

Supporting Information

Asymmetric Transfer Hydrogenation of α -Substituted- β -Keto Carbonitriles via Dynamic Kinetic Resolution

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Content

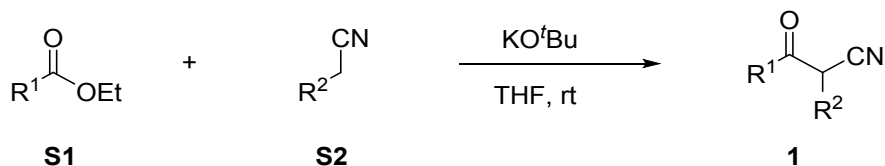
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1. General Information

Unless otherwise mentioned, all experiments were carried out under an atmosphere of argon or using standard Schlenk techniques. Solvents and reagents were purchased from commercial suppliers and used without further purification. Column Chromatography was performed with silica gel Merck 60 (300-400 mesh). NMR spectra were recorded on a Bruker DPX 400 spectrometer at 400 MHz for ^1H NMR, 101 MHz for ^{13}C NMR and a Bruker DPX 600 spectrometer at 600 MHz for ^1H NMR, 151 MHz for ^{13}C NMR. CDCl_3 and d^6 -DMSO was the solvent used for the NMR analysis, with tetramethylsilane (TMS) as the internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Chemical shifts were reported relative to TMS (0.00 ppm) for ^1H NMR and relative to CDCl_3 (77.0 ppm) for ^{13}C NMR. HPLC analysis was carried out on Agilent 1260 Series instrument using a chiral stationary phase. PE refers to petroleum ether, and EA refers to ethyl acetate.

2. General Experimental Details

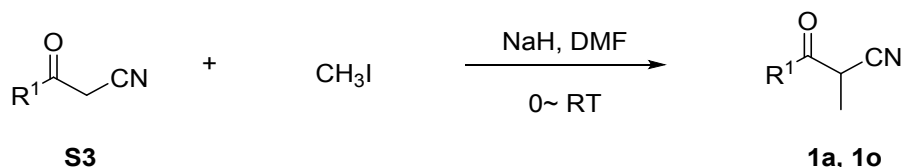
2.1 General Procedure for the Synthesis of Substrate



Scheme S1. Synthetic route of compound **1**.

Procedure A : Preparation of ketones 1b~1n, 1q~1u, 1y, 1z.^{1, 2}

To a solution of KO^tBu (2.48 g, 22 mmol, 2.2 equiv.) in THF (40 mL) was added ethyl ester **S1** (10 mmol, 1.0 equiv.) at ambient temperature with stirring for 10 min and then the corresponding cyanide **S2** (10 mmol, 1.0 equiv.) was added immediately to the above THF solution. The mixture was stirred at room temperature for 1~16 h until the start materials was consumed completely. The mixture was quenched by H₂O (15 mL) and EtOAc (20 mL), and then treated with 2 M HCl to adjust the pH to 7. After above process, the mixture was extracted by EtOAc (30 mL*2), the combined organic layer was washed by saturated NaHCO₃ (aq.) and brine, dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The crude product was purified by chromatography (PE:EA from 30:1 to 5:1). Compound **1** was obtained with medium to high yield (75% ~ 96%).

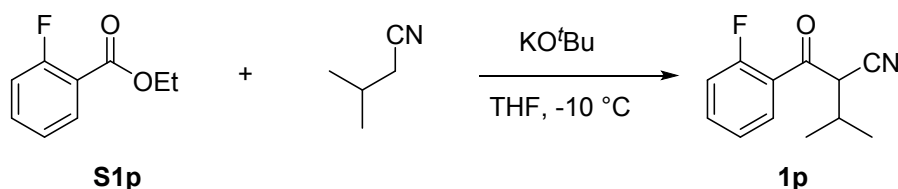


Scheme S2. Synthetic route of compound **1a** and **1o**.³

Procedure B : Preparation of ketones 1a, 1o

To a solution of DMF (20 mL) was cooled to 0 °C and NaH (600 mg, 60% in oil, 1.5

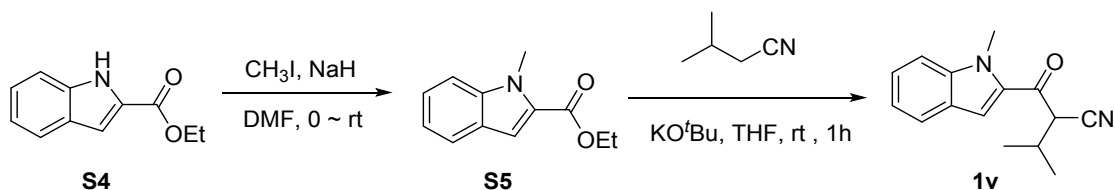
equiv.) was added slowly, the mixture was stirred for 5 min, the corresponding cyanide **S3** (10 mmol, 1.0 equiv.) was added at the temperature and the mixture was stirred for 30 min, CH₃I was added slowly by syringe and then the mixture was stirred at room temperature for 4 hours until the start materials was consumed completely. The mixture was quenched by 2 mL H₂O at 0 °C, and then treated with 2 M HCl to adjust the pH to 7. After above process, the mixture was extracted by EtOAc (30 mL*2), the combined organic layer was washed by saturated NaHCO₃ (aq.) and brine, dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The crude product was purified by chromatography (PE:EA from 30:1 to 5:1). Compound **1a** and **1o** was obtained as yellow oil (75% ~ 90% yield).



Scheme S3. Synthetic route of compound **1p**.²

Procedure C : Preparation of ketones **1p**

To a solution of KO^tBu (2.48 g, 22 mmol, 2.2 equiv.) in THF (40 mL) was cooled to -10 °C, 3-methylbutanenitrile (0.83 g, 10 mmol, 1.0 equiv.) was added with stirring for 10 min and then the corresponding ethyl ester **S1p** (1.68 g, 10 mmol, 1.0 equiv.) was added immediately to the above THF solution at -10 C. The mixture was stirred at -10 °C for 1 h until the start materials was consumed completely. The mixture was quenched by H₂O (15 mL) and EtOAc (20 mL), and then treated with 2 M HCl to adjust the pH to 7. After above process, the mixture was extracted by EtOAc (50 mL*2), the combined organic layer was washed by saturated NaHCO₃ (aq.) and brine, dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The crude product was purified by chromatography (PE:EA from 30:1 to 5:1). Compound **1p** was obtained with 85% yield.

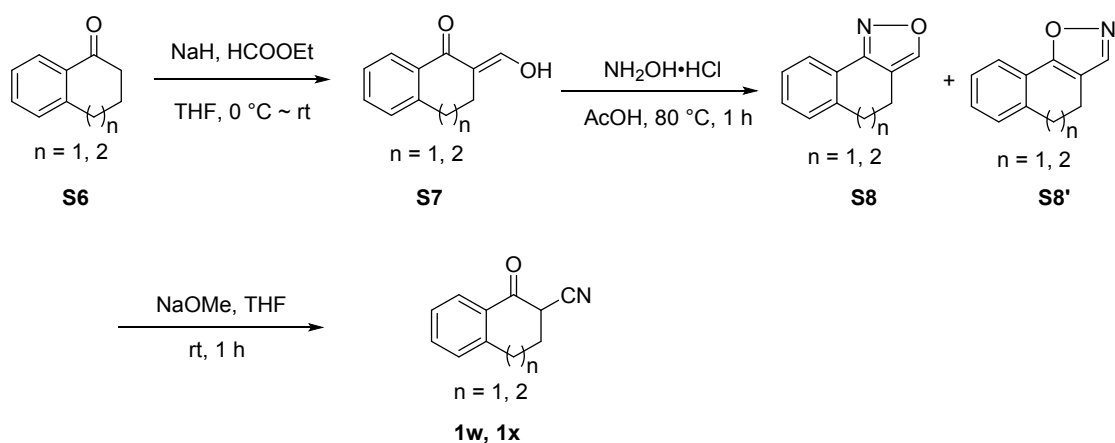


Scheme S4. Synthetic route of compound **1v**.⁴

Procedure D : Preparation of ketones 1v

Step 1: To a solution of NaH (600 mg, 60% in oil, 1.5 equiv.) in DMF (10 mL) was cooled to 0 °C. Ethyl 1H-indole-2-carboxylate **S4** (1.89 g, 10 mmol, 1.0 equiv.) was added slowly to the mixture with stirring 20 min. Then CH₃I (7.1 g, 5.0 equiv.) was added into the mixture and the mixture was stirred at room temperature for 2 h. TLC indicated the ethyl ester was consumed completely and the mixture was quenched by H₂O (10 mL), extracted by EtOAc (50 mL*2), the combined organic layer was washed by saturated NH₄Cl (aq.) and brine, dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The crude product was purified by chromatography (PE:EA from 50:1 to 9:1). Ethyl 1-methyl-1H-indole-2-carboxylate **S5** was obtained with an equivalent yield.

Step 2: To a solution of KO^tBu (2.48 g, 22 mmol, 2.2 equiv.) in THF (40 mL) was added Ethyl 1-methyl-1H-indole-2-carboxylate **S5** (2.03 g, 10 mmol, 1.0 equiv.) at ambient temperature with stirring for 10 min and then 3-methylbutanenitrile (10 mmol, 1.0 equiv.) was added immediately to the above THF solution. The mixture was stirred at room temperature for 1 h until the start materials was consumed completely. The mixture was quenched by 15 mL H₂O and 20 mL EtOAc, and then treated with 2 M HCl to adjust the pH to 7. After above process, the mixture was extracted by EtOAc (30 mL*2), the combined organic layer was washed by saturated NaHCO₃ (aq.) and brine, dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The crude product was purified by chromatography (PE:EA from 30:1 to 6:1). Compound **1v** was obtained as a white solid (75% yield).



Scheme S5. Synthetic route of compound **1w**, **1x**.^{5, 6}

Procedure E : Preparation of ketones **1w**, **1x**

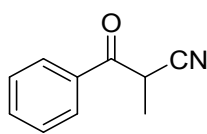
Step 1: To a solution of NaH (800 mg, 60% in oil, 1.0 equiv.) in THF (50 mL) was cooled to 0 °C. The corresponding ketone **S6** (20 mmol, 1.0 equiv.) was added slowly to the mixture with stirring 10 min. Then ethyl formate (3 g, 40 mmol, 2.0 equiv.) was added into the mixture and the mixture was stirred at room temperature for 3 h. TLC indicated the ethyl ester was consumed completely and the mixture was quenched by H₂O (20 mL), HCl (3 M, 10 mL) was added into the mixture and extracted by EtOAc (50 mL*2), the combined organic layer was washed by saturated NH₄Cl (aq.) (20 mL*1) and brine (20 mL*1), dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The crude product was purified by chromatography (PE:EA from 50:1 to 9:1). **S7** was obtained as a yellow solid (85 ~ 90% yield)

Step 2: To a solution of **S7** and NH₂OH·HCl (2.0 equiv.) in AcOH (10 mL) was stirred at 80 °C for 2 h. TLC (PE/EA = 10/1) indicated that the start material was consumed completely and two main spots with lower polarity were detected. The mixture was concentrated under vacuum to remove most AcOH. Saturated NaHCO₃ (aq.) (20 mL) was added into the mixture and extracted by EtOAc (50 mL*2), the combined organic layer was washed by brine (20 mL*1), dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The crude product was purified by chromatography (PE:EA from 50:1 to 9:1). Isomers **S8** and **S8'** was obtained as a

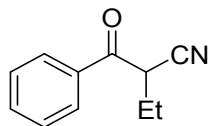
yellow solid (88 ~ 92% yield).

Step 3: To a solution of **S8** and **S8'** in THF was added NaOMe (3.0 equiv.), and the mixture was stirred at room temperature for 1 h. H₂O (20 mL) and EtOAc (50 mL) was added into the mixture and then treated with 2 M HCl to adjust the pH to 7. The red solution was changed into yellow. The solution was extracted by EtOAc (50 mL*2) and the combined organic layer was washed by brine (20 mL*1), dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The crude product was purified by chromatography (PE:EA from 20:1 to 4:1). **1w**, **1x** was obtained as a white solid (45% ~ 60% yield).

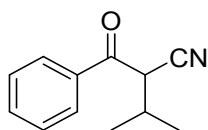
2.2 Characterization Data of 1



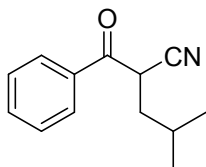
2-methyl-3-oxo-3-phenylpropanenitrile (1a)³: yellow oil, 1.20 g, 75% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.11 – 7.94 (m, 2H), 7.71 – 7.63 (m, 1H), 7.61 – 7.47 (m, 2H), 4.39 (q, *J* = 7.2 Hz, 1H), 1.65 (d, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 190.8, 134.5, 133.6, 129.1, 128.7, 118.1, 33.6, 14.9. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₀H₁₀NO⁺ = 160.0757; Found 160.0756.



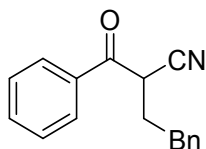
2-benzoylbutanenitrile (1b)¹: white solid, 1.56 g, 90% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.00 – 7.93 (m, 2H), 7.69 – 7.61 (m, 1H), 7.56 – 7.49 (m, 2H), 4.35 (dd, *J* = 8.1, 5.6 Hz, 1H), 2.19 – 1.94 (m, 2H), 1.16 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 190.8, 134.4, 133.9, 129.0, 128.6, 117.2, 41.4, 23.5, 11.4. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₁H₁₂NO⁺ = 174.0913; Found 174.0913.



2-benzoyl-3-methylbutanenitrile (1c)⁷: white solid, 1.72 g, 92% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.03 – 7.89 (m, 2H), 7.72 – 7.61 (m, 1H), 7.59 – 7.48 (m, 2H), 4.37 (dd, *J* = 5.4, 3.1 Hz, 1H), 2.56 – 2.36 (m, 1H), 1.18 (dd, *J* = 6.8, 1.5 Hz, 3H), 1.10 (dd, *J* = 6.8, 2.8 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 191.2, 134.3, 129.0, 128.5, 116.1, 47.8, 29.8, 21.3, 18.6, 18.6. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₁₂H₁₃NNaO⁺ = 210.0889; Found 210.0887.

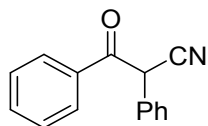


2-benzoyl-4-methylpentanenitrile (1d)⁷: colorless oil, 1.81 g, 90% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.05 – 7.93 (m, 2H), 7.73 – 7.61 (m, 1H), 7.61 – 7.47 (m, 2H), 4.43 (dd, *J* = 9.8, 5.2 Hz, 1H), 2.00 – 1.88 (m, 2H), 1.85 – 1.73 (m, 1H), 1.02 (dd, *J* = 14.4, 6.3 Hz, 6H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 191.0, 134.3, 133.8, 129.0, 128.6, 117.3, 38.4, 38.3, 26.3, 22.6, 21.2. HRMS (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₃H₁₆NO⁺ = 202.1226; Found 202.1227.

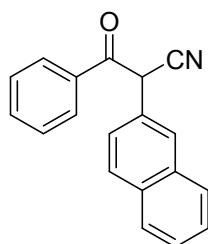


2-benzoyl-4-phenylbutanenitrile (1e)⁷: white solid, 2.20 g, 88% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.99 – 7.92 (m, 2H), 7.69 – 7.60 (m, 1H), 7.55 – 7.47 (m, 2H), 7.39 – 7.26 (m, 5H), 4.58 – 4.47 (m, 1H), 3.44 – 3.17 (m, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 190.0, 135.9, 134.6, 134.0, 129.1, 129.0, 128.9, 128.8, 127.6, 116.9,

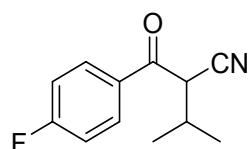
41.8, 35.5. **HRMS** (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{16}H_{14}NO^+$ = 236.1070; Found 236.1069.



3-oxo-2,3-diphenylpropanenitrile (1f)¹: white solid, 2.10 g, 95% yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.01 – 7.91 (m, 2H), 7.69 – 7.56 (m, 1H), 7.56 – 7.31 (m, 7H), 5.66 – 5.54 (m, 1H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 188.9, 134.4, 133.6, 130.3, 129.6, 129.2, 129.1, 129.0, 128.2, 116.5, 46.6. **HRMS** (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{15}H_{12}NO^+$ = 222.0913; Found 222.0913.

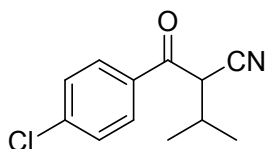


2-(naphthalen-2-yl)-3-oxo-3-phenylpropanenitrile (1g)⁸: white solid, 2.52 g, 93% yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.06 – 7.96 (m, 3H), 7.93 – 7.82 (m, 3H), 7.64 – 7.44 (m, 6H), 5.79 (s, 1H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 188.9, 134.4, 133.6, 133.4, 133.1, 129.8, 129.3, 129.0, 128.0, 127.9, 127.8, 127.6, 127.1, 127.0, 125.0, 116.6, 46.9. **HRMS** (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{19}H_{14}NO^+$ = 272.1070; Found 272.1069.

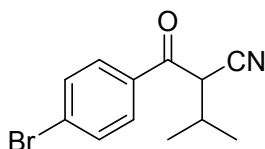


2-(4-fluorobenzoyl)-3-methylbutanenitrile (1h): white solid, 1.64 g, 80% yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.05 – 7.92 (m, 2H), 7.25 – 7.16 (m, 2H), 4.21 (d, J = 5.6 Hz, 1H), 2.54 – 2.37 (m, 1H), 1.15 (dd, J = 14.9, 6.7 Hz, 6H). **¹³C NMR** (101

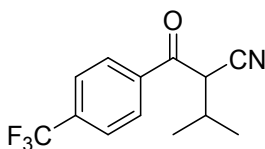
MHz, Chloroform-*d*) δ 189.5, 166.4 (d, $J = 258.6$ Hz), 131.5 (d, $J = 10.1$ Hz), 130.8, (d, $J = 3.0$ Hz), 116.4 (d, $J = 22.2$ Hz), 116.0, 47.8, 29.9, 21.3, 18.8. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -102.3. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{13}\text{FNO}^+ = 206.0976$; Found 206.0975.



2-(4-chlorobenzoyl)-3-methylbutanenitrile (1i): white solid, 1.87 g, 85% yield. **^1H NMR** (400 MHz, Chloroform-*d*) δ 7.93 – 7.85 (m, 2H), 7.53 – 7.47 (m, 2H), 4.29 (d, $J = 5.4$ Hz, 1H), 2.51 – 2.37 (m, 1H), 1.18 (d, $J = 6.8$ Hz, 3H), 1.11 (d, $J = 6.7$ Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 190.0, 140.9, 132.6, 130.0, 129.4, 115.9, 47.8, 29.8, 21.2, 18.7. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{13}\text{ClNO}^+ = 222.0680$; Found 222.0681.

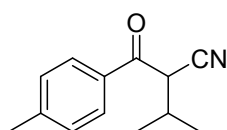


2-(4-bromobenzoyl)-3-methylbutanenitrile (1j): white solid, 2.30 g, 87% yield. **^1H NMR** (400 MHz, Chloroform-*d*) δ 7.85 – 7.79 (m, 2H), 7.72 – 7.66 (m, 2H), 4.24 (dd, $J = 5.6, 2.1$ Hz, 1H), 2.53 – 2.39 (m, 1H), 1.19 (d, $J = 6.8$ Hz, 3H), 1.13 (d, $J = 6.7$ Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 190.2, 133.1, 132.5, 130.1, 129.8, 115.9, 47.8, 29.8, 21.3, 18.8. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{13}\text{BrNO}^+ = 266.0175$; Found 266.0175.

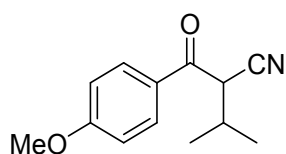


3-methyl-2-(4-(trifluoromethyl)benzoyl)butanenitrile (1k): white solid, 2.32 g, 91% yield. **^1H NMR** (400 MHz, Chloroform-*d*) δ 8.08 (d, $J = 8.2$ Hz, 2H), 7.81 (d, $J = 8.2$

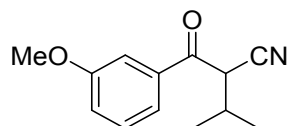
Hz, 2H), 4.36 – 4.28 (m, 1H), 2.55 – 2.41 (m, 1H), 1.21 (d, $J = 6.8$ Hz, 3H), 1.14 (dd, $J = 6.7, 2.1$ Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 190.38, 137.09, 135.67, 135.34, 129.00, 126.23, 126.19, 126.16, 126.12, 124.59, 121.88, 115.65, 48.17, 29.74, 21.30, 18.73, 18.71. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 190.4, 137.1, 135.5 (q, $J = 35.4$ Hz), 129.0, 126.2 (q, $J = 3.5$ Hz), 123.3 (q, $J = 272.7$ Hz), 115.7, 48.2, 29.7, 21.3, 18.7. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.3. HRMS (ESI-TOF) m/z : $[\text{M-H}]^-$ Calcd for $\text{C}_{13}\text{H}_{11}\text{F}_3\text{NO}^- = 254.0798$; Found 254.0799.



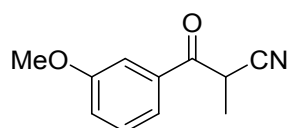
3-methyl-2-(4-methylbenzoyl)butanenitrile (1l): white solid, 1.93 g, 96% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.87 – 7.81 (m, 2H), 7.34 – 7.29 (m, 2H), 4.26 (d, $J = 5.6$ Hz, 1H), 2.51 – 2.39 (m, 4H), 1.16 (d, $J = 6.8$ Hz, 3H), 1.12 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 190.6, 145.5, 131.9, 129.8, 128.8, 116.3, 47.7, 30.0, 21.7, 21.4, 18.9. HRMS (ESI-TOF) m/z : $[\text{M+H}]^+$ Calcd for $\text{C}_{13}\text{H}_{16}\text{NO}^+ = 202.1226$; Found 202.1226.



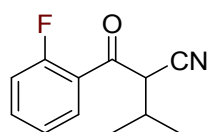
2-(4-methoxybenzoyl)-3-methylbutanenitrile (1m): white solid, 1.62 g, 75% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.98 – 7.90 (m, 2H), 7.04 – 6.96 (m, 2H), 4.23 (d, $J = 5.8$ Hz, 1H), 3.92 (s, 3H), 2.53 – 2.41 (m, 1H), 1.16 (dd, $J = 9.8, 6.7$ Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 189.4, 164.4, 131.1, 127.2, 116.5, 114.2, 55.6, 47.4, 30.0, 21.3, 18.9. HRMS (ESI-TOF) m/z : $[\text{M+H}]^+$ Calcd for $\text{C}_{13}\text{H}_{16}\text{NO}_2^+ = 218.1176$; Found 218.1175.



2-(3-methoxybenzoyl)-3-methylbutanenitrile (1n): white solid, 1.95 g, 90% yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.53 – 7.40 (m, 3H), 7.23 – 7.16 (m, 1H), 4.31 (d, $J = 5.5$ Hz, 1H), 3.89 (s, 3H), 2.53 – 2.42 (m, 1H), 1.19 (d, $J = 6.8$ Hz, 3H), 1.13 (d, $J = 6.7$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 191.0, 160.1, 135.7, 130.0, 121.0, 120.7, 116.1, 113.0, 55.5, 47.9, 30.0, 21.3, 18.7. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{16}\text{NO}_2^+$ = 218.1176; Found 218.1175.

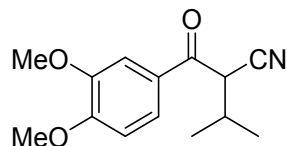


3-(3-methoxyphenyl)-2-methyl-3-oxopropanenitrile (1o): white solid, 2.72 g, 72% yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.59 – 7.41 (m, 3H), 7.23 – 7.17 (m, 1H), 4.40 (q, $J = 7.2$ Hz, 1H), 3.88 (s, 3H), 1.65 (d, $J = 7.2$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 190.7, 160.1, 134.9, 130.0, 121.1, 120.9, 118.1, 113.0, 55.5, 33.8, 15.0. **HRMS** (ESI-TOF) m/z : $[\text{M}-\text{H}]^-$ Calcd for $\text{C}_{11}\text{H}_{10}\text{NO}_2^-$ = 188.0717; Found 188.0713.

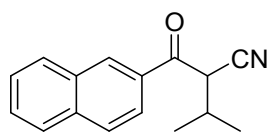


2-(2-fluorobenzoyl)-3-methylbutanenitrile (1p): colorless oil, 1.74 g, 85% yield. $^1\text{H NMR}$ (600 MHz, Chloroform-*d*) δ 7.89 (t, $J = 7.6$ Hz, 1H), 7.66 – 7.59 (m, 1H), 7.31 (t, $J = 7.6$ Hz, 1H), 7.19 (dd, $J = 11.5, 8.4$ Hz, 1H), 4.38 (d, $J = 4.3$ Hz, 1H), 2.42 (dq, $J = 12.6, 6.3$ Hz, 1H), 1.21 (d, $J = 6.8$ Hz, 3H), 1.04 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, Chloroform-*d*) δ 189.4 (d, $J = 4.5$ Hz), 161.3 (d, $J = 255.2$ Hz), 136.0 (d, $J = 9.1$ Hz), 131.4 (d, $J = 3.0$ Hz), 125.2 (d, $J = 3.0$ Hz), 123.1 (d, $J = 12.1$ Hz), 116.8 (d, $J = 24.2$ Hz), 115.5, 52.3 (d, $J = 9.1$ Hz), 29.0, 21.5, 18.1.

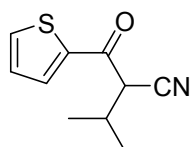
¹⁹F NMR (376 MHz, Chloroform-*d*) δ -110.2. **HRMS** (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₂H₁₃FNO⁺ = 206.0976; Found 206.0976.



2-(3,4-dimethoxybenzoyl)-3-methylbutanenitrile (1q): white solid, 2.12 g, 86% yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.61 – 7.47 (m, 2H), 6.93 (d, *J* = 8.3 Hz, 1H), 4.25 (d, *J* = 5.9 Hz, 1H), 3.97 (d, *J* = 9.7 Hz, 6H), 2.54 – 2.41 (m, 1H), 1.19 – 1.11 (m, 6H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 189.4, 154.4, 149.5, 127.5, 123.4, 116.6, 110.7, 110.1, 56.2, 56.0, 47.2, 30.2, 21.3, 19.0. **HRMS** (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₄H₁₈NO₃⁺ = 248.1281; Found 248.1280.

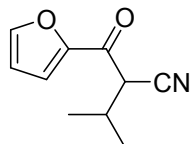


2-(2-naphthoyl)-3-methylbutanenitrile (1r): white solid, 1.94 g, 82% yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.53 – 8.43 (m, 1H), 8.07 – 7.88 (m, 4H), 7.75 – 7.58 (m, 2H), 4.46 (d, *J* = 5.7 Hz, 1H), 2.57 (pd, *J* = 6.8, 5.7 Hz, 1H), 1.21 (dd, *J* = 18.9, 6.7 Hz, 6H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 191.1, 136.0, 132.3, 131.8, 130.6, 129.7, 129.3, 129.1, 127.9, 127.3, 123.8, 116.3, 47.8, 30.1, 21.4, 18.9. **HRMS** (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₆H₁₆NO⁺ = 238.1226; Found 238.1225.

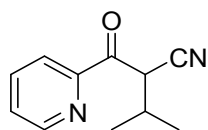


3-methyl-2-(thiophene-2-carbonyl)butanenitrile (1s): white solid, 1.54 g, 80% yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.87 – 7.84 (m, 1H), 7.82 – 7.77 (m, 1H), 7.23 – 7.20 (m, 1H), 4.06 (dd, *J* = 6.2, 1.7 Hz, 1H), 2.61 – 2.44 (m, 1H), 1.19 (t, *J* = 6.9 Hz, 6H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 183.6, 141.4, 136.0, 133.4, 128.6,

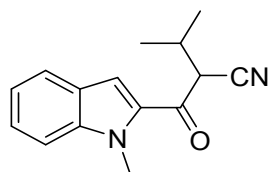
116.2, 48.7, 30.7, 21.2, 19.3. **HRMS** (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{10}H_{12}NOS^+$ = 194.0634; Found 194.0635.



2-(furan-2-carbonyl)-3-methylbutanenitrile (1t): white solid, 1.40 g, 79% yield. **1H NMR** (400 MHz, Chloroform-*d*) δ 7.68 (d, J = 1.7 Hz, 1H), 7.46 – 7.38 (m, 1H), 6.68 – 6.60 (m, 1H), 4.14 (d, J = 6.0 Hz, 1H), 2.59 – 2.41 (m, 1H), 1.19 – 1.10 (m, 6H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 179.7, 150.6, 147.5, 119.5, 115.9, 113.2, 47.8, 29.9, 21.1, 19.0. **HRMS** (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{10}H_{12}NO_2^+$ = 178.0863; Found 178.0862..

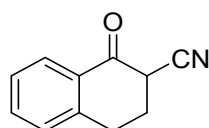


3-methyl-2-picolinoylbutanenitrile (1u): white solid, 1.61 g, 86% yield. **1H NMR** (400 MHz, Chloroform-*d*) δ 8.75 – 8.67 (m, 1H), 8.15 – 8.09 (m, 1H), 7.96 – 7.87 (m, 1H), 7.62 – 7.53 (m, 1H), 5.16 (d, J = 5.2 Hz, 1H), 2.60 – 2.46 (m, 1H), 1.20 (d, J = 6.7 Hz, 3H), 1.09 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 192.8, 150.7, 149.2, 137.4, 128.2, 123.0, 116.6, 46.1, 29.5, 21.4, 18.5. **HRMS** (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{11}H_{13}N_2O^+$ = 189.1022; Found 189.1022.

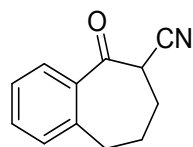


3-methyl-2-(1-methyl-1H-indole-2-carbonyl)butanenitrile (1v): white solid, 1.92 g, 80% yield. **1H NMR** (400 MHz, Chloroform-*d*) δ 7.77 – 7.71 (m, 1H), 7.50 – 7.40 (m, 2H), 7.37 (s, 1H), 7.26 – 7.19 (m, 1H), 4.22 (d, J = 6.3 Hz, 1H), 4.10 (s, 3H), 2.57 (m,

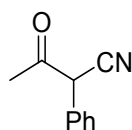
1H), 1.20 (dd, $J = 9.9, 6.7$ Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.1, 140.8, 132.4, 127.2, 125.6, 123.3, 121.4, 116.6, 113.0, 110.6, 49.0, 32.3, 31.1, 21.3, 19.3. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}^+$ = 241.1335; Found 241.1334.



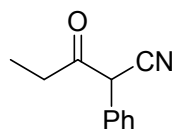
1-oxo-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (1w)⁹: white solid, 1.02 g, 60% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 8.14 – 8.05 (m, 1H), 7.63 – 7.54 (m, 1H), 7.39 (t, $J = 7.6$ Hz, 1H), 7.31 (d, $J = 7.7$ Hz, 1H), 3.78 (dd, $J = 11.3, 4.5$ Hz, 1H), 3.24 – 3.04 (m, 2H), 2.67 – 2.55 (m, 1H), 2.55 – 2.39 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.8, 142.9, 134.8, 130.3, 128.9, 128.2, 127.4, 116.7, 40.7, 27.8, 27.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{10}\text{NO}^+$ = 172.0757; Found 172.0757.



5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carbonitrile (1x)¹⁰: colorless oil, 0.83 g, 45% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.74 (m, 1H), 7.53 – 7.47 (m, 1H), 7.41 – 7.33 (m, 1H), 7.30 – 7.24 (m, 1H), 3.97 (dd, $J = 9.8, 4.6$ Hz, 1H), 3.18 – 2.86 (m, 2H), 2.37 – 2.09 (m, 3H), 2.02 – 1.86 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.2, 141.1, 136.5, 133.3, 130.2, 129.6, 127.2, 117.2, 42.5, 32.5, 27.2, 24.2. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{12}\text{NO}^+$ = 186.0913; Found 186.0914.



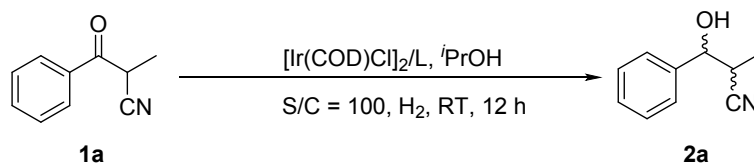
3-oxo-2-phenylbutanenitrile (1y)¹: white powder, 1.19 g, 75% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.53 – 7.38 (m, 5H), 4.71 (s, 1H), 2.29 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 196.4, 129.7, 129.6, 129.3, 127.9, 116.1, 51.5, 26.9. **HRMS** (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₀H₁₀NO⁺ = 160.0757; Found 160.0757.



3-oxo-2-phenylpentanenitrile (1z)²: white powder, 1.38 g, 80% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.33 (m, 5H), 4.70 (s, 1H), 2.78 – 2.45 (m, 2H), 1.04 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 199.4, 129.9, 129.6, 129.2, 127.9, 116.3, 50.6, 33.1, 7.6. **HRMS** (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₁H₁₂NO⁺ = 174.0913; Found 174.0913.

3. Detailed Optimization of the Reaction Conditions.

Table S1. Evaluation of the effects of ligand in Ir-catalyzed asymmetric hydrogenation of **1a**^a



entry	ligand	base	temp. (°C)	H ₂ (bar)	conv. (%) ^b	ee (%) ^c	dr ^c
1	f-amphox	KO ^t Bu (10 mol%)	25	50	<5	-	-
2	f-ampha	KO ^t Bu (10 mol%)	25	50	<5	-	-
3	f-amphol	KO ^t Bu (10 mol%)	25	50	<5	-	-
4	f-amphox	KO ^t Bu (10 mol%)	25	80	<5	-	-
5	f-amphol	KO ^t Bu (10 mol%)	25	80	<5	-	-
6	f-amphox	KO ^t Bu (105 mol%)	50	50	<5	-	-
7	f-ampha	KO ^t Bu (105 mol%)	50	50	<5	-	-
8	f-amphol	KO ^t Bu (105 mol%)	50	50	<5	-	-

^a Reaction conditions: 0.1 mmol of substrate **1a**, 0.25 mol % [Ir(COD)Cl]₂, 1 mol % ligand pre-complexed in *i*PrOH, *i*PrOH (1.0 mL). ^b Conversions were determined by ¹H NMR spectroscopy. ^c Diastereomeric ratio (dr) were determined by ¹H NMR spectroscopy. ^d Enantiomeric excesses (ee) were determined by HPLC analysis using a chiral stationary phase.

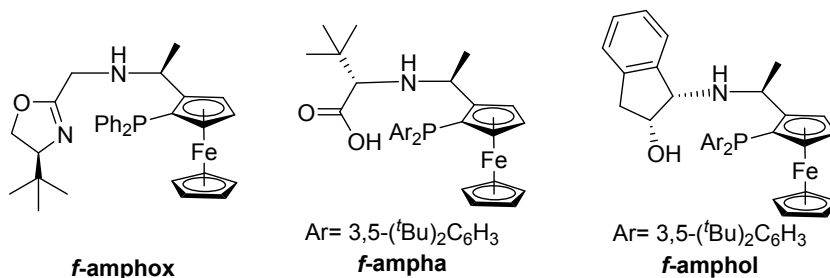
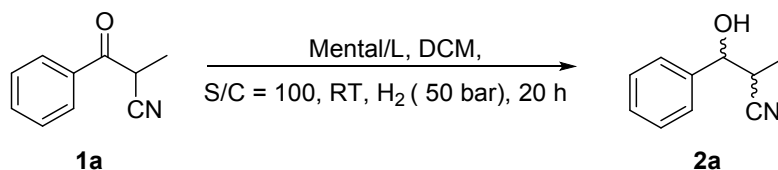
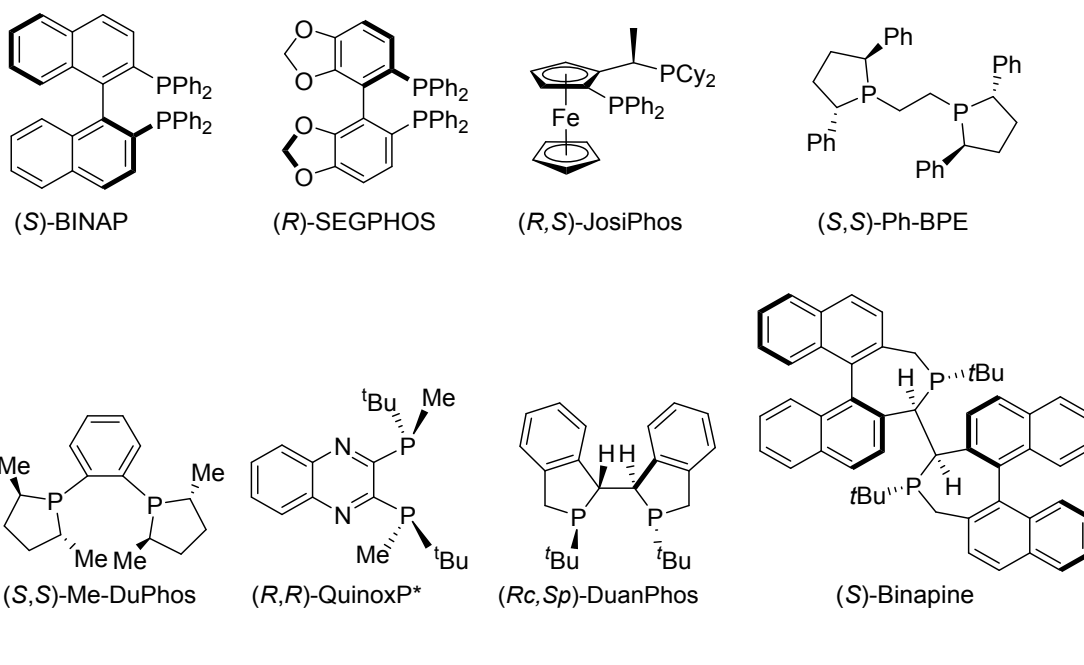


Table S2. Evaluation of ligand in Rh-catalyzed asymmetric hydrogenation of **1a**^a



entry	metal	ligand	conv. (%) ^b	ee (%) ^c	dr ^d
1	[Rh(NBD) ₂] ₂ BF ₄	(<i>R</i> _C , <i>S</i> _P)-Duanphos	<5	-	-
2	[Rh(NBD) ₂] ₂ BF ₄	(<i>S</i>)-Binapine	<5	-	-
3	[Rh(NBD) ₂] ₂ BF ₄	(<i>S</i>)-BINAP	<5	-	-
4	[Rh(NBD) ₂] ₂ BF ₄	(<i>R</i>)-SEGPHOS	<5	-	-
5	[Rh(NBD) ₂] ₂ BF ₄	(<i>R</i> , <i>S</i>)-Josiphos	<5	-	-
6	[Rh(NBD) ₂] ₂ BF ₄	(<i>S</i> , <i>S</i>)-Ph-BPE	<5	-	-
7	[Rh(NBD) ₂] ₂ BF ₄	(<i>S</i> , <i>S</i>)-Me-DuPhos	<5	-	-
8	[Rh(NBD) ₂] ₂ BF ₄	(<i>R</i> , <i>R</i>)-QuinoxP*	<5	-	-

^a Reaction conditions: 0.1 mmol of substrate **1a**, 1 mol % [Rh(NBD)₂]₂BF₄, 1.1 mol % ligand pre-complexed in DCM, DCM (1.0 mL). ^b Conversions were determined by ¹H NMR spectroscopy. ^c Diastereomeric ratio (dr) were determined by ¹H NMR spectroscopy. ^d Enantiomeric excesses (ee) were determined by HPLC analysis using a chiral stationary phase.

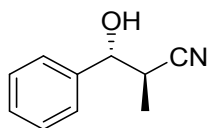


4. General Procedure of Asymmetric Transfer Hydrogenation of **1** via DKR

To a 10 mL Schleck tube charged with a magnetic stirring bar were added successively substrate **1** (0.2 mmol), formic acid/trimethylamine azeotropic mixture (5/2) (50 μ L), the catalyst (1.5 mg) and the solvent (2 mL). The mixture was then stirred at room temperature for the indicated reaction time. After completion, the reaction solution was concentrated and the residue was passed through a short column of silica gel (eluent: EA:PE = 2:1) to remove the metal complex. The ee or dr values of compounds **2** were determined by HPLC analysis on a chiral stationary phase. The physical data were identical in all respect to those previously reported.

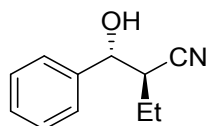
It should be emphasized that cat.1, cat.2, cat.3, cat.5, cat.6 were purchased from commercial suppliers and used without further purification, cat.4 were synthesized according to the literature.²⁷

Characterization Data of **2**

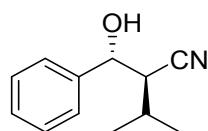


(2R,3R)-3-hydroxy-2-methyl-3-phenylpropanenitrile (2a): white solid; 31 mg, 97% yield; >99% ee, 96:4 dr; $[\alpha]^{20}_D = +80.0$ (c 0.5, CHCl_3); **The absolute configurations of 2a was assigned as (2R,3R) by comparing the NMR and specific rotation with the known compound.**¹¹ HPLC (Chiralpak IB column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 15.7$ min, $t_2 = 16.7$ min, $t_3 = 18.6$ min, $t_4 = 20.4$ min (major). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.31 (m, 5H), 4.71 (dd, $J = 6.7, 2.9$ Hz, 1H), 2.91 (p, $J = 7.1$ Hz, 1H), 2.60 (d, $J = 3.5$ Hz, 1H), 1.24 (d, $J = 7.2$ Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 140.0, 128.8, 128.8,

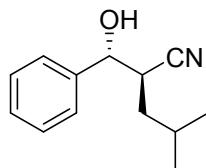
126.2, 121.0, 75.1, 34.5, 14.7. **HRMS** (ESI-TOF) m/z : $[M+Cl]^-$ Calcd for $C_{10}H_{11}ClNO^- = 196.0535$; Found 196.0527.



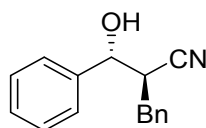
(R)-2-((R)-hydroxy(phenyl)methyl)butanenitrile (2b)¹¹: white solid, 34 mg, 97% yield, >99% ee, 96:4 dr; $[\alpha]^{20}_D = +55.0$ (c 0.5, $CHCl_3$); **The absolute configurations of 2b was assigned as (R,R) by X-ray**; **HPLC** (Chiralpak IA column, hexane/isopropanol = 93/7; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 9.6$ min, $t_2 = 10.6$ min, $t_3 = 11.8$ min, $t_4 = 12.6$ min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.50 – 7.32 (m, 5H), 4.78 (dd, $J = 6.6, 3.0$ Hz, 1H), 2.82 – 2.71 (m, 1H), 2.59 (d, $J = 3.5$ Hz, 1H), 1.68 – 1.46 (m, 2H), 1.08 (t, $J = 7.4$ Hz, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 140.3, 128.8, 128.7, 126.2, 120.1, 73.9, 42.7, 22.4, 11.6. **HRMS** (ESI-TOF) m/z : $[M+Cl]^-$ Calcd for $C_{11}H_{13}ClNO^- = 210.0691$; Found 210.0684.



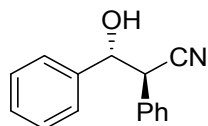
(R)-2-((R)-hydroxy(phenyl)methyl)-3-methylbutanenitrile (2c)¹²: white solid, 37 mg, 98% yield, >99% ee, 98:2 dr; $[\alpha]^{20}_D = +29.4$ (c 0.5, $CHCl_3$); **HPLC** (Chiralpak IB column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 12.3$ min, $t_2 = 13.7$ min, $t_3 = 16.9$ min, $t_4 = 18.8$ min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.51 – 7.28 (m, 5H), 4.84 (d, $J = 7.3$ Hz, 1H), 2.70 (dd, $J = 7.3, 5.2$ Hz, 1H), 2.66 (s, 1H), 1.81 – 1.56 (m, 1H), 1.10 (d, $J = 6.7$ Hz, 3H), 1.05 (d, $J = 6.8$ Hz, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 140.6, 128.9, 128.7, 126.1, 119.1, 72.5, 48.6, 27.4, 21.5, 18.7. **HRMS** (ESI-TOF) m/z : $[M+Cl]^-$ Calcd for $C_{12}H_{15}ClNO^- = 224.0848$; Found 224.0842.



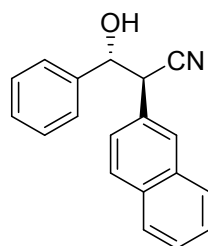
(R)-2-((R)-hydroxy(phenyl)methyl)-4-methylpentanenitrile (2d): white solid, 40 mg, 99% yield, >99% ee, 99:1 dr; $[\alpha]_D^{20} = +15.0$ (c 0.5, CHCl_3); **HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 8.1$ min, $t_2 = 10.7$ min, $t_3 = 13.2$ min (major), $t_4 = 14.4$ min. **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.50 – 7.34 (m, 5H), 4.78 (dd, $J = 5.9, 2.6$ Hz, 1H), 2.97 – 2.87 (m, 1H), 2.44 (brs, 1H), 1.94 – 1.80 (m, 1H), 1.80 – 1.66 (m, 1H), 1.26 – 1.15 (m, 1H), 0.96 (d, $J = 6.6$ Hz, 3H), 0.90 (d, $J = 6.6$ Hz, 3H). **$^{13}\text{C NMR}$** (101 MHz, Chloroform-*d*) δ 140.4, 128.8, 128.8, 126.1, 120.1, 74.4, 39.2, 37.7, 26.0, 23.0, 21.1. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Cl}]^-$ Calcd for $\text{C}_{13}\text{H}_{17}\text{ClNO}$ = 238.1004; Found 238.0999.



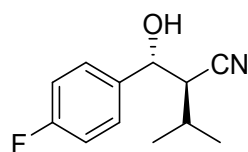
(R)-2-((R)-hydroxy(phenyl)methyl)-4-phenylbutanenitrile (2e)¹³: white solid, 49 mg, 98% yield, >99% ee, 97:3 dr; $[\alpha]_D^{20} = +17.8$ (c 0.5, CHCl_3); **HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 11.5$ min, $t_2 = 14.9$ min, $t_3 = 15.9$ min, $t_4 = 18.9$ min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.53 – 7.09 (m, 10H), 4.84 – 4.66 (m, 1H), 3.10 – 2.99 (m, 1H), 2.99 – 2.84 (m, 2H), 2.65 (d, $J = 3.9$ Hz, 1H). **$^{13}\text{C NMR}$** (101 MHz, Chloroform-*d*) δ 140.2, 136.7, 128.9, 128.8, 128.8, 128.7, 127.2, 126.0, 119.5, 72.8, 43.2, 35.2. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Cl}]^-$ Calcd for $\text{C}_{16}\text{H}_{15}\text{ClNO}$ = 272.0848; Found 272.0846.



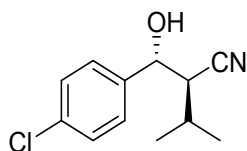
(2R,3R)-3-hydroxy-2,3-diphenylpropanenitrile (2f)¹⁴: white solid, 44 mg, 97% yield, >99% ee, 97:3 dr; $[\alpha]_D^{20} = -6.2$ (c 0.5, CHCl₃); **HPLC** (Chiralpak IE column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 11.4$ min, $t_2 = 12.9$ min, $t_3 = 15.1$ min (major), $t_4 = 24.6$ min. **¹H NMR** (600 MHz, Chloroform-*d*) δ 7.37 – 7.15 (m, 10H), 4.97 (dd, $J = 6.0, 2.5$ Hz, 1H), 4.05 (d, $J = 5.8$ Hz, 1H), 2.63 – 2.54 (m, 1H). **¹³C NMR** (151 MHz, Chloroform-*d*) δ 139.3, 132.4, 128.9, 128.7, 128.5, 128.5, 128.4, 126.2, 118.7, 76.3, 47.3. **HRMS** (ESI-TOF) m/z : $[M-H]^+$ Calcd for C₁₅H₁₂NO⁻ = 222.0924; Found 222.0919.



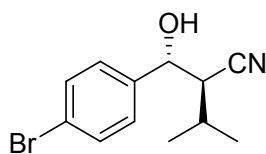
(2R,3R)-3-hydroxy-2-(naphthalen-2-yl)-3-phenylpropanenitrile (2g)¹⁴: white solid, 54 mg, 99% yield, >99% ee, 97:3 dr; $[\alpha]_D^{20} = -24.6$ (c 0.5, CHCl₃); **HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 13.0$ min, $t_2 = 14.9$ min, $t_3 = 17.9$ min, $t_4 = 26.5$ min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.92 – 7.75 (m, 4H), 7.55 (dt, $J = 6.3, 3.4$ Hz, 2H), 7.38 – 7.27 (m, 6H), 5.09 (dd, $J = 5.6, 1.8$ Hz, 1H), 4.25 (d, $J = 5.5$ Hz, 1H), 2.62 (d, $J = 3.5$ Hz, 1H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 139.3, 133.0, 132.9, 129.8, 128.7, 128.7, 128.6, 128.5, 127.9, 127.8, 127.7, 126.7, 126.2, 125.6, 118.7, 76.2, 47.5. **HRMS** (ESI-TOF) m/z : $[M-H]^+$ Calcd for C₁₉H₁₄NO⁻ = 272.1081; Found 272.1080.



