Copper and neocuproine catalysed synthesis of cinnamyl ether derivatives directly from secondary and tertiary cinnamyl alcohols

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Supporting Information

Contents:

1. General information

Instrumentation

^{1}H NMR spectra were recorded on JEOL JNM-ECZS 400 MHz spectrometers. ^{13}C NMR spectra were recorded on JEOL JNM-ECZS 101 MHz spectrometer. Chemical shifts (δ values) were reported in parts per million (ppm), with coupling constants in Hz. Chemical shifts (δ) were reported with respect to the corresponding solvent residual peak at 7.26 ppm for $CDCl_3$, 3.31 for CD_3OD, 1.94 for CD_3CN and 2.50 DMSO-d_6 for ^{1}H-NMR. ^{13}C-NMR spectra were reported in ppm using the central peak of $CDCl_3$ (77.16 ppm), CD_3OD (49.00), CD_3CN (118.26) and 39.52 DMSO-d_6. Spectra were processed with MestReNova 14.0. HPLC-MS Spectra were obtained on Aglient 6120 electron spray ionization-quadrupole mass spectrometer (ESI-MS). HRMS spectra were acquired with Agilent 1100 Series LC/MSD and AB SCIEX TripleTOF 5600+ mass spectrometers. HPLC analyses were recorded on Agilent 1260 liquid chromatography (C18, mobile phase A: water; mobile phase B: acetonitrile).

Solvents

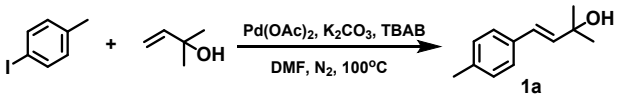
Experiments were performed under air or an atmosphere of nitrogen, using anhydrous solvents. (Petroleum ether (PE), ethyl acetate (EA), dichloromethane (DCM) and methyl alcohol (MeOH)) were used as received for column chromatography.

Others

Bulk chemicals were purchased from Adamas, TCI, or J&K and used as received unless otherwise stated. All glassware is oven-dried before the usage. The reactions were monitored by thin-layer chromatography (TLC) using plates coated with silica gel (HSGF254) form Qingdao Ocean chemical and visualization of the spots was achieved by exposure to 254 nm UV light or iodine fumigation. Column chromatography was performed using 300-400 mesh silica with the corresponding solvent system.

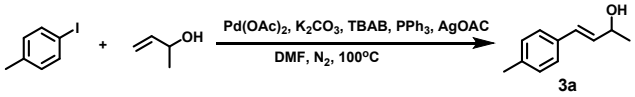
2. Experimental procedures and methods.

2.1 General procedure A for the preparation of tertiary cinnamyl alcohols



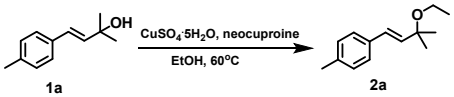
According to the modified Heck's method,[1] a mixture of 1-iodo-4-methylbenzene (10.0 g, 45.9 mmol), 2-methylbut-3-en-2-ol (5.9 g, 68.9 mmol), K_2CO_3 (9.5 g, 68.9 mmol), Tetrabutylammonium bromide (TBAB) (4.5 g, 13.8 mmol), palladium(II) acetate (260 mg, 1.2 mmol) and DMF (100 mL) in a three-neck flask under N_2 atmosphere was stirred at 100℃ for 12 hours. Then, the reaction mixture was cooled followed by the addition of H_2O (50 mL) and extraction with EA (50 mL × 3). The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by silica gel column chromatography (EA/PE = 1:4, retention factor values (R_f) = 0.2) to afford compound **1a**.

2.2 General procedure B for the preparation of secondary cinnamyl alcohols



According to the modified Jeffery's method,[2] a mixture of 1-iodo-4-methylbenzene (1.5 g, 6.9 mmol), but-3-en-2-ol (0.75 g, 10.4 mmol), K_2CO_3 (1.4 g, 10.4 mmol), Tetrabutyl ammonium bromide (TBAB, 0.68 g, 2.1 mmol), PPh_3 (0.14g, 0.52 mmol), silver acetate (0.58g, 3.5mmol), palladium(II) acetate (38 mg, 0.17 mmol) and DMF (20 mL) in a three-neck flask under N_2 atmosphere was stirred at 100℃ for 12 hours. Then, the reaction mixture was cooled to room temperature, then H_2O (30mL) was added and the mixture wasextracted by EA (20mL × 3). The organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The combined crude product was purified by silica gel column chromatography (EA/PE = 1:9, R_f = 0.2) to afford compound **3a**.

2.3 General procedure C for the preparation of secondary and tertiary cinnamyl ether



In a 25 mL round-bottom flask, (*E*)-2-methyl-4-(p-tolyl)but-3-en-2-ol (**1a**, 0.35 g, 2.0 mmol) was dissolved in EtOH (5 mL), then $CuSO_4{\cdot}5H_2O$ (25 mg, 0.1 mmol) and neocuproine (21 mg, 0.1 mmol) were added subsequently. The reaction was stirred at 60 ℃ for 1 hour. TLC (EA/PE = 1:9) and LC-MS indicated the completion of the transformation. After cooling to room temperature, the reaction mixture was poured into water (40 mL), extracted with EA (3 × 20 mL), washed with brine (30 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by silica gel chromatography (EA/PE = 1:19, R_f = 0.2) to afford compound **2a**.

2.4 Establishment of HPLC standard method

A HPLC method was established to calculate the conversion ratio. The UV absorption characteristics of **1a**, **2a**, and **2aa** are different. If the peak area ratio was used for yield calculation directly, it will bring non-negligible error. A method for calculating the concentration through a standard curve was developed.

HPLC method: EC-C18; water/acetonitrile gradient elute (Table S1); flow rate = 1.0 mL/min; □ = 254 nm; mobile phase A, H_2O; mobile phase B, MeCN. Compounds **1a**, **2a** and **2aa** were well separated by the HPLC method. The results were demonstrated in Figure S1.

Table S1. Time table of the gradient elution conditions of the HPLC method

Time	A % (H_2O)	B % (MeCN)	Flow rate
2 min	40	60	1 mL/min
9 min	20	80	1 mL/min
10 min	40	60	1 mL/min
11 min	60	40	1 mL/min
12 min	80	20	1 mL/min

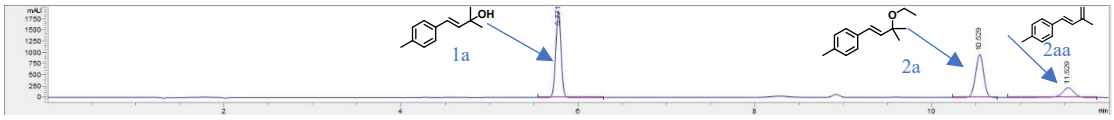


Figure S1. HPLC analysis of compound **1a** (left), **2a** (middle) and **2aa** (right). The relative position was determined by the standard sample after structure identification. t_R**1a** = 5.771 min, t_R**2a** = 10.529 min, tR**2aa** = 11.529 min.

Then, five different concentrations of compounds **1a**, **2a**, and **2aa** were performed by HPLC method. The standard curves of compounds **1a**, **2a**, and **2aa** were achieved and shown in Figure S2, Figure S3, and Figure S4, respectively. A mixture of EtOH solution of these three compounds (**1a**, **2a**, and **2aa**; 0.54 mmol/L) was subjected to HPLC by this method, and the result was shown in Figure S5. Calculated concentrations and actual concentrations were stated in Table S2. The concentrations calculated by the standard curve are matching the actual concentrations. These results show that it is reliable to calculate the concentration through their respective standard curves.

entry	C (mmol/L)	Area (mAu)
1	0.1	1244.4
2	0.25	3178.1
3	0.5	5438.4
4	1	9712.4
5	2	18040.7

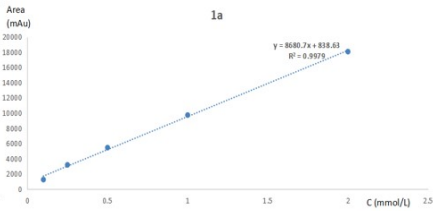


Figure S2. Standard curve of compound **1a**.

entry	C (mmol/L)	Area (mAu)
1	0.1	1133.6
2	0.25	3131.3
3	0.5	5399.8
4	1	11228.6
5	2	21805.9

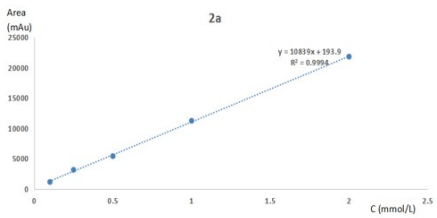


Figure S3. Standard curve of compound **2a**.

entry	C (mmol/L)	Area (mAu)
1	0.1	378.9
2	0.25	848.3
3	0.5	1586.9
4	1	3267
5	2	6342

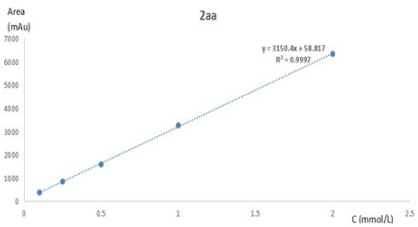
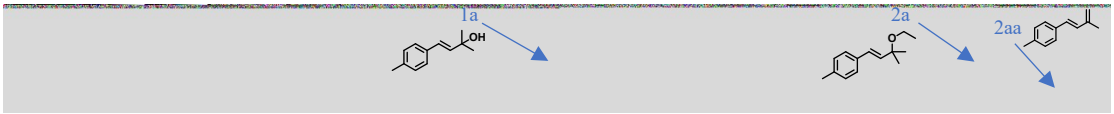


Figure S4. Standard curve of compound **2aa**.



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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.771	MM	0.0573	5558.62646	1616.48865	41.6839
2	10.529	MM	0.1053	6017.52100	952.25348	45.1251
3	11.529	MM	0.1406	1759.04700	208.52325	13.1910

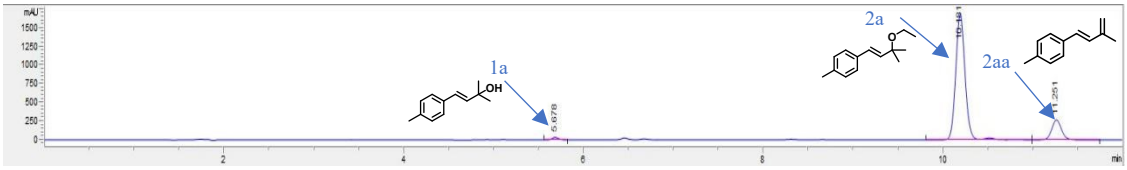
Figure S5. HPLC analysis report of compound **1a** (left) (0.54 mmol/L), **2a** (middle) (0.54 mmol/L) and **2aa** (right) (0.54 mmol/L). The relative position was determined by the standard sample after structure identification. t_R**1a** = 5.771 min, t_R**2a** = 10.529 min, t_R**2aa** = 11.529 min.

Table S2. Calculated concentration by standard curve compared with the actual concentration of 1a (0.54 mmol/L), 2a (0.54 mmol/L), and 2aa (0.54 mmol/L)

Compound	Area (mAu)	calculated concentration	Accuracy rate
1a	5558.6	0.54	100%
2a	6017.5	0.53	98.1%
2aa	1759	0.53	98.1%

2.5 Yield calculation example

Here we choose entry 2 in **Table 1** as an example to illustrate how to calculate yield. After the reaction was continued for 1 h, reaction solution (15 μL) was diluted by MeOH (985 μL) and then subjected to HPLC by method. The peak areas (mAu·s) of compounds **1a**, **2a**, and **2aa** were shown in **Figure S6**. The molar concentration of these three compounds could be easily calculated by the formula of the standard curve. Thus, the HPLC yields of compounds **2a** and **2aa** were 64 and 36%, respectively (**Table S3**).



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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.678	BB	0.0727	157.83096	33.63662	1.1001
2	10.181	BV R	0.1106	1.22040e4	1697.79785	85.0610
3	11.251	BBA	0.1168	1985.50830	266.96539	13.8389

Figure S6. HPLC reports of entry 2 in **Table 1**. HPLC method, tR**1a** = 5.678 min, tR**2a** = 10.181 min, tR**2aa** = 11.251 min.

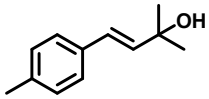
Table S3. Calculated Yield of 2a and 2aa about Entry 2 in Table 1

Compound	Area (mAu)	Calculated concentration	Yield (%)
1a	157.83096	0	0
2a	12204	1.1	64%
2aa	1985.5	0.6	36%

3 Characterization data for the substrates and products

3.1 Characterization data for the substrates

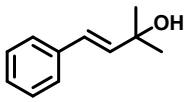
(*E*)-2-methyl-4-(p-tolyl)but-3-en-2-ol (1a)[3]



Synthesis procedure was depicted in 2.1 general procedure A.

Brown solid (5.76 g, 71%). m.p.= 67.4-68.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 7.9 Hz, 2H), 6.54 (d, J = 16.1 Hz, 1H), 6.29 (d, J = 16.1 Hz, 1H), 2.32 (s, 3H), 1.57 (s, 1H), 1.41 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.34, 136.57, 134.18, 129.36, 126.39, 126.32, 71.16, 29.98, 21.26. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{12}H_{16}ONa$ 199.1093, found: 199.1091.

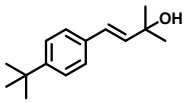
(*E*)-2-methyl-4-phenylbut-3-en-2-ol (1b)[4]



Following general procedure A, iodobenzene (5 g, 25 mmol), 2-methylbut-3-en-2-ol (3.23 g, 37.5 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **1b.**

Brown oil (3.45 g, 84.1%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.35 (m, 2H), 7.31 (td, J = 7.5, 1.3 Hz, 2H), 7.25 – 7.19 (m, 1H), 6.58 (d, J = 16.1 Hz, 1H), 6.35 (d, J = 16.1 Hz, 1H), 1.78 (s, 1H), 1.42 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.64, 137.03, 128.68, 127.53, 126.52, 126.46, 71.17, 29.97. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{11}H_{14}ONa$ 185.0937, found: 185.0938.

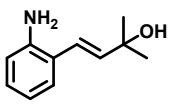
(*E*)-4-(4-(tert-butyl)phenyl)-2-methylbut-3-en-2-ol (1c)[5]



Following general procedure A, 1-(tert-butyl)-4-iodobenzene (2 g, 25 mmol) and 2-methylbut-3-en-2-ol (3.23 g, 37.5 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **1c**.

Brown oil (1.04 g, 67.9%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (m, 4H), 6.58 (d, J = 16.1 Hz, 1H), 6.34 (d, J = 16.1 Hz, 1H), 1.98 (s, 1H), 1.43 (s, 6H), 1.33 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 150.61, 136.99, 134.27, 126.26, 126.18, 125.61, 71.18, 34.65, 31.43, 30.01. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{15}H_{22}ONa$ 241.1563, found: 241.1561.

(*E*)-4-(2-aminophenyl)-2-methylbut-3-en-2-ol (1d)[6]

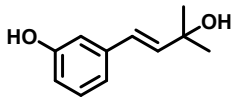


According to a reported literature[6], a mixture of 2-iodoaniline (1.0 g, 4.57 mmol), 2-methylbut-3-en-2-ol (1.97 g, 22.85 mmol), palladium acetate (0.1 g, 0.457 mmol) and DPPF (0.67 g, 0.91 mmol) [with K_2CO_3 (0.95 g, 6.86 mmol) in the case of basic conditions] in H_2O (25 mL) at 100 °C under N_2 atmosphere for 3 h. Then the reaction

mixture was cooled to room temperature, extracted with DCM (20 mL × 3), and the organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo, The combined crude product was purified by silica gel column chromatography (EA/PE = 3:7) to afford **1d**.

Brown oil (0.52 g, Yield: 64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.21 (m, 1H), 7.05 (td, J = 7.6, 1.6 Hz, 1H), 6.75 (td, J = 7.5, 1.2 Hz, 1H), 6.69 – 6.61 (m, 2H), 6.20 (d, J = 15.8 Hz, 1H), 3.18 (s, 3H), 1.40 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 143.63, 139.57, 128.47, 127.39, 123.50, 121.75, 119.20, 116.32, 71.35, 30.14. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{11}H_{15}NONa$ 200.1046, found: 200.1045.

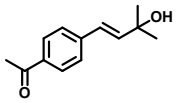
(*E*)-3-(3-hydroxy-3-methylbut-1-en-1-yl)phenol (1e)



Following general procedure A, 3-iodophenol (2 g, 9.1 mmol) and 2-methylbut-3-en-2-ol (1.17 g, 13.64 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:4) to afford **1e.**

Brown oil (1.25 g, 77.2%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.07 (t, J = 7.8 Hz, 1H), 6.84 – 6.78 (m, 2H), 6.61 (ddd, J = 8.1, 2.5, 1.0 Hz, 1H), 6.46 (d, J = 16.1 Hz, 1H), 6.28 (d, J = 16.1 Hz, 1H), 1.34 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Methanol-d_4) δ 157.32, 138.77, 137.20, 129.16, 126.13, 117.68, 113.99, 112.50, 70.06, 28.58. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{11}H_{14}O_2Na$ 201.0886, found: 201.0888.

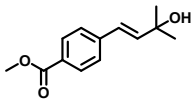
(*E*)-1-(4-(3-hydroxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one (1f)[7]



Following general procedure A, 1-(4-iodophenyl)ethan-1-one (1.0 g, 4.06 mmol) and 2-methylbut-3-en-2-ol (0.52 g, 6.09 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 3:17) to afford **1f.**

Yellow oil (0.43 g, 51.8%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 – 7.82 (m, 2H), 7.43 – 7.37 (m, 2H), 6.60 (d, J = 16.1 Hz, 1H), 6.44 (d, J = 16.1 Hz, 1H), 2.54 (s, 3H), 1.40 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 197.87, 141.95, 140.71, 135.87, 128.84, 126.54, 125.49, 71.09, 29.89, 26.63. LC-MS (ESI): m/z [M + Na]$^+$
calcd for $C_{13}H_{16}O_2Na$ 227.1; found 227.1

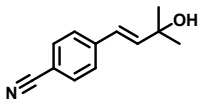
Methyl (*E*)-4-(3-hydroxy-3-methylbut-1-en-1-yl)benzoate (1g)



Following general procedure A, methyl 4-iodobenzoate (0.86 g, 3.28 mmol) and 2-methylbut-3-en-2-ol (0.42 g, 4.92 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19 to 1:9) to afford **1g.**

Brown oil (0.58 g, 80.6%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 8.6 Hz, 1H), 7.42 – 7.40 (m, 1H), 7.40 – 7.37 (m, 1H), 6.60 (d, J = 16.1 Hz, 1H), 6.44 (d, J = 16.1 Hz, 1H), 3.88 (s, 3H), 1.80 (s, 1H), 1.41 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 167.06, 141.66, 140.31, 130.01, 128.88, 126.39, 125.65, 71.17, 52.17, 29.91. HRMS (Q-TOF): m/z calcd for [M+Na]$^+$ $C_{13}H_{16}O_3Na$ 243.0992, found: 243.1001.

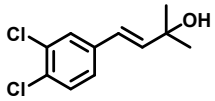
(*E*)-4-(3-hydroxy-3-methylbut-1-en-1-yl)benzonitrile (1h)[7]



Following general procedure A, 4-iodobenzonitrile (2 g, 7.7 mmol) and 2-methylbut-3-en-2-ol (0.99 g, 11.6 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **1h.**

Brown oil (0.73 g, 44.8%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (d, J = 8.5 Hz, 2H), 7.45 – 7.40 (m, 2H), 6.60 (d, J = 16.1 Hz, 1H), 6.45 (d, J = 16.0 Hz, 1H), 1.71 (s, 1H), 1.41 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 141.73, 141.55, 132.48, 127.00, 125.07, 119.07, 110.64, 71.17, 29.93. HRMS (Q-TOF): m/z calcd for $[M+Na]^+$ $C_{12}H_{13}NONa$ 210.0889, found: 210.0886.

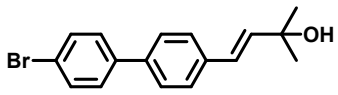
(*E*)-4-(3,4-dichlorophenyl)-2-methylbut-3-en-2-ol (1i)



Following general procedure A, 1,2-dichloro-4-iodobenzene (1.0 g, 3.66 mmol) and 2-methylbut-3-en-2-ol (0.47 g, 5.49 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford **1i.**

Brown oil (0.48 g, 56.5%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, J = 2.1 Hz, 1H), 7.30 (d, J = 8.3 Hz, 1H), 7.12 (dd, J = 8.3, 2.1 Hz, 1H), 6.45 (d, J = 16.1 Hz, 1H), 6.29 (d, J = 16.0 Hz, 1H), 2.23 (s, 1H), 1.38 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 139.65, 137.27, 132.65, 130.97, 130.48, 128.15, 125.73, 124.32, 71.11, 29.90. HRMS (Q-TOF): m/z calcd for $[M+Na]^+$ $C_{11}H_{12}C_{l2}ONa$ 253.0157, found: 253.0164.

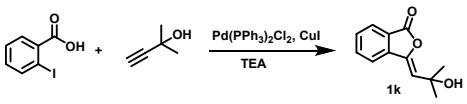
(*E*)-4-(4'-bromo-[1,1'-biphenyl]-4-yl)-2-methylbut-3-en-2-ol (1j)



Following general procedure A, 4-bromo-4'-iodo-1 1'-biphenyl (0.3 g, 0.83 mmol) and 2-methylbut-3-en-2-ol (0.1 g, 1.24 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **1j.**

Brown solid (0.21 g, 79.8%). m.p.= 157.5-159.1 °C. ^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 7.61 – 7.52 (m, 6H), 7.49 – 7.44 (m, 2H), 6.58 (d, J = 16.1 Hz, 1H), 6.44 (d, J = 16.1 Hz, 1H), 1.31 (d, J = 1.1 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Acetonitrile-d_3) δ 139.17, 138.23, 137.19, 131.91, 128.62, 127.02, 126.89, 124.90, 121.04, 117.37, 70.11, 29.28. HRMS (Q-TOF): m/z calcd for $[M+Na]^+$ $C_{17}H_{17}BrONa$ 339.0355, found: 339.0362.

3-(2-hydroxy-2-methylpropylidene)isobenzofuran-1(3*H*)-one (1k) [8]

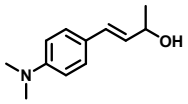


A suspension of 2-iodobenzoic acid (5 g, 0.02 mol), 2-methylbut-3-yn-2-ol (1.85 g, 0.022 mol), $Pd(PPh_3)_2Cl_2$, (0.28 g, 0.4 mmol), CuI(0.19 g, 10 mmol) and TEA (60 mL) in a round-bottom flask under N_2 atmosphere was stirred at room temperature for 12 h. Then, H_2O (50 mL) was added, and the mixture was extracted with EA (50

mL × 3). The organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo, and the combined crude product was purified by silica gel column chromatography (EA/PE= 1:9 to 1:4) to afford compound **1k**.

Brown oil (3.6 g, 90%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.06 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 7.5 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.49 (t, J = 8.2 Hz, 1H), 6.74 (s, 1H), 5.49 (s, 1H), 1.38 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.61, 162.25, 137.70, 135.77, 129.21, 128.65, 126.76, 119.74, 99.94, 69.98, 28.76. LC-MS (ESI): m/z $[M + H]^+$ calcd for $C_{12}H_{13}O_3$ 205.2; found 205.2.

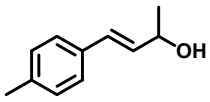
(*E*)-4-(4-(dimethylamino)phenyl)but-3-en-2-ol (3a)[9]



To a 100 mL three-necked flask was added a solution of (*E*)-3-(4-(dimethylamino)phenyl)acrylaldehyde (0.5 g, 2.85 mmol) in dry THF (15 mL) followed by dropwise addition of CH_3MgBr (8.5 mL,1 mol/L) at 0 ℃ under N_2 atmosphere for 3 hours. The mixture was quenched with saturated aqueous NH_4Cl (20 mL), extracted with EA (15 mL × 3), the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The combined crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford **3a**.

Orange solid (0.48 g, 89%). m.p.= 83.6-84.9 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 (dd, J = 8.2, 1.4 Hz, 2H), 6.69 – 6.64 (m, 2H), 6.45 (d, J = 15.8 Hz, 1H), 6.05 (dd, J = 15.8, 6.8 Hz, 1H), 4.43 (t, J = 6.4 Hz, 1H), 2.94 (s, 6H), 1.74 (s, 1H), 1.34 (d, J = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 150.27, 129.74, 129.44, 127.53, 125.25, 112.59, 69.44, 40.61, 23.59. LC-MS (ESI): m/z $[M + H]^+$ calcd for $C_{12}H_{18}NO$ 192.2; found 192.2.

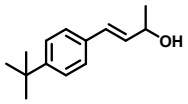
(*E*)-4-(p-tolyl)but-3-en-2-ol (3b)[10]



Synthesis procedure was depicted in 2.2 general procedure B.

Yellow oil (320 mg, 88%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.20 (m, 2H), 7.11 (d, J = 7.9 Hz, 2H), 6.52 (d, J = 15.9 Hz, 1H), 6.20 (dd, J = 15.9, 6.5 Hz, 1H), 4.46 (p, J = 6.4 Hz, 1H), 2.33 (s, 3H), 1.77 (d, J = 10.2 Hz, 1H), 1.36 (d, J = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.56, 133.99, 132.65, 129.44, 129.38, 126.47, 69.11, 23.50, 21.27. HRMS (Q-TOF): m/z calcd for $[M+Na]^+$ $C_{11}H_{14}O$ Na 185.0937, found: 185.0937.

(*E*)-4-(4-(tert-butyl)phenyl)but-3-en-2-ol (3c)

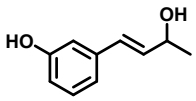


Following general procedure B, 1-(tert-butyl)-4-iodobenzene (0.5 g, 1.9 mmol) and but-3-en-2-ol (0.21 g, 2.9 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **3c.**

Light yellow oil (0.3 g, 76%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.29 (m, 4H), 6.54 (dd, J = 15.9, 1.2 Hz, 1H), 6.22 (dd, J = 15.9, 6.5 Hz, 1H), 4.47 (pd, J = 6.4, 1.2 Hz, 1H), 1.82 (s, 1H), 1.36 (d, J = 6.4 Hz, 3H), 1.31

(s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 150.87, 134.00, 132.94, 129.28, 126.28, 125.61, 69.12, 34.66, 31.38, 23.52. HRMS (Q-TOF): m/z calcd for $[M+Na]^+$ $C_{14}H_{20}ONa$ 227.1406, found: 227.1420.

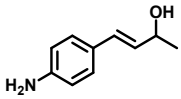
(*E*)-3-(3-hydroxybut-1-en-1-yl)phenol (3d)



Following general procedure B, 3-iodophenol (0.5 g, 2.3 mmol), but-3-en-2-ol (0.25 g, 3.5 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE = 1:4) to afford **3d.**

Colorless oil (0.25 g, 67.1%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.29 (d, J = 3.3 Hz, 1H), 7.05 (t, J = 7.8 Hz, 1H), 6.83 – 6.69 (m, 2H), 6.58 (dd, J = 7.9, 2.6 Hz, 1H), 6.41 – 6.31 (m, 1H), 6.14 (dd, J = 15.9, 5.5 Hz, 1H), 4.79 (d, J = 4.3 Hz, 1H), 4.23 (q, J = 5.8 Hz, 1H), 1.15 (d, J = 6.3 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6) δ 158.06, 138.75, 135.75, 130.04, 127.83, 117.68, 114.86, 113.22, 67.10, 24.32. HRMS (Q-TOF): m/z calcd for $[M+Na]^+$ $C_{10}H_{12}O_2Na$ 187.0730, found: 187.0734.

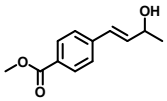
(*E*)-4-(4-aminophenyl)but-3-en-2-ol (3e)[11]



Following general procedure B, 4-iodoaniline (1.0 g, 4.6 mmol), but-3-en-2-ol (0.5 g, 6.9 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE= 1:4) to afford **3e.**

Yellow oil (0.45 g, 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.20 – 7.15 (m, 2H), 6.65 – 6.59 (m, 2H), 6.44 (d, J = 14.8 Hz, 1H), 6.04 (dd, J = 15.8, 6.8 Hz, 1H), 4.43 (pd, J = 6.4, 1.1 Hz, 1H), 1.33 (d, J = 6.3 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 146.18, 129.99, 129.63, 127.72, 115.22, 113.52, 69.37, 23.55. HRMS (Q-TOF): m/z calcd for $[M+H]^+$ $C_{10}H_{14}NO$ 164.1070, found: 164.1067.

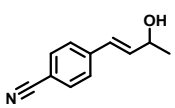
Methyl (*E*)-4-(3-hydroxybut-1-en-1-yl)benzoate (3f)[12]



Following general procedure B, methyl 4-iodobenzoate (0.5 g, 1.9 mmol), but-3-en-2-ol (0.21 g, 2.9 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **3f.**

White solid (0.2 g, 51%). m.p.=71.1-73.0 ^{o}C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 – 7.90 (m, 2H), 7.40 (dd, J = 8.4, 1.8 Hz, 2H), 6.58 (d, J = 16.0 Hz, 1H), 6.36 (ddd, J = 15.9, 6.0, 1.7 Hz, 1H), 4.57 – 4.43 (m, 1H), 3.89 (d, J = 1.7 Hz, 3H), 1.83 (s, 1H), 1.36 (d, J = 6.5 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 167.01, 141.38, 136.37, 130.02, 129.10, 128.35, 126.41, 68.73, 52.16, 23.45. LC-MS (ESI): m/z $[M + H]^+$ calcd for $C_{12}H_{15}O_3$ 207.1; found 207.1.

(*E*)-4-(3-hydroxybut-1-en-1-yl)benzonitrile (3g)[13]

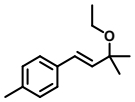


Following general procedure B, 4-iodobenzonitrile (1.5 g, 6.5 mmol) and but-3-en-2-ol (0.7 g, 9.8 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **3g.**

Yellow oil (0.48 g, 44%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 – 7.55 (m, 2H), 7.47 – 7.40 (m, 2H), 6.63 – 6.54 (m, 1H), 6.37 (dd, *J* = 16.0, 5.8 Hz, 1H), 4.51 (p, *J* = 5.8 Hz, 1H), 1.65 (s, 1H), 1.37 (d, *J* = 6.5 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 141.44, 137.60, 132.51, 127.55, 127.01, 119.03, 110.85, 68.50, 23.47. LC-MS (ESI): m/z [M + H]$^+$ calcd for $C_{11}H_{12}NO$ 174.1; found 174.1.

3.2 Characterization data for the products

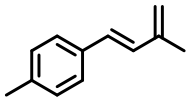
(*E*)-1-(3-ethoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (2a)



Synthesis procedure was depicted in 2.3 general procedure C.

Colorless oil (0.34 g, 90.0%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 6.44 (d, *J* = 16.3 Hz, 1H), 6.17 (d, *J* = 16.3 Hz, 1H), 3.40 (q, *J* = 7.0 Hz, 2H), 2.34 (s, 3H), 1.38 (s, 6H), 1.18 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.34, 134.98, 134.28, 129.37, 128.54, 126.37, 75.00, 58.06, 26.62, 21.26, 16.27. HRMS (Q-TOF): m/z calcd for [M+Na]$^+$ $C_{14}H_{20}ONa$ 227.1406, found: 227.1412.

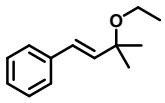
(*E*)-1-methyl-4-(3-methylbuta-1,3-dien-1-yl)benzene (2aa)[14]



To a 25 mL round bottom flask, (*E*)-2-methyl-4-(p-tolyl)but-3-en-2-ol (**1a**, 0.35 g, 2.0 mmol) dissolving in EtOH (10 mL) was added followed by the addition of H_2SO_4 (9.8 mg, 0.1 mmol). The reaction was stirred at 60℃ for 1 hour. After cooling, the reaction mixture was poured into water (40 mL), extracted with EA (3 × 20 mL), washed with brine (30 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by silica gel chromatography and eluted with PE (R_f = 0.8) to afford compound **2aa**.

Colourless oil (0.25 g, 80%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.41 – 7.34 (m, 2H), 7.22 – 7.15 (m, 2H), 6.90 (d, *J* = 16.1 Hz, 1H), 6.56 (d, *J* = 16.1 Hz, 1H), 5.19 – 5.07 (m, 2H), 2.38 (s, 3H), 2.05 – 2.00 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 142.30, 137.41, 134.73, 130.86, 129.49, 128.77, 126.54, 117.00, 21.38, 18.78. LC-MS (ESI): m/z [M + H]$^+$ calcd for $C_{12}H_{15}$ 159.1; found 159.1.

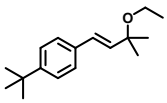
(*E*)-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2b)



Following general procedure C, **1b** (0.32 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 3:97) to afford **2b.**

Yellow oil (0.31 g, 82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.39 (m, 2H), 7.37 – 7.30 (m, 2H), 7.27 – 7.22 (m, 1H), 6.50 (d, *J* = 16.4 Hz, 1H), 6.25 (d, *J* = 16.3 Hz, 1H), 3.42 (q, *J* = 7.0 Hz, 2H), 1.41 (s, 6H), 1.21 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.14, 136.08, 128.74, 128.70, 127.58, 126.52, 74.97, 58.11, 26.65, 16.32. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{13}H_{18}ONa$ 213.1250, found: 213.1264.

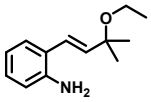
(*E*)-1-(tert-butyl)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2c)



Following general procedure C, **1c** (0.44 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford **2c.**

Light yellow oil (0.37 g, 75.4%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 (s, 4H), 6.53 (d, J = 16.3 Hz, 1H), 6.26 (d, J = 16.4 Hz, 1H), 3.46 (q, J = 7.0 Hz, 2H), 1.44 (s, 6H), 1.38 (s, 9H), 1.24 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 150.67, 135.28, 134.36, 128.53, 126.28, 125.63, 75.01, 58.10, 34.67, 31.47, 26.73, 16.35. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{17}H_{26}ONa$ 269.1876, found: 269.1892.

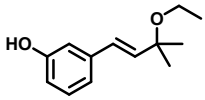
(*E*)-2-(3-ethoxy-3-methylbut-1-en-1-yl)aniline (2d)



Following general procedure C, **1d** (0.35 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford **2d.**

Brown oil (0.22 g, 56%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.23 (m, 1H), 7.07 (td, J = 7.6, 1.6 Hz, 1H), 6.76 (td, J = 7.5, 1.2 Hz, 1H), 6.67 (dd, J = 7.9, 1.2 Hz, 1H), 6.53 (d, J = 16.2 Hz, 1H), 6.10 (d, J = 16.2 Hz, 1H), 3.78 (s, 2H), 3.43 (q, J = 7.0 Hz, 2H), 1.39 (s, 6H), 1.19 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 143.70, 137.90, 128.54, 127.49, 124.06, 123.50, 119.12, 116.20, 75.16, 58.12, 26.75, 16.28. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{13}H_{19}NONa$ 228.1359, found: 228.1363.

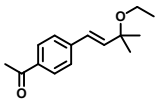
(*E*)-3-(3-ethoxy-3-methylbut-1-en-1-yl)phenol (2e)



Following general procedure C, **1e** (0.36 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **2e.**

Colorless oil (0.26 g, 55%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 – 7.15 (m, 2H), 6.98 (t, J = 2.1 Hz, 1H), 6.90 (dt, J = 7.7, 1.3 Hz, 1H), 6.77 (ddd, J = 8.1, 2.5, 0.9 Hz, 1H), 6.44 (d, J = 16.3 Hz, 1H), 6.22 (d, J = 16.2 Hz, 1H), 3.47 (q, J = 7.0 Hz, 2H), 1.41 (s, 6H), 1.19 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 156.57, 138.32, 135.39, 129.95, 129.09, 119.26, 115.19, 112.63, 75.94, 58.54, 26.44, 16.06. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{13}H_{18}O_2Na$ 229.1199, found: 229.1208.

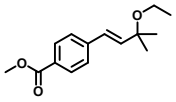
(*E*)-1-(4-(3-ethoxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one (2f)



Following general procedure C, **1f** (0.41 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:49 to 1:19) to afford **2f.**

Colorless oil (0.28 g, 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 – 7.86 (m, 2H), 7.43 (d, J = 8.2 Hz, 2H), 6.50 (d, J = 16.3 Hz, 1H), 3.38 (q, J = 7.0 Hz, 2H), 2.56 (s, 3H), 1.37 (d, J = 1.2 Hz, 6H), 1.16 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 197.63, 141.82, 139.22, 136.03, 128.84, 127.62, 126.52, 74.96, 58.19, 26.64, 26.45, 16.19. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{15}H_{20}O_2Na$ 255.1356, found: 255.1375.

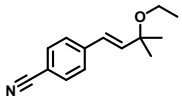
Methyl (*E*)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzoate (2g)



Following general procedure C, **1g** (0.44 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:49) to afford **2g.**

White oil (0.23 g, 46%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 – 7.91 (m, 2H), 7.43 – 7.38 (m, 2H), 6.49 (d, J = 16.3 Hz, 1H), 6.32 (d, J = 16.3 Hz, 1H), 3.88 (s, 3H), 3.38 (q, J = 7.0 Hz, 2H), 1.36 (s, 6H), 1.16 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 166.95, 141.62, 138.93, 129.99, 128.95, 127.72, 126.33, 74.93, 58.17, 52.09, 26.46, 16.19. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{15}H_{20}O_3Na$ 271.1305, found: 271.1324.

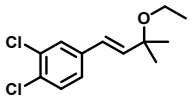
(*E*)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzonitrile (2h)



Following general procedure C, **1h** (0.37 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **2h.**

Colorless oil (0.28 g, 66%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 – 7.53 (m, 2H), 7.46 – 7.38 (m, 2H), 6.46 (d, J = 16.3 Hz, 1H), 6.32 (dd, J = 16.4, 0.7 Hz, 1H), 3.36 (q, J = 7.0 Hz, 2H), 1.35 (s, 6H), 1.15 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 141.66, 140.31, 132.45, 127.01, 126.96, 119.04, 110.67, 74.89, 58.22, 26.39, 16.16. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{14}H_{17}NONa$ 238.1202, found: 238.1217.

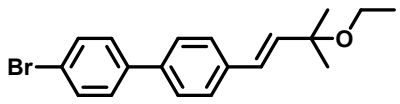
(*E*)-1,2-dichloro-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2i)



Following general procedure C, **1i** (0.48 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:48) to afford **2i.**

Light yellow oil (0.31 g, 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (d, J = 2.1 Hz, 1H), 7.33 (d, J = 8.3 Hz, 1H), 7.18 (d, J = 2.1 Hz, 1H), 6.36 (d, J = 16.3 Hz, 1H), 6.20 (d, J = 16.3 Hz, 1H), 3.37 (q, J = 7.0 Hz, 2H), 1.35 (s, 6H), 1.16 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 138.29, 137.28, 132.71, 131.05, 130.48, 128.15, 126.33, 125.67, 74.83, 58.15, 26.45, 16.19. HRMS (Q-TOF): m/z [M+H]$^+$ calcd for $C_{13}H_{17}Cl_2O$ 259.0651, found: 259.0612.

(*E*)-4-bromo-4'-(3-ethoxy-3-methylbut-1-en-1-yl)-1,1'-biphenyl (2j)

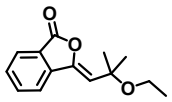


Following general procedure C, **1j** (0.63 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford **2j.**

White oil (0.36 mg, 52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 – 7.48 (m, 4H), 7.45 (dd, J = 8.5, 3.5 Hz, 4H), 6.50 (d, J = 16.3 Hz, 1H), 6.28 (d, J = 16.3 Hz, 1H), 3.41 (q, J = 7.0 Hz, 2H), 1.40 (s, 6H), 1.19 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 139.71, 139.03, 136.58, 136.55, 131.98, 128.57, 128.04, 127.14,

127.01, 121.61, 75.02, 58.14, 26.59, 16.26. HRMS (Q-TOF): m/z $[M+Na]^+$ calcd for $C_{19}H_{21}BrONa$ 367.0668, found: 367.0712.

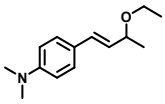
3-(2-ethoxy-2-methylpropylidene)isobenzofuran-1(3*H*)-one (2k)



Following general procedure C, **1k** (0.63 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE =1:19) to afford **2k.**

White solid. (0.36 mg, 52%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.03 (dt, J = 7.9, 0.9 Hz, 1H), 7.86 (dt, J = 7.7, 0.9 Hz, 1H), 7.79 (ddd, J = 7.8, 7.3, 1.1 Hz, 1H), 7.60 (td, J = 7.5, 0.9 Hz, 1H), 5.99 (s, 1H), 3.38 (q, J = 7.0 Hz, 2H), 1.43 (s, 6H), 1.07 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 166.84, 144.50, 140.23, 135.60, 130.94, 125.41, 123.21, 121.49, 114.68, 74.75, 58.32, 27.71, 16.48. LC-MS (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{17}O_3$ 233.1; found 233.1. HRMS (Q-TOF): m/z $[M+Na]^+$ calcd for $C_{14}H_{16}O_3Na$ 255.0992, found: 255.0993.

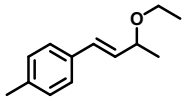
(*E*)-4-(3-ethoxybut-1-en-1-yl)-N,N-dimethylaniline (4a)



Following general procedure C, **3a** (0.38 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:48) to afford **4a.**

Yellow oil (0.44 g, 62%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.33 – 7.27 (m, 2H), 6.71 – 6.66 (m, 2H), 6.44 (d, J = 15.9 Hz, 1H), 5.92 (dd, J = 15.9, 7.9 Hz, 1H), 4.03 – 3.92 (m, 1H), 3.59 (dq, J = 9.3, 7.0 Hz, 1H), 3.40 (dq, J = 9.3, 7.0 Hz, 1H), 2.96 (s, 6H), 1.35 (d, J = 6.4 Hz, 3H), 1.22 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 150.26, 131.13, 127.82, 127.50, 125.33, 112.57, 76.84, 63.40, 40.61, 22.10, 15.56. HRMS (Q-TOF): m/z $[M+H]^+$ calcd for $C_{14}H_{22}NO$ 220.1696, found: 220.1710.

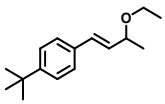
(*E*)-1-(3-ethoxybut-1-en-1-yl)-4-methylbenzene (4b)[15]



Following general procedure C, **3b** (0.32 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:99) to afford **4b.**

Colorless oil (0.22 g, 58.3%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.32 – 7.26 (m, 2H), 7.13 (d, J = 7.9 Hz, 2H), 6.48 (d, J = 15.9 Hz, 1H), 6.07 (dd, J = 15.9, 7.6 Hz, 1H), 3.99 (m, 1H), 3.57 (dq, J = 9.3, 7.1 Hz, 1H), 3.41 (dq, J = 9.3, 7.0 Hz, 1H), 2.34 (s, 3H), 1.34 (d, J = 6.4 Hz, 3H), 1.22 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 137.49, 134.05, 131.18, 130.85, 129.36, 126.45, 76.53, 63.62, 21.89, 21.27, 15.54. HRMS (Q-TOF): m/z $[M+Na]^+$ calcd for $C_{13}H_{18}ONa$ 213.1250, found: 213.1246.

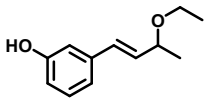
(*E*)-1-(tert-butyl)-4-(3-ethoxybut-1-en-1-yl)benzene (4c)



Following general procedure C, **3c** (0.41 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:48) to afford **4c.**

Colorless oil (0.37 g, 77%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (d, J = 8.0 Hz, 4H), 6.48 (d, J = 15.9 Hz, 1H), 6.07 (dd, J = 16.1, 7.8 Hz, 1H), 3.99 (q, J = 7.3, 6.8 Hz, 1H), 3.60 – 3.51 (m, 1H), 3.44 – 3.35 (m, 1H), 1.32 (s, 3H), 1.30 (s, 9H), 1.19 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 150.82, 134.02, 131.44, 130.72, 126.24, 125.58, 76.53, 63.59, 31.37, 30.28, 21.93, 15.51. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{16}H_{24}ONa$ 255.1719, found: 255.1734.

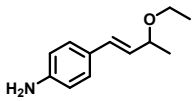
(*E*)-3-(3-ethoxybut-1-en-1-yl)phenol (4d)



Following general procedure C, **3d** (0.33 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:4) to afford **4d.**

Colorless oil (0.18 g, 48%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.17 (t, J = 7.8 Hz, 1H), 6.94 – 6.91 (m, 1H), 6.89 (dt, J = 7.6, 1.3 Hz, 1H), 6.74 (ddd, J = 8.1, 2.5, 1.0 Hz, 1H), 6.46 (d, J = 15.9 Hz, 1H), 6.09 (dd, J = 15.9, 7.8 Hz, 1H), 4.04 (tt, J = 7.2, 6.3 Hz, 1H), 3.62 (dq, J = 9.4, 7.0 Hz, 1H), 3.45 (dq, J = 9.4, 7.0 Hz, 1H), 2.04 (s, 1H), 1.34 (d, J = 6.4 Hz, 3H), 1.22 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 156.41, 138.15, 131.79, 131.25, 129.93, 119.46, 119.41, 115.21, 112.59, 63.89, 21.73, 15.34. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{12}H_{16}O_2Na$ 215.1043, found: 215.1054.

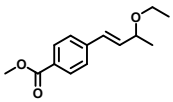
(*E*)-4-(3-ethoxybut-1-en-1-yl)aniline (4e)



Following general procedure C, **3e** (0.33 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **4e.**

Yellow oil (0.17 g, 46%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 – 7.15 (m, 2H), 6.67 – 6.59 (m, 2H), 6.38 (d, J = 15.9 Hz, 1H), 5.89 (dd, J = 15.9, 7.8 Hz, 1H), 4.01 – 3.90 (m, 1H), 3.55 (dq, J = 9.4, 7.1 Hz, 1H), 3.37 (dq, J = 9.4, 7.0 Hz, 1H), 1.30 (d, J = 6.4 Hz, 3H), 1.18 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 146.11, 130.94, 128.45, 127.68, 127.48, 115.19, 76.71, 63.45, 22.00, 15.50. HRMS (Q-TOF): m/z [M+H]$^+$ calcd for $C_{12}H_{18}NO$ 192.1383, found: 192.1395.

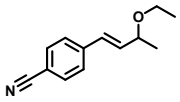
Methyl (*E*)-4-(3-ethoxybut-1-en-1-yl)benzoate (4f)



Following general procedure C, **3f** (0.41 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:48) to afford **4f.**

Yellow oil (0.2 g, 43%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 – 7.93 (m, 2H), 7.45 – 7.38 (m, 2H), 6.54 (d, J = 16.0 Hz, 1H), 6.24 (dd, J = 16.0, 7.3 Hz, 1H), 4.02 (ddd, J = 7.4, 6.4, 1.1 Hz, 1H), 3.89 (s, 3H), 3.55 (dq, J = 9.2, 7.0 Hz, 1H), 3.42 (dq, J = 9.2, 7.0 Hz, 1H), 1.32 (d, J = 6.4 Hz, 4H), 1.20 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 166.99, 141.36, 135.07, 130.01, 129.74, 129.07, 126.39, 76.15, 63.93, 52.15, 21.63, 15.51. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{14}H_{18}O_3Na$ 257.1148, found: 257.1171.

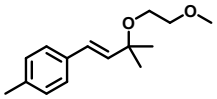
(*E*)-4-(3-ethoxybut-1-en-1-yl)benzonitrile (4g)



Following general procedure C, **3g** (0.35 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purifie by silica gel column chromatography (EA/PE = 1:48) to afford **4g.**

Yellow oil (0.16 g, 41%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, J = 7.8 Hz, 2H), 7.44 (d, J = 7.8 Hz, 2H), 6.52 (d, J = 15.8 Hz, 1H), 6.25 (dd, J = 16.0, 6.9 Hz, 1H), 4.10 – 3.97 (m, 1H), 3.60 – 3.49 (m, 1H), 3.43 (t, J = 7.8 Hz, 1H), 1.32 (d, J = 5.9 Hz, 3H), 1.24 (t, J = 8.7 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 141.39, 136.41, 132.49, 128.87, 127.00, 119.04, 110.84, 75.90, 64.06, 21.49, 15.50. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{13}H_{15}NONa$ 224.1046, found: 224.1063.

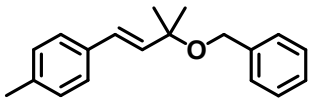
(*E*)-1-(3-(2-methoxyethoxy)-3-methylbut-1-en-1-yl)-4-methylbenzene (5a)



Following general procedure C, **1a** (0.35 g, 2 mmol) and 2-methoxyethan-1-ol (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford **5a.**

Colorless oil (0.45 g, 96%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (d, J = 8.2 Hz, 2H), 7.15 – 7.08 (m, 2H), 6.47 (d, J = 16.4 Hz, 1H), 6.18 (d, J = 16.3 Hz, 1H), 3.51 (d, J = 0.7 Hz, 4H), 3.38 (s, 3H), 2.33 (s, 3H), 1.40 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.39, 134.55, 134.20, 129.36, 129.00, 126.41, 75.34, 72.70, 62.14, 59.12, 26.50, 21.25. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{16}H_{24}ONa$ 257.1512, found: 257.1544.

