

# Supporting Information

## Iron-Catalyzed $\beta$ -Hydroxymethylative Carbonylation of Styrene under Photo-Irradiation

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# equal contribution to this paper

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## 1. General information

Unless otherwise noted, all of the reagents were purchased from commercial suppliers and used without purification. All commercially available compounds were purchased from Energy Chemical, Bidepharm or Adamas. TLC was carried out on SiO<sub>2</sub> (silica gel 60 F254, Merck), and the spots were located with UV light (254 nm). Flash chromatography was carried out on SiO<sub>2</sub> (silica gel 60, 200-300 mesh). NMR spectra were measured on a Bruker magnetic resonance spectrometer (<sup>1</sup>H at 400 MHz, <sup>13</sup>C at 100 MHz). Chemical shifts are reported in ppm using tetramethylsilane as internal standard (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet). CDCl<sub>3</sub> and TMS were used as a solvent and an internal standard, respectively. For light-promoted reactions, we use RLH-18 8-position Photo Reaction System, which manufactured by Beijing Rogertech Co.ltd base in Beijing PRC. This Photo reactor we used have equipped 8 blue light 10W LED, other LEDs could be selected and replaced each position. This blue light 10W LED's energy peak wavelength is 453.6nm, peak width at half-height is 20.4nm, irradiance@5W is 246mW./cm<sup>2</sup>. Irradiation vessel is general glass test tube, LED irradiate through a high-reflection channel to the test tube, path length is 2cm. no filter between LED and test tube. And the temperature of the heated reactor was set to indicate temperature.

## 2. The spectrum of our lamp and the visible-light irradiation instrument

All reactions have been studied in borosilicate glass vessels irradiated by a blue light LED strips purchased from Beijing Rogertech Co.ltd without using filters.

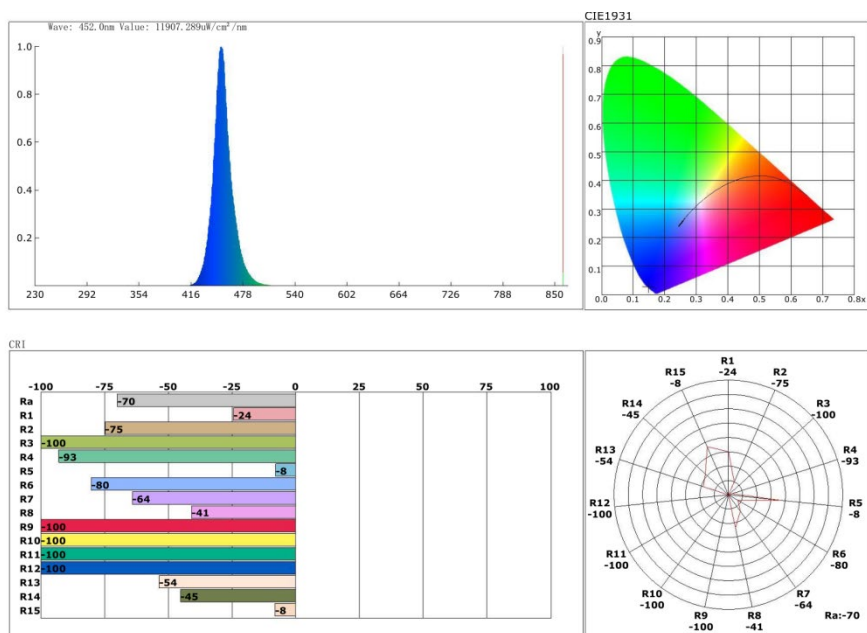
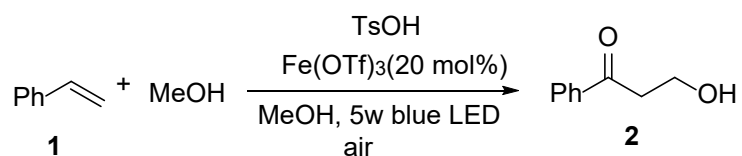


Figure S1. The spectrum of our blue LED.  $\lambda_{\text{max}} = 460 \text{ nm}$ .



Figure S2. Photograph of the reaction setup

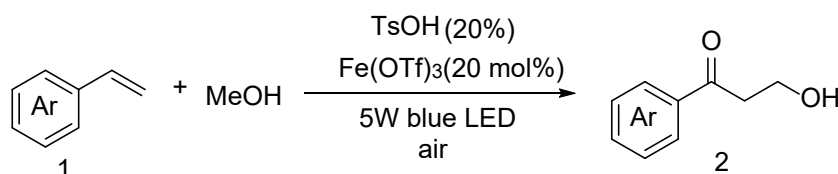
### 3. Optimization of the Reaction Condition



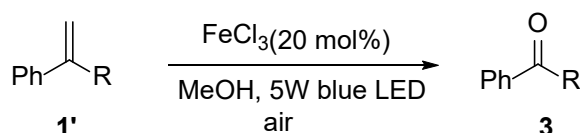
Entry	[Fe]	Temp	additive	Yields of <b>2a</b> (%) <sup>b</sup>
1	$\text{FeCl}_3$	rt	-	16
2	$\text{Fe}(\text{OTf})_3$	rt	-	63
3	$\text{Fe}(\text{NO}_3)_3$	rt	-	NR
4	$\text{Fe}(\text{TPP})\text{Cl}$	rt	-	NR
5	$\text{Fe}(\text{OAc})_2$	rt	-	NR
6	$\text{Fe}(\text{BF}_4)_2$	rt	-	NR
7	$\text{Fe}(\text{OTf})_3$	40	-	67
8	$\text{Fe}(\text{OTf})_3$	50	-	56
9	$\text{Fe}(\text{OTf})_3$	rt	LiCl	55
10	$\text{Fe}(\text{OTf})_3$	rt	TBAC	62
11	$\text{Fe}(\text{OTf})_3$	rt	TsOH	72
12 <sup>c</sup>	$\text{Fe}(\text{OTf})_3$	rt	TsOH	63
13 <sup>d</sup>	$\text{Fe}(\text{OTf})_3$	rt	TsOH	60
14 <sup>e</sup>	$\text{Fe}(\text{OTf})_3$	rt	TsOH	NR

<sup>a</sup>Standard conditions: 1-phenylethene **1a** (0.2 mmol), [Fe] (0.2 equiv), additive (0.2 equiv), 5 W blue LED in 2 mL MeOH were stirred. <sup>b</sup>Isolated yield based on **1a**. <sup>c</sup>3w LED was used. <sup>d</sup> 7 W LED was used. <sup>e</sup> No LED was used. NR = No reaction.

## 4. Experimental procedures



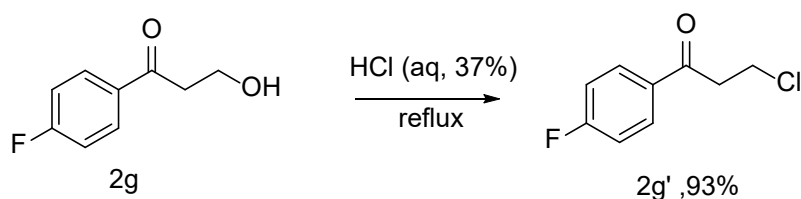
In a test tube, Substrate (0.2 mmol, 1.0 equiv.), Fe(OTf)<sub>3</sub> (0.2 equiv.), TsOH (0.2 equiv.) were dissolved in MeOH (3.0 mL), and the reaction mixture was stirred under 5W blue LEDs at 40 °C for 12 hour. After the reaction completed, the reaction mixture was purified by column chromatography on silica gel to give desired product.



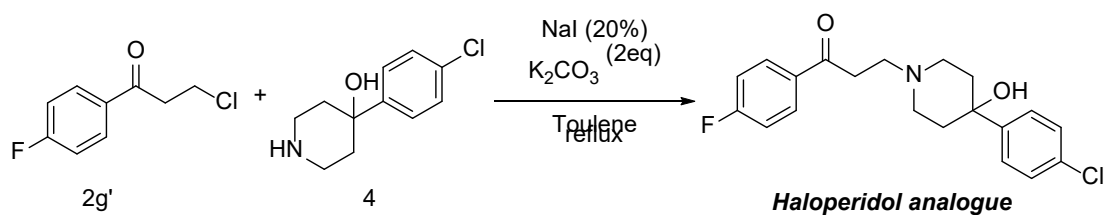
In a test tube, Substrate (0.2 mmol, 1.0 equiv.), FeCl<sub>3</sub> (0.2 equiv.), were dissolved in MeOH (3.0 mL), and the reaction mixture was stirred under 5W blue LEDs at 40 °C for 12 hours. After the reaction completed, the reaction mixture was purified by column chromatography on silica gel to give desired product.

## 5. Synthetic applications

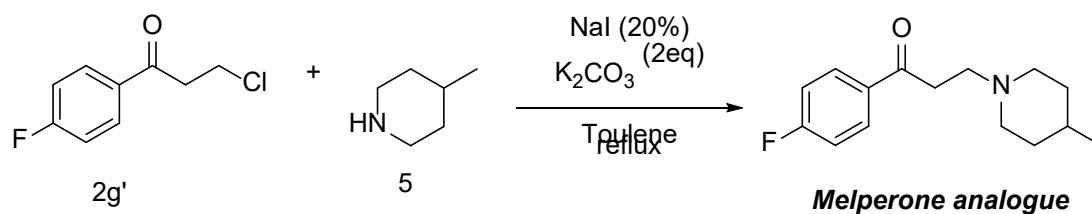
### 5.1 Synthesis of *Haloperidol*, *Melperone* and *Lenperone* analogue



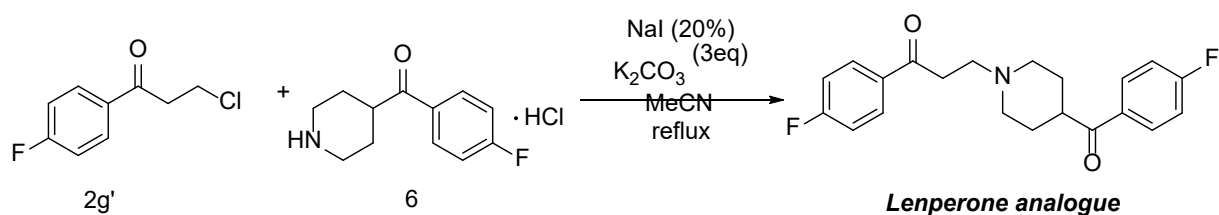
To a 20 mL vial were added the 2g (1mmol, 1.0 equiv.) HCl (aq, 37%) (1mL). Stir the mixture at 90°C for 8 h. After completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel to afford the desired product 3-chloro-1-(4-fluorophenyl)propan-1-one (2g') (eluent: PE/EA = 30/1): White solid<sup>[1]</sup>.(173 mg, 93% ).



To a 20 mL vial were added the 2g'(0.2mmol, 1.0 eq), 4(0.3 mmol, 1.5 eq), NaI (0.04 mmol, 0.02 eq), and K<sub>2</sub>CO<sub>3</sub>(0.4 mmol, 2 eq), and add 2 mL of toluene. Reflux the mixture for 20 h. After completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel to afford the desired product haloperidol.(eluent: PE/EA = 1/1): White solid.(51 mg, 71% ).

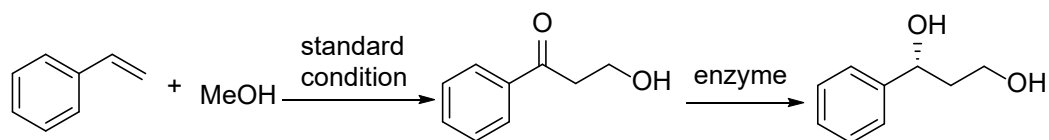


To a 20 mL vial were added the 2g'(0.2mmol, 1.0 eq), 5(0.3 mmol, 1.5 eq), NaI (0.04 mmol, 0.02 eq), and K<sub>2</sub>CO<sub>3</sub>(0.4 mmol, 2 eq), and add 2 mL of toluene. Reflux the mixture for 20 h. After completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel to afford the desired product haloperidol.(eluent: PE/EA = 1/1): White solid.(32 mg, 64% ).



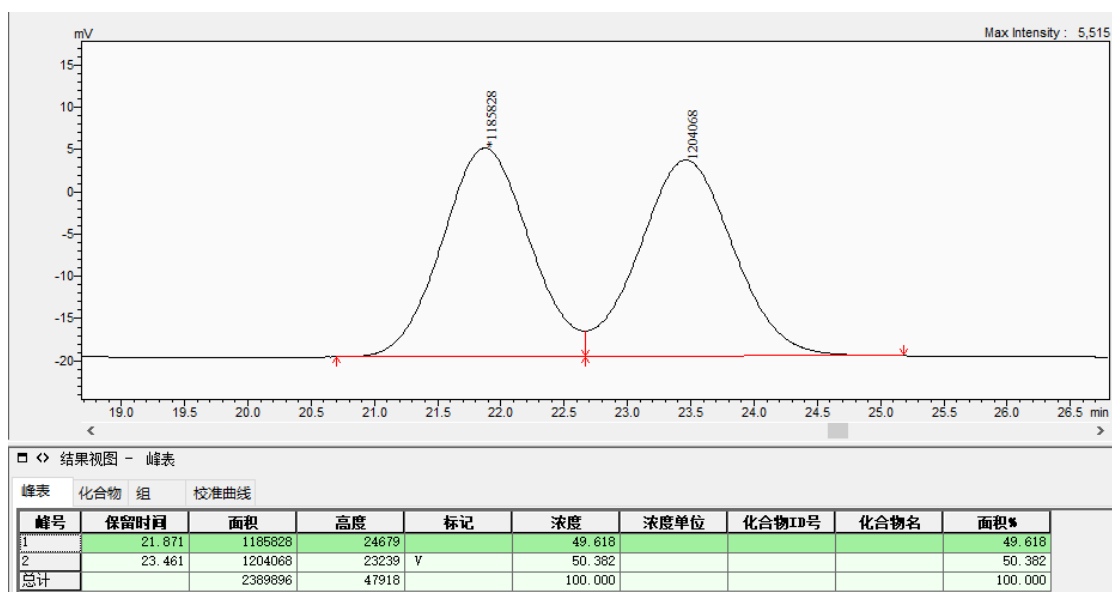
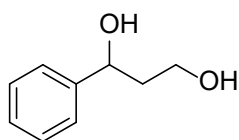
To a 20 mL vial were added the 2g'(0.2mmol, 1.0 eq), 6(0.3 mmol, 1.5 eq), NaI (0.04 mmol, 0.02 eq), and K<sub>2</sub>CO<sub>3</sub>(0.6 mmol, 3 eq), and add 2 mL of MeCN. Reflux the mixture for 20 h. After completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel to afford the desired product haloperidol.(eluent: PE/EA = 1/1): White solid.(49 mg, 69% ).

## 5.2 Synthesis of (R)-1-phenylpropane-1,3-diol

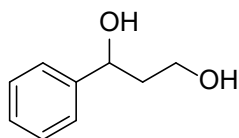


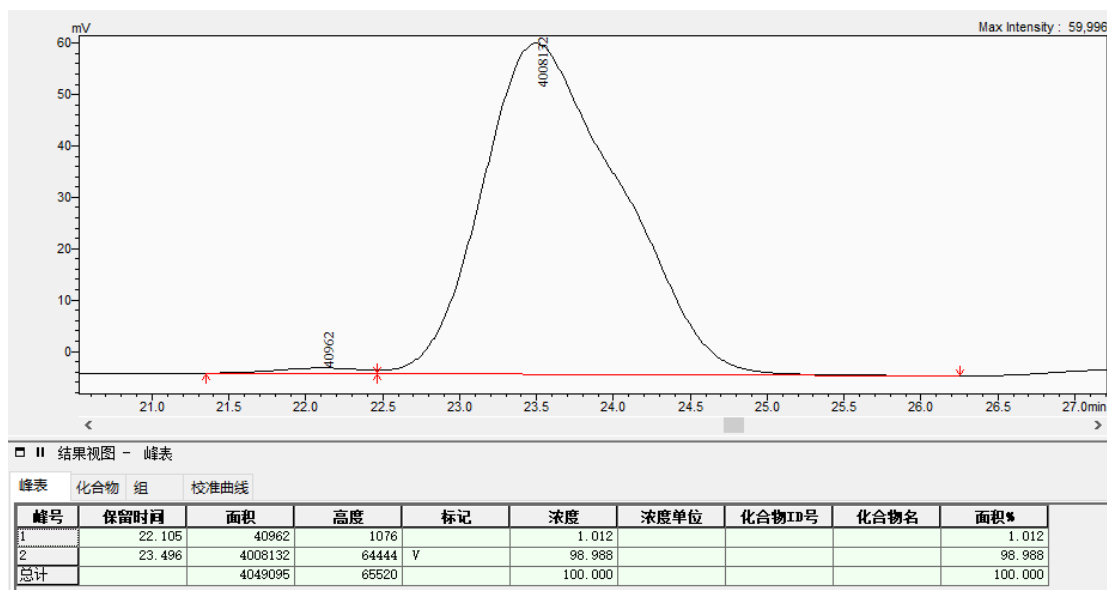
Colorless oil, 98% ee;  $[\alpha]^{25}_D = +23.8$  ( $c = 1.00$  in  $\text{CHCl}_3$ ); HPLC (OD-H, elute: Hexane/*i*-PrOH = 98/2, detector: 254 nm, flow rate: 1.0 mL/min),  $t_1 = 22.1$  min (minor),  $t_2 = 23.5$  min (major)<sup>[1]</sup>.

HPLC trace of racemic 1-phenylpropane-1,3-diol

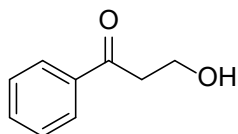


HPLC trace of enantioenriched 1-phenylpropane-1,3-diol

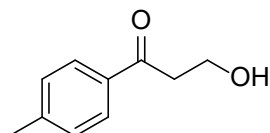




## 6. Characterization for all compounds

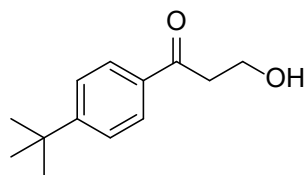


**3-Hydroxy-1-phenylpropan-1-one (2a)<sup>1</sup>:** The title compound was prepared according to the general procedure. Colorless oil (21.6mg, 72%; eluent: 3:1 ethyl acetate/ Petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.96-7.94 (m, 2H), 7.59-7.56 (m, 1H), 7.48-7.44 (m, 2H), 4.02 (t, *J* = 5.3 Hz, 2H), 3.22 (t, *J* = 5.3 Hz, 2H), 2.55 (s, 1H).; <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 200.5, 136.6, 133.5, 128.7, 128.0, 58.0, 40.4.

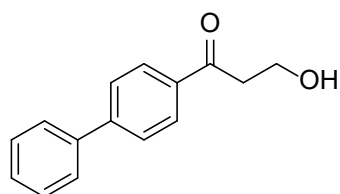


**3-Hydroxy-1-(p-tolyl)propan-1-one (2b)<sup>1</sup>:** The title compound was prepared according to the general procedure. Colorless oil (19mg, 57%; eluent: 3:1 ethyl acetate/ Petroleum ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.86-7.84 (m, 2H), 7.27-7.25 (m, 2H), 4.01 (t, *J* = 5.3 Hz, 2H), 3.19 (t, *J* = 5.3 Hz, 2H), 2.41 (s, 3H), 2.32 (s, 1H).; <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 200.2, 144.4, 134.2, 129.4, 128.2, 58.1, 40.2, 21.7.

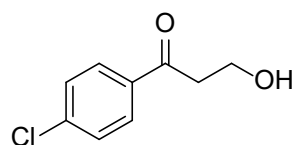




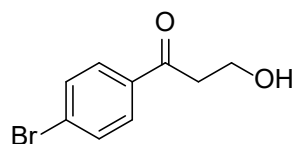
**4-(Tert-butylphenyl)-3-hydroxypropan-1-one (2c):** The title compound was prepared according to the general procedure. Colorless oil (22mg, 54%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.90-7.89 (m, 2H), 7.49-7.47 (m, 2H), 4.01 (t,  $J = 4.9$  Hz, 2H), 3.20 (t,  $J = 4.9$  Hz, 2H), 2.64 (s, 1H) 1.33 (s, 9H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  200.2, 157.3, 134.1, 128.0, 125.6, 58.2, 40.2, 35.2, 31.1.



**[1,1-Biphenyl]-4-yl)-3-hydroxypropan-1-one (2d)<sup>[4]</sup>:** The title compound was prepared according to the general procedure. Colorless oil (25mg, 56%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04-8.02 (m, 2H), 7.70-7.61 (m, 4H), 7.49-7.38 (m, 3H), 4.05 (t,  $J = 5.2$  Hz, 2H), 3.25 (t,  $J = 5.2$  Hz, 2H), 2.43 (s, 1H).;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  200.1, 146.2, 139.7, 135.3, 129.0, 128.7, 128.3, 127.3, 127.3, 58.1, 40.4.

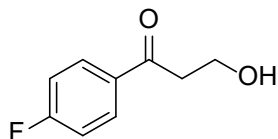


**(4-Chlorophenyl)-3-hydroxypropan-1-one (2e)<sup>1</sup>:** The title compound was prepared according to the general procedure. Colorless oil (24mg, 63%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.89-7.87 (m, 2H), 7.44-7.42 (m, 2H), 4.01 (t,  $J = 5.0$  Hz, 2H), 3.18 (t,  $J = 5.0$  Hz, 2H), 2.58 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.1, 140.0, 134.9, 129.5, 129.0, 57.9, 40.4.

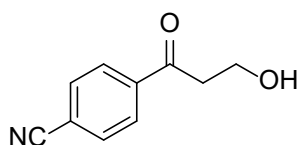


**(4-Bromophenyl)-3-hydroxypropan-1-one (2f)<sup>1</sup>:** The title compound was prepared according to the general procedure. Colorless oil (28mg, 62%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.81-7.79 (m, 2H), 7.61-7.59

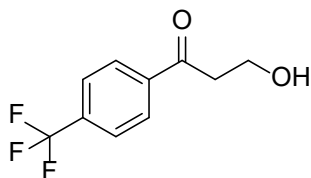
(m, 2H), 4.00 (t,  $J = 18$  Hz, 2H), 3.17 (t,  $J = 18$  Hz, 2H), 2.28 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.3, 138.4, 135.3, 132.0, 129.6, 57.9, 40.4.



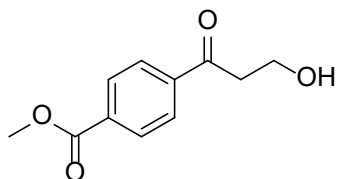
**(4-Fluorophenyl)-3-hydroxypropan-1-one (2g)**<sup>1</sup>: The title compound was prepared according to the general procedure. Colorless oil (22mg, 66%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00-7.96 (m, 2H), 7.15-7.11 (m, 2H), 4.01 (t,  $J = 4.9$  Hz, 2H), 3.19 (t,  $J = 4.9$  Hz, 2H), 2.27 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  198.8, 165.9, 130.8, 130.7, 115.9, 115.7, 58.0, 40.3.



**4-(3-Hydroxypropanoyl)benzotrile (2h)**<sup>1</sup>: The title compound was prepared according to the general procedure. White solid (26mg, 72%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.03-8.02 (m, 2H), 7.77-7.75 (m, 2H), 4.03 (t,  $J = 4.8$  Hz, 2H), 3.22 (t,  $J = 4.8$  Hz, 2H), 2.45 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  198.8, 139.5, 132.6, 128.5, 117.8, 116.7, 57.7, 40.9.

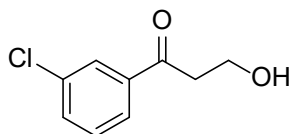


**3-Hydroxy-1-(4-(trifluoromethyl)phenyl)propan-1-one (2i)**: The title compound was prepared according to the general procedure. Colorless oil (27mg, 61%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07-8.05 (m, 2H), 7.75-7.73 (m, 2H), 4.04 (t,  $J = 5.0$  Hz, 2H), 3.24 (t,  $J = 5.0$  Hz, 2H), 2.25 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.3, 139.2, 134.9, 128.4, 125.8, 125.78, 125.7, 125.7, 57.8, 40.8. HRMS (ESI-TOF): ( $[\text{M}+\text{H}]^+$ ) calcd for  $\text{C}_{10}\text{H}_{10}\text{F}_3\text{O}_2^+$ : 219.0628; found: 219.0640.

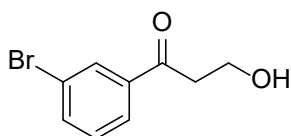


**Methyl 4-(3-hydroxypropanoyl)benzoate (2j)**<sup>1</sup>: The title compound was prepared according to the general procedure. Colorless oil (29mg, 70%; eluent: 3:1 et

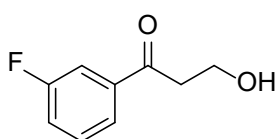
hyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.11-8.09 (m, 2 H), 7.99-7.98 (m, 2H), 4.02 (t,  $J = 4.8$  Hz, 2H), 3.93 (s, 3H), 3.23 (t,  $J = 4.8$  Hz, 2H), 2.45 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.8, 166.1, 139.7, 134.2, 129.9, 127.9, 57.8, 52.5, 40.9.



