

Transformation of Alkynes into Chiral Alcohols via TfOH-Catalyzed Hydration and Ru-Catalyzed Tandem Asymmetric Hydrogenation

Sensheng Liu,[†] Huan Liu,[†] Haifeng Zhou,^{*,†,‡} Qixing Liu,[†] and Jinliang Lv^{*,‡}

[†]Research Center of Green Pharmaceutical Technology and Process, Hubei Key Laboratory of Natural Products Research and Development, College of Biological and Pharmaceutical Sciences, China Three Gorges University, Yichang 443002, China

[‡]Yichang Humanwell Pharmaceutical Co., Ltd, Yichang, 443005, China

1. General Information.....	S2
2. Optimization of the Hydration Step.....	S2
3. General Procedure for the Synthesis of Racemic Aryl Alcohols.....	S2
4. Reaction Conditions for the Tandem Reactions.....	S2
5. General Procedure for the Hydration and Asymmetric Hydrogenation of Aryl Alkynes.....	S4
6. General Procedure for the Hydration and Asymmetric Hydrogenation of 1,3-diethynylbenzene.....	S4
7. General Procedure for the Hydration and Asymmetric Hydrogenation of 1,4-diethynylbenzene.....	S4
8. General Procedure for the Hydration and Asymmetric Hydrogenation of 1,3,5-triethynylbenzene.....	S5
9. General Procedure for Gram Scale Reaction.....	S5
10. Analytical Data of the Products.....	S6
11. ¹ H NMR and ¹³ C NMR Spectra of the Products.....	S12
12. HPLC Spectra of Products.....	S33

1. General Information

Unless otherwise noted, all reagents, catalysts and solvents were purchased from commercial suppliers and used without further purification. Column Chromatography was performed with silica gel (200-300 mesh). NMR spectra were recorded on Bruker ADVANCE III (400 MHz) spectrometers. CDCl_3 was used for the NMR analysis with tetramethylsilane as the internal standard. Chemical shifts were reported up field to TMS (0.00 ppm) for ^1H NMR and relative to CDCl_3 (77.0 ppm) for ^{13}C NMR. HPLC analysis was conducted on a Waters 2489 Series instrument with chiral column OJ-H, AD-H, AS-H and OD-H. Optical rotations were measured on a MCP-500. Melting points were determined using X-4 made by Peking Taike Apparatus Co., Ltd. HRMS spectra were acquired using an Agilent 6210 ESI/TOF mass spectrometer.

2. Optimization of the Hydration Step^a



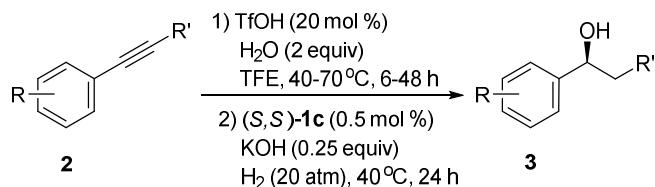
entry	T/°C	t/h	yield (%)
1 ^b	25	45	100
2	25	24	76.5
3	40	12	99.9
4	40	6	99.9
5	40	4	99.3
6	40	2	98.9
7 ^c	40	12	37.6

^aReaction conditions: phenylacetylene (0.5 mmol), TfOH (20 mol %), H_2O (2.0 equiv), TFE (1 mL), the yield was determined by GC with an internal standard (mesitylene). ^bThe same reaction conditions as reference: *Org. Lett.* **2016**, *18*, 2184–2187. ^cHexafluoro-2-propanol (HFIP) was used as solvent.

3. General Procedure for the Synthesis of Racemic Aryl Alcohols

The aryl ketone (0.2 mmol) was dissolved in 1.0 mL MeOH, and NaBH_4 (0.4 mmol) was added slowly. The mixture was stirred at room temperature until the starting material was disappeared. And then 5.0 mL of H_2O was added slowly, the residue was extracted 3 times with ethyl acetate. The combined organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The product was further purified by silica gel column.

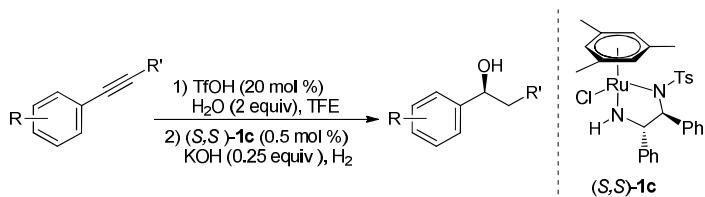
4. Reaction Conditions for Hydration and Asymmetric Hydrogenation Steps^a



entry	substrate	product	hydration step			asymmetric hydrogenation step				yield (%)	ee (%)
			T/ °C	t/h	(S,S)- 1c (mol %)	KOH (equiv)	t/h	H ₂ (atm)	T/ °C		
1	2a : R = H, R' = H	3a	40	6	0.5	0.25	24	20	40	96	99
2	2b : R = 2-F, R' = H	3b	70	12	0.5	0.25	24	20	40	90	93
3	2c : R = 3-F, R' = H	3c	70	12	0.5	0.25	24	20	40	81	99
4	2d : R = 4-F, R' = H	3d	70	12	0.5	0.25	24	20	40	96	95
5	2e : R = 4-Cl, R' = H	3e	70	12	0.5	0.25	24	20	40	94	91
6	2f : R = 2,5-Cl, R' = H	3f	70	12	0.5	0.25	24	20	40	79	87
7	2g : R = 3-Br, R' = H	3g	70	12	0.5	0.25	24	20	40	82	95
8	2h : R = 4-Br, R' = H	3h	70	12	0.5	0.25	24	20	40	89	97
9 ^b	2i : R = 4-NO ₂ , R' = H	3i	70	48	0.5	0.25	24	20	40	62	81
10	2j : R = 4-Me, R' = H	3j	40	6	0.5	0.25	24	20	40	85	99
11	2k : R = 4-Et, R' = H	3k	40	6	0.5	0.25	24	20	40	82	99
12	2l : R = 4-n-Pr, R' = H	3l	40	6	0.5	0.25	24	20	40	83	97
13	2m : R = 4-MeO, R' = H	3m	40	6	0.5	0.25	24	20	40	87	97
14	2n : 2-ethynyl naphthalene	3n	40	6	0.5	0.25	24	20	40	90	93
15	2o : R = H, R' = Me	3o	40	48	0.5	0.25	24	20	40	79	99
16	2p : R = H, R' = Et	3p	40	48	0.5	0.25	24	20	40	72	93
17	2q : R = H, R' = n-Bu	3q	40	48	0.5	0.25	24	20	40	75	94
18	2r : R = H, R' = Ph	3r	40	48	0.5	0.25	24	20	40	83	97

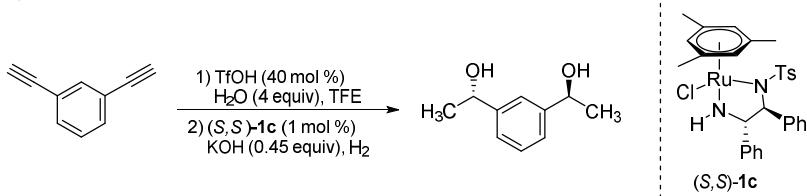
^aReaction conditions: phenylacetylene (0.5 mmol), TfOH (20 mol %), H₂O (2.0 equiv), TFE (1 mL), isolated yield. ^bHexafluoro-2-propanol (HFIP) was used as solvent.

5. General Procedure for the Hydration and Asymmetric Hydrogenation of Alkynes



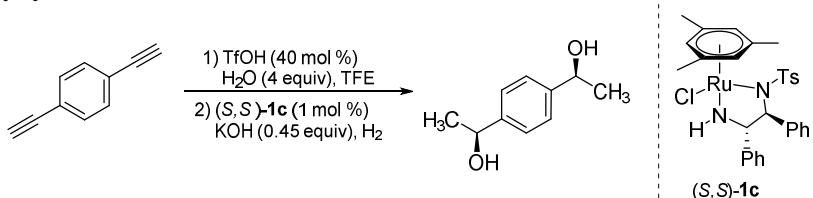
Under nitrogen atmosphere, the alkyne (0.5 mmol), TfOH (0.1 mmol, 10 uL), H₂O (1 mmol, 18.0 uL), and TFE (1.0 mL) were added into a 10 mL glass tube. The reaction mixture was stirred at 40–70 °C for 6–48 h. After the hydration reaction was complete, KOH (0.125 mmol, 7.0 mg) and (S,S)-1c (0.0025 mmol, 1.59 mg) were added. The glass tube was put into a stainless steel autoclave. The final pressure of the hydrogen gas was adjusted to 20 atm after purging the autoclave with hydrogen gas 3 times. The reaction mixture was stirred at 40 °C for 24 h. The solvent was removed under reduced pressure. Water (2 mL) was added and extracted 3 times with ethyl acetate, and the combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was further purified by silica gel column.

6. General Procedure for the Hydration and Asymmetric Hydrogenation of 1,3-diethynylbenzene



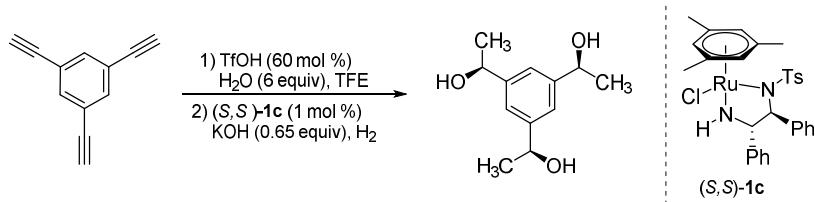
Under nitrogen atmosphere, 1,3-diethynylbenzene (0.5 mmol), TfOH (0.2 mmol, 20 uL), H₂O (2 mmol, 36 uL), and TFE (1.0 mL) were added into a 10 mL glass tube. The reaction mixture was stirred at 70 °C for 48 h. After the hydration reaction was complete, KOH (0.225 mmol, 12.6 mg) and (S,S)-1c (0.005 mmol, 3.18 mg) were added. The glass tube was put into a stainless steel autoclave. The final pressure of the hydrogen gas was adjusted to 40 atm after purging the autoclave with hydrogen gas 3 times. The reaction mixture was stirred at 40 °C for 24 h. The solvent was removed under reduced pressure. Water (2 mL) was added and extracted 3 times with ethyl acetate, and the combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was further purified by silica gel column to give a colourless oil (74 mg, 89% yield, >99% ee, >99% de).

7. General Procedure for the Hydration and Asymmetric Hydrogenation of 1,4-diethynylbenzene



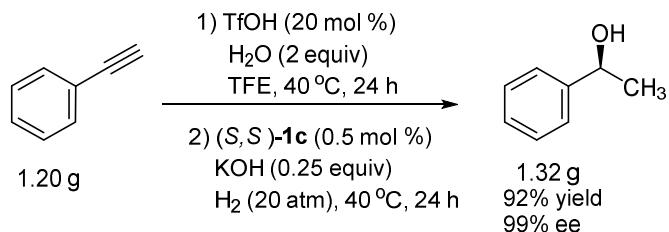
Under nitrogen atmosphere, 1,4-diethynylbenzene (0.5 mmol), TfOH (0.2 mmol, 20 uL), H₂O (2 mmol, 36 uL), and TFE (1.0 mL) were added into a 10 mL glass tube. The reaction mixture was stirred at 70 °C for 48 h. After the hydration reaction was complete, KOH (0.225 mmol, 12.6 mg) and (S,S)-1c (0.005 mmol, 3.18 mg) were added. The glass tube was put into a stainless steel autoclave. The final pressure of the hydrogen gas was adjusted to 40 atm after purging the autoclave with hydrogen gas 3 times. The reaction mixture was stirred at 40 °C for 24 h. The solvent was removed under reduced pressure. Water (2 mL) was added and extracted 3 times with ethyl acetate, and the combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was further purified by silica gel column to give a white solid (76 mg, 92% yield, >99% ee, 90% de).

8. General Procedure for the Hydration and Asymmetric Hydrogenation of 1,3,5-Triethynylbenzene



Under nitrogen atmosphere, 1,3,5-triethynylbenzene (0.5 mmol), TfOH (0.3 mmol, 30 uL), H₂O (3 mmol, 54 uL), and TFE (1.0 mL) were added into a 10 mL glass tube. The reaction mixture was stirred 70 °C for 48 h. After the hydration reaction was complete, KOH (0.325 mmol, 18.2 mg) and (S,S)-1c (0.005 mmol, 3.18 mg) were added. The glass tube was put into a stainless steel autoclave. The final pressure of the hydrogen gas was adjusted to 40 atm after purging the autoclave with hydrogen gas 3 times. The reaction mixture was stirred at 40 °C for 24 h. The solvent was removed under reduced pressure. Water (2 mL) was added and extracted 3 times with ethyl acetate, and the combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was further purified by silica gel column to give colourless oil (95 mg, 91% yield, 94% ee, 99% de).

9. General Procedure for Gram Scale Reaction

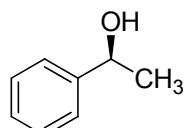


Under nitrogen atmosphere, phenylacetylene (12 mmol, 1.2 g), TfOH (2.4 mmol, 0.24 mL), H₂O (24 mmol, 0.43 mL), and TFE (8.0 mL) were added into a 30 mL glass tube. The reaction mixture was stirred at 40 °C for 24 h. After the hydration reaction was complete, KOH (3 mmol,

168.0 mg) and (*S,S*)-**1c** (0.6 mmol, 38.2 mg) were added. The glass tube was put into a stainless steel autoclave. The final pressure of the hydrogen gas was adjusted to 20 atm after purging the autoclave with hydrogen gas 3 times. The reaction mixture was stirred at 40 °C for 24 h. The solvent was removed under reduced pressure. Water (2 mL) was added and extracted 3 times with ethyl acetate, and the combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was further purified by silica gel column to give a colourless oil (1.32 g, 92% yield, 99% ee).

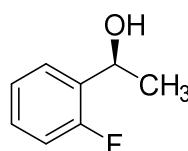
10. Analytical Data of the Products

(*S*)-1-phenylethanol (**3a**, CAS: 1445-91-6, know compound)^[1]



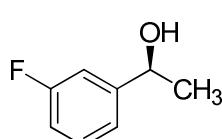
Colourless oil; 96% yield (59 mg), 99% ee. Purified by flash column chromatography (PE: EA = 10:1). ([α]²⁰_D -56.6 (c 0.8, CHCl₃)). **1H NMR** (400 MHz, CDCl₃): δ = 7.43-7.37 (m, 4H), 7.34-7.30 (m, 1H), 4.93 (q, *J* = 6.4 Hz, 1H), 2.03 (s, 1H), 1.54 (d, *J* = 6.4 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ = 145.83, 128.53, 127.50, 125.41, 70.44, 25.19. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 97:3 (v/v), 1.0 mL/min, 254 nm, 30 °C), t_R = 11.58 min (minor), t_S = 13.82 min (major).

(*S*)-1-(2-fluorophenyl)ethanol (**3b**, CAS: 171032-87-4, know compound)^[3]



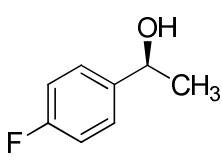
Colourless oil; 90% yield (63 mg), 93% ee. Purified by flash column chromatography (PE: EA = 10:1). ([α]²⁰_D -43.4 (c 0.9, CHCl₃)). **1H NMR** (400 MHz, CDCl₃): δ = 7.53-7.49 (m, 1H), 7.17-7.11 (m, 1H), 7.30-7.24 (m, 1H), 7.20-7.16 (m, 1H), 7.07-7.02 (m, 1H), 5.21 (q, *J* = 2.8 Hz, 1H), 2.47 (d, *J* = 3.2 Hz, 1H), 1.53 (d, *J* = 6.4 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ = 159.69 (d, *J* = 243.6 Hz, 1C), 132.68 (d, *J* = 13.2 Hz, 1C), 128.75 (d, *J* = 8.3 Hz, 1C), 126.64 (d, *J* = 4.5 Hz, 1C), 124.32 (d, *J* = 3.5 Hz, 1C), 115.27 (d, *J* = 21.8 Hz, 1C), 64.43 (d, *J* = 3.1 Hz, 1C), 24.01. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 98:2 (v/v), 1.0 mL/min, 254 nm, 30 °C), t_R = 10.71 min (minor), t_S = 11.56 min (major).

(*S*)-1-(3-fluorophenyl)ethanol (**3c**, CAS: 126534-32-5, know compound)^[3]



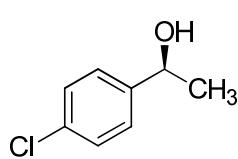
Colourless oil; 81% yield (58 mg), >99% ee. Purified by flash column chromatography (PE: EA = 10:1). ([α]²⁰_D -49.0 (c 1.0, CHCl₃)). **1H NMR** (400 MHz, CDCl₃): δ = 7.36-7.30 (m, 1H), 7.17-7.11 (m, 2H), 7.01-6.96 (m, 1H), 4.92 (q, *J* = 6.4 Hz, 1H), 2.14 (s, 1H), 1.51 (d, *J* = 6.4 Hz, 3H); **13C NMR** (100 MHz, CDCl₃): δ = 163.00 (d, *J* = 244.2 Hz, 1C), 148.52 (d, *J* = 6.5 Hz, 1C), 129.99 (d, *J* = 8.0 Hz, 1C), 120.95 (d, *J* = 2.7 Hz, 1C), 114.21 (d, *J* = 21.0 Hz, 1C), 112.31 (d, *J* = 21.6 Hz, 1C), 69.80 (d, *J* = 1.8 Hz, 1C), 25.22. HPLC (Chiralcel OJ-H column, n-hexane/2-propanol = 95:5 (v/v), 1.0 mL/min, 200 nm, 30 °C), t_S = 7.77 min (major).

(*S*)-1-(4-fluorophenyl)ethanol (**3d**, CAS: 101219-73-2, know compound)^[3]



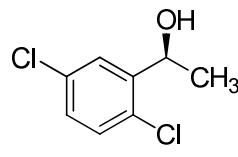
Colourless oil; 96% yield (67 mg), 95% ee. Purified by flash column chromatography (PE: EA = 10:1). ($[\alpha]^{20}_D$ -65.0 (*c* 1.0, CHCl₃)). **¹H NMR** (400 MHz, CDCl₃): δ = 7.37-7.34 (m, 2H), 7.05 (t, *J* = 8.8 Hz, 2H), 4.90 (q, *J* = 6.8 Hz, 1H), 2.27 (s, 1H), 1.49 (d, *J* = 6.4 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ = 162.10 (d, *J* = 243.6 Hz, 1C), 141.53 (d, *J* = 3.2 Hz, 1C), 127.06 (d, *J* = 8.0 Hz, 2C), 115.24 (d, *J* = 21.2 Hz, 2C), 69.74, 25.27. HPLC (Chiralcel AS-H column, n-hexane/2-propanol = 98:2 (v/v), 1.0 mL/min, 220 nm, 30 °C), t_R = 13.86 min (minor), t_S = 15.67 min (major).

(*S*)-1-(4-chlorophenyl)ethanol (**3e**, CAS: 99528-42-4, know compound)^[3]



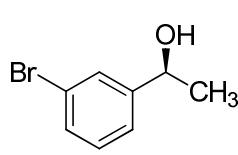
Colourless oil; 94% yield (73 mg), 91% ee. Purified by flash column chromatography (PE: EA = 10:1). ($[\alpha]^{20}_D$ -59.3 (*c* 1.0, CHCl₃)). **¹H NMR** (400 MHz, CDCl₃): δ = 7.37-7.32 (m, 4H), 4.90 (q, *J* = 6.4 Hz, 1H), 2.05 (s, 1H), 1.50 (d, *J* = 6.4 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ = 144.25, 133.07, 128.61, 126.81, 69.75, 25.29. HPLC (Chiralcel OJ-H column, n-hexane/2-propanol = 97:3 (v/v), 1.0 mL/min, 220 nm, 30 °C), t_S = 10.76 min (major), t_R = 11.92 min (minor).

(*S*)-1-(2,5-dichlorophenyl)ethanol (**3f**, CAS: 691881-93-3, know compound)



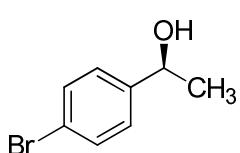
Colourless oil; 79% yield (74 mg), 87% ee. Purified by flash column chromatography (PE: EA = 10:1). ($[\alpha]^{20}_D$ -72.5 (*c* 0.8, CHCl₃)). **¹H NMR** (400 MHz, CDCl₃): δ = 7.51 (d, *J* = 8.4 Hz, 1H), 7.43 (d, *J* = 2.0 Hz, 1H), 7.27 (dd, *J*₁ = 8.4 Hz, *J*₂ = 8.4 Hz, 1H), 5.21 (q, *J* = 6.4 Hz, 1H), 2.78 (s, 1H), 1.45 (d, *J* = 6.4 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ = 141.72, 133.34, 132.09, 129.06, 127.48, 127.41, 66.50, 23.58. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 99:1 (v/v), 1.0 mL/min, 220 nm, 30 °C), t_S = 18.96 min (major), t_R = 21.04 min (minor).

(*S*)-1-(3-bromophenyl)ethanol (**3g**, CAS: 134615-22-8, know compound)^[2]



Colourless oil; 82% yield (82 mg), 95% ee. Purified by flash column chromatography (PE: EA = 10:1). ($[\alpha]^{20}_D$ -48.9 (*c* 1.0, CHCl₃)). **¹H NMR** (400 MHz, CDCl₃): δ = 7.54 (t, *J* = 2.0 Hz, 1H), 7.43-7.40 (m, 1H), 7.30-7.28 (m, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 4.84 (q, *J* = 6.4 Hz, 1H), 2.56 (s, 1H), 1.48 (d, *J* = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ = 148.14, 130.44, 130.11, 128.58, 124.05, 122.59, 69.69, 25.23. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 95:5 (v/v), 1.0 mL/min, 220 nm, 30 °C), t_S = 8.48 min (major), t_R = 9.40 min (minor).

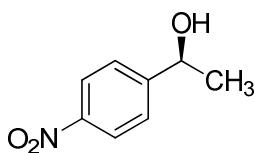
(*S*)-1-(4-bromophenyl)ethanol (**3h**, CAS: 100760-04-1, know compound)^[3]



Colourless oil; 89% yield (88 mg), 97% ee. Purified by flash column chromatography (PE: EA = 10:1). ($[\alpha]^{20}_D$ -31.9 (*c* 0.9, CHCl₃)). **¹H NMR**

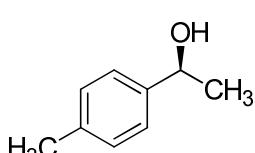
(400 MHz, CDCl₃): δ = 7.50 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 4.90 (q, J = 6.4 Hz, 1H), 2.04 (s, 1H), 1.50 (d, J = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 144.78, 131.56, 127.16, 121.17, 69.79, 25.26. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 95:5 (v/v), 1.0 mL/min, 254 nm, 30 °C), t_S = 8.37 min (major), t_R = 9.10 min (minor).

(S)-1-(4-nitrophenyl)ethanol (**3i**, CAS: 6531-13-1, know compound)^[1]



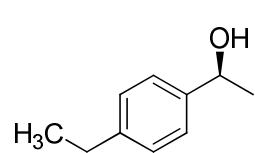
Colourless oil; 62% yield (52 mg), 81% ee. Purified by flash column chromatography (PE: EA = 10:1). ([α]_D²⁰ -22.2 (*c* 0.8, CHCl₃)). ¹H NMR (400 MHz, CDCl₃): δ = 8.21 (d, J = 8.8 Hz, 2H), 7.56 (d, J = 8.4 Hz, 2H), 5.05 (q, J = 6.8 Hz, 1H), 2.37 (s, 1H), 1.54 (d, J = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 153.17, 147.13, 126.15, 123.76, 69.50, 25.51. HPLC (Chiralcel OJ-H column, n-hexane/2-propanol = 95:5 (v/v), 1.0 mL/min, 254 nm, 30 °C), t_S = 30.10 min (major), t_R = 32.23 min (minor).

(S)-1-(p-tolyl)ethanol (**3j**, CAS: 51154-54-2, know compound)^[3]



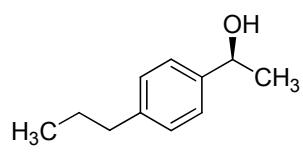
Colourless oil; 85% yield (57 mg), 99% ee. Purified by flash column chromatography (PE: EA = 10:1). ([α]_D²⁰ -60.1 (*c* 1.0, CHCl₃)). ¹H NMR (400 MHz, CDCl₃): δ = 7.31 (d, J = 7.6 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 4.91 (q, J = 6.4 Hz, 1H), 2.39 (s, 3H), 1.97 (s, 1H), 1.52 (d, J = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 142.90, 137.16, 129.18, 125.38, 70.26, 25.10, 21.12. HPLC (Chiralcel OJ-H column, n-hexane/2-propanol = 98:2 (v/v), 1.0 mL/min, 220 nm, 30 °C), t_S = 10.22 min (major), t_R = 11.66 min (minor).