(R)-2-((R)-(4-fluorophenyl)(hydroxy)methyl)-3-methylbutanenitrile (2h): white solid, 41 mg, 99% yield, >99% ee, 98:2 dr; $[\alpha]_D^{20} = +55.4$ (c 0.5, CHCl₃); **HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 5.3$ min, $t_2 = 5.8$ min, $t_3 = 10.6$ min, $t_4 = 12.6$ min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.44 – 7.33 (m, 2H), 7.15 – 7.05 (m, 2H), 4.87 (d, $J = 7.1$ Hz, 1H), 2.77 (s, 1H), 2.67 (dd, $J = 7.1, 5.3$ Hz, 1H), 1.78 – 1.65 (m, 1H), 1.12 (d, $J = 6.8$ Hz, 3H), 1.08 (d, $J = 6.7$ Hz, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 162.8 (d, $J = 252.5$ Hz), 136.5 (d, $J = 10.1$ Hz), 127.9 (d, $J = 10.1$ Hz), 119.0, 115.8 (d, $J = 20.2$ Hz), 71.8, 48.7, 27.4, 21.4, 18.8. **¹⁹F NMR** (376 MHz, Chloroform-*d*) δ -112.9. **HRMS** (ESI-TOF) m/z : $[M+Cl]^-$ Calcd for C₁₂H₁₄ClFNO⁻ = 242.0753; Found 242.0750.

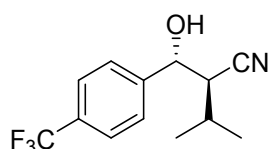


(R)-2-((R)-(4-chlorophenyl)(hydroxy)methyl)-3-methylbutanenitrile (2i) white solid, 44 mg, 98% yield, >99% ee, 98:2 dr; $[\alpha]_D^{20} = +61.8$ (c 0.5, CHCl₃); **HPLC** (Chiralpak ID column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 6.3$ min, $t_2 = 6.8$ min, $t_3 = 8.0$ min, $t_4 = 8.7$ min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.42 – 7.31 (m, 4H), 4.87 (d, $J = 6.9$ Hz, 1H), 2.71 – 2.65 (m, 1H), 2.65 – 2.50 (m, 1H), 1.80 – 1.70 (m, 1H), 1.13 (d, $J = 6.6$ Hz, 3H), 1.08 (d, $J = 6.7$ Hz, 3H). **¹³C NMR** (151 MHz, Chloroform-*d*) δ 139.1, 134.6, 129.1, 127.5, 118.8, 71.9, 48.7, 27.5, 21.4, 18.9. **HRMS** (ESI-TOF) m/z : $[M+Cl]^-$ Calcd for C₁₂H₁₄Cl₂NO⁻ = 258.0458; Found 258.0455.

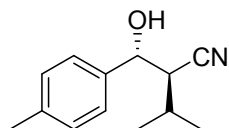


(R)-2-((R)-(4-bromophenyl)(hydroxy)methyl)-3-methylbutanenitrile (2j) white solid, 52 mg, 97% yield, >99% ee, 98:2 dr; $[\alpha]_D^{20} = +43.6$ (c 0.5, CHCl₃); **HPLC**

(Chiralpak ID column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 11.5$ min, $t_2 = 12.6$ min, $t_3 = 16.2$ min, $t_4 = 17.5$ min (major). $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.61 – 7.50 (m, 2H), 7.31 – 7.26 (m, 2H), 4.86 (dd, $J = 7.0, 3.7$ Hz, 1H), 2.67 (dd, $J = 6.9, 5.5$ Hz, 1H), 2.63 – 2.53 (m, 1H), 1.82 – 1.71 (m, 1H), 1.13 (d, $J = 6.7$ Hz, 3H), 1.09 (d, $J = 6.7$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 139.6, 132.0, 127.8, 122.7, 118.8, 71.9, 48.6, 27.5, 21.4, 18.9. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Cl}]^-$ Calcd for $\text{C}_{12}\text{H}_{14}\text{BrClNO}^- = 301.9953$; Found 301.9951.

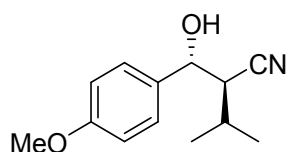


(*R*)-2-((*R*)-hydroxy(4-(trifluoromethyl)phenyl)methyl)-3-methylbutanenitrile (2k) white solid, 50 mg, 97% yield, >99% ee, 98:2 dr; $[\alpha]_{\text{D}}^{20} = +30.6$ (c 0.5, CHCl_3); **HPLC** (Chiralpak IA column, hexane/isopropanol = 97/3; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 15.4$ min, $t_2 = 16.9$ min, $t_3 = 20.4$ min, $t_4 = 31.1$ min (major). $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.68 (d, $J = 8.1$ Hz, 2H), 7.53 (d, $J = 8.0$ Hz, 2H), 4.96 (dd, $J = 6.7, 3.2$ Hz, 1H), 2.93 – 2.76 (m, 1H), 2.69 (t, $J = 6.2$ Hz, 1H), 1.86 – 1.73 (m, 1H), 1.15 (d, $J = 6.7$ Hz, 3H), 1.10 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 144.6, 130.9 (q, $J = 32.8$ Hz), 126.5, 125.8 (q, $J = 3.5$ Hz), 123.9 (q, $J = 272.7$ Hz), 118.6, 71.8, 48.8, 27.6, 21.3, 19.1. $^{19}\text{F NMR}$ (376 MHz, Chloroform-*d*) δ -62.7. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Cl}]^-$ Calcd for $\text{C}_{13}\text{H}_{14}\text{ClF}_3\text{NO}^- = 292.0721$; Found 292.0721.

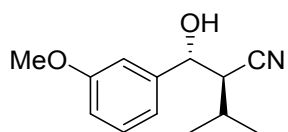


(*R*)-2-((*R*)-hydroxy(*p*-tolyl)methyl)-3-methylbutanenitrile (2l) white solid, 40 mg, 98% yield, >99% ee, 99:1 dr; $[\alpha]_{\text{D}}^{20} = +46.0$ (c 0.5, CHCl_3); **HPLC** (Chiralpak IC column, hexane/isopropanol = 85/15; flow rate = 1.0 mL/min; UV detection at 220

nm; $t_1 = 5.4$ min, $t_2 = 6.4$ min, $t_3 = 10.9$ min, $t_4 = 13.8$ min (major). $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.28 – 7.23 (m, 2H), 7.22 – 7.15 (m, 2H), 4.81 (dd, $J = 7.6, 2.8$ Hz, 1H), 2.71 (dd, $J = 7.5, 5.0$ Hz, 1H), 2.36 (s, 3H), 2.35 – 2.25 (m, 1H), 1.75 – 1.64 (m, 1H), 1.09 (d, $J = 6.7$ Hz, 3H), 1.05 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 138.7, 137.6, 129.6, 126.1, 119.2, 72.6, 48.6, 27.4, 21.5, 21.1, 18.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{13}\text{H}_{17}\text{NNaO}^+$ = 226.1202; Found 226.1200.

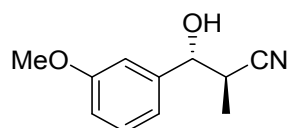


(*R*)-2-((*R*)-hydroxy(4-methoxyphenyl)methyl)-3-methylbutanenitrile (2m) white solid, 43 mg, 98% yield, >99% ee, 99:1 dr; $[\alpha]_D^{20} = +54.8$ (c 0.5, CHCl_3); **HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 10.7$ min, $t_2 = 12.0$ min, $t_3 = 23.9$ min, $t_4 = 29.1$ min (major). $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.31 – 7.27 (m, 2H), 6.99 – 6.84 (m, 2H), 4.79 (d, $J = 7.6$ Hz, 1H), 3.81 (s, 3H), 2.69 (dd, $J = 7.6, 5.0$ Hz, 1H), 2.54 (s, 1H), 1.72 – 1.60 (m, 1H), 1.08 (d, $J = 6.8$ Hz, 3H), 1.04 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 159.8, 132.6, 127.4, 119.3, 114.2, 72.3, 55.3, 48.5, 27.3, 21.5, 18.5. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{13}\text{H}_{17}\text{NNaO}_2^+$ = 242.1151; Found 242.1148.

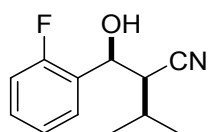


(*R*)-2-((*R*)-hydroxy(3-methoxyphenyl)methyl)-3-methylbutanenitrile (2n) white solid, 43 mg, 98% yield, >99% ee, 99:1 dr; $[\alpha]_D^{20} = +52.8$ (c 0.5, CHCl_3); **HPLC** (Chiralpak IC column, hexane/isopropanol = 85/15; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 6.3$ min, $t_2 = 8.8$ min, $t_3 = 10.8$ min, $t_4 = 16.6$ min (major). $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.35 – 7.27 (m, 1H), 6.97 – 6.87 (m, 3H), 4.85 – 4.77 (m, 1H), 3.83 (s, 3H), 2.87 (s, 1H), 2.71 (dd, $J = 7.3, 5.2$ Hz, 1H), 1.78 – 1.67

(m, 1H), 1.11 (d, $J = 6.7$ Hz, 3H), 1.06 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (101 MHz, Chloroform- d) δ 159.9, 142.2, 129.9, 119.1, 118.4, 114.0, 111.7, 72.4, 55.2, 48.5, 27.3, 21.4, 18.7. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{13}\text{H}_{17}\text{NNaO}_2^+$ = 242.1151; Found 242.1149.

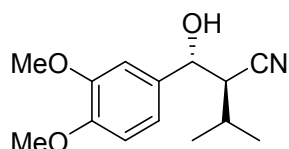


(2*R*,3*R*)-3-hydroxy-3-(3-methoxyphenyl)-2-methylpropanenitrile (2o) white solid, 37 mg, 97% yield, >99% ee, 95:5 dr; $[\alpha]_D^{20} = +64.8$ (c 0.5, CHCl_3); **The absolute configurations of 2o was assigned as (2*R*, 3*R*) by X-ray Diffraction; HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 15.2$ min, $t_2 = 20.3$ min, $t_3 = 21.6$ min, $t_4 = 29.7$ min (major). ^1H NMR (400 MHz, Chloroform- d) δ 7.38 – 7.29 (m, 1H), 7.02 – 6.87 (m, 3H), 4.71 (dd, $J = 6.8, 2.4$ Hz, 1H), 3.84 (s, 3H), 2.93 (p, $J = 7.1$ Hz, 1H), 2.60 (s, 1H), 1.27 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, Chloroform- d) δ 159.9, 141.6, 129.8, 121.0, 118.5, 114.3, 111.7, 75.1, 55.3, 34.5, 14.8. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Cl}]^-$ Calcd for $\text{C}_{11}\text{H}_{13}\text{ClNO}_2^-$ = 226.0640; Found 226.0634.



Syn-(2-fluorophenyl)(hydroxy)methyl-3-methylbutanenitrile (2p) white solid, 39 mg, 95% yield, 71% ee, 95:5 dr; $[\alpha]_D^{20} = -52.6$ (c 1.0, CHCl_3). **The relative configuration of 2p was assigned syn- by X-ray Diffraction; HPLC** (Chiralpak IC column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_1 = 9.0$ min (major), $t_2 = 10.4$ min, $t_3 = 15.4$ min, $t_4 = 22.2$ min. ^1H NMR (400 MHz, Chloroform- d) δ 7.6 – 7.5 (m, 1H), 7.4 – 7.3 (m, 1H), 7.2 – 7.2 (m, 1H), 7.2 – 7.0 (m, 1H), 5.2 (dd, $J = 8.5, 4.9$ Hz, 1H), 3.0 (dd, $J = 8.5, 4.4$ Hz, 1H), 2.3 (dq, $J = 5.0, 1.2$ Hz, 1H), 2.2 (pd, $J = 6.8, 4.4$ Hz, 1H), 1.1 (dd, $J = 6.8, 5.7$ Hz, 6H). ^{13}C NMR (101

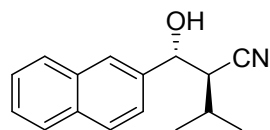
MHz, Chloroform-*d*) δ 160.1 (d, $J = 247.5$ Hz), 130.5, (d, $J = 8.1$ Hz), 128.3 (d, $J = 4.0$ Hz), 127.8 (d, $J = 3.0$ Hz), 124.8 (d, $J = 3.0$ Hz), 118.1, 115.8 (d, $J = 22.2$ Hz), 66.7 (d, $J = 2.0$ Hz), 46.9 (d, $J = 1.0$ Hz), 26.4, 21.7, 17.9. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -118.0. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Cl}]^-$ Calcd for $\text{C}_{12}\text{H}_{14}\text{ClFNO}^-$ = 242.0753; Found 242.0749.



(*R*)-2-((*R*)-(3,4-dimethoxyphenyl)(hydroxy)methyl)-3-methylbutanenitrile (2q)

white solid, 49 mg, 98% yield, >99% ee, 99:1 dr; $[\alpha]_{\text{D}}^{20} = +42.6$ (c 0.5, CHCl_3).

HPLC (Chiralpak IA column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 28.2$ min, $t_2 = 30.2$ min, $t_3 = 33.7$ min, $t_4 = 42.6$ min (major). **^1H NMR** (400 MHz, Chloroform-*d*) δ 6.99 – 6.82 (m, 3H), 4.81 (dd, $J = 7.4$, 2.6 Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 2.71 (dd, $J = 7.4$, 5.1 Hz, 1H), 2.51 (d, $J = 3.7$ Hz, 1H), 1.79 – 1.70 (m, 1H), 1.12 (d, $J = 6.8$ Hz, 3H), 1.08 (d, $J = 6.8$ Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 149.4, 149.3, 133.1, 119.2, 118.7, 111.0, 108.8, 72.5, 56.0, 55.9, 48.6, 27.4, 21.5, 18.7. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{14}\text{H}_{19}\text{NNaO}_3^+$ = 272.1257; Found 272.1254.

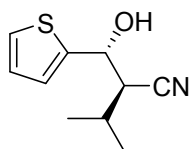


(*R*)-2-((*R*)-hydroxy(naphthalen-2-yl)methyl)-3-methylbutanenitrile (2r)

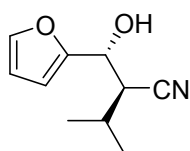
white solid, 47 mg, 98% yield, >99% ee, 98:2 dr; $[\alpha]_{\text{D}}^{20} = +46.0$ (c 0.5, CHCl_3).

HPLC (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 8.2$ min, $t_2 = 10.0$ min, $t_3 = 16.5$ min, $t_4 = 20.0$ min (major). **^1H NMR** (400 MHz, Chloroform-*d*) δ 7.9 – 7.8 (m, 4H), 7.6 – 7.4 (m, 3H), 5.0 (d, $J = 7.4$ Hz, 1H), 2.8 (dd, $J = 7.5$, 5.0 Hz, 2H), 1.8 – 1.6 (m, 1H), 1.1 (d, $J = 6.7$ Hz, 3H), 1.1 (d, $J = 6.8$ Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 137.8, 133.4, 133.0,

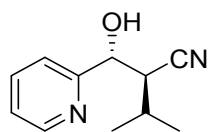
128.9, 128.0, 127.7, 126.5, 126.5, 125.7, 123.3, 119.1, 72.8, 48.4, 27.4, 21.5, 18.6.
HRMS (ESI-TOF) m/z : $[M+Cl]^-$ Calcd for $C_{16}H_{17}ClNO^-$ = 274.1004; Found 274.1002.



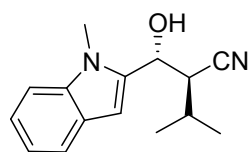
(R)-2-((R)-hydroxy(thiophen-2-yl)methyl)-3-methylbutanenitrile (2s) yellow oil, 38 mg, 97% yield, >99% ee, >99:1 dr; $[\alpha]_D^{20} = +40.6$ (c 0.5, $CHCl_3$); **HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 8.1$ min, $t_2 = 10.3$ min, $t_3 = 14.7$ min, $t_4 = 18.1$ min (major)). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.39 – 7.31 (m, 1H), 7.14 – 7.07 (m, 1H), 7.07 – 6.96 (m, 1H), 5.12 (d, $J = 7.5$ Hz, 1H), 3.04 (s, 1H), 2.80 (dd, $J = 7.6, 5.0$ Hz, 1H), 1.87 – 1.73 (m, 1H), 1.11 (d, $J = 6.8$ Hz, 3H), 1.09 (d, $J = 6.8$ Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 143.9, 126.9, 125.8, 125.3, 118.8, 68.6, 48.8, 27.5, 21.4, 18.4. **HRMS** (ESI-TOF) m/z : $[M+Cl]^-$ Calcd for $C_{10}H_{13}ClNOS^+$ = 230.0412; Found 230.0407.



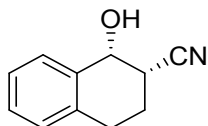
(R)-2-((R)-furan-2-yl(hydroxy)methyl)-3-methylbutanenitrile (2t) yellow oil, 35 mg, 98% yield, >99% ee, >99:1 dr; $[\alpha]_D^{20} = +52.2$ (c 0.5, $CHCl_3$); **HPLC** (Chiralpak IC column, hexane/isopropanol = 85/15; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 6.1$ min, $t_2 = 6.5$ min, $t_3 = 11.0$ min, $t_4 = 11.7$ min (major)). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.43 (d, $J = 2.3$ Hz, 1H), 6.46 – 6.36 (m, 2H), 4.90 (d, $J = 7.3$ Hz, 1H), 2.99 (dd, $J = 7.3, 5.3$ Hz, 1H), 2.83 (s, 1H), 1.83 – 1.70 (m, 1H), 1.11 (s, 3H), 1.09 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 152.5, 142.8, 118.9, 110.5, 108.1, 66.3, 45.9, 27.4, 21.3, 18.7. **HRMS** (ESI-TOF) m/z : $[M+Cl]^-$ Calcd for $C_{10}H_{13}ClNO_2^+$ = 214.0640; Found 214.0634.



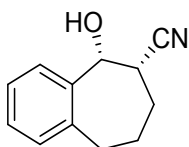
(R)-2-((R)-hydroxy(pyridin-2-yl)methyl)-3-methylbutanenitrile (2u) yellow oil, 37 mg, 97% yield, >99% ee, 96:4 dr; $[\alpha]^{20}_D = +45.6$ (c 0.5, CHCl_3); **HPLC** (Chiralpak ID column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 9.9$ min, $t_2 = 12.8$ min, $t_3 = 15.1$ min, $t_4 = 21.9$ min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 8.60 (dt, $J = 4.7, 1.4$ Hz, 1H), 7.77 (td, $J = 7.7, 1.7$ Hz, 1H), 7.43 – 7.35 (m, 1H), 7.34 – 7.26 (m, 1H), 4.97 (d, $J = 4.2$ Hz, 1H), 2.81 (dd, $J = 7.4, 4.2$ Hz, 1H), 2.18 – 2.01 (m, $J = 6.8$ Hz, 1H), 1.16 (t, $J = 6.8$ Hz, 6H). **$^{13}\text{C NMR}$** (101 MHz, Chloroform-*d*) δ 158.3, 148.6, 137.2, 123.3, 120.7, 118.7, 70.7, 48.0, 27.9, 20.9, 20.3. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{15}\text{N}_2\text{O}^+$ = 191.1179; Found 191.1176.



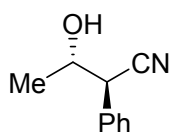
(R)-2-((R)-hydroxy(1-methyl-1H-indol-2-yl)methyl)-3-methylbutanenitrile (2v) white solid, 46 mg, 96% yield, >99% ee, 90:10 dr; $[\alpha]^{20}_D = +48.0$ (c 0.5, CHCl_3); **HPLC** (Chiralpak IE column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 9.8$ min, $t_2 = 11.2$ min, $t_3 = 12.4$ min (major), $t_4 = 14.4$ min. **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.7 – 7.6 (m, 1H), 7.3 – 7.2 (m, 2H), 7.2 – 7.1 (m, 1H), 6.5 (s, 1H), 5.0 (t, $J = 6.8$ Hz, 1H), 3.8 (s, 3H), 3.1 (dd, $J = 7.3, 5.0$ Hz, 1H), 2.5 (d, $J = 6.5$ Hz, 1H), 1.9 (pd, $J = 6.8, 5.0$ Hz, 1H), 1.1 (t, $J = 6.5$ Hz, 6H). **$^{13}\text{C NMR}$** (151 MHz, Chloroform-*d*) δ 138.1, 137.3, 126.8, 122.5, 121.0, 120.0, 119.0, 109.3, 100.7, 65.9, 46.2, 30.2, 27.9, 21.5, 18.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}^+$ = 243.1492; Found 243.1489.



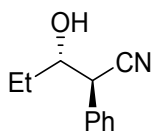
(1R,2S)-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (2w)¹⁵: white solid, 34 mg, 98% yield, >99% ee, >99:1 dr; $[\alpha]_D^{20} = +6.4$ (c 0.5, CHCl₃); **HPLC** (Chiralpak IC column, hexane/isopropanol = 80/20; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 8.9$ min, $t_2 = 11.6$ min, $t_3 = 14.9$ min, $t_4 = 22.0$ min (major). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.50 – 7.42 (m, 1H), 7.35 – 7.27 (m, 2H), 7.22 – 7.11 (m, 1H), 4.96 (dd, $J = 6.5, 4.0$ Hz, 1H), 3.20 – 3.12 (m, 1H), 3.12 – 3.01 (m, 1H), 2.91 – 2.78 (m, 1H), 2.50 (d, $J = 6.8$ Hz, 1H), 2.44 – 2.30 (m, 1H), 2.20 – 2.08 (m, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 135.1, 134.8, 129.1, 128.8, 128.7, 126.8, 120.0, 67.2, 34.2, 27.0, 21.7. **HRMS** (ESI-TOF) m/z : $[M+H]^+$ Calcd for C₁₁H₁₂NO⁺ = 174.0913; Found 174.0912.



(5R,6S)-5-hydroxy-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carbonitrile (2x): white solid, 36 mg, 96% yield, >99% ee, >99:1 dr; $[\alpha]_D^{20} = -22.0$ (c 0.5, CHCl₃); **HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 13.3$ min, $t_2 = 15.6$ min, $t_3 = 16.8$ min, $t_4 = 25.2$ min (major). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.52 – 7.40 (m, 1H), 7.32 – 7.23 (m, 2H), 7.18 – 7.12 (m, 1H), 5.13 (s, 1H), 3.20 (s, 1H), 3.12 – 3.00 (m, 1H), 2.77 – 2.65 (m, 1H), 2.47 – 2.33 (m, 2H), 2.18 – 2.06 (m, 1H), 1.85 – 1.72 (m, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 140.3, 139.2, 129.8, 128.4, 126.6, 126.3, 120.1, 73.7, 37.8, 34.8, 30.5, 24.9. **HRMS** (ESI-TOF) m/z : $[M+Na]^+$ Calcd for C₁₂H₁₃NNaO⁺ = 210.0889; Found 210.0888.

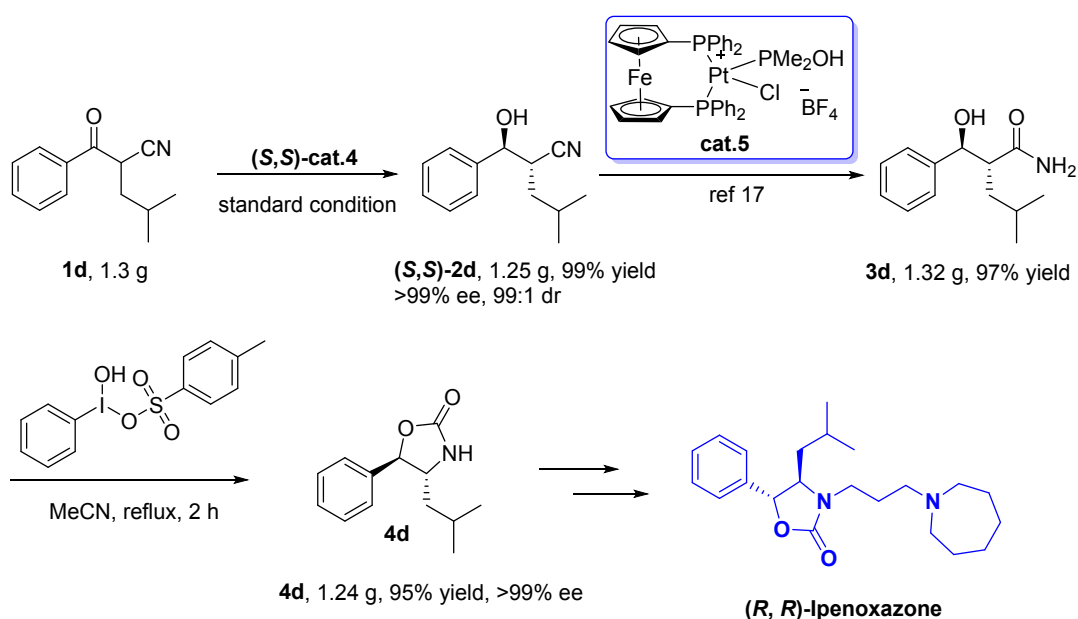


(2*R*,3*S*)-3-hydroxy-2-phenylbutanenitrile (2y): white solid, 31 mg, 96% yield, >99% ee, 93:7 dr; $[\alpha]_D^{20} = +42.4$ (c 0.5, CHCl₃); **The absolute configurations of 2y was assigned as (2*R*, 3*S*) by X-ray**; **HPLC** (Chiralpak IC column, hexane/isopropanol = 85/15; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 13.3$ min, $t_2 = 15.6$ min, $t_3 = 16.8$ min, $t_4 = 25.2$ min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.52 – 7.32 (m, 5H), 4.22 – 4.06 (m, 1H), 3.84 (d, $J = 5.1$ Hz, 1H), 2.30 (s, 1H), 1.35 (d, $J = 6.3$ Hz, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 132.8, 129.1, 128.5, 128.2, 118.9, 69.8, 46.4, 20.9. **HRMS** (ESI-TOF) m/z : $[M+Cl]^-$ Calcd for C₁₀H₁₁CINO⁺ = 196.0535; Found 196.0527.



(2*R*,3*S*)-3-hydroxy-2-phenylpentanenitrile (2z) white solid, 34 mg, 97% yield, >99% ee, 81:19 dr; $[\alpha]_D^{20} = +22.2$ (c 1.0, CHCl₃); **HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 10.4$ min, $t_2 = 13.5$ min, $t_3 = 14.4$ min, $t_4 = 20.6$ min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.5 – 7.3 (m, 5H), 4.0 – 3.9 (m, 1H), 3.9 – 3.8 (m, 1H), 2.3 (d, $J = 5.2$ Hz, 1H), 1.8 – 1.5 (m, 2H), 1.1 – 1.0 (m, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 133.0, 129.1, 128.4, 128.1, 118.8, 75.0, 44.9, 27.7, 10.0. **HRMS** (ESI-TOF) m/z : $[M+H]^+$ Calcd for C₁₁H₁₄NO⁺ = 176.1070; Found 176.1069.

5. Synthetic Applications

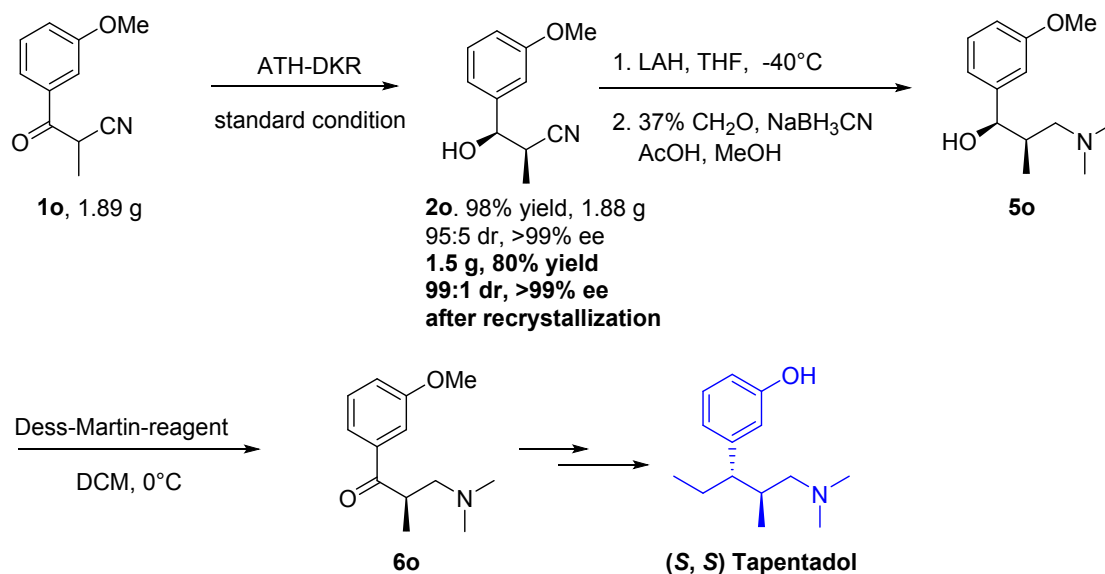


Step 1: In a nitrogen filled glovebox, to a 50 mL Schleck tube charged with a magnetic stirring bar were added successively substrate **1d** (6.2 mmol, 1.25 g), formic acid/trimethylamine azeotropic mixture (5/2 molar ratio) (1.5 mL), the catalyst (**cat.5**, 46 mg, 0.062 mmol) and the solvent (30 mL). The mixture was then stirred at room temperature for 12 h. After completion, The reaction solution was concentrated and the residue was passed through a short column of silica gel (eluent: EA:PE = 2:1) to remove the metal complex. Compounds (S,S) -**2d**¹⁶ was obtained as a white solid (1.25 g, 99% yield, >99% ee, 99:1 dr); $[\alpha]_D^{20} = -19.8$ (c 0.5, CHCl_3); **HPLC** (Chiralpak IC column, hexane/isopropanol = 90/10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_1 = 8.1$ min, $t_2 = 10.7$ min (major), $t_3 = 13.2$ min, $t_4 = 14.4$ min. $^1\text{H NMR}$ and $^{13}\text{C NMR}$ was the same as **2d**. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Cl}]^-$ Calcd for $\text{C}_{13}\text{H}_{17}\text{ClNO}^- = 238.1004$; Found 238.0999.

Step 2¹⁷: In a nitrogen filled glovebox, to a 10 mL vial charged with a magnetic stirring bar were added **cat.5** (9.1 mg, 0.01 mmol), AgBF_4 (2 mg, 0.01 mmol), THF (2 mL), the mixture was stirred for 1 h, then water (2 mL) was added into the vial and stirred for another 5 min. The vial was taken outside of the glovebox and nitriles **2d'**

(6.2 mmol, 1.25 g) were added. The reaction mixture was then warmed up to 40 °C and was stirred for 12 hours. After then, it was diluted with water (5 mL) and extracted by ethyl acetate twice (10 mL for each). The combined organic layer was washed with brine (10 mL), and then solvent was removed by rotary evaporator to produce the crude products, which were purified by flash chromatography (SiO₂, 80% EtOAc in petroleum ether). The products **3d** were obtained as a white solid (1.32 g, 97% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.4 – 7.3 (m, 5H), 5.7 (d, *J* = 20.2 Hz, 2H), 4.8 (d, *J* = 5.9 Hz, 1H), 3.8 (s, 1H), 2.7 – 2.5 (m, 1H), 1.9 – 1.5 (m, 3H), 1.3 – 1.2 (m, 2H), 0.9 (dd, *J* = 10.7, 6.5 Hz, 6H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 177.5, 142.7, 128.5, 127.7, 126.0, 75.4, 51.6, 39.1, 25.8, 23.2, 21.9.

Step 3¹⁸: To a solution of **3d** (1.32 g, 6 mmol, 1.0 equiv.), [hydroxyl (tosyloxy)iodo]benzene (2.9 g, 7.5 mmol, 1.25 equiv.) in CH₃CN (15.0 mL) was heated at reflux for 2 h. The reaction was allowed to cool down and concentrated. The resulting product was treated with sat. NaHCO₃ (10 mL), extracted with DCM (5 mL × 3), and concentrated as a white solid which was purified with flash chromatography (30% EtOAc in petroleum ether) to yield **4d** (1.24 g, 95% yield, >99% ee) as a white solid. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.5 – 7.4 (m, 5H), 7.0 (s, 1H), 5.1 (d, *J* = 6.7 Hz, 1H), 3.9 – 3.8 (m, 1H), 1.8 – 1.6 (m, 2H), 1.6 – 1.5 (m, 1H), 0.9 (dd, *J* = 8.8, 6.5 Hz, 6H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 159.6, 138.2, 128.9, 128.8, 125.9, 84.2, 59.1, 44.2, 25.0, 23.0, 21.8. [α]²⁵_D = +28.4 (c 1.0, CHCl₃); **HPLC** (Chiralpak IC column, hexane/isopropanol = 95/5; flow rate = 1.0 mL/min; UV detection at 220 nm; t₁ = 16.2 min (major), t₂ = 17.5 min. **HRMS** (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₃H₁₈NO₂⁺ = 220.1332; Found 220.1331.



Step 1: In a nitrogen filled glovebox, to a 50 mL Schleck tube charged with a magnetic stirring bar were added successively substrate **1d** (10 mmol, 1.89 g), formic acid/trimethylamine azeotropic mixture (5/2 molar ratio) (2.5 mL), the catalyst (**cat.4**, 74 mg, 0.1 mmol) and the solvent (50 mL). The mixture was then stirred at room temperature for 12 h. After completion, the reaction solution was concentrated and the residue was passed through a short column of silica gel (eluent: EA:PE = 2:1) to remove the metal complex. Compounds **2o** was obtained as a white solid (1.88 g, 98% yield, >99% ee, 95:5 dr). Pure compounds **2o** (1.50 g, 80% yield, >99% ee, 99:1 dr) were obtained after recrystallization (isopropanol/*n*-hexane)

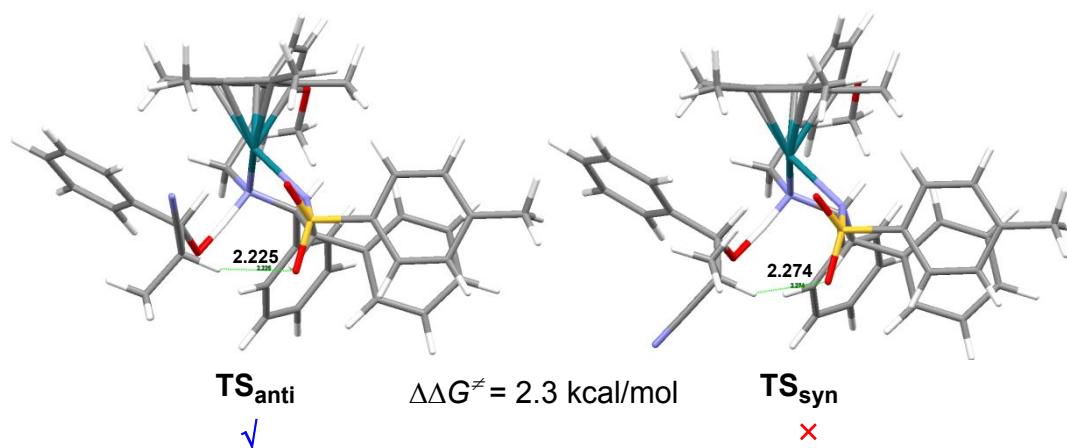
Step 2¹⁹: To a suspension solution of LAH in THF was cooled to -40 °C, a solution of **2o** (1 g, 5.2 mmol, 1.0 equiv.) in THF was added into the mixture by springe, then the mixture was stirred at -40 °C for 2 h. TLC showed **2o** was consumed completely and then the mixture was warmed to room temperature. The mixture was quenched by 1 mL H₂O slowly and filtered by Celite, washed by DCM (30 mL × 3), combined the organic layer and concentrated in vacuum to obtained the crude. The crude was dissolved in MeOH (20 mL) and cooled to 0 °C, CH₂O (1.2 mL, 37% wt in water) was added into the mixture and the mixture was stirred at room temperature for 30 min, then NaBH₃CN (0.69 g, 10.4 mmol, 2.0 equiv.) and AcOH (1.3 mL) was added

into the mixture. The mixture was stirred at 0 °C for 2 h. After then, it was diluted with water (5 mL) and extracted by ethyl acetate twice (10 mL for each). The combined organic layer was washed with brine (10 mL), and then solvent was removed by rotary evaporator to produce the crude products, which were purified by flash chromatography (SiO₂, 3% MeOH in DCM). The products **5o** were obtained as a colorless oil (0.93 g, 80% yield). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.3 – 7.2 (m, 1H), 6.9 (dt, *J* = 4.8, 1.7 Hz, 2H), 6.8 – 6.8 (m, 1H), 4.4 (d, *J* = 9.3 Hz, 1H), 3.8 (s, 3H), 2.7 (t, *J* = 12.0 Hz, 1H), 2.4 (s, 7H), 2.0 – 1.9 (m, 1H), 0.6 (d, *J* = 6.8 Hz, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 159.5, 145.5, 129.0, 119.7, 112.8, 112.6, 83.0, 67.6, 55.1, 45.6, 36.4, 15.3.

Step 3²⁰: To a solution of **5o** (0.23 g, 1 mmol, 1.0 equiv.) in DCM was cooled to 0 °C and the Dess-Martin reagent (0.51 g, 1.2 mmol, 1.2 equiv.) was added into the mixture and stirred for 1 h. TLC showed the **5o** was consumed completely and the mixture was quenched by sat. NaHCO₃ (aq.) (10 mL) and extracted by DCM (20 mL × 2), combined organic layers and dried over anhydrous Na₂SO₄, concentrated in vacuum. The crude product was purified by chromatography (Al₂O₃, PE/EA = 10/1 ~2/1). **6o** (180 mg) was obtained with 82% yield. **¹H NMR** (600 MHz, Chloroform-*d*) δ 7.6 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.5 – 7.5 (m, 1H), 7.4 (t, *J* = 7.9 Hz, 1H), 7.1 – 7.1 (m, 1H), 3.9 (s, 3H), 3.7 (td, *J* = 7.2, 6.2 Hz, 1H), 2.8 (dd, *J* = 12.3, 7.5 Hz, 1H), 2.4 – 2.3 (m, 1H), 2.2 (s, 6H), 1.2 (d, *J* = 7.0 Hz, 3H). **¹³C NMR** (151 MHz, Chloroform-*d*) δ 203.3, 159.9, 138.0, 129.6, 120.8, 119.5, 112.7, 62.8, 55.4, 45.9, 39.3, 16.7. **HPLC** (Chiralpak IC column, hexane/isopropanol = 80/20; flow rate = 1.0 mL/min; UV detection at 220 nm; *t*₁ = 5.8 min (major), *t*₂ = 8.8 min. **HRMS** (ESI-TOF) *m/z*: [M+H]⁺ Calcd for C₁₃H₂₀NO₂⁺ = 222.1489; Found 222.1487.

6. Computational Details

Geometries of transition states for the *anti*- and *syn*- products were optimized in gas phase by DFT calculation using the Gaussian 16 package.²¹ All the structures are optimized using the B3LYP-D3(BJ) functional²² with the basis set lan2dz for Rh,²³ 6-31G* for other main group atoms.²⁴ Polarization functions ($\zeta_f = 1.350$) were added for Rh.²⁵ Geometric structures of all species were optimized at $T = 298.15$ K. Frequency calculations were performed to verify the optimized transition states to have only one imaginary and to obtain relative Gibbs free energies (within the harmonic approximation) at 298.15 K. Transition state structures were confirmed to connect appropriate reactants or products by intrinsic reaction coordinate (IRC) calculations.²⁶



TS_{anti}

E = -2832.284946; G = -2831.498379; Frequency = -1145.94.

Rh	0.78220200	-0.67893600	-0.81919100
S	-1.78303600	-2.20689700	0.39551500
O	-1.84759900	-2.46574800	1.85063500
O	-1.12266700	-3.19690500	-0.47334500
O	1.59223200	6.12443400	-1.92409600
N	-1.10743200	-0.74484200	0.06824600
N	0.97460700	0.78907900	0.58231500
C	-1.32473400	0.28190200	1.10849900
C	-0.34537100	1.42308000	0.78718200
C	-2.74577500	0.80884200	1.14814000
C	-3.39804700	1.18815300	-0.03007300
C	-4.70025100	1.67902000	0.00812200
C	-5.36567000	1.80428300	1.23071400
C	-4.71844400	1.43627600	2.41039000
C	-3.41442400	0.93971000	2.36655200
C	-0.32496000	2.49397000	1.85641800

C	0.15881400	2.21941900	3.14312600
C	0.17610000	3.22259300	4.11221200
C	-0.29218400	4.50407400	3.81176900
C	-0.78033400	4.78012500	2.53366300
C	-0.79214100	3.77825500	1.56210700
C	-3.48061700	-2.05298200	-0.15684700
C	-4.50165400	-1.90617100	0.77884900
C	-5.79775400	-1.65704600	0.33641800
C	-6.08942200	-1.55307000	-1.02924500
C	-5.05013700	-1.73854700	-1.95117300
C	-3.74895500	-1.98712200	-1.52296500
C	-7.48605900	-1.21766600	-1.48980000
C	2.06093800	1.73738400	0.28301400
C	1.86012100	2.55375500	-0.97846300
C	1.85088700	3.94694300	-0.85949300
C	1.64419200	4.76730000	-1.97320000
C	1.45797300	4.18414100	-3.23336500
C	1.45473000	2.80199300	-3.35224600
C	1.64984100	1.96305500	-2.24233800
C	1.71113300	6.74904400	-0.65289700
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7. References

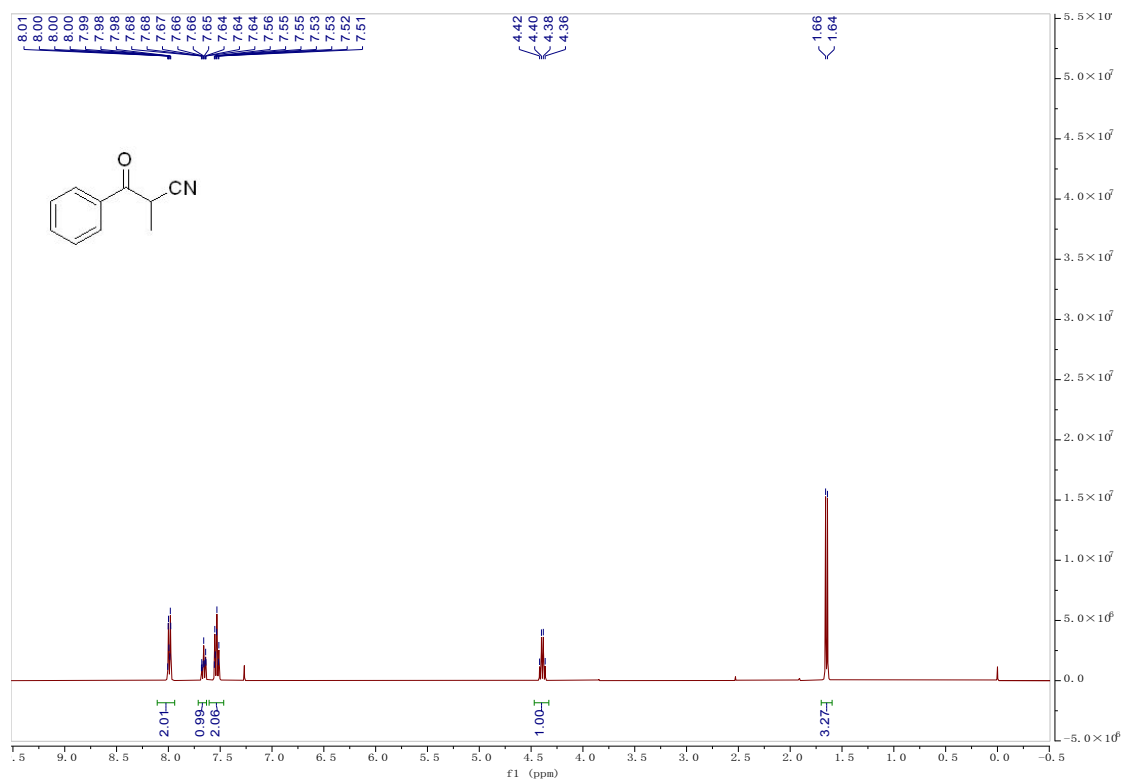
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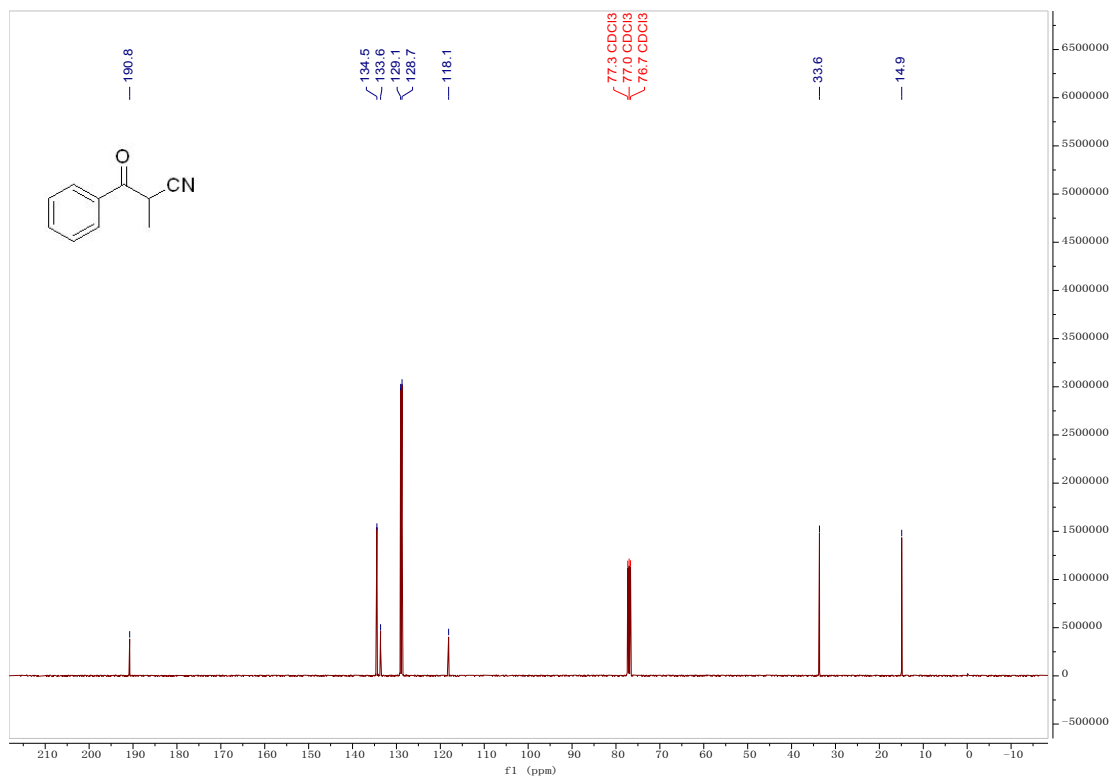
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8. NMR Spectroscopic Data