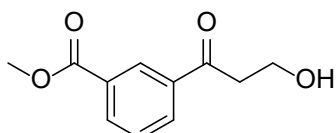
**1-(3-Chlorophenyl)-3-hydroxypropan-1-one (2k)**<sup>3</sup>: The title compound was prepared according to the general procedure. Colorless oil (24mg, 67%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.91 (s, 1H), 7.82-7.80 (m, 1H), 7.55-7.54 (m, 1H), 7.42-7.38 (m, 1H), 4.01 (t,  $J = 4.6$  Hz, 2H), 3.18 (t,  $J = 4.6$  Hz, 2H), 2.65 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.0, 138.1, 135.0, 133.4, 130.0, 128.1, 126.2, 57.8, 40.6.



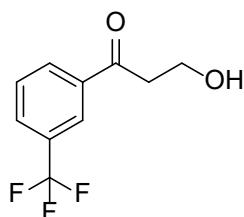
**1-(3-Bromophenyl)-3-hydroxypropan-1-one (2l)**<sup>1</sup>: The title compound was prepared according to the general procedure. Colorless oil (28mg, 62%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 (s, 1H), 7.87-7.85 (m, 1H), 7.70-7.68 (m, 1H), 7.36-7.32 (m, 1H), 4.01 (t,  $J = 5.1$  Hz, 2H), 3.18 (t,  $J = 5.1$  Hz, 2H), 2.70 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.0, 138.3, 136.3, 131.1, 130.3, 126.6, 123.0, 57.8, 40.6.



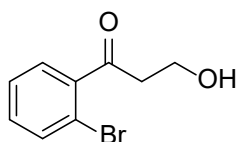
**1-(3-Fluorophenyl)-3-hydroxypropan-1-one (2m)**: The title compound was prepared according to the general procedure. Colorless oil (22mg, 66%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.75-7.73 (m, 1H), 7.64-7.65 (m, 1H), 7.48-7.43 (m, 1H), 7.30-7.26 (m, 1H), 4.03 (t,  $J = 5.2$  Hz, 2H), 3.20 (t,  $J = 5.2$  Hz, 2H), 2.61 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.1, 164.1, 161.6, 138.7, 130.4, 130.4, 123.9, 123.9, 120.6, 120.4, 114.9, 114.6, 57.8, 40.7. HRMS (ESI-TOF): ( $[\text{M}+\text{Na}]^+$ ) calcd for  $\text{C}_9\text{H}_9\text{FNaO}_2^+$ : 191.0479; found: 191.0486.



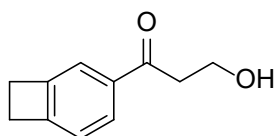
**Methyl 3-(3-hydroxypropanoyl)benzoate (2n):** The title compound was prepared according to the general procedure. Colorless oil (29mg, 70%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.59 (s, 1H), 8.25-8.23 (m, 1H), 8.16-8.17 (m, 1H), 7.58-7.54 (m, 1H), 4.04 (t,  $J = 5.2$  Hz, 2H), 3.95 (s, 3H), 3.27 (t,  $J = 5.2$  Hz, 2H), 2.71 (s, 1H).;  $^{13}\text{C}$  { $^1\text{H}$ } NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.5, 166.2, 136.8, 134.2, 132.1, 130.8, 129.3, 129.0, 57.9, 52.5, 40.6. IR (film): 3367, 2996, 2946, 2266, 1721, 1687, 1018, 857, 831, 728  $\text{cm}^{-1}$ . HRMS (ESI-TOF): ( $[\text{M}+\text{Na}]^+$ ) calcd for  $\text{C}_{11}\text{H}_{12}\text{NaO}_4^+$ : 231.0628; found: 231.0641.



**3-Hydroxy-1-(3-(trifluoromethyl)phenyl)propan-1-one (2o):** The title compound was prepared according to the general procedure. Yellow oil (25mg, 59%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.20 (s, 1H), 8.14-8.12 (m, 1H), 7.83-7.81 (m, 1H), 7.63-7.59 (m, 1H), 4.04 (t,  $J = 5.0$  Hz, 2H), 3.24 (t,  $J = 5.0$  Hz, 2H), 2.71 (s, 1H).;  $^{13}\text{C}$  { $^1\text{H}$ } NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  198.9, 137.1, 131.2, 131.1, 129.9, 129.9, 129.8, 129.8, 129.4, 124.9, 124.9, 124.9, 124.8, 122.2, 57.7, 40.6. HRMS (ESI-TOF): ( $[\text{M}+\text{H}]^+$ ) calcd for  $\text{C}_{10}\text{H}_{10}\text{F}_3\text{O}_2^+$ : 219.0628; found: 219.0642.

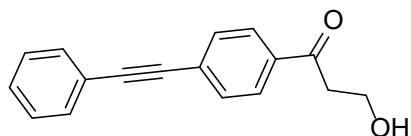


**1-(2-Bromophenyl)-3-hydroxypropan-1-one (2p)<sup>1</sup>:** The title compound was prepared according to the general procedure. Colorless oil (21mg, 46%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.63-7.61 (m, 1H), 7.46-7.44 (m, 1H), 7.40-7.36 (m, 1H), 7.33-7.29 (m, 1H), 4.01 (t,  $J = 5.0$  Hz, 2H), 3.20 (t,  $J = 5.0$  Hz, 2H), 2.53 (s, 1H).;  $^{13}\text{C}$  { $^1\text{H}$ } NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  204.2, 140.8, 133.9, 132.0, 128.9, 127.5, 118.8, 58.1, 44.7.

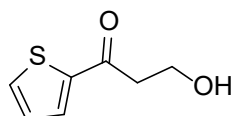


**1-(Bicyclo[4.2.0]octa-1(6),2,4-trien-3-yl)-3-hydroxypropan-1-one (2q)<sup>1</sup>:** The title compound was prepared according to the general procedure. Colorless oil (15mg,

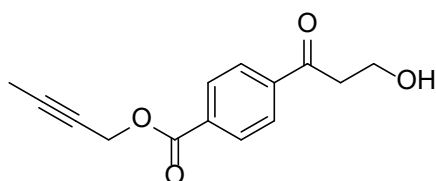
42%; eluent:3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.86-7.84 (m, 1H), 7.64 (s, 1H), 7.14-7.12 (m, 1H), 4.00 (t,  $J = 5.1$  Hz, 2H), 3.21–3.15 (m, 6H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  200.8, 152.6, 146.2, 135.8, 127.5, 122.6, 122.1, 58.2, 40.3, 30.0, 29.4.



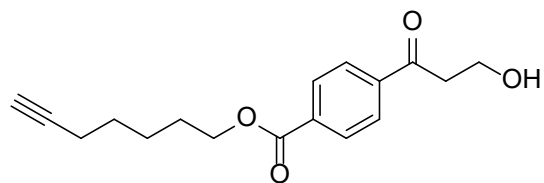
**3-Hydroxy-1-(4-(phenylethynyl)phenyl)propan-1-one (2r):** The title compound was prepared according to the general procedure. White solid (31mg, 61%; eluent: 10% ethyl acetate/ Petroleum ether); mp: 106-114°C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95-7.93 (m, 2H), 7.62-7.54 (m, 4H), 7.37-7.38 (m, 3H), 4.03 (t,  $J = 4.5$  Hz, 2H), 3.21 (t,  $J = 4.5$  Hz, 2H), 2.69 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.6, 135.6, 131.8, 131.7, 128.9, 128.6, 128.5, 128.0, 122.5, 93.0, 88.5, 58.0, 40.4. IR (KBr): 3576, 3053, 2982, 2365, 1736, 1638, 1424, 1043, 802, 782  $\text{cm}^{-1}$ ; HRMS (ESI-TOF): ( $[\text{M}+\text{Na}]^+$ ) calcd for  $\text{C}_{17}\text{H}_{14}\text{NaO}_2^+$ : 273.0886; found: 273.0902.



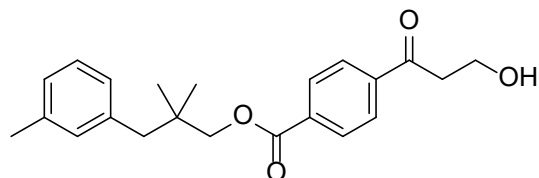
**3-Hydroxy-1-(thiophen-2-yl)propan-1-one (2s)<sup>1</sup>:** The title compound was prepared according to the general procedure. Yellow oil (20mg, 64%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.75-7.73 (m, 1H), 7.67-7.65 (m, 1H), 7.14-7.15 (m, 1H), 4.01 (t,  $J = 5.2$  Hz, 2H), 3.17 (t,  $J = 5.2$  Hz, 2H), 2.30 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  193.2, 143.8, 134.2, 132.5, 128.2, 58.2, 41.1.



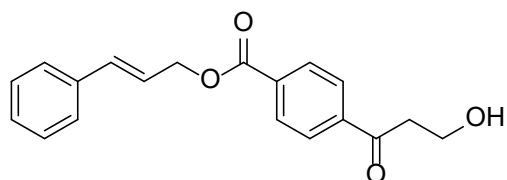
**Prop-1-yn-1-yl 4-(3-hydroxypropanoyl)benzoate (2t):** The title compound was prepared according to the general procedure. Colorless oil (34mg, 74%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.14-8.12 (m, 2H), 8.00-7.98 (m, 2H), 4.89 (s, 2H), 4.02 (t,  $J = 5.0$  Hz, 2H), 3.23 (t,  $J = 5.0$  Hz, 2H), 1.86 (s, 3H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.8, 165.1, 139.9, 133.8, 130.1, 127.9, 83.7, 72.9, 57.8, 53.8, 40.9, 3.7. IR (film): 3462, 2957, 2255, 1728, 1676, 1409, 1279, 1109, 871, 769  $\text{cm}^{-1}$ . HRMS (ESI-TOF): ( $[\text{M}+\text{Na}]^+$ ) calcd for  $\text{C}_{14}\text{H}_{14}\text{NaO}_4^+$ : 269.0784; found: 269.0791.



**Hept-6-yn-1-yl 4-(3-hydroxypropanoyl)benzoate (2u):** The title compound was prepared according to the general procedure. Colorless oil (32mg, 56%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.13-8.11 (m, 2H), 8.01-7.99 (m, 2H), 4.34 (t,  $J = 6.5$  Hz, 2H), 4.04 (t,  $J = 5.0$  Hz, 2H), 3.24 (t,  $J = 5.0$  Hz, 2H), 2.26-2.17 (s, 2H), 1.94 (s, 1H), 1.85 – 1.77 (m, 2H), 1.64-1.52 (m, 4H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.9, 165.6, 139.7, 134.5, 129.9, 127.9, 84.1, 68.5, 65.4, 57.9, 40.8, 28.1, 28.0, 25.1, 18.3. IR (film): 3303, 3062, 3024, 2930, 2827, 1742, 1680, 1490, 1454, 1432, 1264, 1030, 831, 741, 699, 632  $\text{cm}^{-1}$ . HRMS (ESI-TOF): ( $[\text{M}+\text{Na}]^+$ ) calcd for  $\text{C}_{17}\text{H}_{20}\text{NaO}_4^+$ : 311.1254; found: 311.1262.

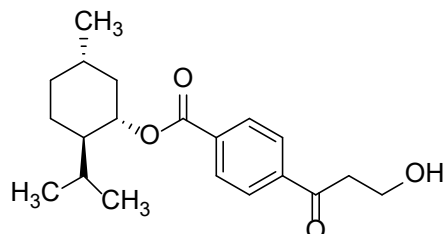


**2,2-Dimethyl-3-(m-tolyl)propyl 4-(3-hydroxypropanoyl)benzoate (2v):** The title compound was prepared according to the general procedure. Colorless oil (37mg, 52%; eluent: 3:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17-8.16 (m, 2H), 8.06-8.04 (m, 2H), 7.21-7.15 (m, 1H), 7.04-7.02 (m, 1H), 6.96-6.95 (m, 2H), 4.07 (s, 4H), 3.32-3.28 (m, 2H), 2.67 (s, 2H), 2.31 (s, 3H), 1.04 (s, 6H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.8, 197.9, 165.5, 139.8, 137.8, 137.5, 134.5, 131.3, 129.9, 128.1, 127.9, 127.5, 127.0, 72.7, 57.9, 45.3, 40.9, 35.3, 24.6, 21.4. IR (film): 3535, 3009, 2929, 2294, 1721, 1693, 1450, 1439, 1379, 1275, 1040, 858, 745, 671  $\text{cm}^{-1}$ . HRMS (ESI-TOF): ( $[\text{M}+\text{Na}]^+$ ) calcd for  $\text{C}_{22}\text{H}_{26}\text{NaO}_4^+$ : 377.1723; found: 377.1741.

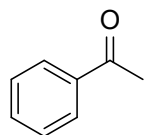


**4,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl 4-(3-hydroxypropanoyl)benzoate (2w):** The title compound was prepared according to the general procedure. Colorless oil (42mg, 62%; eluent: 3:1 ethyl acetate/ Petroleum ether)  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19-8.17 (m, 2H), 8.03-8.01 (m, 2H), 7.44-7.42 (m, 2H), 7.36-7.26 (m, 3H),

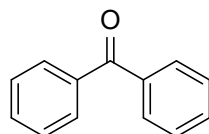
6.77-6.75 (m, 1H), 6.48-6.35 (m, 1H), 5.02-5.00 (d,  $J = 6.4$  Hz, 2H), 4.05 (t,  $J = 4.8$  Hz, 2H), 3.26 (t,  $J = 4.8$  Hz, 2H), 2.63 (s, 1H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.9, 165.4, 139.8, 136.0, 134.9, 134.3, 130.0, 128.7, 128.25, 128.0, 126.7, 122.7, 66.1, 57.9, 40.8. IR (film): 3445, 1716, 1684, 1676, 1484, 1387, 1268, 1092, 984, 856, 760, 731  $\text{cm}^{-1}$ . HRMS (ESI-TOF): ( $[\text{M}+\text{Na}]^+$ ) calcd for  $\text{C}_{19}\text{H}_{18}\text{NaO}_4^+$ : 333.1097; found: 333.1111.



**2,2-Dichloro-2-cyclopropyl-1-phenylethan-1-one (2x):** The title compound was prepared according to the general procedure. Colorless oil (42mg, 64%; eluent: 3:1 ethyl acetate/ Petroleum ether)  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.13-8.11 (m, 2H), 8.01-7.99 (m, 2H), 4.97-4.91 (m, 1H), 4.04 (t,  $J = 4.3$  Hz, 2H), 3.24 (t,  $J = 4.3$  Hz, 2H), 2.63 (s, 1H), 2.11 (d,  $J = 11.3$  Hz, 1H), 1.93-1.91 (m, 1H), 1.73 (d,  $J = 11.5$  Hz, 2H), 1.55 (t,  $J = 10.9$  Hz, 2H), 1.24 -1.09 (m, 2H), 0.96-0.90 (m, 7H), 0.78 (d,  $J = 6.7$  Hz, 3H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.9, 165.1, 139.6, 134.9, 129.8, 127.9, 75.5, 57.9, 47.2, 40.8, 34.2, 31.4, 26.5, 23.6, 22.0, 20.7, 16.5. IR (film): 3376, 2930, 1739, 1678, 1446, 1375, 1080, 876, 760, 711  $\text{cm}^{-1}$ . HRMS (ESI-TOF): ( $[\text{M}+\text{Na}]^+$ ) calcd for  $\text{C}_{20}\text{H}_{28}\text{NaO}_4^+$ : 355.1880; found: 355.1884.

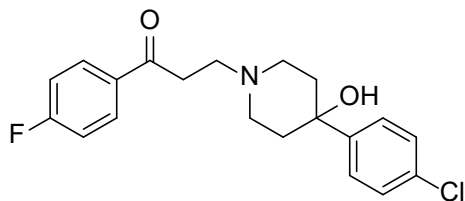


**Acetophenone (3a)**<sup>5</sup>: The title compound was prepared according to the general procedure. Colorless oil (20mg, 83%; eluent: 20:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96-7.94 (m, 2H), 7.54-7.57 (m, 1H), 7.44-7.47 (m, 2H), 2.60 (s, 3H).;  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  198.2, 137.1, 133.1, 128.6, 128.3, 26.6.

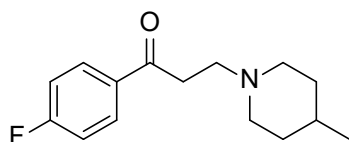


**Benzophenone (3b)**<sup>5</sup>: The title compound was prepared according to the general procedure. Colorless oil (27mg, 75%; eluent: 20:1 ethyl acetate/ Petroleum ether);  $^1\text{H}$

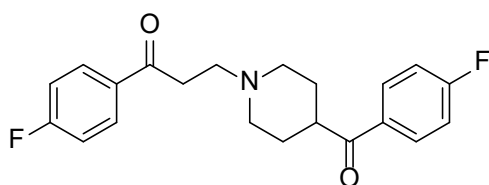
NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.81-7.79 (m, 2H), 7.56-7.60 (m, 1H), 7.49-7.46 (m, 2H);  
<sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  196.8, 137.6, 132.4, 130.1, 128.3.



**3-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)-1-(4-fluorophenyl)propan-1-one (4a)**<sup>6-7</sup>: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.01-7.98 (m, 2H), 7.44-7.42 (m, 2H), 7.32-7.29 (m, 2H), 7.16-7.11 (m, 2H), 3.23-3.19 (m, 2H), 2.93-2.84 (m, 4H), 2.60-2.54 (m, 2H), 2.16-2.00 (m, 3H), 1.76-1.73 (m, 2H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  197.4, 167.0, 146.7, 132.9, 130.7, 128.4, 126.1, 115.6, 70.9, 53.1, 49.5, 38.3, 36.2.



**1-(4-fluorophenyl)-3-(4-methylpiperidin-1-yl)propan-1-one (4b)**<sup>6-7</sup>: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.98-7.96 (m, 2H), 7.12-7.08 (m, 2H), 3.17-3.14 (m, 2H), 2.91-2.88 (m, 2H), 2.80-2.77 (m, 2H), 2.04-1.98 (m, 2H), 1.64-1.61 (m, 2H), 1.43-1.21 (m, 3H), 0.91 (d, *J* = 4Hz, 3H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  197.70, 165.7 (d, *J* = 253Hz), 133.3, 130.6 (d, *J* = 10Hz), 115.6 (d, *J* = 22Hz), 54.1, 53.5, 36.4, 34.2, 30.6, 21.8.



**3-(4-(4-fluorobenzoyl)piperidin-1-yl)-1-(4-fluorophenyl)propan-1-one (4c)**<sup>6-7</sup>: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.00-7.93 (m, 4H), 7.14-7.10 (m, 4H), 3.24-3.17 (m, 3H), 3.04-3.01 (m, 2H), 2.88-2.84 (m, 2H), 2.25-2.20 (m, 2H), 1.87-1.79 (m, 4H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  200.82, 197.51, 165.7 (d, *J* = 253Hz), 165.6 (d, *J* = 253Hz), 133.3 (d, *J* = 3Hz), 132.3 (d, *J* = 3Hz), 130.8 (dd, *J* = 22Hz), 115.9 (d, *J* = 5Hz), 115.64 (d, *J* = 5Hz), 53.3, 53.3, 43.3, 36.4, 28.6.

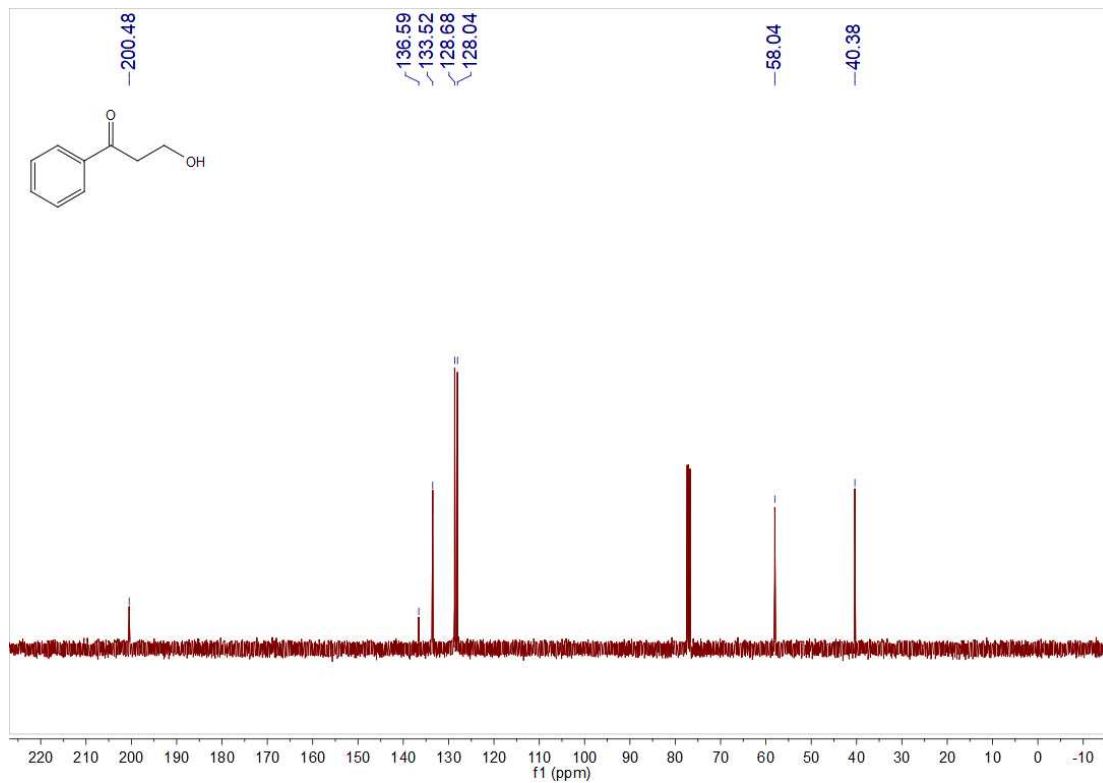


## 7. References

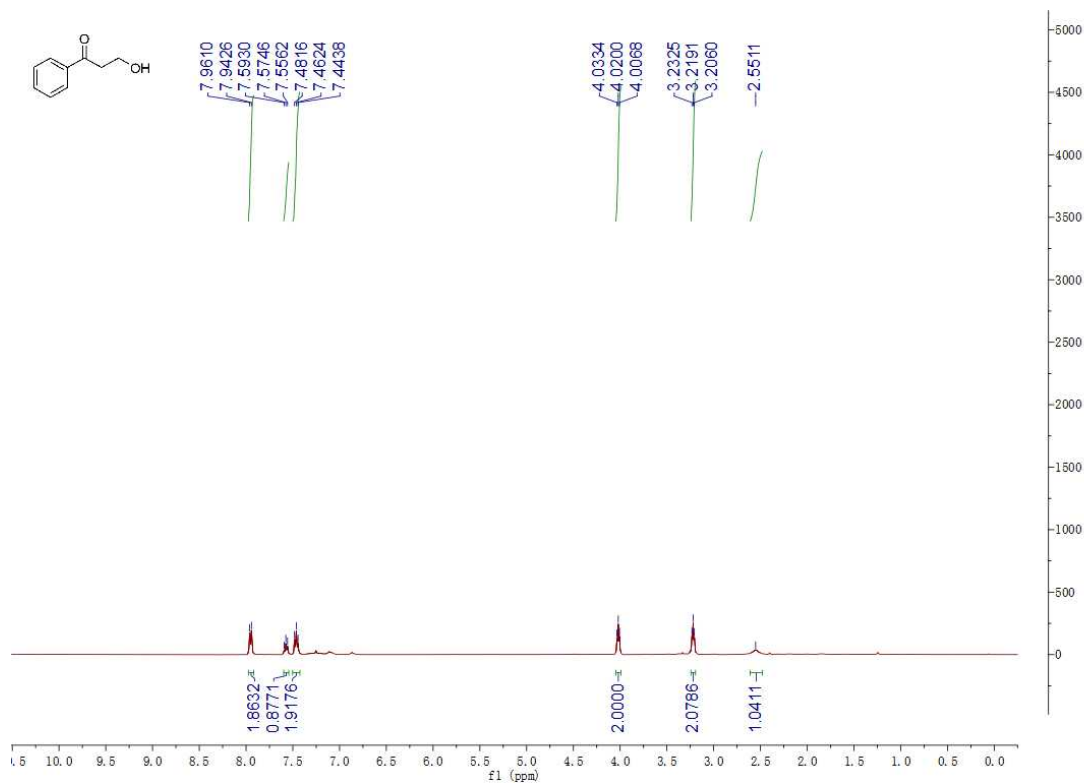
- [1]. (a) Zhang, W.; Wang, N.-X.; Bai, C.-B.; Wang, Y.-J.; Lan, X.-W.; Xing, Y.; Li, Y.-H.; Wen, J.-L. *Sci. Rep.* 2015, **5**, 15250; (b) Zhang, Y.; He, L.; Shi, L. *Adv. Synth. Catal.* **2018**, *360*, 1926.
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- [7]. Tim J. F.; Barrie K.; David A. S. *et al. J. Med. Chem.* **2019**, *62*, 21, 9488.

