

Supporting Information

Ir-Catalyzed chemo-, regio- and enantioselective allylic enolization of 6,6-dimethyl-3-((trimethylsilyl)oxy)cyclohex-2-en-1-one involving keto-enol isomerization

Xiao-Lin Wang, Ji-Teng Chen, Sheng-Cai Zheng* and Xiao-Ming Zhao*

School of Chemical Technology and Engineering, Tongji University, 1239 Siping Road, Shanghai, P.R. China, 200092

Table of Contents

1. General.....	S2
2. General Procedure for the Synthesis of 3	S3
3. Procedure for the Synthesis of 5	S9
4. References.....	S10
5. X-ray Crystallographic Information of 3j	S11
6. Copies of NMR spectra of compounds 3 and 5	S13
7. HPLC Spectra of compounds 3 and 5	S31

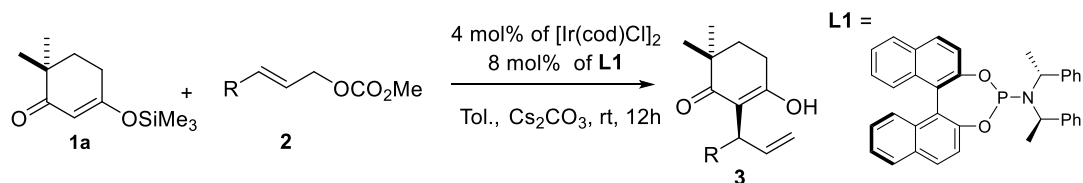
1. General

All manipulations were carried out under the argon atmosphere using standard Schlenk techniques. All glassware was oven or flame dried immediately prior to use. All solvents were purified and dried according to standard methods prior to use, unless stated otherwise.

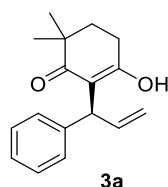
^1H NMR spectra were obtained at 400 MHz or 600 MHz and recorded relative to the tetramethylsilane signal (0 ppm) or residual protio-solvent (7.26 ppm for CDCl_3 , 1.94 ppm for CD_3CN , 2.50 ppm for DMSO-d_6). ^{13}C NMR spectra were obtained at 100 MHz or 150 MHz, and chemical shifts were recorded relative to the solvent resonance (CDCl_3 , 77.16 ppm, CD_3CN , 1.32 ppm, 39.52 ppm for DMSO-d_6). ^{19}F NMR spectra were obtained at 376 MHz or 565 MHz. Data for NMR are recorded as follows: chemical shift (δ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, coupling constant(s) in Hz, integration).

The phosphoramidite ligands¹, substituted allylic carbonates², were prepared according to the known procedures. Other chemicals were purchased from commercial suppliers and used without further purification, unless mentioned.

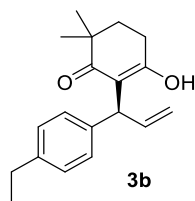
2. General Procedure for the Synthesis of 3



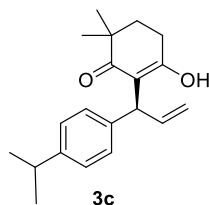
[Ir(COD)Cl]₂ (0.004 mmol, 4 mol%), phosphoramidite ligand **L1** (0.008 mmol, 8 mol%) were dissolved in THF (0.5 mL) and *n*-propylamine (0.3 mL) in a dry Schlenk tube filled with argon. The reaction mixture was heated at 50 °C for 30 min and then the volatile solvents were removed under vacuum to give a yellow solid. After that, allylic carbonate **2** (0.20 mmol), cesium carbonate (Cs₂CO₃, 0.12 mmol), and toluene (1.0 mL) were added. In another dry Schlenk tube, 6, 6-dimethyl-3-((trimethylsilyl)oxy) cyclohex-2-en-1-one **1a**³ was prepared from 4, 4-dimethylcyclohexane-1, 3-cyclohexanedione (0.10 mmol) and hexamethyldisilazane (HMDS) (0.15 mmol) in DCM (2.0 mL) stirring for 2.5 h at room temperature, and the solvent was removed under vacuum to give a light-yellow liquid which was transferred through syringe into the above mentioned Schlenk tube. The reaction was stirring at room temperature for 12 h. Then the mixture was washed with brine. After the organic phase was collected, the aqueous phase was extracted with DCM. The combined organic phase was dried over anhydrous Na₂SO₄ and concentrated on a rotary evaporator. The crude residue was purified by flash column chromatography (petroleum ether/ethyl acetate) to give the desired products **3**.



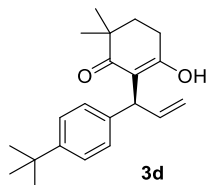
(S)-3-Hydroxy-6,6-dimethyl-2-(1-phenylallyl)cyclohex-2-en-1-one (3a), white solid; **m.p.**: 103-105 °C; 75% yield (19.2 mg); **HPLC** *ee*: 91% [Daicel CHIRALPAK AD-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; *t_R* = 6.77 (minor), 8.22 (major) min]. [α]_D²⁰ = +22.3 (c 1.0, CHCl₃). **¹H NMR** (600 MHz, CD₃CN) δ 7.28 – 7.24 (m, 2H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.17 – 7.13 (m, 1H), 6.49 – 6.43 (m, 1H), 5.11 – 5.05 (m, 2H), 4.88 (d, *J* = 7.8 Hz, 1H), 2.57 – 2.54 (m, 2H), 1.82 (t, *J* = 6.0 Hz, 2H), 1.06 (d, *J* = 6.0 Hz, 6H). **¹³C NMR** (150 MHz, CD₃CN) δ 212.6, 172.2, 144.4, 140.2, 128.5, 127.9, 126.1, 115.9, 115.4, 44.2, 39.8, 34.7, 27.7, 24.8, 24.8. **IR** (KBr): ν_{max} (cm⁻¹) = 3648, 3523, 3442, 1715, 1627, 1400, 1275, 1260, 764, 749. **HRMS** (ESI⁺) calcd for C₁₇H₂₀NaO₂ [M+Na]⁺: 279.1356, Found: 279.1362.



(S)-2-(1-(4-Ethylphenyl)allyl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one (3b), pale yellow wax; 71% yield (20.2 mg); **HPLC** *ee*: 90% [Daicel CHIRALCEL OJ-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; t_R = 8.45 (major), 12.06 (minor) min]. $[\alpha]_D^{20}$ = +12.7 (c 1.0, CHCl₃). **¹H NMR** (600 MHz, CD₃CN) δ 7.11 (d, J = 2.4 Hz, 4H), 6.49 – 6.42 (m, 1H), 5.10 – 5.04 (m, 2H), 4.85 (d, J = 8.4 Hz, 1H), 2.63 – 2.59 (m, 2H), 2.58 – 2.53 (m, 2H), 1.82 (t, J = 6.6 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H), 1.06 (d, J = 3.2 Hz, 6H). **¹³C NMR** (150 MHz, CD₃CN) δ 202.3, 170.1, 141.9, 141.3, 140.4, 127.9, 127.8, 115.9, 115.1, 43.7, 39.7, 34.5, 28.5, 27.1, 24.7, 24.7, 15.8. **IR** (KBr): ν_{max} (cm⁻¹) = 3443, 3418, 3012, 1655, 1621, 1412, 1234, 1231, 745. **HRMS** (ESI⁺) calcd for C₁₉H₂₄NaO₂ [M+Na]⁺: 307.1669, Found: 307.1680.

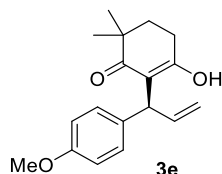


(S)-3-Hydroxy-2-(1-(4-isopropylphenyl)allyl)-6,6-dimethylcyclohex-2-en-1-one (3c), pale yellow solid; **m.p.**: 99–101°C; 78% yield (23.2 mg); **HPLC** *ee*: 90% [Daicel CHIRALPAK AD-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; t_R = 6.56 (minor), 7.41 (major) min]. $[\alpha]_D^{20}$ = -5.5 (c 1.0, CHCl₃). **¹H NMR** (600 MHz, DMSO-*d*₆) δ 10.45 (s, 1H), 7.10 – 7.00 (m, 4H), 6.44 – 6.38 (m, 1H), 5.02 – 4.93 (m, 2H), 4.76 (d, J = 9.0 Hz, 1H), 2.52 – 2.50 (m, 3H), 1.73 (t, J = 6.6 Hz, 2H), 1.17 (d, J = 7.2 Hz, 6H), 0.99 (d, J = 3.6 Hz, 6H). **¹³C NMR** (150 MHz, DMSO-*d*₆) δ 201.1, 170.6, 145.4, 141.5, 140.5, 127.3, 126.0, 115.0, 114.9, 43.5, 34.2, 33.4, 26.9, 25.3, 25.2, 24.5, 24.4. **IR** (KBr): ν_{max} (cm⁻¹) = 3498, 3431, 3011, 1676, 1632, 1413, 1265, 1243, 743. **HRMS** (ESI⁺) calcd for C₂₀H₂₆NaO₂ [M+Na]⁺: 321.1825, Found: 321.1823.

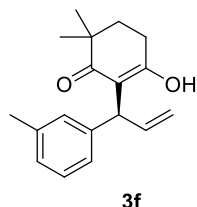


(S)-2-(1-(4-(Tert-butyl)phenyl)allyl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one (3d), pale yellow solid; **m.p.**: 91–94°C; 90% yield (28.1 mg); **HPLC** *ee*: 94% [Daicel CHIRALCEL OJ-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 95/5; flow rate = 0.5 mL/min; detection wavelength = 254 nm; t_R = 16.86 (minor), 19.18 (major) min]. $[\alpha]_D^{20}$ = +15.8 (c 1.0, CHCl₃). **¹H NMR** (600 MHz, DMSO-*d*₆) δ 10.45 (s, 1H), 7.22 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 7.8 Hz, 2H), 6.43 – 6.37 (m, 1H),

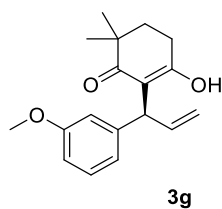
5.02 – 4.94 (m, 2H), 4.75 (d, $J = 8.4$ Hz, 1H), 2.50 – 2.49 (m, 2H), 1.72 (t, $J = 6.0$ Hz, 2H), 1.24 (s, 9H), 0.99 (s, 6H). **^{13}C NMR** (150 MHz, DMSO- d_6) δ 201.1, 170.6, 147.6, 141.1, 140.5, 127.1, 124.9, 114.9, 114.8, 43.4, 34.4, 34.2, 31.7, 26.9, 25.3, 25.2. **IR** (KBr): ν_{max} (cm^{-1}) = 3586, 3523, 3441, 3129, 1650, 1400, 1275, 1269, 764, 752. **HRMS** (ESI $^{+}$) calcd for $\text{C}_{21}\text{H}_{27}\text{NaO}_2$ $[\text{M}+\text{Na}]^{+}$: 353.1887, Found: 353.1908.



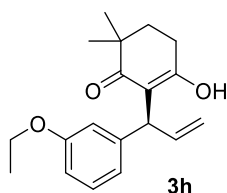
(S)-3-Hydroxy-2-(1-(4-methoxyphenyl)allyl)-6,6-dimethylcyclohex-2-en-1-one (3e), yellow solid; **m.p.:** 75-77°C; 70% yield (20.1 mg); **HPLC** *ee*: 83% [Daicel CHIRALPAK AD-H (0.46 cm \times 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; t_{R} = 10.52 (minor), 12.24 (major) min]. $[\alpha]_{\text{D}}^{20} = +6.8$ (c 1.0, CHCl_3). **^1H NMR** (600 MHz, CD_3CN) δ 7.01 (d, $J = 9.0$ Hz, 2H), 6.71 (d, $J = 9.0$ Hz, 2H), 6.36 - 6.30 (m, 1H), 5.00 – 4.89 (m, 2H), 4.71 (d, $J = 7.8$ Hz, 1H), 3.65 (s, 3H), 2.45 – 2.42 (m, 2H), 1.70 (t, $J = 6.0$ Hz, 2H), 0.95 (d, $J = 4.2$ Hz, 6H). **^{13}C NMR** (150 MHz, CD_3CN) δ 202.2, 176.0, 158.2, 140.6, 135.9, 128.8, 116.0, 115.0, 113.7, 55.3, 43.3, 39.7, 34.5, 27.6, 24.7, 24.7. **IR** (KBr): ν_{max} (cm^{-1}) = 3523, 3129, 3006, 2990, 1607, 1509, 1400, 1275, 1260, 764, 749. **HRMS** (ESI $^{+}$) calcd for $\text{C}_{18}\text{H}_{22}\text{NaO}_3$ $[\text{M}+\text{Na}]^{+}$: 309.1461, Found: 309.1462.



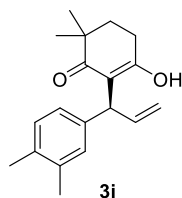
(S)-3-Hydroxy-6,6-dimethyl-2-(1-(m-tolyl)allyl)cyclohex-2-en-1-one (3f), yellow solid; **m.p.:** 87-89°C; 70% yield (21.1 mg); **HPLC** *ee*: 82% [Daicel CHIRALPAK IC (0.46 cm \times 25 cm); *n*-hexane/2-propanol = 95/5; flow rate = 0.5 mL/min; detection wavelength = 254 nm; t_{R} = 22.16 (minor), 23.36 (major) min]. $[\alpha]_{\text{D}}^{20} = +7.9$ (c 1.0, CHCl_3). **^1H NMR** (600 MHz, DMSO- d_6) δ 10.46 (s, 1H), 7.08 (t, $J = 7.8$ Hz, 1H), 6.93 (s, 1H), 6.90 (d, $J = 7.8$ Hz, 2H), 6.44 – 6.37 (m, 1H), 5.03 – 4.96 (m, 2H), 4.75 (d, $J = 8.4$ Hz, 1H), 2.51 – 2.50 (m, 2H), 2.23 (s, 3H), 1.73 (t, $J = 6.6$ Hz, 2H), 0.99 (d, $J = 3.0$ Hz, 6H). **^{13}C NMR** (150 MHz, DMSO) δ 201.0, 170.7, 144.2, 140.4, 136.9, 128.1, 128.0, 126.2, 124.5, 115.1, 114.9, 43.7, 34.2, 26.9, 25.2, 25.1, 21.6. **IR** (KBr): ν_{max} (cm^{-1}) = 3509, 3440, 3127, 1628, 1607, 1440, 1275, 1234, 765. **HRMS** (ESI $^{+}$) calcd for $\text{C}_{18}\text{H}_{22}\text{NaO}_2$ $[\text{M}+\text{Na}]^{+}$: 293.1512, Found: 293.1513.



(S)-3-Hydroxy-2-(1-(3-methoxyphenyl)allyl)-6,6-dimethylcyclohex-2-en-1-one (3g), yellow solid; **m.p.:** 83-85°C; 60% yield (20.0 mg); **HPLC** *ee*: 92% [Daicel CHIRALCEL OJ-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 95/5; flow rate = 1.0 mL/min; detection wavelength = 254 nm; *t_R* = 23.39 (major), 26.21 (minor) min]. $[\alpha]_D^{20} = +16.9$ (c 1.0, CHCl₃). **¹H NMR** (600 MHz, CD₃CN) δ 7.87 (s, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.80 (d, *J* = 9.0 Hz, 1H), 6.77 – 6.70 (m, 2H), 6.47 – 6.41 (m, 1H), 5.09 – 5.05 (m, 2H), 4.85 (d, *J* = 8.4 Hz, 1H), 3.75 (s, 3H), 2.57 – 2.54 (m, 2H), 1.82 (t, *J* = 6.0 Hz, 2H), 1.07 (d, *J* = 3.0 Hz, 6H). **¹³C NMR** (150 MHz, CD₃CN) δ 202.2, 170.1, 160.1, 145.9, 140.1, 129.4, 120.1, 115.8, 115.4, 113.5, 111.2, 55.2, 44.0, 40.0, 34.4, 27.0, 24.7. **IR** (KBr): ν_{\max} (cm⁻¹) = 3651, 3511, 3112, 1677, 1609, 1412, 1212, 1205, 722. **HRMS** (ESI⁺) calcd for C₁₈H₂₂NaO₃ [M+Na]⁺: 309.1461, Found: 309.1469.

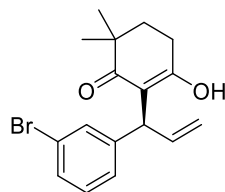


(S)-2-(1-(3-Ethoxyphenyl)allyl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one (3h), yellow solid; **m.p.:** 83-85°C; 76% yield (22.8 mg); **HPLC** *ee*: 89% [Daicel CHIRALPAK AD-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; *t_R* = 8.08 (major), 8.64 (minor) min]. $[\alpha]_D^{20} = -21.5$ (c 1.0, CHCl₃). **¹H NMR** (600 MHz, DMSO-*d*₆) δ 10.45 (s, 1H), 7.12 – 7.07 (m, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 6.65 – 6.63 (m, 2H), 6.42 – 6.36 (m, 1H), 5.00 – 4.97 (m, 2H), 4.75 (d, *J* = 9.0 Hz, 1H), 3.93 (dd, *J* = 6.6, 2.4 Hz, 2H), 2.50 – 2.49 (m, 2H), 1.72 (t, *J* = 6.6 Hz, 2H), 1.29 (t, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 3.6 Hz, 6H). **¹³C NMR** (150 MHz, DMSO-*d*₆) δ 201.0, 172.3, 159.7, 146.3, 140.5, 129.7, 120.4, 116.1, 115.6, 114.4, 112.1, 63.9, 44.4, 40.0, 34.8, 27.8, 25.1, 15.1. **IR** (KBr): ν_{\max} (cm⁻¹) = 3498, 3465, 3009, 1665, 1620, 1342, 1298, 1213, 734. **HRMS** (ESI⁺) calcd for C₁₉H₂₄NaO₃ [M+Na]⁺: 323.1618, Found: 323.1617.



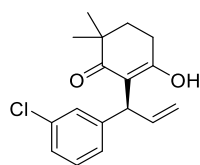
(S)-2-(1-(3,4-Dimethylphenyl)allyl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one (3i), yellow solid; **m.p.:** 108-110°C; 70% yield (19.9 mg); **HPLC** *ee*: 91% [Daicel CHIRALPAK AD-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; *t_R* = 6.07 (minor), 6.71 (major) min]. $[\alpha]_D^{20} = -30.2$ (c 1.0, CHCl₃). **¹H NMR** (600 MHz, CD₃CN) δ 7.75 (s, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.96 (s, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 6.47 – 6.41

(m, 1H), 5.09 – 5.02 (m, 2H), 4.82 (d, $J = 8.4$ Hz, 1H), 2.55 – 2.52 (m, 2H), 2.21 (s, 6H), 1.81 (t, $J = 6.0$ Hz, 2H), 1.06 (s, 6H). **^{13}C NMR** (150 MHz, CD_3CN) δ 200.6, 172.4, 141.5, 140.5, 136.4, 129.6, 129.0, 125.2, 116.0, 115.0, 43.6, 39.7, 34.5, 27.5, 24.8, 24.7, 19.5, 18.9. **IR** (KBr): ν_{max} (cm^{-1}) = 3521, 3422, 3123, 1710, 1676, 1423, 1211, 1201, 725. **HRMS** (ESI^+) calcd for $\text{C}_{19}\text{H}_{24}\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 307.1669, Found: 307.1661.



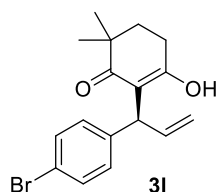
3j

(S)-2-(1-(3-Bromophenyl)allyl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one (3j), white solid; **m.p.**: 90–92°C; 70% yield (23.4 mg); **HPLC** *ee*: 81% [Daicel CHIRALPAK AD-H (0.46 cm \times 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; t_{R} = 6.42 (minor), 7.12 (major) min]. $[\alpha]_{\text{D}}^{20} = +15.8$ (c 1.0, CHCl_3). **^1H NMR** (600 MHz, $\text{DMSO}-d_6$) δ 10.73 (s, 1H), 7.30 (d, $J = 7.8$ Hz, 1H), 7.25 (s, 1H), 7.18 (t, $J = 7.2$ Hz, 1H), 7.10 (d, $J = 7.8$ Hz, 1H), 6.38 – 6.32 (m, 1H), 5.09 – 4.99 (m, 2H), 4.78 (d, $J = 8.4$ Hz, 1H), 2.53 – 2.50 (m, 2H), 1.72 (t, $J = 6.6$ Hz, 2H), 0.98 (d, $J = 5.4$ Hz, 6H). **^{13}C NMR** (150 MHz, $\text{DMSO}-d_6$) δ 201.0, 171.2, 147.3, 139.2, 130.4, 130.1, 128.5, 126.5, 121.7, 116.1, 114.2, 43.5, 34.1, 26.8, 25.2, 25.1. **IR** (KBr): ν_{max} (cm^{-1}) = 3508, 3441, 3116, 1670, 1628, 1400, 1273, 1261, 763, 748. **HRMS** (ESI^+) calcd for $\text{C}_{17}\text{H}_{19}\text{BrNaO}_2$ $[\text{M}+\text{Na}]^+$: 357.0461, Found: 357.0457.



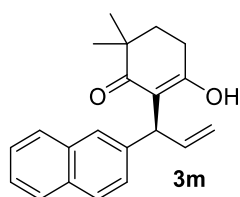
3k

(S)-2-(1-(3-Chlorophenyl)allyl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one (3k), pale yellow wax; 69% yield (20.0 mg); **HPLC** *ee*: 87% [Daicel CHIRALPAK AD-H (0.46 cm \times 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; t_{R} = 5.89 (minor), 6.56 (major) min]. $[\alpha]_{\text{D}}^{20} = +8.9$ (c 1.0, CHCl_3). **^1H NMR** (600 MHz, CD_3CN) δ 7.27 – 7.20 (m, 2H), 7.19 – 7.11 (m, 2H), 6.43 – 6.38 (m, 1H), 5.13 – 5.07 (m, 2H), 4.85 (d, $J = 8.4$ Hz, 1H), 2.59 – 2.55 (m, 2H), 1.82 (t, $J = 6.6$ Hz, 2H), 1.05 (d, $J = 8.4$ Hz, 6H). **^{13}C NMR** (150 MHz, CD_3CN) δ 201.9, 178.5, 147.1, 139.3, 133.7, 130.0, 127.7, 126.3, 125.9, 115.9, 115.4, 43.8, 39.7, 34.4, 27.3, 24.6, 24.5. **IR** (KBr): ν_{max} (cm^{-1}) = 3613, 3524, 34426, 3009, 1660, 1392, 1275, 1260, 765, 746. **HRMS** (ESI^+) calcd for $\text{C}_{17}\text{H}_{19}\text{ClNaO}_2$ $[\text{M}+\text{Na}]^+$: 313.0966, Found: 313.0996.

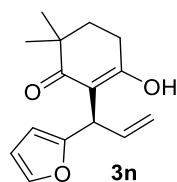


3l

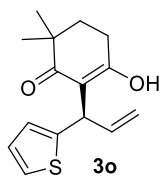
(S)-2-(1-(4-Bromophenyl)allyl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one (3l), yellow solid; **m.p.:** 93-95°C; 62% yield (20.7 mg); **HPLC** *ee*: 86% [Daicel CHIRALPAK AD-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; *t_R* = 7.09 (minor), 8.95 (major) min]. $[\alpha]_D^{20} = +39.9$ (c 1.0, CHCl₃). **¹H NMR** (600 MHz, DMSO-*d*₆) δ 10.61 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.39 – 6.32 (m, 1H), 5.03 – 4.99 (m, 2H), 4.75 (d, *J* = 8.4 Hz, 1H), 2.51 (t, *J* = 1.8 Hz, 2H), 1.72 (t, *J* = 6.0 Hz, 2H), 0.97 (d, *J* = 7.8 Hz, 6H). **¹³C NMR** (150 MHz, DMSO-*d*₆) δ 201.0, 171.0, 143.9, 139.5, 131.0, 129.7, 118.6, 115.8, 114.5, 43.2, 34.2, 26.8, 25.2, 25.1. **IR** (KBr): ν_{\max} (cm⁻¹) = 3648, 3526, 3442, 3207, 1704, 1628, 1416, 1386, 1270, 1010, 655. **HRMS** (ESI⁺) calcd for C₁₇H₁₉BrNaO₂ [M+Na]⁺: 357.0461, Found: 357.0448.