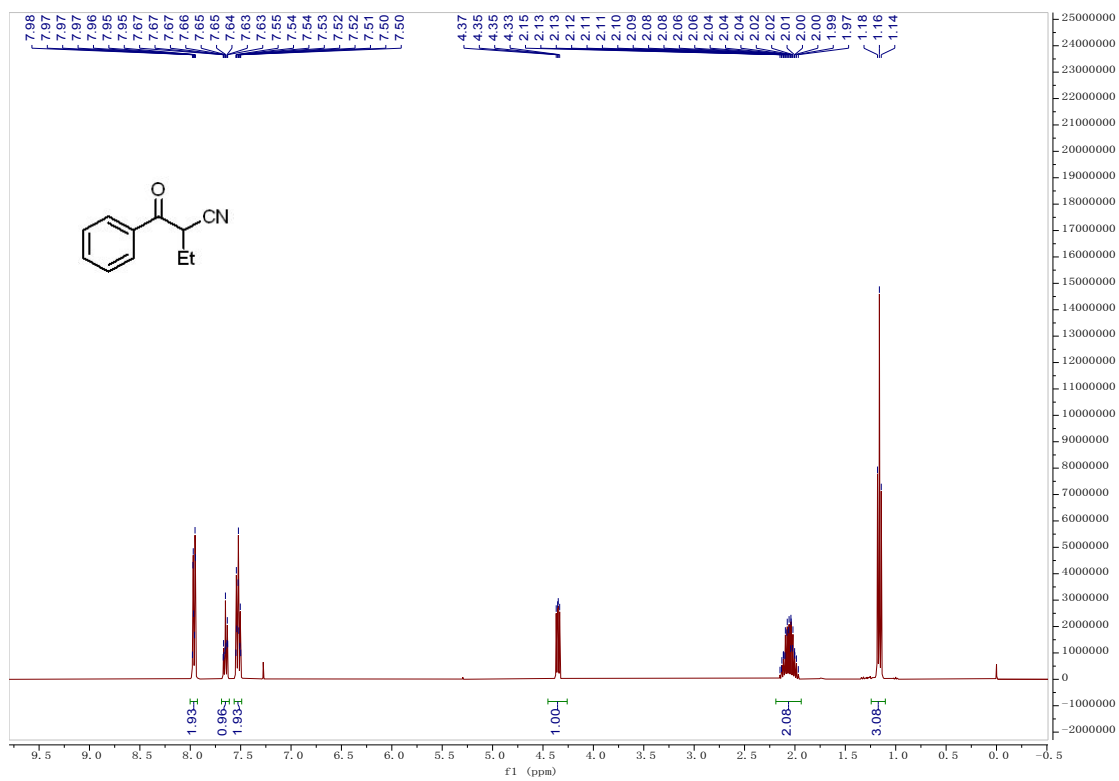
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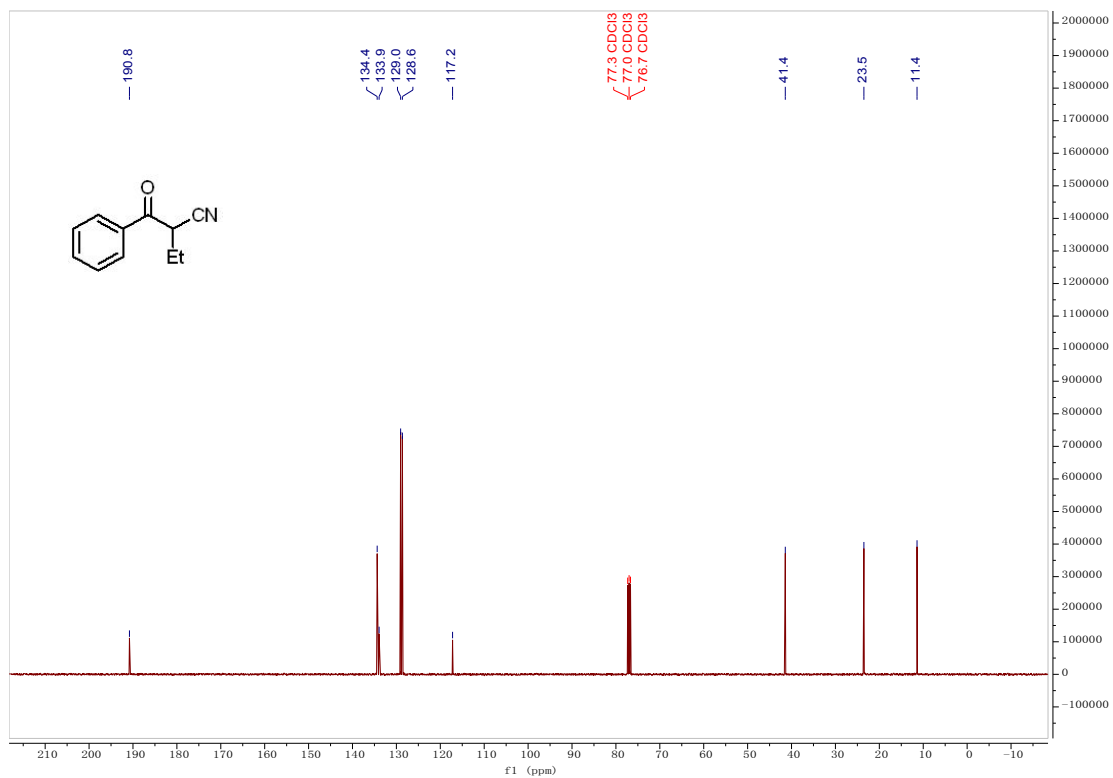
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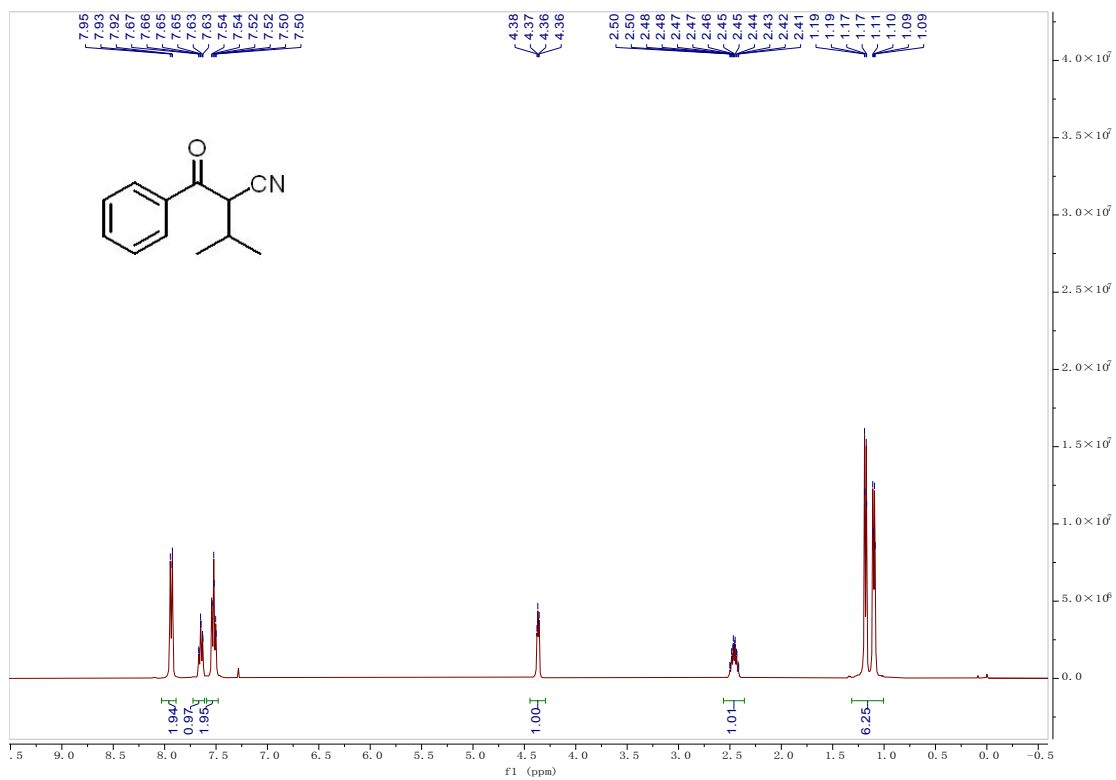
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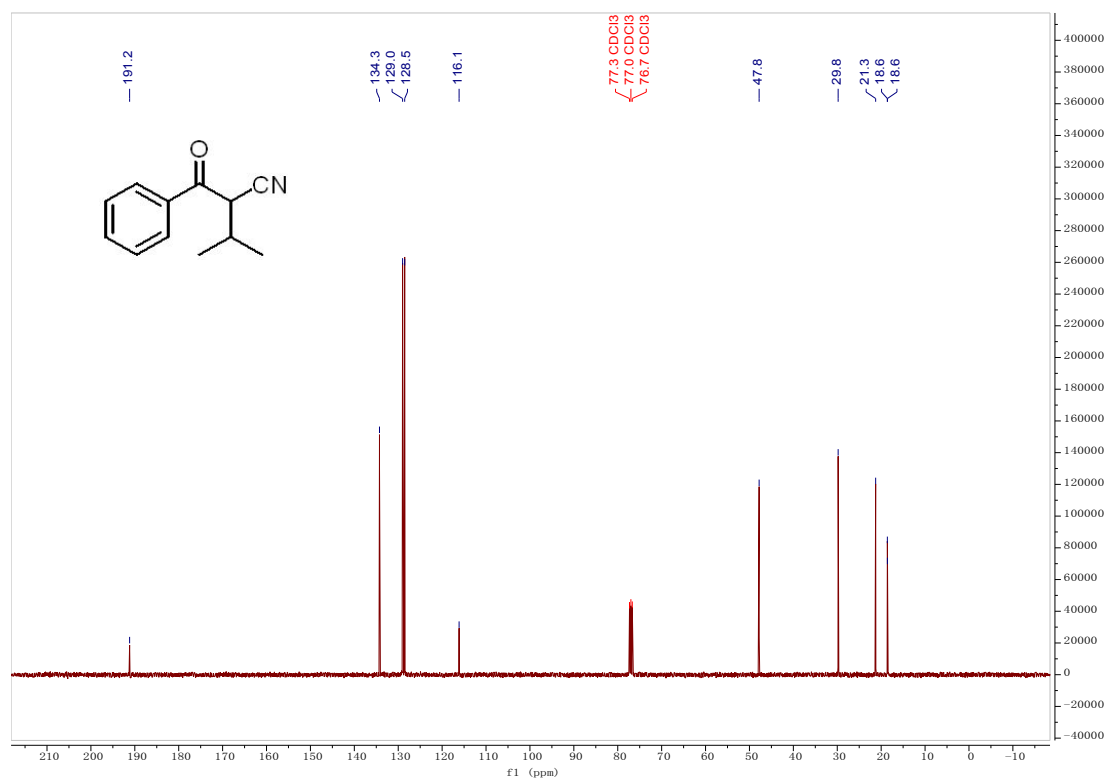
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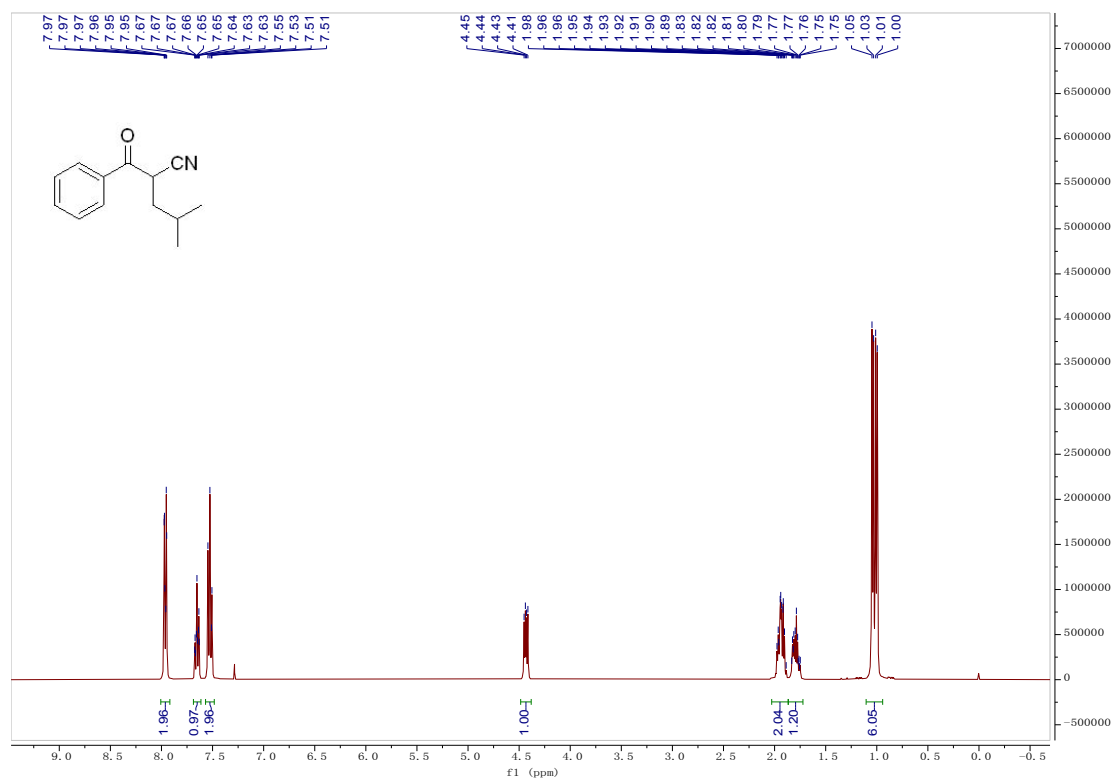
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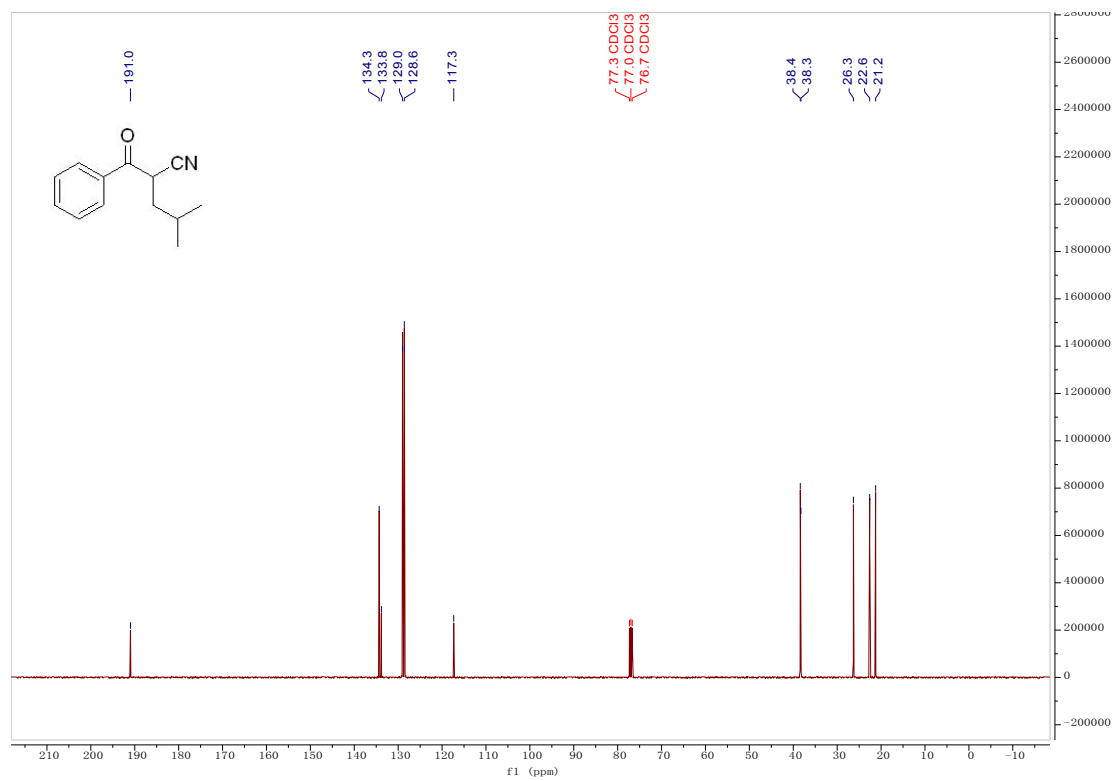
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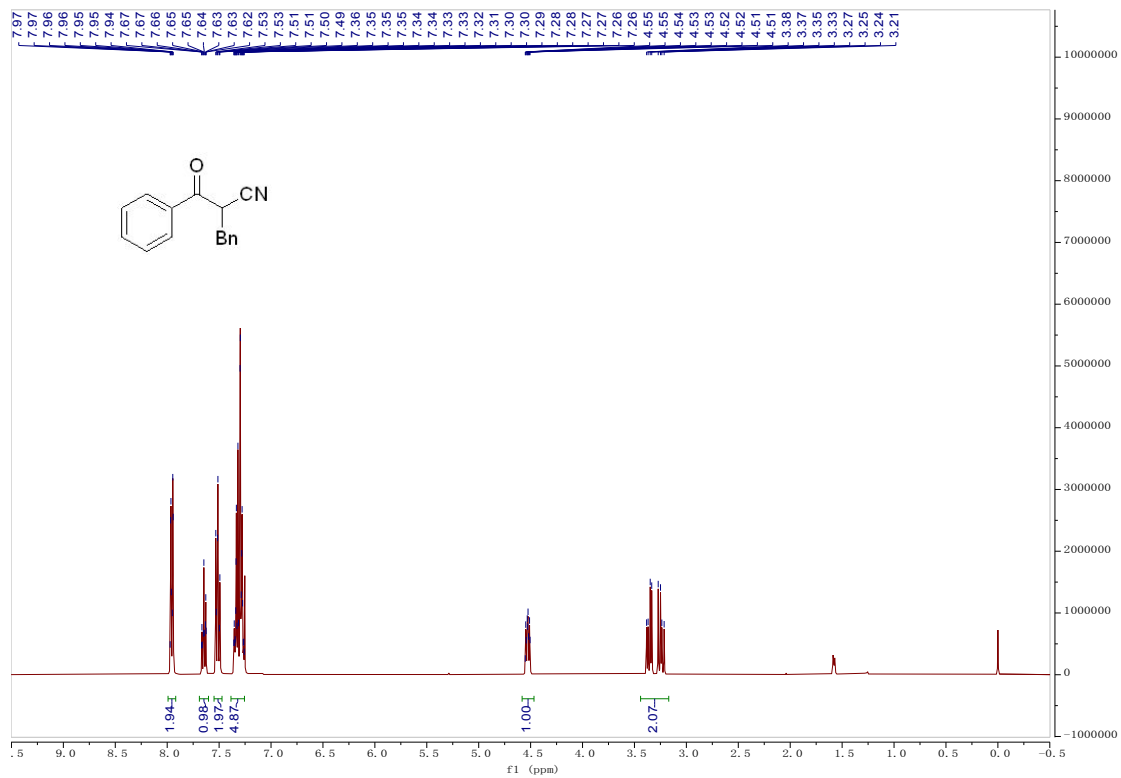
¹H NMR of 1d (400 MHz, Chloroform-*d*)



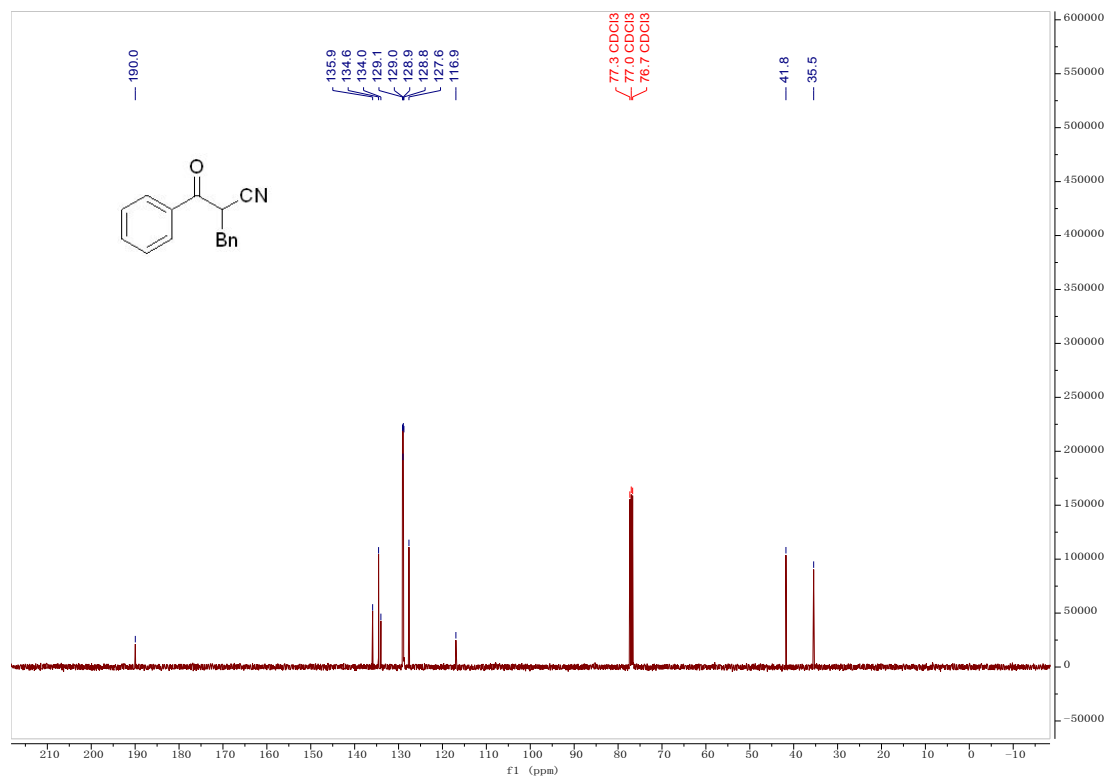
¹³C NMR of 1d (101 MHz, Chloroform-*d*)



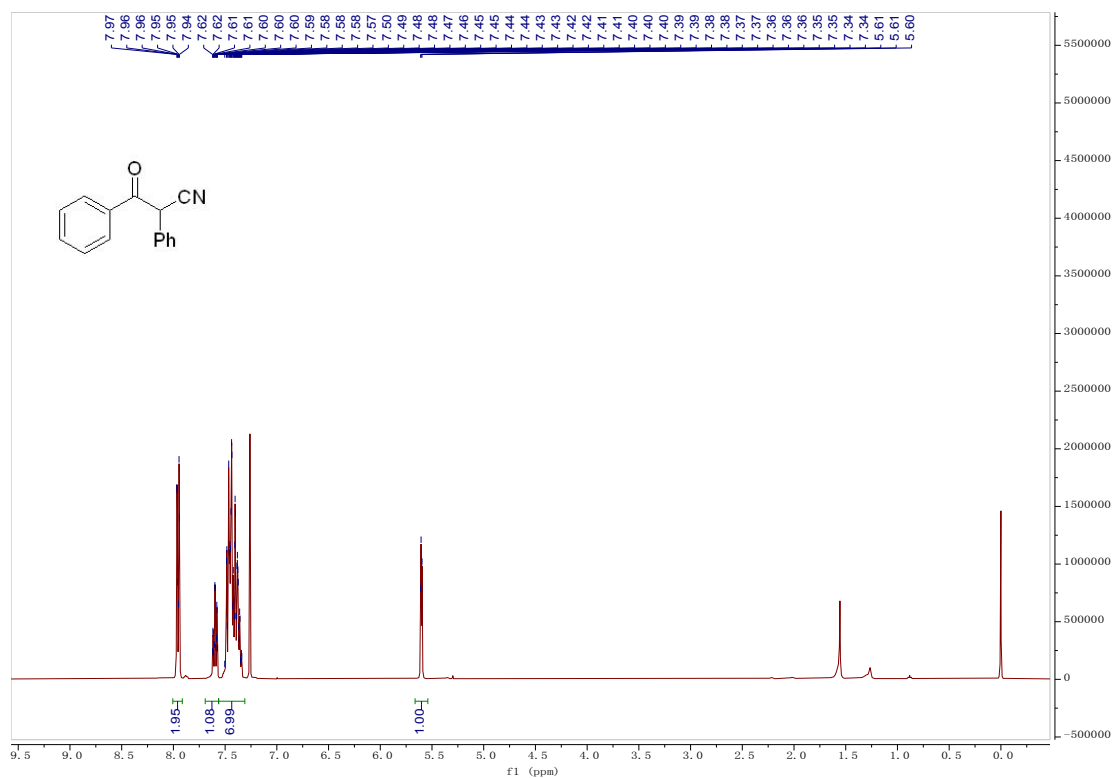
¹H NMR of 1e (400 MHz, Chloroform-*d*)



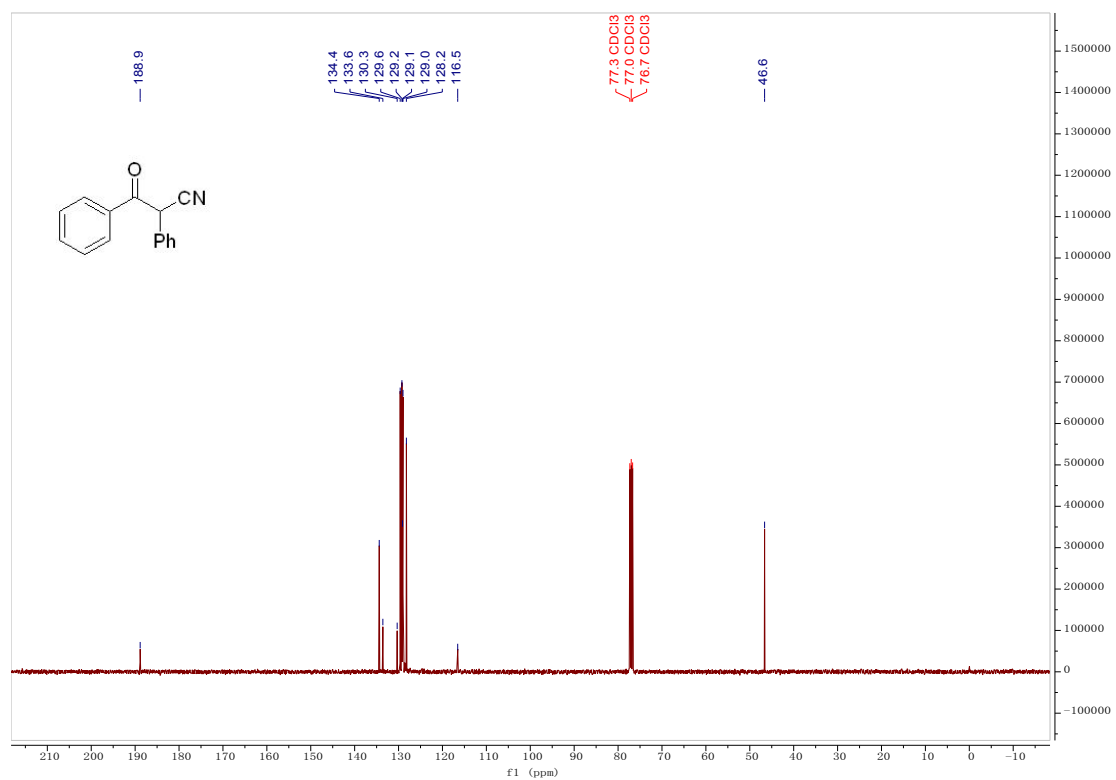
¹³C NMR of 1e (101 MHz, Chloroform-*d*)



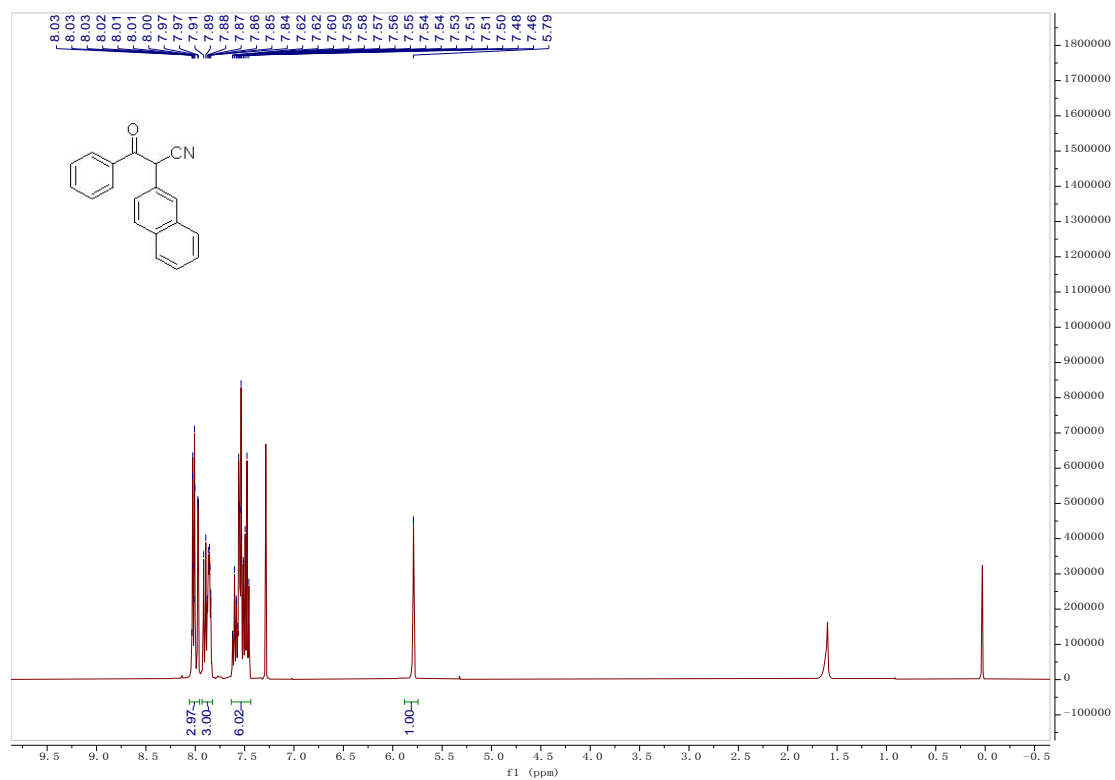
¹H NMR of 1f (400 MHz, Chloroform-*d*)



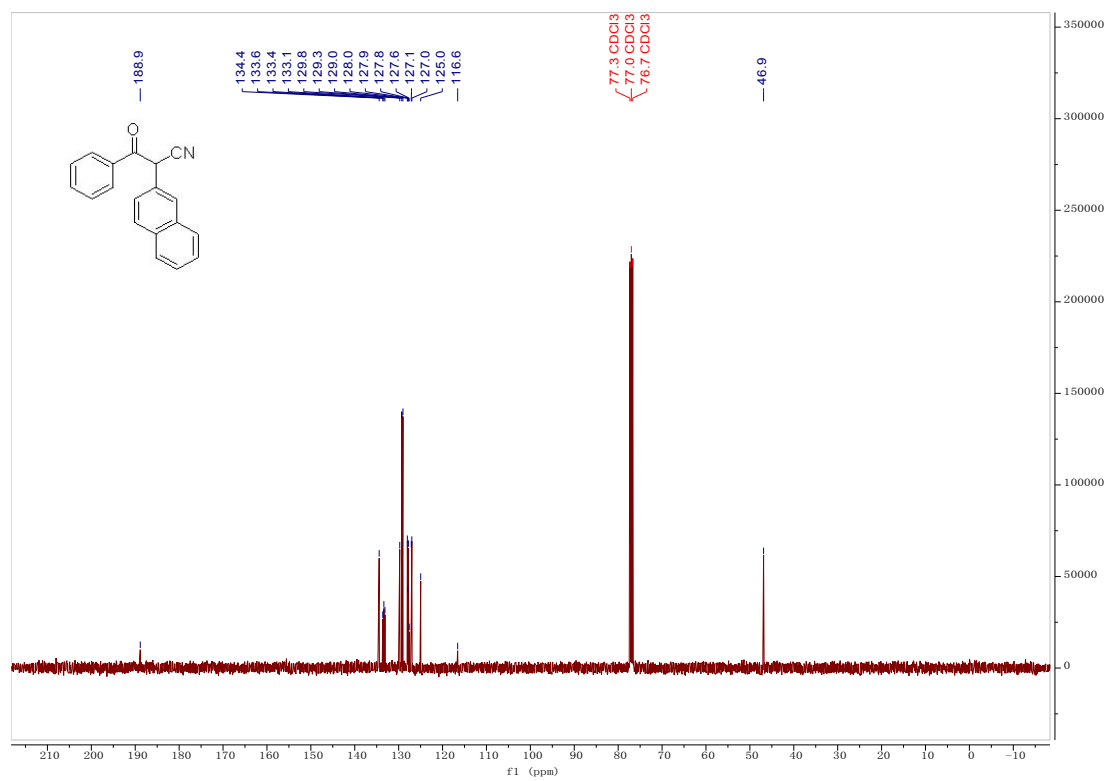
¹³C NMR of 1f (101 MHz, Chloroform-*d*)



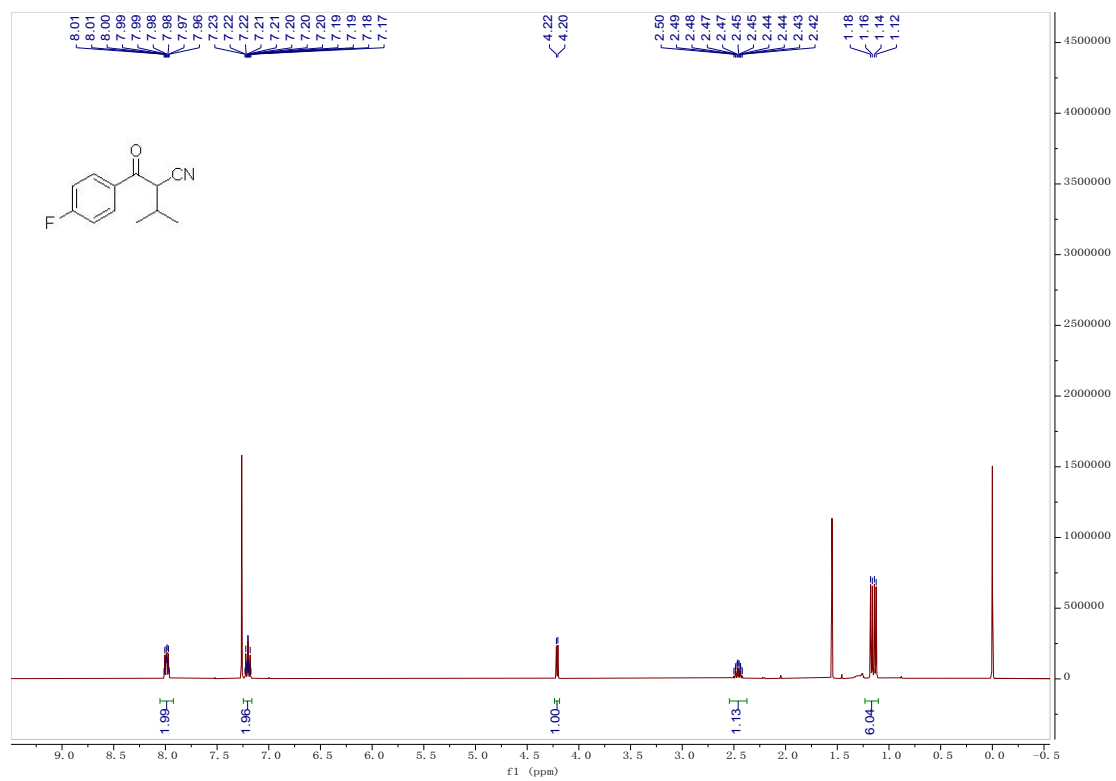
¹H NMR of 1g (400 MHz, Chloroform-*d*)



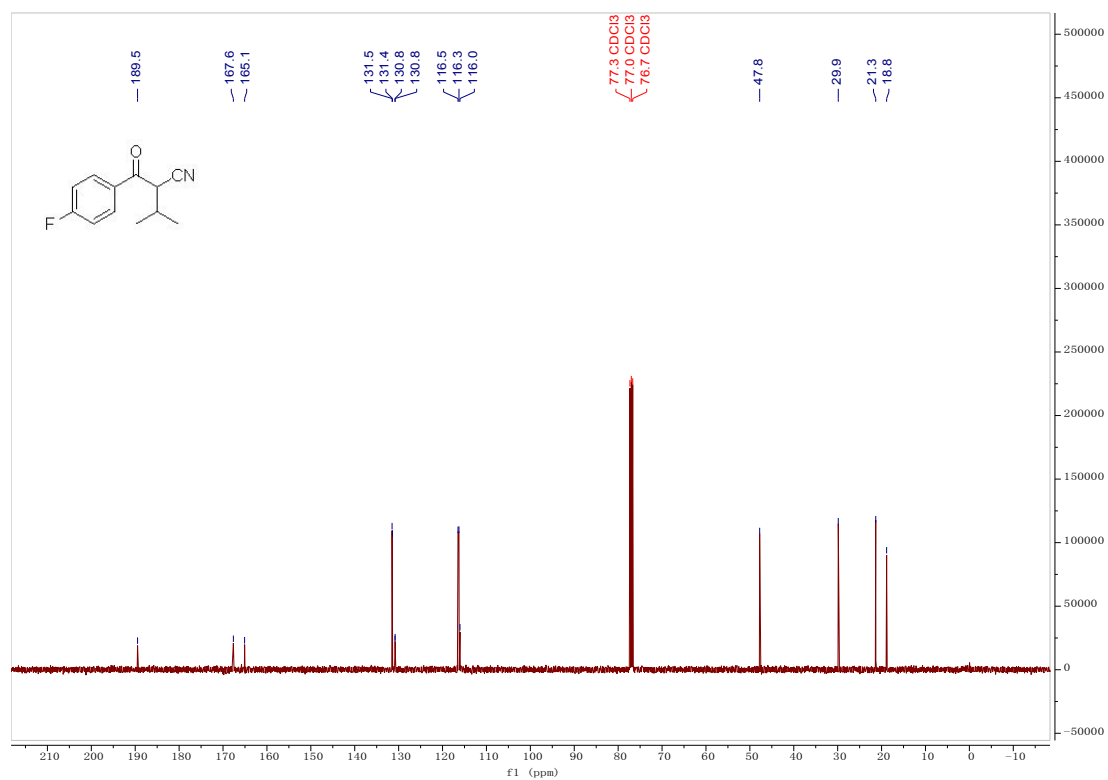
¹³C NMR of 1g (101 MHz, Chloroform-*d*)



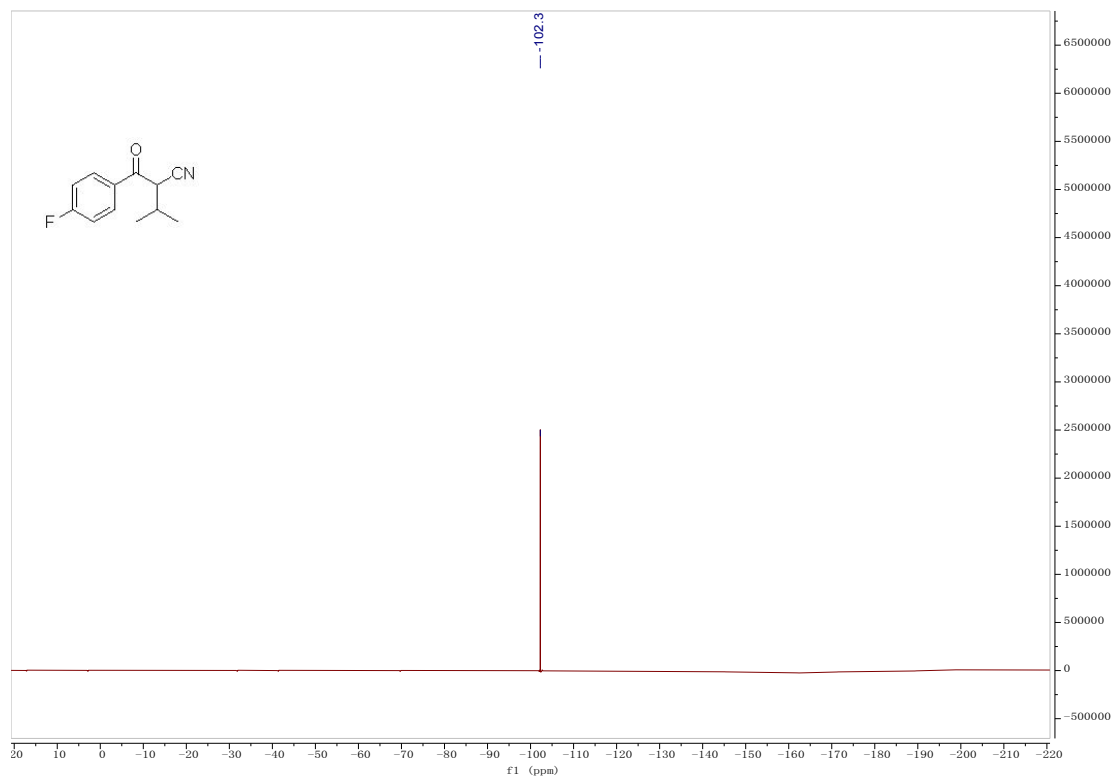
¹H NMR of 1h (400 MHz, Chloroform-*d*)



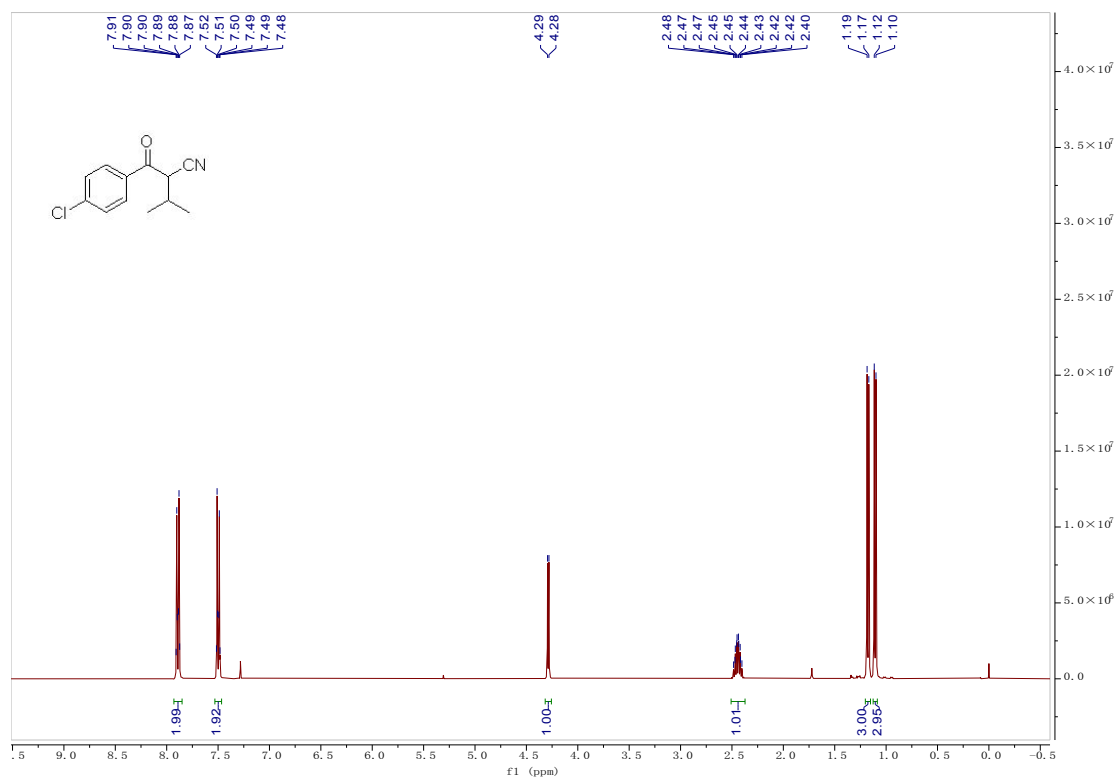
¹³C NMR of 1h (101 MHz, Chloroform-*d*)



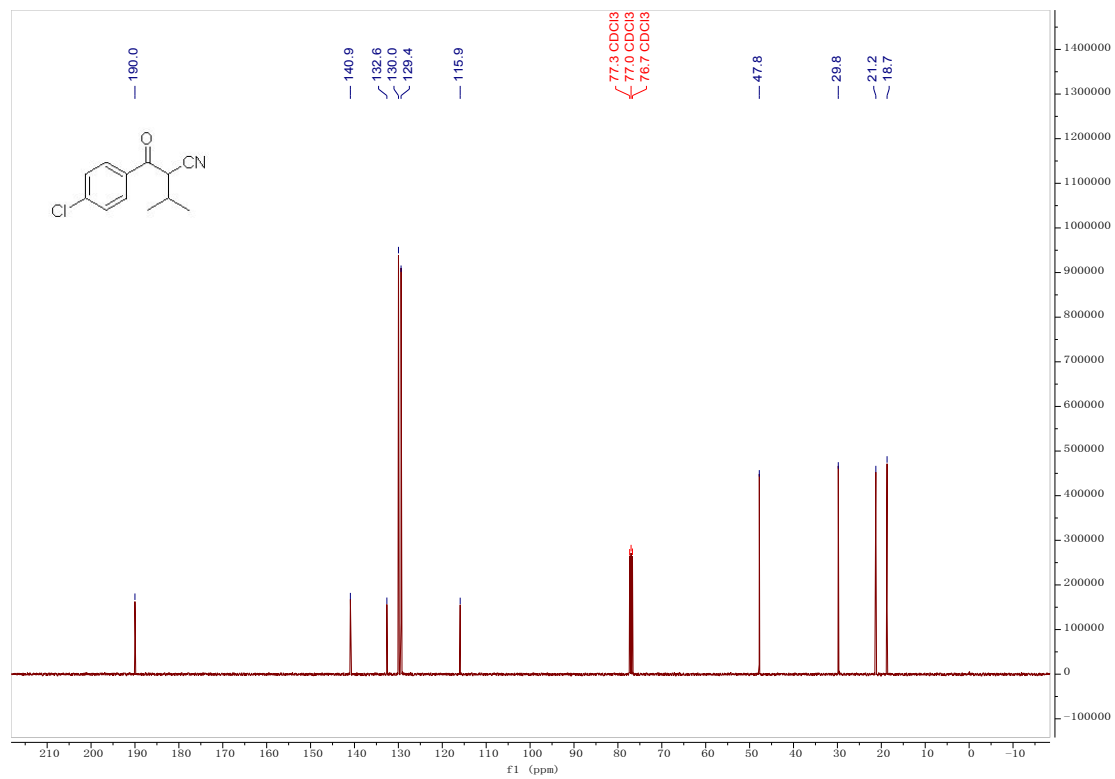
¹³C NMR of 1h (376 MHz, Chloroform-*d*)



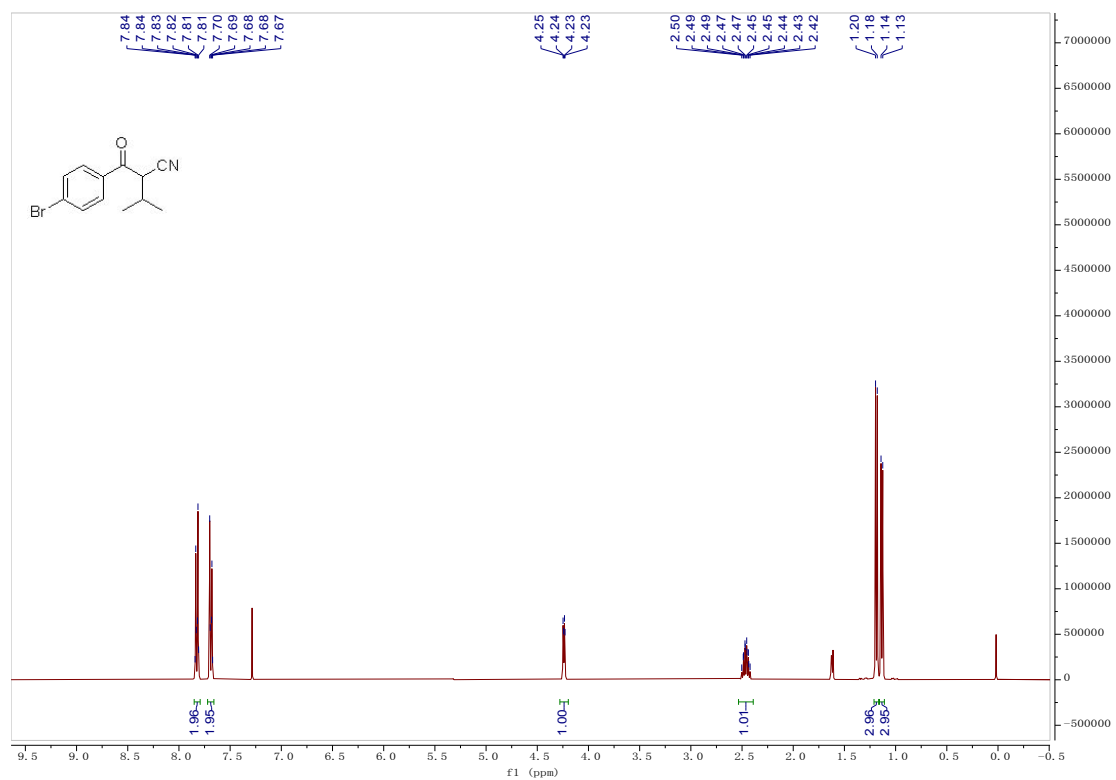
¹H NMR of 1i (400 MHz, Chloroform-*d*)



