

Supporting Information

Organocatalytic Enantioselective Cross-Aldol Reaction of *o*-Hydroxyarylketones and Trifluoromethyl Ketones

Pei Wang,[†] Hong-Feng Li,[†] Jia-Zhen Zhao,[†] Zhi-Hong Du,[†] Chao-Shan Da^{†,‡,¶,*}

[†]Institute of Biochemistry and Molecular Biology, School of Life Sciences, Lanzhou University, Lanzhou 730000, China.

[‡]State Key Laboratory of Organic Chemistry, Lanzhou University, Lanzhou 730000, China.

[¶]Key Lab of Preclinical Study for New Drugs of Gansu Province, Lanzhou University, Lanzhou 730000, China.

Table of Contents

1. General.....	S2
2. Optimization of the Reaction Conditions.....	S2
3. The self disproportionation of enantiomer (<i>S</i>)- 4aa	S3
4. Preparation and characterization of catalysis 1	S5
5. General procedure of the catalytic cross-aldol reaction	S8
6. Gram-scale procedure for the preparation of (<i>S</i>)- 4ga	S8
7. Characterization of compounds 4	S8
8. Asymmetric cross-aldol reaction of acetophenone with trifluoroacetophenone ..	S26
9. Asymmetric cross-aldol reaction of <i>o</i> -hydroxyacetophenones with trichloroacetophenone.....	S27
10. Preparation and characterization of 6 and 8	S28
11. Determination of the absolute configuration by 5 X-ray crystallography	S31
12. Copies of NMR spectra.....	S36
13. Reference.....	S81

1. General

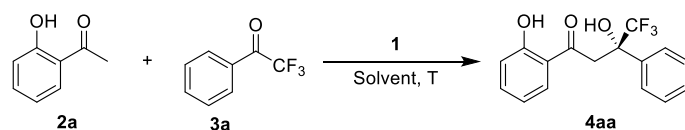
Instrumentations

All reactions were performed under an argon atmosphere and solvents were dried according to the established procedures ahead of use. The reactions were monitored by TLC (thin layer chromatography) method; column and preparative TLC purification were carried out using silica gel. Melting points were uncorrected and recorded on X-4 melting point apparatus. ^1H NMR and ^{13}C NMR spectra were measured on 400/600 MHz and 100/150 MHz spectrometers, and ^{19}F NMR spectra was measured on 376/564 MHz spectrometers (NMR in CDCl_3 with TMS as an internal standard) respectively, and recorded as ppm. HR-MS were measured with APEX II 47e mass spectrometer. Enantiomeric excess were decided with chiral HPLC equipped with a 2996 UV detector.

Materials

All commercial reagents were purchased with the analysis purity grade. They were used without further purification unless specified. All solvents used, mainly petroleum ether (PE) and ethyl acetate (EtOAc) were distilled. Anhydrous DCM and CH_3CN were freshly distilled from CaH_2 , THF, Et_2O and toluene were freshly distilled from sodium/benzophenone before use. Anhydrous methanol and ethanol were distilled from Mg.

2. Optimization of the Reaction Conditions^a



entry	3 (equiv) ^b	1 (mol%)	solvent ^c	°C	yield (%) ^d	ee (%) ^e
1	5.0	1a (10)	THF	rt	33	63
2	5.0	1a (10)	DCE	rt	55	88
3	5.0	1a (10)	Tol	rt	67	91
4	5.0	1a (10)	<i>n</i> -Hex	rt	49	88
5	2.5	1a (10)	Tol	rt	31	90
6	7.5	1a (10)	Tol	rt	53	90

^aReaction conditions: 0.25 mmol of **2a**, 0.5 mL of solvent. ^bEuivalent to the amount of **3a**. ^cDCE= $\text{ClCH}_2\text{CH}_2\text{Cl}$, *n*-Hex=*n*-hexane, and Tol=toluene. ^dIsolated yield. ^eDetermined by HPLC analysis on a chiral stationary phase.

3. The self disproportionation of enantiomer (*S*)-**4aa**

In the past years, it has been reported that chiral compounds containing trifluoromethyl group like (*S*)-**4aa** will possibly occur self-disproportionation.¹ We herein indeed found the self-proportionation of (*S*)-**4aa**. (*S*)-**4aa** with 89% ee was separated into two fractions with clear boundary using common HPLC (0.5 μ m silicon column). The two parts were separately collected. Chiral HPLC analysis showed that the less polar but big fraction has higher enantioselectivity of 92.2%, while the small and more polar fraction showed lower enantioselectivity of 79.8%. This phenomenon is displayed in the following chromatographical figures in detail. The ee was determined by chiral HPLC analysis. CHIRALPAK OJ-H; Hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 270.0 nm.

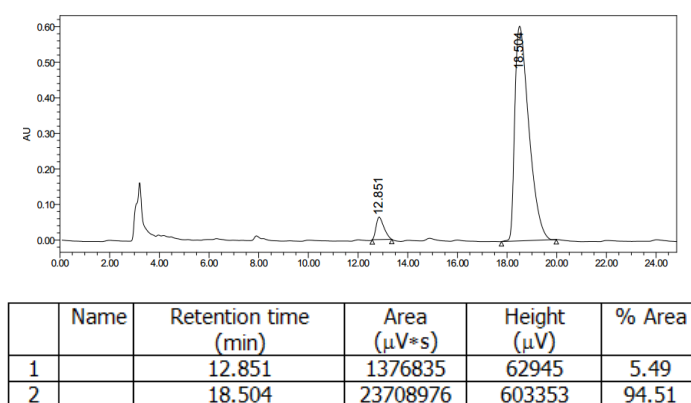


Figure S1. The HPLC chromatography of (*S*)-**4aa** of 89% ee.

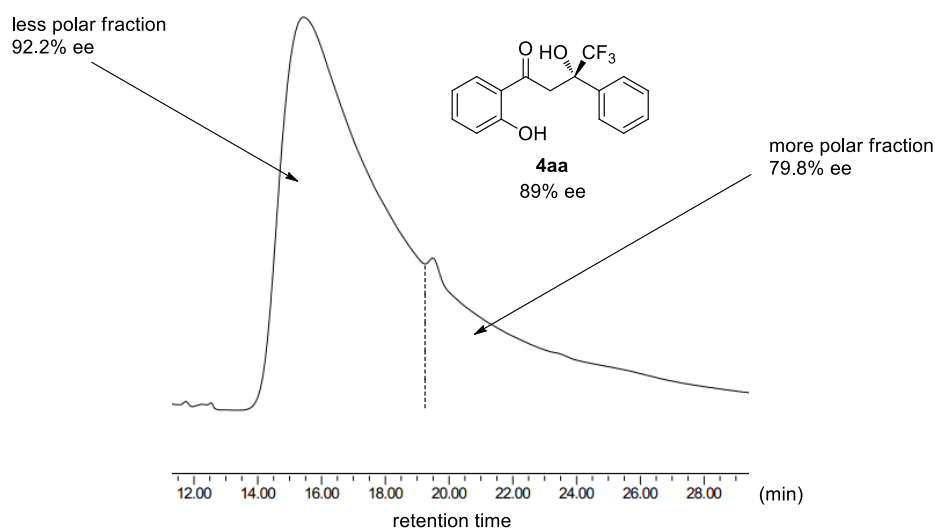


Figure S2. HPLC chromatography of (*S*)-**4aa** (89% ee) showing self-disproportionation. (*S*)-**4aa** was separated into two fractions with clear boundary. (Hexane/2-propanol = 29/1; flow rate 0.3 mL/min. HPLC was performed on a 25 x 0.4 cm i. d. silica gel, 5 μ m).

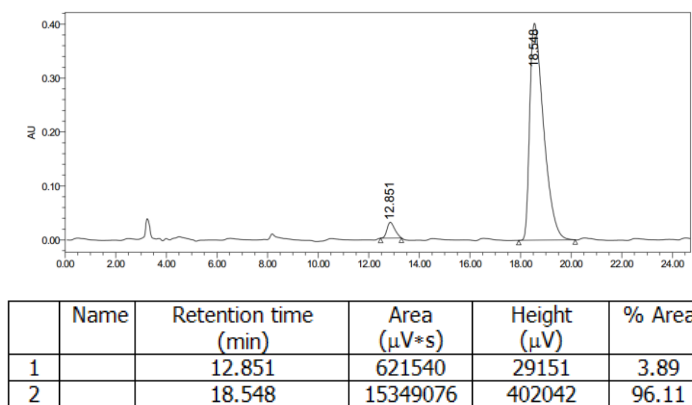


Figure S3. Chiral HPLC chromatography of the big fraction, showing 92.2% ee.

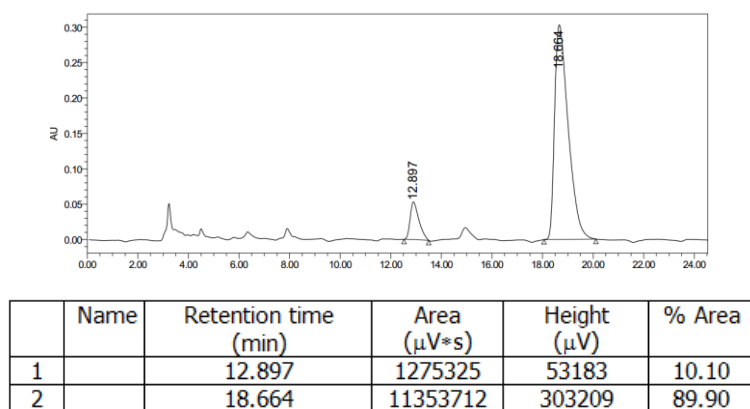
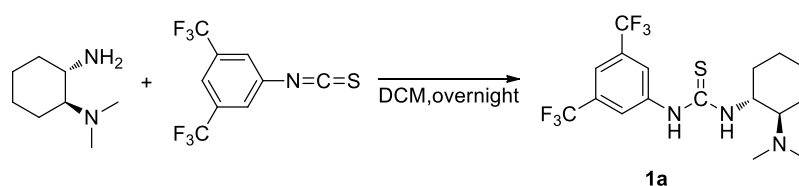


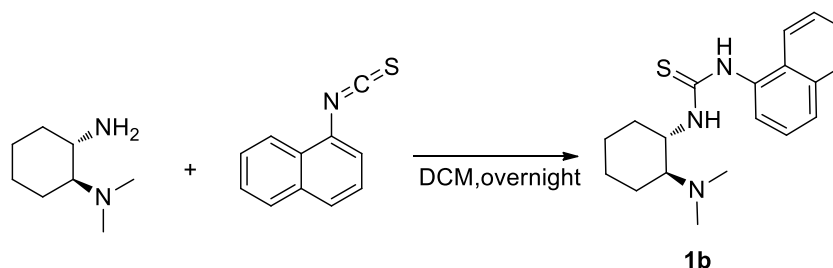
Figure S4. Chiral HPLC chromatography of the small fraction, showing 79.8% ee.

4. Preparation and characterization of catalysis 1

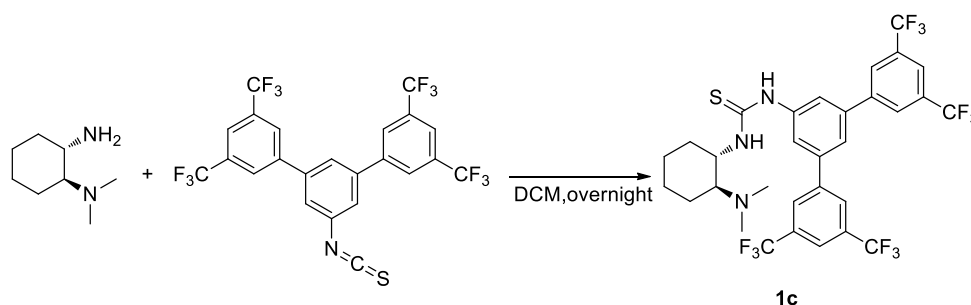


Bifunctional organocatalyst **1a** was prepared by the literature procedure.²

1a: white solid, mp 161.5-163.6°C, $[\alpha]_D^{26} = -35.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 7.98 (s, 2 H), 7.60 (s, 1 H), 3.52-3.59 (m, 1 H), 2.34-2.37 (m, 1 H), 2.29 (s, 6 H), 1.84-1.90 (m, 2 H), 1.69 (d, $J=12.0$ Hz, 1 H), 0.90-1.33 (m, 5 H); ¹⁹F NMR (CDCl₃, 564 MHz) δ -63.66 (s, 6 F).

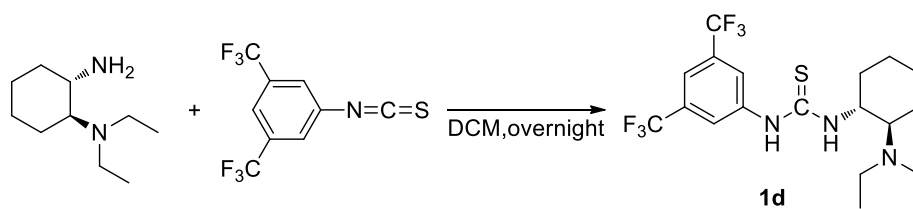


1b: white solid, mp 77.2-79.8°C, $[\alpha]_D^{26} = -48.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 8.62 (br, 1 H), 8.06 (b, $J=8.0$ Hz, 1 H), 7.81-7.89 (m, 2 H), 7.45-7.46 (m, 4 H), 6.87 (br, 1 H), 2.69 (b, $J=8.0$ Hz, 1 H), 2.15 (m, 1 H), 1.99 (s, 6 H), 1.73 (b, $J=12.0$ Hz, 2 H), 1.57 (d, $J=16.0$ Hz, 1 H), 1.22-1.32 (m, 2 H), 1.00-1.17 (m, 2 H), 0.68 (d, $J=12.0$ Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 180.9, 134.4, 132.7, 129.8, 128.1, 127.9, 126.8, 126.5, 125.3, 124.7, 122.8, 66.4, 56.0, 39.5, 32.4, 25.0, 24.4, 21.4; HRMS: (ESI+) m/z calcd for [C₁₉H₂₅N₃S + H⁺] 328.1842, found 328.1846.



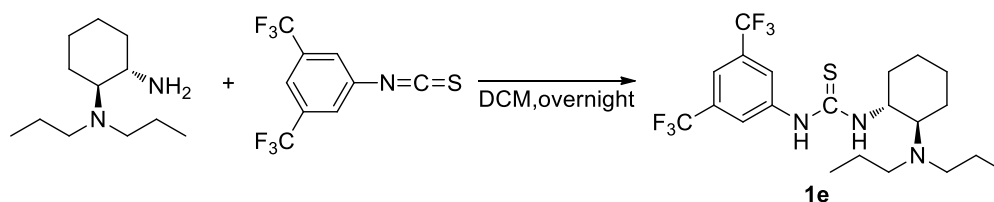
Bifunctional organocatalyst **1c** was prepared by the literature procedure.³

1c: white solid, mp 106.9-108.7°C, $[\alpha]_D^{21} = +6.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 7.98 (s, 4 H), 7.89 (s, 2 H), 7.73 (s, 2 H), 7.49 (s, 1 H), 4.10-4.33 (m, 1 H), 2.58 (br, 1 H), 2.29-2.34 (m, 6 H), 1.85-1.93 (m, 2 H), 1.70-1.74 (m, 1 H), 1.17-1.47 (m, 5 H); ¹⁹F NMR (CDCl₃, 564 MHz) δ -63.21 (s, 12 F).



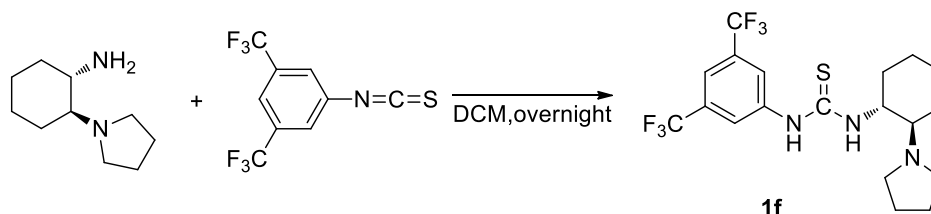
Bifunctional organocatalyst **1d** was prepared by the literature procedure.⁴

1d: white solid, mp 143.7-144.3°C, $[\alpha]_D^{26} = -25.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 7.84 (s, 2 H), 7.70 (s, 1 H), 3.77 (br, 1 H), 2.64 (s, 3 H), 2.39 (s, 3 H), 1.83-1.94 (m, 3 H), 1.19-1.36 (m, 11 H); ¹⁹F NMR (CDCl₃, 564 MHz) δ -63.44 (s, 6 F).



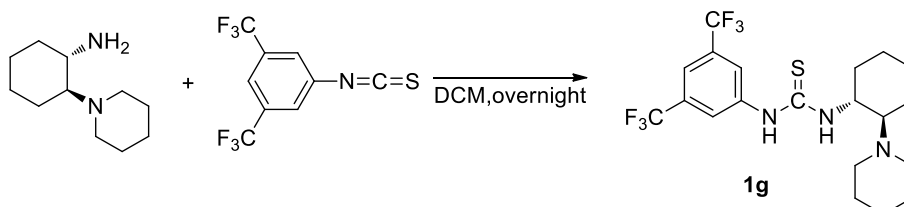
Bifunctional organocatalyst **1e** was prepared by the literature procedure.⁵

1e: white solid, mp 139.5-141.2°C, $[\alpha]_D^{26} = -18.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 7.74 (s, 2H), 7.68 (s, 1 H), 3.71 (s, 1 H), 2.85 (br, 1H), 2.26-2.47 (m, 5 H), 1.72-1.89 (m, 3 H), 1.11-1.31 (m, 8 H), 0.70-0.72 (m, 6 H); ¹⁹F NMR (CDCl₃, 564 MHz) δ -63.53 (s, 6 F).



Bifunctional organocatalyst **1f** was prepared by the literature procedure.⁶

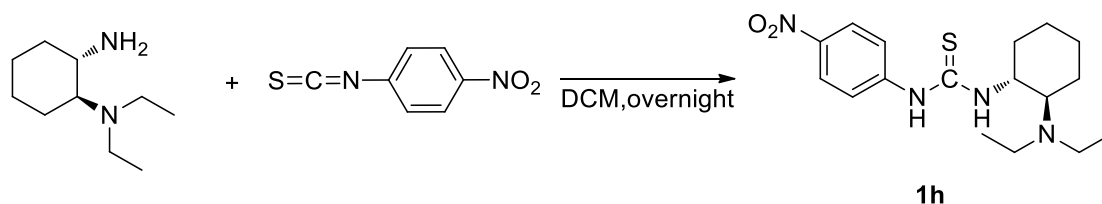
1f: white solid, mp 116.4-118.2°C, $[\alpha]_D^{26} = +3.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 9.89 (br, 1 H), 8.17 (s, 2 H), 7.54 (s, 2 H), 4.64 (s, 1 H), 3.29-3.48 (m, 4 H), 2.40 (d, *J*=12.0 Hz, 1 H), 2.00-2.14 (m, 5 H), 1.85-1.87 (m, 1 H), 1.35-1.50 (m, 4 H), 0.79-0.89 (m, 3 H); ¹⁹F NMR (CDCl₃, 564 MHz) δ -63.46 (s, 6 F).



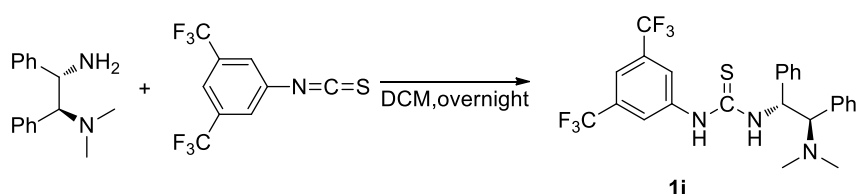
Bifunctional organocatalyst **1g** was prepared by the literature procedure.⁶

1g: white solid, mp 148.4-150.5°C, $[\alpha]_D^{26} = -23.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 7.79 (s, 2 H), 7.68 (s, 1 H), 3.74 (br, 1 H), 2.58-2.68 (m, 4 H), 2.41 (s, 2

H), 1.73-1.89 (m, 3 H), 1.18-1.29 (m, 5 H), 0.93 (s, 6 H); ^{19}F NMR (CDCl_3 , 564 MHz) δ -63.44 (s, 6 F).

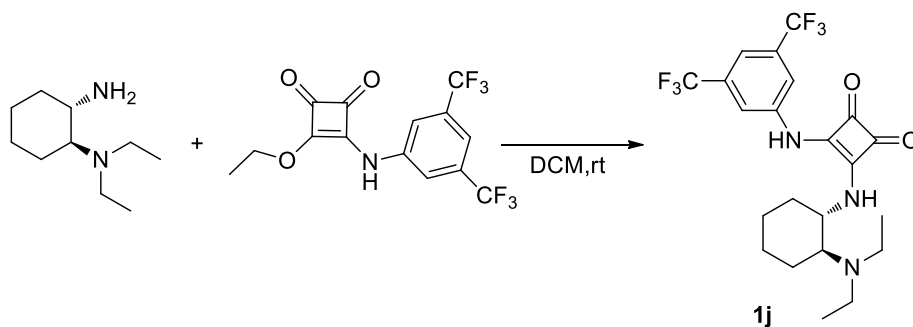


1h: yellow solid, mp 109.9-111.7°C, $[\alpha]_{\text{D}}^{26} = -41.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 8.19 (d, $J=8.0$ Hz, 2 H), 7.47 (d, $J=8.0$ Hz, 2 H), 3.84 (t, $J=12.0$ Hz, 1 H), 2.53-2.75 (m, 4 H), 2.32-2.39 (m, 2 H), 1.70-1.89 (m, 3 H), 1.06-1.23 (m, 4 H), 0.93-0.96 (m, 6 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 197.8, 145.4, 130.5, 129.7, 126.9, 100.0, 44.9, 34.1, 31.2, 26.9, 26.0, 25.3, 15.7; HRMS: (ESI+) m/z calcd for $[\text{C}_{17}\text{H}_{26}\text{N}_4\text{O}_2\text{S}_1 + \text{H}^+]$ 351.1849, found 351.1855.



Bifunctional organocatalyst **1i** was prepared by the literature procedure.⁷

1i: white solid, mp 83.0-85.6°C, $[\alpha]_{\text{D}}^{26} = -157.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 8.29 (br, 1 H), 7.67-7.72 (m, 3 H), 7.25-7.26 (m, 3 H), 7.15 (s, 5 H), 5.36 (br, 1 H), 3.81 (d, $J=12.0$ Hz, 1 H), 2.21 (s, 6 H); ^{19}F NMR (CDCl_3 , 564 MHz) δ -63.42 (s, 6 F).



1j: white solid, mp 232.5-233.1°C, $[\alpha]_{\text{D}}^{21} = -16.2$ (c 0.50, EtOH); ^1H NMR (CDCl_3 , 400 MHz) δ 10.15 (s, 1 H), 8.09 (s, 2 H), 7.65 (s, 1 H), 7.59 (br, 1 H), 3.92 (s, 1 H), 2.52-2.58 (m, 2 H), 2.42-2.45 (m, 1 H), 2.27-2.32 (m, 2 H), 2.02-2.09 (m, 1 H), 1.69-1.83 (m, 3 H), 1.17-1.40 (m, 5 H), 0.86-0.89 (m, 6 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 194.2, 192.7, 143.2, 126.4, 123.7, 119.8, 65.4, 56.7, 26.7, 26.0, 16.0; ^{19}F NMR (CDCl_3 , 564 MHz) δ -63.66 (s, 6 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{22}\text{H}_{25}\text{F}_6\text{N}_3\text{O}_2 + \text{H}^+]$ 478.1924, found 478.1929.

5. General procedure of the catalytic cross-aldol reaction

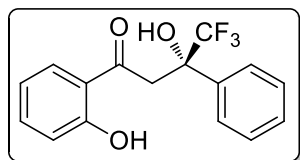
To *o*-hydroxy arylketones **2** (1.25 mmol) and the catalyst **1c** (7.7 mg, 0.0175 mmol) in dry toluene (0.5 mL) was added trifluoromethyl ketones **3** (0.25 mmol) at 0 °C. The mixture was stirred for 3 to 6 days at 0 °C to complete checked by thin layer chromatography. The mixture was directly submitted to flash silica gel column chromatography (petroleum ether:ethyl acetate = 20:1 to 5:1) to furnish the product **4**.

6. Gram-scale procedure for the preparation of (*S*)-4ga.

To 1-(5-bromo-2-hydroxyphenyl)ethanone **2g** (15.0 mmol, 3.225 g) and the catalyst **1d** (92.4 mg, 0.21 mmol) in dry toluene (6.0 mL) was added trifluoroacetophenone **3a** (3.0 mmol, 430 μ L) at 0 °C. The mixture was stirred for 6 days at 0 °C to complete checked by thin layer chromatography. The mixture was directly submitted to flash silica gel column chromatography (petroleum ether:ethyl acetate = 20:1 to 5:1) to furnish the product (*S*)-**4ga** (white solid, 1.12 g, 96% yield, 94% ee).

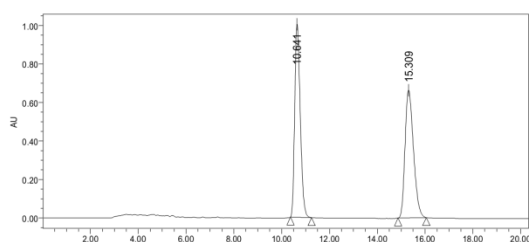
7. Characterization of compounds 4.

(*S*)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)-3-phenylbutan-1-one (**4aa**)⁸

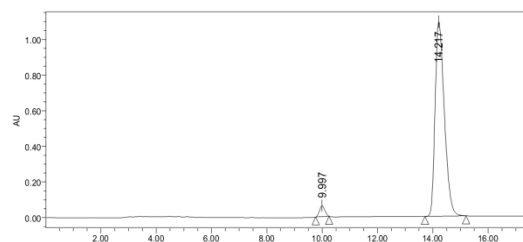


64.8 mg, 84% yield, white solid, mp 107.9-108.7 °C, $[\alpha]_D^{26} = +107.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.50 (s, 1 H), 7.82 (d, *J*=4.0 Hz, 1 H), 7.52-7.56 (m, 3 H), 7.34-7.41 (m, 3 H), 6.98 (t, *J*=8.0 Hz, 2 H), 5.19 (s, 1 H), 4.13 (d, *J*=16.0 Hz, 1 H), 3.67 (d, *J*=16.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 205.8, 164.3, 139.3, 138.7, 131.3, 130.4, 130.0, 127.7, 121.0, 120.7, 120.5, 77.8, 41.3; ¹⁹F NMR (CDCl₃, 564 MHz) δ -81.01 (s, 3 F).

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 10.0 min (minor) and 14.2 min (major).

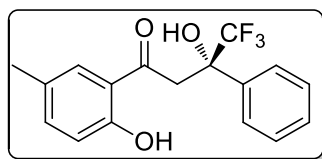


	Name	Retention time (min)	Area (μ V*s)	Height (μ V)	% Area
1		10.641	16105547	1005883	49.83
2		15.309	16216784	664737	50.17



	Name	Retention time (min)	Area (μ V*s)	Height (μ V)	% Area
1		9.997	820056	60621	3.14
2		14.217	25329098	1090788	96.86

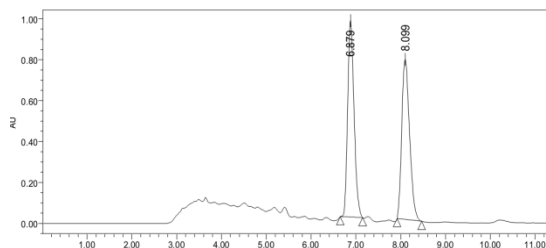
(*S*)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxy-5-methylphenyl)-3-phenylbutan-1-one (**4ba**)



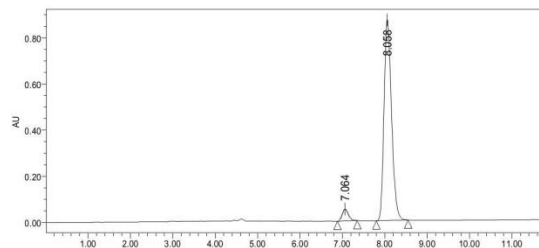
65.6 mg, 81% yield, white solid, mp 113.1-113.6 °C, $[\alpha]_D^{26} = +138.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.35 (s, 1 H), 7.56-7.61 (m, 3 H), 7.34-7.38 (m, 4 H), 6.87 (d, *J*=8.0 Hz, 1 H), 5.23 (s, 1 H), 4.13 (d, *J*=16.0 Hz, 1 H), 3.64 (d, *J*=16.0 Hz, 1 H), 2.36 (s, 3 H); ¹³C NMR (CDCl₃, 100 MHz) δ 204.1, 160.8, 139.0, 137.3, 129.2, 128.8, 128.5, 126.2, 125.8,

123.0, 118.8, 71.0, 39.8, 20.5; ^{19}F NMR (CDCl_3 , 376 MHz) δ -80.14 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{17}\text{H}_{15}\text{F}_3\text{O}_3 + \text{Na}^+]$ 347.0866, found 347.0871.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 7.1 min (minor) and 8.1 min (major).

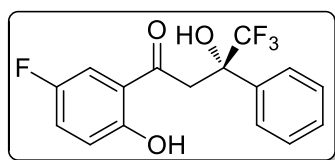


	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		6.879	9489801	964226	50.09
2		8.099	9456655	783776	49.91



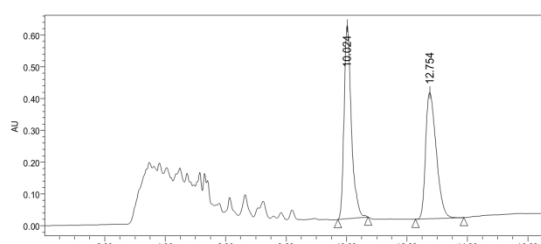
	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		7.064	395762	44634	3.57
2		8.058	10696790	874527	96.43

(S)-4,4,4-trifluoro-1-(5-fluoro-2-hydroxyphenyl)-3-hydroxy-3-phenylbutan-1-one (4ca)

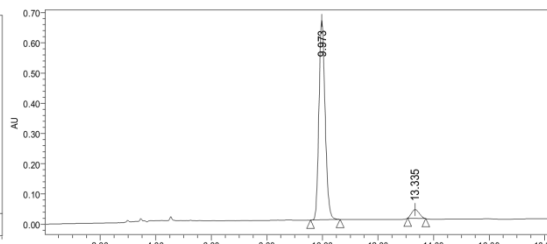


74.6 mg, 91% yield, white solid, mp 120.1-120.8 $^{\circ}\text{C}$, $[\alpha]_{\text{D}}^{26} = +90.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.27 (s, 1 H), 7.58-7.59 (m, 2 H), 7.46-7.49 (m, 1 H), 7.28-7.42 (m, 3 H), 7.27-7.32 (m, 1 H), 6.94-6.97 (m, 1 H), 5.01 (s, 1 H), 4.05 (d, $J=16.0$ Hz, 1 H), 3.64 (d, $J=16.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 203.4, 159.1, 156.1, 153.7, 137.0, 129.0, 128.6, 126.1, 125.8, 125.5, 122.8, 120.6, 120.5, 118.5, 114.6, 114.4, 76.3, 40.3; ^{19}F NMR (CDCl_3 , 376 MHz) δ -80.11 (s, 3 F), -122.52 (s, 1 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{16}\text{H}_{12}\text{F}_4\text{O}_3 + \text{Na}^+]$ 351.0615, found 351.0620.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 10.0 min (major) and 13.3 min (minor).

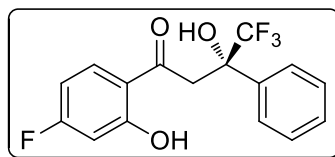


	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		10.024	10157877	609113	51.27
2		12.754	9655445	397856	48.73



	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		9.973	10239941	661418	94.84
2		13.335	557053	28857	5.16

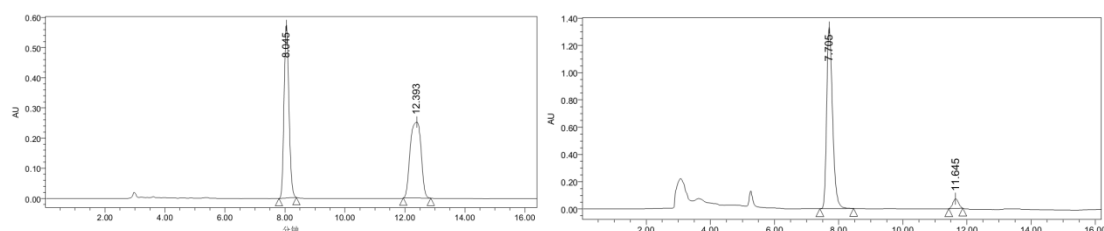
(S)-4,4,4-trifluoro-1-(4-fluoro-2-hydroxyphenyl)-3-hydroxy-3-phenylbutan-1-one (4da)



70.6 mg, 86% yield, white solid, mp 109.4-109.9 $^{\circ}\text{C}$, $[\alpha]_{\text{D}}^{21} = +145.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.81 (s, 1 H), 7.82-7.86 (m, 1 H), 7.57-7.59 (m, 2 H),

7.37-7.39 (m, 3 H), 6.63-6.72 (m, 2 H), 5.12 (s, 1 H), 4.04 (d, $J=16.0$ Hz, 1 H), 3.63 (d, $J=16.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 203.0, 169.5, 166.9, 166.6, 137.1, 132.5, 132.3, 128.9, 128.6, 126.2, 116.5, 108.3, 108.0, 105.7, 105.4, 40.1; ^{19}F NMR (CDCl_3 , 376 MHz) δ -80.09 (s, 3 F), -96.10 (s, 1 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{16}\text{H}_{12}\text{F}_4\text{O}_3 + \text{Na}^+]$ 351.0615, found 351.0613.

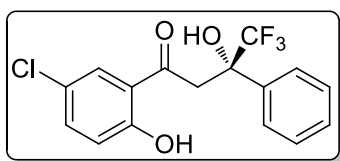
The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 258.7 nm; retention time: 7.7 min (major) and 11.6 min (minor).



	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		8.045	6354242	574164	50.05
2		12.393	6342045	252361	49.95

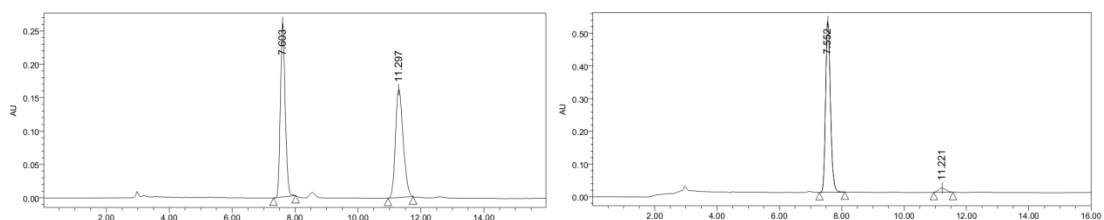
	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		7.705	16857288	1335116	95.06
2		11.645	876615	71251	4.94

(S)-1-(5-chloro-2-hydroxyphenyl)-4,4,4-trifluoro-3-hydroxy-3-phenylbutan-1-one (4ea)



86.0 mg, >99% yield, white solid, mp 139.6-140.4 °C, $[\alpha]_{\text{D}}^{26} = +193.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.40 (s, 1 H), 7.75 (s, 1 H), 7.57-7.59 (m, 2 H), 7.48 (d, $J=8.0$ Hz, 1 H), 7.38-7.40 (m, 3 H), 6.94 (d, $J=8.0$ Hz, 1 H), 4.95 (s, 1 H), 4.08 (d, $J=20.0$ Hz, 1 H), 3.65 (d, $J=16.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 203.4, 161.3, 137.7, 136.9, 129.0, 128.8, 128.6, 126.1, 125.7, 124.3, 122.9, 120.7, 119.8, 76.3, 40.4; ^{19}F NMR (CDCl_3 , 376 MHz) δ -80.11 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{16}\text{H}_{12}\text{ClF}_3\text{O}_3 + \text{Na}^+]$ 367.0319, found 367.0320.

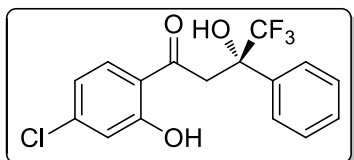
The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 255.1 nm; retention time: 10.0 min (major) and 13.3 min (minor).



	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		7.603	2765190	262140	50.07
2		11.297	2757671	161612	49.93

	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		7.552	5628202	523067	96.33
2		11.221	214237	12711	3.67

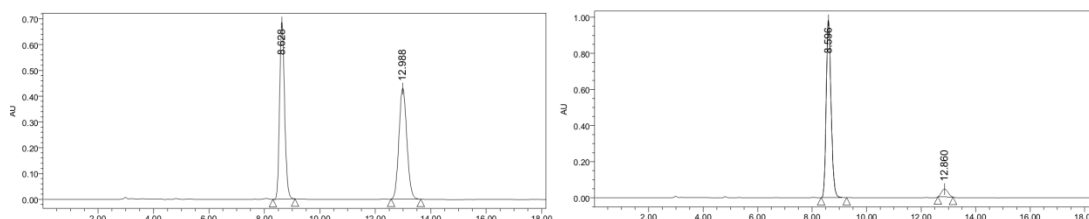
(S)-1-(4-chloro-2-hydroxyphenyl)-4,4,4-trifluoro-3-hydroxy-3-phenylbutan-1-one (4fa)



77.4 mg, 90% yield, white solid, mp 126.5-127.4 °C, $[\alpha]_{\text{D}}^{26} = +147.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400

MHz) δ 11.62 (s, 1 H), 7.74 (d, $J=8.0$ Hz, 1 H), 7.57-7.58 (m, 2 H), , 7.37-7.39 (m, 3 H), 6.94-6.99 (m, 3H), 5.05 (s, 1 H), 4.06 (d, $J=20.0$ Hz, 1 H), 3.64 (d, $J=20.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 203.5, 163.4, 143.9, 137.0, 130.8, 129.0, 128.6, 126.1, 123.0, 119.1, 40.2; ^{19}F NMR (CDCl_3 , 376 MHz) δ -80.11 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{16}\text{H}_{12}\text{ClF}_3\text{O}_3 + \text{H}^+]$ 345.0500, found 345.0502.

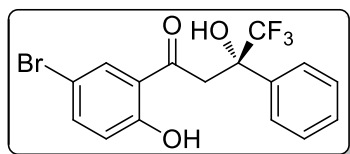
The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 265.8 nm; retention time: 8.6 min (major) and 12.9 min (minor).



	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		8.628	8523641	688093	49.94
2		12.988	8543703	430187	50.06

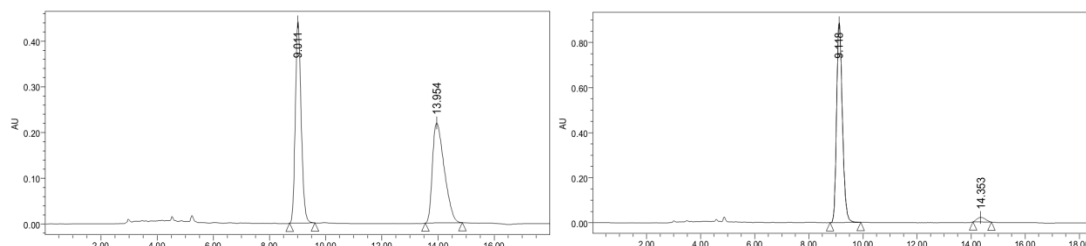
	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		8.596	1219054	984907	94.35
2		12.860	730613	43807	5.65

(S)-1-(5-bromo-2-hydroxyphenyl)-4,4,4-trifluoro-3-hydroxy-3-phenylbutan-1-one (4ga)



93.4 mg, 96% yield, white solid, mp 114.5-114.8 °C, $[\alpha]_{\text{D}}^{26} = +198.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.43 (s, 1 H), 7.90 (s, 1 H), 7.58-7.63 (m, 3 H), 7.39-7.41 (m, 3 H), 6.89 (d, $J=8.0$ Hz, 1 H), 4.93 (s, 1 H), 4.10 (d, $J=16.0$ Hz, 1 H), 3.65 (d, $J=16.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 203.3, 171.7, 161.7, 140.5, 136.9, 131.8, 129.0, 128.6, 126.1, 121.1, 120.3, 111.1, 40.3; ^{19}F NMR (CDCl_3 , 376 MHz) δ -80.11 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{16}\text{H}_{12}\text{BrF}_3\text{O}_3 + \text{Na}^+]$ 410.9814, found 410.9821.

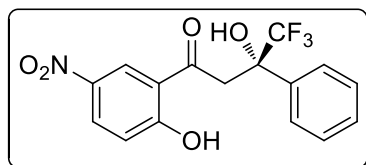
The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 256.3 nm; retention time: 9.1 min (major) and 14.4 min (minor).



	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		9.011	6379391	440968	50.02
2		13.954	6373776	218724	49.98

	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		9.118	13213775	888033	96.72
2		14.353	447964	20462	3.28

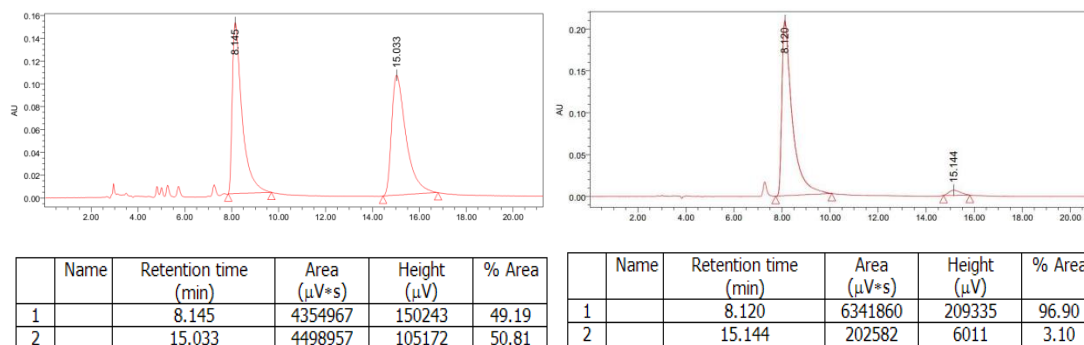
(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxy-5-nitrophenyl)-3-phenylbutan-1-one (4ha)



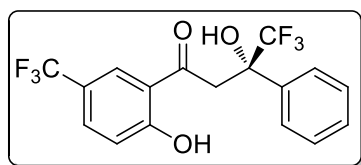
88.7 mg, >99% yield, slightly yellow solid, mp 136.1-136.6 °C, $[\alpha]_{\text{D}}^{26} = +123.0$ (c 1.0, CHCl_3); ^1H

NMR (CDCl₃, 400 MHz) δ 12.08 (s, 1 H), 8.77 (s, 1 H), 8.38-8.41 (m, 1 H), 7.58-7.60 (m, 2 H), 7.39-7.42 (m, 3 H), 7.10 (d, J =8.0 Hz, 1 H), 4.68 (s, 1 H), 4.19 (d, J =20.0 Hz, 1 H), 3.78 (d, J =20.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 203.8, 167.1, 139.9, 136.6, 132.0, 129.2, 128.7, 126.4, 126.0, 120.2, 118.1, 41.0; ¹⁹F NMR (CDCl₃, 376 MHz) δ -79.94 (s, 3 F); HRMS: (ESI+) m/z calcd for [C₁₆H₁₂F₃NO₅ + H⁺] 356.0740, found 356.0738.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 297.1 nm; retention time: 8.1 min (major) and 15.1 min (minor).

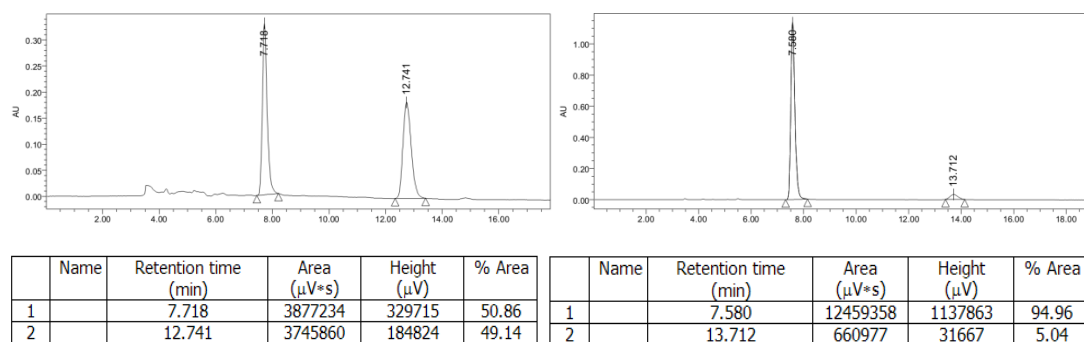


(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxy-5-(trifluoromethyl)phenyl)-3-phenylbutan-1-one (4ia)

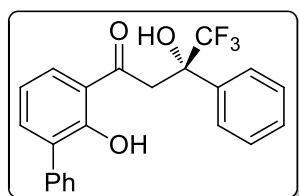


80.3 mg, 88% yield, white solid, mp 153.0-154.0 °C, $[\alpha]_D^{21}$ = +150.0 (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.78 (s, 1 H), 8.03 (s, 1 H), 7.58-7.60 (m, 2 H), 7.38-7.40 (m, 3 H), 7.08 (d, J =8.0 Hz, 1 H), 4.84 (s, 1 H), 4.13 (d, J =16.0 Hz, 1 H), 3.71 (d, J =16.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 203.9, 165.0, 136.8, 134.0, 129.1, 128.7, 127.3, 126.1, 120.1, 118.6, 40.6; ¹⁹F NMR (CDCl₃, 376 MHz) δ -61.81 (s, 3 F), -80.05 (s, 3 F); HRMS: (ESI+) m/z calcd for [C₁₇H₁₂F₆O₃ + H⁺] 379.0763, found 379.0765.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 251.6 nm; retention time: 7.6 min (major) and 13.7 min (minor).