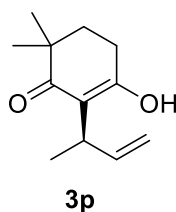
(S)-3-Hydroxy-6,6-dimethyl-2-(1-(naphthalen-2-yl)allyl)cyclohex-2-en-1-one (3m), white solid; **m.p.:** 139-141°C; 90% yield (27.5 mg); **HPLC** *ee*: 90% [Daicel CHIRALPAK AD-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; *t_R* = 10.39 (major), 9.68 (minor) min]. $[\alpha]_D^{20} = -46.6$ (c 1.0, CHCl₃). **¹H NMR** (600 MHz, DMSO-*d*₆) δ 10.59 (s, 1H), 7.80 (t, *J* = 7.9 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.59 (s, 1H), 7.46 – 7.39 (m, 2H), 7.29 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.55 – 6.48 (m, 1H), 5.08 (dq, *J* = 13.6, 2.5 Hz, 2H), 4.96 (d, *J* = 8.5 Hz, 1H), 2.51 (t, *J* = 1.9 Hz, 2H), 1.75 (t, *J* = 6.4 Hz, 2H), 0.99 (d, *J* = 7.6 Hz, 6H). **¹³C NMR** (150 MHz, DMSO-*d*₆) δ 201.2, 170.9, 142.1, 140.0, 133.4, 127.9, 127.7, 127.5, 126.8, 126.2, 125.4, 125.1, 115.6, 114.8, 43.9, 34.2, 26.8, 25.3, 25.1. **IR** (KBr): ν_{\max} (cm⁻¹) = 3523, 3440, 3127, 3007, 1641, 1625, 1605, 1400, 1276, 1268, 769, 752. **HRMS** (ESI⁺) calcd for C₂₁H₂₂NaO₂ [M+Na]⁺: 329.1512, Found: 329.1515.



(R)-2-(1-(Furan-2-yl)allyl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one (3n), brown solid; **m.p.:** 100-102°C; 61% yield (15.0 mg); **HPLC** *ee*: 92% [Daicel CHIRALPAK IG (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 220 nm; *t_R* = 7.28 (minor), 8.92 (major) min]. $[\alpha]_D^{20} = -4.6$ (c 1.0, CHCl₃). **¹H NMR** (600 MHz, CD₃CN) δ 7.23 (s, 1H), 6.26 – 6.21 (m, 1H), 6.20 – 6.19 (m, 1H), 5.88 (d, *J* = 3.2 Hz, 1H), 5.00 – 4.94 (m, 2H), 4.82 (d, *J* = 7.8 Hz, 1H), 2.43 (td, *J* = 6.6, 1.8 Hz, 2H), 1.70 (t, *J* = 6.6 Hz, 2H), 0.96 (s, 6H). **¹³C NMR** (150 MHz, CD₃CN) δ 200.3, 173.5, 157.1, 141.2, 138.0, 115.3, 113.3, 110.8, 105.3, 39.6, 38.5, 34.5, 27.6, 24.7. **IR** (KBr): ν_{\max} (cm⁻¹) = 3524, 3442, 3129, 1627, 1590, 1400, 1277, 1260, 764, 747. **HRMS** (ESI⁺) calcd for C₁₅H₁₈NaO₃ [M+Na]⁺: 269.1148, Found: 269.1168.

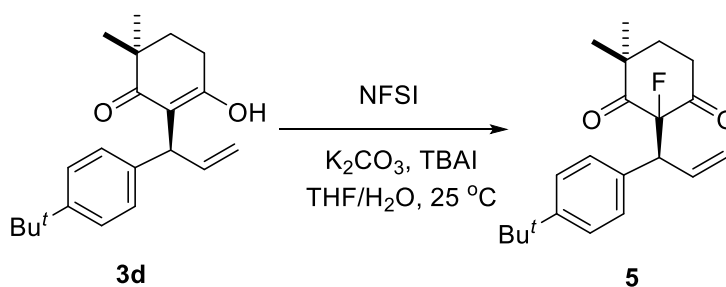


(R)-3-Hydroxy-6,6-dimethyl-2-(1-(thiophen-2-yl)allyl)cyclohex-2-en-1-one 3o, yellow solid; **m.p.:** 99-101°C; 63% yield (16.5 mg); **HPLC ee:** 93% [Daicel CHIRALPAK IG (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 220 nm; t_R = 7.62 (minor), 10.17 (major) min]. $[\alpha]_D^{20}$ = +4.8 (c 1.0, CHCl₃). **¹H NMR** (600 MHz, CD₃CN) δ 7.16 (d, J = 5.4 Hz, 1H), 6.90 (dd, J = 4.8, 3.6 Hz, 1H), 6.75 (dd, J = 3.6, 1.8 Hz, 1H), 6.51 – 6.45 (m, 1H), 5.12 (dt, J = 15.6, 1.2 Hz, 1H), 5.08 – 5.03 (m, 2H), 2.56 (td, J = 6.6, 1.8 Hz, 2H), 1.82 (t, J = 6.6 Hz, 2H), 1.08 (d, J = 3.0 Hz, 6H). **¹³C NMR** (150 MHz, CD₃CN) δ 148.7, 140.0, 127.0, 123.9, 123.7, 116.0, 115.2, 40.3, 39.7, 34.4, 27.2, 24.6. **IR** (KBr): ν_{\max} (cm⁻¹) = 3510, 3442, 3128, 3002, 1647, 1400, 1275, 1261, 761, 742. **HRMS** (ESI⁺) calcd for C₁₅H₁₈NaO₂S [M+Na]⁺: 285.0920, Found: 285.0913.

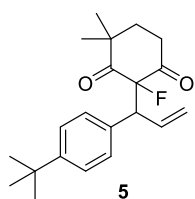


(R)-2-(But-3-en-2-yl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one (3p), white wax; 60% yield (11.6 mg); **HPLC ee:** 91% [Daicel CHIRALCEL OJ-H (0.46 cm × 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; t_R = 6.56 (major), 7.71 (minor) min]. $[\alpha]_D^{20}$ = +24.6 (c 1.0, CHCl₃). **¹H NMR** (600 MHz, DMSO-*d*₆) δ 10.28 (s, 1H), 6.06 – 6.01 (m, 1H), 4.84 (dt, J = 17.4, 1.8 Hz, 1H), 4.76 (dt, J = 10.2, 1.8 Hz, 1H), 3.62 – 3.57 (m, 1H), 2.44 (t, J = 6.6 Hz, 2H), 1.67 (t, J = 6.6 Hz, 2H), 1.11 (d, J = 7.2 Hz, 3H), 0.97 (s, 6H). **¹³C NMR** (150 MHz, DMSO-*d*₆) δ 201.4, 169.7, 143.5, 115.8, 112.1, 34.3, 32.9, 25.3, 25.3, 18.8. **IR** (KBr): ν_{\max} (cm⁻¹) = 3586, 3523, 3442, 3209, 1665, 1608, 1409, 1311, 1215, 1112, 756. **HRMS** (ESI⁺) calcd for C₁₂H₁₈NaO₂ [M+Na]⁺: 217.1199, Found: 217.1195.

3. Procedure for the Synthesis of 5⁴



A round bottom flask equipped with a magnetic stir bar was charged with 2-(1-(4-(tert-butyl)phenyl)allyl)-3-hydroxy-6,6-dimethylcyclohex-2-en-1-one **3d** (31.2 mg, 0.1 mmol), and then a mixture of tetrahydrofuran and water (2.0 mL) in 7/3 proportion was added via a glass syringe and followed by the addition of TBAI (3.7 mg, 0.01 mmol) and K₂CO₃ (34.5 mg, 0.25 mmol). The resulting reaction mixture was stirred for 30 min at room temperature and then NFSI (34.7 mg, 0.11 mmol) was added. The reaction was allowed to stir for another 2 h, then quenched with water (5.0 mL) and extracted with ethyl acetate (3 x 5.0 mL). The combined organic layers were washed with brine and dried over anhydrous Na₂SO₄, filtered and concentrated. The crude product was purified by flash column chromatography over silica gel using 5% ethyl acetate in petroleum ether as eluent to afford the pure product **5** in 86% yield.



2-(1-(4-(Tert-butyl)phenyl)allyl)-2-fluoro-4,4-dimethylcyclohexane-1,3-dione (5), white solid; **m.p.:** 102-104°C; 86% yield (28.4 mg); **HPLC** *ee*: 99% [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 90/10; flow rate = 1.0 mL/min; detection wavelength = 254 nm; *t_R* = 5.478 (major), 7.106 (minor) min]. [α]_D²⁰ = +32.5 (c 1.0, CHCl₃). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.24 – 6.15 (m, 1H), 5.22 (d, *J* = 10.0 Hz, 1H), 5.08 (d, *J* = 17.2 Hz, 1H), 4.12 (dd, *J* = 28.0, 8.8 Hz, 1H), 2.65 (t, *J* = 8.0 Hz, 2H), 2.12 – 2.04 (m, 1H), 1.78 – 1.72 (m, 1H), 1.32 (s, 3H), 1.28 (s, 9H), 1.13 (s, 3H). **¹³C NMR** (100 MHz, Chloroform-*d*) δ 205.3 (d, *J* = 14.8 Hz), 200.6 (d, *J* = 15.8 Hz), 151.1, 133.3 (d, *J* = 6.0 Hz), 132.6, 128.2 (d, *J* = 2.1 Hz), 125.9, 119.0, 103.7 (d, *J* = 208.3 Hz), 53.9 (d, *J* = 21.3 Hz), 44.4, 34.8, 34.5, 31.2, 30.8, 25.9, 25.4. **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -174.1. **IR** (KBr): ν_{max} (cm⁻¹) = 3652, 3542, 3212, 3098, 1675, 1623, 1521, 1476, 1298, 1279, 765, 749. **HRMS** (ESI⁺) calcd for C₂₁H₂₇FNao₂ [M+Na]⁺: 353.1887, Found: 353.1908.

4. References

1. a) A. Alexakis, S. Rosset, J. Allamand, S. March, F. Guillen, C. Benhaim, *Synlett*. **2001**, 9, 1375. b) R. Naasz, L. A. Arnold, A. J. Minnaard, B. L. Feringa, *Angew. Chem. Int. Ed.* **2001**, 40, 927. c) D. Polet, A. Alexakis, *Synthesis*. **2004**, 15, 2586.
3. P. G. M. Wuts, S. W. Ashford, A. M. Anderson, J. R. Atkins, *Org. Lett.* **2003**, 5, 1483.
4. D. T. W. Chu, S. N. Huckin, *Can. J. Chem.* **1980**, 58, 138.
5. K. Jain, K. Das. *Synthetic Communications*. **2018**, 48, 1.

5. X-ray Crystallographic Information of 3j

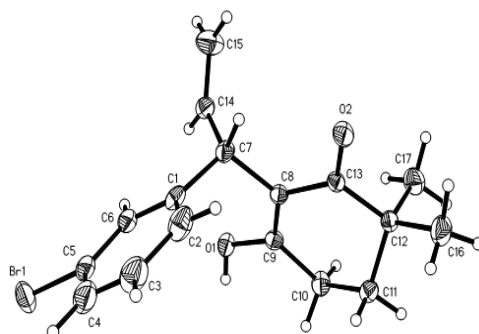


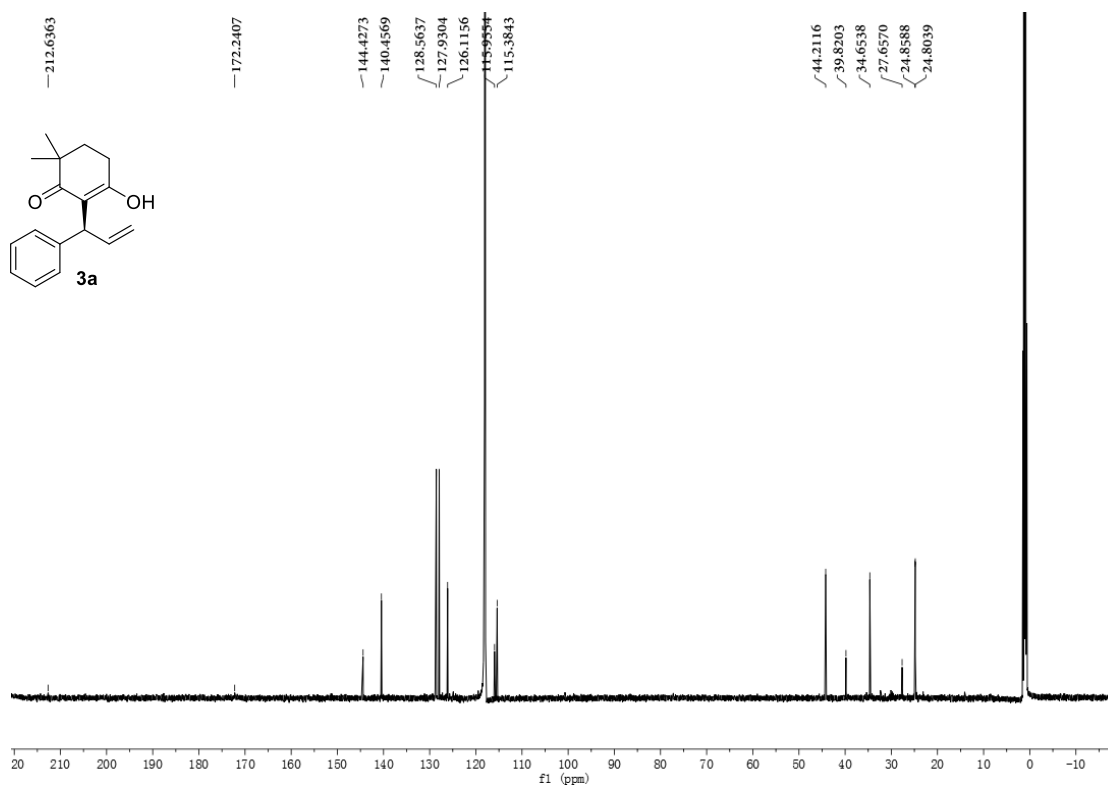
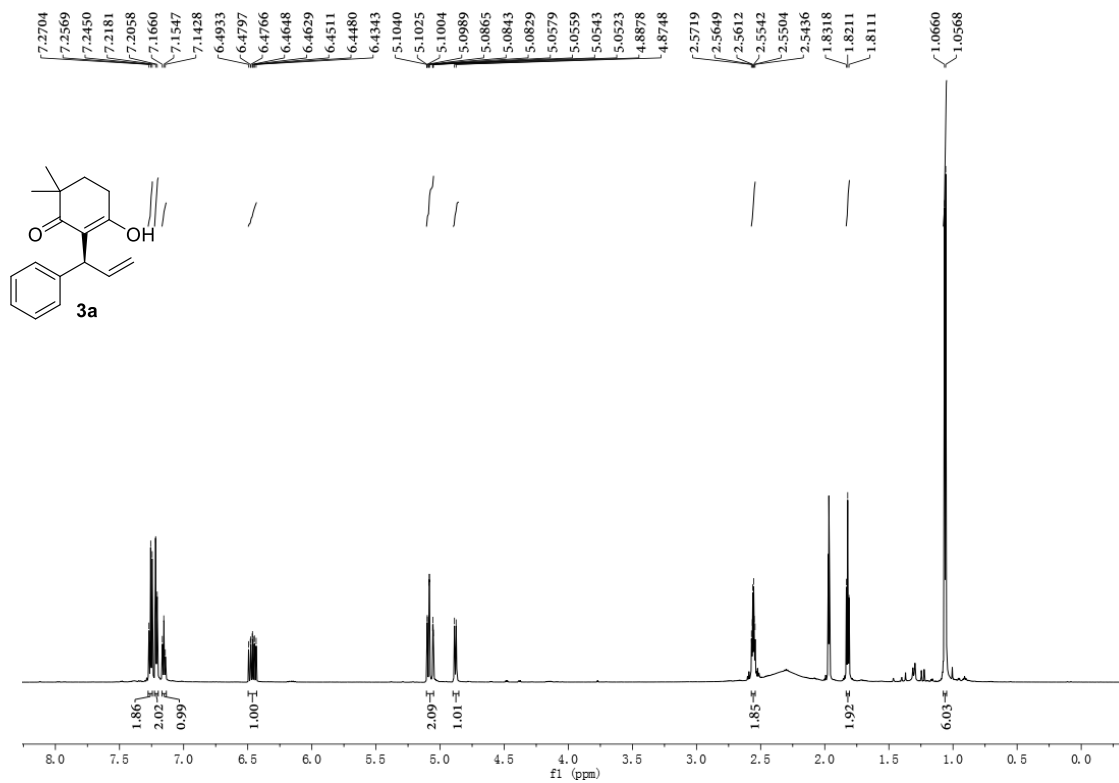
Table 1. Crystal data and structure refinement for compound 3j. (CCDC : 2098319)

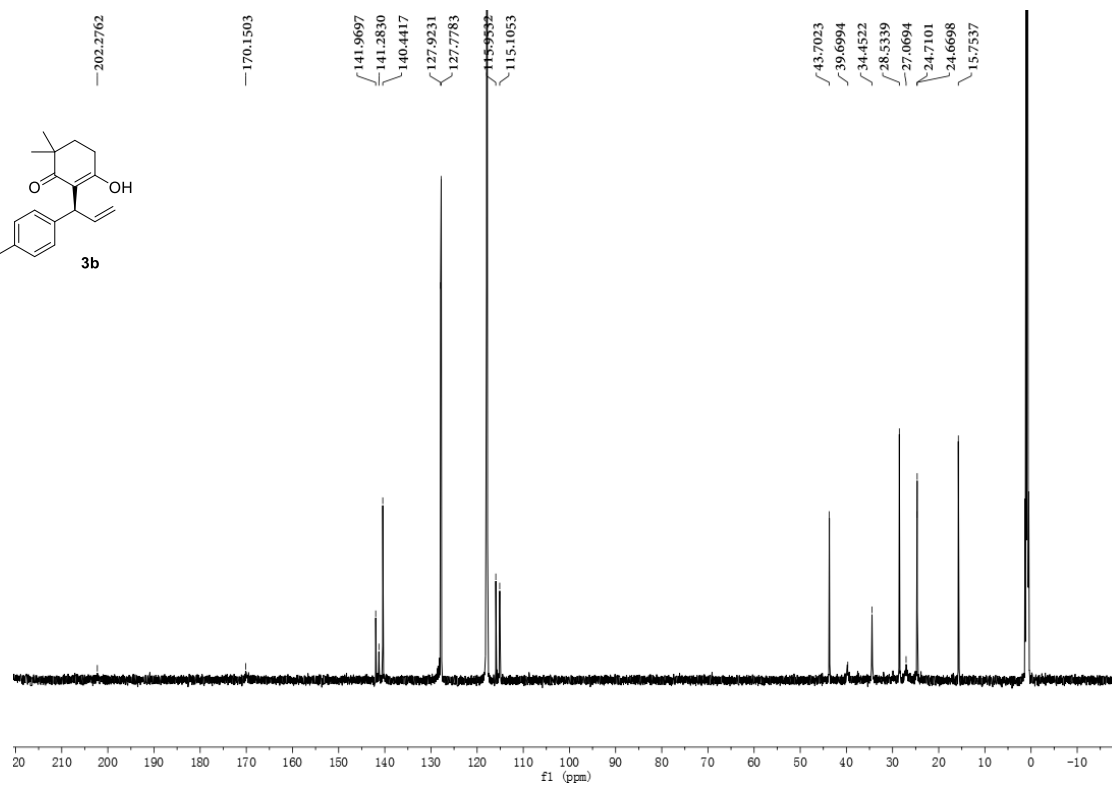
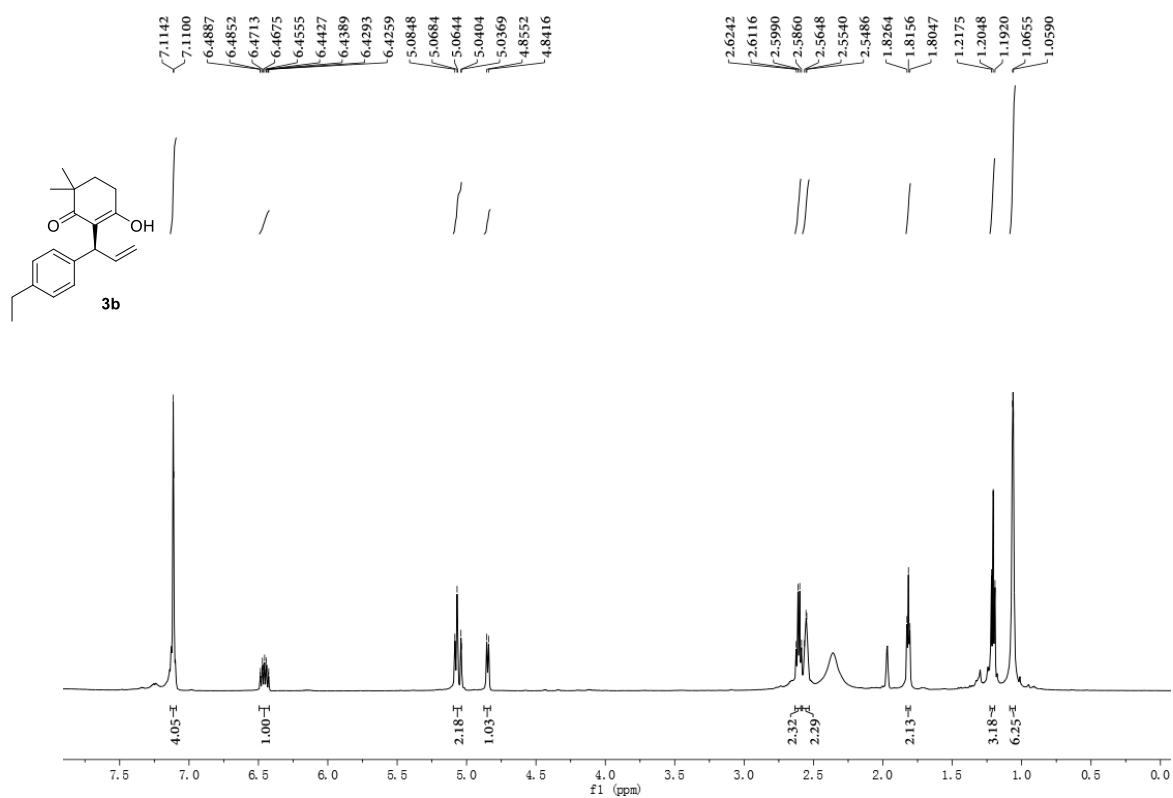
CCDC 2098319 (**3j**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

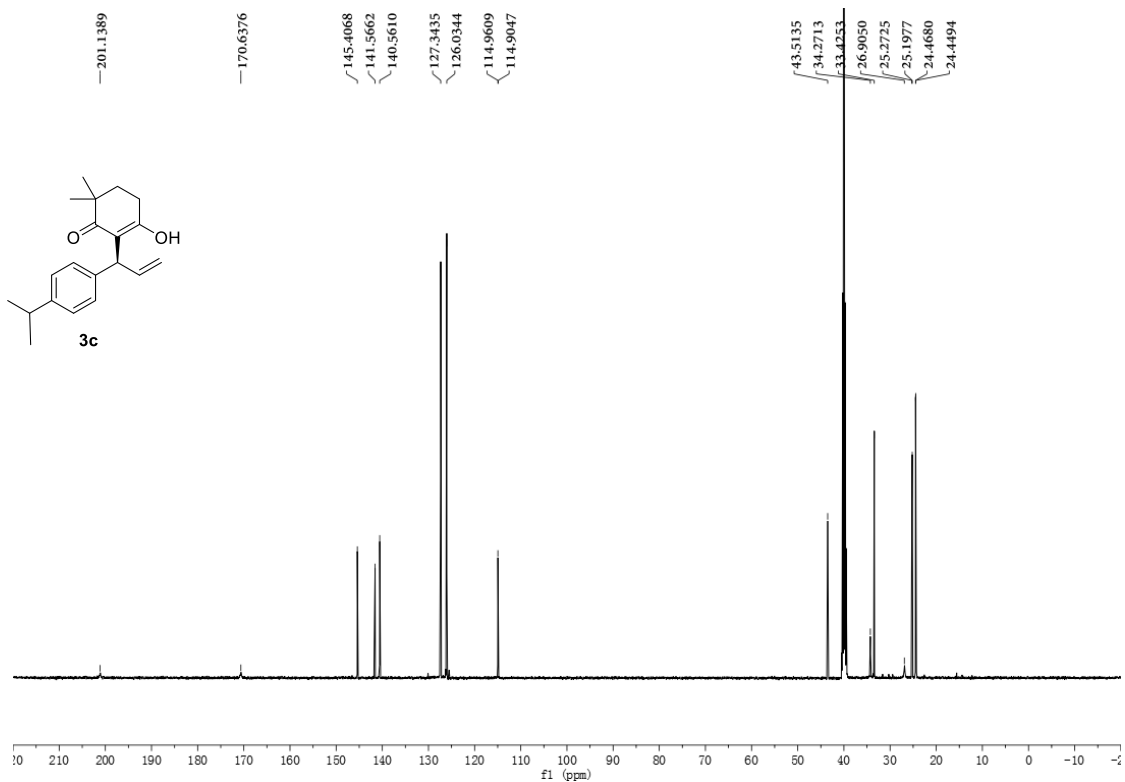
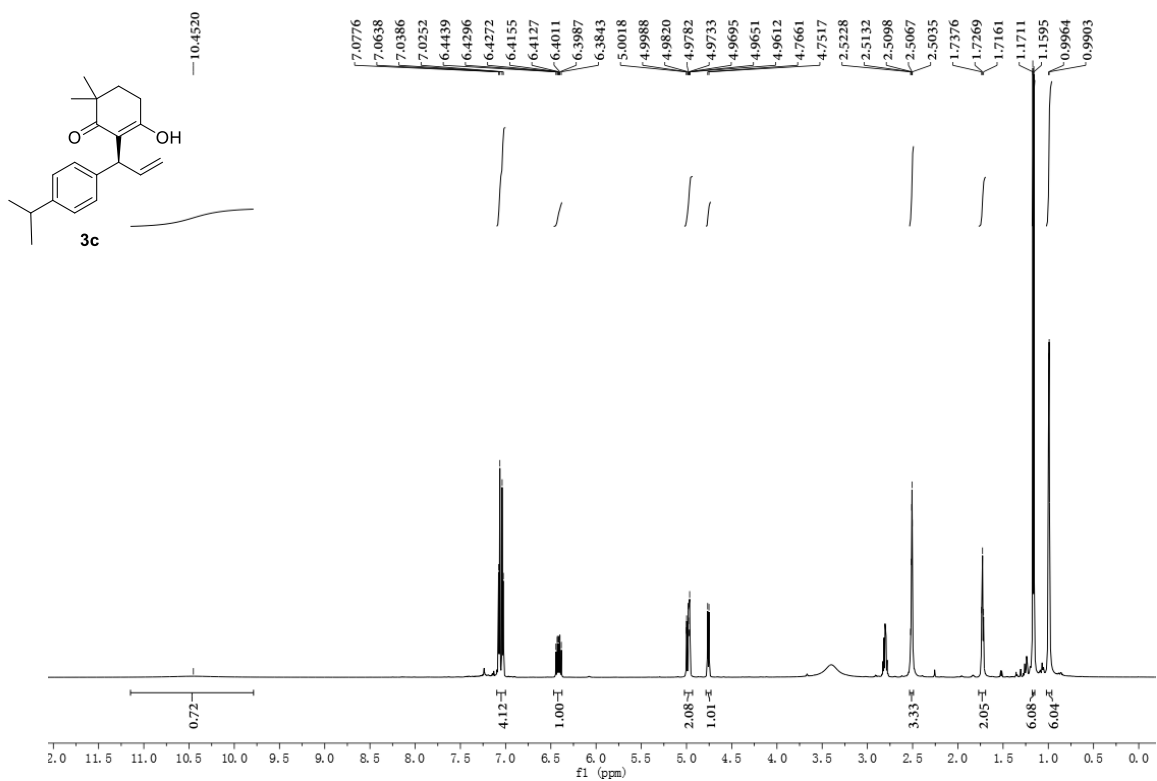
Empirical formula	C ₁₇ H ₁₉ BrO ₂
Formula weight	335.23
Temperature [K]	288(2)
Crystal system	monoclinic
Space group (number)	<i>P</i> 2 ₁ (4)
<i>a</i> [Å]	10.4035(3)
<i>b</i> [Å]	13.6608(4)
<i>c</i> [Å]	11.3206(4)
α [°]	90
β [°]	97.2470(10)
γ [°]	90
Volume [Å ³]	1596.03(9)
<i>Z</i>	4
ρ_{calc} [gcm ⁻³]	1.395
μ [mm ⁻¹]	2.574
<i>F</i> (000)	688
Crystal size [mm ³]	0.220×0.210×0.080
Crystal colour	colourless
Crystal shape	block
Radiation	MoK α (λ =0.71073 Å)
2 θ range [°]	5.69 to 50.04 (0.84 Å)
Index ranges	-12 ≤ <i>h</i> ≤ 12 -16 ≤ <i>k</i> ≤ 16 -13 ≤ <i>l</i> ≤ 13
Reflections collected	26284