## 8. Copies of $^1\text{H}$ and $^{13}\text{C}$ NMR spectra of products

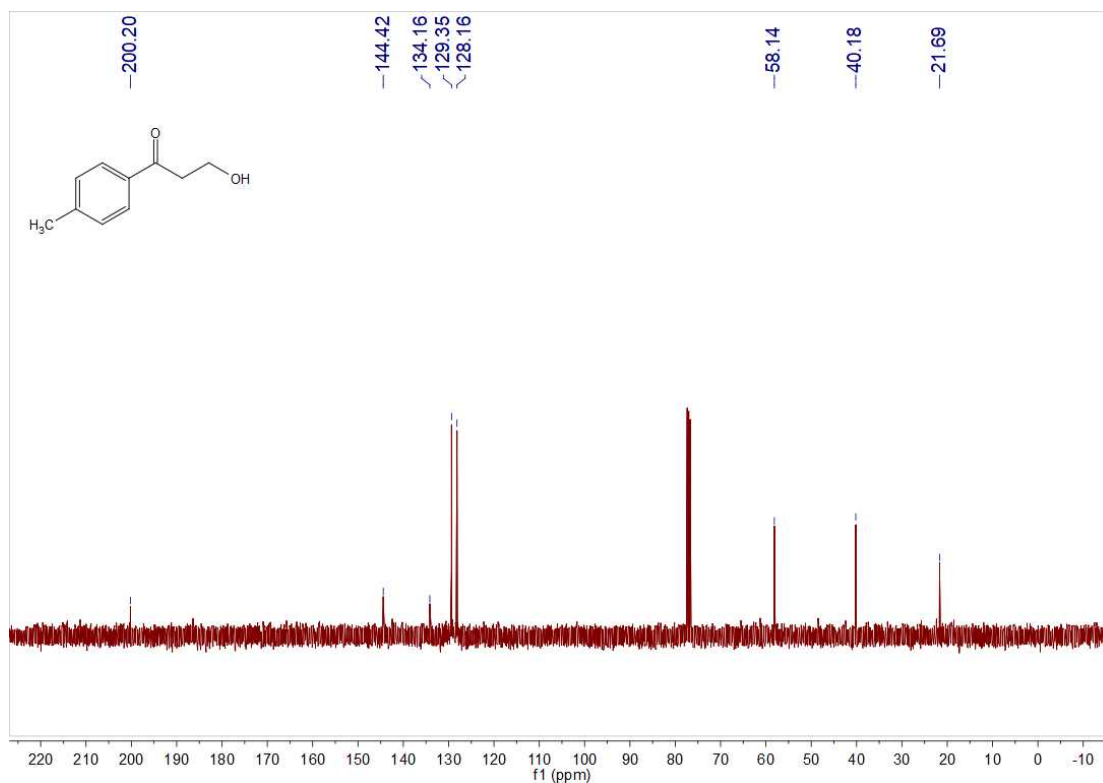
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ ) of compound 2a



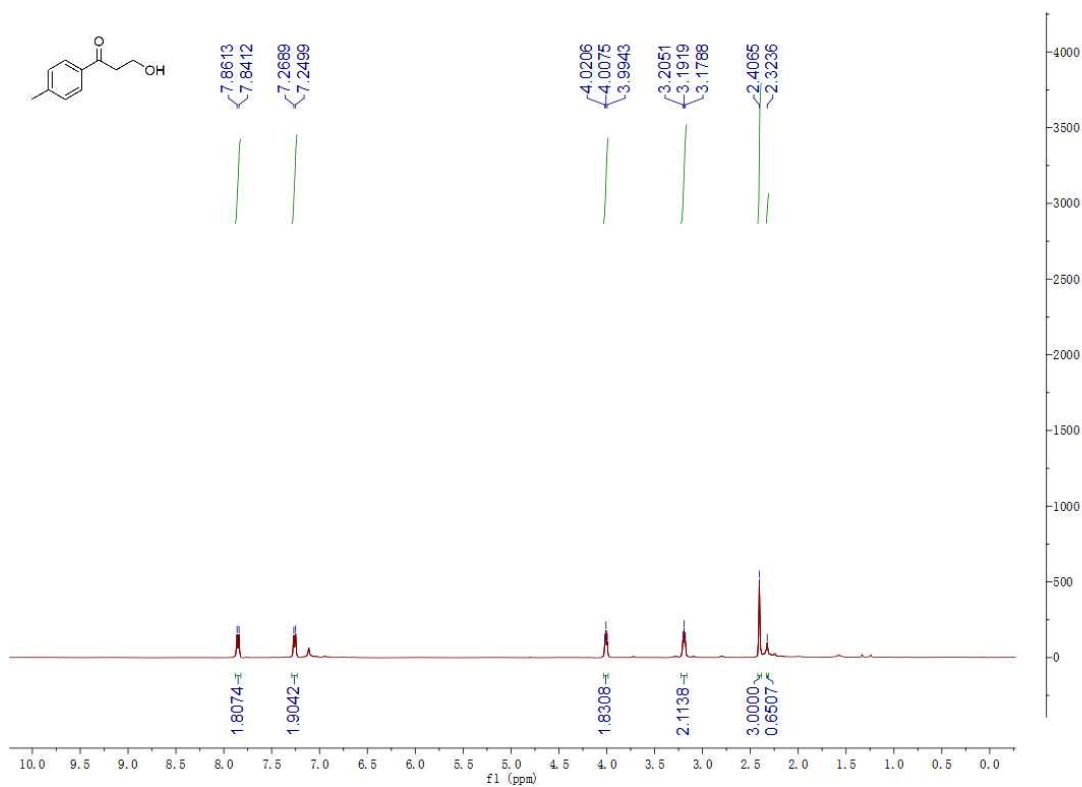
$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of compound 2a



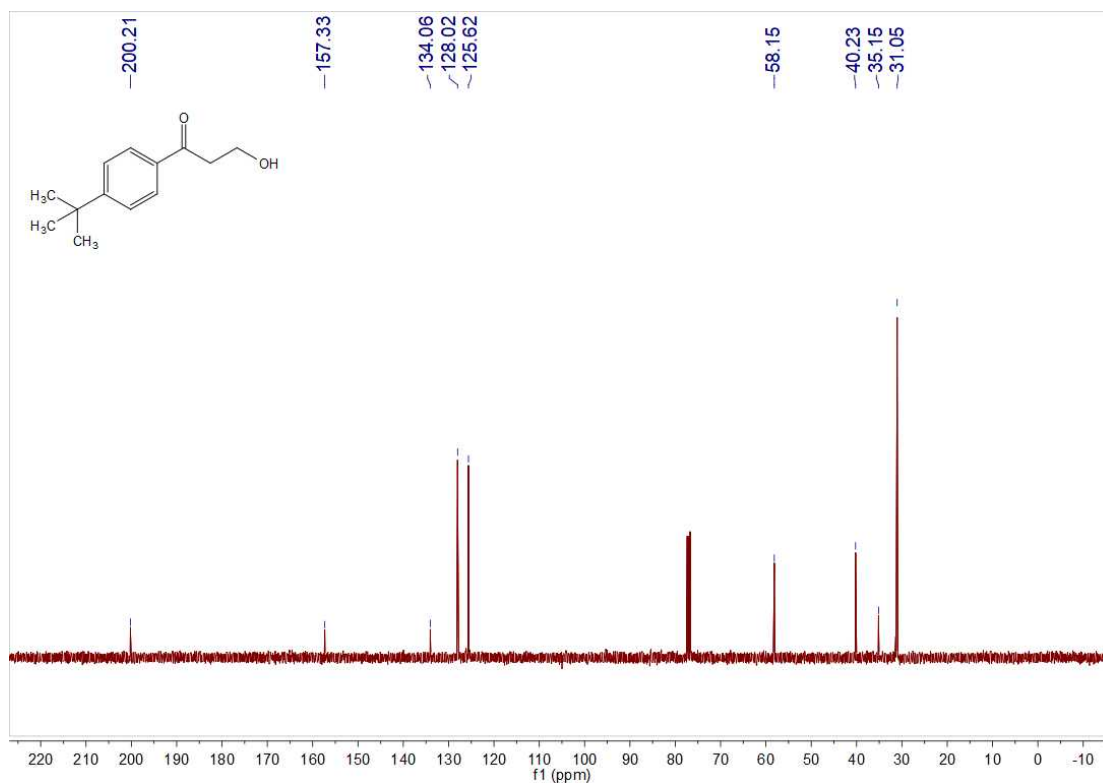
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2b**



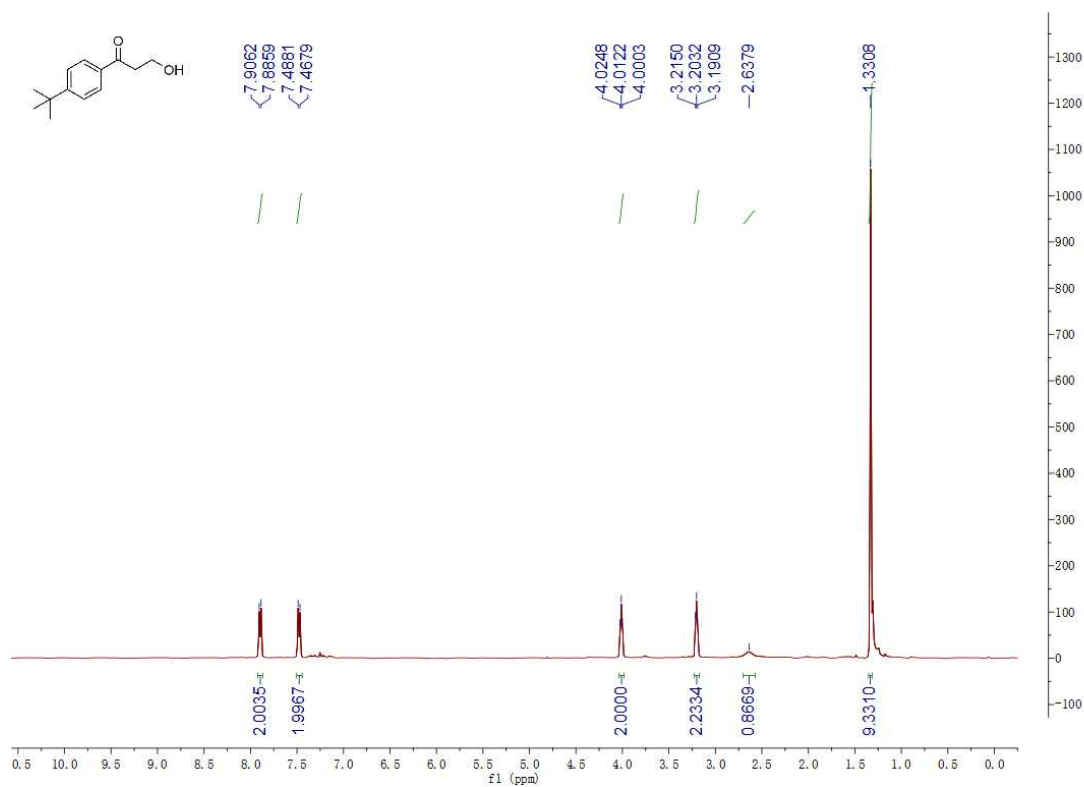
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2b**



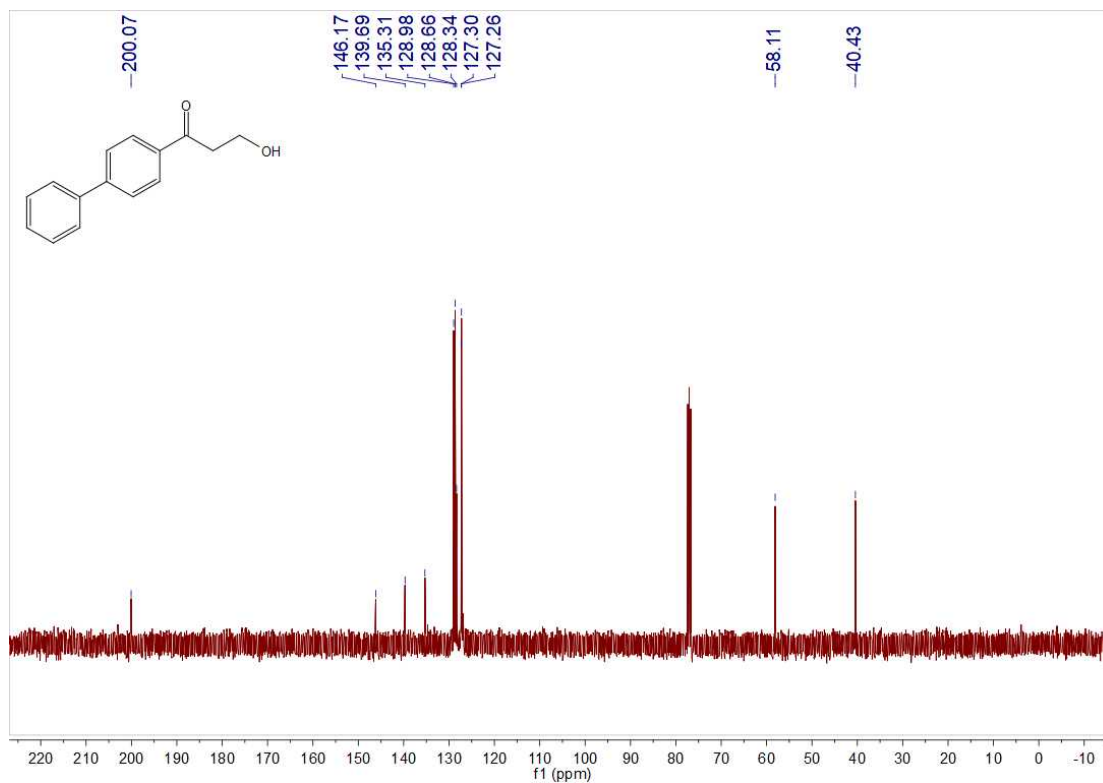
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2c**



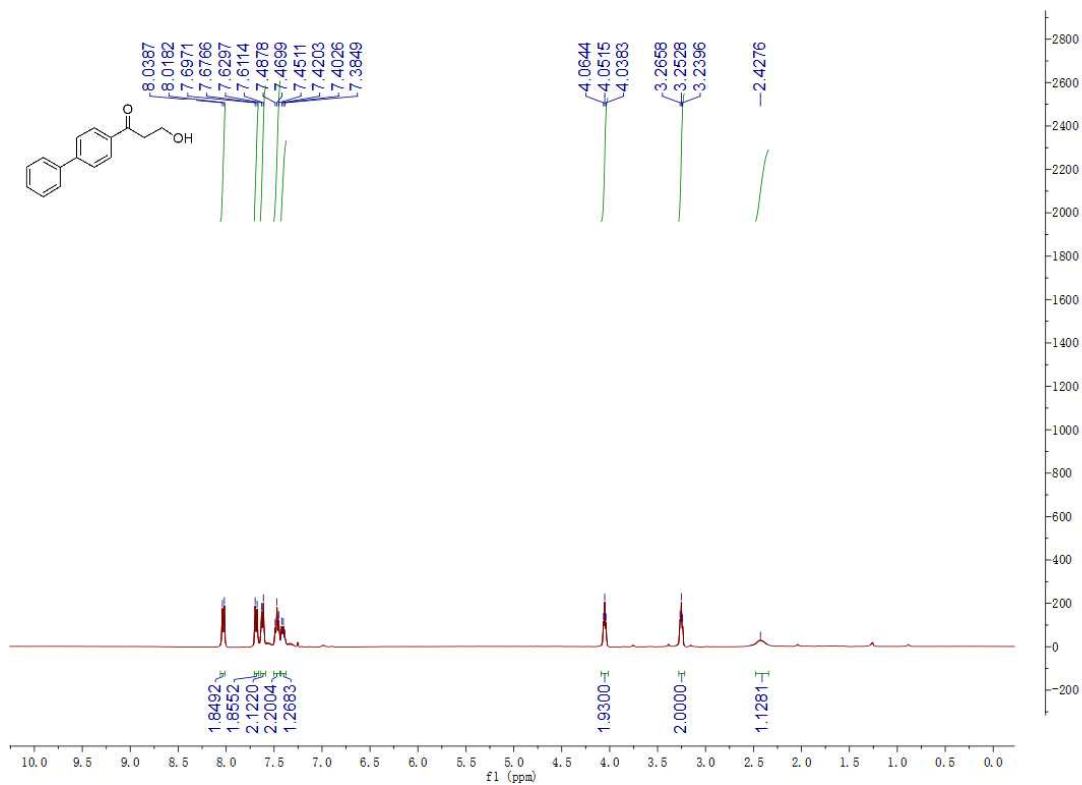
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2c**



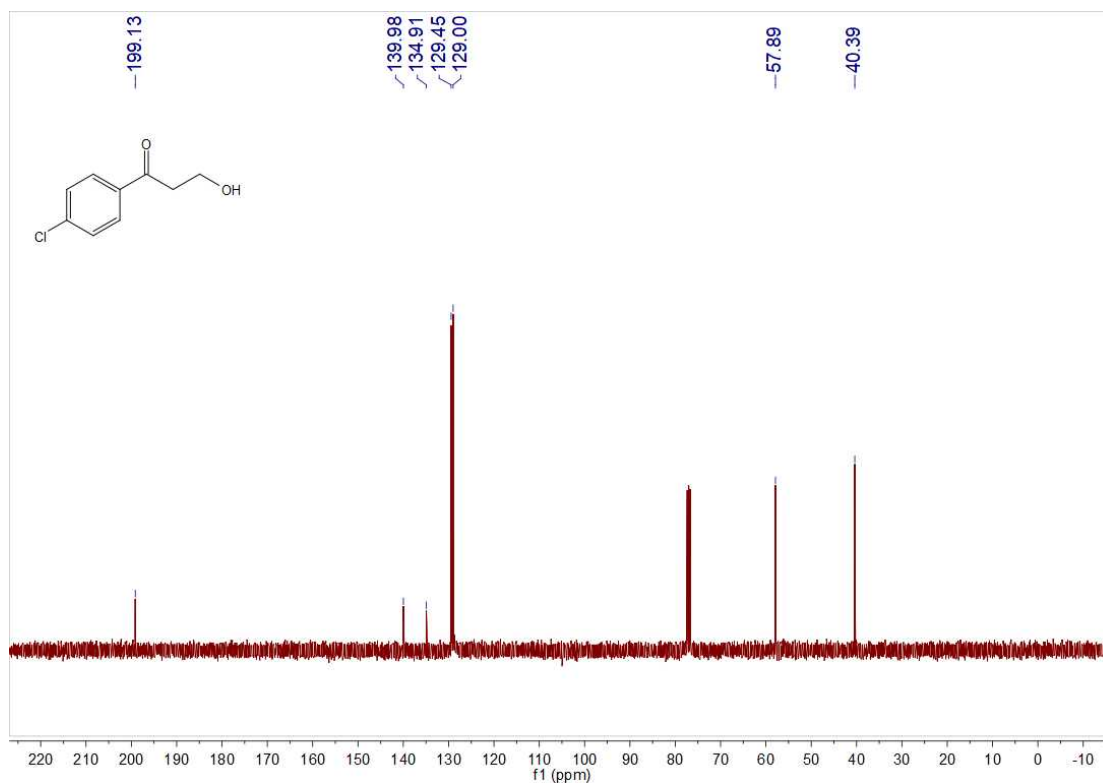
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2d**



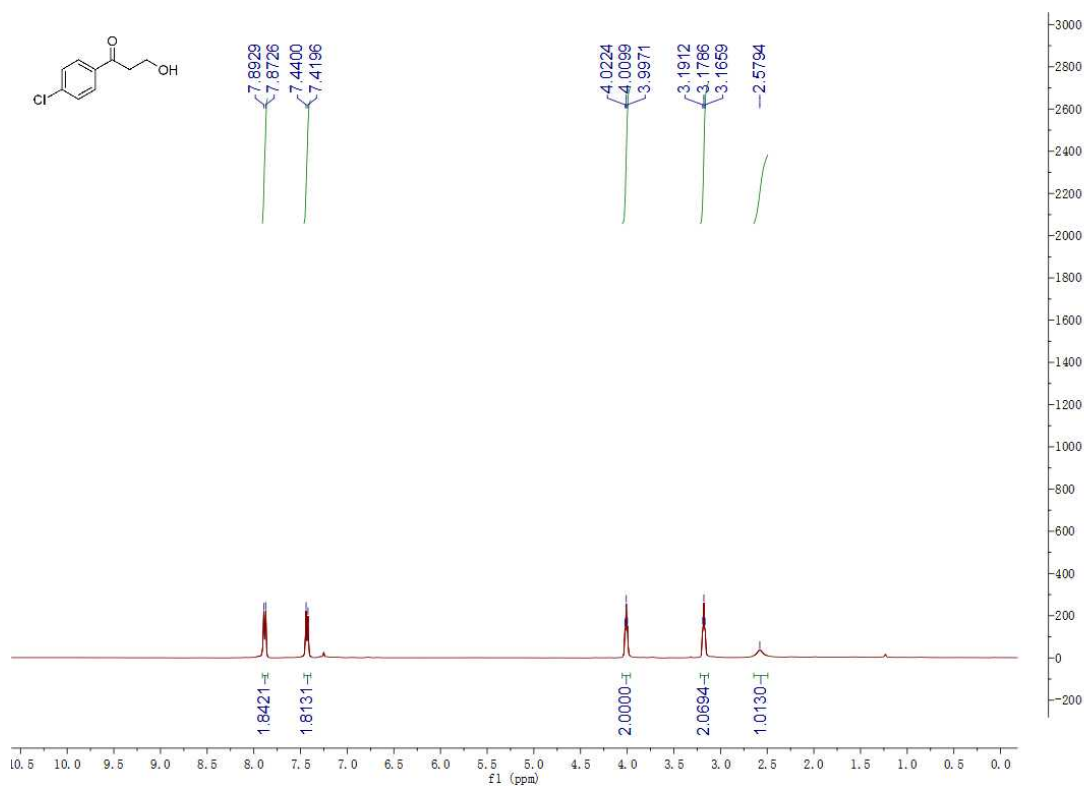
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2d**



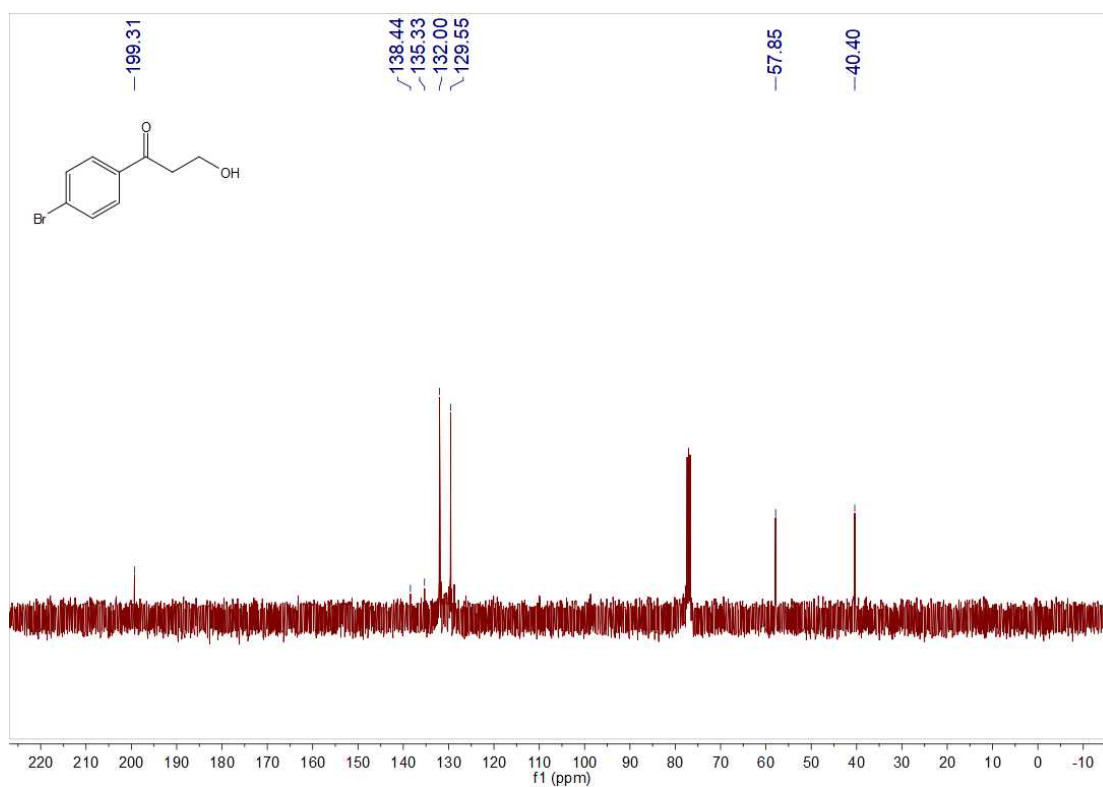
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2e**