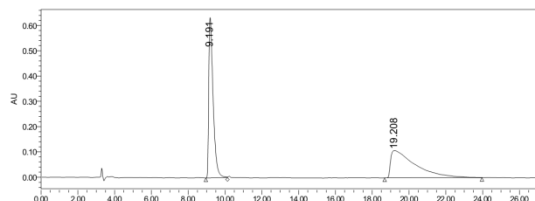
(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxy-[1,1'-biphenyl]-3-yl)-3-phenylbutan-1-one (4ja)



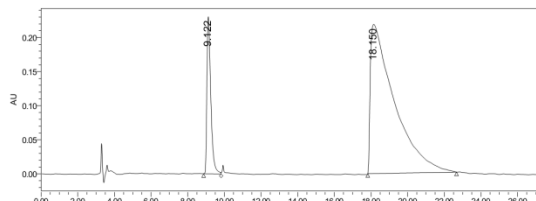
39.1 mg, 40% yield, white solid, mp 123.7-125.5 °C, $[\alpha]_D^{21}$ = +27.0 (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ

12.02 (s, 1 H), 7.84 (d, $J=8.0$ Hz, 1 H), 7.60-7.62 (m, 3 H), 7.50-7.52 (m, 2 H), 7.33-7.43 (m, 6 H), 7.05 (t, $J=8.0$ Hz, 1 H), 5.18 (s, 1 H), 4.18 (d, $J=20.0$ Hz, 1 H), 3.72 (d, $J=16.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 204.7, 160.3, 138.7, 137.2, 136.4, 131.8, 129.3, 129.2, 128.9, 128.6, 128.2, 127.7, 126.2, 119.4, 128.6, 40.2; ^{19}F NMR (CDCl_3 , 376 MHz) δ -80.11 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{22}\text{H}_{17}\text{F}_3\text{O}_3 + \text{H}^+]$ 387.1203, found 387.1201.

The ee was determined by HPLC analysis. CHIRALPAK IC; Hexane/DCM = 75/25; flow rate 1.0 mL/min; 251.6 nm; retention time: 9.1 min (minor) and 18.2 min (major).

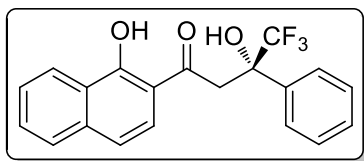


	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		9.191	10454983	633974	50.92
2		19.208	10077182	108248	49.08



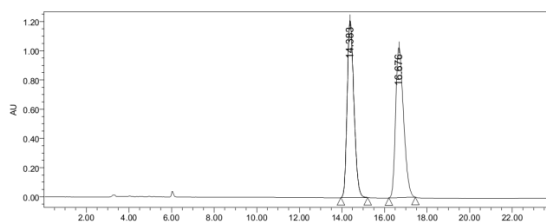
	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		9.122	3410071	230542	14.62
2		18.150	19908082	218779	85.38

(S)-4,4,4-trifluoro-3-hydroxy-1-(1-hydroxynaphthalen-2-yl)-3-phenylbutan-1-one (4ka)

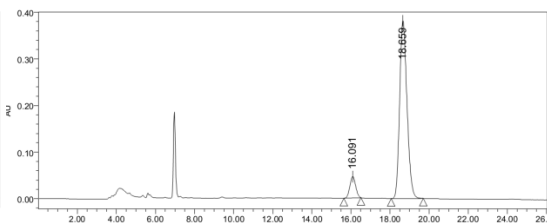


45.1 mg, 50% yield, yellow solid, mp 128.6-129.1 °C, $[\alpha]_{\text{D}}^{26} = +34.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 13.27 (s, 1 H), 8.40 (d, $J=8.0$ Hz, 1 H), 7.76 (d, $J=8.0$ Hz, 1 H), 7.62-7.69 (m, 4 H), 7.51-7.54 (m, 1 H), 7.31-7.38 (m, 4 H), 5.35 (s, 1 H), 4.18 (d, $J=16.0$ Hz, 1 H), 3.70 (d, $J=16.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 203.7, 163.7, 137.8, 137.4, 131.0, 128.8, 128.5, 127.5, 126.4, 126.3, 125.1, 124.7, 123.3, 119.2, 112.9, 75.5, 39.9; ^{19}F NMR (CDCl_3 , 376 MHz) δ -80.12 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{20}\text{H}_{15}\text{F}_3\text{O}_3 + \text{Na}^+]$ 383.0866, found 383.0859.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 258.7 nm; retention time: 16.1 min (minor) and 18.7 min (major).

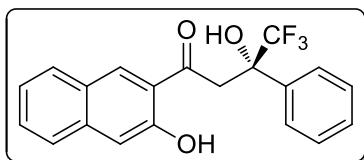


	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		14.383	26648858	1212636	50.01
2		16.676	26638113	1029370	49.99



	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		16.091	950861	46053	8.63
2		18.659	10065676	381405	91.37

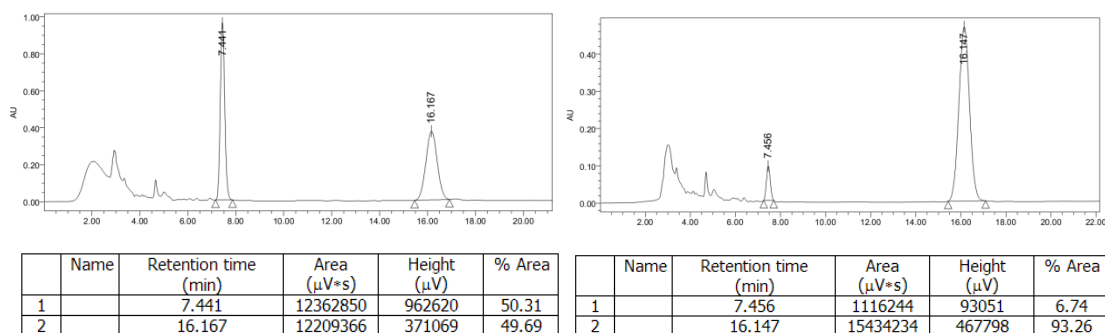
(S)-4,4,4-trifluoro-3-hydroxy-1-(3-hydroxynaphthalen-2-yl)-3-phenylbutan-1-one (4la)



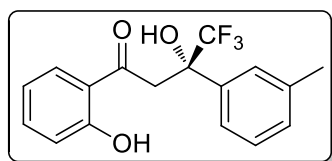
61.2 mg, 68% yield, yellow solid, mp 186.0-187.2 °C, $[\alpha]_{\text{D}}^{26} = +234.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400

MHz) δ 10.72 (s, 1 H), 8.43 (s, 1 H), 7.88 (d, $J=8.0$ Hz, 1 H), 7.62-7.67 (m, 3 H), 7.56 (t, $J=8.0$ Hz, 1 H), 7.36-7.40 (m, 4 H), 5.12 (s, 1 H), 4.35 (d, $J=20.0$ Hz, 1 H), 3.83 (d, $J=20.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 204.6, 156.7, 138.7, 137.1, 133.2, 130.5, 129.6, 129.0, 128.6, 126.8, 126.2, 125.8, 124.6, 123.0, 120.8, 112.1, 76.4, 40.3; ^{19}F NMR (CDCl_3 , 564 MHz) δ -80.61 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{20}\text{H}_{15}\text{F}_3\text{O}_3 + \text{Na}^+]$ 383.0866, found 383.0860.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 255.1 nm; retention time: 7.5 min (minor) and 16.1 min (major).

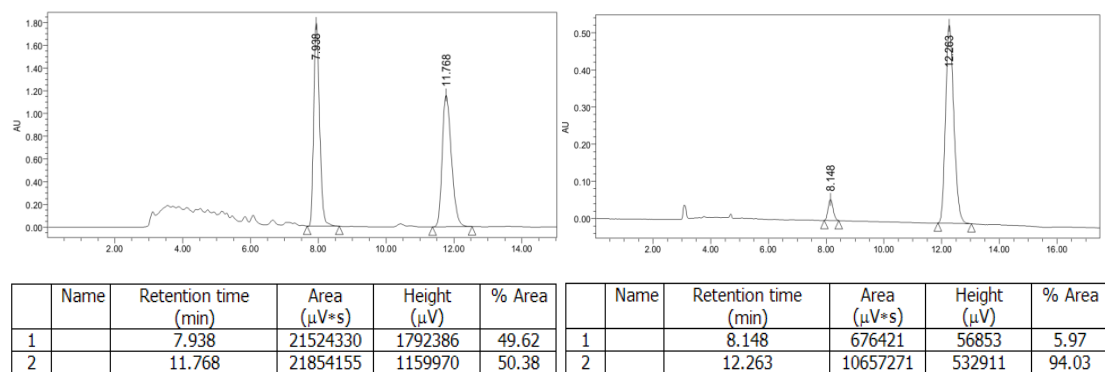


(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)-3-(m-tolyl)butan-1-one (4ab)

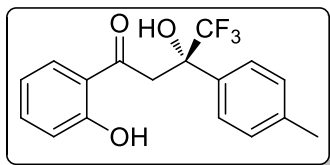


56.9 mg, 70% yield, white solid, mp 114.9-115.6 °C, $[\alpha]_{\text{D}}^{26} = +122.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.52 (s, 1 H), 7.82 (d, $J=8.0$ Hz, 1 H), 7.53 (t, $J=8.0$ Hz, 1 H), 7.44 (s, 1 H), 7.34 (d, $J=8.0$ Hz, 1 H), 7.24 (t, $J=8.0$ Hz, 1 H), 7.16 (d, $J=8.0$ Hz, 1 H), 6.95-6.99 (m, 2 H), 5.16 (s, 1 H), 4.10 (d, $J=16.0$ Hz, 1 H), 3.65 (d, $J=16.0$ Hz, 1 H), 2.35 (s, 3 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 204.3, 162.8, 138.3, 137.8, 137.1, 129.8, 129.7, 128.3, 126.9, 125.8, 123.2, 119.5, 119.3, 119.0, 76.3, 39.9, 21.6; ^{19}F NMR (CDCl_3 , 564 MHz) δ -81.01 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{17}\text{H}_{15}\text{F}_3\text{O}_3 + \text{Na}^+]$ 347.0866, found 347.0872.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 8.1 min (minor) and 12.3 min (major).

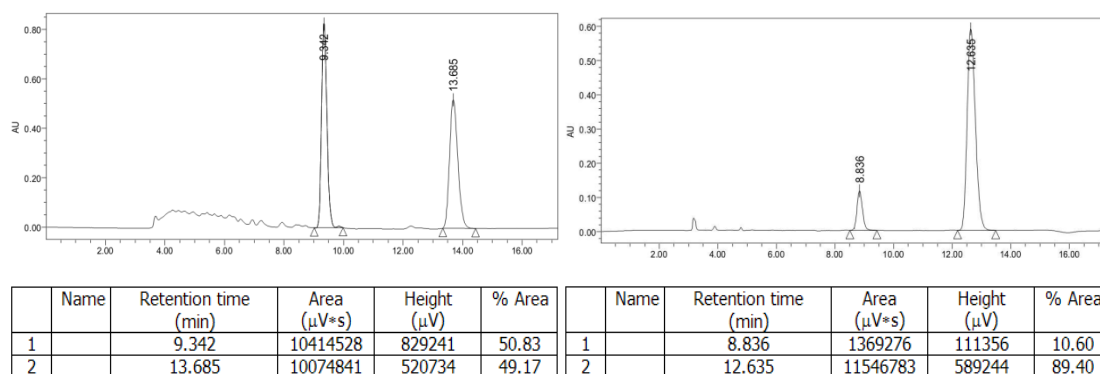


(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)-3-(p-tolyl)butan-1-one (4ac)

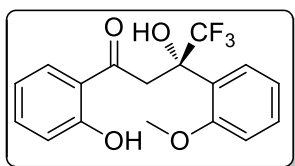


64.0 mg, 79% yield, white solid, mp 110.4-110.8 °C, $[\alpha]_D^{26} = +74.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.52 (s, 1 H), 7.82 (d, *J*=8.0 Hz, 1 H), 7.53 (t, *J*=8.0 Hz, 1 H), 7.47 (d, *J*=8.0 Hz, 2 H), 7.17 (d, *J*=8.0 Hz, 2 H), 6.95-6.99 (m, 2 H), 5.13 (s, 1 H), 4.12 (d, *J*=16.0 Hz, 1 H), 3.63 (d, *J*=16.0 Hz, 1 H), 2.33 (s, 3 H); ¹³C NMR (CDCl₃, 100 MHz) δ 204.4, 162.8, 138.8, 137.8, 134.2, 129.8, 129.2, 126.1, 123.0, 119.5, 119.3, 119.0, 76.3, 39.8, 21.0; ¹⁹F NMR (CDCl₃, 376 MHz) δ -80.08 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₇H₁₅F₃O₃ + Na⁺] 347.0866, found 347.0870.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 8.8 min (minor) and 12.6 min (major).

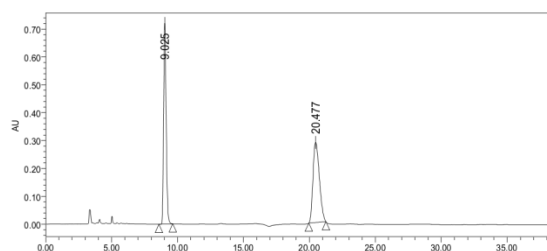


(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)-3-(2-methoxyphenyl)butan-1-one (4ad)

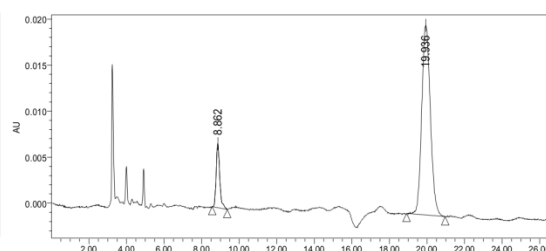


47.6 mg, 54% yield, white solid, mp 98.7-99.1 °C, $[\alpha]_D^{26} = +89.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.66 (s, 1 H), 7.87 (d, *J*=8.0 Hz, 1 H), 7.78 (d, *J*=8.0 Hz, 1 H), 7.51 (t, *J*=8.0 Hz, 1 H), 7.34 (t, *J*=8.0 Hz, 1 H), 7.05 (t, *J*=8.0 Hz, 1 H), 6.97 (t, *J*=8.0 Hz, 2 H), 6.85 (d, *J*=8.0 Hz, 1 H), 5.23 (s, 1 H), 4.69 (d, *J*=16.0 Hz, 1 H), 3.61 (s, 3 H), 3.49 (d, *J*=16.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 203.9, 162.5, 156.6, 137.0, 130.5, 130.1, 130.0, 126.1, 124.1, 121.1, 118.2, 118.7, 111.6, 76.3, 55.4, 41.2; ¹⁹F NMR (CDCl₃, 564 MHz) δ -81.28 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₇H₁₅F₃O₄ + Na⁺] 363.0815, found 363.0819.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 255.1 nm; retention time: 8.9 min (minor) and 19.9 min (major).

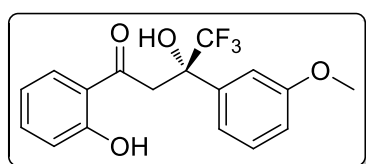


	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		9.025	9652626	723742	49.94
2		20.477	9675001	287953	50.06



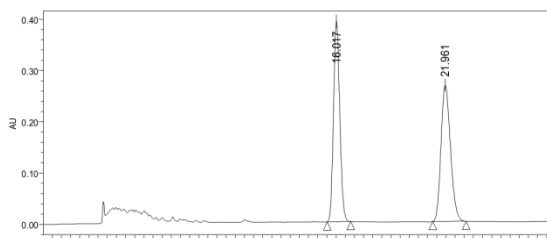
	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		8.862	92866	6983	12.35
2		19.936	659067	20627	87.65

(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)-3-(3-methoxyphenyl)butan-1-one (4ae)

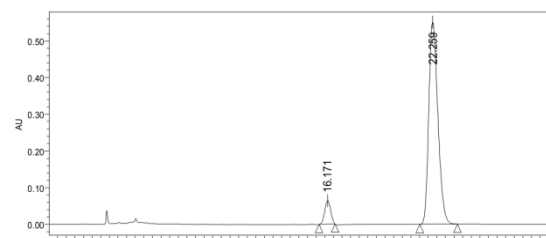


66.2 mg, 74% yield, white solid, mp 78.3-78.5 °C, $[\alpha]_D^{26} = +122.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.52 (s, 1 H), 7.81 (d, *J*=8.0 Hz, 1 H), 7.53 (t, *J*=8.0 Hz, 1 H), 7.27 (t, *J*=8.0 Hz, 1 H), 7.21 (s, 1 H), 7.10 (d, *J*=8.0 Hz, 1 H), 6.95-6.99 (m, 2 H), 6.88 (d, *J*=8.0 Hz, 1 H), 5.22 (s, 1 H), 4.12 (d, *J*=16.0 Hz, 1 H), 3.79 (s, 3 H), 3.63 (d, *J*=20.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 204.2, 162.8, 159.6, 138.8, 137.8, 129.8, 129.5, 119.5, 119.2, 119.0, 118.3, 113.9, 112.7, 76.6, 76.3, 55.2, 39.9; ¹⁹F NMR (CDCl₃, 564 MHz) δ -80.63 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₇H₁₅F₃O₄ + Na⁺] 363.0815, found 363.0819.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 255.1 nm; retention time: 8.9 min (minor) and 19.9 min (major).

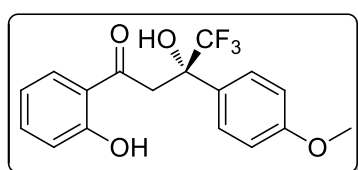


	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		16.017	9264339	390837	49.29
2		21.961	9532272	265788	50.71



	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		16.171	1546594	64537	7.13
2		22.259	20138930	550652	92.87

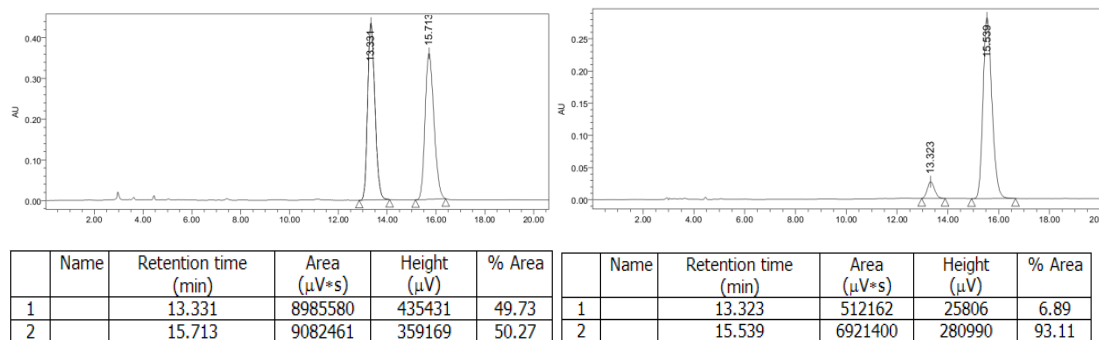
(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)butan-1-one (4af)



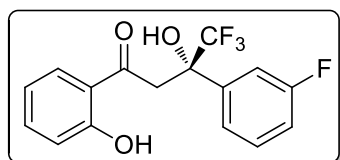
70.0 mg, 78% yield, white solid, mp 69.9-70.6 °C, $[\alpha]_D^{26} = +70.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.54 (s, 1 H), 7.82 (d, *J*=8.0 Hz, 1 H), 7.49-7.56 (m, 3 H), 6.96-7.00 (m, 2 H), 6.89 (d, *J*=8.0 Hz, 2 H), 5.15 (s, 1 H), 4.12 (d, *J*=16.0 Hz, 1 H), 3.79 (s, 3 H), 3.62 (d, *J*=20.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ

204.4, 162.8, 159.8, 137.8, 129.8, 129.0, 127.5, 125.8, 123.0, 119.5, 119.3, 119.0, 113.8, 76.1, 55.2, 39.7; ^{19}F NMR (CDCl_3 , 376 MHz) δ -80.07 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{17}\text{H}_{15}\text{F}_3\text{O}_4 + \text{Na}^+]$ 363.0815, found 363.0821.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 13.3 min (minor) and 15.5 min (major).

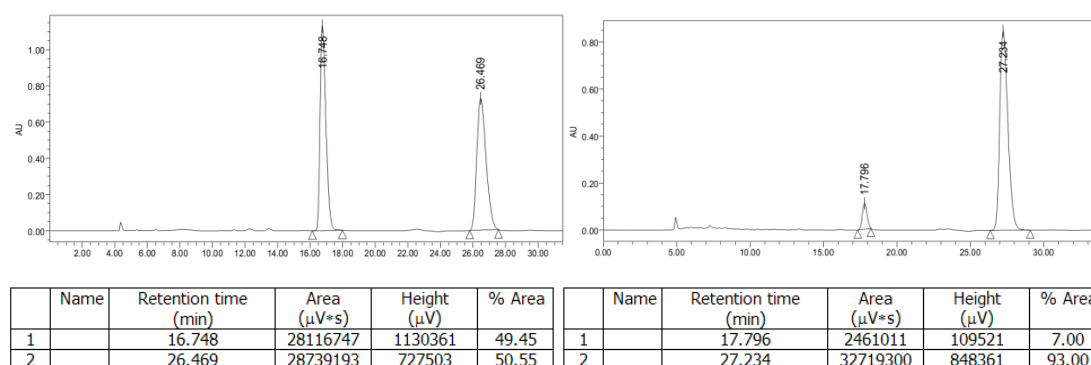


(S)-4,4,4-trifluoro-3-(3-fluorophenyl)-3-hydroxy-1-(2-hydroxyphenyl)butan-1-one (4a)

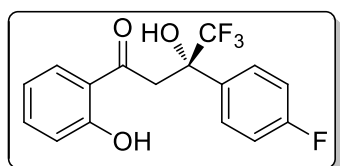


76.3 mg, 93% yield, white solid, mp 114.4-115.5 °C, $[\alpha]_{\text{D}}^{26} = +67.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.46 (s, 1 H), 7.80 (d, $J=8.0$ Hz, 1 H), 7.55 (t, $J=8.0$ Hz, 1 H), 7.33-7.38 (m, 3 H), 6.97-7.07 (m, 3 H), 5.28 (s, 1 H), 4.06 (d, $J=16.0$ Hz, 1 H), 3.63 (d, $J=20.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 204.0, 164.0, 162.9, 161.6, 139.9, 138.0, 130.1, 130.0, 129.8, 125.6, 122.7, 121.8, 119.6, 119.1, 116.1, 115.9, 114.1, 113.8, 39.9; ^{19}F NMR (CDCl_3 , 564 MHz) δ -81.01 (s, 3 F), -122.63 (s, 1 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{16}\text{H}_{12}\text{F}_4\text{O}_3 + \text{Na}^+]$ 351.0615, found 351.0618.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 17.8 min (minor) and 27.2 min (major).



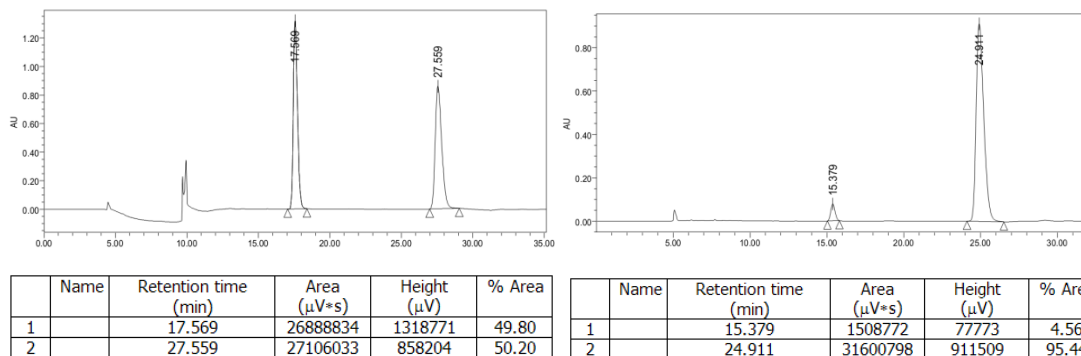
(S)-4,4,4-trifluoro-3-(4-fluorophenyl)-3-hydroxy-1-(2-hydroxyphenyl)butan-1-one (4ah)



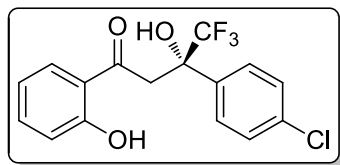
61.8 mg, 75% yield, white solid, mp 110.3-111.1 °C, $[\alpha]_{\text{D}}^{26} = +125.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.48 (s, 1 H), 7.80 (d, $J=8.0$ Hz, 1 H), 7.52-7.59 (m, 3 H), 6.97-7.08 (m, 4 H), 5.26 (s, 1 H), 4.08 (d,

$J=16.0$ Hz, 1 H), 3.65 (d, $J=16.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 204.2, 164.2, 162.9, 161.7, 138.0, 133.0, 129.8, 128.3, 128.2, 125.7, 122.8, 119.6, 119.1, 115.6, 115.4, 76.4, 76.1, 39.8; ^{19}F NMR (CDCl_3 , 564 MHz) δ -81.73 (s, 3 F), -114.21 (s, 1 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{16}\text{H}_{12}\text{F}_4\text{O}_3 + \text{Na}^+]$ 351.0615, found 351.0617.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 15.4 min (minor) and 24.9 min (major).

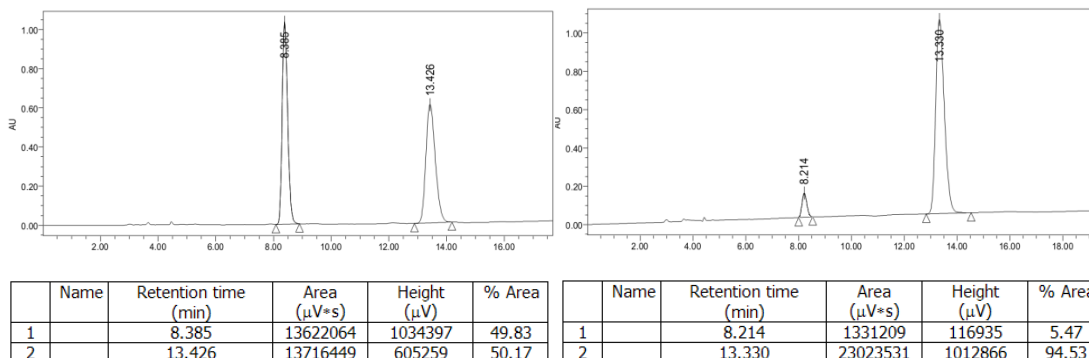


(S)-3-(4-chlorophenyl)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)butan-1-one (4ai)

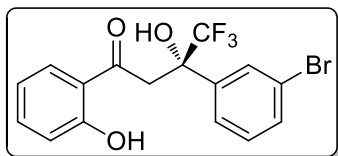


74.5 mg, 86% yield, white solid, mp 108.6-109.7 °C, $[\alpha]_{\text{D}}^{26} = +94.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.46 (s, 1 H), 7.80 (d, $J=8.0$ Hz, 1 H), 7.52-7.57 (m, 3 H), 7.35 (d, $J=8.0$ Hz, 2 H), 6.96-6.99 (m, 2 H), 5.24 (s, 1 H), 4.07 (d, $J=16.0$ Hz, 1 H), 3.66 (d, $J=20.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 204.1, 162.9, 138.0, 135.8, 135.1, 129.7, 128.8, 127.7, 125.6, 122.7, 119.6, 119.1, 76.4, 76.1, 39.7; ^{19}F NMR (CDCl_3 , 564 MHz) δ -81.01 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{16}\text{H}_{12}\text{ClF}_3\text{O}_3 + \text{H}^+]$ 367.0319, found 367.0322.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 8.2 min (minor) and 13.3 min (major).

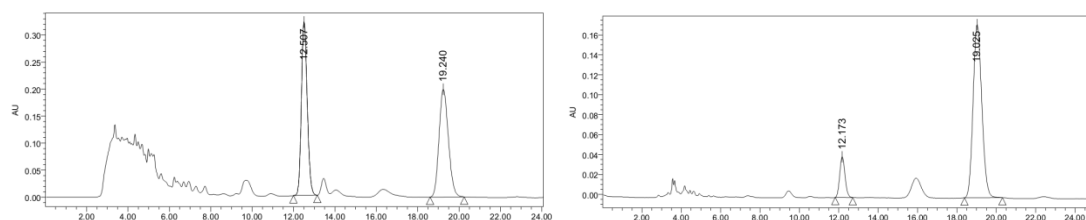


(S)-3-(3-bromophenyl)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)butan-1-one (4aj)



80.7 mg, 83% yield, white solid, mp 155.1-156.4 °C, $[\alpha]_D^{26} = +92.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.46 (s, 1 H), 7.79-7.80 (m, 2 H), 7.47-7.57 (m, 3 H), 7.24 (t, *J*=8.0 Hz, 1 H), 6.97-7.01 (m, 2 H), 5.29 (s, 1 H), 4.02 (d, *J*=16.0 Hz, 1 H), 3.68 (d, *J*=16.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 203.9, 162.9, 130.6, 138.1, 132.1, 130.0, 129.8, 129.7, 125.6, 124.8, 122.9, 122.7, 119.6, 119.1, 76.3, 76.0, 39.8; ¹⁹F NMR (CDCl₃, 564 MHz) δ -81.01 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₆H₁₂BrF₃O₃ + H⁺] 388.9995, 390.9975, found 388.9995, 390.9974.

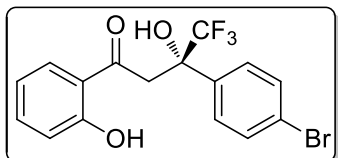
The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 12.2 min (minor) and 19.0 min (major).



	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		12.507	6309362	321747	50.26
2		19.240	6242845	199417	49.74

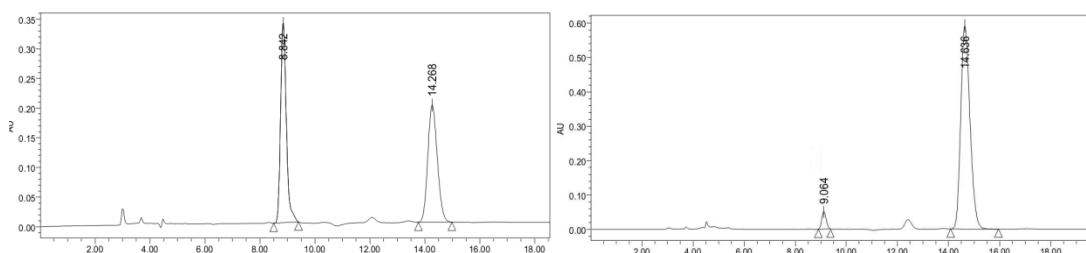
	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		12.173	763104	40892	12.50
2		19.025	5342559	173739	87.50

(S)-3-(4-bromophenyl)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)butan-1-one (4ak)



88.4 mg, 91% yield, white solid, mp 132.6-133.5 °C, $[\alpha]_D^{26} = +82.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.46 (s, 1 H), 7.79 (d, *J*=8.0 Hz, 1 H), 7.45-7.56 (m, 5 H), 6.96-6.99 (m, 2 H), 5.24 (s, 1 H), 4.07 (d, *J*=16.0 Hz, 1 H), 3.65 (d, *J*=16.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 204.0, 162.9, 138.1, 136.4, 131.7, 129.7, 128.0, 125.5, 123.3, 122.7, 119.6, 119.1, 76.4, 76.2, 39.7; ¹⁹F NMR (CDCl₃, 376 MHz) δ -80.23 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₆H₁₂BrF₃O₃ + H⁺] 388.9995, 390.9974, found 388.9995, 390.9975.

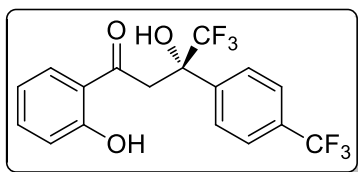
The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 9.1 min (minor) and 14.6 min (major).



	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		8.842	4874793	337342	50.66
2		14.268	4748503	197625	49.34

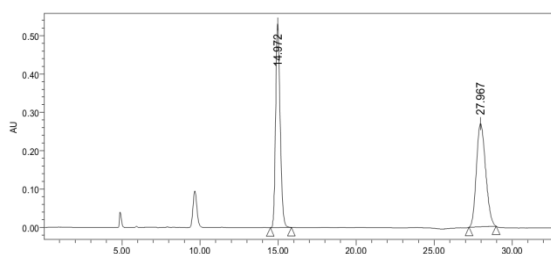
	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		9.064	781088	62549	5.00
2		14.636	14843701	590670	95.00

(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)-3-(4-(trifluoromethyl)phenyl)butan-1-one (4al)

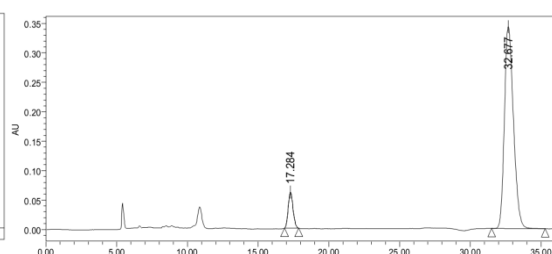


77.5 mg, 82% yield, white solid, mp 136.2-136.4 °C, $[\alpha]_D^{26} = +77.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.42 (s, 1 H), 7.81 (d, *J*=8.0 Hz, 1 H), 7.74 (d, *J*=8.0 Hz, 2 H), 7.65 (d, *J*=8.0 Hz, 2 H), 7.56 (t, *J*=8.0 Hz, 1 H), 6.97-7.01 (m, 2 H), 5.31 (s, 1 H), 4.11 (d, *J*=16.0 Hz, 1 H), 3.72 (d, *J*=16.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 203.9, 162.9, 141.3, 138.2, 131.3, 131.0, 129.7, 126.8, 125.6, 125.5, 125.1, 122.7, 119.7, 119.2, 119.1, 76.2, 39.8; ¹⁹F NMR (CDCl₃, 564 MHz) δ -62.86 (s, 3 F), -80.11 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₇H₁₂F₆O₃ + Na⁺] 401.0583, found 401.0585.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 17.3 min (minor) and 32.7 min (major).

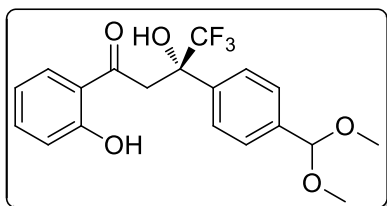


	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		14.972	10767339	531581	49.34
2		27.967	11053518	269325	50.66



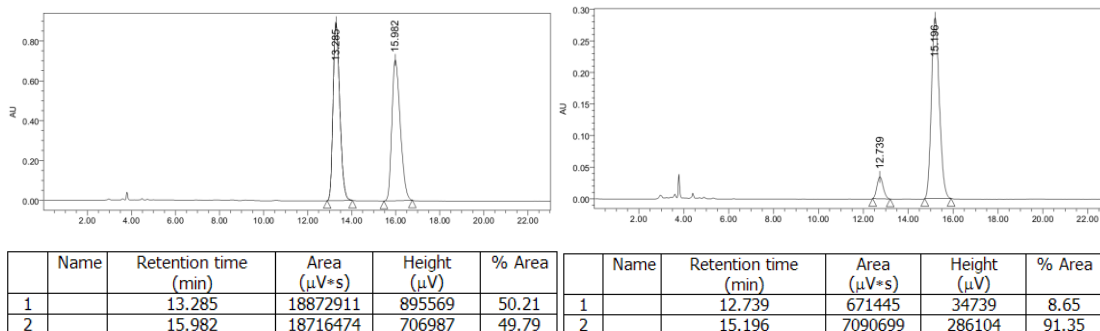
	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		17.284	1446624	61198	8.69
2		32.677	15207955	342790	91.31

(S)-3-(4-(dimethoxymethyl)phenyl)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)butan-1-one (4am)

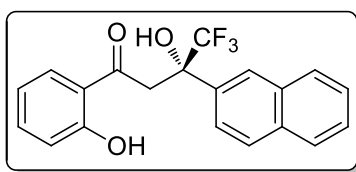


45.1 mg, 47% yield, white solid, mp 103.3-104.4 °C; ¹H NMR (CDCl₃, 400 MHz) δ 11.49 (s, 1H), 7.81 (d, *J*=8.0 Hz, 1H), 7.60 (d, *J*=8.0 Hz, 2H), 7.54 (t, *J*=8.0 Hz, 1H), 7.46 (d, *J*=8.0 Hz, 2H), 6.96-6.99 (m, 2H), 5.38 (s, 1H), 5.24 (s, 1H), 4.12 (d, *J*=20.0 Hz, 1H), 3.66 (d, *J*=16.0 Hz, 1H), 3.32 (s, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 202.7, 161.3, 137.3, 136.4, 135.9, 128.3, 124.7, 121.4, 118.0, 117.7, 117.5, 101.1, 74.8, 51.3, 38.4; ¹⁹F NMR (CDCl₃, 564 MHz) δ -81.47 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₉H₁₉F₃O₅ + Na⁺] 407.1077, found 407.1070.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 12.7 min (minor) and 15.2 min (major).

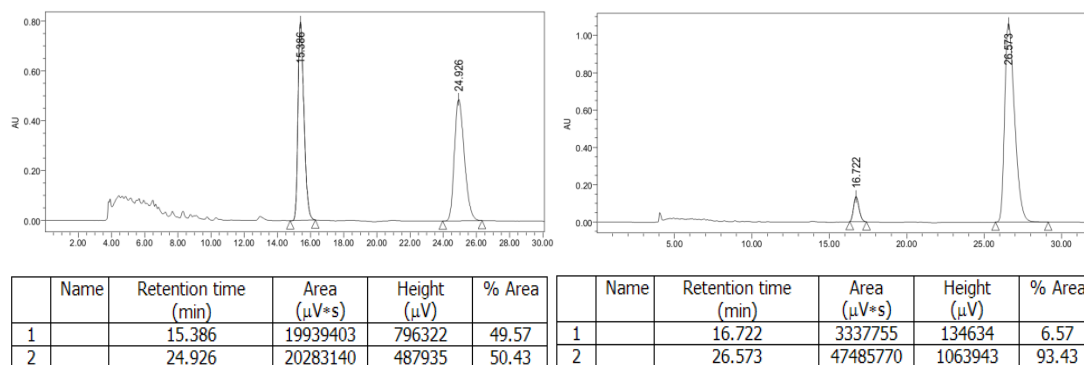


(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)-3-(naphthalen-2-yl)butan-1-one (4an)

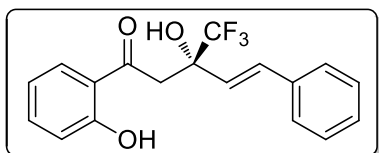


63.1 mg, 70% yield, white solid, mp 137.9-138.5 °C, $[\alpha]_D^{26} = +116.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.47 (s, 1 H), 8.12 (s, 1 H), 7.82-7.88 (m, 4 H), 7.66 (d, *J*=8.0 Hz, 1 H), 7.49-7.55 (m, 3 H), 6.94-7.01 (m, 2 H), 5.36 (s, 1 H), 4.25 (d, *J*=16.0 Hz, 1 H), 3.75 (d, *J*=20.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 204.2, 178.4, 162.8, 150.4, 137.9, 134.6, 133.1, 132.8, 129.8, 128.4, 128.3, 127.5, 126.8, 126.5, 126.2, 123.3, 119.5, 119.0, 72.2, 39.9; ¹⁹F NMR (CDCl₃, 564 MHz) δ -81.19 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₂₀H₁₅F₃O₃ + Na⁺] 383.0866, found 383.0871.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 16.7 min (minor) and 26.6 min (major).

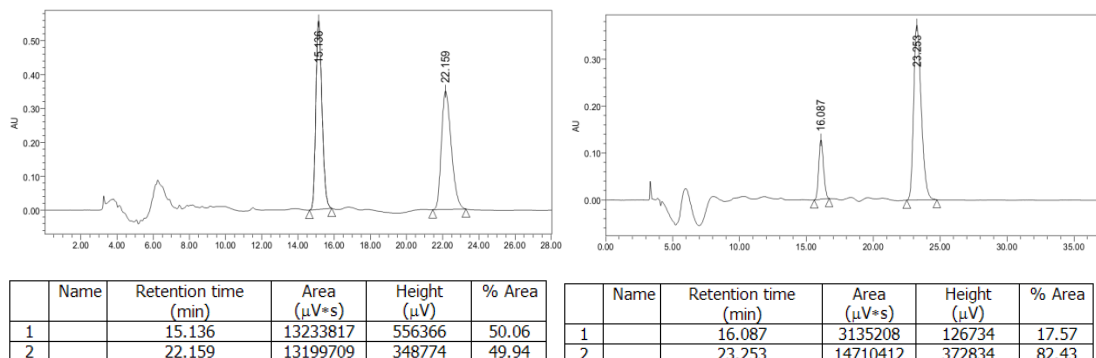


(S)-3-hydroxy-1-(2-hydroxyphenyl)-5-phenyl-3-(trifluoromethyl)pent-4-en-1-one (4ao)

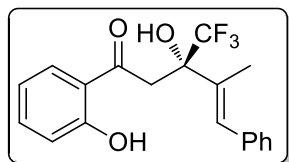


50.8 mg, 60% yield, white solid, mp 170.8-171.7 °C, $[\alpha]_D^{26} = -39.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.70 (s, 1 H), 7.67 (d, *J*=8.0 Hz, 1 H), 7.55 (t, *J*=8.0 Hz, 1 H), 7.28-7.39 (m, 4 H), 6.96-7.02 (m, 3 H), 6.21 (d, *J*=16.0 Hz, 1 H), 5.14 (s, 1 H), 3.55 (s, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 204.4, 163.0, 147.4, 137.9, 135.3, 134.2, 130.1, 128.6, 125.9, 124.1, 123.1, 119.5, 119.3, 119.0, 75.7, 75.4, 39.6; ¹⁹F NMR (CDCl₃, 564 MHz) δ -81.23 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₈H₁₅F₃O₃ + H⁺] 337.1046, found 337.1042.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 257.5 nm; retention time: 16.1 min (minor) and 23.3 min (major).

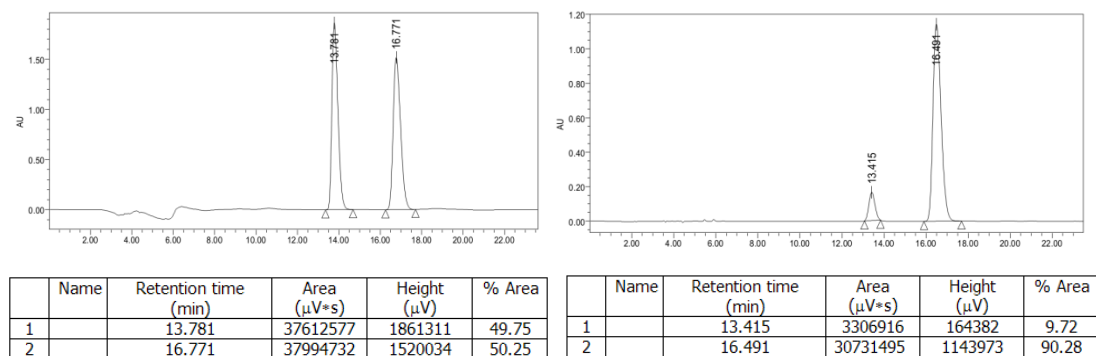


(S)-3-hydroxy-1-(2-hydroxyphenyl)-4-methyl-5-phenyl-3-(trifluoromethyl)pent-4-en-1-one (4ap)

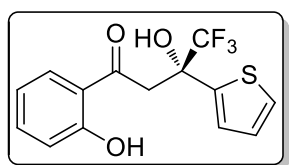


58.6 mg, 67% yield, white solid, mp 81.1-82.2 °C, $[\alpha]_D^{26} = +48.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.73 (s, 1 H), 7.78 (d, *J*=8.0 Hz, 1 H), 7.55 (t, *J*=8.0 Hz, 1 H), 7.32 (t, *J*=8.0 Hz, 1 H), 7.17-7.25 (m, 3 H), 6.95-7.03 (m, 3 H), 4.81 (s, 1 H), 3.93 (d, *J*=16.0 Hz, 1 H), 3.47 (d, *J*=20.0 Hz, 1 H), 1.93 (s, 3 H); ¹³C NMR (CDCl₃, 100 MHz) δ 204.5, 162.9, 137.8, 130.6, 129.9, 128.9, 128.1, 127.0, 126.1, 123.2, 119.6, 119.2, 119.1, 77.8, 39.2, 15.1; ¹⁹F NMR (CDCl₃, 564 MHz) δ -80.74 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₉H₁₇F₃O₃ + Na⁺] 373.1022, found 373.1019.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 253.9 nm; retention time: 13.4 min (minor) and 16.5 min (major).



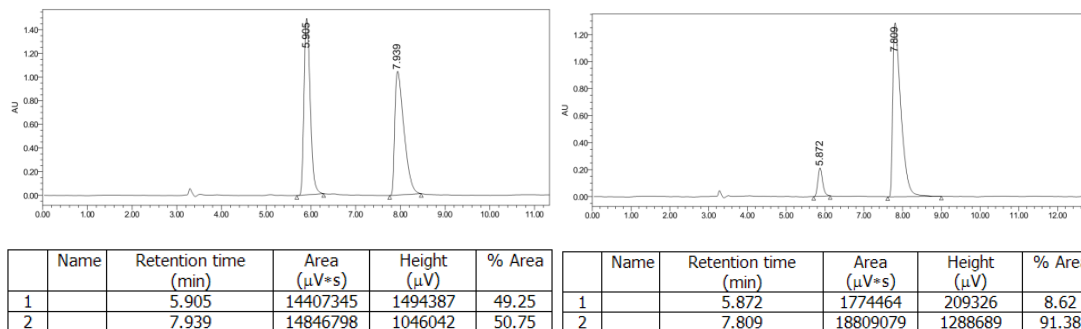
(S)-4,4,4-trifluoro-3-hydroxy-1-(2-hydroxyphenyl)-3-(thiophen-2-yl)butan-1-one (4aq)



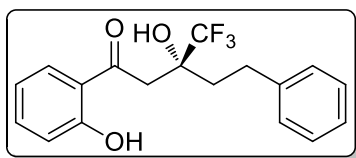
40.3 mg, 51% yield, white solid, mp 104.6-105.8 °C, $[\alpha]_D^{26} = +98.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.52 (s, 1 H), 7.78 (d, *J*=8.0 Hz, 1 H), 7.55 (t, *J*=8.0 Hz, 1 H), 7.32 (d, *J*=8.0 Hz, 1 H), 7.11-7.12 (m, 1 H), 6.96-7.00 (m, 3 H), 5.76 (s, 1 H), 4.03 (d, *J*=16.0 Hz, 1 H), 3.62 (d,

$J=16.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 204.2, 162.9, 141.4, 138.0, 129.9, 127.2, 126.7, 126.0, 125.1, 119.6, 119.0, 40.5; ^{19}F NMR (CDCl_3 , 564 MHz) δ -82.04 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{14}\text{H}_{11}\text{F}_3\text{O}_3 + \text{Na}^+]$ 339.0273, found 339.0278.