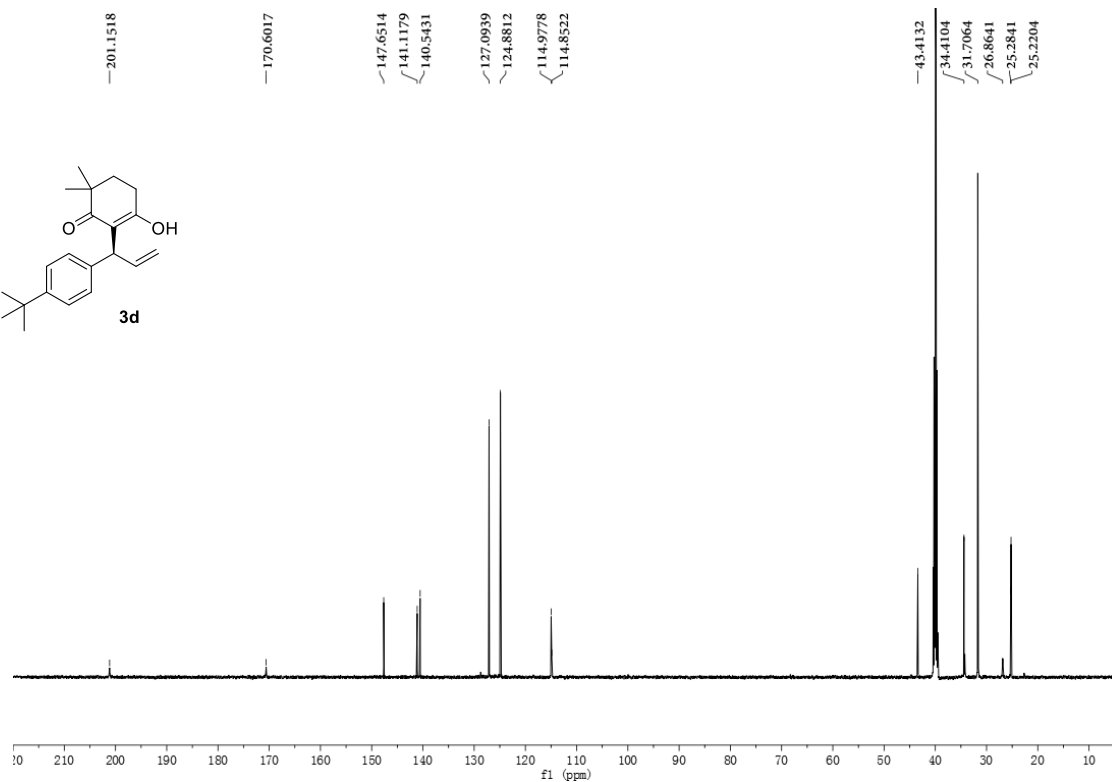
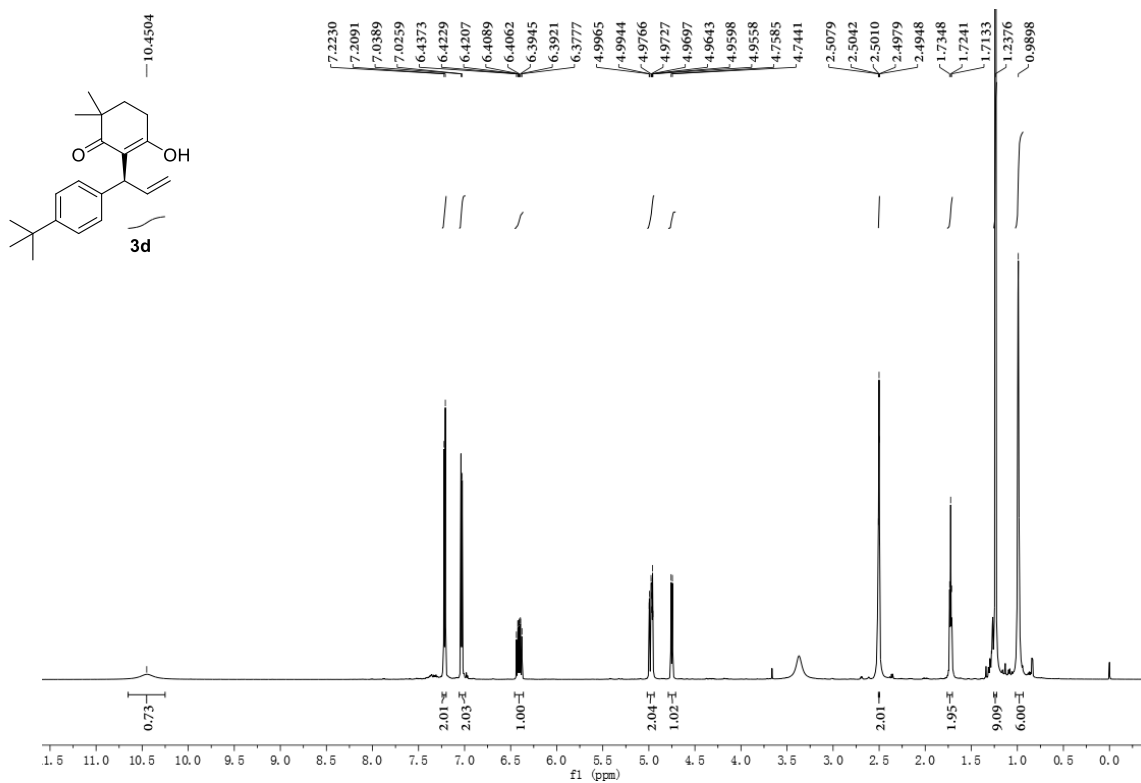
Independent reflections	5605
	$R_{\text{int}} = 0.0286$
	$R_{\text{sigma}} = 0.0452$
Completeness to	99.7 %
$\Theta = 25.019^\circ$	
Data / Restraints / Parameters	5605/395/431
Goodness-of-fit on F^2	1.065
Final R indexes	$R_1 = 0.0553$
$[I \geq 2\sigma(I)]$	$wR_2 = 0.1612$
Final R indexes	$R_1 = 0.0674$
[all data]	$wR_2 = 0.1715$
Largest peak/hole [$\text{e}\text{\AA}^{-3}$]	1.18/-0.68
Flack X parameter	0.020(5)

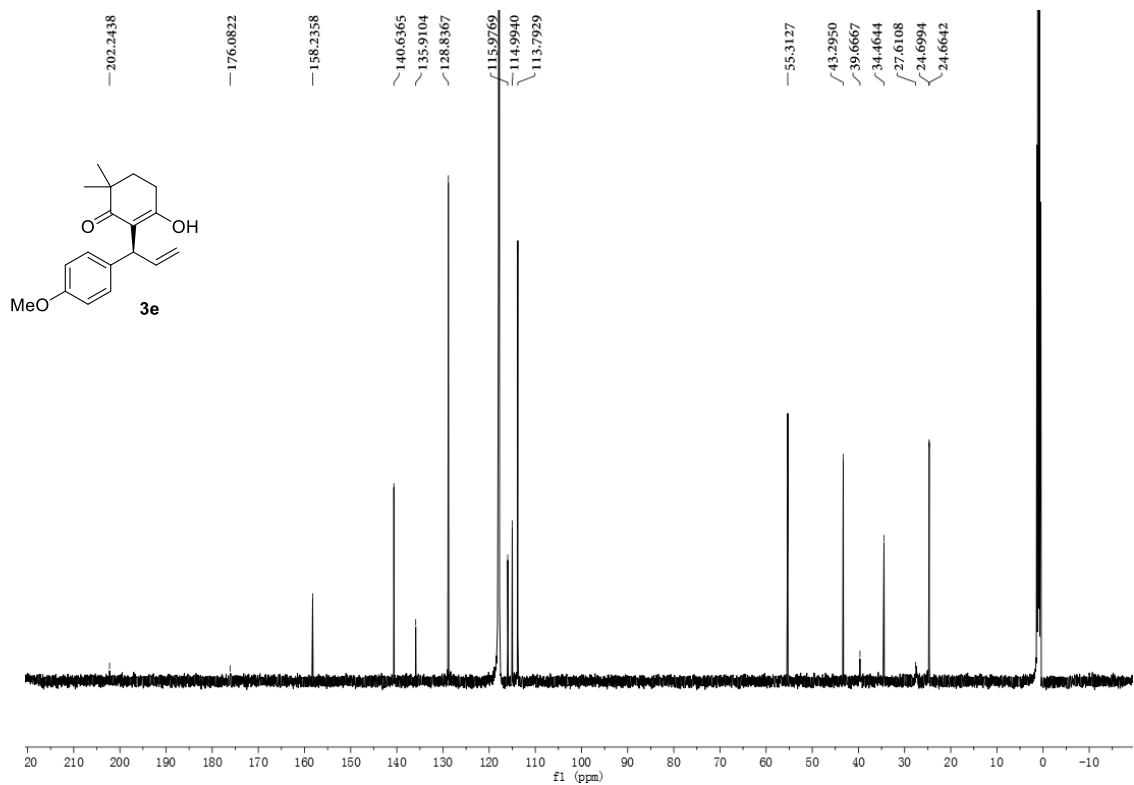
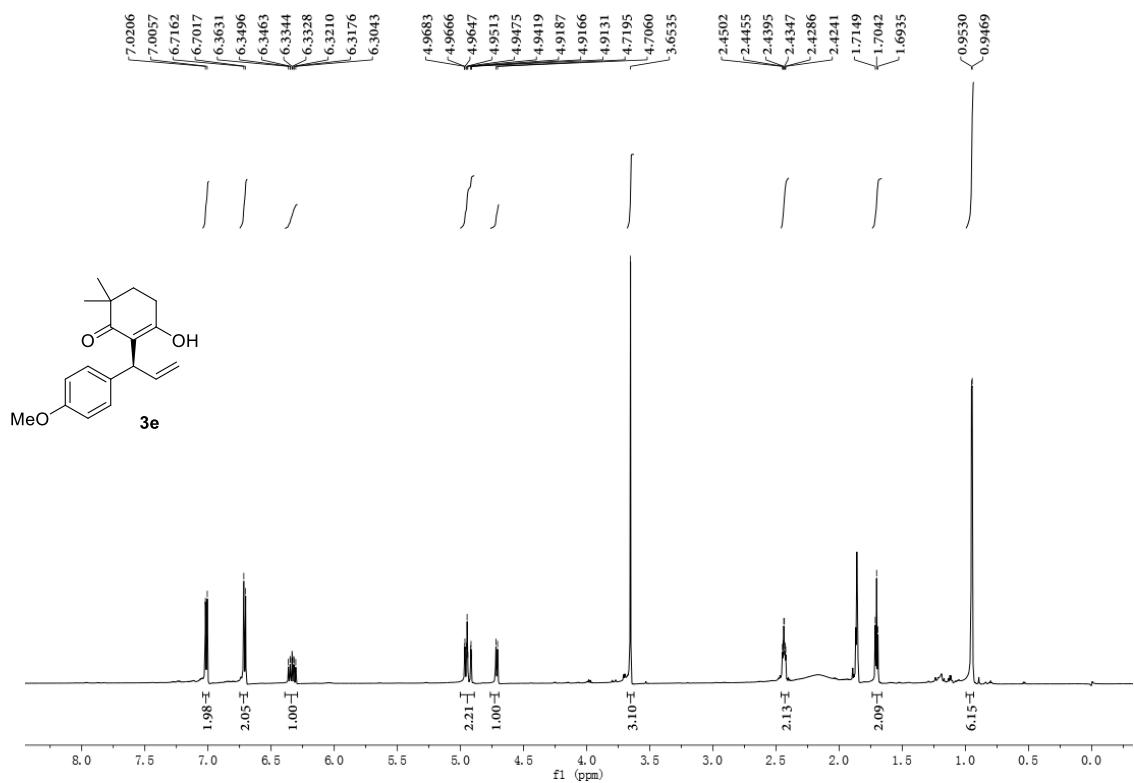
6. Copies of NMR spectra of compounds 3 and 5

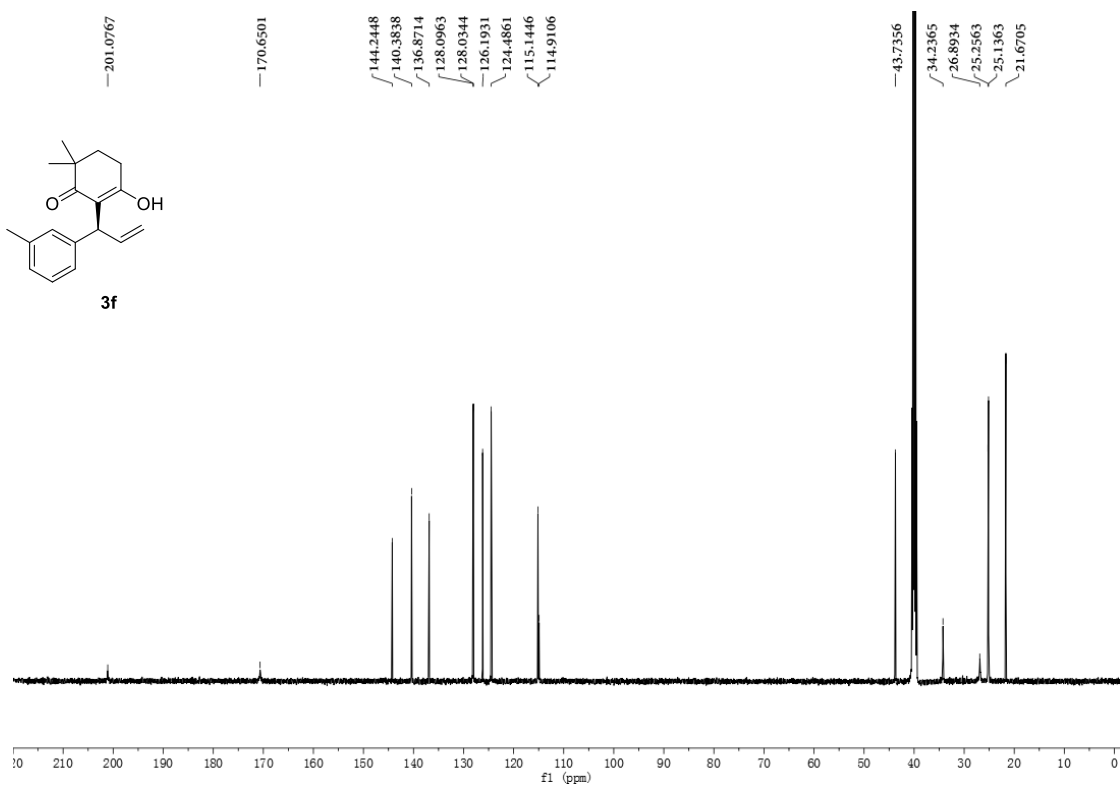
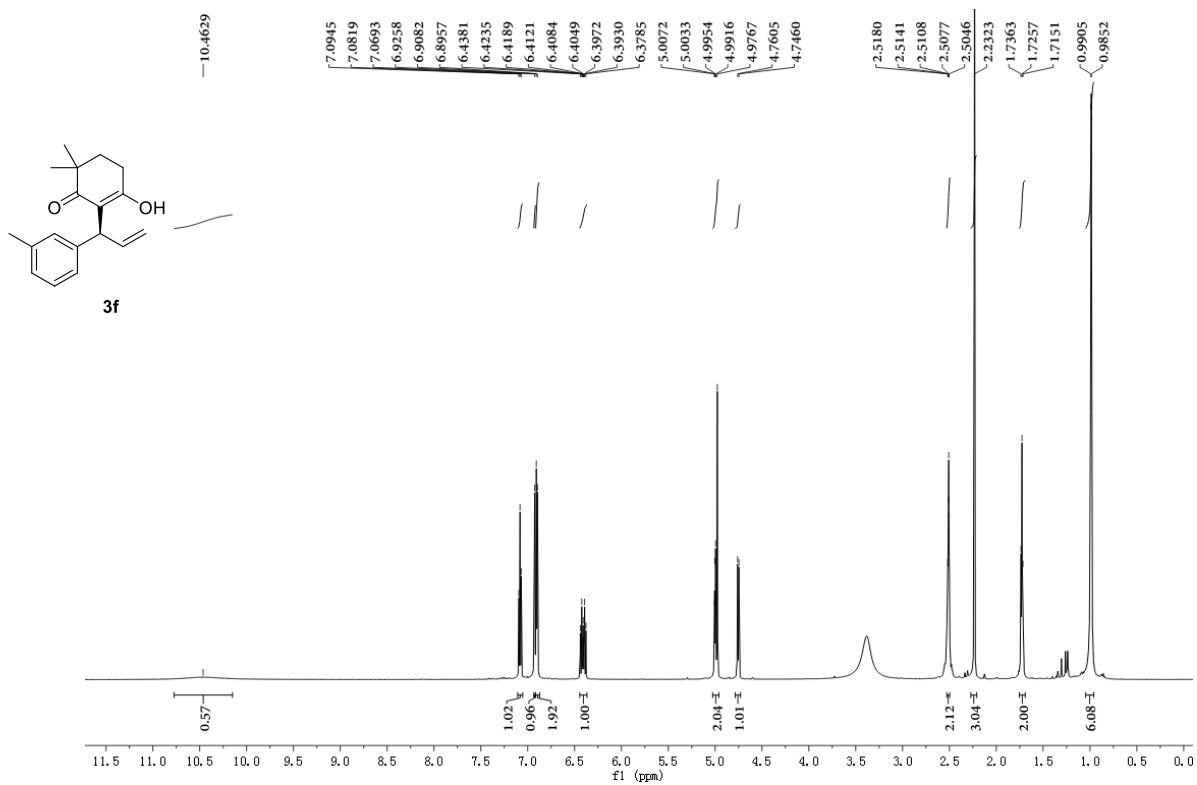


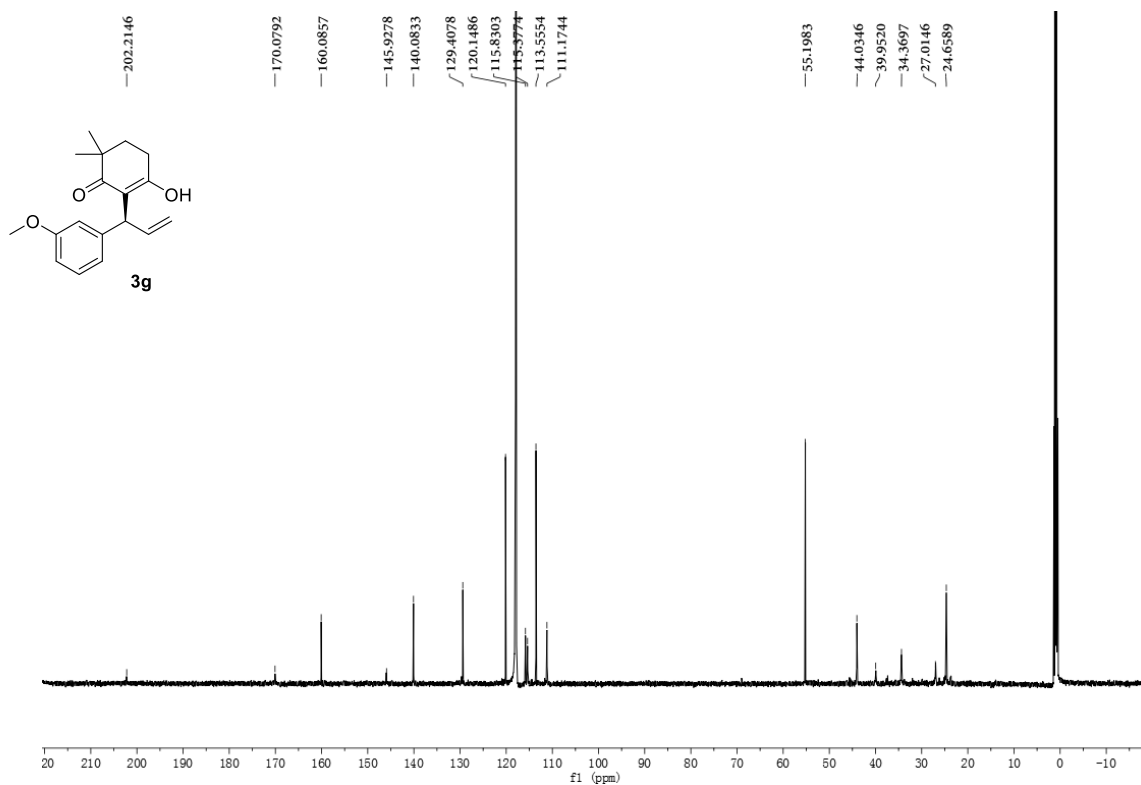
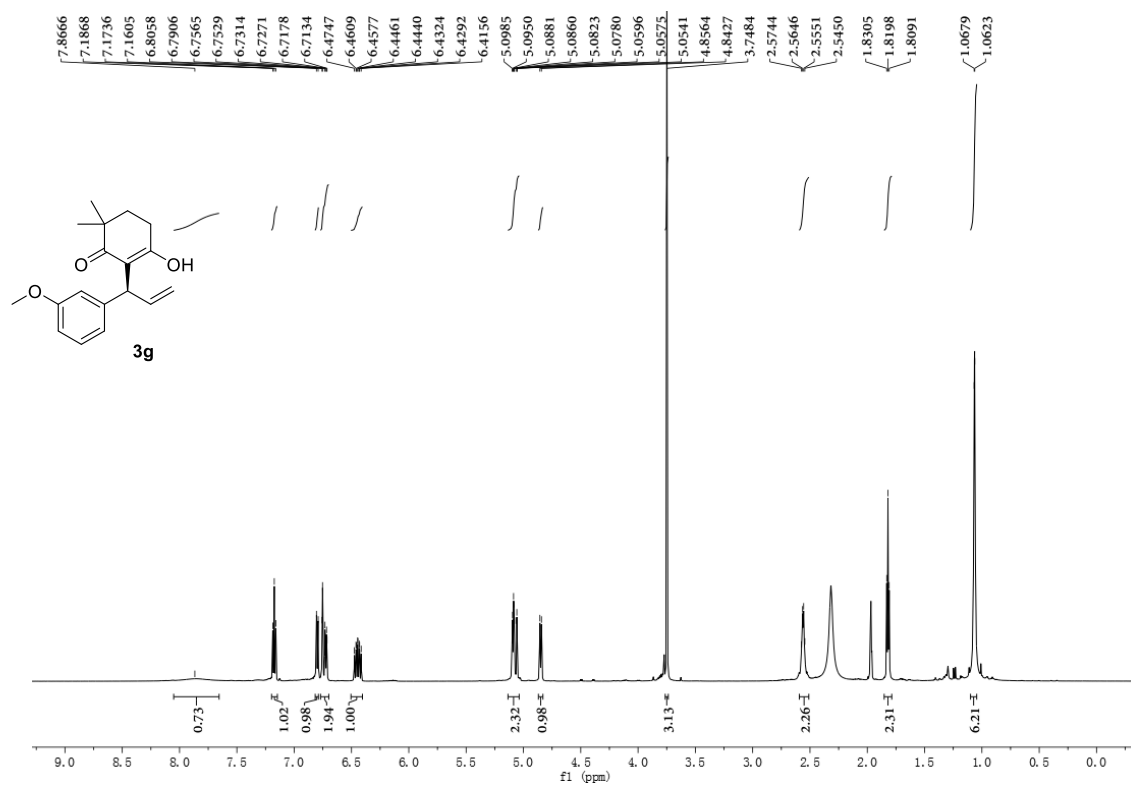