(S)-1-(4-ethylphenyl)ethanol (**3k**, CAS: 101219-72-1, know compound)^[2]



Colourless oil; 82% yield (61.2 mg), 99% ee. Purified by flash column chromatography (PE: EA = 10:1). ([α]_D²⁰ -50.1 (*c* 1.0, CHCl₃)). ¹H NMR (400 MHz, CDCl₃): δ = 7.34 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 7.6 Hz, 2H), 4.92 (q, J = 6.8 Hz, 1H), 2.68 (q, J = 7.6 Hz, 2H), 1.79 (s, 1H), 1.53 (d, J = 6.4 Hz, 3H), 1.27 (t, J = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 143.26, 143.09, 128.02, 125.45, 70.33, 28.55, 25.06, 15.66. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 99:1 (v/v), 1.0 mL/min, 254 nm, 30 °C), t_R = 19.09 min (minor), t_S = 20.50 min (major).

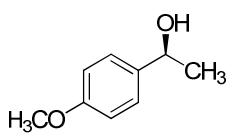
(S)-1-(4-propylphenyl)ethanol (**3l**, CAS: 473700-93-5, know compound)^[2]



Colourless oil; 83% yield (68 mg), 97% ee. Purified by flash column chromatography (PE: EA = 10:1). ([α]_D²⁰ -49.1 (*c* 1.0, CHCl₃)). ¹H NMR (400 MHz, CDCl₃): δ = 7.33 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 4.92 (q, J = 6.8 Hz, 1H), 2.62 (q, J = 7.2 Hz, 2H), 1.91 (s, 1H), 1.73-1.65 (m, 2H),

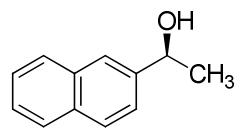
1.53 (d, $J = 6.4$ Hz, 3H), 0.99 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 143.08$, 142.03, 128.59, 125.35, 70.31, 37.74, 25.03, 24.60, 13.87. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 97:3 (v/v), 1.0 mL/min, 254 nm, 30 °C), $t_R = 8.16$ min (minor), $t_S = 9.04$ min (major).

(S)-1-(4-methoxyphenyl)ethanol (**3m**, CAS: 1572-97-0, know compound)^[1]



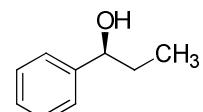
Colourless oil; 87% yield (66 mg), 97% ee. Purified by flash column chromatography (PE: EA = 10:1). ($[\alpha]^{20}_D -52.4$ (c 1.0, CHCl_3)). ^1H NMR (400 MHz, CDCl_3): $\delta = 7.32$ (d, $J = 8.4$ Hz, 2H), 6.91 (d, $J = 8.8$ Hz, 2H), 4.86 (q, $J = 6.4$ Hz, 1H), 3.83 (s, 3H), 2.22 (s, 1H), 1.50 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 158.92$, 138.07, 126.70, 113.83, 69.93, 55.31, 25.05. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 95:5 (v/v), 1.0 mL/min, 220 nm, 30 °C), $t_R = 11.62$ min (minor), $t_S = 13.49$ min (major).

(S)-1-(naphthalen-2-yl)ethanol (**3n**, CAS: 27544-18-9, know compound)^[1]



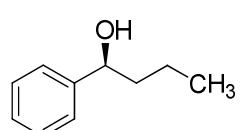
White solid, m. p. = 70-72 °C, 90% yield (77 mg), 93% ee. Purified by flash column chromatography (PE: EA = 3:1). ($[\alpha]^{20}_D -42.5$ (c , 0.70, acetone)). ^1H NMR (400 MHz, CDCl_3): $\delta = 7.89$ -7.85 (m, 4H), 7.56-7.49 (m, 3H), 5.11 (q, $J = 7.2$ Hz, 1H), 2.08 (s, 1H), 1.62 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 143.21$, 133.34, 132.94, 128.34, 127.96, 127.70, 126.18, 125.83, 123.85, 123.83, 70.56, 25.17. HPLC (Chiralcel OJ-H column, n-hexane/2-propanol = 95:5 (v/v), 1.0 mL/min, 230 nm, 30 °C), $t_S = 24.01$ min (major), $t_R = 32.61$ min (minor).

(S)-1-phenylpropan-1-ol (**3o**, CAS: 613-87-6, know compound)^[3]



Colourless oil; 79% yield (54 mg), 99% ee. Purified by flash column chromatography (PE: EA = 10:1). ($[\alpha]^{20}_D -48.6$ (c 1.0, CHCl_3)). ^1H NMR (400 MHz, CDCl_3): $\delta = 7.42$ -7.37 (m, 4H), 7.35-7.31 (m, 1H), 4.64 (t, $J = 6.8$ Hz, 1H), 1.91-1.78 (m, 3H), 0.96 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 144.59$, 128.43, 127.54, 125.99, 76.07, 31.92, 10.19. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 95:5 (v/v), 1.0 mL/min, 254 nm, 30 °C), $t_S = 8.57$ min (major), $t_R = 9.60$ min (minor).

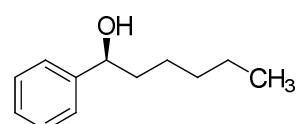
(S)-1-phenylbutan-1-ol (**3p**, CAS: 22135-49-5, know compound)^[3]



Yellow oil; 72% yield (54 mg), 93% ee. Purified by flash column chromatography (PE: EA = 10:1). ($[\alpha]^{20}_D -48.1$ (c 0.8, CHCl_3)). ^1H NMR (400 MHz, CDCl_3): $\delta = 7.38$ (d, $J = 4.4$ Hz, 4H), 7.33-7.30 (m, 1H), 4.74-4.70 (m, 1H), 1.90-1.81 (m, 2H), 1.79-1.64 (m, 1H), 1.49-1.45 (m, 1H), 1.38-1.29 (m, 1H), 0.97 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 144.93$, 128.45, 127.52, 125.92, 74.47,

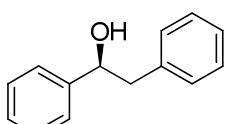
41.27, 19.08, 14.01. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 98:2 (v/v), 1.0 mL/min, 254 nm, 30 °C), t_S = 14.10 min (major), t_R = 15.61 min (minor).

(*S*)-1-phenylhexan-1-ol (**3q**, CAS: 138381-77-8, know compound)^[1]



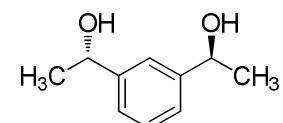
Colourless oil; 75% yield (67 mg), 94% ee. Purified by flash column chromatography (PE: EA = 10:1). ($[\alpha]^{20}_D$ -46.5 (*c* 1.0, CHCl₃)). ¹**H NMR** (400 MHz, CDCl₃): δ = 7.38 (dd, *J* = 2.0 Hz, *J*₂ = 5.2 Hz, 4H), 7.33-7.31 (m, 1H), 4.68 (t, *J* = 6.4 Hz, 1H), 2.14 (s, 1H), 1.85-1.80 (m, 1H), 1.77-1.73 (m, 1H), 1.48-1.44 (m, 1H), 1.37-1.31 (m, 5H), 0.93 (t, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 145.00, 128.42, 127.46, 125.94, 74.70, 39.10, 31.77, 25.54, 22.61, 14.07. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 99:1 (v/v), 1.0 mL/min, 220 nm, 30 °C), t_R = 19.48 min (minor), t_S = 20.63 min (major).

(*S*)-1,2-diphenylethanol (**3r**, CAS: 5773-56-8, know compound)^[4]



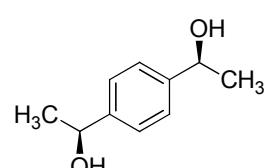
White solid, m. p. = 60-61 °C; 83% yield (82 mg), 97% ee. Purified by flash column chromatography (PE: EA = 5:1). ($[\alpha]^{20}_D$ -52.4 (*c* 1.0, CHCl₃)). ¹**H NMR** (400 MHz, CDCl₃): δ = 7.41-7.24 (m, 10H), 4.97-4.93 (m, 1H), 3.12-3.00 (m, 2H), 1.99 (d, *J* = 2.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 143.81, 138.04, 129.53, 128.54, 128.45, 127.65, 126.66, 125.91, 75.38, 46.14. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 95:5 (v/v), 1.0 mL/min, 220 nm, 30 °C), t_R = 11.21 min (minor), t_S = 12.25 min (major).

(1*S*,1'*S*)-1,1'-(1,3-phenylene)diethanol (**3s**, CAS: 143329-81-1, know compound)^{[5],[6]}



Colourless oil; 89% yield (74 mg, de > 99%), >99% ee, Purified by flash column chromatography (PE: EA = 5:1). ($[\alpha]^{20}_D$ -61.5 (*c*, 1.0, acetone)). ¹**H NMR** (400 MHz, CDCl₃): δ = 7.38 (d, *J* = 6.0 Hz, 1H), 7.31 (d, *J* = 6.8 Hz, 1H), 7.24 (t, *J* = 6.8 Hz, 2H), 4.86 (q, *J* = 6.8 Hz, 2H), 2.78 (s, 2H), 1.48 (d, *J* = 6.4 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 146.11, 146.08, 128.55, 128.53, 124.55, 124.51, 122.49, 122.37, 70.28, 70.25, 25.15, 25.10. HPLC (Chiralcel OJ-H column, n-hexane/2-propanol = 95:5 (v/v), 1.0 mL/min, 254 nm, 30 °C), $t_{S,S}$ = 17.70 min (major), $t_{R,R}$ = 20.84 min (minor).

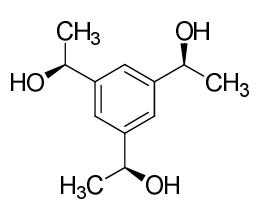
(1*S*,1'*S*)-1,1'-(1,4-phenylene)diethanol (**3t**, CAS: 143394-10-9, know compound)^{[5],[6]}



White solid, m. p. = 128-130 °C; 92% yield (76 mg, de > 98%), 93% ee, Purified by flash column chromatography (PE: EA = 5:1). ($[\alpha]^{20}_D$ -87.5 (*c* 1.0, acetone)). ¹**H NMR** (400 MHz, CDCl₃): δ = 7.38 (s, 4H), 4.93 (q, *J* = 6.4 Hz, 2H), 2.03 (s, 2H), 1.52 (d, *J* = 6.4 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 145.06, 125.58, 70.18, 70.16, 25.19. HPLC (Chiralcel OD-H column, n-hexane/2-propanol = 90:10 (v/v), 1.0 mL/min, 210 nm, 30 °C), $t_{R,R}$ = 12.28 min (minor), $t_{S,S}$ =

13.21 min (major), $t_{meso} = 17.22$ min (minor).

(*1S,1'S,1"S*)-1,1',1"-(*benzene-1,3,5-triyl*)triethanol (**3u**, unknown compound)

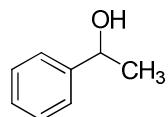


Colourless oil; 91% yield (95 mg, de > 98%), 93% ee, Purified by flash column chromatography (PE: EA = 2:1). $[\alpha]^{20}_D -46.2$ (*c*, 1.0, acetone)). **¹H NMR** (400 MHz, CDCl₃): δ = 7.43–7.41 (m, 3H), 4.90 (q, *J* = 6.4 Hz, 3H), 2.04 (s, 3H), 1.51 (d, *J* = 6.4 Hz, 9H); **¹³C NMR** (100 MHz, CDCl₃): δ = 146.39, 146.38, 128.23, 128.21, 123.07, 123.04, 122.30, 69.96, 69.94, 25.21, 25.19. HPLC (Chiralcel OJ-H column, n-hexane/2-propanol = 80:20 (v/v), 1.0 mL/min, 254 nm, 30 °C), $t_{R,R,R} = 4.21$ min (minor), $t_{S,S,S} = 5.28$ min (major). **HRMS** (ESI) m/z [M-H]⁻ calcd for C₁₂H₁₈O₃ 209.1183, found: 209.1182.

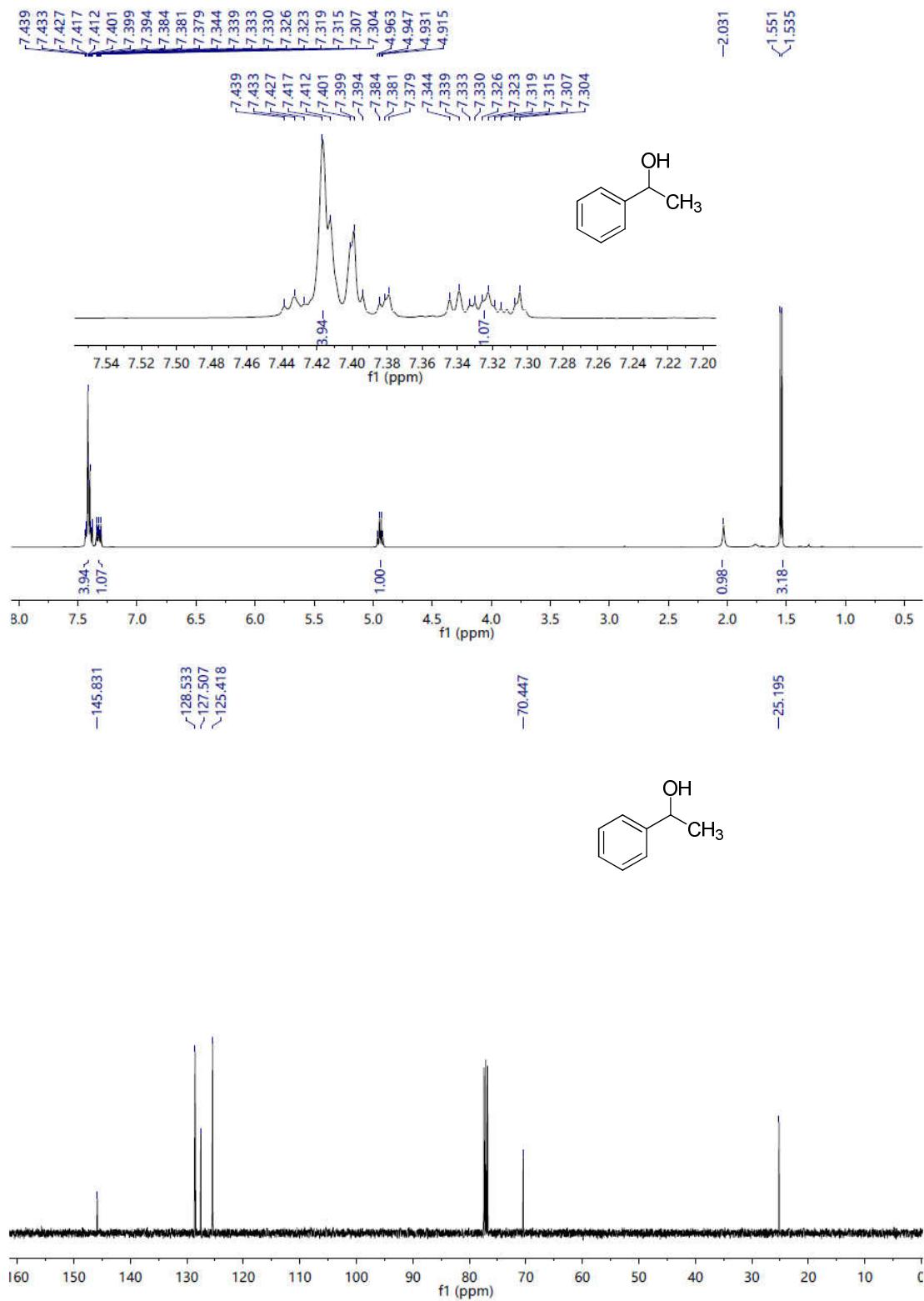
Reference:

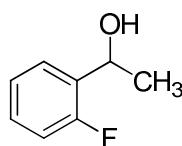
- [1] Zhang, Z.; Jain, P.; Antilla, J. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 10961–10964.
- [2] Li, F.; Wang, N.; Lu, L.; Zhu, G. *J. Org. Chem.* **2015**, *80*, 3538–3546.
- [3] Chen, X.; Lu, Z. *Org. Lett.* **2016**, *18*, 4658–4661.
- [4] Li, J.; Wang, C.; Xue, D.; Wei, Y.; Xiao, J. *Green Chem.* **2013**, *15*, 2685–2689.
- [5] Shimada, Y.; Miyake, Y.; Matsuzawa, H.; Nishibayashi Y., *Chem. Asian J.* **2007**, *2*, 393 – 396.
- [6] Uchiyama, M.; Katoh, N.; Mimura, R.; Yokota, N.; Shimogaichi, Y.; Shimazaki, M.; Ohta, A. *Tetrahedron: Asymmetry*, **1997**, *8*, 3467–3474.

11. ^1H NMR and ^{13}C NMR Spectra of the Products

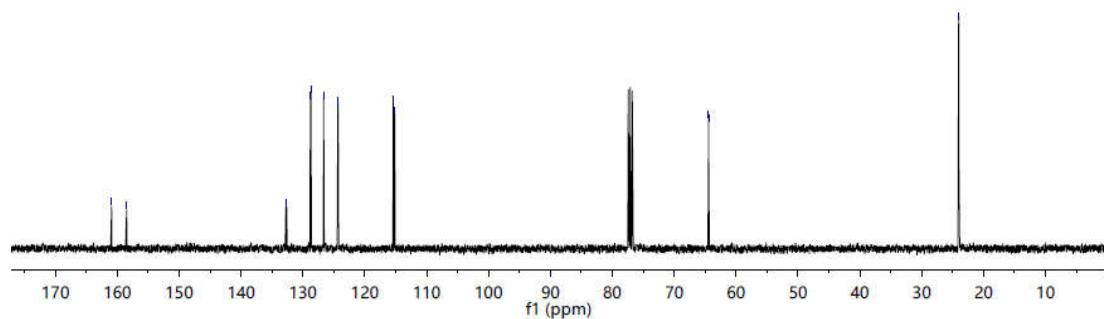
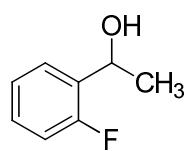
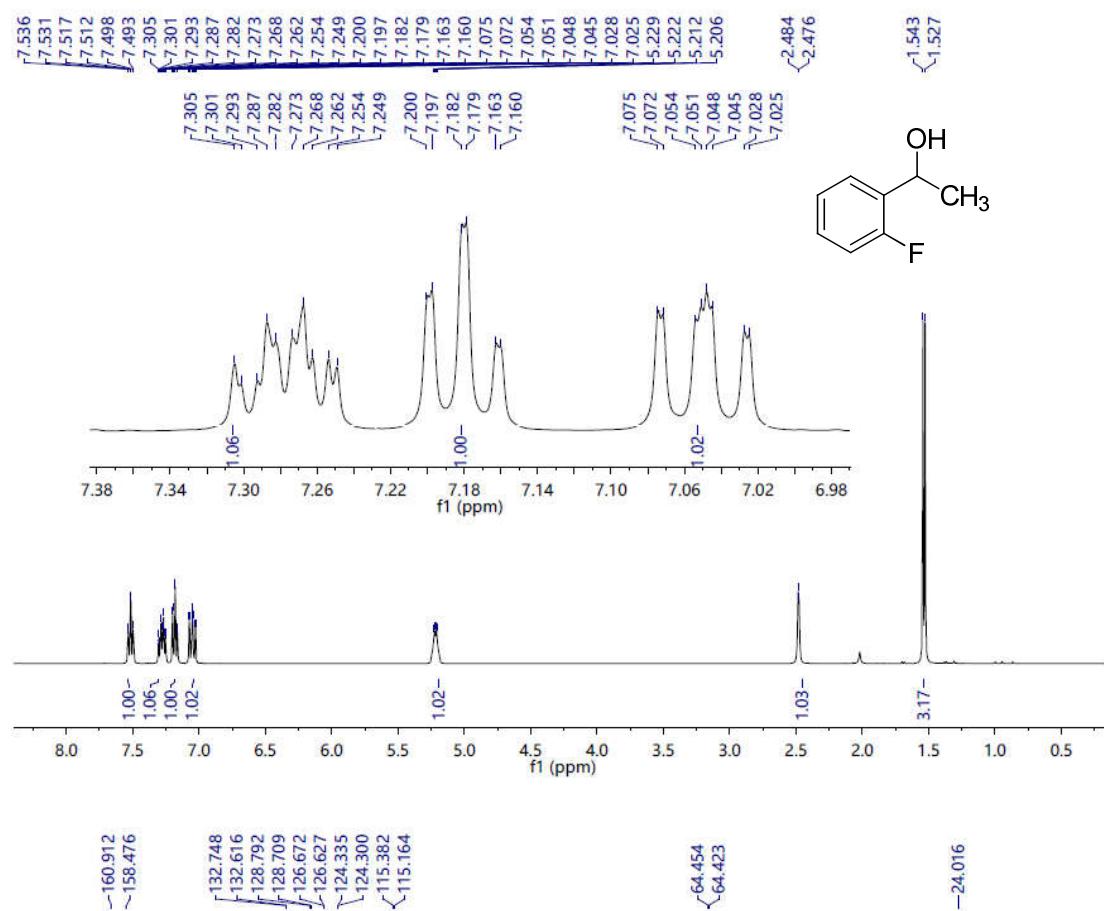