The ee was determined by HPLC analysis. CHIRALPAK IC; Hexane/Dichloromethane = 65/35; flow rate 1.0 mL/min; 258.8 nm; retention time: 5.9 min (minor) and 7.8 min (major).

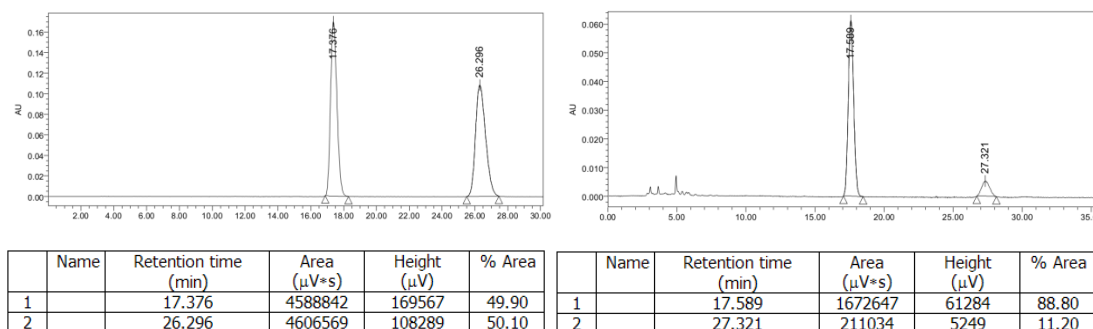


(S)-3-hydroxy-1-(2-hydroxyphenyl)-5-phenyl-3-(trifluoromethyl)pentan-1-one (4ar)

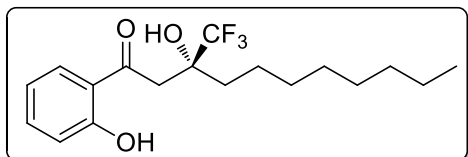


49.1 mg, 58% yield, white solid, mp 119.6-120.7 °C, $[\alpha]_{\text{D}}^{26} = +7.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.78 (s, 1 H), 7.70 (d, $J=8.0$ Hz, 1 H), 7.56 (t, $J=8.0$ Hz, 1 H), 7.28-7.32 (m, 2 H), 7.18-7.22 (m, 3 H), 7.03 (d, $J=8.0$ Hz, 1 H), 6.95 (t, $J=8.0$ Hz, 1 H), 5.29 (s, 1 H), 3.56 (d, $J=16.0$ Hz, 1 H), 3.12 (d, $J=16.0$ Hz, 1 H), 3.75-2.92 (m, 2 H), 2.17-2.24 (m, 1 H), 2.00-2.08 (m, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 205.7, 163.0, 140.9, 137.9, 130.1, 128.6, 128.3, 127.2, 126.2, 124.3, 119.5, 119.3, 119.0, 75.7, 75.4, 37.5, 37.0, 29.2; ^{19}F NMR (CDCl_3 , 564 MHz) δ -81.01 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{19}\text{H}_{17}\text{F}_3\text{O}_3 + \text{H}^+]$ 339.1203, found 339.1196.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 93/7; flow rate 1.0 mL/min; 337.1 nm; retention time: 17.6 min (major) and 27.3 min (minor).



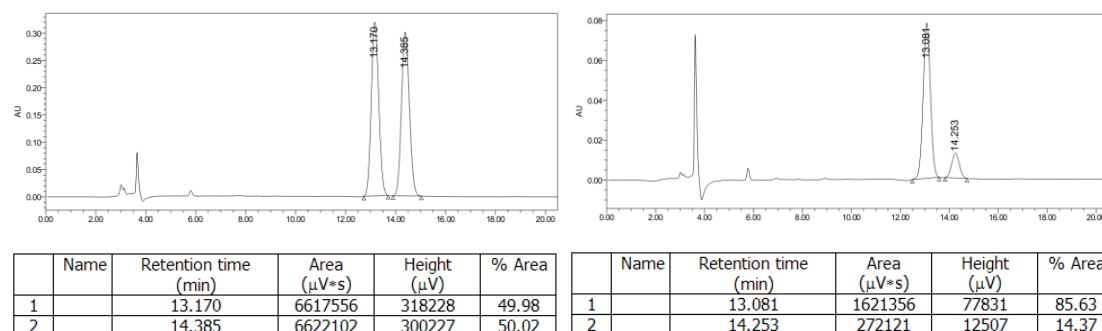
(S)-3-hydroxy-1-(2-hydroxyphenyl)-3-(trifluoromethyl)undecan-1-one (4as)



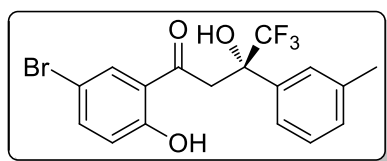
34.6 mg, 40% yield, white solid, mp 47.8-48.6 °C, $[\alpha]_{\text{D}}^{26} = +107.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.79 (s, 1 H), 7.70-7.73 (m, 1 H), 7.51-7.56 (m, 1 H), 7.00-7.02

(m, 1 H), 6.92-6.96 (m, 1 H), 5.09 (s, 1 H), 3.50 (d, $J=16.0$ Hz, 1 H), 3.05 (d, $J=16.0$ Hz, 1 H), 1.80-1.88 (m, 1 H), 1.68-1.76 (m, 1 H), 1.48-1.57 (m, 1 H), 1.36-1.44 (m, 1 H), 1.26-1.32 (m, 10 H), 0.85-0.88 (m, 3 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 207.4, 164.6, 139.3, 131.7, 120.9, 120.6, 77.4, 77.2, 38.9, 36.7, 33.3, 31.3, 30.9, 30.7, 24.4, 24.1, 15.6; ^{19}F NMR (CDCl_3 , 564 MHz) δ -81.15 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{18}\text{H}_{25}\text{F}_3\text{O}_3 + \text{Na}^+]$ 369.1648, found 369.1654.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 255.8 nm; retention time: 13.1 min (major) and 14.3 min (minor).

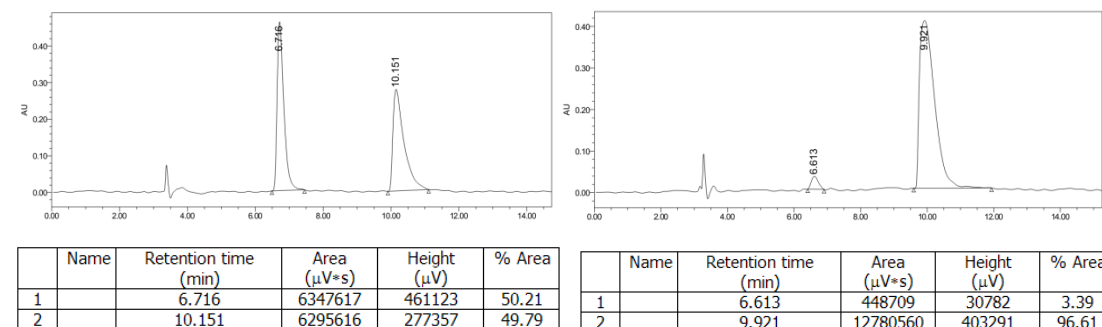


(S)-1-(5-bromo-2-hydroxyphenyl)-4,4,4-trifluoro-3-hydroxy-3-(m-tolyl)butan-1-one (4gb)

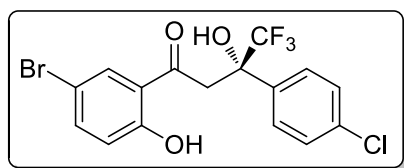


97.5 mg, 97% yield, white solid, mp 139.8-140.6 °C, $[\alpha]_{\text{D}}^{21} = +185.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 11.44 (s, 1 H), 7.89 (d, $J=4.0$ Hz, 1 H), 7.59-7.61 (m, 1 H), 7.42 (s, 1 H), 7.24-7.34 (m, 2 H), 7.17 (d, $J=8.0$ Hz, 1 H), 6.88 (d, $J=8.0$ Hz, 1 H), 4.89 (s, 1 H), 4.05 (d, $J=16.0$ Hz, 1 H), 3.63 (d, $J=20.0$ Hz, 1 H), 2.37 (s, 3 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 203.4, 161.7, 140.4, 138.4, 136.8, 131.9, 129.8, 128.4, 126.9, 125.7, 123.1, 122.9, 121.1, 120.5, 111.1, 76.3, 40.5, 21.6; ^{19}F NMR (CDCl_3 , 564 MHz) δ -81.41 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{17}\text{H}_{14}\text{BrF}_3\text{O}_3 + \text{H}^+]$ 403.0150, 405.0131, found 403.0155, 405.0135.

The ee was determined by HPLC analysis. CHIRALPAK IC; Hexane/Dichloromethane = 75/25; flow rate 1.0 mL/min; 257.6 nm; retention time: 6.6 min (minor) and 9.9 min (major).

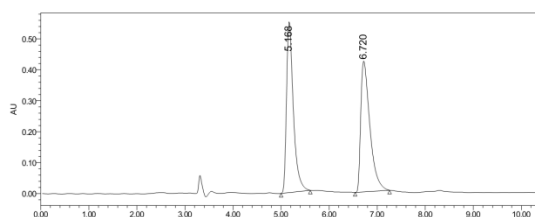


(S)-1-(5-bromo-2-hydroxyphenyl)-3-(4-chlorophenyl)-4,4,4-trifluoro-3-hydroxybutan-1-one (4gi)

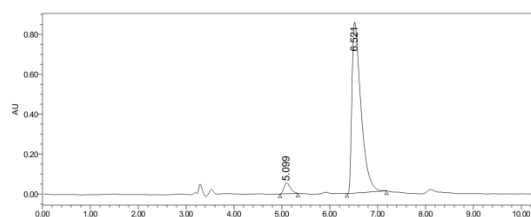


84.4 mg, 80% yield, white solid, mp 177.7-178.2°C, $[\alpha]_D^{21} = +191.0$ (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.37 (s, 1 H), 7.87 (d, *J*=4.0 Hz, 1 H), 7.60-7.63 (m, 1 H), 7.52 (d, *J*=8.0 Hz, 2 H), 7.37 (d, *J*=8.0 Hz, 2 H), 6.90 (d, *J*=8.0 Hz, 1 H), 6.88 (d, *J*=8.0 Hz, 1 H), 4.98 (s, 1 H), 4.02 (d, *J*=20.0 Hz, 1 H), 3.64 (d, *J*=16.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 203.1, 161.8, 140.6, 135.6, 135.2, 131.8, 128.9, 127.7, 125.5, 122.6, 121.2, 120.3, 111.2, 76.1, 40.2; ¹⁹F NMR (CDCl₃, 564 MHz) δ -81.01 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₆H₁₁BrClF₃O₃ + H⁺] 422.9605, 424.9584, found 422.9603, 424.9582.

The ee was determined by HPLC analysis. CHIRALPAK IC; Hexane/Dichloromethane = 65/35; flow rate 1.0 mL/min; 258.8 nm; retention time: 5.1 min (minor) and 6.5 min (major).

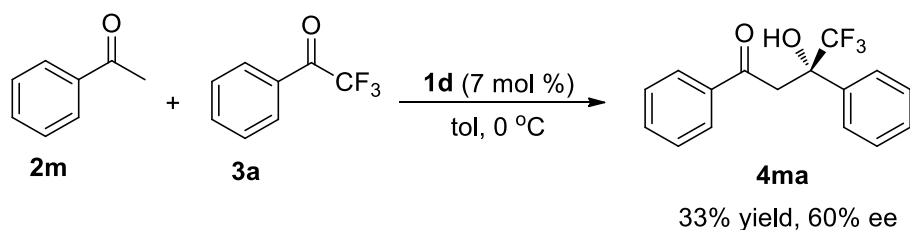


	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		5.168	5460866	551920	49.46
2		6.720	5580603	422671	50.54



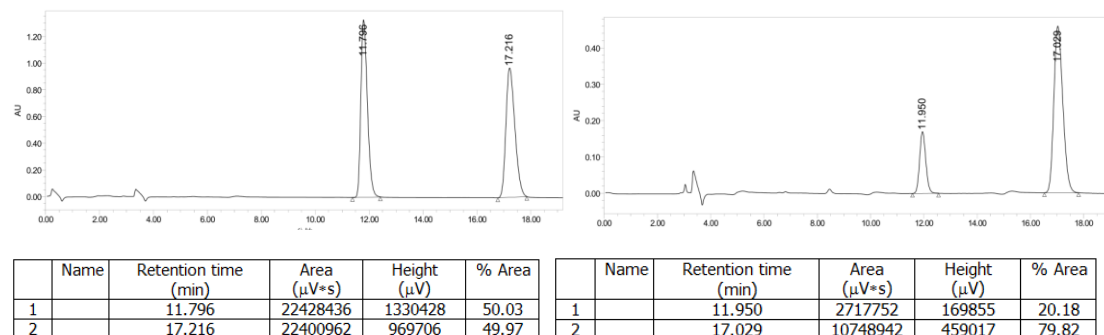
	Name	Retention time (min)	Area (μV*s)	Height (μV)	% Area
1		5.099	502442	53415	4.29
2		6.521	11214712	856974	95.71

8. Asymmetric cross-aldol reaction of acetophenone with trifluoroacetophenone

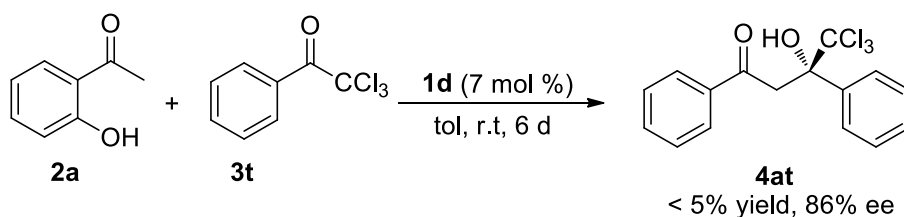


(S)-4ma⁸: 24.3 mg, 33% yield, colourless oil, $[\alpha]_{\text{D}}^{21} = +9.7$ (c 0.96, CHCl_3); ^1H NMR (CDCl_3 , 600 MHz) δ 7.94-7.92 (m, 2 H), 7.64-7.60 (m, 3 H), 7.51-7.48 (m, 2 H), 7.37-7.31 (m, 3 H), 5.68 (s, 1 H), 4.03 (d, $J=16.8$ Hz, 1 H), 3.65 (d, $J=17.4$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 199.6, 137.7, 136.3, 134.4, 128.9, 128.7, 128.4, 128.2, 126.3, 125.5, 123.6, 76.6, 76.4, 40.2; ^{19}F NMR (CDCl_3 , 564 MHz) δ -80.63 (s, 3 F).

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 98/2; flow rate 1.0 mL/min; 245.1 nm; retention time: 11.9 min (minor) and 17.0 min (major).

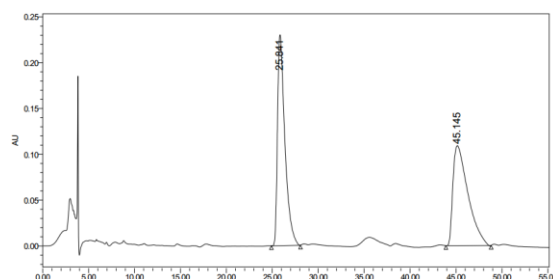


9. Asymmetric cross-aldol reaction of *o*-hydroxyacetophenones with trichloroacetophenone

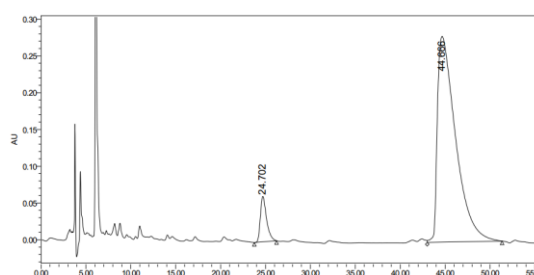


(S)-4at: < 5% yield, white solid, mp 130.0-130.4 °C; ^1H NMR (CDCl_3 , 600 MHz) δ 11.46 (s, 1 H), 7.90-7.88 (m, 1 H), 7.75-7.73 (m, 2 H), 7.55-7.52 (m, 1 H), 7.33-7.30 (m, 3 H), 7.00-6.95 (m, 2 H), 5.49 (s, 1 H), 4.69 (d, $J=17.4$ Hz, 1 H), 3.91 (d, $J=16.8$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 204.8, 162.8, 137.9, 137.7, 129.8, 128.8, 128.5, 127.7, 119.5, 119.4, 119.0, 115.4, 84.3, 41.7; HRMS: (ESI+) m/z calcd for $[\text{C}_{16}\text{H}_{13}\text{Cl}_3\text{O}_3 + \text{H}^+]$ 359.0003, 360.9974, found 359.0002, 360.9972.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; CHIRALPAK OD-H; Hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 256.9 nm; retention time: 24.7 min (minor) and 44.7 min (major).

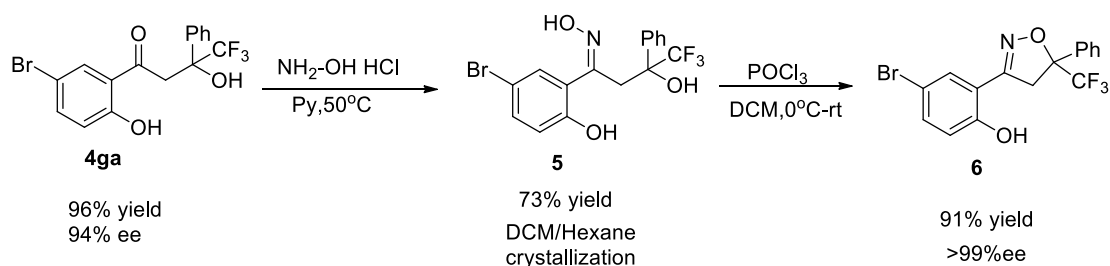


	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		25.841	12843900	229997	50.91
2		45.145	12386737	108968	49.09



	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		24.702	2957872	61760	6.98
2		44.666	39396984	279821	93.02

10. Preparation and characterization of **6** and **8**



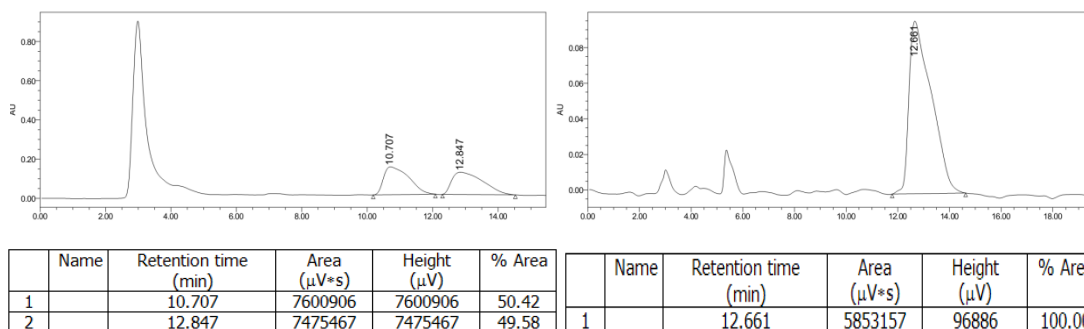
Optical active compound **4ga** (0.39 g, 1.0 mmol) and hydroxylamine hydrochloride (139 mg, 2.0 mmol) was added into pyridine (3 mL) at argon atmosphere. The mixture was stirred to 50 °C overnight, then was condensed under vacuo. The residue prepared by silicon column chromatography (petroleum ether: ethyl acetate = 5:1) to give desired the product **5** (0.29 g, 73% yield). The oxime **5** was recrystallized by hexane and dichloromethane to obtain yellow single crystal **5**.⁹

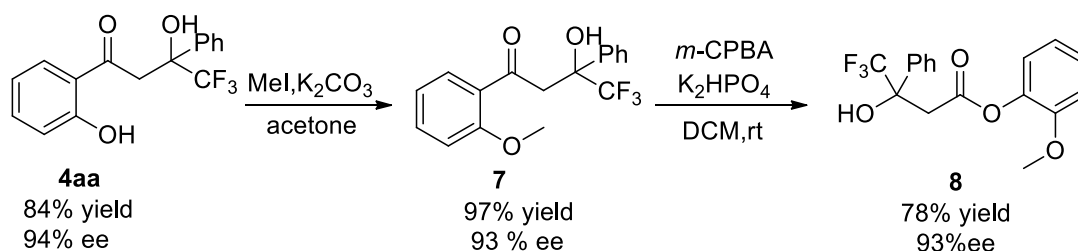
To the solution of single crystal **5** (40 mg, 0.1 mmol) in dichloromethane (1 mL) was slowly added POCl₃ (46.6 μL, 0.5 mmol) at ice bath. The mixture was stirred 6h and quenched with ice water at 0 °C. The aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL). The combined organics were washed with brine, dried over anhydrous Na₂SO₄, filtered, and condensed under vacuo. The residue was purified by silicon column chromatography (petroleum ether: ethyl acetate = 8:1) to give the desired product **6** (35.1 mg, 91% yield).

5: white solid, mp 149.6-149.8 °C, [α]_D²¹ = - 97.0 (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 11.96 (s, 1 H), 8.87 (br, 1 H), 7.58 (d, *J*=8.0 Hz, 2 H), 7.29-7.35 (m, 3 H), 7.16-7.18 (m, 1 H), 6.71-6.73 (m, 1 H), 4.61 (s, 1 H), 4.09 (d, *J*=12.0 Hz, 1 H), 3.28 (d, *J*=16.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 159.3, 157.3, 137.4, 135.3, 132.2, 130.5, 130.1, 126.9, 120.3, 120.0, 112.4, 33.9; ¹⁹F NMR (CDCl₃, 564 MHz) δ -79.09 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₆H₁₃BrF₃N₁O₃ + H⁺] 404.0109, 406.0089, found 404.0108, 406.0087.

6: white solid, mp 77.9-78.2 °C, [α]_D²¹ = - 44.0 (c 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 7.74 (d, *J*=4.0 Hz, 1 H), 7.63-7.66 (m, 2 H), 7.29-7.44 (m, 5 H), 5.84 (s, 1 H), 3.78 (s, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 163.6, 149.2, 141.7, 136.7, 129.2, 128.7, 128.6, 126.7, 123.0, 117.8, 112.1, 76.3, 33.9; ¹⁹F NMR (CDCl₃, 564 MHz) δ -81.11 (s, 3 F); HRMS: (ESI+) *m/z* calcd for [C₁₆H₁₁BrF₃N₁O₂ + H⁺] 385.9998, 387.9978, found 385.9999, 387.9978.

The ee was determined by HPLC analysis. CHIRALPAK AD-H; Hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 281.8 nm; retention time: 12.7 min (major).



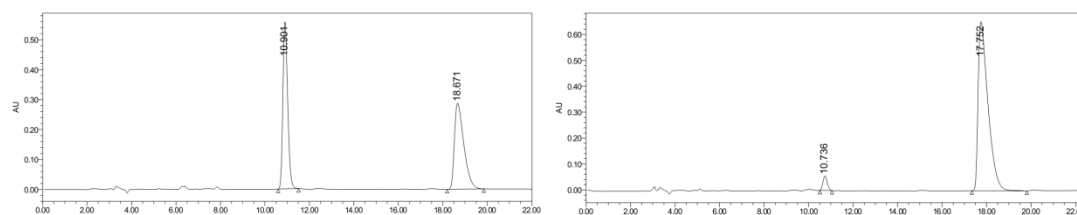


Optical active compound **4aa** (0.31 g, 1.0 mmol) and anhydrous potassium carbonate (345 mg, 2.5 mmol) was added to acetone (3 mL) at argon atmosphere. The mixture was stirred for 4h. The mixture was condensed under vacuo and the residue was purified by silicon column chromatography (petroleum ether: ethyl acetate = 10:1) to give the desired product **7** (315 mg, 97% yield).

To the solution of **7** (162 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (0.81 g, 4.0 mmol, 85%) and KH_2PO_4 (0.17 g, 1.25 mmol). The mixture was stirred for 24h at room temperature and then poured to the saturated NaHCO_3 solution. The aqueous layer was extracted with CH_2Cl_2 (3×5 mL). The combined organics were washed with brine, dried over Na_2SO_4 , filtered, and condensed under vacuo. The residue was purified by silicon column chromatography (petroleum ether: ethyl acetate = 20:1) to give the desired product **8** (132 mg, 78% yield).

7: white solid, mp 93.4-93.9 °C, $[\alpha]_D^{21} = +177.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 7.51-7.69 (m, 1 H), 7.49-7.52 (m, 2 H), 6.94-7.01 (m, 2 H), 5.71 (s, 1 H), 4.10 (d, $J=16.0$ Hz, 1 H), 3.97 (s, 3 H), 3.72 (d, $J=20.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 203.2, 160.4, 139.5, 136.4, 131.9, 129.9, 129.7, 128.7, 127.9, 127.5, 124.7, 122.3, 113.1, 57.1, 46.8; ^{19}F NMR (CDCl_3 , 564 MHz) δ -80.76 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{17}\text{H}_{15}\text{F}_3\text{O}_3 + \text{H}^+]$ 325.1046, found 325.1042.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 97/3; flow rate 1.0 mL/min; 248.7 nm; retention time: 10.7 min (minor) and 17.8 min (major).

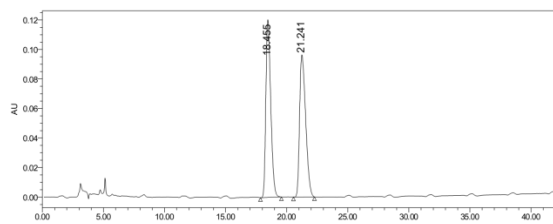


	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		10.901	8348014	558062	49.75
2		18.671	8432892	287191	50.25

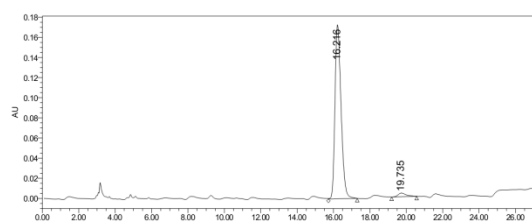
	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		10.736	766269	56231	3.67
2		17.752	20099116	652413	96.33

8: white solid, mp 71.4-71.7 °C, $[\alpha]_D^{21} = -51.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 7.68 (d, $J=8.0$ Hz, 1 H), 7.38-7.46 (m, 3 H), 7.16-7.20 (m, 1 H), 6.83-6.91 (m, 1 H), 6.01 (s, 1 H), 3.66 (s, 1 H), 3.53 (d, $J=16.0$ Hz, 1 H), 3.43 (d, $J=16.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.7, 152.1, 140.2, 138.3, 130.5, 129.9, 129.0, 128.2, 123.8, 122.2, 113.9, 77.2, 76.9, 39.9; ^{19}F NMR (CDCl_3 , 564 MHz) δ -81.01 (s, 3 F); HRMS: (ESI+) m/z calcd for $[\text{C}_{17}\text{H}_{15}\text{F}_3\text{O}_4 + \text{Na}^+]$ 363.0815, found 363.0820.

The ee was determined by HPLC analysis. CHIRALPAK OD-H; Hexane/2-propanol = 97/3; flow rate 1.0 mL/min; 270.0 nm; retention time: 16.3 min (major) and 19.7 min (minor).



	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		18.455	3347188	120289	50.16
2		21.241	3325779	96243	49.84



	Name	Retention time (min)	Area ($\mu\text{V}\cdot\text{s}$)	Height (μV)	% Area
1		16.216	4011001	172842	97.29
2		19.735	111595	3606	2.71

11. Determination of the absolute configuration by 5 X-ray crystallography

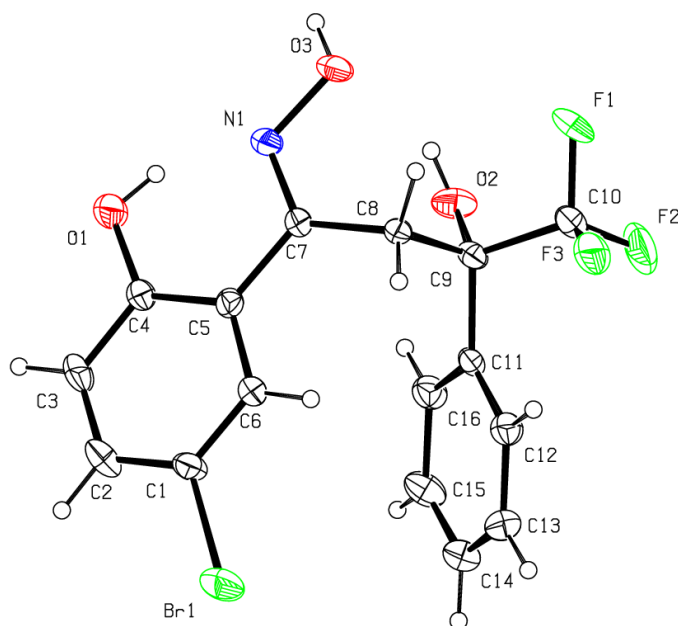
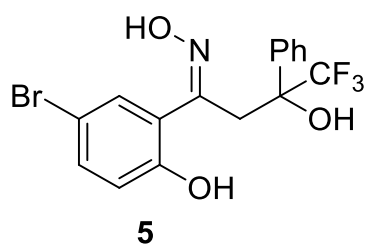


Table S1 Crystal data and structure refinement for 1.

Identification code	1
Empirical formula	C ₁₆ H ₁₃ NO ₃ BrF ₃
Formula weight	404.18
Temperature/K	296.15
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	5.8132(14)
b/Å	8.851(2)
c/Å	31.166(8)
α /°	90.00
β /°	90.00
γ /°	90.00
Volume/Å ³	1603.5(7)
Z	4

$\rho_{\text{calc}}/\text{g}/\text{cm}^3$	1.674
μ/mm^{-1}	2.610
F(000)	808.0
Crystal size/ mm^3	$0.3 \times 0.28 \times 0.2$
Radiation	MoK α ($\lambda = 0.71073$)
2 Θ range for data collection/ $^\circ$	2.62 to 53.14
Index ranges	$-7 \leq h \leq 7, -11 \leq k \leq 10, -32 \leq l \leq 39$
Reflections collected	9138
Independent reflections	3330 [$R_{\text{int}} = 0.0590, R_{\text{sigma}} = 0.0846$]
Data/restraints/parameters	3330/0/220
Goodness-of-fit on F^2	1.004
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0450, wR_2 = 0.0947$
Final R indexes [all data]	$R_1 = 0.0725, wR_2 = 0.1037$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.50/-0.63
Flack parameter	0.017(12)

Table S2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 1. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Atom	x	y	z	U_{eq}
Br1	13640.7(9)	-912.3(5)	1426.04(18)	65.6(2)
C1	11215(8)	49(4)	1727.5(13)	39.4(10)
C2	9983(8)	-758(5)	2023.3(15)	48.4(11)
C3	8310(9)	-61(4)	2249.9(14)	48.3(11)
C4	7799(7)	1460(4)	2178.2(13)	34.6(10)
C5	9049(7)	2293(4)	1877.2(11)	30.1(9)
C6	10779(8)	1545(4)	1652.8(13)	37.6(10)
C7	8546(7)	3899(4)	1788.0(11)	33.6(8)
C8	9675(6)	4783(4)	1435.8(12)	29.7(8)
C9	8263(7)	4751(4)	1014.9(12)	33.3(9)
C10	8938(9)	6144(4)	750.6(14)	47.7(11)
C11	8667(7)	3286(4)	769.6(11)	29.4(8)
C12	10710(7)	3001(5)	566.0(13)	37.9(10)
C13	11057(9)	1653(5)	355.8(14)	46.1(11)
C14	9399(8)	564(5)	355.6(14)	48.0(12)
C15	7344(8)	822(5)	561.9(15)	52.1(12)

C16	6962 (7)	2176 (5)	769.6 (14)	40.4 (10)
F1	8198 (6)	7402 (3)	948.2 (9)	72.2 (9)
F2	7975 (7)	6118 (3)	365.8 (9)	87.5 (11)
F3	11164 (6)	6295 (3)	700.8 (9)	63.7 (8)
N1	6996 (7)	4500 (4)	2036.2 (11)	46.7 (10)
O1	6077 (6)	2081 (3)	2421.5 (10)	54.4 (8)
O2	5855 (4)	4876 (3)	1096.1 (10)	47.3 (8)
O3	6538 (7)	6007 (3)	1934.3 (10)	59.7 (9)

Table S3 Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 1. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\dots]$.

Atom	U ₁₁	U ₂₂	U ₃₃	U ₂₃	U ₁₃	U ₁₂
Br1	73.7 (3)	44.8 (3)	78.3 (4)	2.5 (3)	14.7 (3)	27.5 (3)
C1	48 (2)	27 (2)	42 (2)	-2.6 (18)	-3 (2)	11 (2)
C2	53 (3)	27 (2)	65 (3)	13 (2)	-4 (2)	2 (2)
C3	63 (3)	28 (2)	54 (3)	16 (2)	10 (2)	-4 (2)
C4	43 (2)	25 (2)	36 (2)	3.2 (18)	7.6 (18)	-3.9 (17)
C5	39 (2)	27.0 (19)	24.6 (19)	-0.6 (16)	-0.6 (17)	-3.5 (17)
C6	52 (3)	27 (2)	33 (2)	3.8 (18)	6.9 (19)	5.0 (18)
C7	48 (2)	24.2 (18)	29 (2)	2.9 (16)	5.7 (19)	1 (2)
C8	41 (2)	20.0 (17)	28 (2)	-1.4 (18)	4.7 (18)	-1.0 (15)
C9	40 (2)	21.7 (18)	39 (2)	2.6 (17)	4.6 (18)	4.1 (18)
C10	75 (3)	28 (2)	40 (3)	4.1 (19)	-3 (2)	10 (2)
C11	39 (2)	20.4 (17)	29 (2)	4.0 (15)	-2.8 (19)	2.5 (17)
C12	40 (3)	34 (2)	40 (2)	2 (2)	5.3 (18)	-0.7 (18)
C13	53 (3)	44 (2)	41 (2)	-3 (2)	10 (2)	12 (2)
C14	63 (3)	31 (2)	50 (3)	-3 (2)	3 (2)	5 (2)
C15	62 (3)	25 (2)	69 (3)	-3 (3)	-2 (2)	-8 (2)
C16	38 (2)	35 (2)	48 (3)	3 (2)	6.1 (19)	0.5 (18)
F1	113 (3)	21.7 (13)	82 (2)	7.8 (13)	10.9 (19)	18.3 (16)
F2	156 (3)	54.1 (18)	52.8 (18)	22.4 (15)	-29.0 (19)	8 (2)
F3	82 (2)	38.5 (15)	70.4 (19)	14.7 (13)	25.2 (17)	-7.7 (16)
N1	71 (3)	24.3 (17)	45 (2)	2.8 (16)	24.5 (19)	7.3 (16)
O1	69 (2)	36.3 (16)	58 (2)	10.7 (15)	31.3 (18)	4.5 (17)
O2	34.4 (16)	42.5 (17)	65 (2)	-12.7 (16)	4.4 (13)	8.1 (14)
O3	91 (3)	25.9 (14)	63 (2)	4.1 (15)	37.7 (19)	17.0 (19)

Table S4 Bond Lengths for 1.

Atom	Atom	Length/ $\text{\AA}$	Atom	Atom	Length/ $\text{\AA}$
Br1	C1	1.896 (4)	C9	C11	1.524 (5)
C1	C2	1.368 (6)	C9	O2	1.427 (5)

C1	C6	1.368 (5)	C10	F1	1.343 (5)
C2	C3	1.351 (6)	C10	F2	1.324 (5)
C3	C4	1.396 (6)	C10	F3	1.310 (6)
C4	C5	1.397 (5)	C11	C12	1.370 (6)
C4	O1	1.371 (5)	C11	C16	1.395 (5)
C5	C6	1.392 (6)	C12	C13	1.376 (6)
C5	C7	1.477 (5)	C13	C14	1.363 (6)
C7	C8	1.500 (5)	C14	C15	1.376 (6)
C7	N1	1.301 (5)	C15	C16	1.380 (6)
C8	C9	1.548 (6)	N1	O3	1.397 (4)
C9	C10	1.534 (6)			

Table S5 Bond Angles for 1.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C2	C1	Br1	119.3 (3)	O2	C9	C8	111.6 (3)
C2	C1	C6	121.5 (4)	O2	C9	C10	106.5 (3)
C6	C1	Br1	119.2 (4)	O2	C9	C11	107.8 (4)
C3	C2	C1	119.4 (4)	F1	C10	C9	109.8 (4)
C2	C3	C4	120.6 (4)	F2	C10	C9	111.4 (4)
C3	C4	C5	120.4 (4)	F2	C10	F1	107.1 (4)
O1	C4	C3	116.9 (4)	F3	C10	C9	113.4 (4)
O1	C4	C5	122.7 (4)	F3	C10	F1	106.6 (4)
C4	C5	C7	122.1 (4)	F3	C10	F2	108.2 (4)
C6	C5	C4	117.5 (3)	C12	C11	C9	121.5 (4)
C6	C5	C7	120.4 (3)	C12	C11	C16	119.1 (3)
C1	C6	C5	120.6 (4)	C16	C11	C9	119.3 (4)
C5	C7	C8	123.6 (3)	C11	C12	C13	120.5 (4)
N1	C7	C5	114.7 (3)	C14	C13	C12	120.6 (4)
N1	C7	C8	121.7 (3)	C13	C14	C15	119.8 (4)
C7	C8	C9	112.2 (3)	C14	C15	C16	120.2 (4)
C10	C9	C8	107.7 (3)	C15	C16	C11	119.8 (4)
C11	C9	C8	111.1 (3)	C7	N1	O3	112.8 (3)
C11	C9	C10	112.0 (3)				

Table S6 Torsion Angles for 1.

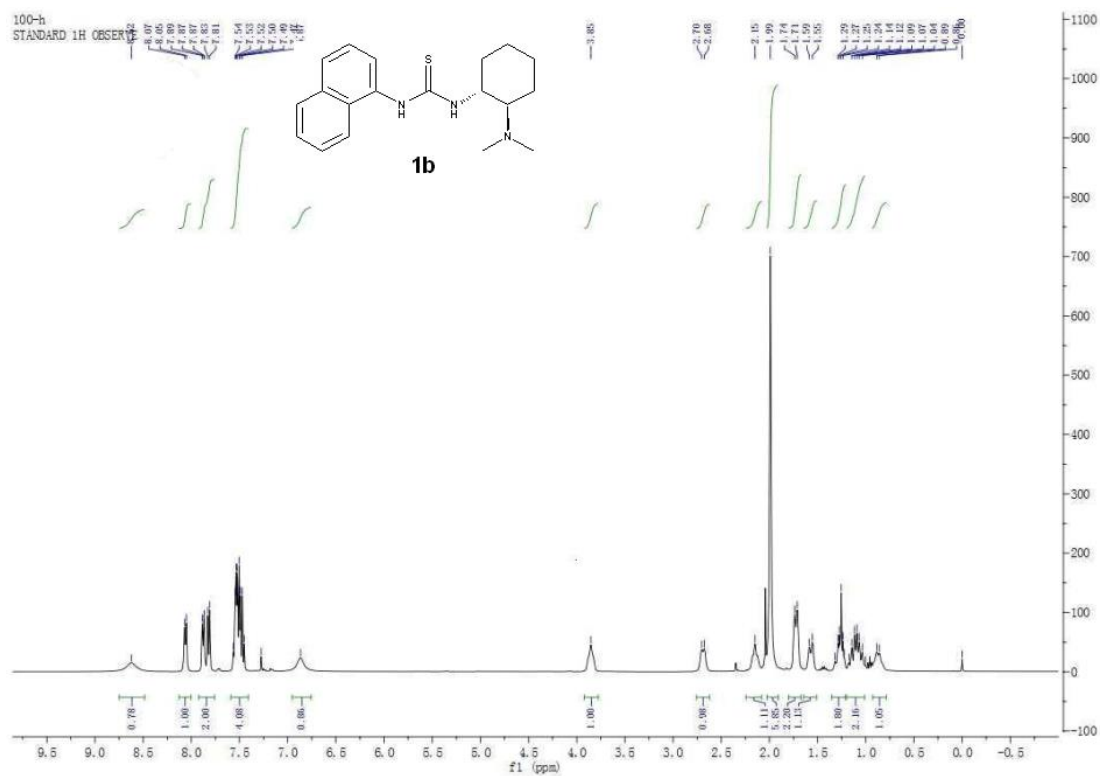
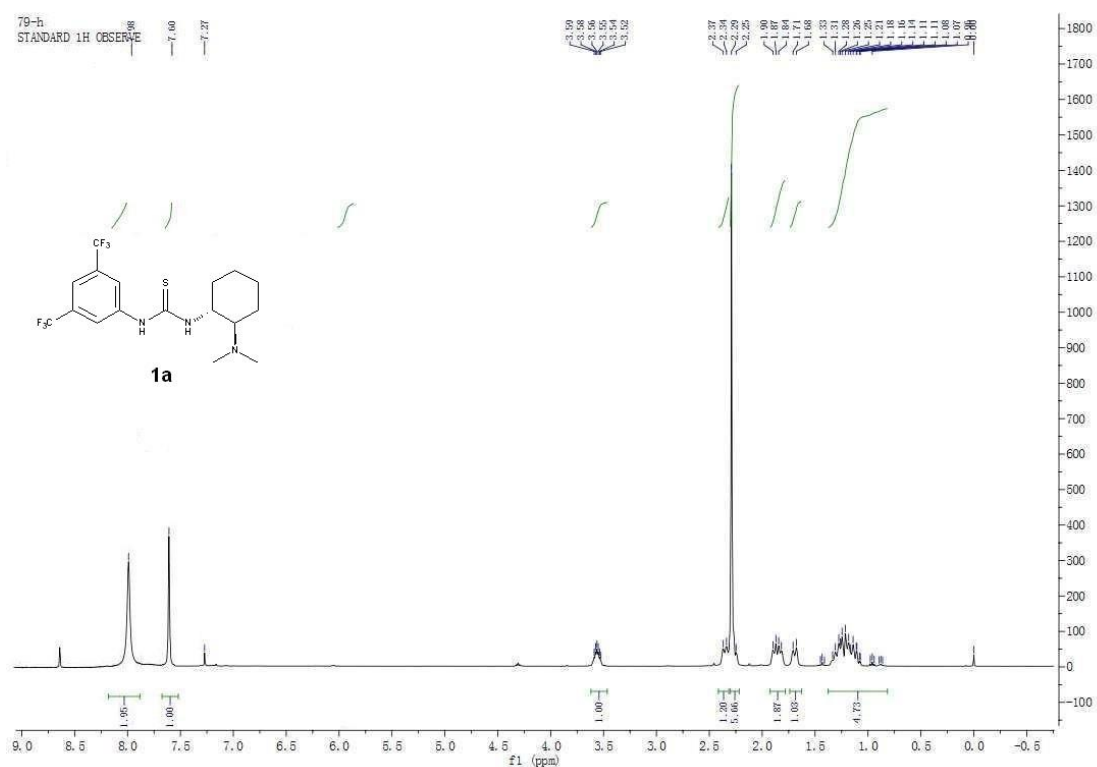
A	B	C	D	Angle/°	A	B	C	D	Angle/°
Br1	C1	C2	C3	177.6 (4)	C8	C9	C11	C12	-71.6 (4)
Br1	C1	C6	C5	-178.3 (3)	C8	C9	C11	C16	105.2 (4)
C1	C2	C3	C4	1.3 (7)	C9	C11	C12	C13	178.3 (4)
C2	C1	C6	C5	-0.2 (7)	C9	C11	C16	C15	-177.6 (4)
C2	C3	C4	C5	-1.5 (7)	C10	C9	C11	C12	49.0 (5)