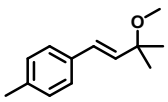
(*E*)-1-(3-(benzyloxy)-3-methylbut-1-en-1-yl)-4-methylbenzene (5b)



Following general procedure C, **1a** (0.35 g, 2.0 mmol) and benzyl alcohol (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford **5b.**

Colorless oil (0.45 g, 85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.26 (m, 7H), 7.14 (d, J = 8.0 Hz, 2H), 6.53 (d, J = 16.3 Hz, 1H), 6.26 (d, J = 16.4 Hz, 1H), 4.43 (s, 2H), 2.34 (s, 3H), 1.47 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 139.84, 137.52, 134.66, 134.14, 129.41, 129.15, 128.69, 128.41, 127.56, 127.26, 127.10, 126.44, 75.76, 65.24, 26.70, 21.30. LC-MS (ESI): m/z [M + Na]$^+$ calcd for $C_{19}H_{22}ONa$ 289.2, found 289.2. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{19}H_{22}ONa$ 289.1563, found: 289.1566.

(*E*)-1-(3-methoxy-3-methylbut-1-en-1-yl)-4-methylbenzene （5c）[3]

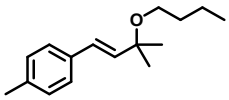


Following general procedure C, **1a** (0.35 g, 2.0 mmol) and MeOH (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to give the product **5c.**

Light yellow oil (0.25 g, 65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (d, J = 8.1 Hz, 2H), 7.15 – 7.10 (m, 2H), 6.46 (d, J = 16.4 Hz, 1H), 6.14 (d, J = 16.3 Hz, 1H), 3.20 (s, 3H), 2.33 (s, 3H), 1.37 (s, 6H). ^{13}C{^{1}H} NMR

(101 MHz, Chloroform-*d*) δ 137.42, 134.21, 129.37, 129.11, 126.39, 75.21, 50.56, 26.02, 21.25. HRMS (Q-TOF): m/z $[M+Na]^+$ calcd for $C_{13}H_{18}ONa$ 213.1250, found: 213.1245.

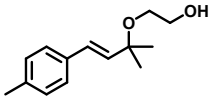
(*E*)-1-(3-butoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (5d)



Following general procedure C, **1a** (0.35 g, 2.0 mmol) and butan-1-ol (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford **5d.**

Colorless oil (0.34 g, 74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, J = 7.9 Hz, 2H), 7.12 (d, J = 7.8 Hz, 2H), 6.43 (d, J = 16.3 Hz, 1H), 6.16 (d, J = 16.3 Hz, 1H), 3.32 (t, J = 6.7 Hz, 2H), 2.33 (s, 3H), 1.55 – 1.48 (m, 2H), 1.36 (s, 9H), 0.90 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.30, 135.17, 134.34, 129.35, 128.49, 126.35, 74.78, 62.51, 32.83, 26.55, 21.24, 19.50, 14.06. HRMS (Q-TOF): m/z $[M+Na]^+$ calcd for $C_{16}H_{24}ONa$ 255.1719, found: 255.1719.

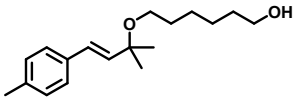
(*E*)-2-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)ethan-1-ol (5e)



Following general procedure C, **1a** (0.35 g, 2.0 mmol) and ethane-1,2-diol (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford **5e.**

Colorless oil (0.25 g, 57%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, J = 8.2 Hz, 2H), 7.16 – 7.08 (m, 2H), 6.45 (d, J = 16.4 Hz, 1H), 6.15 (d, J = 16.3 Hz, 1H), 3.72 – 3.65 (m, 2H), 3.48 – 3.41 (m, 2H), 2.33 (s, 3H), 2.26 (s, 1H), 1.39 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.54, 134.26, 134.03, 129.38, 129.13, 126.42, 75.37, 63.86, 62.44, 26.48, 21.25. HRMS (Q-TOF): m/z $[M+Na]^+$ calcd for $C_{14}H_{20}O_2Na$ 243.1356, found: 243.1385.

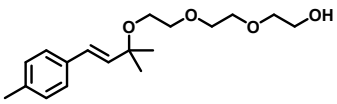
(*E*)-6-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)hexan-1-ol (5f)



Following general procedure C, **1a** (0.35 g, 2.0 mmol) and hexanediol (5mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 3:17) to afford **5f**.

Light yellow oil (0.3 g, 54.5%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.25 (m, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.42 (d, J = 16.4 Hz, 1H), 6.15 (d, J = 16.3 Hz, 1H), 3.59 (t, J = 6.6 Hz, 2H), 3.31 (t, J = 6.7 Hz, 2H), 2.32 (s, 3H), 1.89 (s, 1H), 1.58 – 1.50 (m, 4H), 1.35 (d, J = 4.9 Hz, 10H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.36, 134.97, 134.25, 129.37, 128.61, 126.36, 74.92, 62.91, 62.71, 32.79, 30.62, 26.53, 26.12, 25.71, 21.26. HRMS (Q-TOF): m/z $[M+Na]^+$ calcd for $C_{18}H_{28}O_2Na$ 299.1982, found: 299.2018.

(*E*)-2-(2-(2-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)ethoxy)ethoxy)ethan-1-ol (5g)

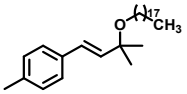


Following general procedure C, **1a** (0.35 g, 2.0 mmol) and 2,2'-(ethane-1,2-diylbis(oxy))bis(ethan-1-ol) (5 mL)

were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:3) to afford **5g.**

Light yellow oil (0.38 g, 62%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 (dd, *J* = 8.1, 2.0 Hz, 2H), 7.13 – 7.02 (m, 2H), 6.42 (dd, *J* = 16.5, 1.9 Hz, 1H), 6.13 (dd, *J* = 16.4, 2.0 Hz, 1H), 3.69 – 3.46 (m, 12H), 3.38 (s, 1H), 2.28 (d, *J* = 2.1 Hz, 3H), 1.34 (d, *J* = 2.2 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.36, 134.32, 134.10, 129.34, 129.06, 126.40, 75.47, 72.76, 71.14, 70.62, 70.36, 62.15, 61.64, 26.42, 21.24. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{18}H_{28}O_4Na$ 331.1880, found: 331.1917.

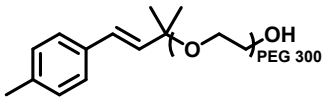
(*E*)-1-methyl-4-(3-methyl-3-(octadecyloxy)but-1-en-1-yl)benzene (5h)



Following general procedure C, **1a** (0.35 g, 2.0 mmol) and 1-Octadecanol (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford **5h.**

Brown solid (0.5 g, 60%). m.p.= 38.0-39.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.43 (d, *J* = 16.4 Hz, 1H), 6.16 (d, *J* = 16.3 Hz, 1H), 3.31 (t, *J* = 6.8 Hz, 2H), 2.33 (s, 3H), 1.36 (s, 6H), 1.25 (d, *J* = 4.2 Hz, 32H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.30, 135.14, 134.32, 129.34, 128.50, 126.35, 74.81, 62.86, 32.02, 30.72, 29.80, 29.63, 29.46, 26.55, 26.32, 22.79, 21.24, 14.21. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{30}H_{52}ONa$ 451.3910, found: 451.3840.

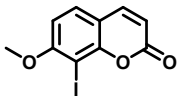
(*E*)-19,19-dimethyl-21-(p-tolyl)-3,6,9,12,15,18-hexaoxahenicos-20-en-1-ol （5i）



Following general procedure C, **1a** (0.35 g, 2.0 mmol) and hexaethylene glycol (5 mL) were used. The crude product was purified by silica gel column chromatography (MeOH/DCM= 1:49) to afford **5i.**

Yellow oil (0.51 g, 58%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.25 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 7.9 Hz, 2H), 6.43 (d, J = 16.3 Hz, 1H), 6.13 (d, J = 16.3 Hz, 1H), 3.70 – 3.55 (m, 24H), 2.31 (s, 3H), 1.35 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 137.39, 134.51, 134.15, 129.34, 128.91, 126.38, 75.38, 72.67, 71.19, 70.65, 70.62, 70.58, 70.36, 62.21, 61.78, 26.49, 21.27. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{30}H_{52}ONa$ 451.3910, found: 451.3910.

8-Iodo-7-methoxy-2*H*-chromen-2-one[7]

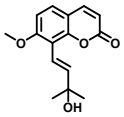


According to a reported literature[7], umbelliferone (5.00 g, 31 mmol) was dissolved in 20% ammonium hydroxide solution (125 mL). A solution of potassium iodide (12.28 g, 74 mmol) and iodine (7.87 g, 31 mmol) in water (240 mL) was added over 60 min. The mixture was stirred for 24 h at room temperature before sulfuric acid (300 mL, 2.5M) was carefully added. The crude product was collected by filtration and was purified by recrystallisation (acetone) to afford a pale brown powder. After that, the pale brown powder was dissolved in acetone (50 mL), then anhydrous potassium carbonate (4.7 g, 34.1 mmol) and the corresponding MeI (2.1 mL, 34.1 mmol) were added. The solution was heated to reflux for 5 h. Water (50 mL) was added and the mixture was extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by silica gel column (EA/PE = 1:4) to afford

the title product.

White solid (1.87g, 20%). m.p.=147.4-148.2°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.56 (d, J = 9.5 Hz, 1H), 7.42 (d, J = 8.6 Hz, 1H), 6.79 (d, J = 8.6 Hz, 1H), 6.24 (d, J = 9.4 Hz, 1H), 3.97 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 161.75, 160.62, 155.09, 143.21, 129.20, 113.97, 113.80, 107.51, 76.09, 57.10.
HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{10}H_7IO_3Na$ 324.9332, found: 324.9335.

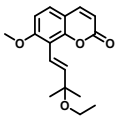
(*E*)-8-(3-hydroxy-3-methylbut-1-en-1-yl)-7-methoxy-2*H*-chromen-2-one (6)[7]



Following general procedure A, 8-Iodo-7-methoxy-2H-chromen-2-one (0.3 g, 1.0 mmol) and 2-methylbut-3-en-2-ol (0.13g, 1.5mmol) were used. The product was purified by silica gel column chromatography (EA/PE = 1:3 to 2:3) to afford **6.**

Brown oil (0.33 g, 56.9%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.62 (d, J = 9.5 Hz, 1H), 7.29 (d, J = 8.7 Hz, 1H), 7.02 (d, J = 16.5 Hz, 1H), 6.92 (d, J = 16.5 Hz, 1H), 6.86 (d, J = 8.7 Hz, 1H), 6.25 (d, J = 9.5 Hz, 1H), 3.95 (s, 3H), 1.47 (s, 6H). ^{13}C{1H} NMR (101 MHz, Chloroform-d) δ 161.13, 160.30, 152.66, 144.59, 144.05, 127.12, 114.38, 113.73, 113.08, 113.02, 107.64, 71.72, 56.21, 29.95. LC-MS (ESI): m/z [M + Na]$^+$ calcd for $C_{15}H_{16}O_4Na$ 283.1; found 283.1.

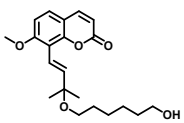
(*E*)-8-(3-ethoxy-3-methylbut-1-en-1-yl)-7-methoxy-2*H*-chromen-2-one (6a)



Following general procedure C, **6** (0.52 g, 2.0 mmol), EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford **6a**.

White solid (0.33 g, 57%). m.p.= 69.7-71.4 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 9.5 Hz, 1H), 7.23 (d, *J* = 8.5 Hz, 1H), 6.81 – 6.72 (m, 3H), 6.16 (d, *J* = 9.3 Hz, 1H), 3.88 (s, 3H), 3.42 (q, *J* = 7.0 Hz, 2H), 1.36 (s, 6H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 160.93, 160.28, 152.56, 143.97, 142.89, 127.16, 116.62, 113.73, 113.03, 112.95, 107.64, 75.76, 58.26, 56.18, 26.58, 16.25. LC-MS (ESI): m/z [M + Na]$^+$ calcd for $C_{17}H_{20}O_4Na$ 311.1; found 311.1. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{17}H_{20}O_4$ Na 311.1254, found: 311.1256.

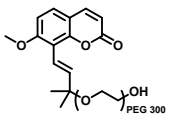
(*E*)-8-(3-((6-hydroxyhexyl)oxy)-3-methylbut-1-en-1-yl)-7-methoxy-2*H*-chromen-2-one (6b)



Following general procedure C, **6** (0.52 g, 2.0 mmol), Hexanediol (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 2:3) to afford **6b**.

Yellow oil (0.45 g, 62%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.57 (d, J = 9.5 Hz, 1H), 7.25 (d, J = 8.6 Hz, 1H), 6.82 (d, J = 8.7 Hz, 1H), 6.74 (d, J = 1.1 Hz, 2H), 6.19 (d, J = 9.5 Hz, 1H), 3.89 (s, 3H), 3.56 (t, J = 6.6 Hz, 2H), 3.36 (t, J = 6.8 Hz, 2H), 2.08 (s, 1H), 1.59 – 1.48 (m, 4H), 1.40 – 1.31 (m, 10H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 161.10, 160.32, 152.56, 144.06, 143.10, 127.16, 116.63, 113.82, 113.06, 113.00, 107.69, 75.67, 62.95, 62.81, 56.21, 32.76, 30.60, 26.53, 26.09, 25.71. LC-MS (ESI): m/z [M + Na]$^+$ calcd for $C_{21}H_{28}O_5Na$ 383.2; found 383.2. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{21}H_{28}O_5Na$ 383.1829, found: 383.1832.

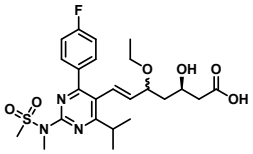
(*E*)-8-(1-hydroxy-19,19-dimethyl-3,6,9,12,15,18-hexaoxahenicos-20-en-21-yl)-7-methoxy-2*H*-chromen-2-one（6c）



Following general procedure C, **6** (0.52 g, 2.0 mmol), Hexaethylene glycol (5 mL) were used. The crude product was purified by silica gel column chromatography (CH_3OH/DCM = 1:19) to afford **6c**.

Yellow oil (0.52 g, 50%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 9.5 Hz, 1H), 7.29 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.77 (s, 2H), 6.24 (d, *J* = 9.5 Hz, 1H), 3.93 (s, 3H), 3.74 – 3.53 (m, 24H), 1.41 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 160.96, 160.35, 152.67, 143.93, 142.64, 127.17, 117.06, 113.82, 113.21, 113.02, 107.64, 76.23, 72.67, 71.19, 70.61, 70.56, 70.28, 62.35, 61.73, 56.23, 26.39. LC-MS (ESI): m/z [M + Na]$^+$ calcd for $C_{27}H_{40}O_{10}Na$ 547.2; found 547.2. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{27}H_{40}O_{10}Na$ 547.2514, found: 547.2515.

(3R,E)-5-ethoxy-7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)-3-hydroxyhept-6-enoic acid (7a)

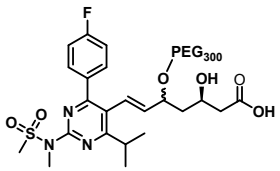


Following general procedure C, **7** (0.96 g, 2.0 mmol), EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 2:3) to afford **7a**.

Yellow oil (0.64 g, 62%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 – 7.61 (m, 2H), 7.13 – 7.05 (m, 2H), 6.64 (dd, *J* = 16.1, 1.6 Hz, 1H), 5.45 (dd, *J* = 16.1, 5.2 Hz, 1H), 4.49 – 4.43 (m, 1H), 4.19 (q, *J* = 7.2 Hz, 3H), 3.57 (s, 3H), 3.52 (s, 3H), 3.37 (p, *J* = 6.6 Hz, 1H), 2.48 – 2.44 (m, 2H), 1.56 (dt, *J* = 14.3, 9.8 Hz, 1H), 1.45 (dt, *J* = 14.3, 3.0 Hz, 1H), 1.27 (dd, *J* = 6.9, 5.6 Hz, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 175.01, 172.77, 163.58, 157.36, 139.46, 134.66, 132.28, 132.19, 122.74, 121.51, 115.21, 114.99, 72.06, 68.57, 61.10, 42.51, 41.94, 41.36, 33.20, 32.21, 21.71, 21.68, 14.23. LC-MS (ESI): m/z [M + H]$^+$ calcd for $C_{24}H_{33}FN_3O_6S$ 510.2; found 510.2. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for $C_{24}H_{32}FN_3O_6SNa$ 532.1888, found: 532.1892. [α]25 D: +7.6 (c = 1.0 g / mL, methanol: water =1:1).

7 (Rosuvastatin): [α]25 D: +14.3 (c = 1.0 g / mL, methanol: water =1:1). (Reference: O'Neil, M. J. The Merck Index –An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013. ISBN: 978-1-84973-670-1. Page: 1540. [α]24 D: +14.8 (c = 1.012 g / mL, methanol: water =1:1)).

(21R)-19-((E)-2-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)vinyl)-1,21-dihydroxy-3,6,9,12,15,18-hexaoxatricosan-23-oic acid（7b）

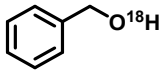


Following general procedure C, **7** (0.96 g, 2.0 mmol), Hexaethylene glycol (5 mL) were used. The crude product

was purified by silica gel column chromatography (EA/PE = 2:3) to afford **7b**.

Yellow oil (1.0 g, 45%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.60 (m, 2H), 7.11 – 7.03 (m, 2H), 6.59 (dd, *J* = 16.1, 1.6 Hz, 1H), 5.44 (dd, *J* = 16.1, 5.2 Hz, 1H), 4.42 (ddd, *J* = 7.8, 4.4, 1.7 Hz, 1H), 4.29 – 4.20 (m, 3H), 3.71 – 3.56 (m, 22H), 3.54 (s, 3H), 3.49 (s, 3H), 3.40 – 3.31 (m, 1H), 2.52 – 2.44 (m, 2H), 1.61 – 1.40 (m, 2H), 1.24 (d, *J* = 6.7 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 175.02, 172.02, 163.53, 157.31, 139.70, 132.30, 132.22, 122.47, 121.64, 115.20, 114.99, 72.87, 71.85, 70.60, 70.55, 70.53, 70.48, 70.43, 70.09, 69.02, 68.47, 63.78, 61.60, 42.49, 42.44, 42.21, 33.20, 32.13, 21.74, 21.71. LC-MS (ESI): m/z [M + Na]+ calcd for $C_{34}H_{52}FN_3O_{12}SNa$ 768.2; found 768.2. HRMS (Q-TOF): m/z [M+Na]$^{+}$ calcd for $C_{34}H_{52}FN_3O_{12}SNa$ 768.3148, found: 768.3164. [α]25 D: +8.2 (c = 1.0 g / mL, methanol: water =1:1).

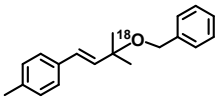
Bn ^{18}OH



Following a reported literature,[16] Benzylbromide (2.00 mL, 16.7 mmol) was heated to 75°C in a sealed flask. Diisopropylethylamine (2.16 g, 16.7 mmol) and heavy water (300 μL, 16.7 mmol) were added and the mixture was stirred for 24 hours. Water (10 mL) and dichloromethane (50 mL) were added and the organic layer was washed two times with brine. The organic layer was dried (Na_2SO_4) and evaporated to dryness. The product was purified by column chromatography (EA/PE = 1:19 to 1:9) to afford Bn ^{18}OH.

Colorless liquid (0.83 g, 45%). Repeat this procedure, 2.0 g product was prepared. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 4.4 Hz, 4H), 7.32 – 7.26 (m, 1H), 4.67 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 140.96, 128.67, 127.77, 127.10, 65.43. HRMS (Q-TOF): m/z [M+H]$^{+}$ calcd for $C_7H_9O^{18}$ 111.0804, found: 111.0817.

(*E*)-1-(3-(Benzyl oxygen 18)-3-methylbut-1-en-1-yl)-4-methylbenzene (8)



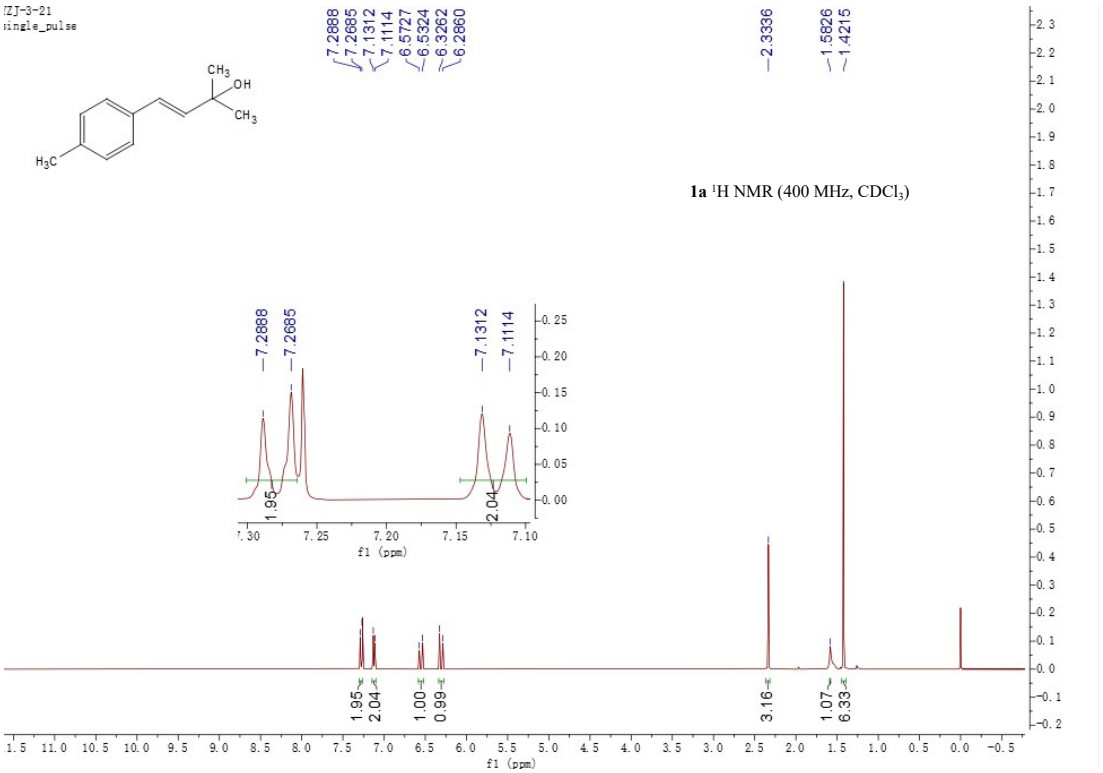
Following general procedure C, **1a** (0.35 g, 2.0 mmol) and Bn ^{18}OH (2g) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford **8.**

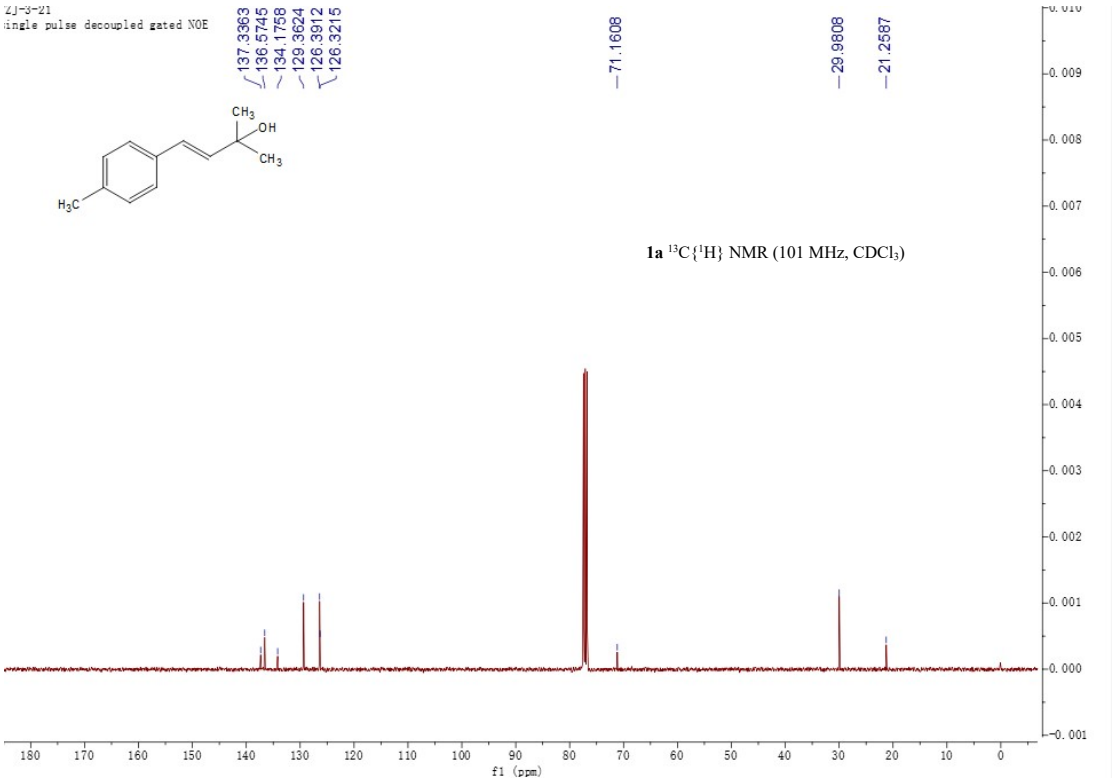
Yellow oil (0.43 g, 80%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.39 – 7.26 (m, 7H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.53 (d, *J* = 16.3 Hz, 1H), 6.26 (d, *J* = 16.4 Hz, 1H), 4.43 (s, 2H), 2.34 (s, 3H), 1.47 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 139.84, 137.52, 134.66, 134.14, 129.41, 129.15, 128.41, 127.56, 127.26, 75.76, 65.24, 26.70, 21.34, 21.30. LC-MS (ESI): m/z [M + Na]$^{+}$ calcd for $C_{19}H_{23}O^{18}Na$ 291.1; found 291.1. HRMS (Q-TOF): m/z [M+H]$^{+}$ calcd for $C_{19}H_{23}O^{18}$ 269.1752, found: 269.2070.

4 Copy of NMR

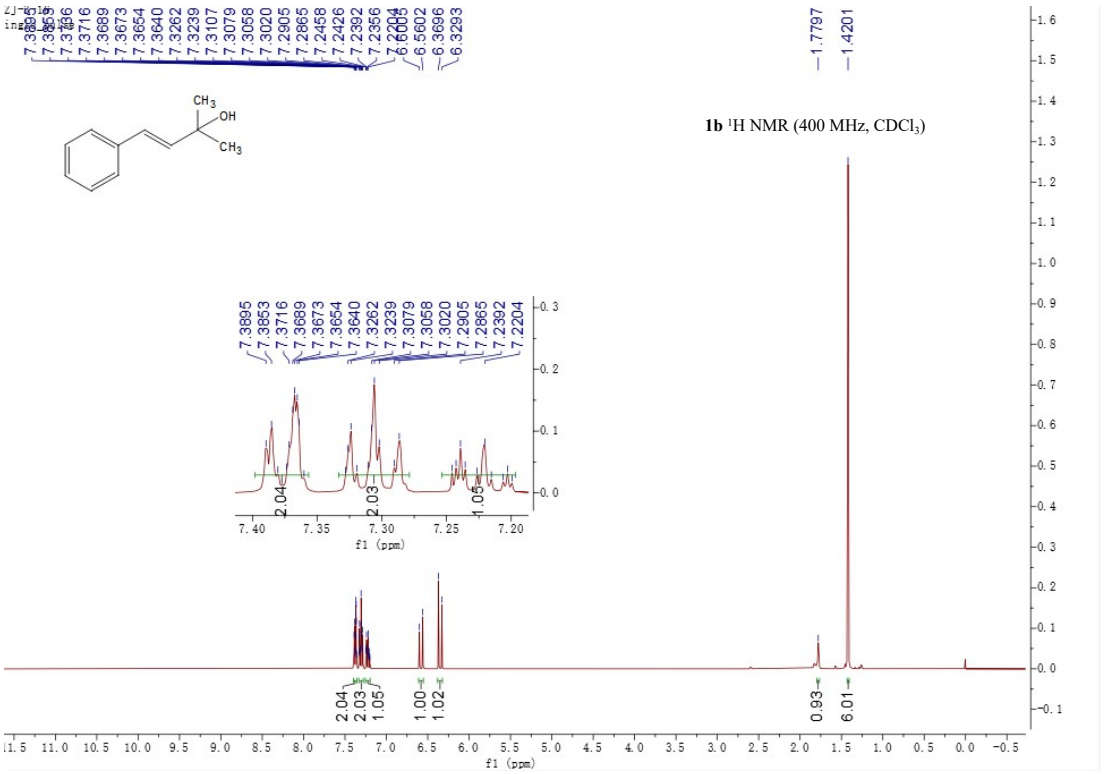
4.1 ^{1}H-NMR and ^{13}C{^{1}H} NMR Spectra of the Substrates

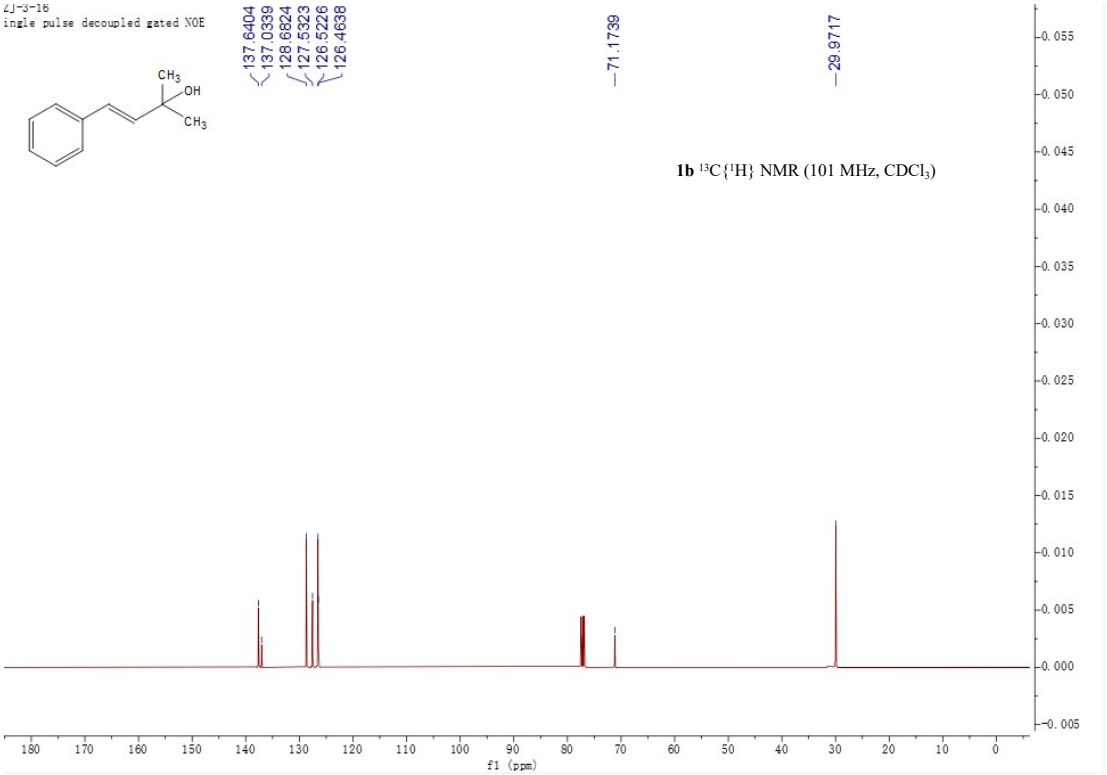
^{1}H-NMR and ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) Spectra of (*E*)-2-methyl-4-(p-tolyl)but-3-en-2-ol (1a)



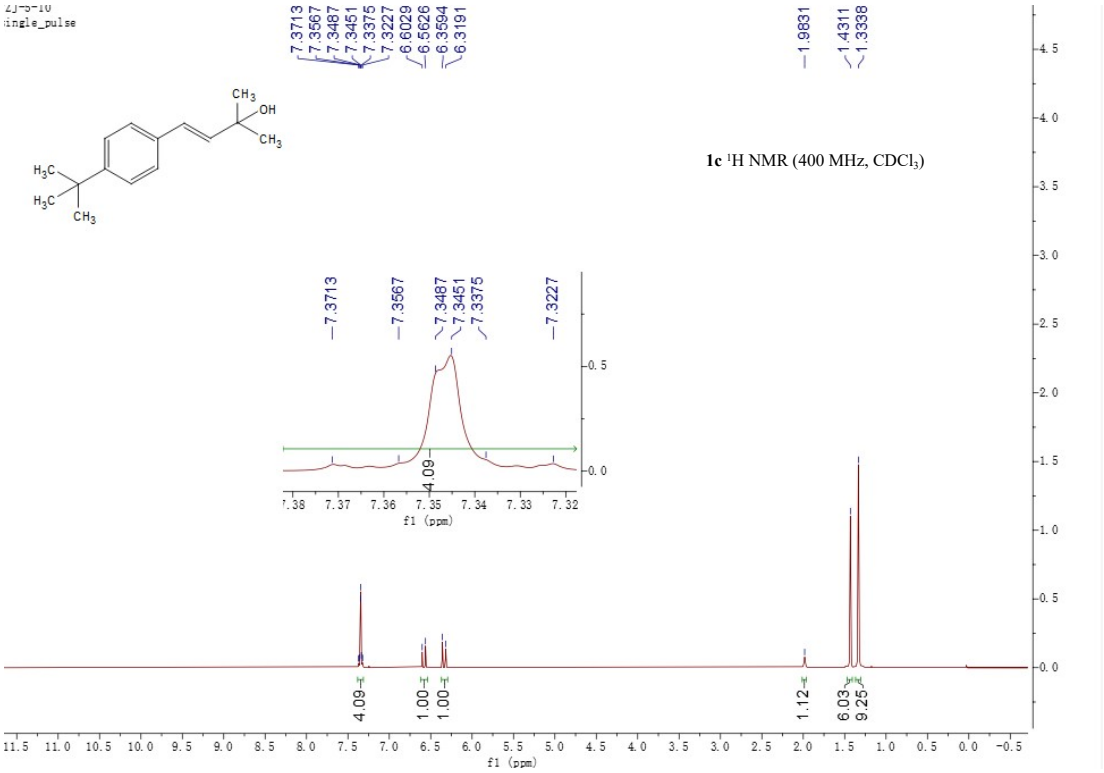


^{1}H-NMR and ^{13}C{^{1}H}NMR Spectra of (*E*)-2-methyl-4-phenylbut-3-en-2-ol (1b)

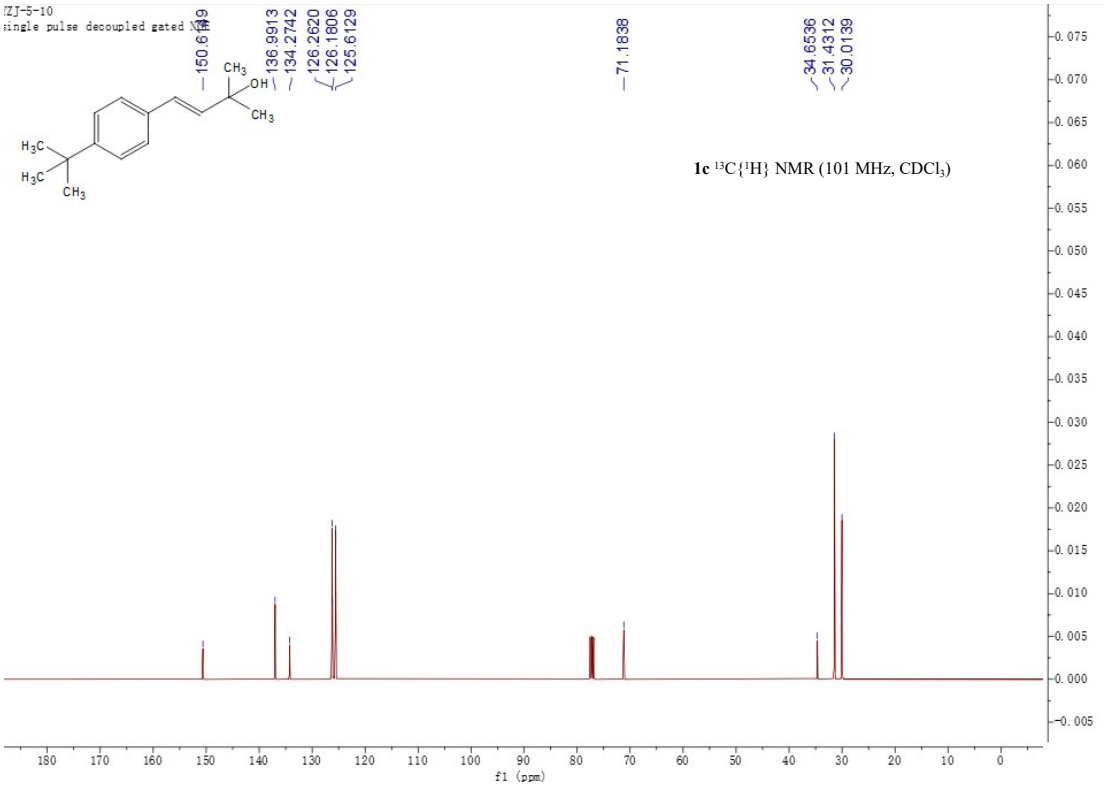




^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(4-(tert-butyl)phenyl)-2-methylbut-3-en-2-ol (1c)

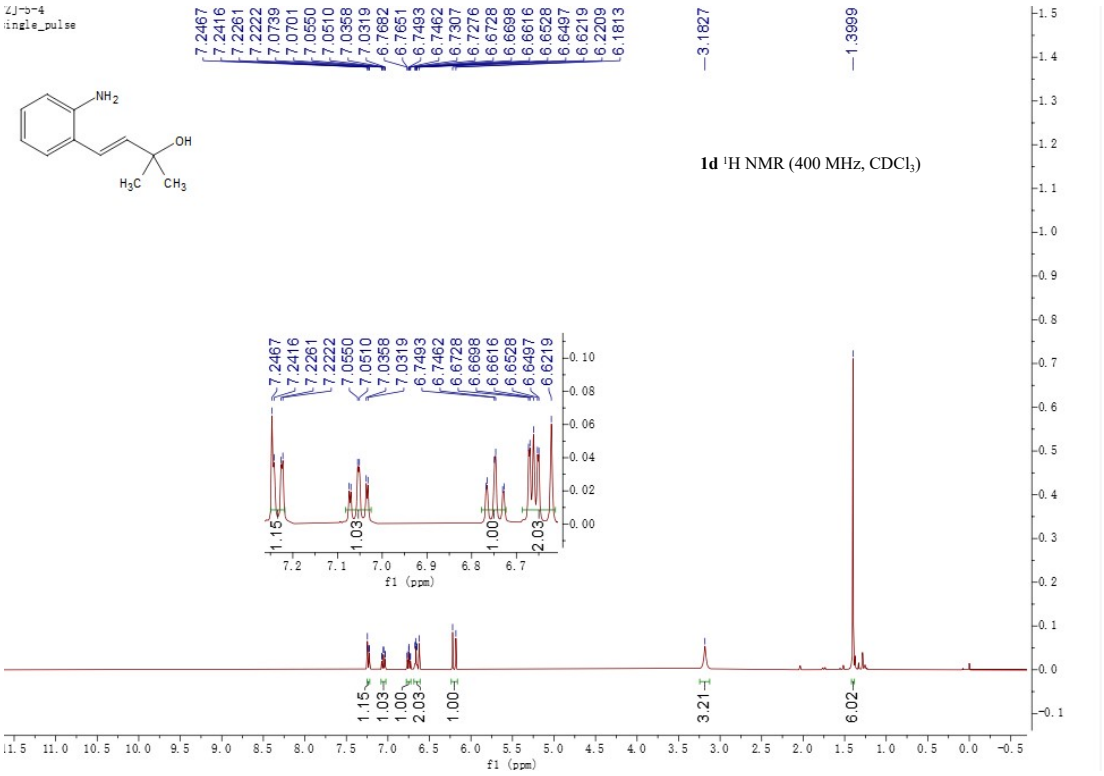


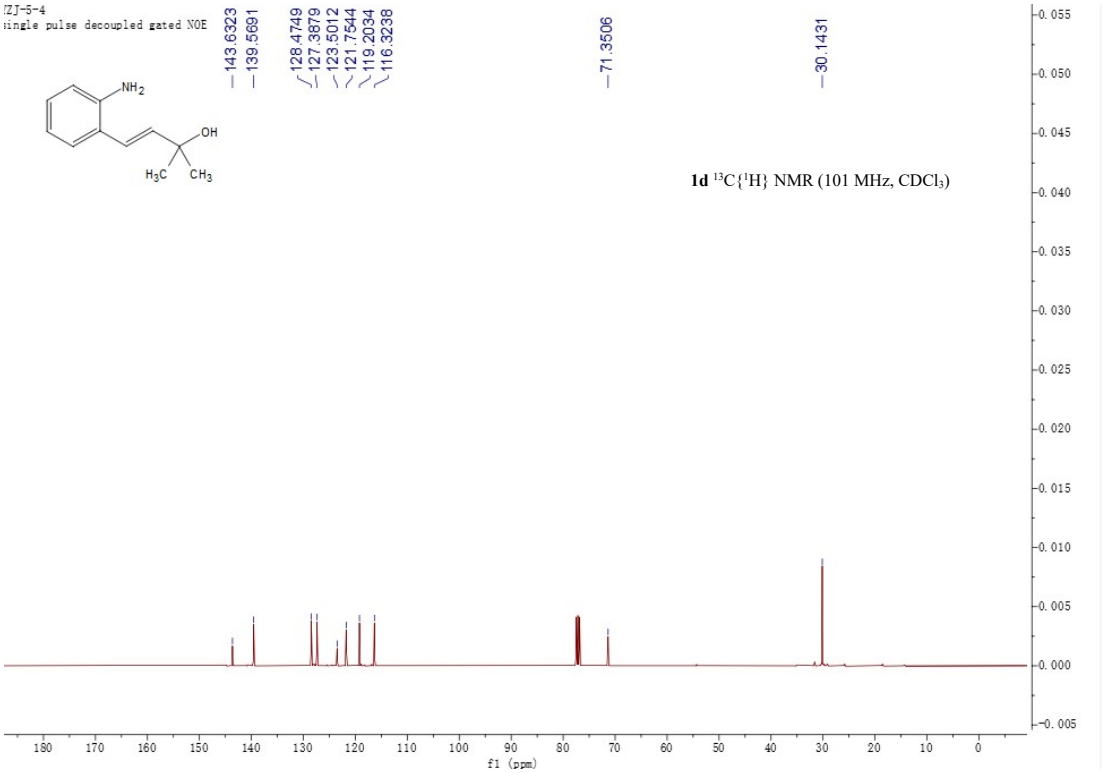
1c ^{1}H NMR (400 MHz, $CDCl_3$)



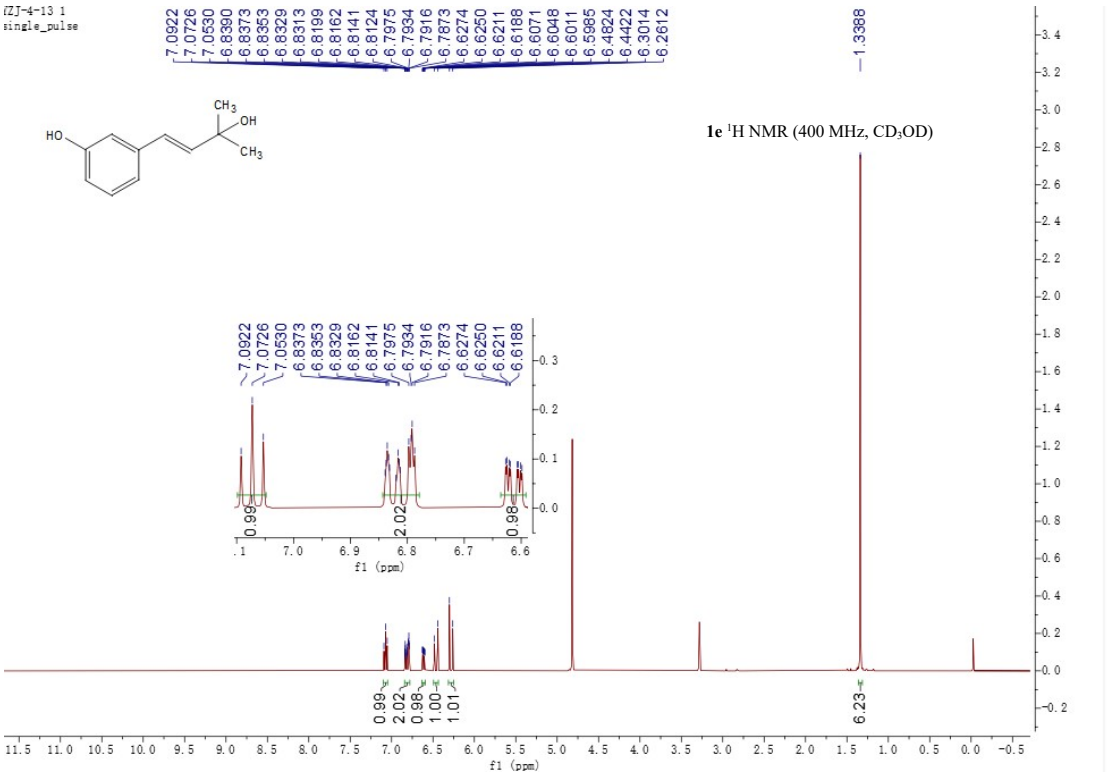
1c ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

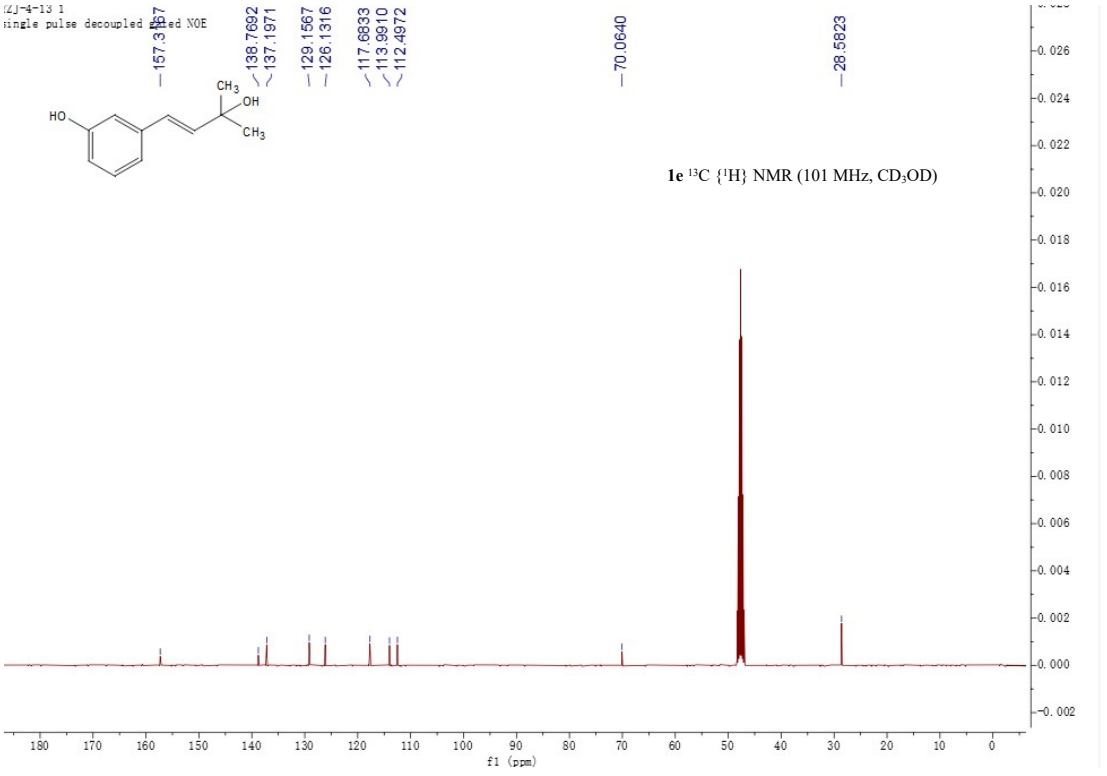
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(2-aminophenyl)-2-methylbut-3-en-2-ol (1d)