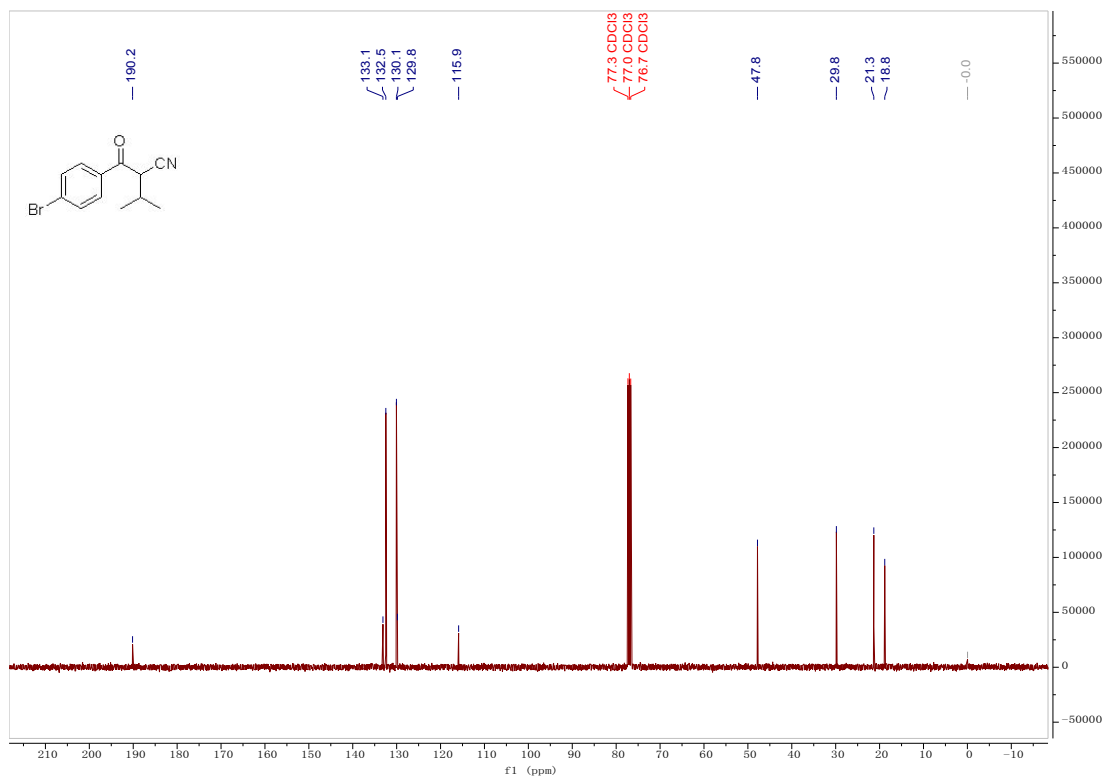
¹³C NMR of 1i (101 MHz, Chloroform-*d*)



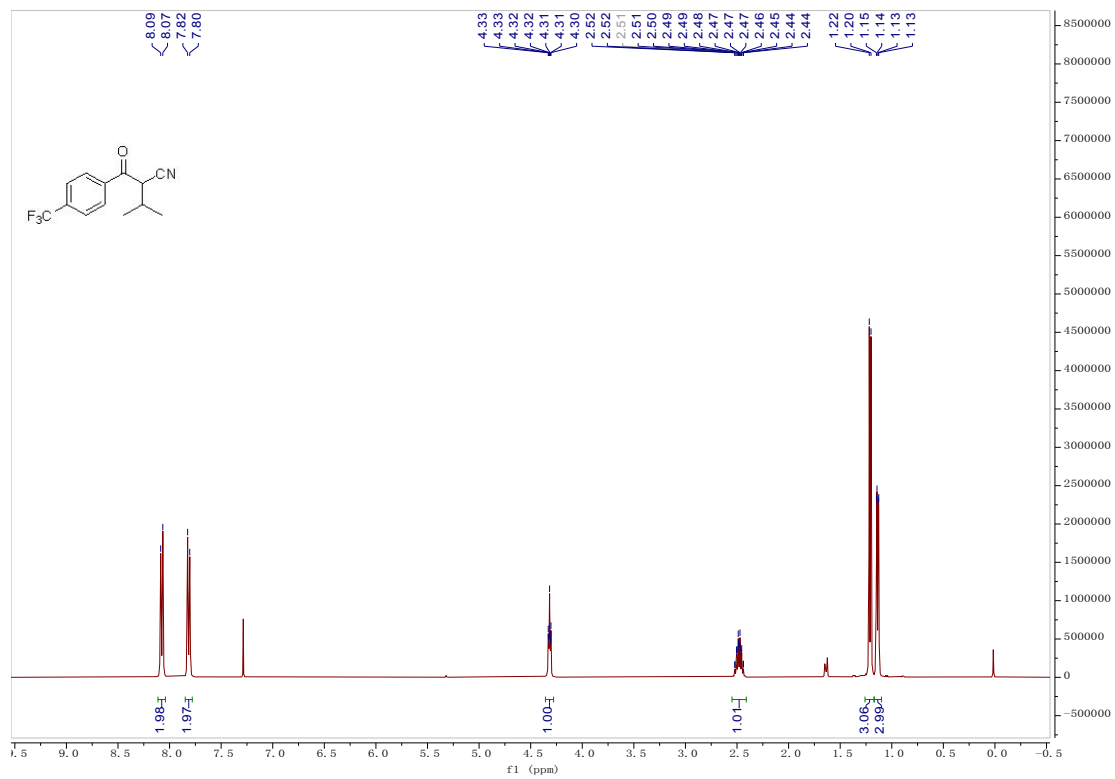
¹H NMR of 1j (400 MHz, Chloroform-*d*)



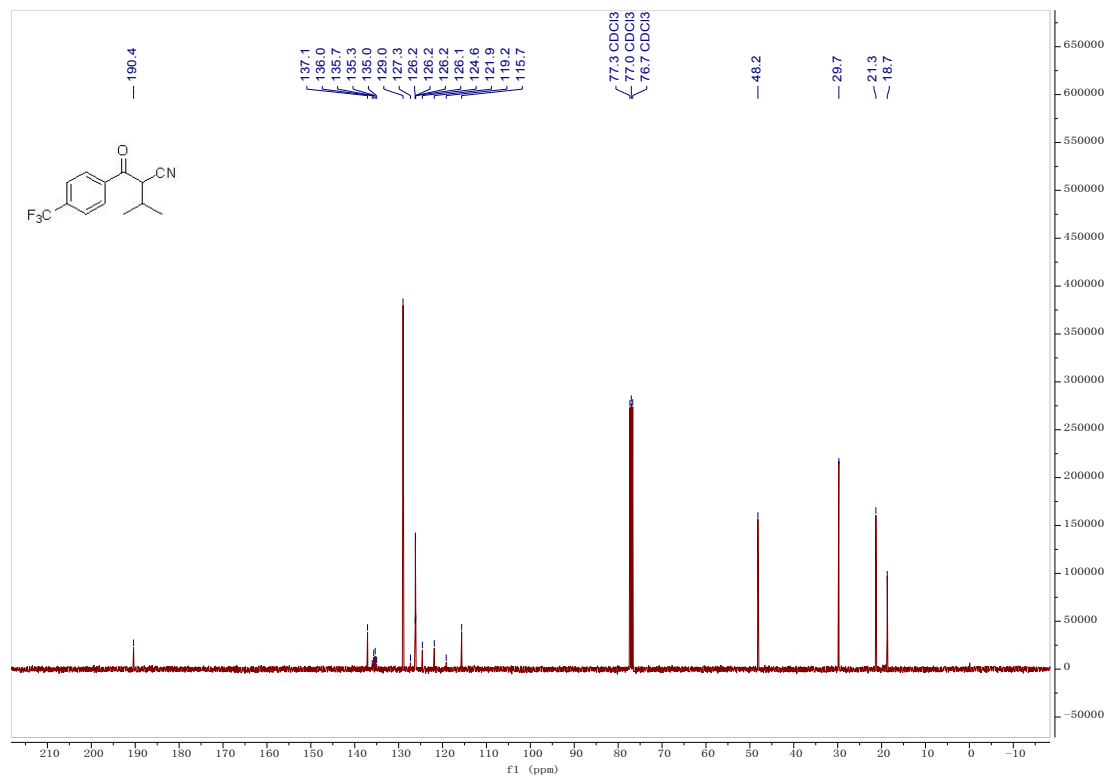
¹³C NMR of 1j (101 MHz, Chloroform-*d*)



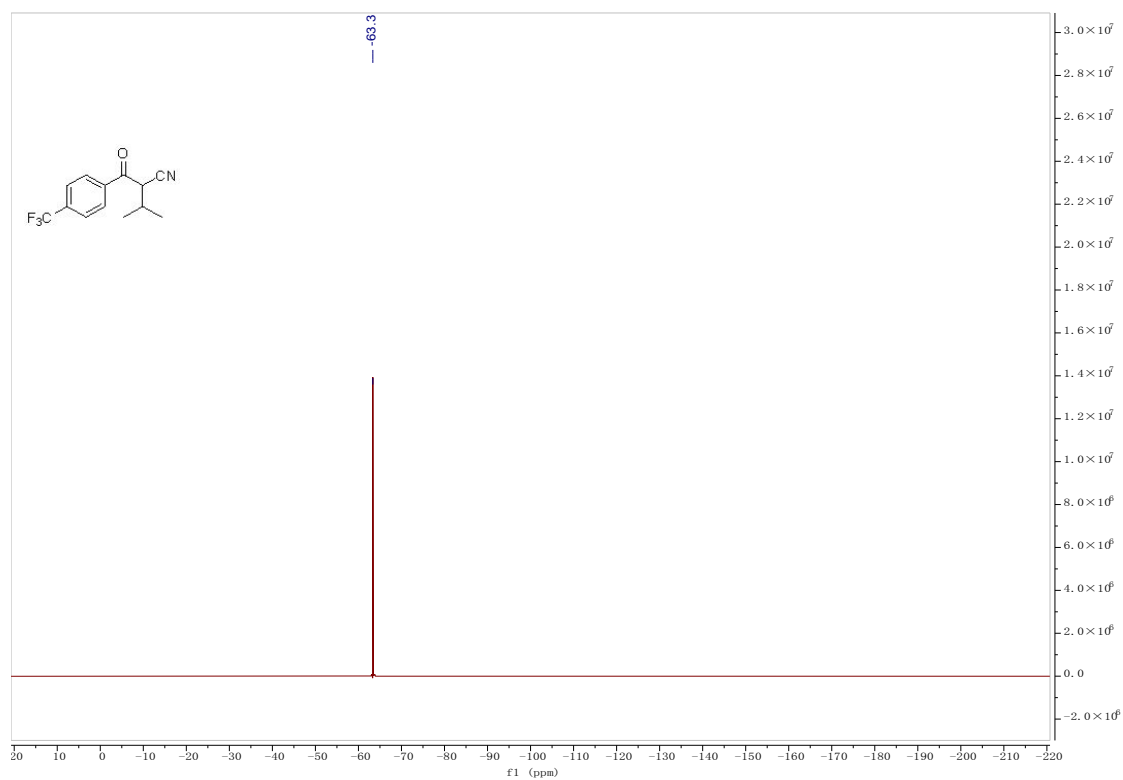
¹H NMR of 1k (400 MHz, Chloroform-*d*)



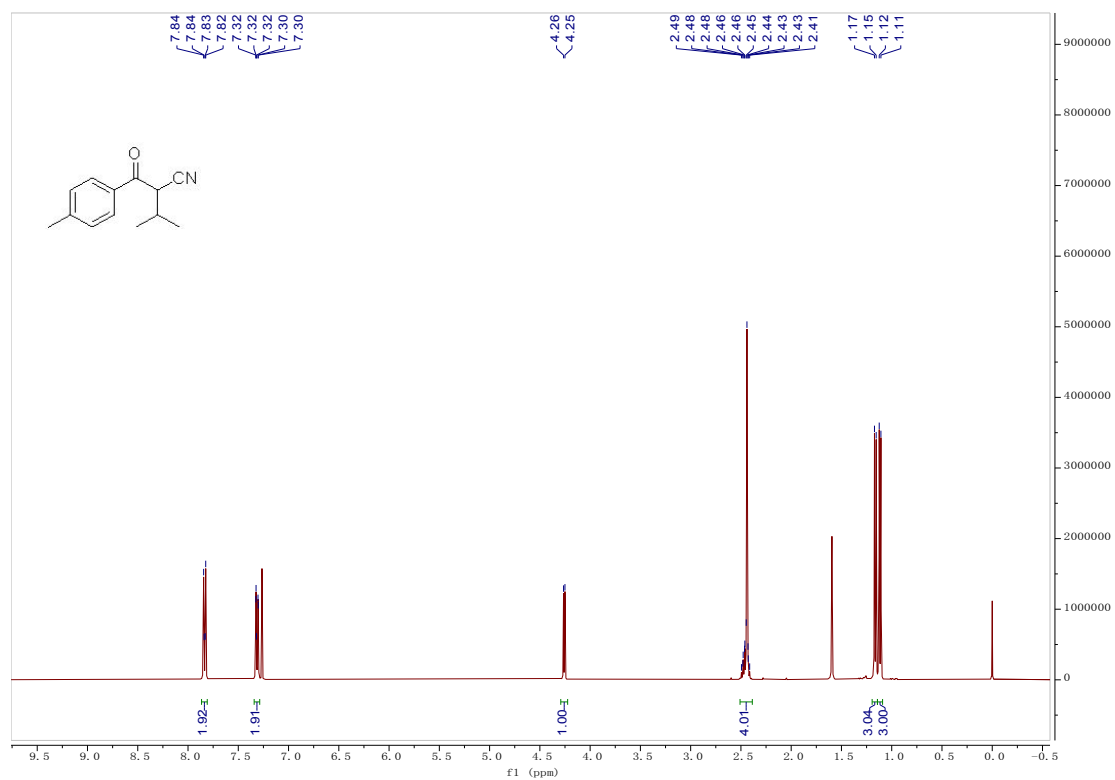
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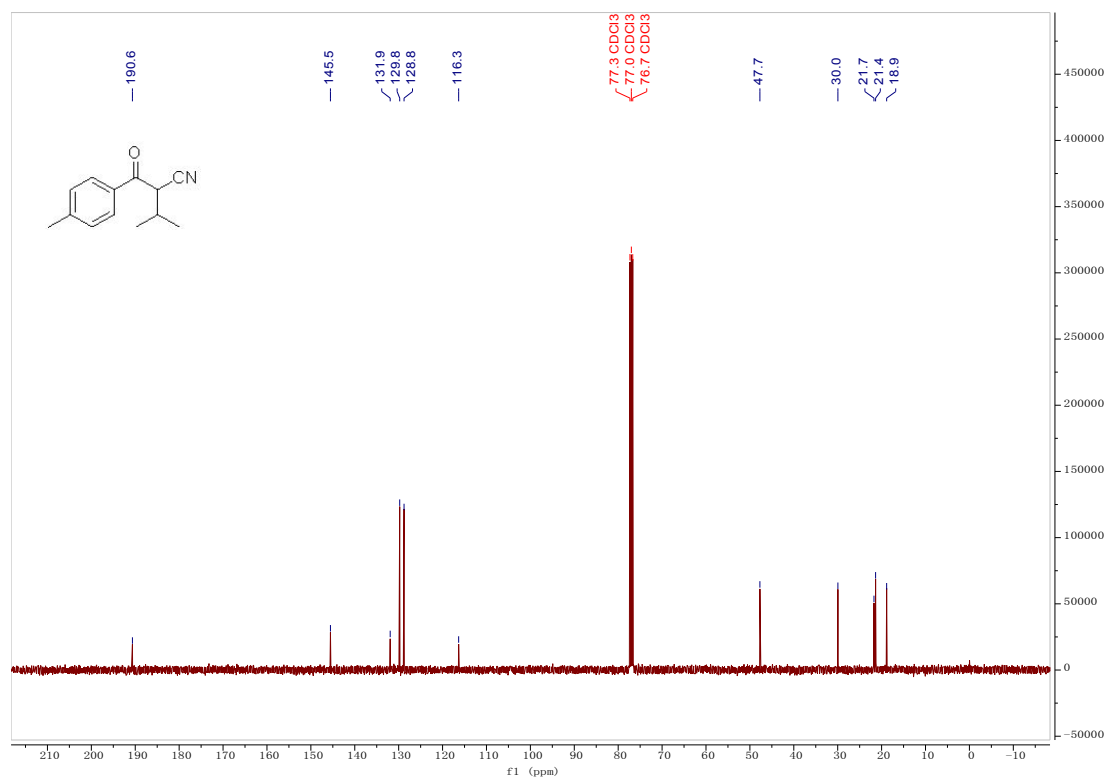
¹⁹F NMR of 1k (376 MHz, Chloroform-*d*)



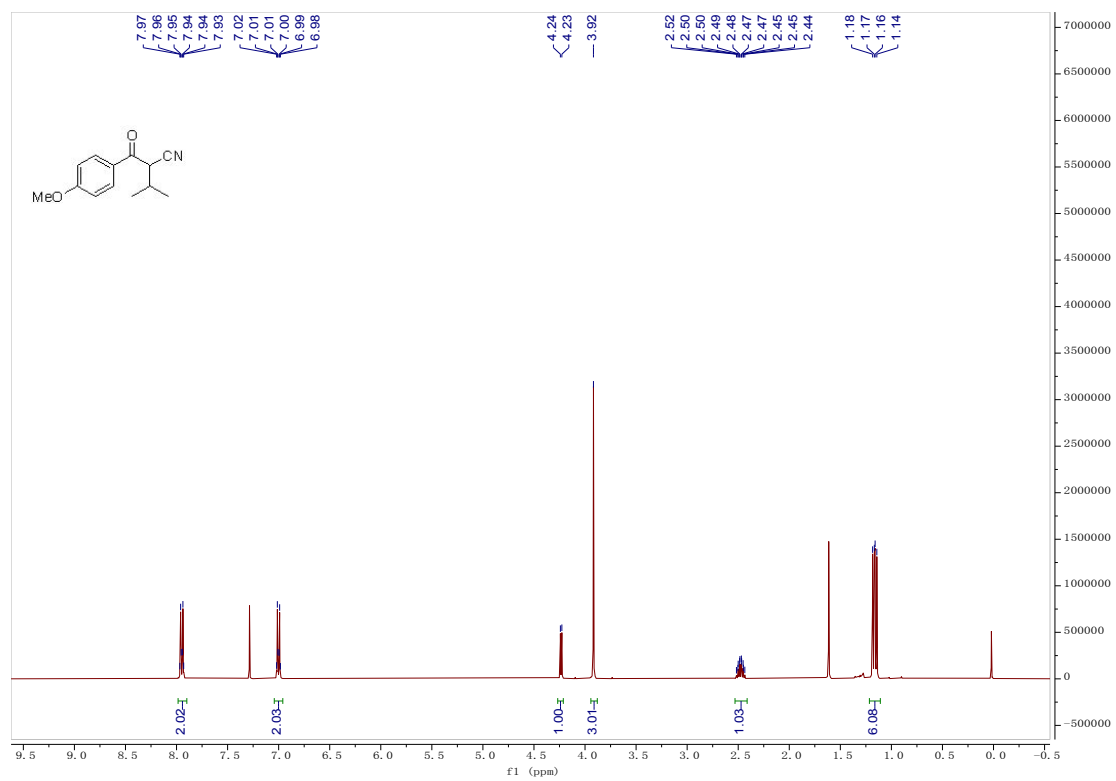
^1H NMR of 11 (400 MHz, Chloroform-*d*)



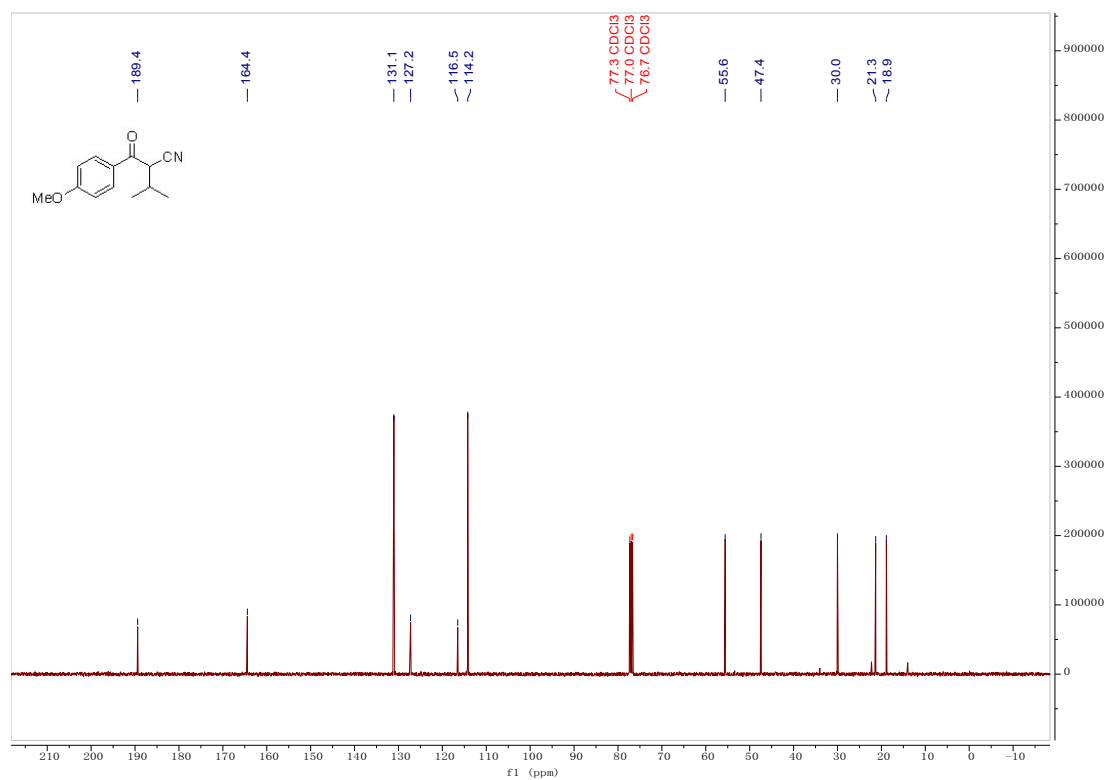
¹³C NMR of 11 (101 MHz, Chloroform-*d*)



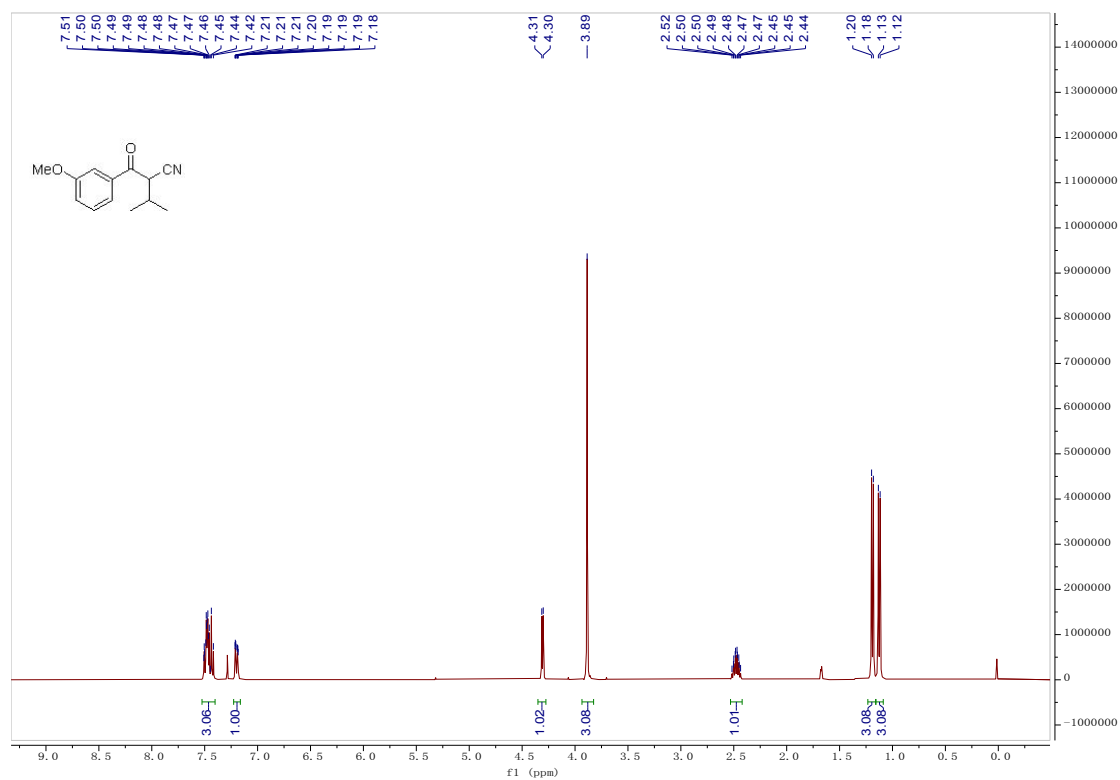
¹H NMR of 1m (400 MHz, Chloroform-*d*)



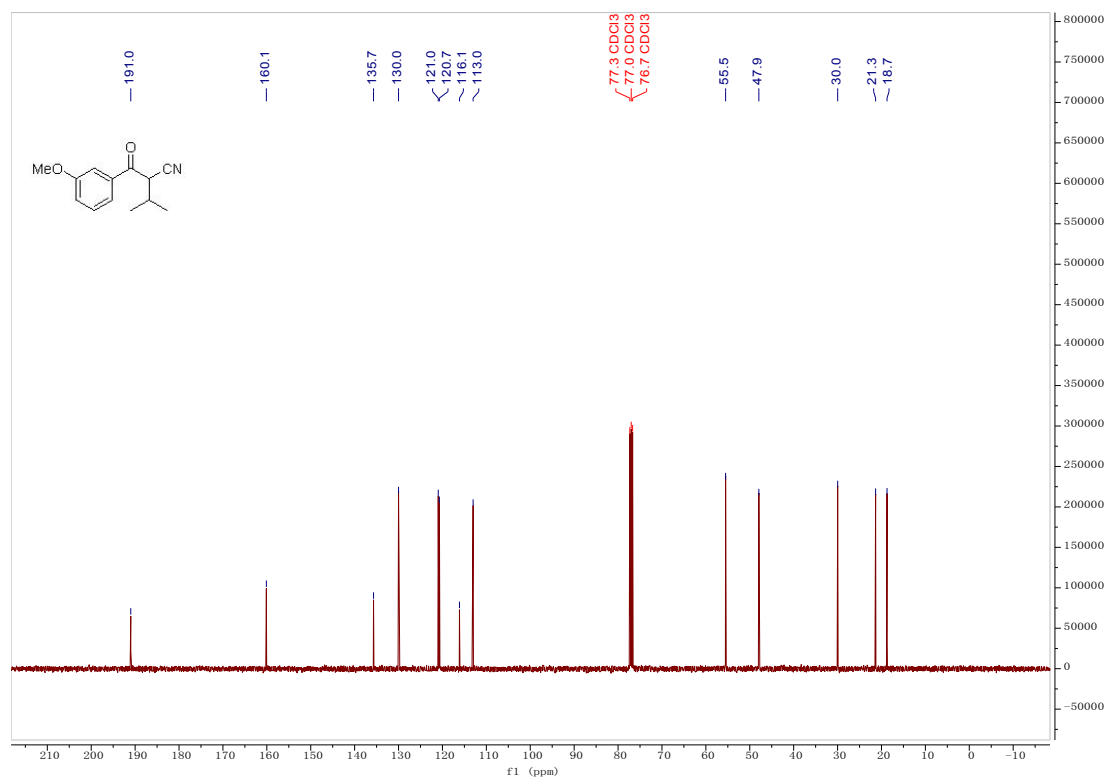
¹³C NMR of 1m (101 MHz, Chloroform-*d*)



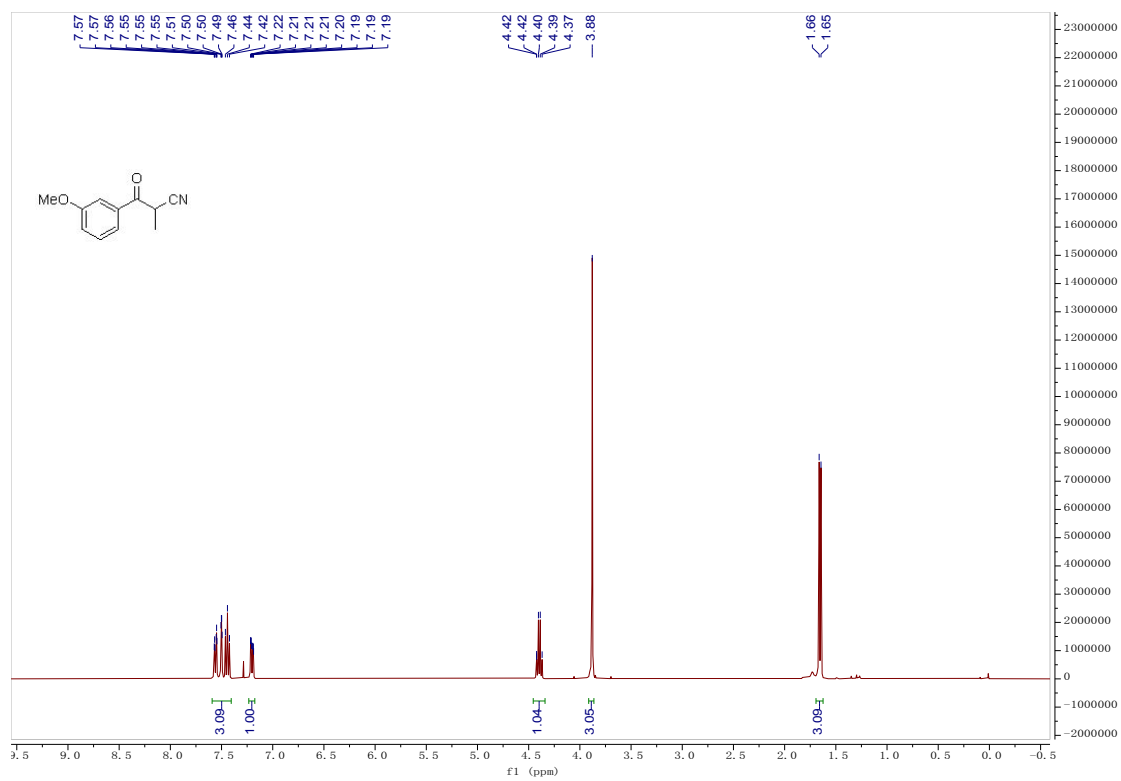
¹H NMR of 1n (400 MHz, Chloroform-*d*)



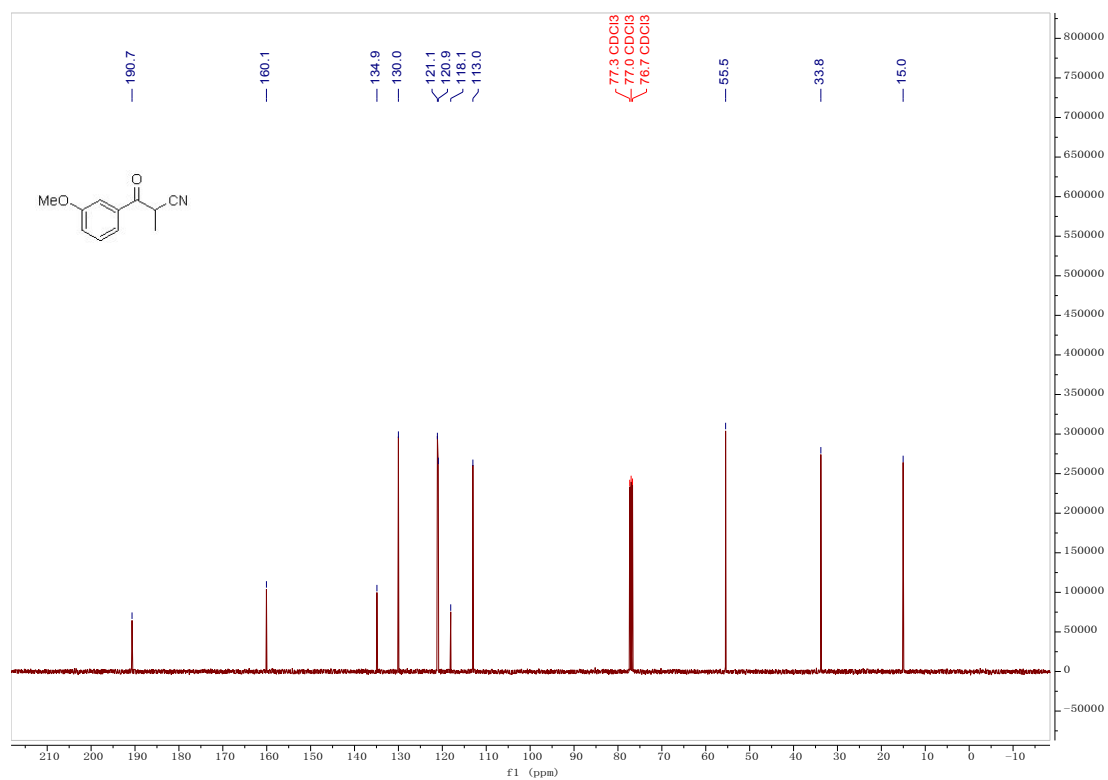
¹³C NMR of 1n (101 MHz, Chloroform-*d*)



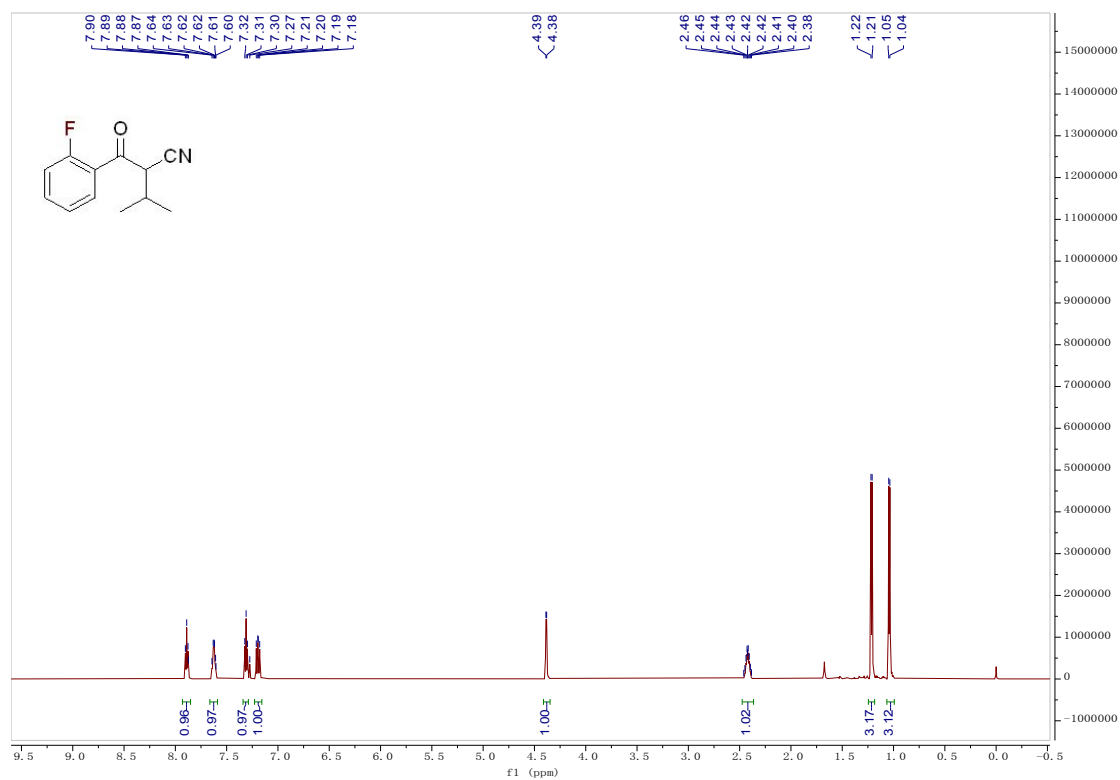
¹H NMR of 1o (400 MHz, Chloroform-*d*)



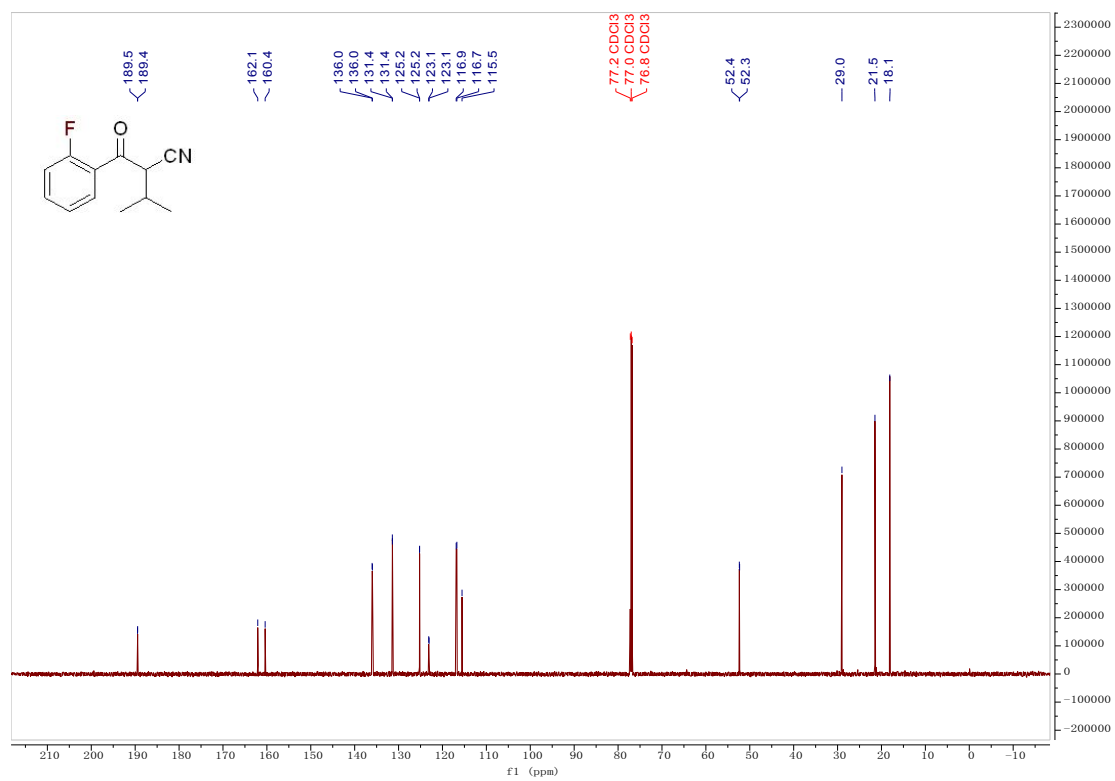
¹³C NMR of 1o (101 MHz, Chloroform-*d*)



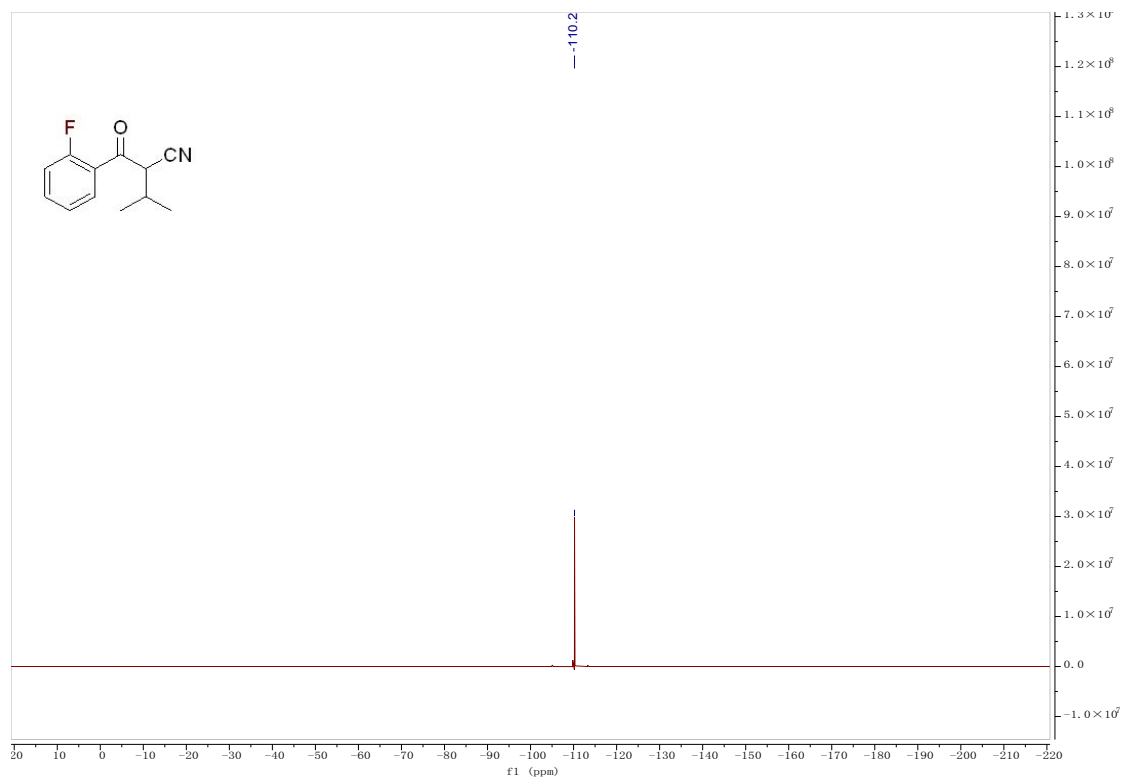
¹H NMR of 1p (600 MHz, Chloroform-*d*)



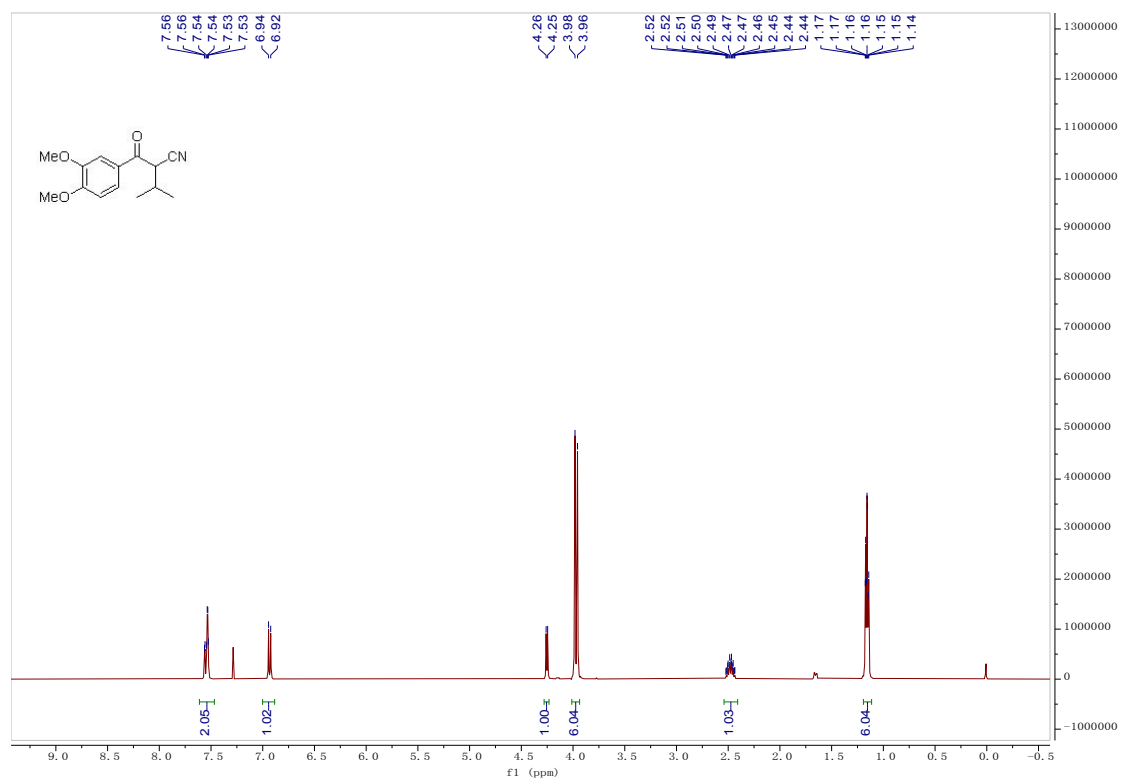
¹³C NMR of 1p (151 MHz, Chloroform-*d*)



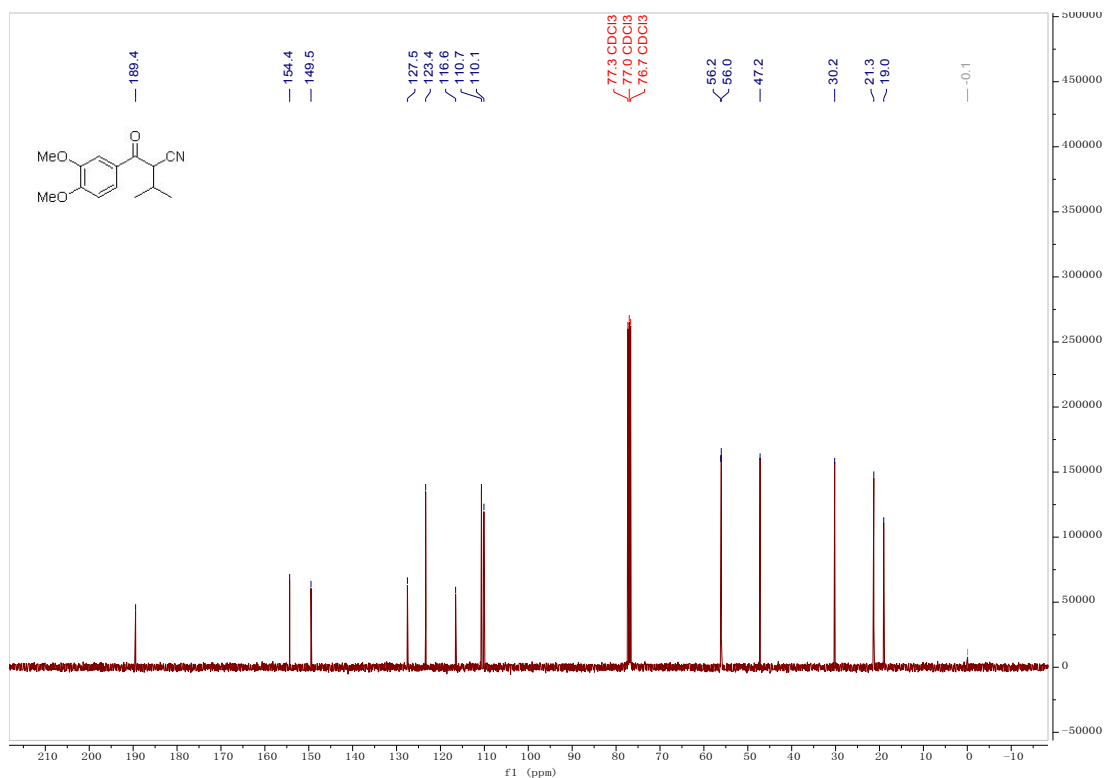
¹⁹F NMR of 1p (376 MHz, Chloroform-*d*)



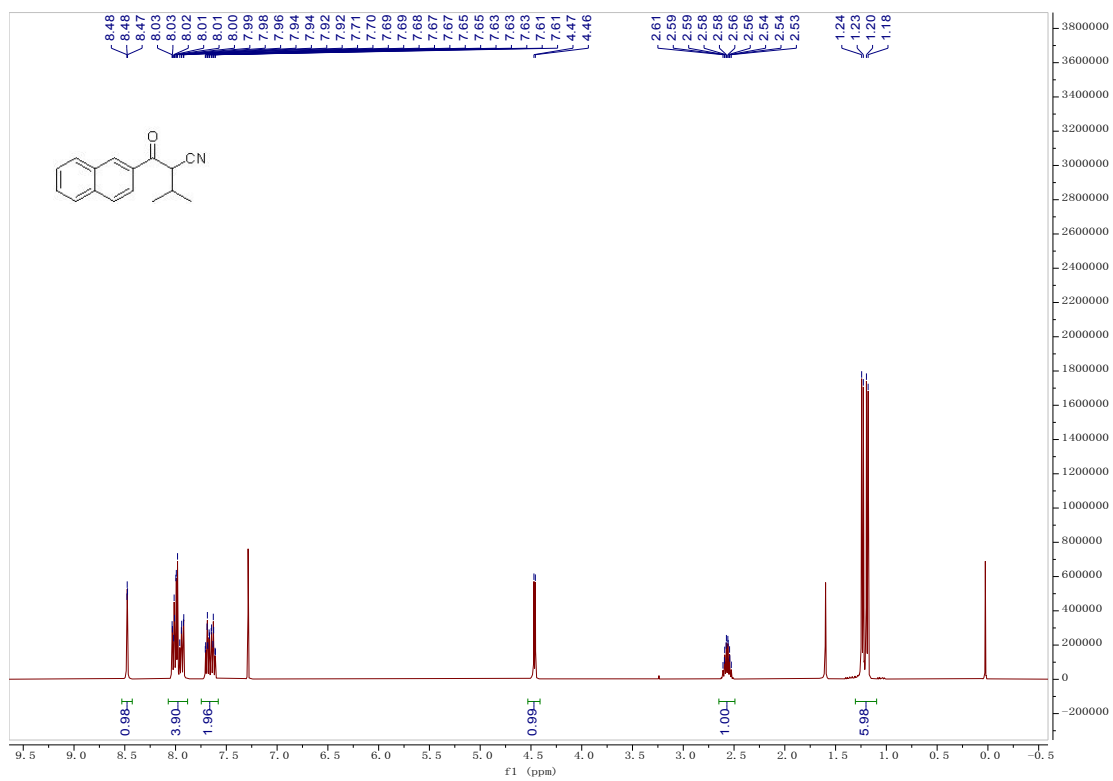
¹H NMR of 1q (400 MHz, Chloroform-*d*)