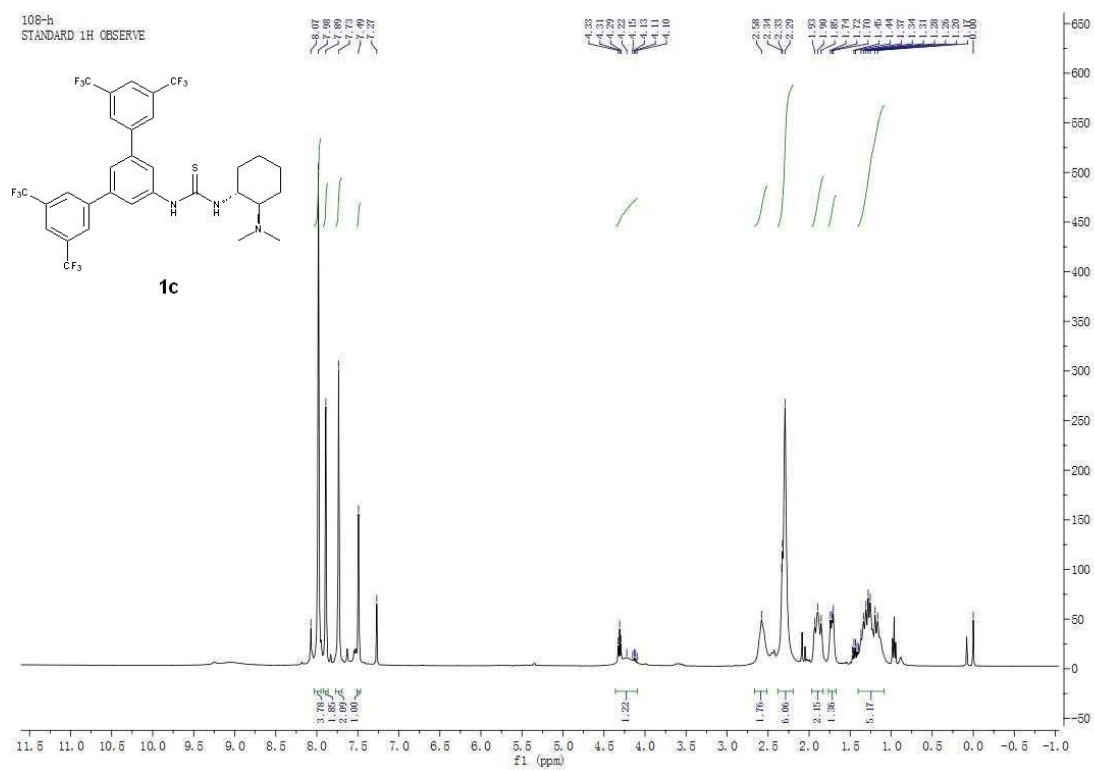
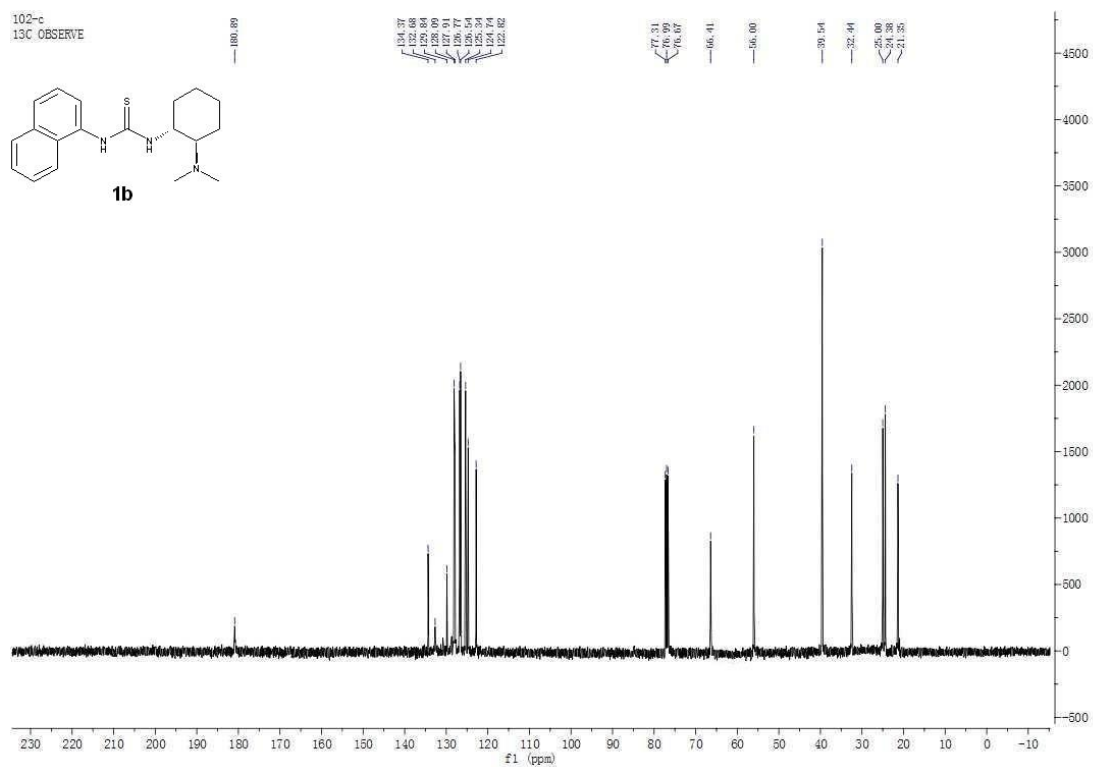
C2 C3C4 O1	180.0 (4)	C10C9 C11C16	-134.2 (4)
C3 C4C5 C6	0.7 (6)	C11C9 C10F1	169.6 (4)
C3 C4C5 C7	179.2 (4)	C11C9 C10F2	51.2 (5)
C4 C5C6 C1	0.1 (6)	C11C9 C10F3	-71.2 (5)
C4 C5C7 C8	-173.3 (4)	C11C12C13C14	-1.6 (6)
C4 C5C7 N1	5.7 (6)	C12C11C16C15	-0.7 (6)
C5 C7C8 C9	92.8 (4)	C12C13C14C15	1.0 (7)
C5 C7N1 O3	-178.7 (4)	C13C14C15C16	-0.2 (7)
C6 C1C2 C3	-0.5 (7)	C14C15C16C11	0.1 (7)
C6 C5C7 C8	5.2 (6)	C16C11C12C13	1.5 (6)
C6 C5C7 N1	-175.9 (4)	N1 C7 C8 C9	-86.0 (5)
C7 C5C6 C1	-178.5 (4)	O1 C4 C5 C6	179.2 (4)
C7 C8C9 C10	156.6 (3)	O1 C4 C5 C7	-2.3 (6)
C7 C8C9 C11	-80.3 (4)	O2 C9 C10F1	52.0 (5)
C7 C8C9 O2	40.1 (4)	O2 C9 C10F2	-66.5 (5)
C8 C7N1 O3	0.3 (6)	O2 C9 C10F3	171.2 (3)
C8 C9C10F1	-67.9 (4)	O2 C9 C11C12	165.8 (4)
C8 C9C10F2	173.6 (4)	O2 C9 C11C16	-17.4 (5)
C8 C9C10F3	51.3 (4)		

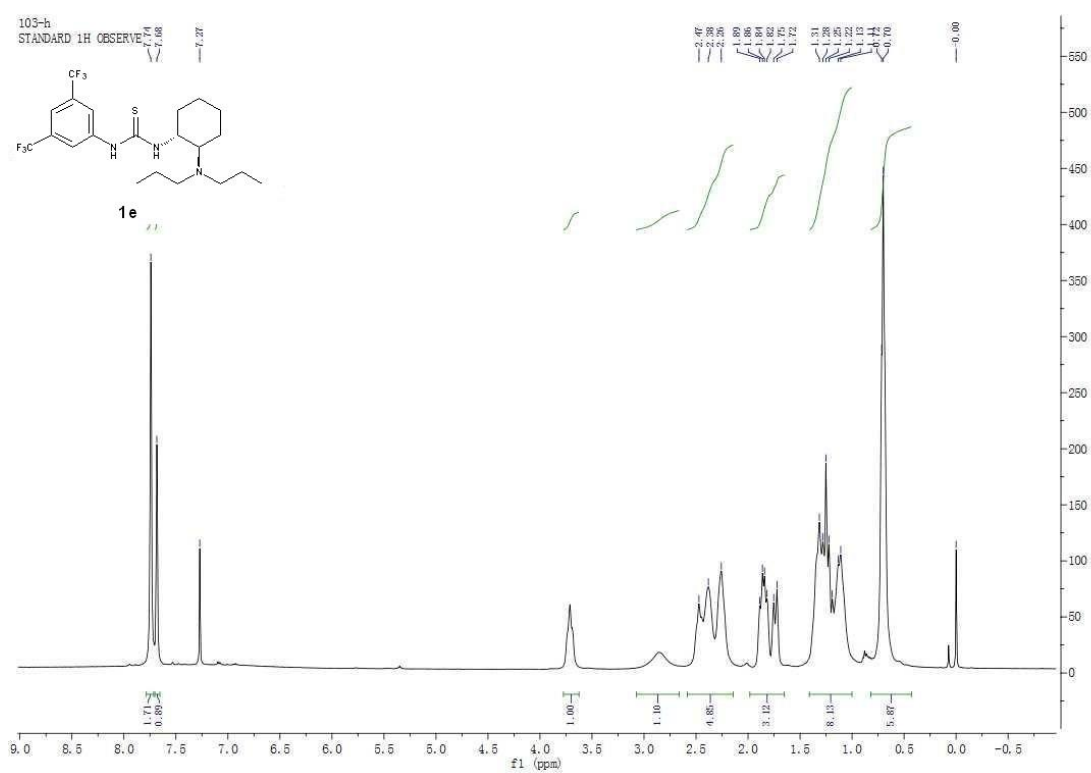
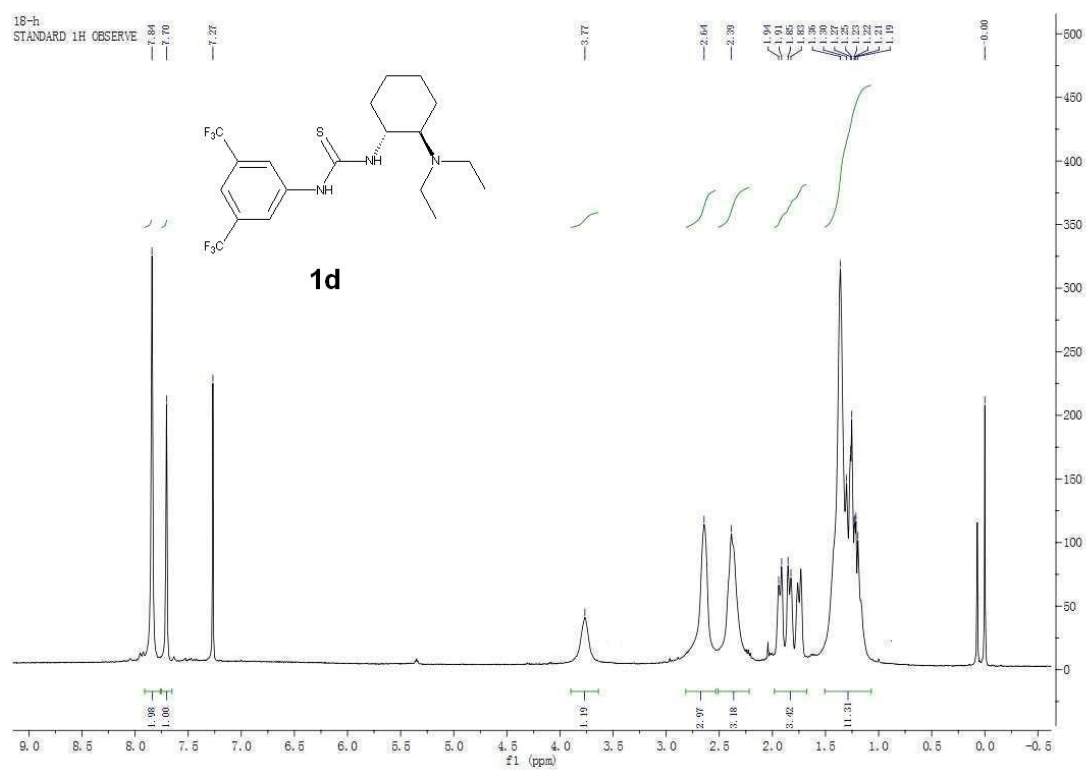
Table S7 Hydrogen Atom Coordinates ($\text{\AA} \times 10^4$) and Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 1.

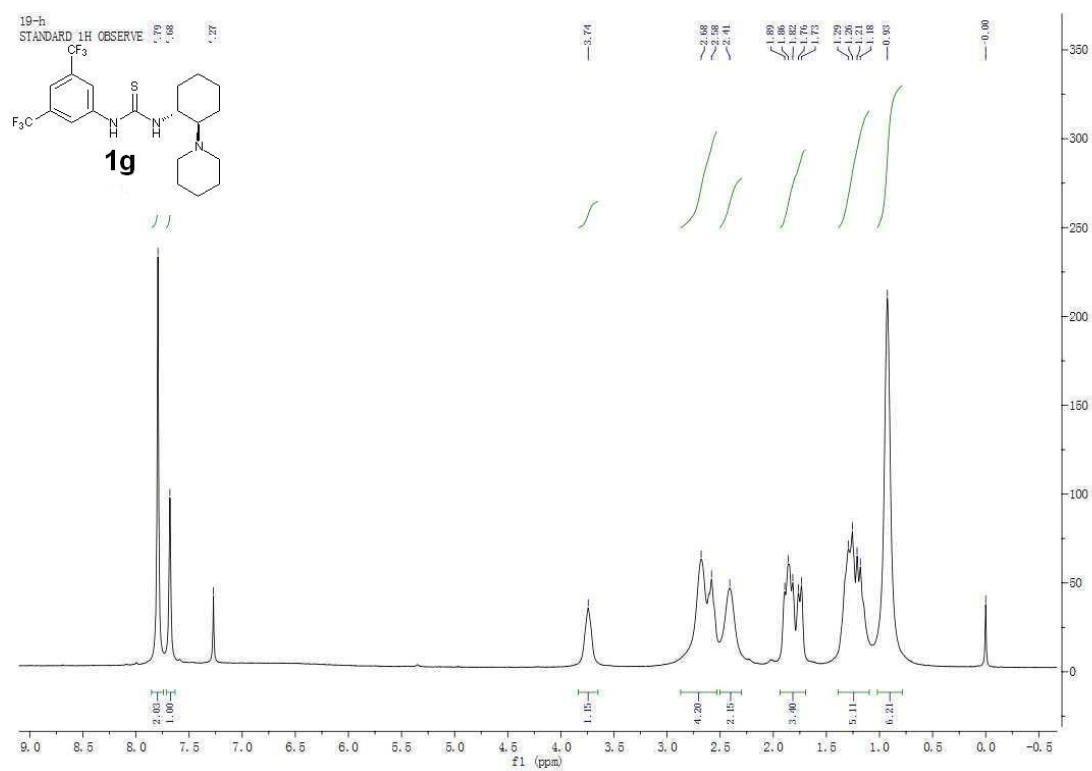
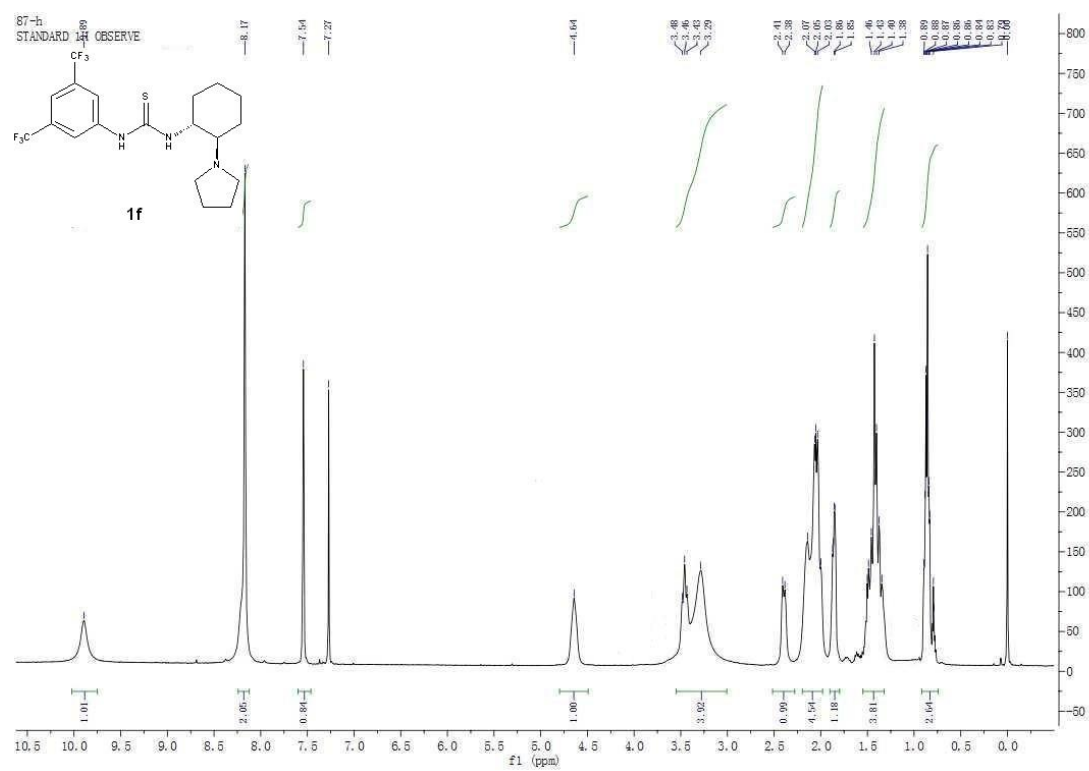
Atom	x	y	z	U(eq)
H2	10295	-1776	2068	58
H3	7490	-599	2456	58
H6	11645	2067	1450	45
H8A	11193	4369	1382	36
H8B	9864	5823	1528	36
H12	11871	3724	570	46
H13	12436	1483	213	55
H14	9656	-350	216	58
H15	6208	82	561	62
H16	5573	2349	909	49
H1	5724	2908	2323	82
H2A	5645	5409	1308	71
H3A	5413	6297	2070	90

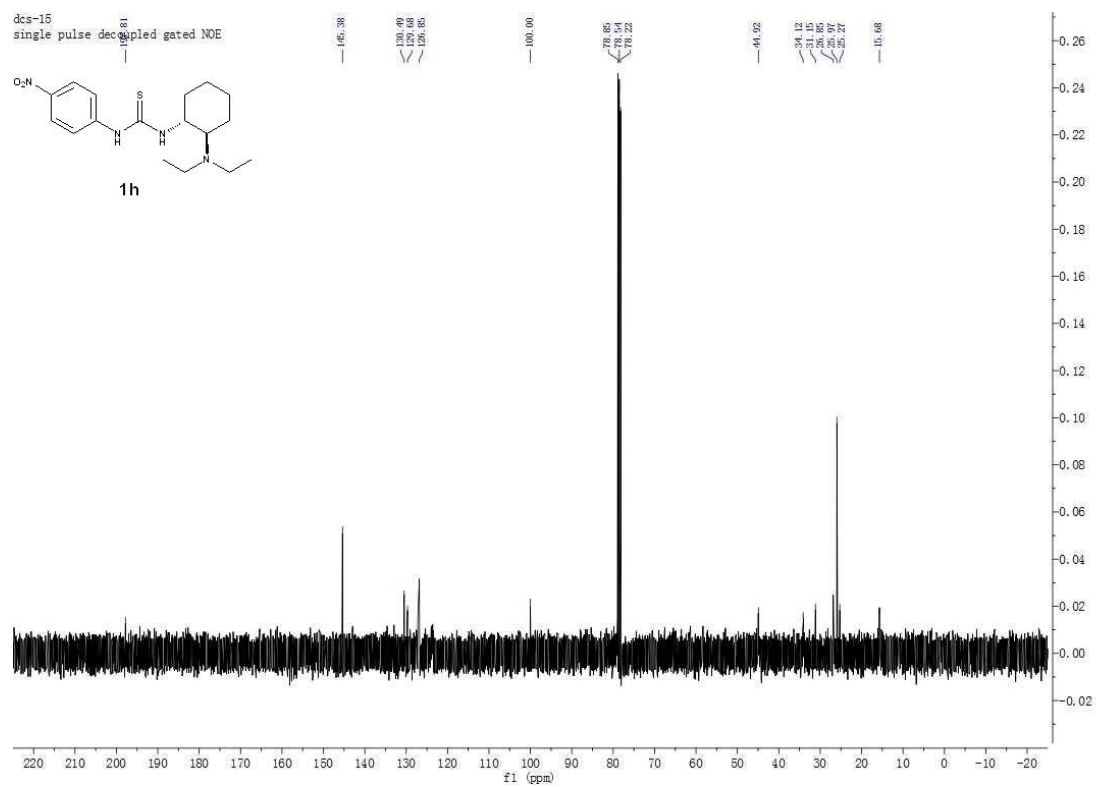
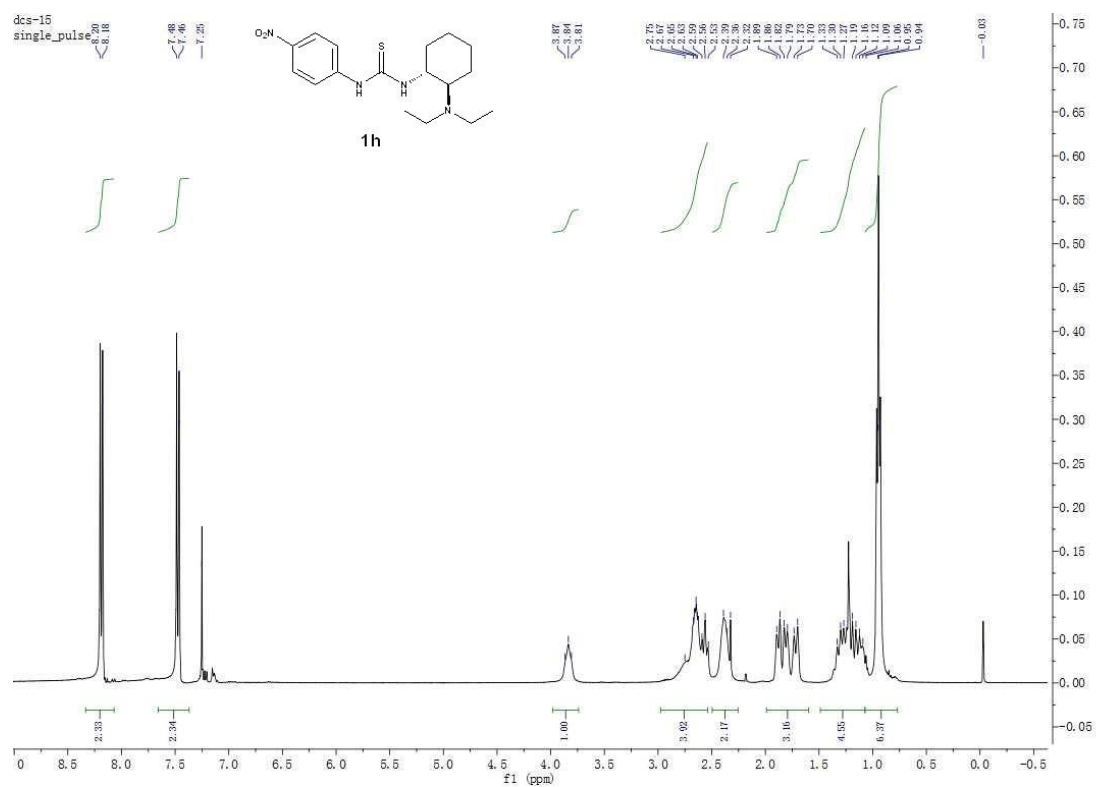
12. Copies of NMR spectra

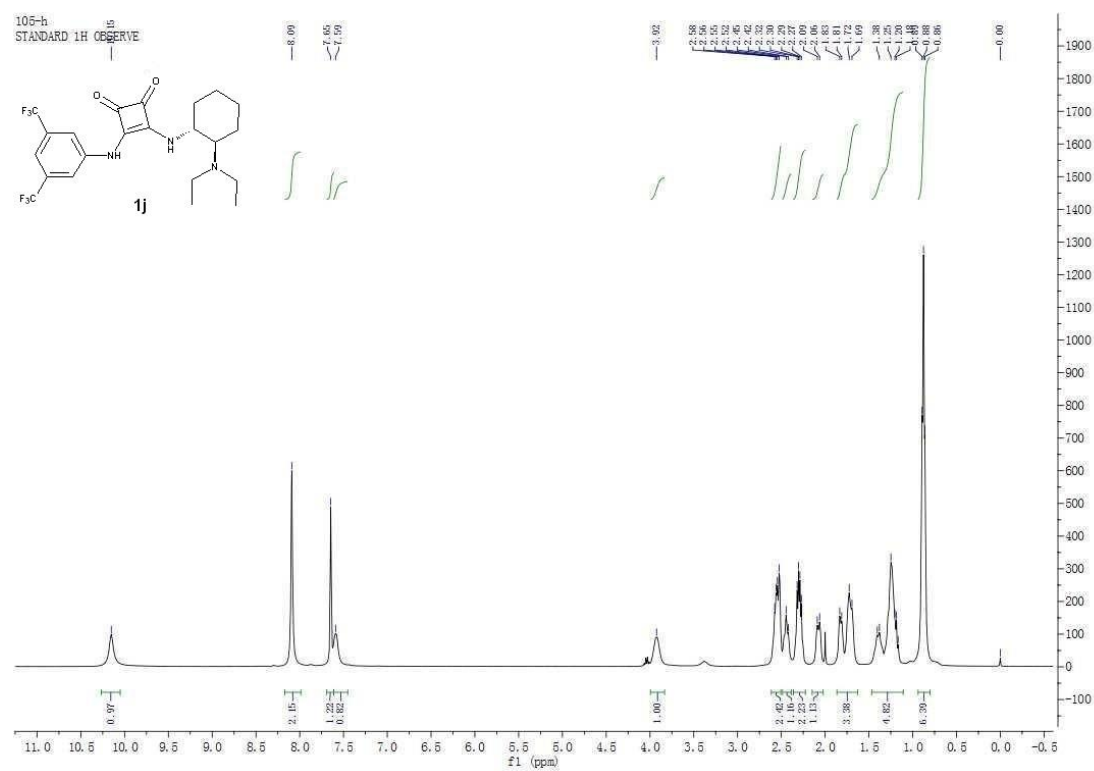
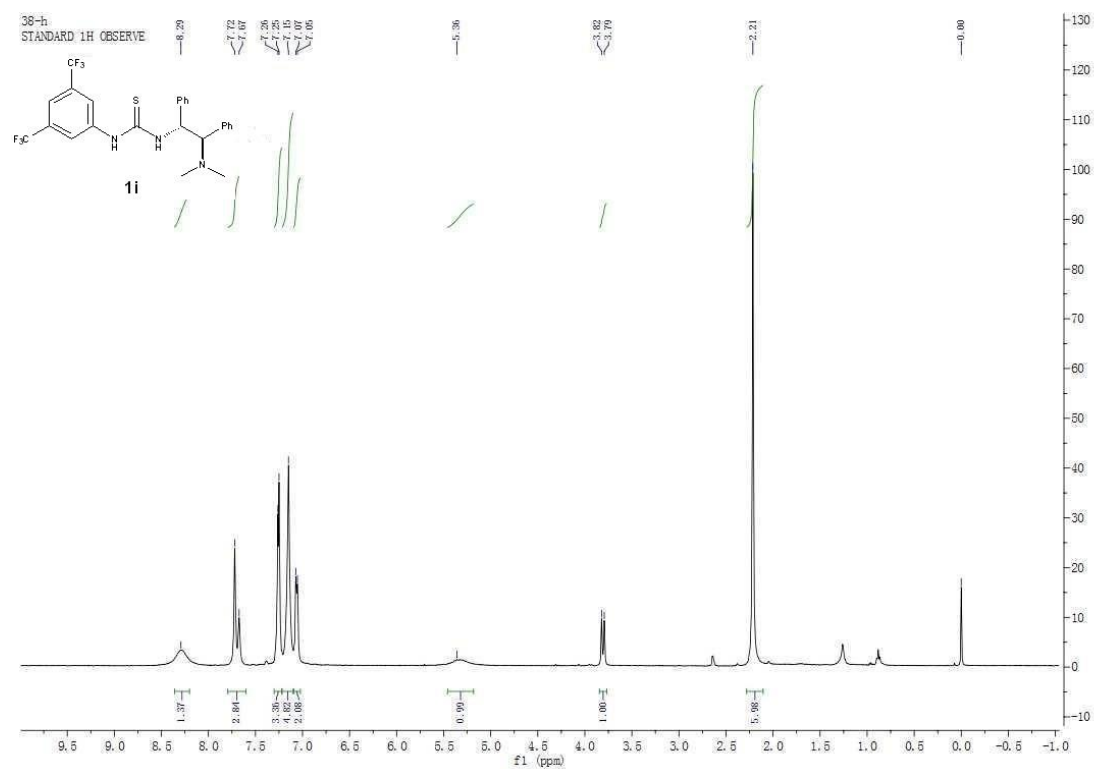


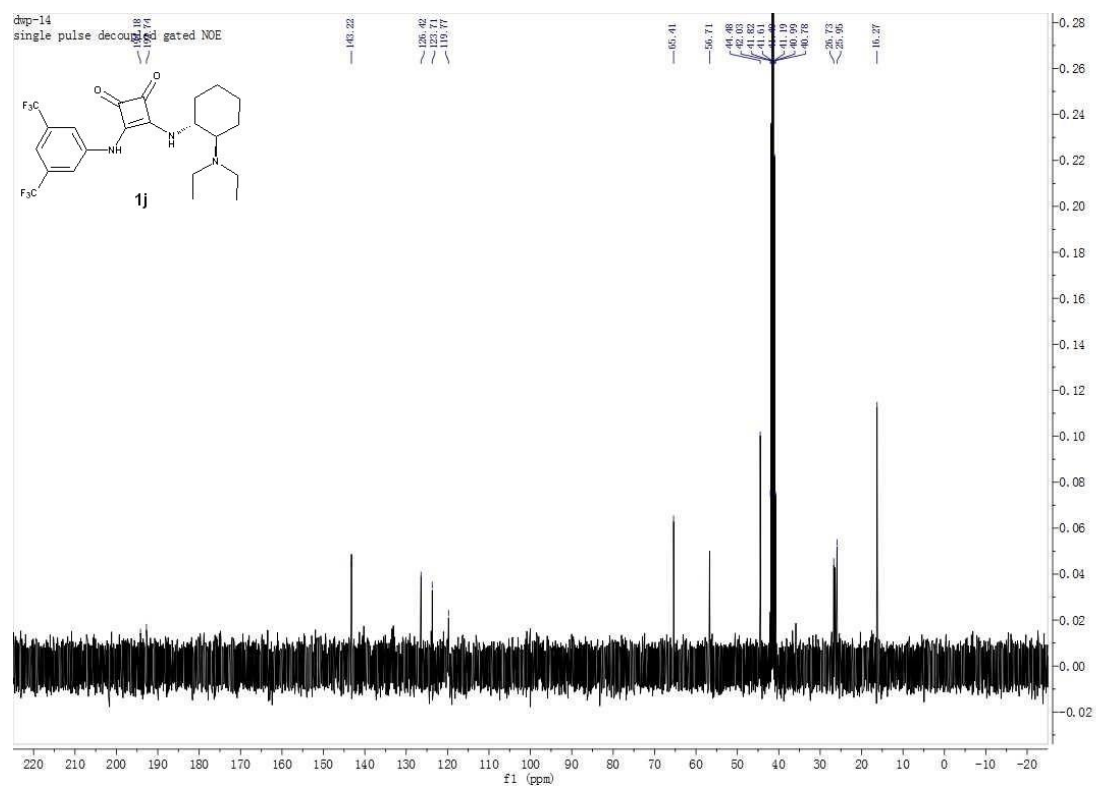


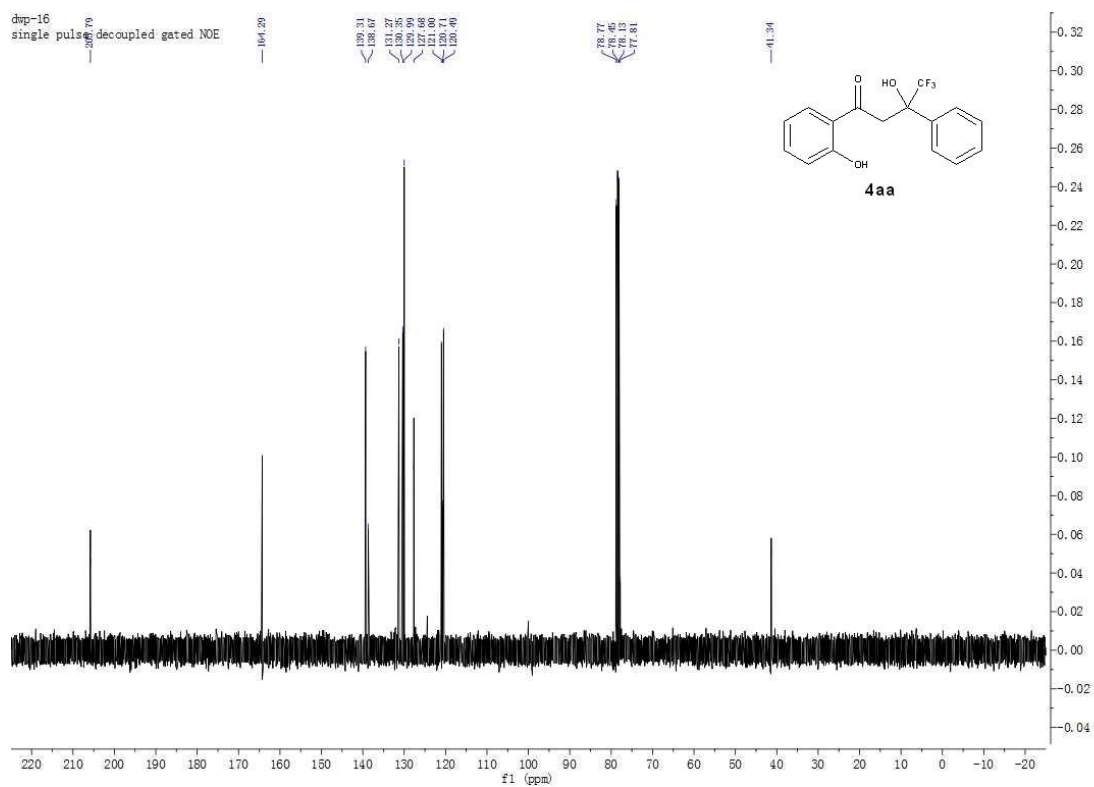
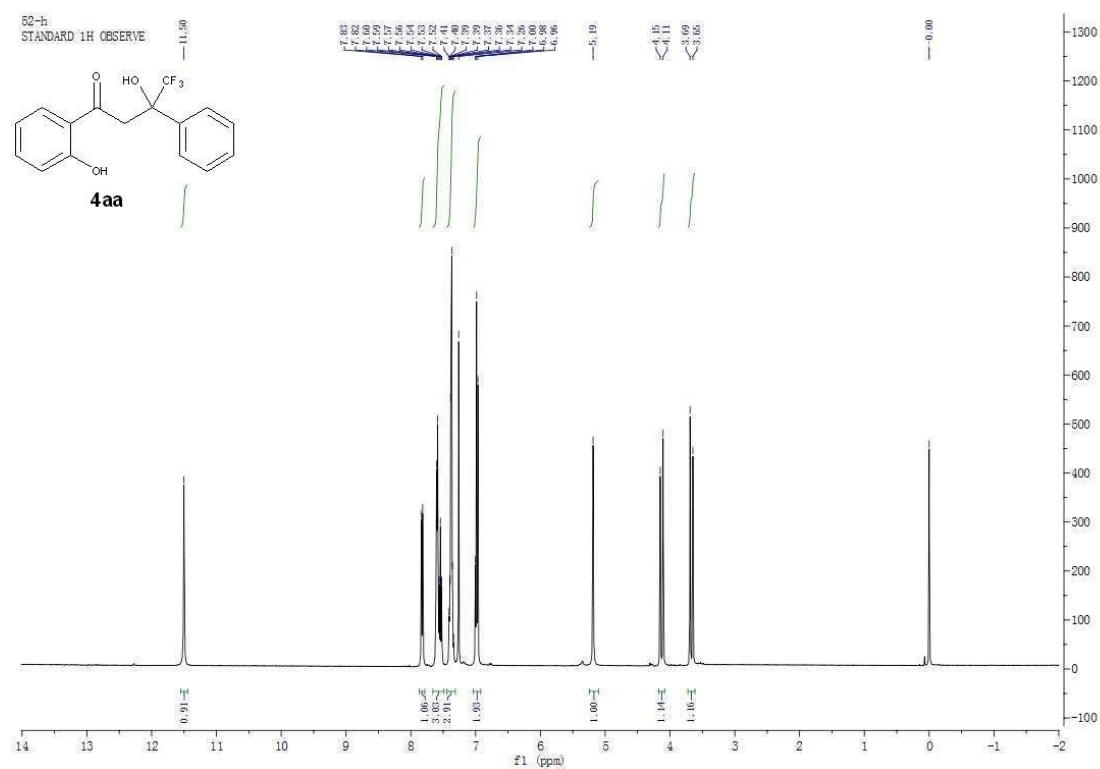


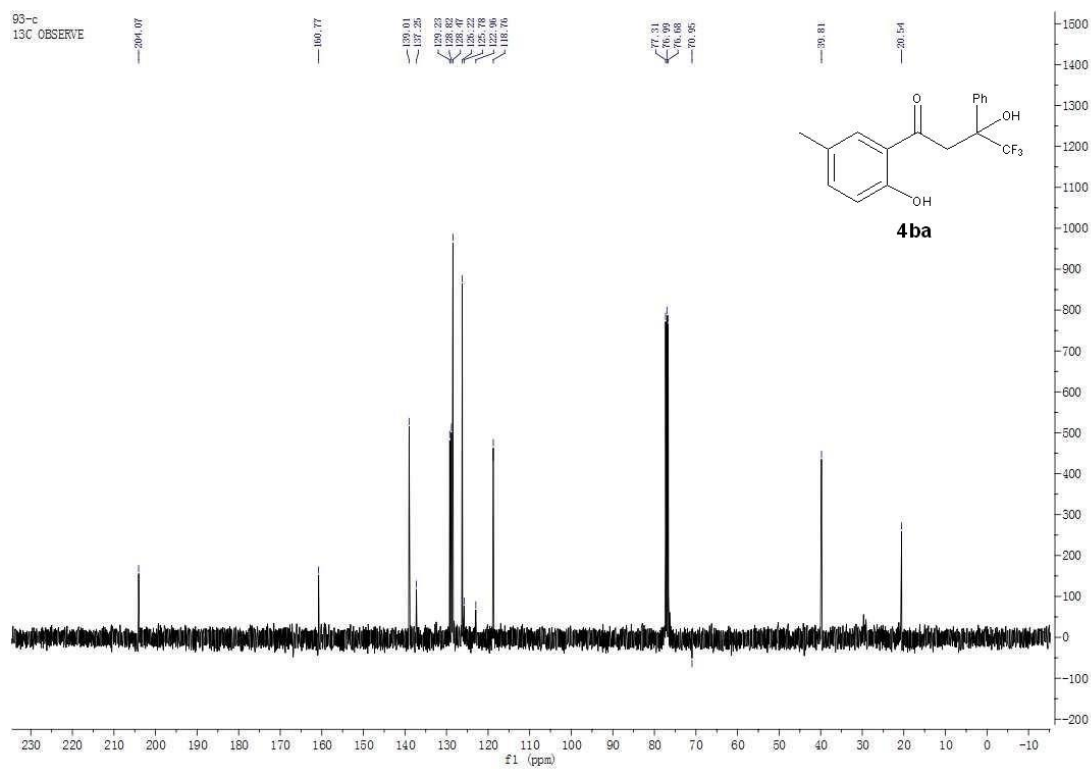
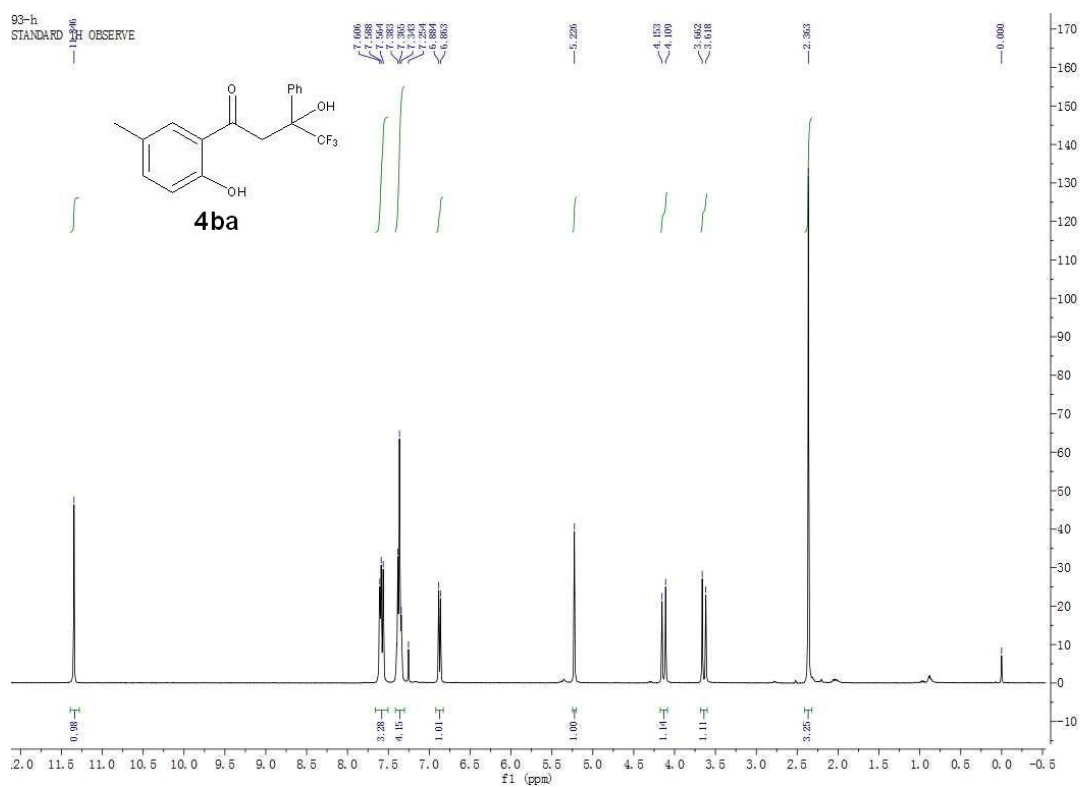


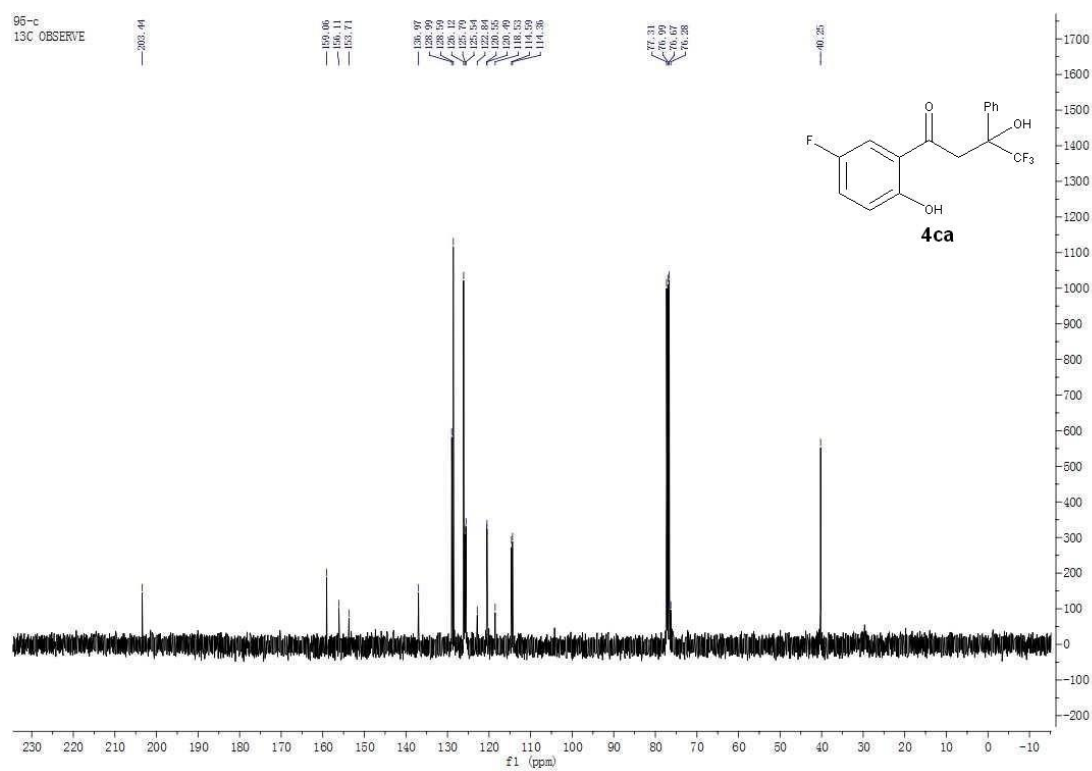
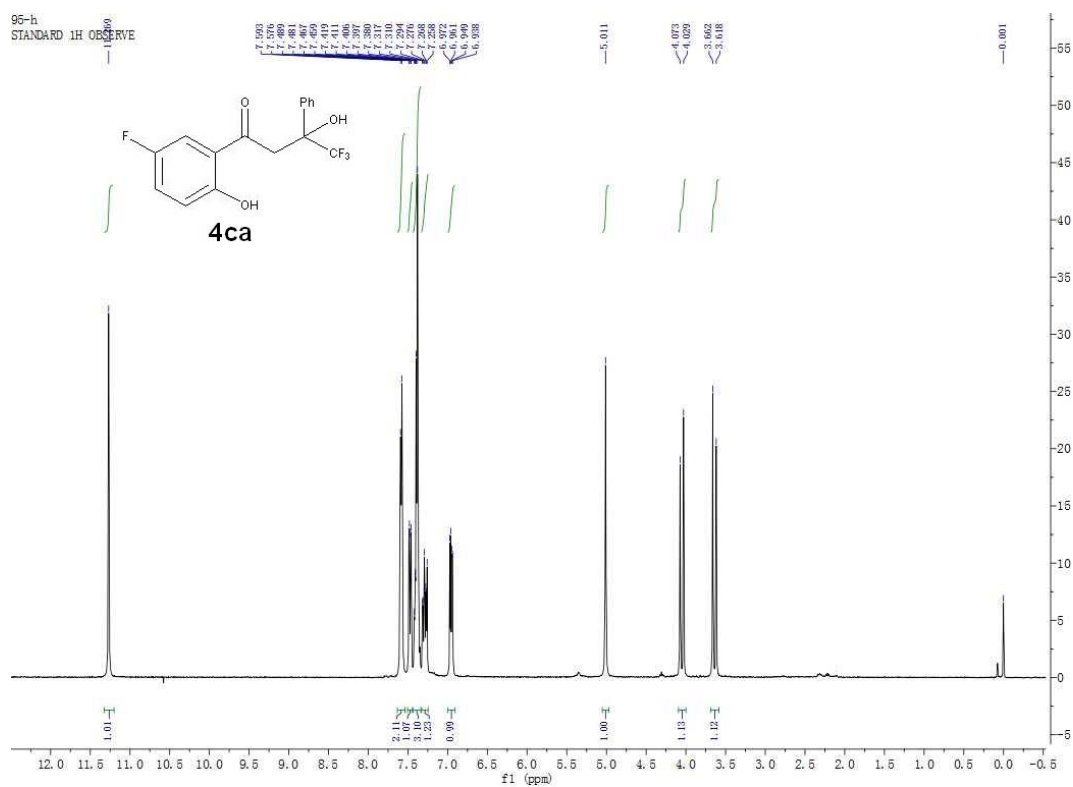