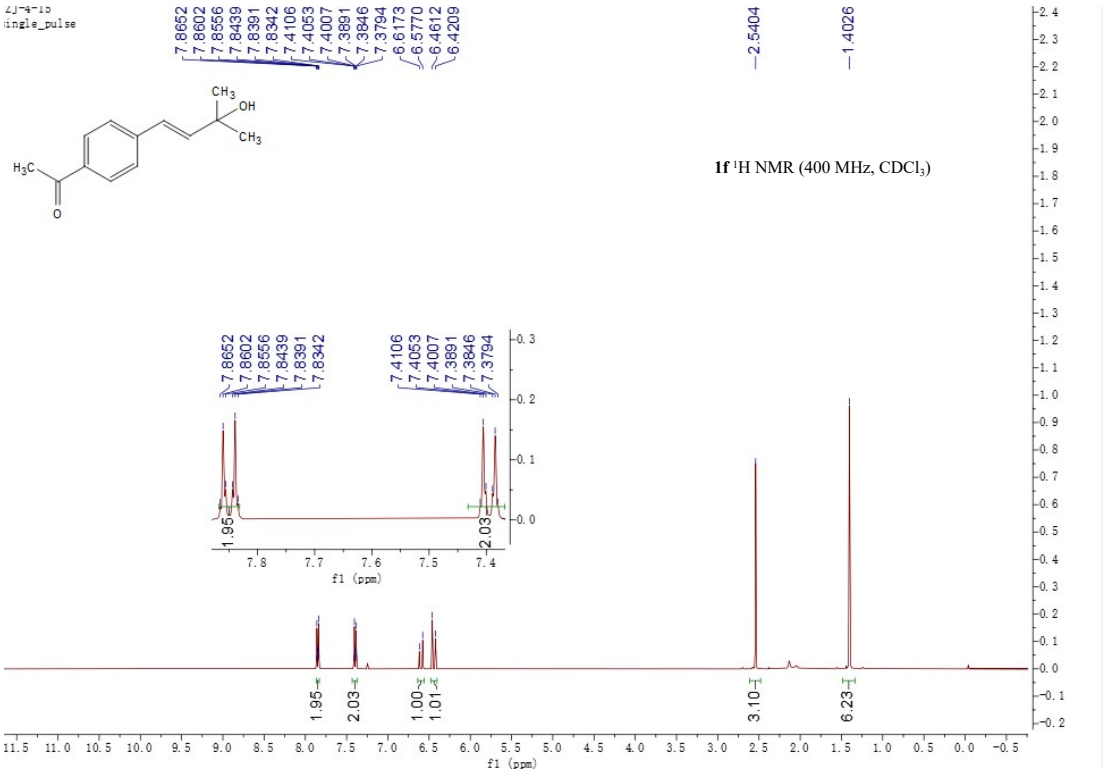


^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-3-(3-hydroxy-3-methylbut-1-en-1-yl)phenol (1e)

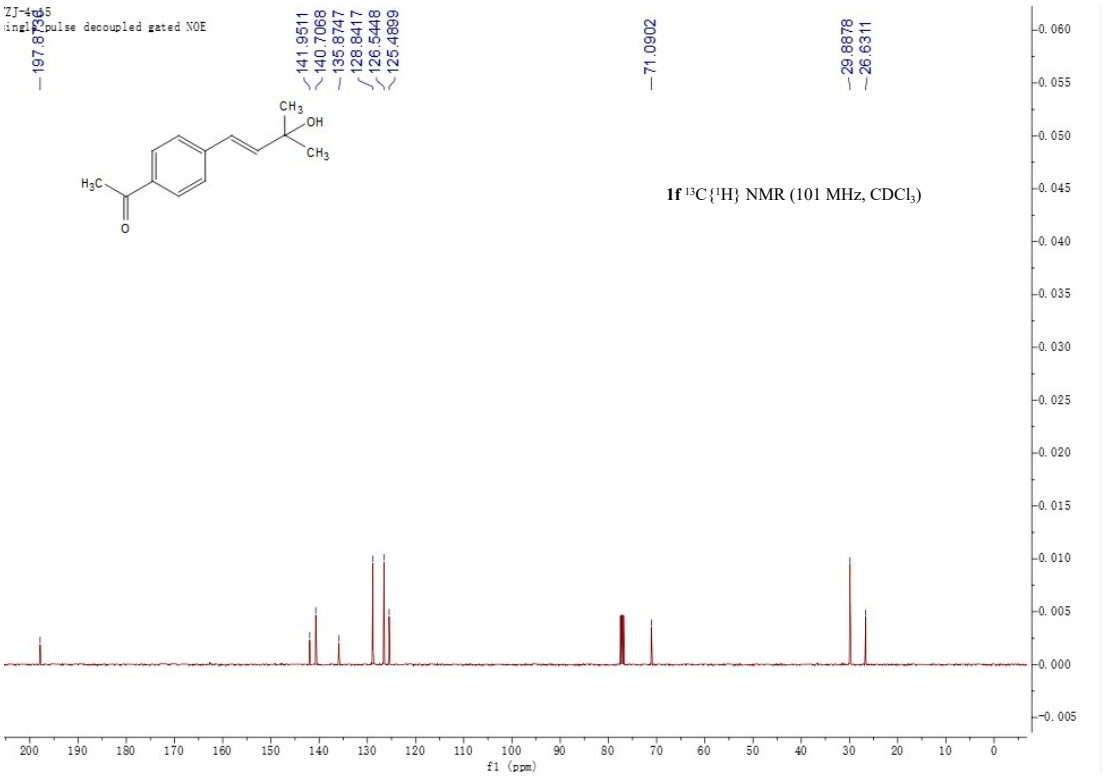




^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(4-(3-hydroxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one (1f)

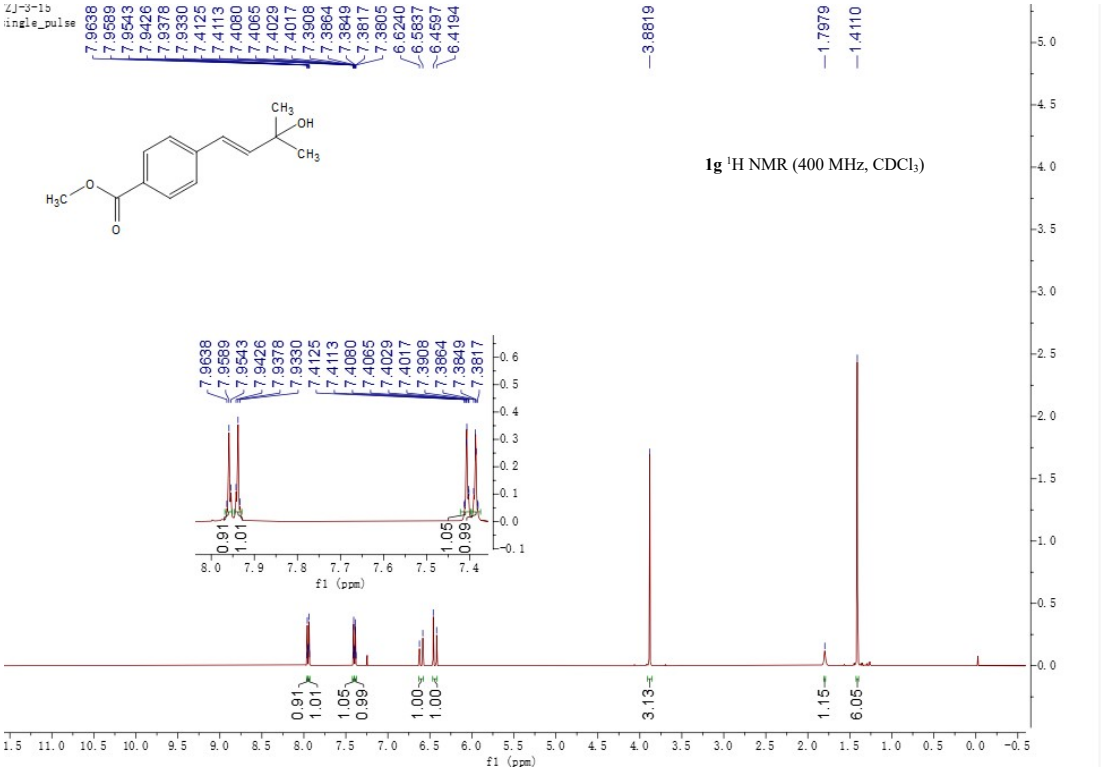


1f ^{1}H NMR (400 MHz, $CDCl_3$)

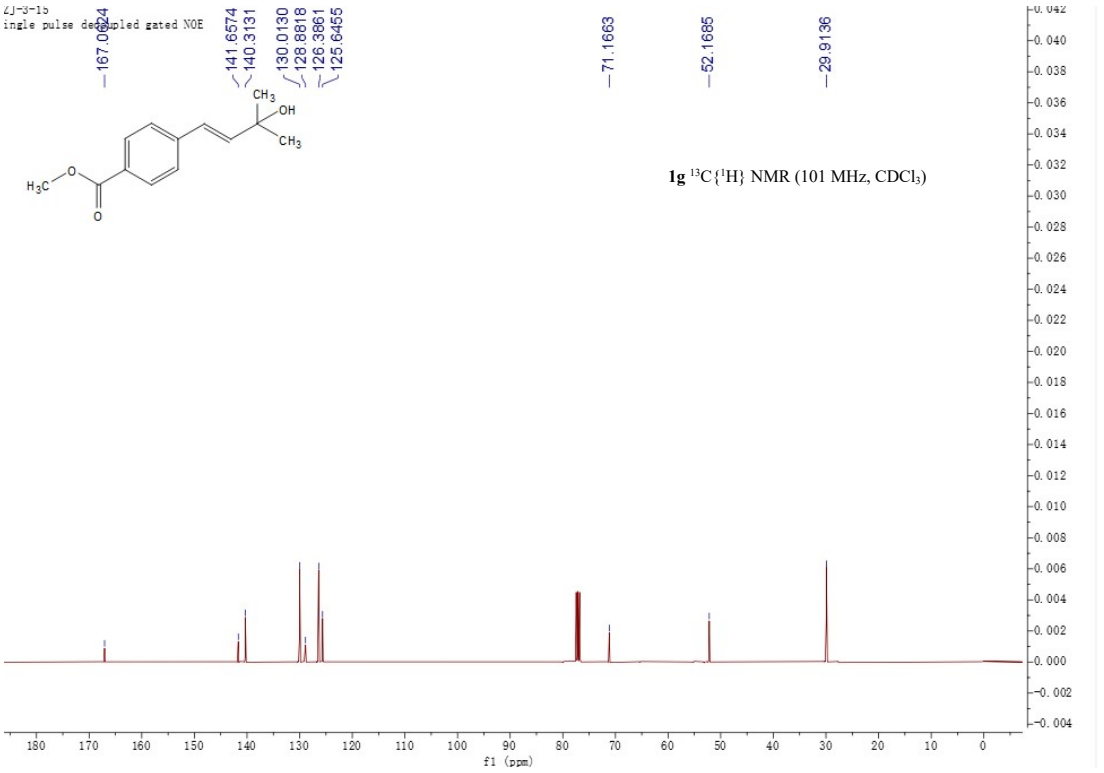


1f ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of methyl (*E*)-4-(3-hydroxy-3-methylbut-1-en-1-yl)benzoate (1g)

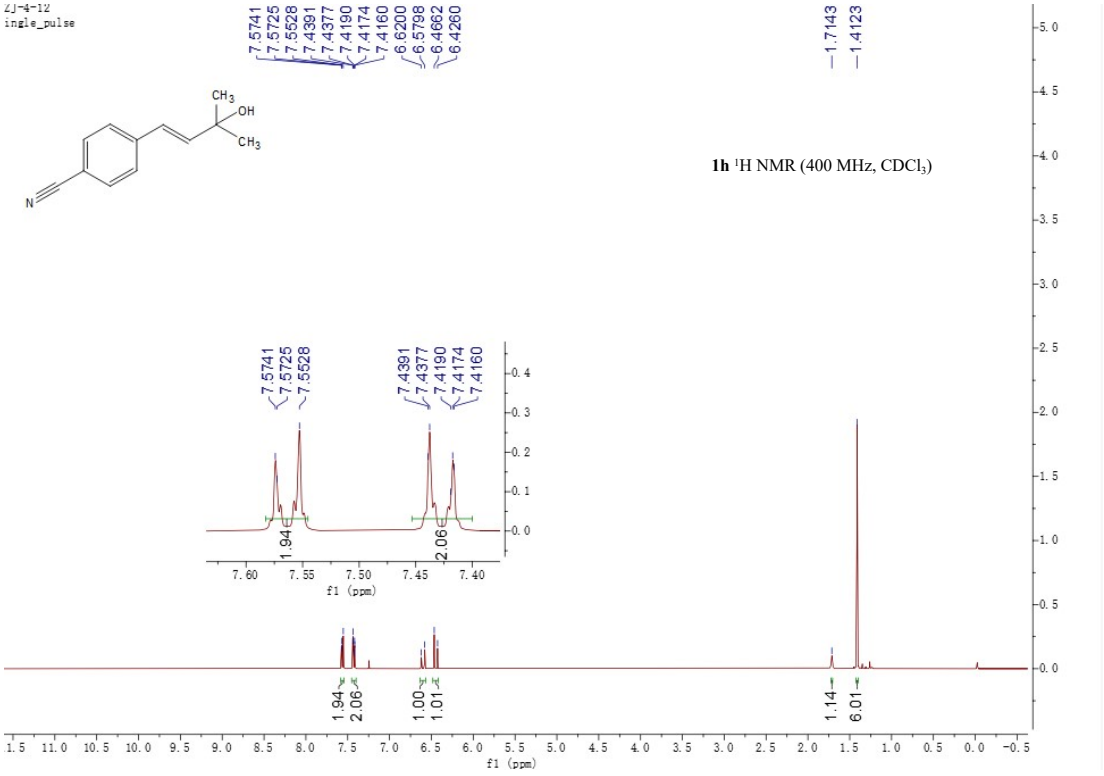


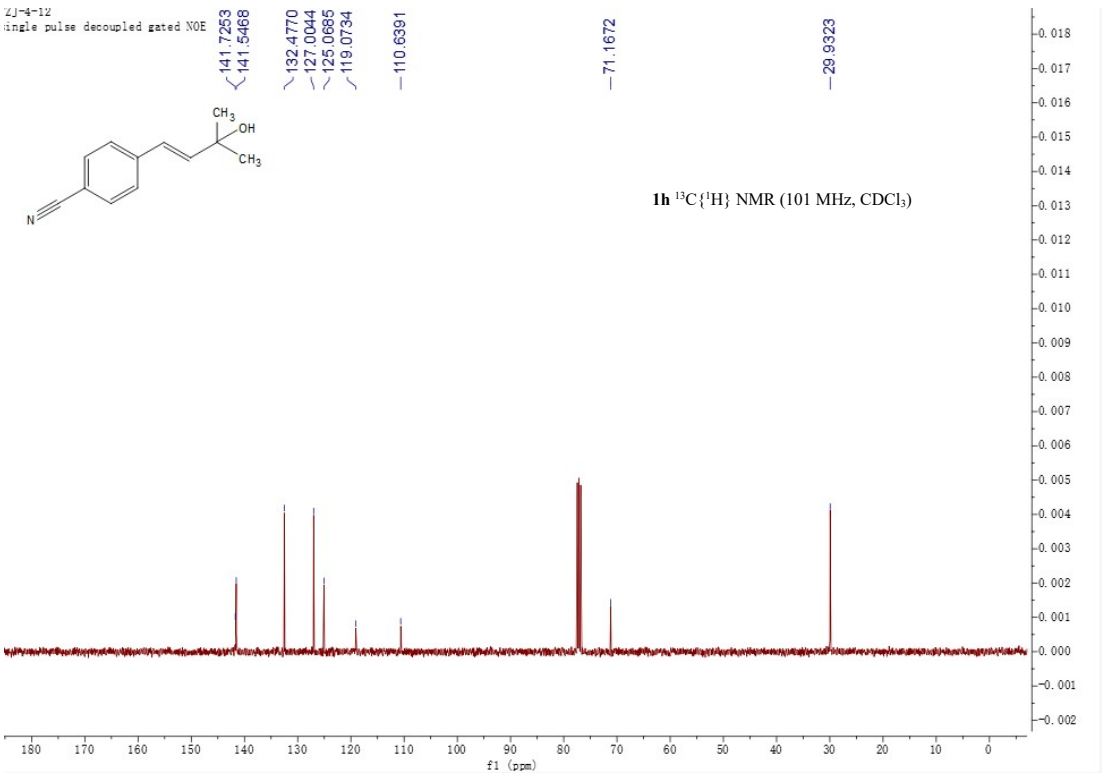
1g ^{1}H NMR (400 MHz, $CDCl_3$)



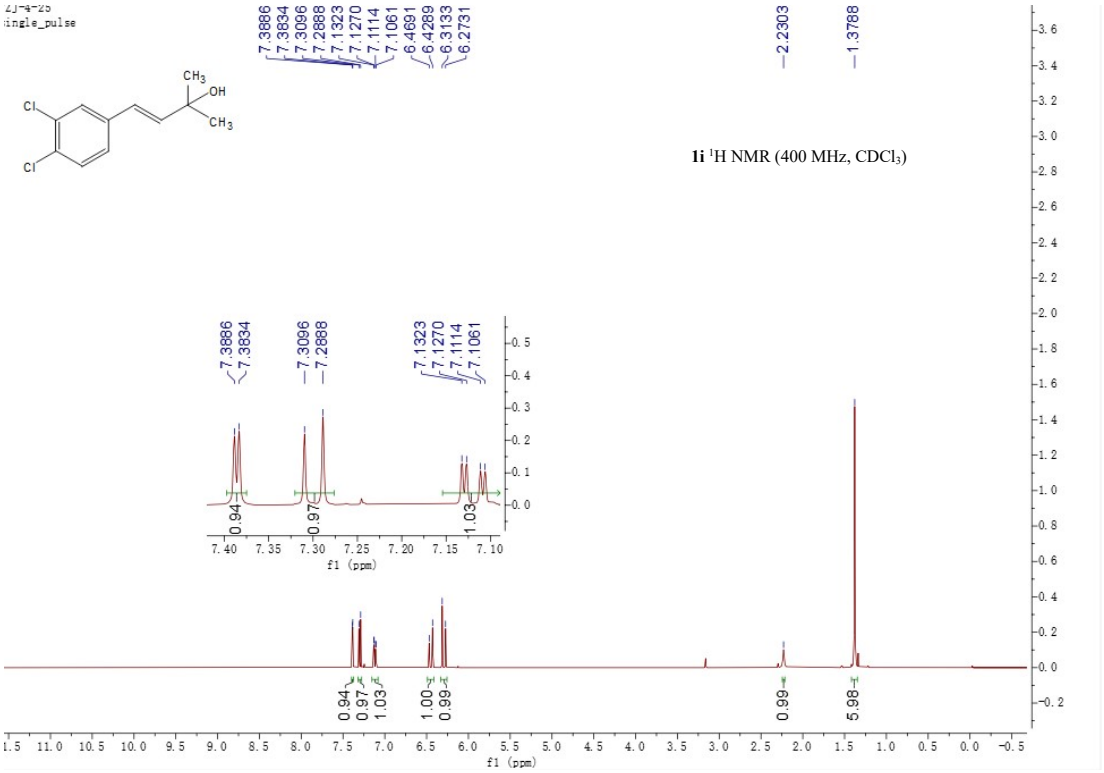
1g ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(3-hydroxy-3-methylbut-1-en-1-yl)benzonitrile (1h)

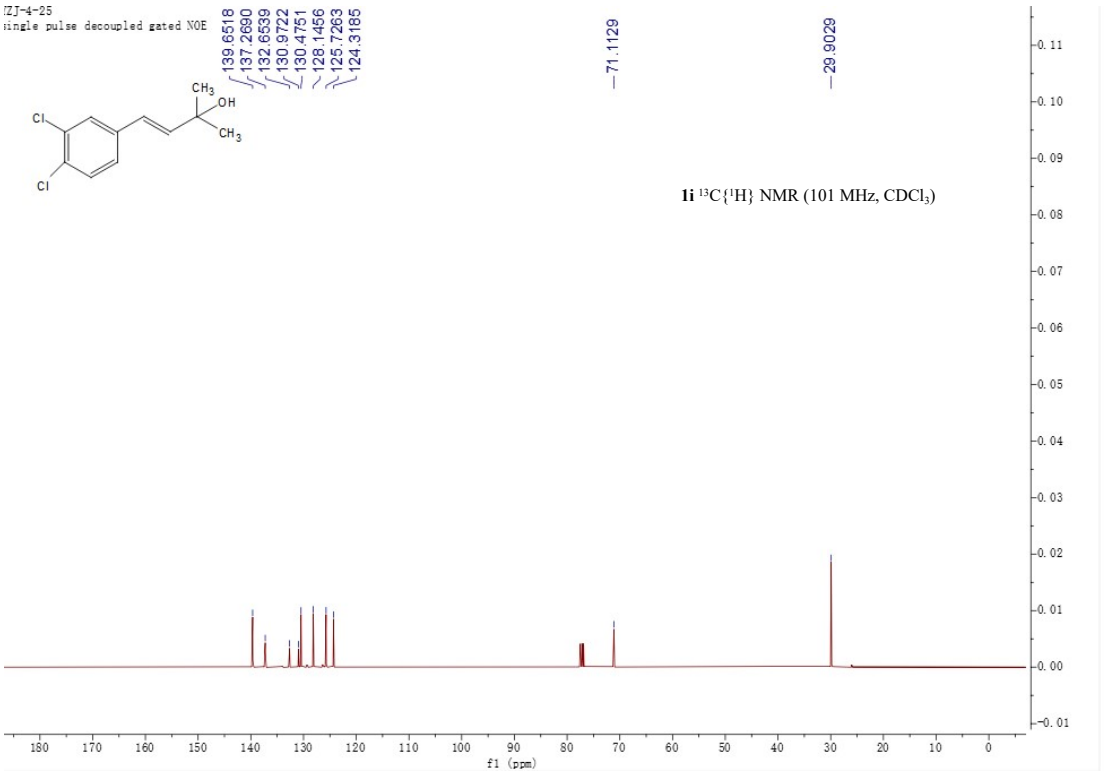




^{1}H-NMR and ^{13}C {^{1}H}NMR Spectra of (*E*)-4-(3,4-dichlorophenyl)-2-methylbut-3-en-2-ol (1i)

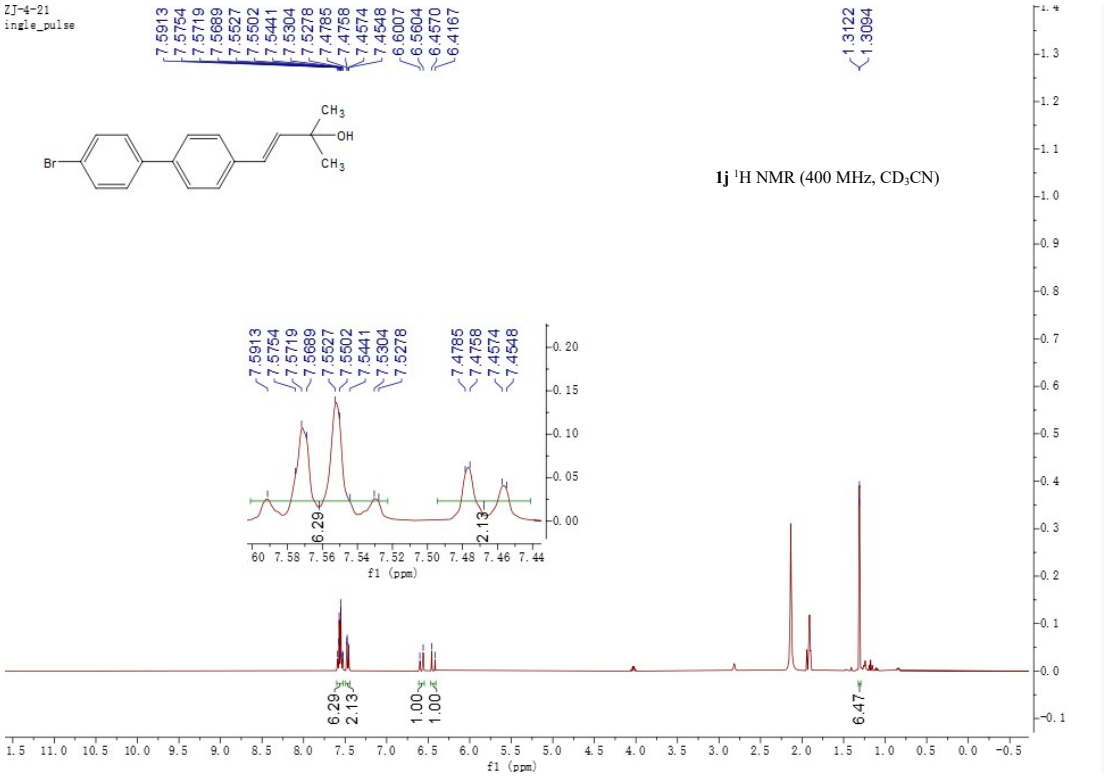


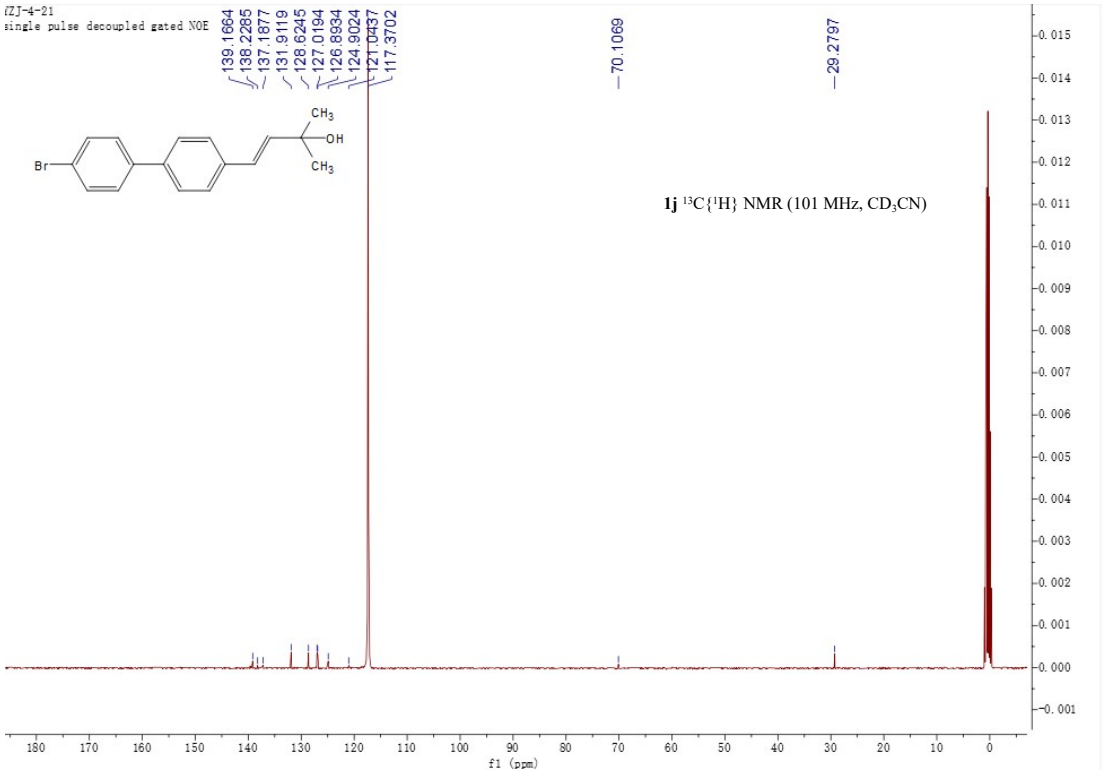
1i ^{1}H NMR (400 MHz, $CDCl_3$)



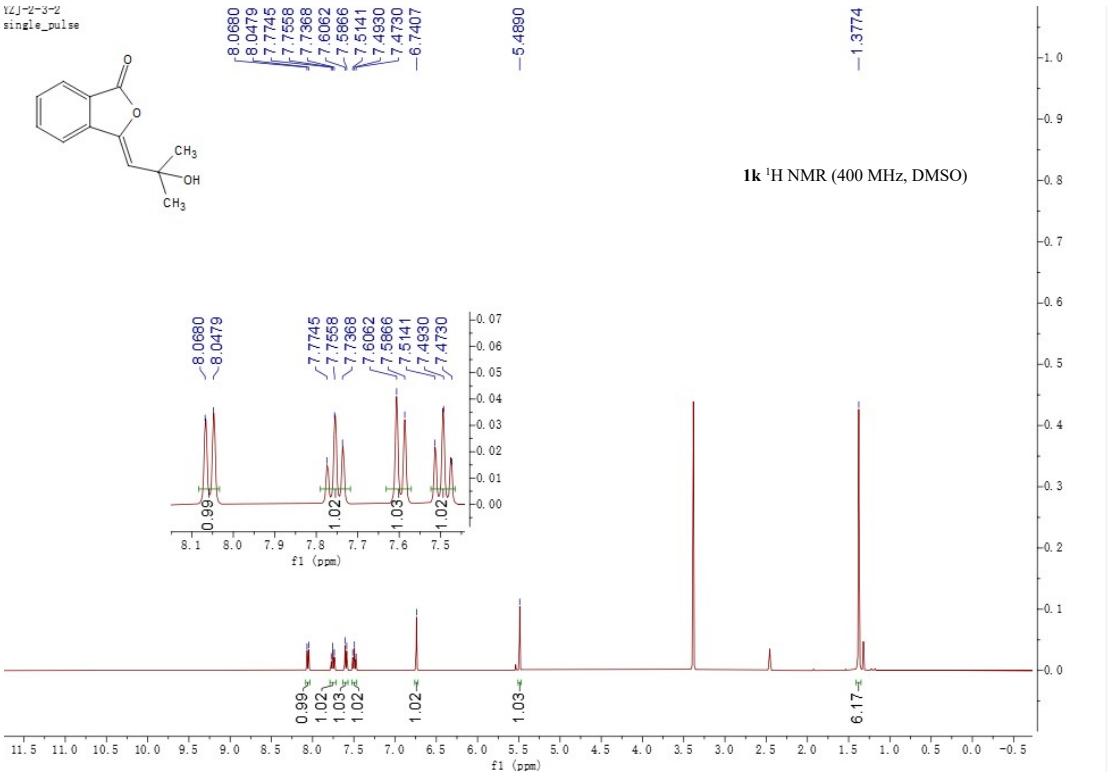
1i ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

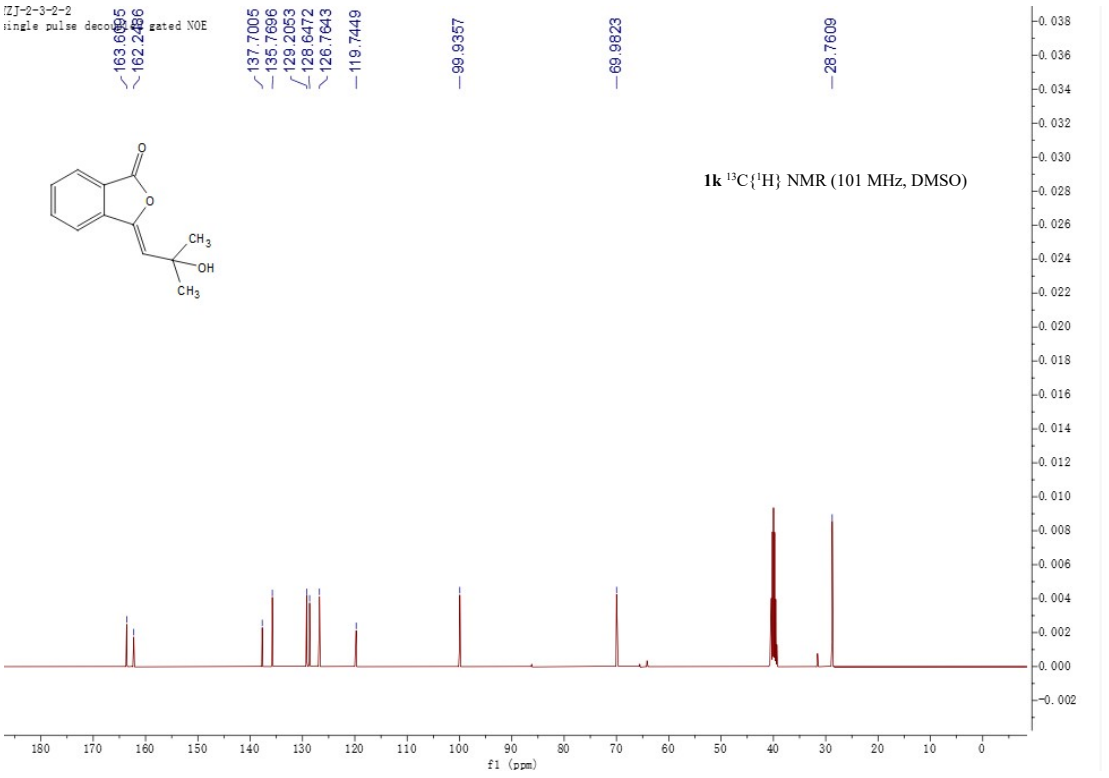
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(4'-bromo-[1,1'-biphenyl]-4-yl)-2-methylbut-3-en-2-ol (1j)



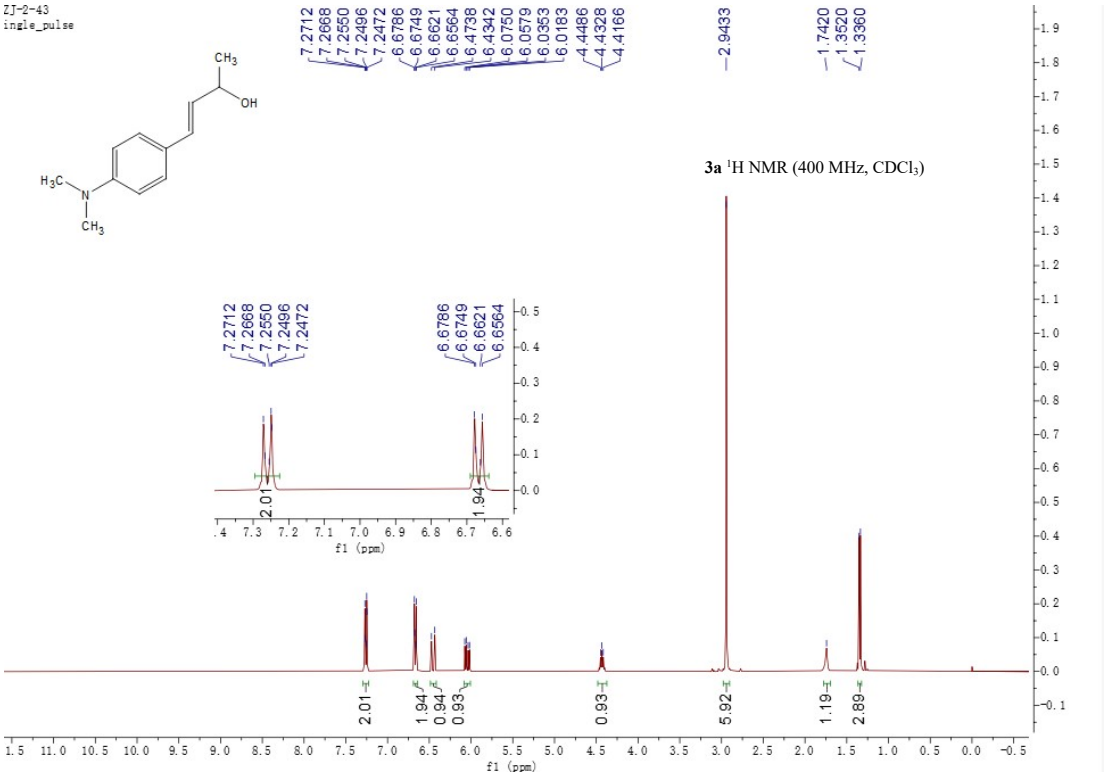


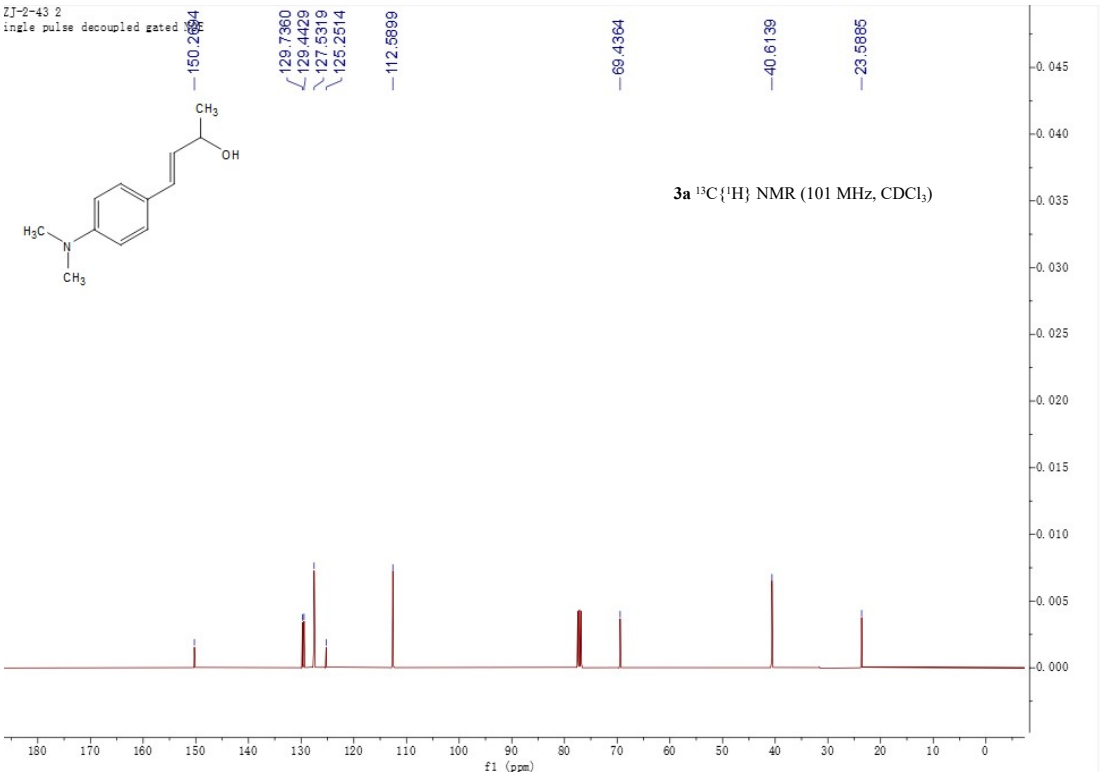
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of 3-(2-hydroxy-2-methylpropylidene)isobenzofuran-1(3*H*)-one (1k)



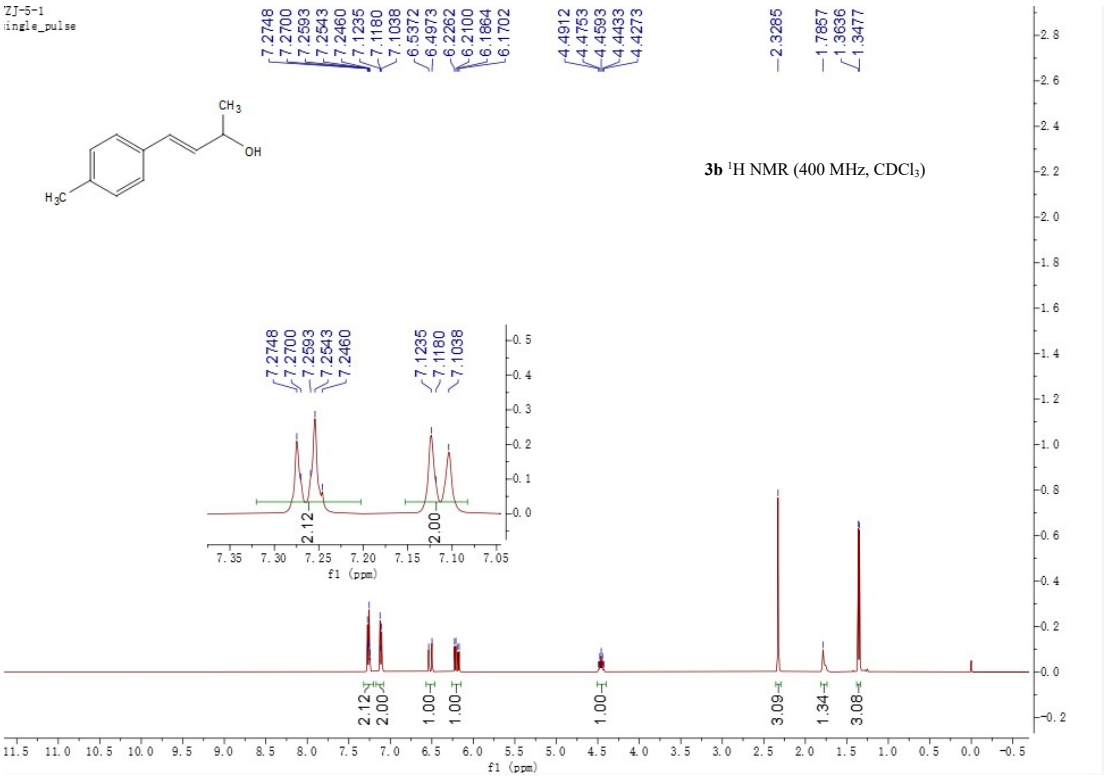


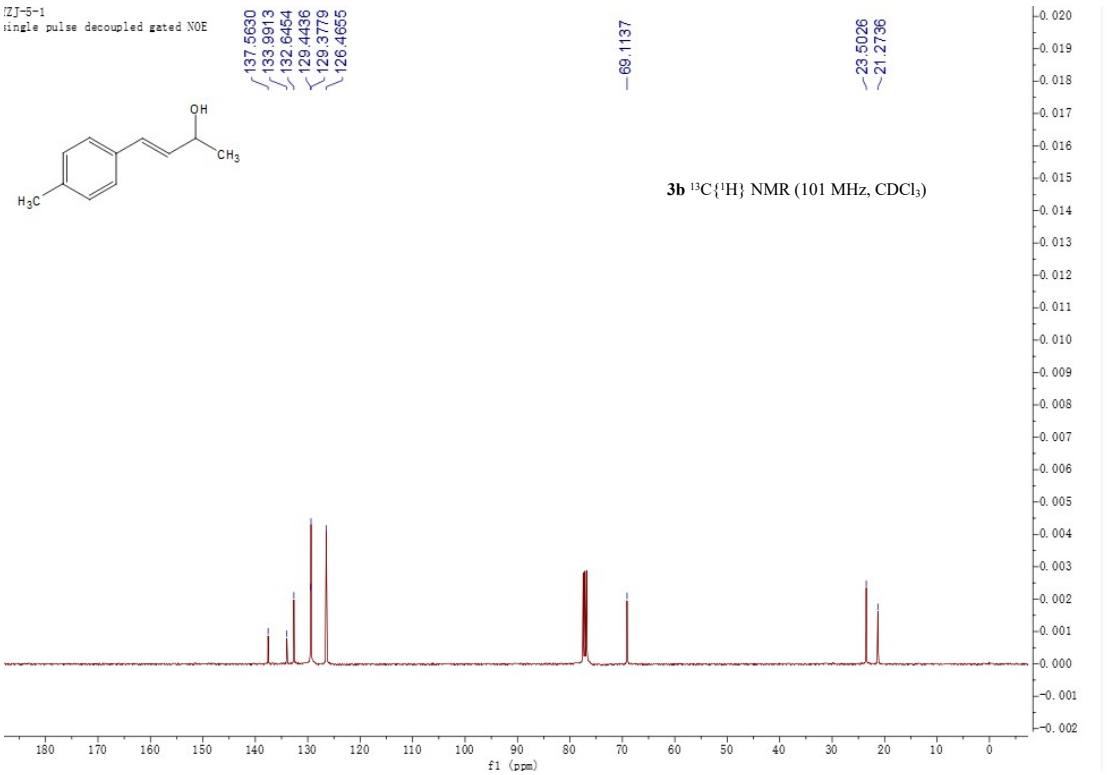
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(4-(dimethylamino)phenyl)but-3-en-2-ol (3a)



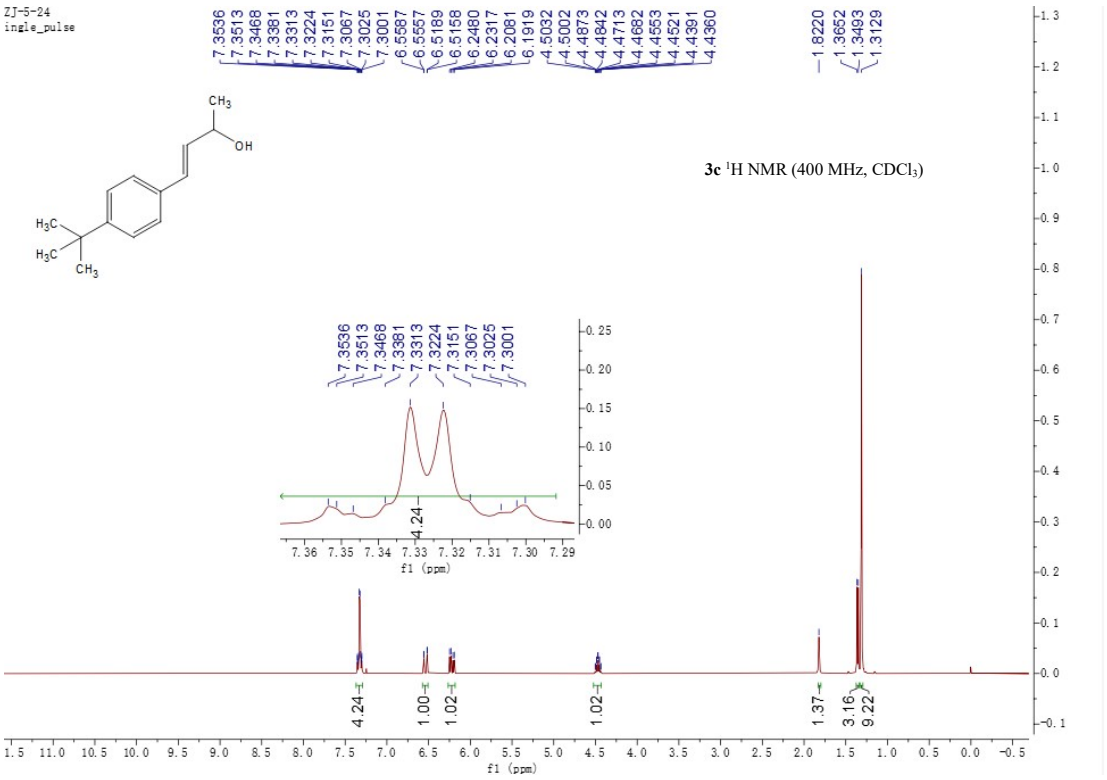


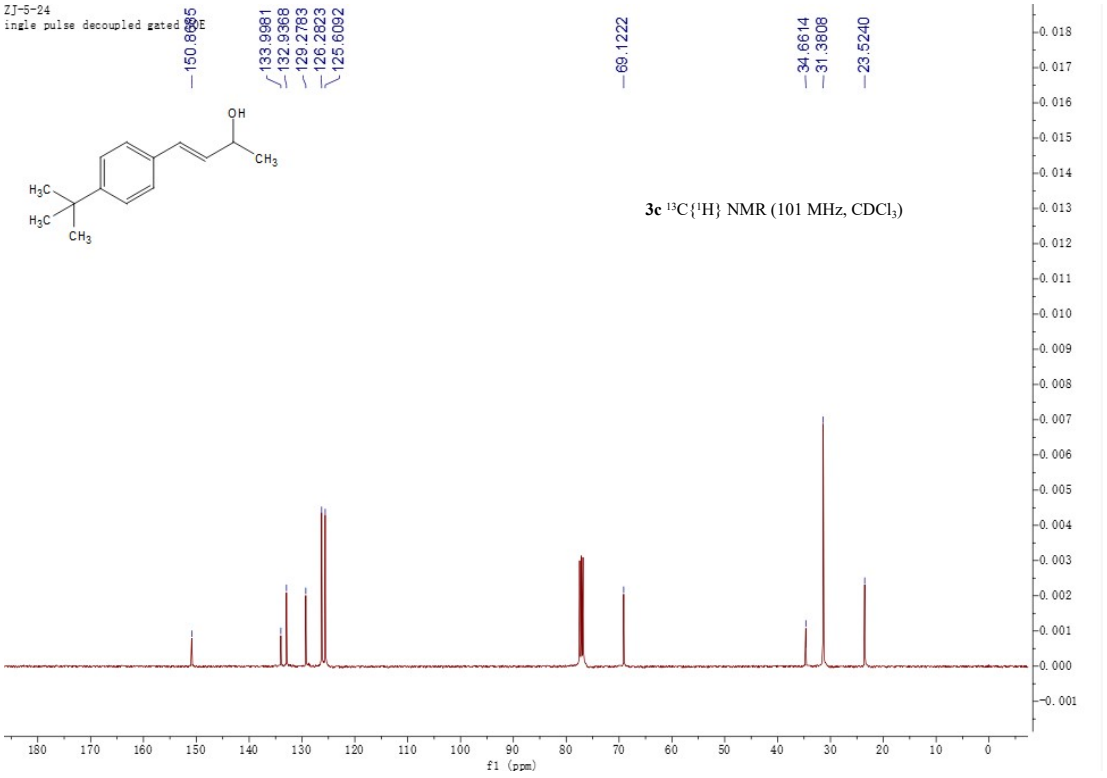
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(p-tolyl)but-3-en-2-ol (3b)