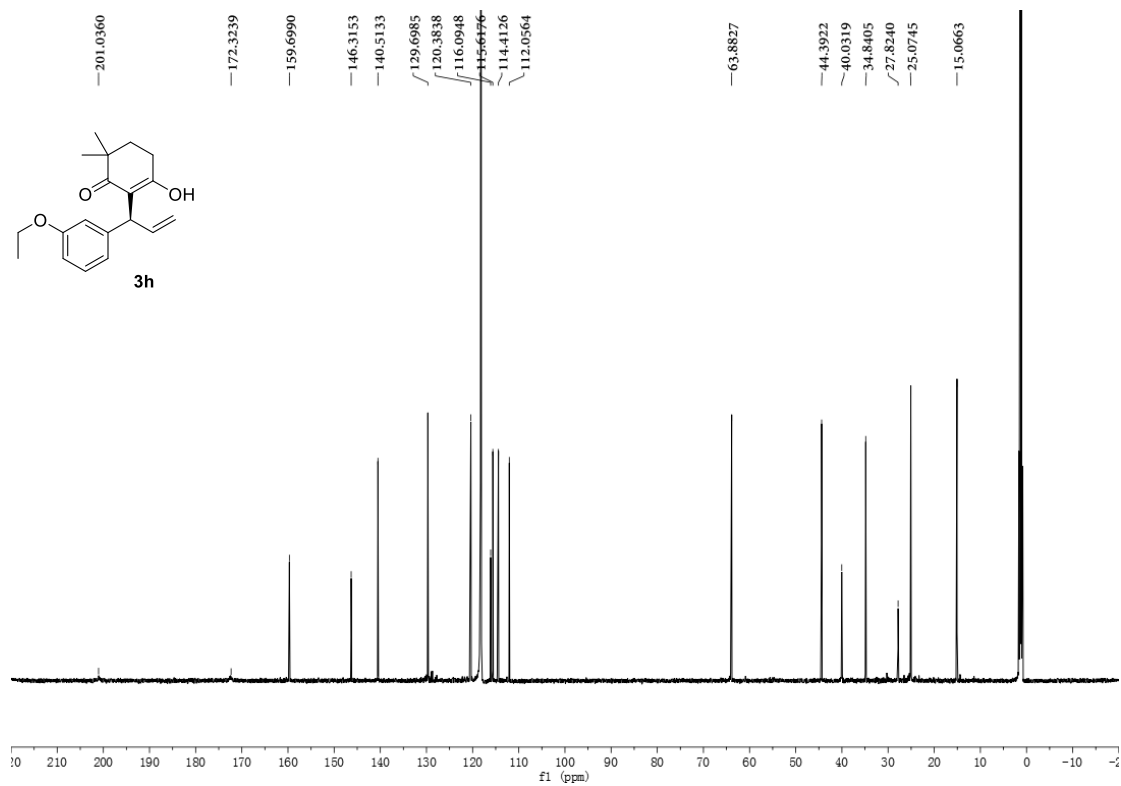
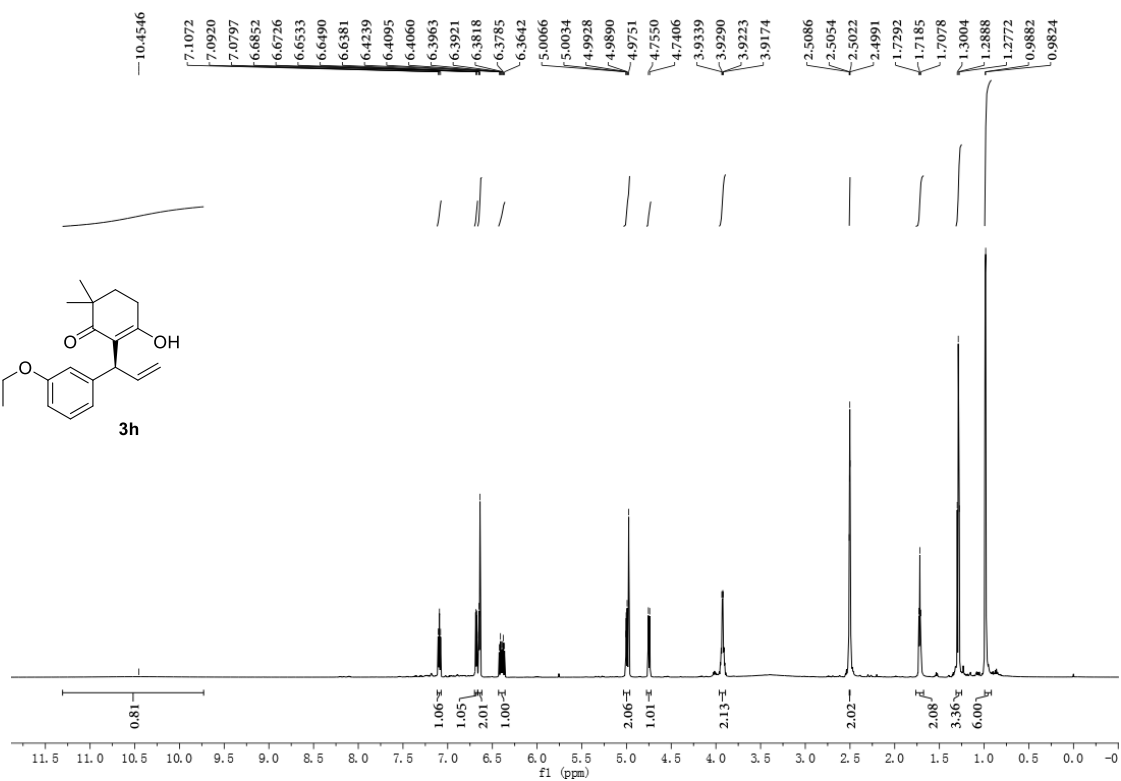


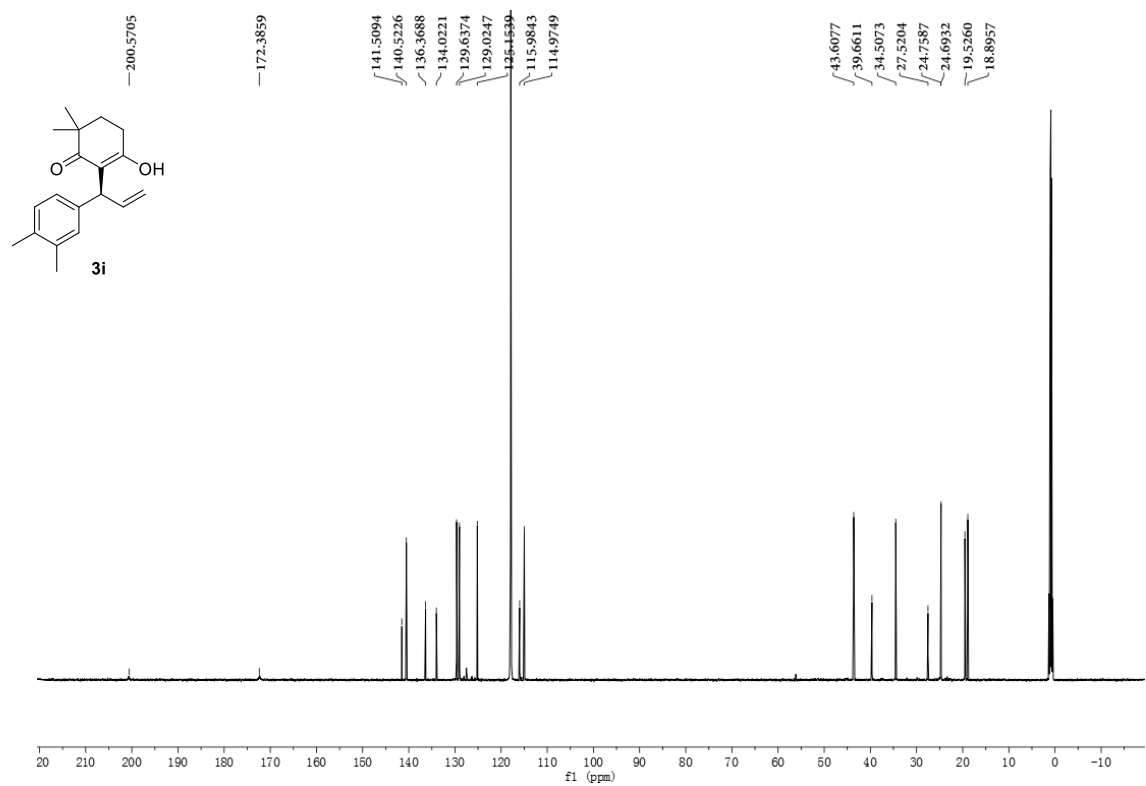
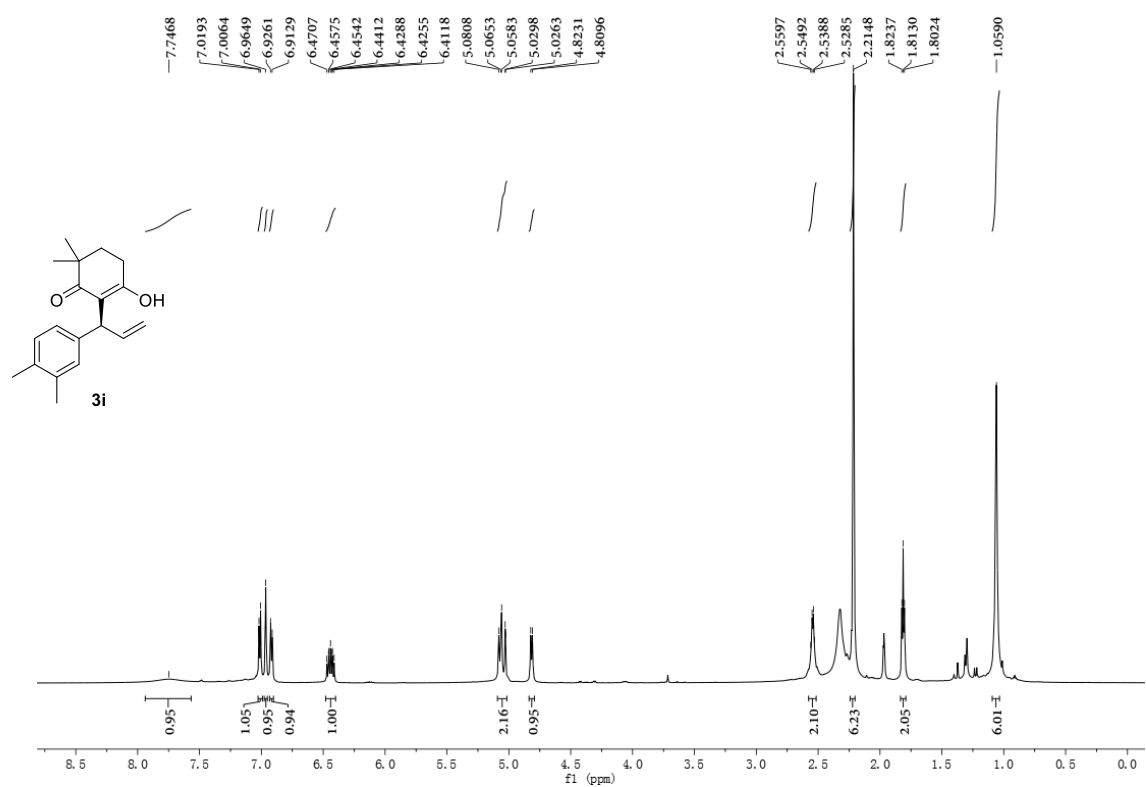


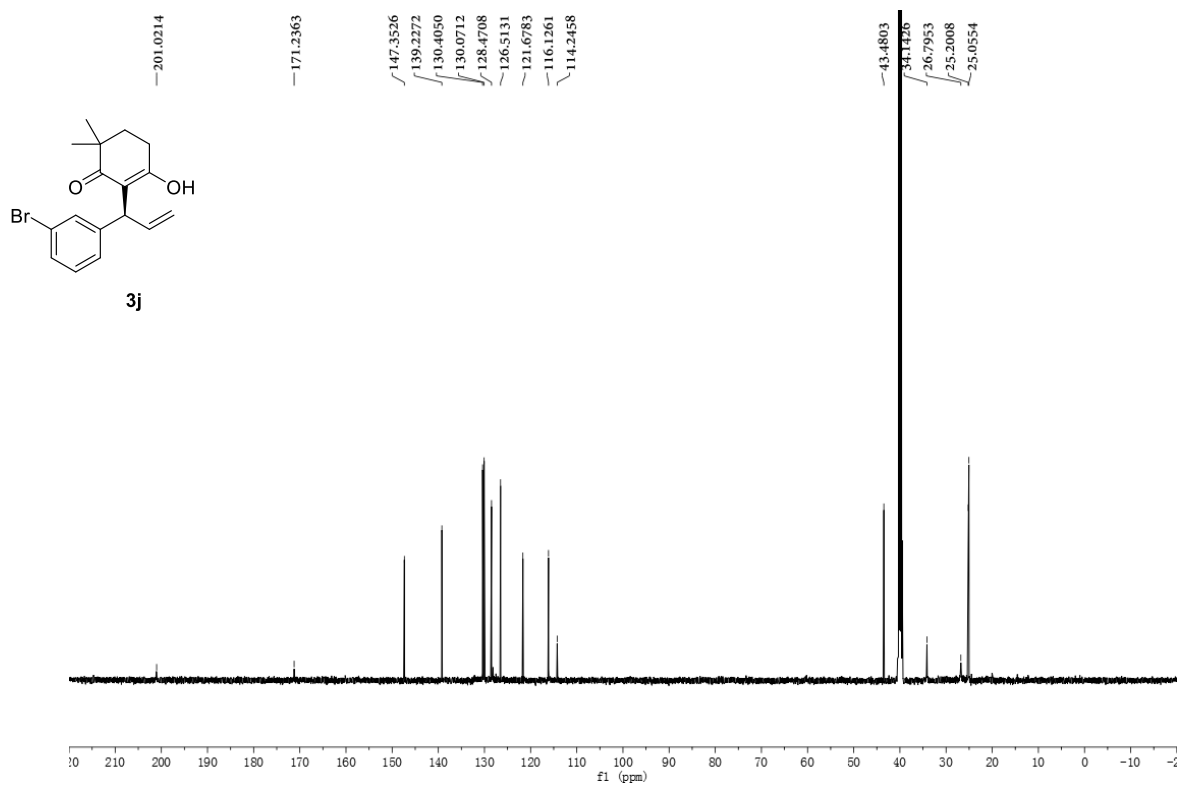
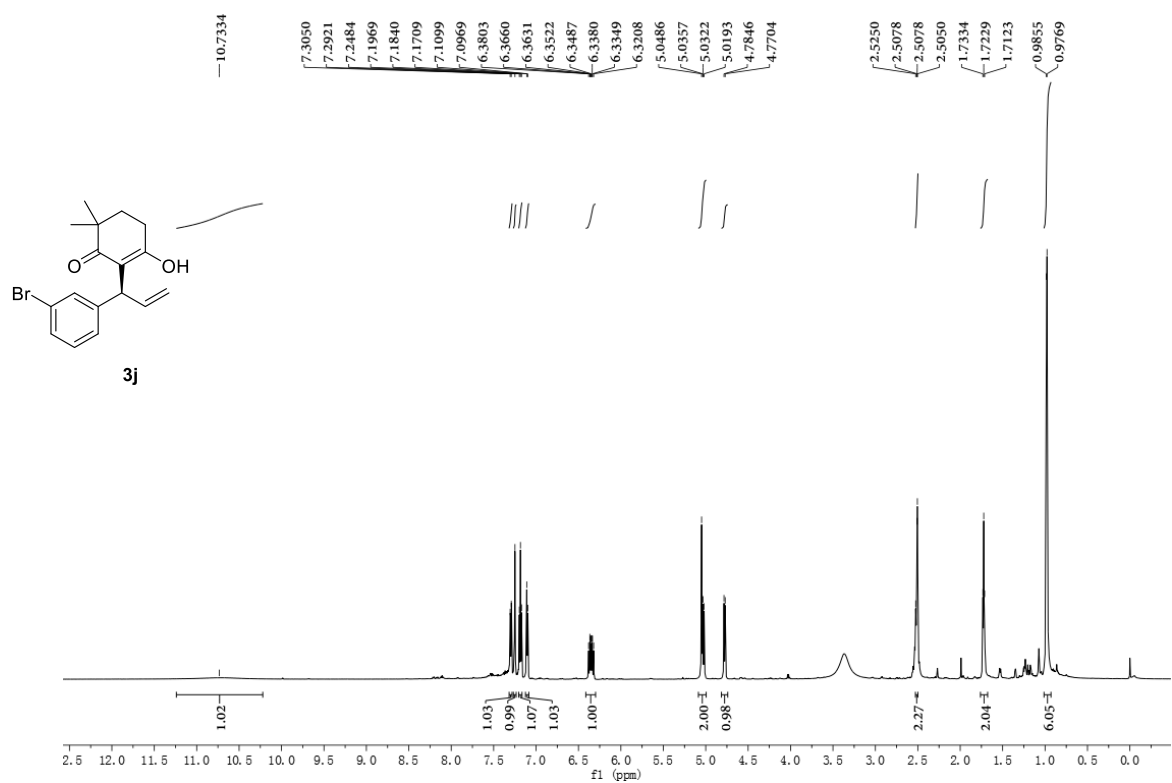


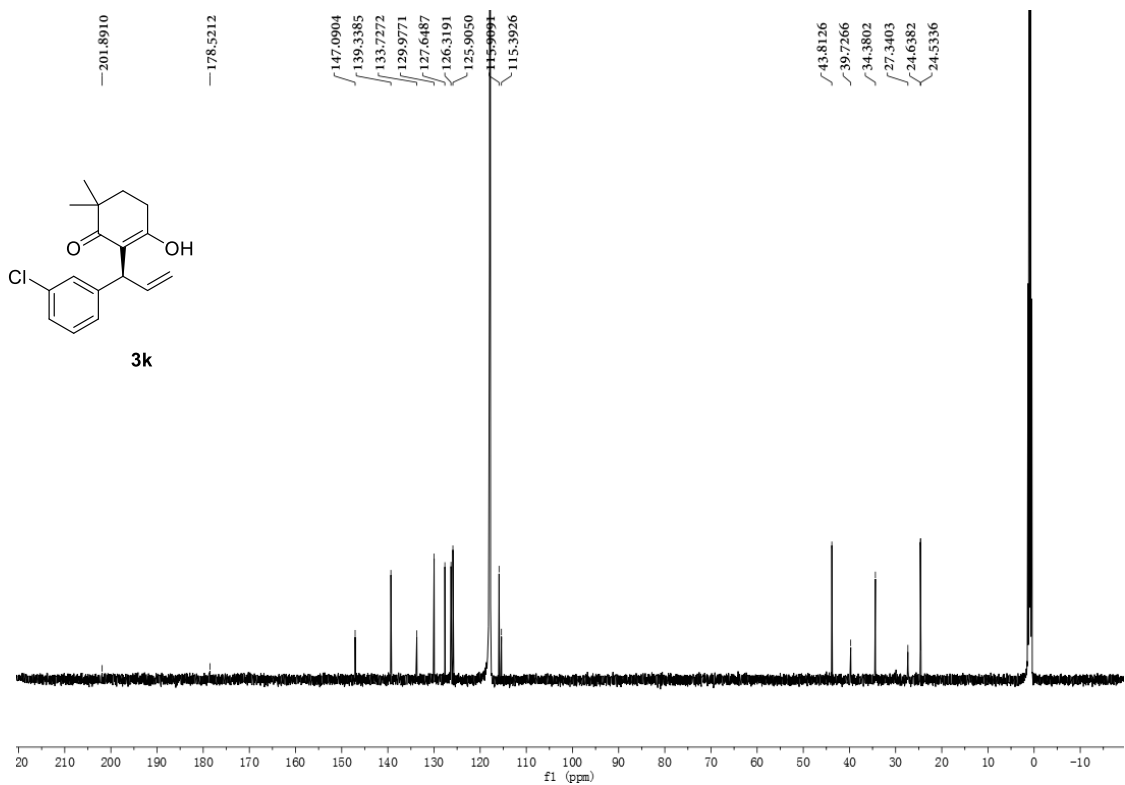
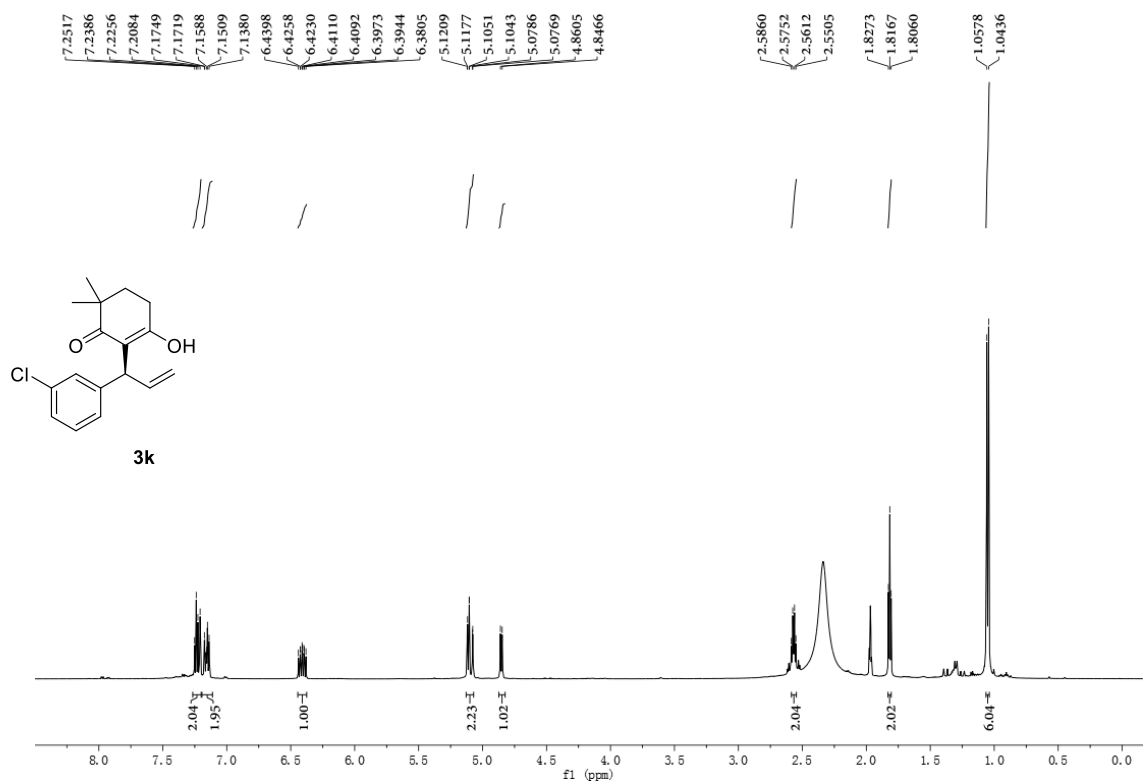