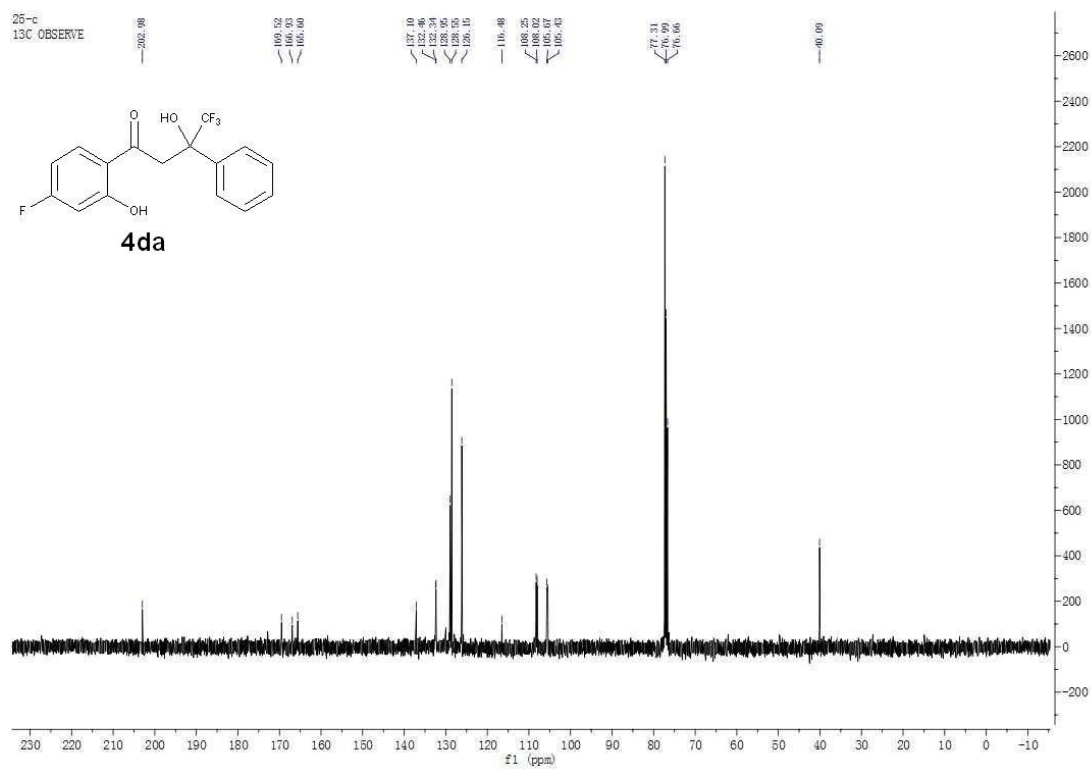
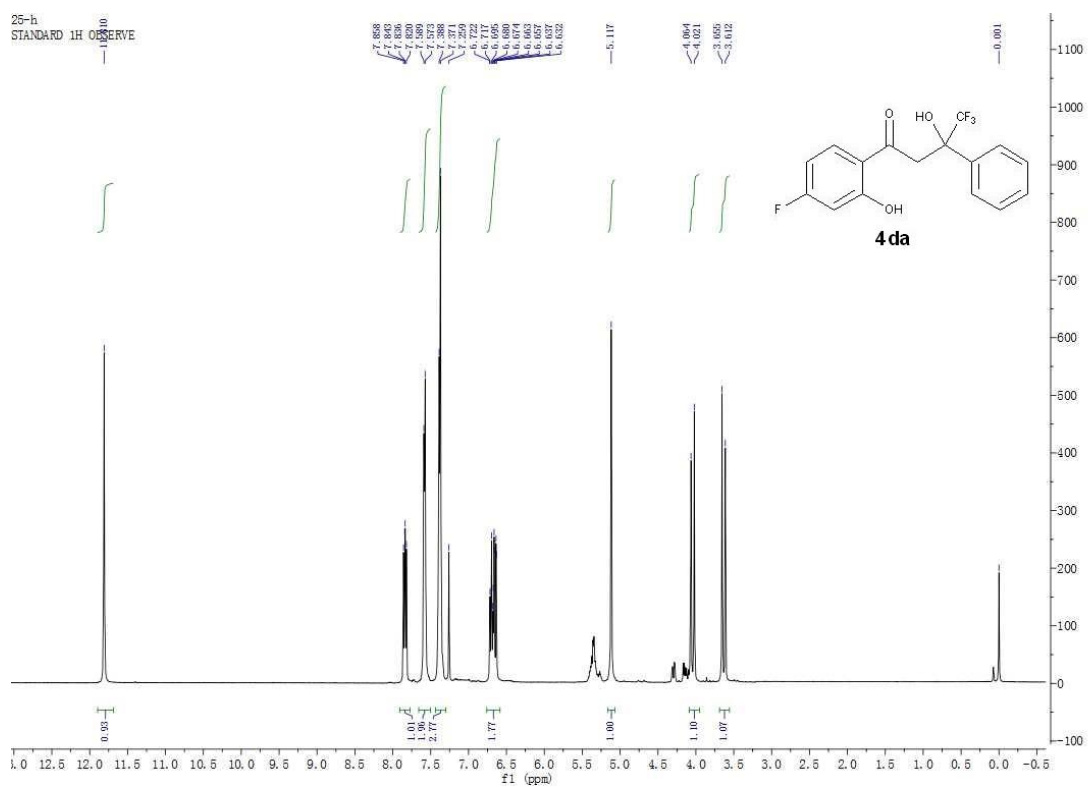


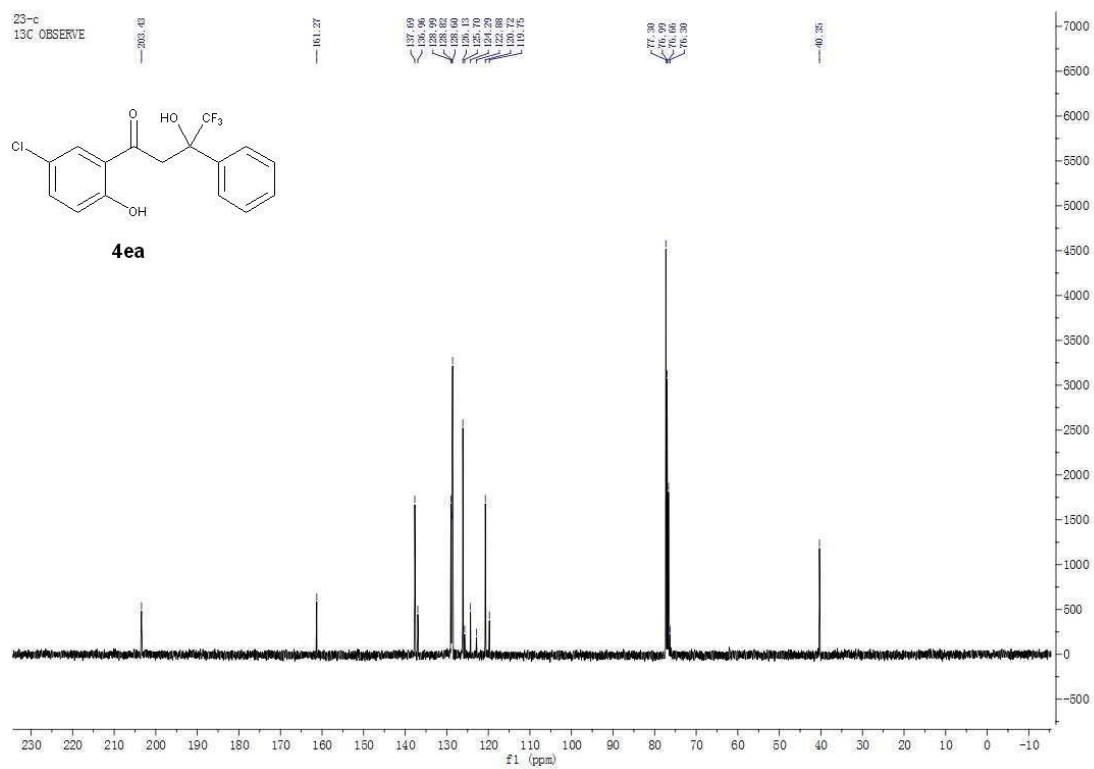
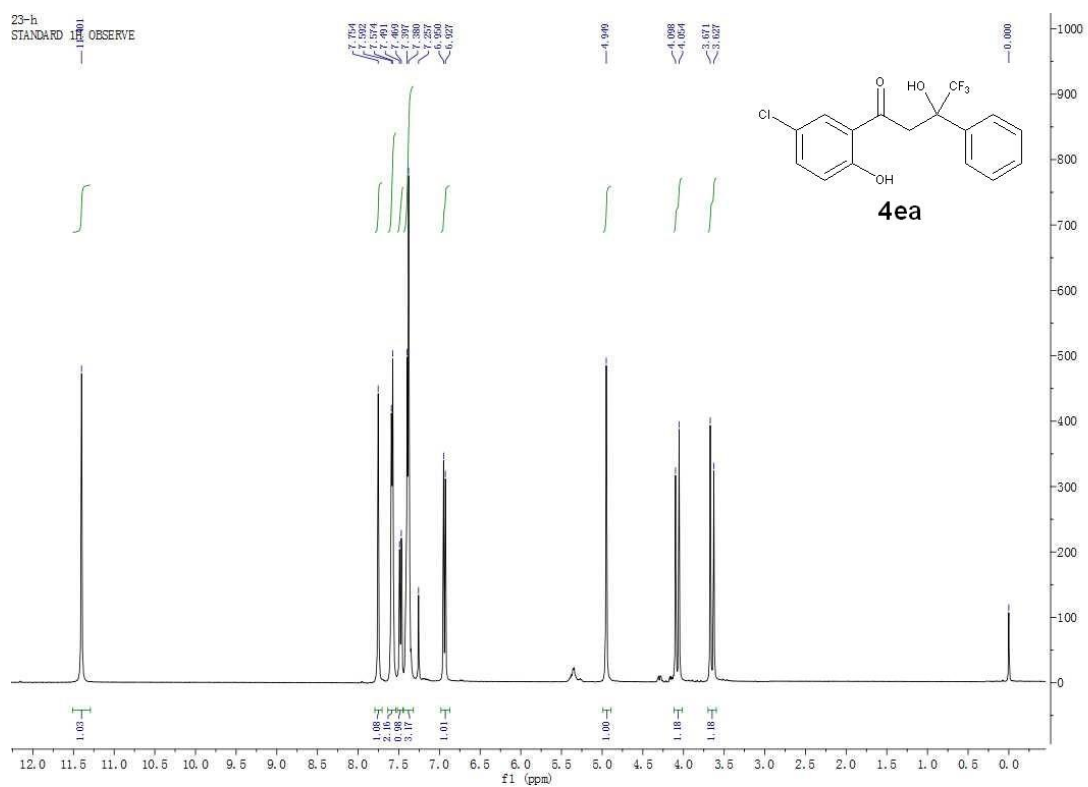


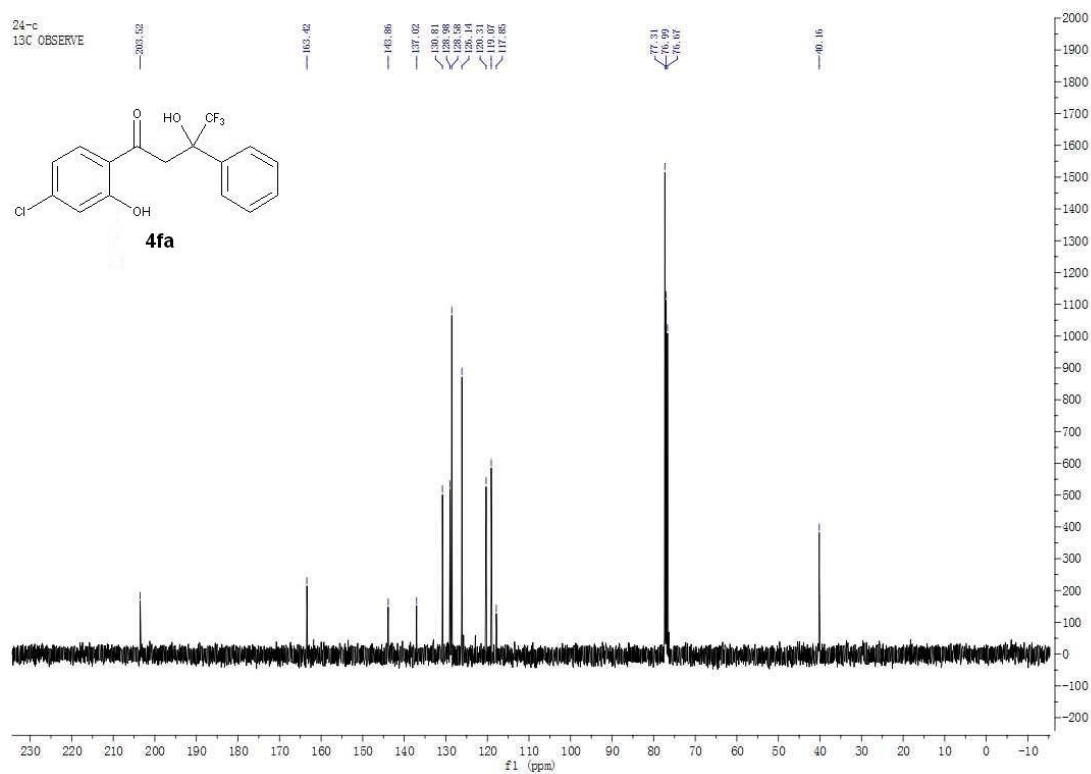
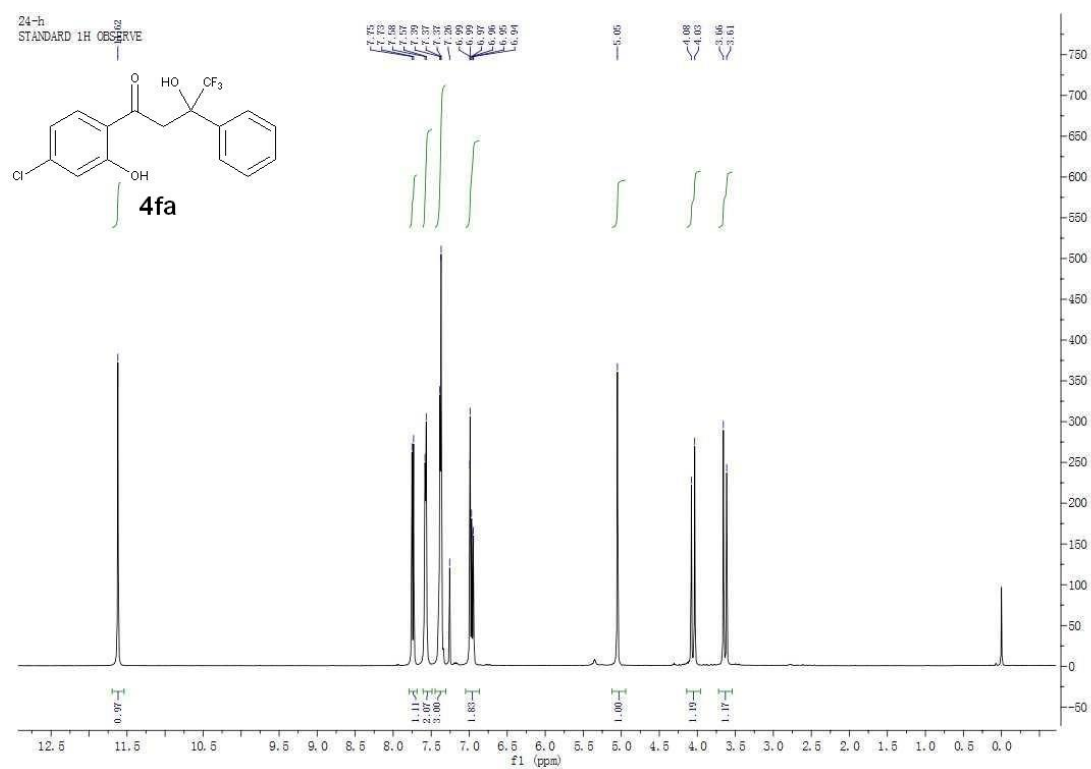


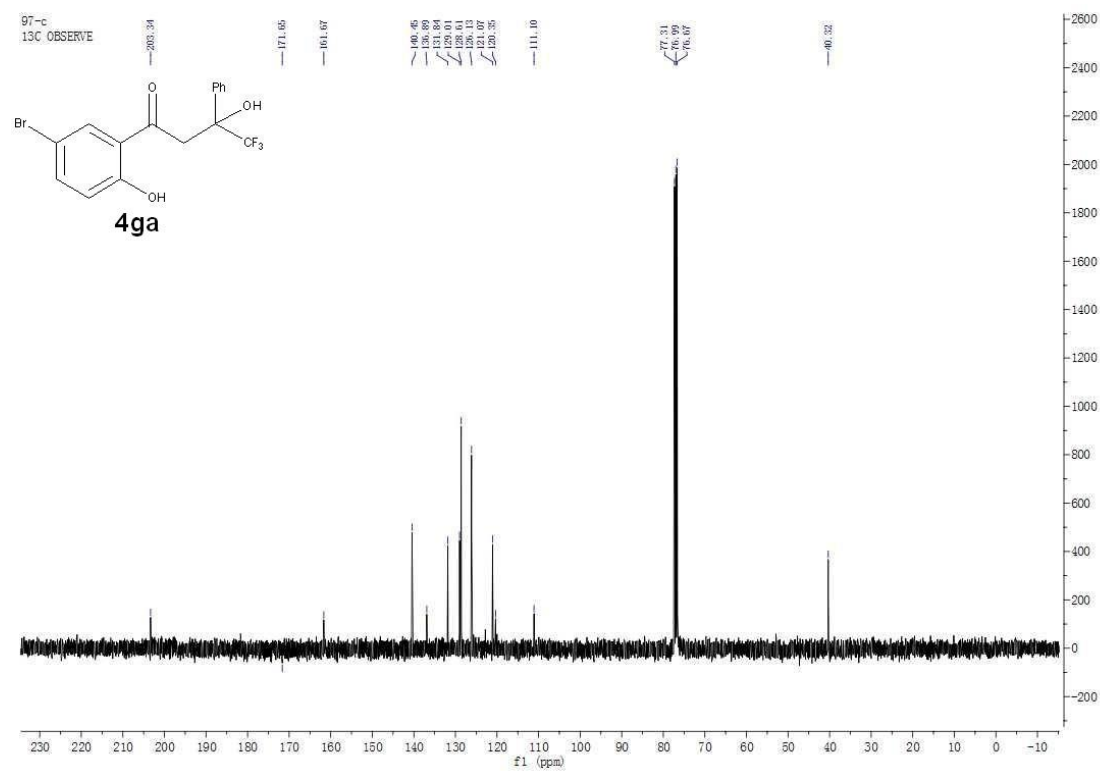
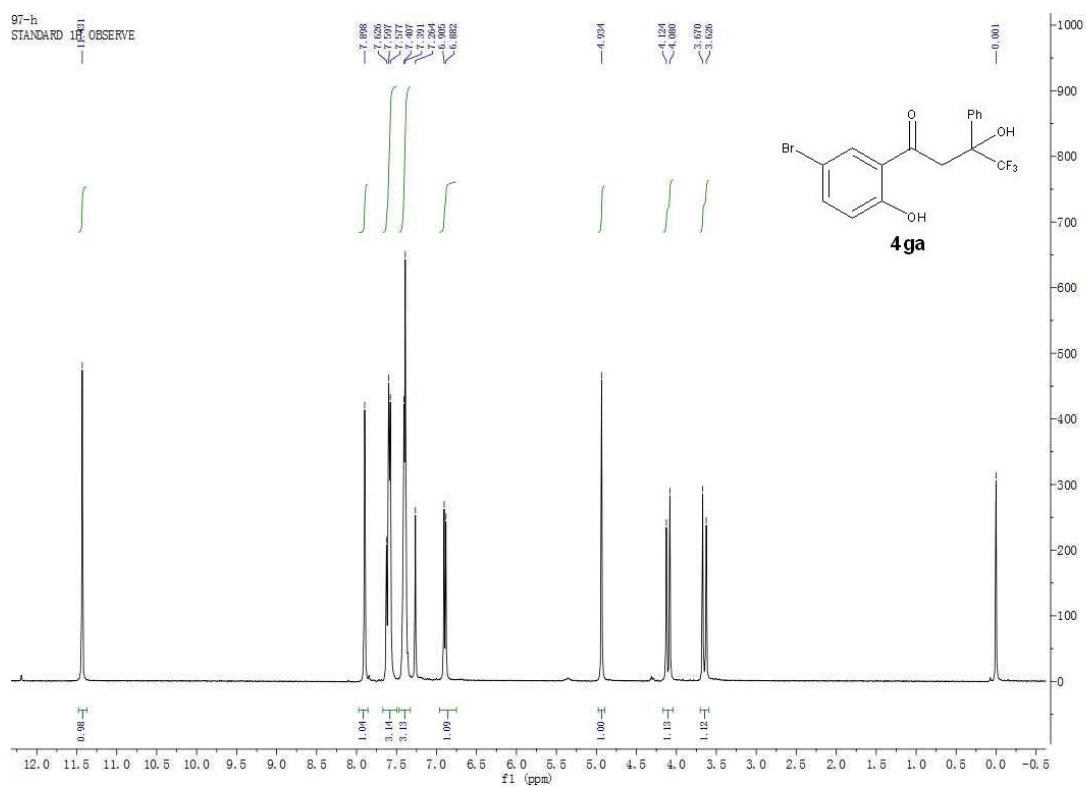


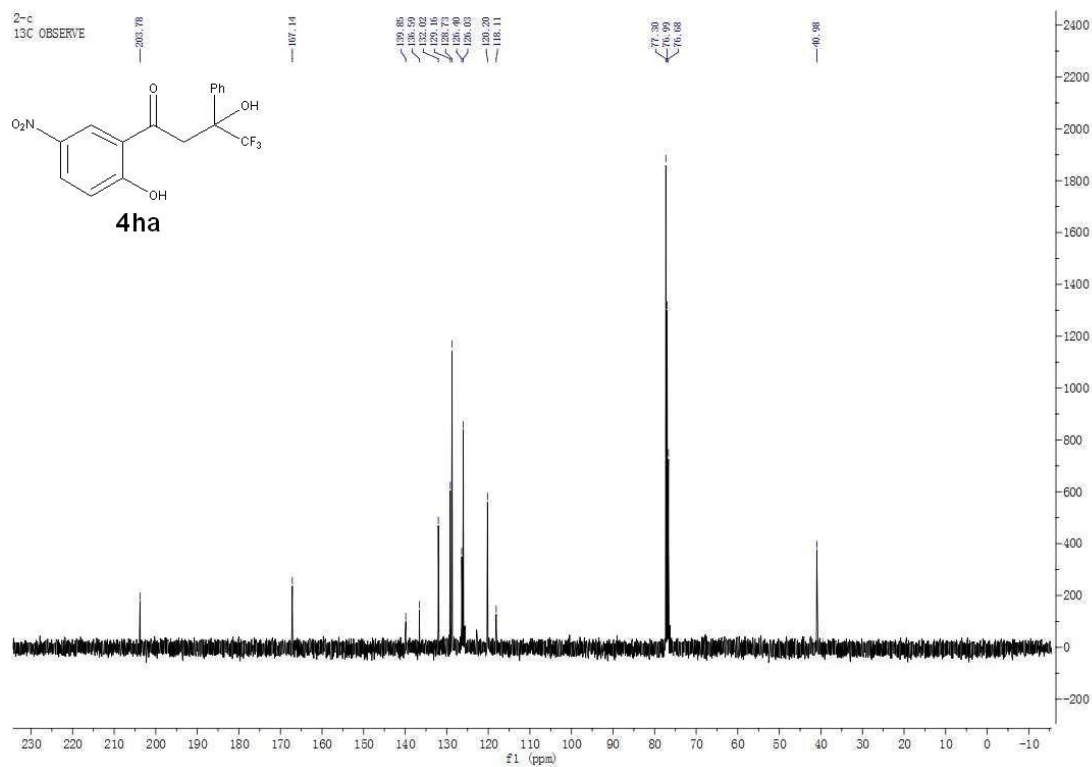


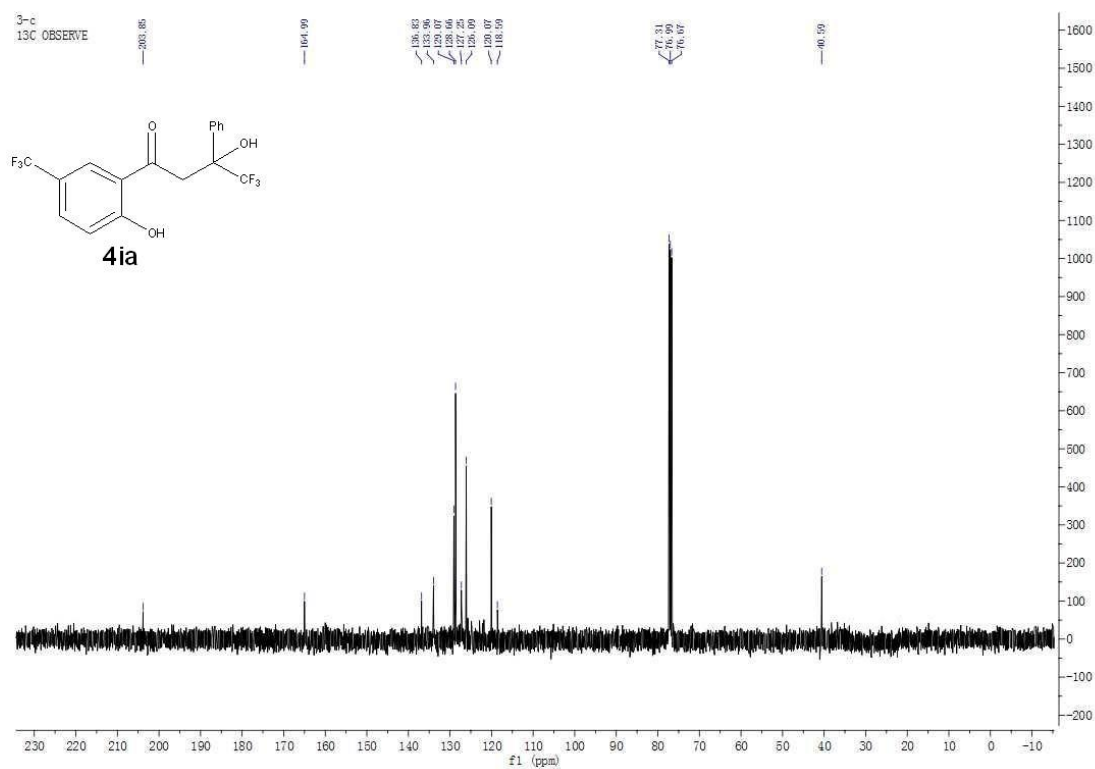
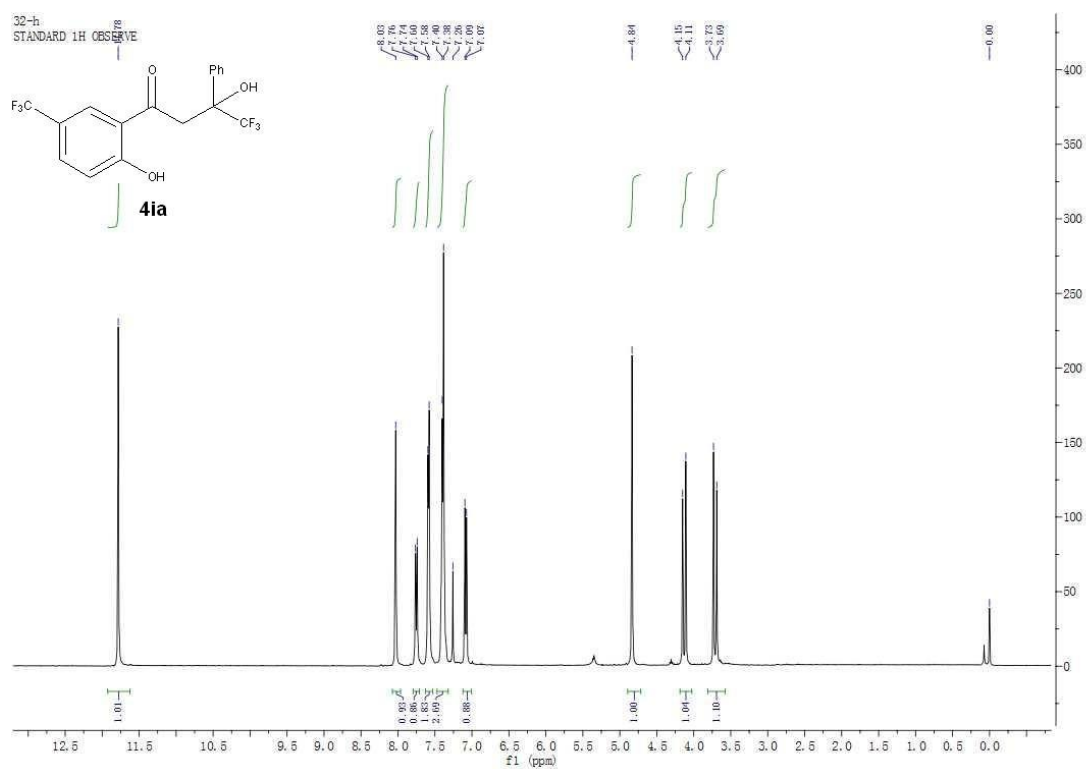


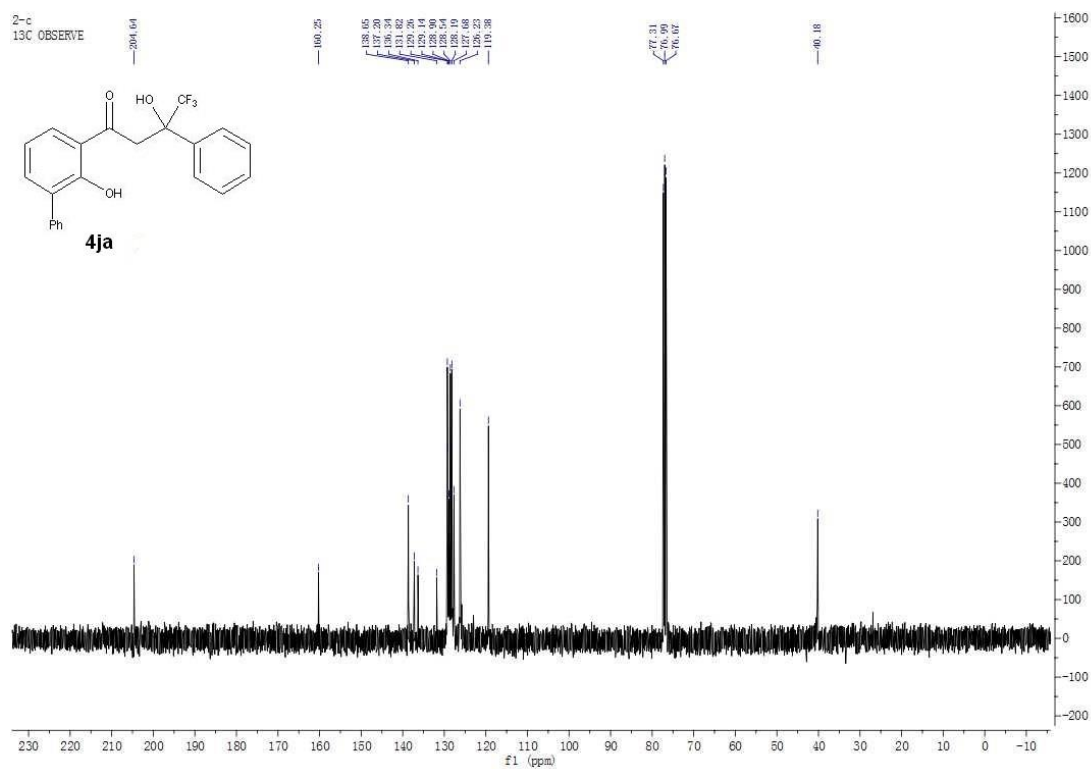
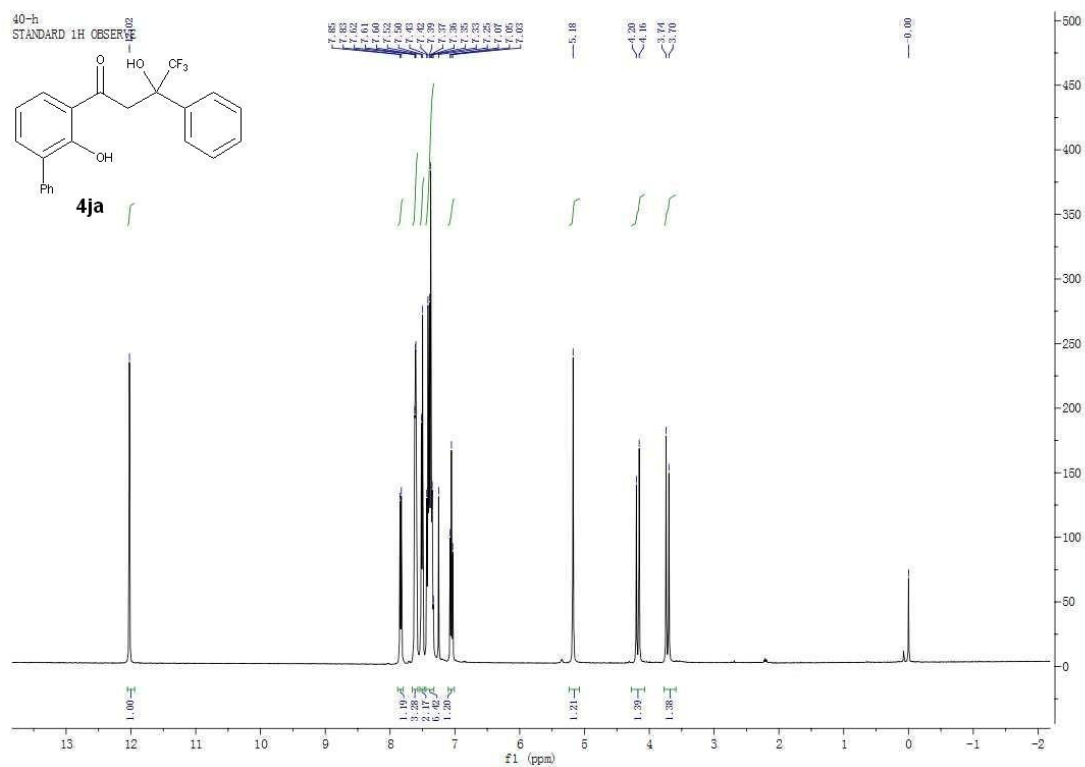


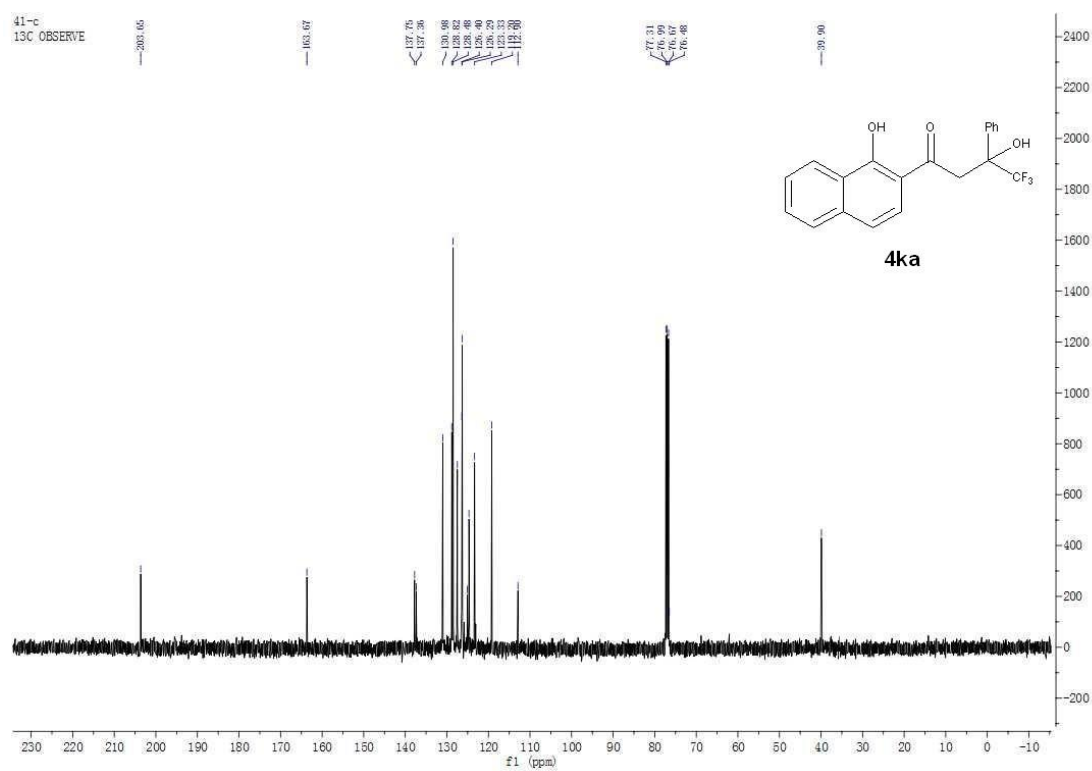
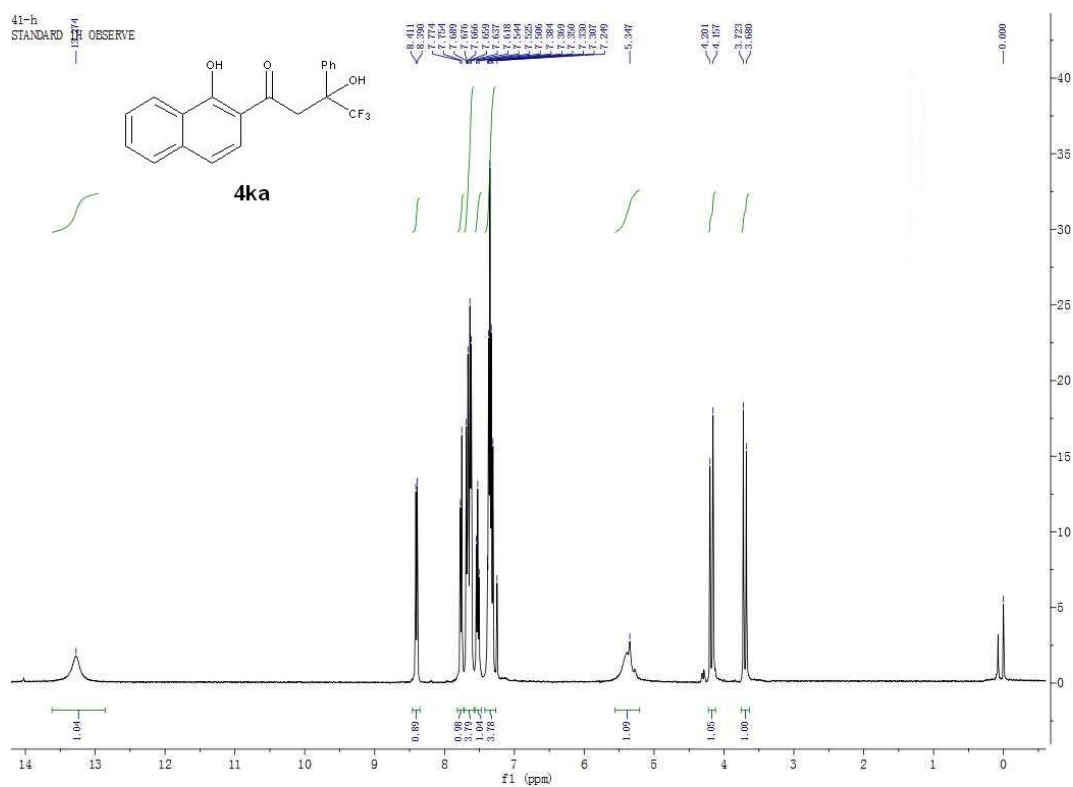


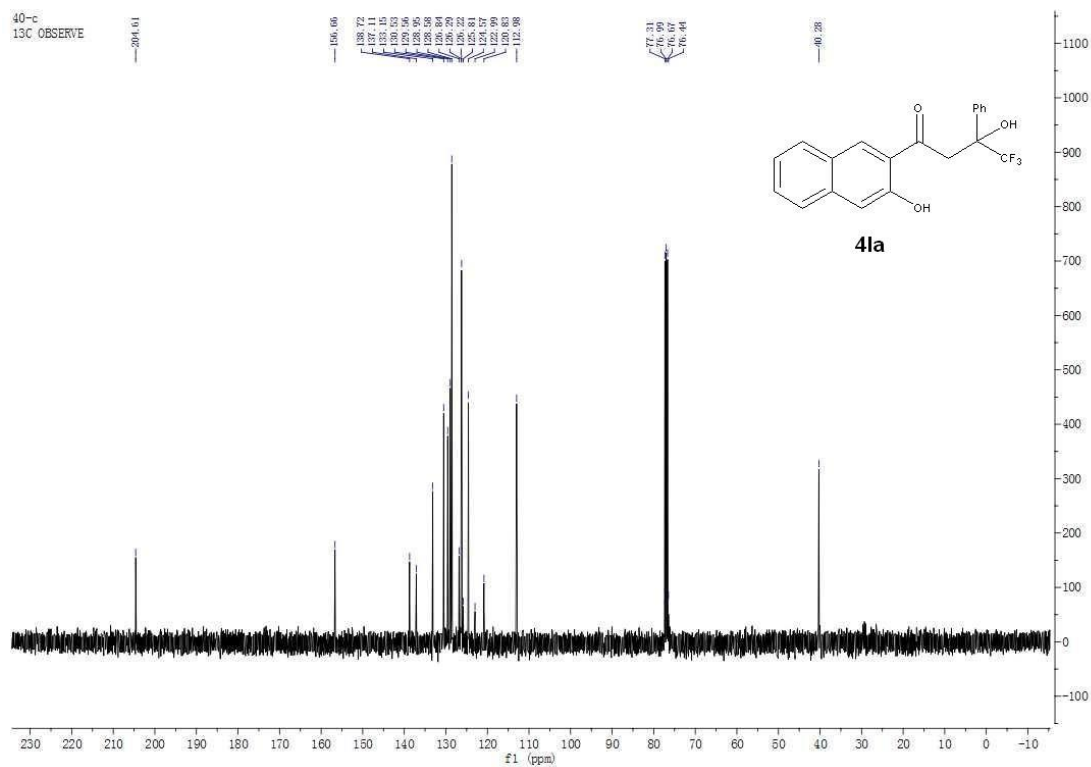
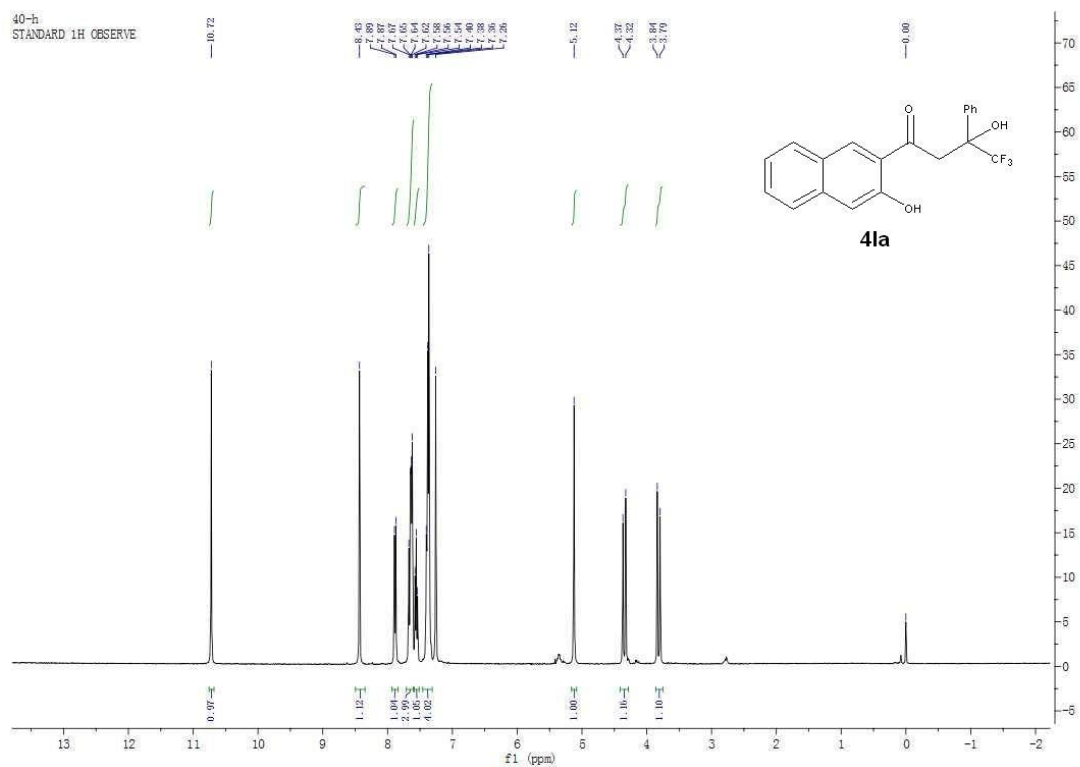