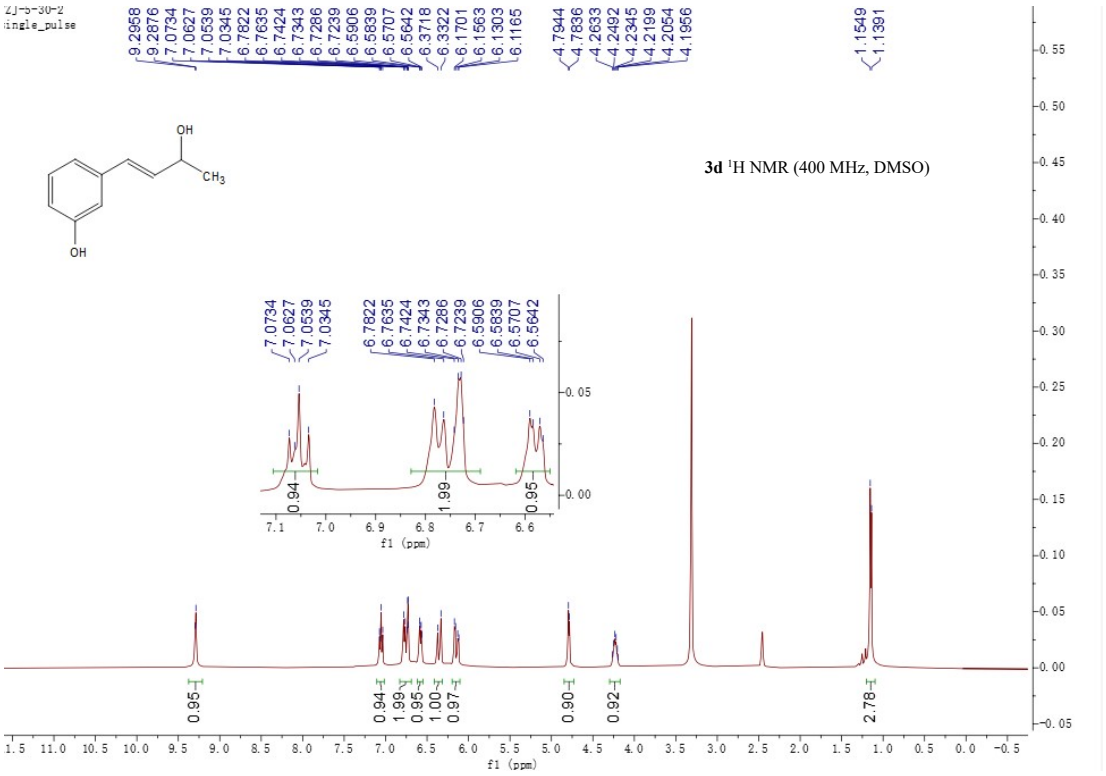


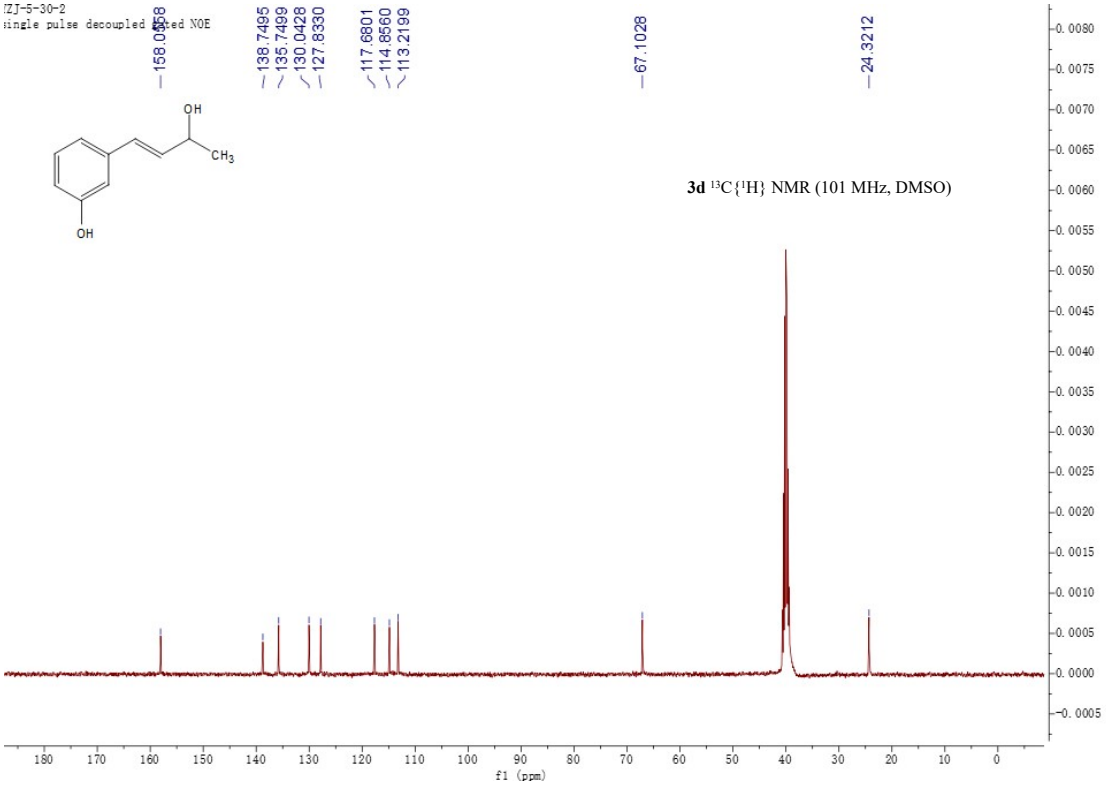
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(4-(tert-butyl)phenyl)but-3-en-2-ol (3c)



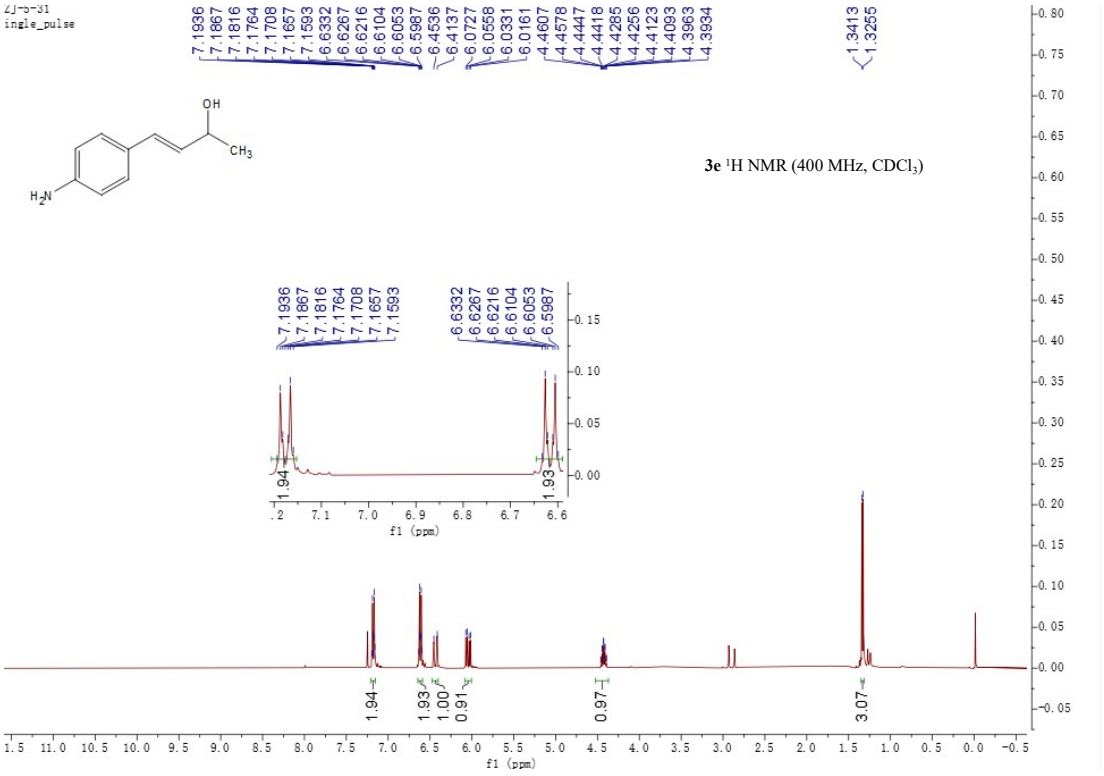


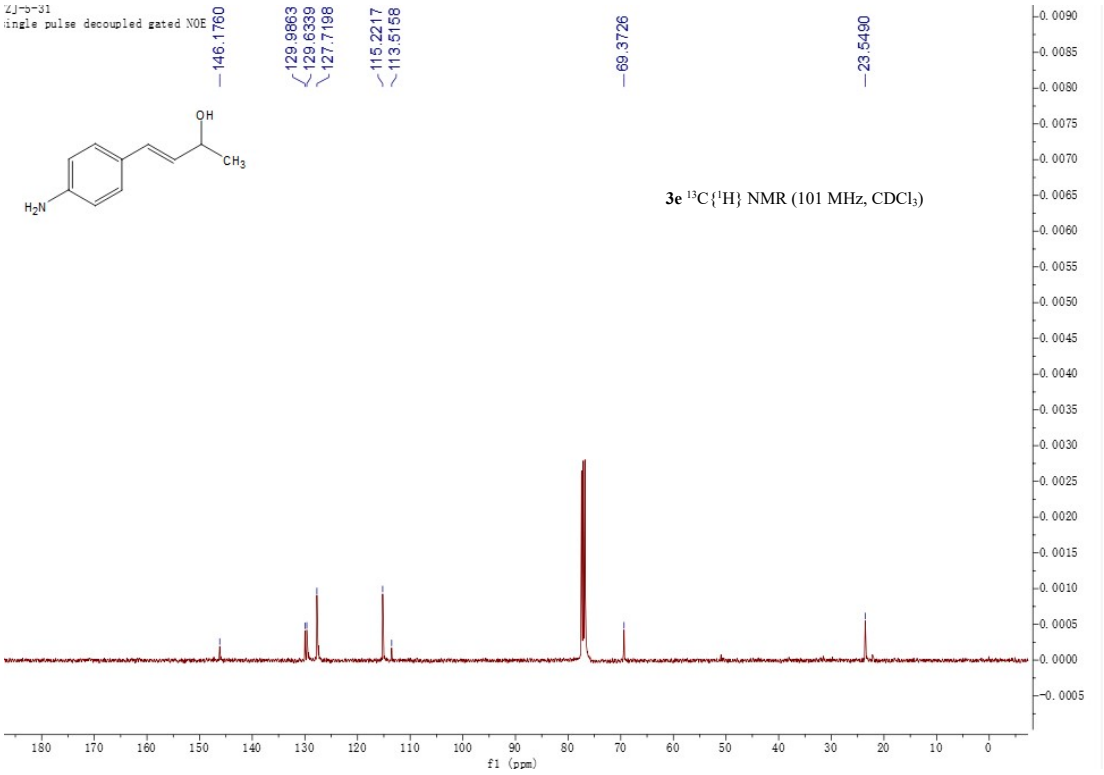
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-3-(3-hydroxybut-1-en-1-yl)phenol (3d)



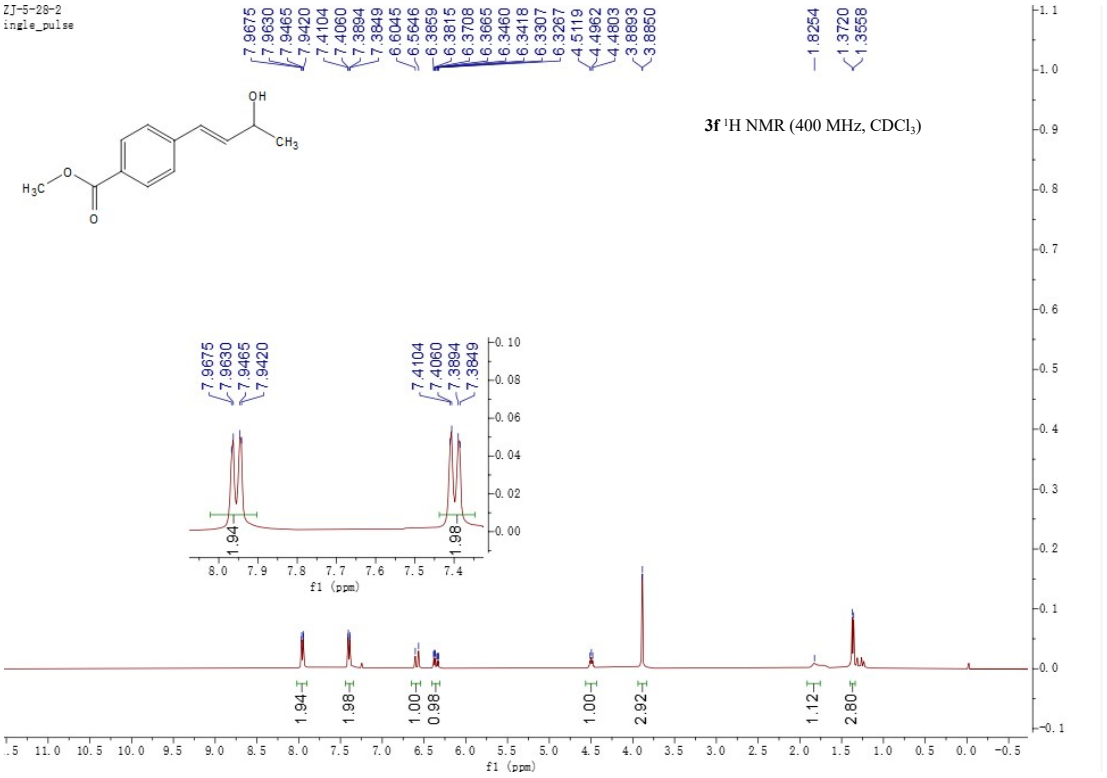


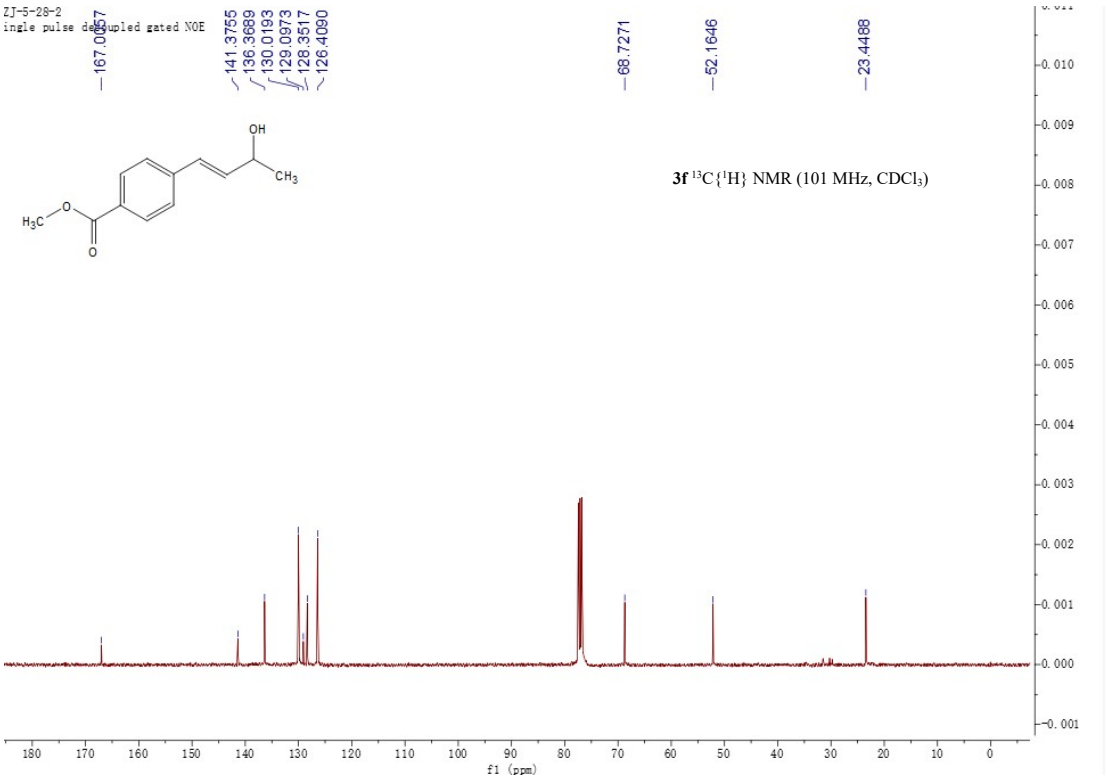
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(4-aminophenyl)but-3-en-2-ol (3e)



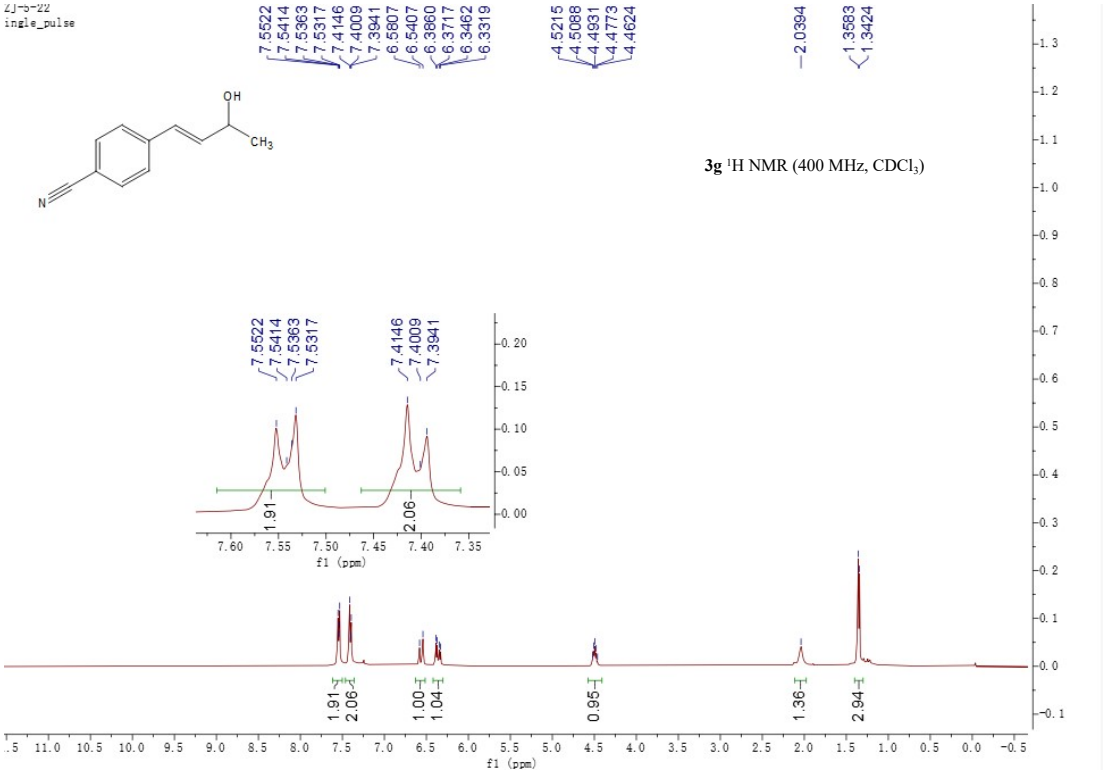


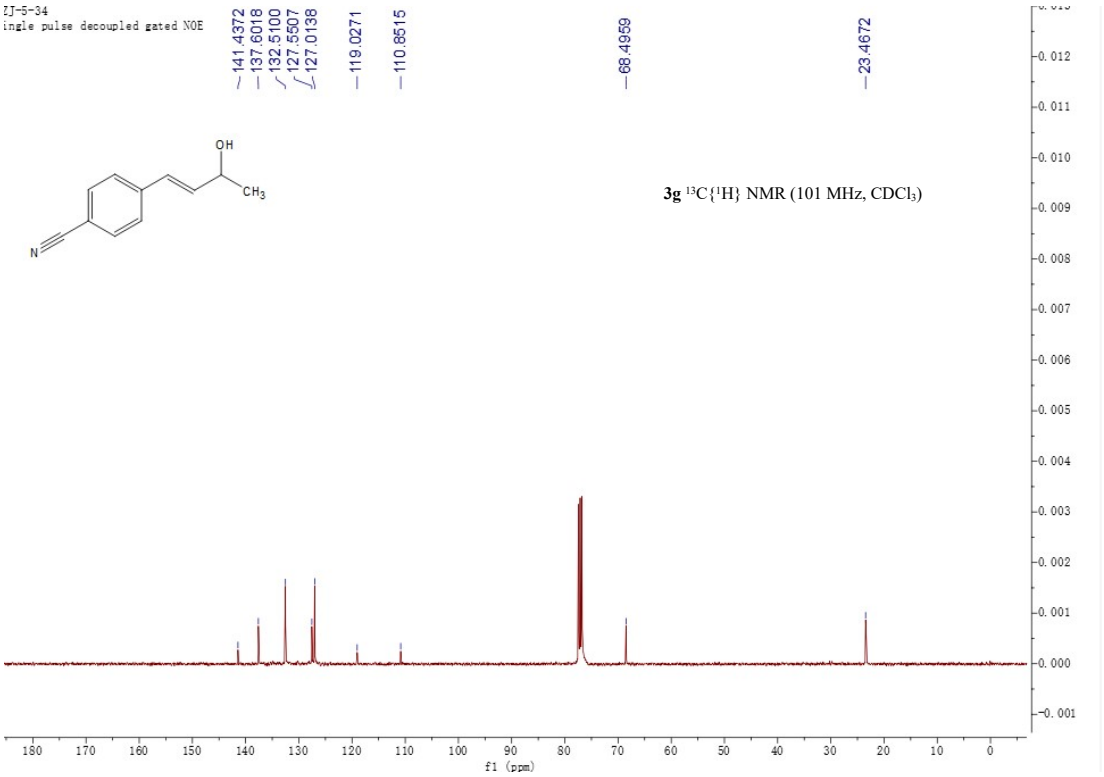
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of methyl (*E*)-4-(3-hydroxybut-1-en-1-yl)benzoate (3f)





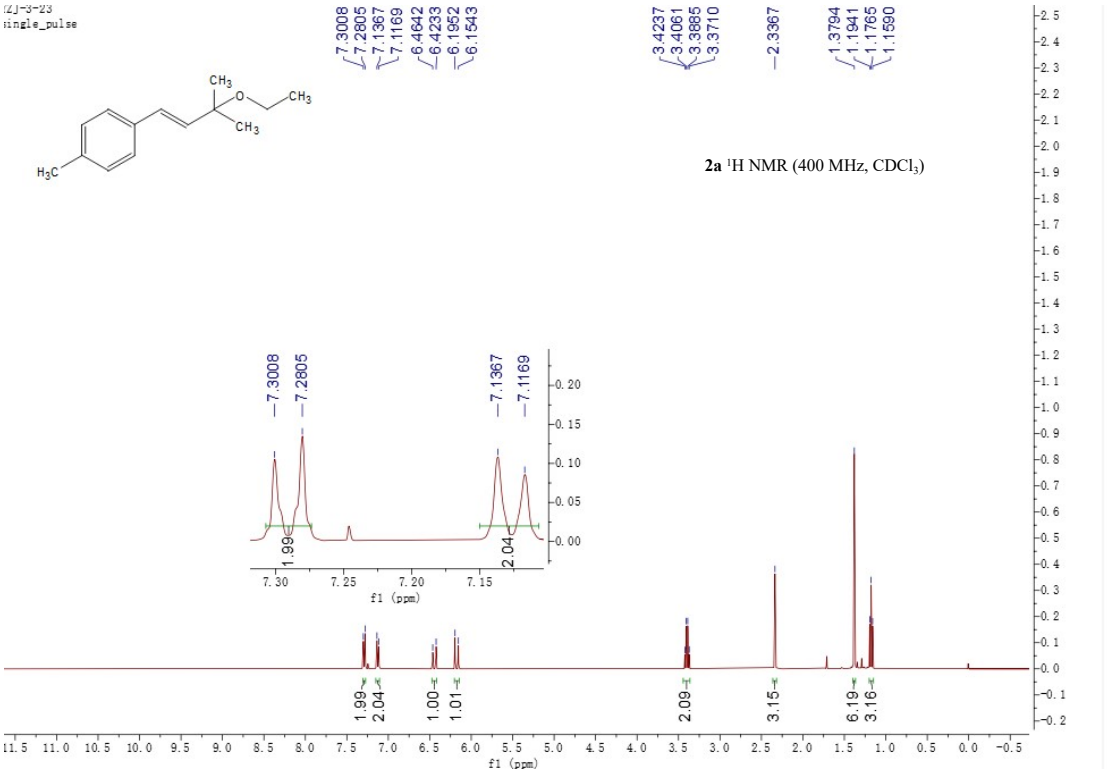
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(3-hydroxybut-1-en-1-yl)benzonitrile (3g)

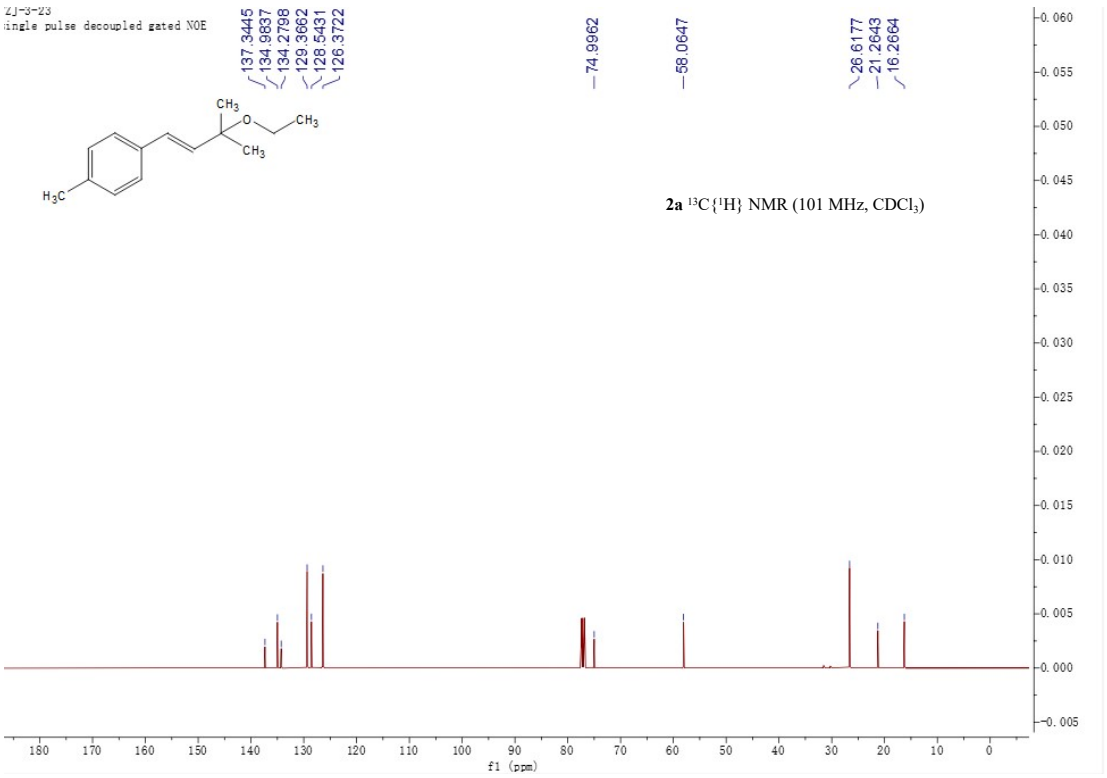




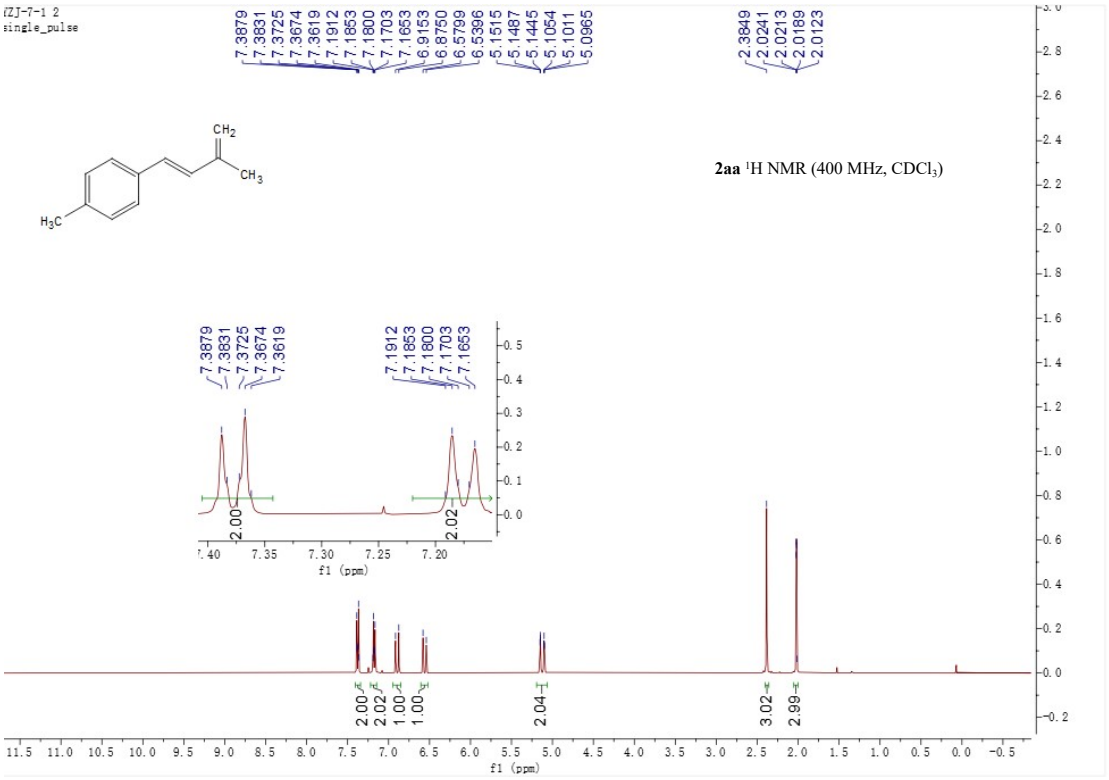
4.2 ^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of the products

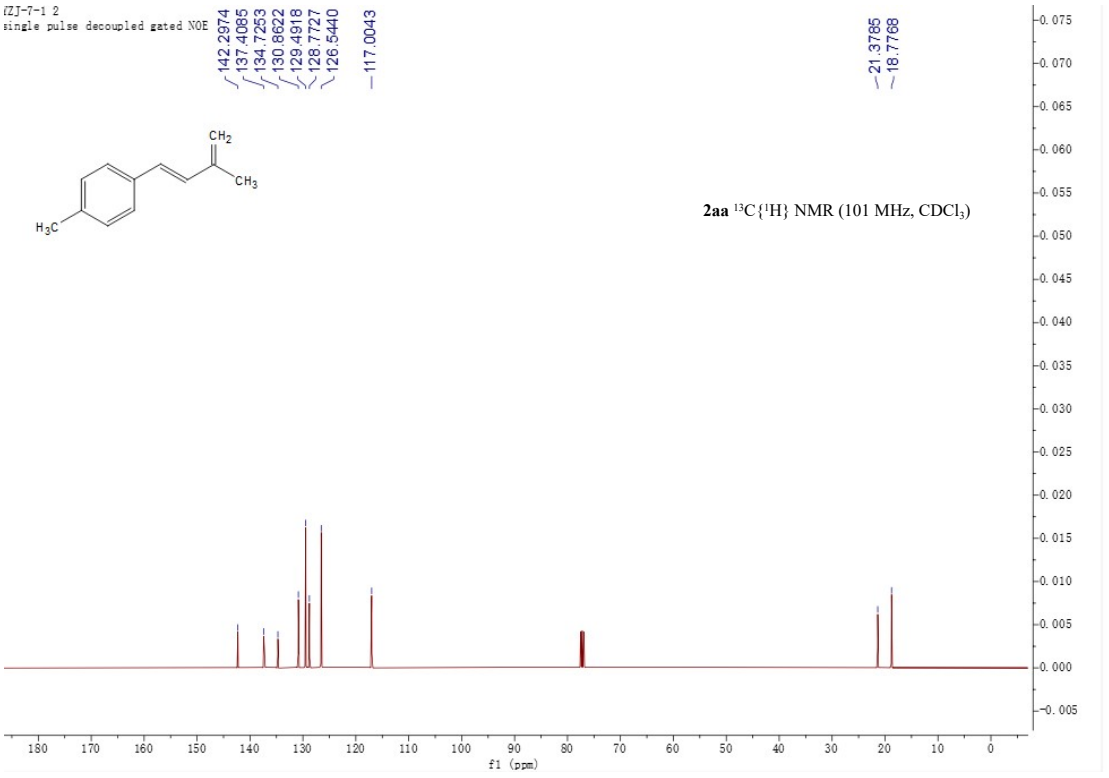
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(3-ethoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (2a)



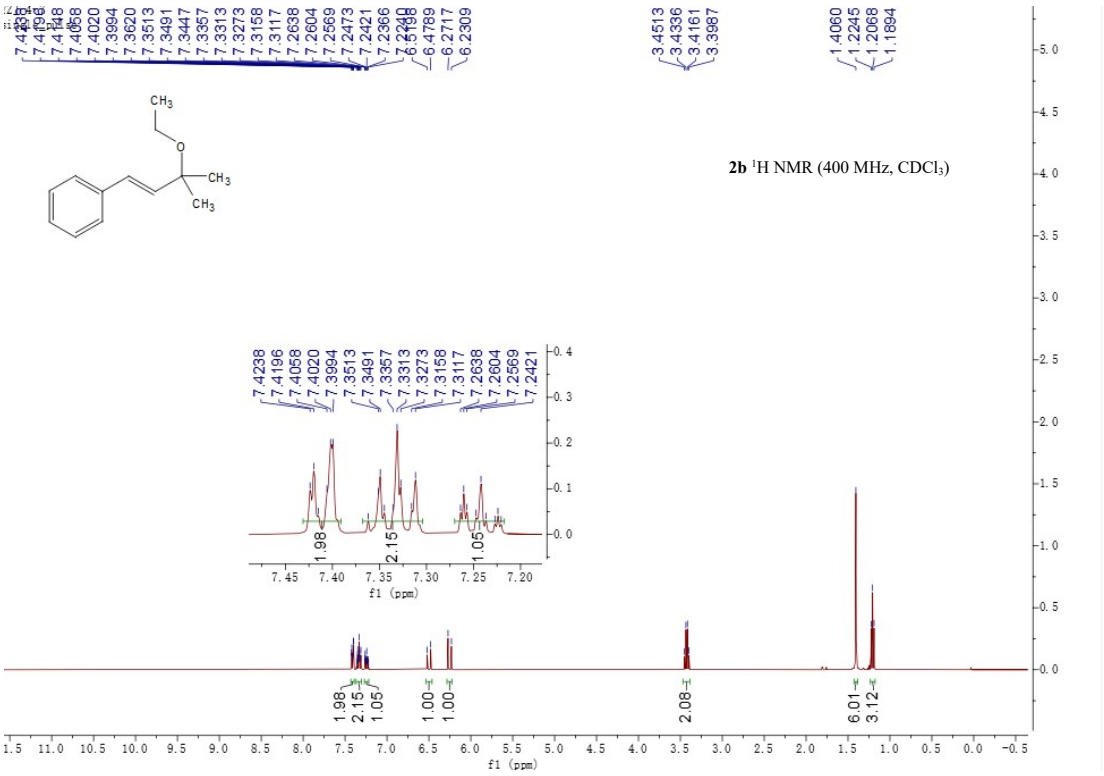


^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-methyl-4-(3-methylbuta-1,3-dien-1-yl)benzene (2aa)

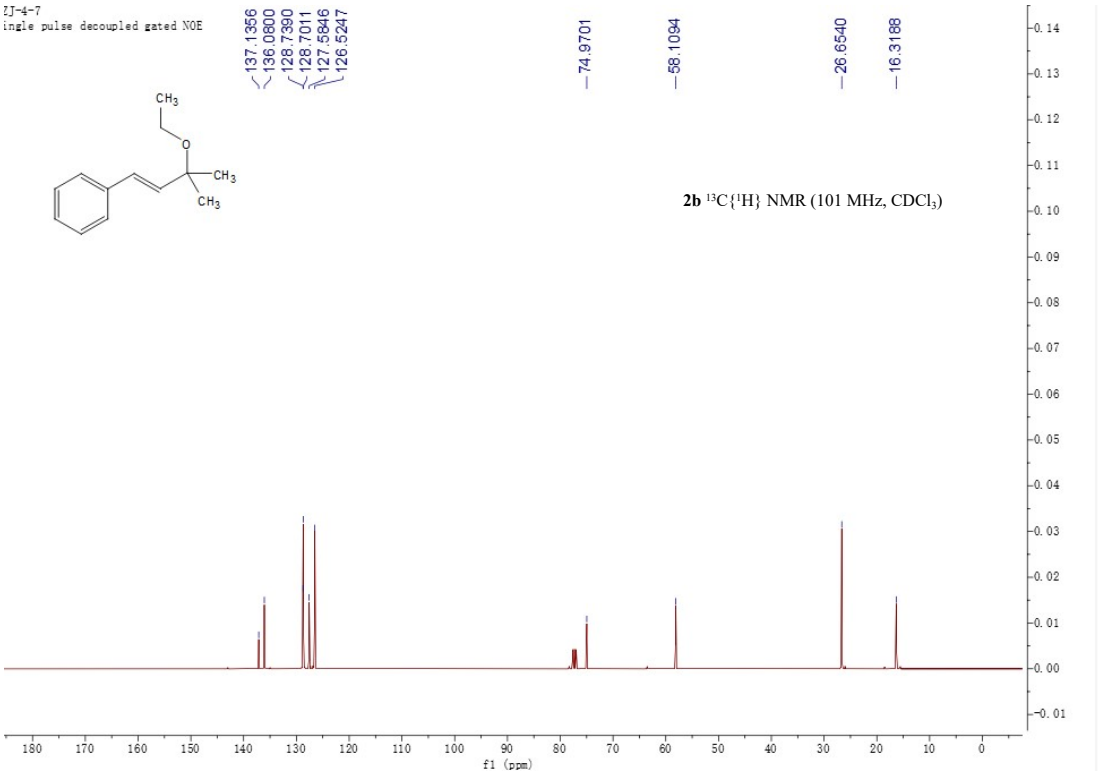




^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2b)

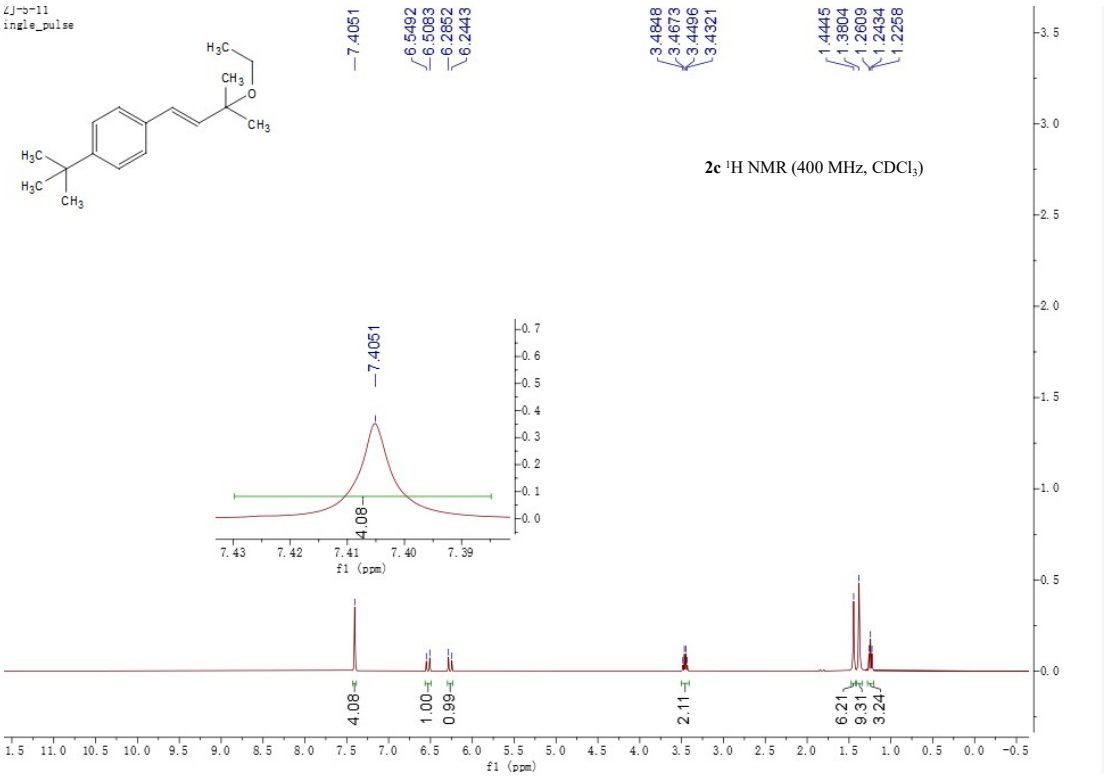


2b ^{1}H NMR (400 MHz, $CDCl_3$)

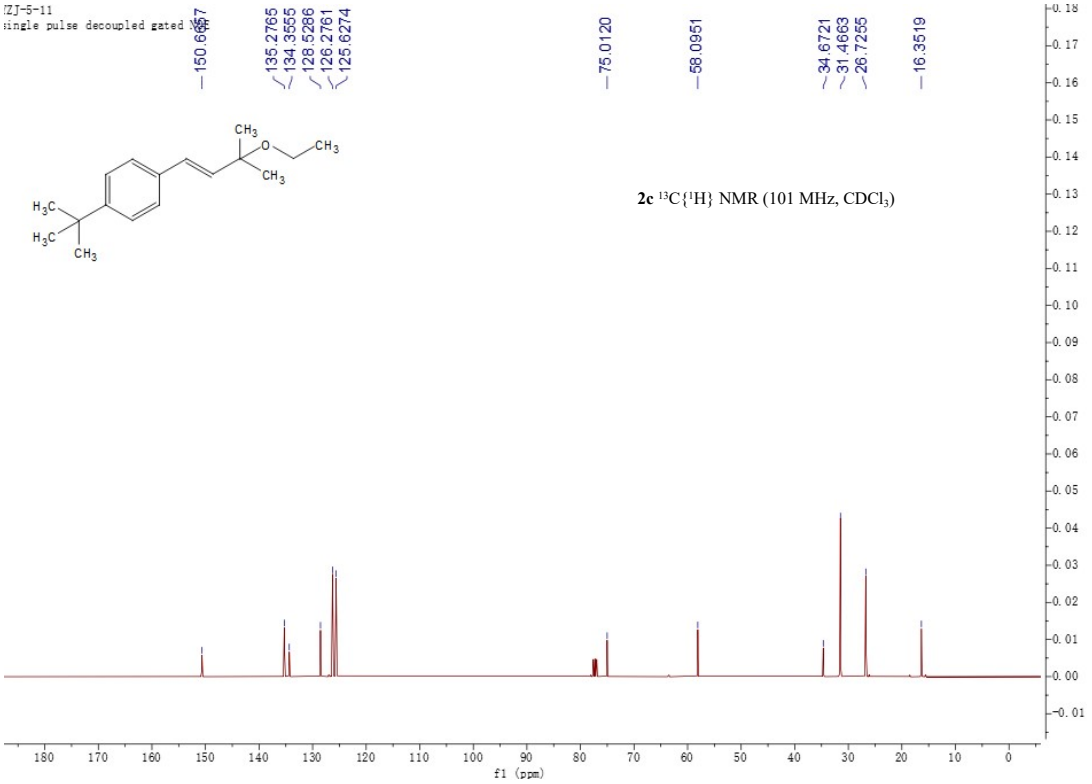


2b ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(tert-butyl)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2c)

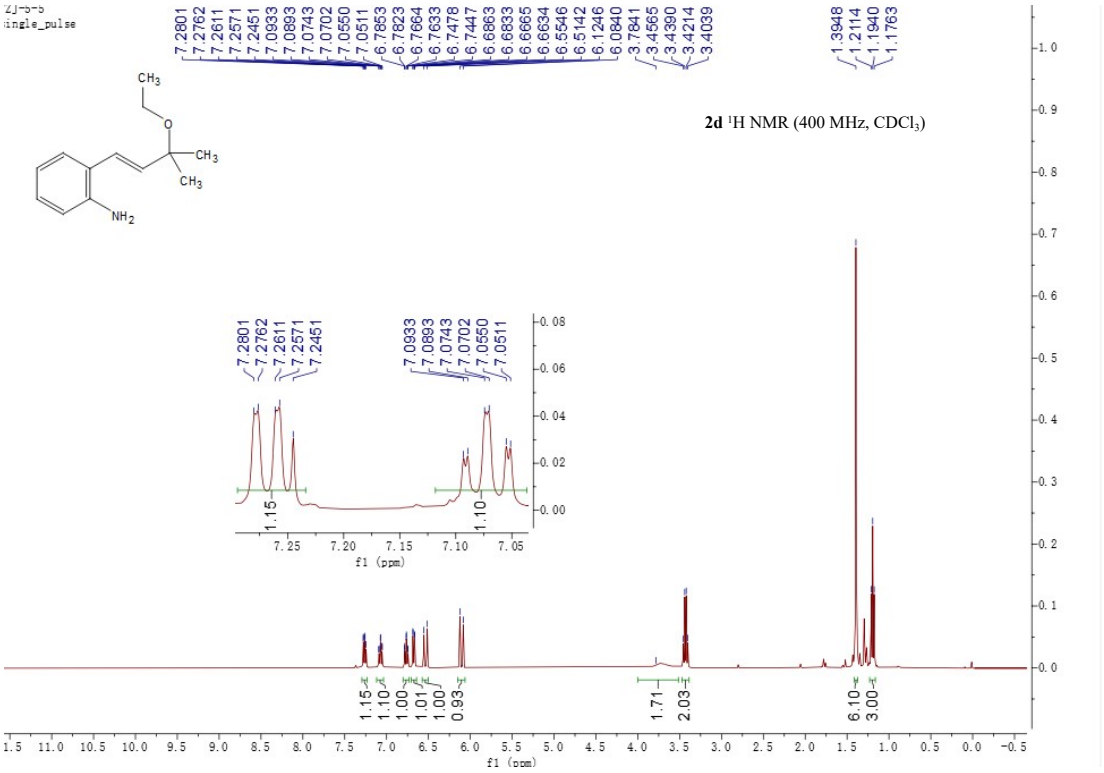


2c ^{1}H NMR (400 MHz, $CDCl_3$)

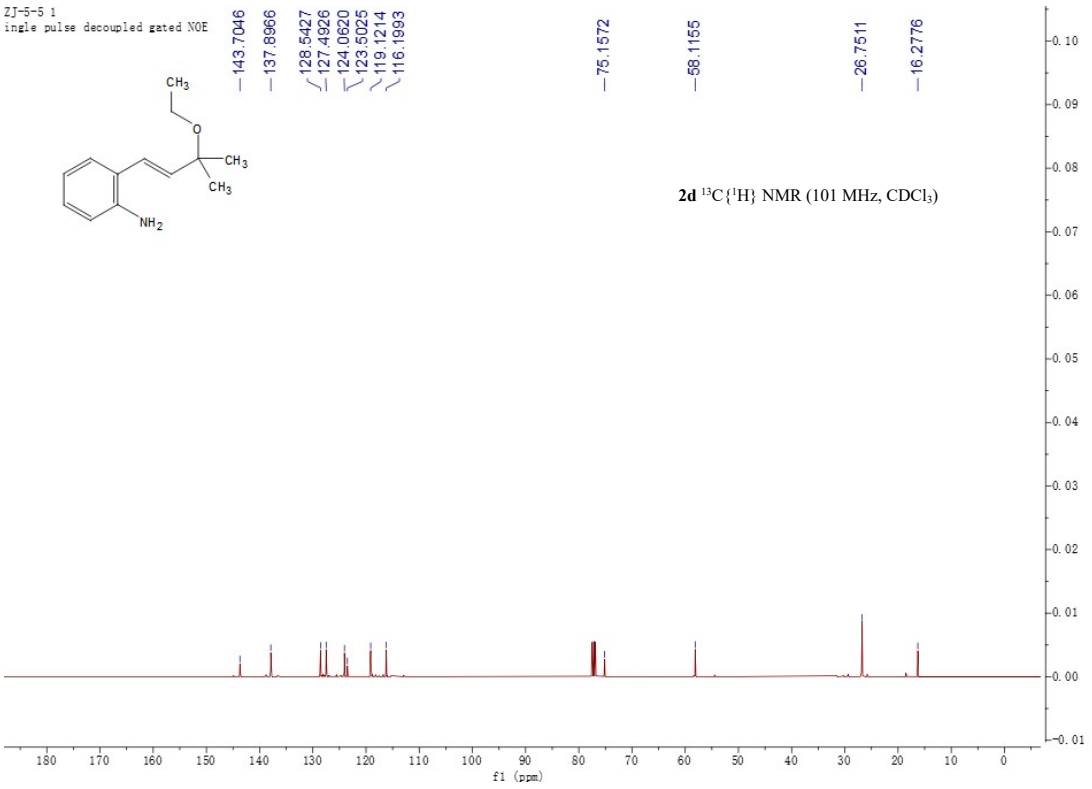


2c ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-2-(3-ethoxy-3-methylbut-1-en-1-yl)aniline (2d)