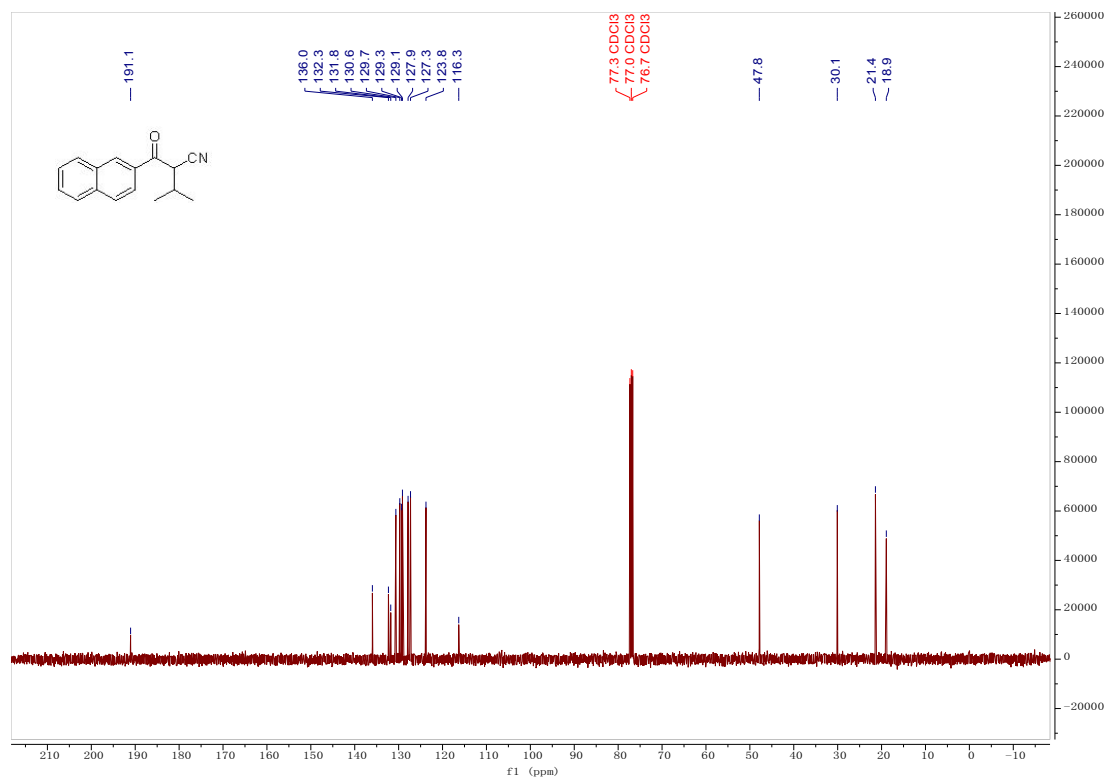
¹³C NMR of 1q (101 MHz, Chloroform-*d*)



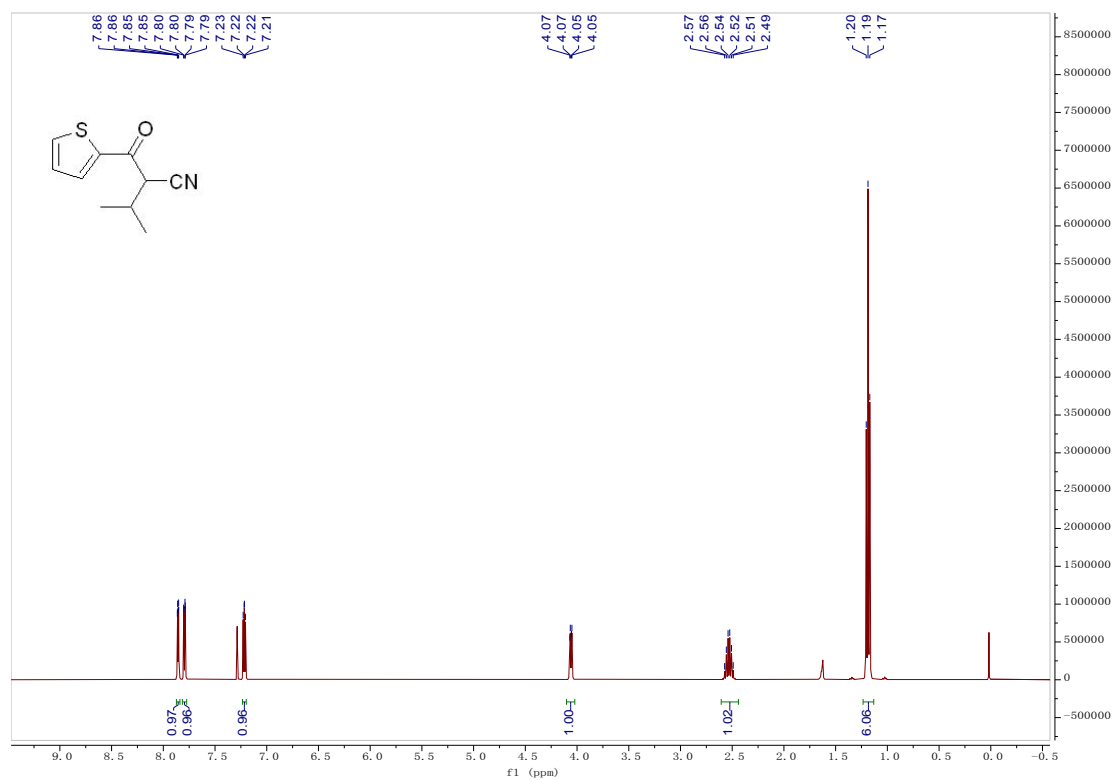
¹H NMR of 1r (400 MHz, Chloroform-*d*)



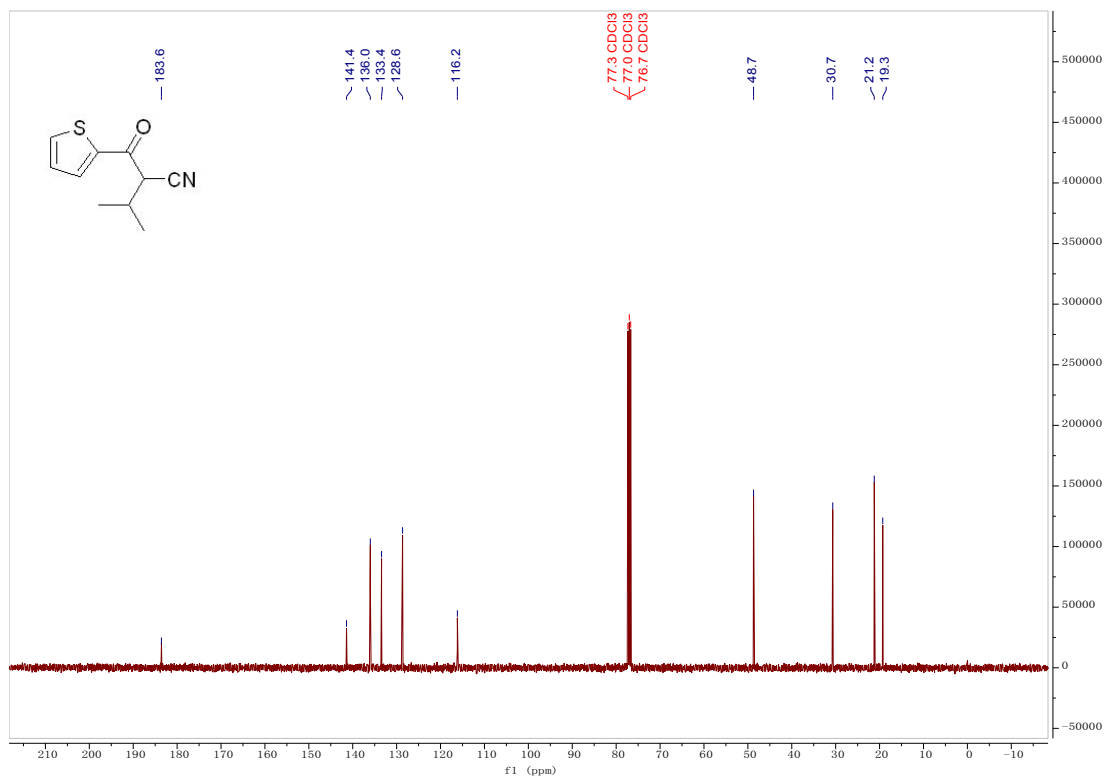
¹³C NMR of 1r (101 MHz, Chloroform-*d*)



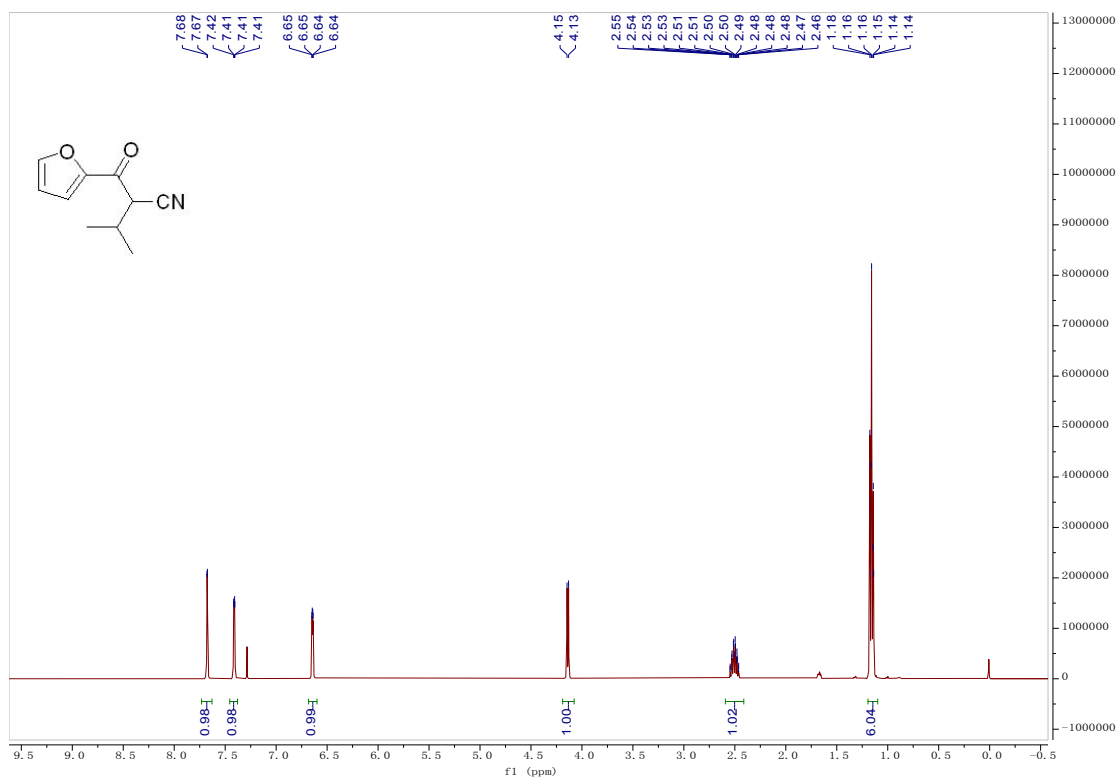
¹H NMR of 1s (400 MHz, Chloroform-*d*)



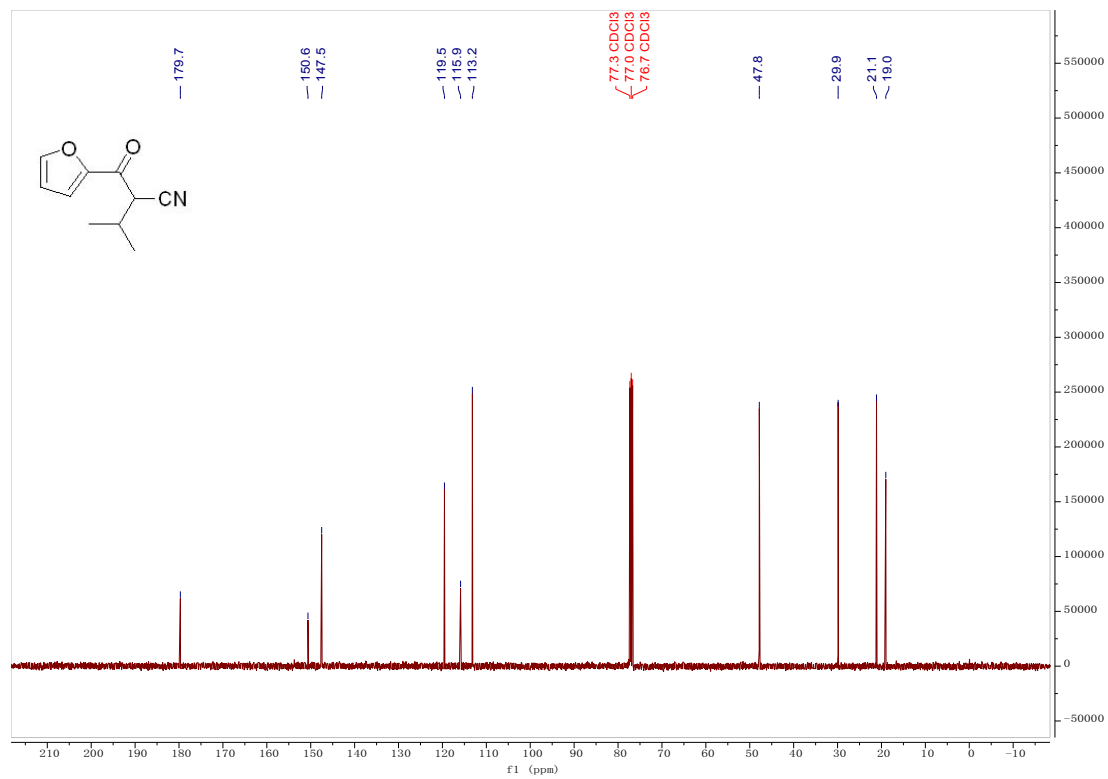
¹³C NMR of 1s (101 MHz, Chloroform-*d*)



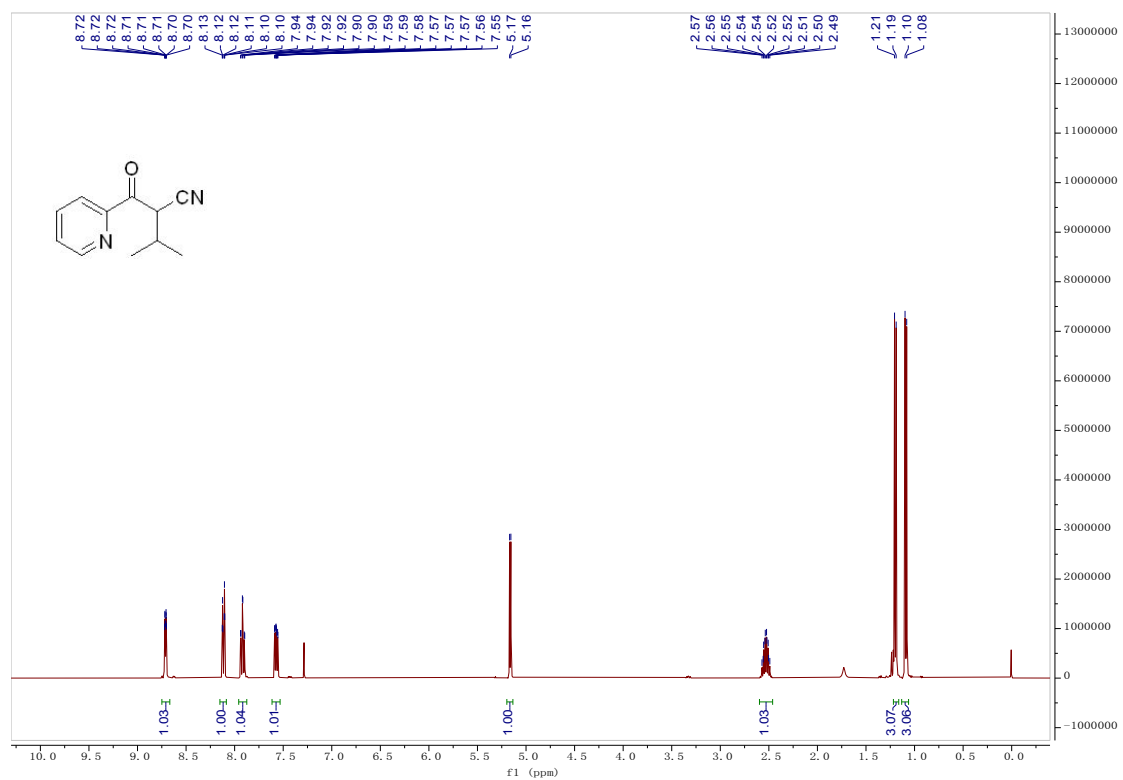
¹H NMR of 1t (400 MHz, Chloroform-d)



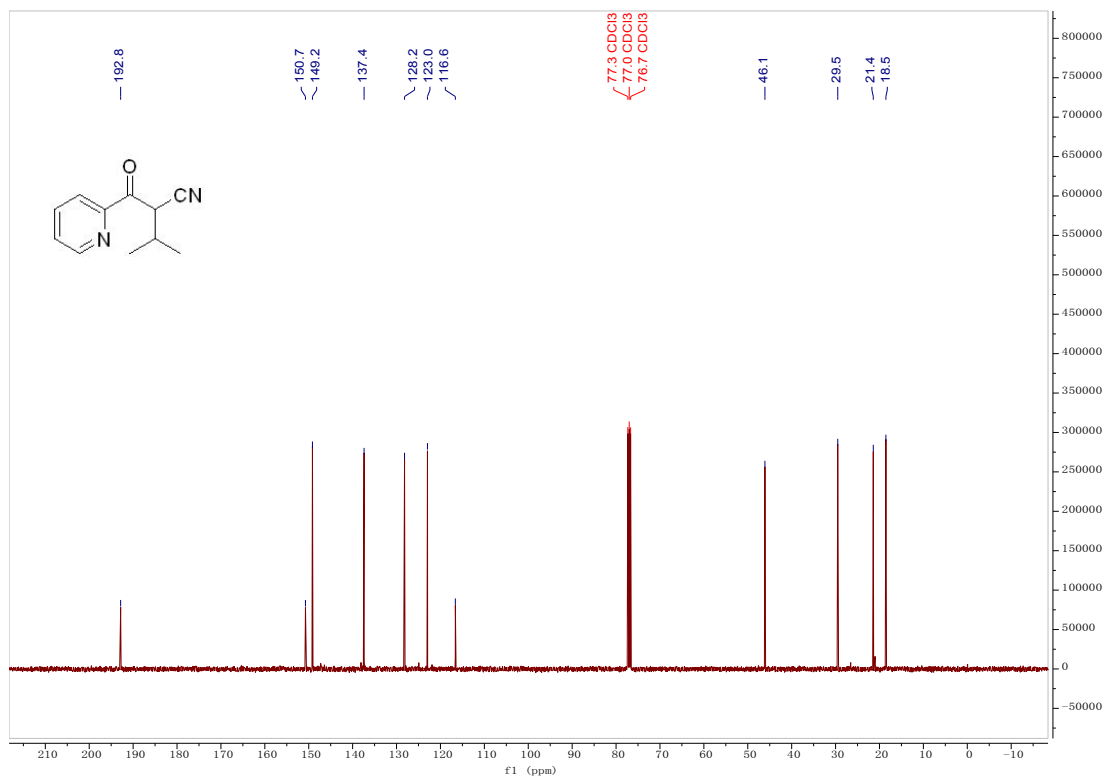
¹³C NMR of 1t (101 MHz, Chloroform-*d*)



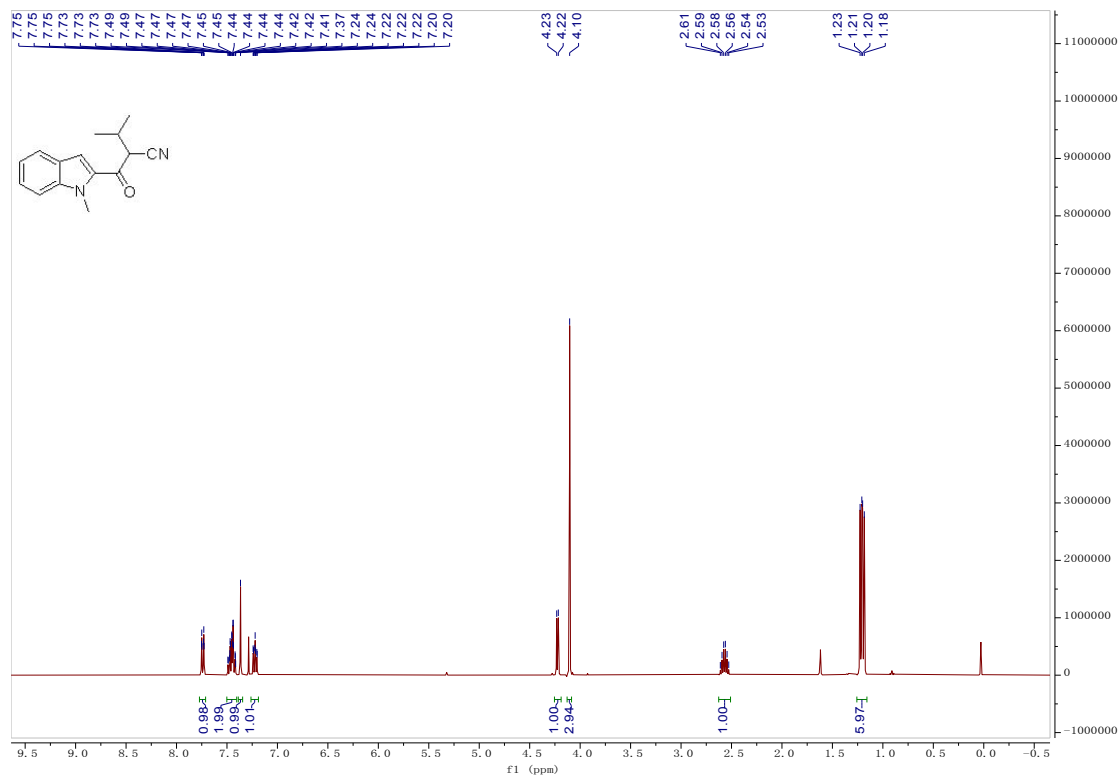
¹H NMR of 1u (400 MHz, Chloroform-*d*)



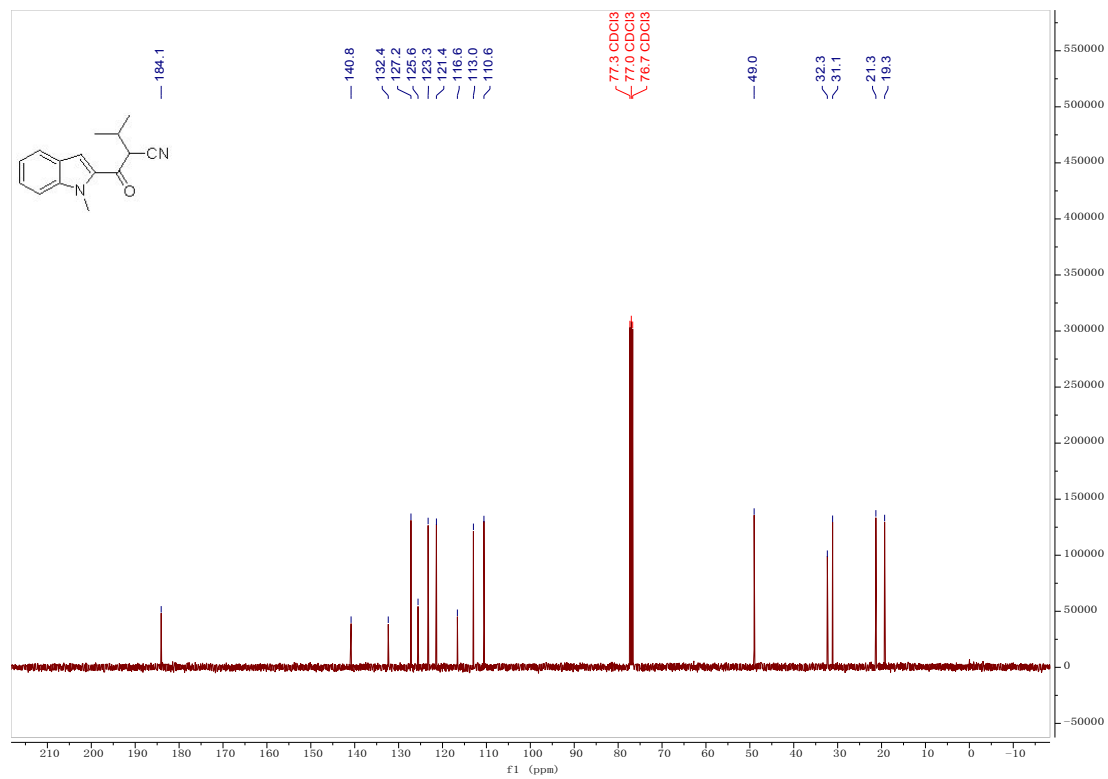
¹³C NMR of 1u (101 MHz, Chloroform-*d*)



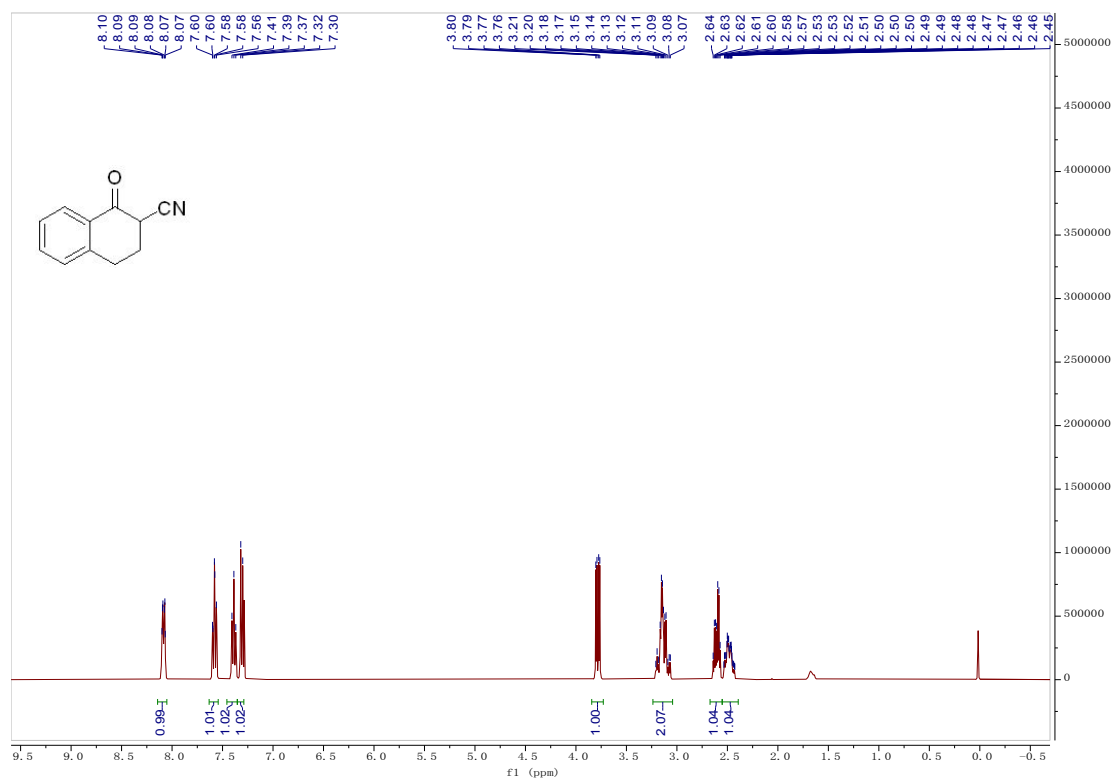
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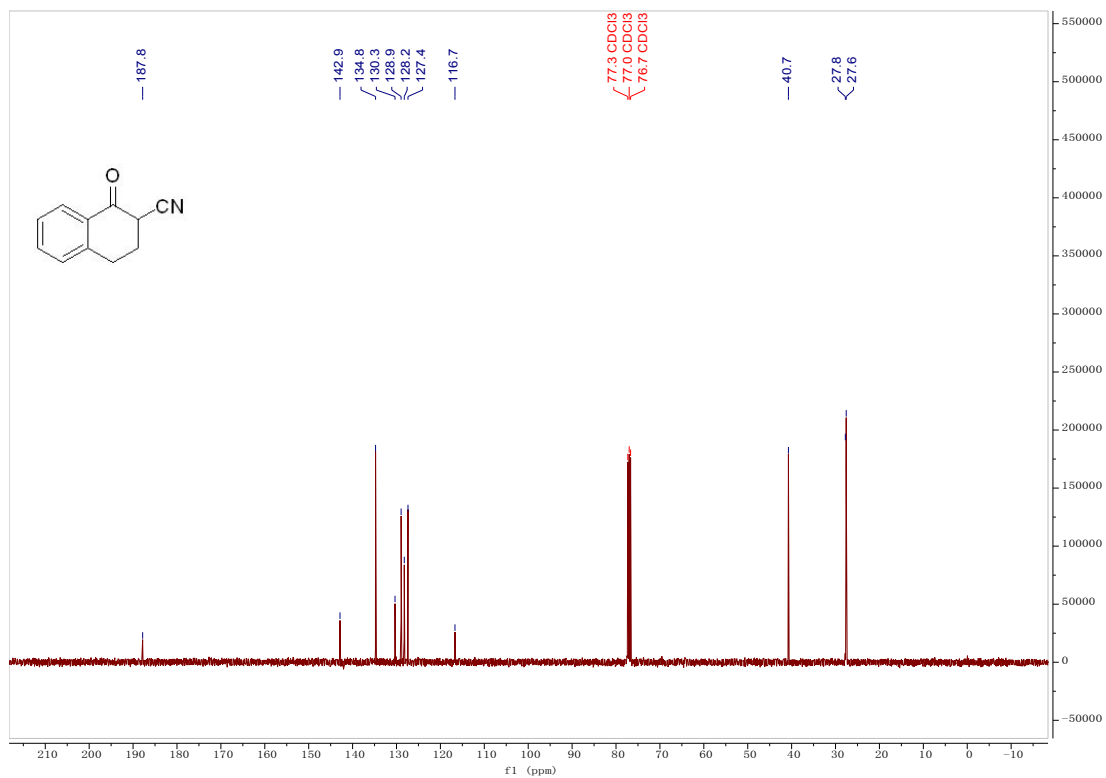
¹³C NMR of 1v (101 MHz, Chloroform-*d*)



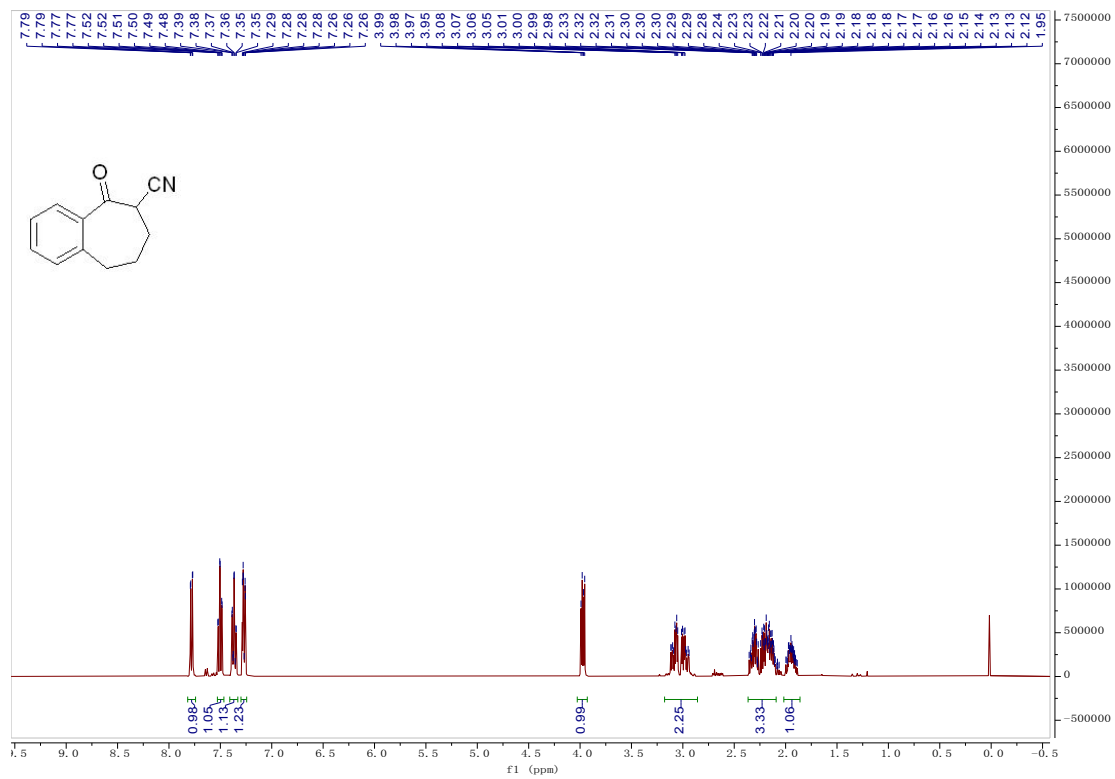
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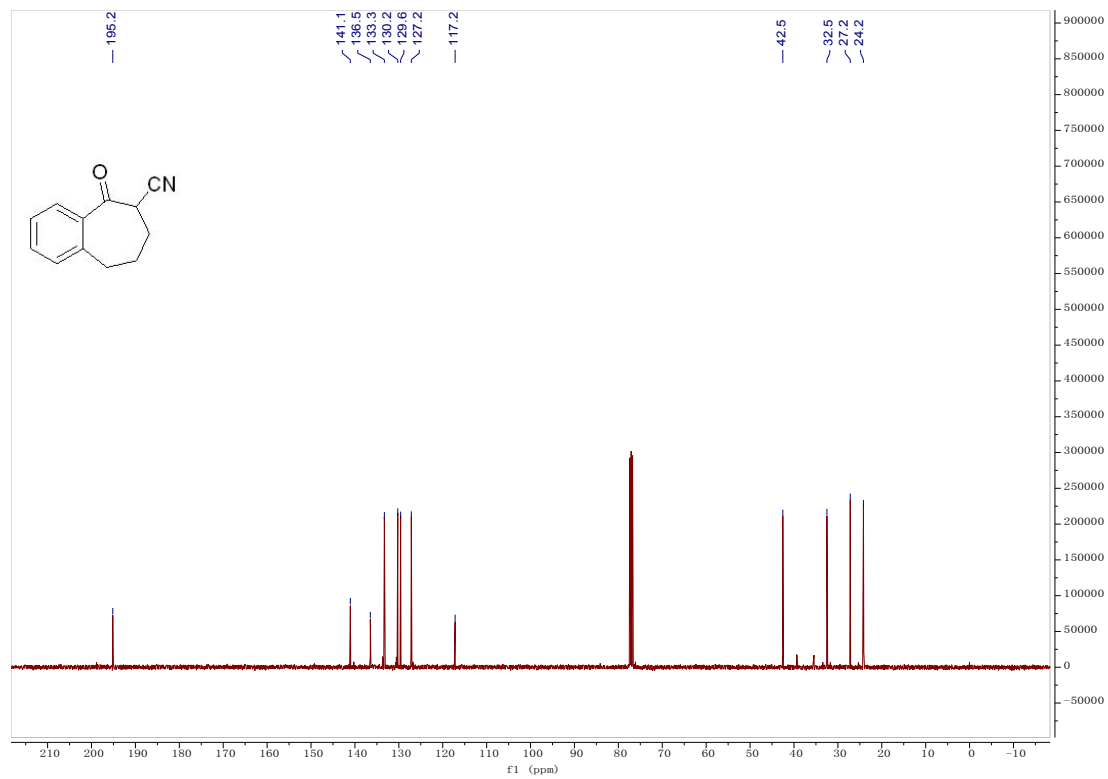
¹³C NMR of 1w (101 MHz, Chloroform-d)



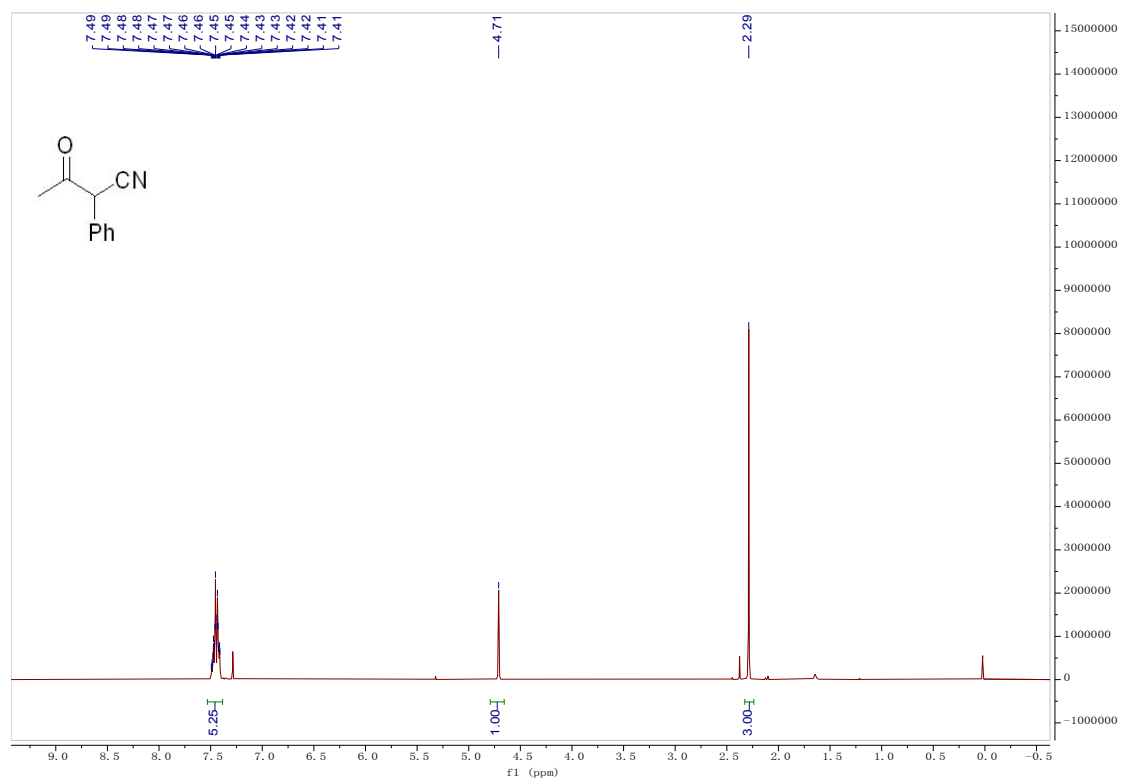
¹H NMR of 1x (400 MHz, Chloroform-d)



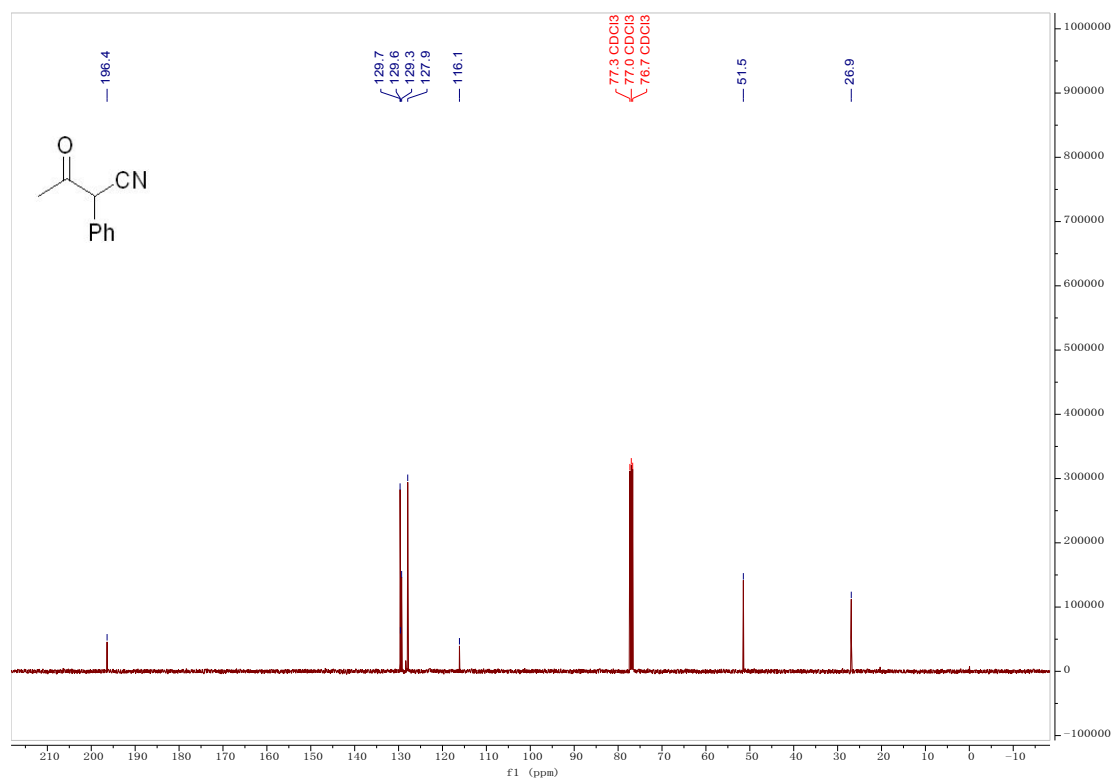
¹³C NMR of 1x (101 MHz, Chloroform-*d*)



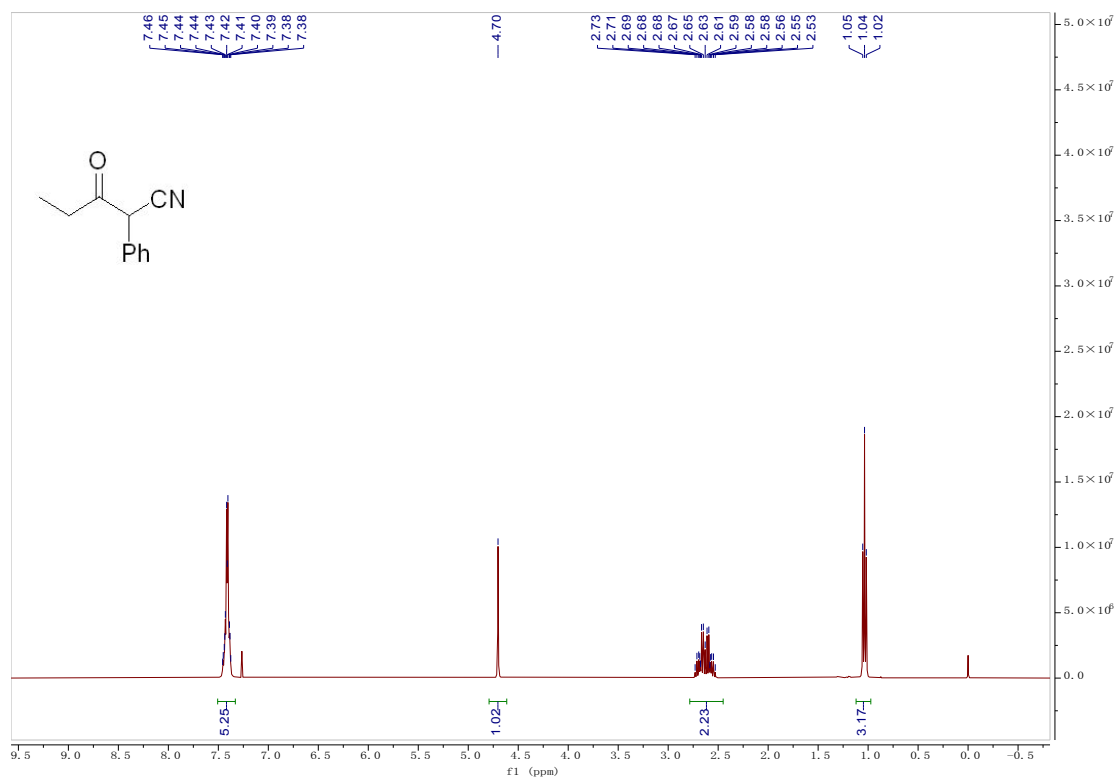
¹H NMR of 1y (400 MHz, Chloroform-*d*)



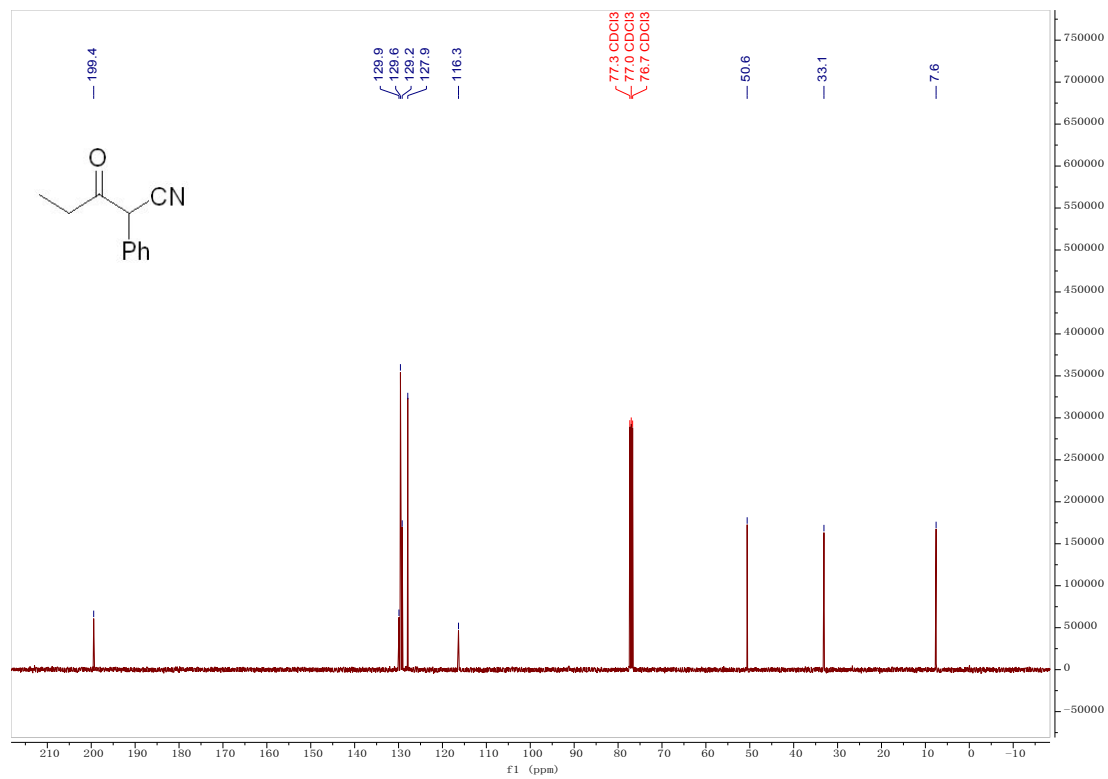
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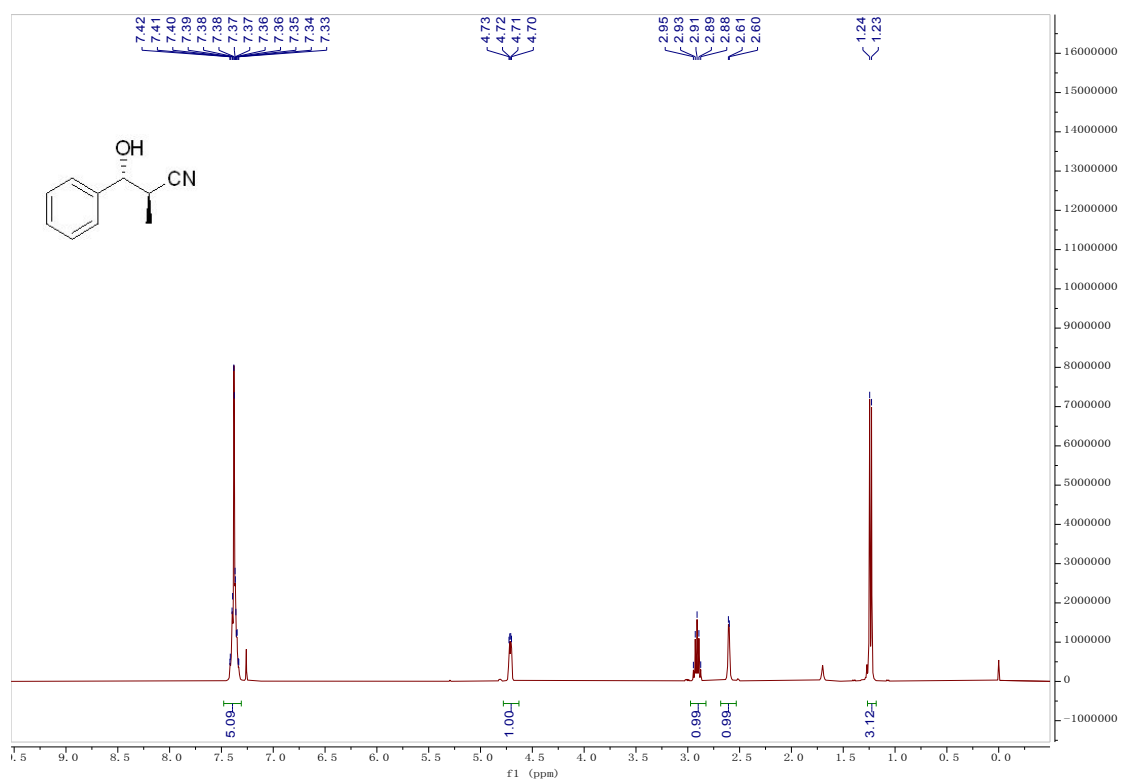
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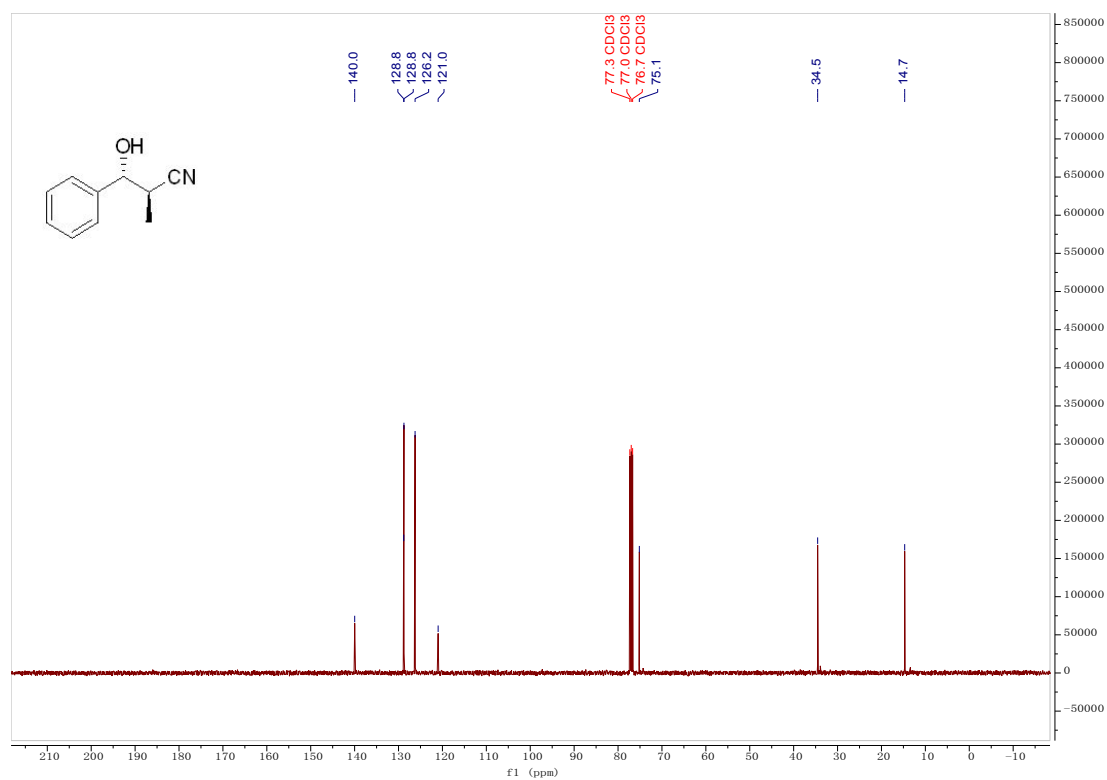
¹³C NMR of 1z (101 MHz, Chloroform-*d*)