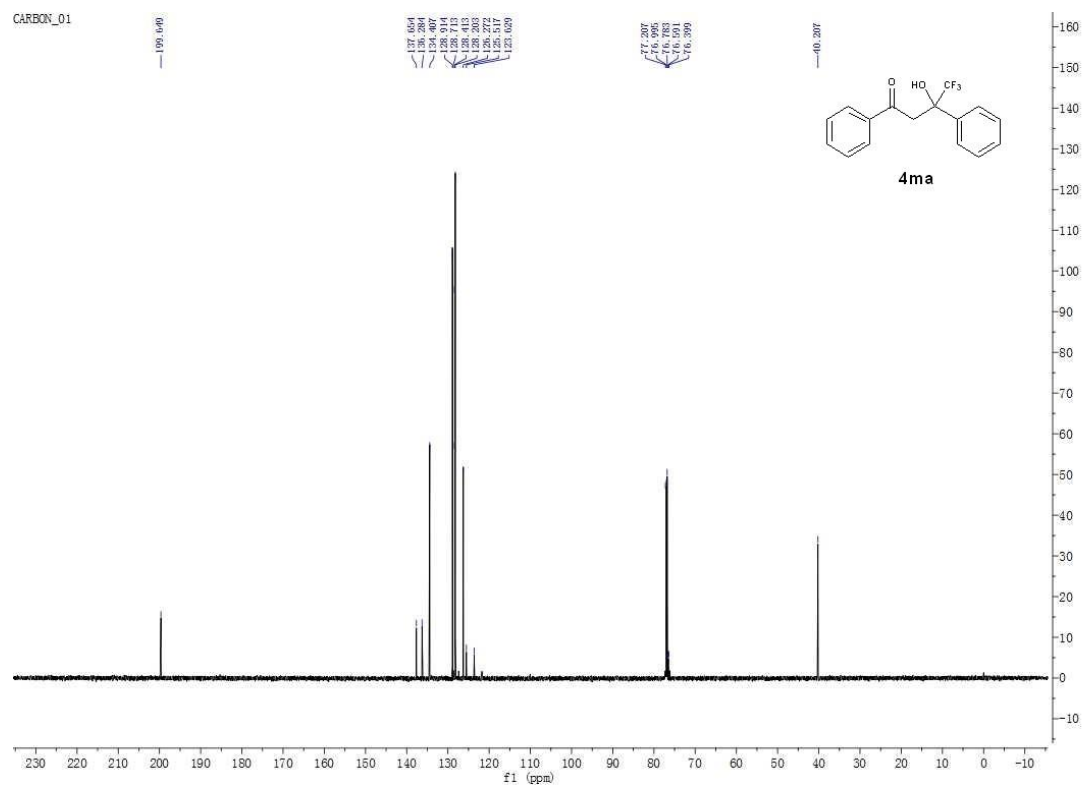
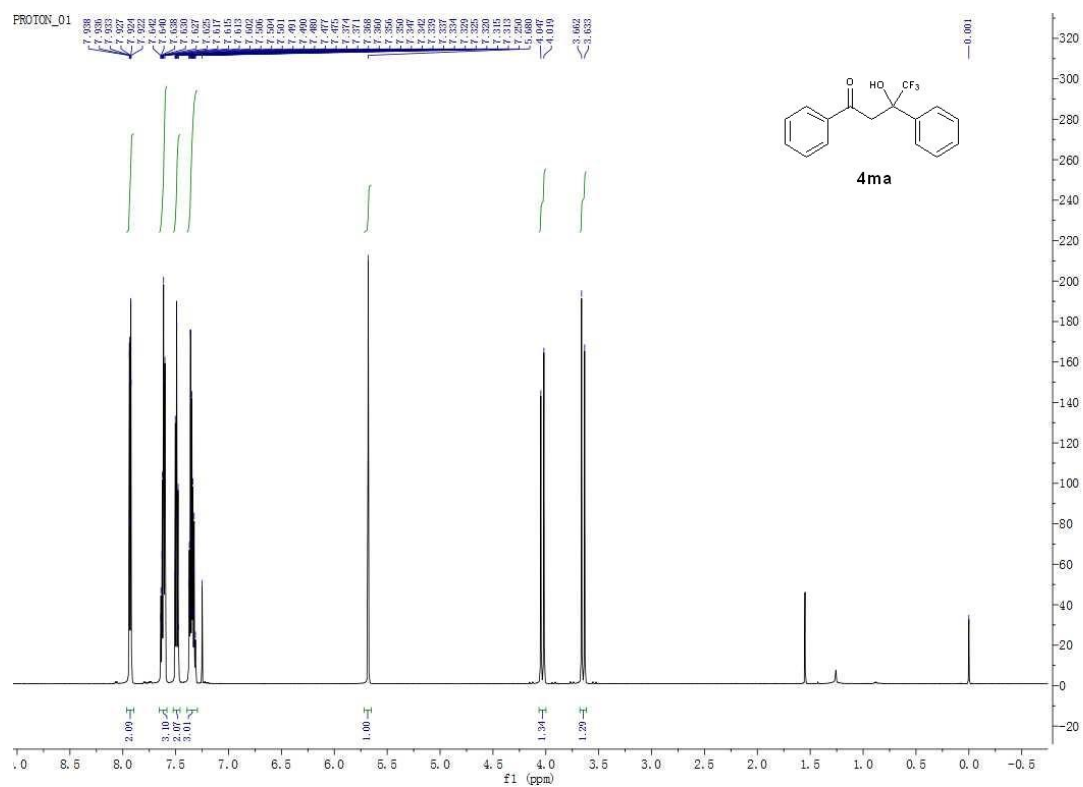


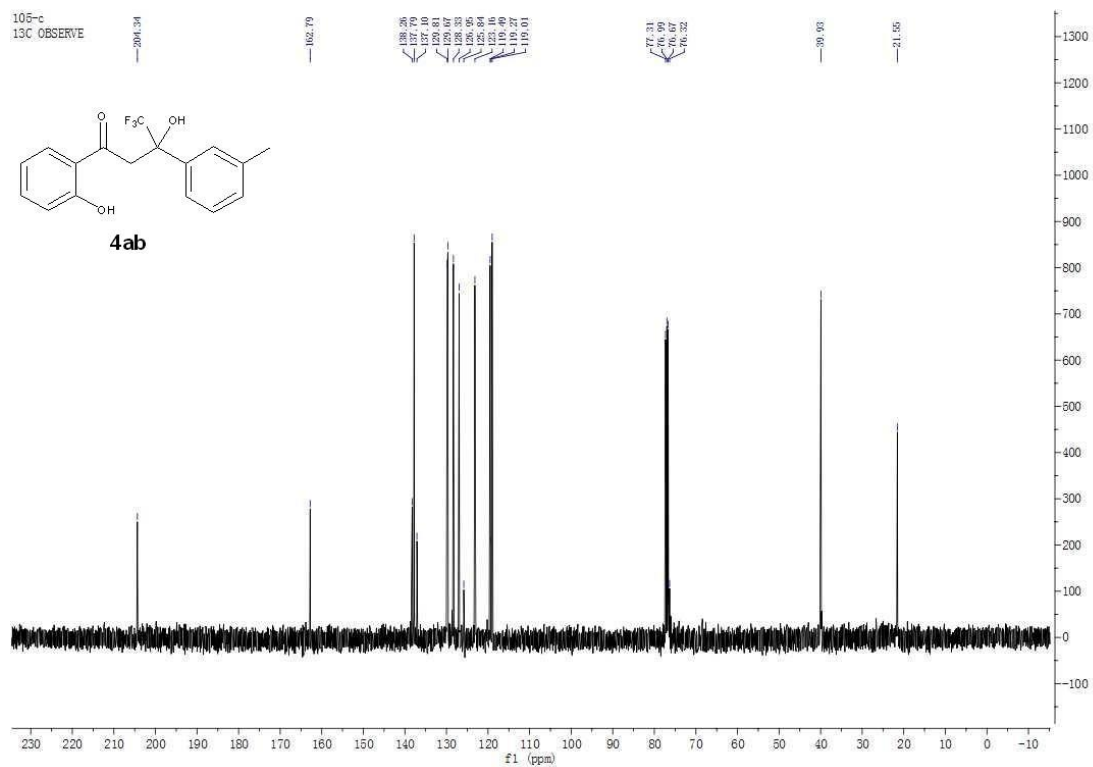
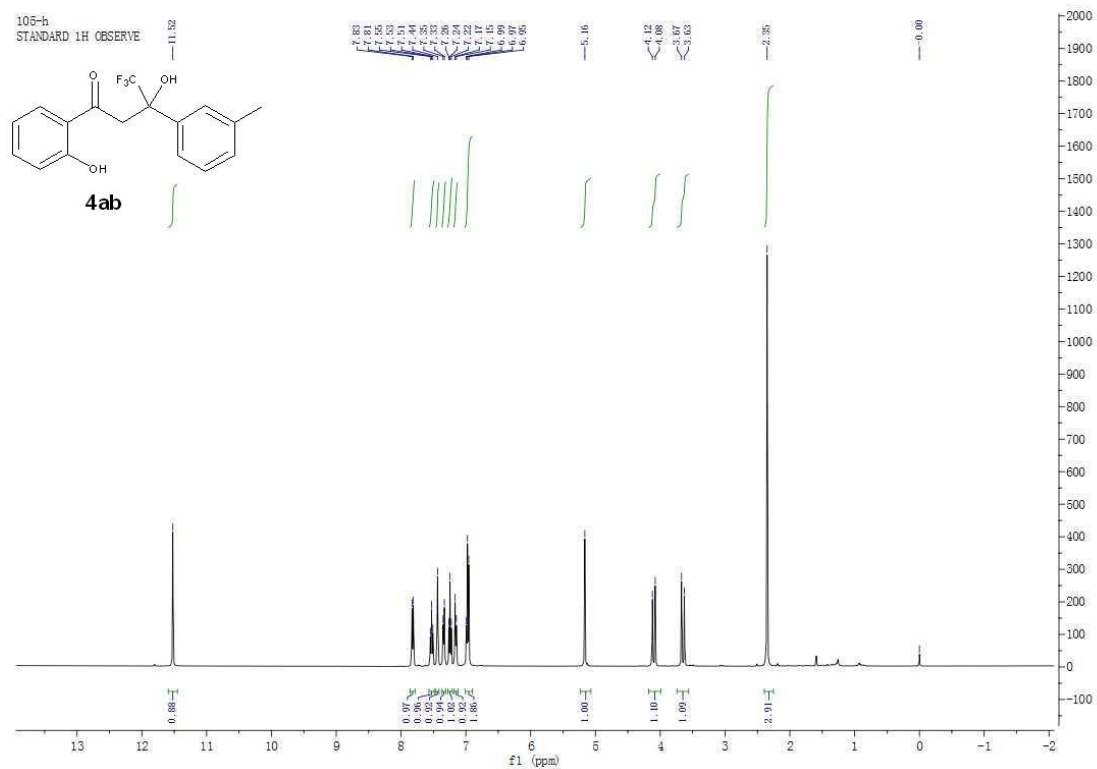


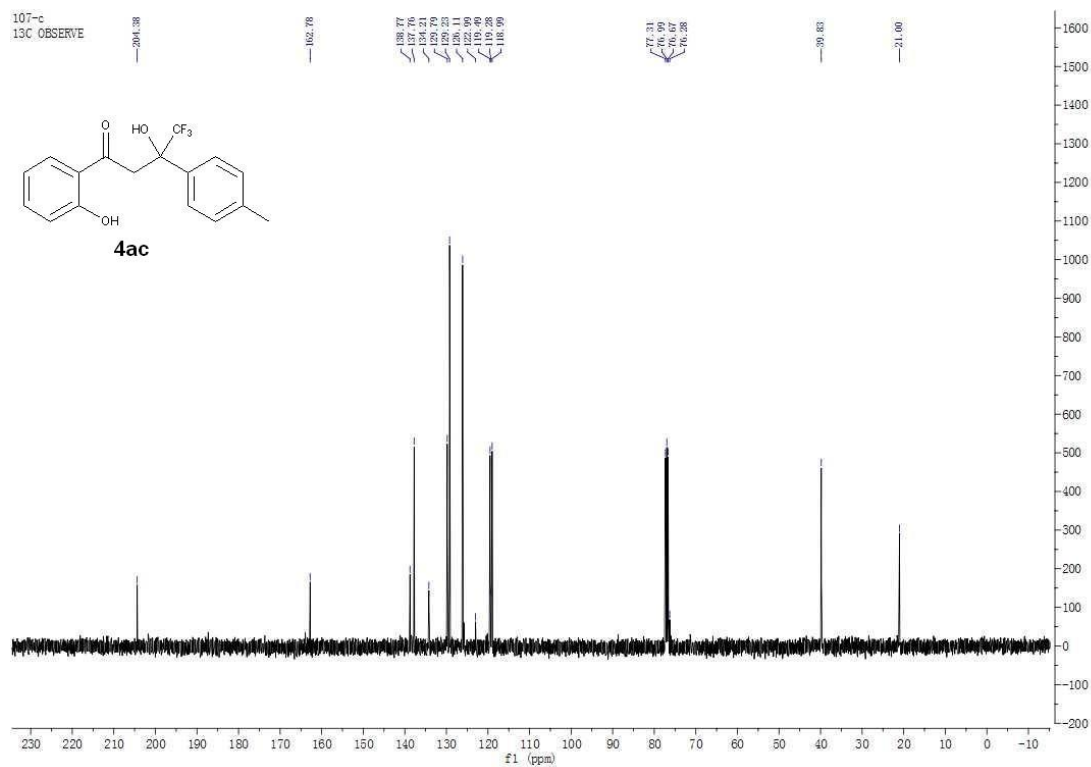
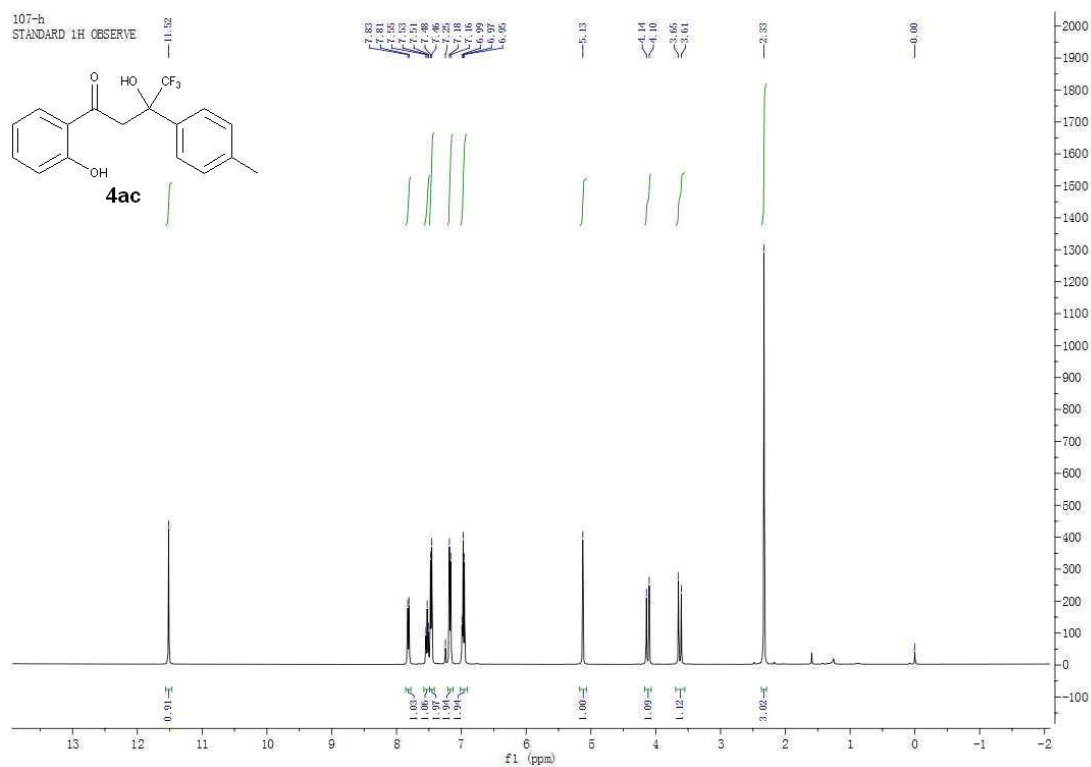


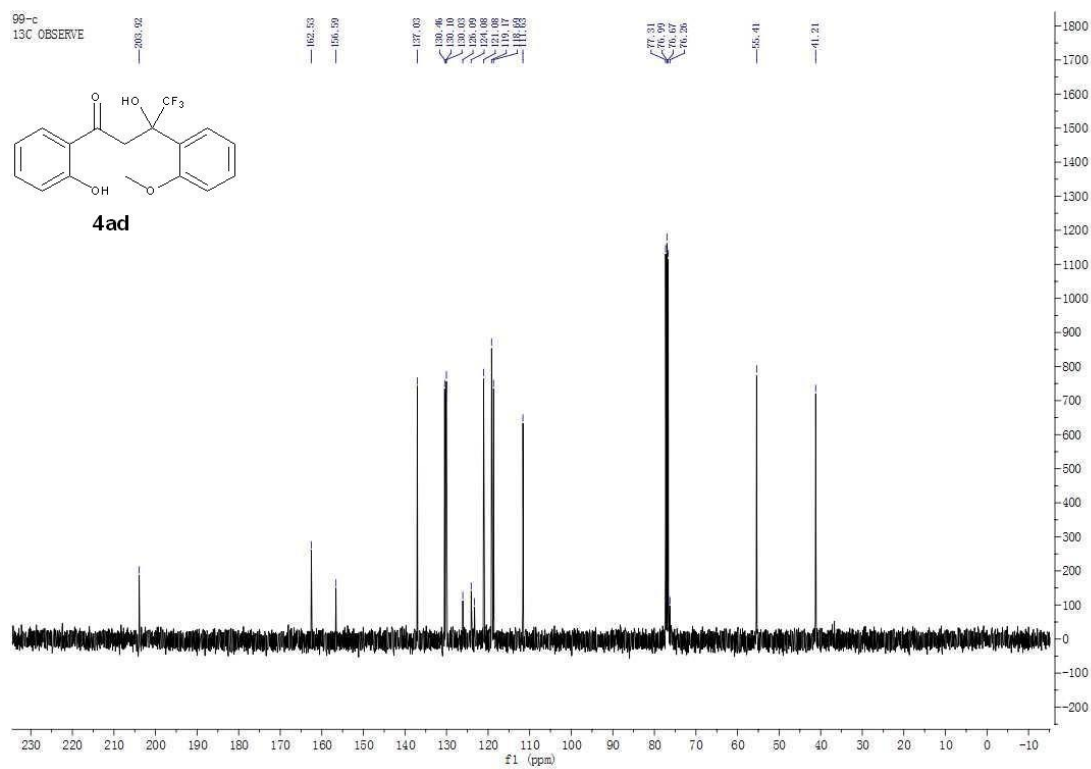
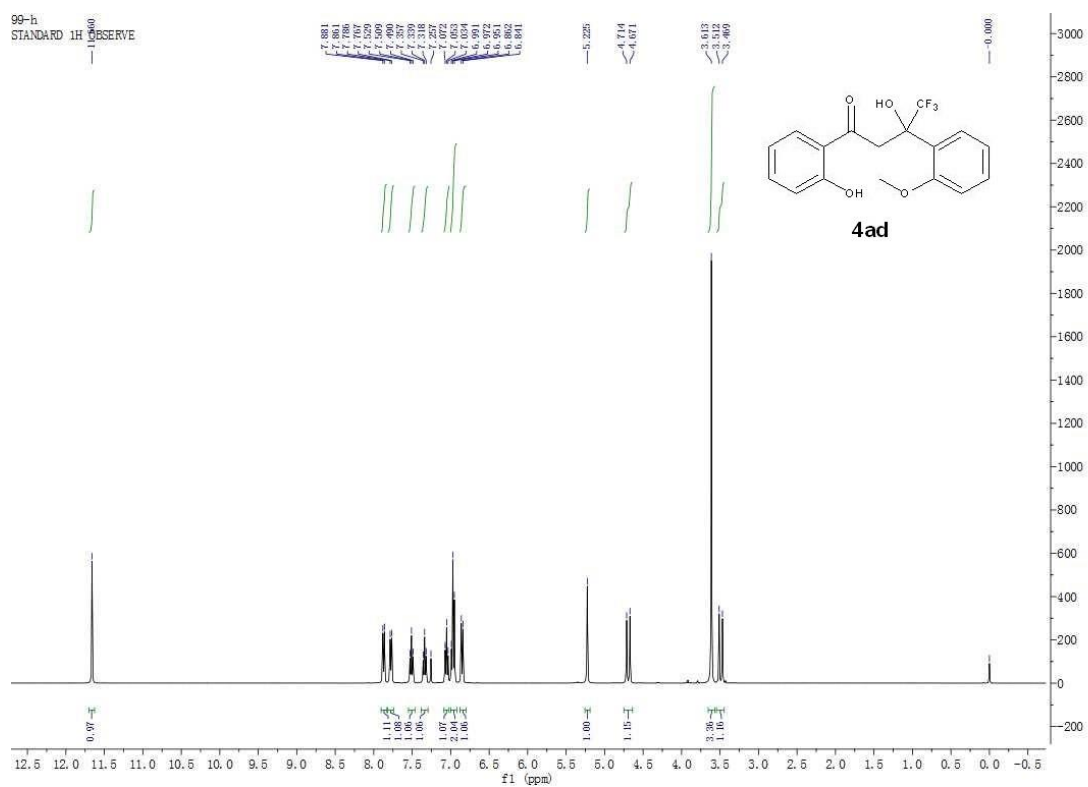


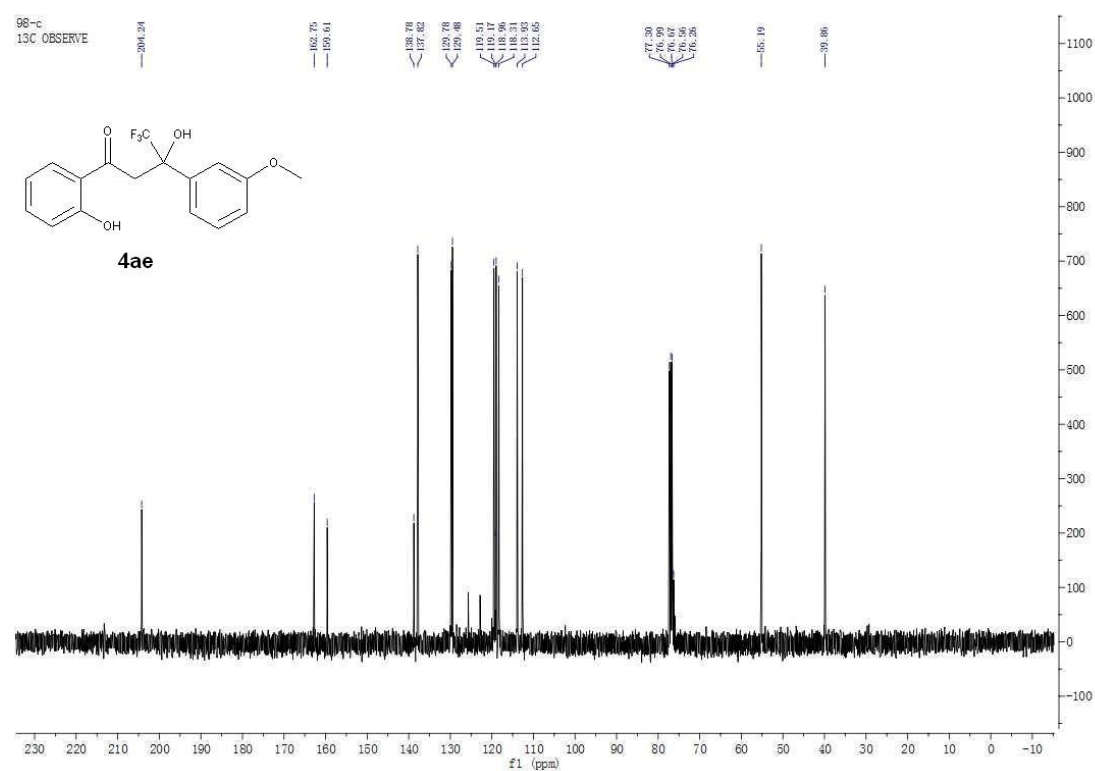
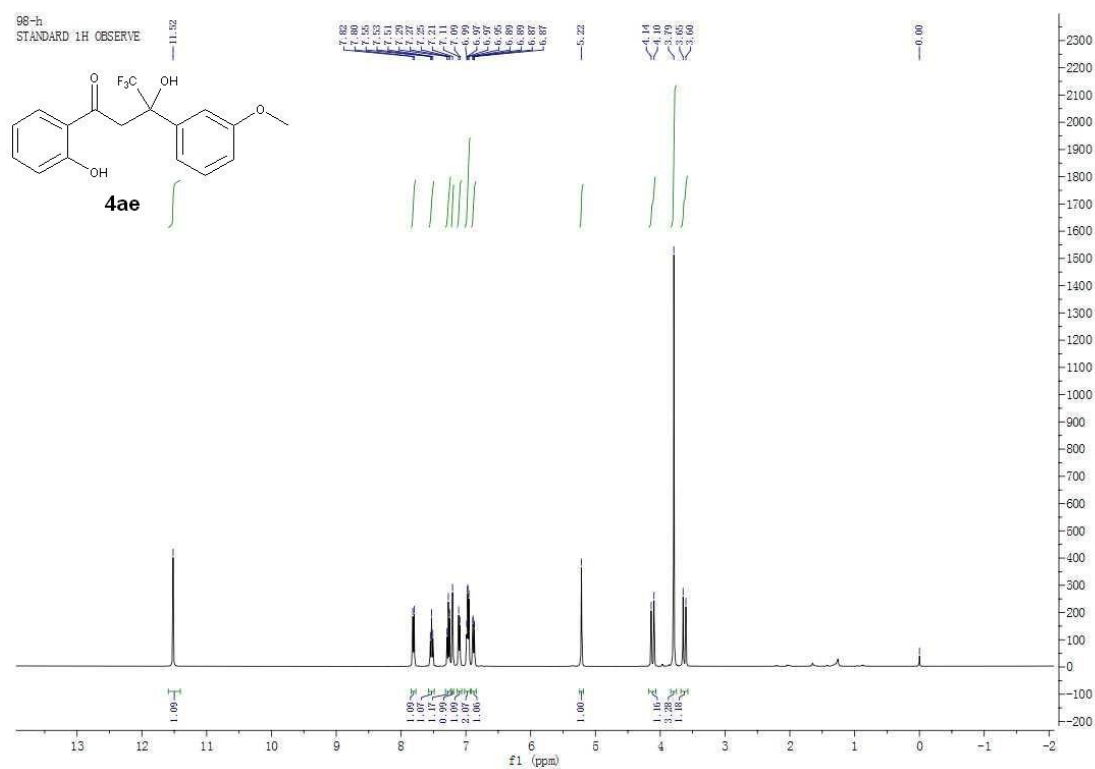


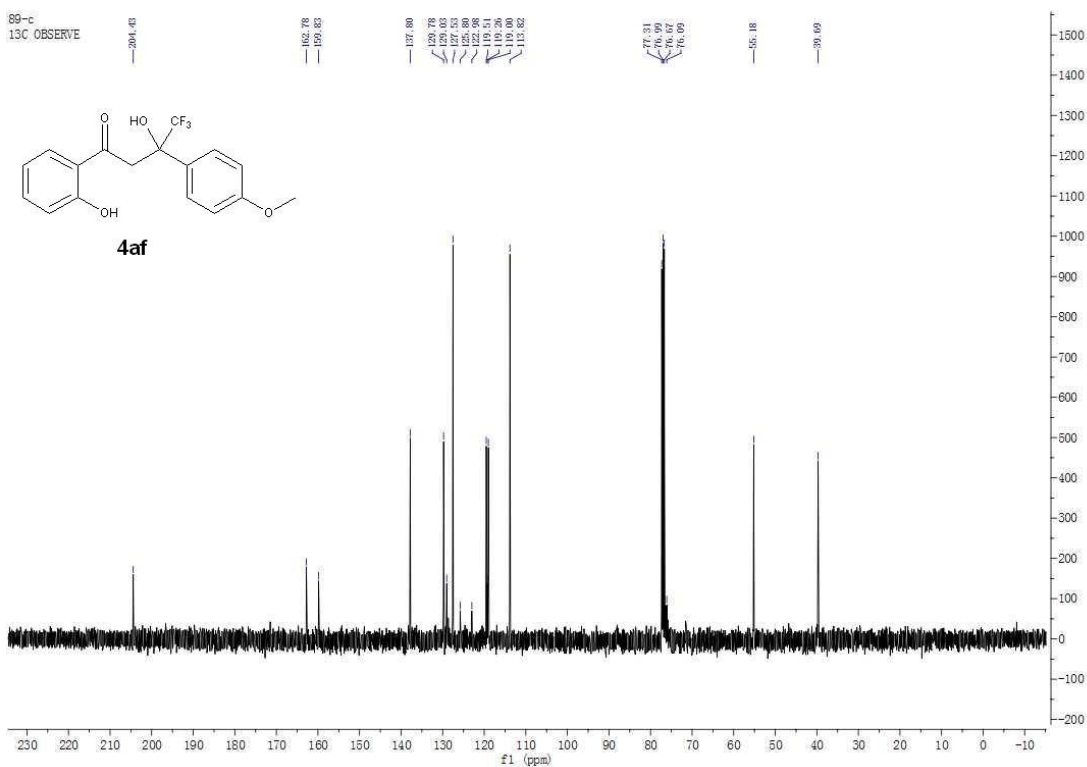


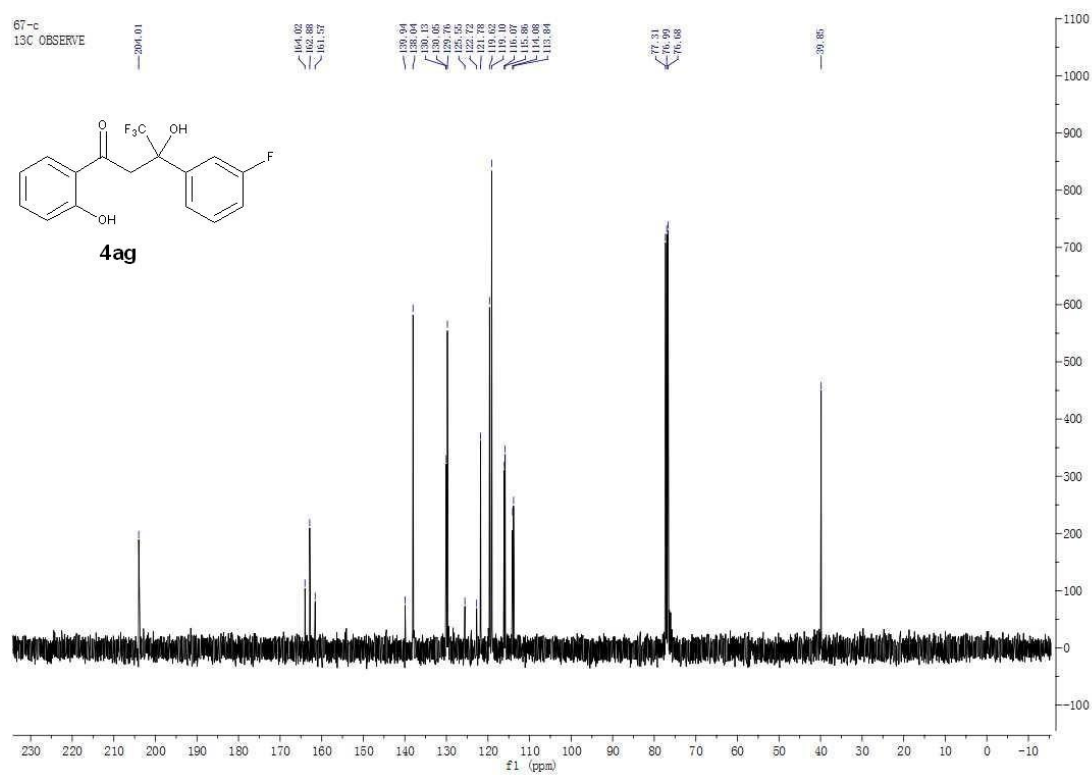
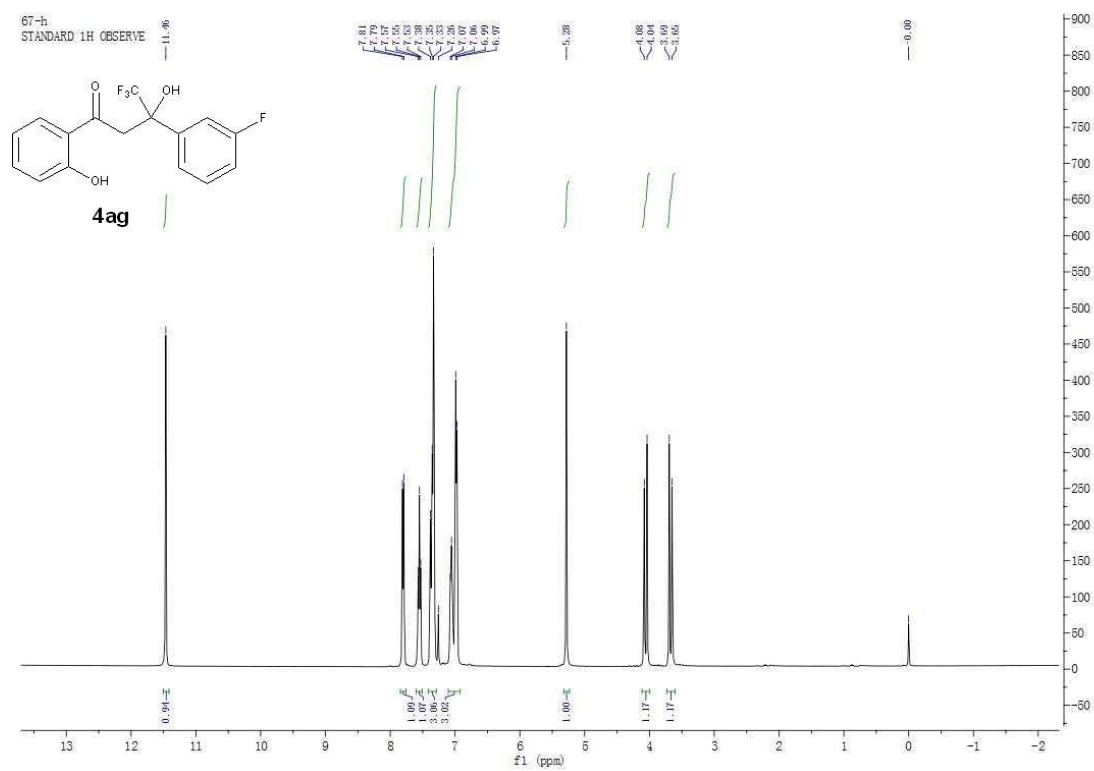


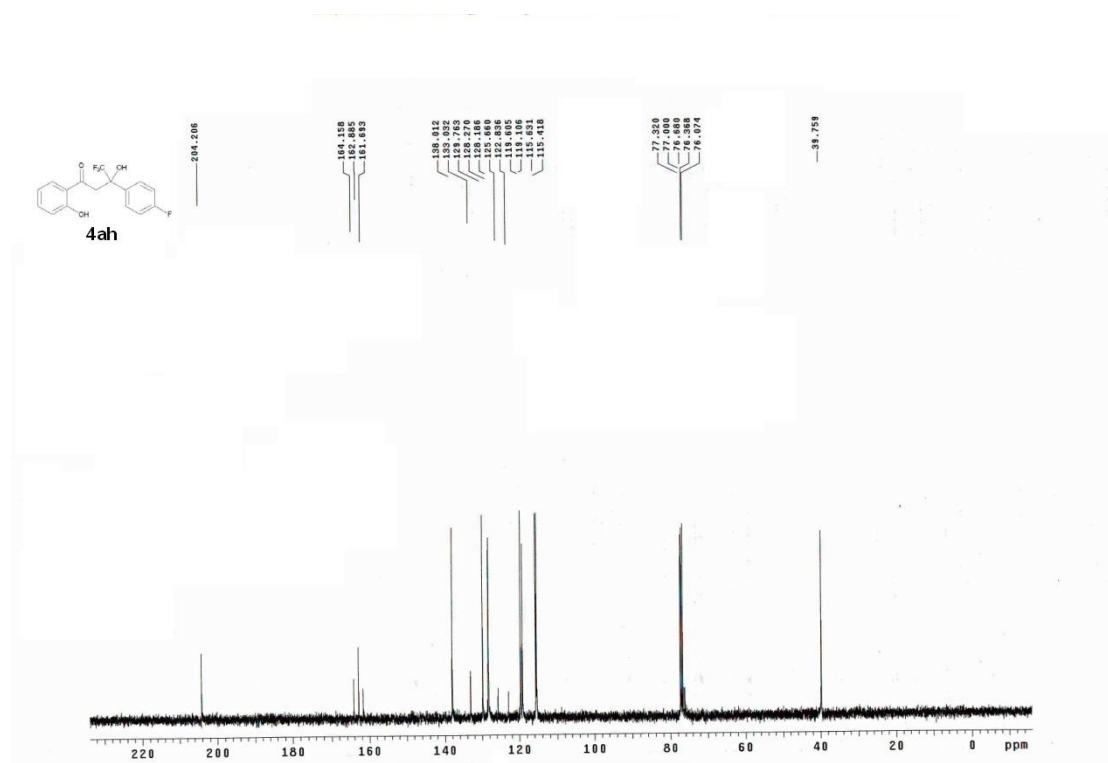
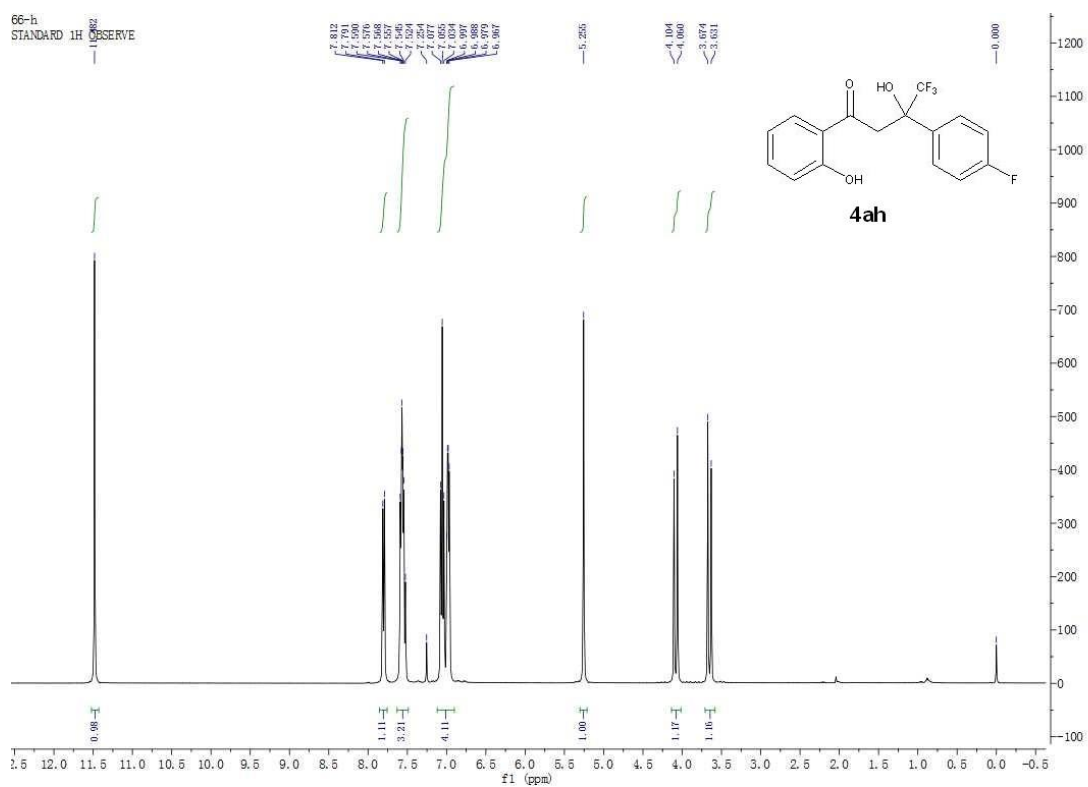


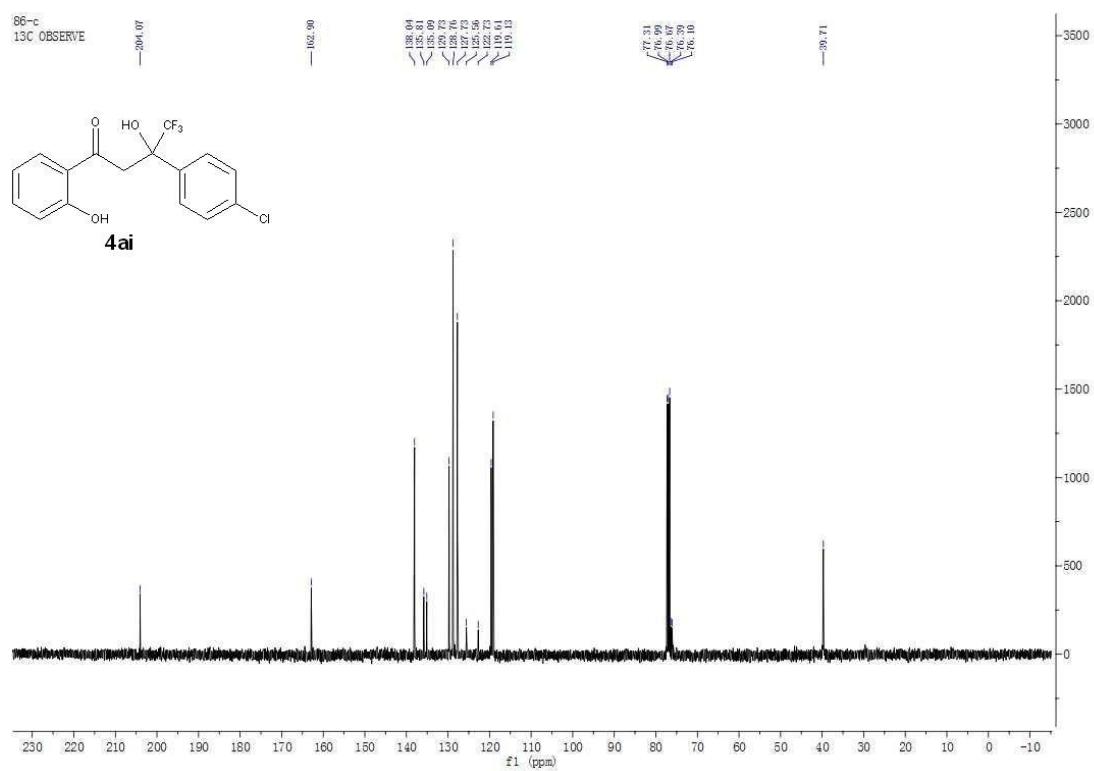
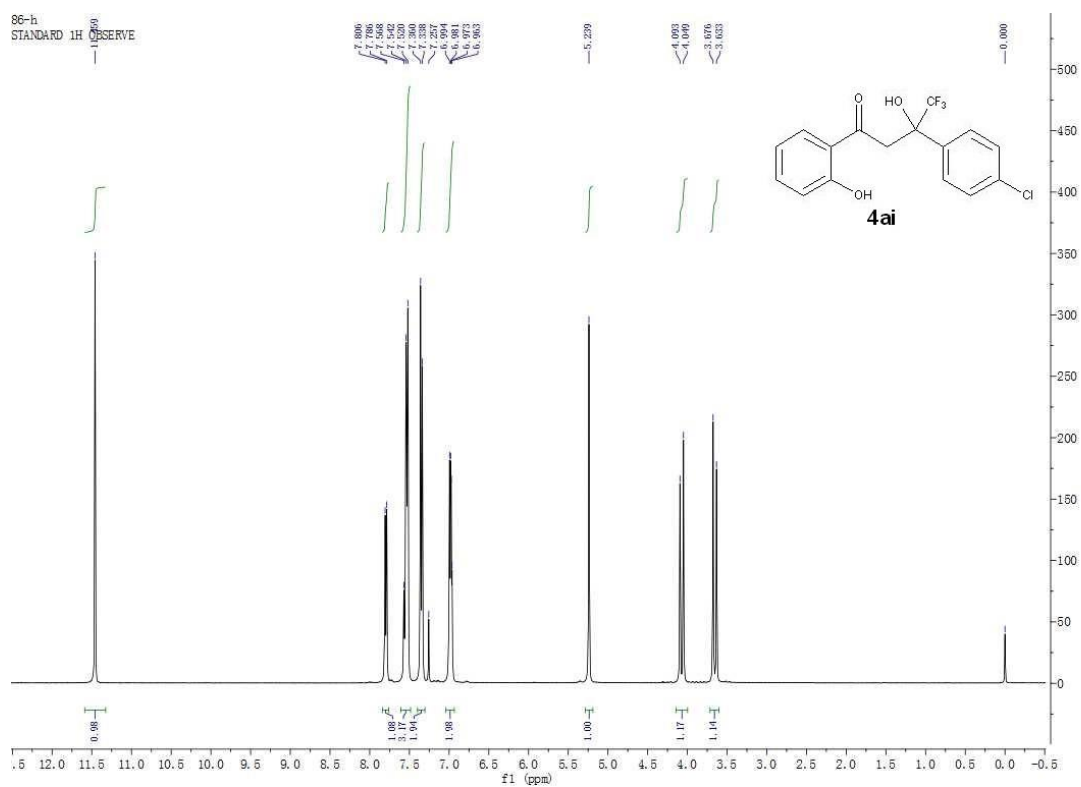