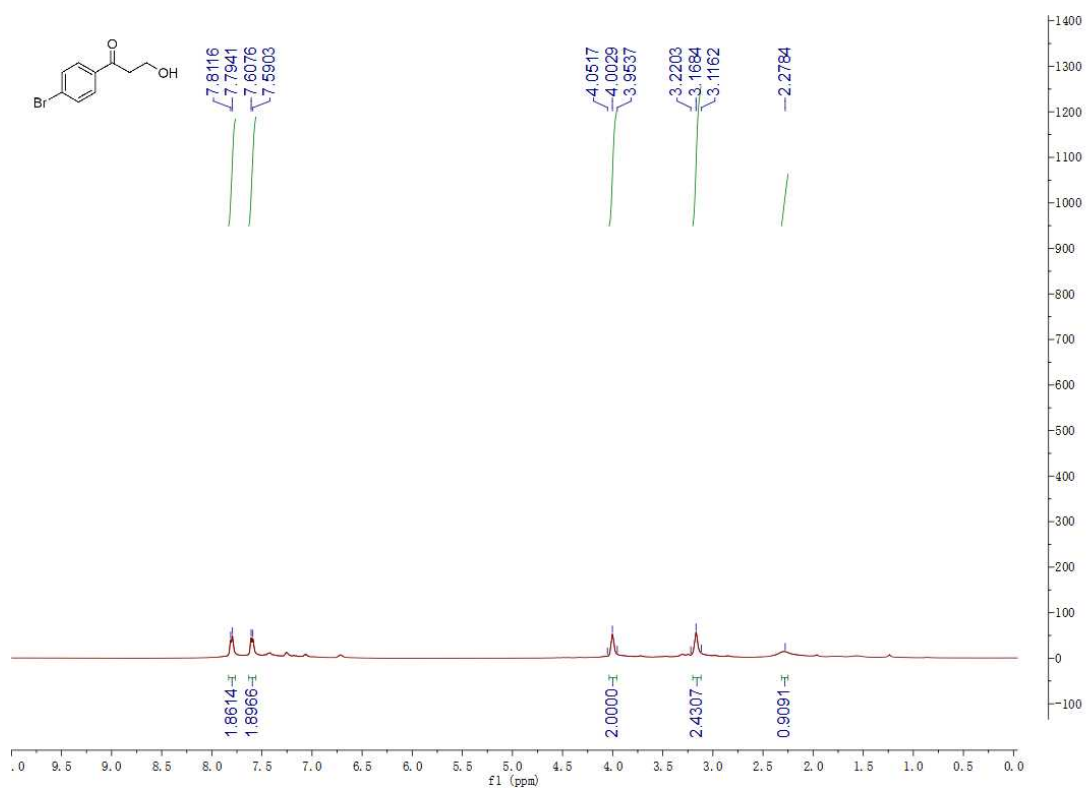
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2e**



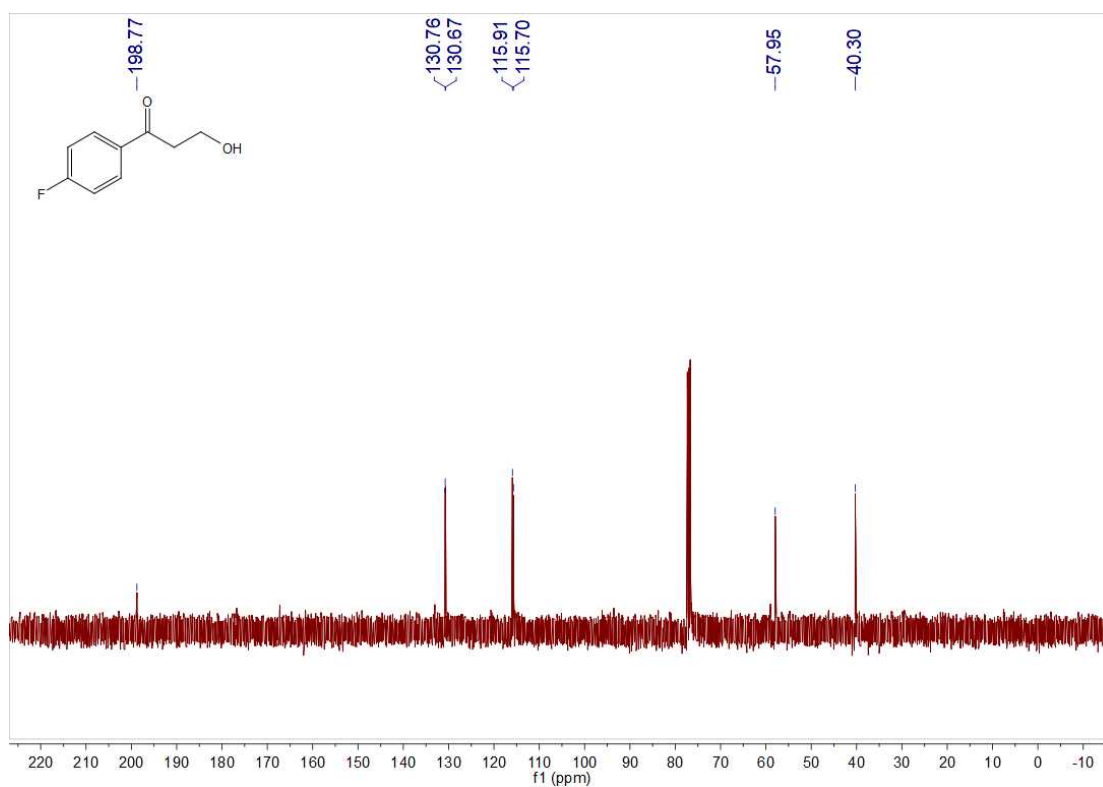
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2f**



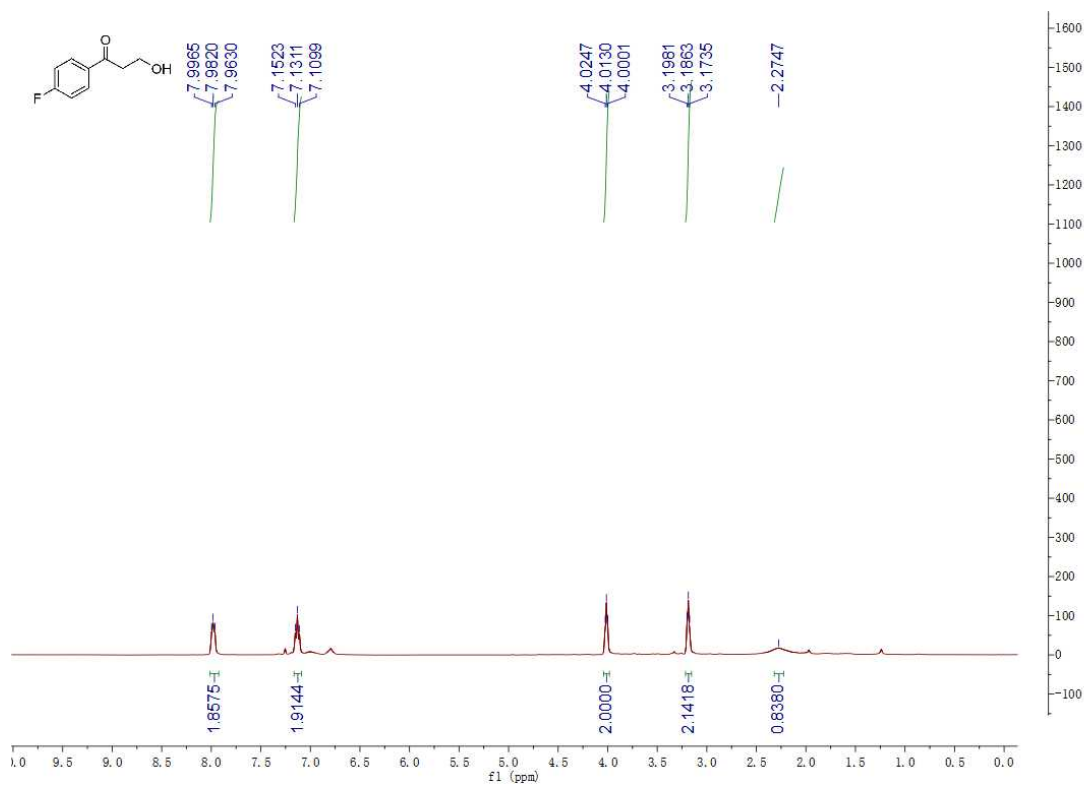
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2f**



<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2g**

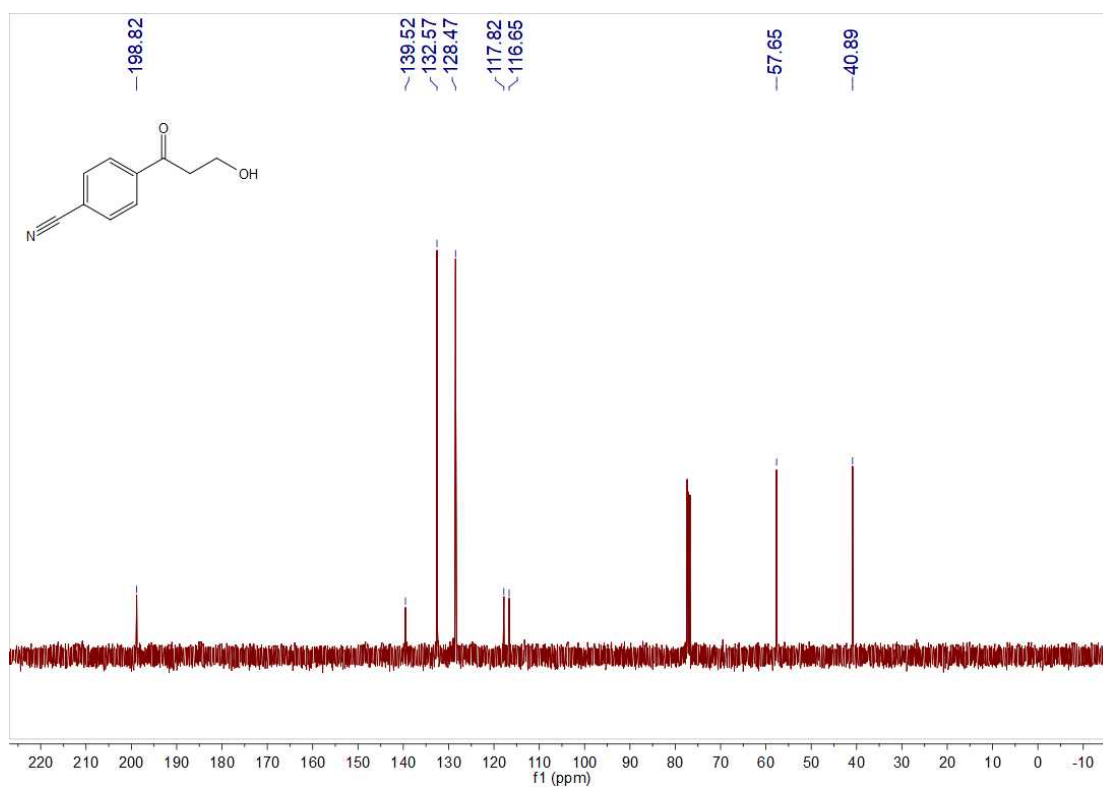


<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2g**

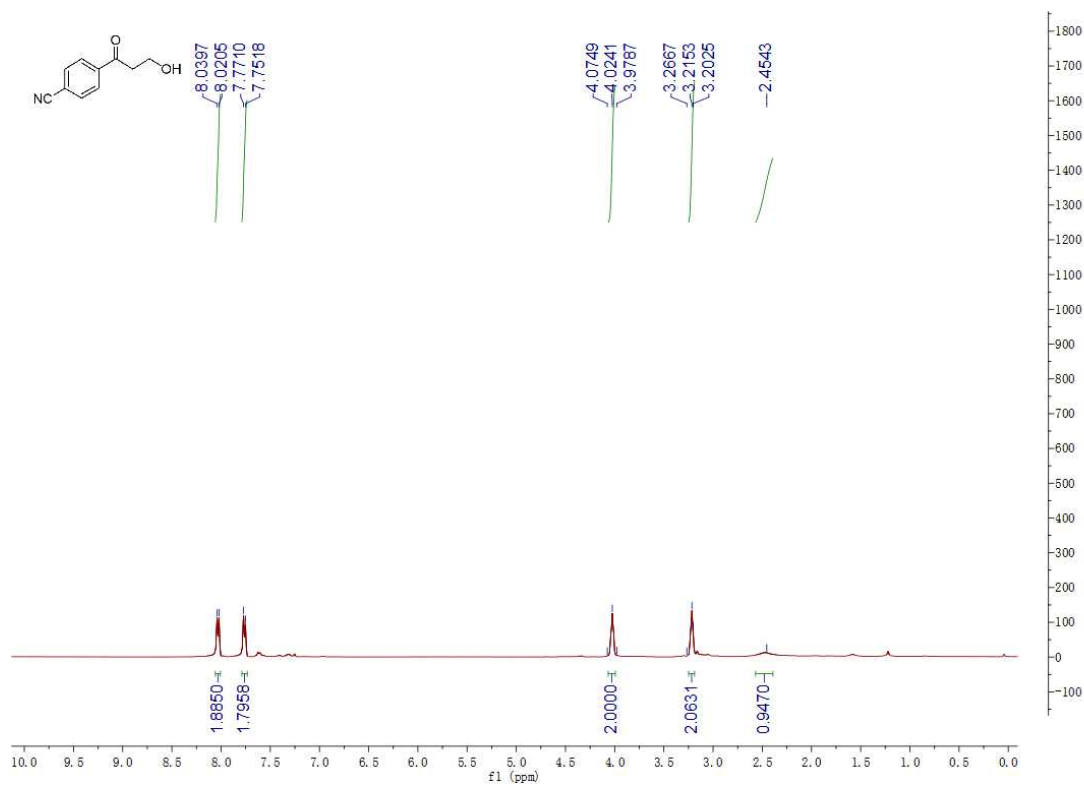




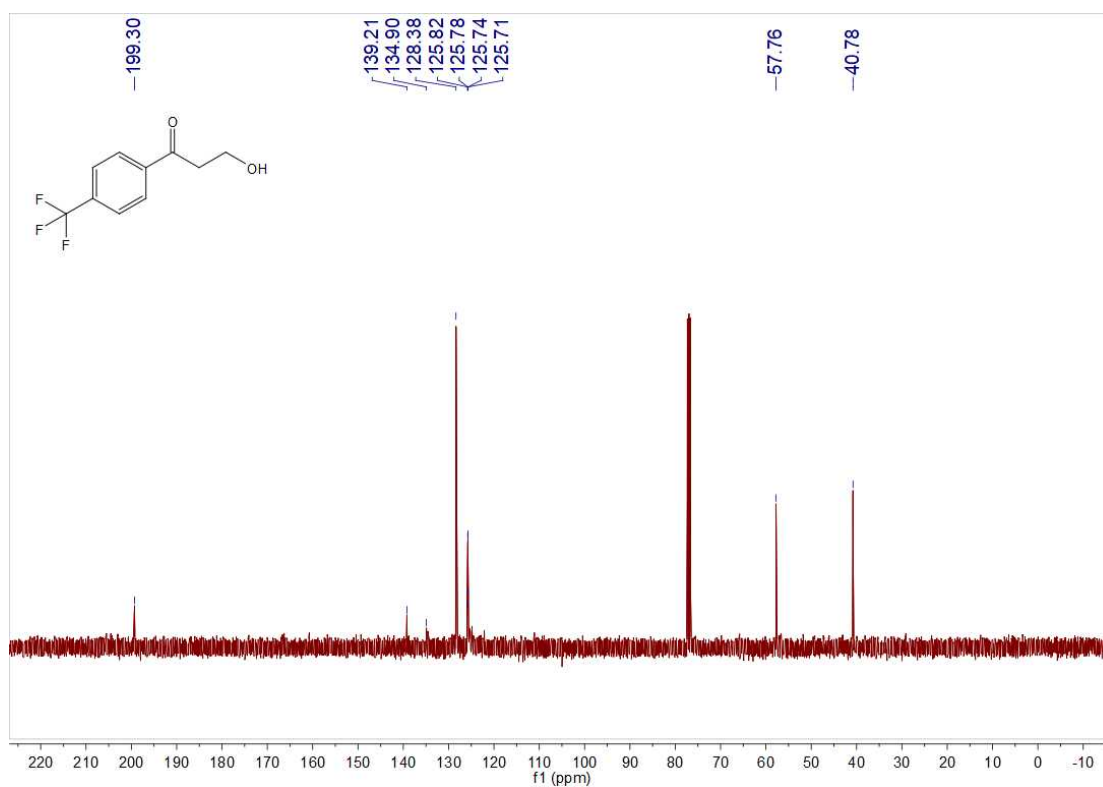
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2h**



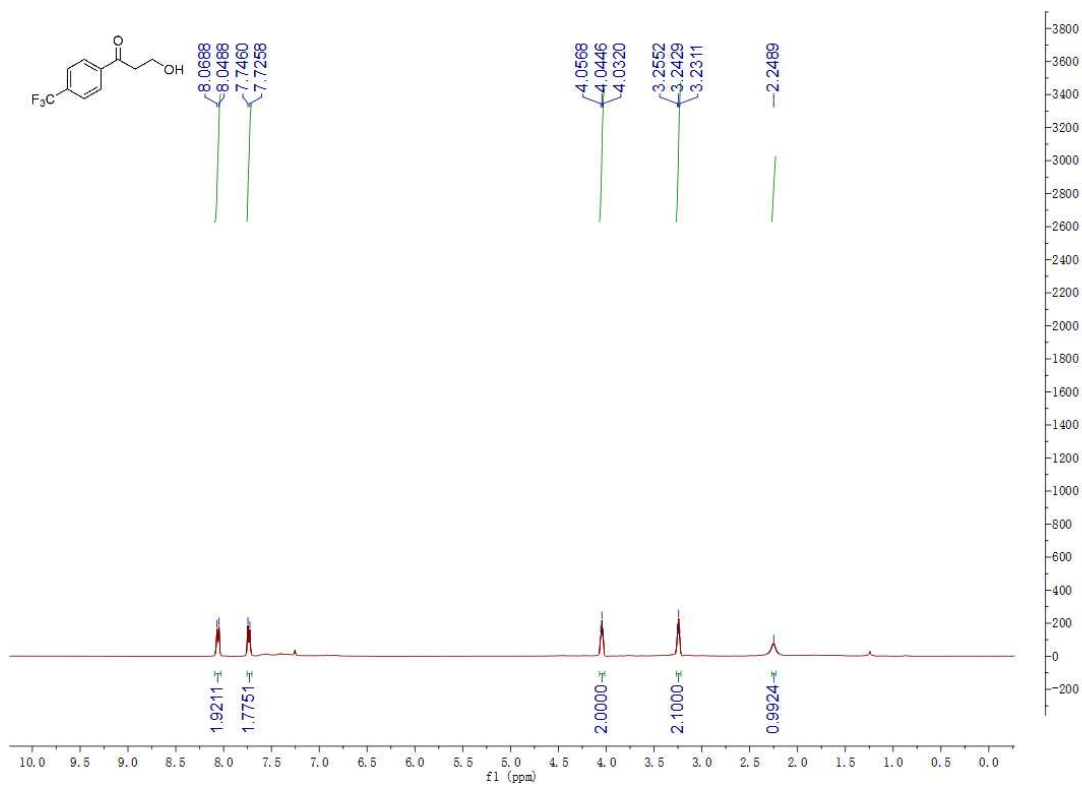
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2h**



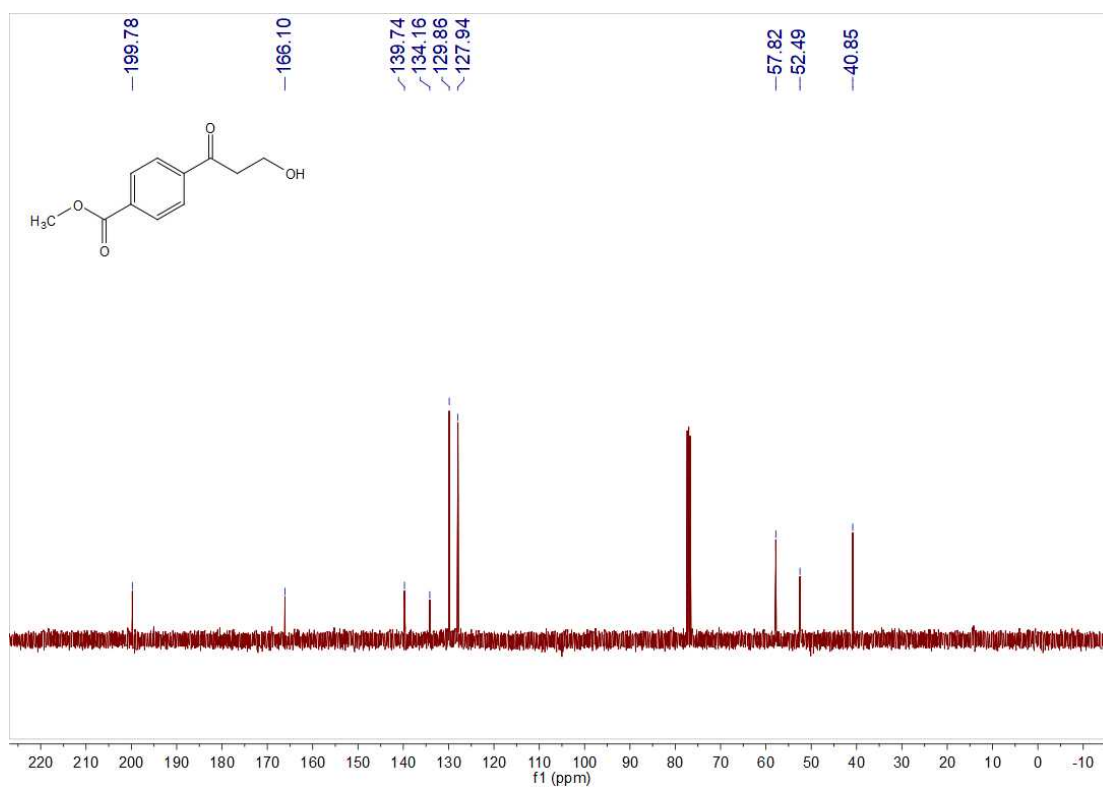
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2i**



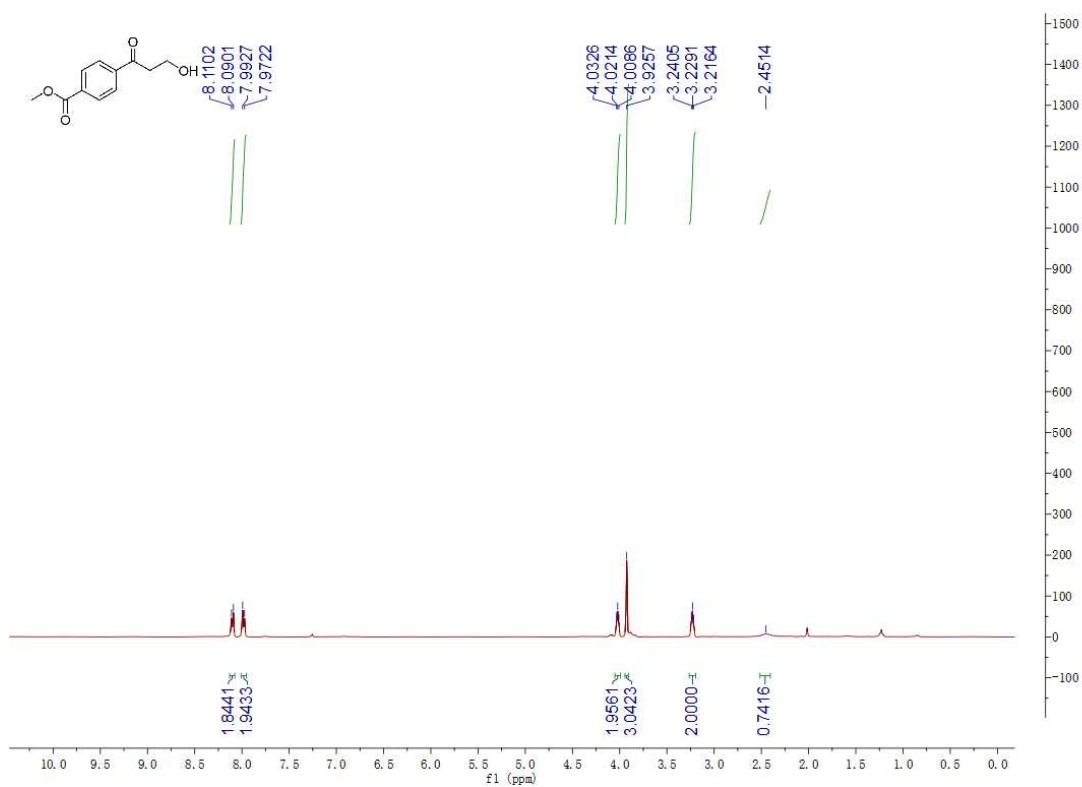
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2i**