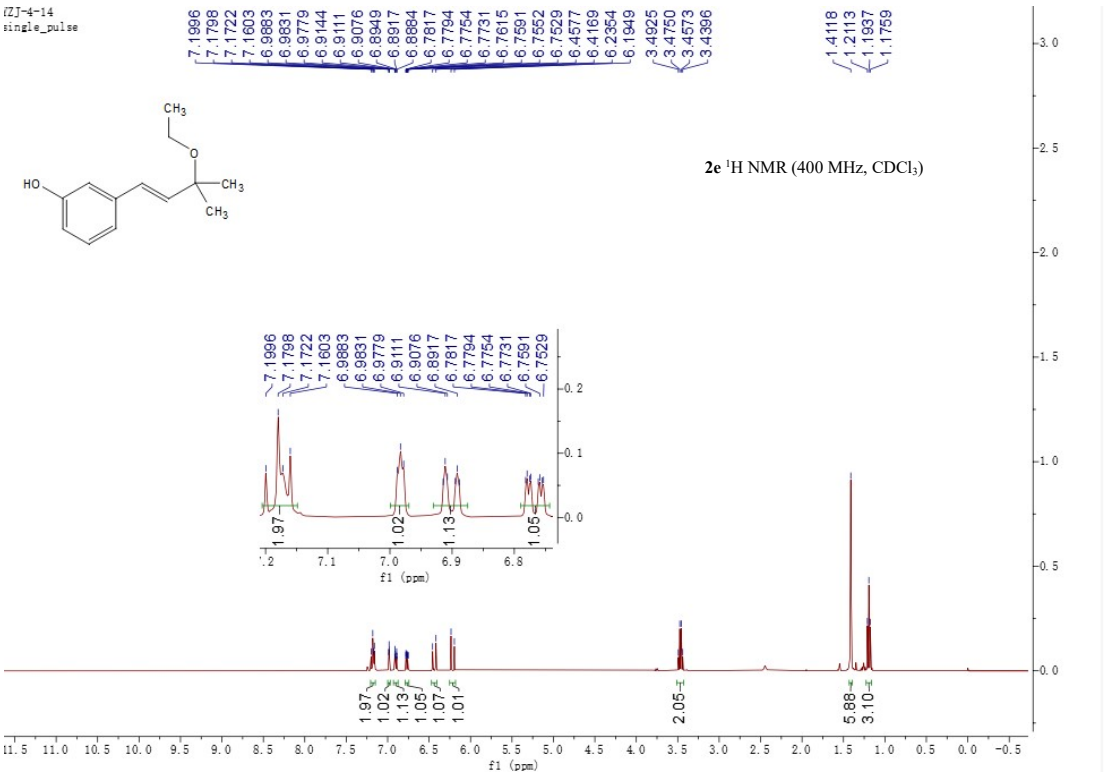


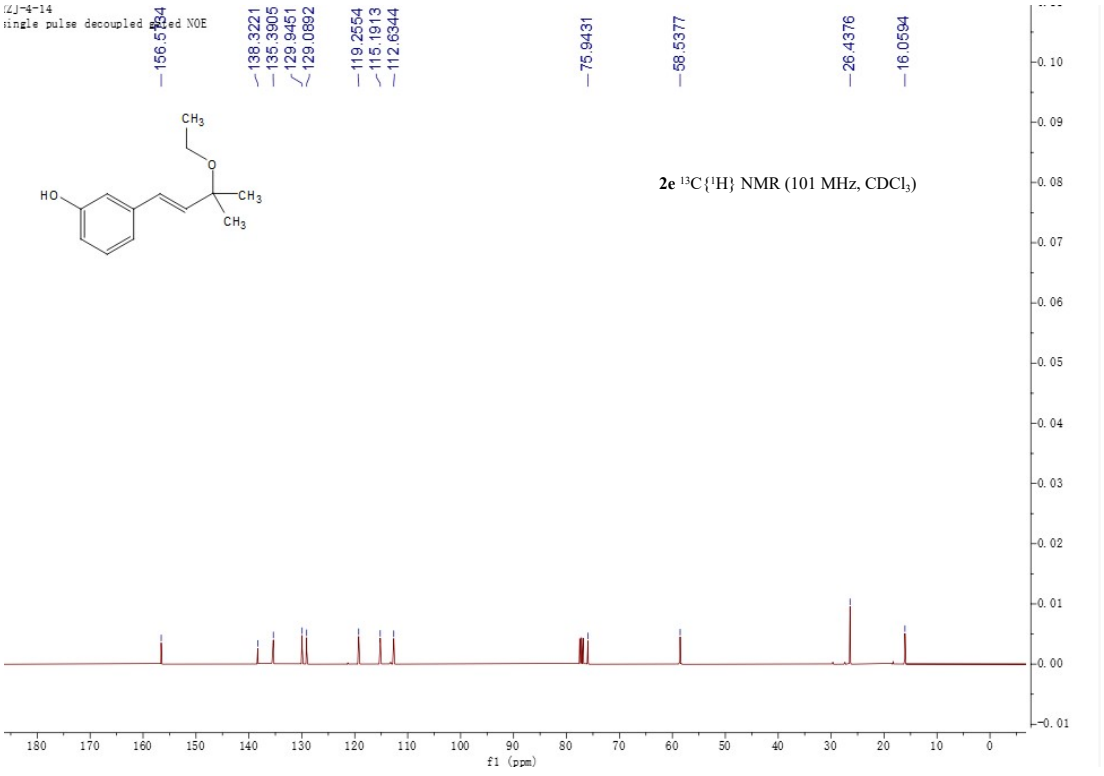
2d ^{1}H NMR (400 MHz, $CDCl_3$)



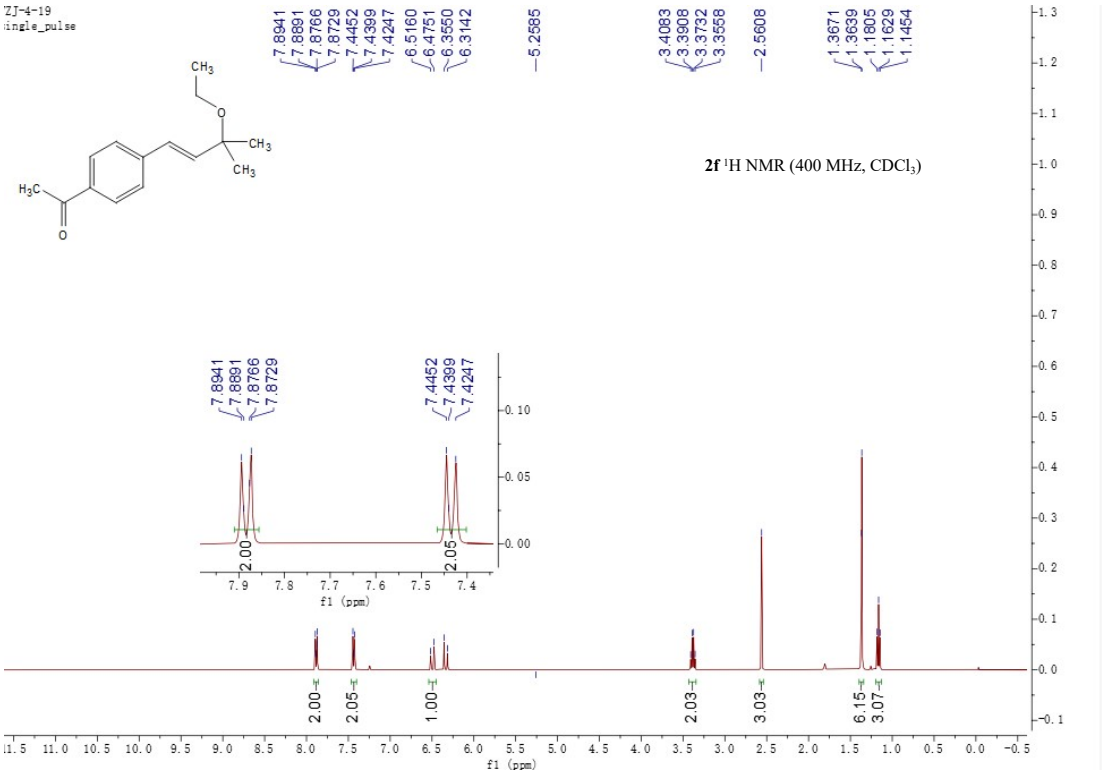
2d ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

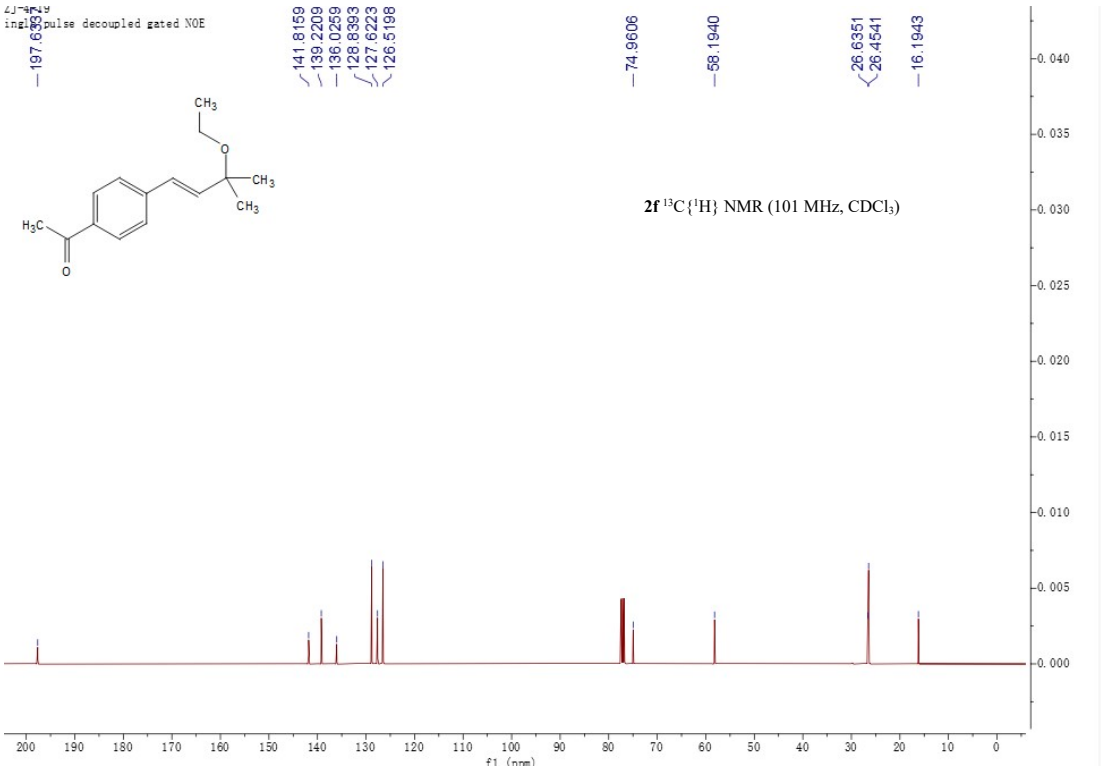
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-3-(3-ethoxy-3-methylbut-1-en-1-yl)phenol (2e)



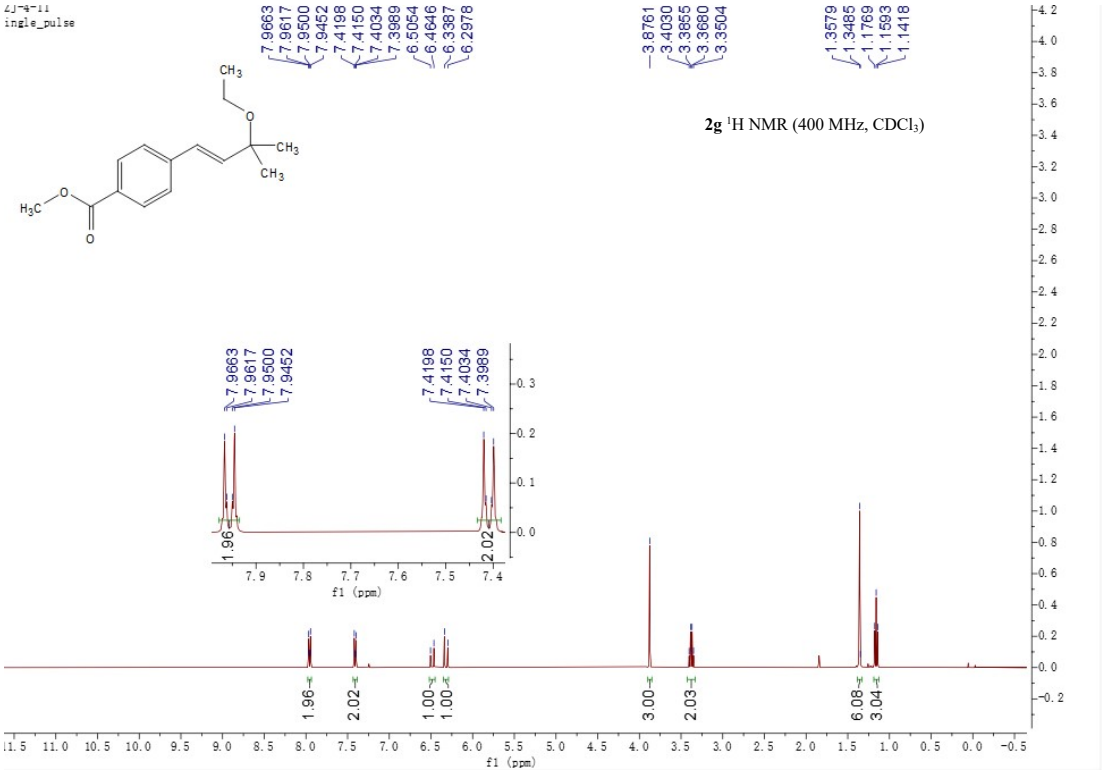


^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(4-(3-ethoxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one (2f)

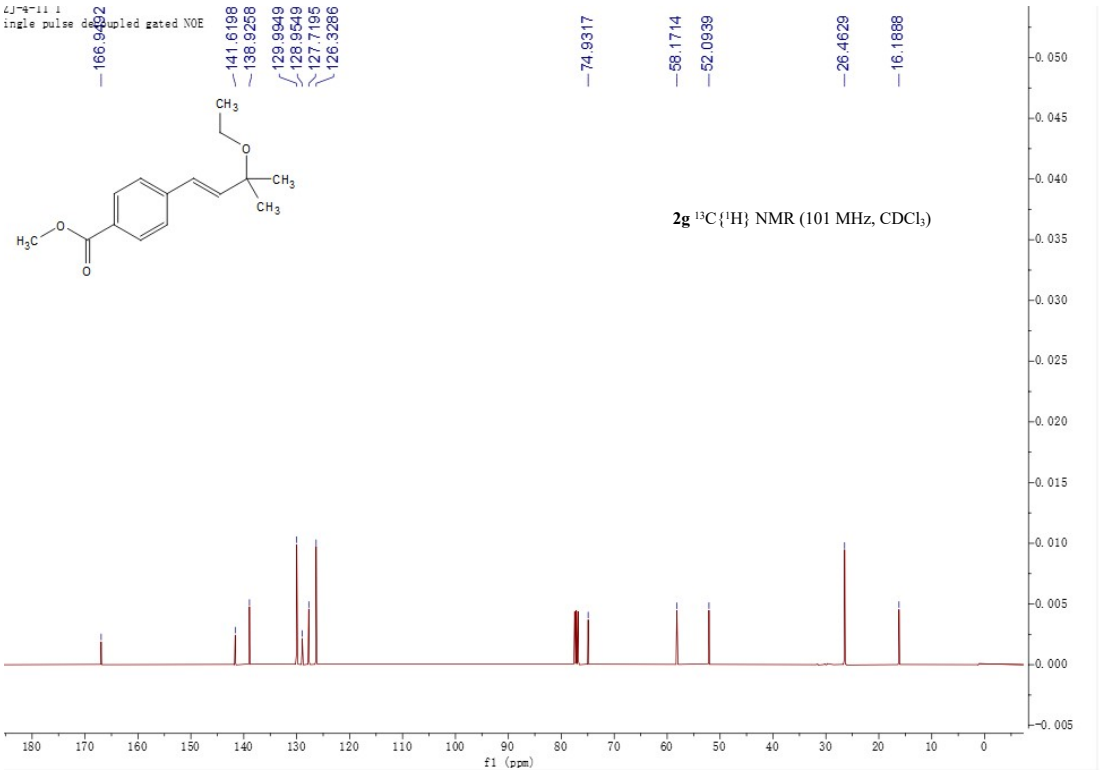




^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of methyl (*E*)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzoate (2g)

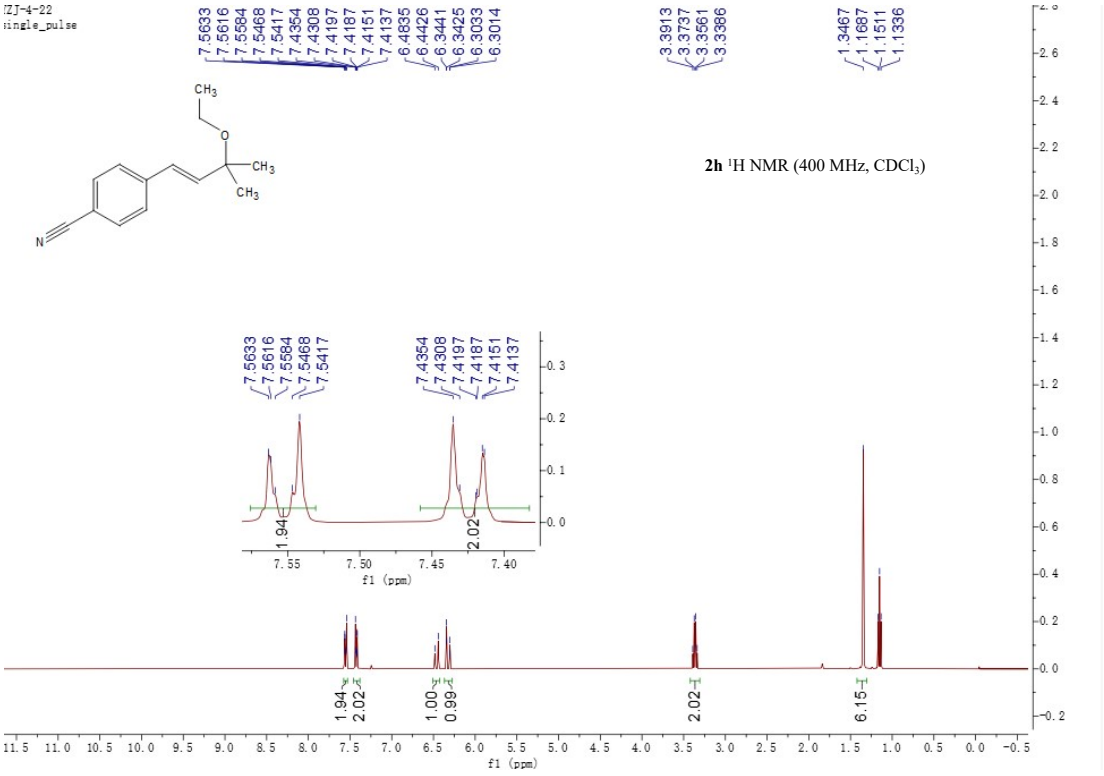


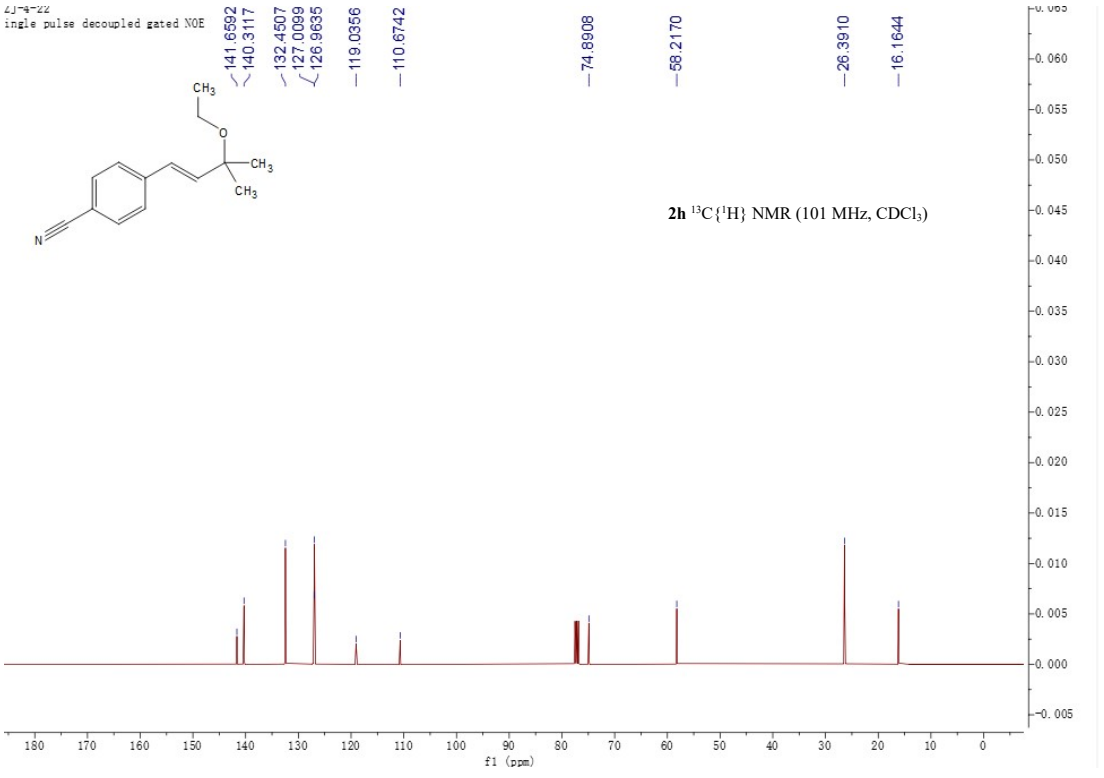
2g ^{1}H NMR (400 MHz, $CDCl_3$)



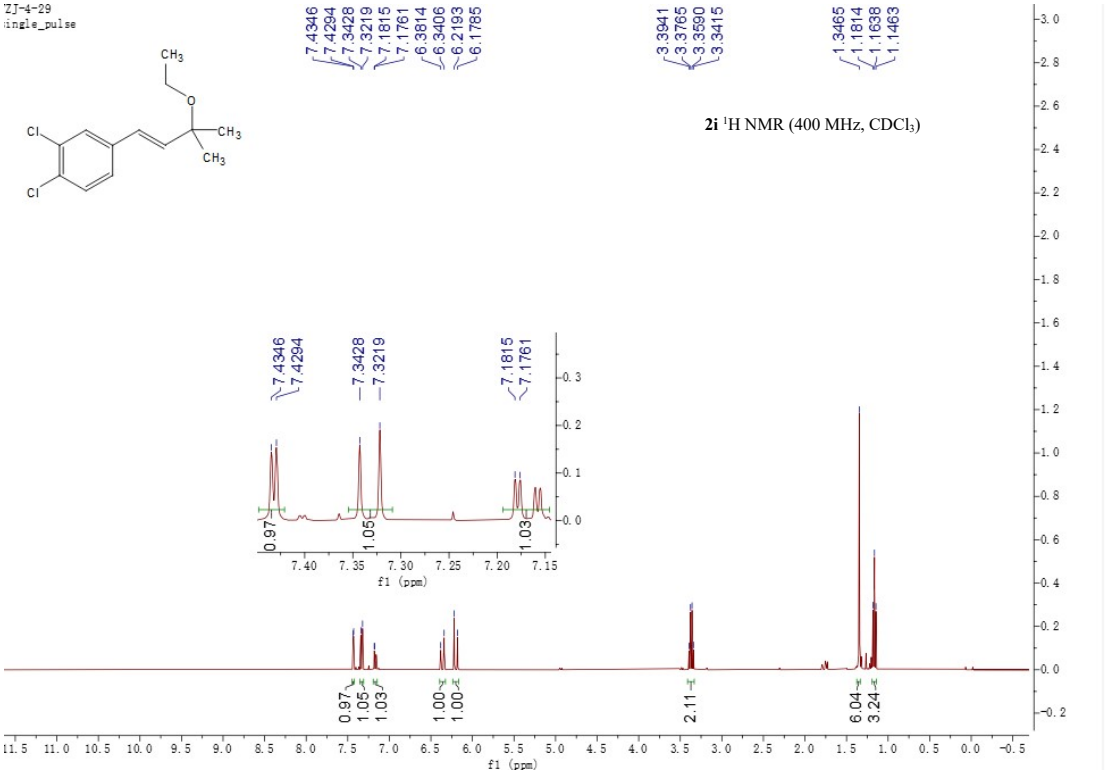
2g ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

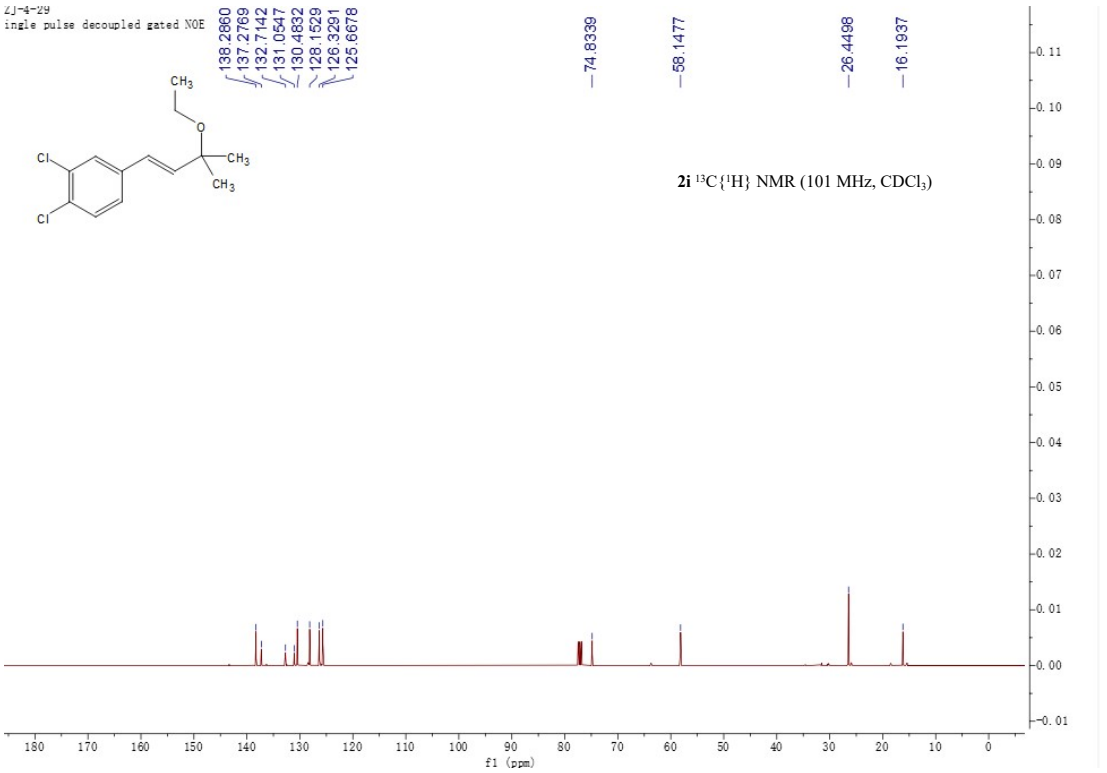
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzonitrile (2h)



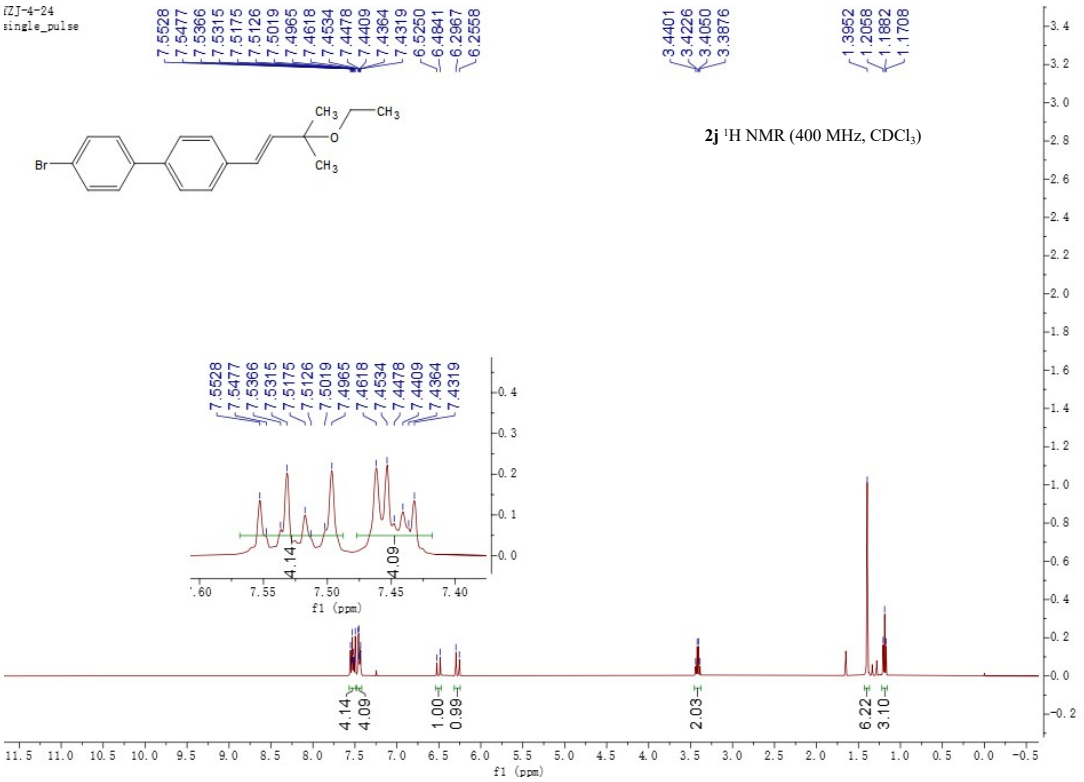


^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1,2-dichloro-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2i)

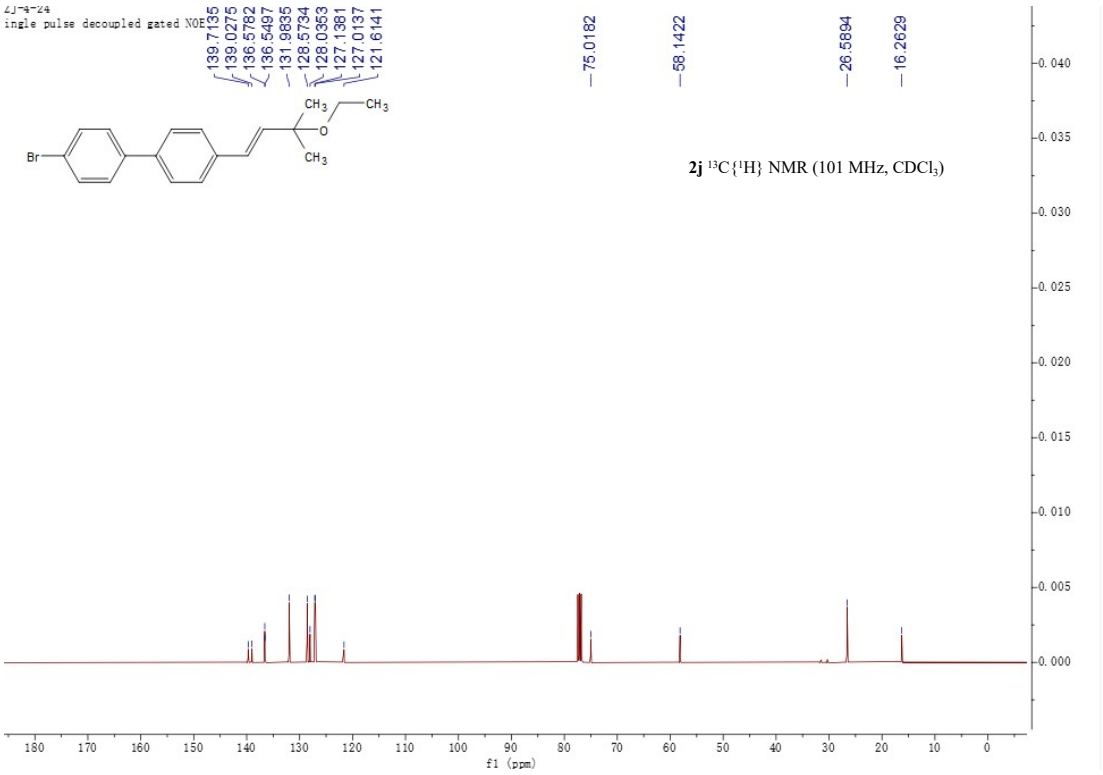




^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-bromo-4'-(3-ethoxy-3-methylbut-1-en-1-yl)-1,1'-biphenyl (2j)

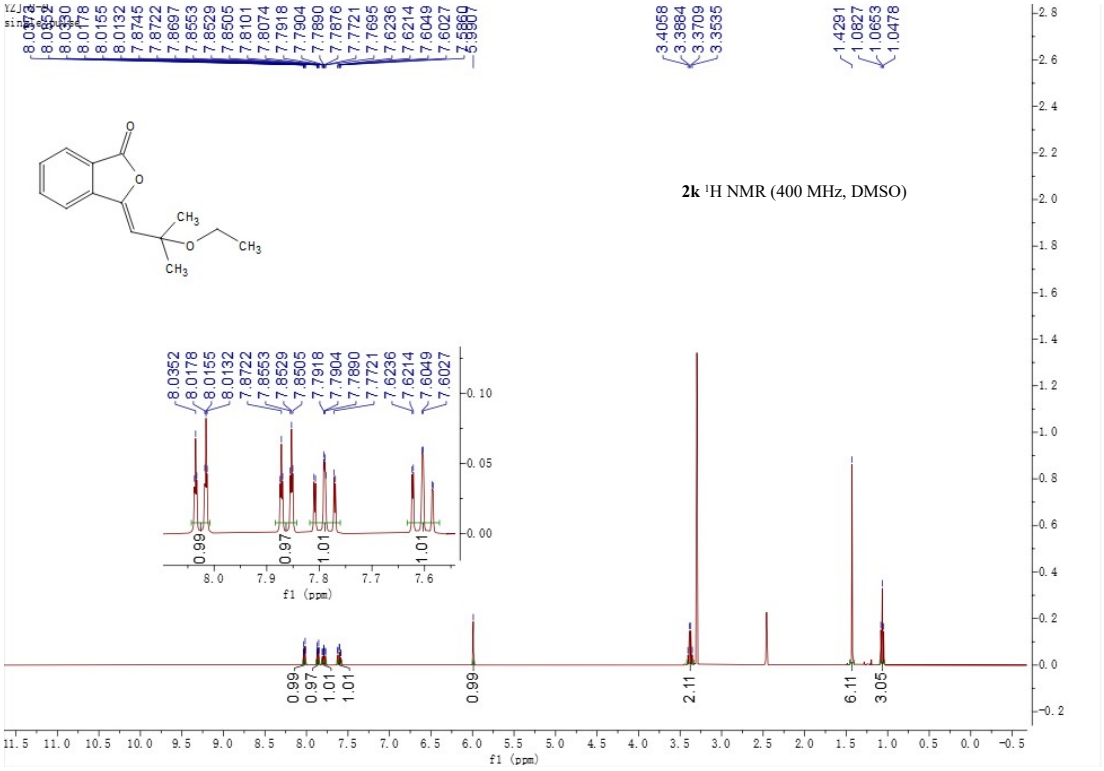


2j ^{1}H NMR (400 MHz, $CDCl_3$)

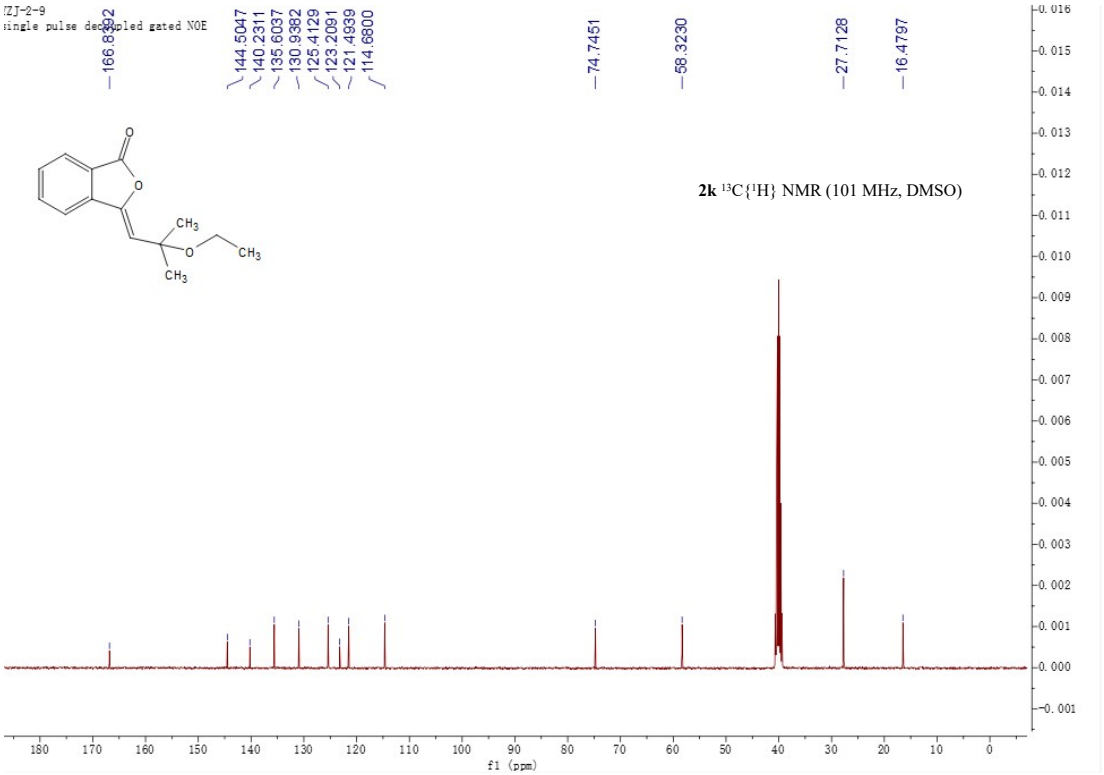


2j ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

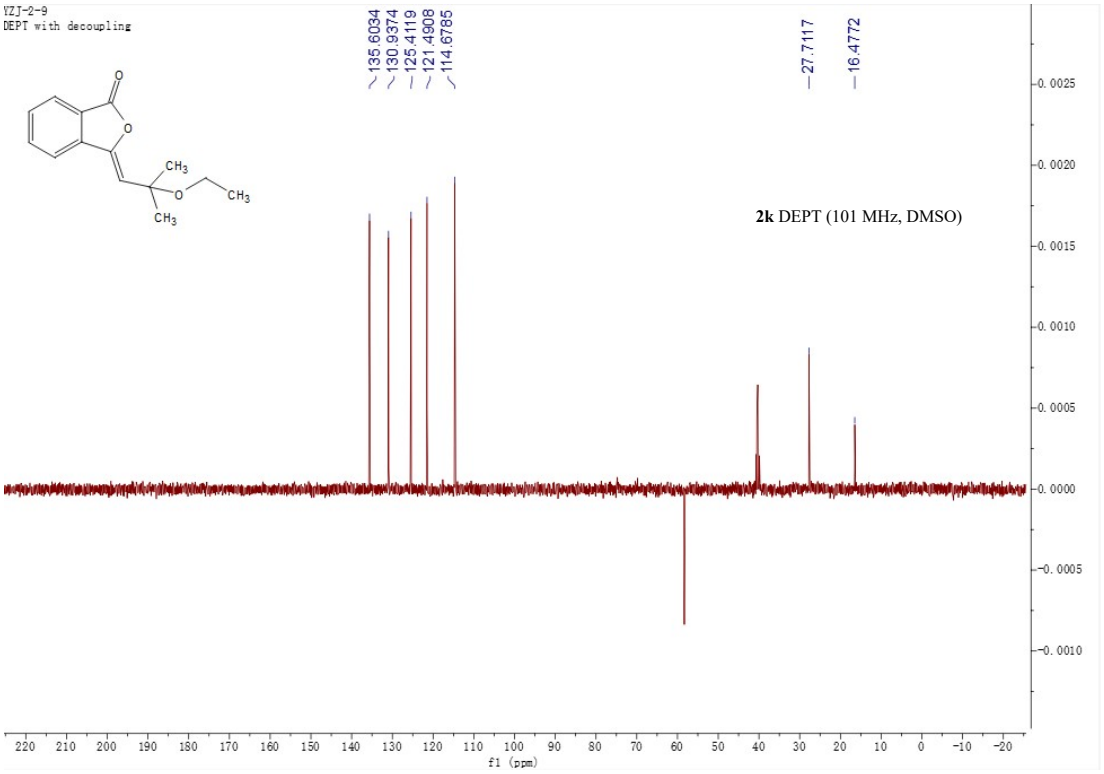
^{1}H-NMR, ^{13}C {^{1}H} NMR, DEPT, HMQC and HMBC Spectra of 3-(2-ethoxy-2-methylpropylidene)isobenzofuran-1(3H)-one (2k)



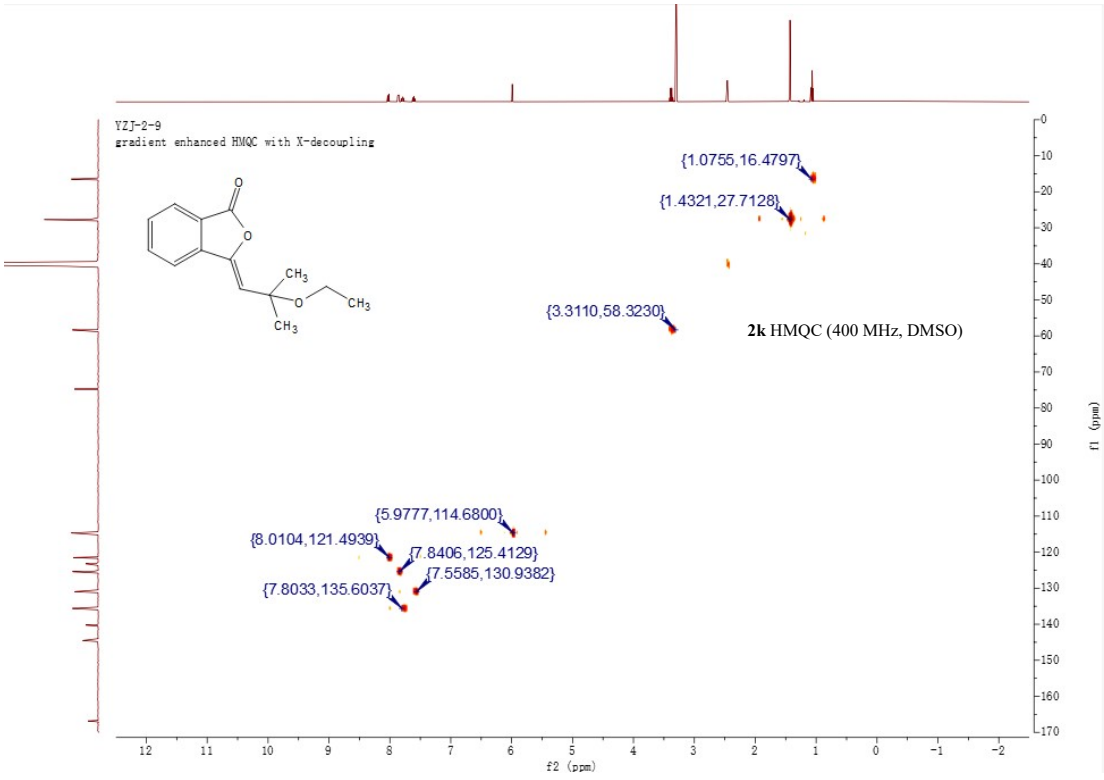
2k ^{1}H NMR (400 MHz, DMSO)



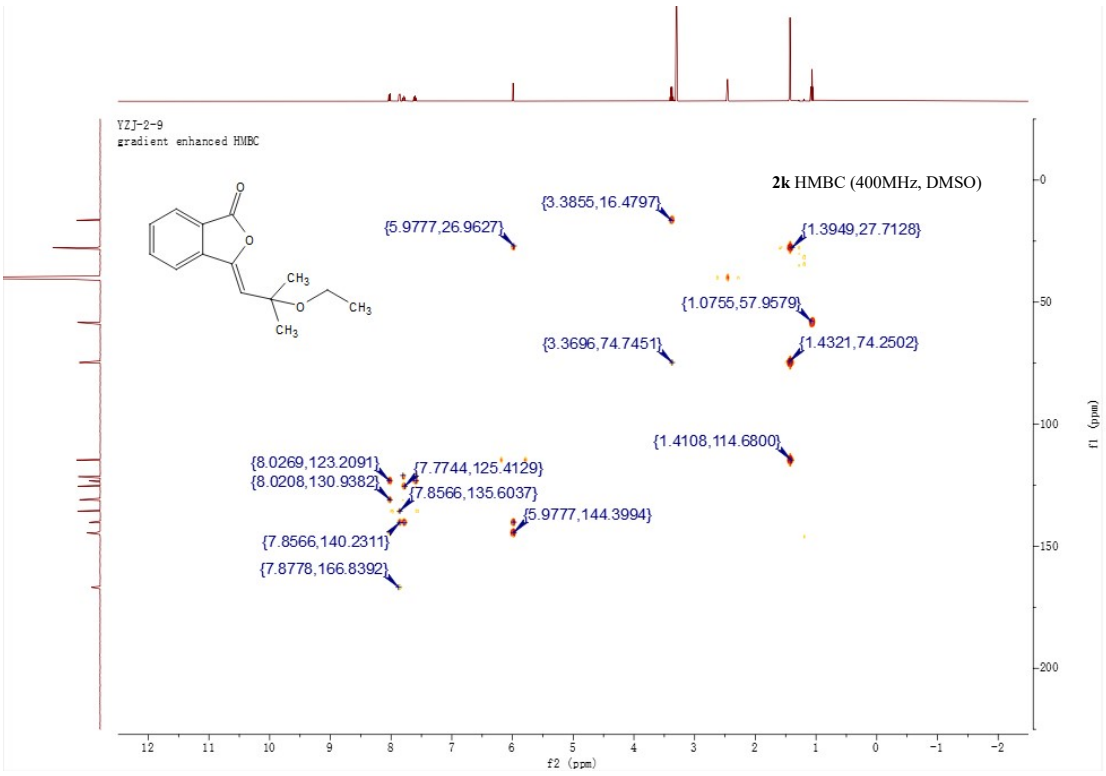
2k ^{13}C{^{1}H} NMR (101 MHz, DMSO)