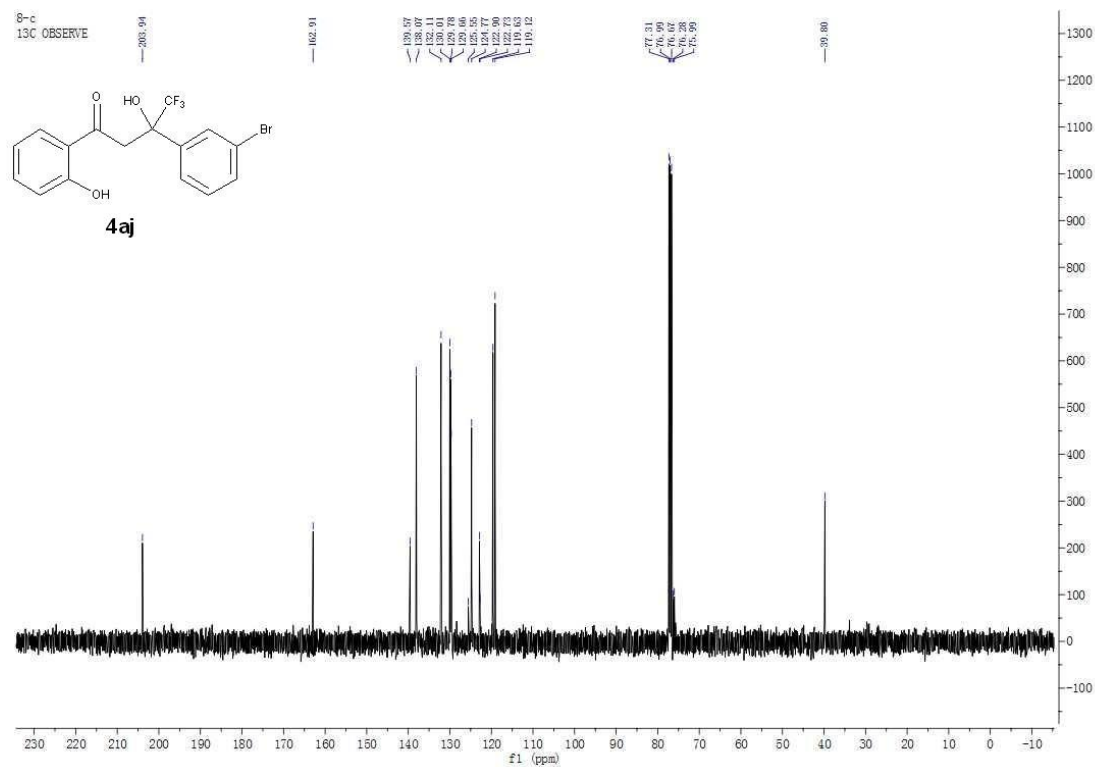
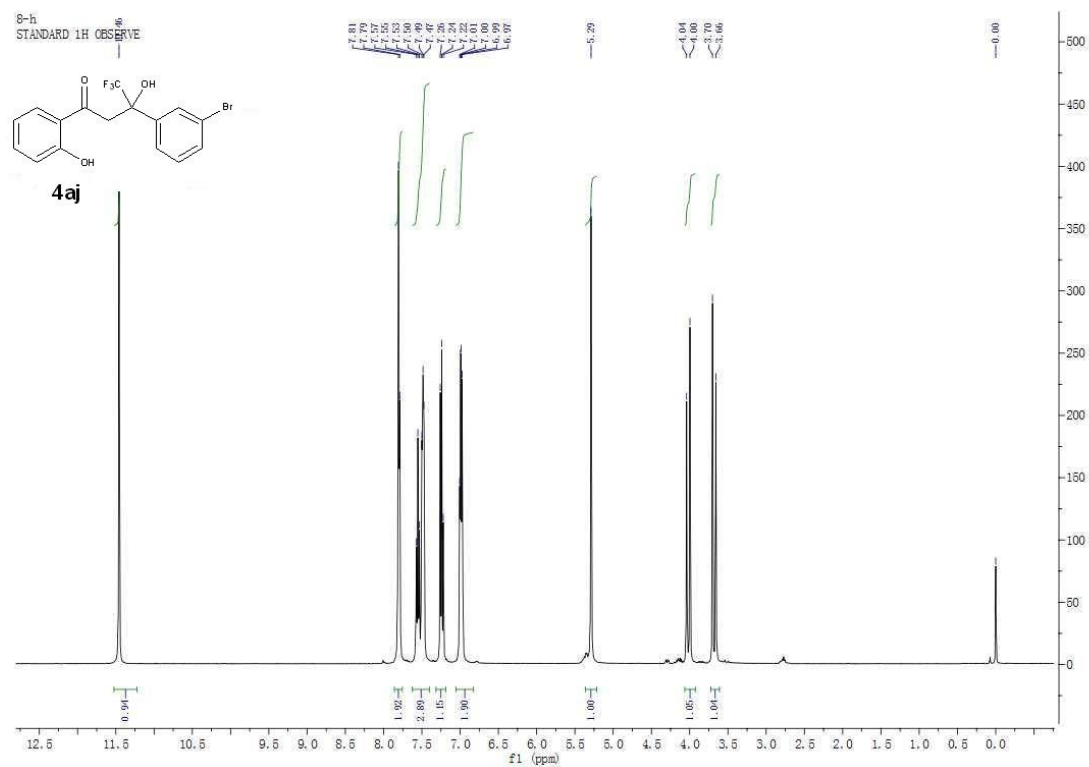


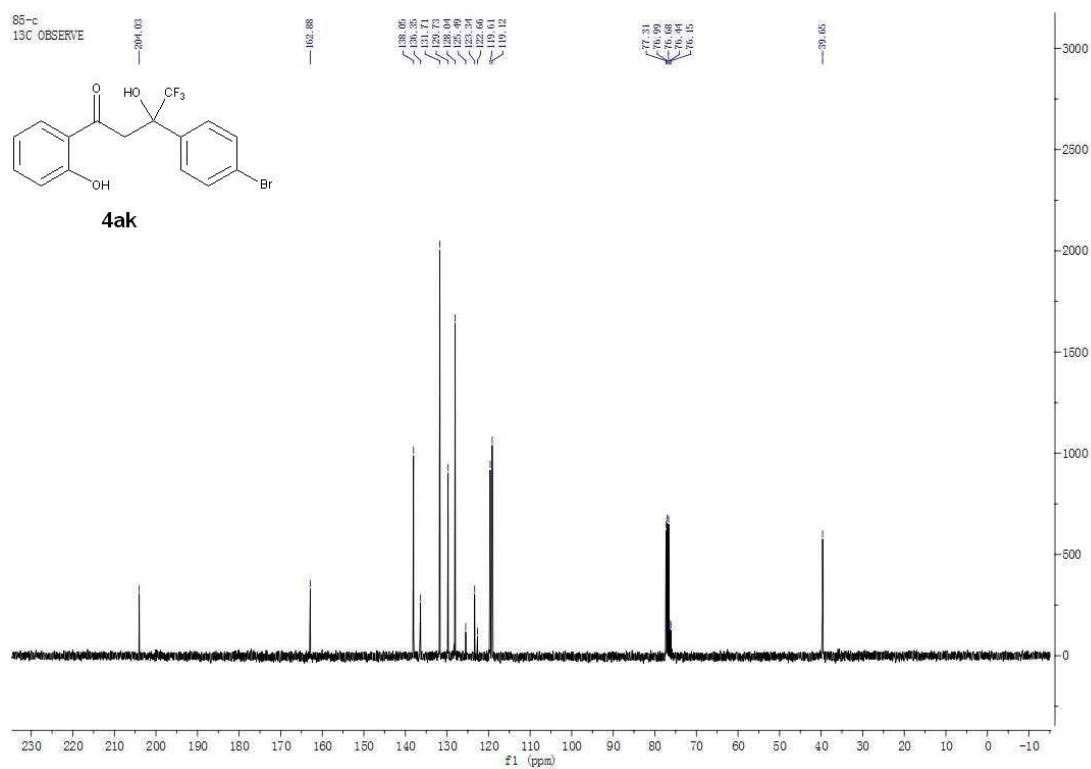
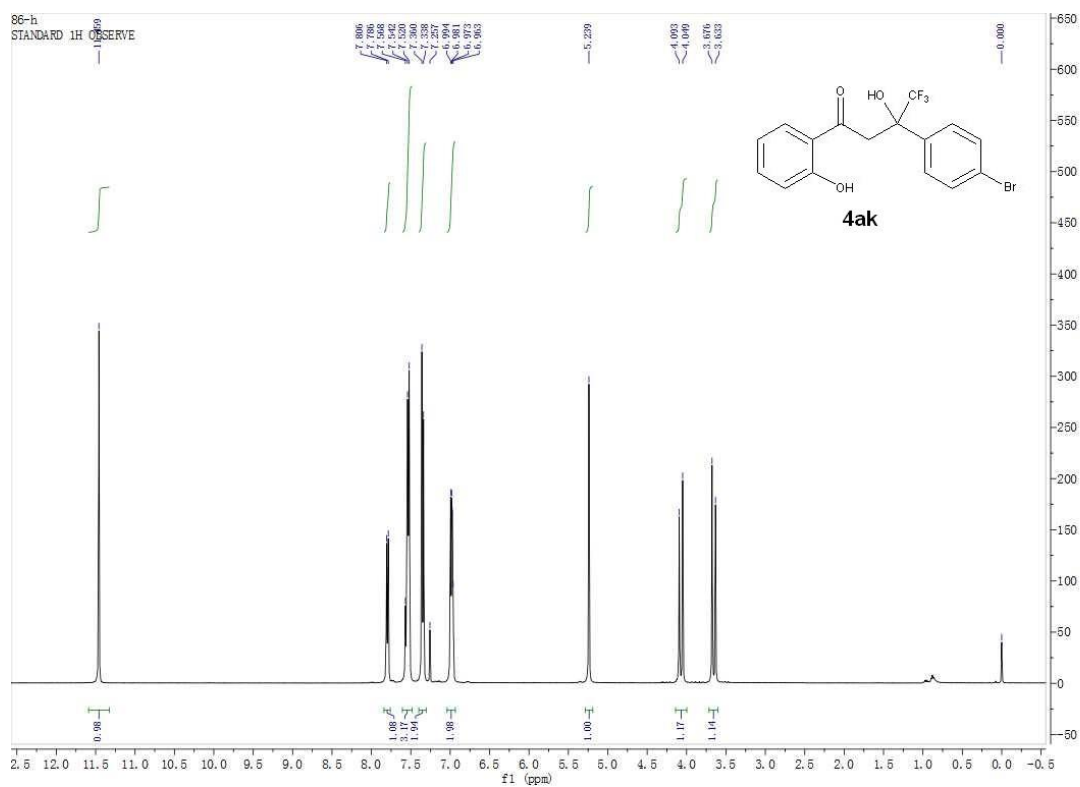


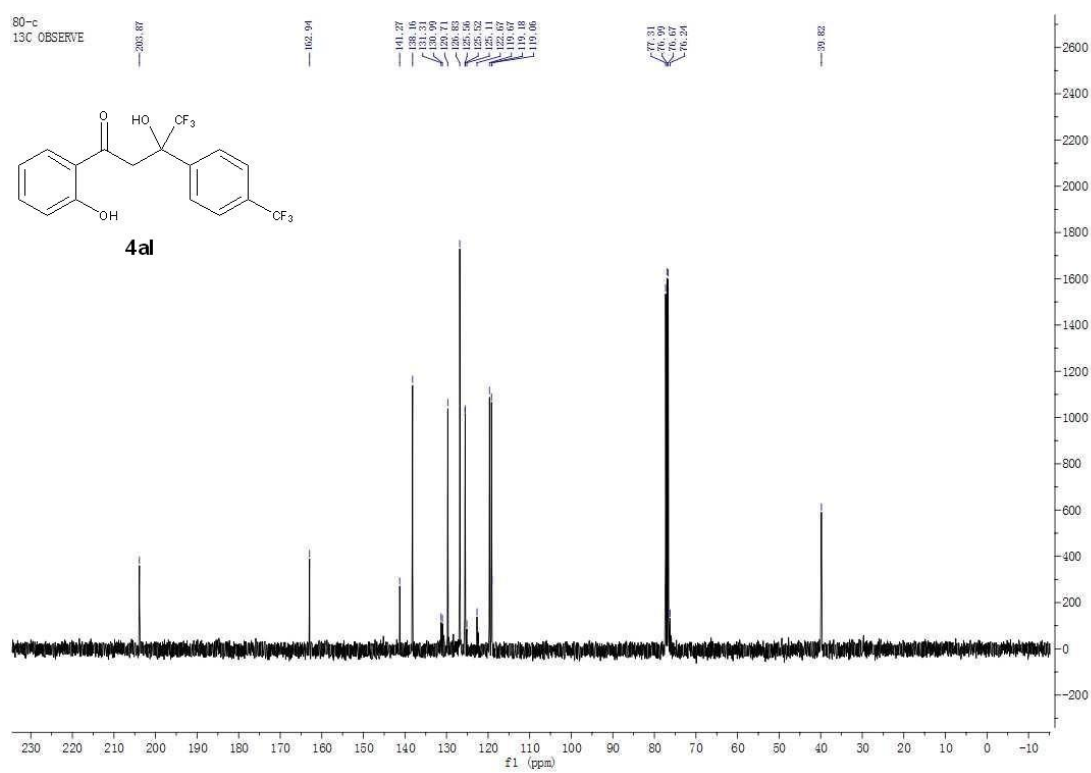
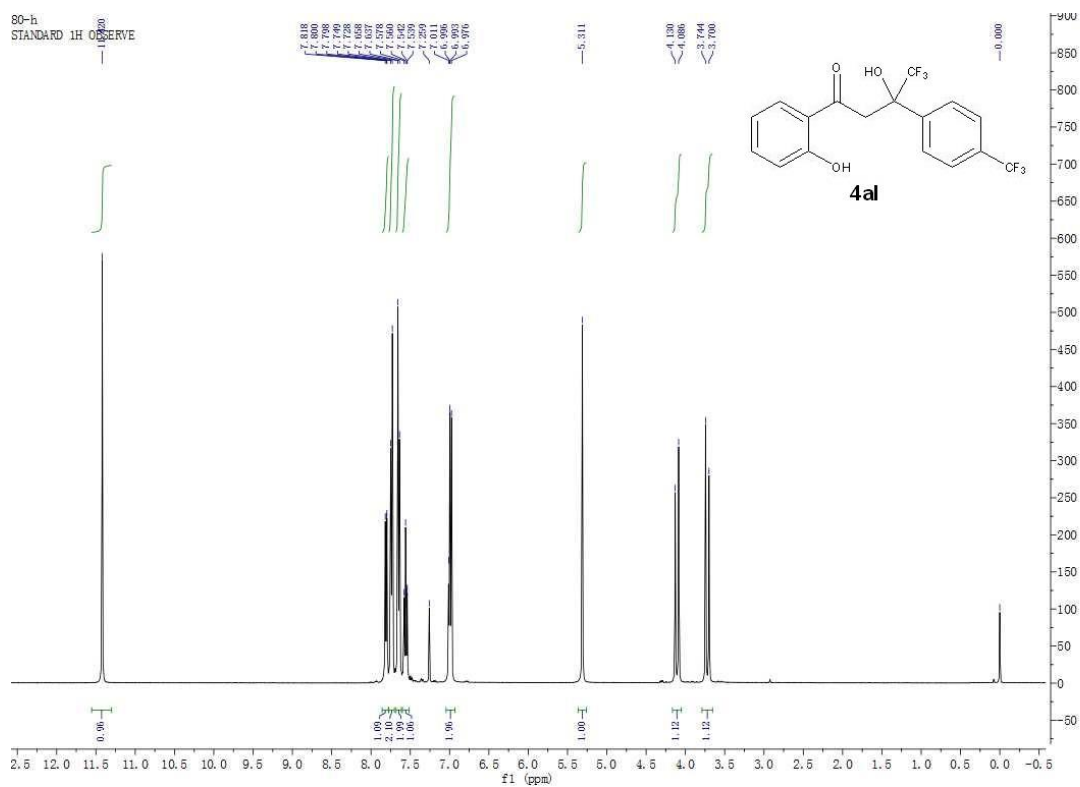


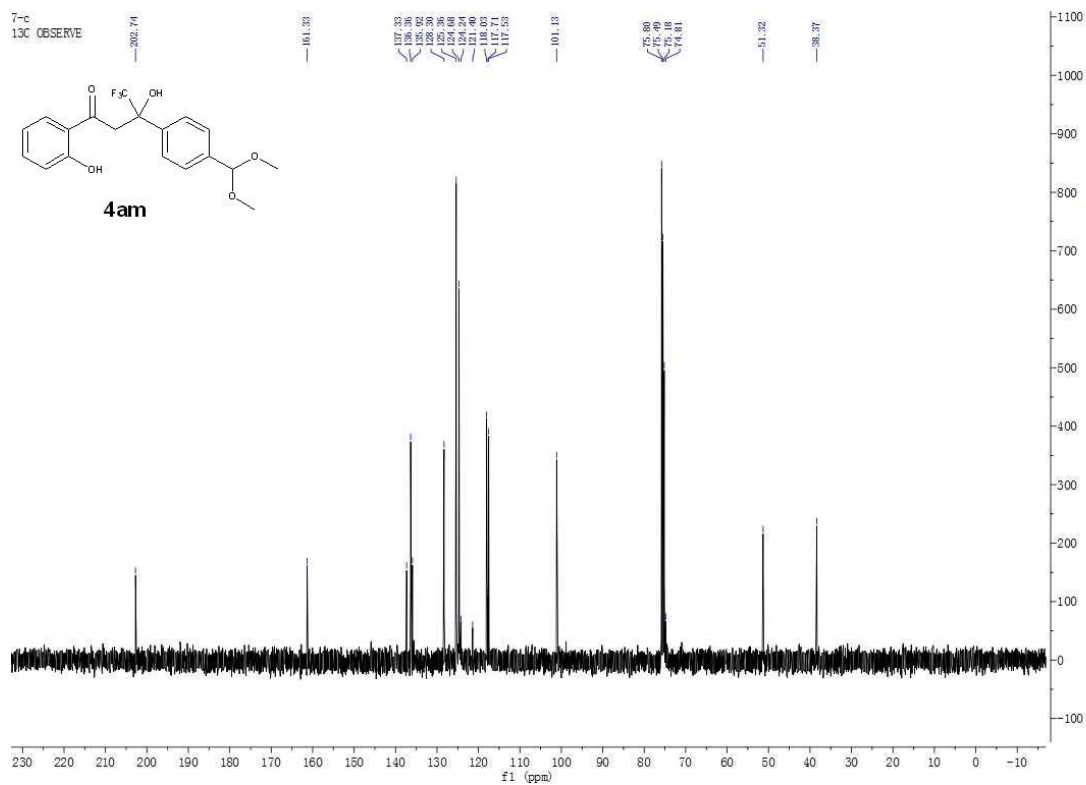
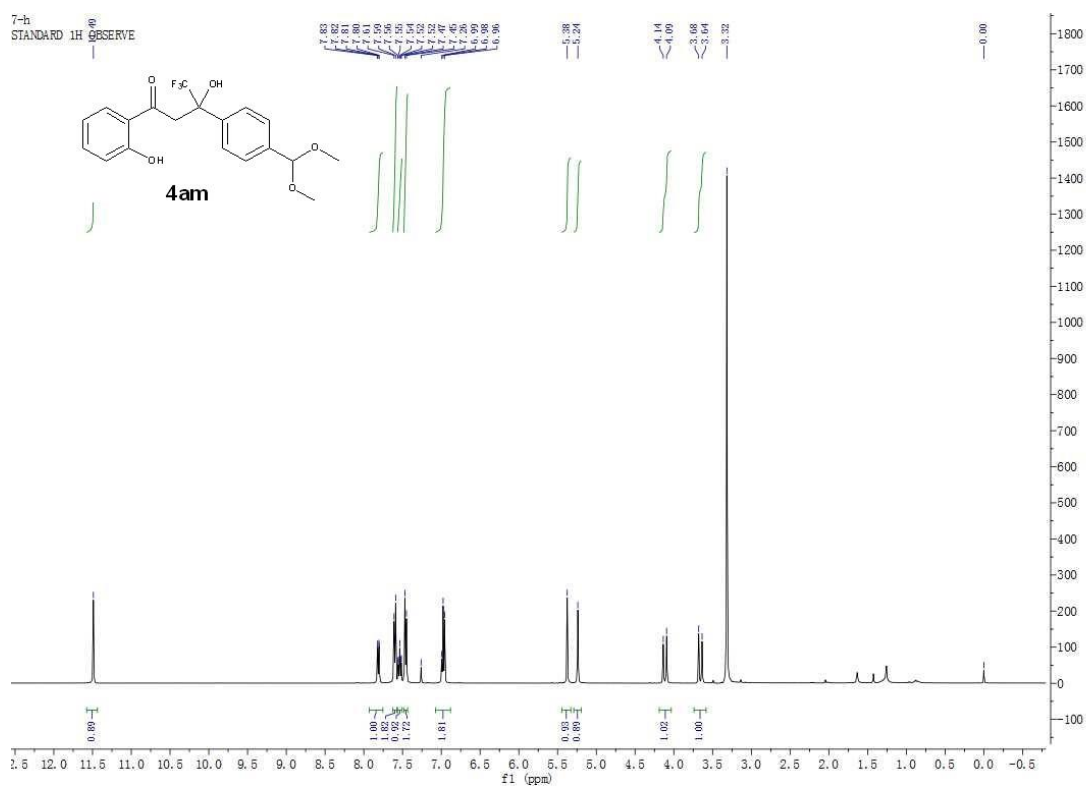


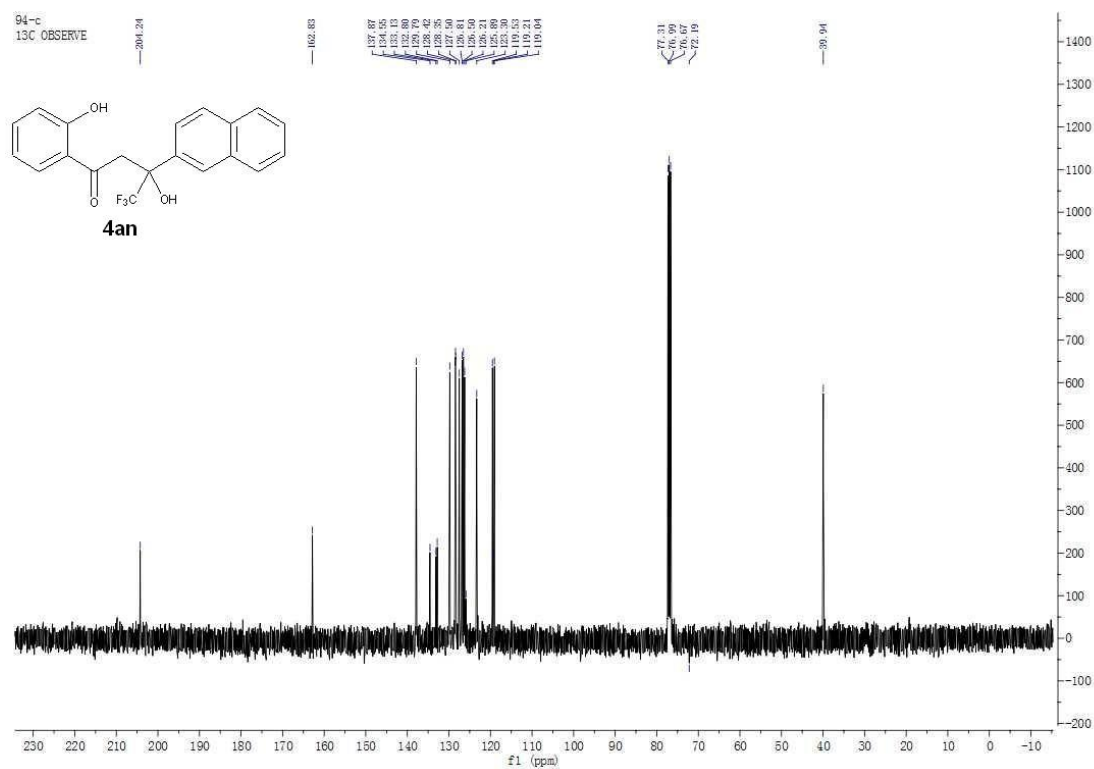
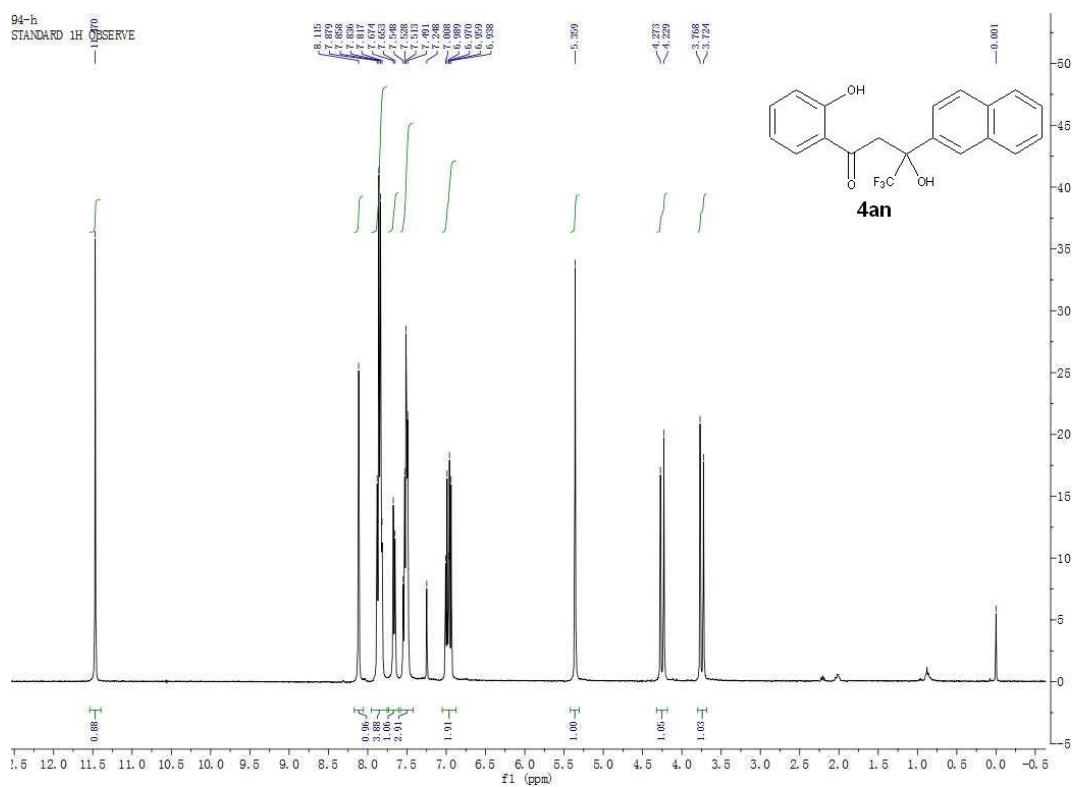


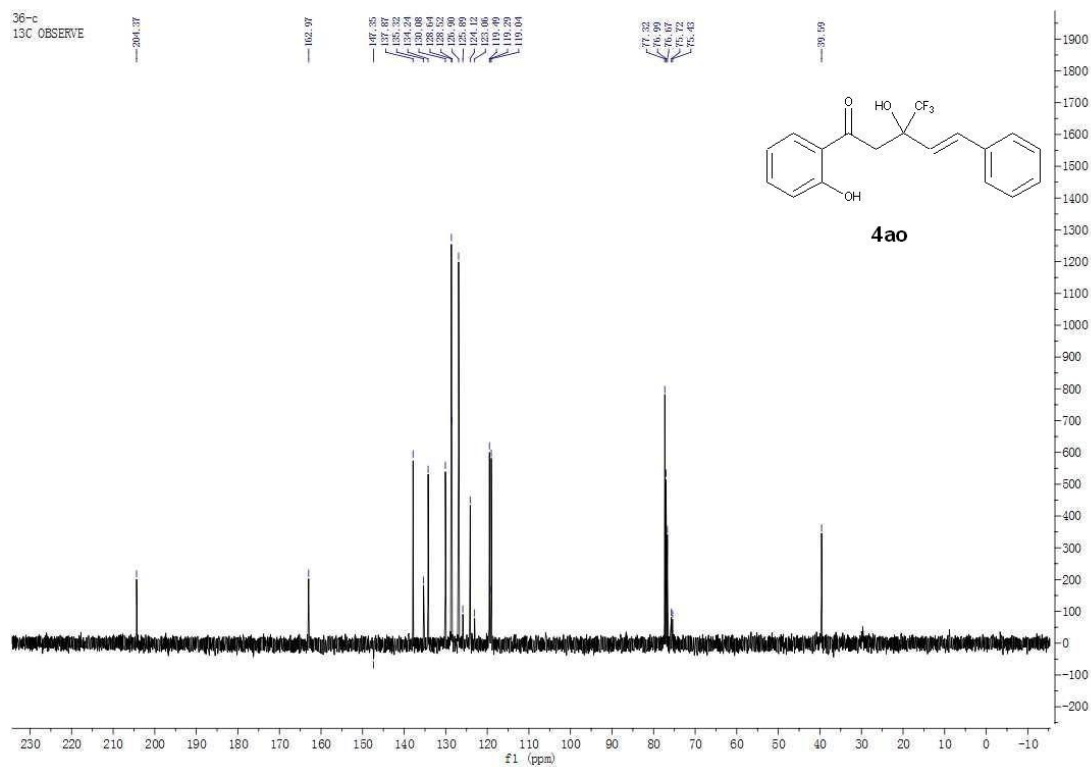
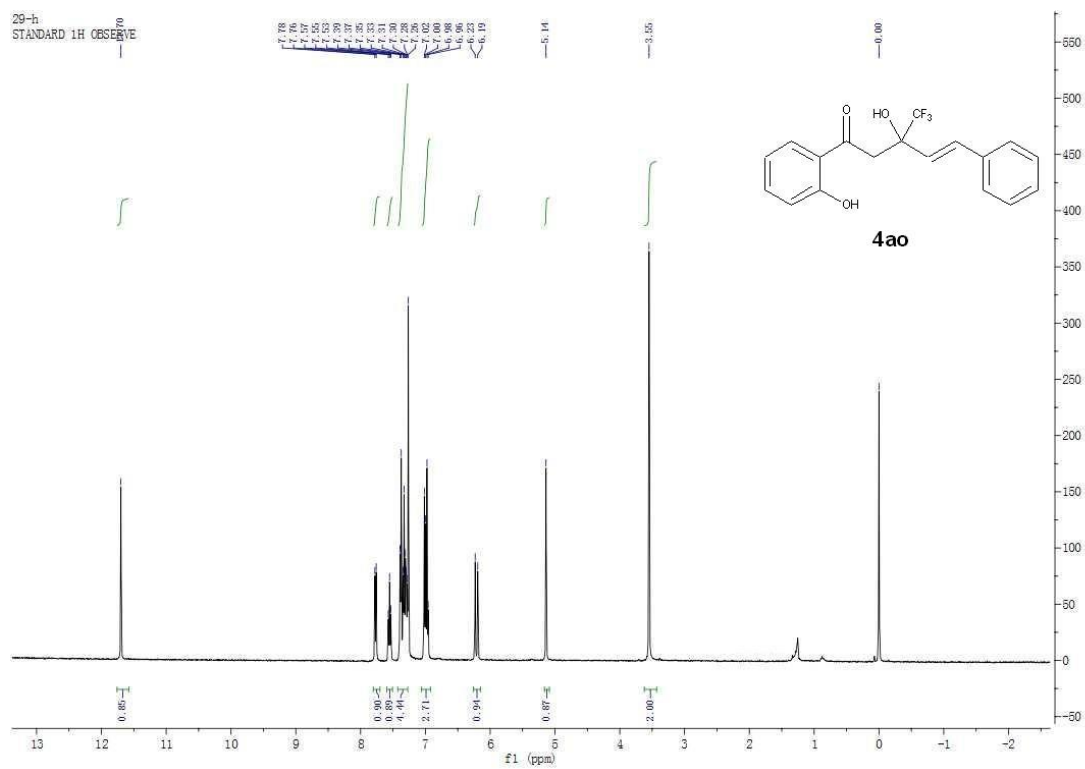


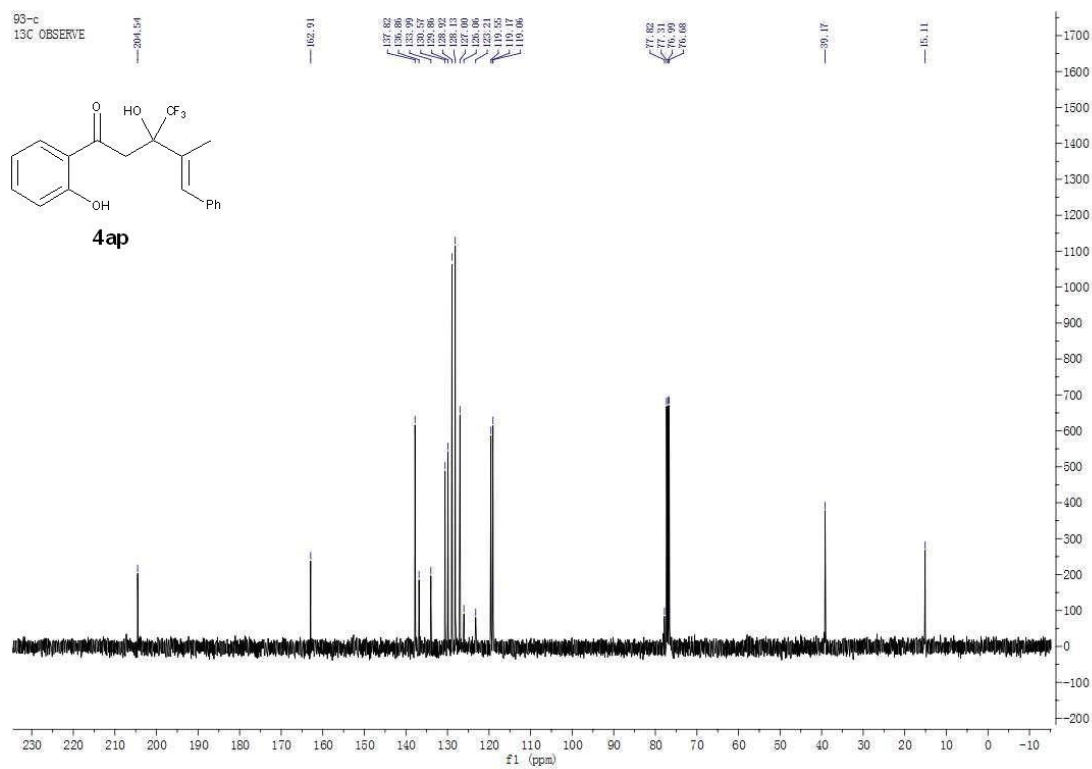
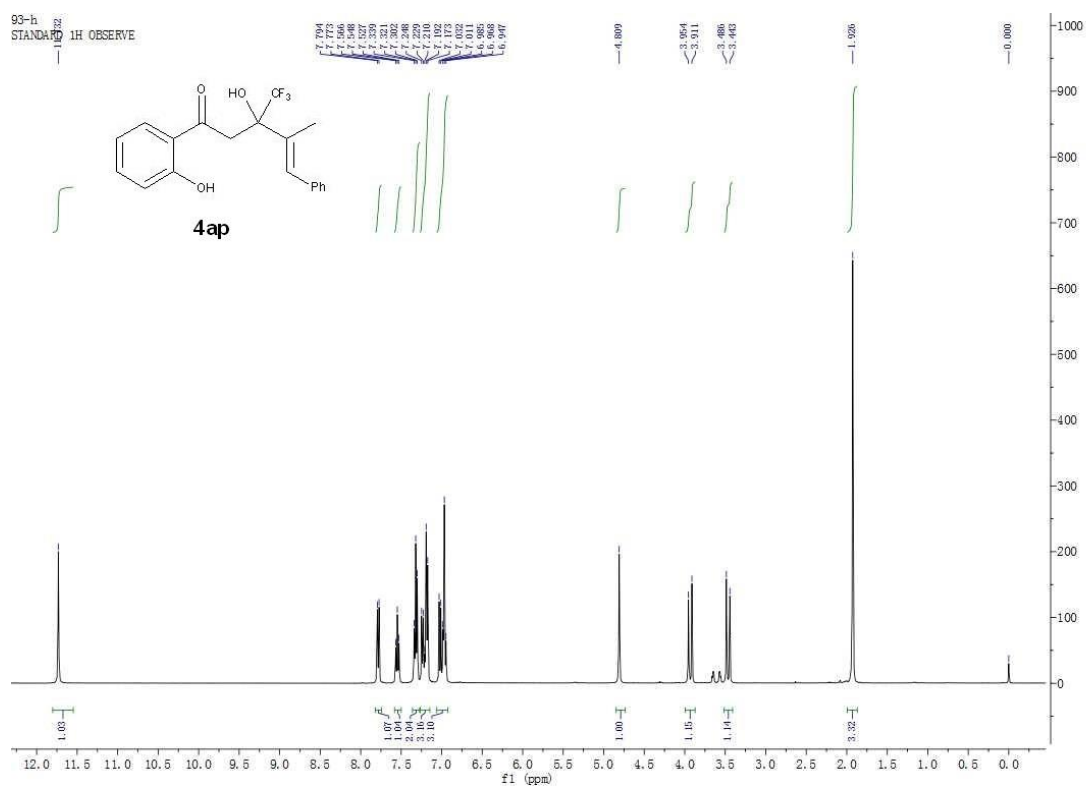


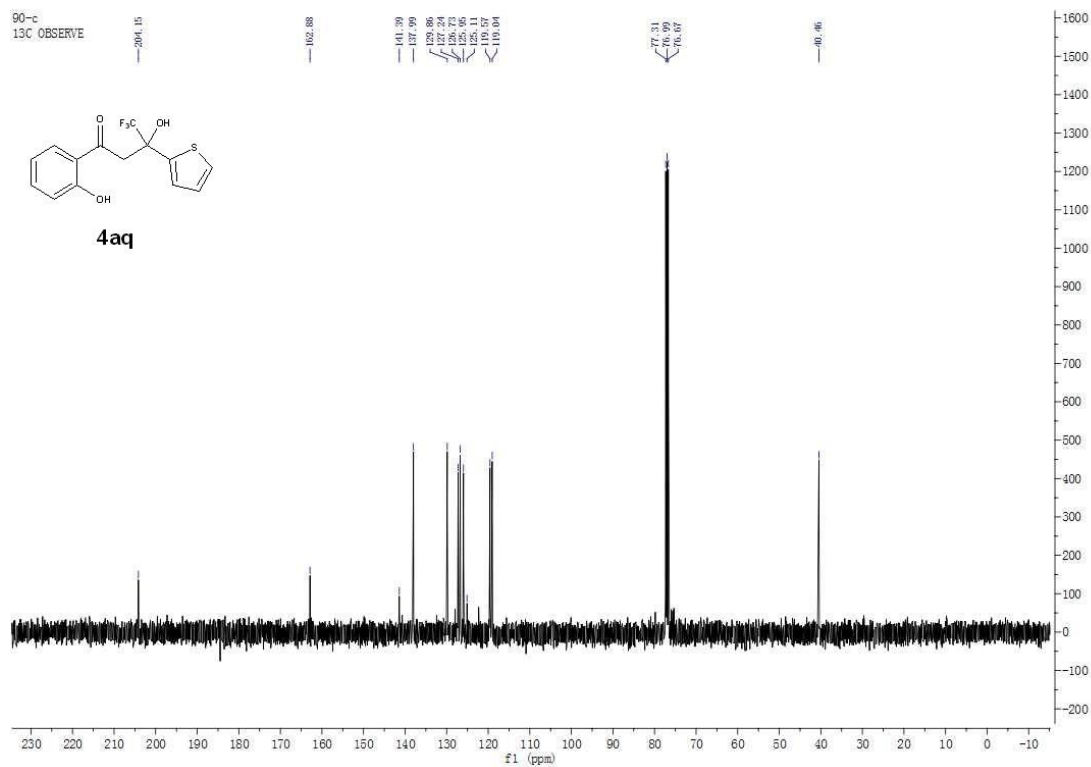
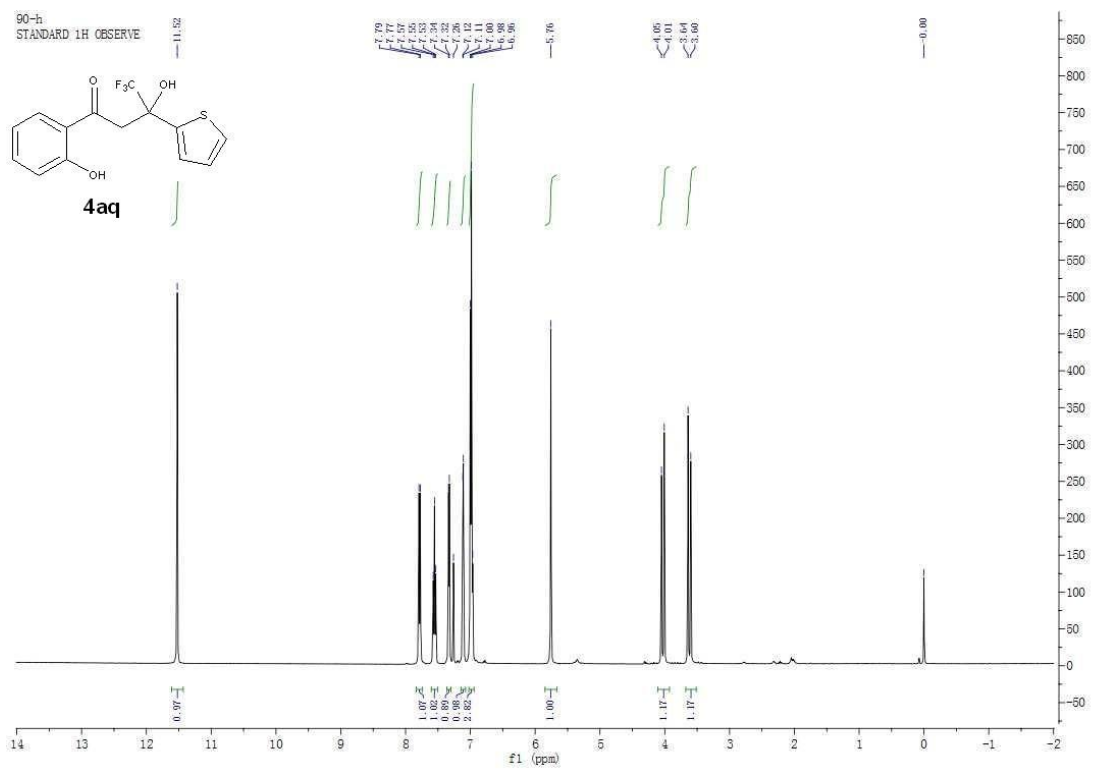


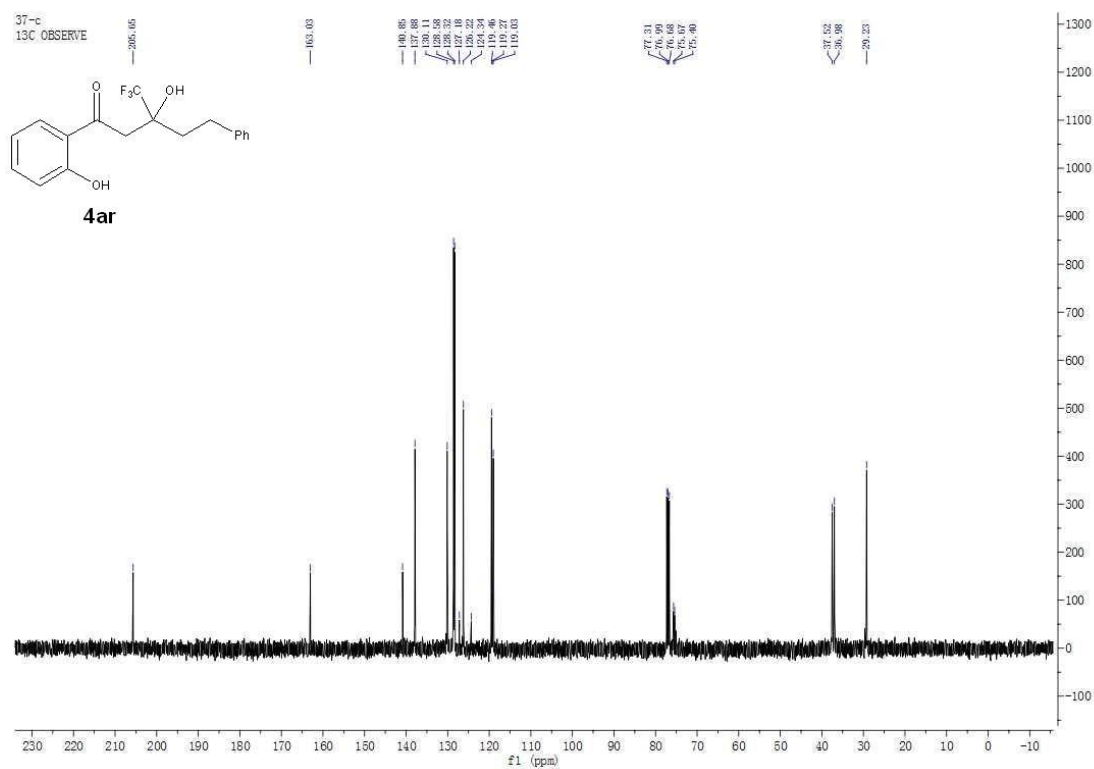
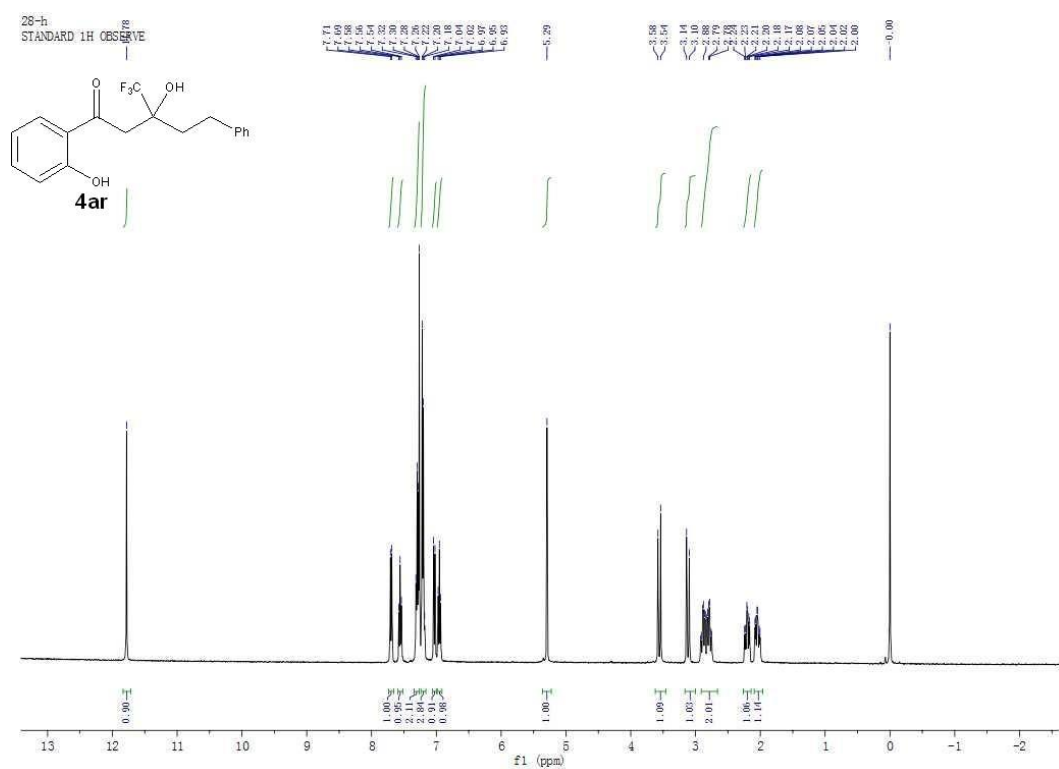