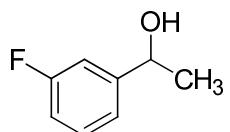
3a



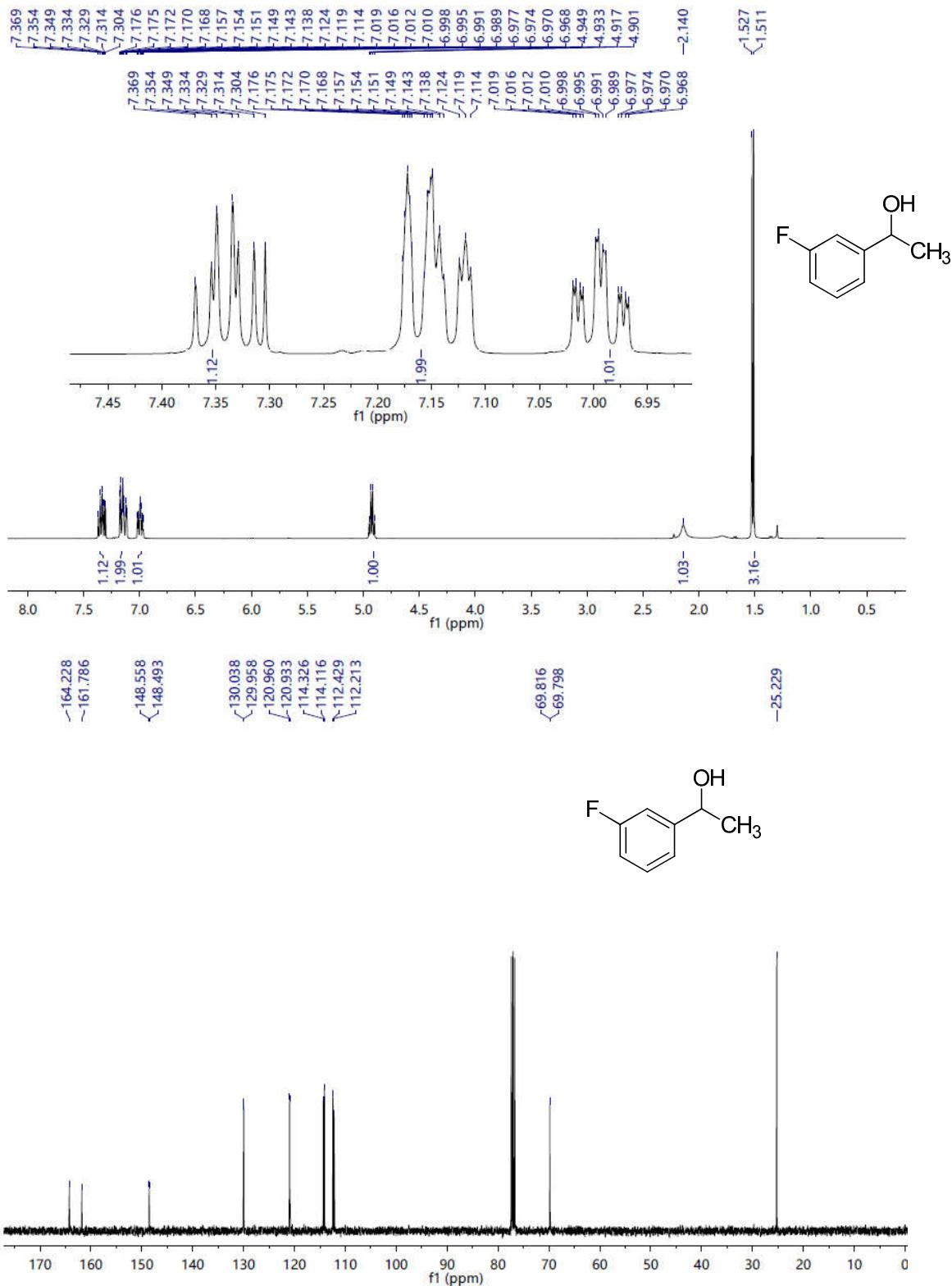


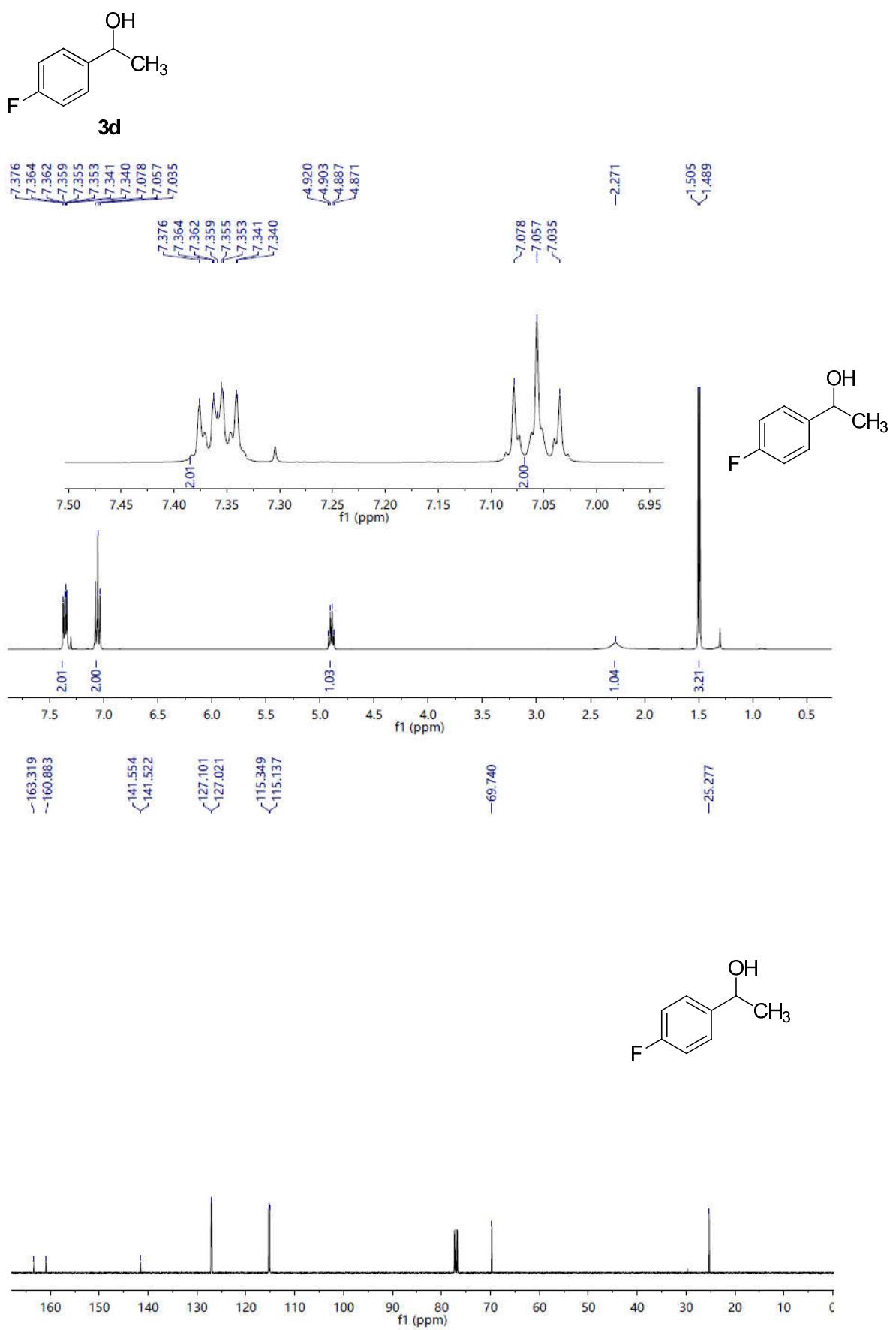
3b

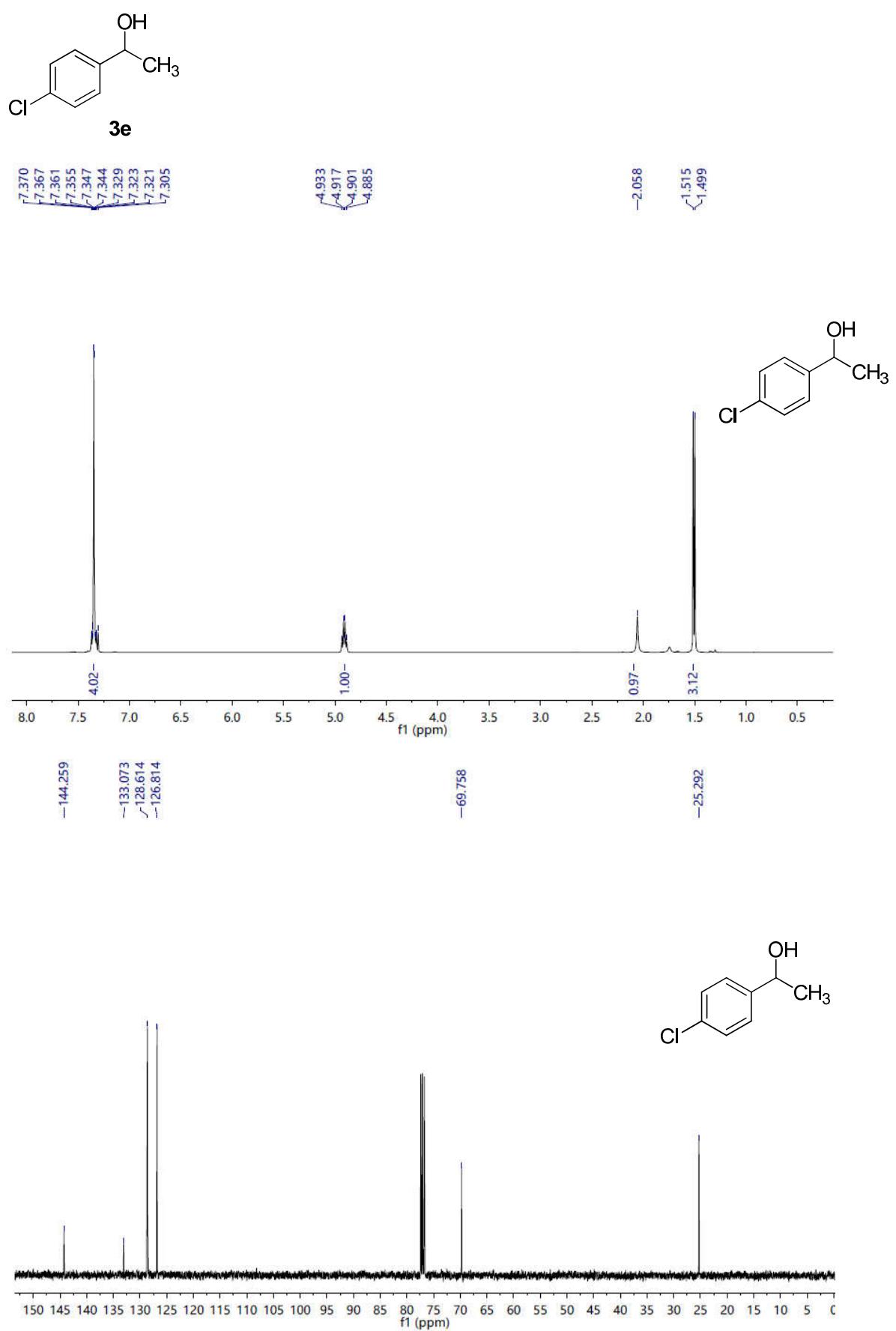


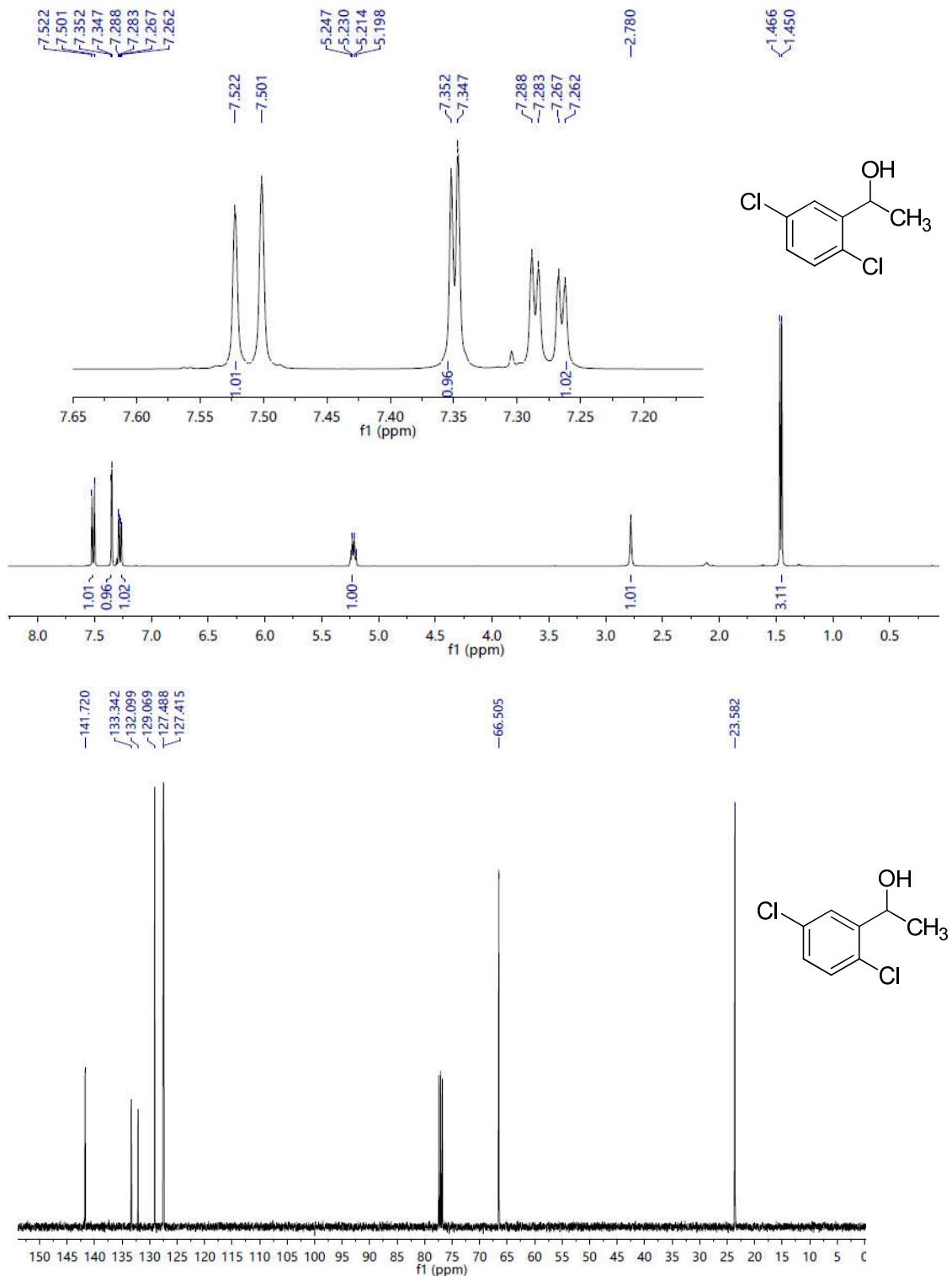
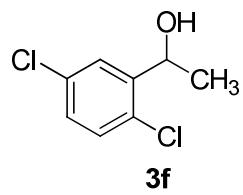


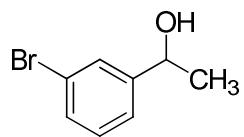
3c



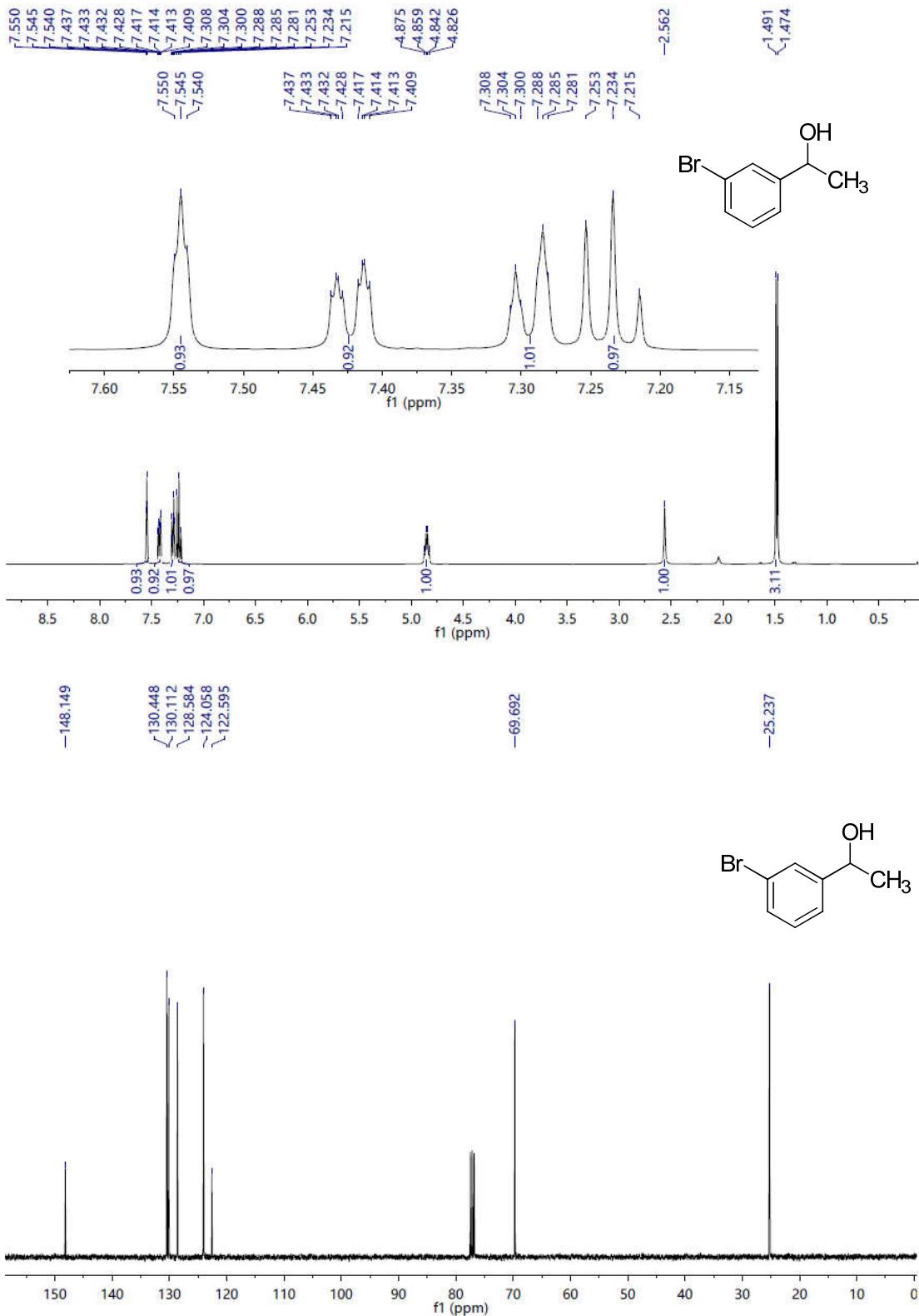


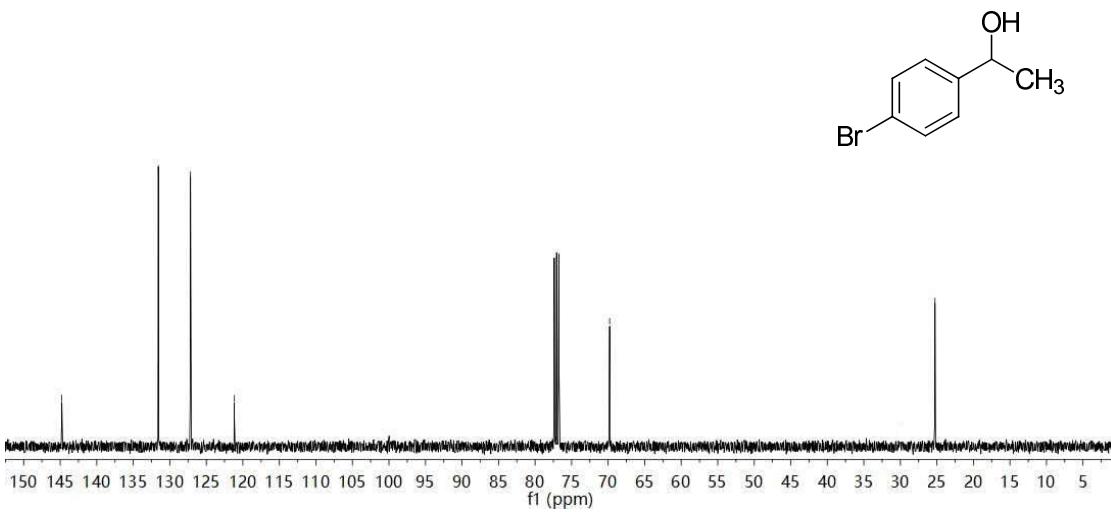
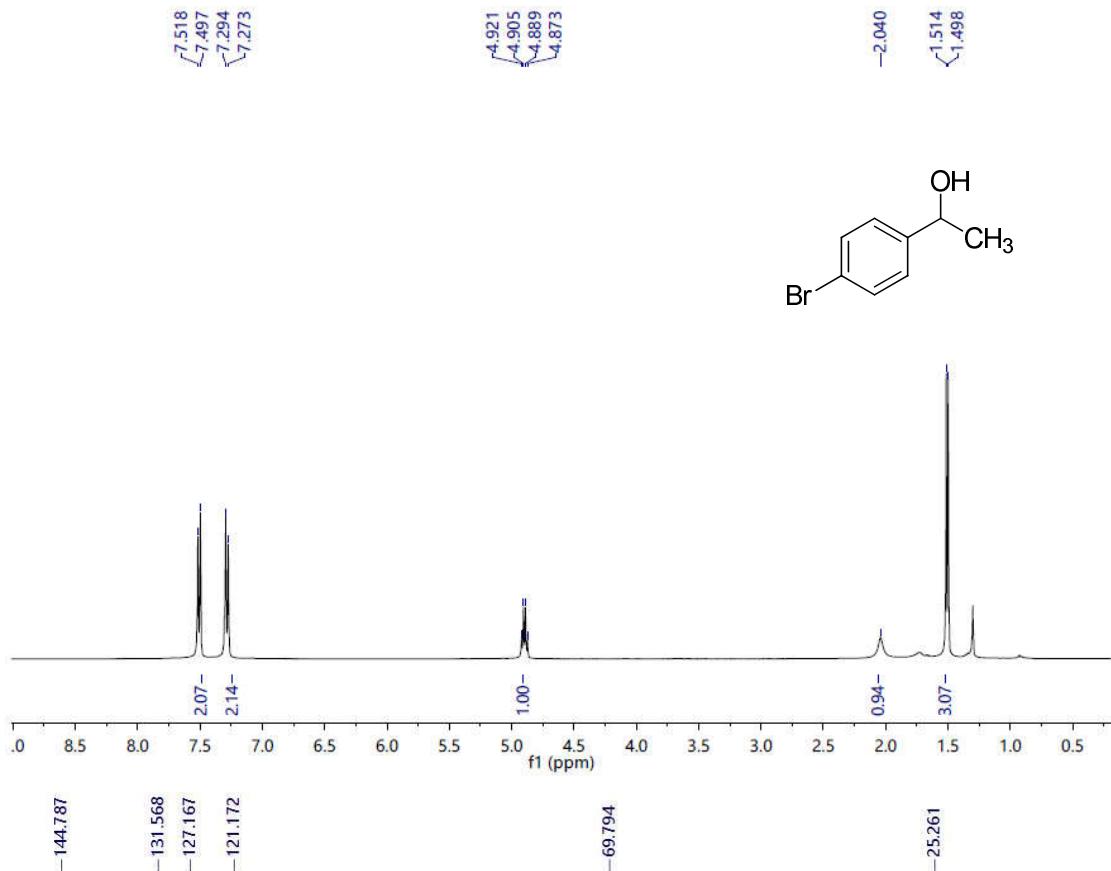
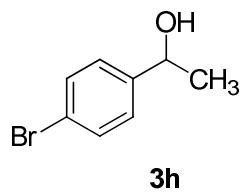


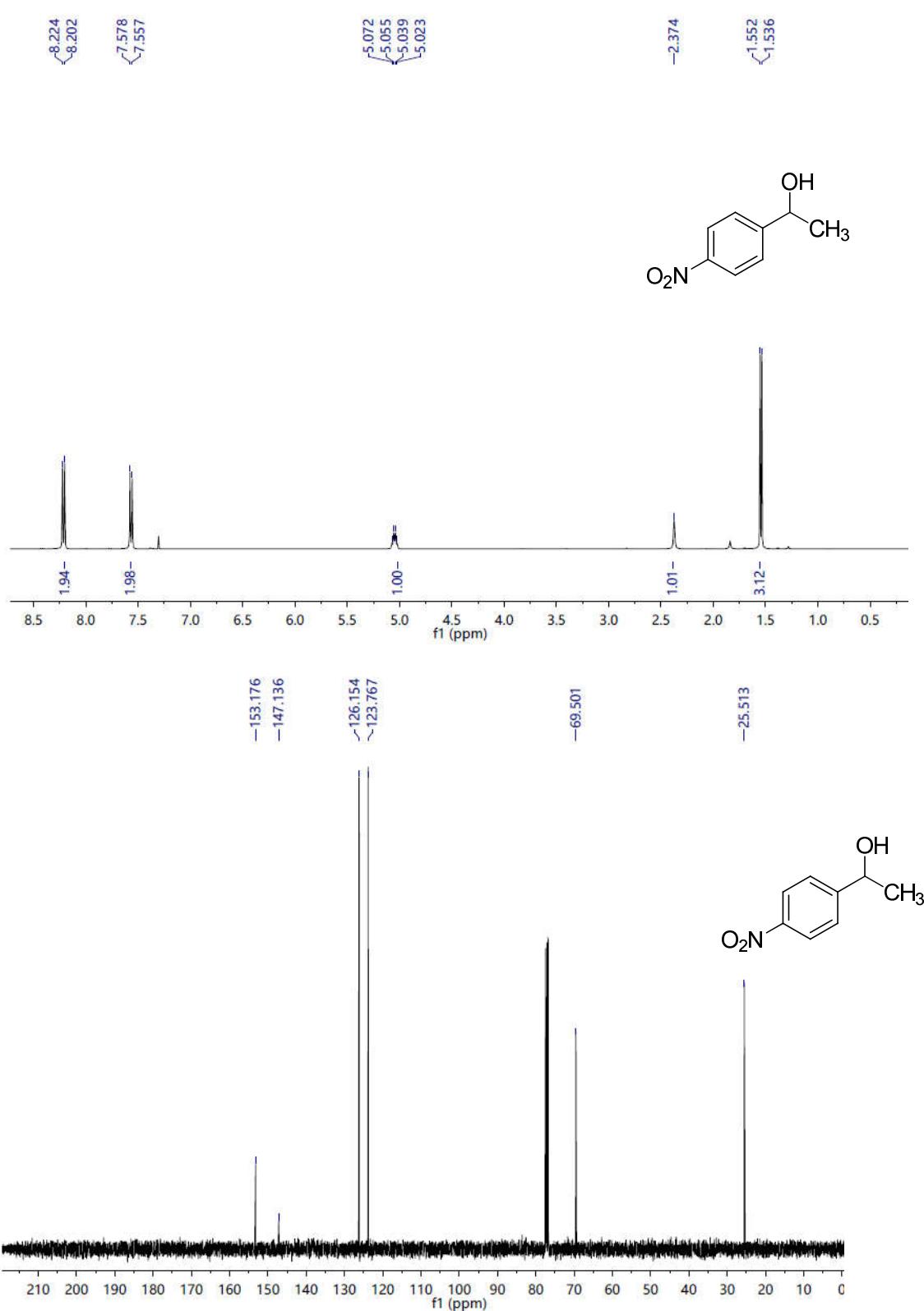
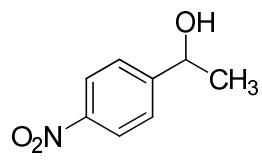