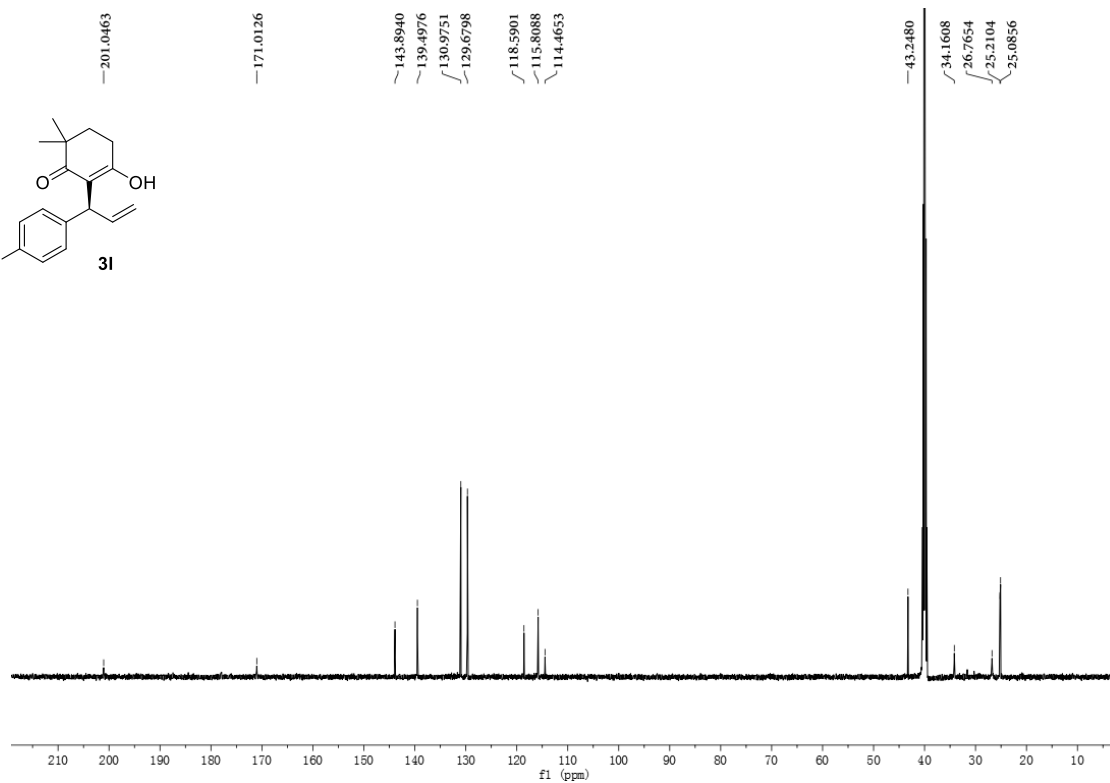
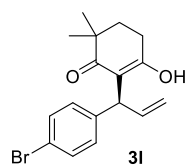
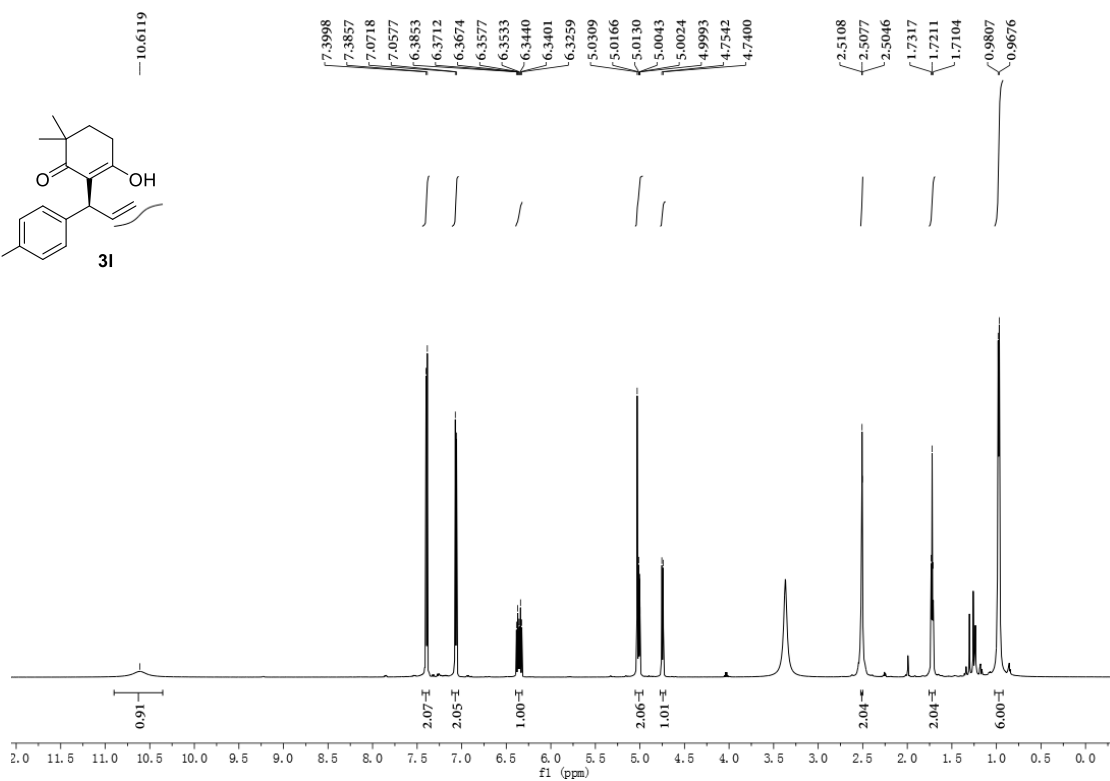
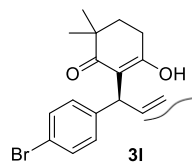


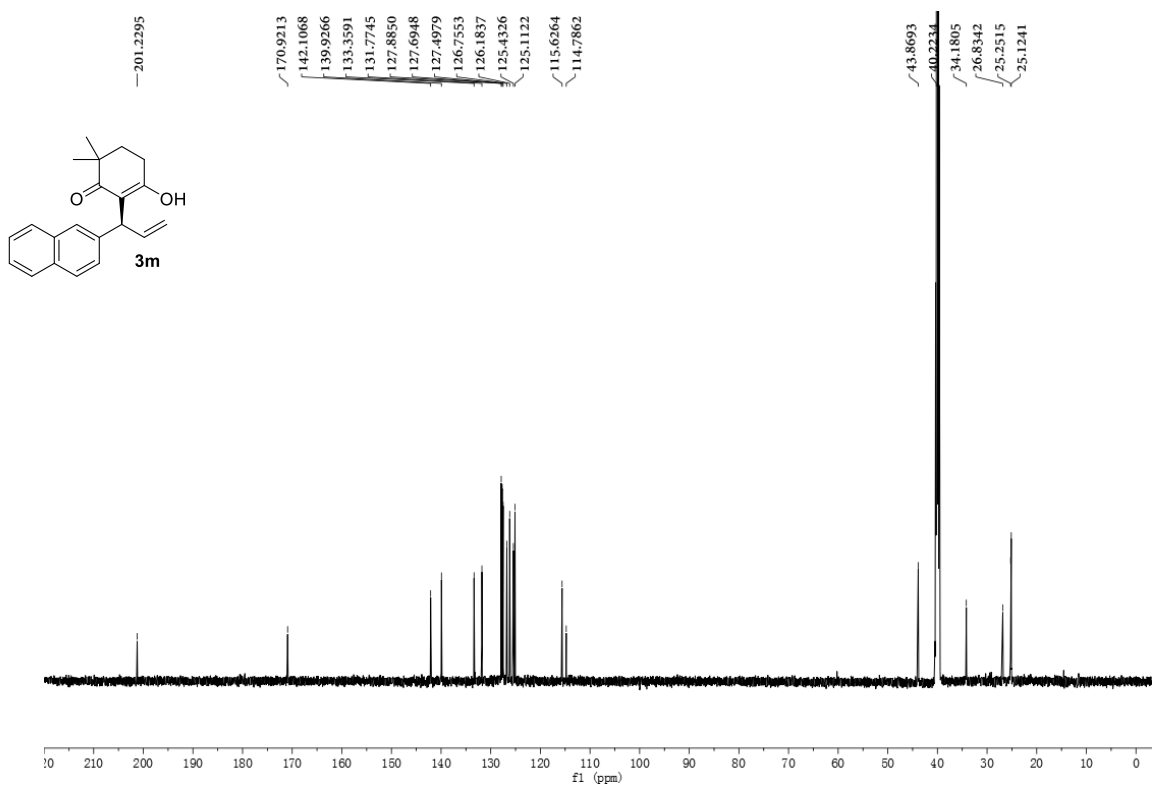
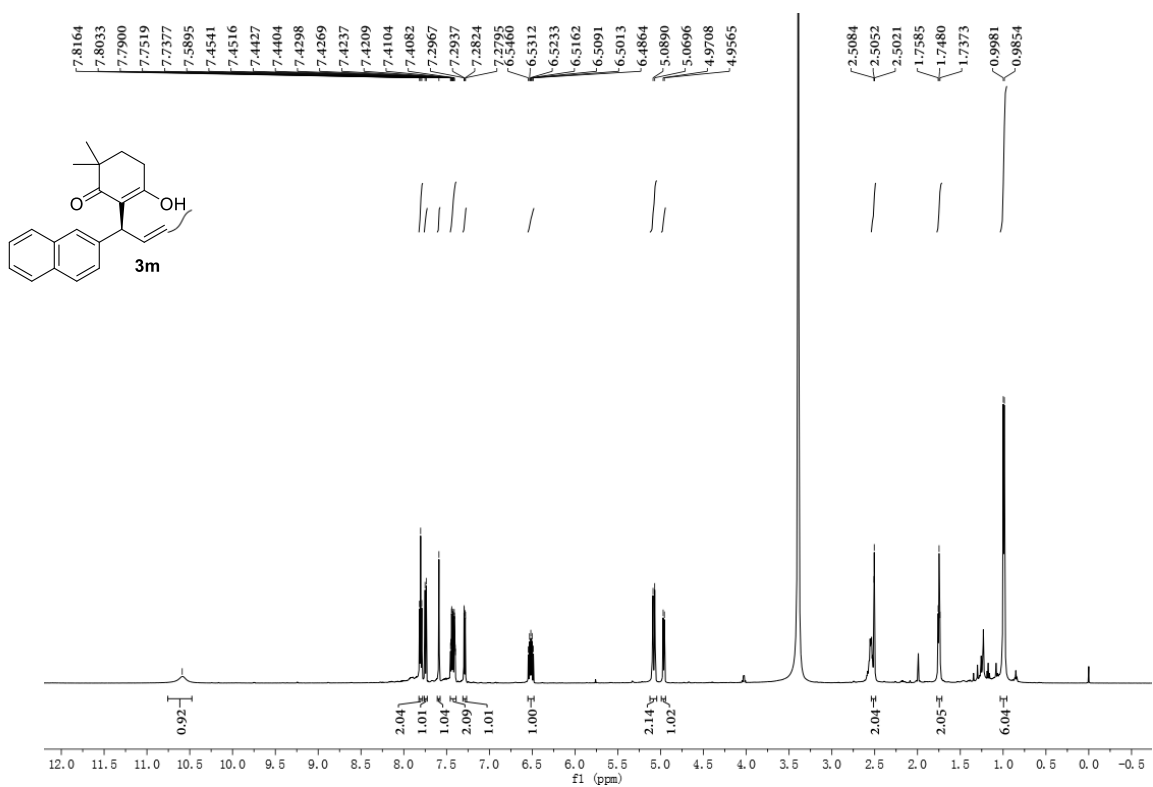


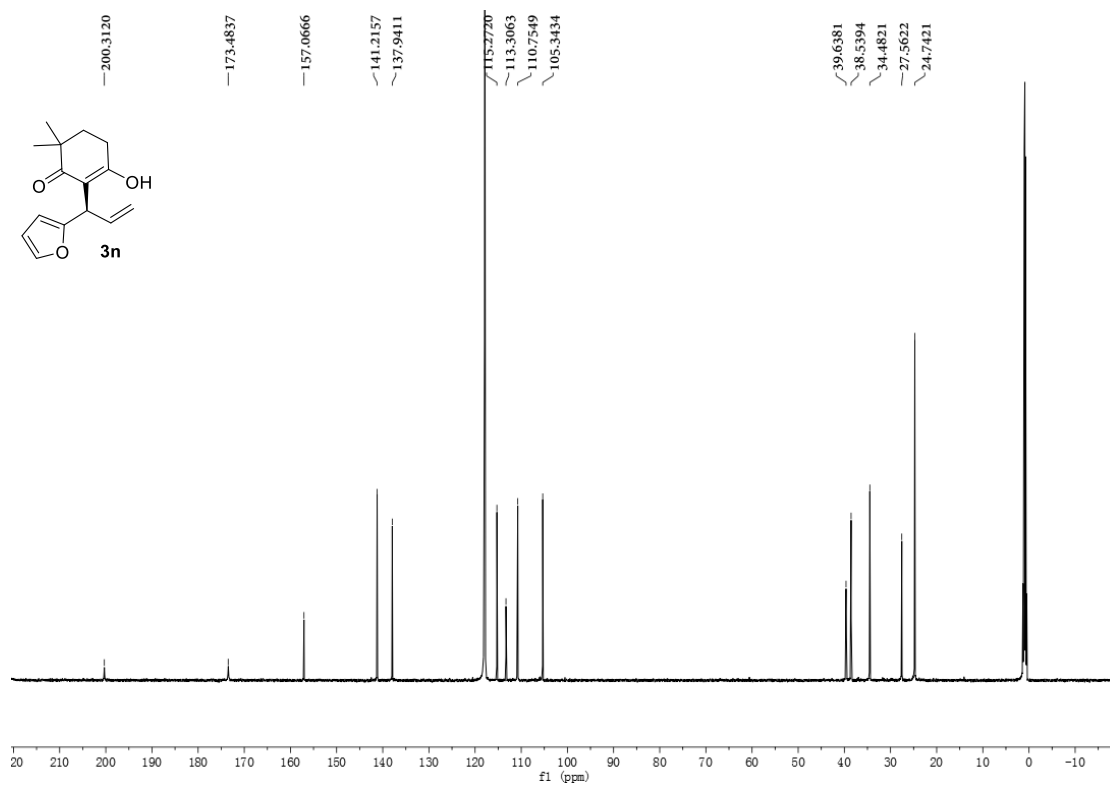
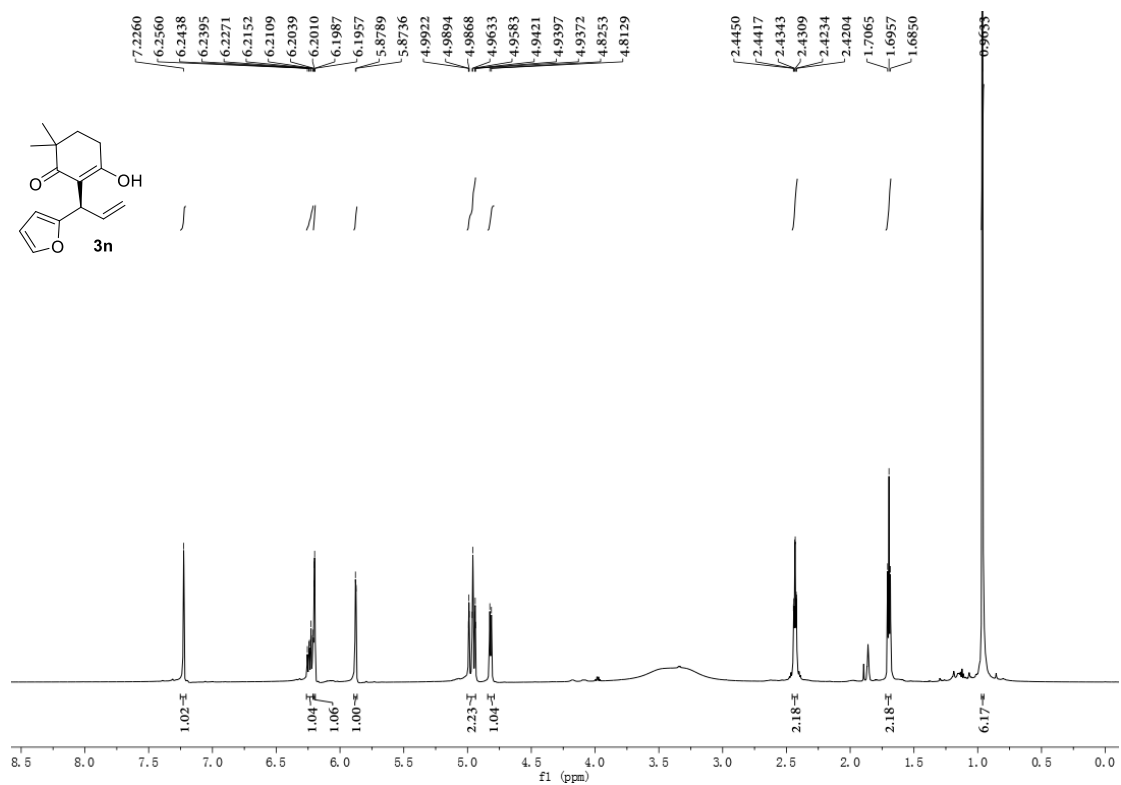


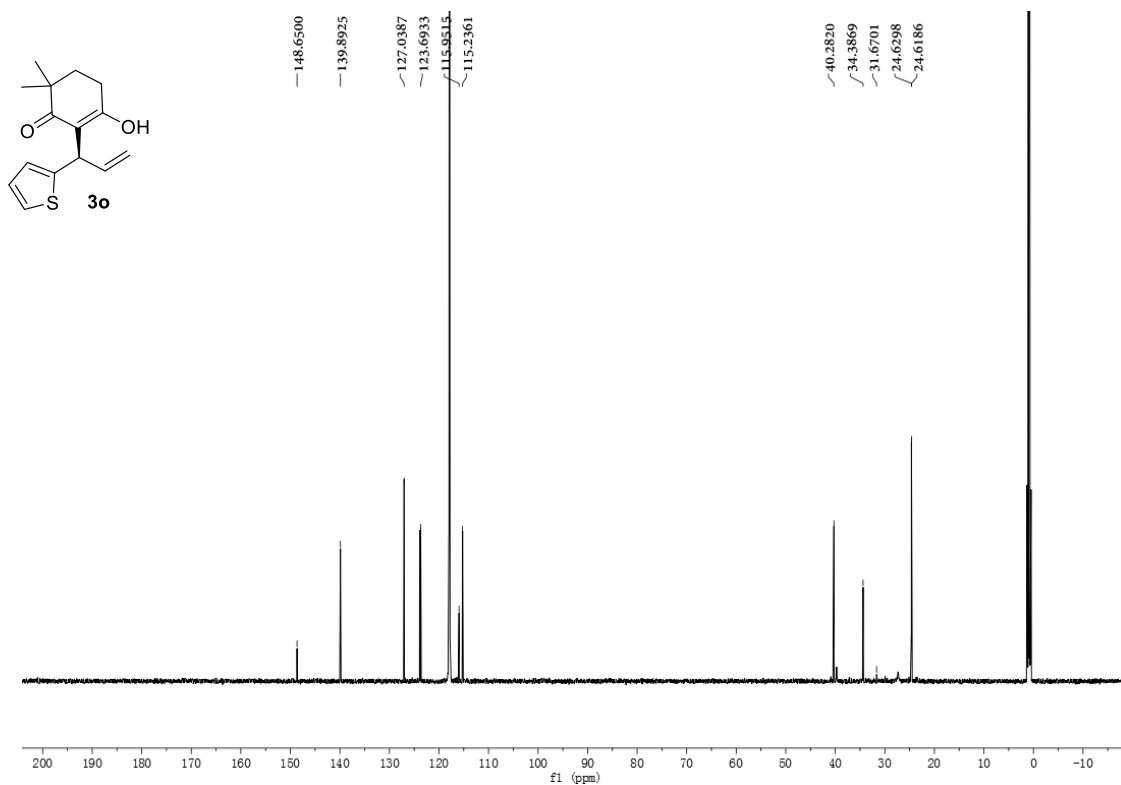
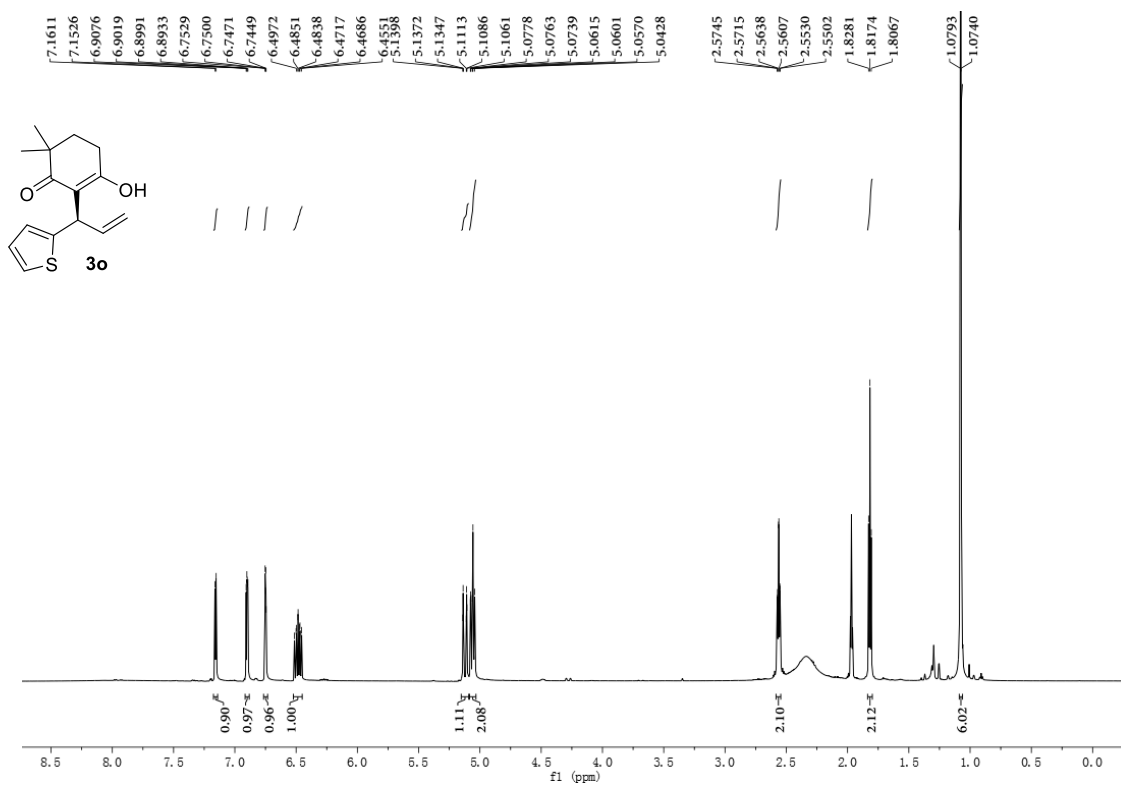


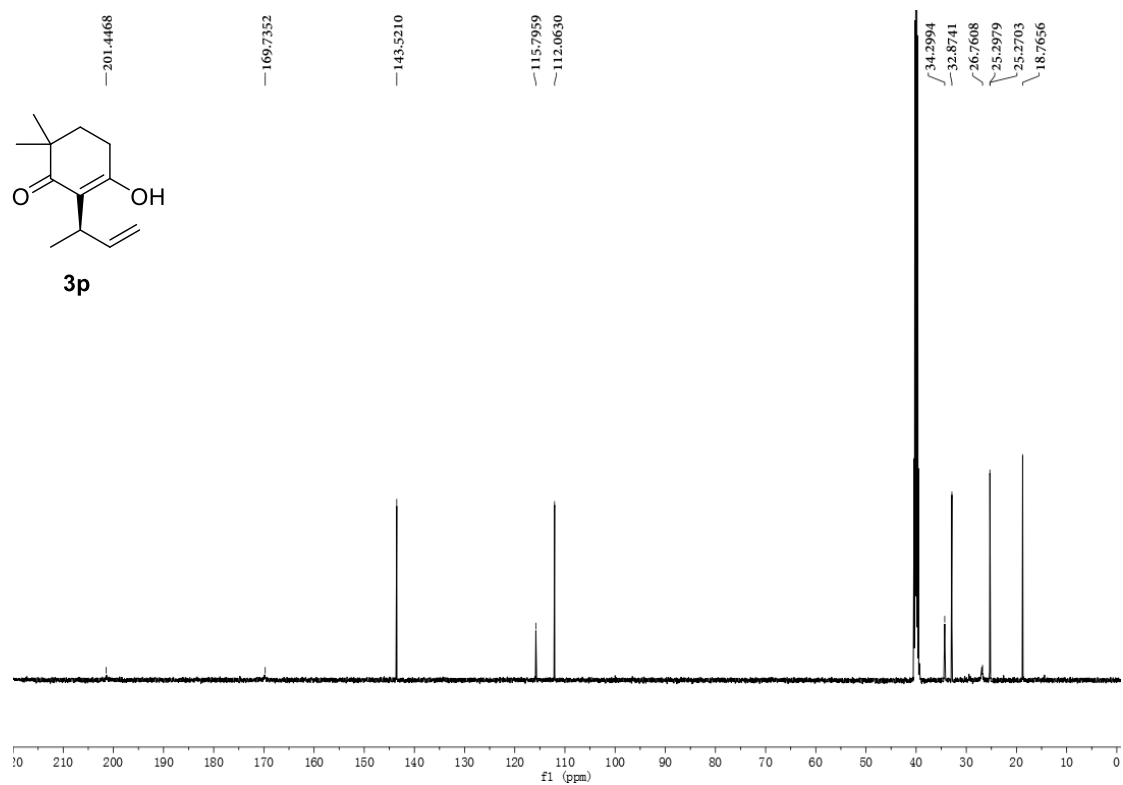
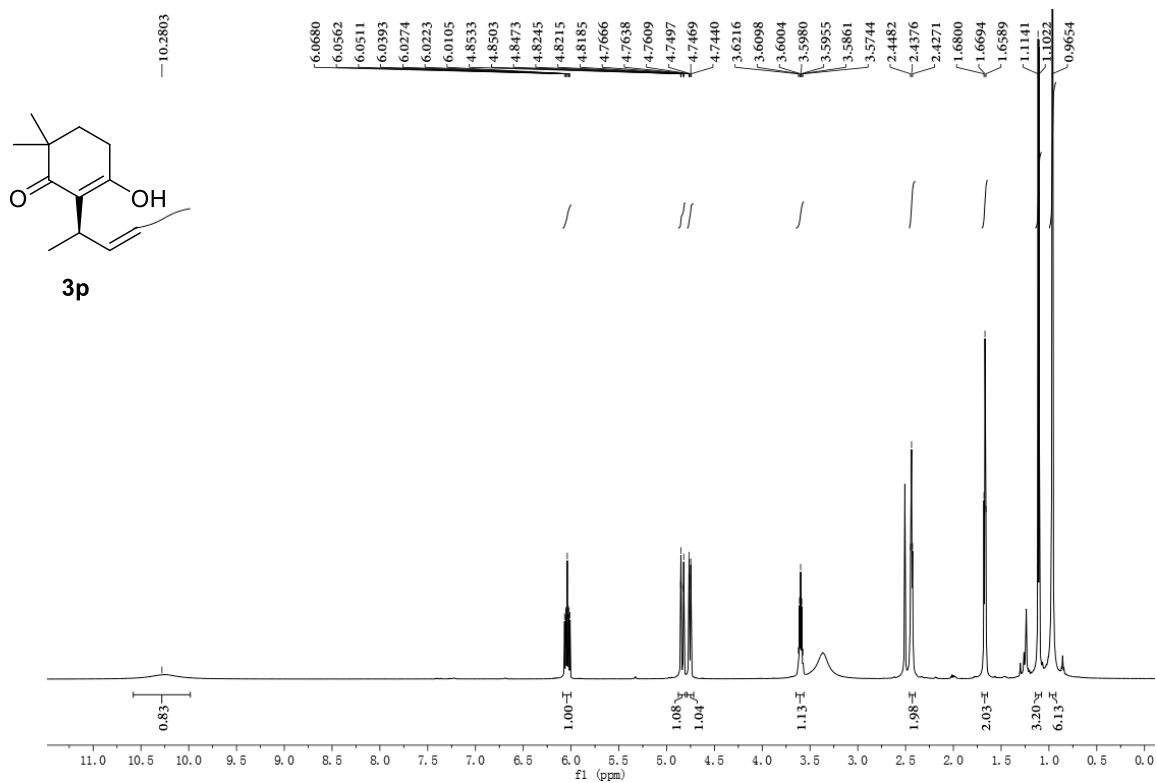