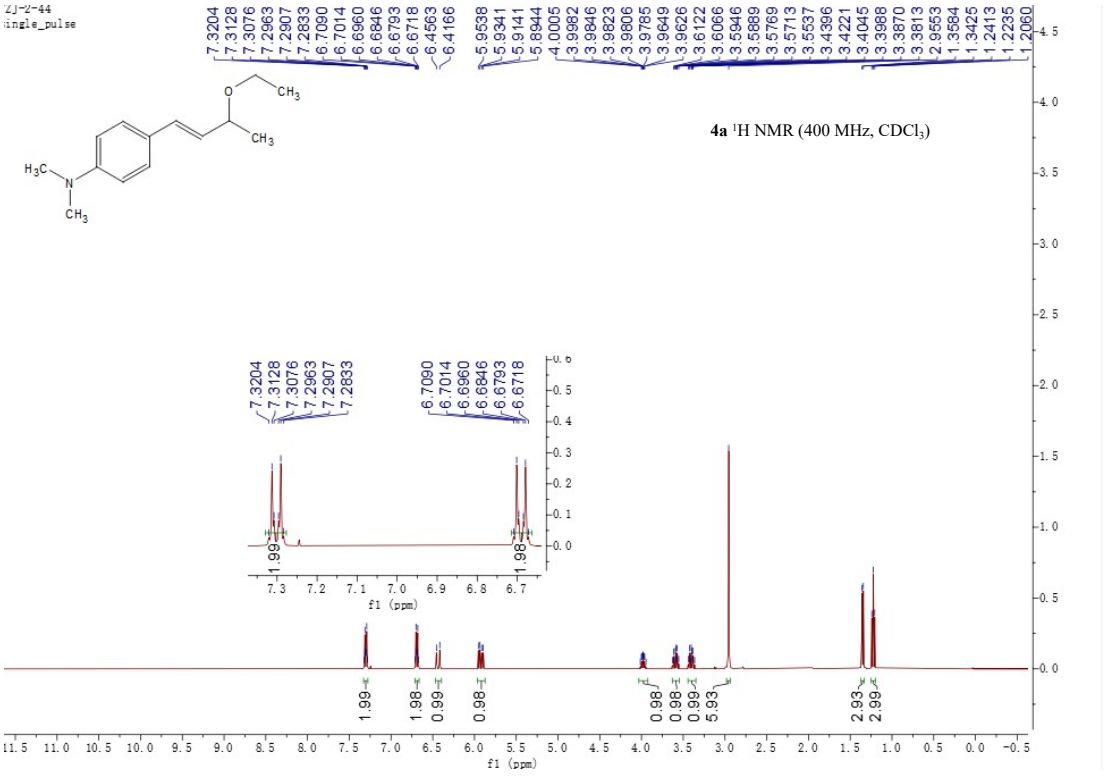
2k DEPT (101 MHz, DMSO)

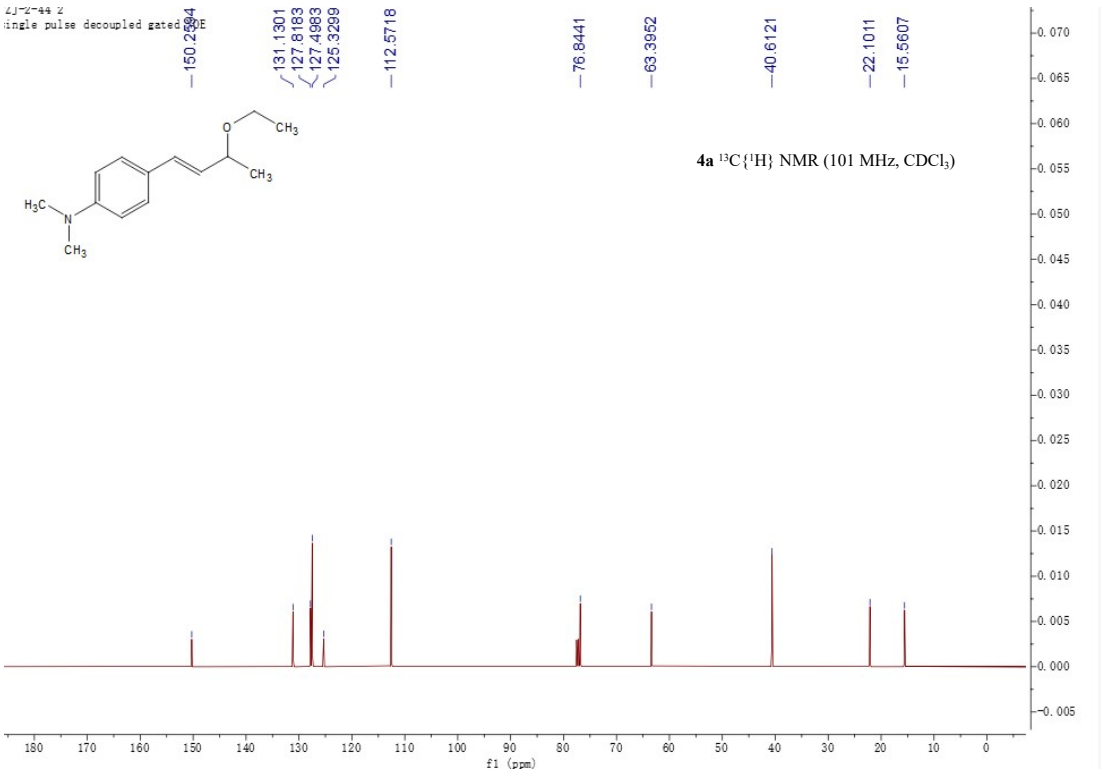


2k HMQC (400 MHz, DMSO)

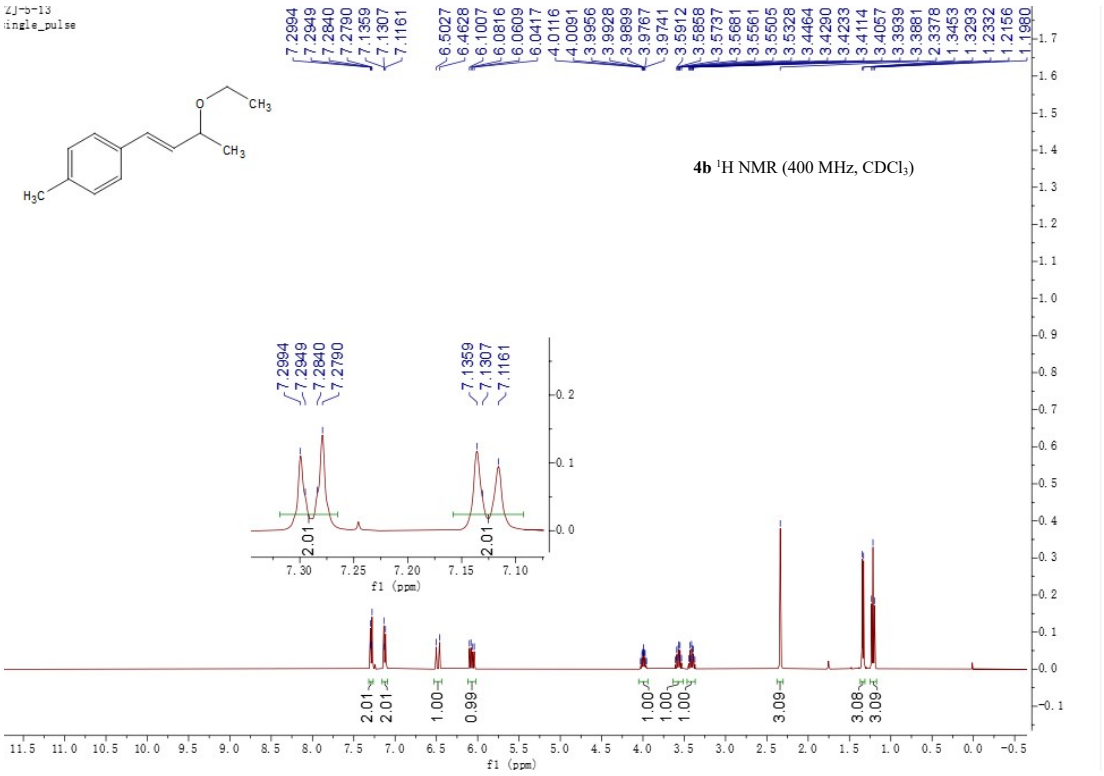

YZJ-2-9
gradient enhanced HMBC
2k HMBC (400MHz, DMSO)
{3.3855,16.4797}
{5.9777,26.9627}
{1.3949,27.7128}
{1.0755,57.9579}
{3.3696,74.7451}
{1.4321,74.2502}
{1.4108,114.6800}
{8.0269,123.2091}
{7.7744,125.4129}
{8.0208,130.9382}
{7.8566,135.6037}
{5.9777,144.3994}
{7.8566,140.2311}
{7.8778,166.8392}
f2 (ppm)
f1 (ppm)

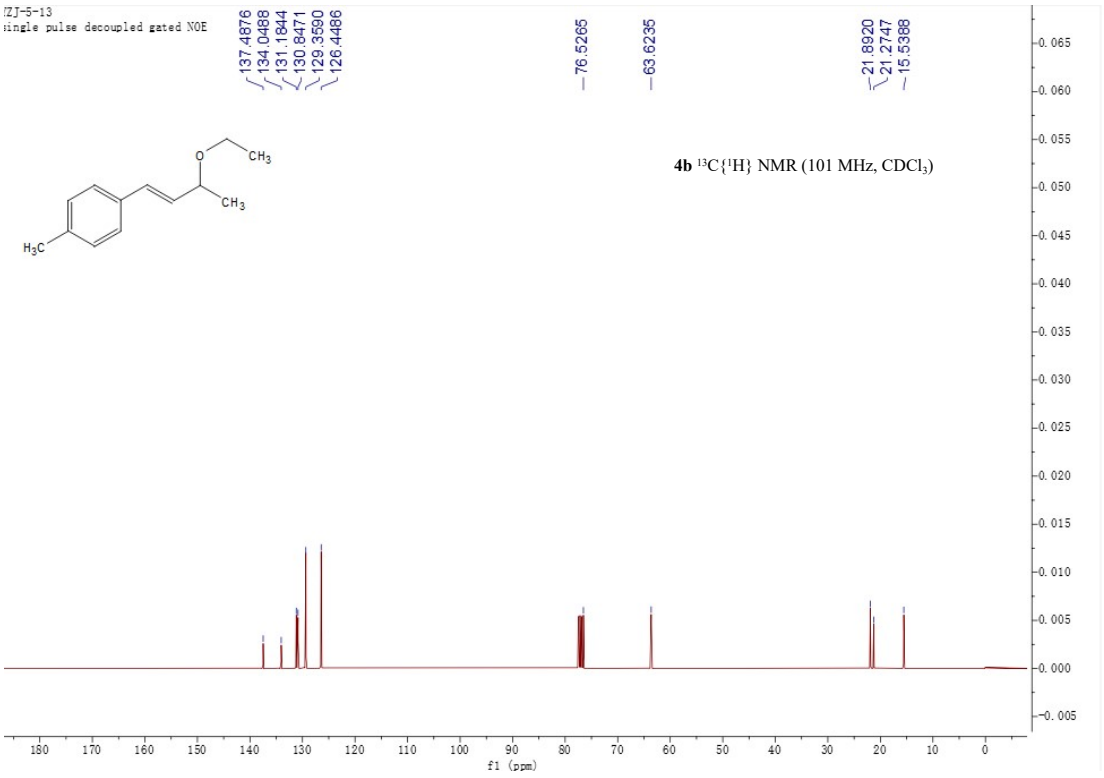
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(3-ethoxybut-1-en-1-yl)-N,N-dimethylaniline (4a)



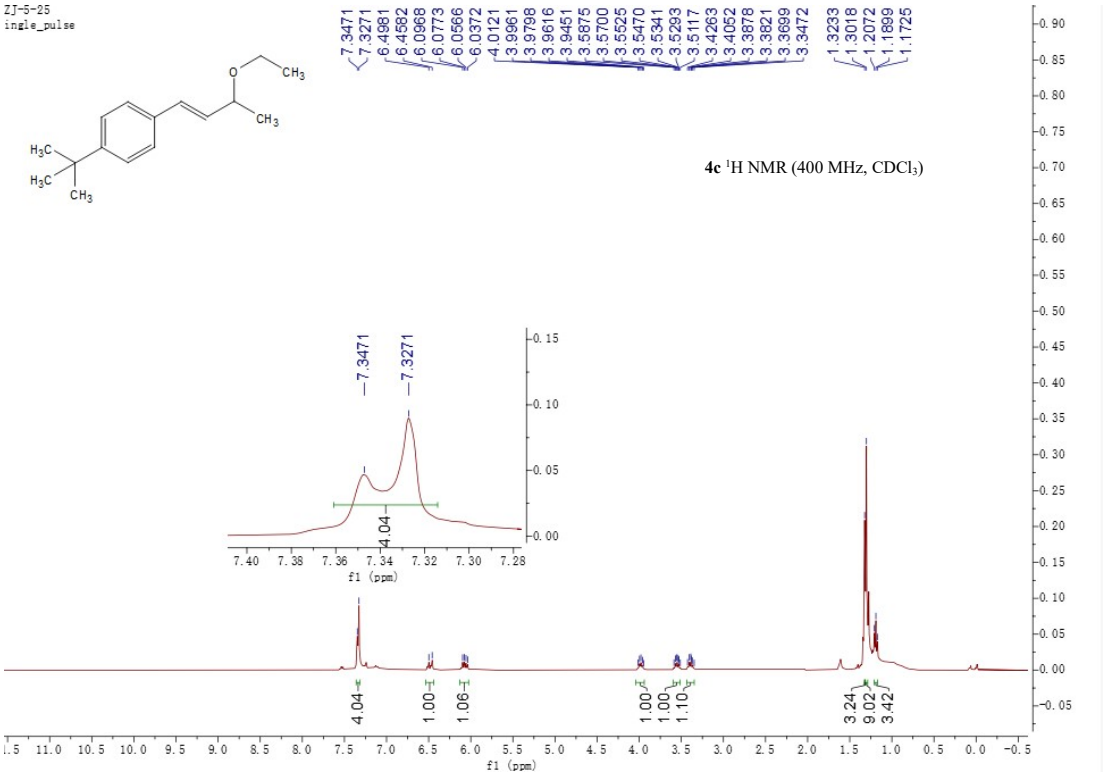


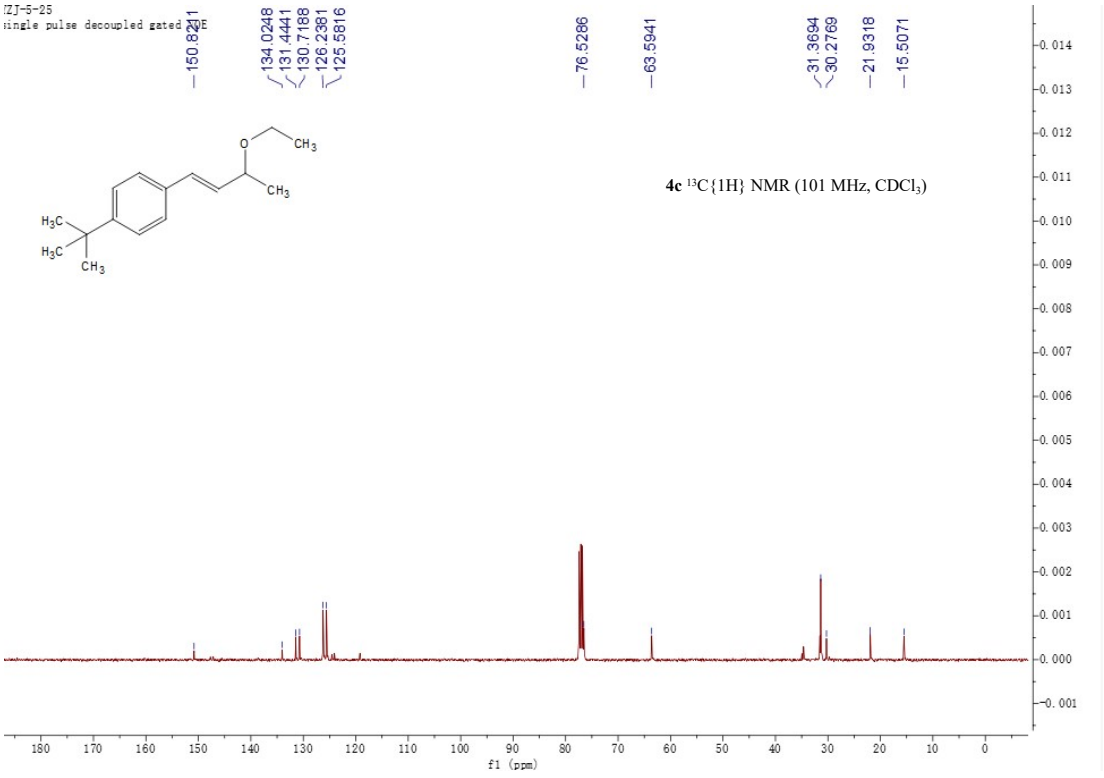
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(3-ethoxybut-1-en-1-yl)-4-methylbenzene (4b)



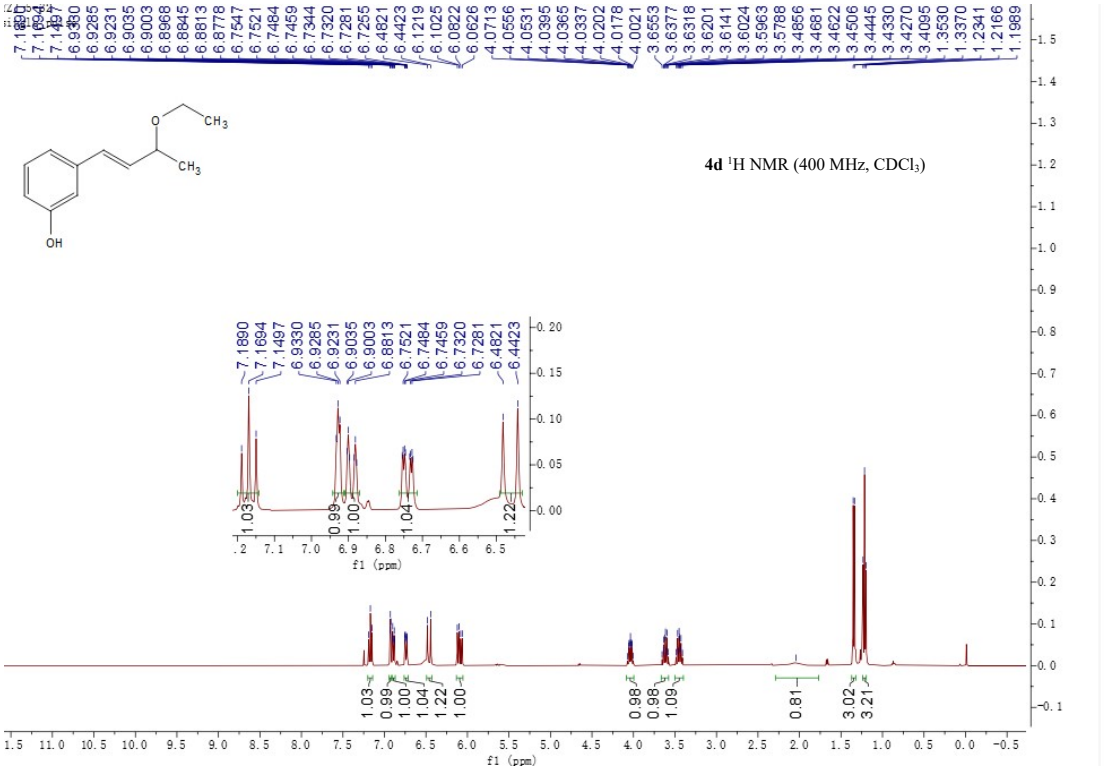


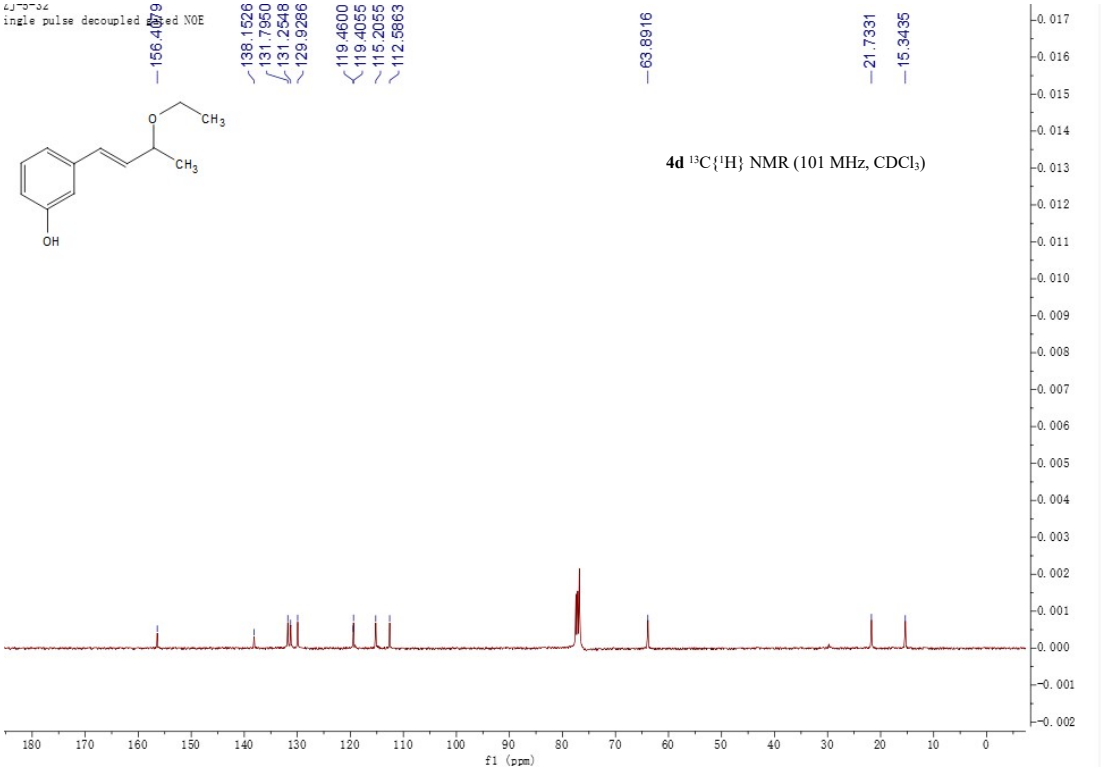
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(tert-butyl)-4-(3-ethoxybut-1-en-1-yl)benzene (4c)



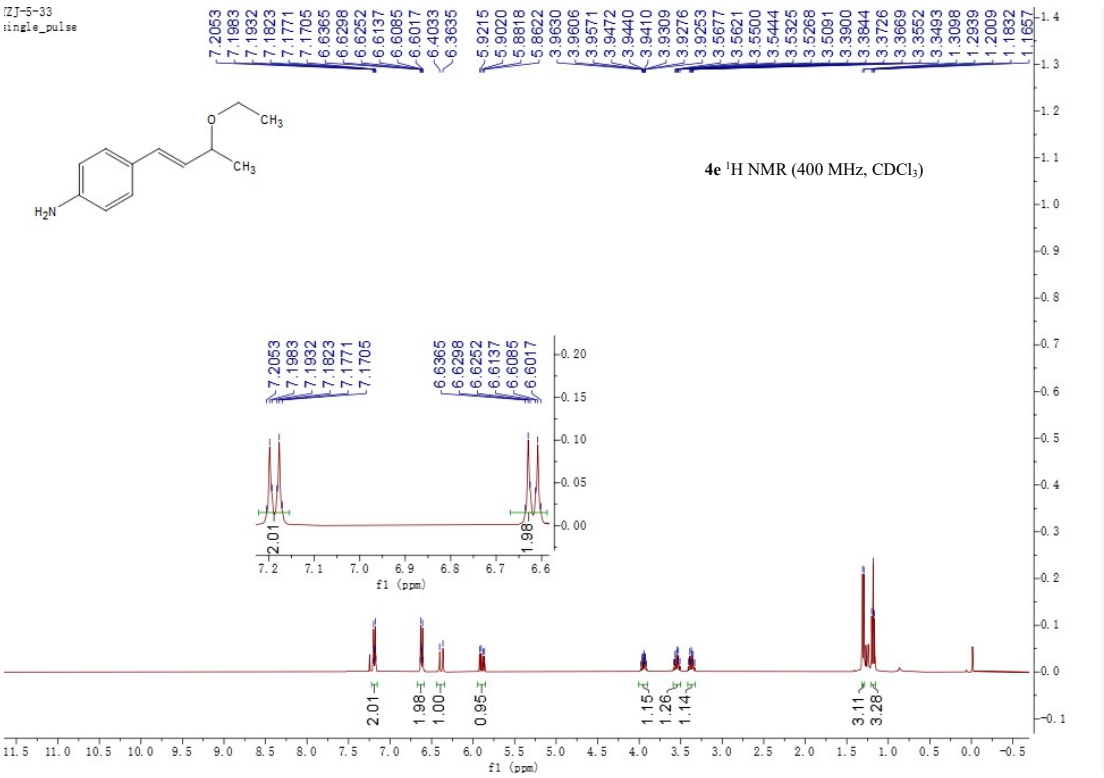


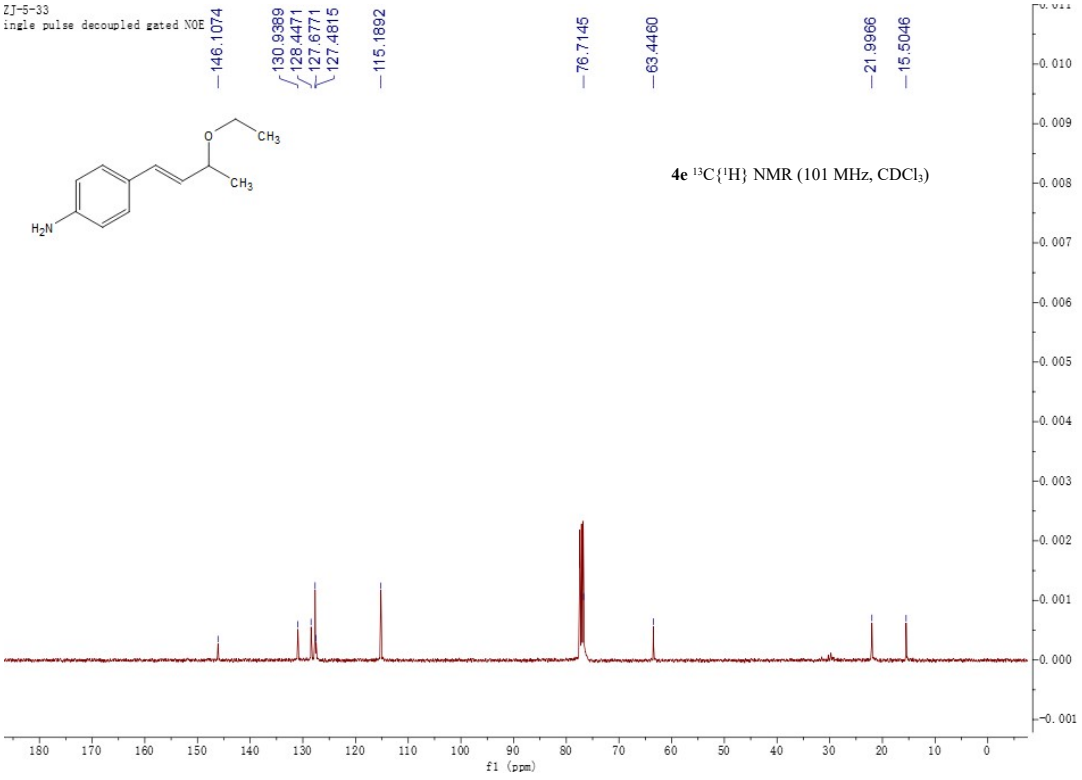
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-3-(3-ethoxybut-1-en-1-yl)phenol (4d)



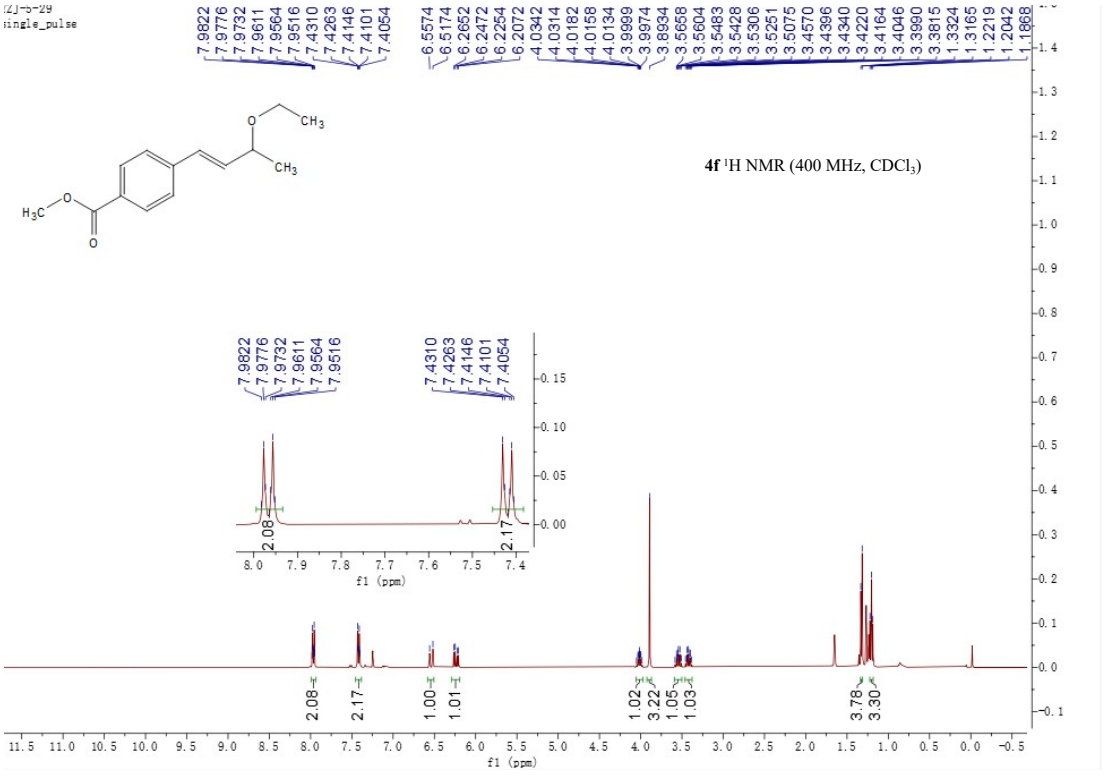


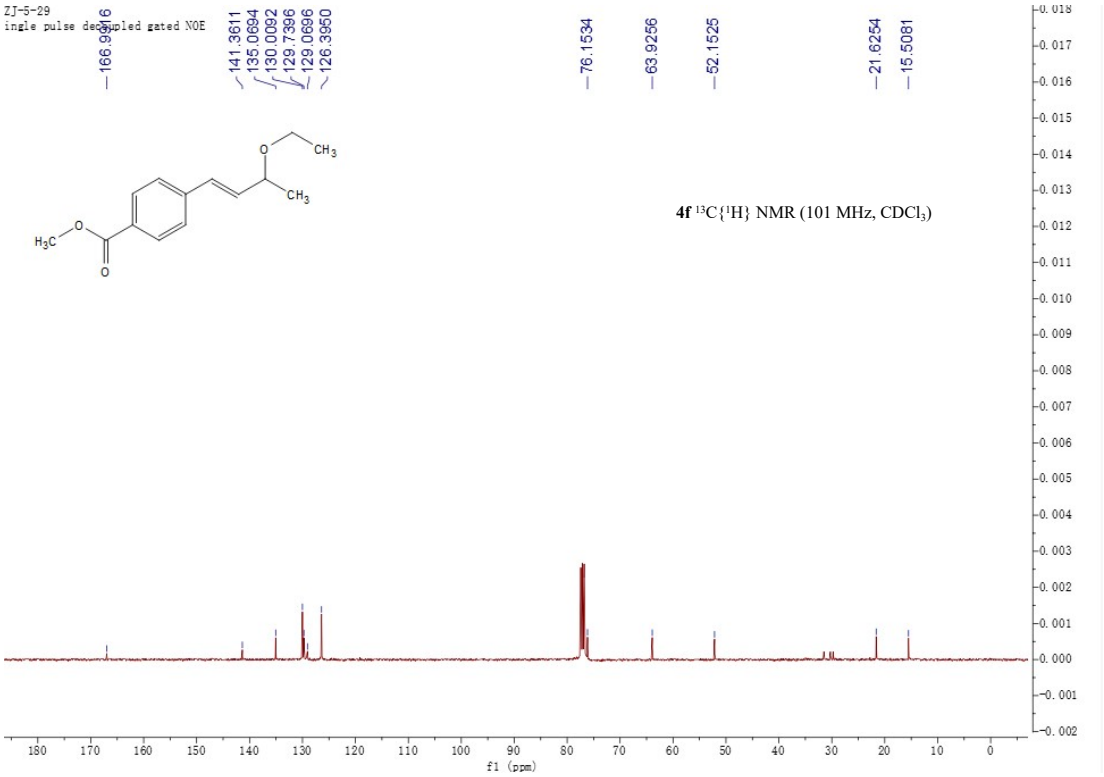
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(3-ethoxybut-1-en-1-yl)aniline (4e)



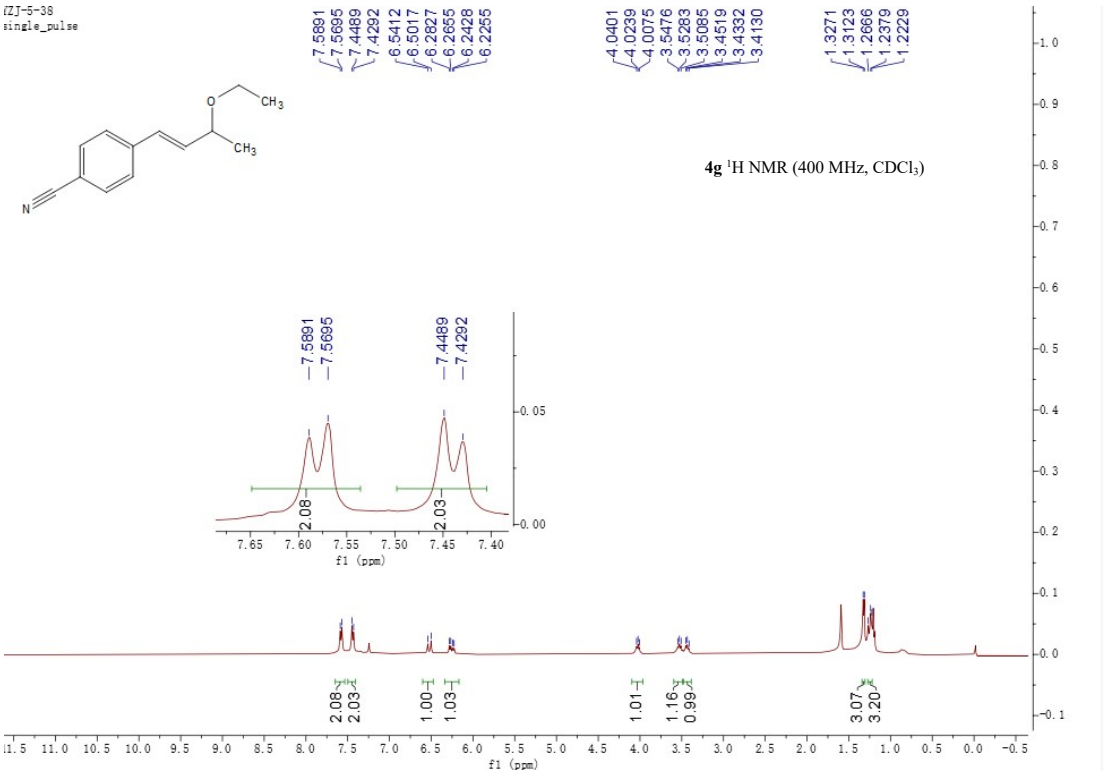


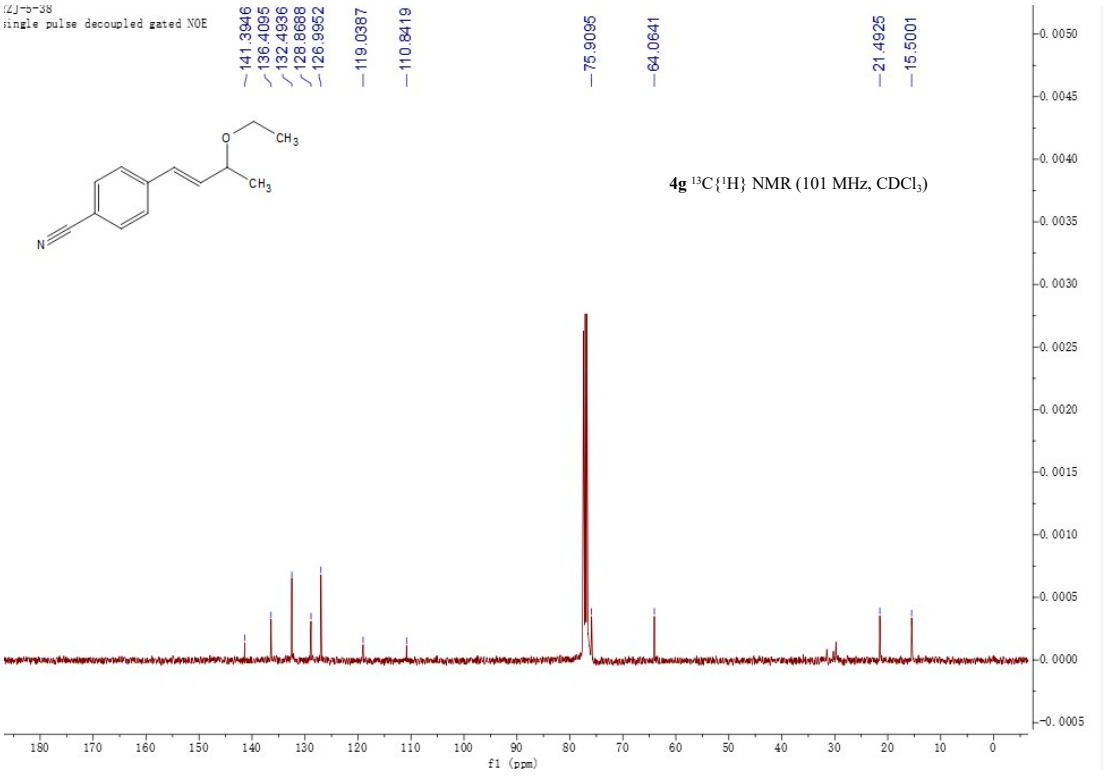
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of methyl (*E*)-4-(3-ethoxybut-1-en-1-yl)benzoate (4f)



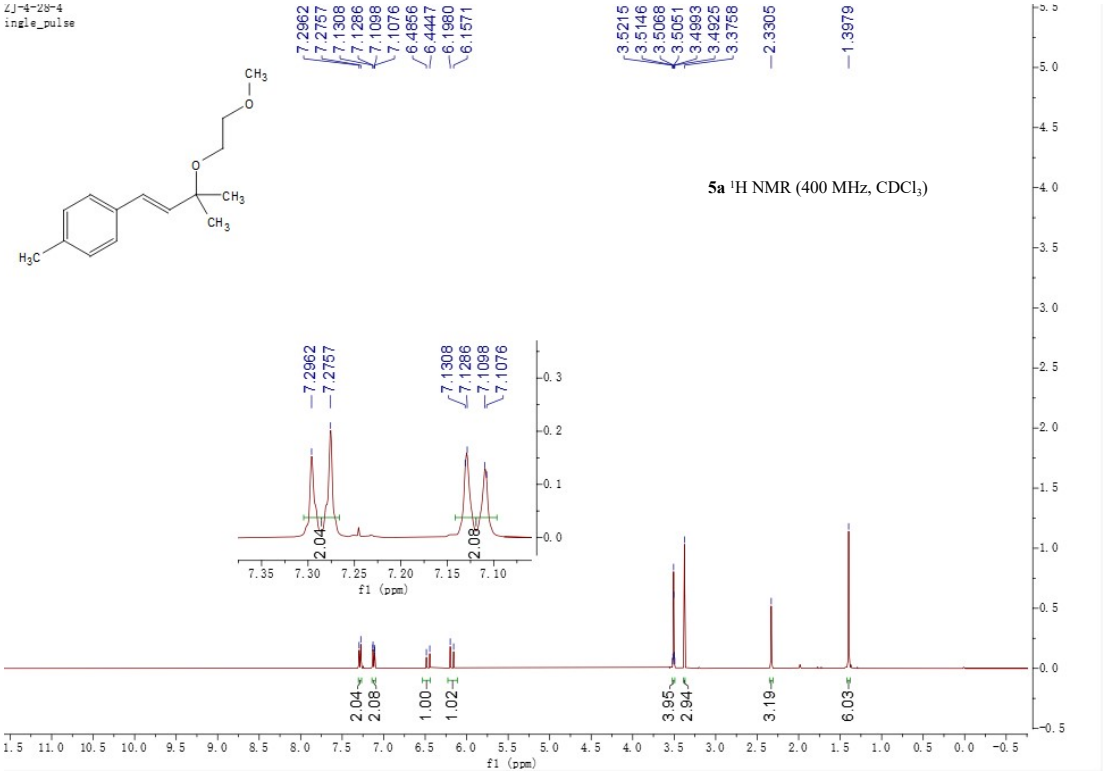


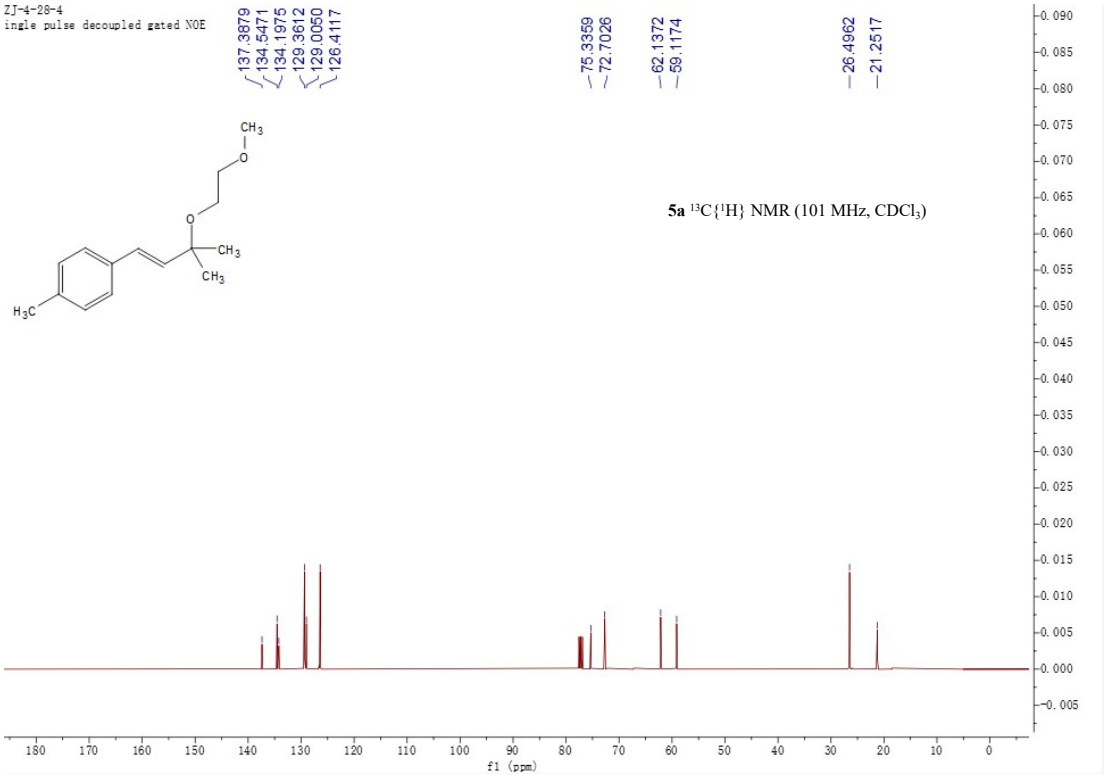
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-4-(3-ethoxybut-1-en-1-yl)benzonitrile (4g)



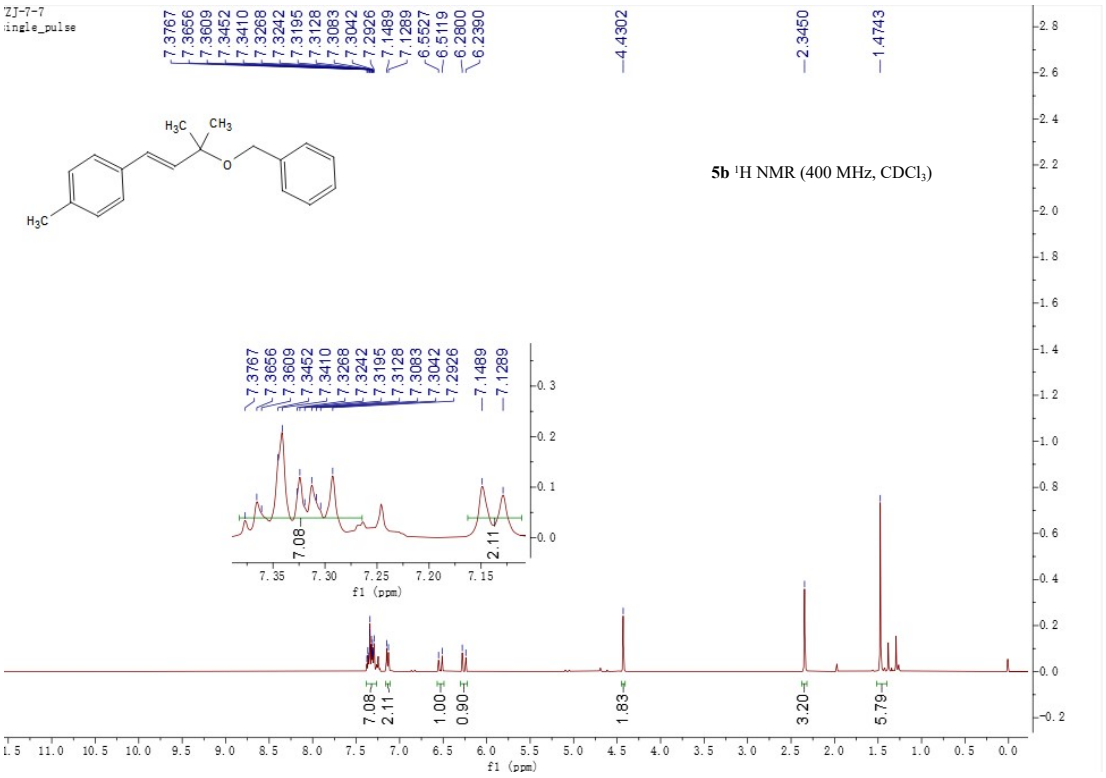


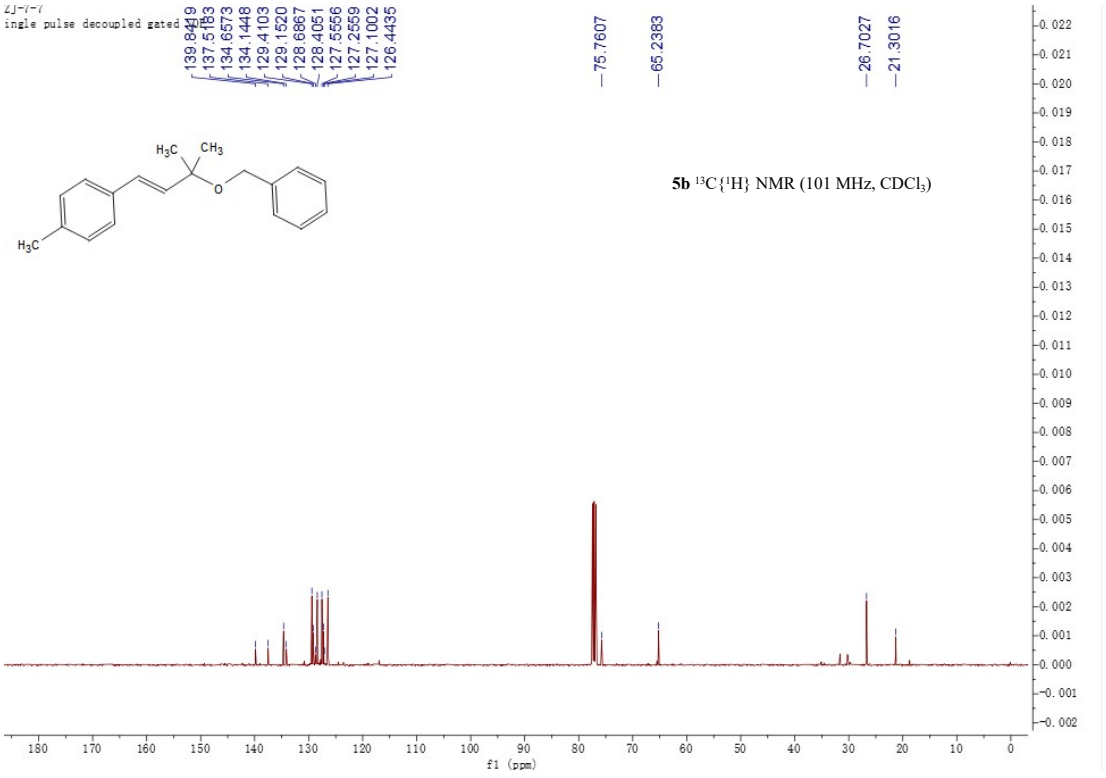
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(3-(2-methoxyethoxy)-3-methylbut-1-en-1-yl)-4-methylbenzene（5a）