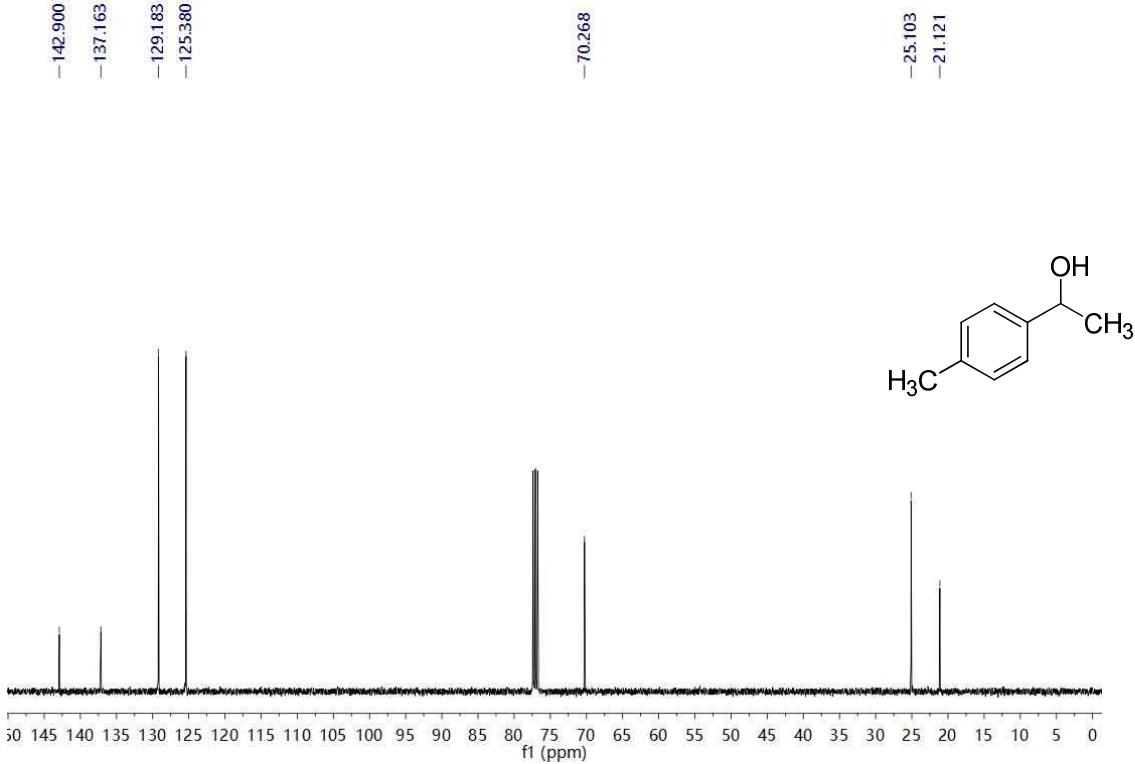
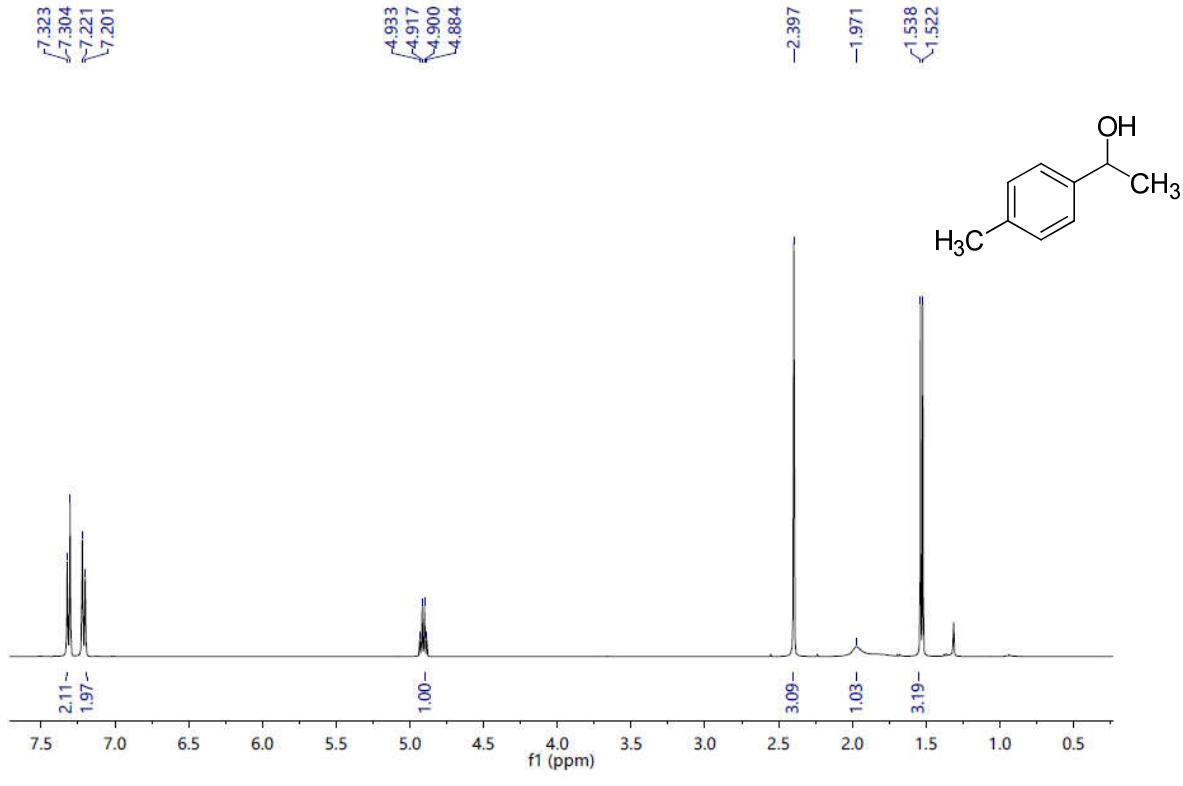
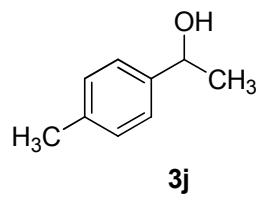


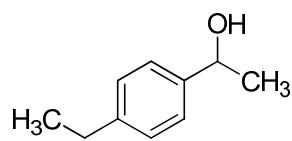
3g



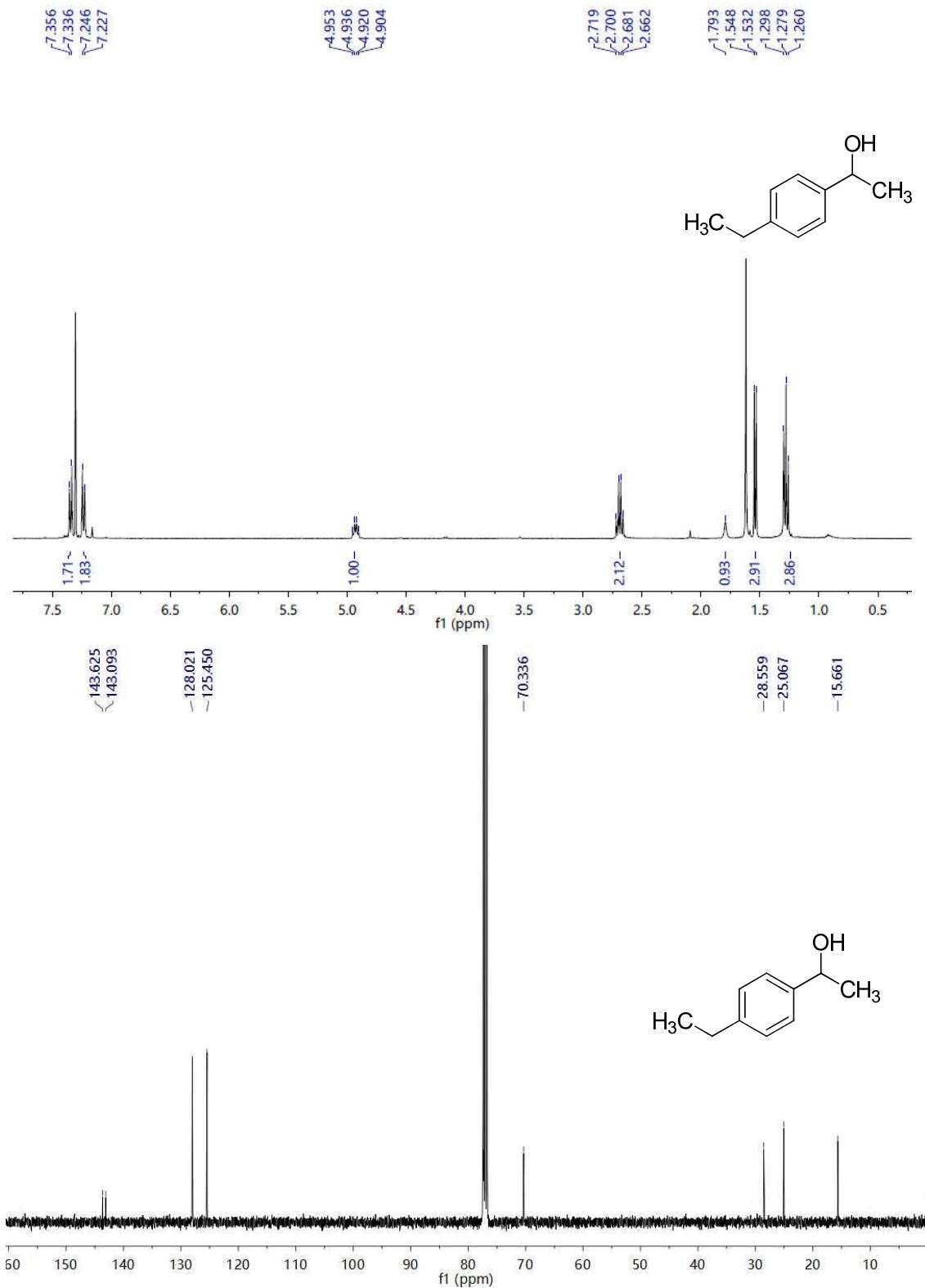


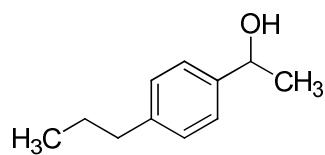




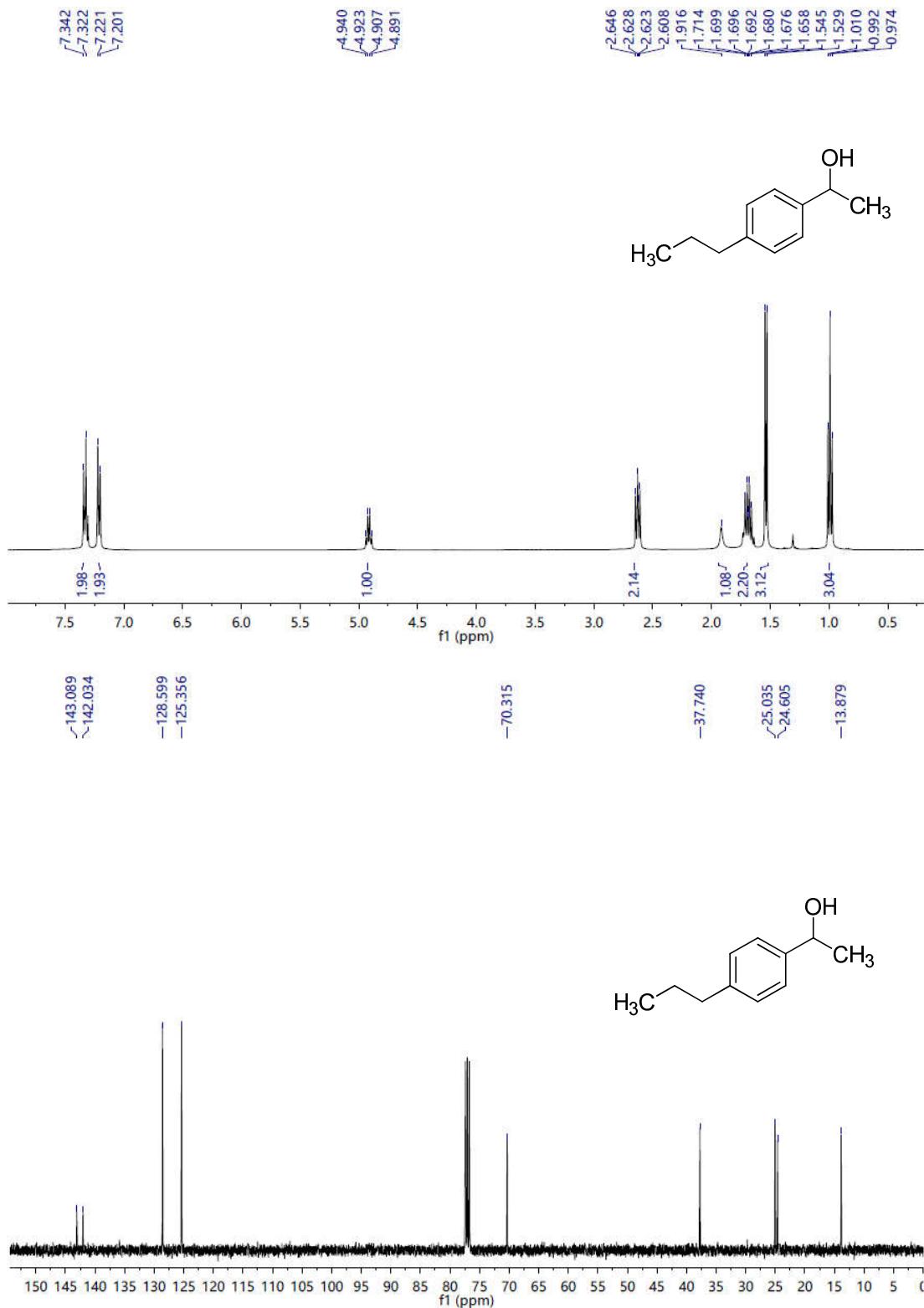


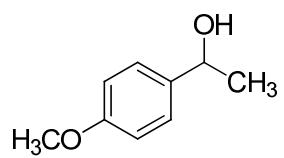
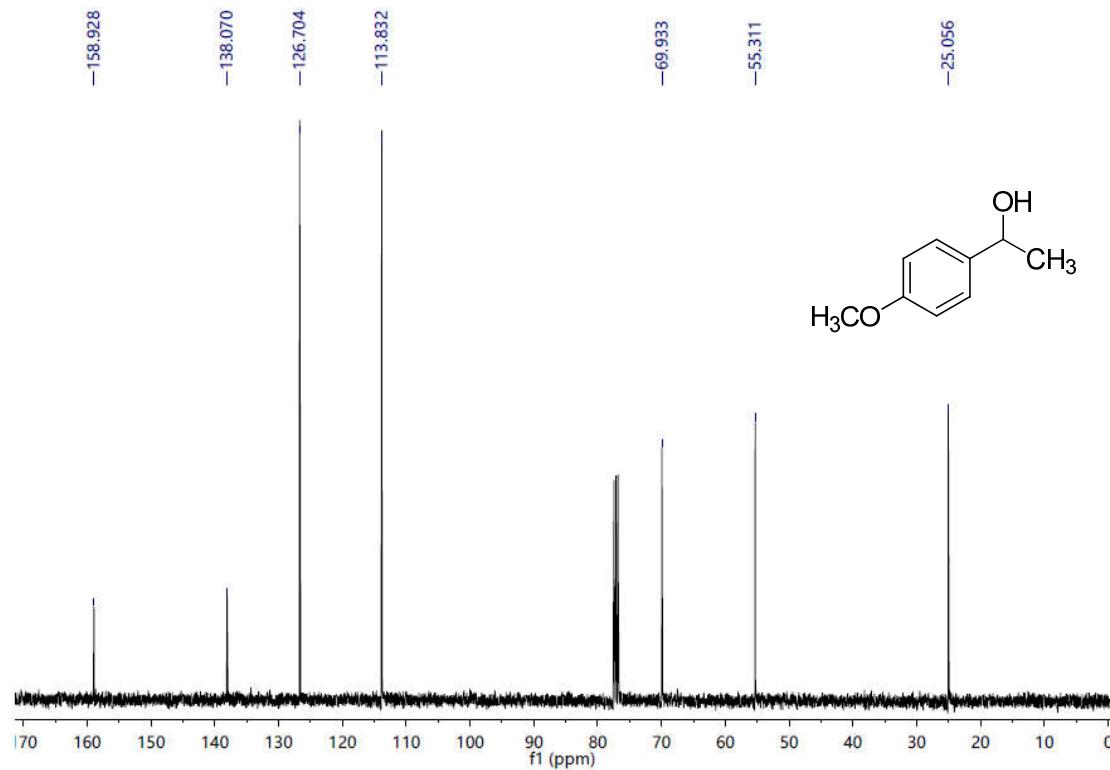
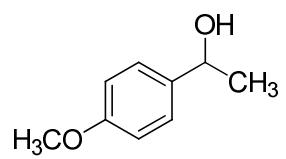
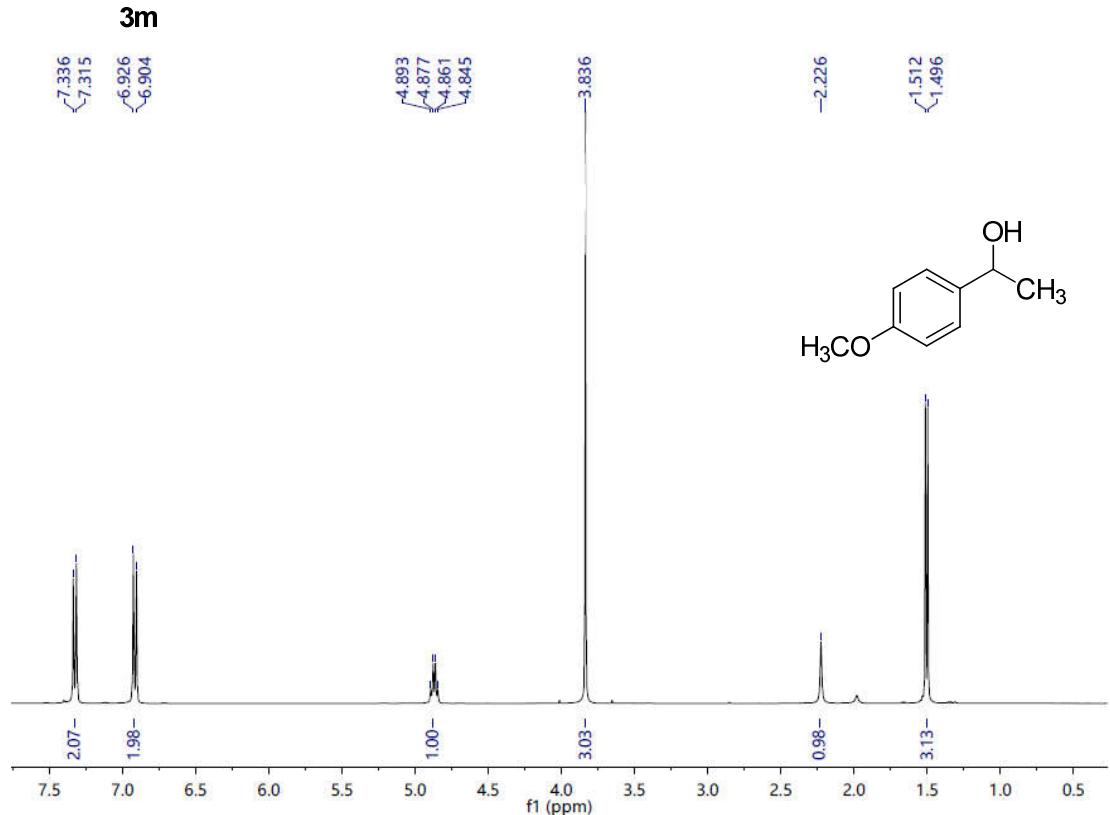
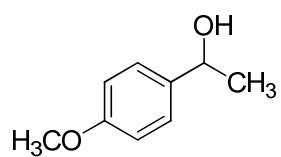
3k

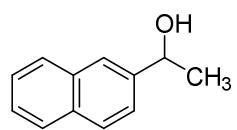




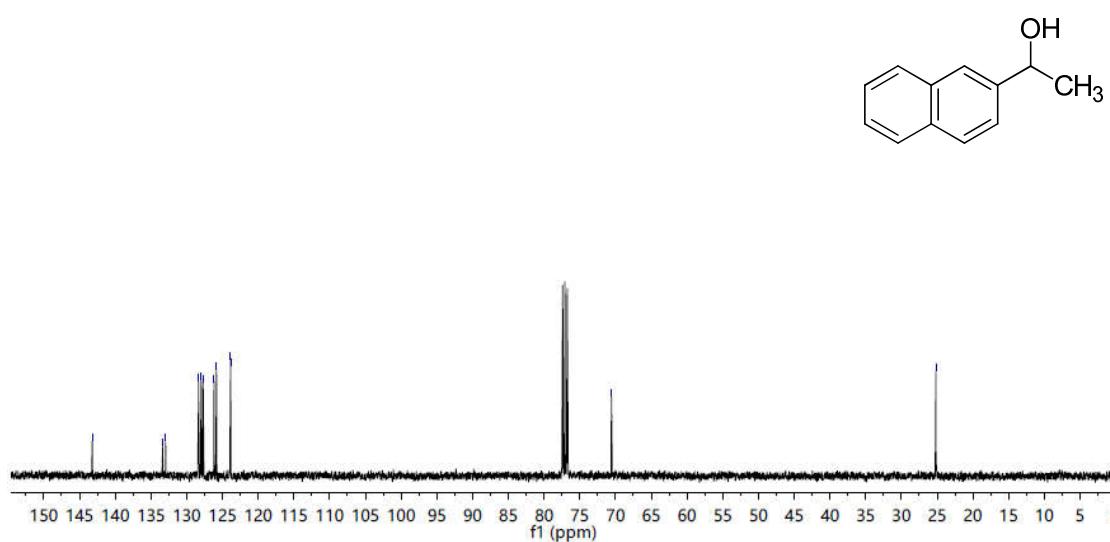
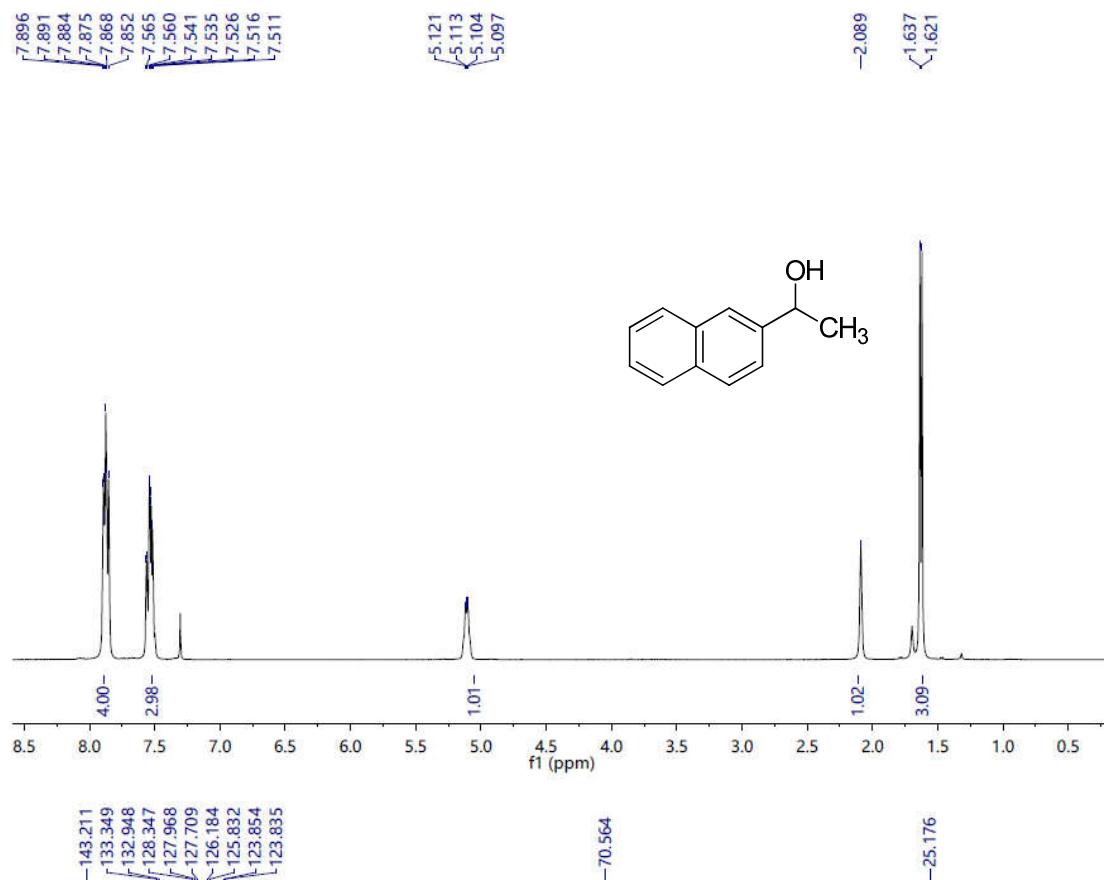
3I