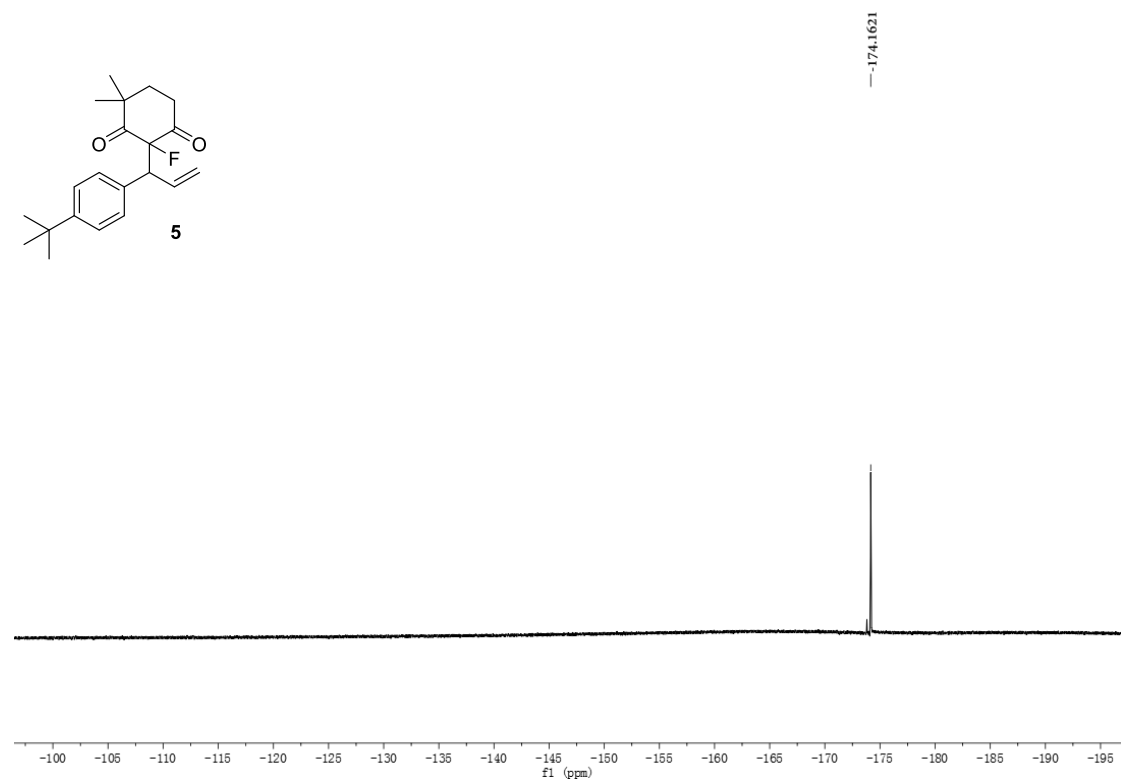
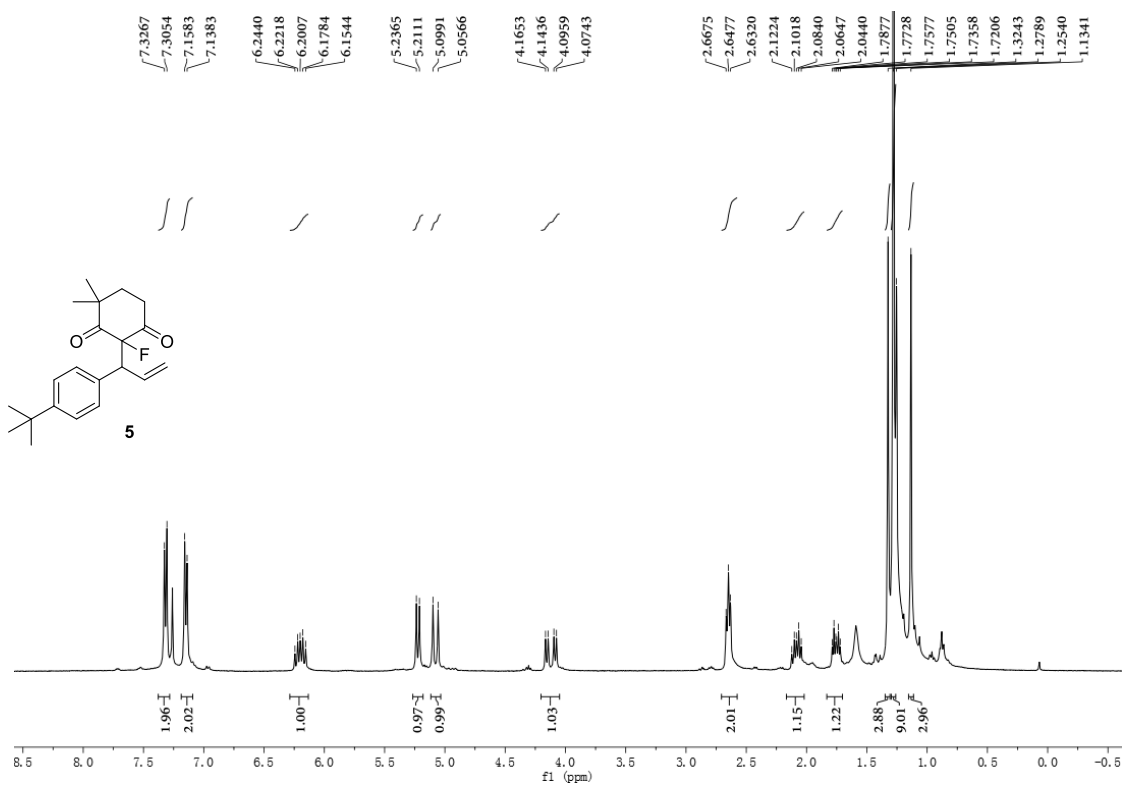


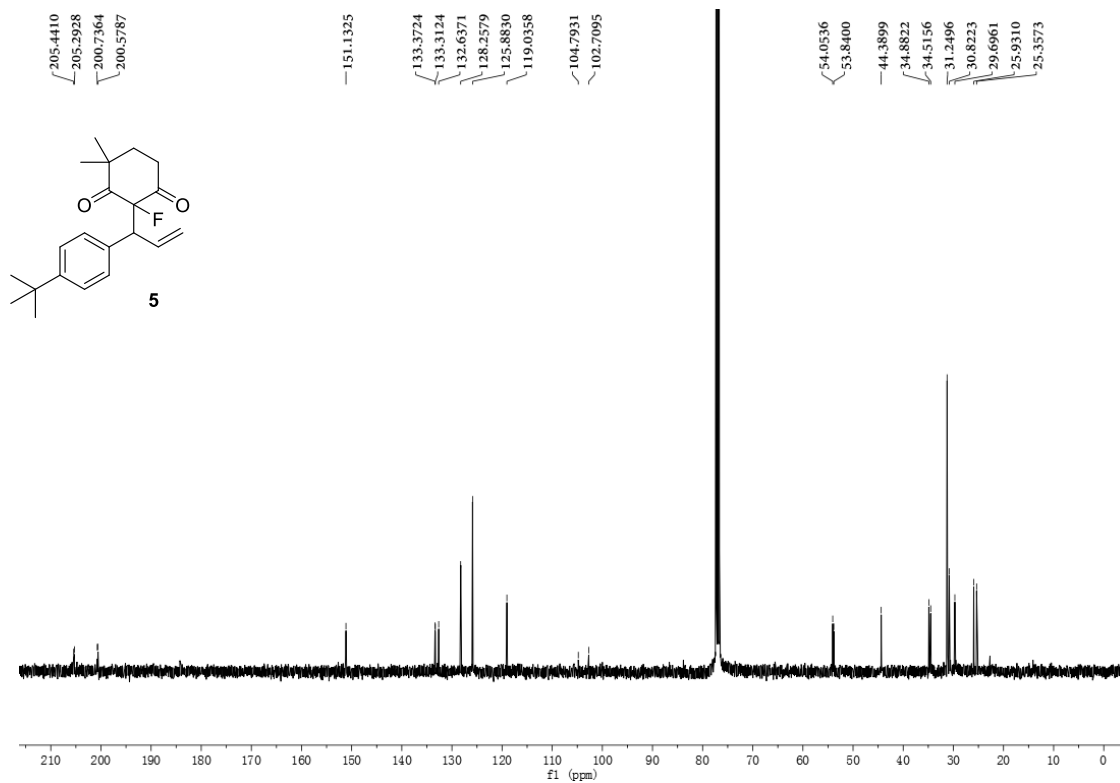




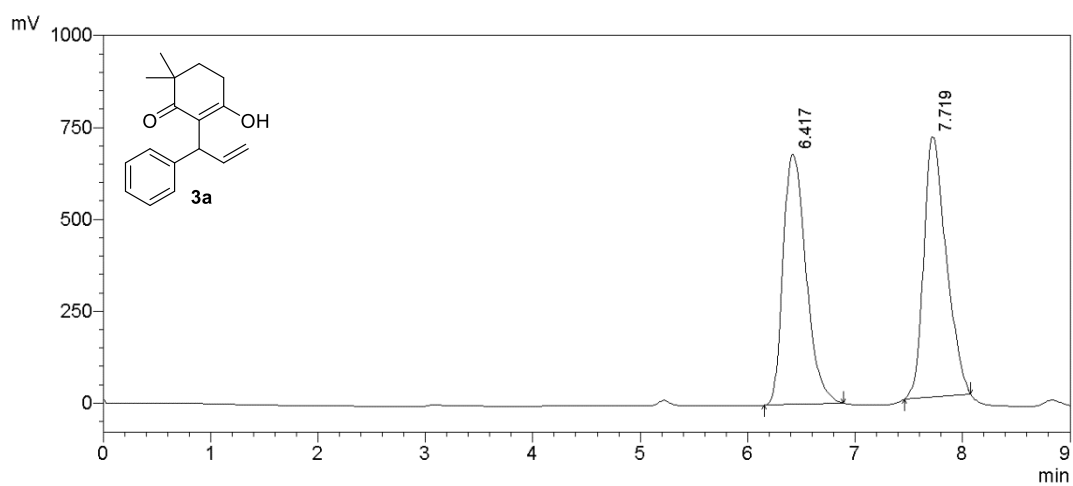




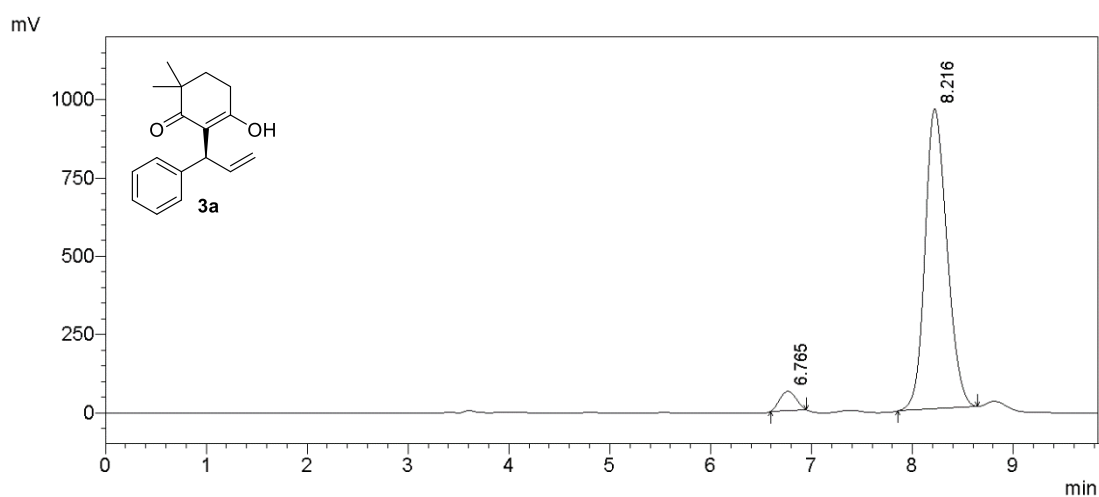




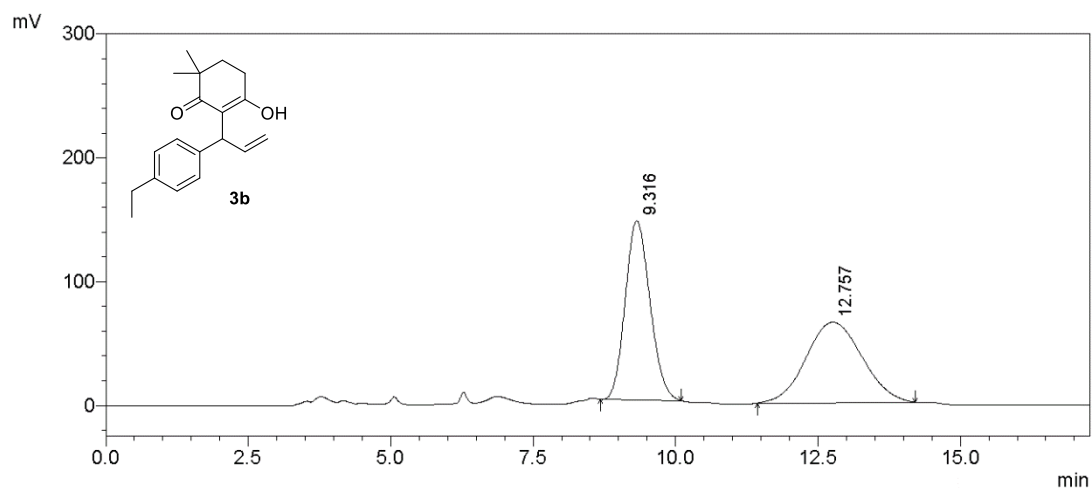
7. HPLC Spectra of compound 3 and 5



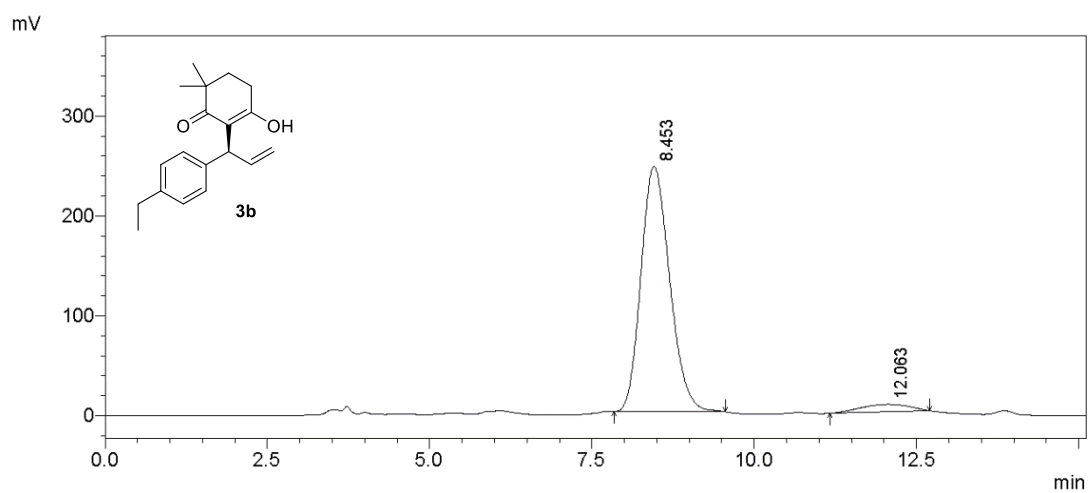
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.417	10142311	49.649
2	7.719	10285810	50.351
Total		20428121	100.000



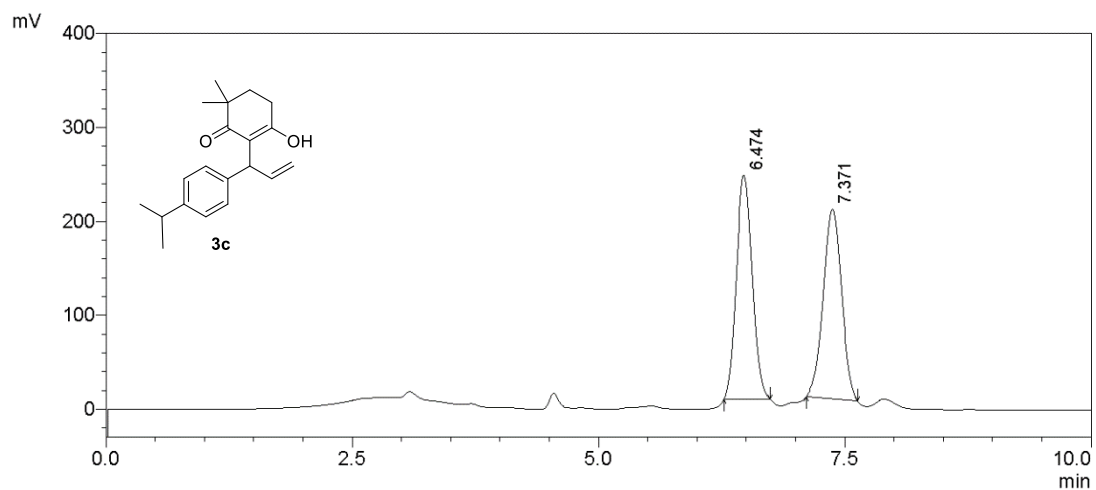
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.765	682551	4.520
2	8.216	14417491	95.480
Total		15100041	100.000



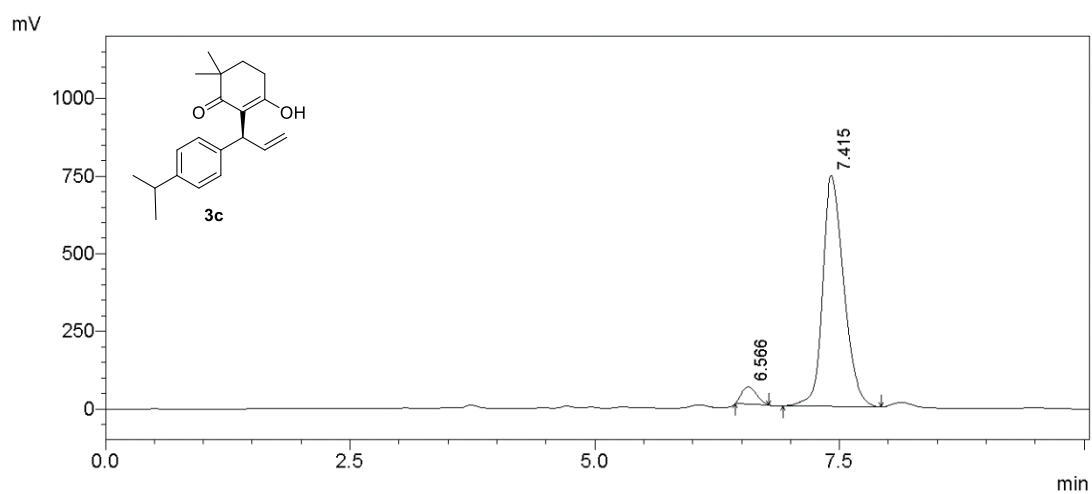
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	9.316	4389402	49.566
2	12.757	4466251	50.434
Total		8855653	100.000



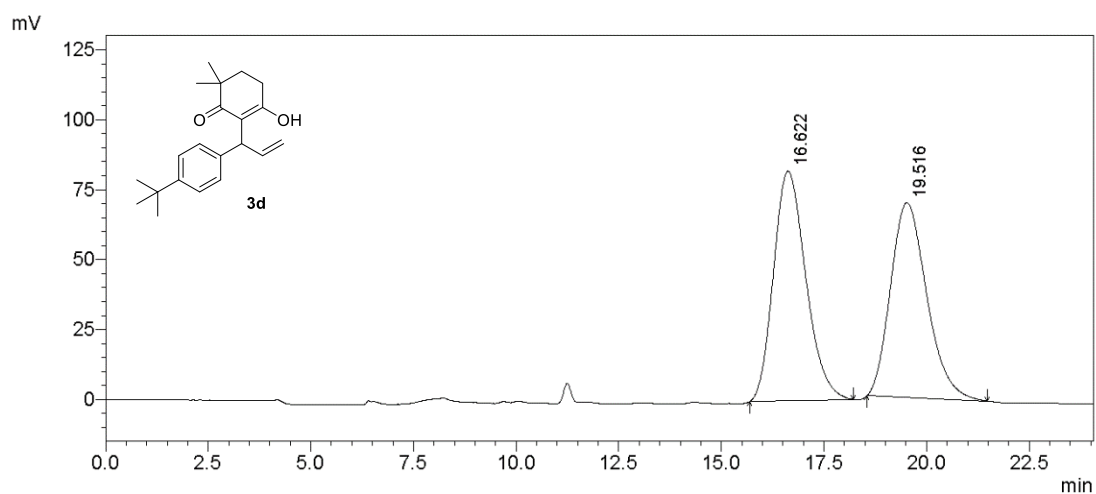
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	8.453	7576165	95.075
2	12.063	392446	4.925
Total		7968611	100.000



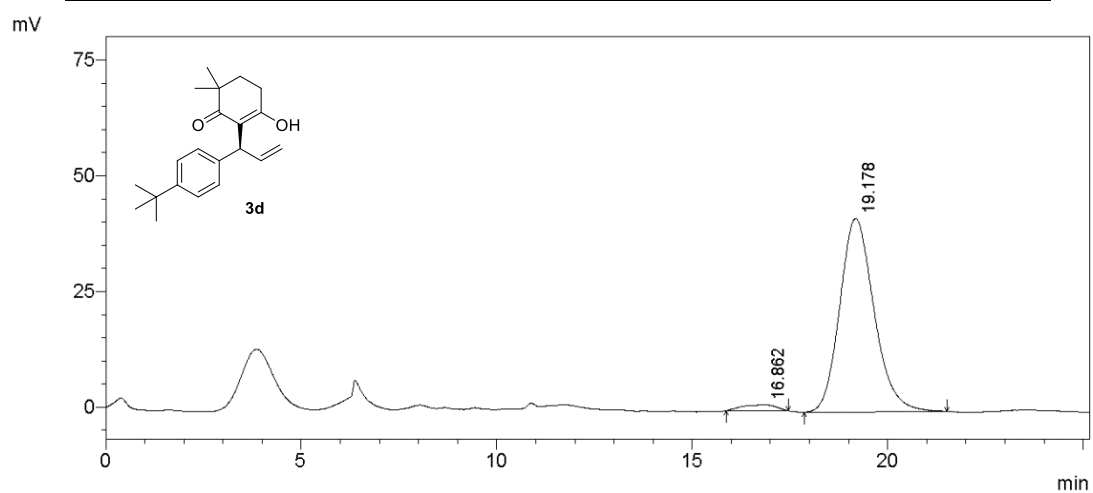
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.474	2698768	50.918
2	7.371	2601480	49.082
Total		5300248	100.000