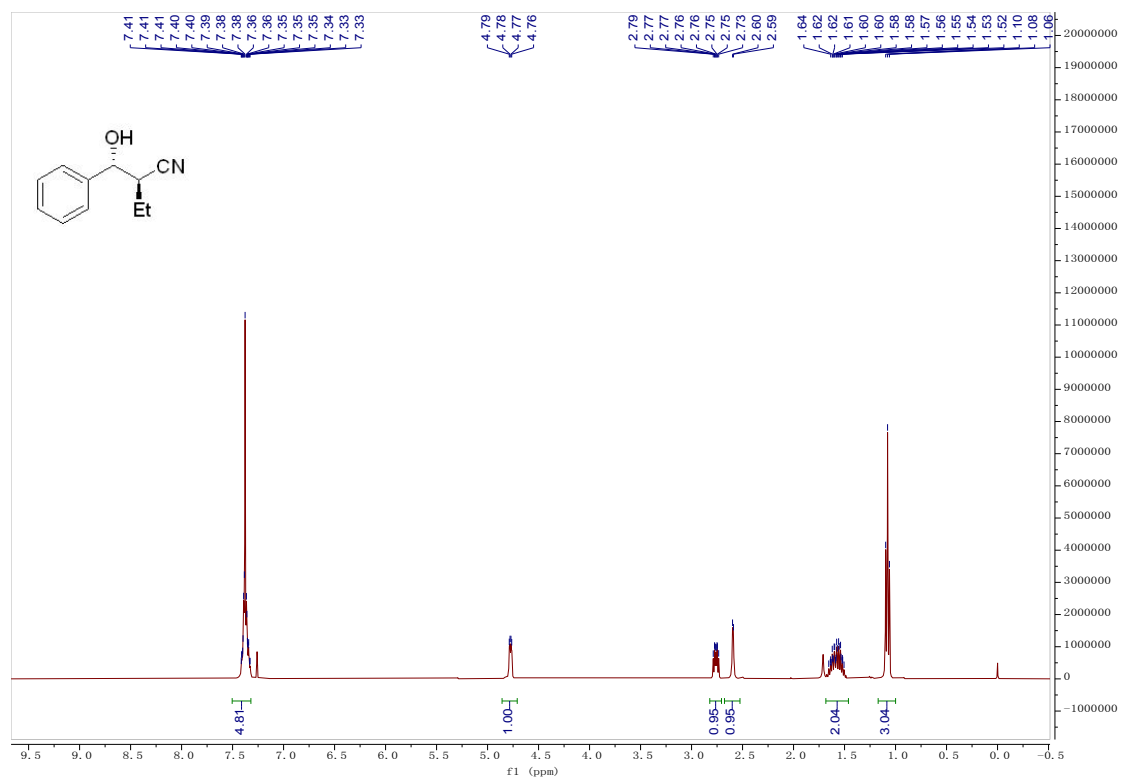
¹H NMR of 2a (400 MHz, Chloroform-*d*)



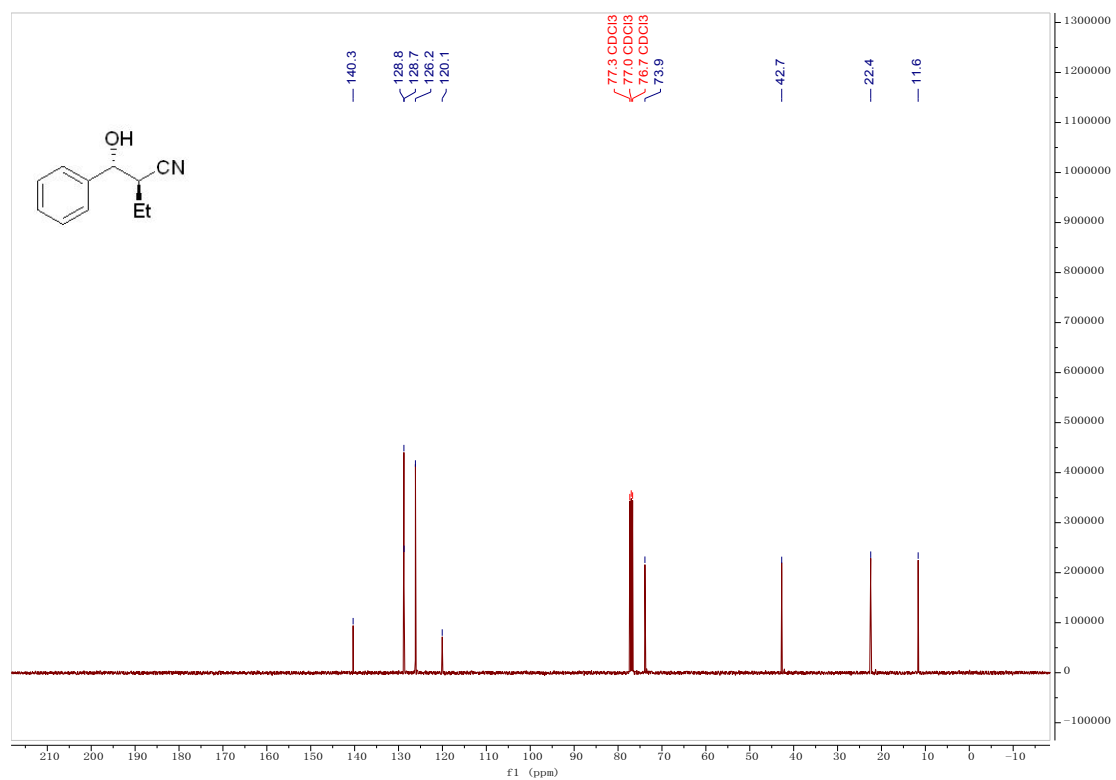
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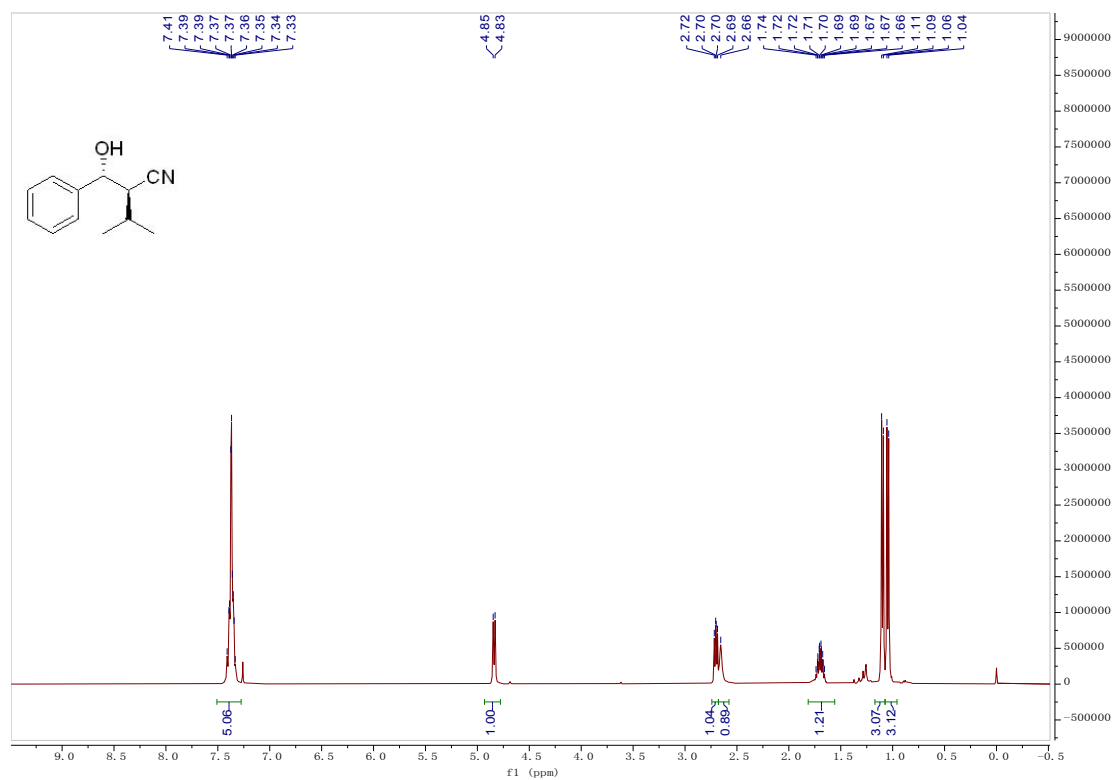
¹H NMR of 2b (400 MHz, Chloroform-*d*)



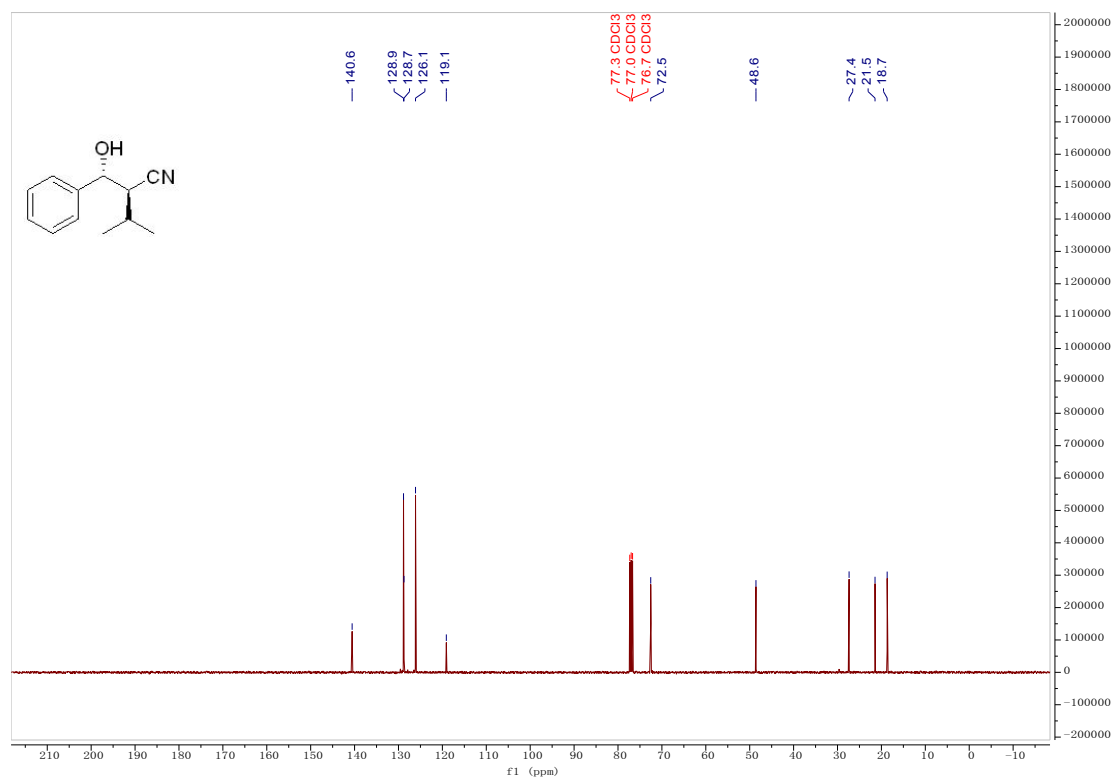
¹³C NMR of 2b (101 MHz, Chloroform-*d*)



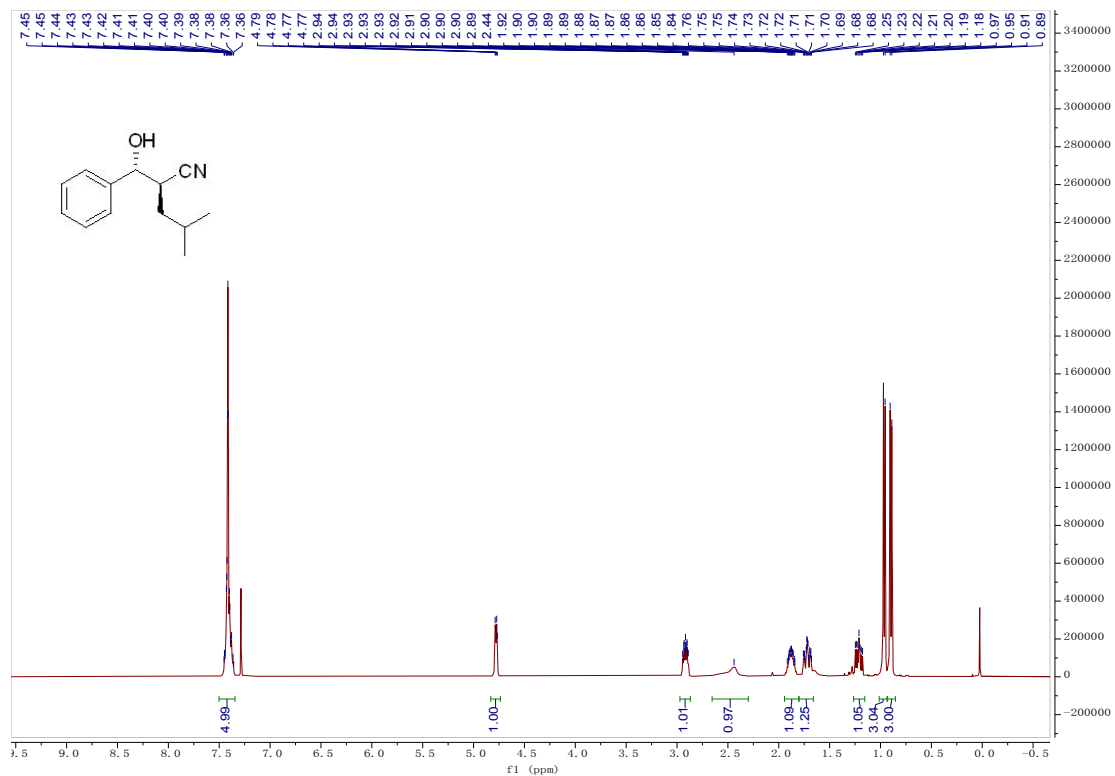
¹H NMR of 2c (400 MHz, Chloroform-*d*)



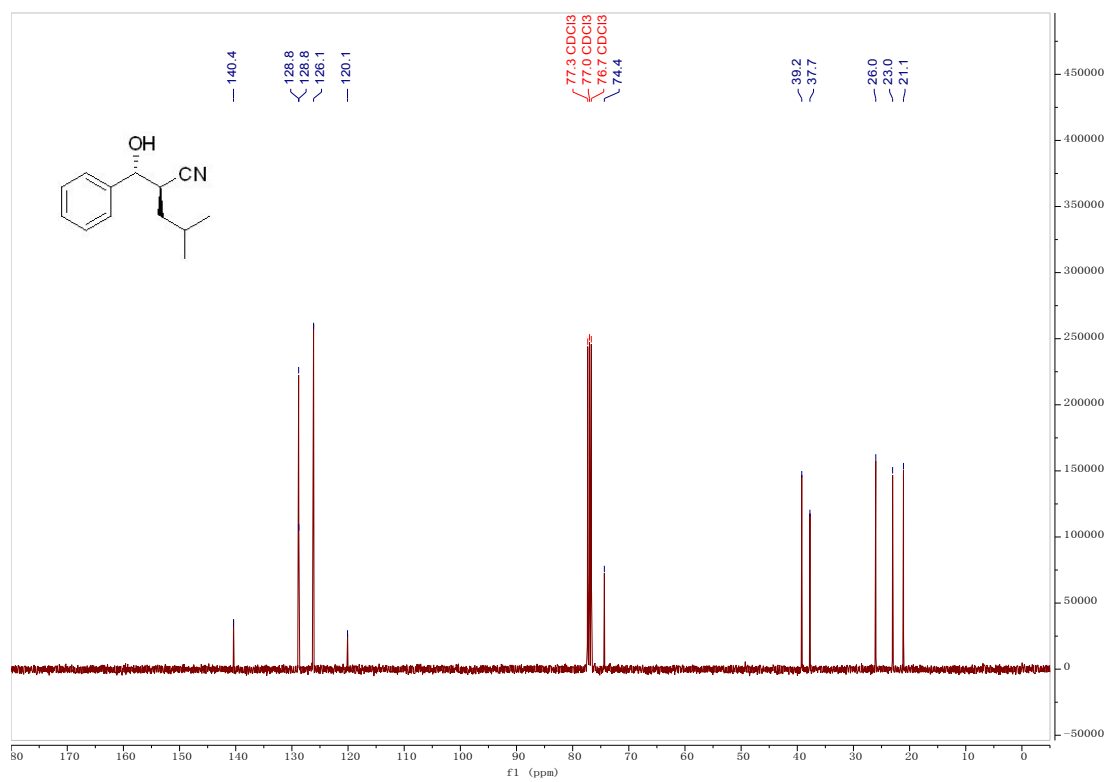
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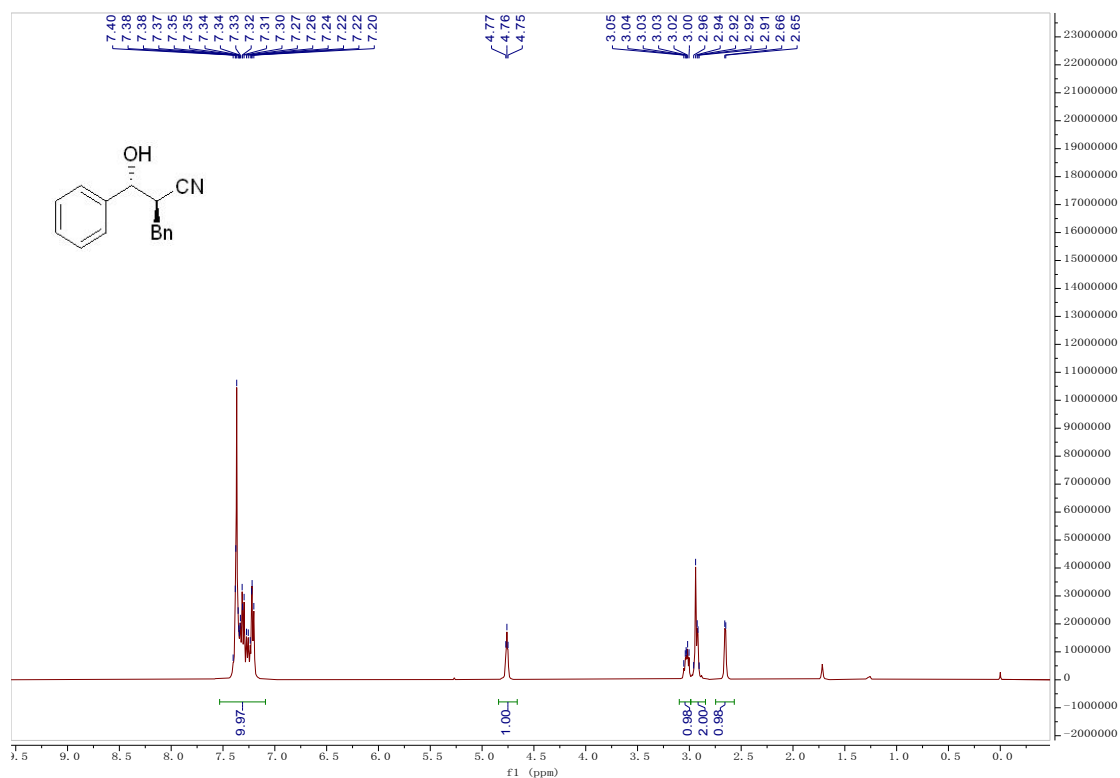
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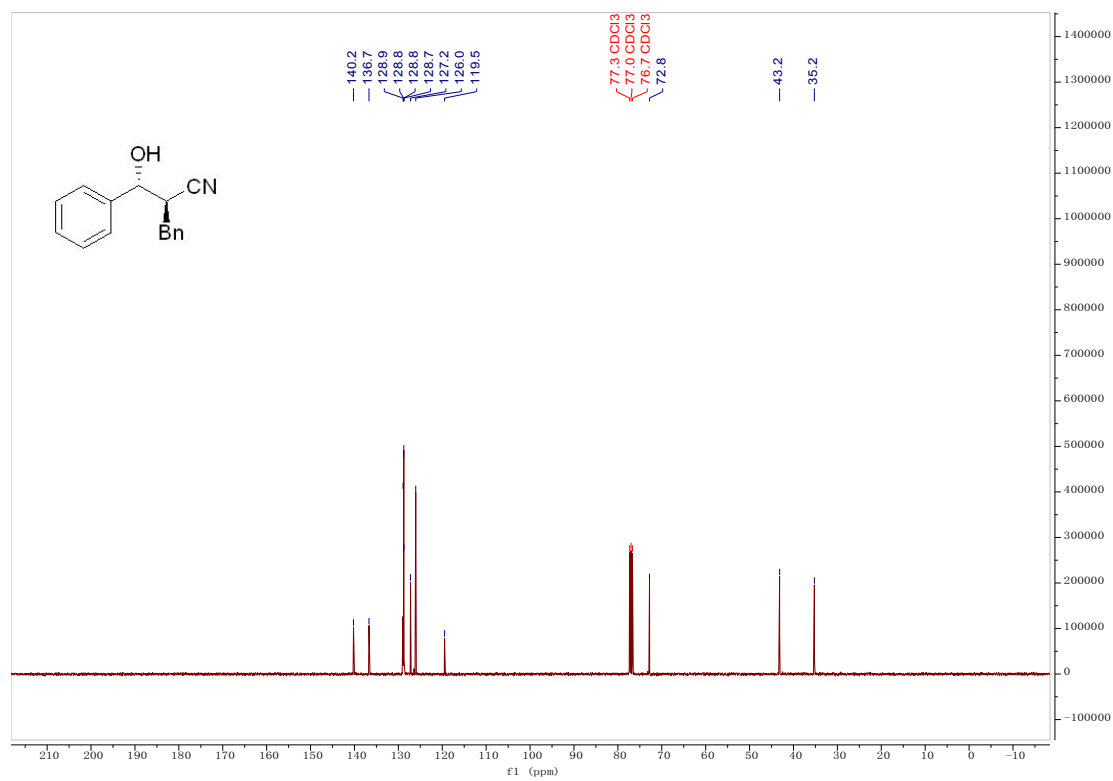
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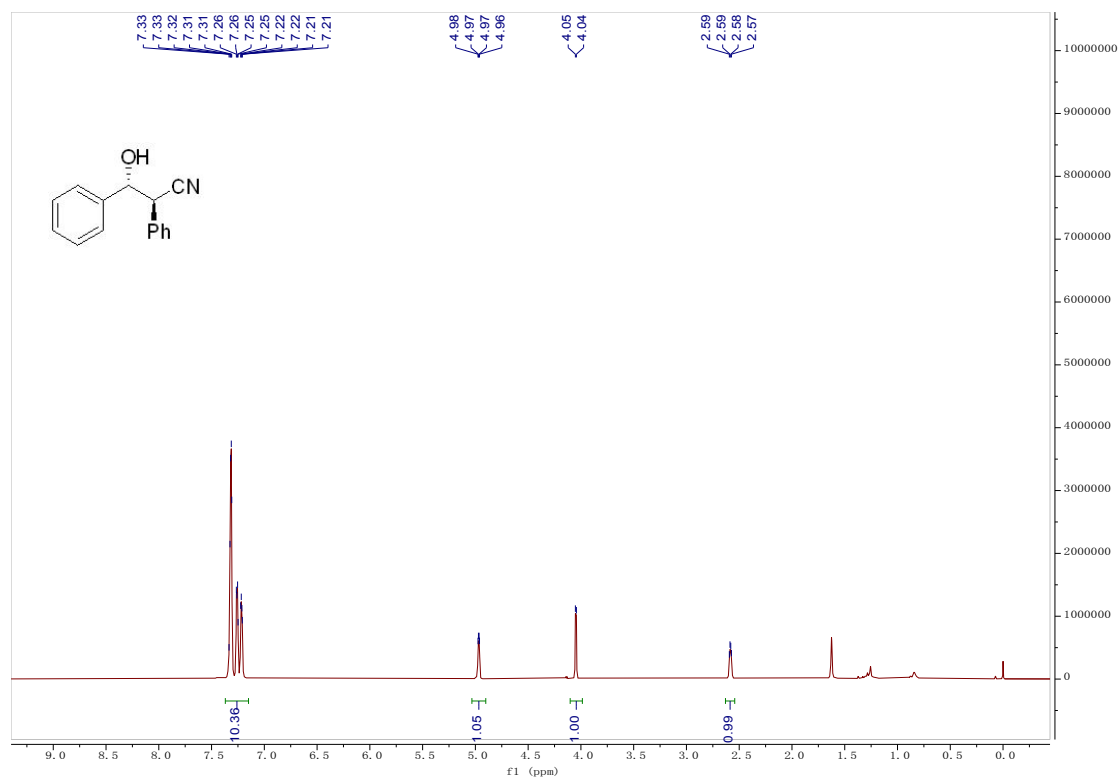
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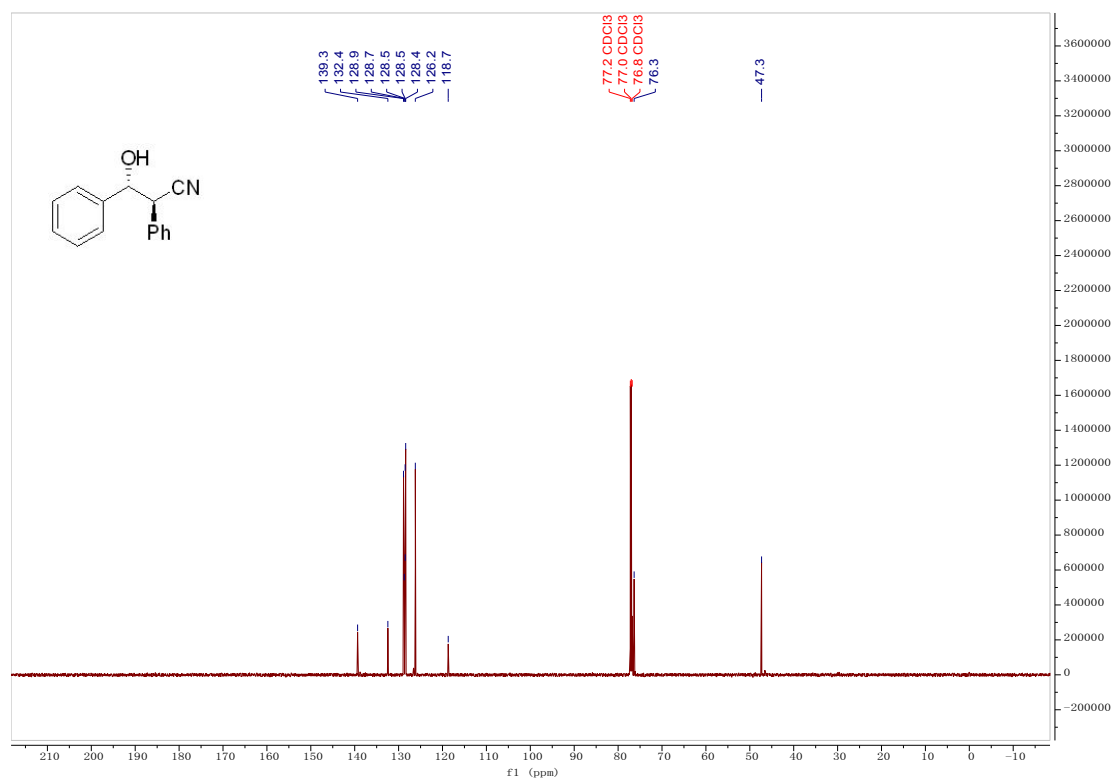
¹³C NMR of 2e (101 MHz, Chloroform-*d*)



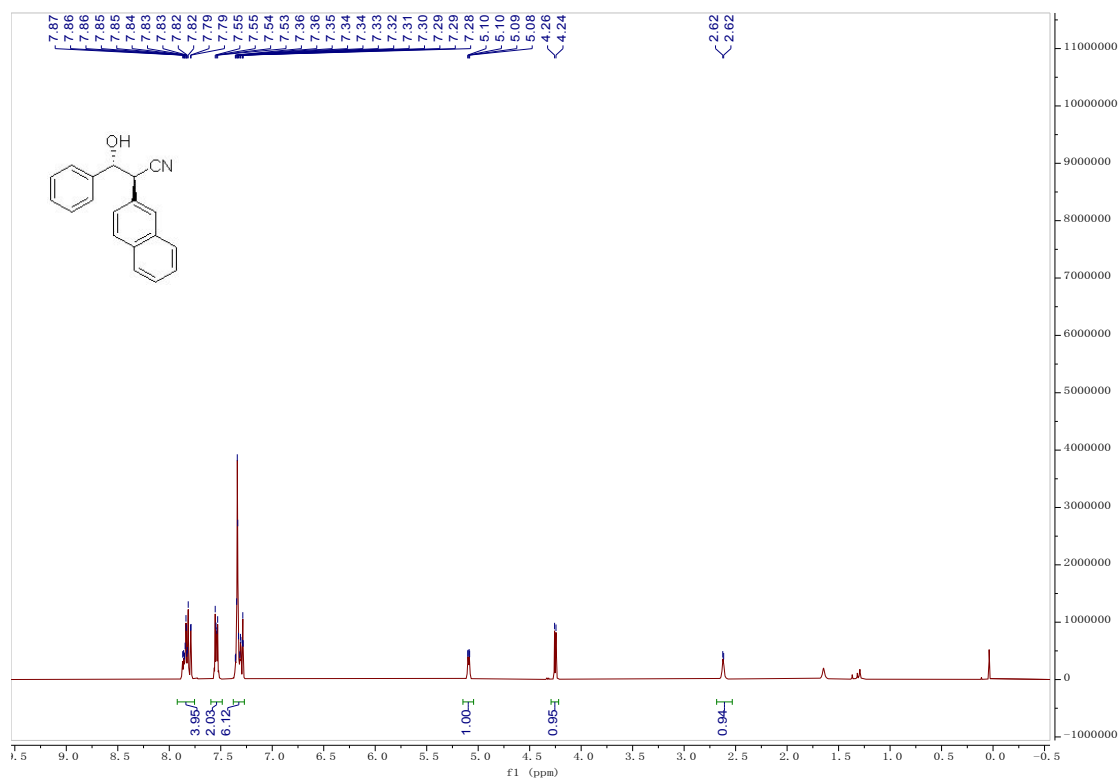
¹H NMR of 2f (600 MHz, Chloroform-*d*)



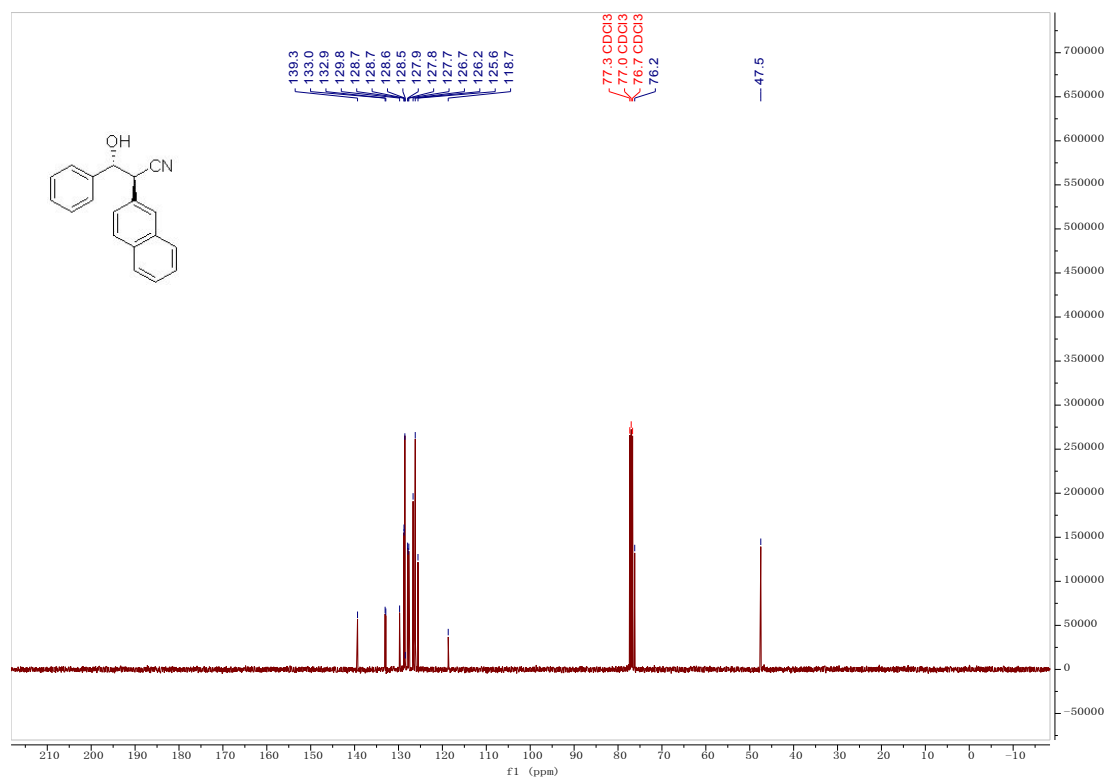
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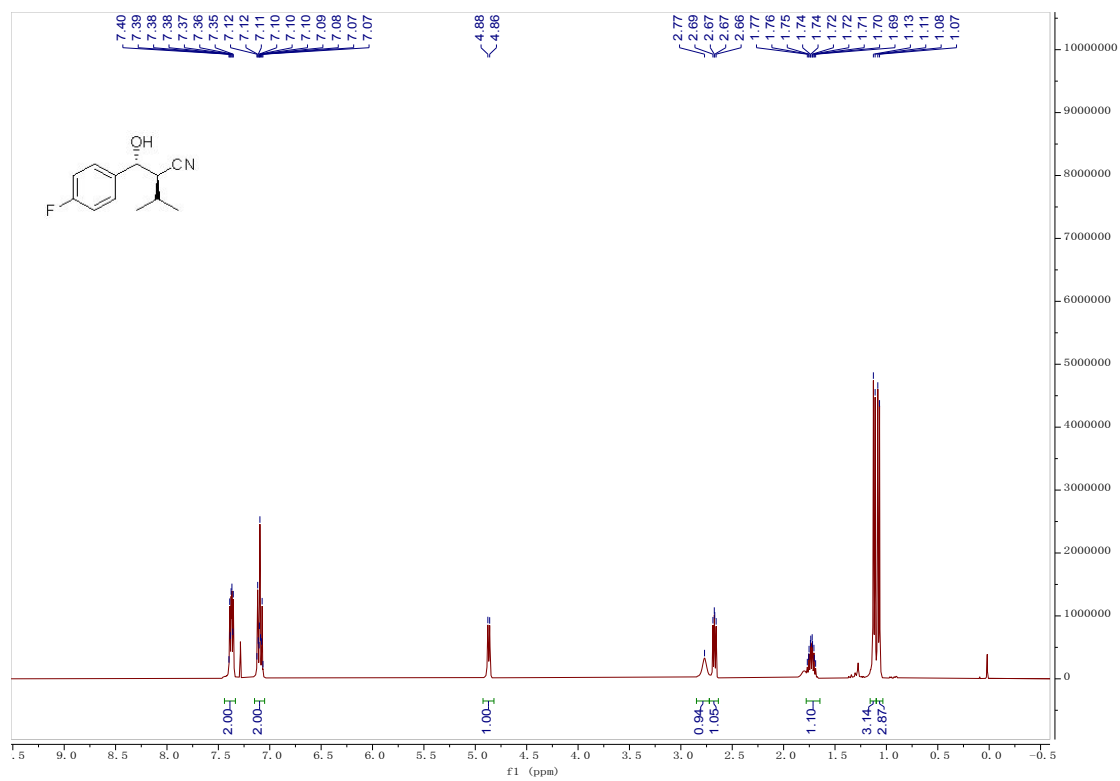
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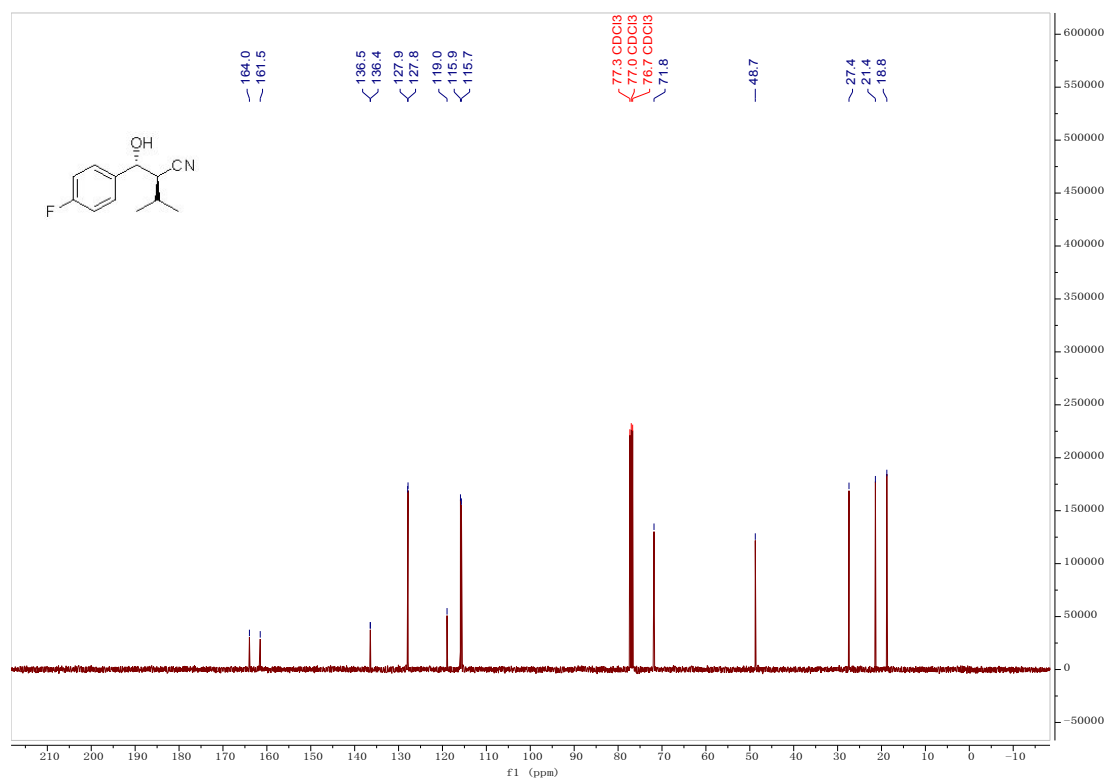
¹³C NMR of 2g (101 MHz, Chloroform-d)



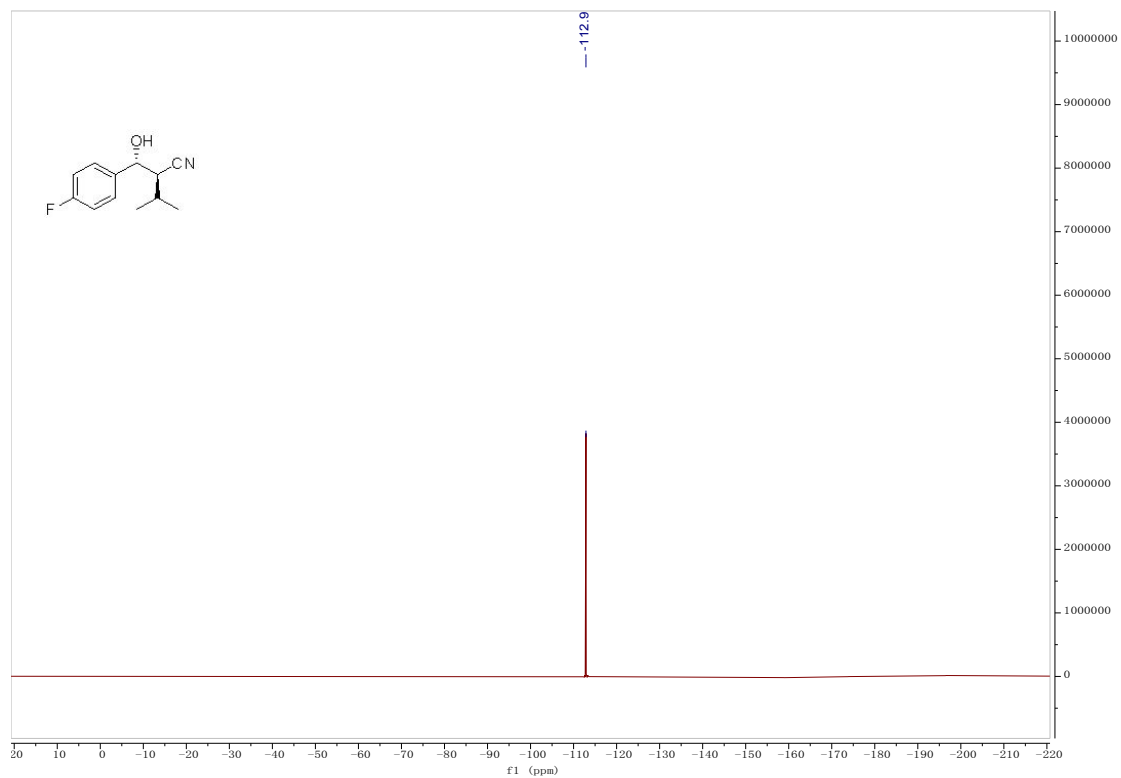
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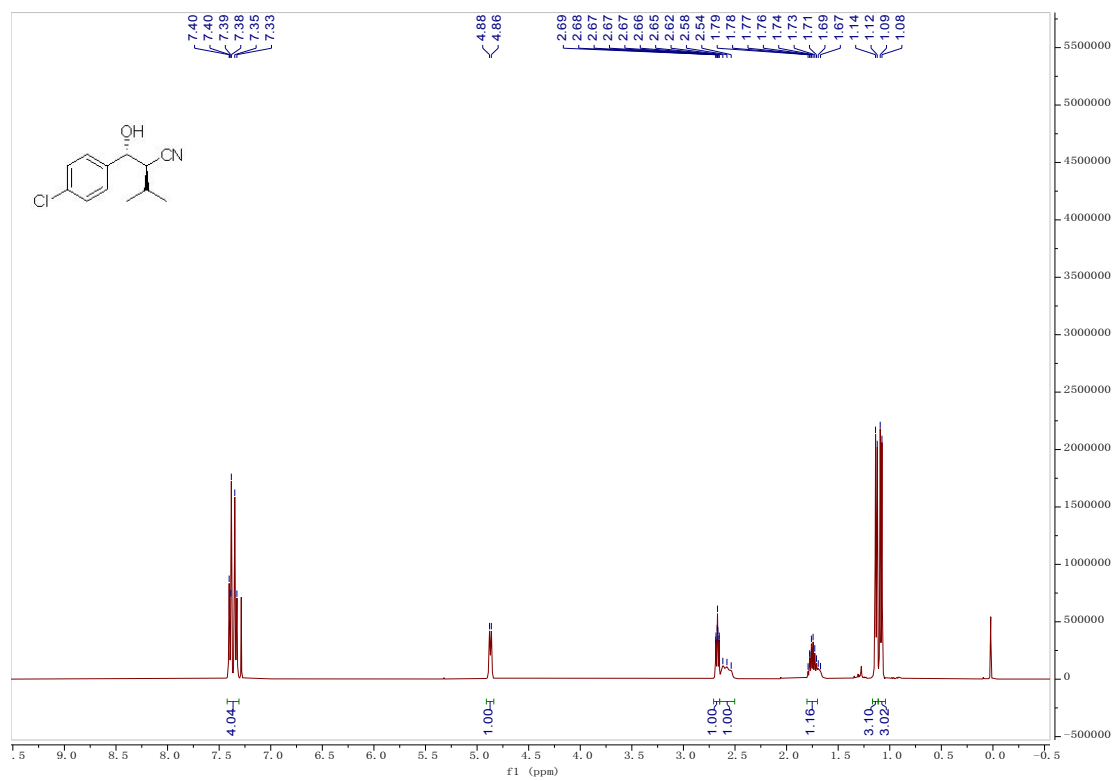
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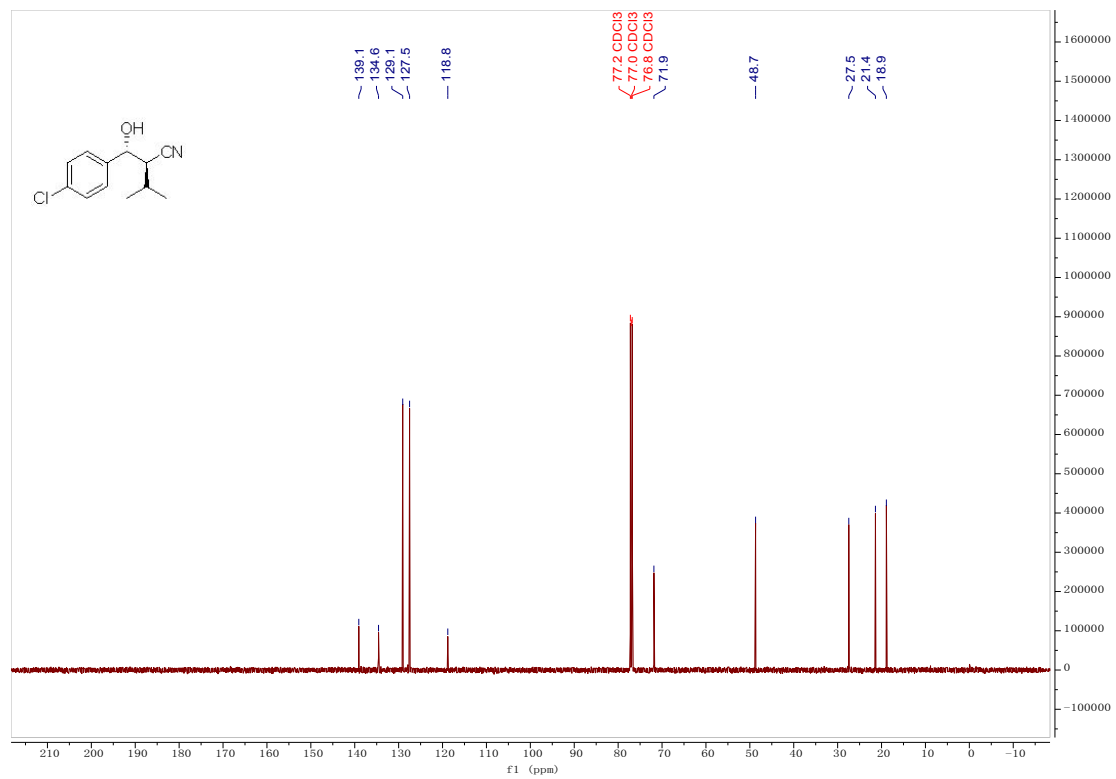
¹⁹F NMR of 2h (376 MHz, Chloroform-*d*)