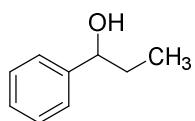




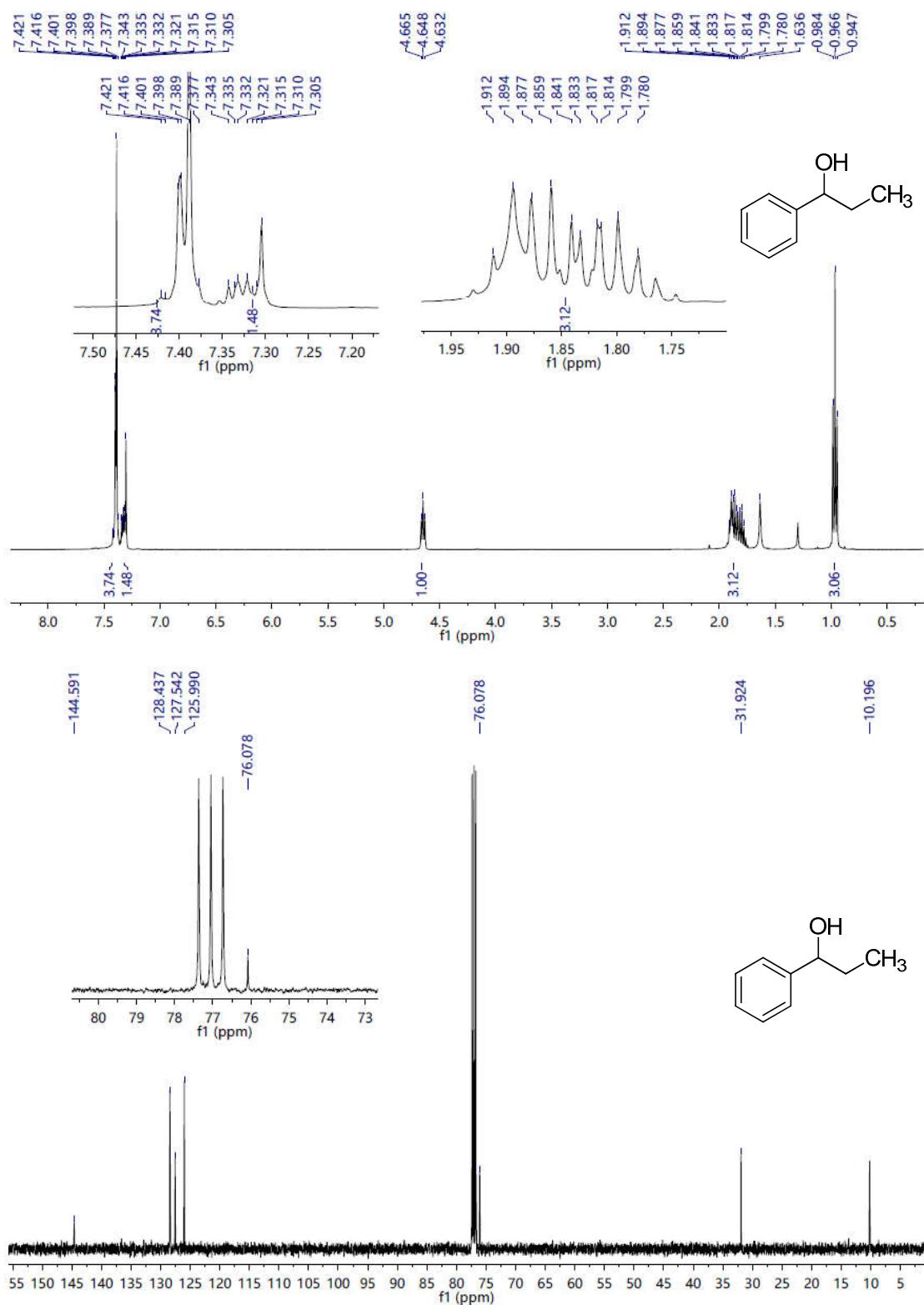


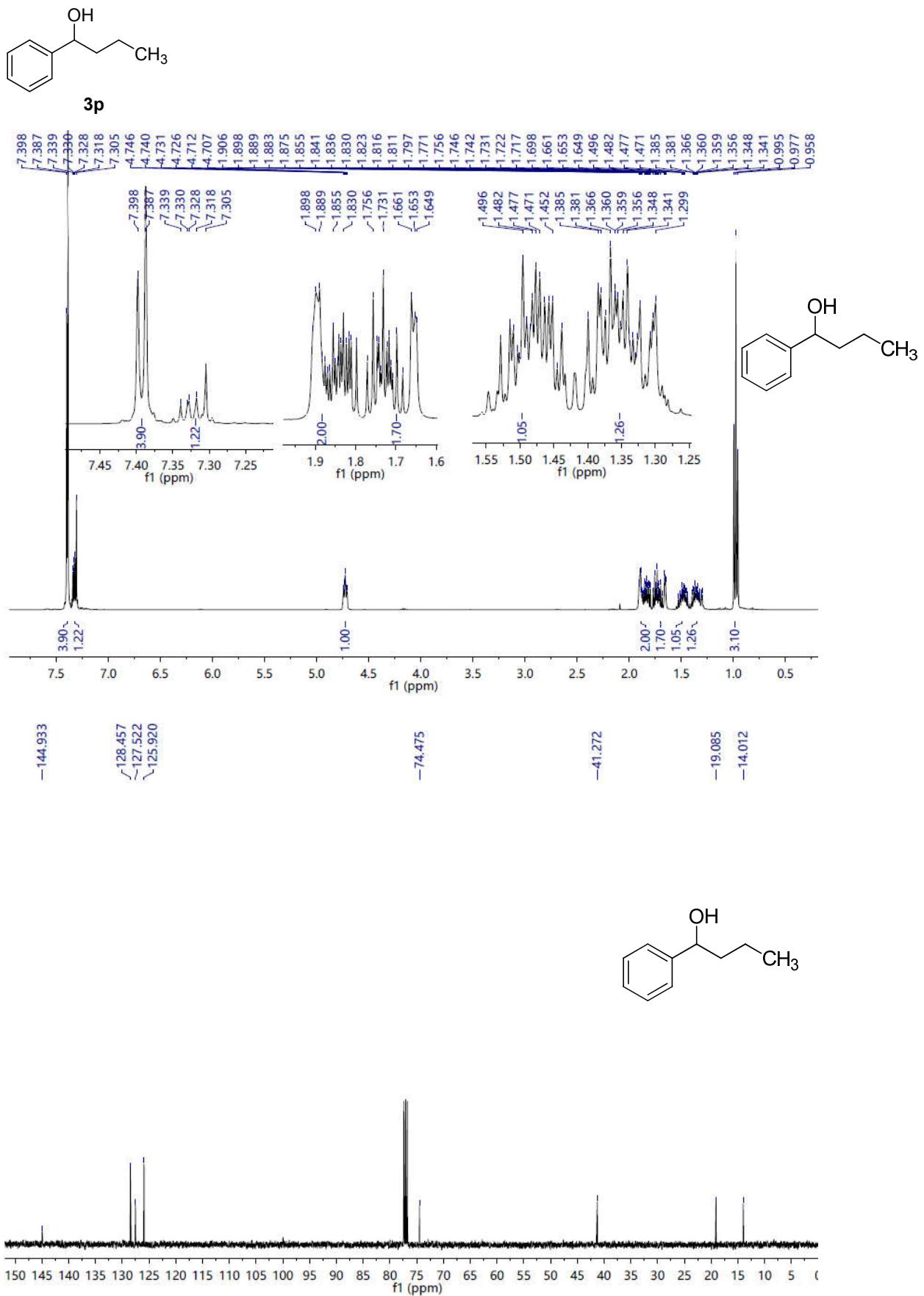
3n

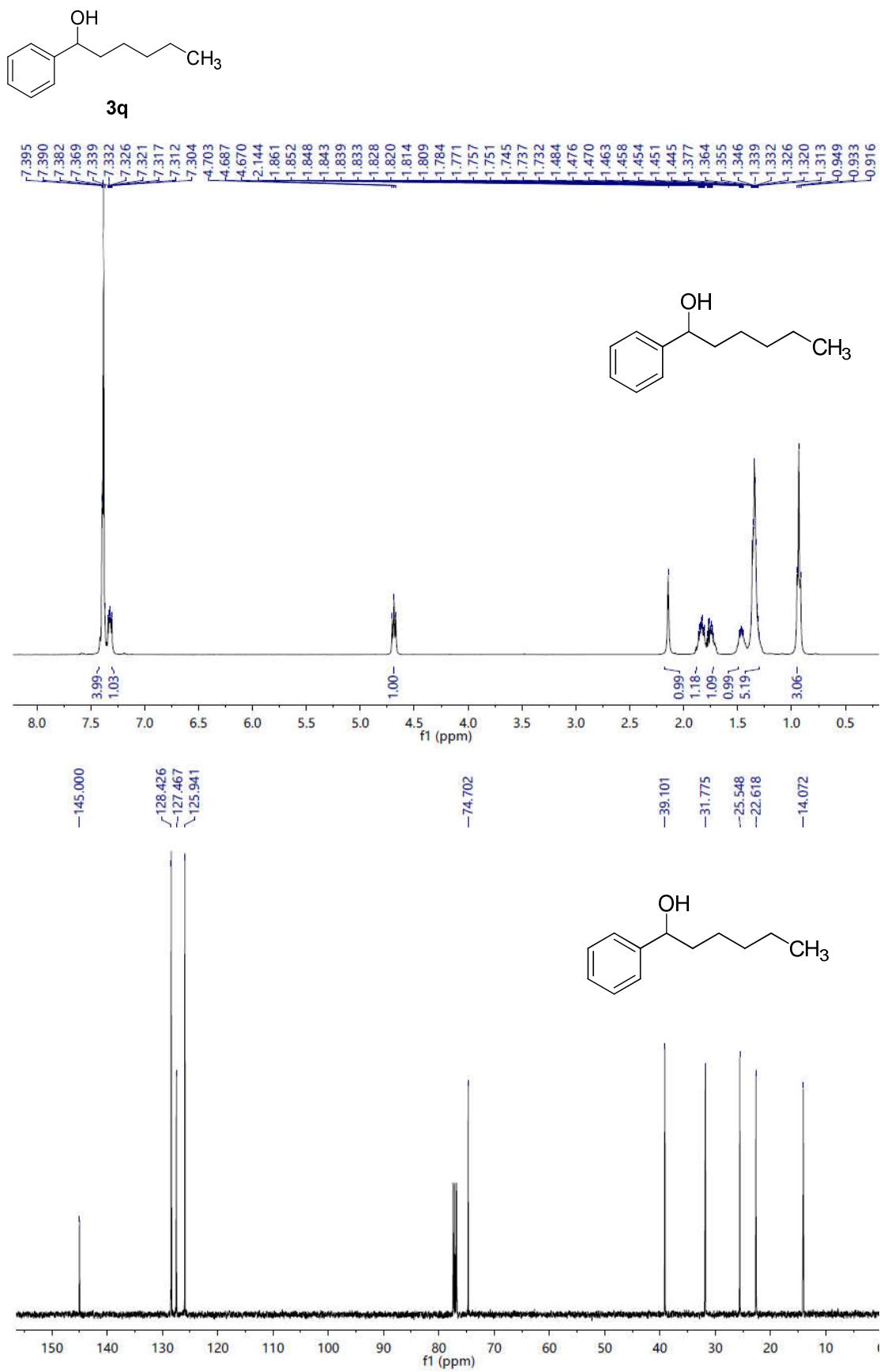


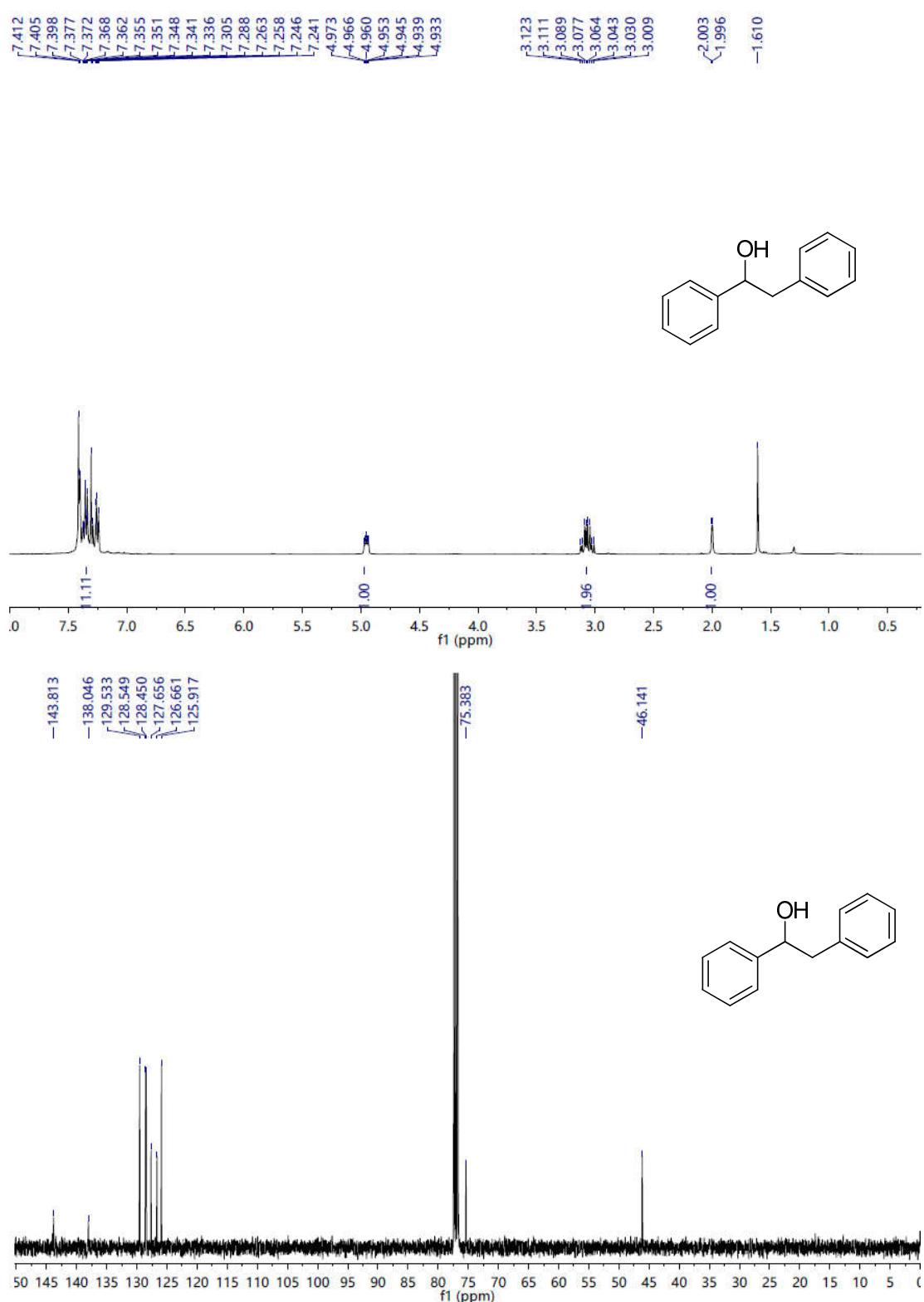
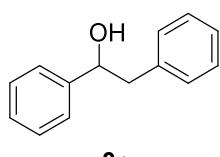


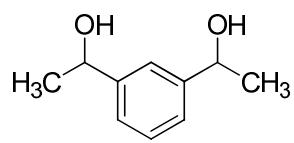
3o



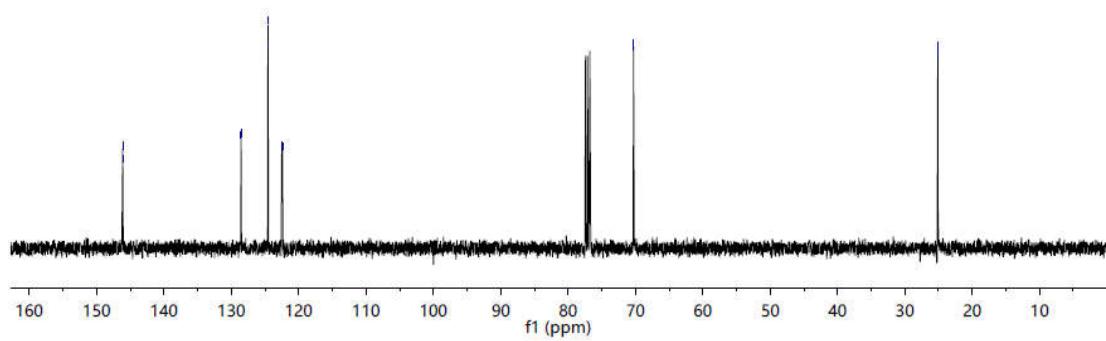
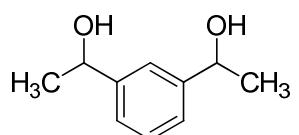
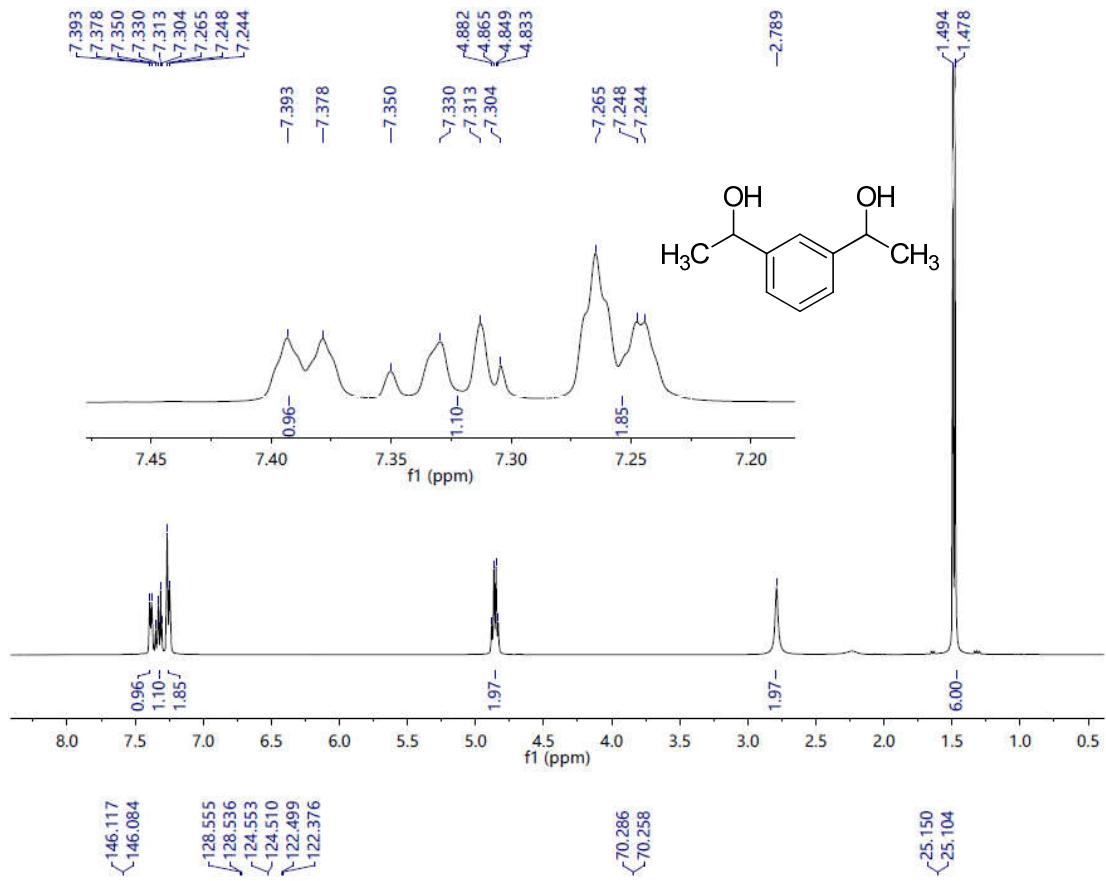


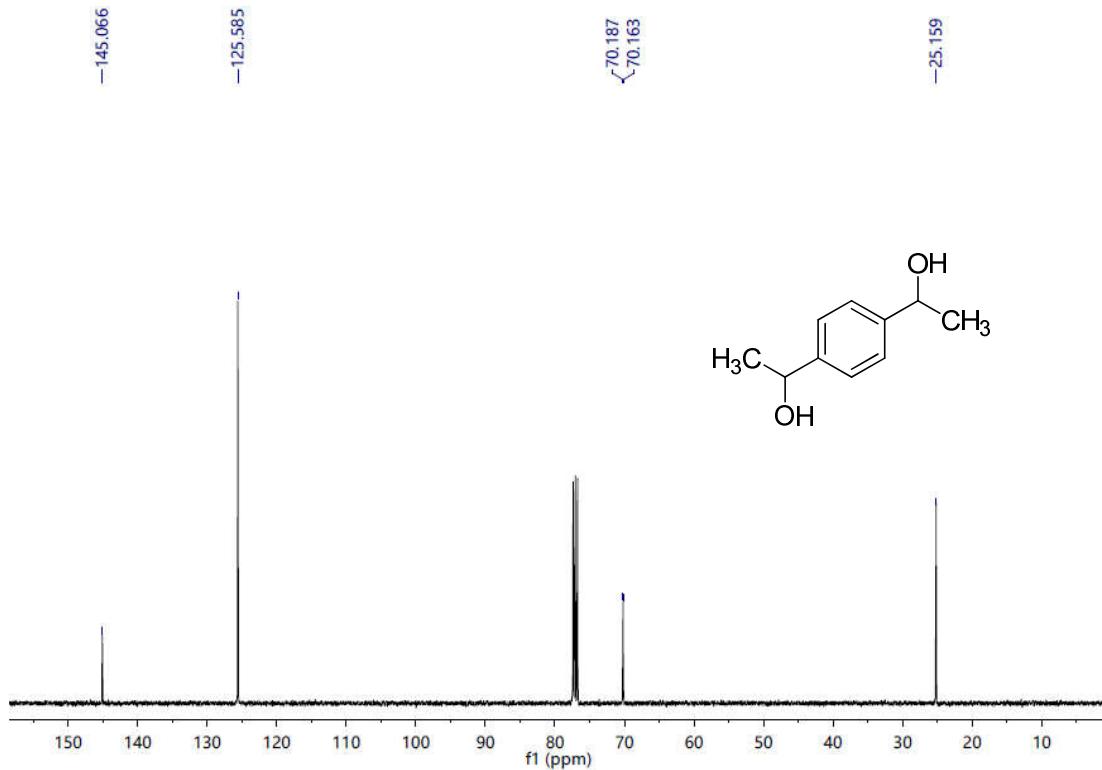
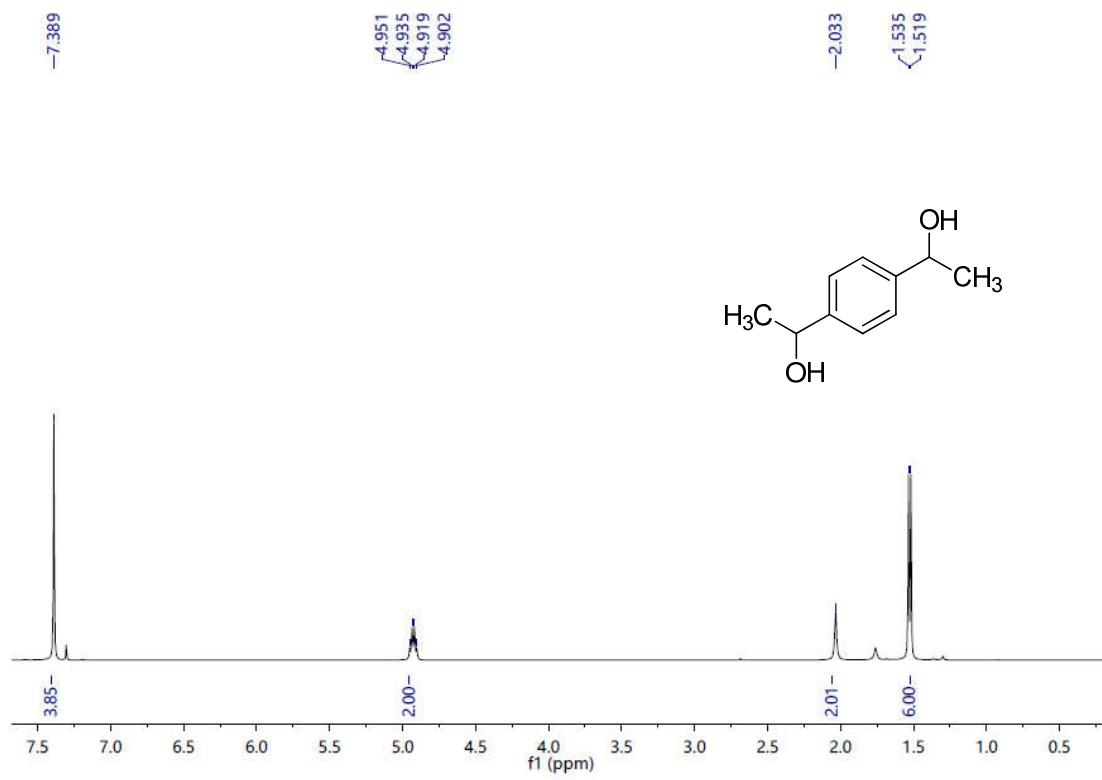
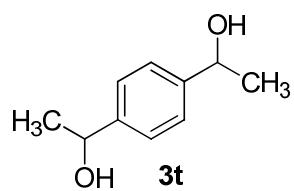