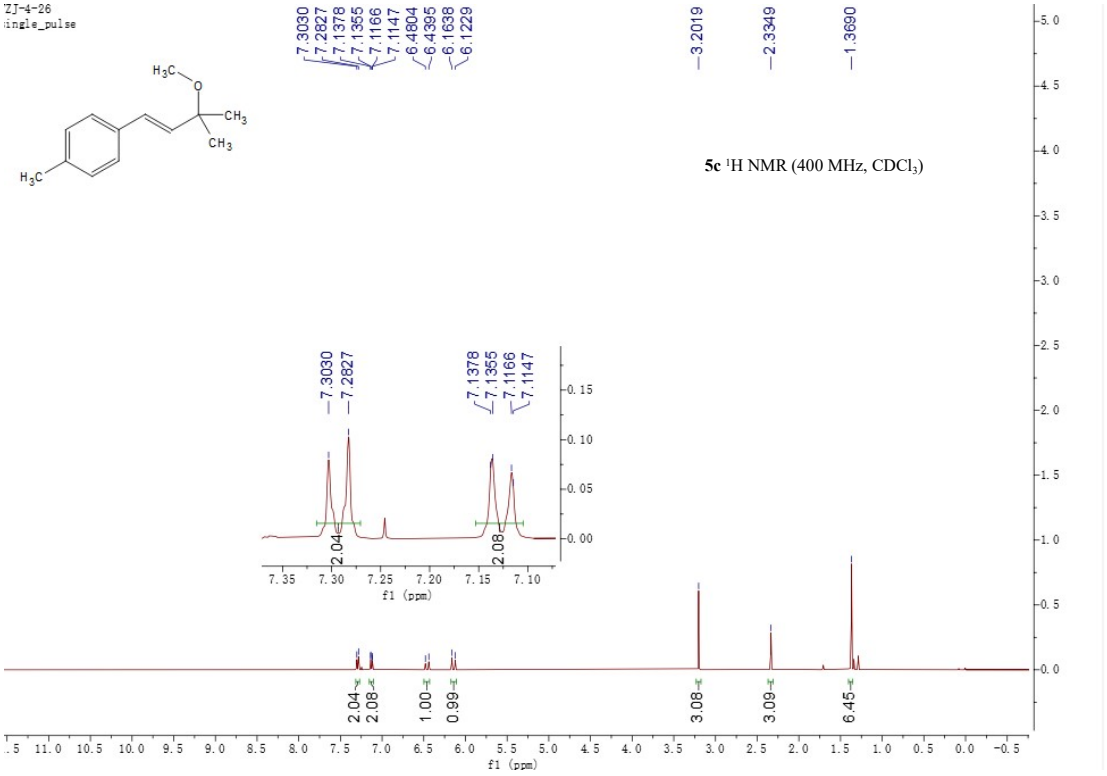


^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(3-(benzyloxy)-3-methylbut-1-en-1-yl)-4-methylbenzene (5b)

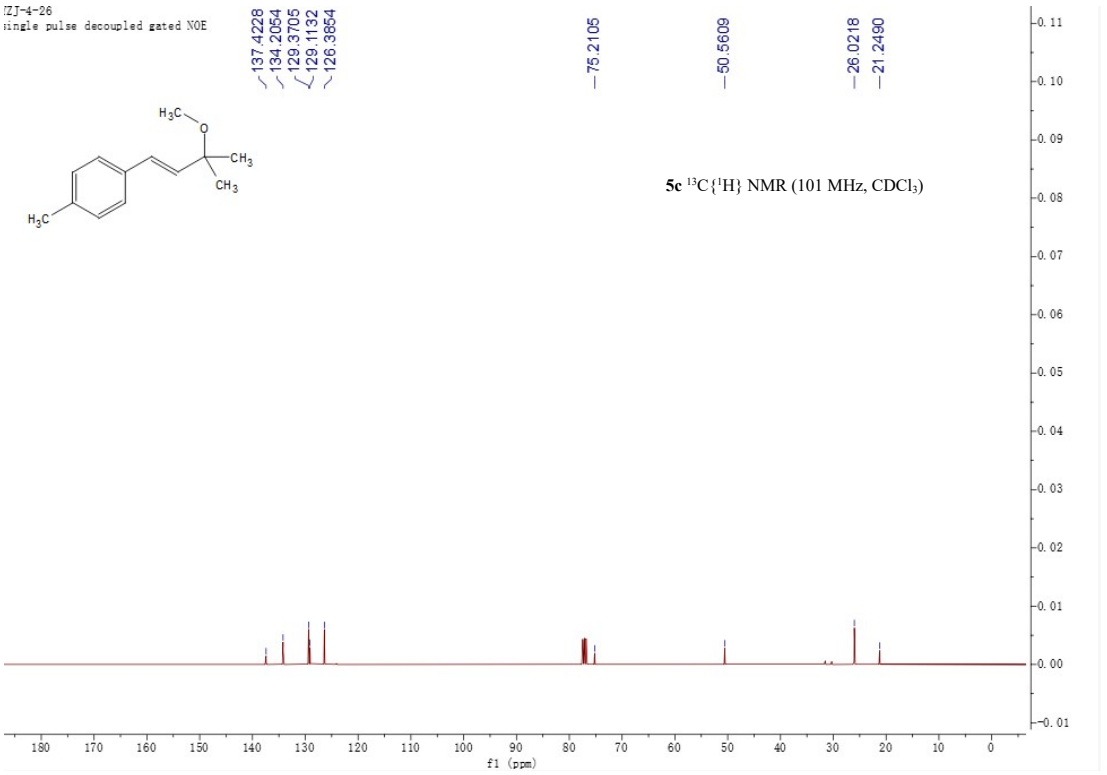




^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(3-methoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (5c)

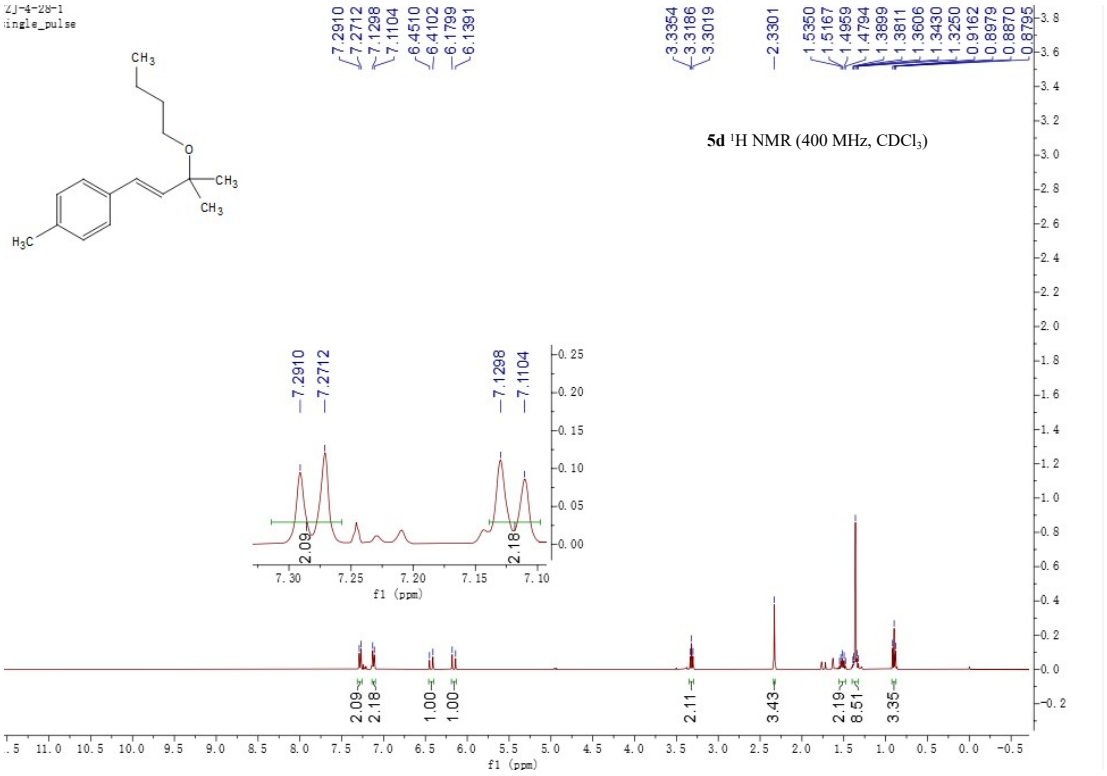


5c ^{1}H NMR (400 MHz, $CDCl_3$)

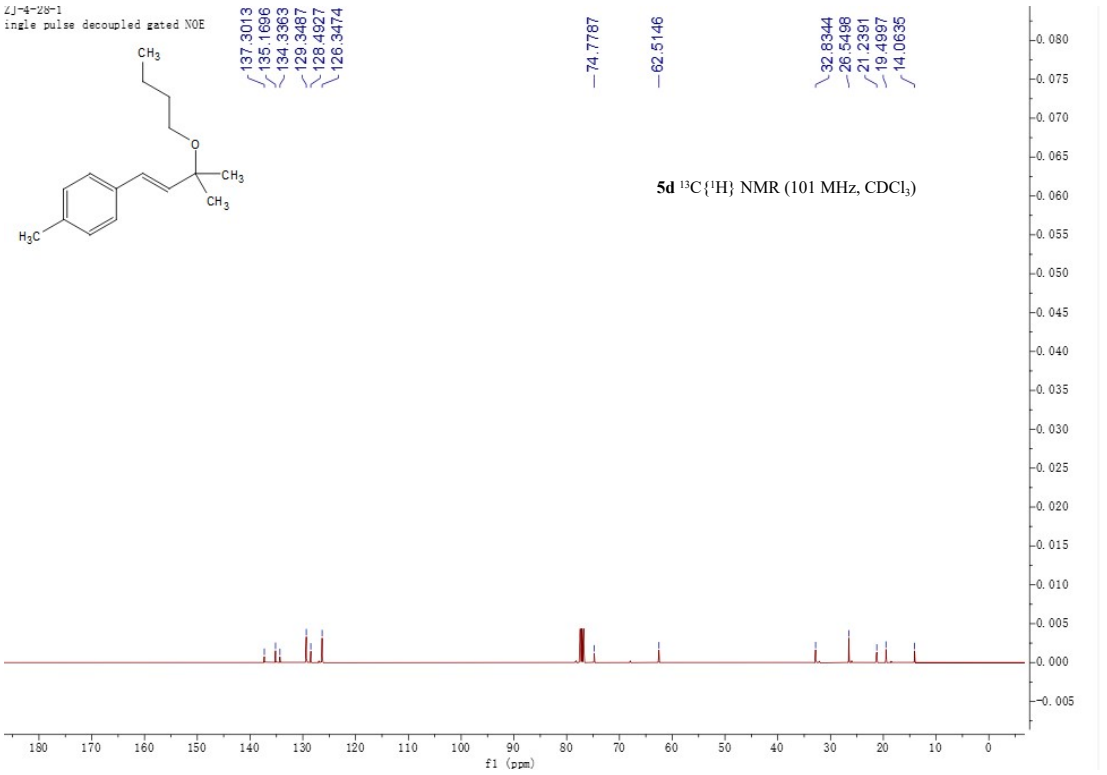


5c ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(3-butoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (5d)

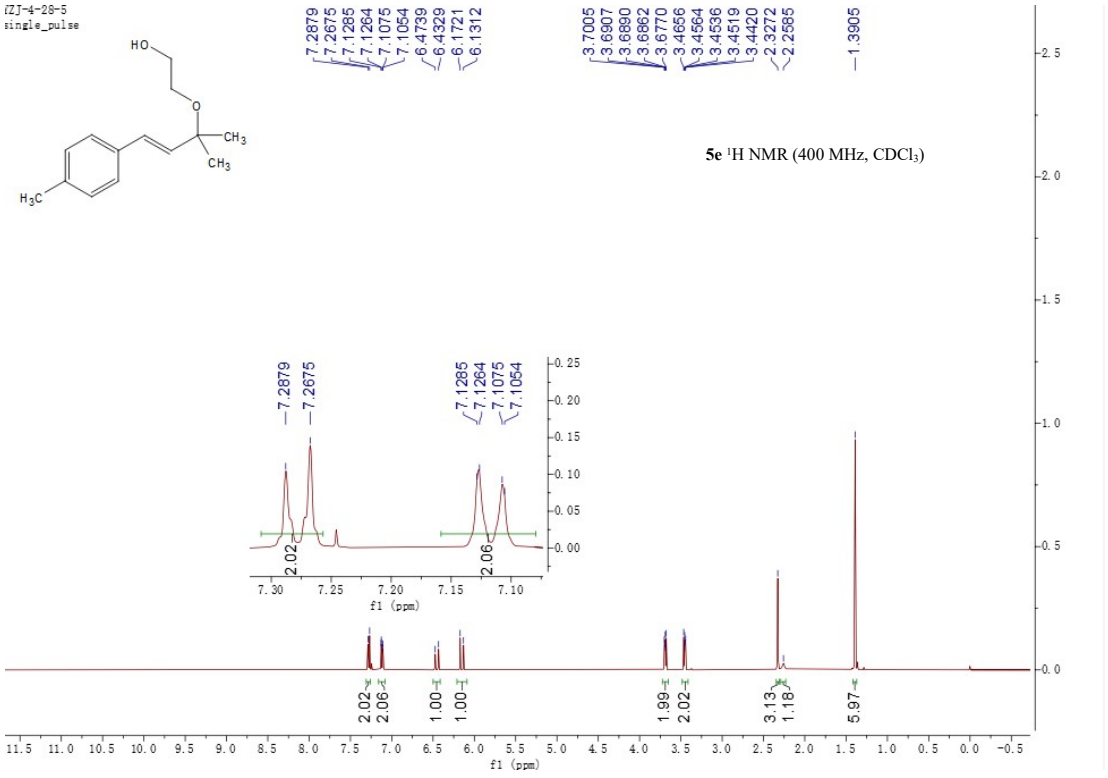


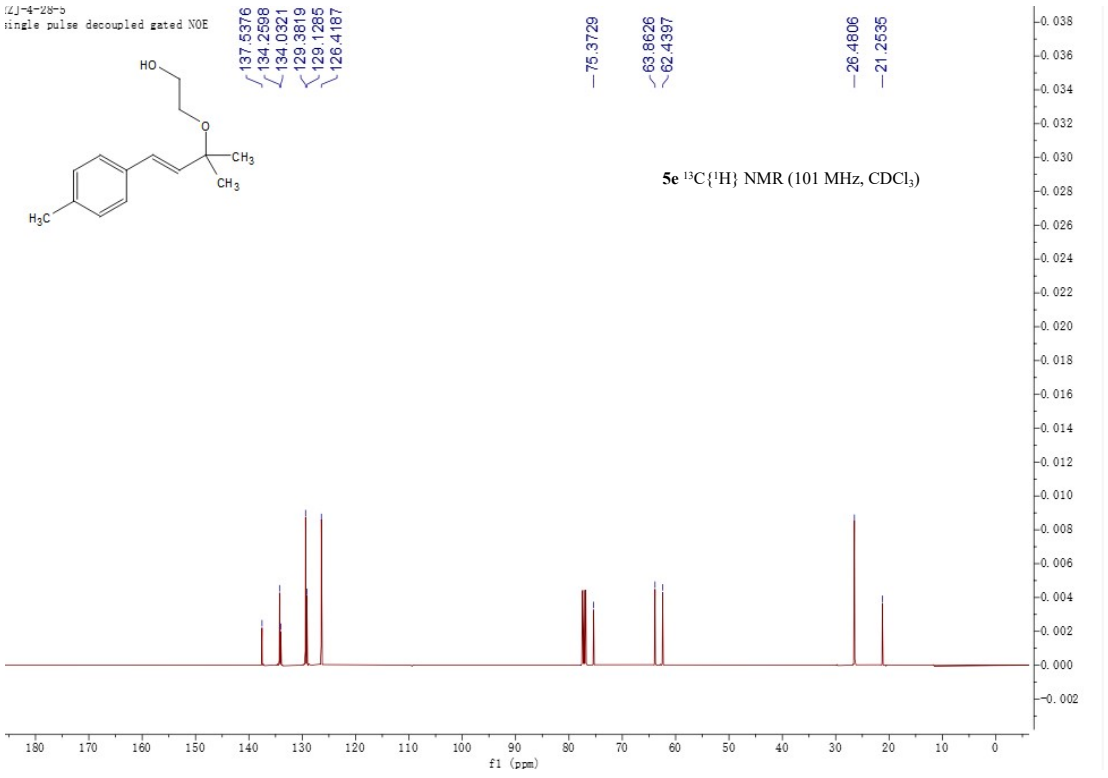
5d ^{1}H NMR (400 MHz, $CDCl_3$)



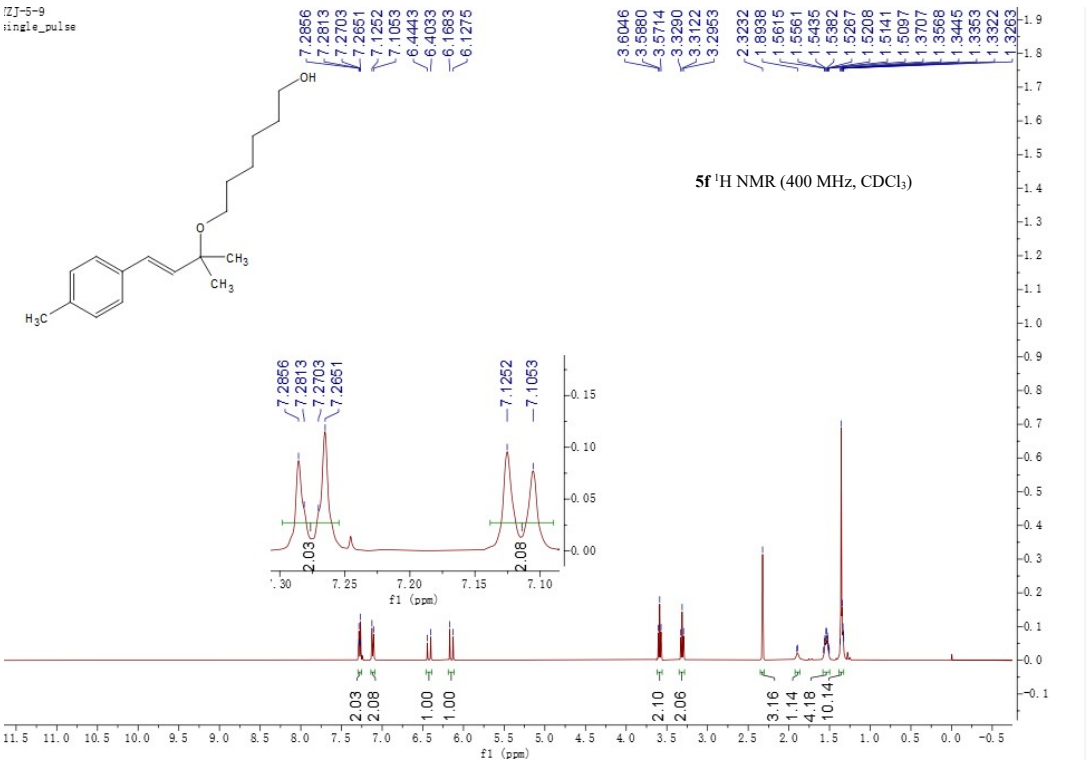
5d ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-2-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)ethan-1-ol（5e）

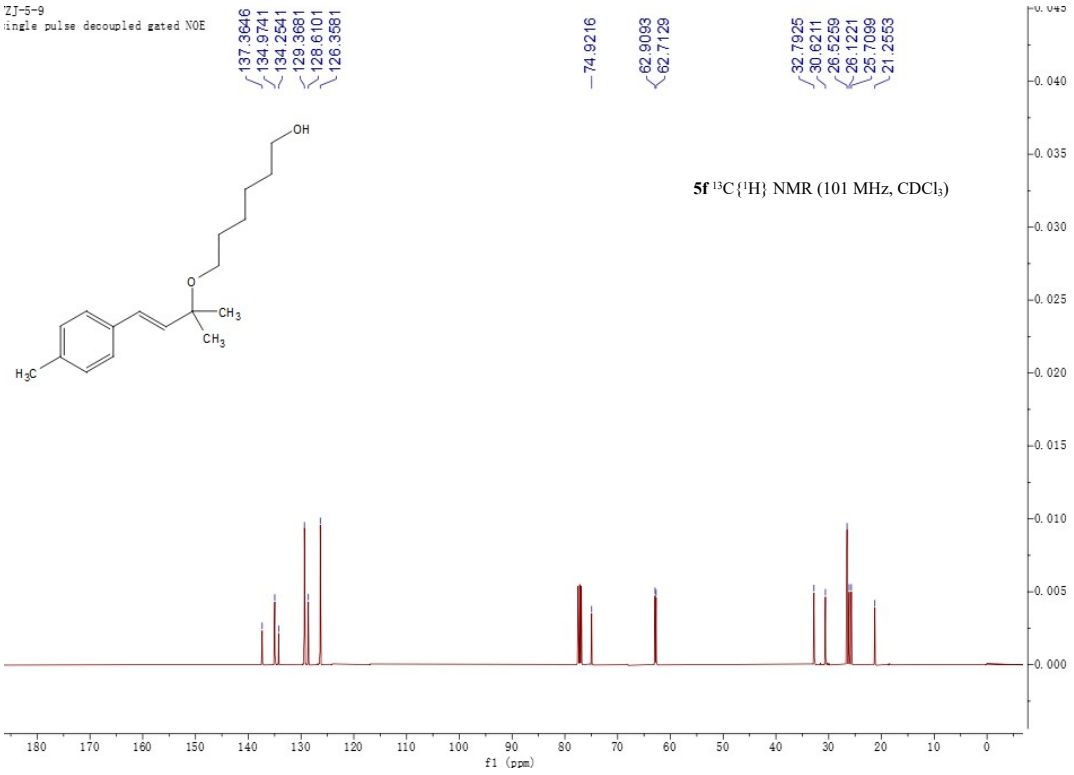




^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-6-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)hexan-1-ol（5f）

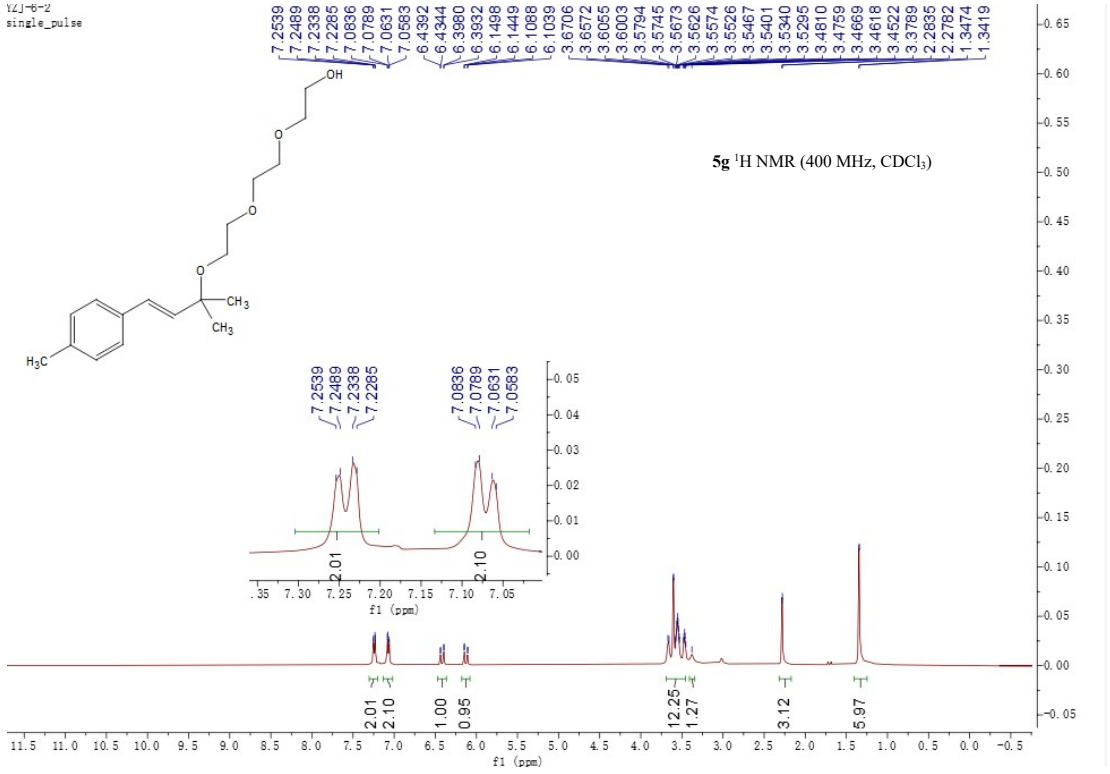


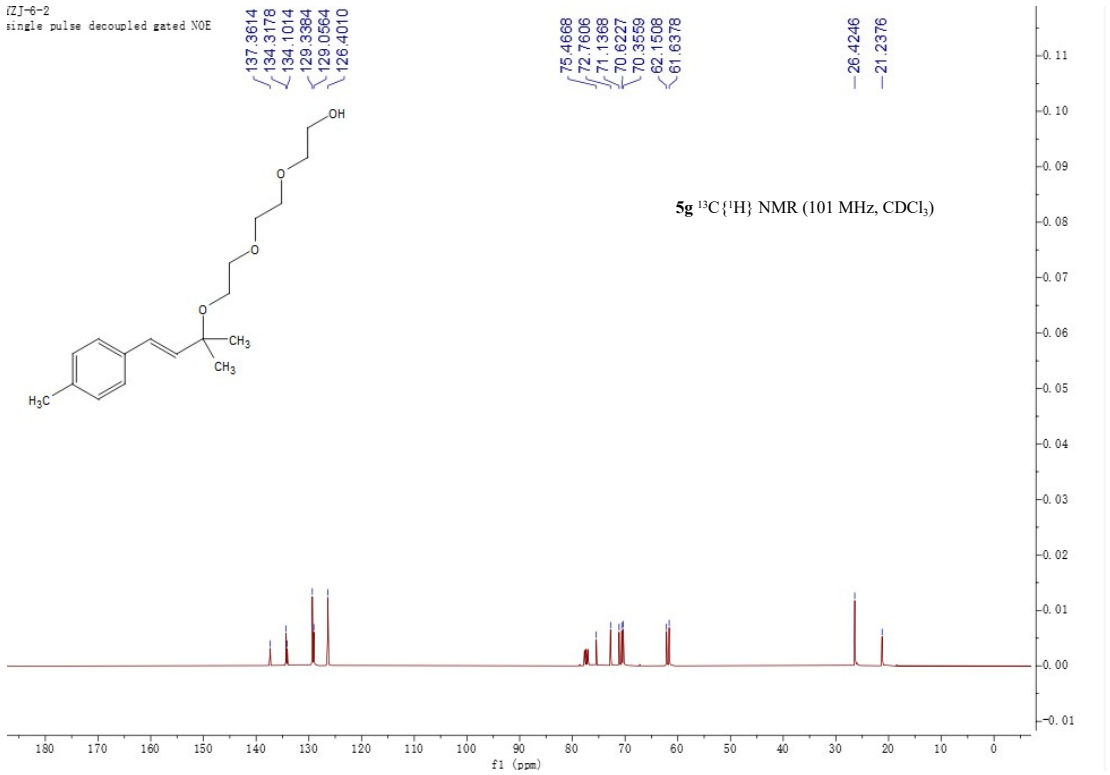
5f ^{1}H NMR (400 MHz, $CDCl_3$)



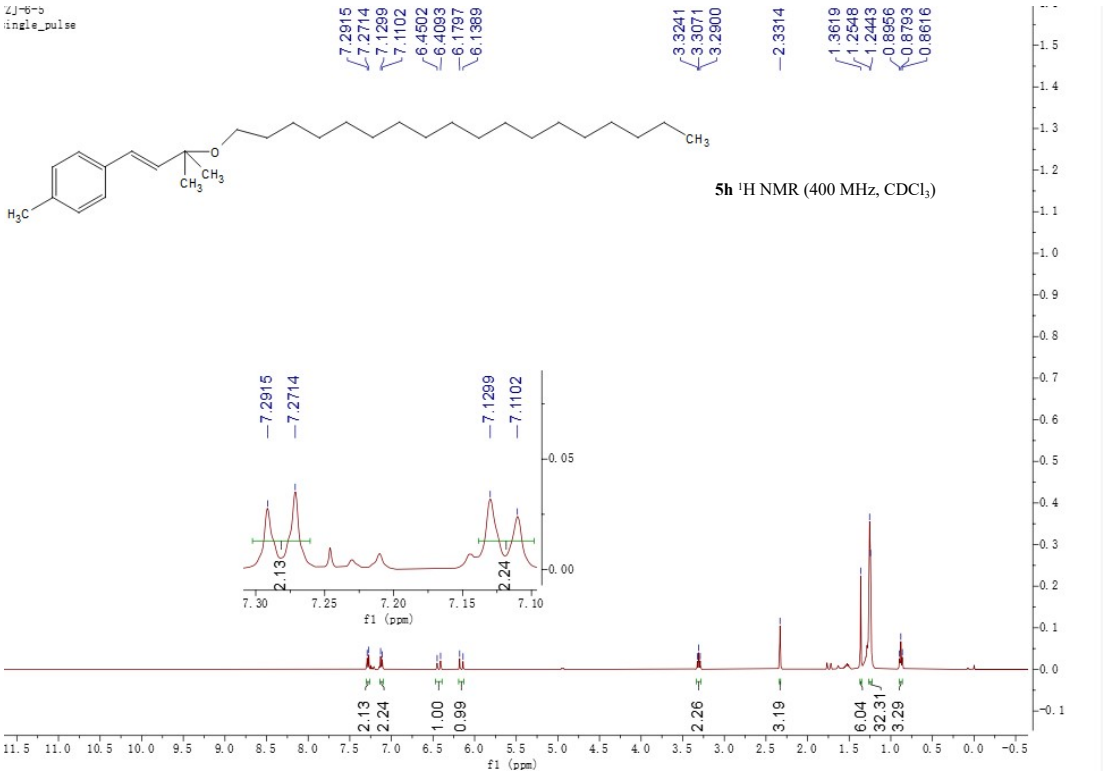
5f ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

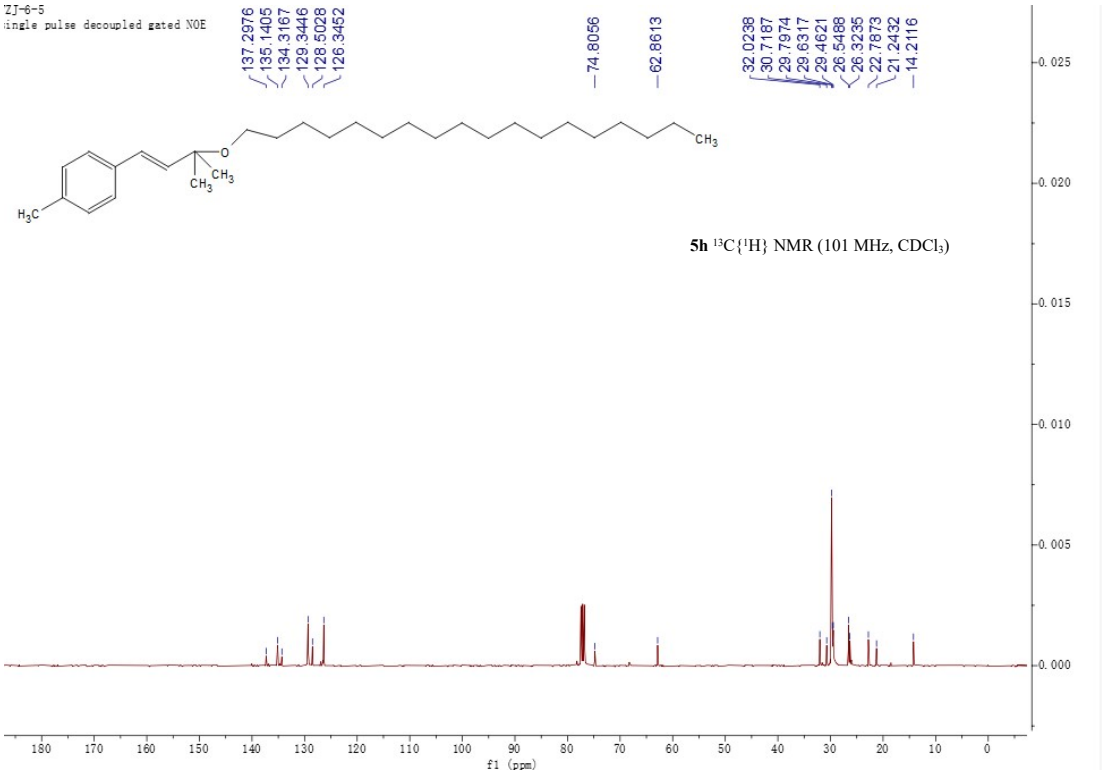
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-2-(2-(2-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)ethoxy)ethoxy)ethan-1-ol (5g)



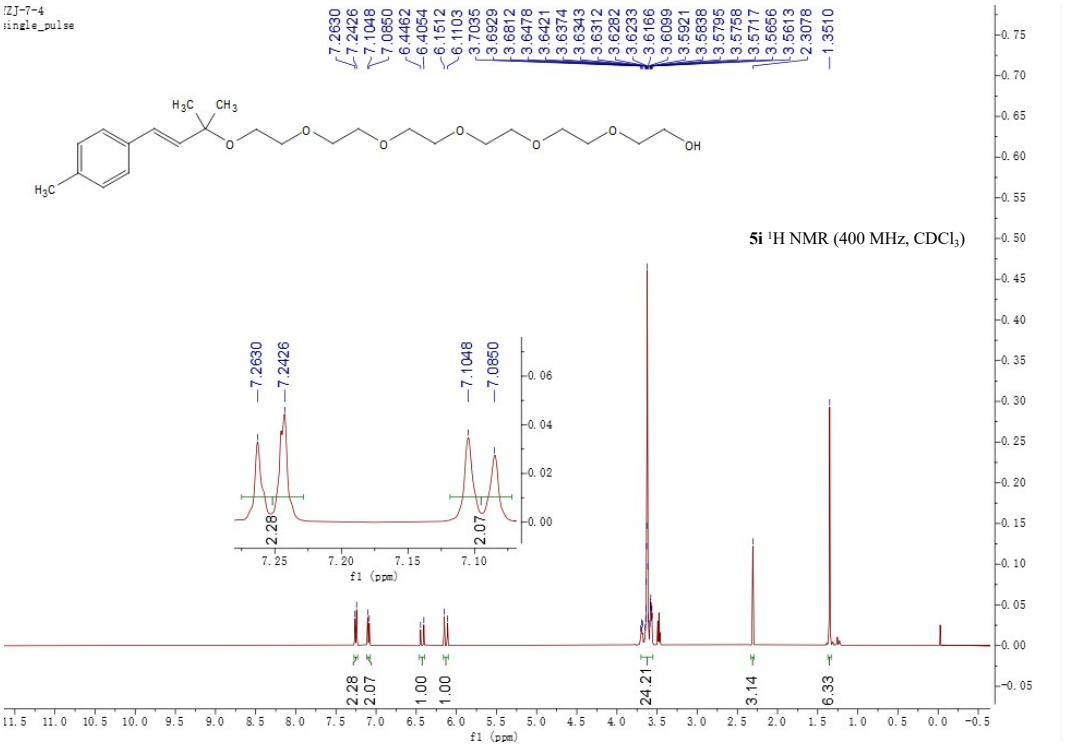


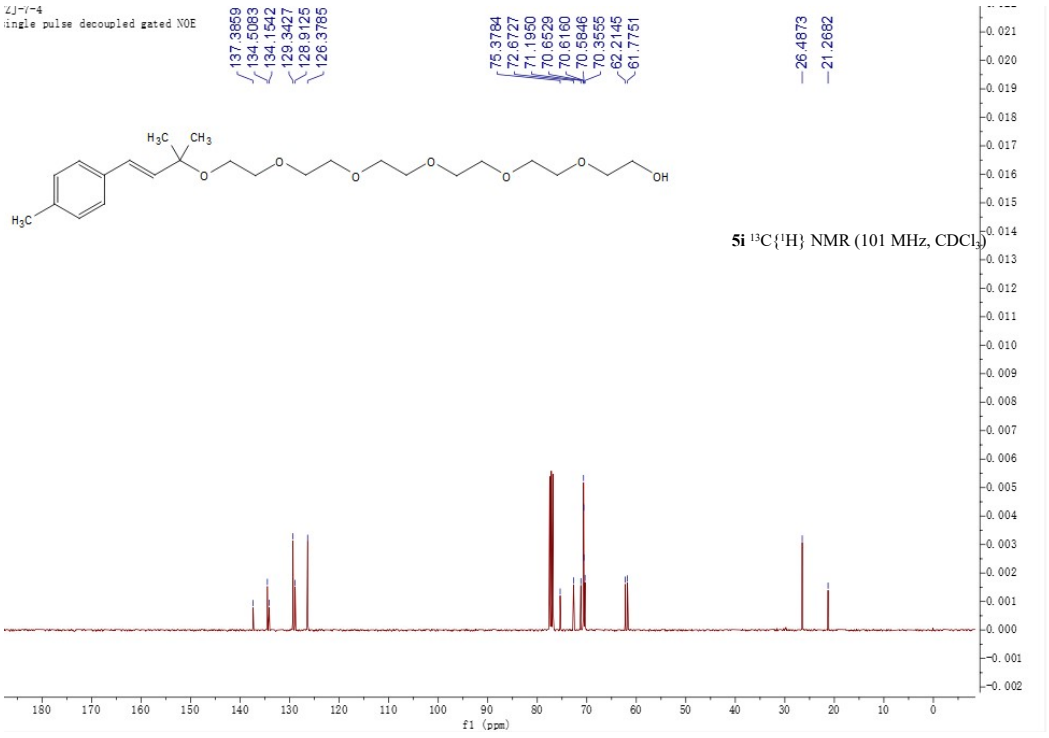
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-methyl-4-(3-methyl-3-(octadecyloxy)but-1-en-1-yl)benzene (5h)



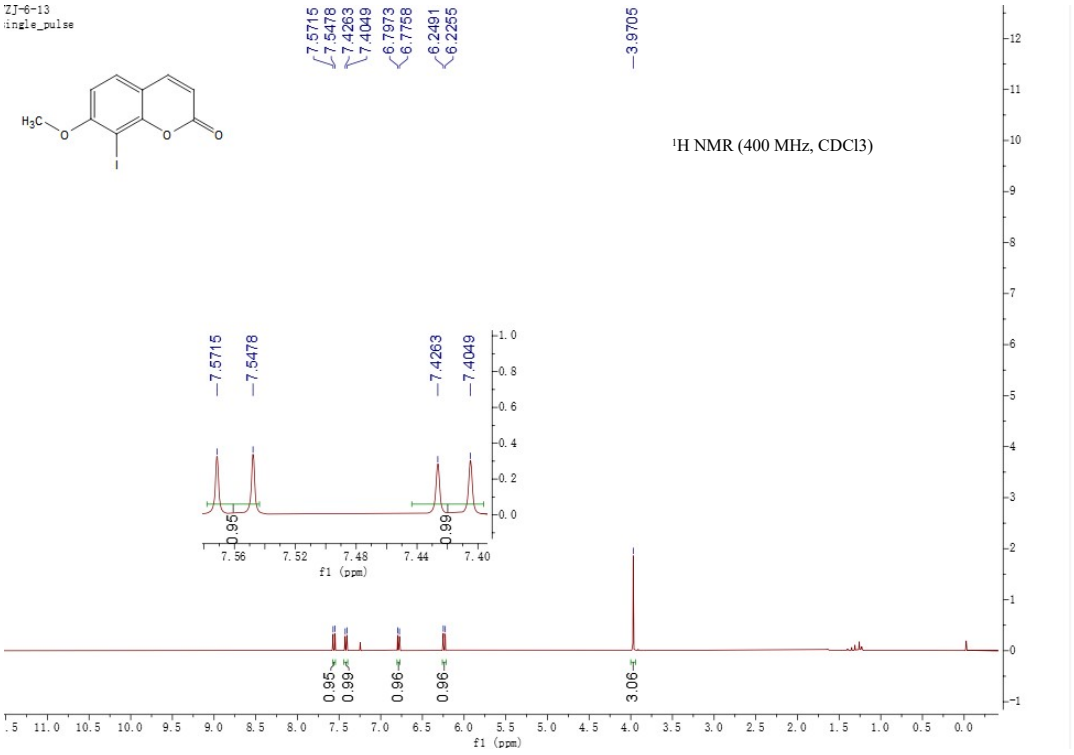


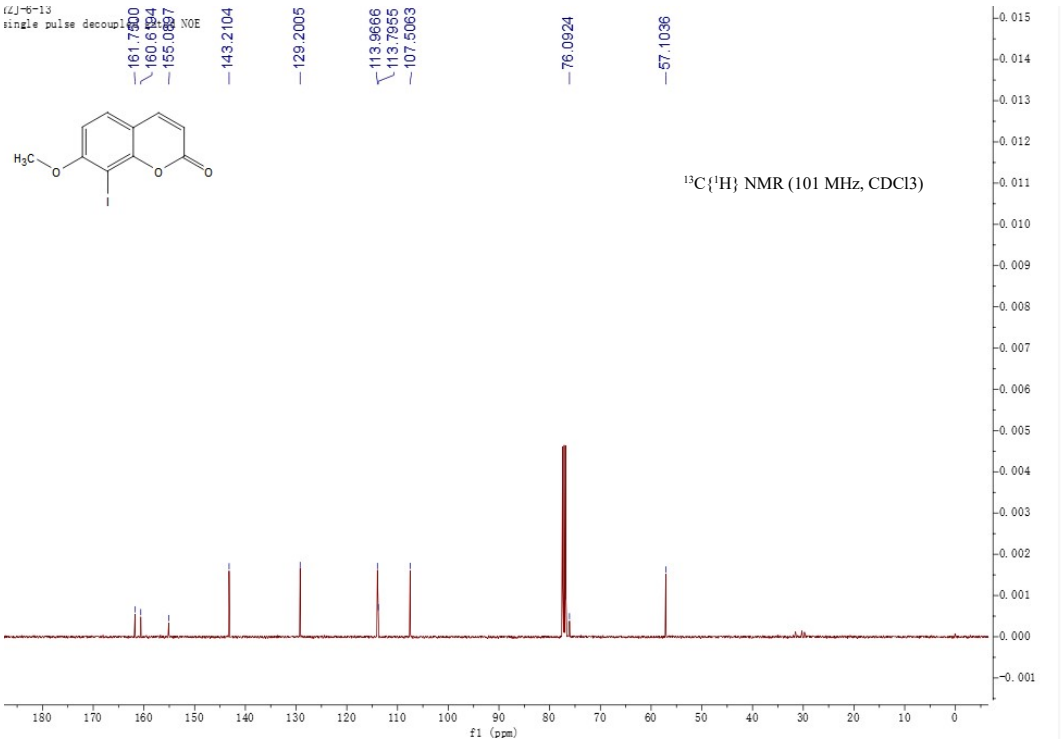
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-19,19-dimethyl-21-(p-tolyl)-3,6,9,12,15,18-hexaoxahenicos-20-en-1-ol（5i）



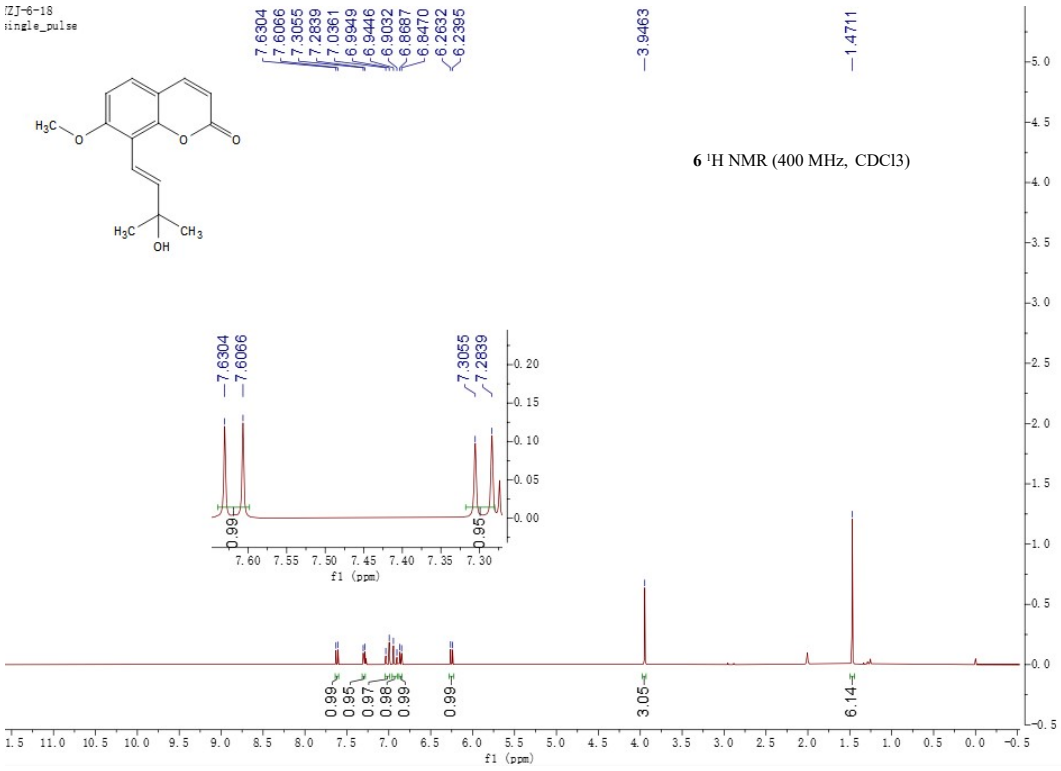


^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of 8-Iodo-7-methoxy-2*H*-chromen-2-one[7]

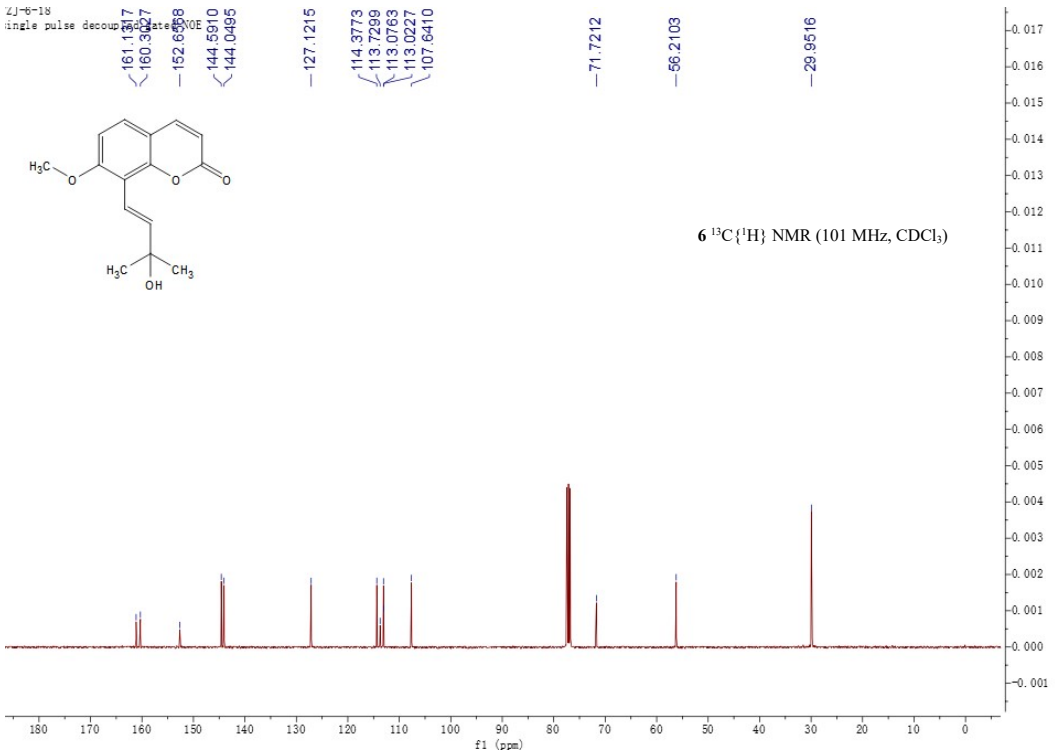




^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-8-(3-hydroxy-3-methylbut-1-en-1-yl)-7-methoxy-2H-chromen-2-one (6)[7]