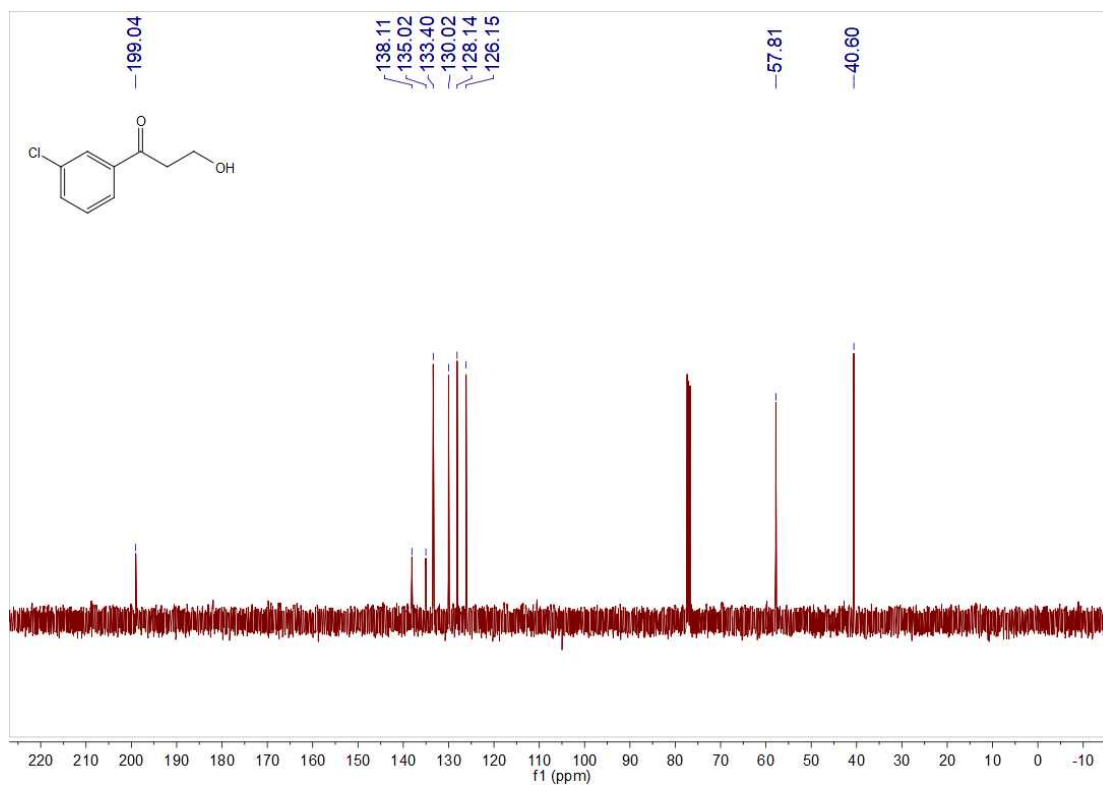
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2j**



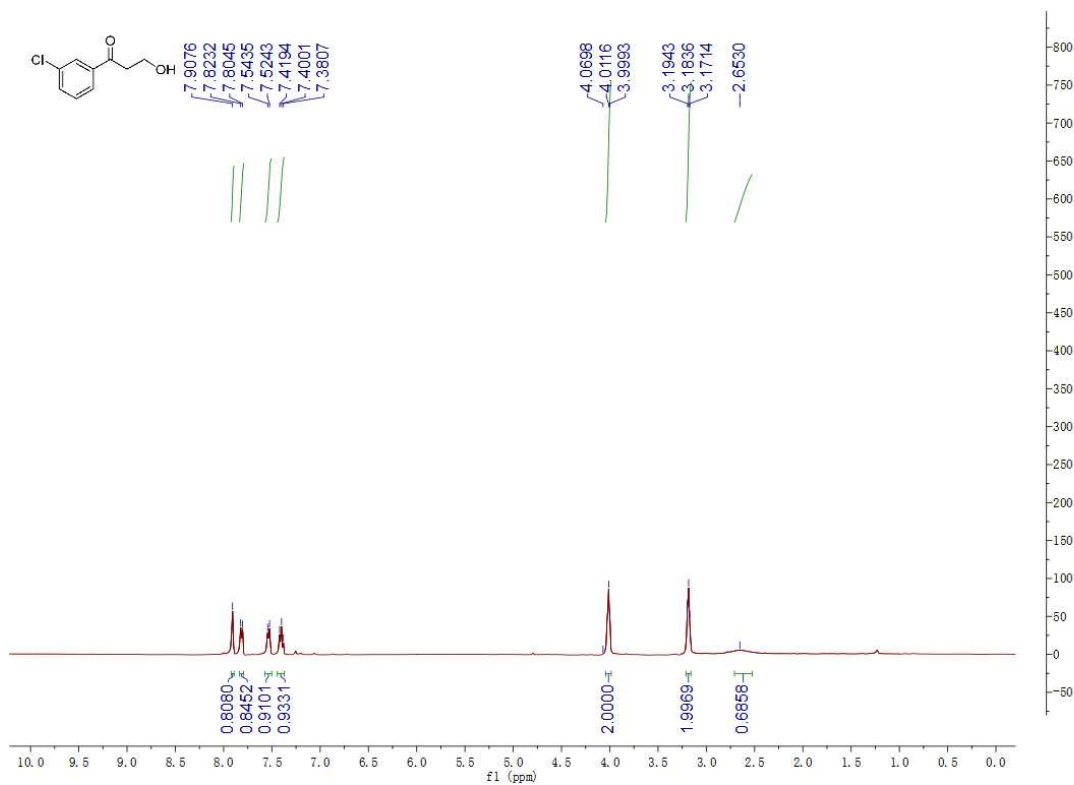
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2j**



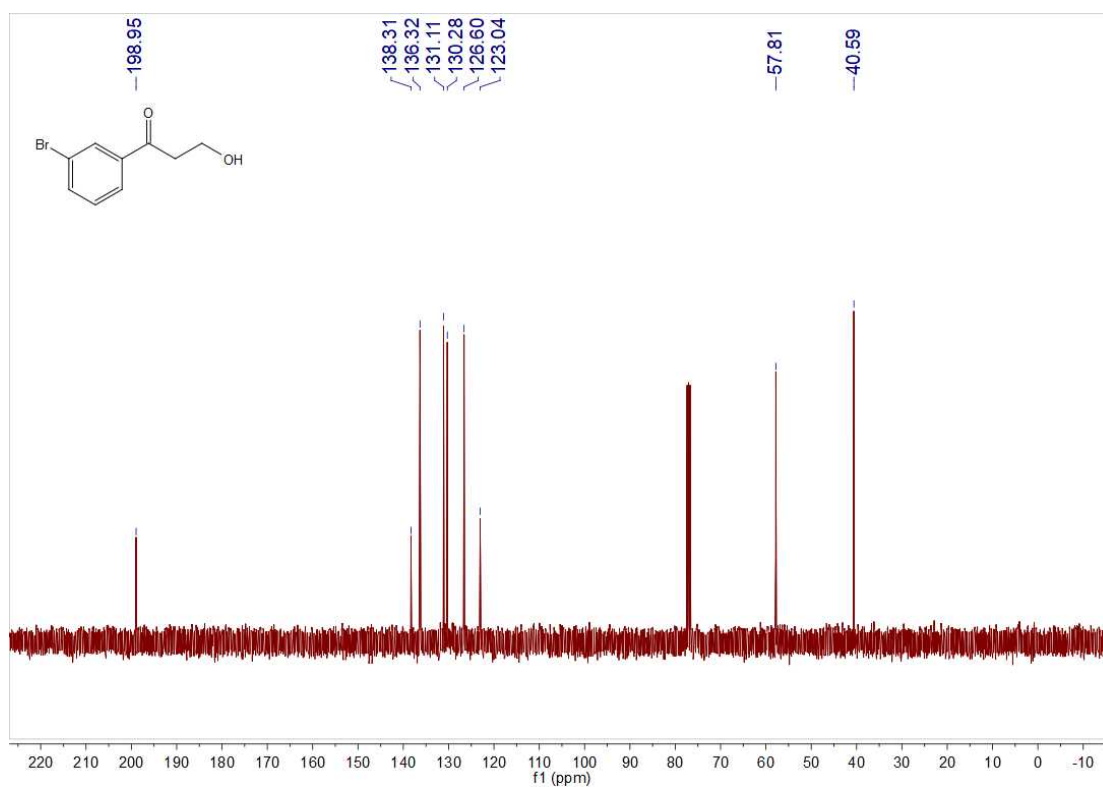
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ ) of compound **2k**



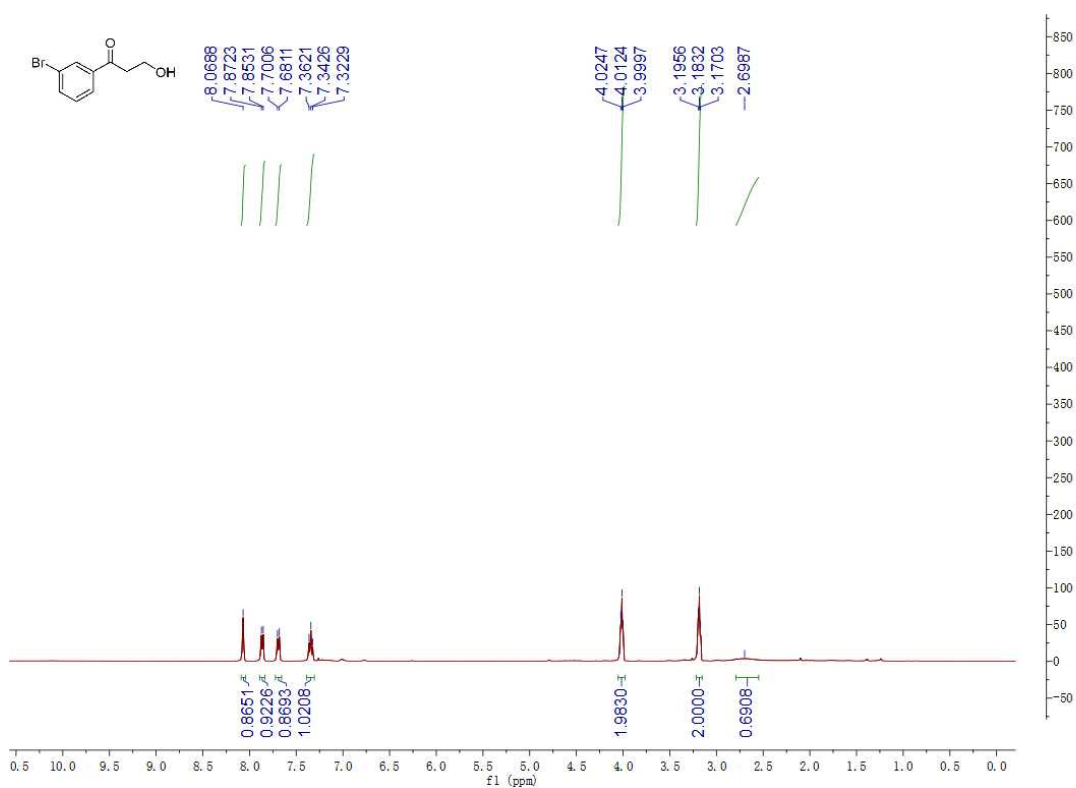
$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of compound **2k**



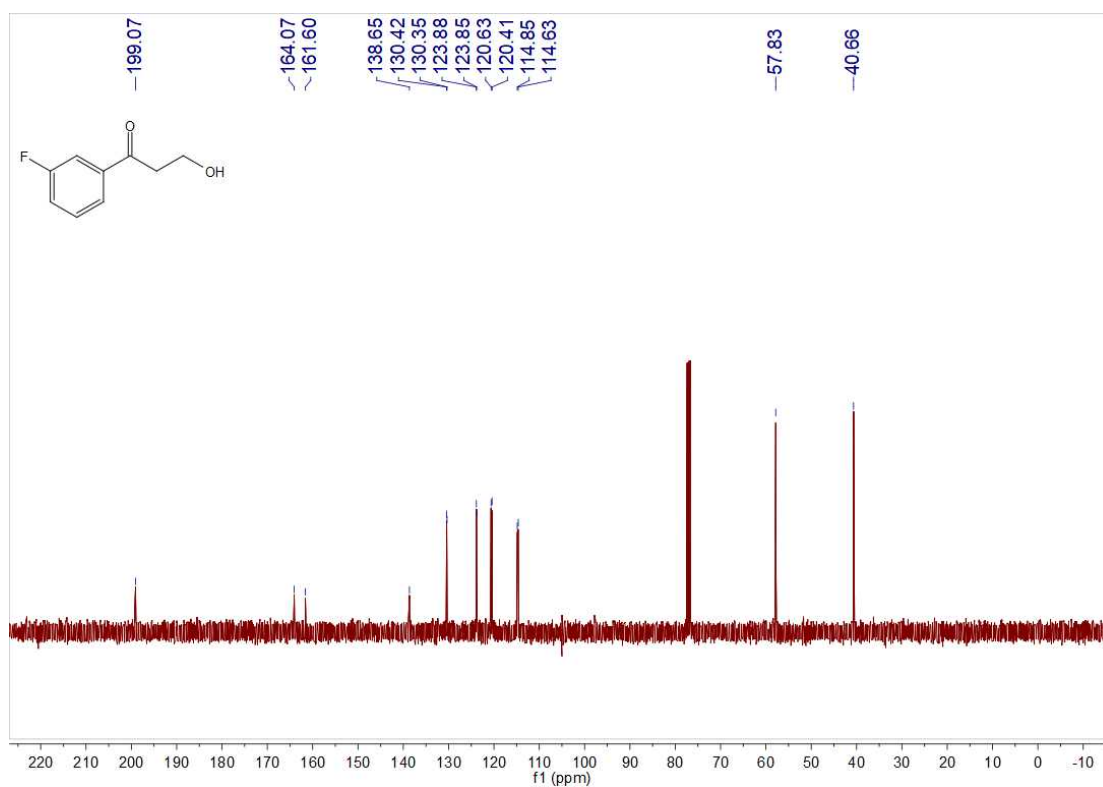
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **21**



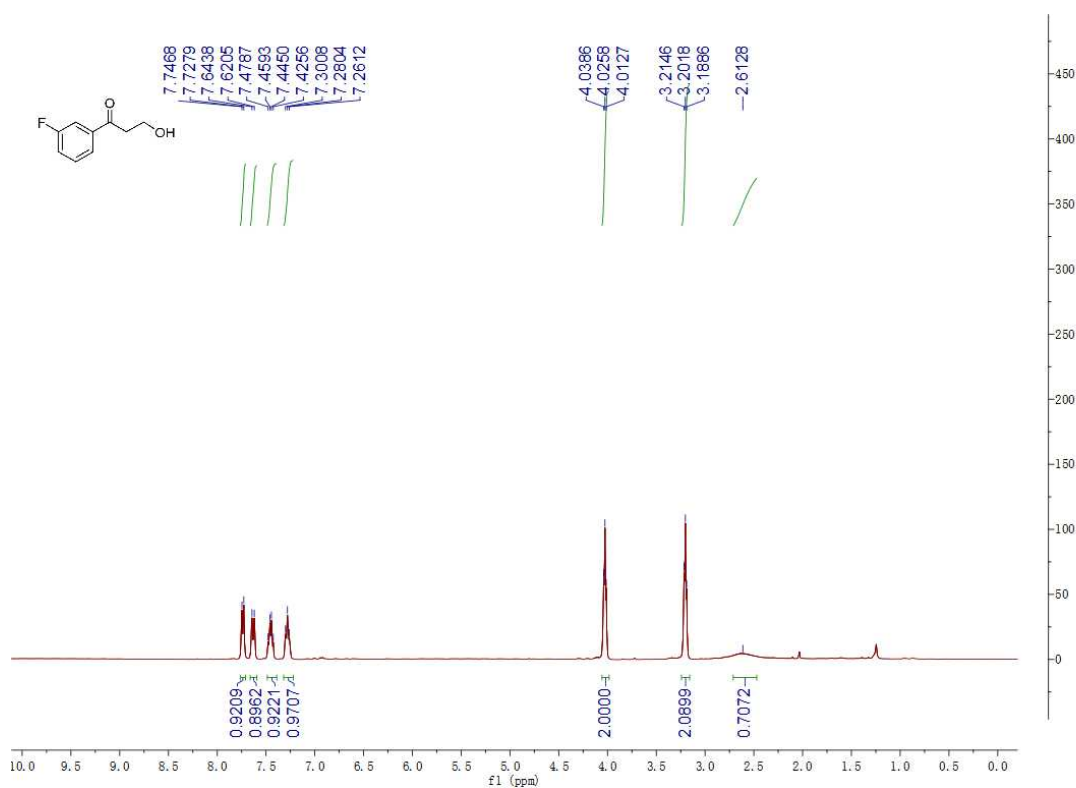
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **21**



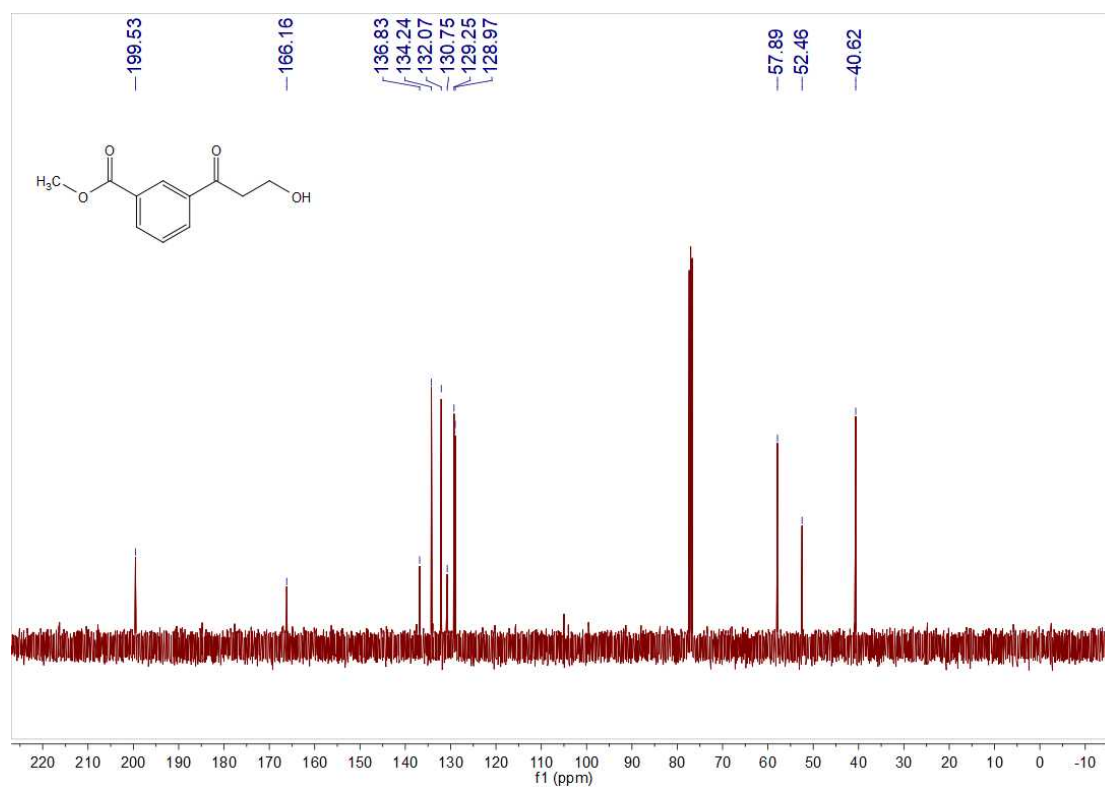
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2m**



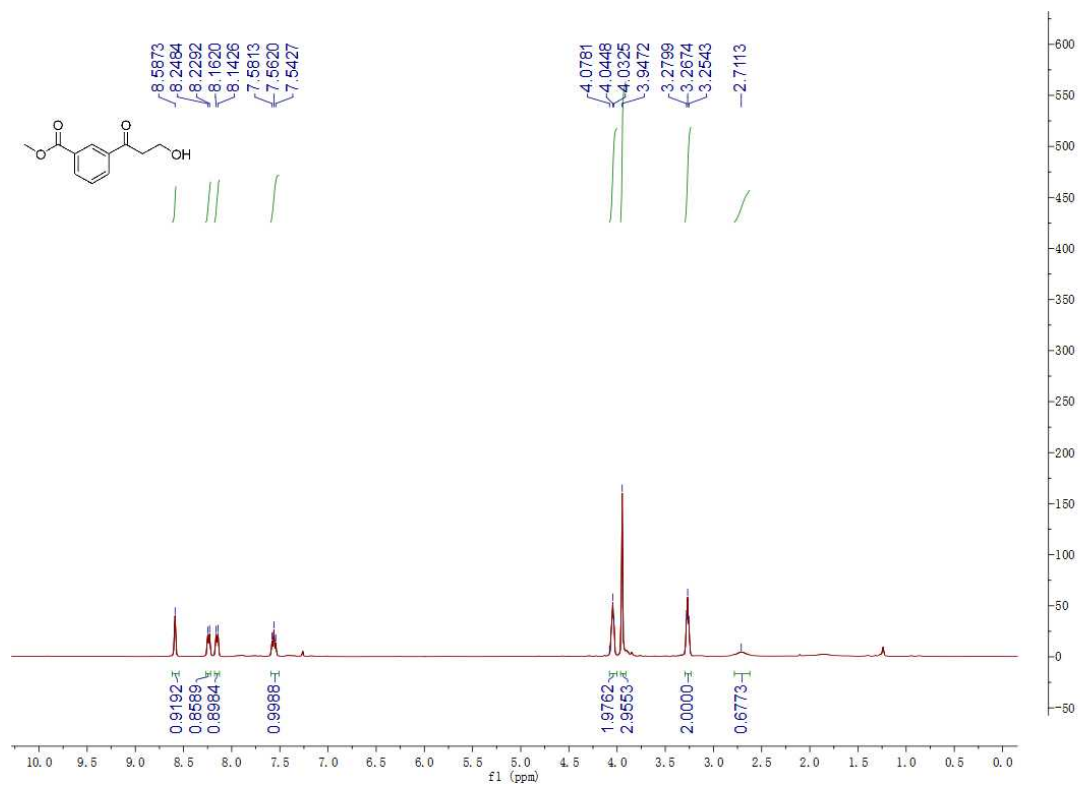
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2m**



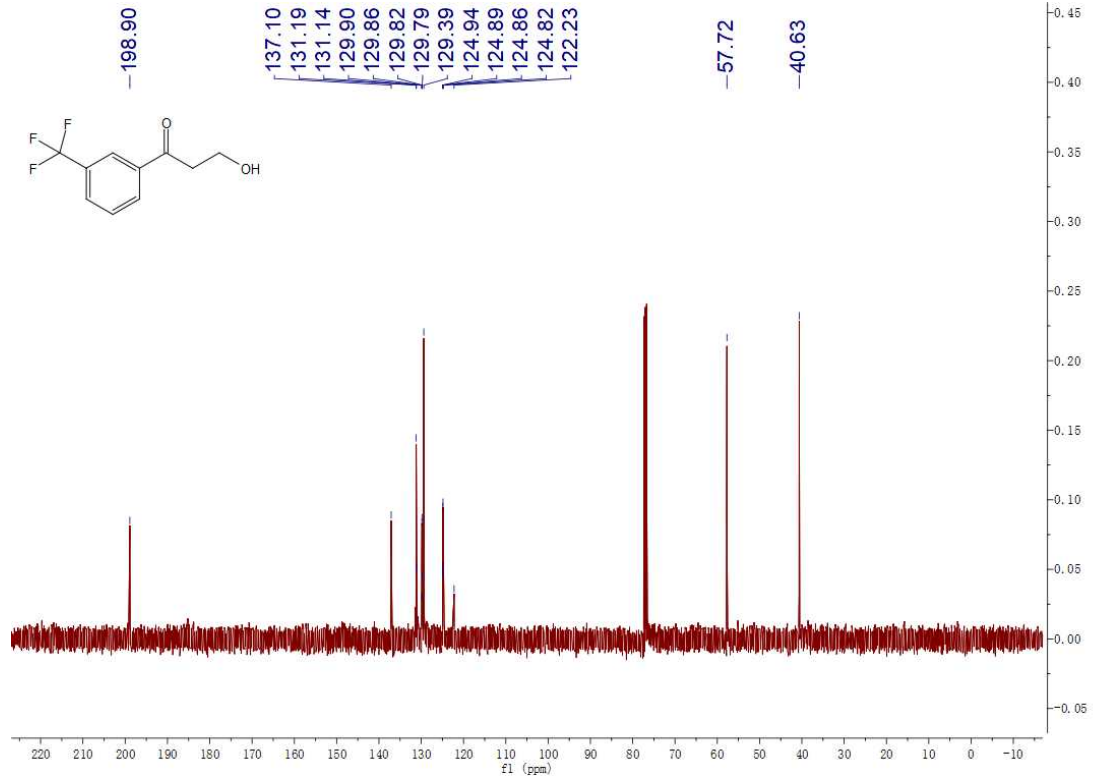
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2n**



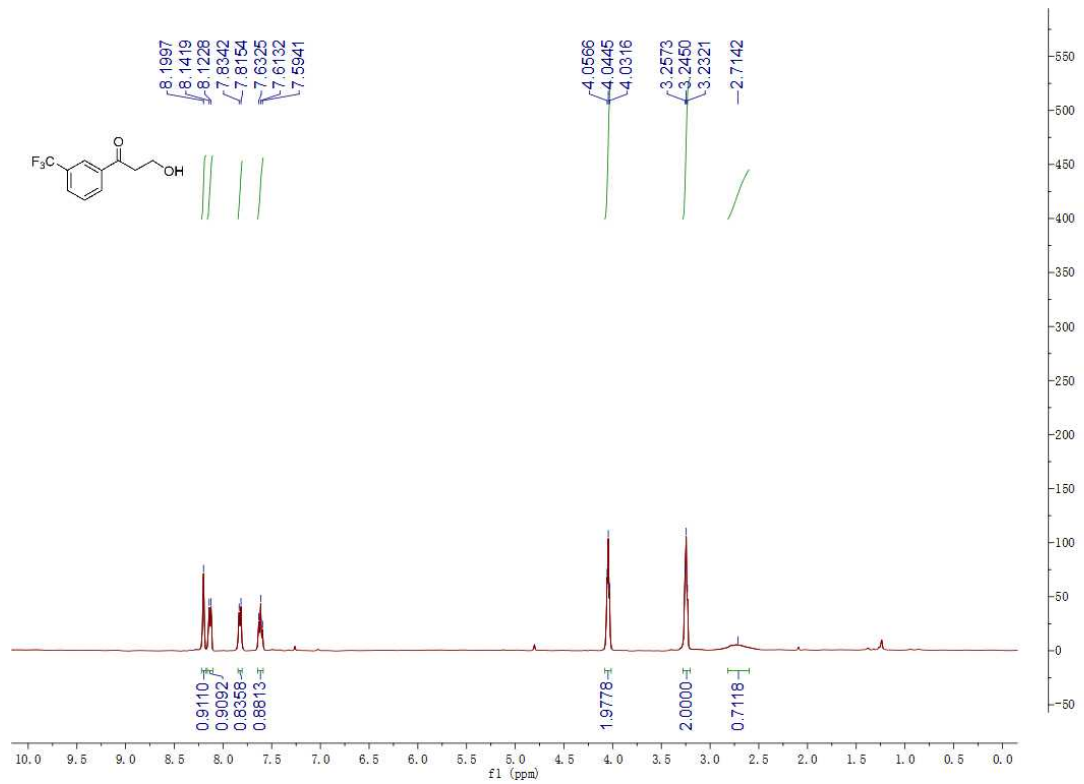
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2n**