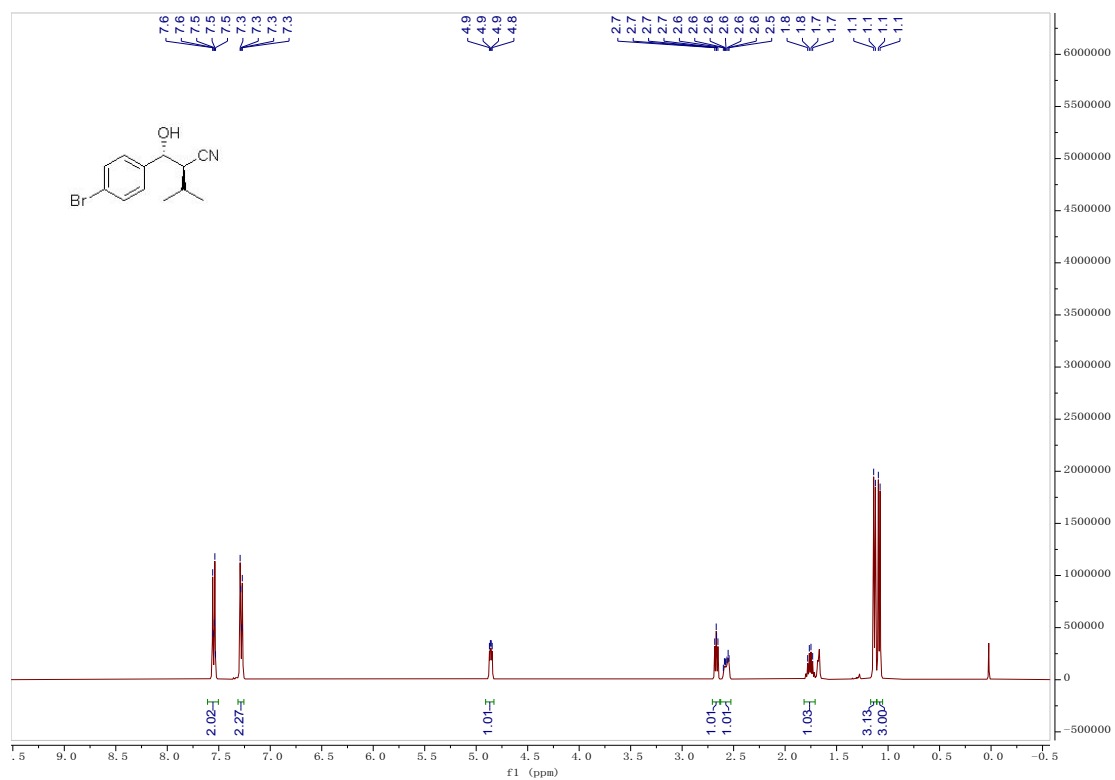
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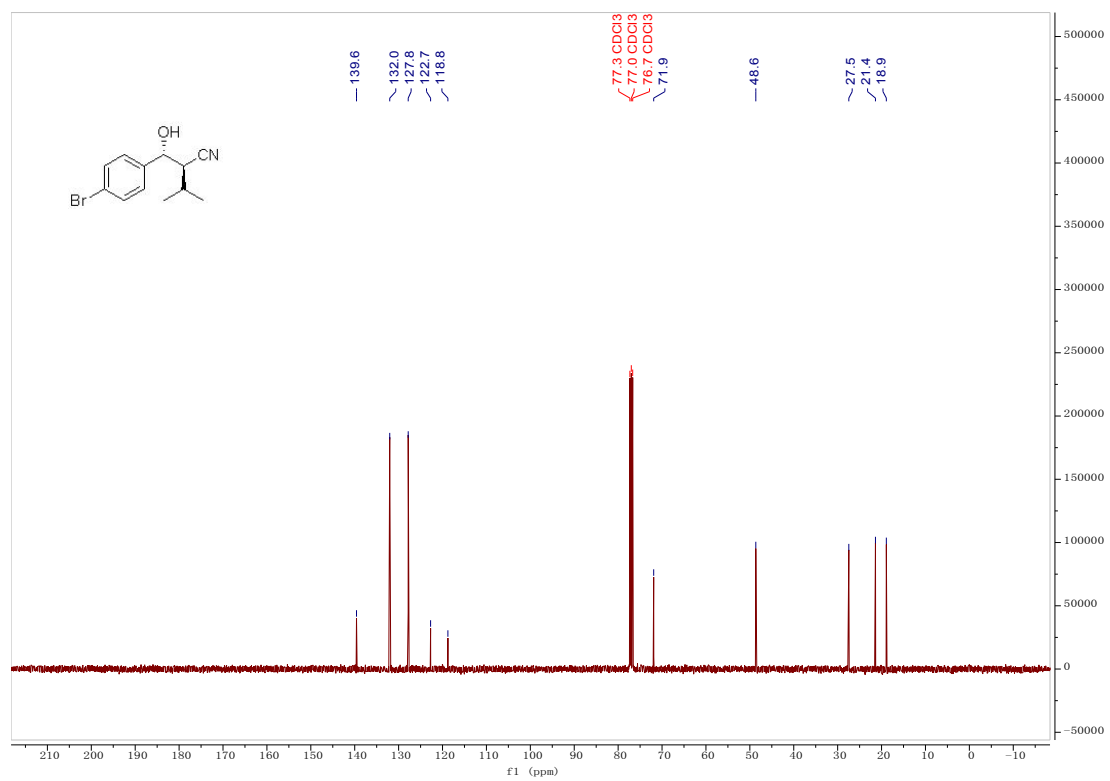
¹³C NMR of 2i (151 MHz, Chloroform-*d*)



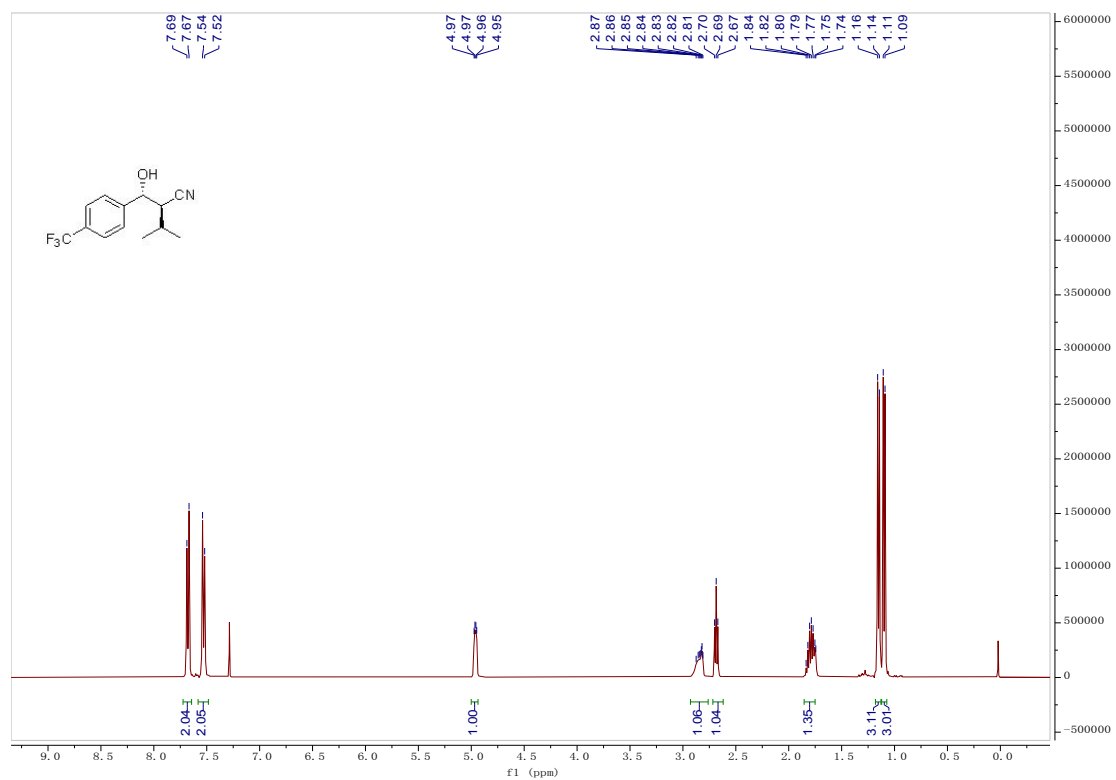
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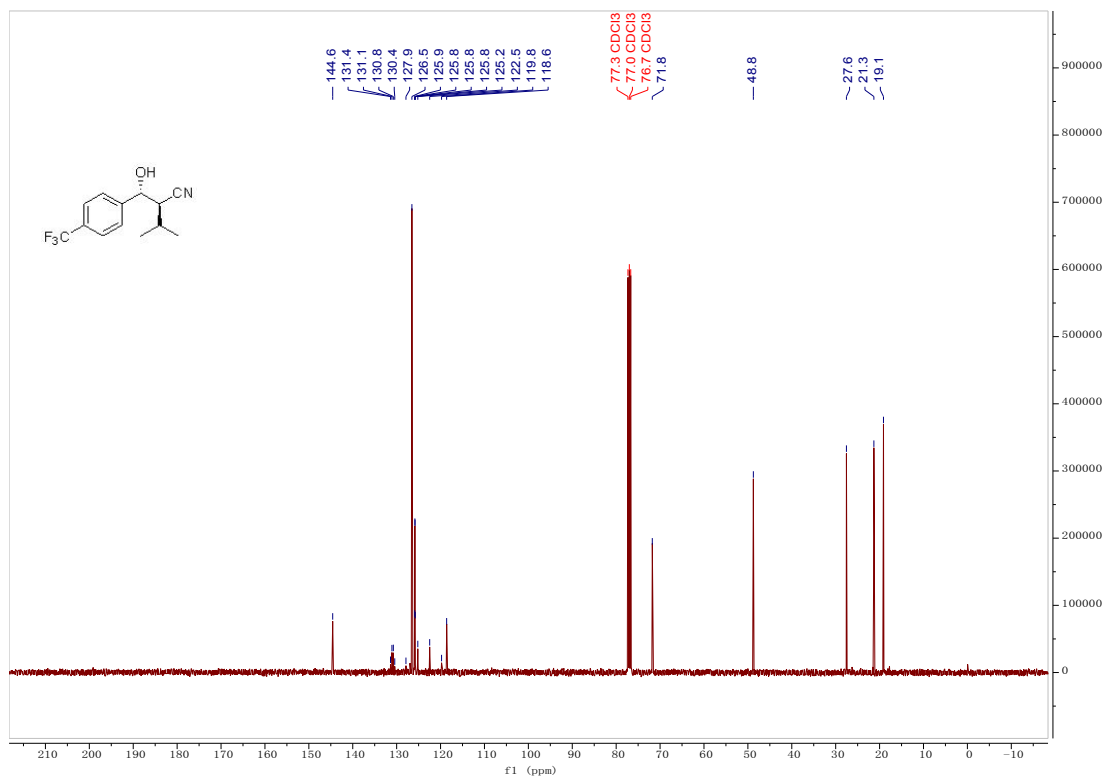
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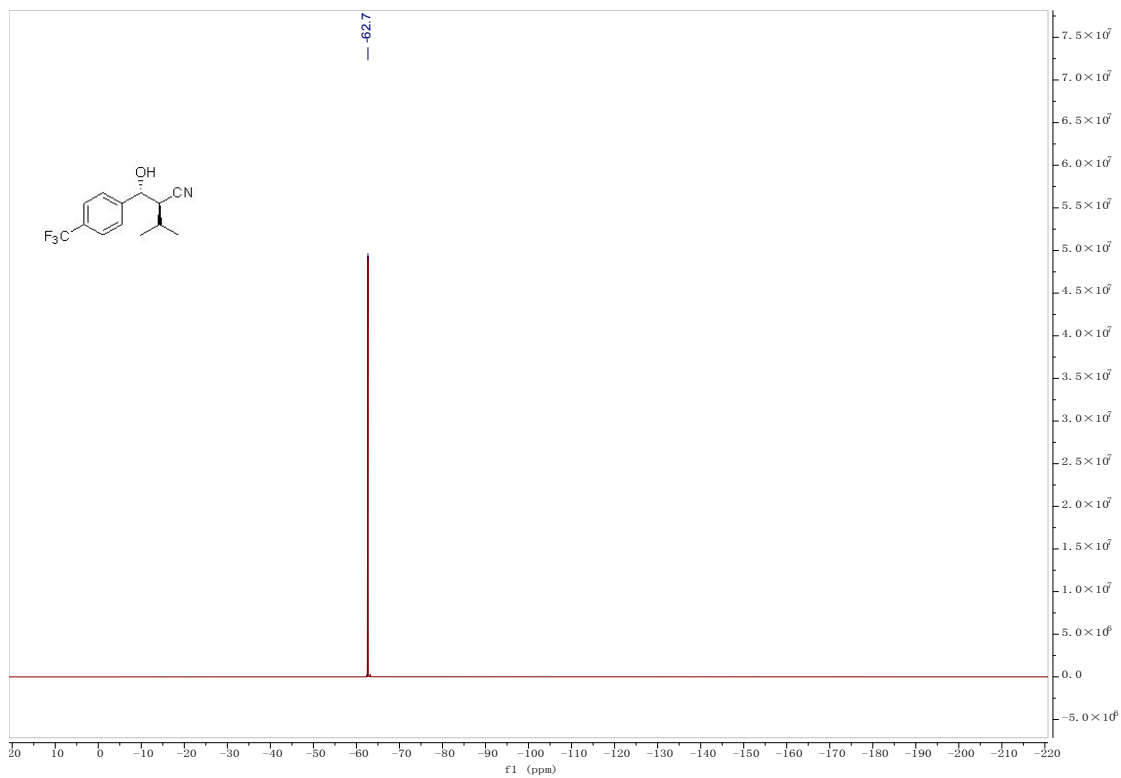
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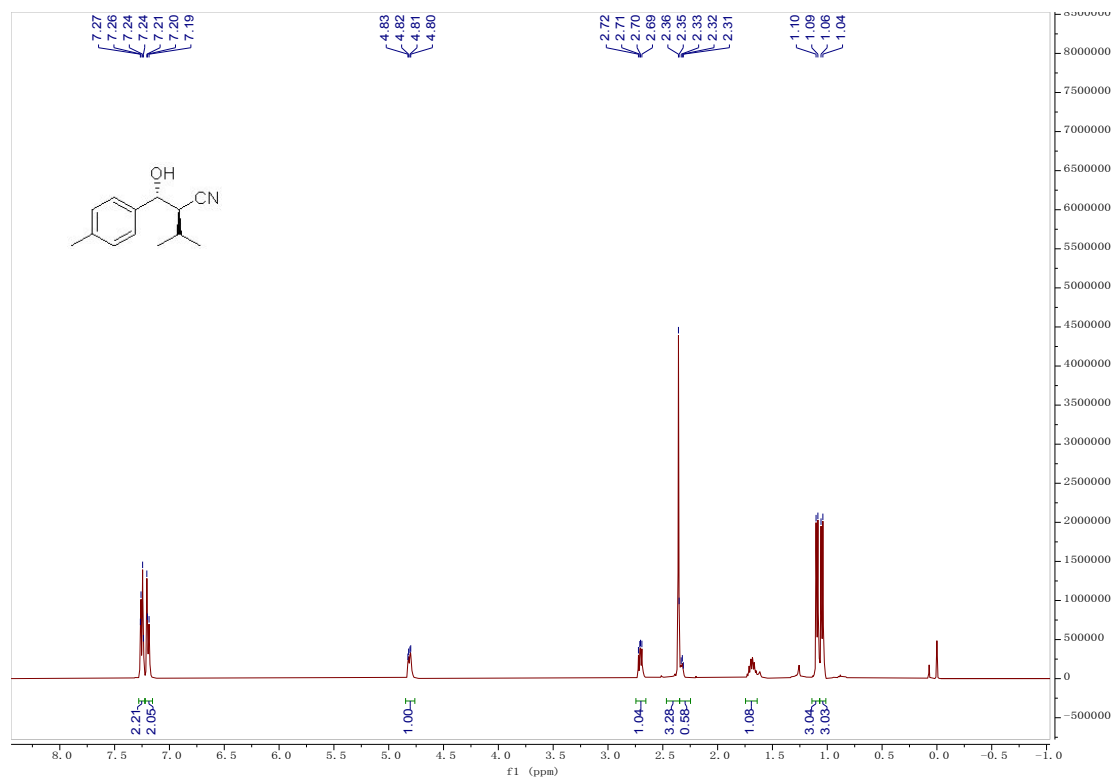
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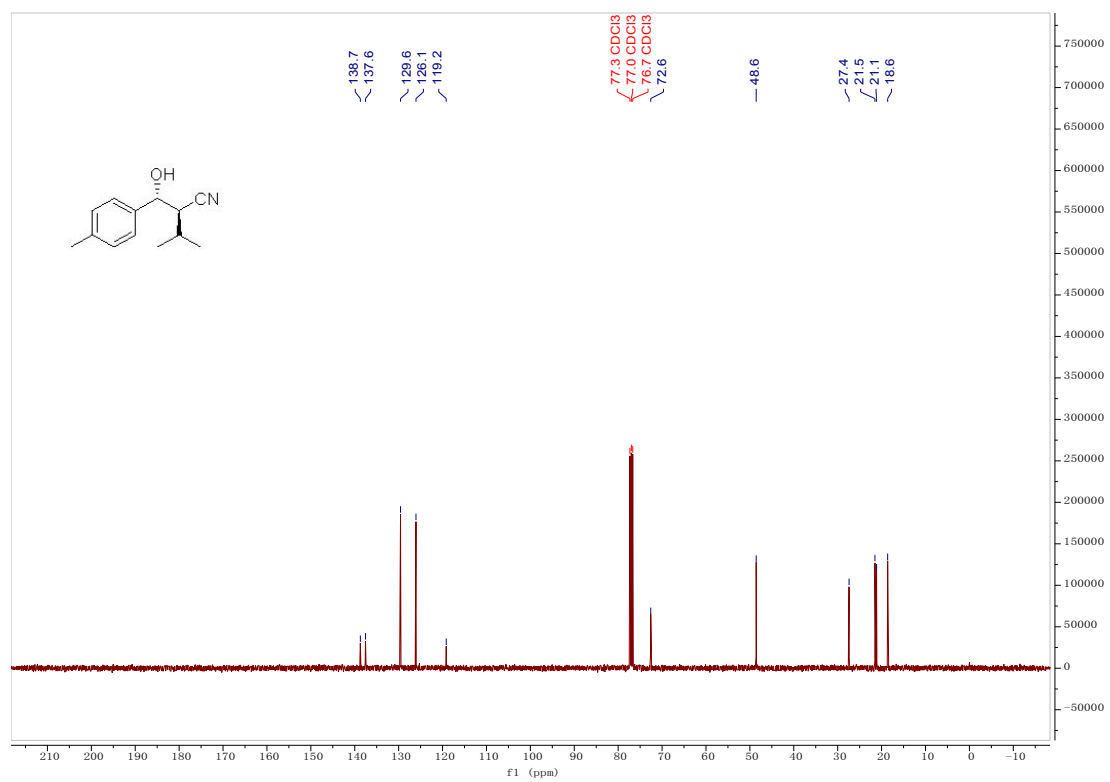
¹⁹F NMR of 2k (376 MHz, Chloroform-*d*)



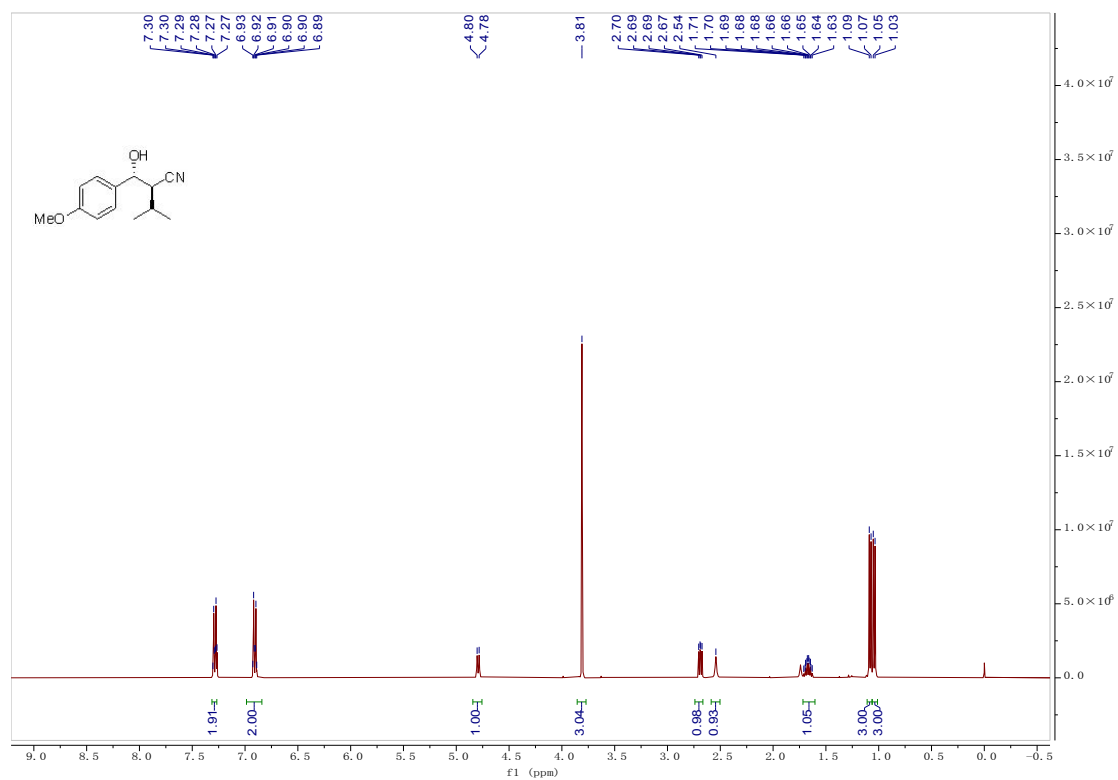
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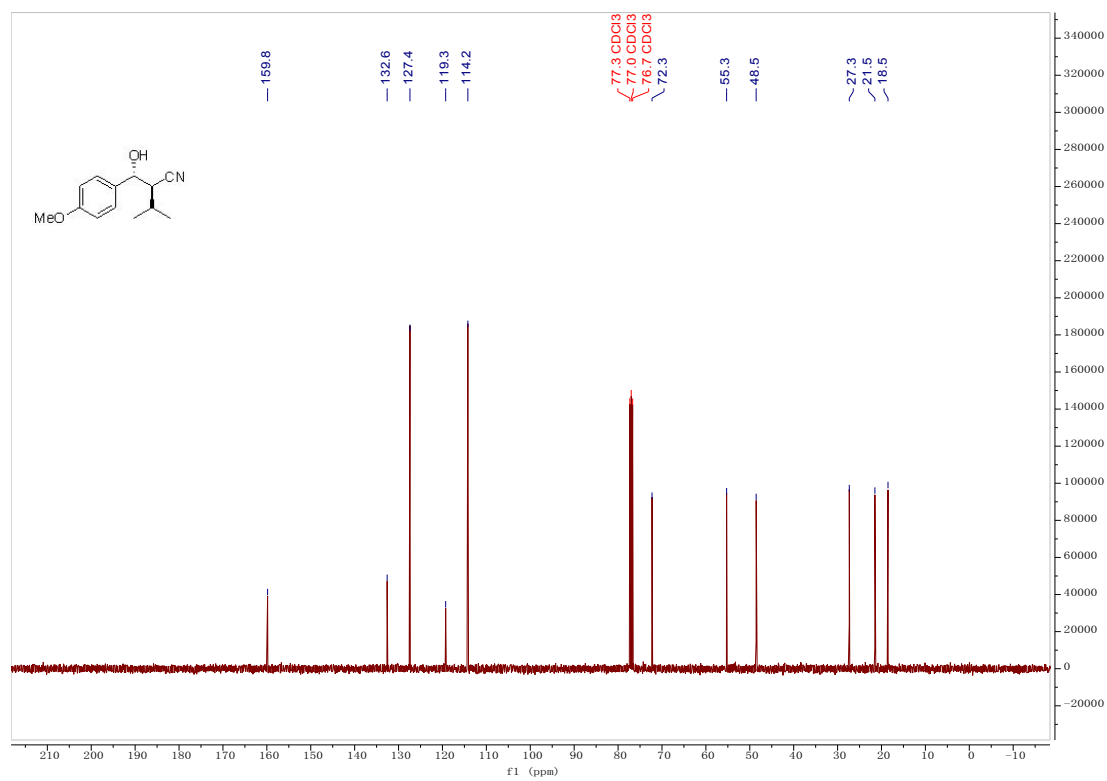
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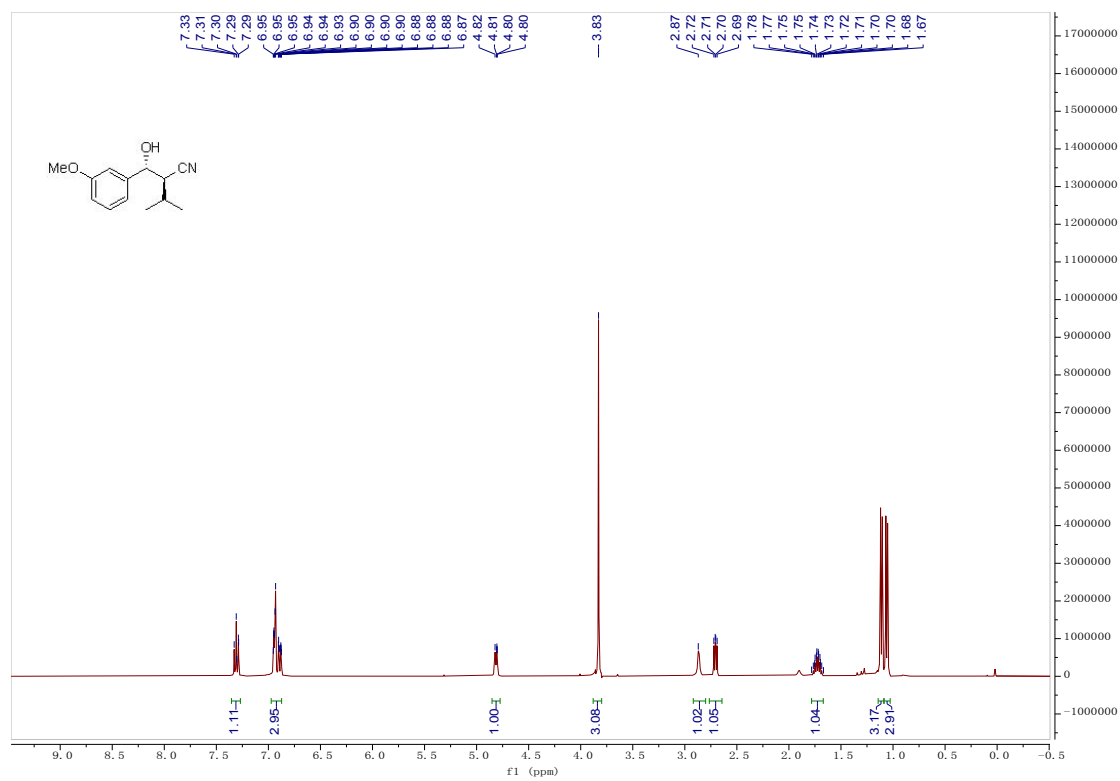
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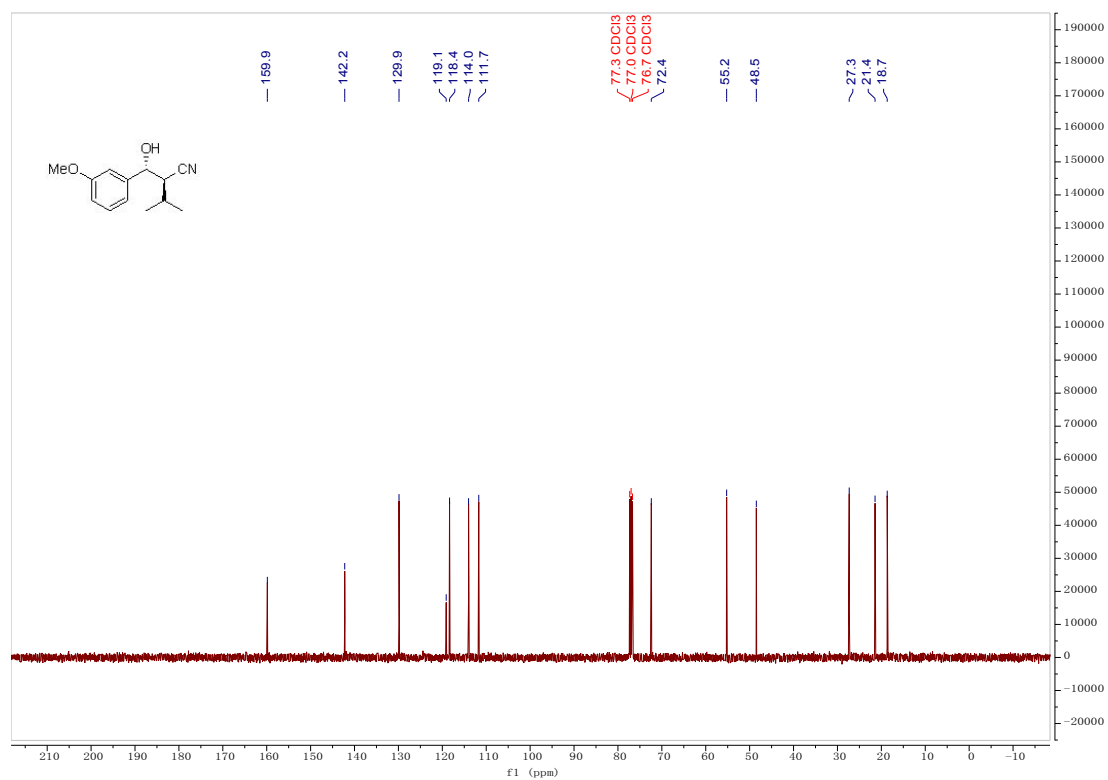
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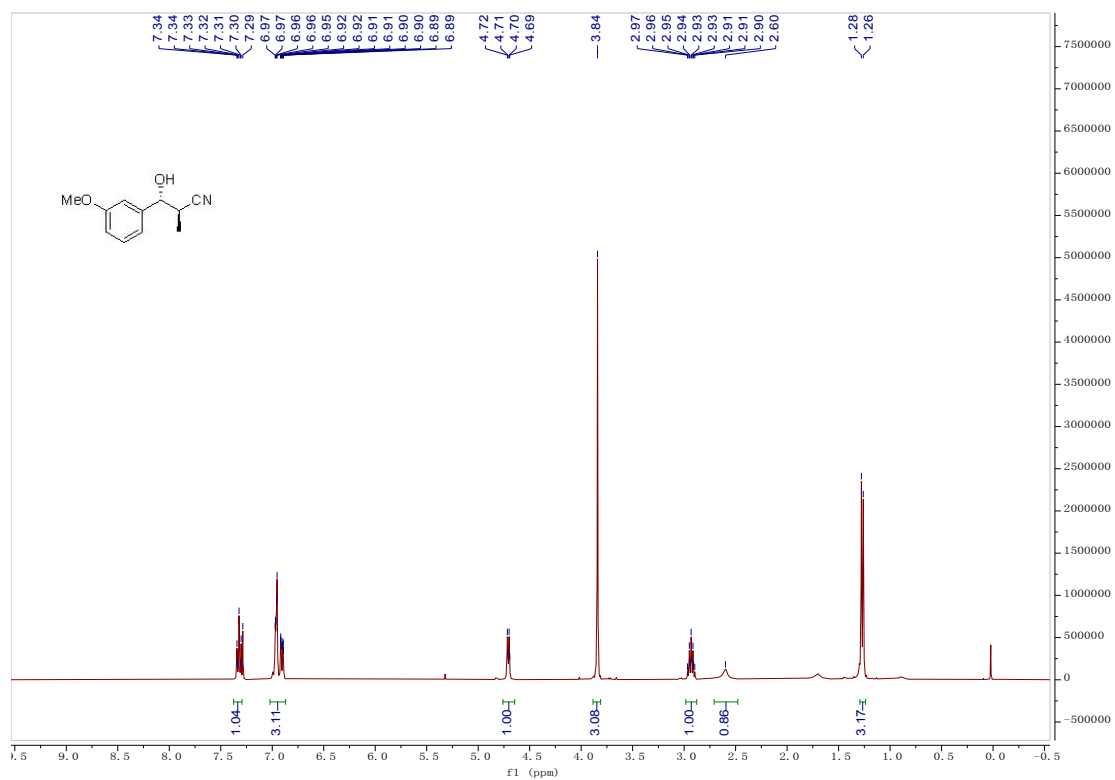
¹H NMR of 2n (400 MHz, Chloroform-*d*)



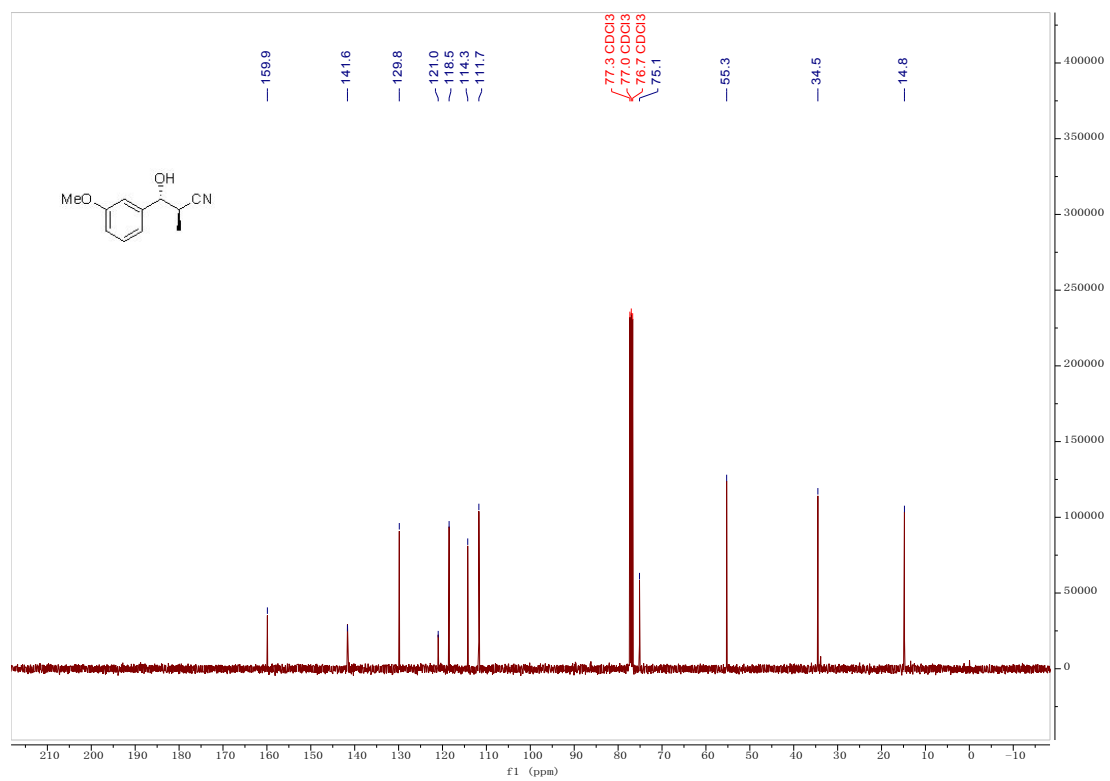
¹H NMR of 2n (101 MHz, Chloroform-*d*)



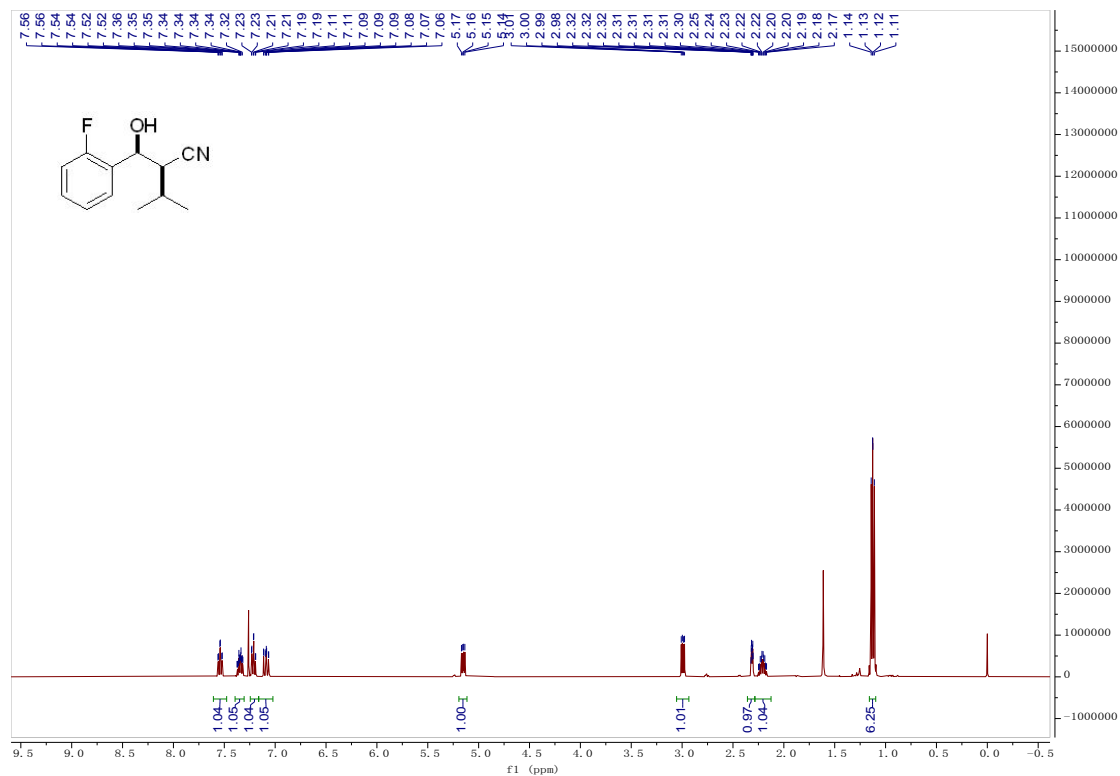
¹H NMR of 2o (400 MHz, Chloroform-*d*)



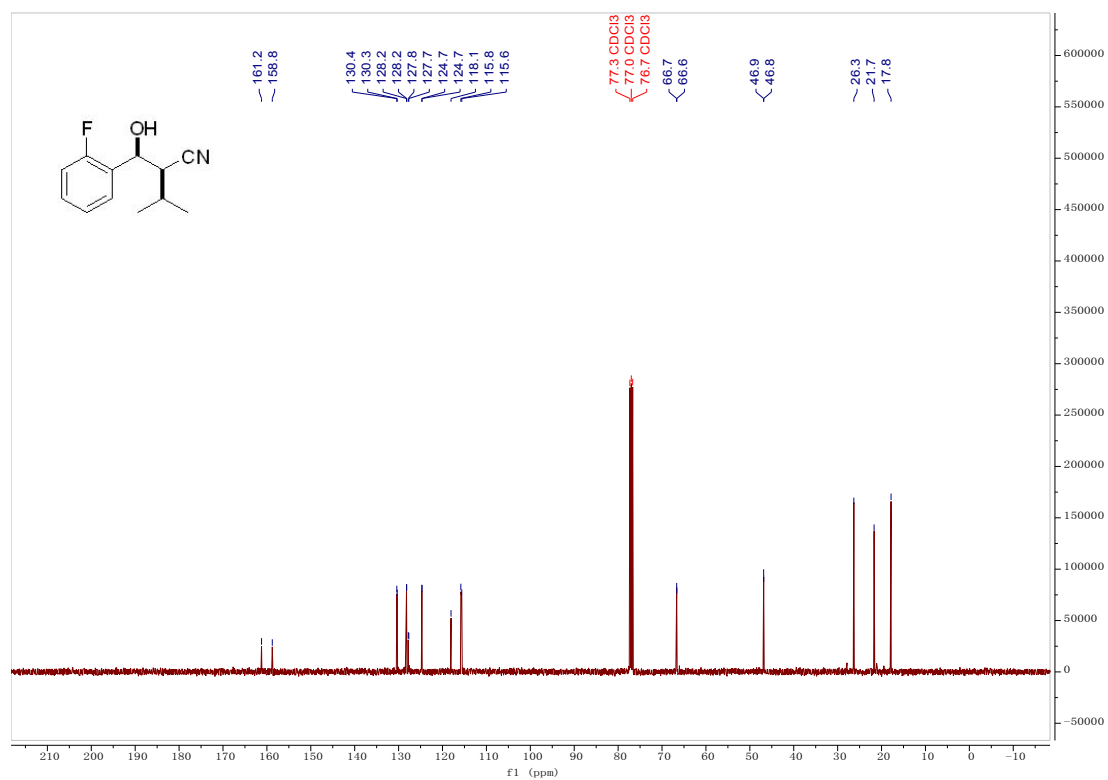
¹³C NMR of 2o (101 MHz, Chloroform-d)



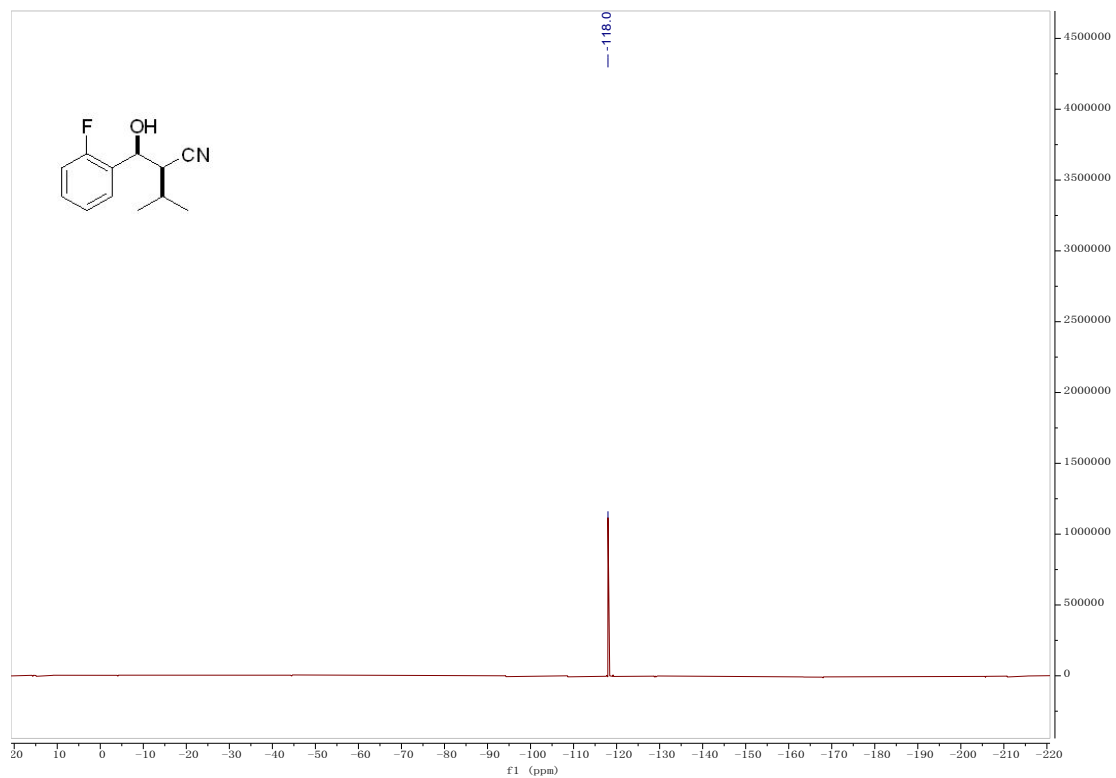
¹H NMR of 2p (400 MHz, Chloroform-*d*)



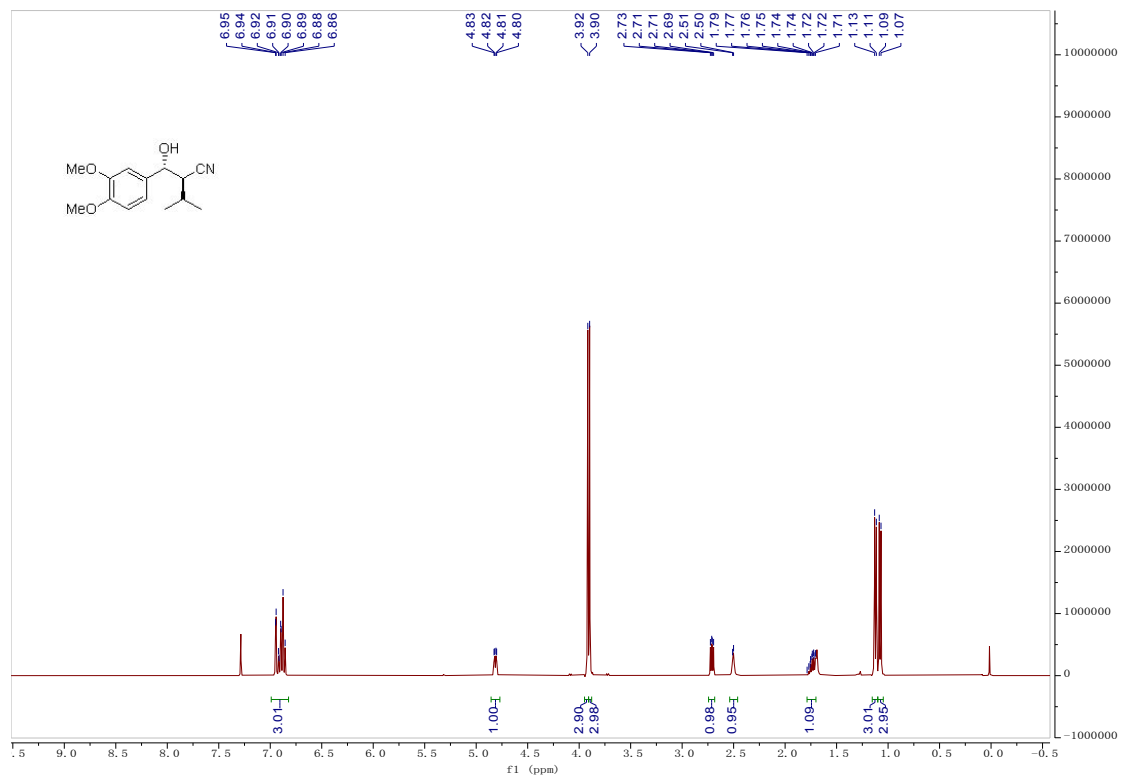
¹³C NMR of 2p (101 MHz, Chloroform-*d*)