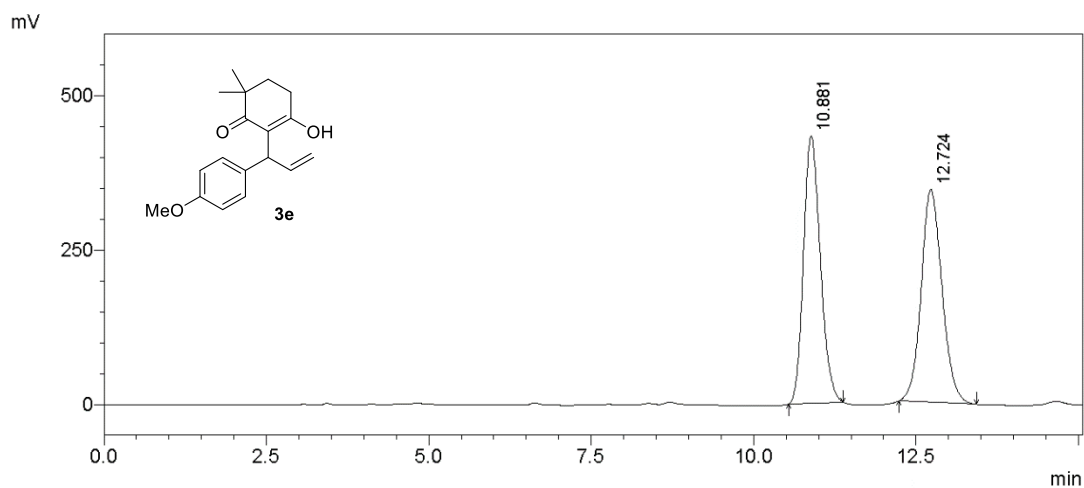
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.564	584142	4.926
2	7.413	11275340	95.074
Total		11859483	100.000



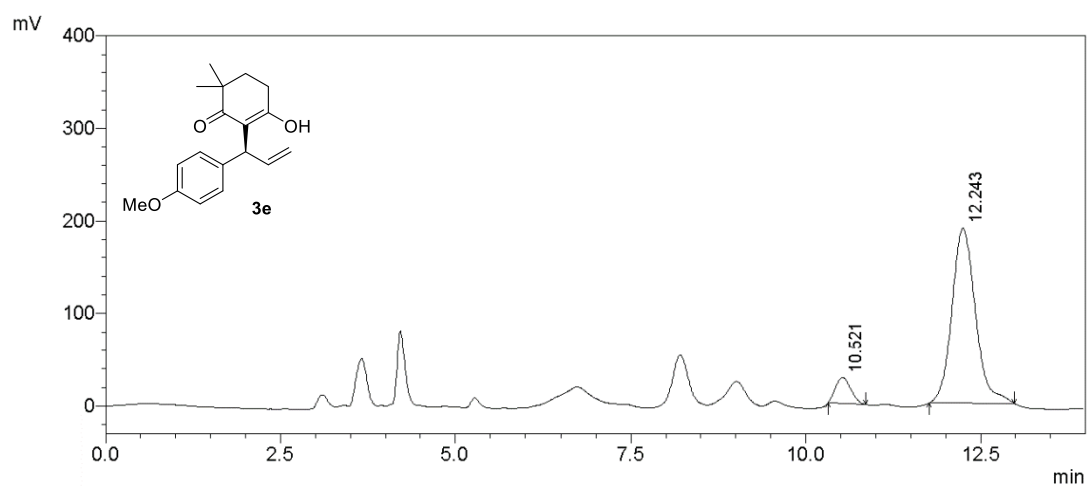
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	16.622	4496572	51.216
2	19.516	4283118	48.784
Total		8779690	100.000



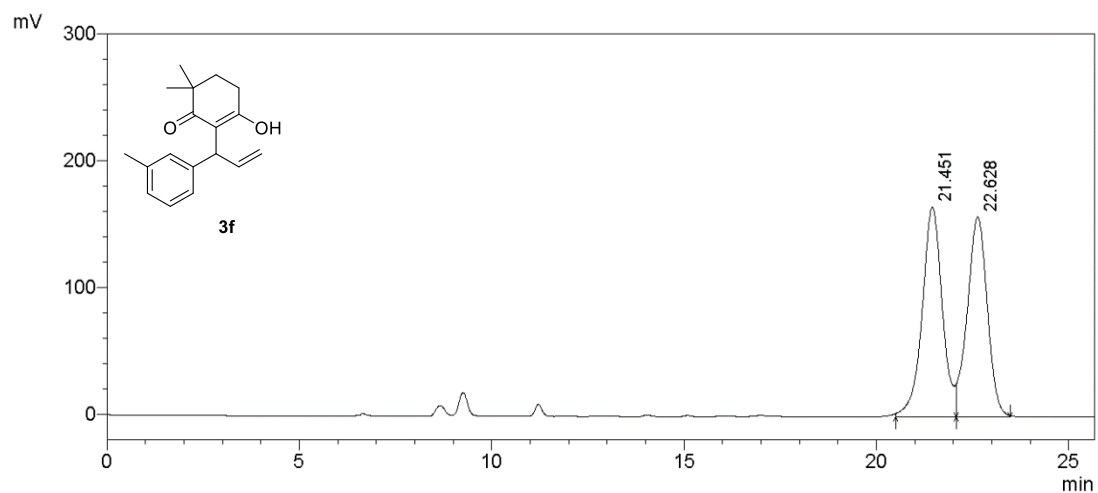
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	16.862	75612	2.875
2	19.178	2553918	97.125
Total		2629530	100.000



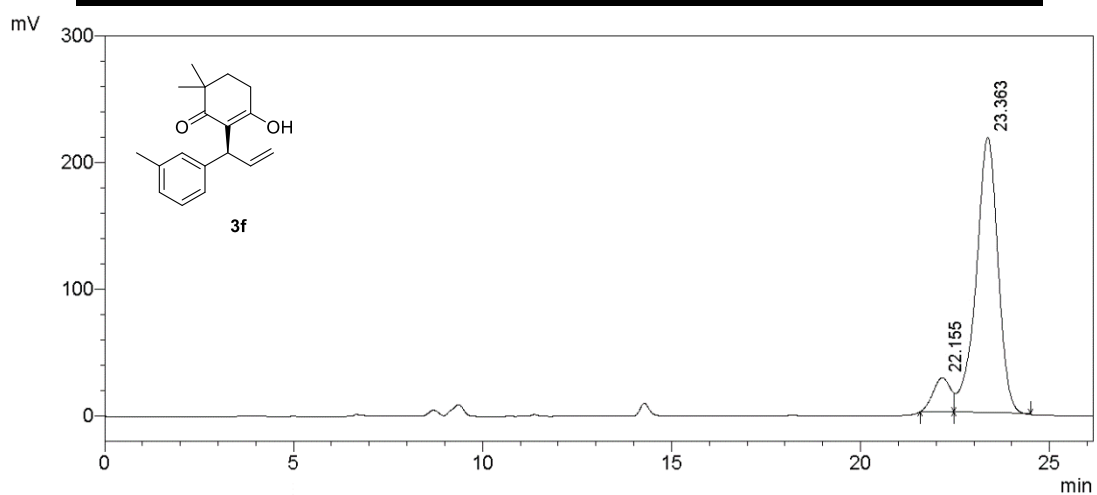
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	10.881	7784212	50.236
2	12.724	7710951	49.764
Total		15495163	100.000



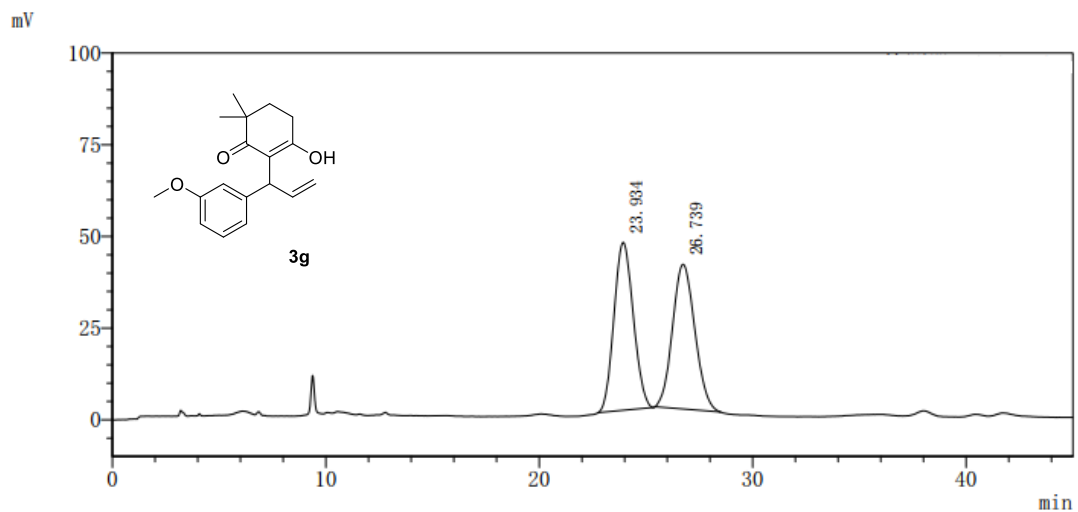
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	10.521	427376	8.799
2	12.243	4429667	91.201
Total		4857043	100.000



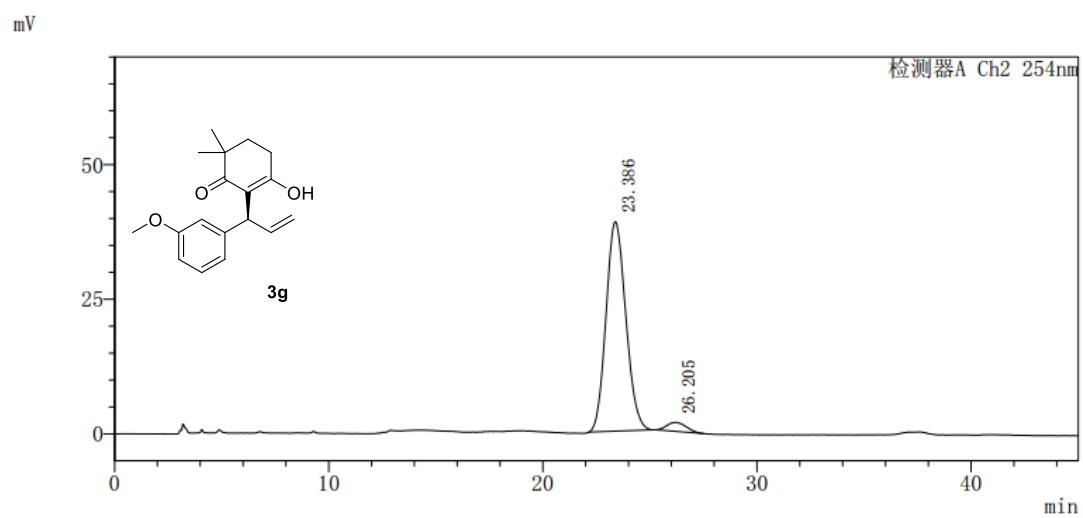
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	21.451	6037062	51.478
2	22.628	5690366	48.522
Total		11727427	100.000



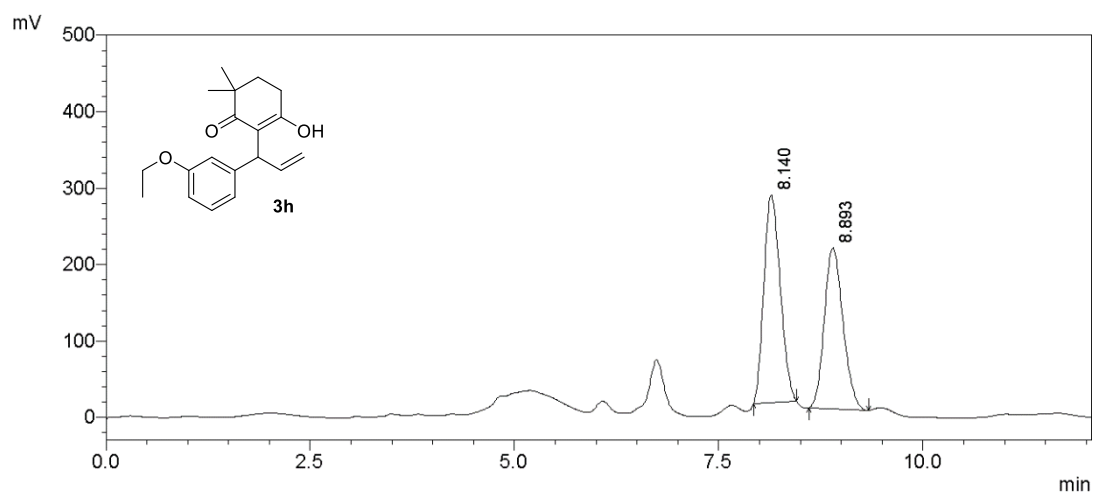
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	22.155	858654	8.949
2	23.363	8736033	91.051
Total		9594687	100.000



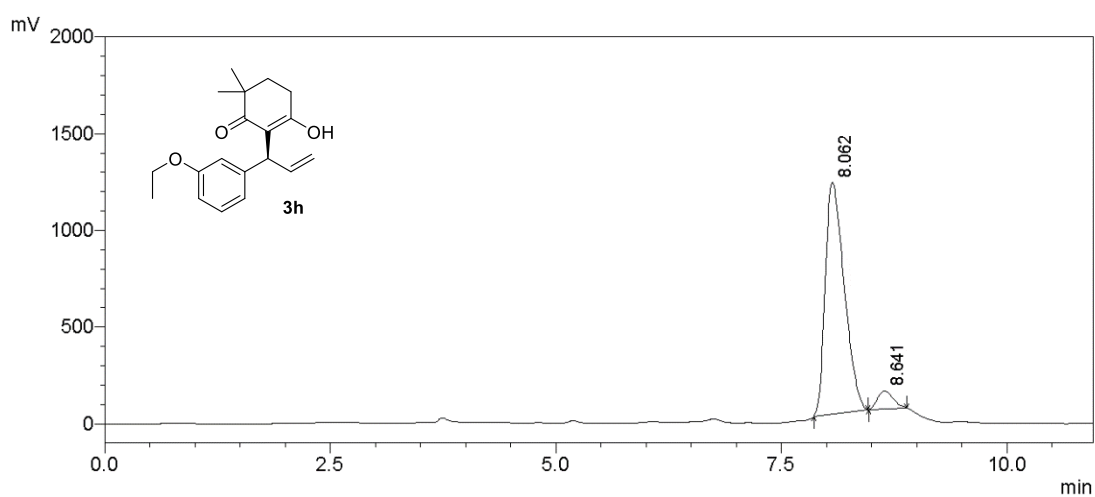
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	23.934	2879674	50.095
2	26.739	2868756	49.905
Total		5748430	100.000



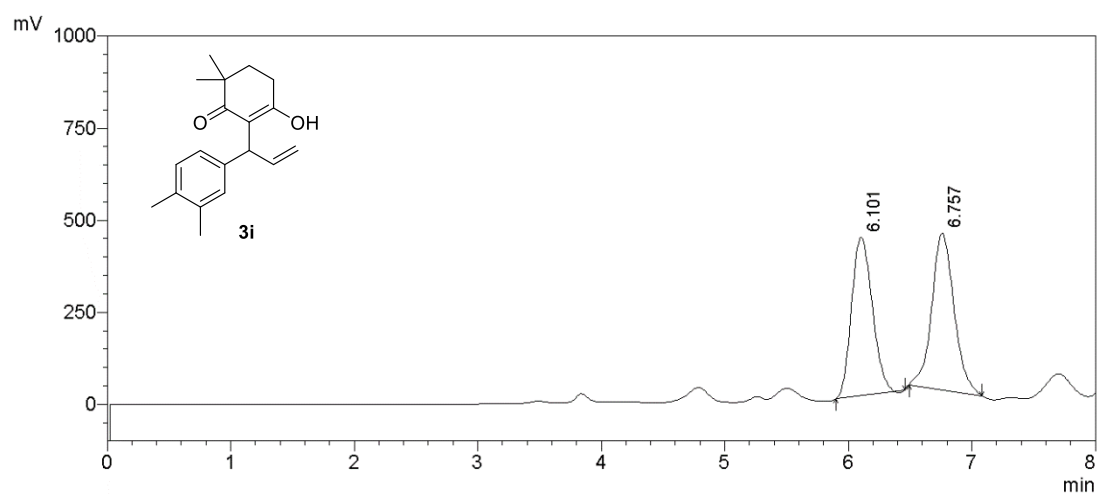
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	23.386	2492475	96.005
2	26.205	103720	3.995
Total		2596195	100.000



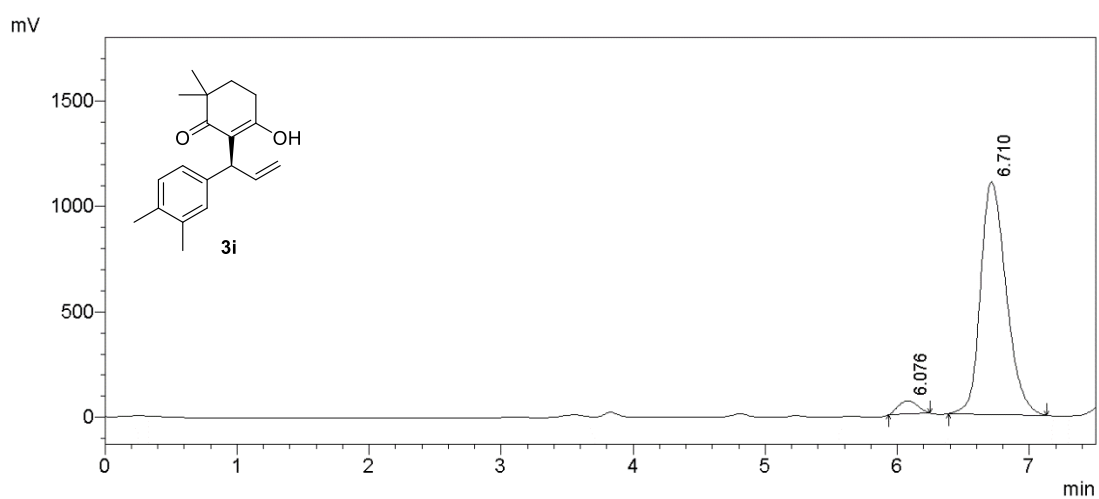
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	8.136	4261033	51.901
2	8.892	3948929	48.099
Total		9594687	100.000



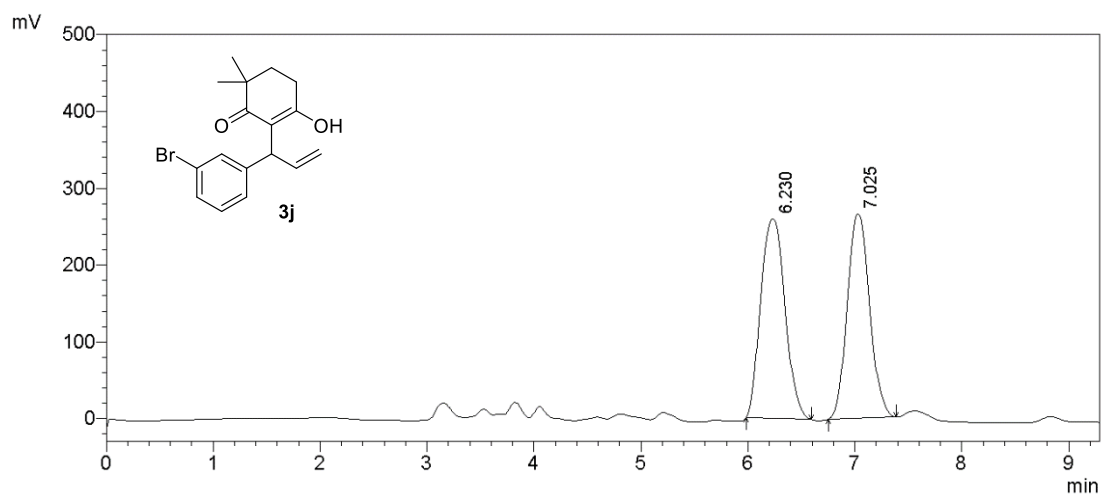
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	8.082	17516935	94.935
2	8.641	1111160	5.065
Total		18628095	100.000



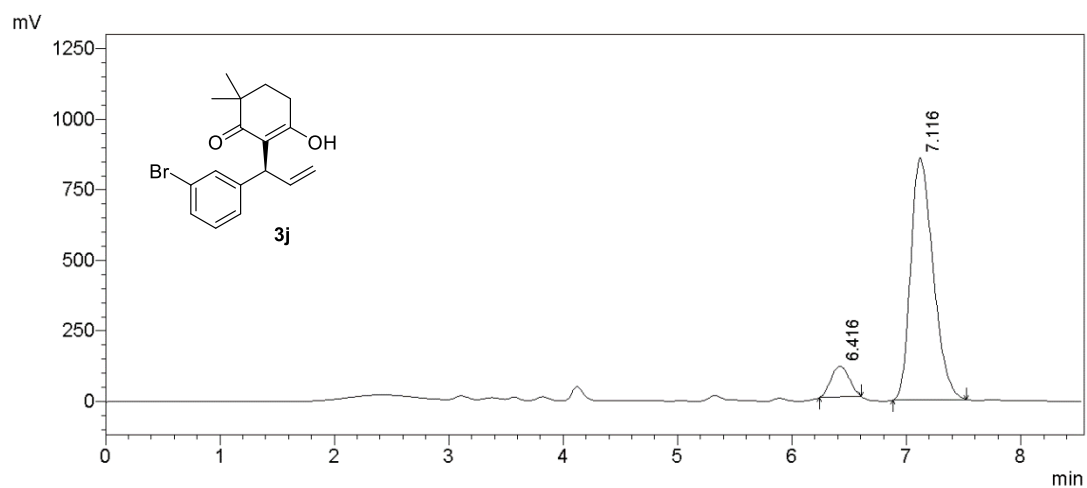
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.098	5948449	47.420
2	6.756	6595691	52.580
Total		12544141	100.000



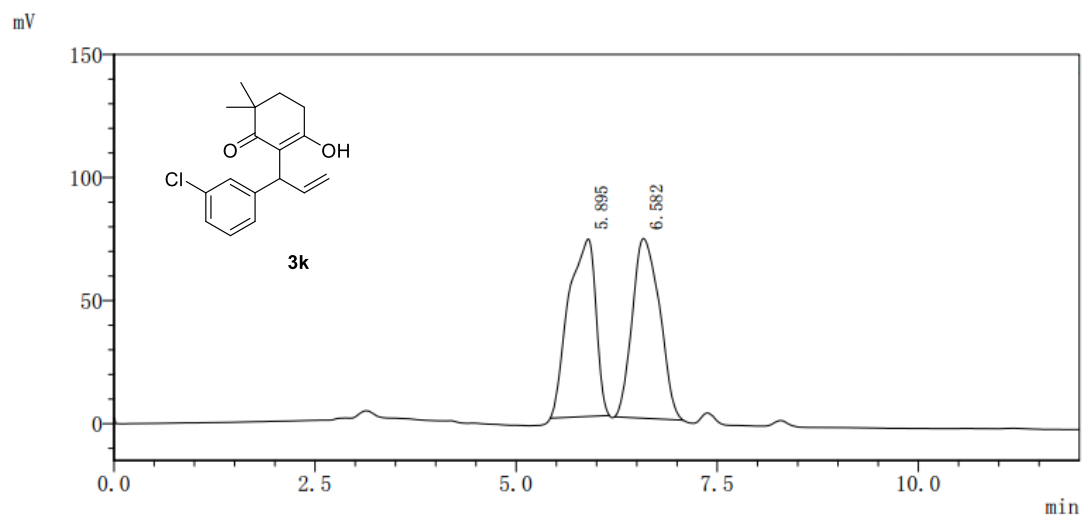
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.073	765687	4.165
2	6.708	17618645	95.835
Total		18384332	100.000