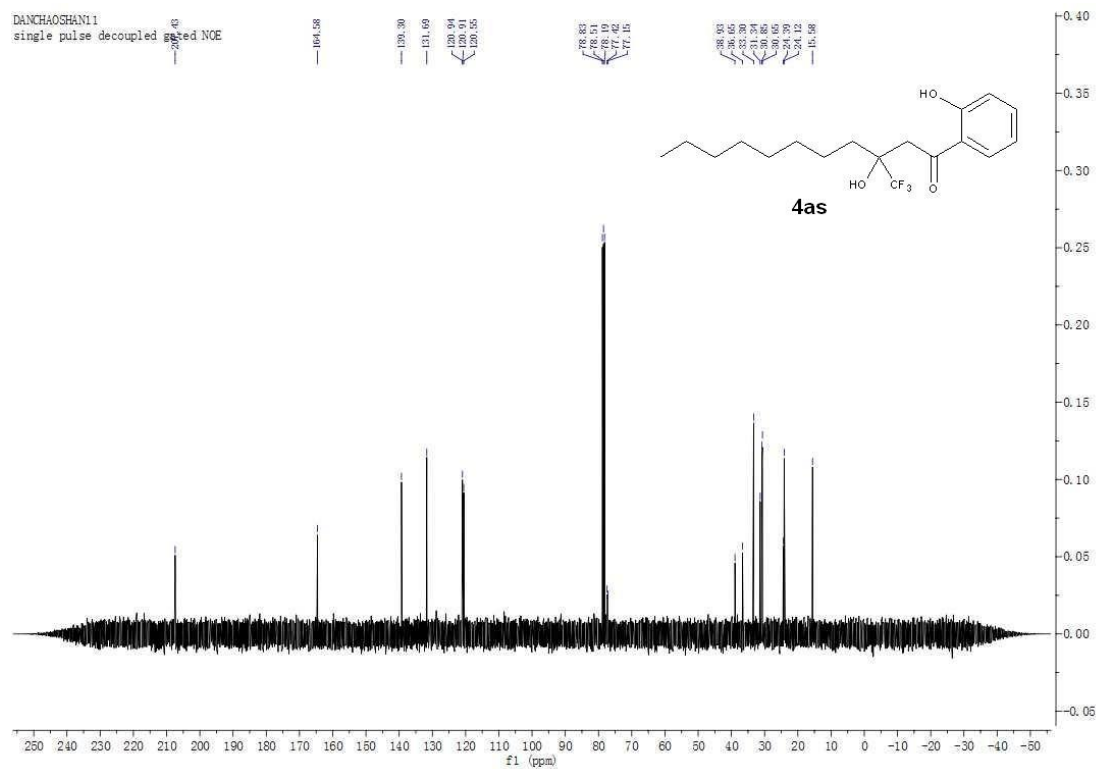
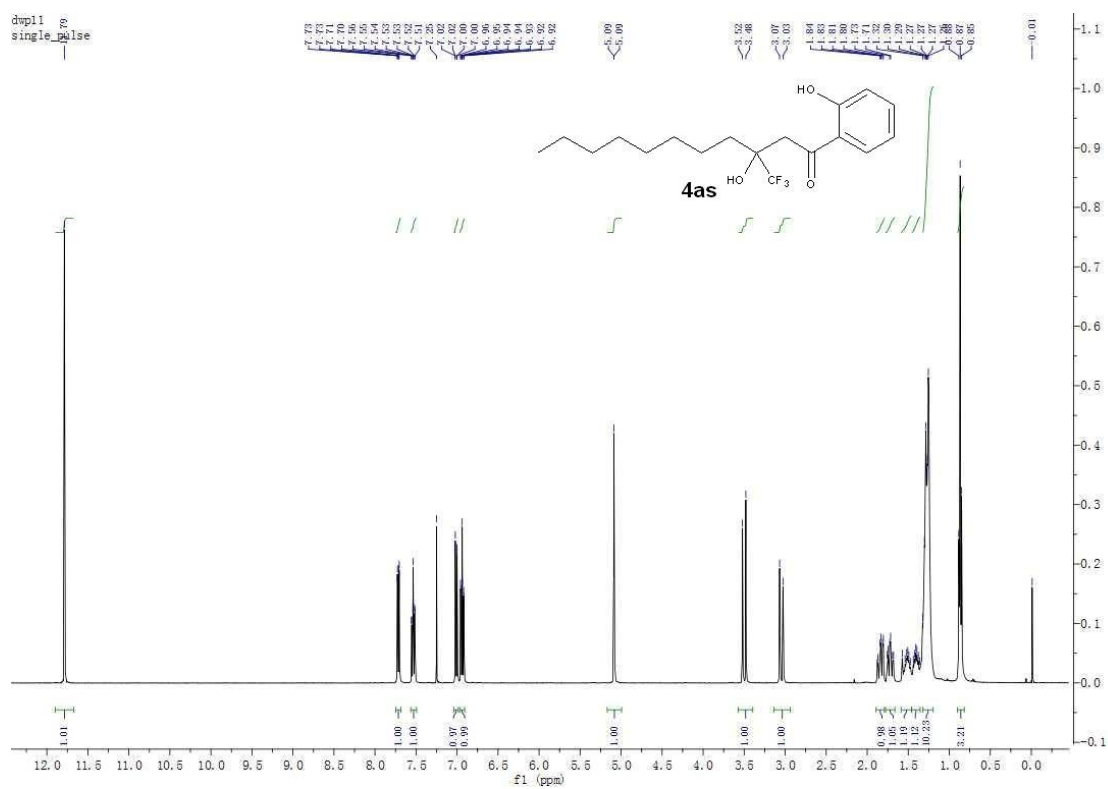


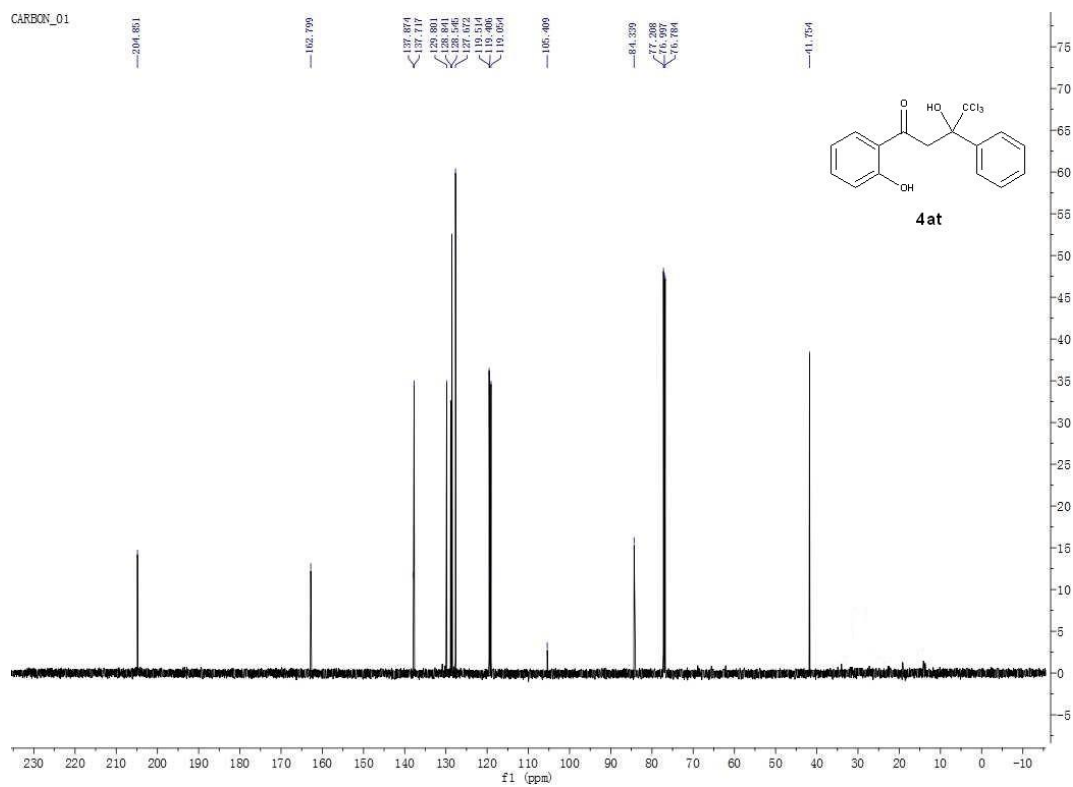
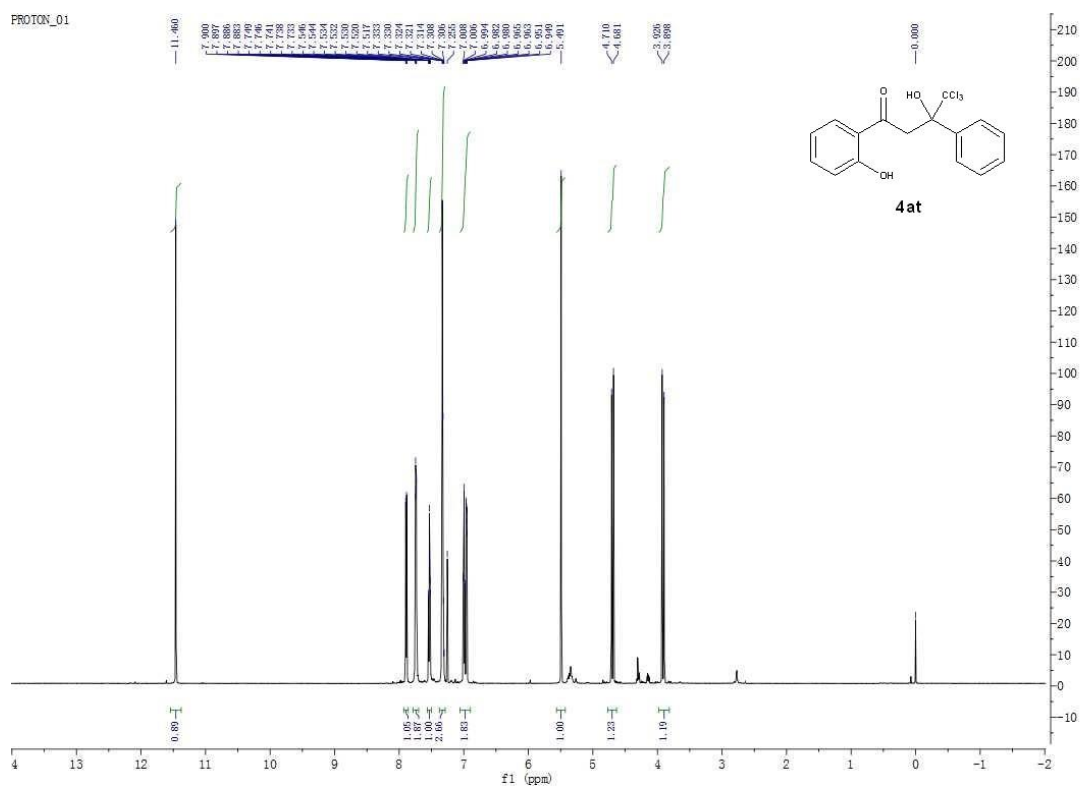


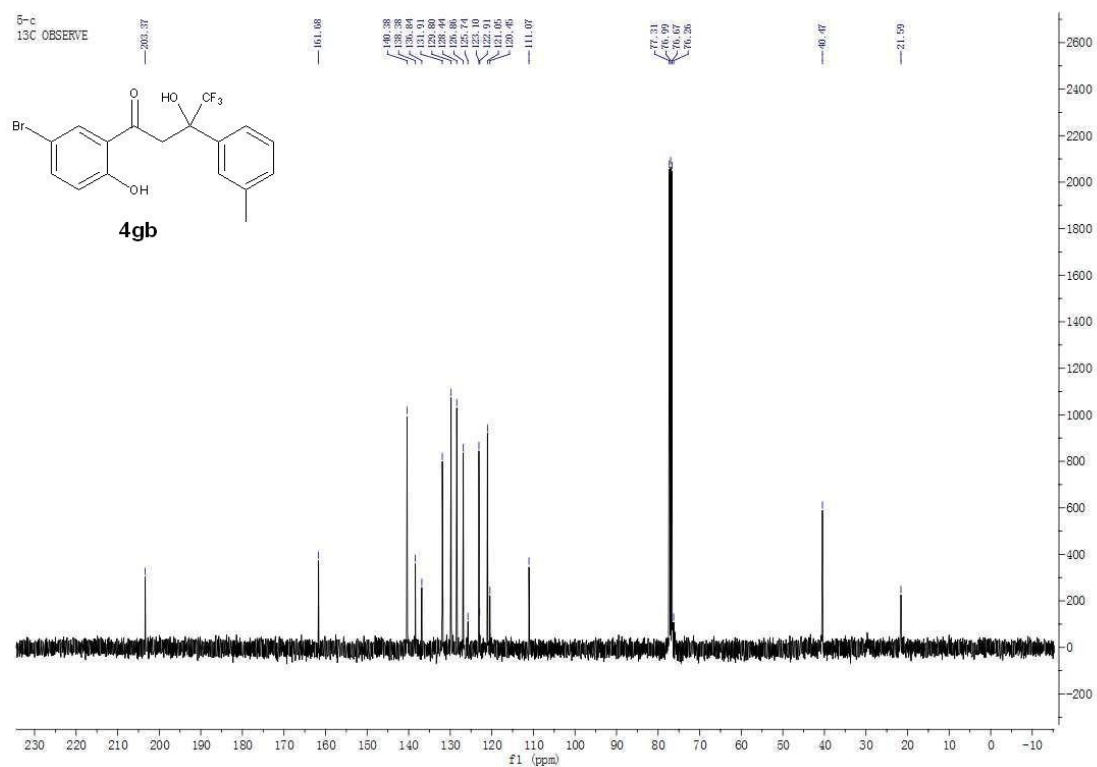
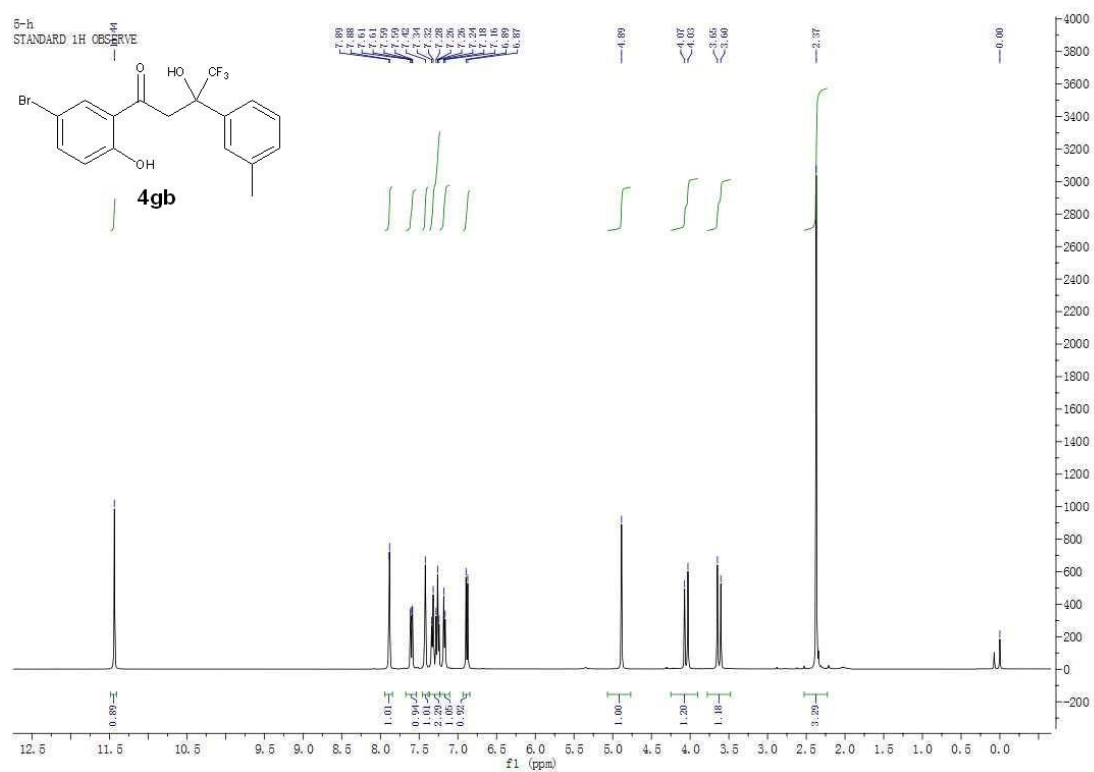


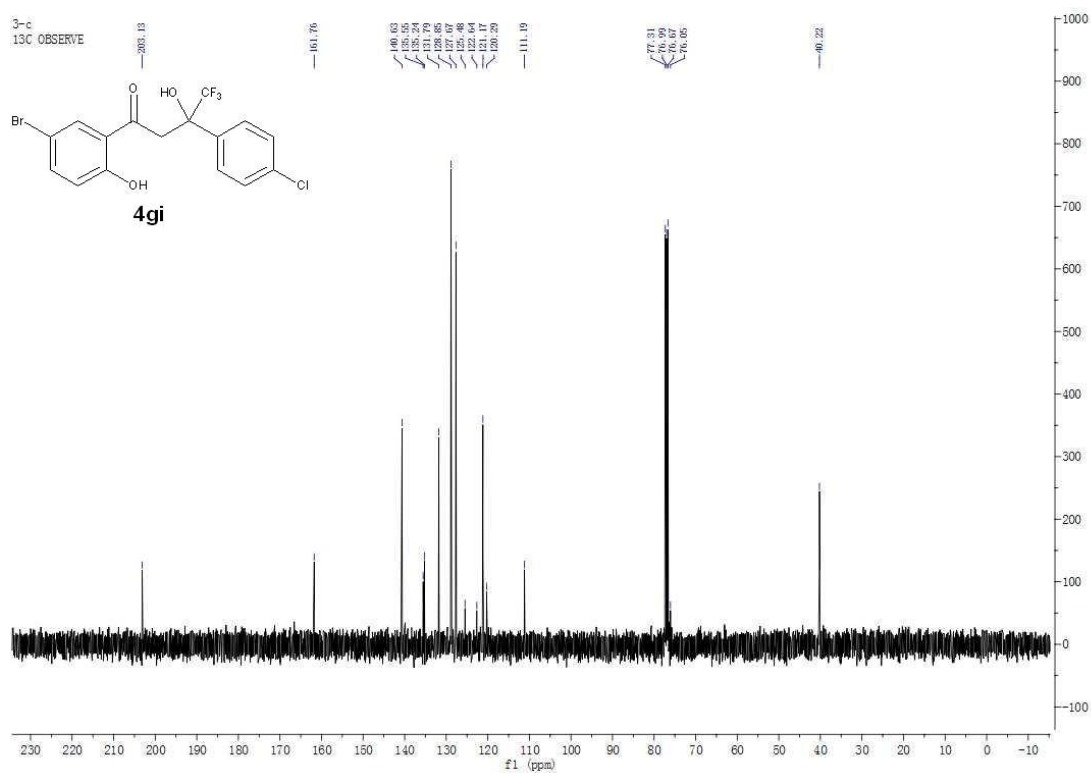
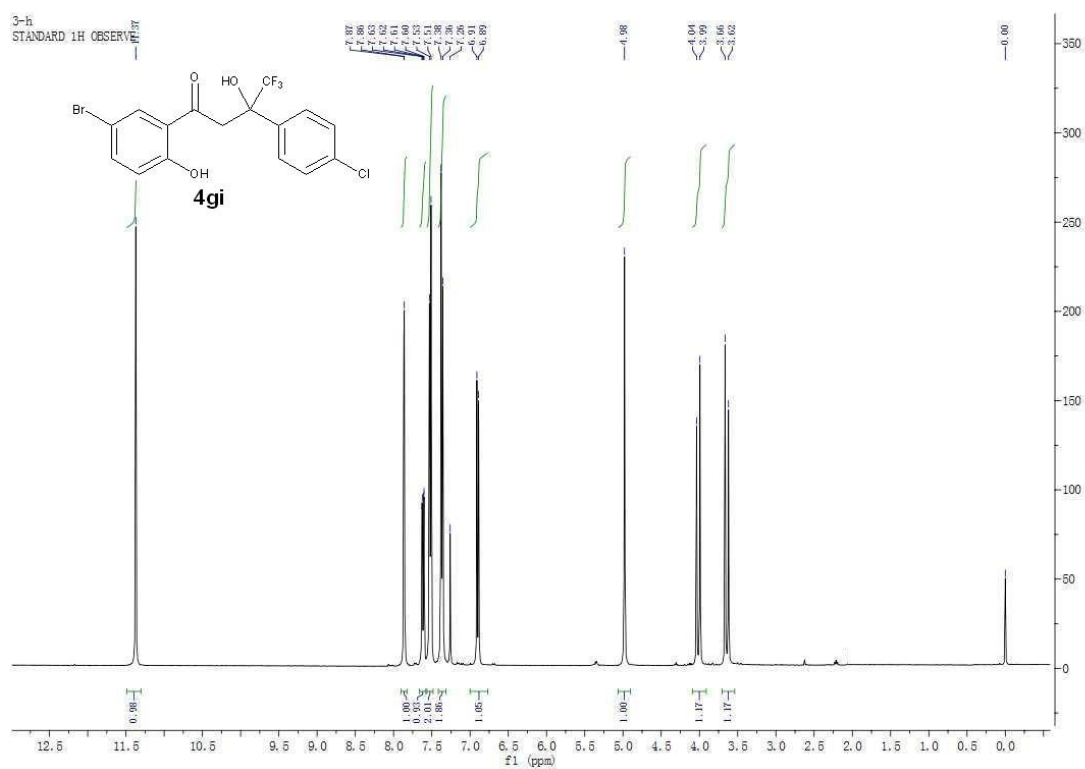


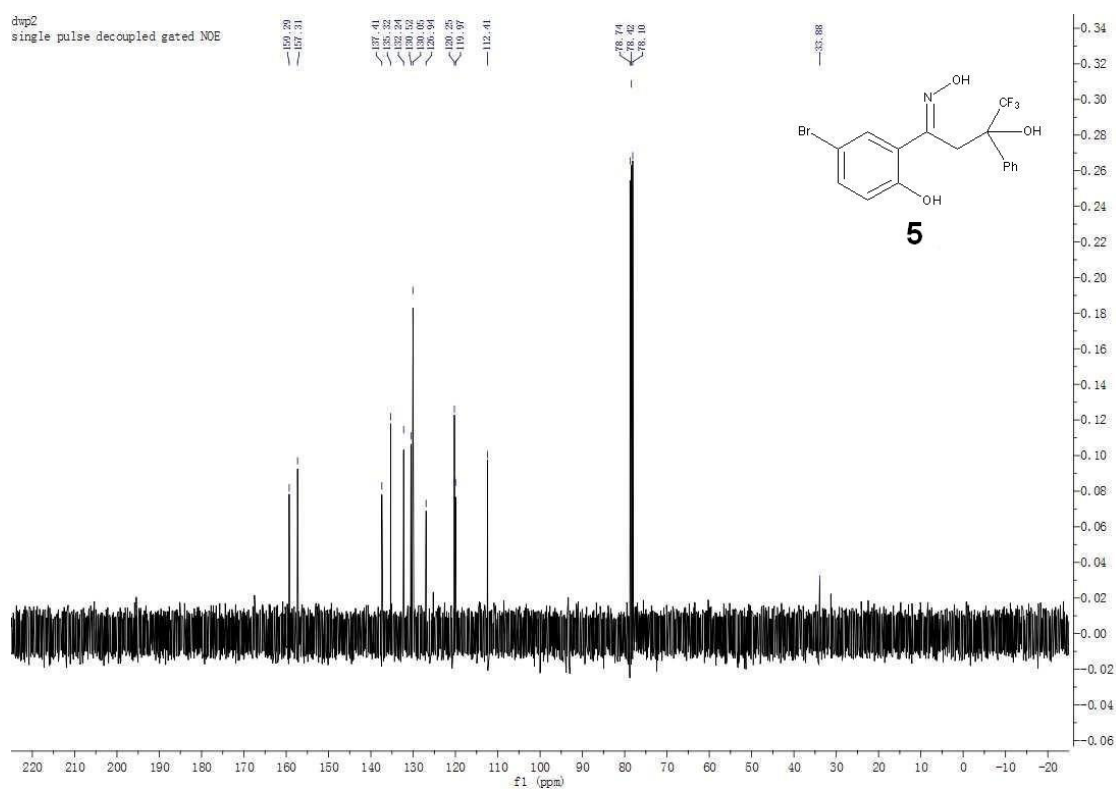
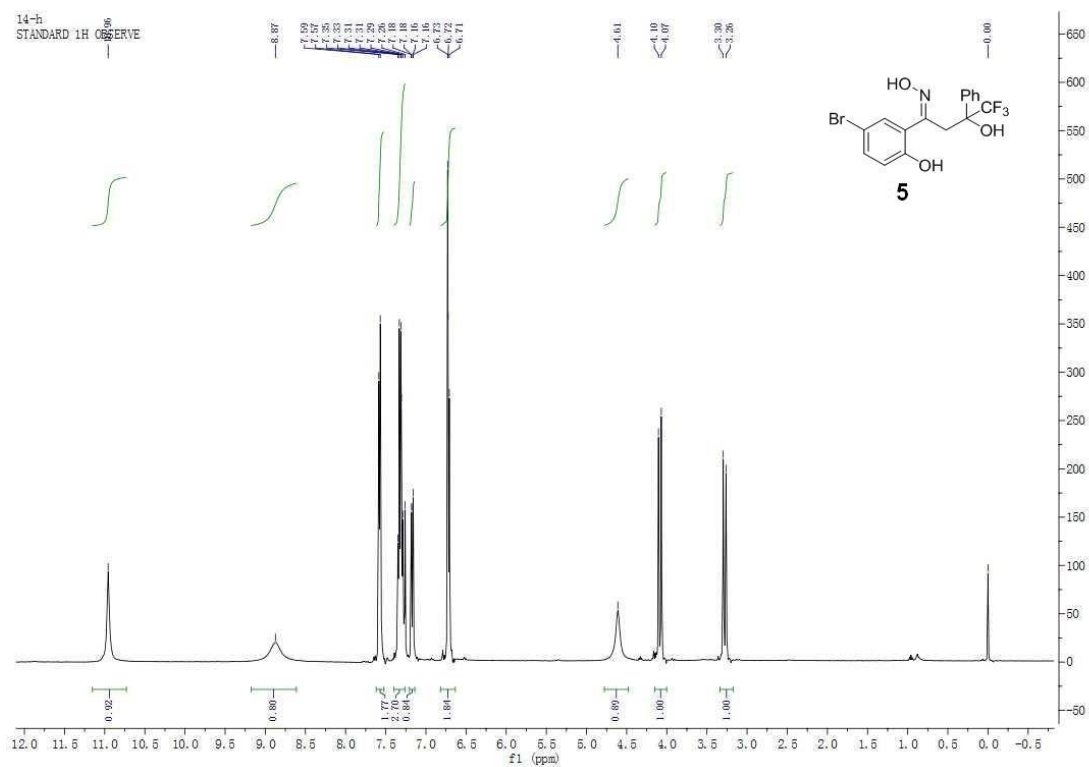


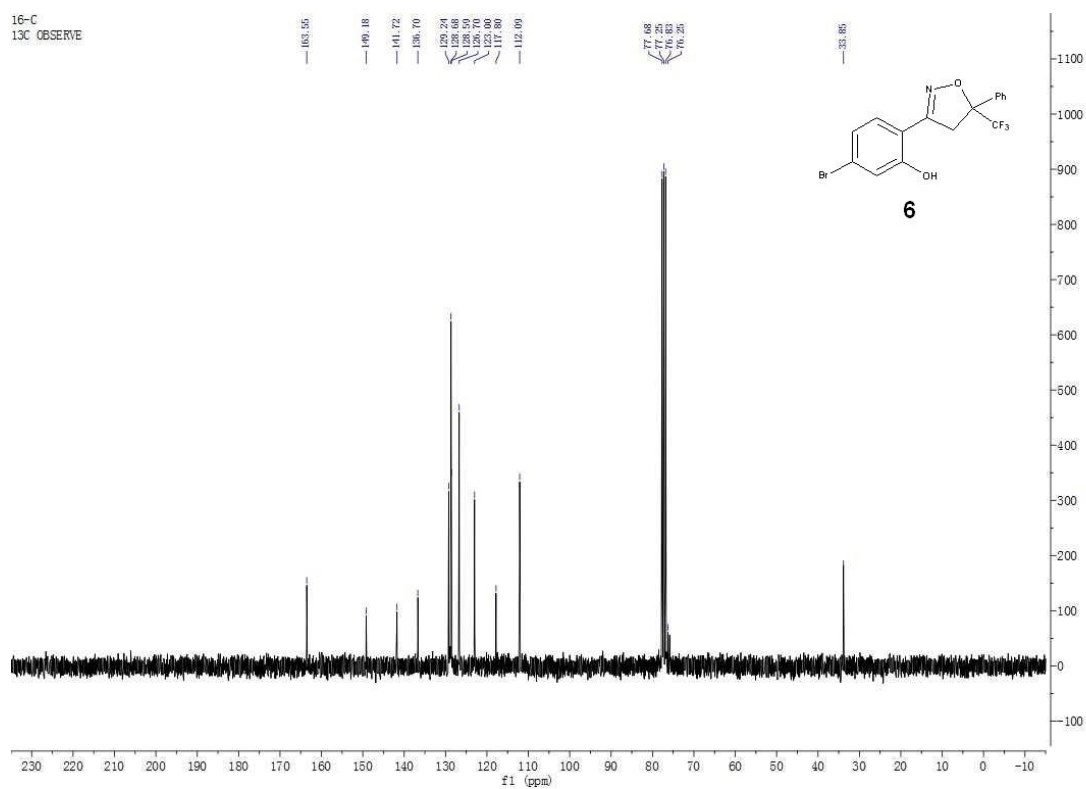
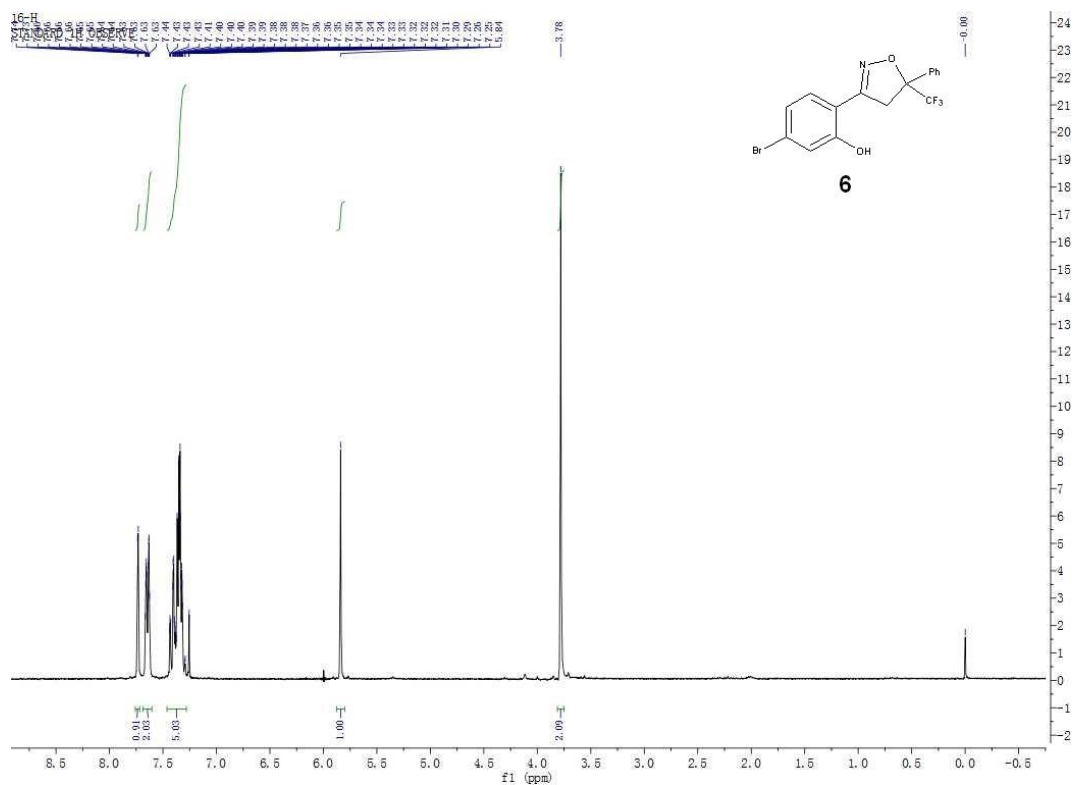


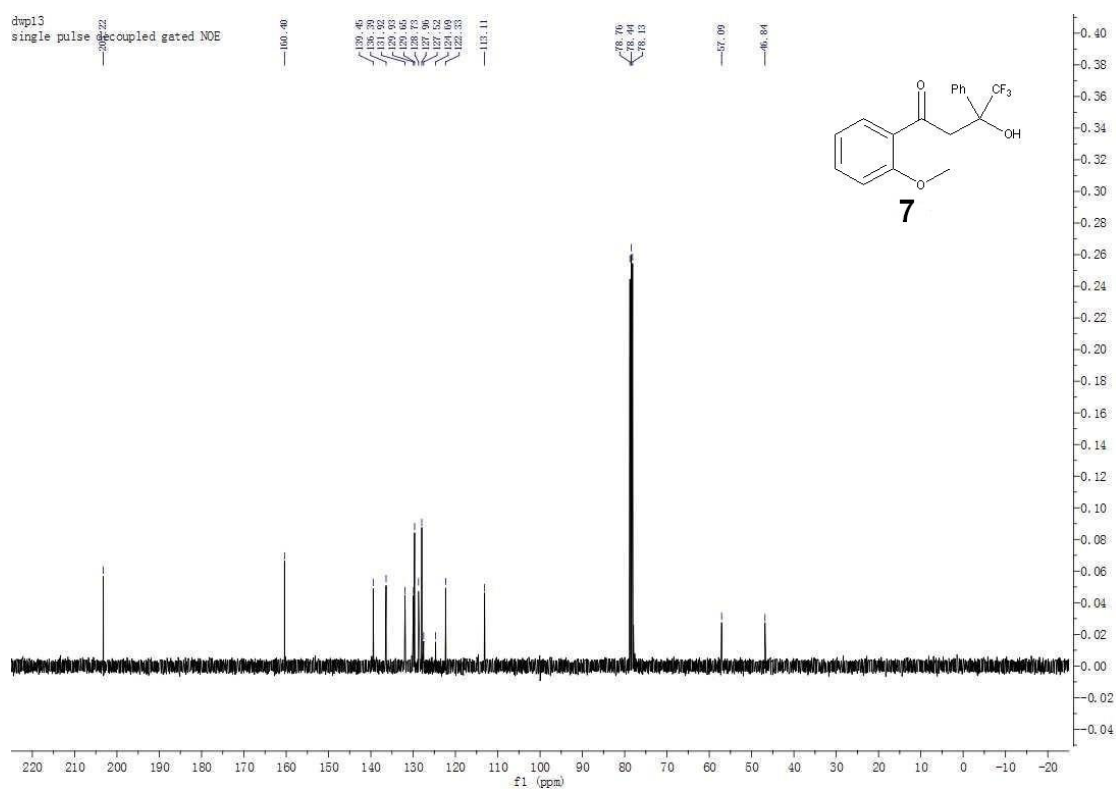
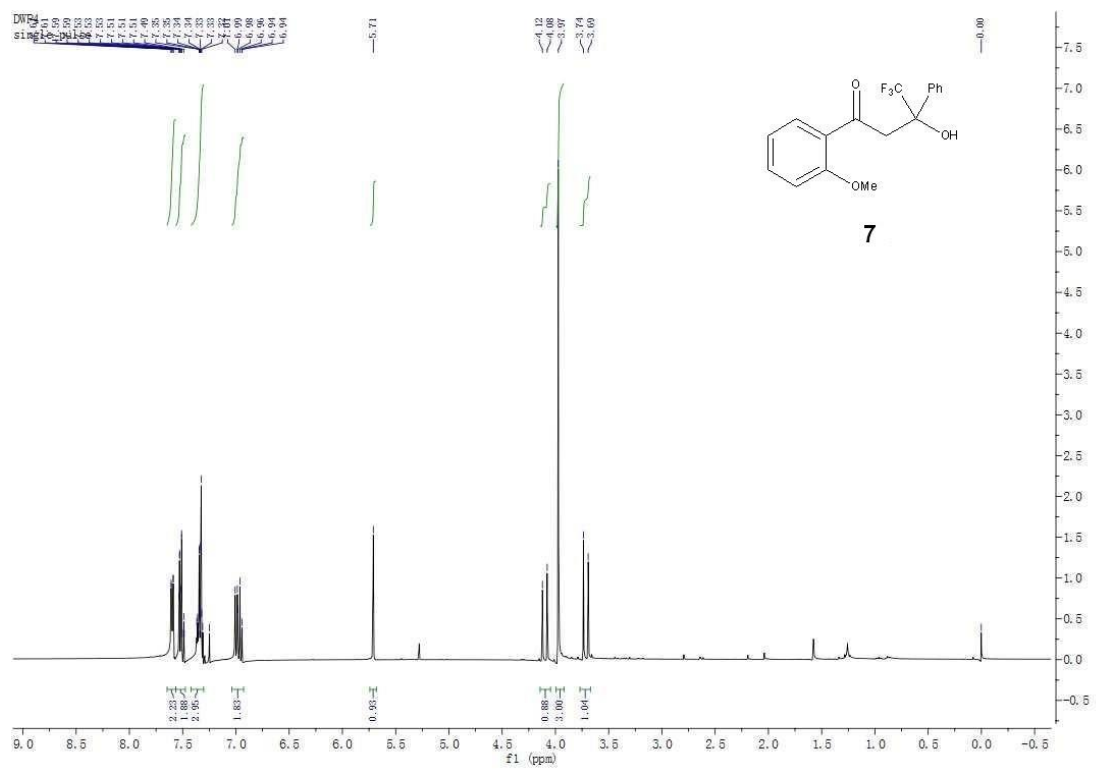


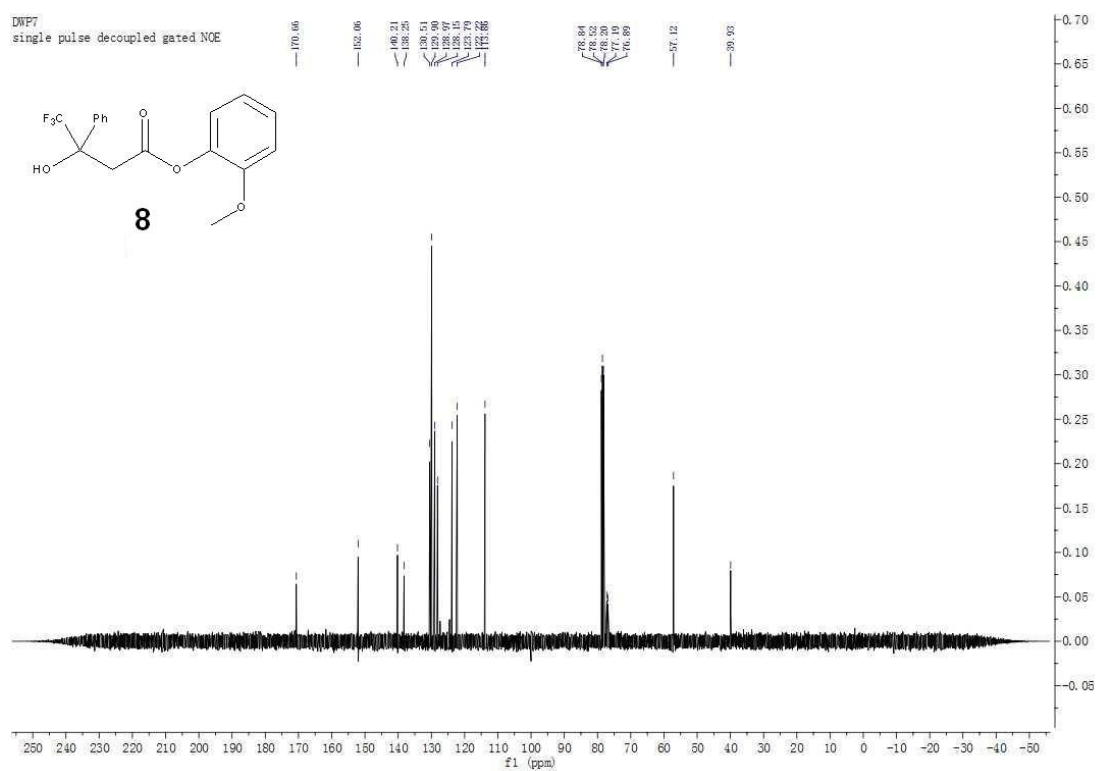
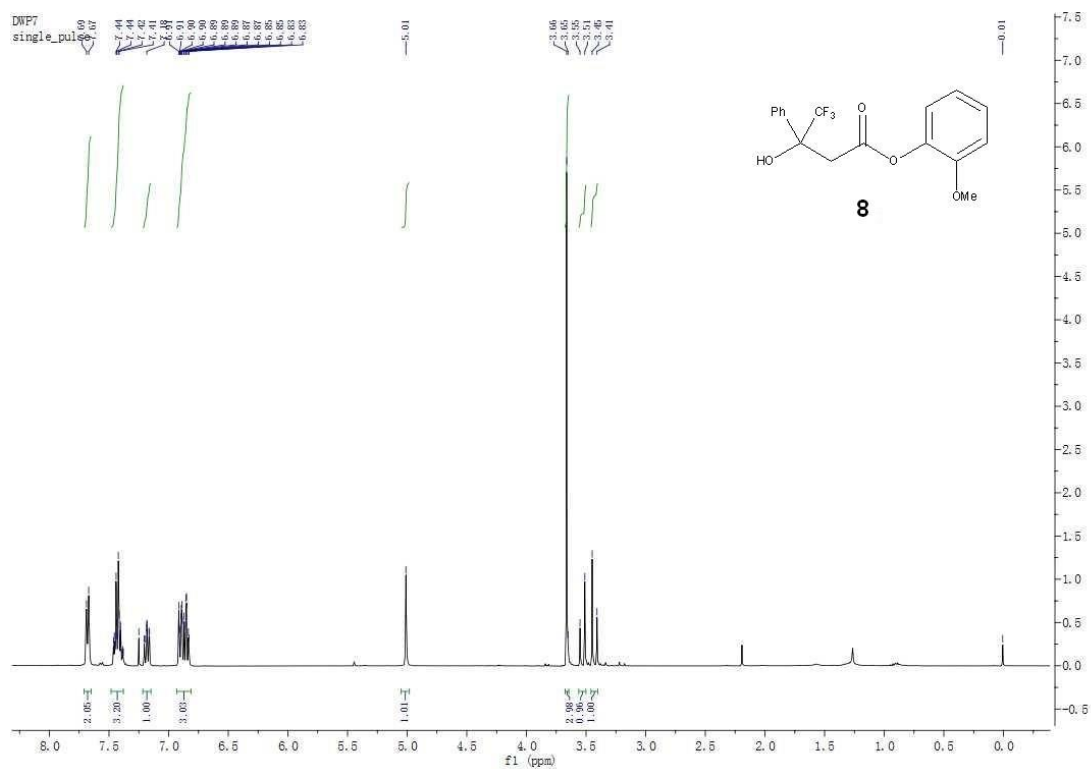












13. Reference:

1. Soloshonok, V. A.; Roussel, C.; Kitagawa, O.; Sorochinsky, A. E. *Chem. Soc. Rev.*, **2012**, *41*, 4180.
2. Fukata, Y.; Okamura, T.; Asano, K.; Matsubara, S. *Org. Lett.* **2014**, *16*, 2184.
3. Li, B. J.; Jiang, L.; Liu, M.; Chen, Y.-C.; Ding, L.-S.; Wu, Y. *Synlett.* **2005**, 603.
4. Amarasinghe, N. R.; Turner, P.; Todd, M. H. *Adv. Synth. Catal.* **2012**, *354*, 2954.
5. Jia, L.-N.; Huang, J.; Peng, L.; Wang, L.-L.; Bai, J.-F.; Tian, F.; He, G.-Y.; Xu, X.-Y.; Wang, L.-X. *Org. Biomol. Chem.* **2012**, *10*, 236.
6. Jing, Z. Z.; Bai, X. B.; Chen, W. C.; Zhang, G.; Zhu, B.; Jiang, Z. Y. *Org. Lett.* **2016**, *18*, 260.
7. Liu, T.-Y.; Long, J.; Li, B.-J.; Jiang, L.; Li, R.; Wu, Y.; Ding, L.-S.; Chen, Y.-C. *Org. Biomol. Chem.* **2006**, *4*, 2097.
8. Tao, R.; Yin, X. J.; Wang, K. H.; Niu, Y. Z.; Wang, Y. L.; Huang, D. F.; Su, Y. P.; Wang, J. X.; Hu, Y. L.; Fu, Y.; Du, Z. Y. *Chin. Chem. Lett.* **2015**, *26*, 1046.
9. Kawai, H.; Okusu, S.; Tokunaga, E.; Shibata, N. *Eur. J. Org. Chem.* **2013**, 6506.