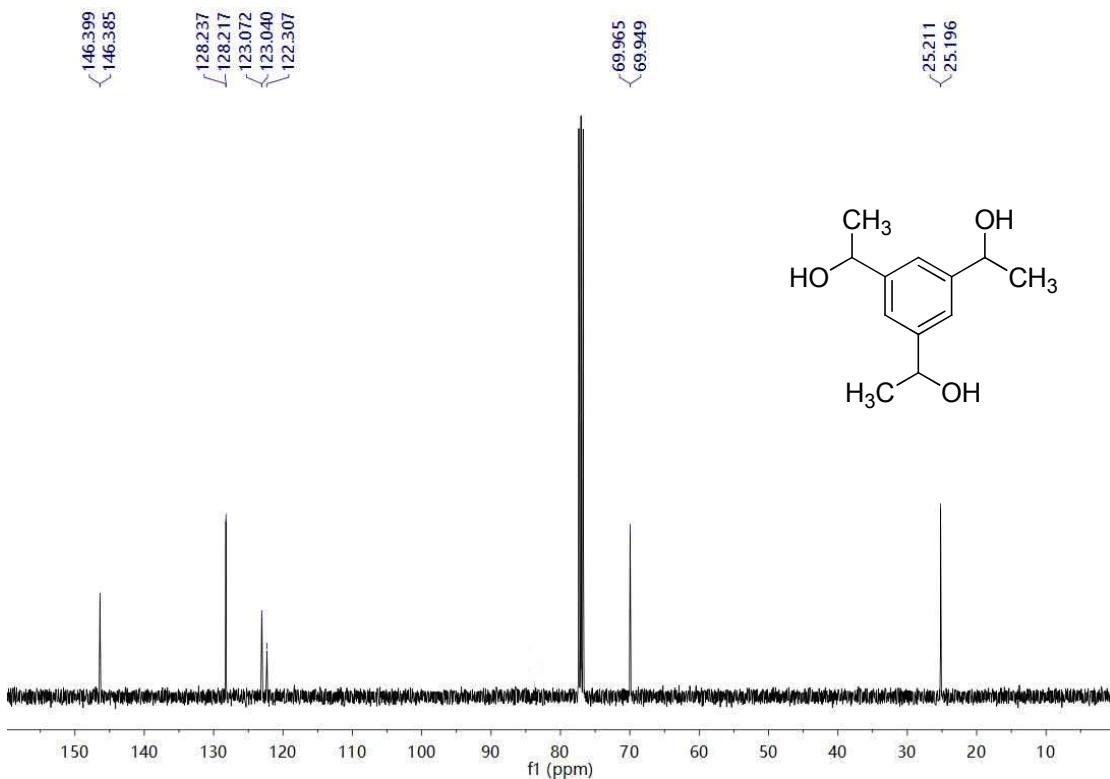
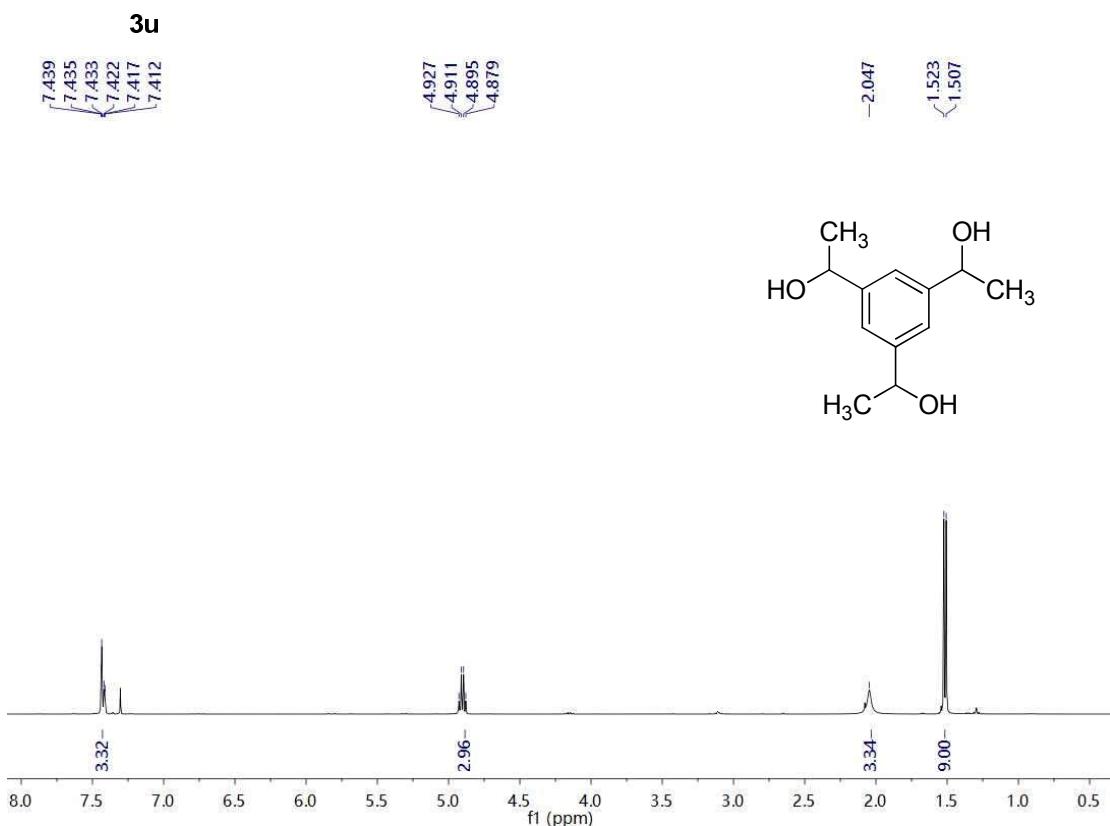
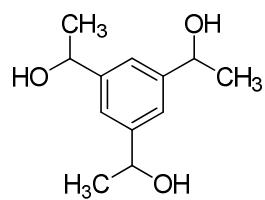




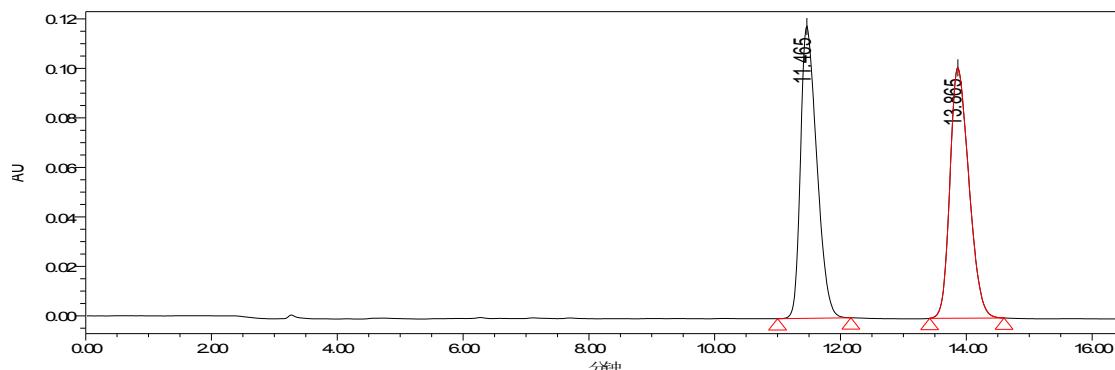
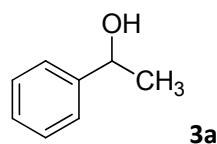
3s



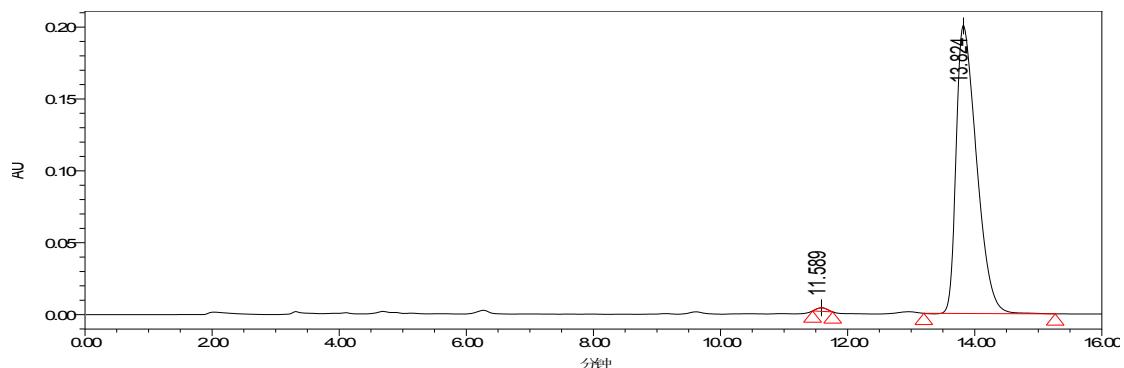
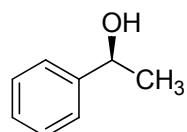




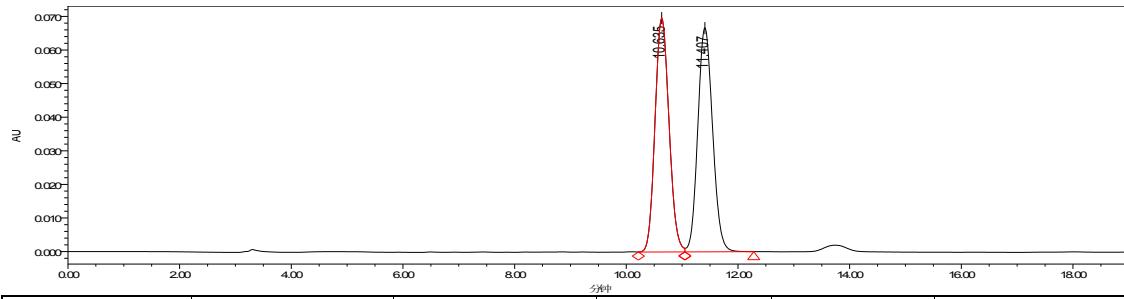
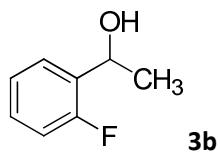
12. HPLC Spectra of the Products



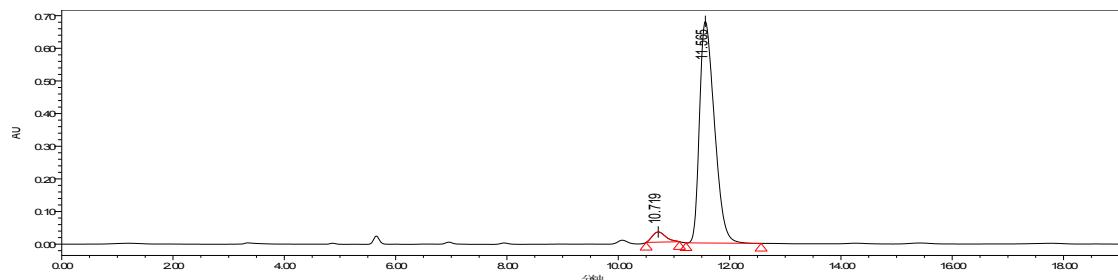
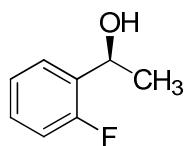
Peak	Ret Time [min]	Area	% Area	Height	Type
1	11.465	2118457	50.01	117993	bb
2	13.865	2117822	49.99	101248	bb



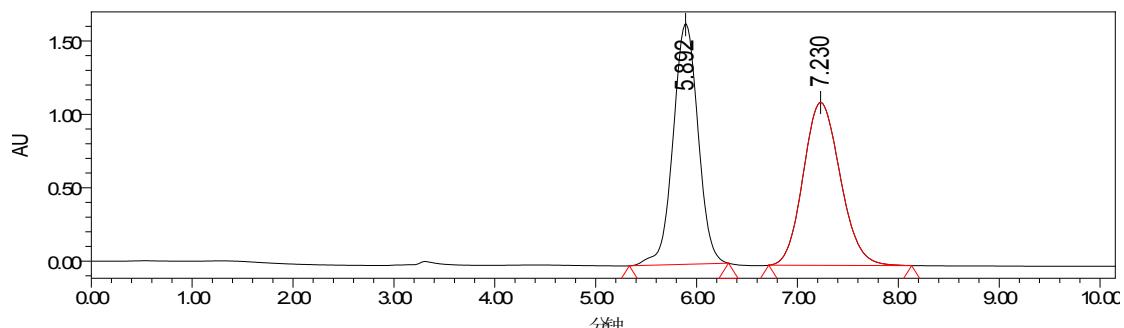
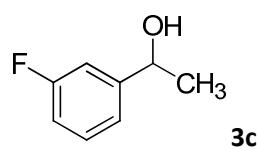
Peak	Ret Time [min]	Area	% Area	Height	Type
1	11.588	23308	0.42	2250	bb
2	13.824	4440217	99.58	200605	bb



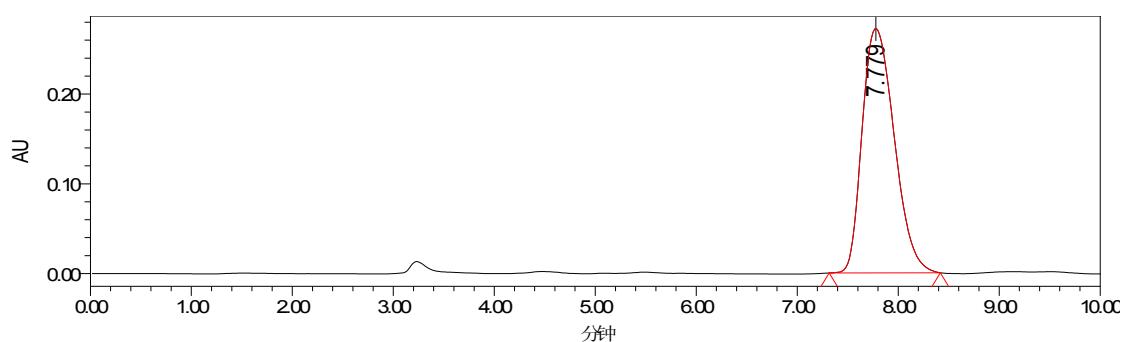
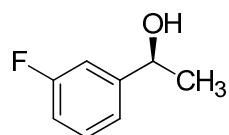
Peak	Ret Time [min]	Area	% Area	Height	Type
1	10.635	1175759	49.76	68837	bb
2	11.407	1187210	50.24	65875	bb



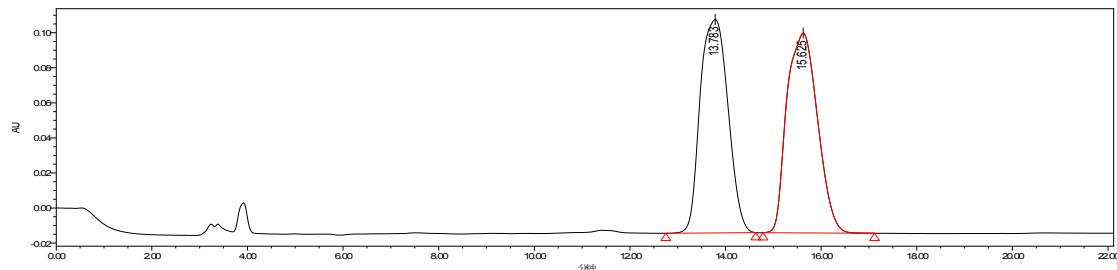
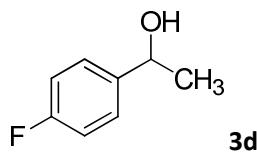
Peak	Ret Time [min]	Area	% Area	Height	Type
1	10.719	521729	3.47	31266	bb
2	11.565	12635160	96.53	679429	bb



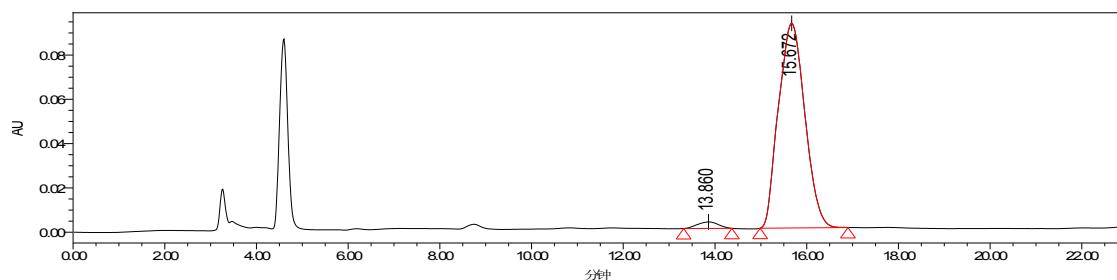
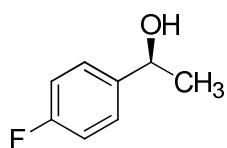
Peak	Ret Time [min]	Area	% Area	Height	Type
1	5.892	28128690	50.12	1639654	bb
2	7.230	27990295	49.88	1105522	bb



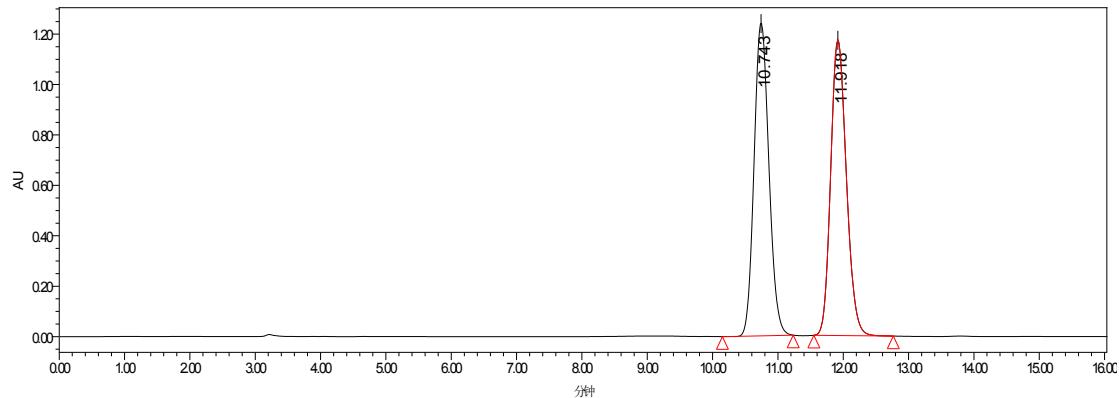
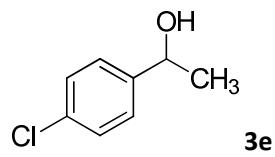
Peak	Ret Time [min]	Area	% Area	Height	Type
1	7.779	6055541	100.00	272838	bb



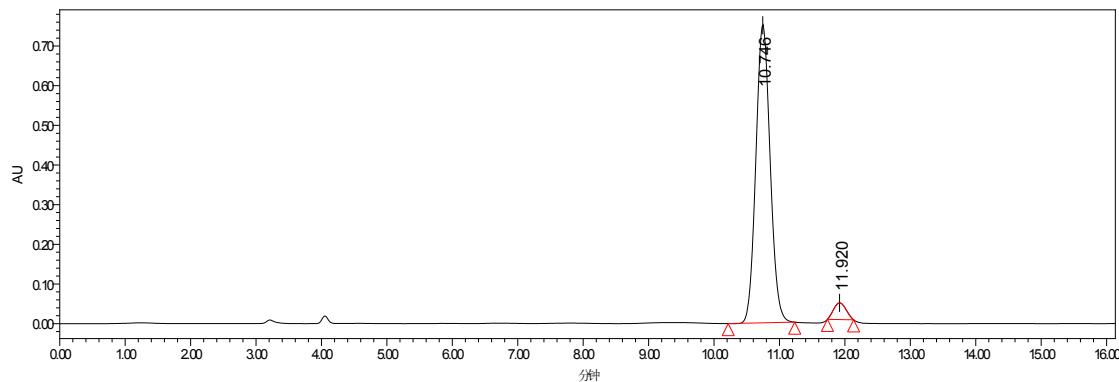
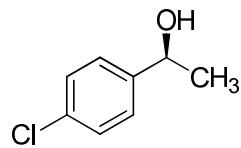
Peak	Ret Time [min]	Area	% Area	Height	Type
1	13.783	4940957	49.31	121737	bb
2	15.625	5078763	50.69	113990	bb



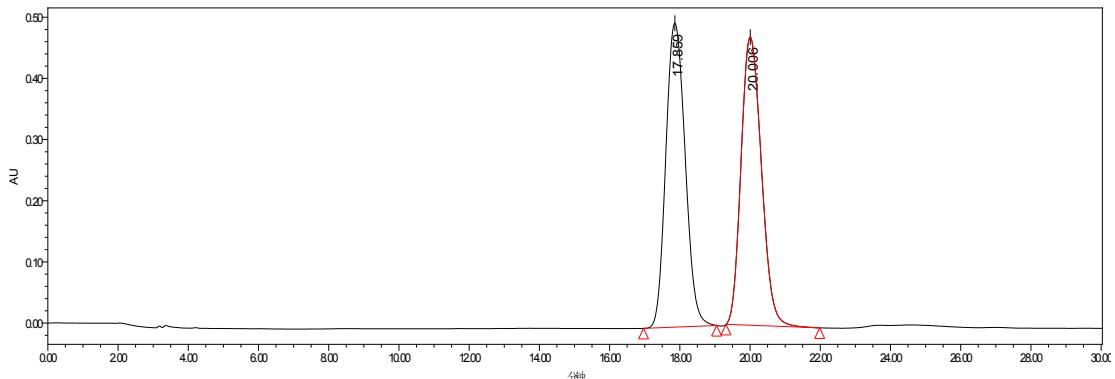
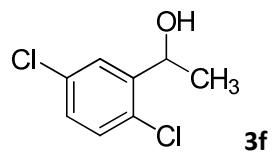
Peak	Ret Time [min]	Area	% Area	Height	Type
1	13.860	93519	2.47	2942	bb
2	15.672	3686501	97.53	92422	bb



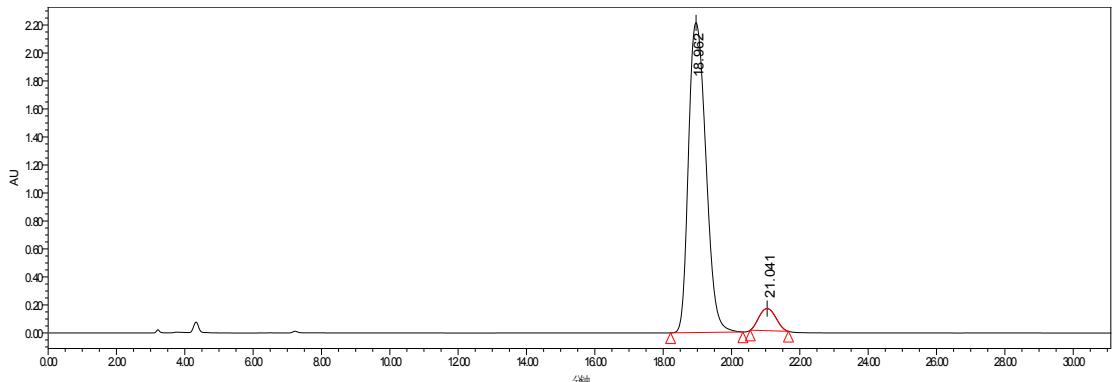
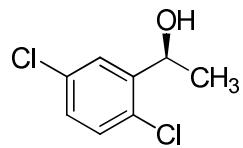
Peak	Ret Time [min]	Area	% Area	Height	Type
1	10.743	19567901	50.04	1241972	bb
2	11.918	19536517	49.96	1172397	bb



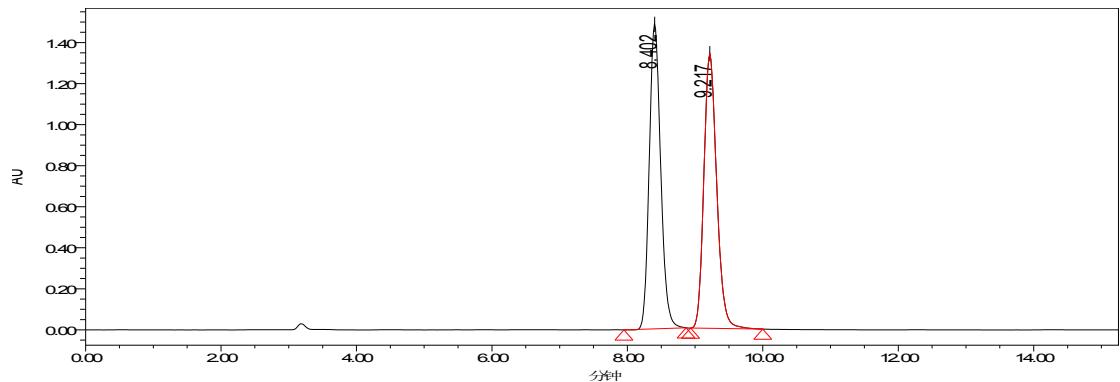
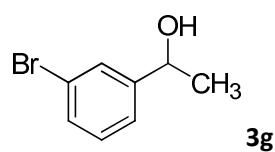
Peak	Ret Time [min]	Area	% Area	Height	Type
1	10.746	11499407	95.91	753199	bb
2	11.920	489961	4.09	39325	bb