<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2o**

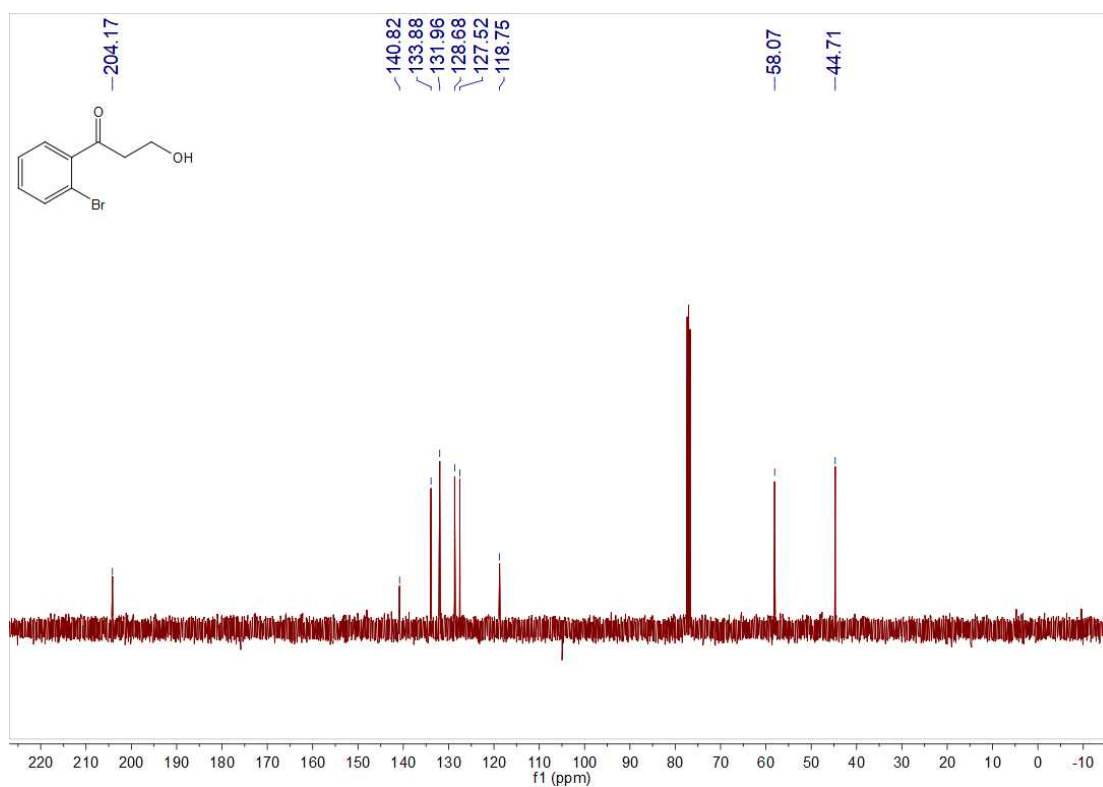


<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2o**

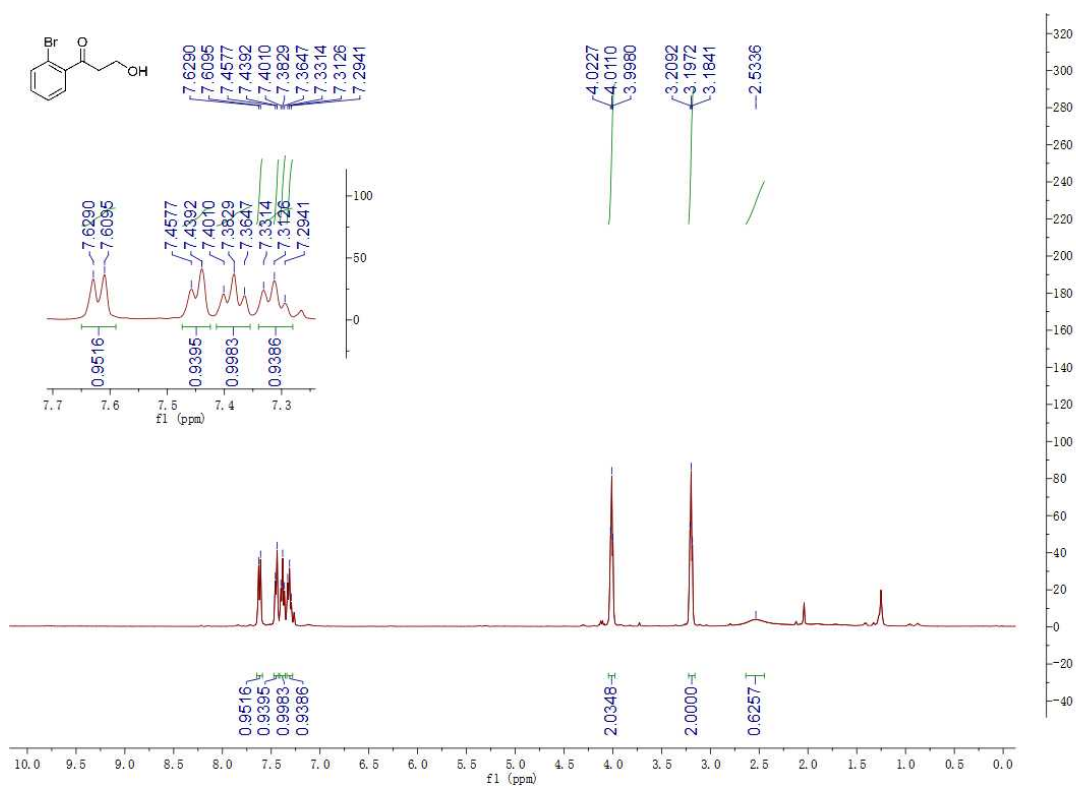




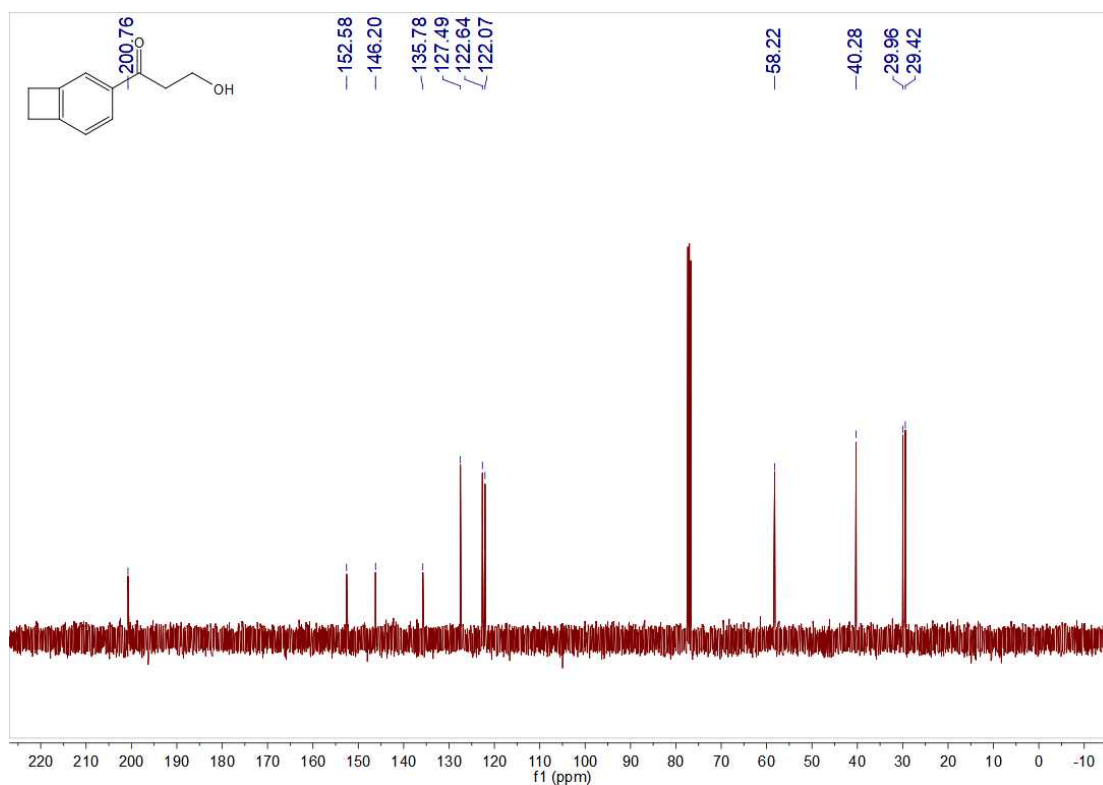
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2p**



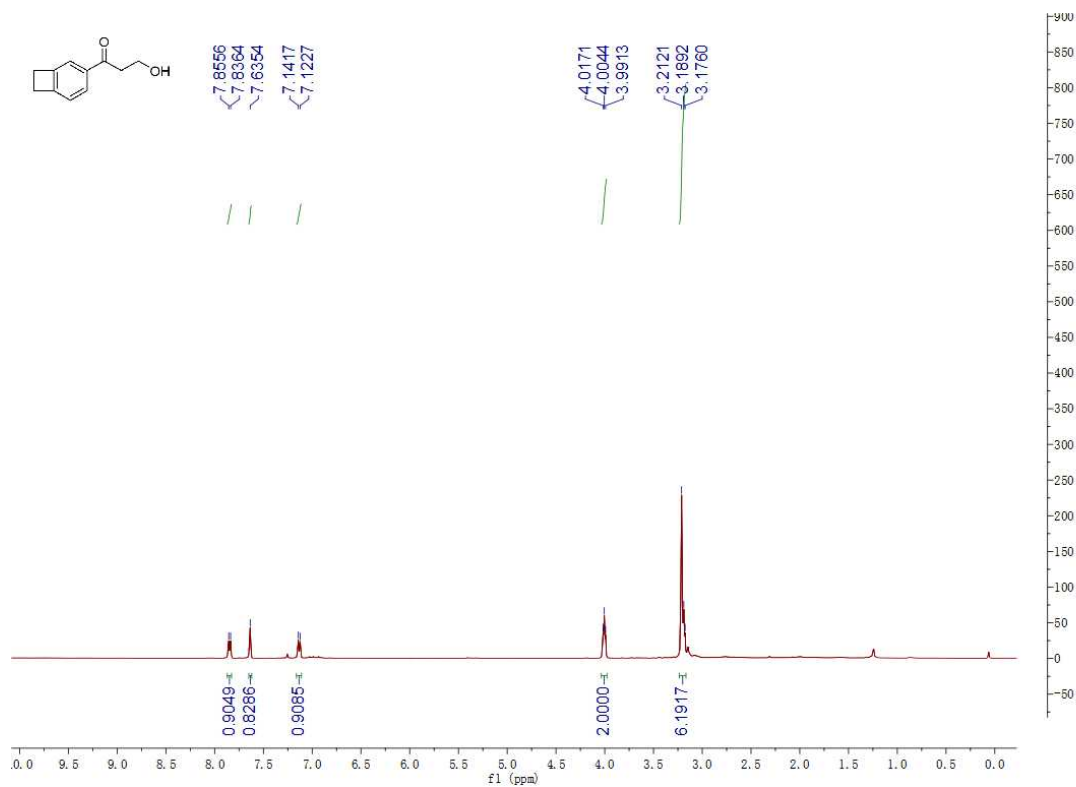
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2p**



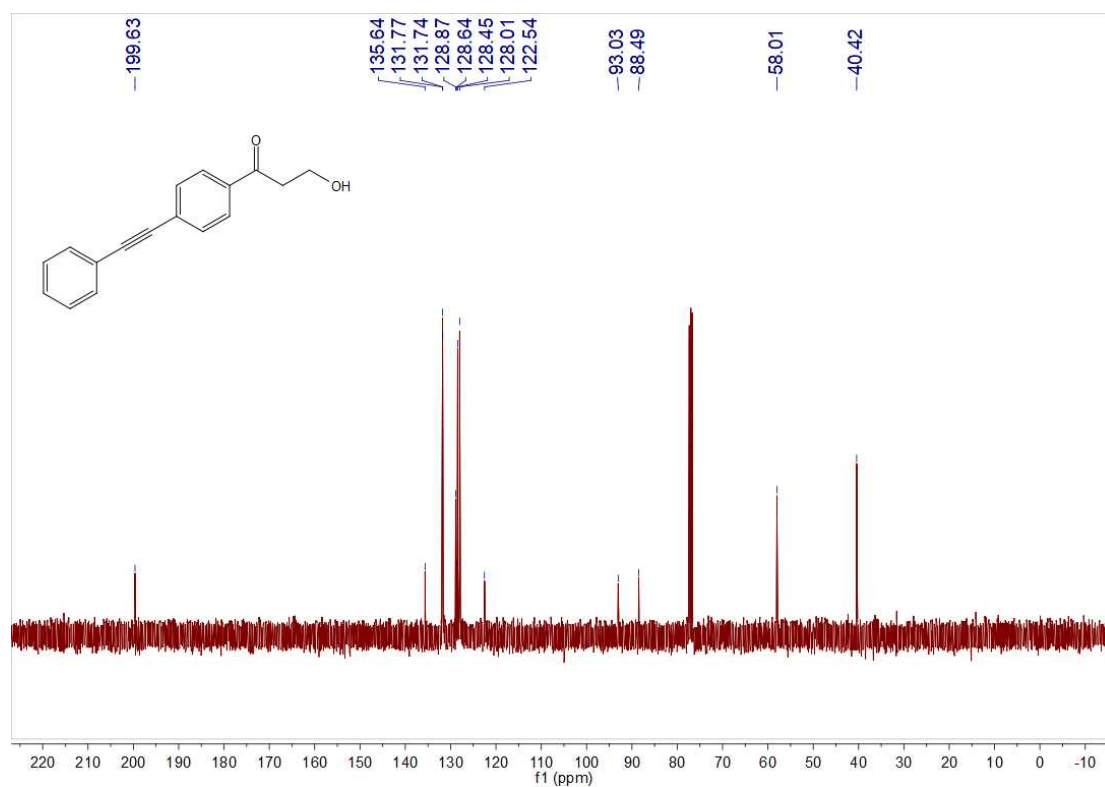
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2q**



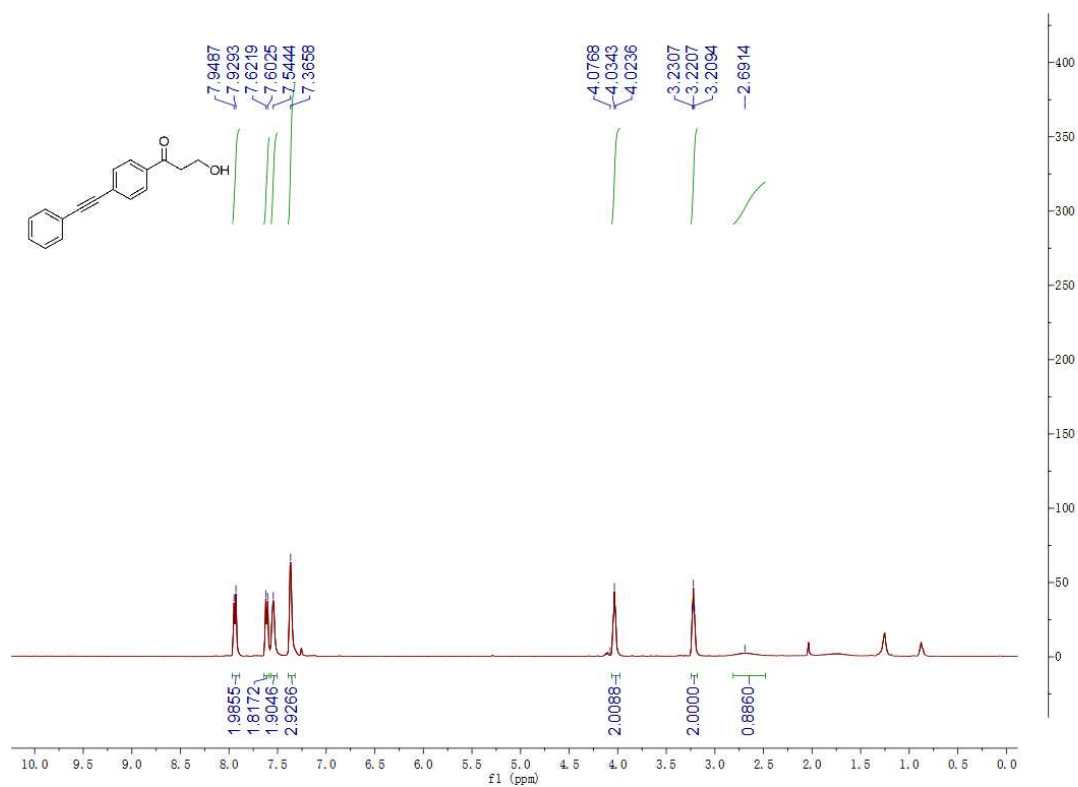
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2q**



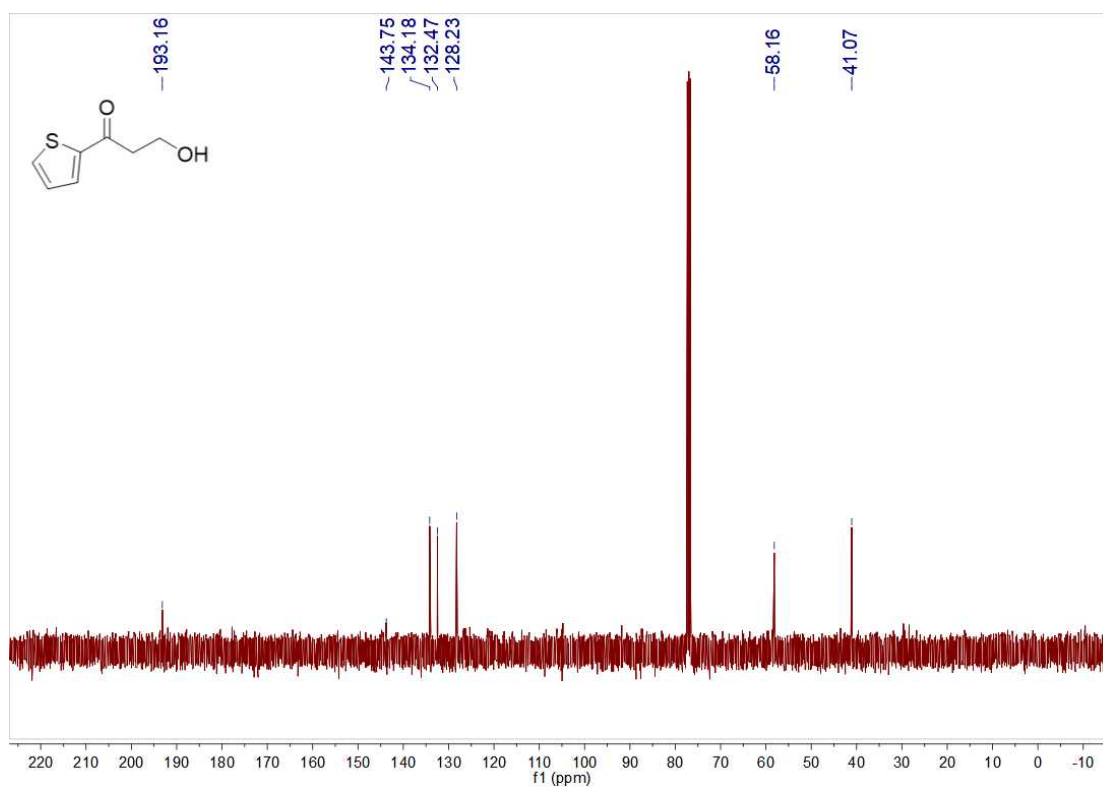
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2r**



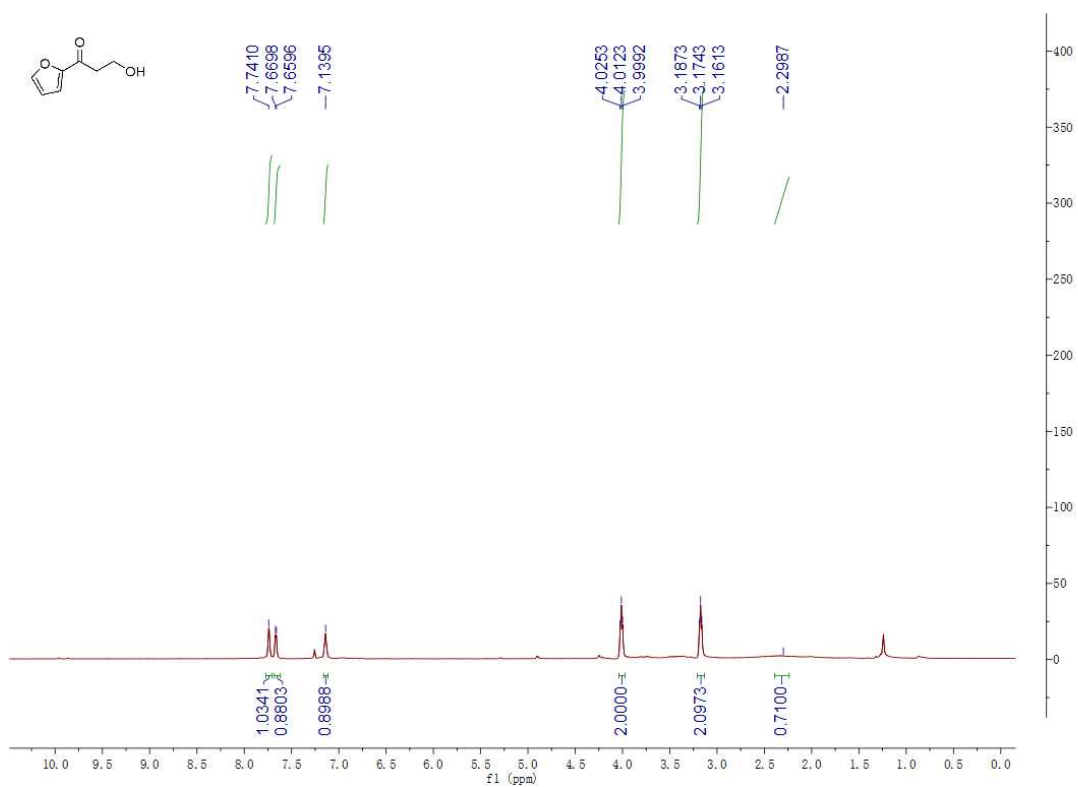
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2r**



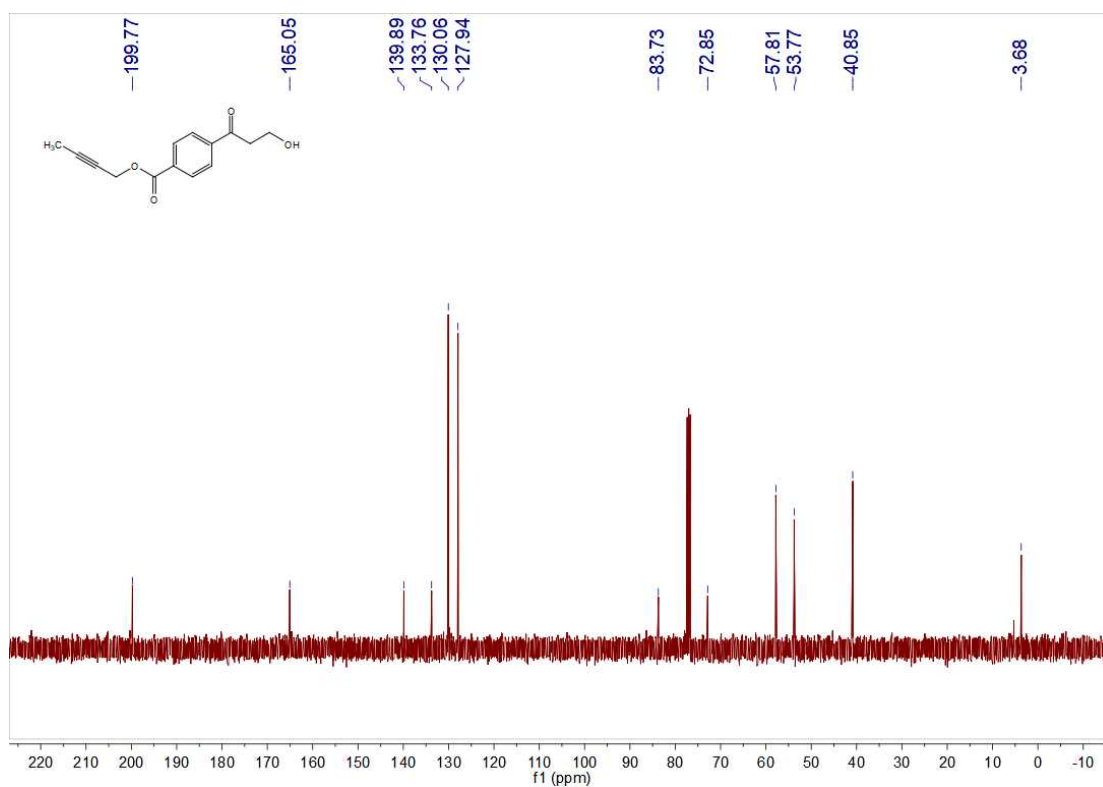
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2s**