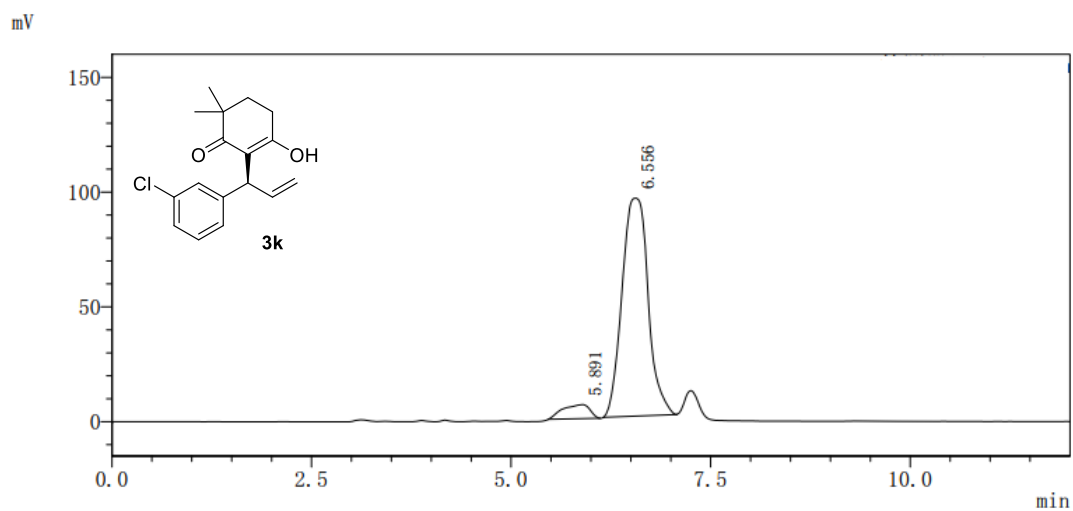
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.232	3728664	51.712
2	7.027	3481768	48.288
Total		7210432	100.000



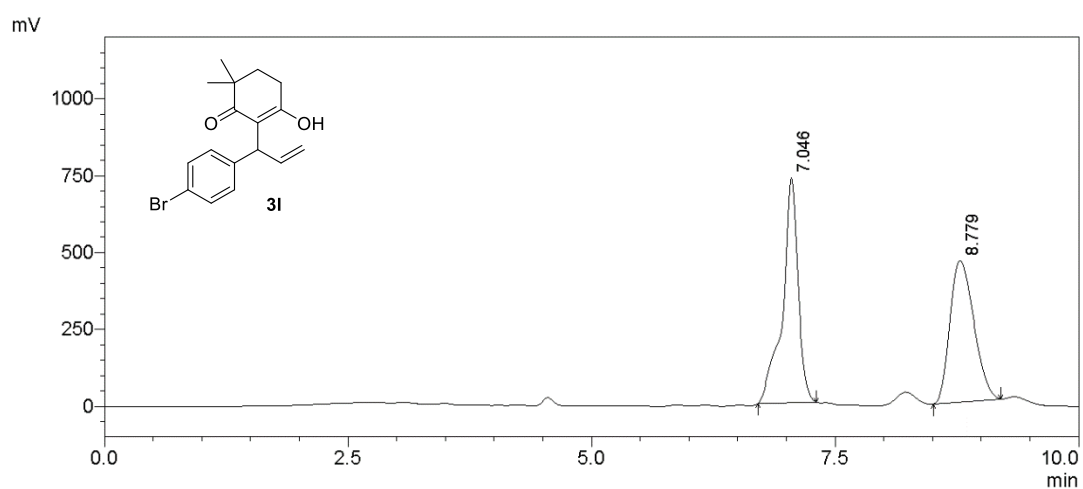
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.416	1226910	9.495
2	7.116	11694158	90.505
Total		12921067	100.000



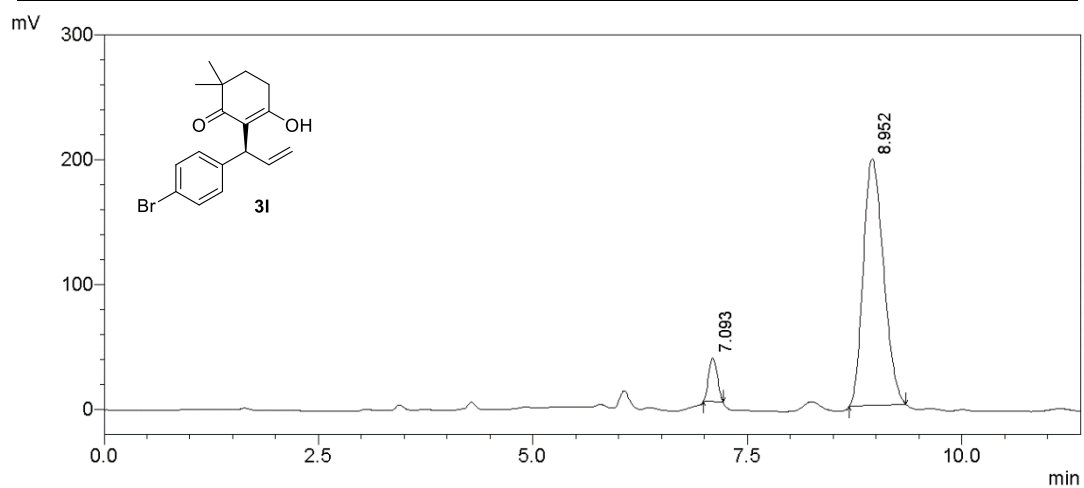
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	5.895	1696141	49.532
2	6.582	1728214	50.468
Total		3424356	100.000



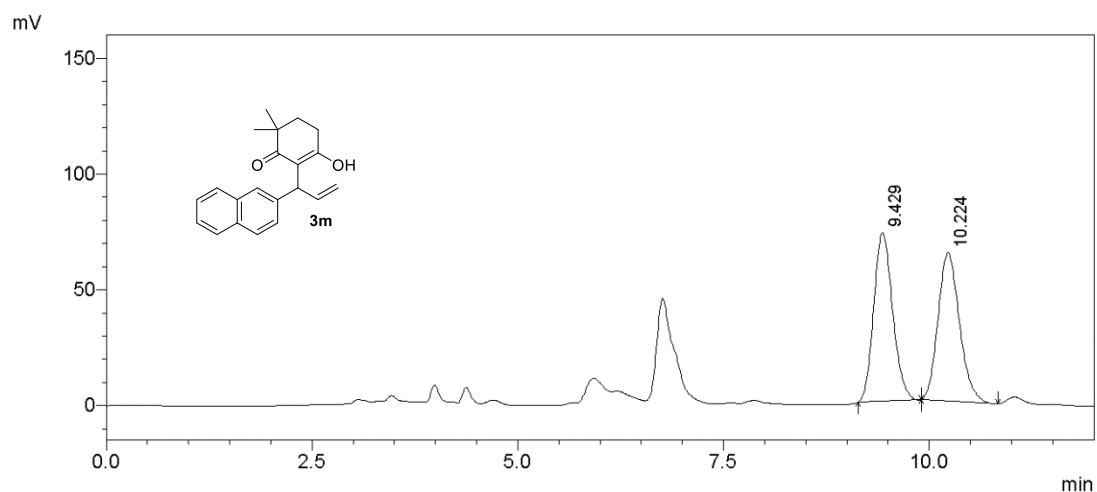
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	5.891	145140	6.286
2	6.556	2163813	93.714
Total		2308953	100.000



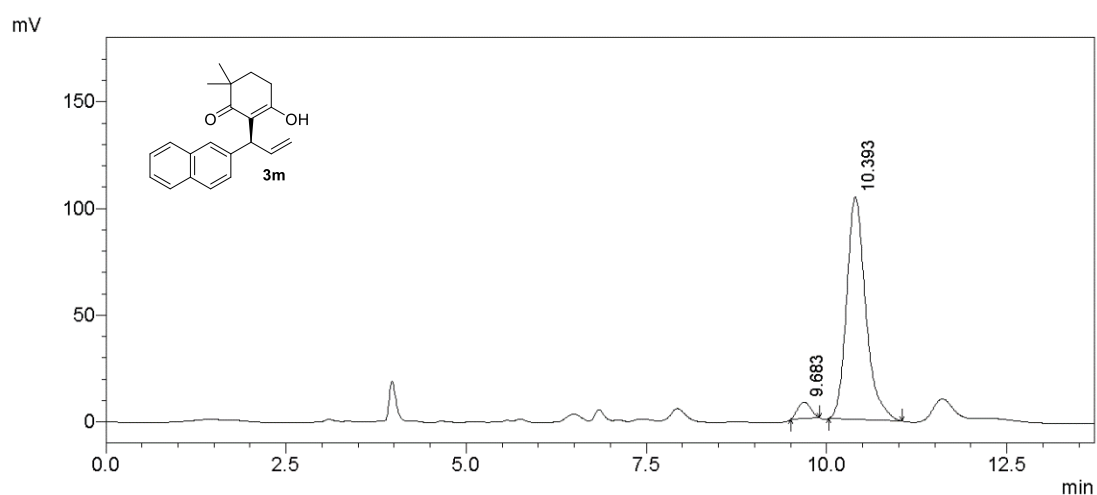
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	7.046	8099342	50.965
2	8.779	7792659	49.035
Total		15892001	100.000



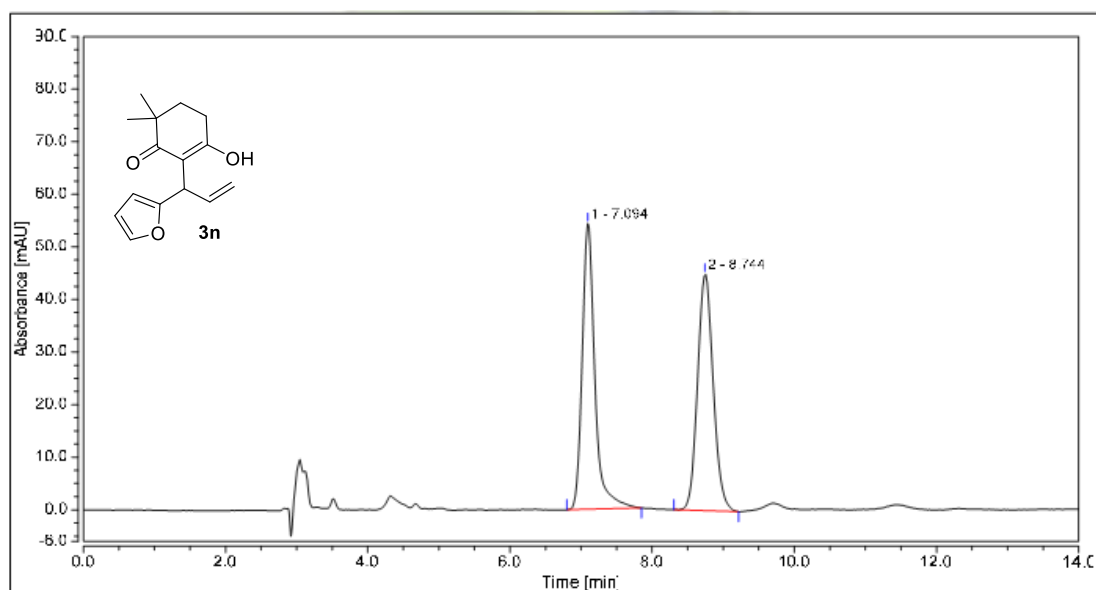
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	7.093	241956	6.922
2	8.952	3253598	93.078
Total		3495553	100.000



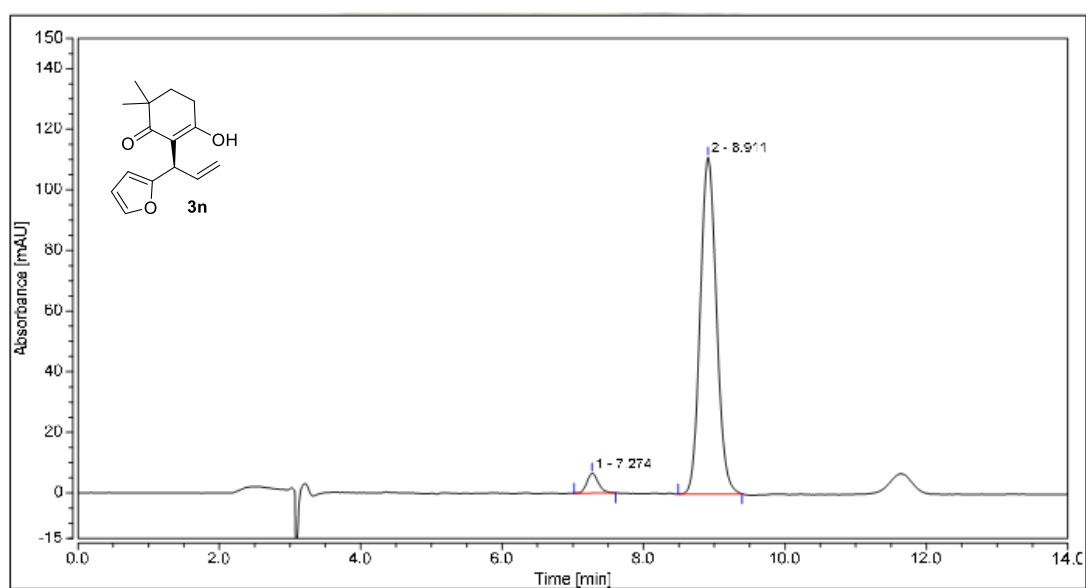
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	9.429	1157171	50.040
2	10.224	1155316	49.960
Total		2312487	100.000



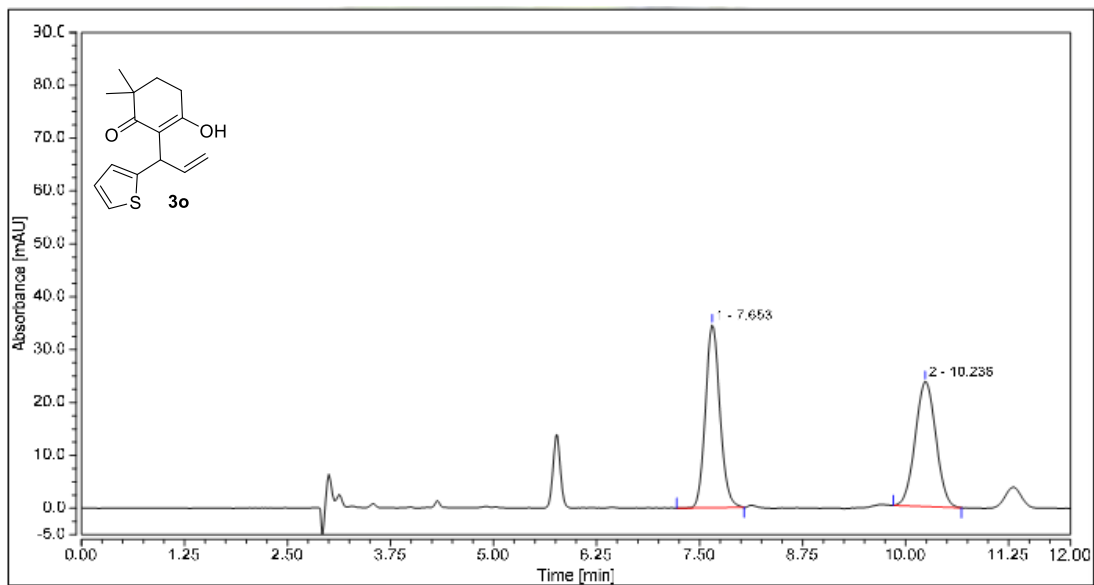
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	9.683	98556	4.871
2	10.393	1924635	95.129
Total		2023191	100.000



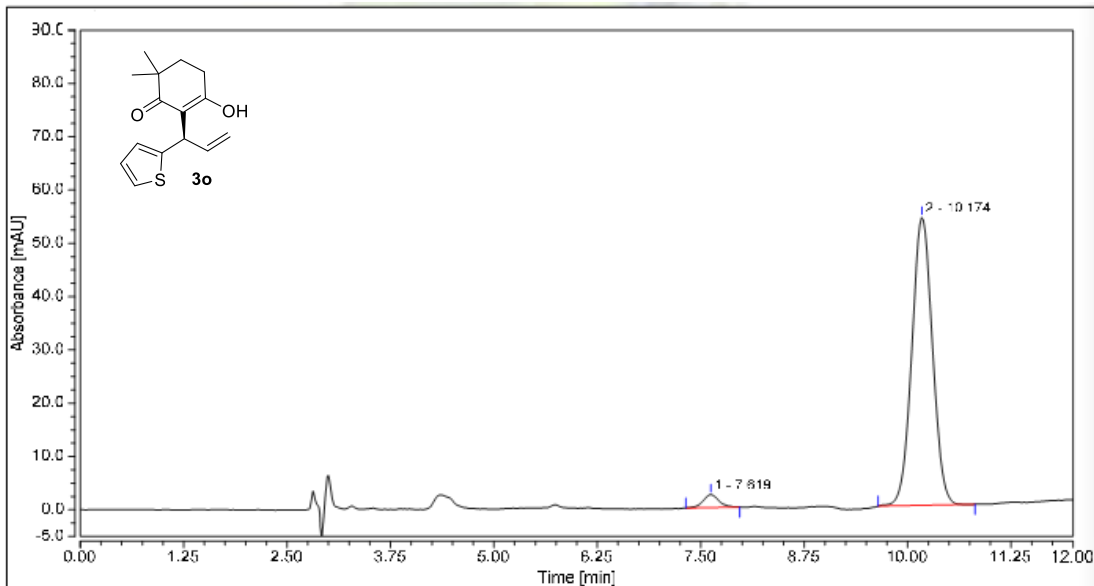
Peak No.	R. Time(min)	Peak Area (mAU*min)	Percent (%)
1	7.094	11.183	49.41
2	8.744	11.449	50.59
Total		22.633	100.000



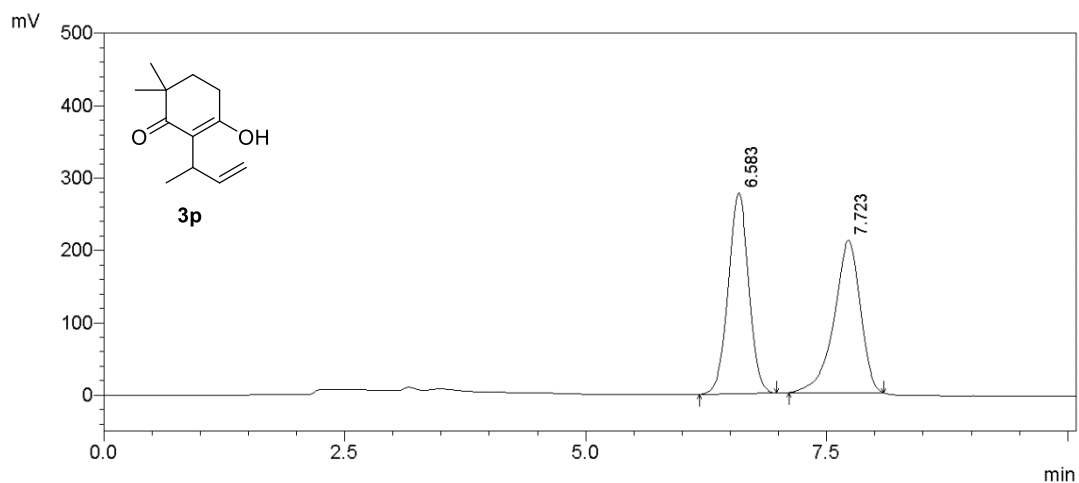
Peak No.	R. Time(min)	Peak Area (mAU*min)	Percent (%)
1	7.274	7006737	3.99
2	8.911	325365	96.01
Total		7332103	100.000



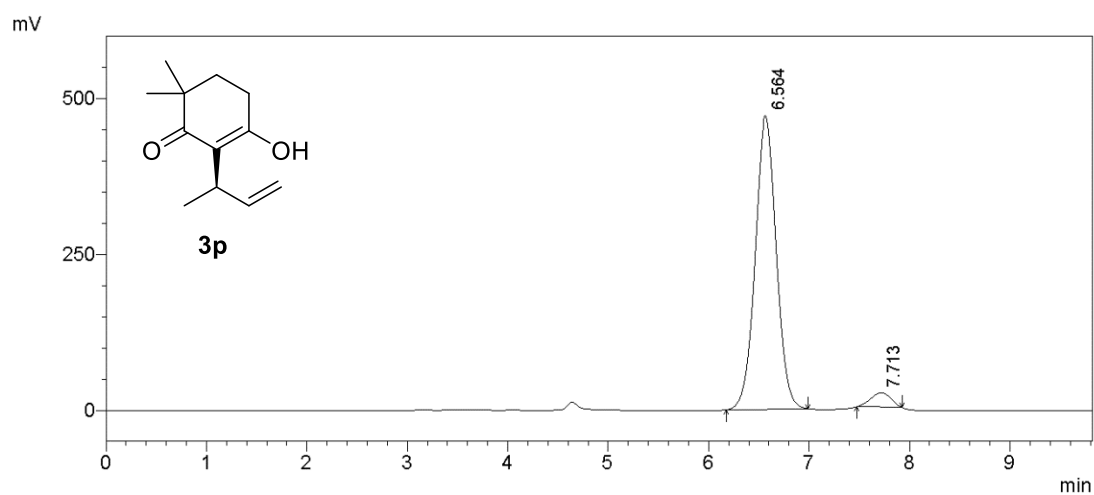
Peak No.	R. Time(min)	Peak Area (mAU*min)	Percent (%)
1	7.653	7.047	50.67
2	10.236	6.860	49.33
Total		13.907	100.000



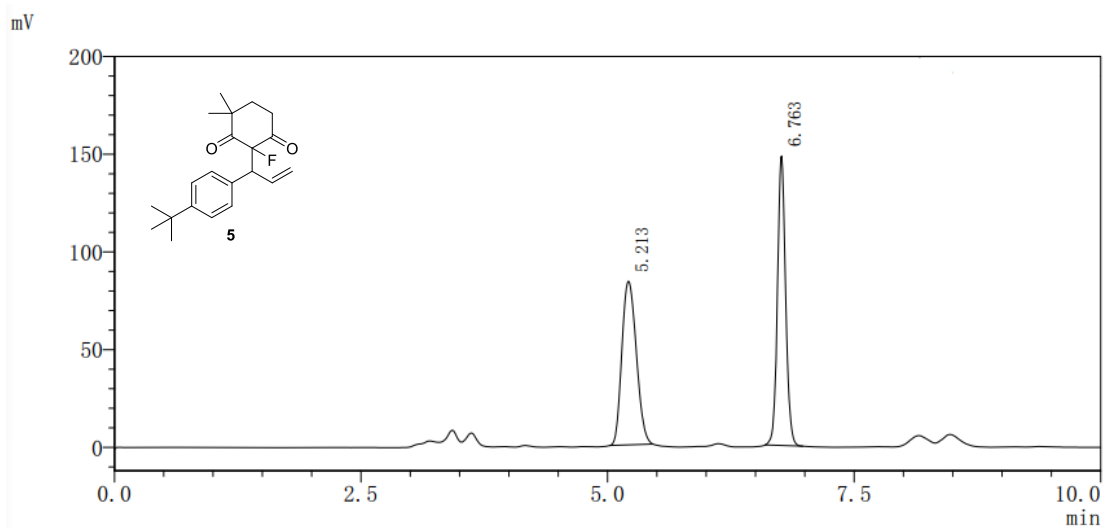
Peak No.	R. Time(min)	Peak Area (mAU*min)	Percent (%)
1	7.819	0.553	3.42
2	10.174	15.619	96.58
Total		16.172	100.000



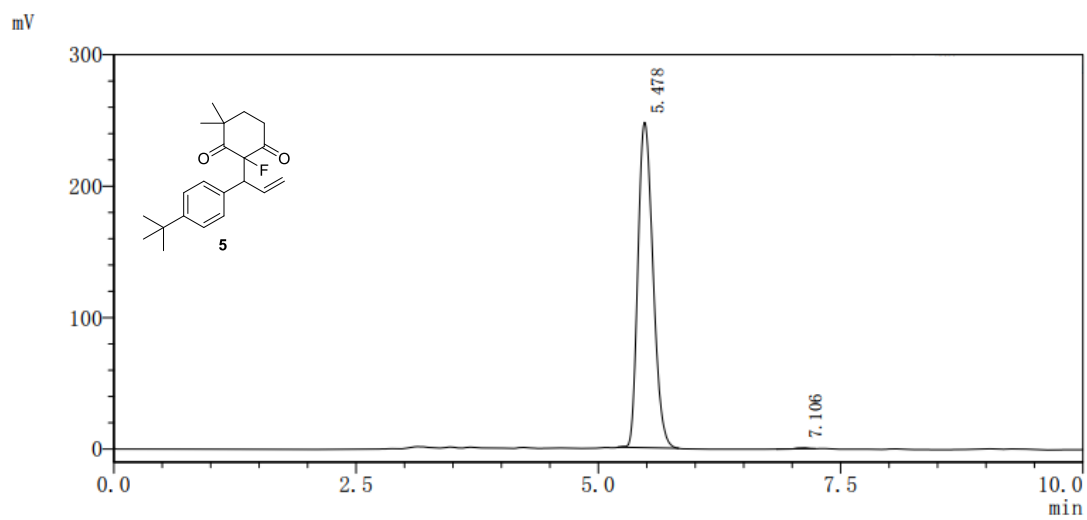
Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.583	4099851	50.677
2	7.723	3990381	49.323
Total		8090232	100.000



Peak No.	R. Time(min)	Peak Area(mV*min)	Percent (%)
1	6.564	7006737	95.562
2	7.713	325365	4.438
Total		7332103	100.000



Peak No.	R. Time(min)	Peak Area(mV*min)	Percent(%)
1	5.213	849932	49.943
2	6.763	851888	50.057
Total		1701820	100.000



Peak No.	R. Time(min)	Peak Area(mV*min)	Percent(%)
1	5.478	2676604	99.814
2	7.106	4988	0.186
Total		2681592	100.000