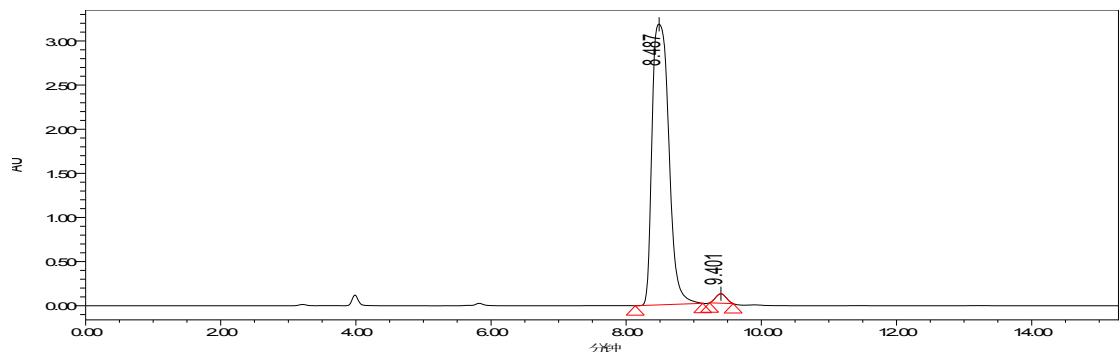
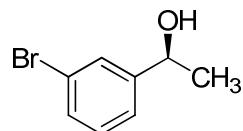
Peak	Ret Time [min]	Area	% Area	Height	Type
1	17.859	19026005	50.16	497090	bb
2	20.006	18904174	49.84	471250	bb



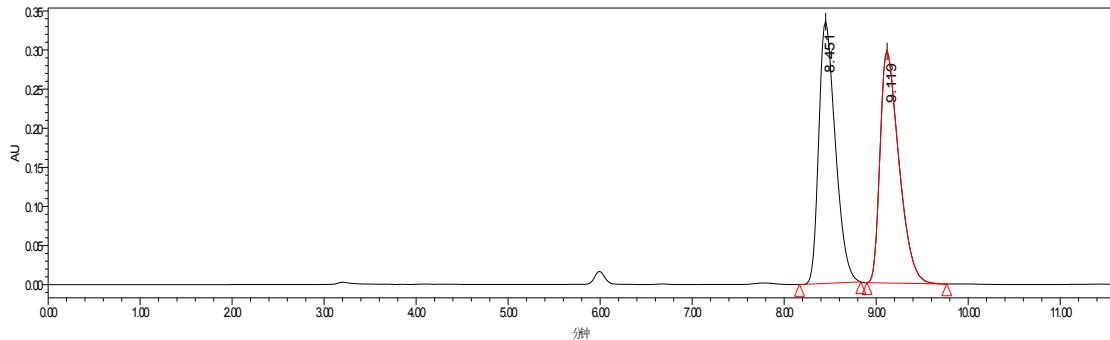
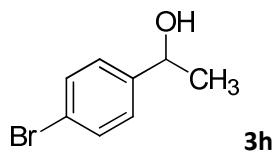
Peak	Ret Time [min]	Area	% Area	Height	Type
1	18.962	78278689	93.51	2213443	bb
2	21.041	5429347	6.49	158324	bb



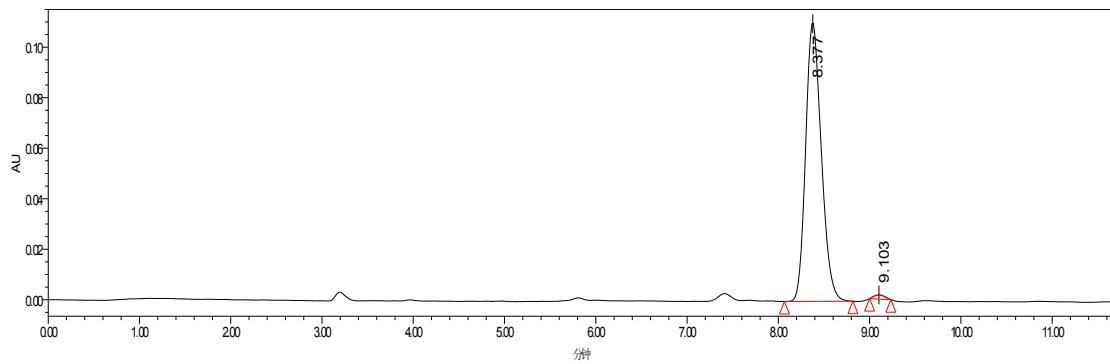
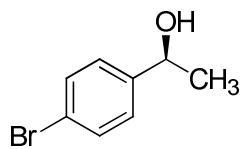
Peak	Ret Time [min]	Area	% Area	Height	Type
1	8.402	17421213	49.76	1487118	bb
2	9.217	17586816	50.24	1337508	bb



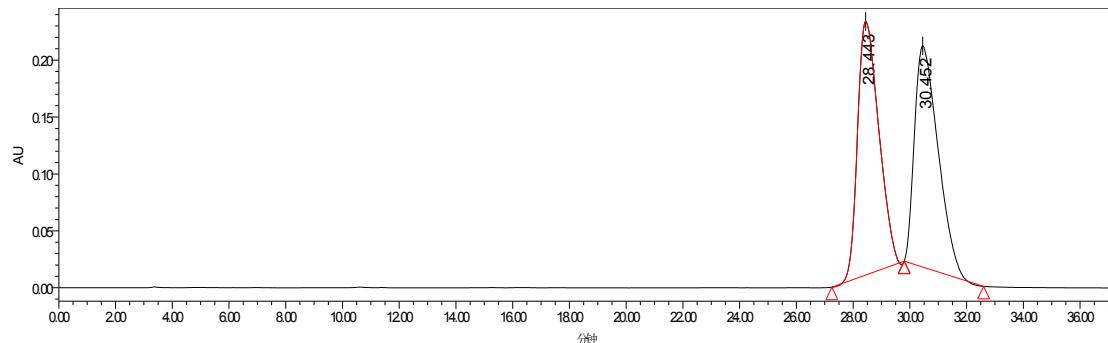
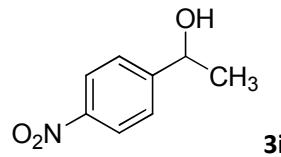
Peak	Ret Time [min]	Area	% Area	Height	Type
1	8.487	54928552	97.93	3181975	bb
2	9.401	1162568	2.07	106985	bb



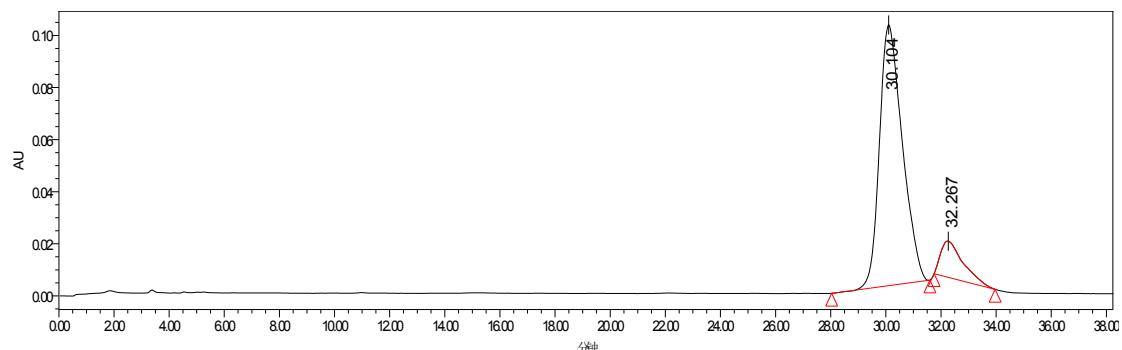
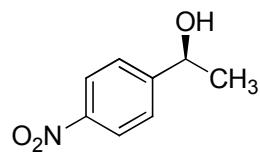
Peak	Ret Time [min]	Area	% Area	Height	Type
1	8.451	4185450	49.83	335018	bb
2	9.119	4214619	50.17	296990	bb



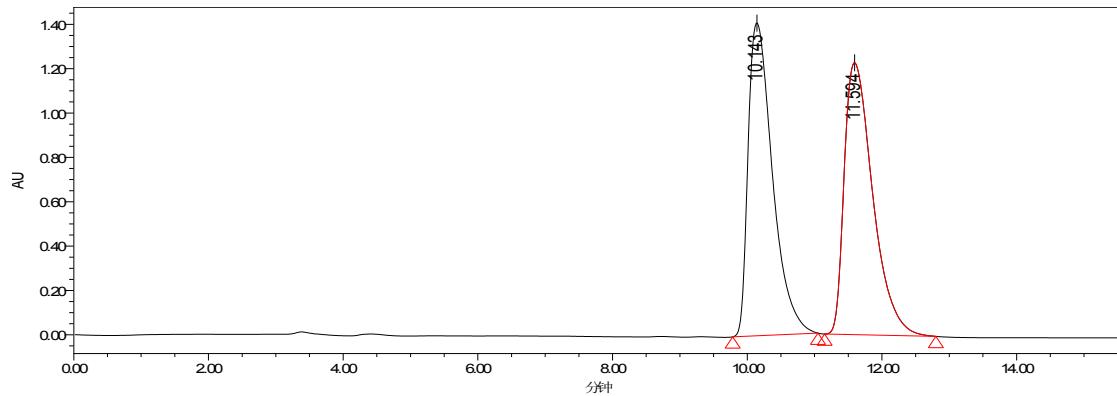
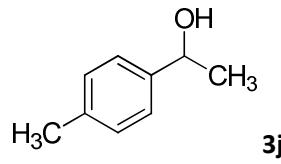
Peak	Ret Time [min]	Area	% Area	Height	Type
1	8.377	1316613	98.97	110411	bb
2	9.103	13768	1.03	1651	bb



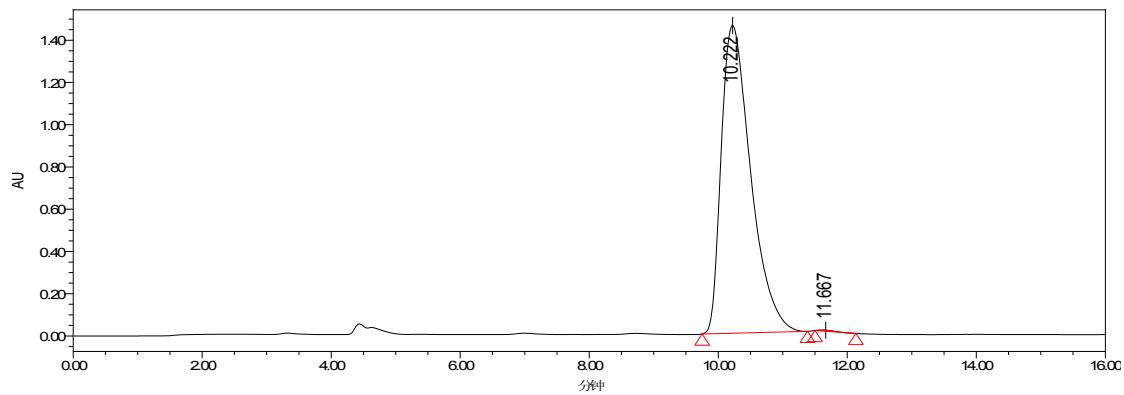
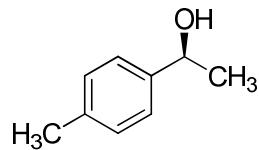
Peak	Ret Time [min]	Area	% Area	Height	Type
1	28.443	11601540	50.71	222898	bb
2	30.452	11276947	49.29	194518	bb



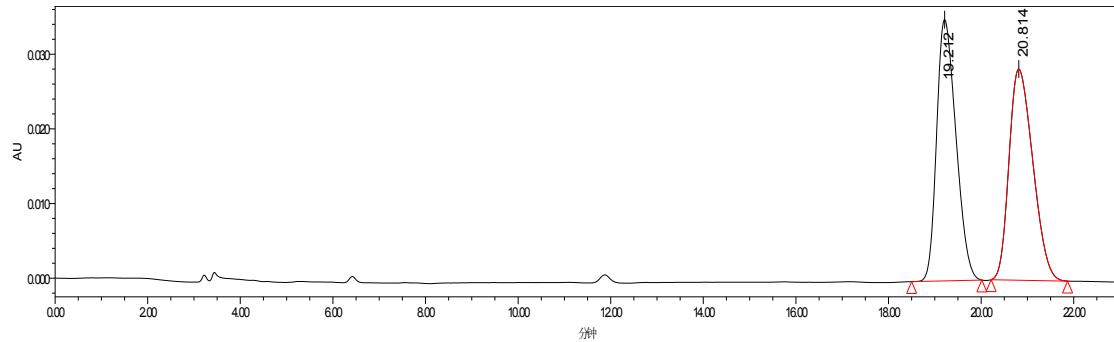
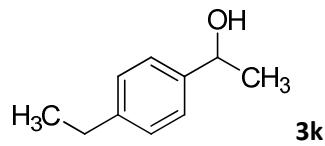
Peak	Ret Time [min]	Area	% Area	Height	Type
1	30.104	5762802	90.97	99893	Bb
2	32.237	572026	9.03	12445	bb



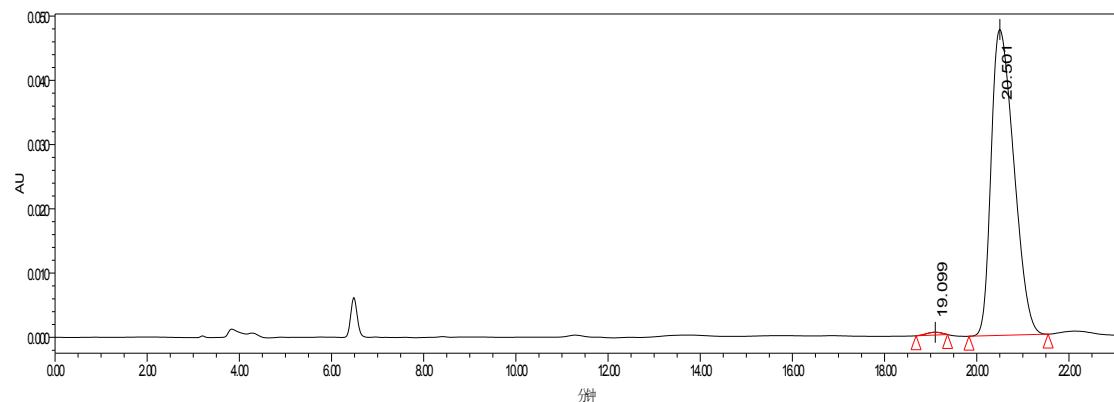
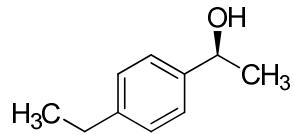
Peak	Ret Time [min]	Area	% Area	Height	Type
1	10.143	35426399	49.58	1410791	bb
2	11.594	36025226	50.42	1226451	bb



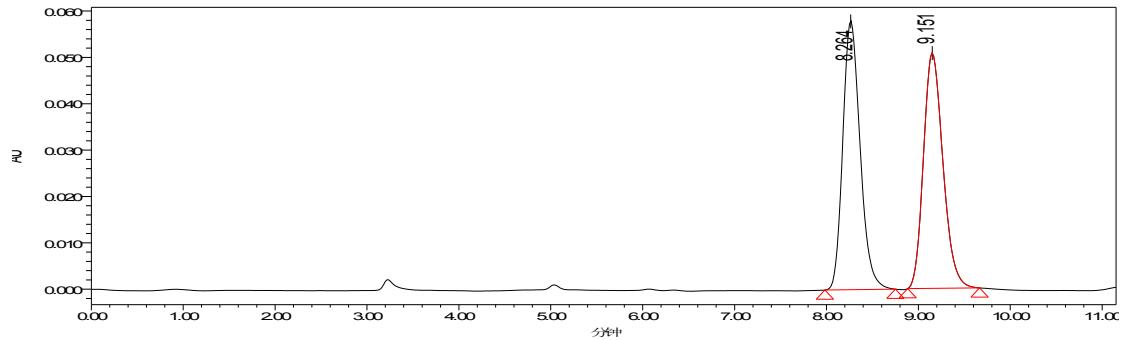
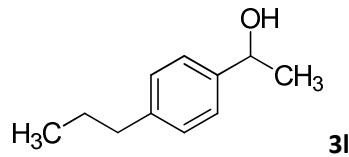
Peak	Ret Time [min]	Area	% Area	Height	Type
1	10.222	46288860	99.81	1457608	bb
2	11.667	87142	0.19	5371	bb



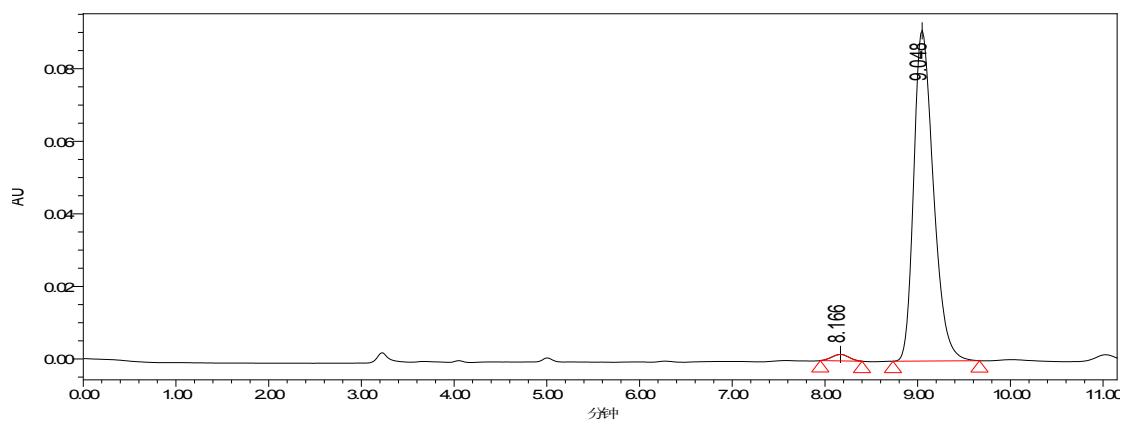
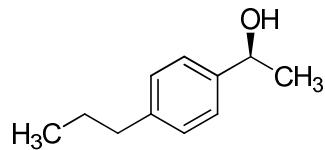
Peak	Ret Time [min]	Area	% Area	Height	Type
1	19.212	1014161	50.09	35004	bb
2	20.814	1010695	49.91	28295	bb



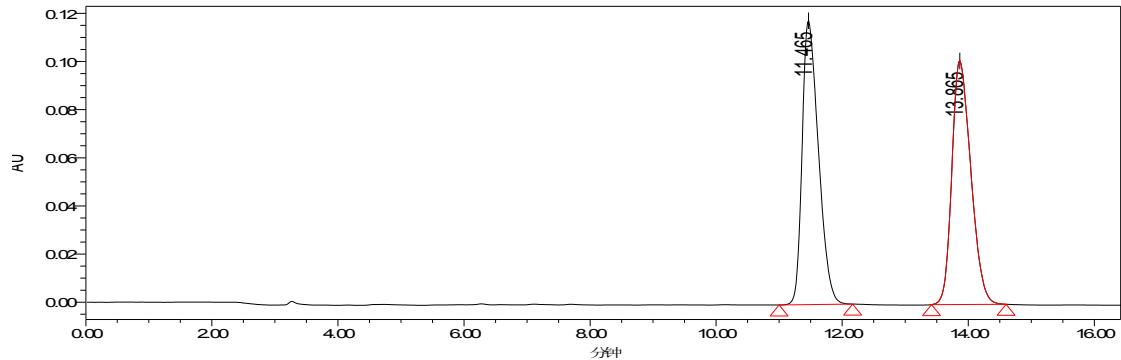
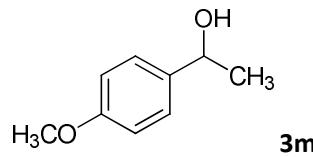
Peak	Ret Time [min]	Area	% Area	Height	Type
1	19.099	5710	0.35	314	bb
2	20.501	1621065	99.65	47502	bb



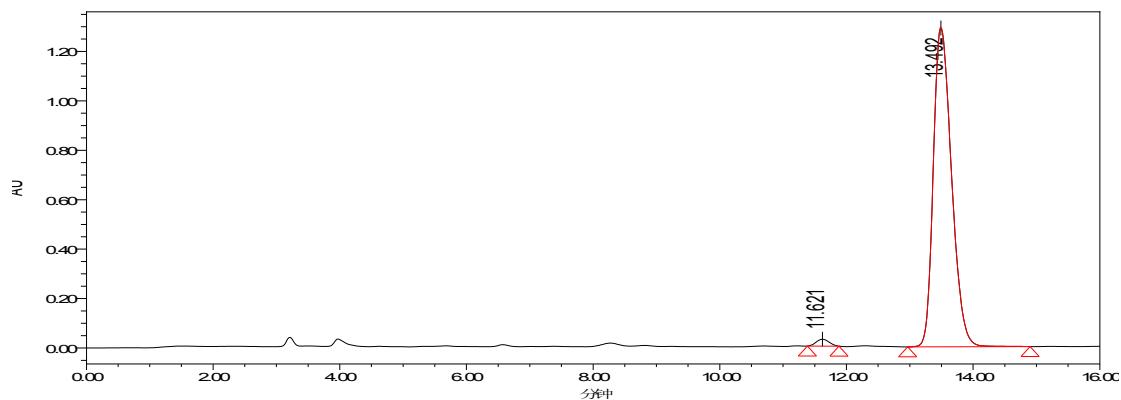
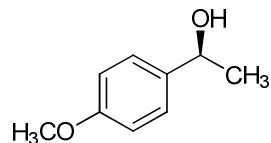
Peak	Ret Time [min]	Area	% Area	Height	Type
1	8.264	760080	50.44	57999	bb
2	9.151	746896	49.56	50788	bb



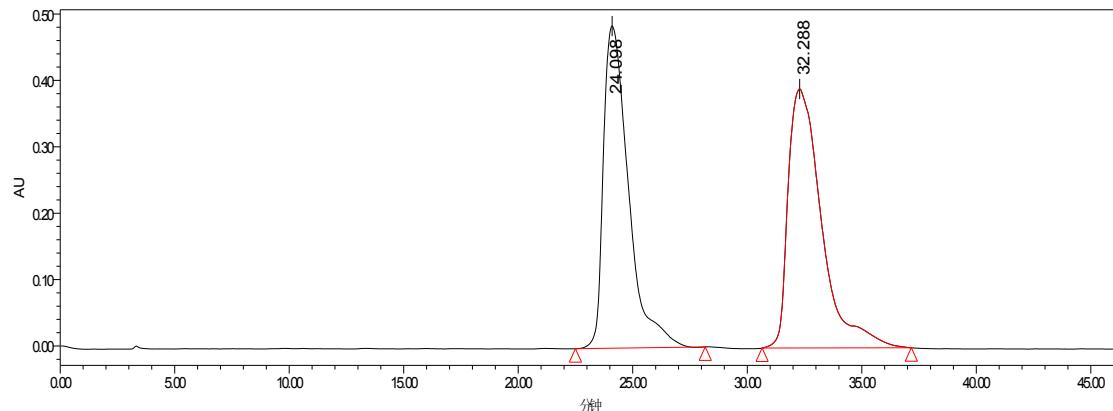
Peak	Ret Time [min]	Area	% Area	Height	Type
1	8.166	14260	1.05	1383	bb
2	9.048	1343951	98.95	91118	bb



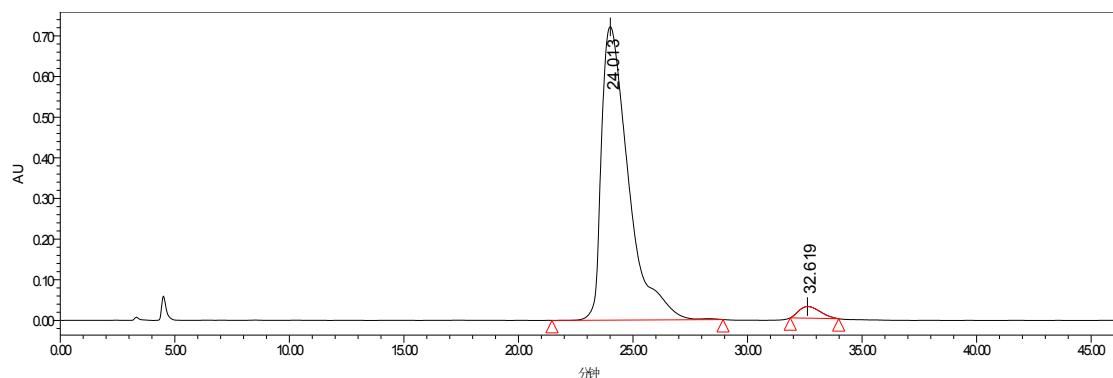
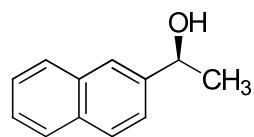
Peak	Ret Time [min]	Area	% Area	Height	Type
1	11.465	2118457	50.01	117993	bb
2	13.665	2117822	49.99	101248	bb