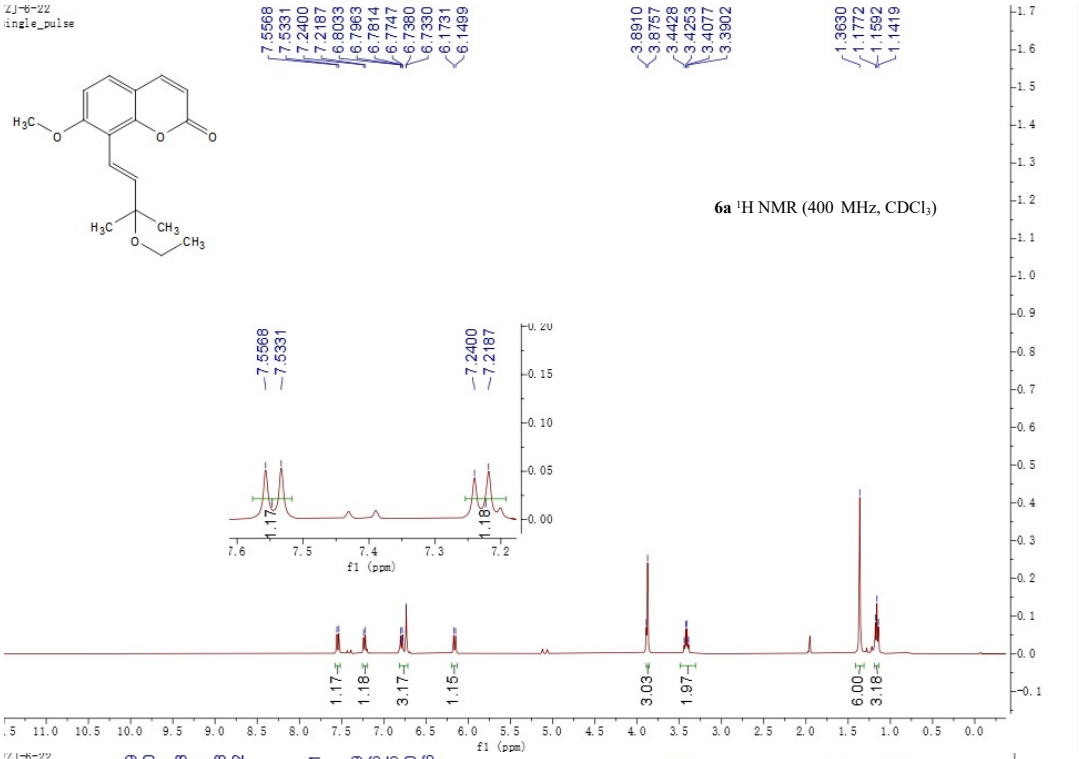


6 ^{1}H NMR (400 MHz, CDCl3)

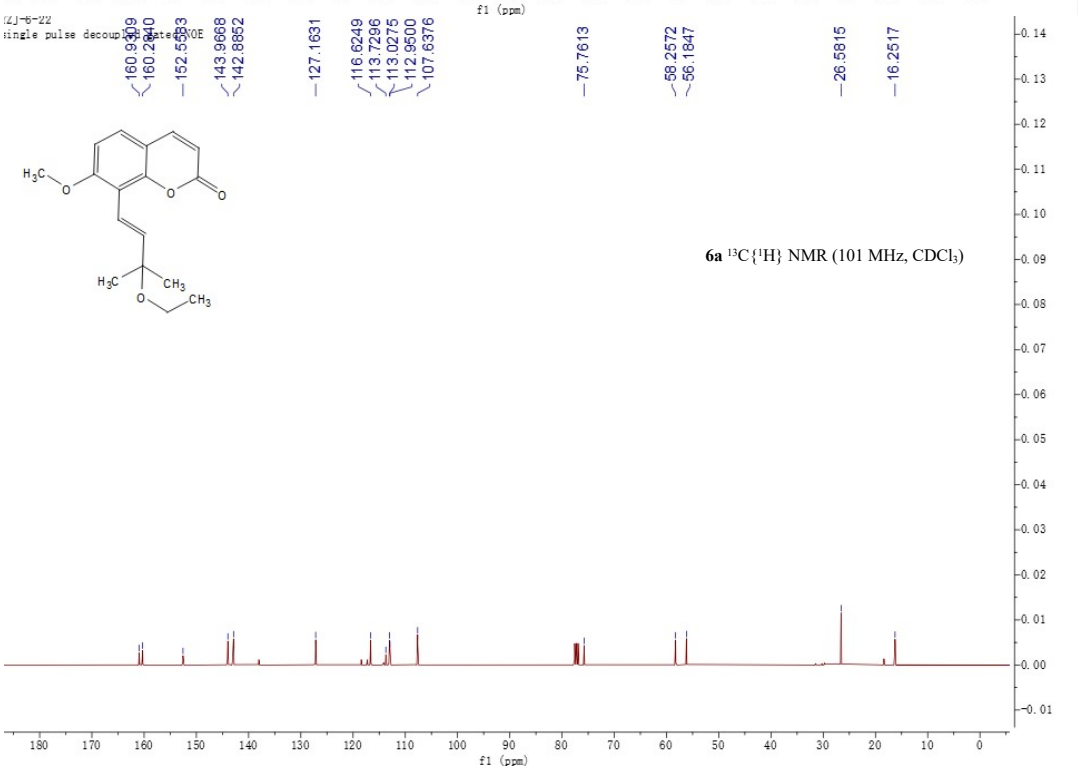


6 ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-8-(3-ethoxy-3-methylbut-1-en-1-yl)-7-methoxy-2*H*-chromen-2-one (6a)

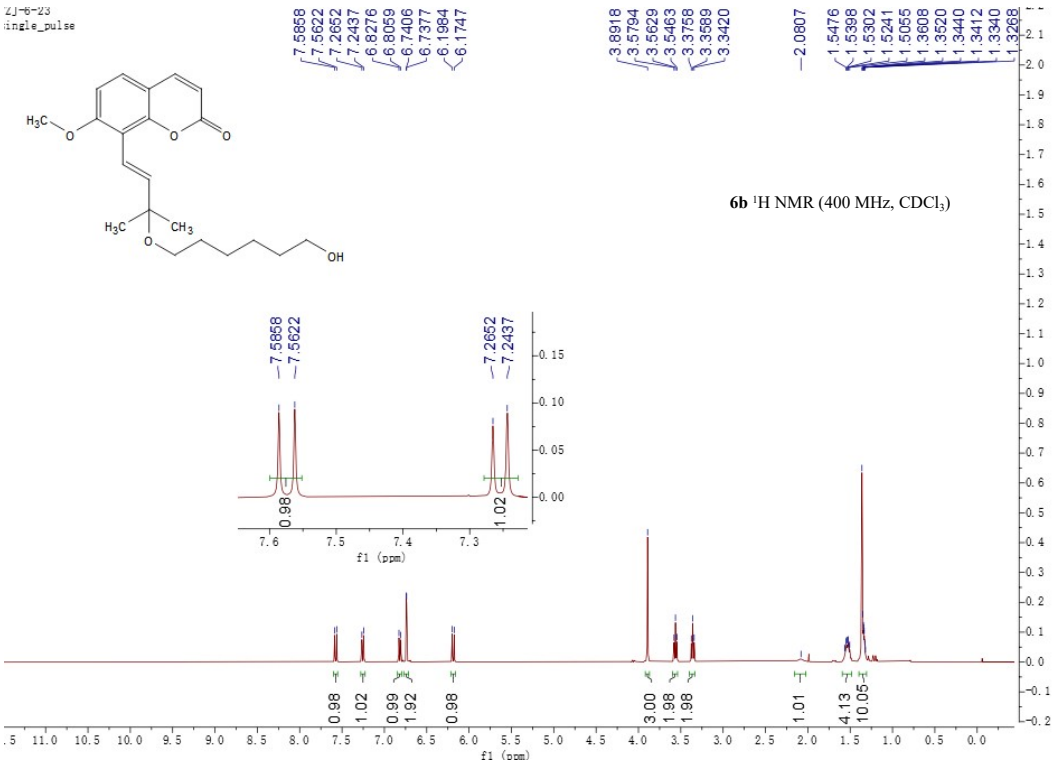


6a ^{1}H NMR (400 MHz, $CDCl_3$)

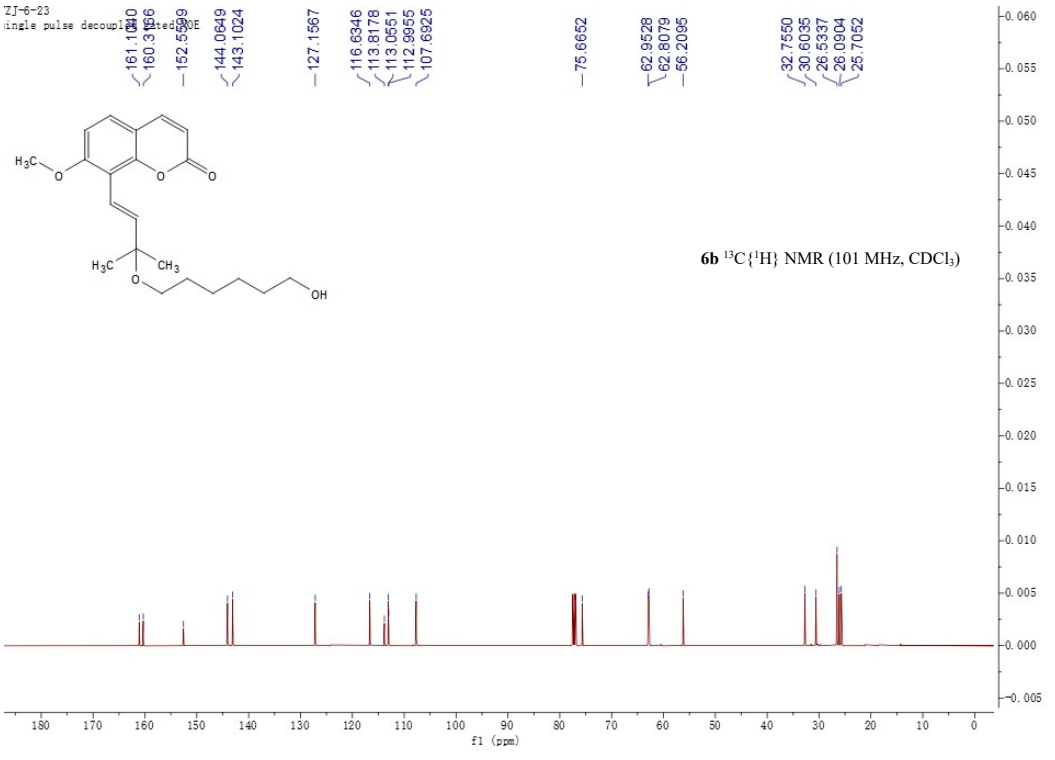


6a ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-8-(3-((6-hydroxyhexyl)oxy)-3-methylbut-1-en-1-yl)-7-methoxy-2*H*-chromen-2-one (6b)

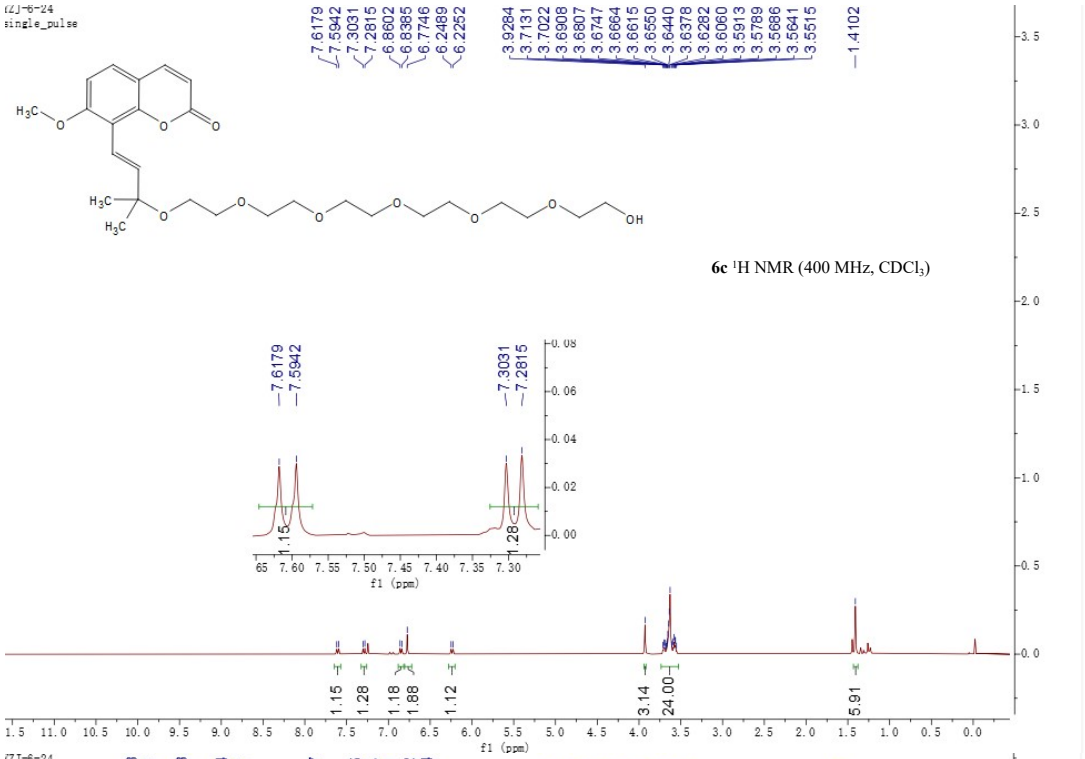


6b ^{1}H NMR (400 MHz, $CDCl_3$)

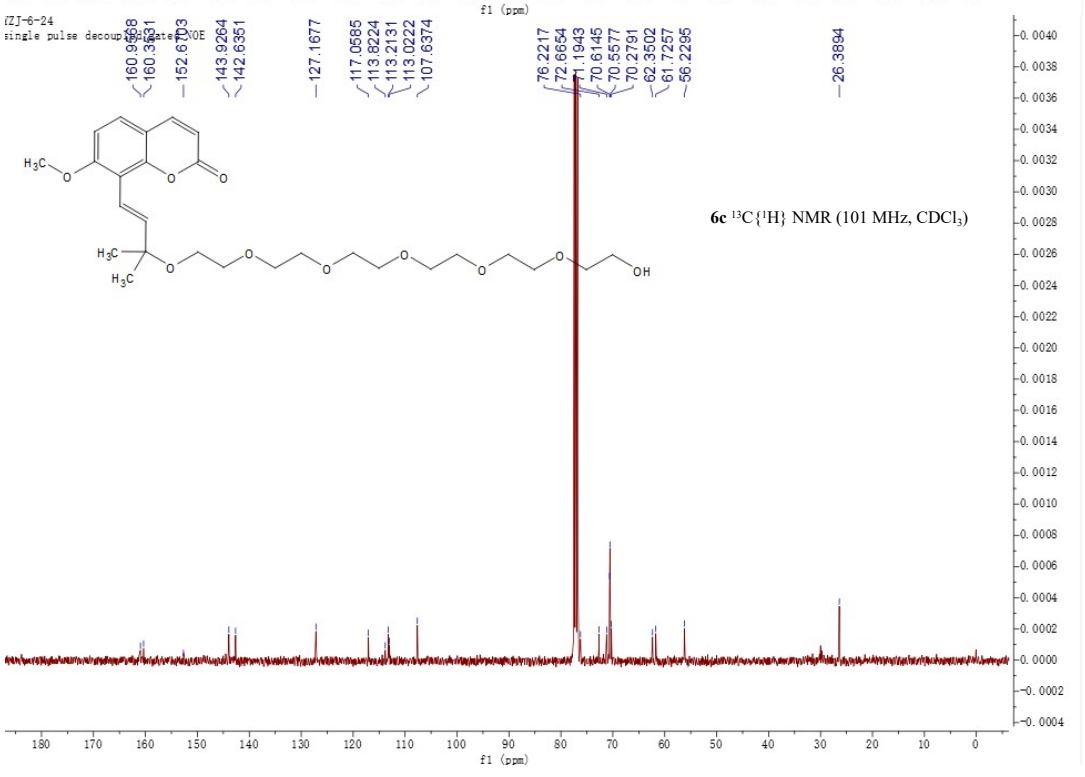


6b ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-8-(1-hydroxy-19,19-dimethyl-3,6,9,12,15,18-hexaoxahenicos-20-en-21-yl)-7-methoxy-2*H*-chromen-2-one （6c）

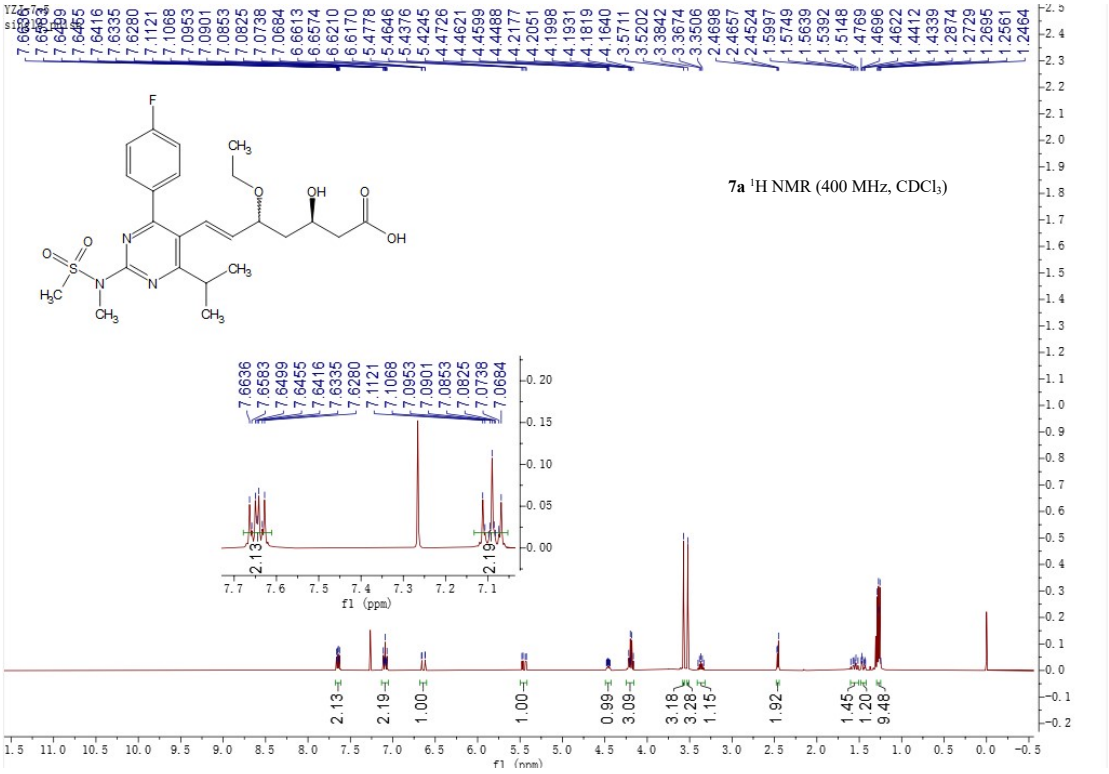


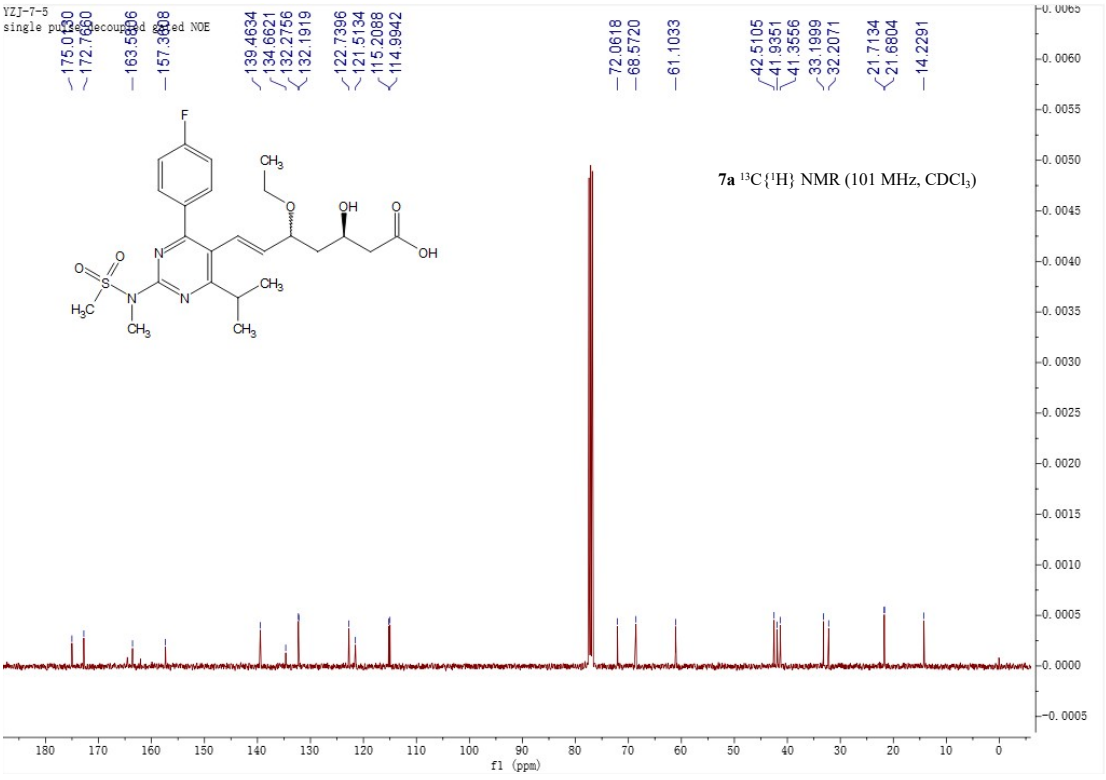
6c ^{1}H NMR (400 MHz, $CDCl_3$)



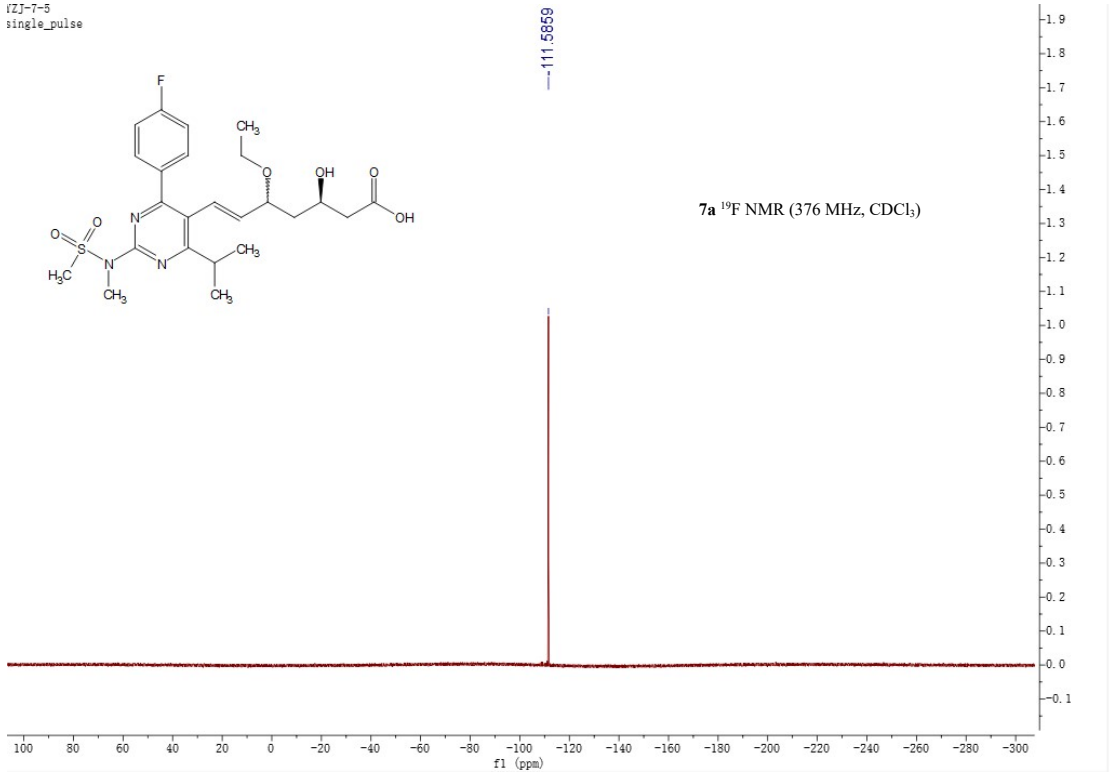
6c ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (3R,E)-5-ethoxy-7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)-3-hydroxyhept-6-enoic acid (7a)

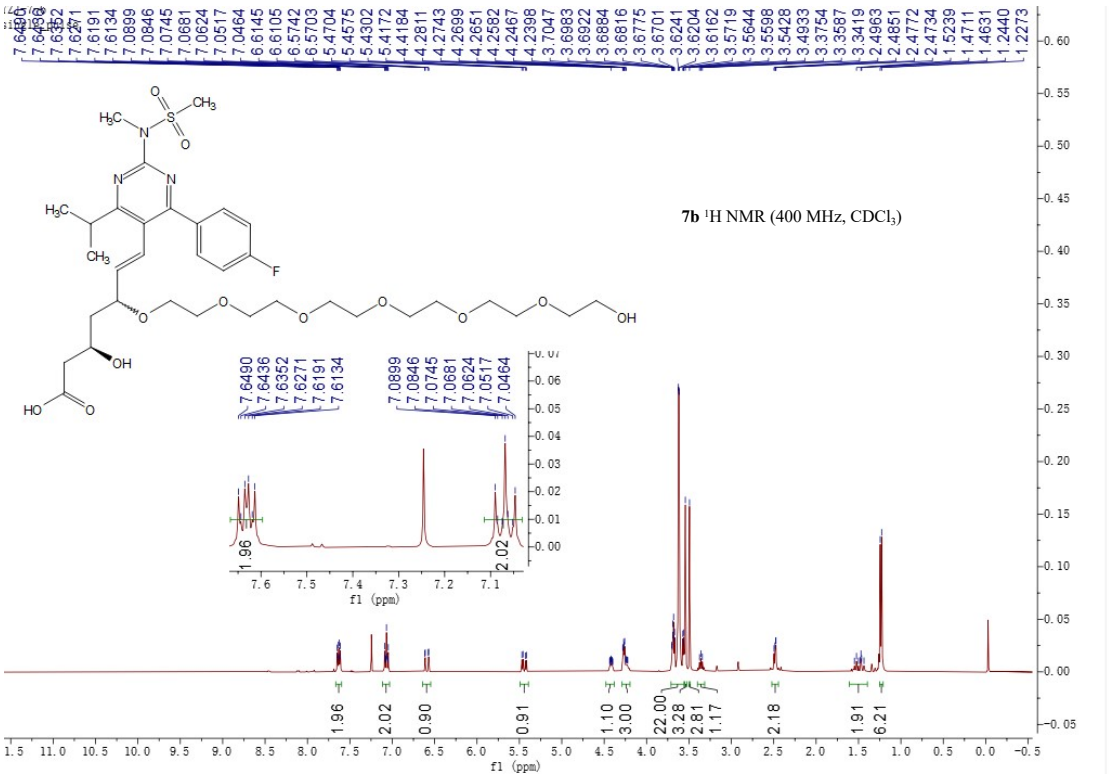


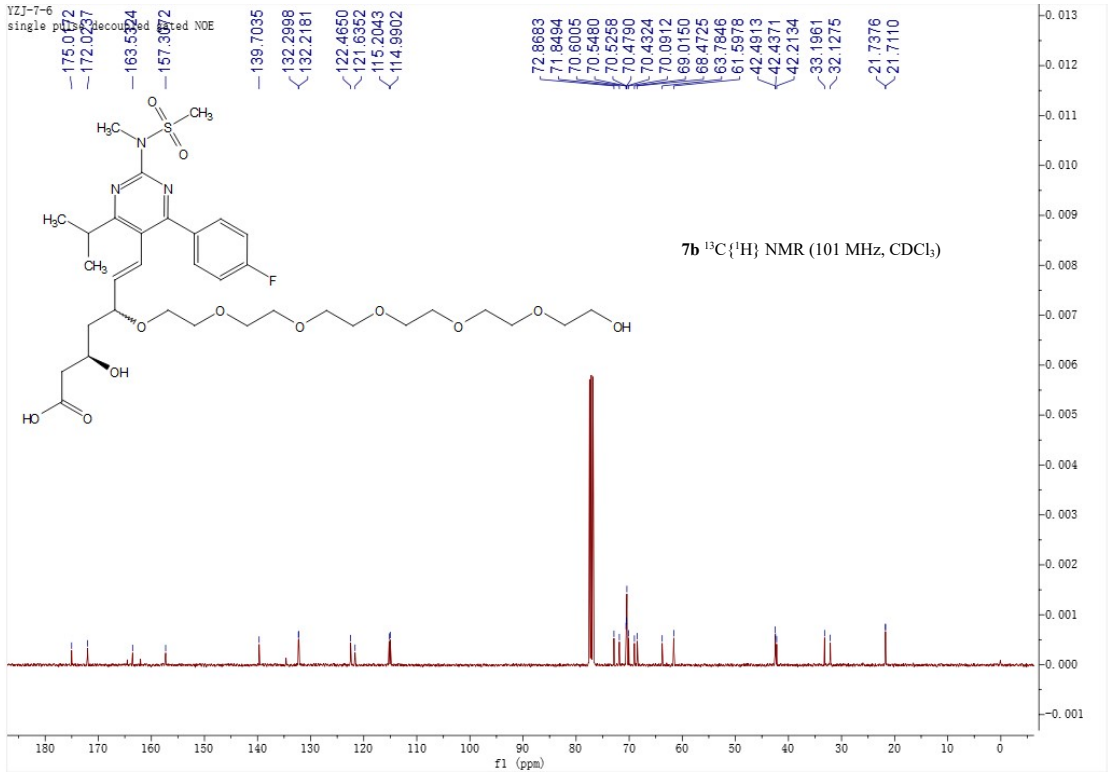


^{19}F NMR of (3R, E)-5-ethoxy-7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)-3-hydroxyhept-6-enoic acid (7a)

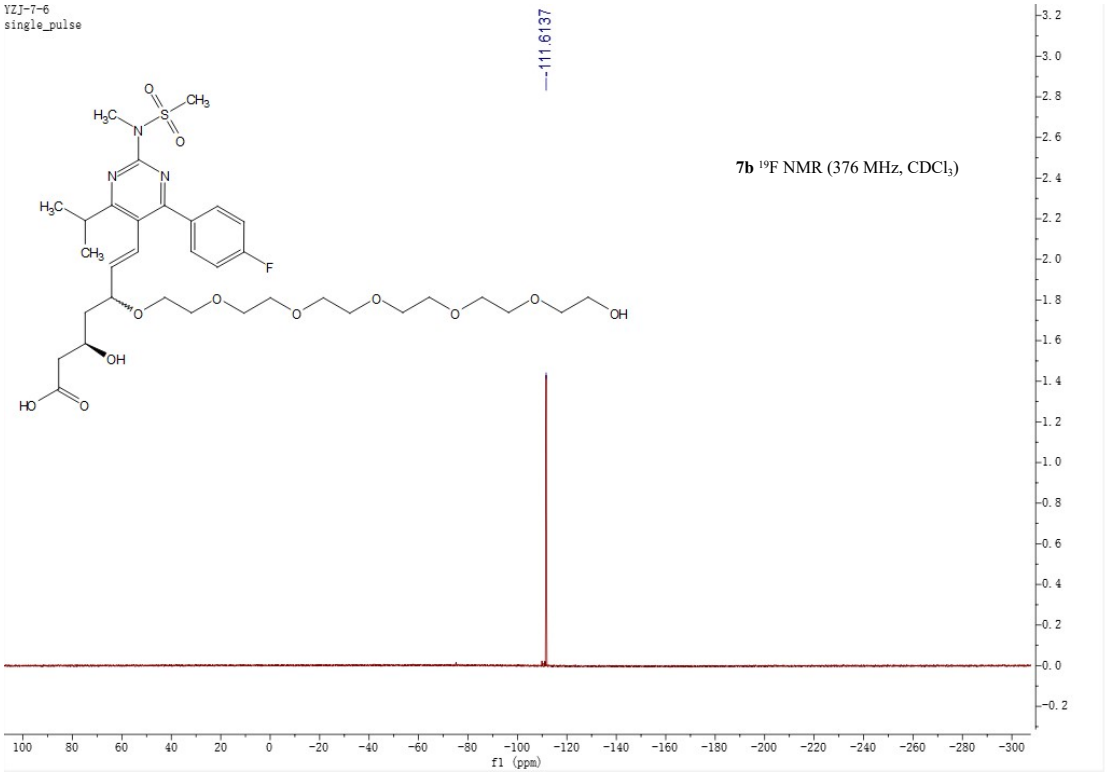


^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (21R)-19-((E)-2-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)vinyl)-1,21-dihydroxy-3,6,9,12,15,18-hexaoxatricosan-23-oic acid（7b）

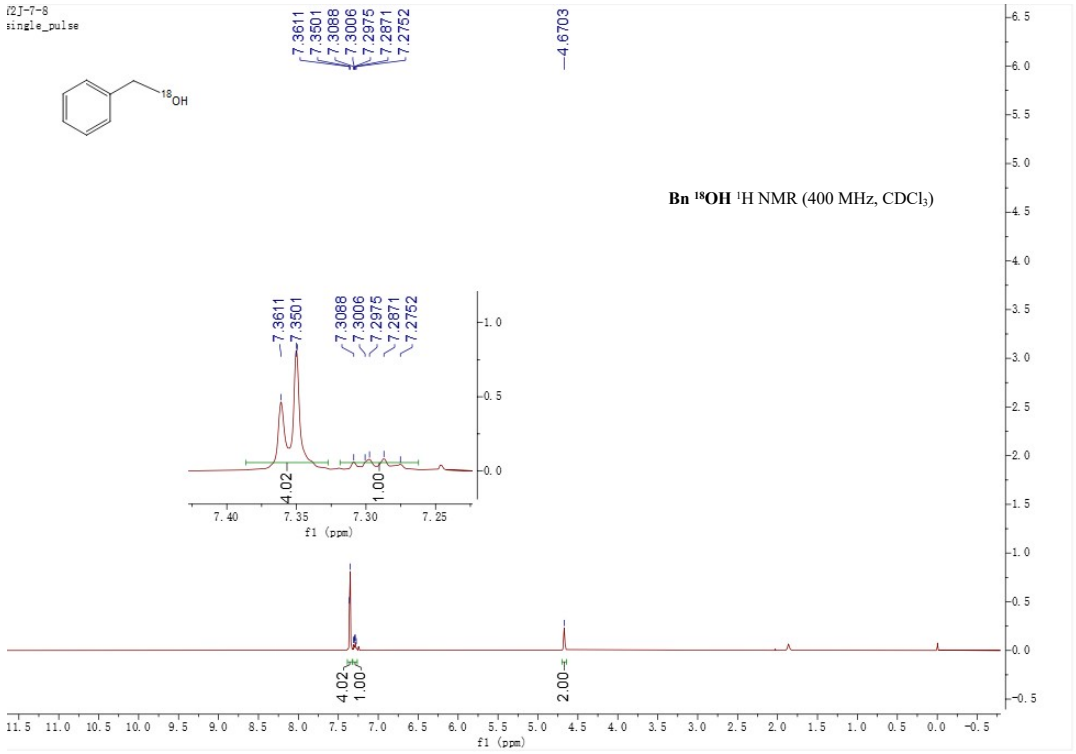




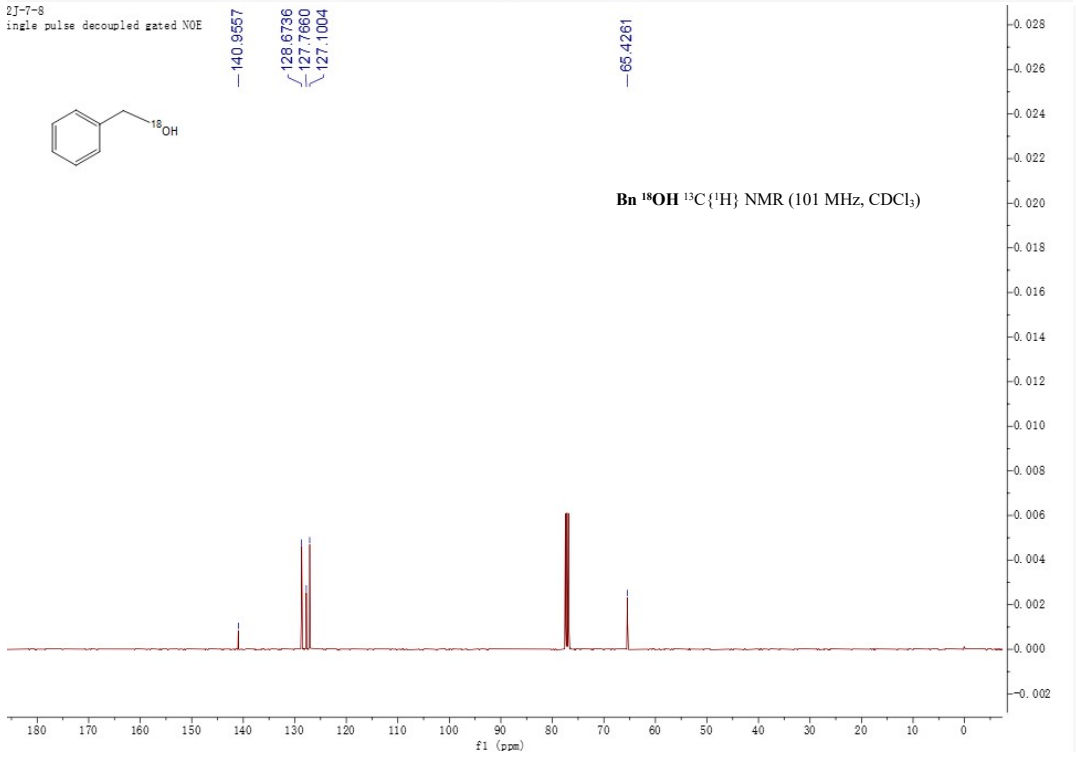
^{19}F NMR of (21R)-19-((E)-2-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)vinyl)-1,21-dihydroxy-3,6,9,12,15,18-hexaoxatricosan-23-oic acid （7b）



^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of Bn ^{18}OH

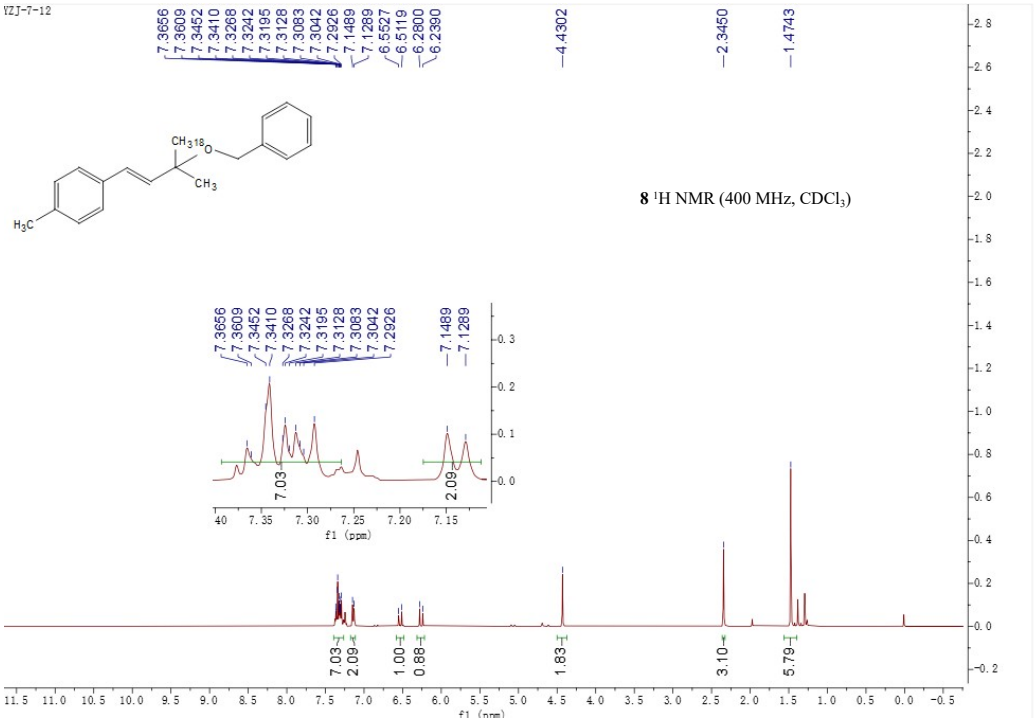


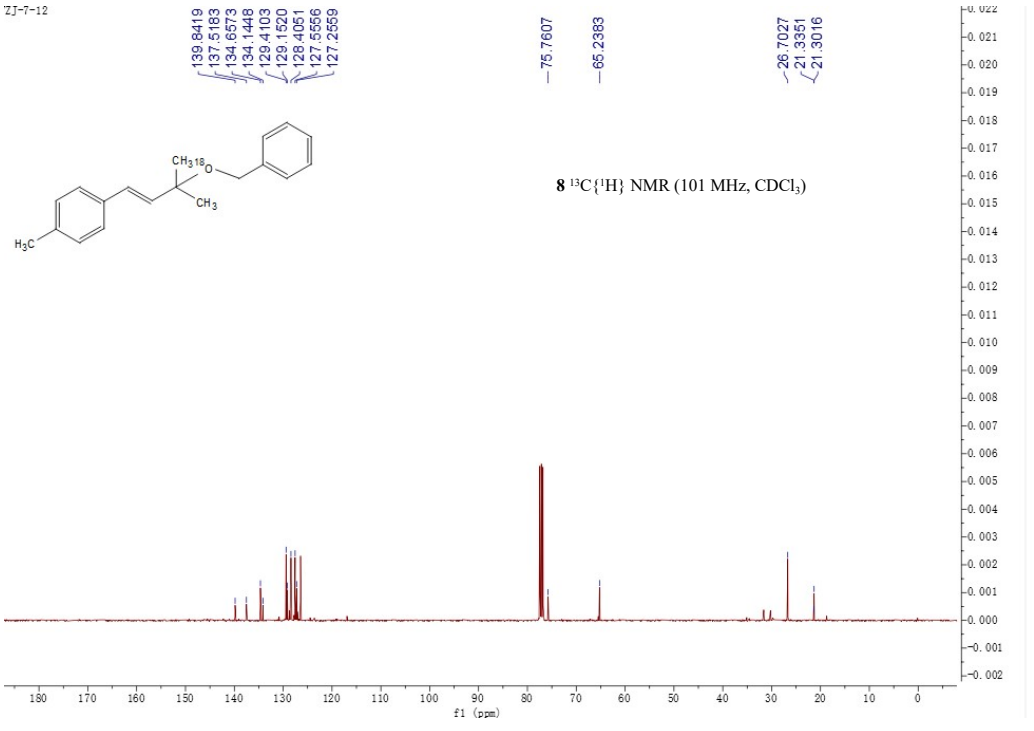
Bn ^{18}OH ^{1}H NMR (400 MHz, $CDCl_3$)



Bn ^{18}OH ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

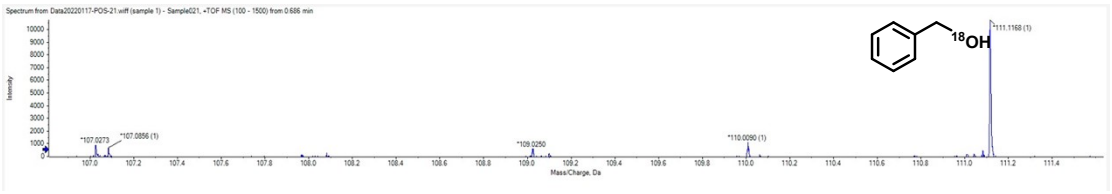
^{1}H-NMR and ^{13}C {^{1}H} NMR Spectra of (*E*)-1-(3-(Benzyl oxygen 18)-3-methylbut-1-en-1-yl)-4-methylbenzene (8)

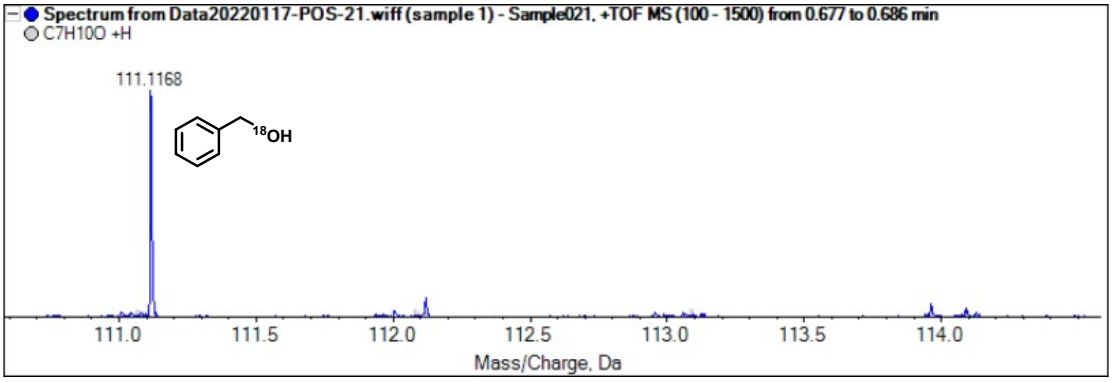




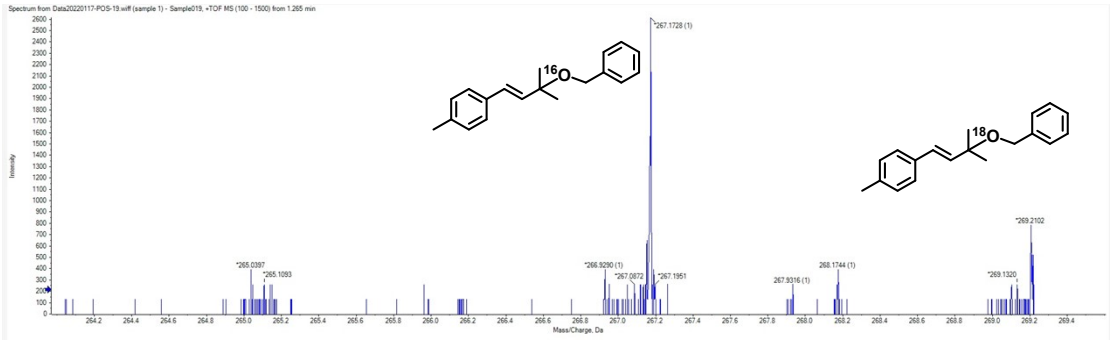
5 Copy of HRMS (Q-TOF) spectra

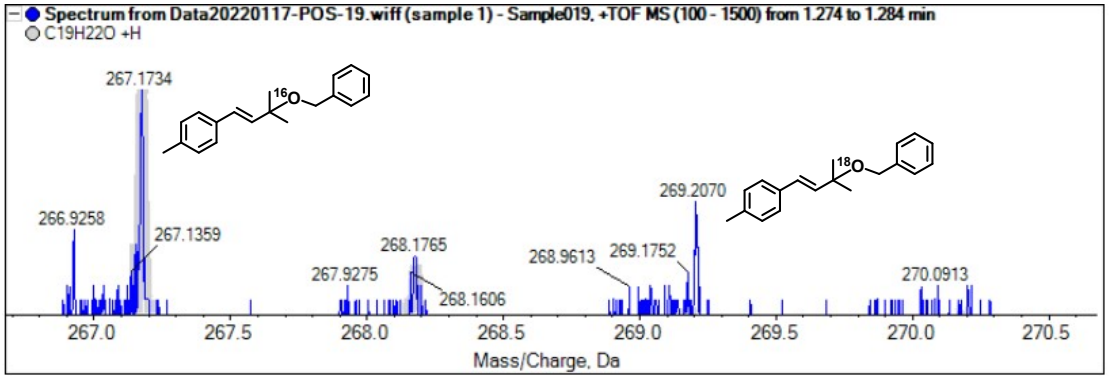
5.1 Copy of HRMS (Q-TOF) spectra (positive) of Bn ^{18}OH



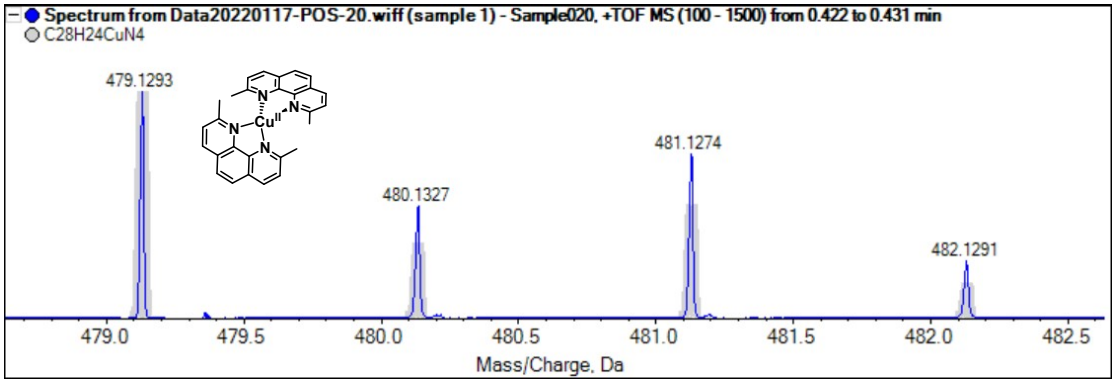


5.2 Copy of HRMS (Q-TOF) spectra (positive) of (*E*)-1-(3-(Benzyl oxygen 18)-3-methylbut-1-en-1-yl)-4-methylbenzene (8)





5.3 Copy of HRMS (Q-TOF) spectra of Cu(neocuproine)$_2$.



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