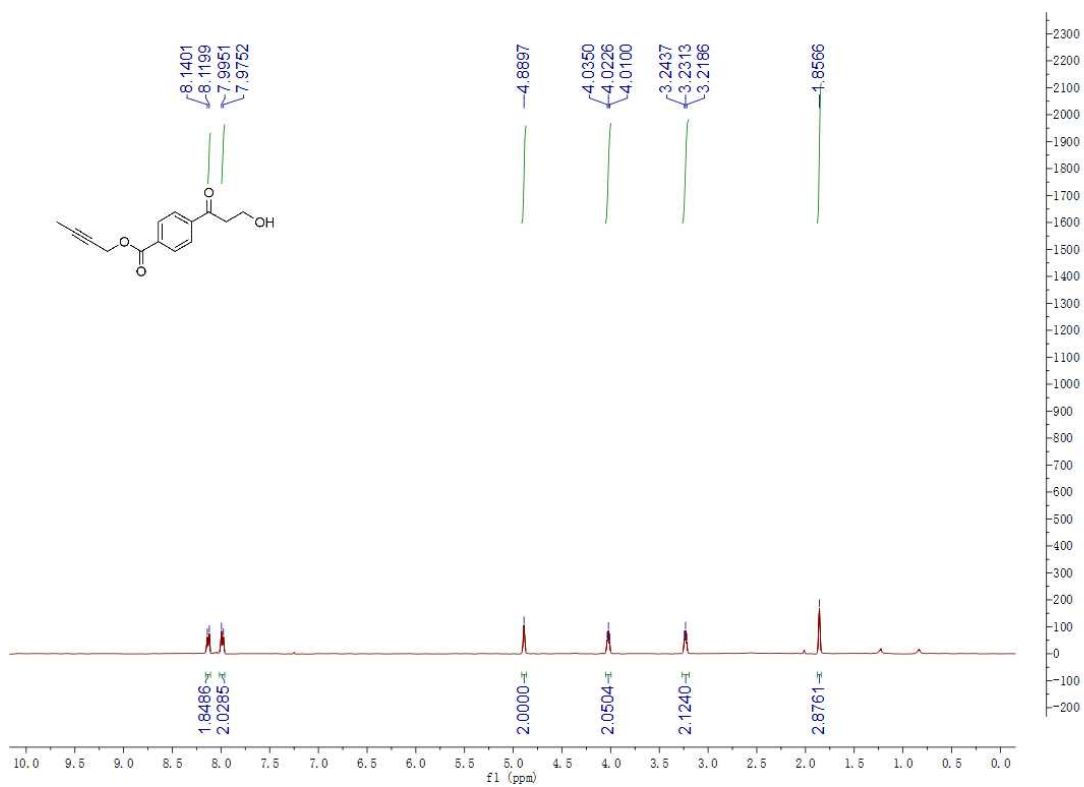
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2s**



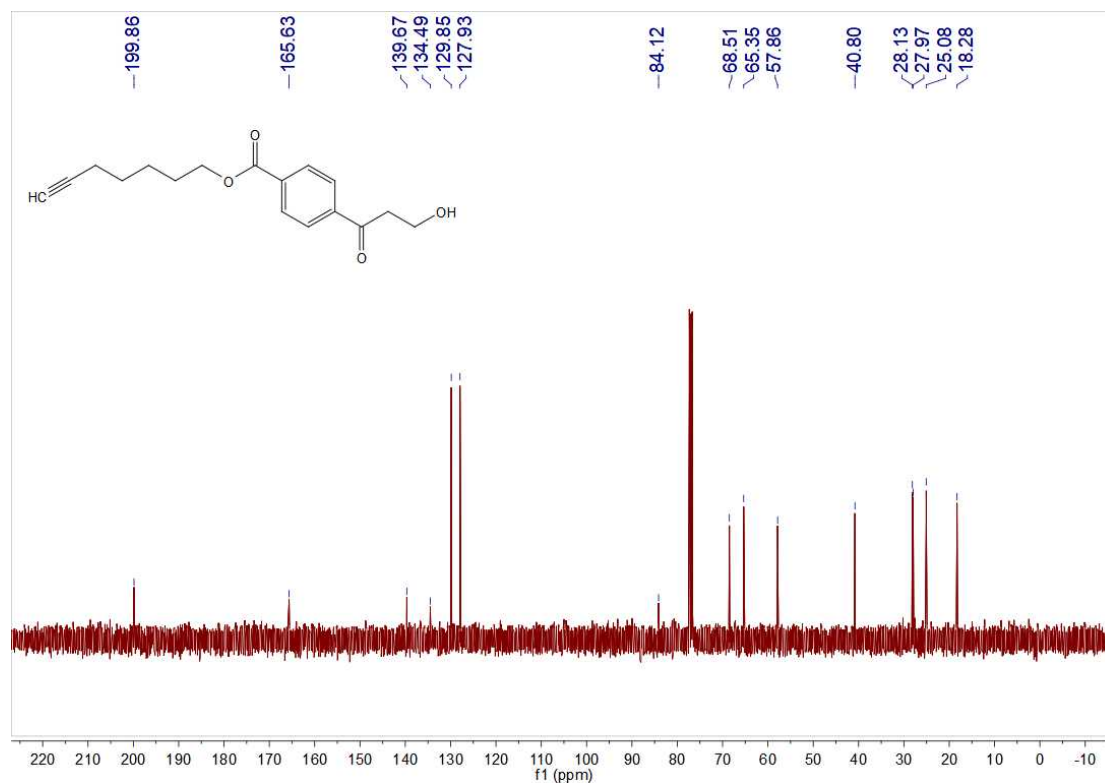
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2t**



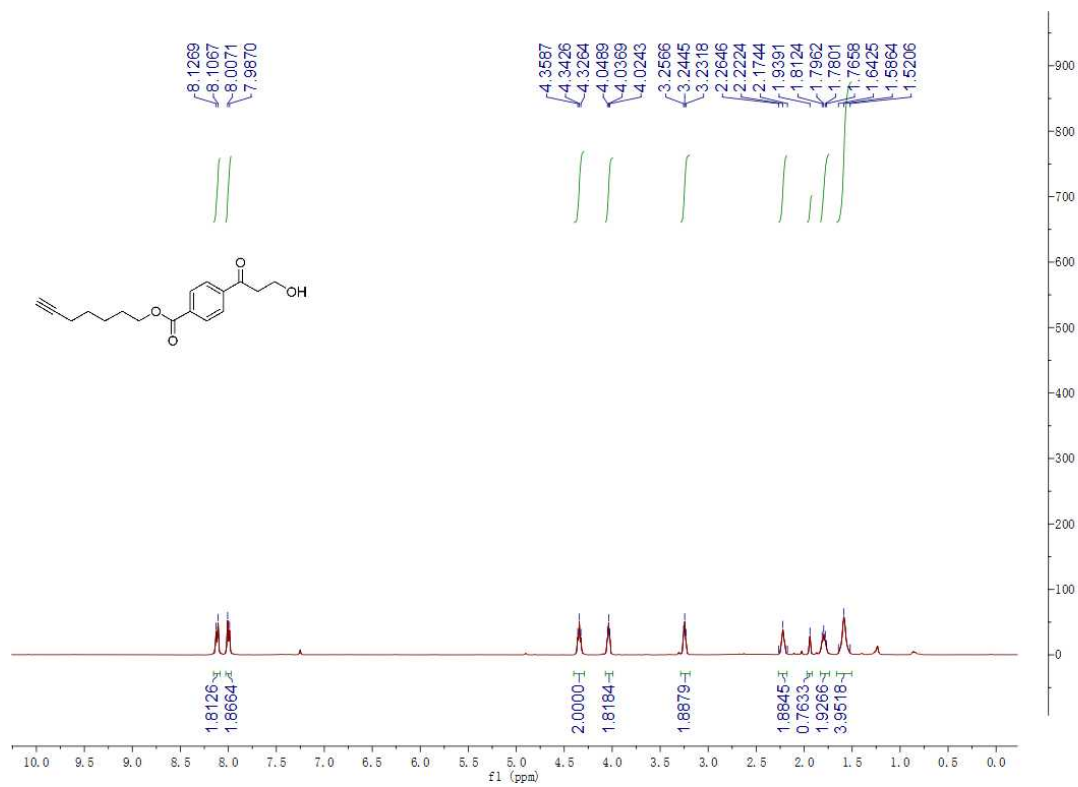
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2t**



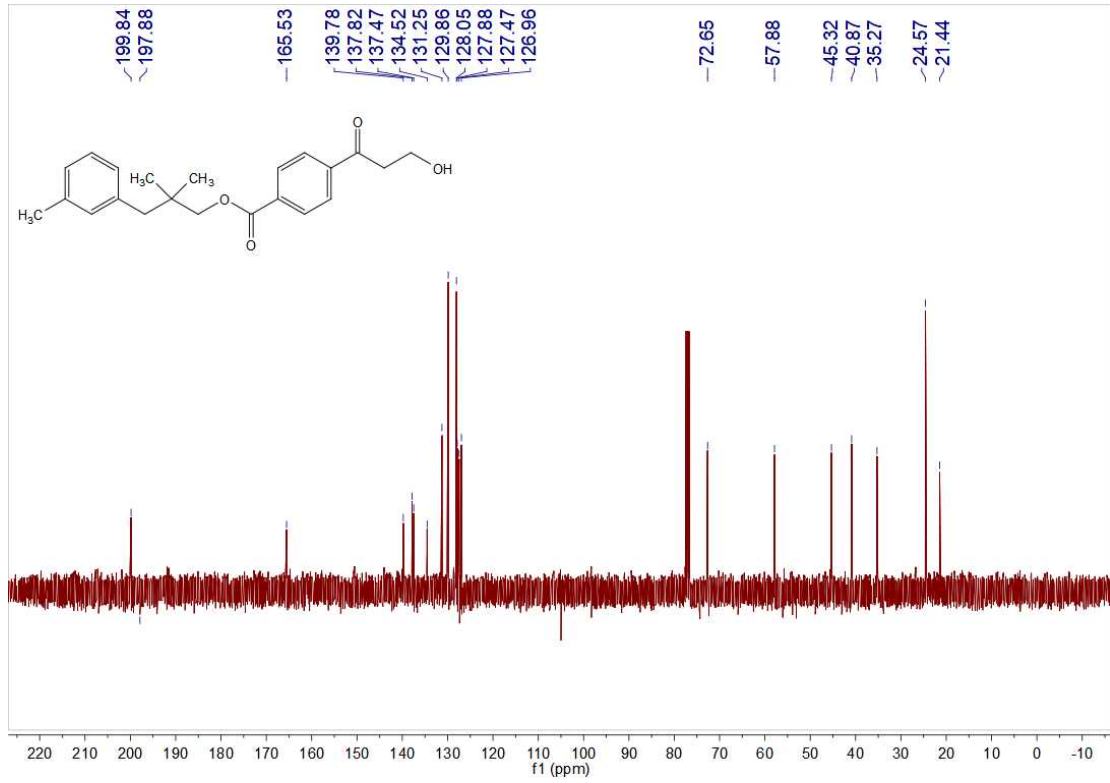
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2u**



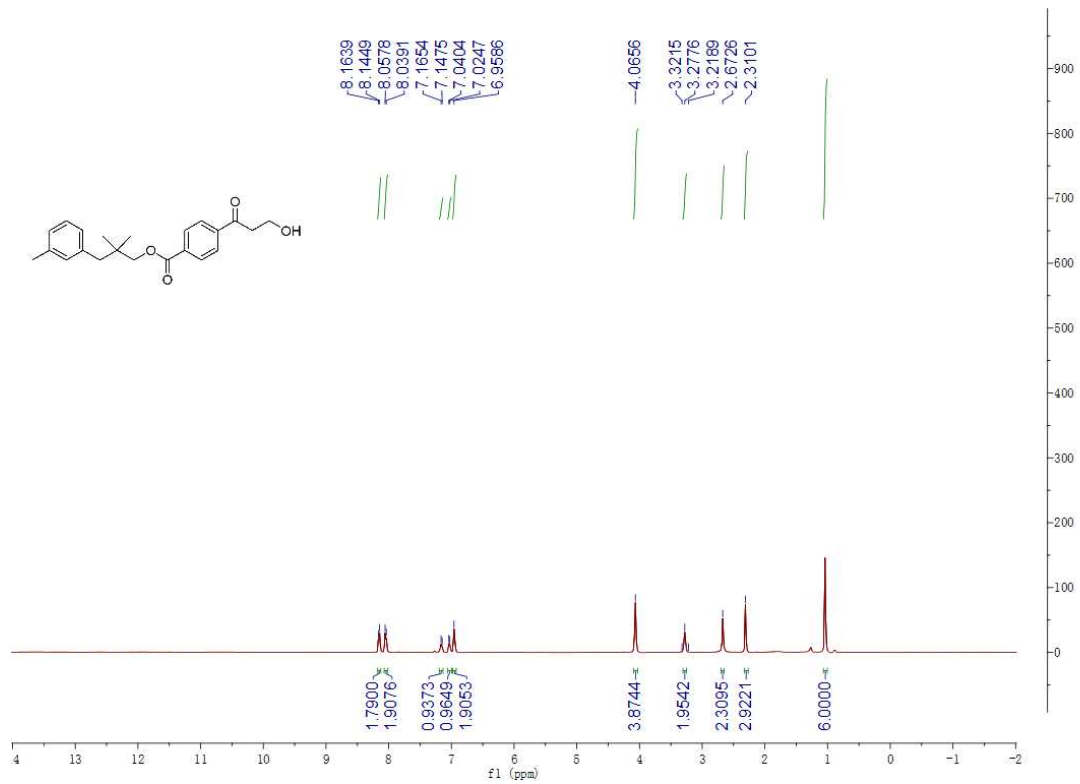
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2u**



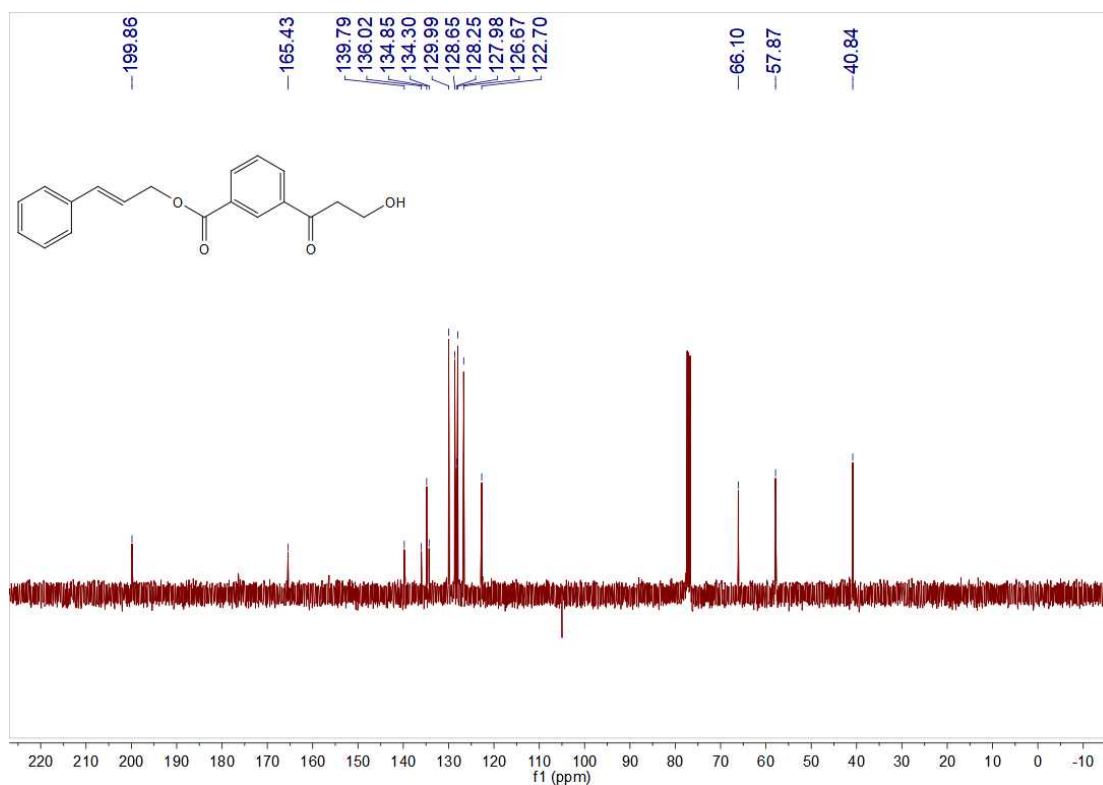
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2v**



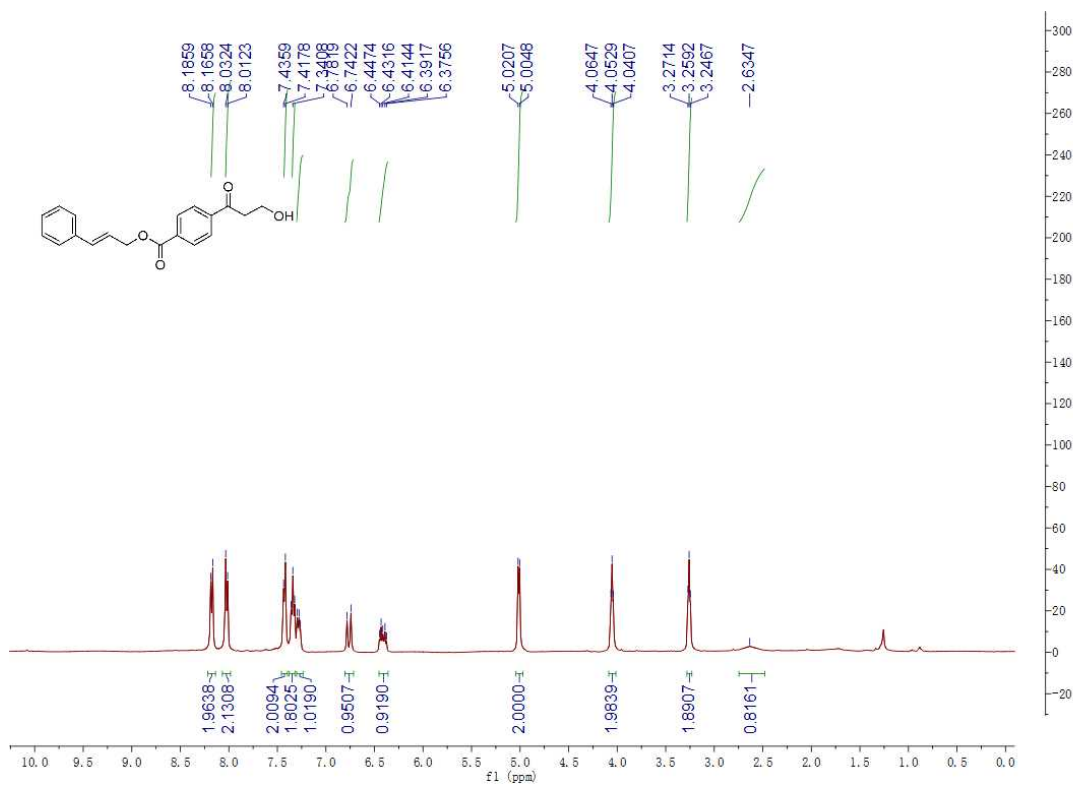
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2v**



<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2w**

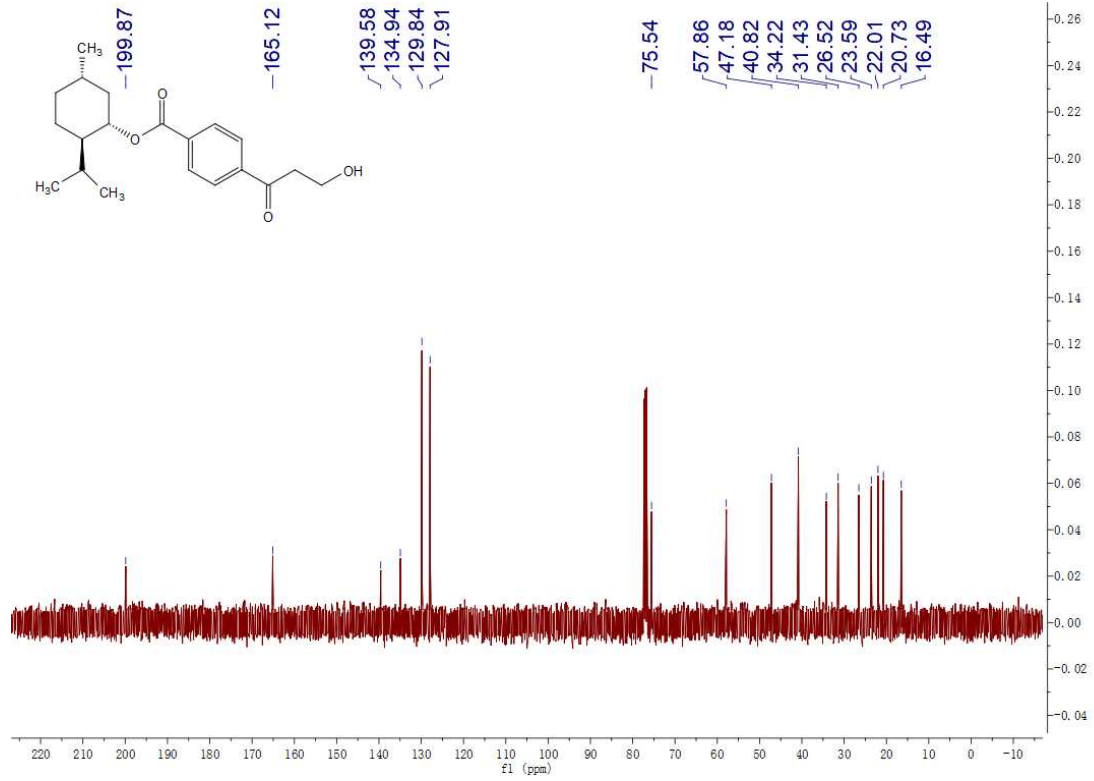


<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2w**

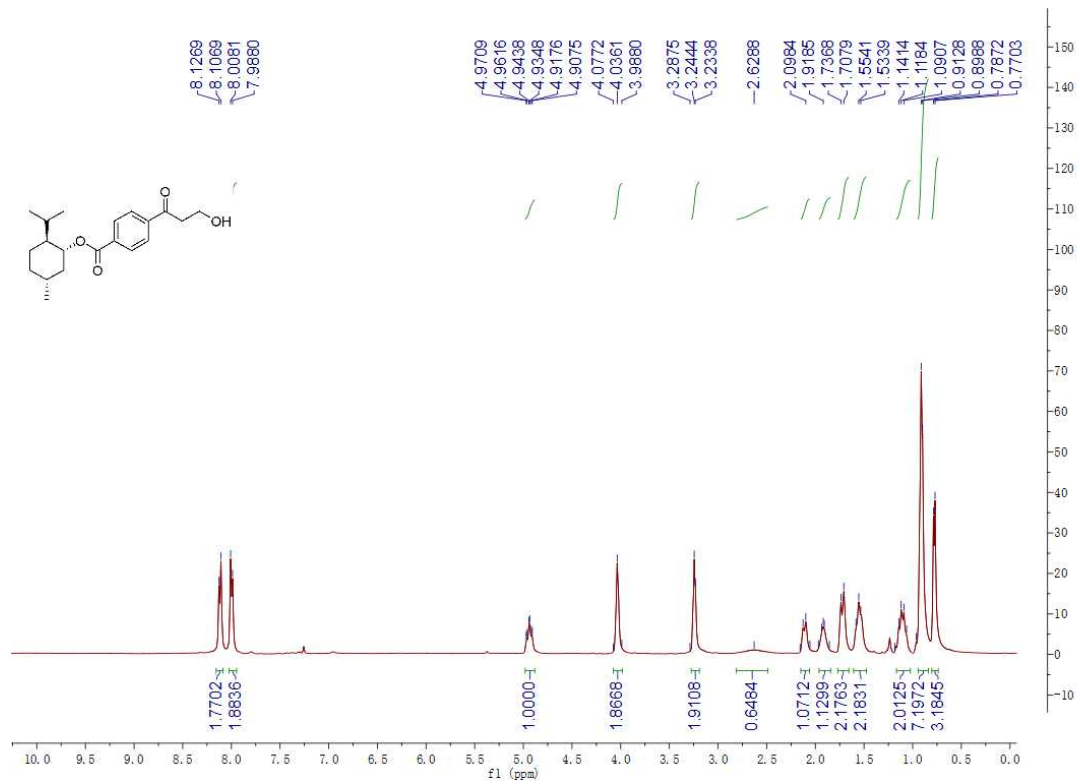




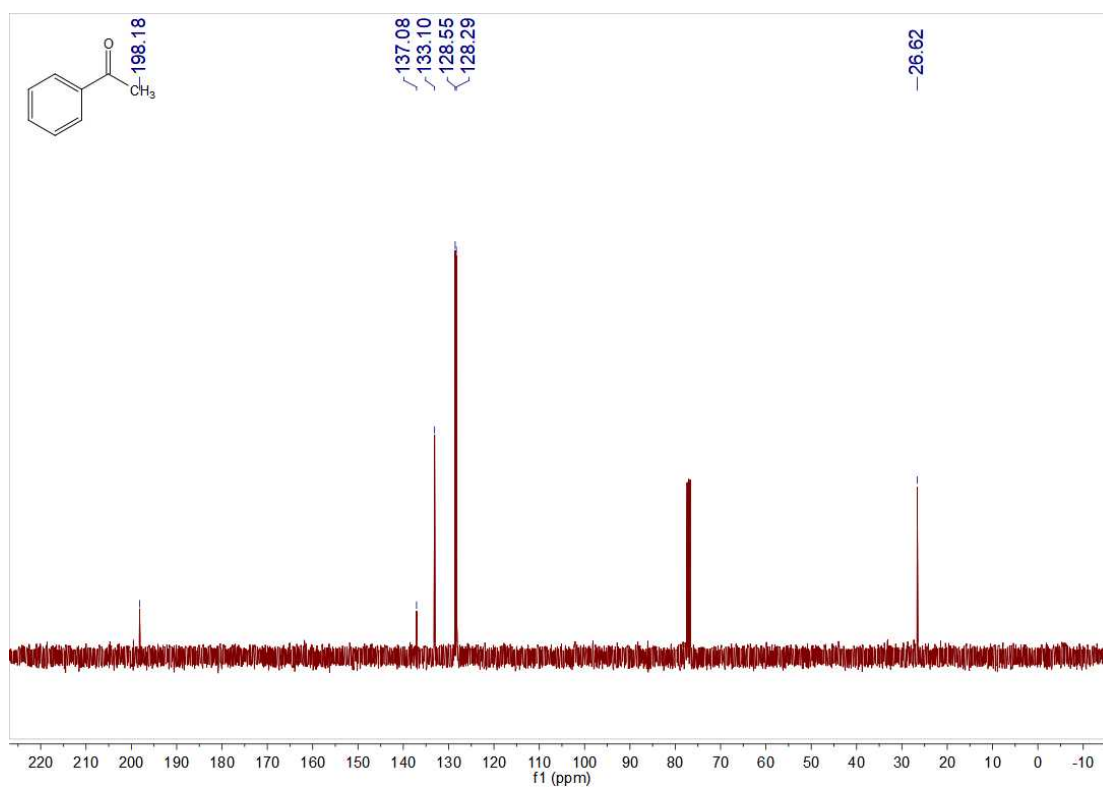
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **2x**