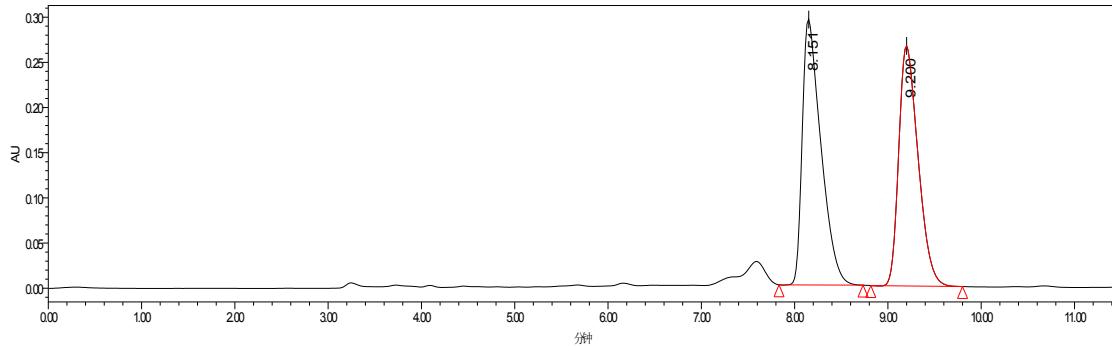
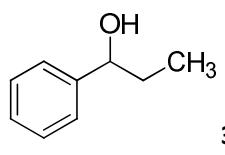
Peak	Ret Time [min]	Area	% Area	Height	Type
1	11.621	269225	1.03	22017	bb
2	13.492	25848382	98.97	1293140	bb



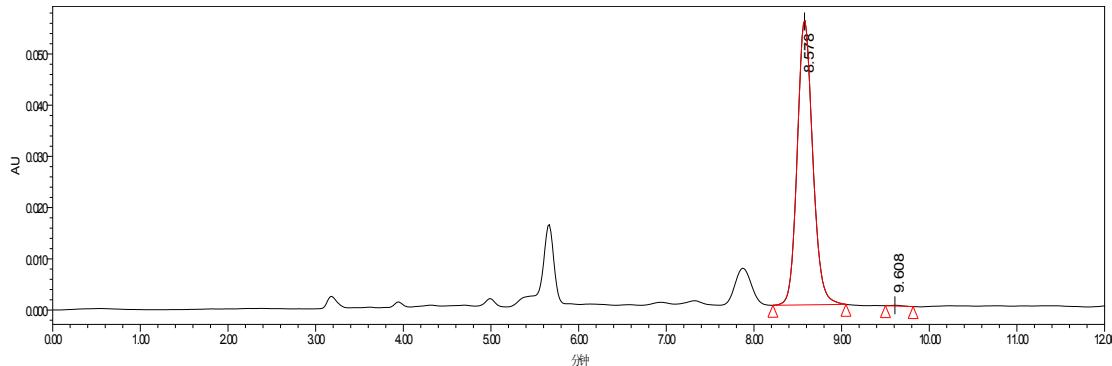
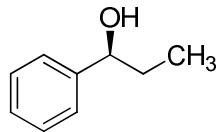
Peak	Ret Time [min]	Area	% Area	Height	Type
1	24.098	36925337	48.20	485298	bb
2	32.288	39684986	51.80	390175	bb



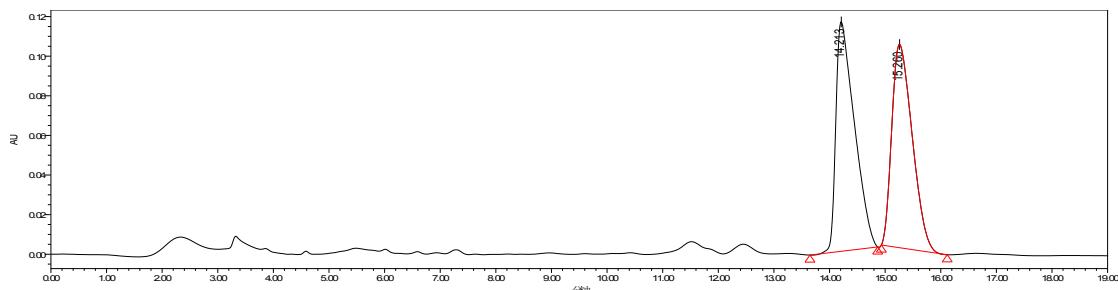
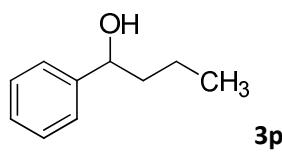
Peak	Ret Time [min]	Area	% Area	Height	Type
1	24.013	59044636	96.94	721648	bb
2	32.619	1865168	3.06	28695	bb



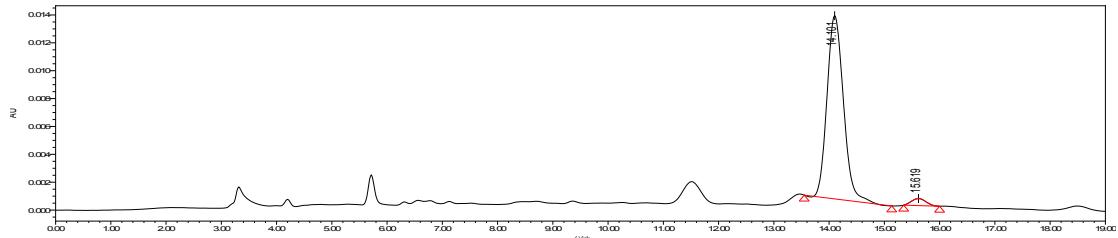
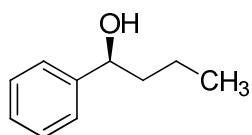
Peak	Ret Time [min]	Area	% Area	Height	Type
1	8.151	4088101	51.68	294285	bb
2	9.200	3823016	48.32	265718	bb



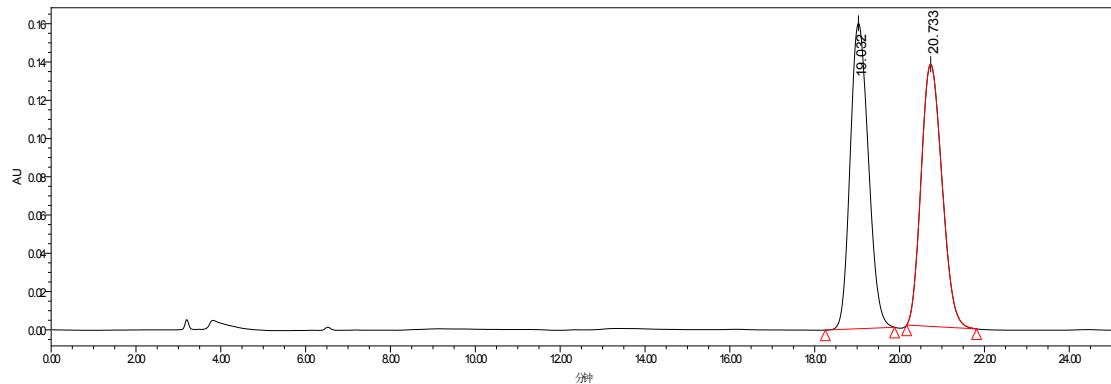
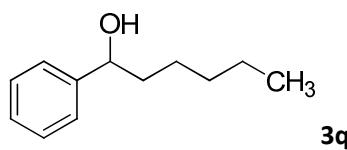
Peak	Ret Time [min]	Area	% Area	Height	Type
1	8.578	682370	99.81	55572	bb
2	9.608	1300	0.19	136	bb



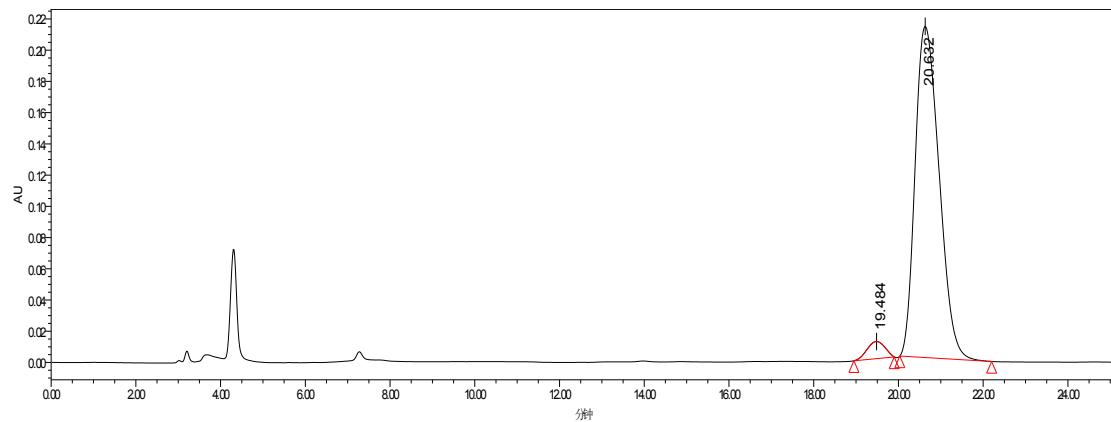
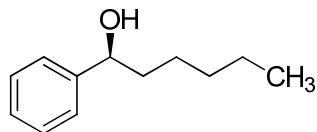
Peak	Ret Time [min]	Area	% Area	Height	Type
1	14.213	2689042	50.61	115927	bb
2	15.260	2623979	49.39	102692	bb



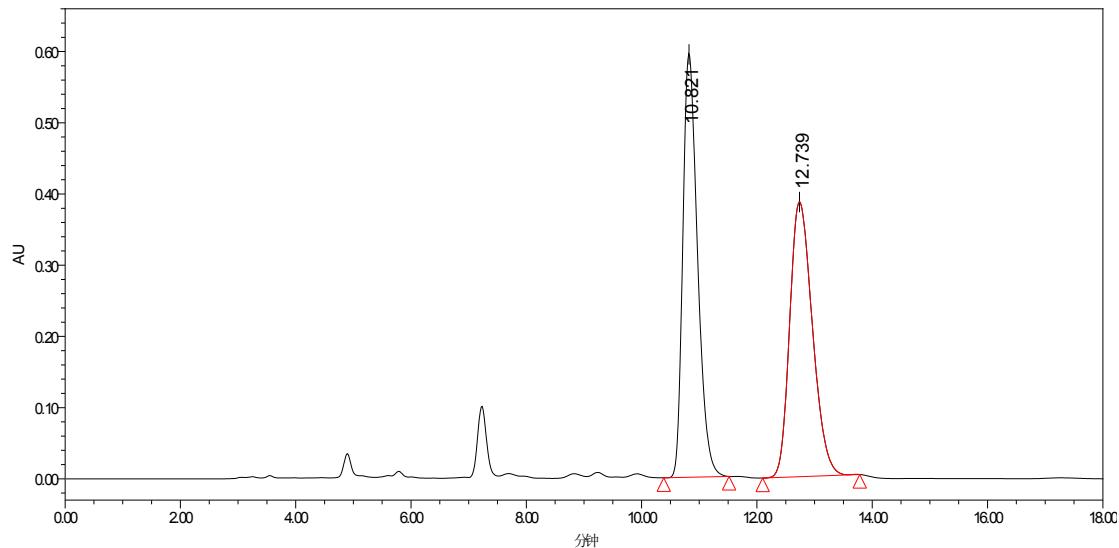
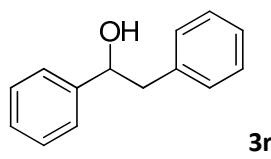
Peak	Ret Time [min]	Area	% Area	Height	Type
1	14.101	272991	96.76	13153	bb
2	15.619	9153	3.24	505	bb



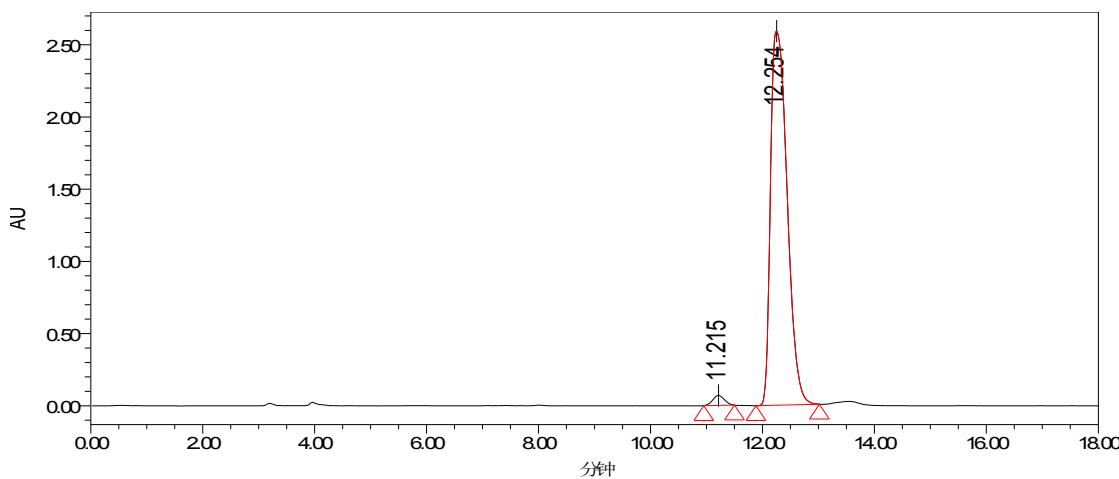
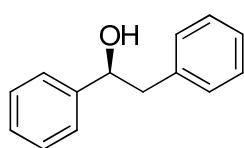
Peak	Ret Time [min]	Area	% Area	Height	Type
1	19.032	4795474	50.02	159947	bb
2	20.733	4791335	49.98	138208	bb



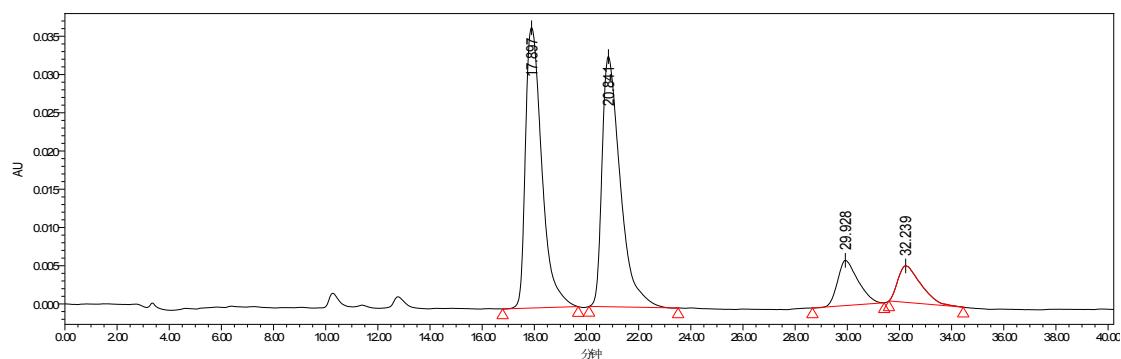
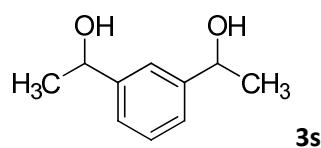
Peak	Ret Time [min]	Area	% Area	Height	Type
1	19.484	247287	2.87	9460	bb
2	20.632	8360926	97.13	212523	bb



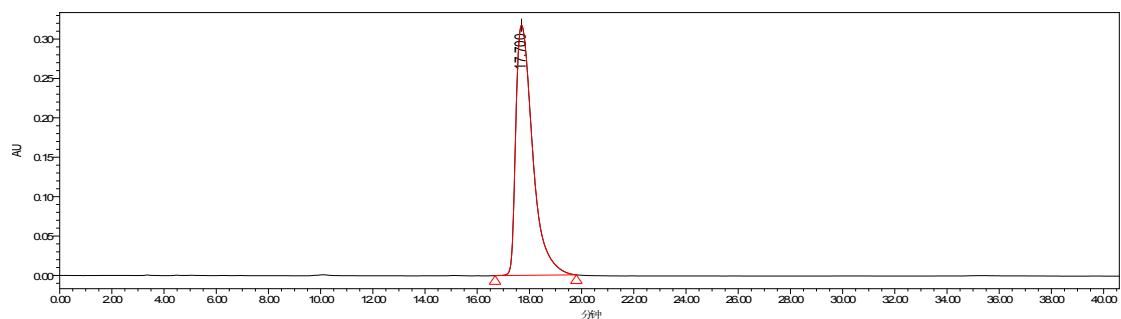
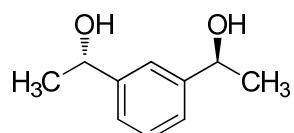
Peak	Ret Time [min]	Area	% Area	Height	Type
1	10.821	10518942	49.12	594959	bb
2	12.739	10894739	50.88	388223	bb



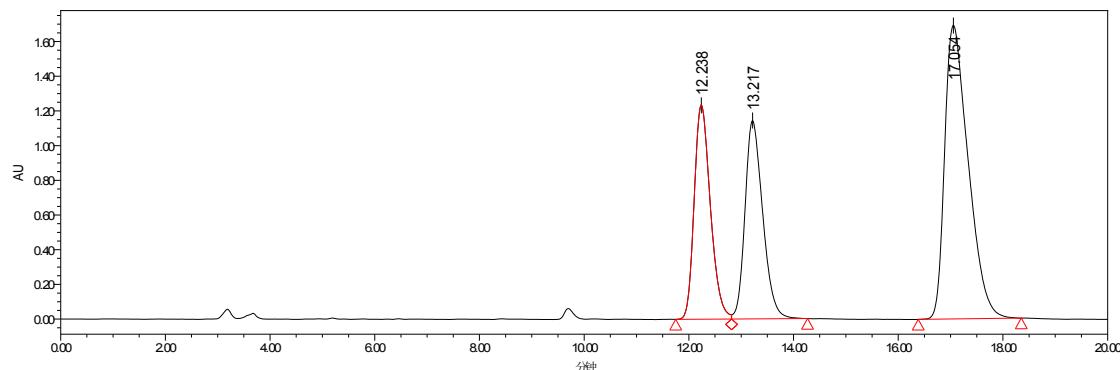
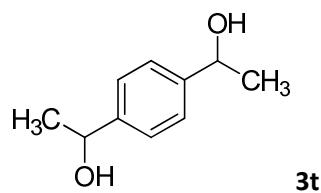
Peak	Ret Time [min]	Area	% Area	Height	Type
1	11.215	752008	1.39	60150	bb
2	12.254	53465877	98.61	2593306	bb



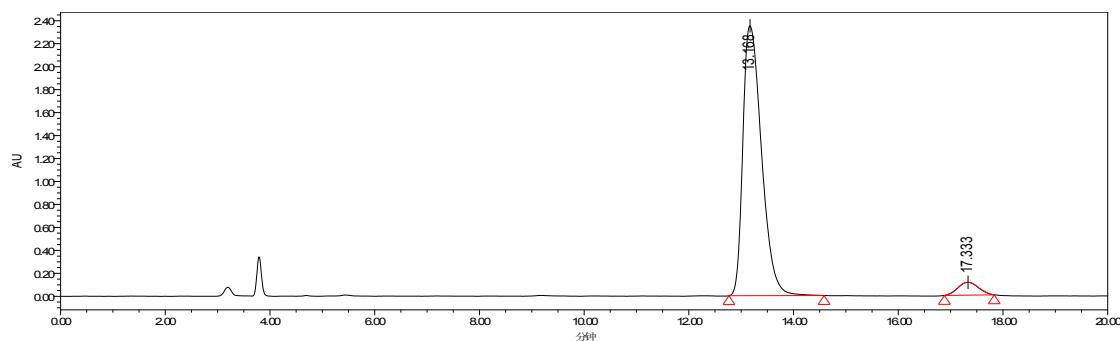
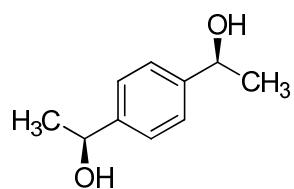
Peak	Ret Time [min]	Area	% Area	Height	Type
1	17.897	1598497	42.08	36650	bb
2	20.841	1586914	41.77	32729	bb
3	29.928	321781	8.47	5918	bb
4	32.239	291888	7.68	4754	bb



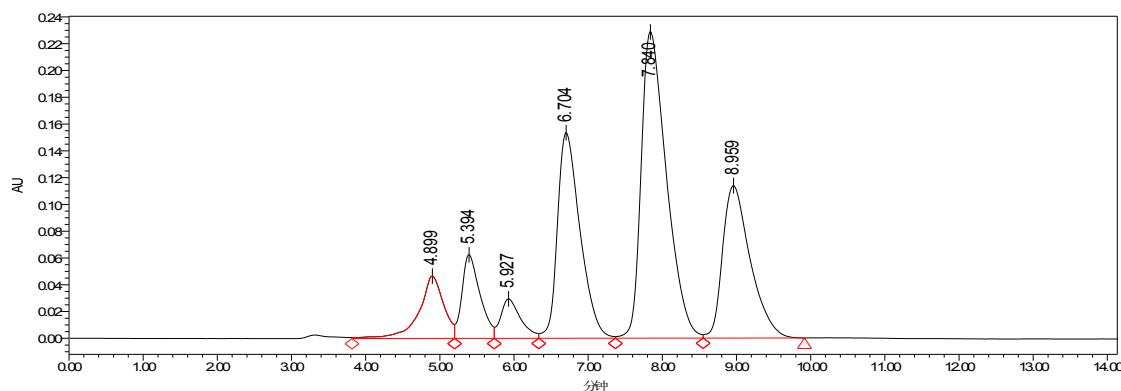
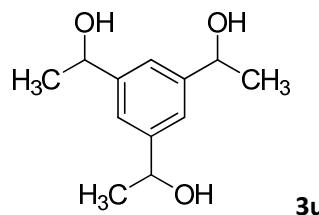
Peak	Ret Time [min]	Area	% Area	Height	Type
1	17.700	14233192	100.00	317550	bb



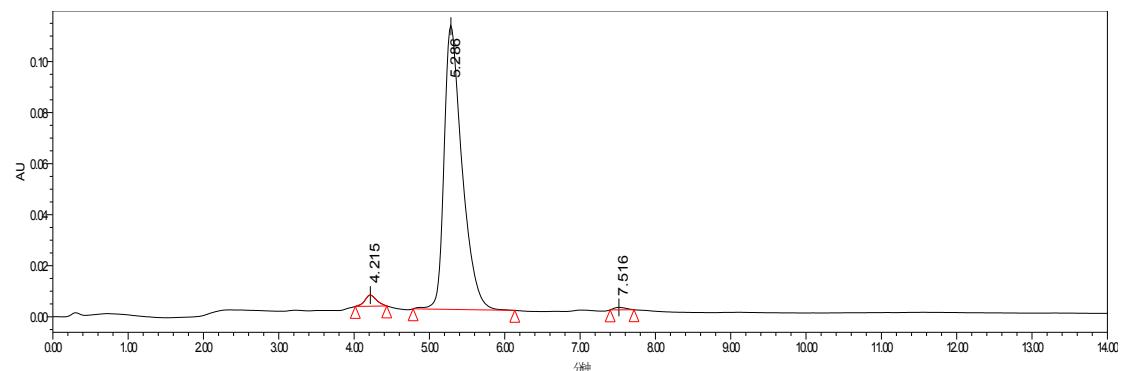
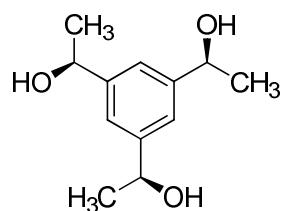
Peak	Ret Time [min]	Area	% Area	Height	Type
1	12.238	26513708	24.93	1234636	BV
2	13.217	26868476	25.27	1143585	VB
3	17.054	52963234	49.80	1692842	BB



Peak	Ret Time [min]	Area	% Area	Height	Type
1	13.168	58124914	95.00	2350971	bb
2	17.333	3057095	5.00	111879	bb



Peak	Ret Time [min]	Area	% Area	Height	Type
1	4.899	1079083	7.54	46623	VV
2	5.394	1054358	7.37	62542	VV
3	5.927	547068	3.82	29502	VV
4	6.704	3248523	22.69	153727	VV
5	7.840	5429110	37.93	229104	VV
6	8.959	2956539	20.65	113905	VB



Peak	Ret Time [min]	Area	% Area	Height	Type
1	4.215	47155	2.48	4366	bb
2	5.286	1843832	96.98	111223	bb
3	7.516	10268	0.54	952	bb