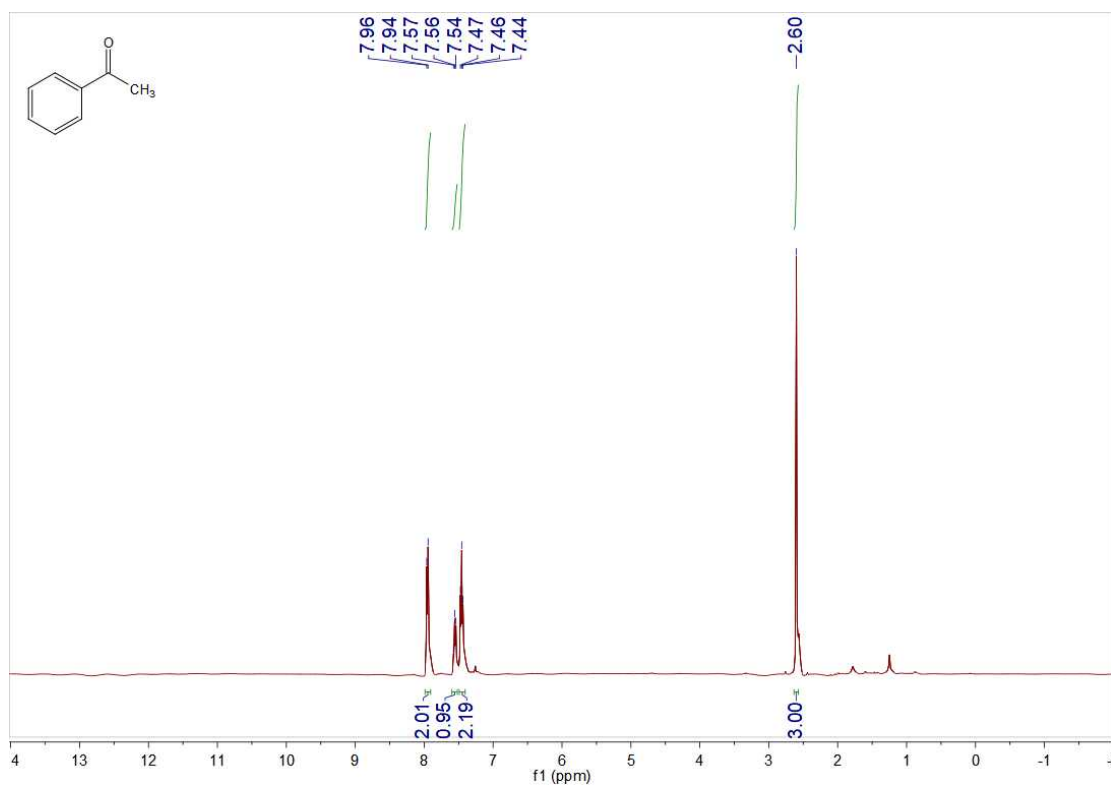
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **2x**



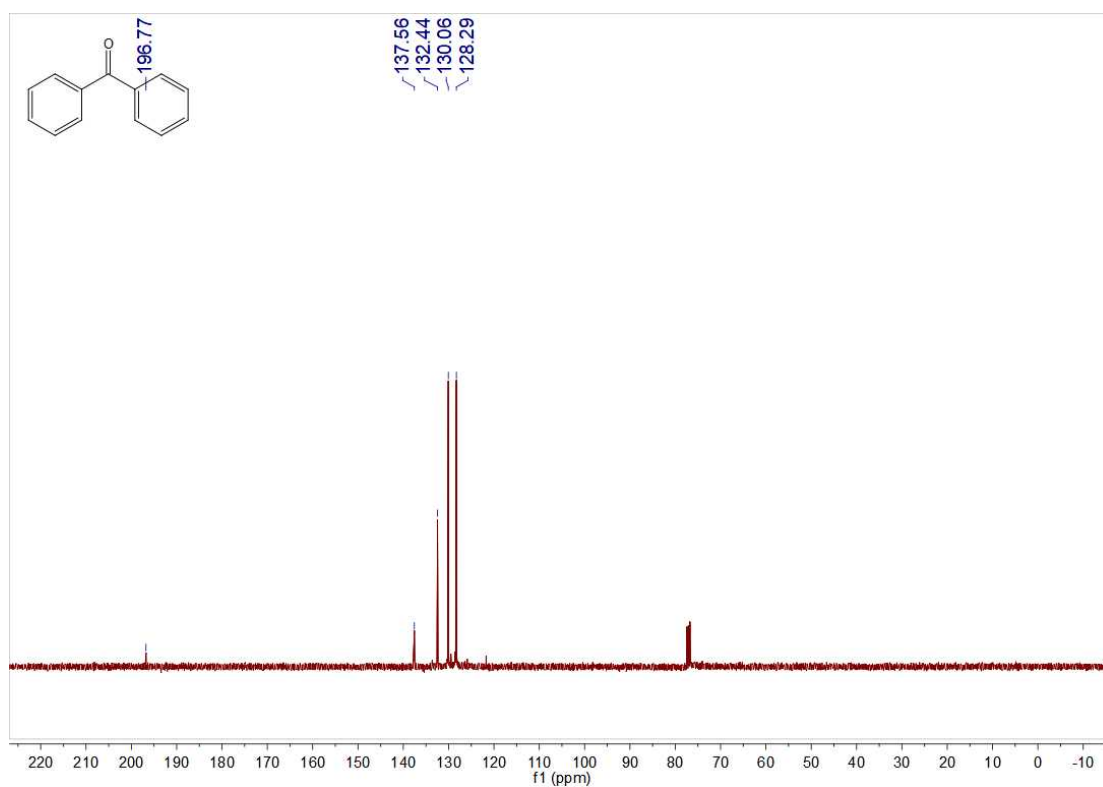
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ ) of compound **3a**



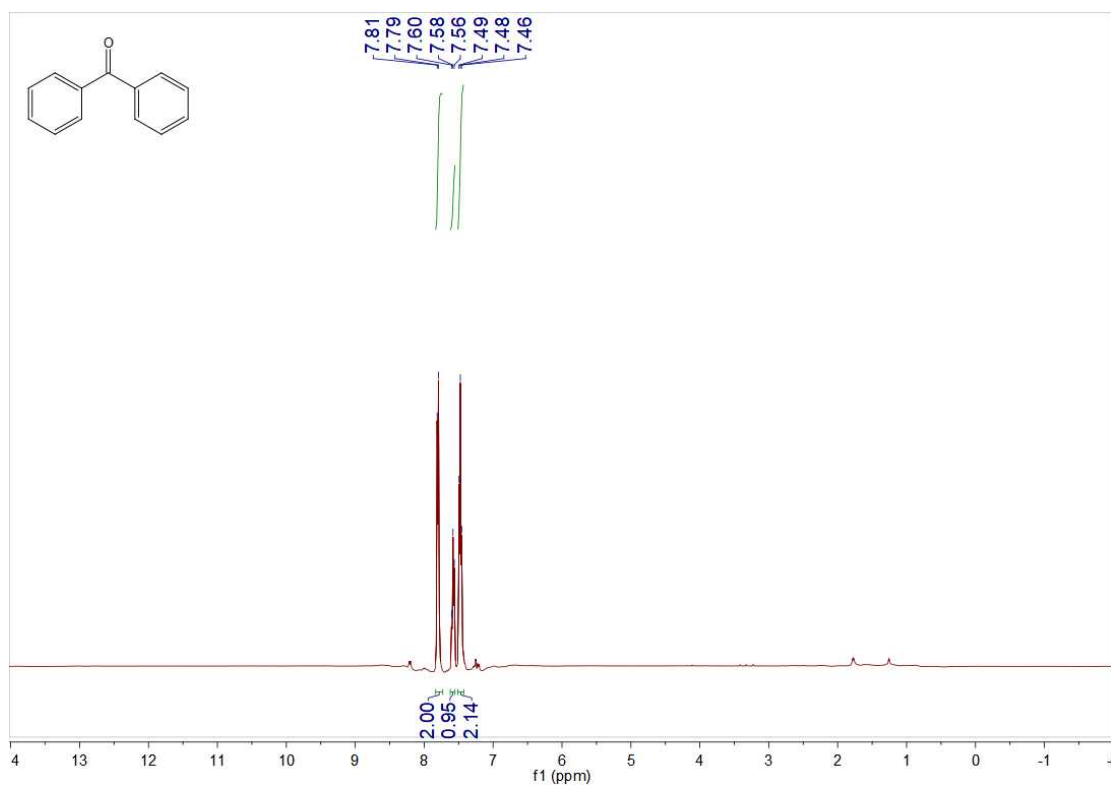
$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of compound **3a**



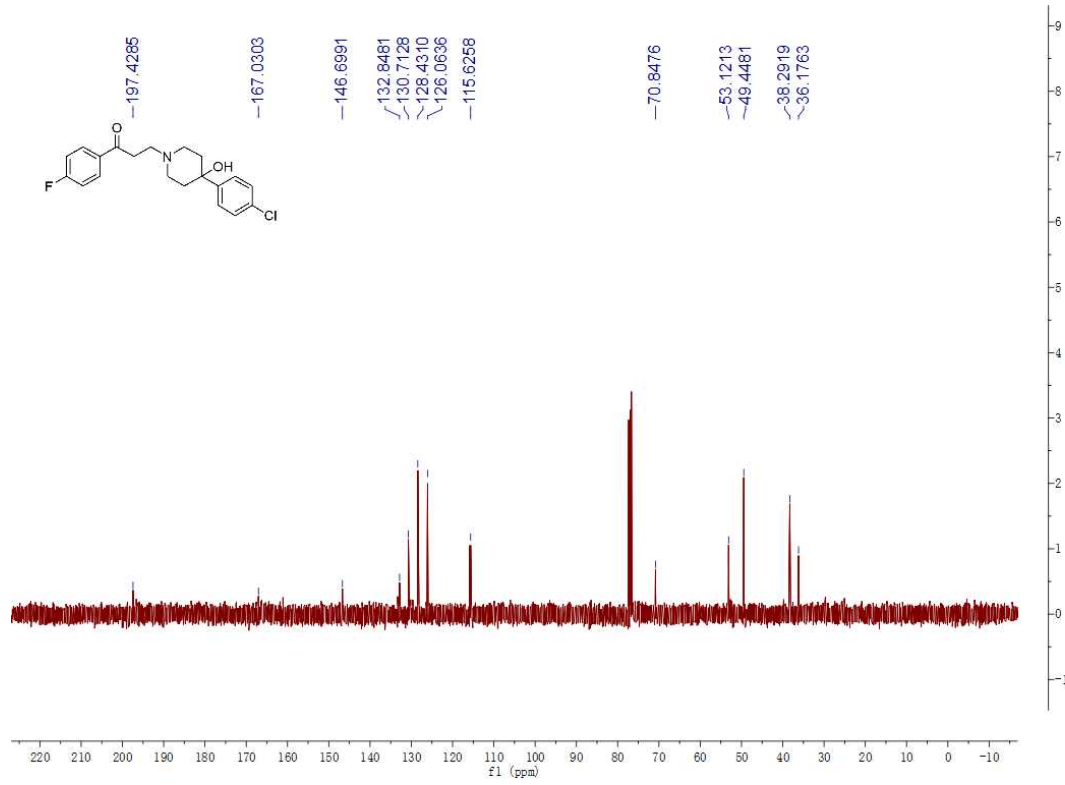
$^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ ) of compound **3b**



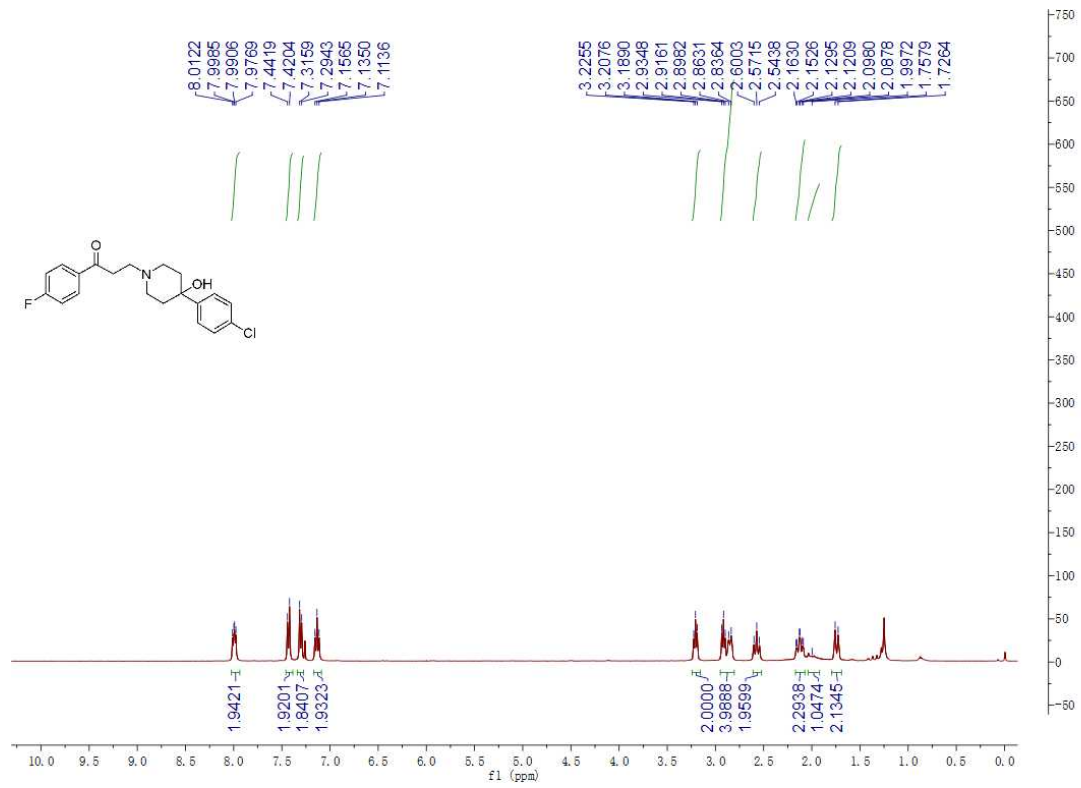
$^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of compound **3b**



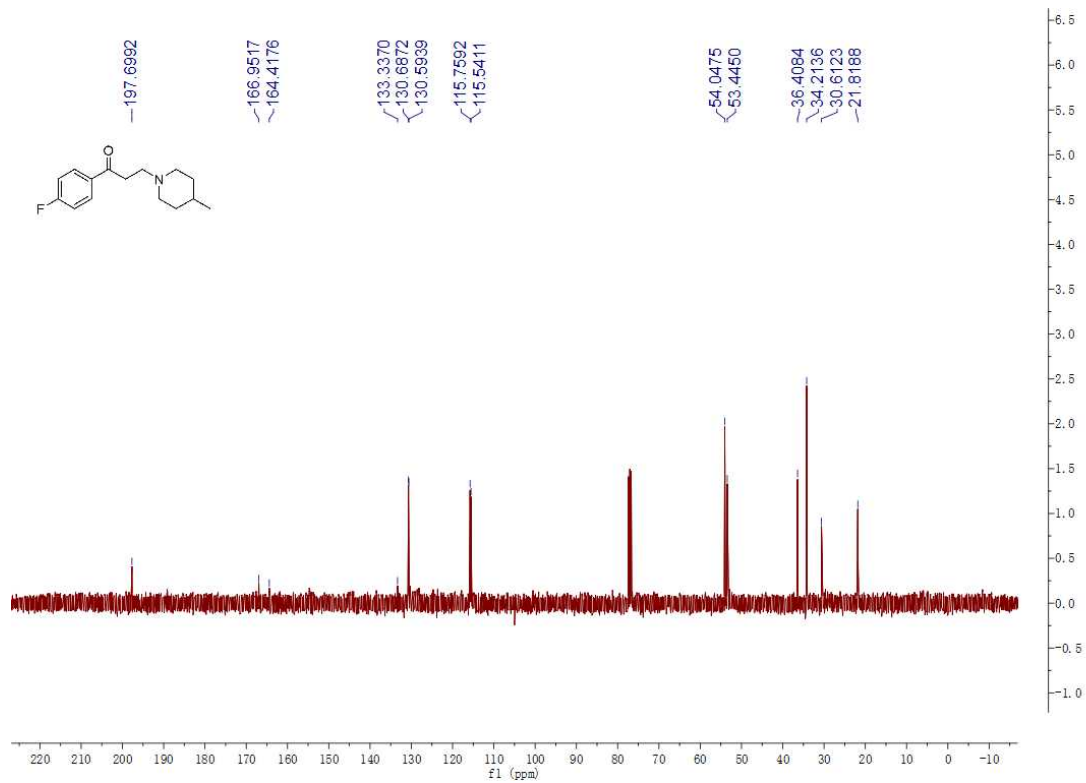
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **4a**



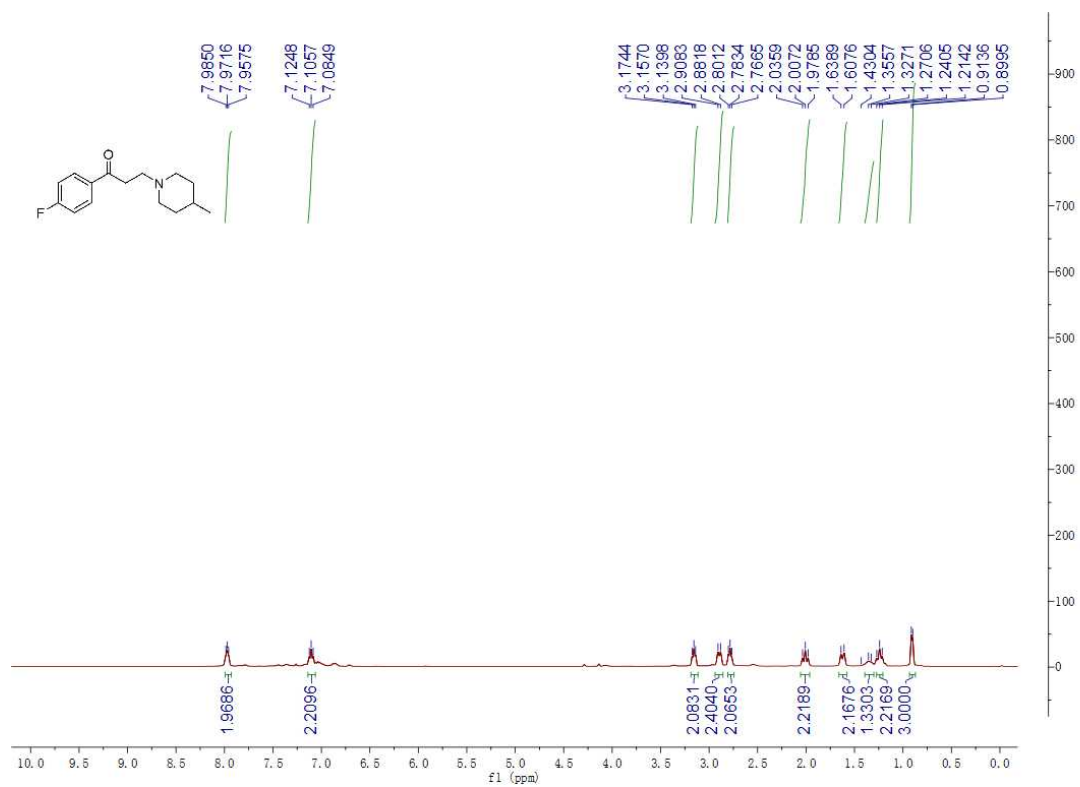
<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **4a**



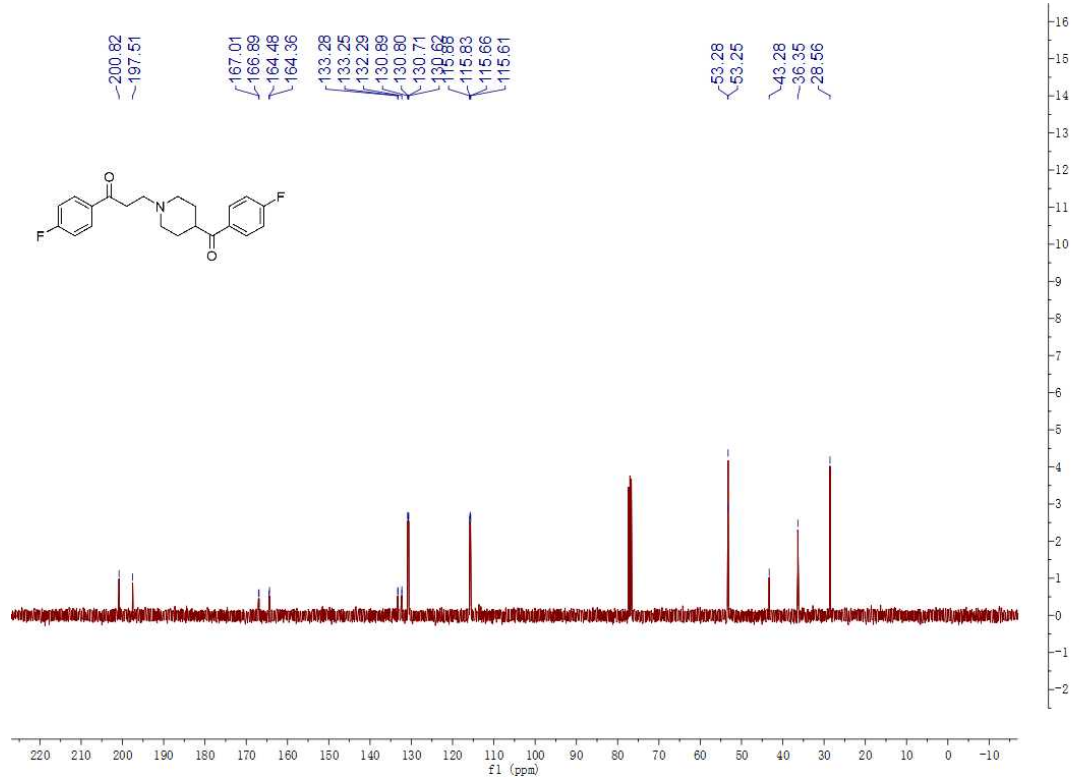
<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **4b**



<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound 4b



<sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **4c**



<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **4c**