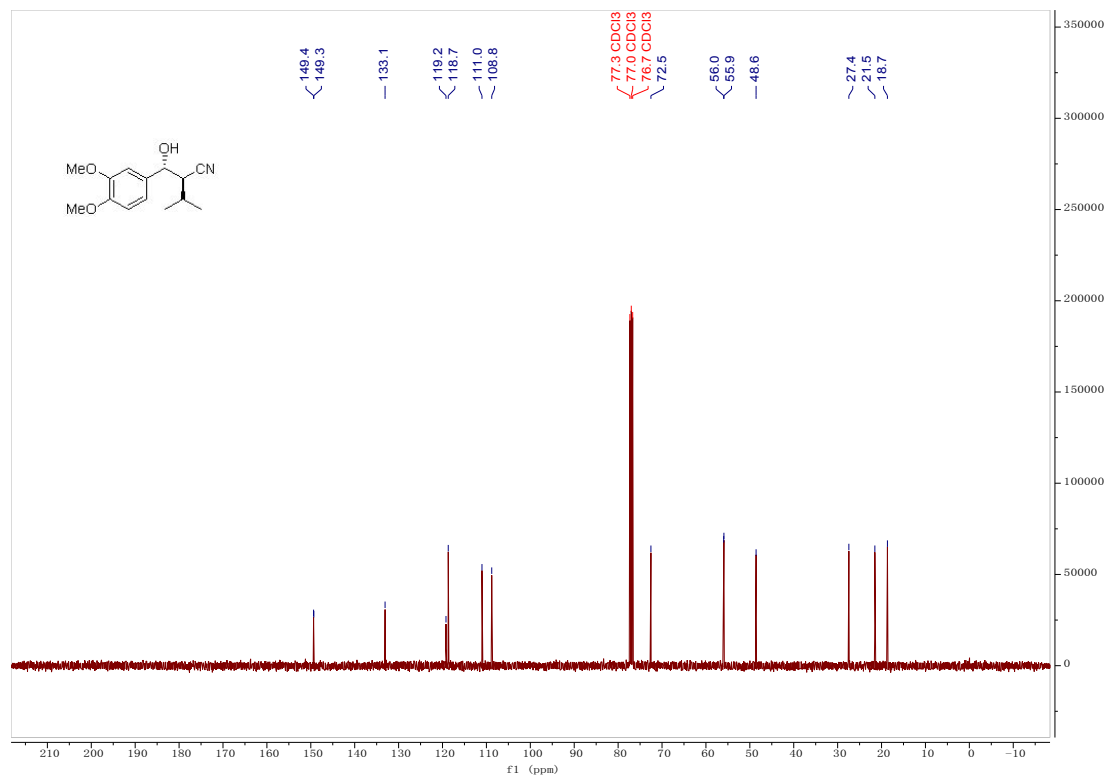
¹⁹F NMR of 2p (376 MHz, Chloroform-*d*)



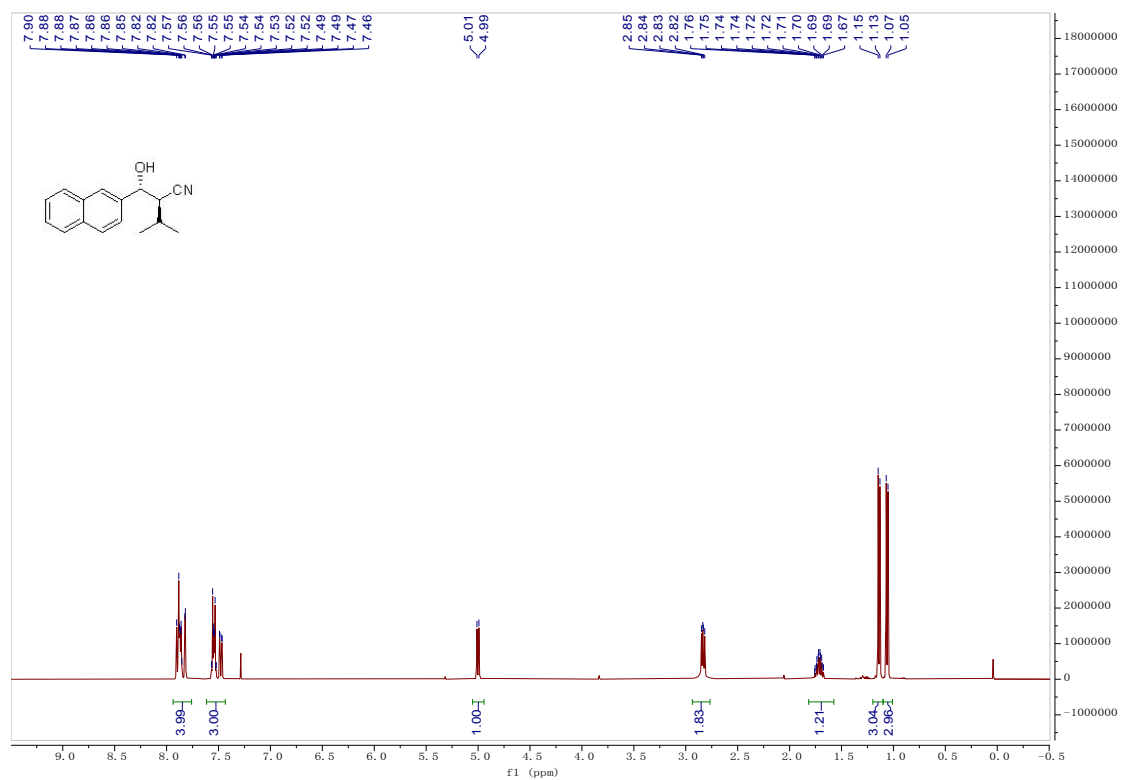
¹H NMR of 2q (400 MHz, Chloroform-*d*)



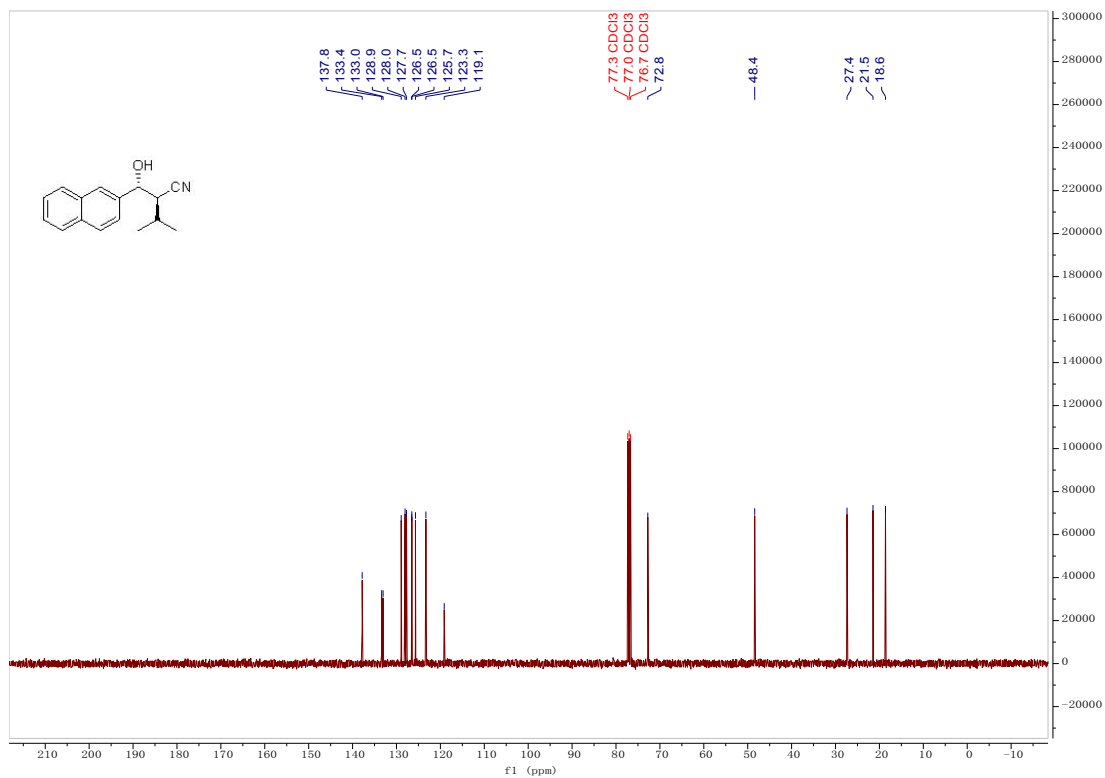
¹³C NMR of 2q (101 MHz, Chloroform-*d*)



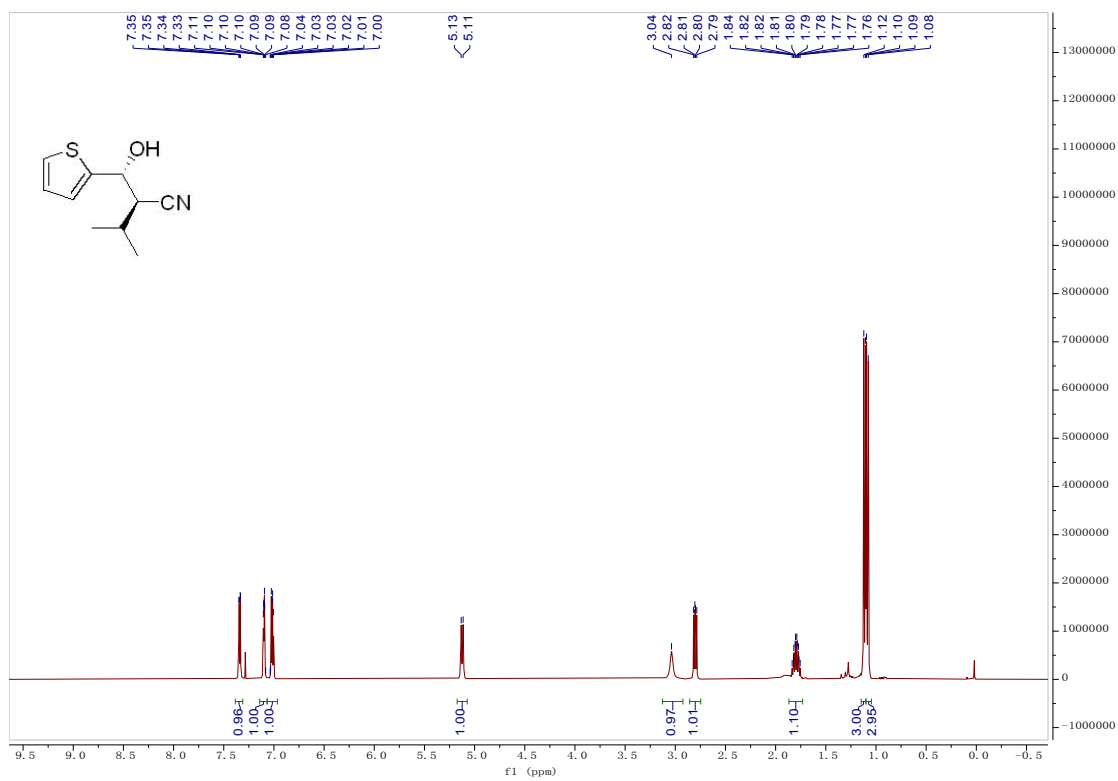
¹H NMR of 2r (400 MHz, Chloroform-*d*)



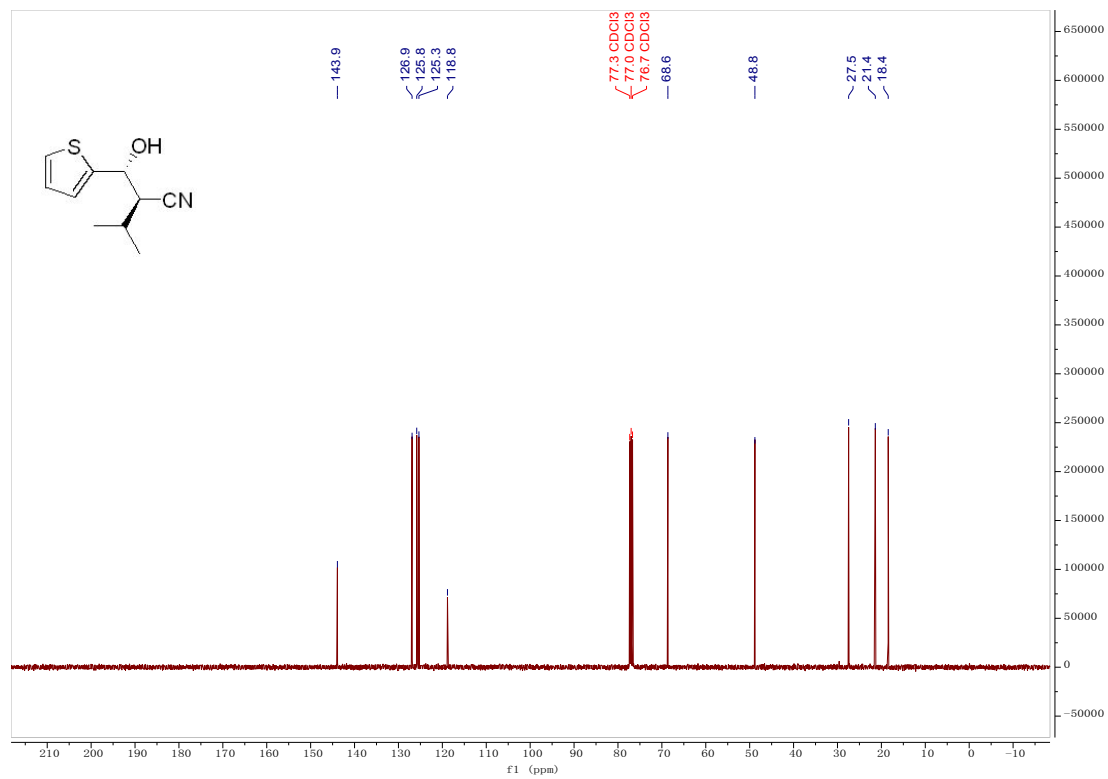
¹³C NMR of 2r (101 MHz, Chloroform-*d*)



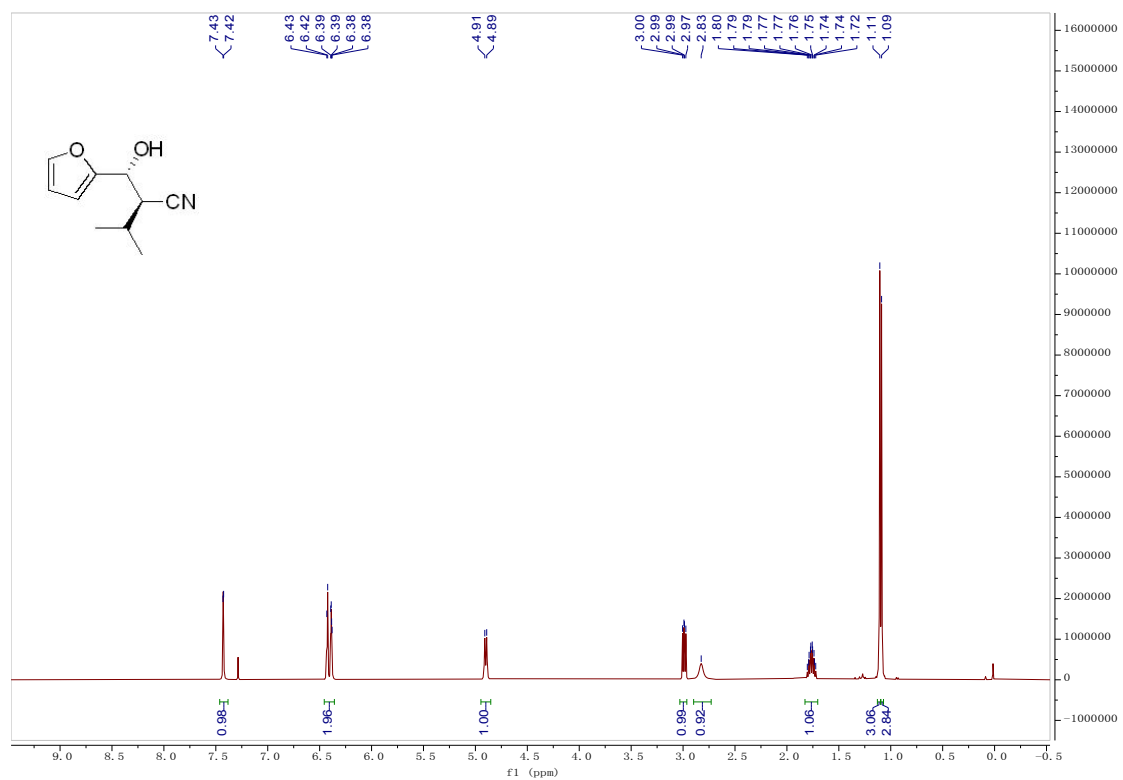
¹H NMR of 2s (400 MHz, Chloroform-d)



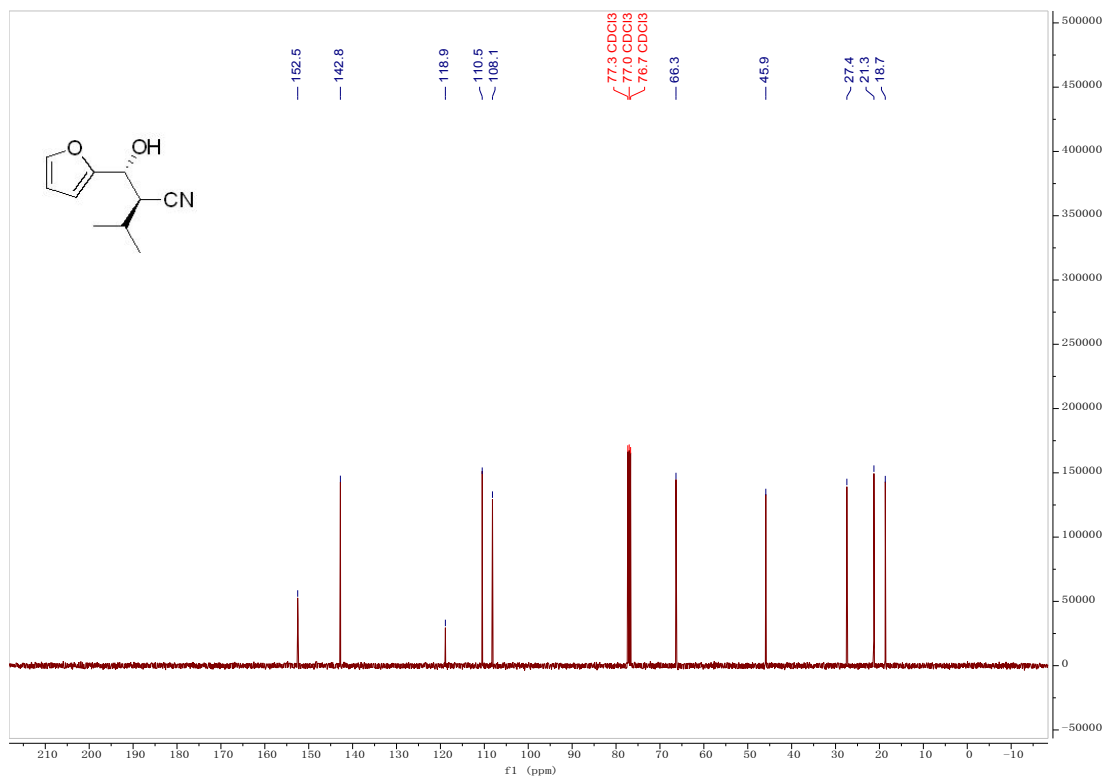
¹³C NMR of 2s (101 MHz, Chloroform-*d*)



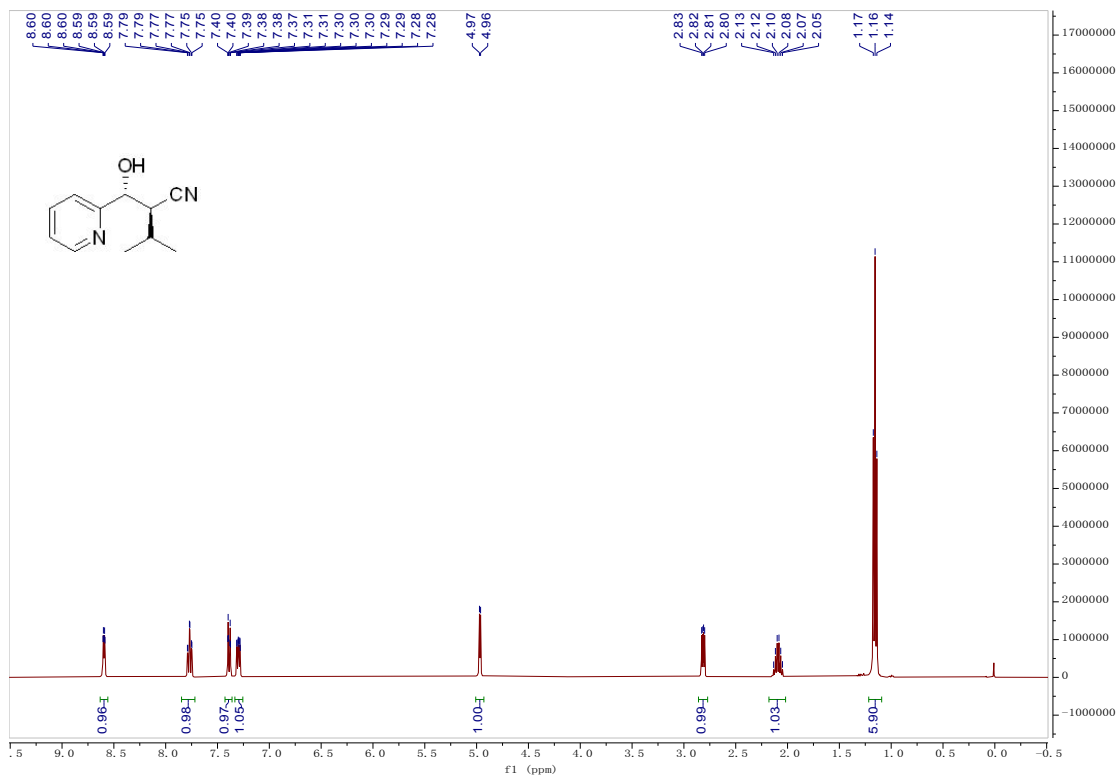
¹H NMR of 2t (400 MHz, Chloroform-*d*)



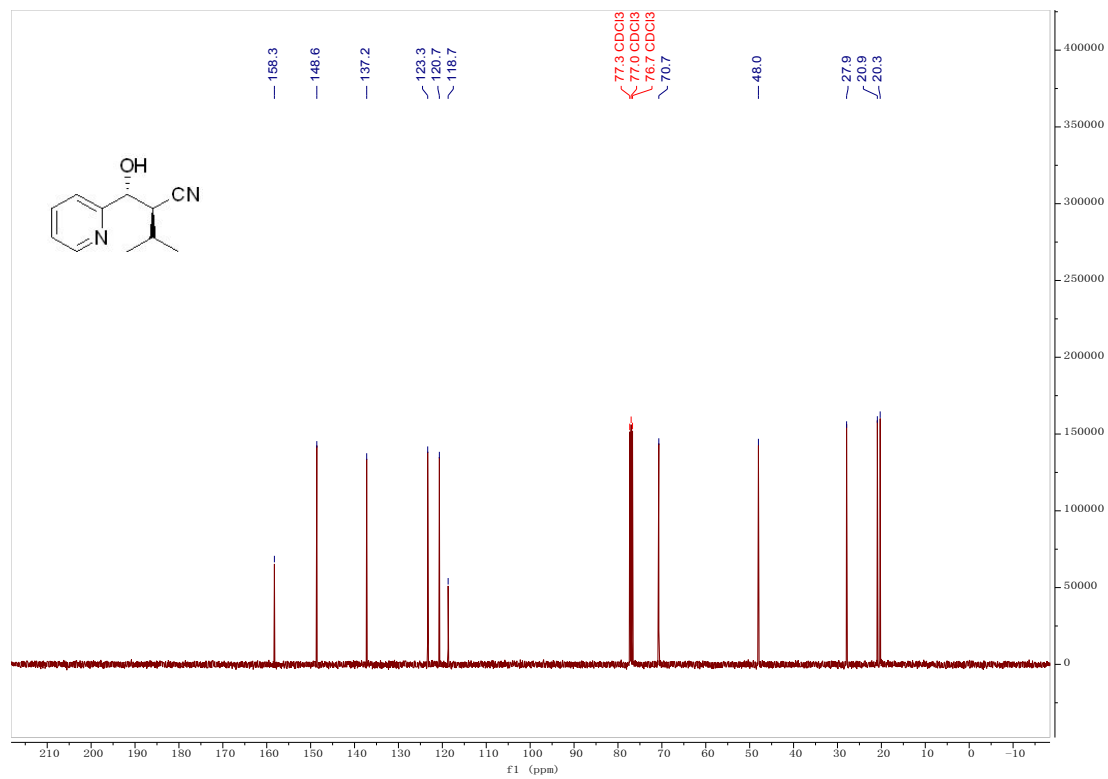
¹³C NMR of 2t (101 MHz, Chloroform-*d*)



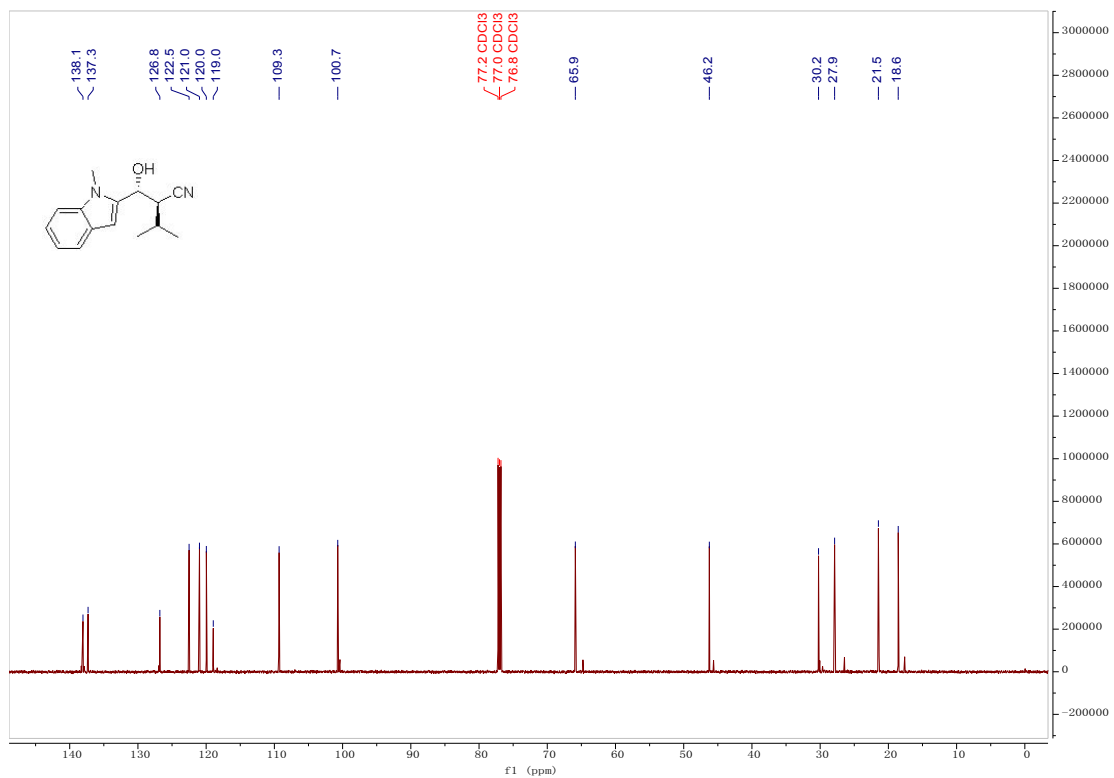
¹H NMR of 2u (400 MHz, Chloroform-*d*)



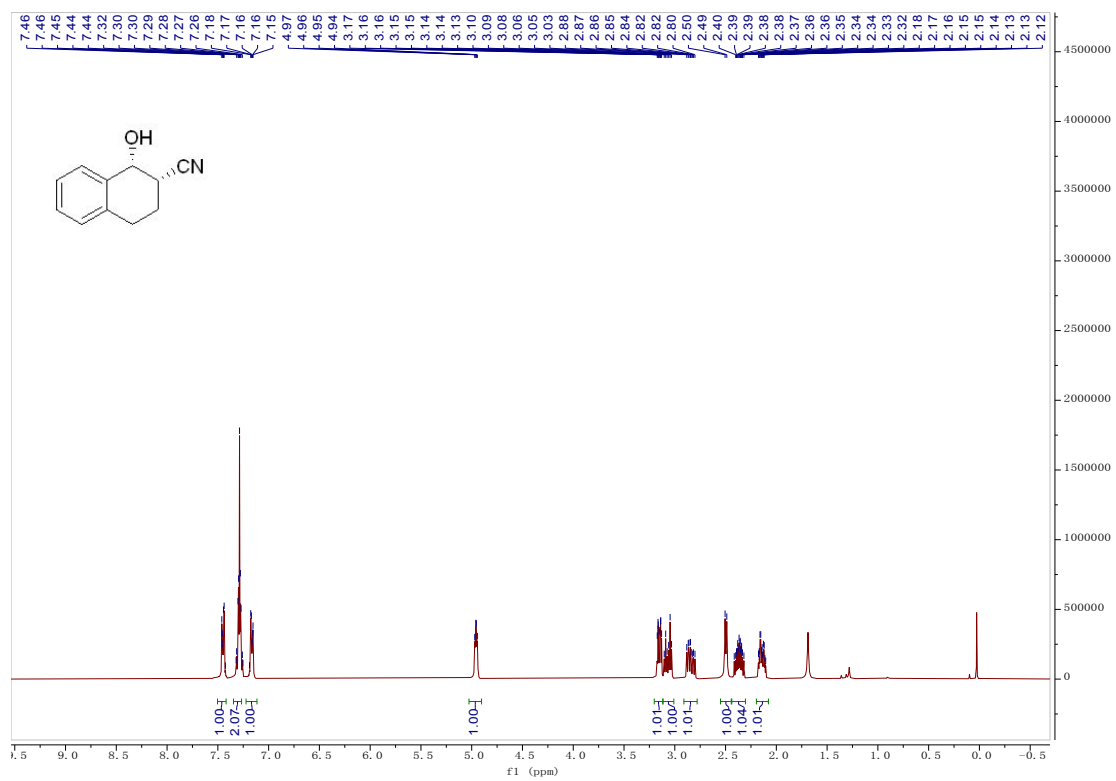
¹³C NMR of 2u (101 MHz, Chloroform-*d*)



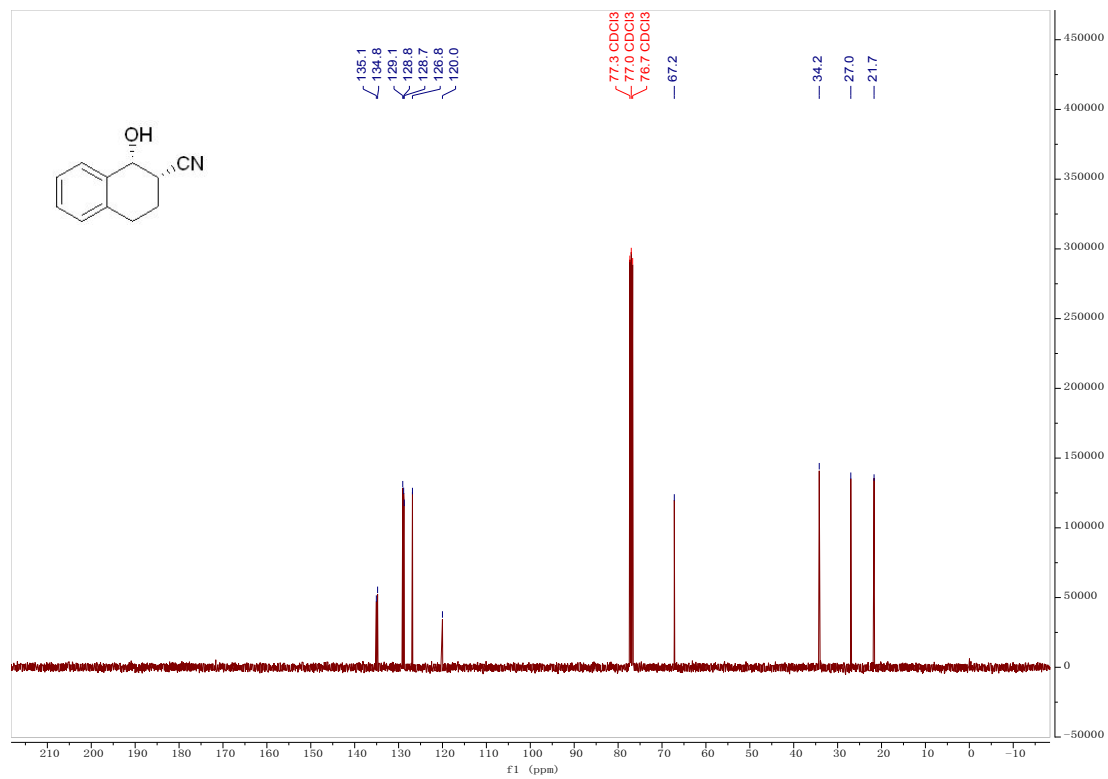
¹H NMR of 2v (400 MHz, Chloroform-*d*)



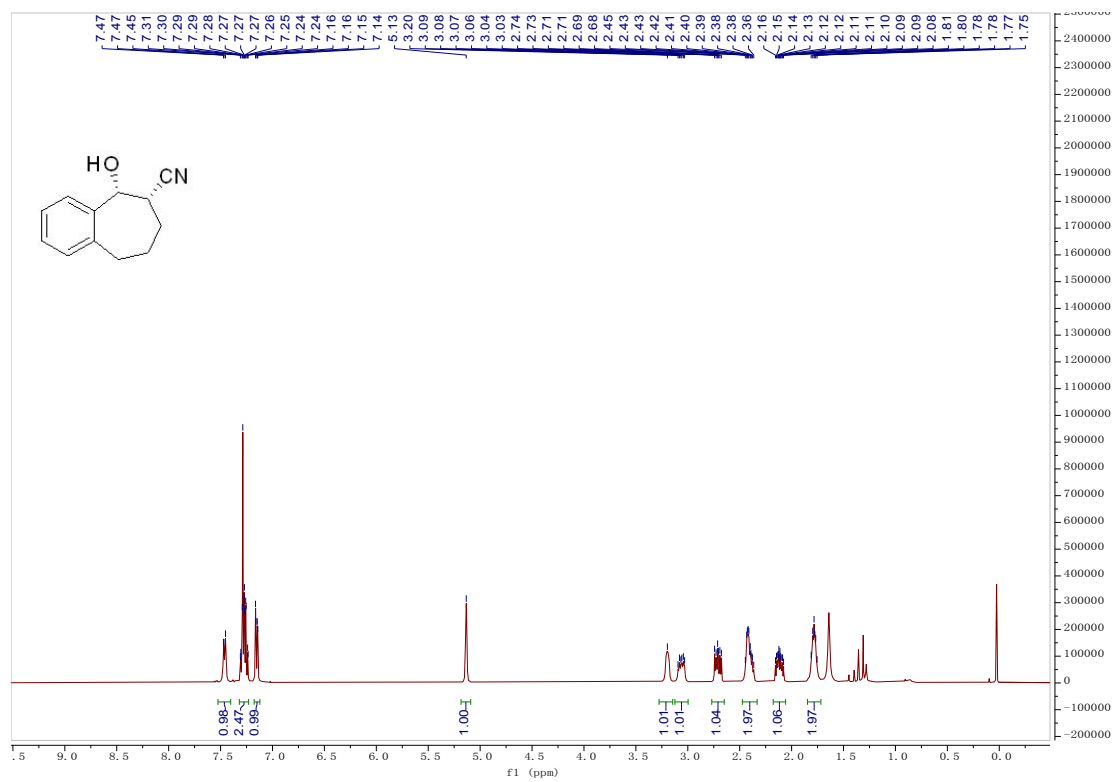
¹H NMR of 2w (400 MHz, Chloroform-*d*)



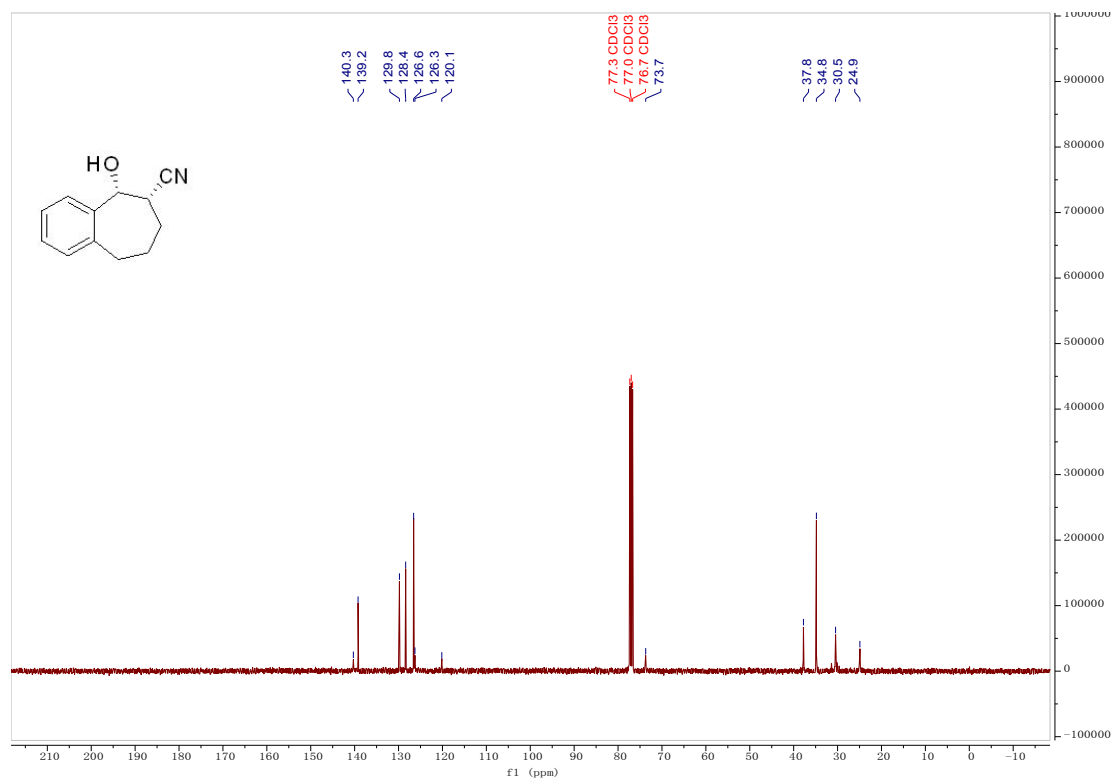
¹³C NMR of 2w (101 MHz, Chloroform-*d*)



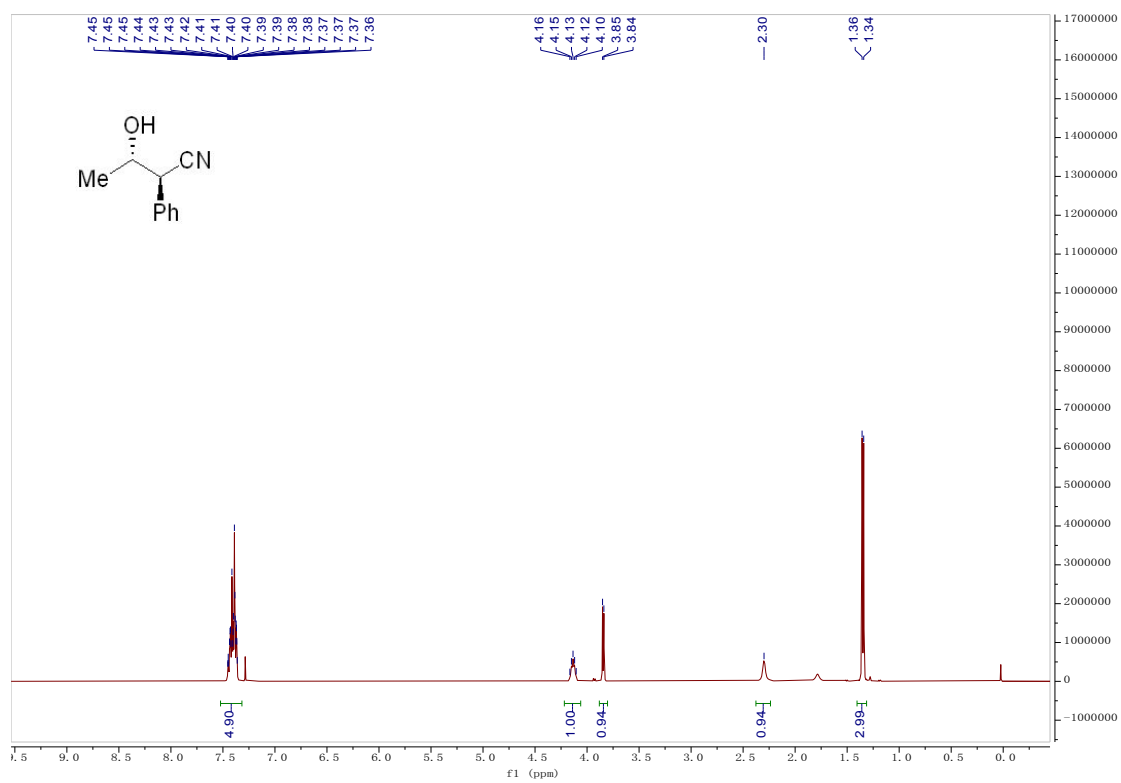
¹H NMR of 2x (400 MHz, Chloroform-*d*)



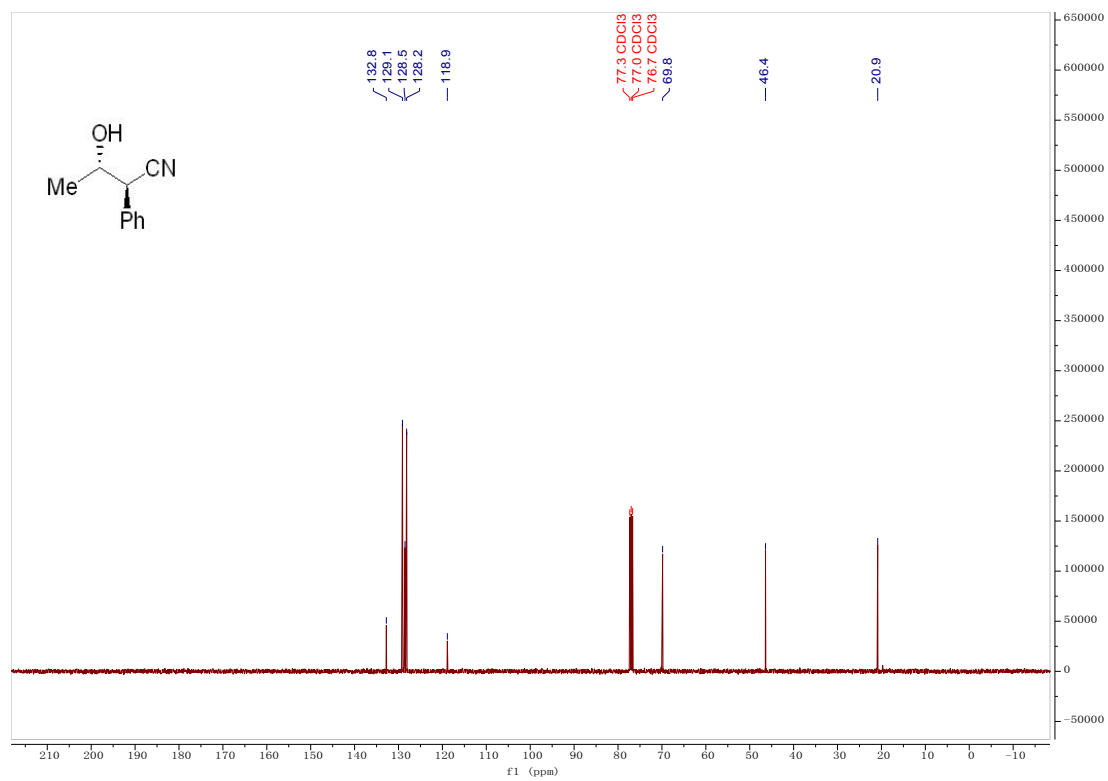
¹³C NMR of 2x (101 MHz, Chloroform-*d*)



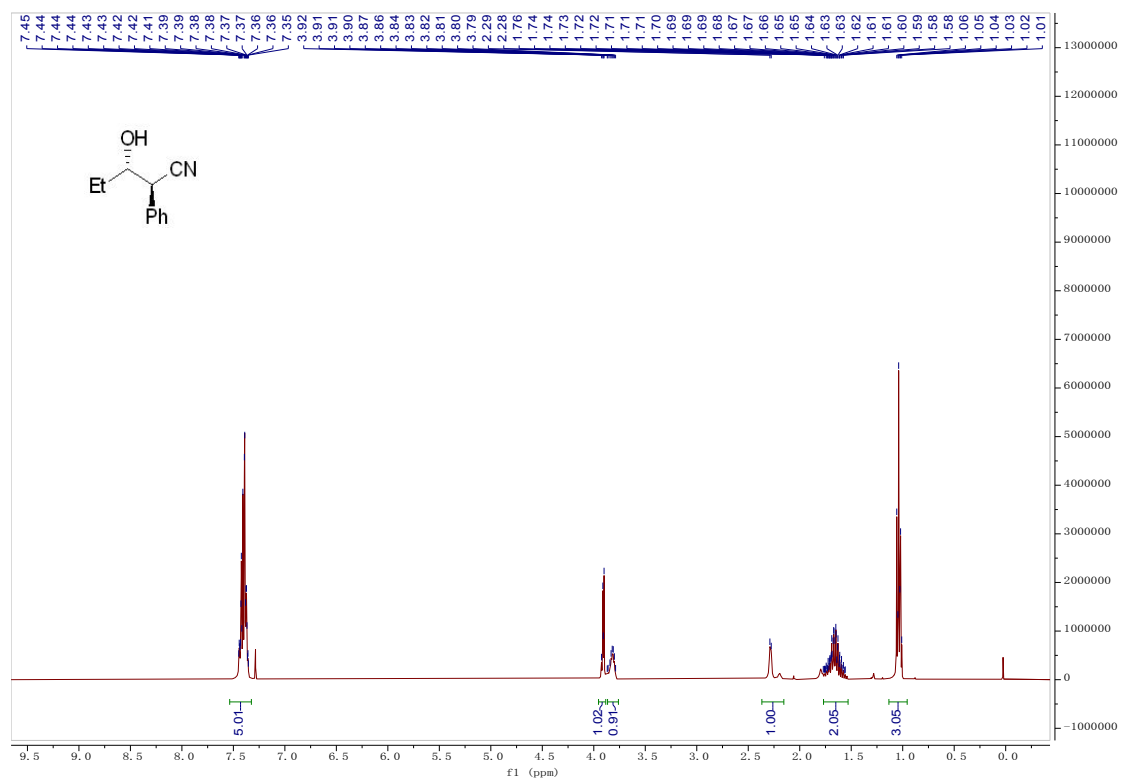
¹H NMR of 2y (400 MHz, Chloroform-d)



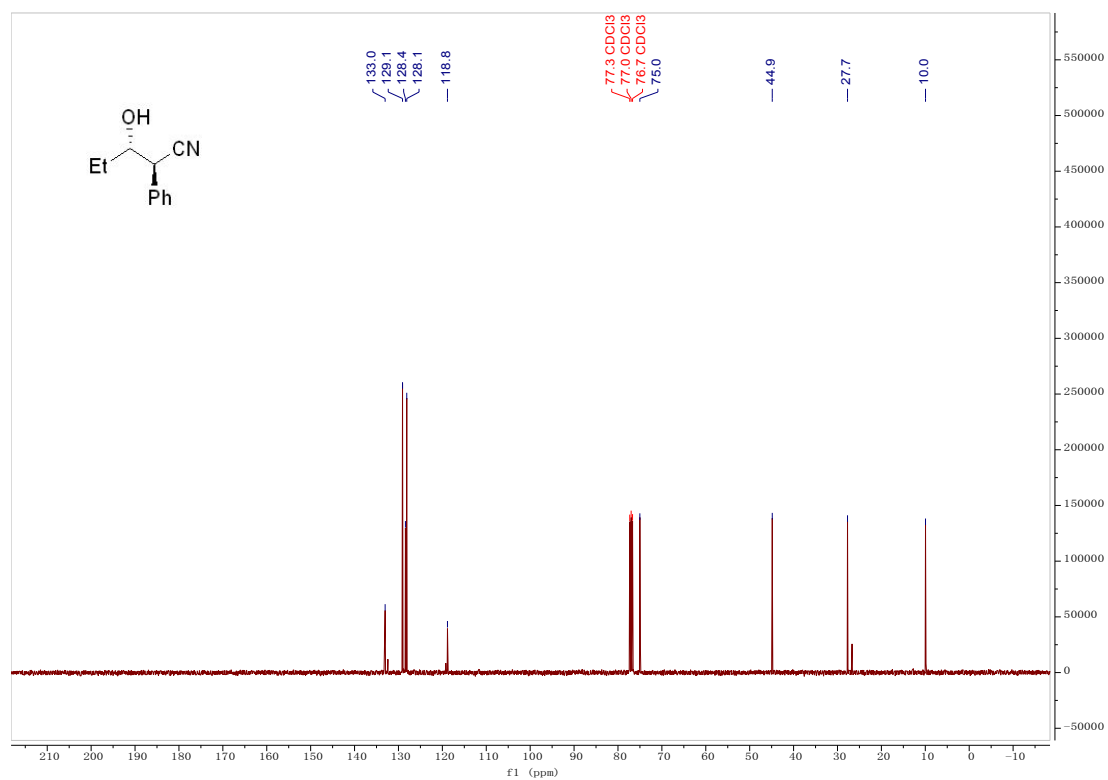
¹³C NMR of 2y (101 MHz, Chloroform-*d*)



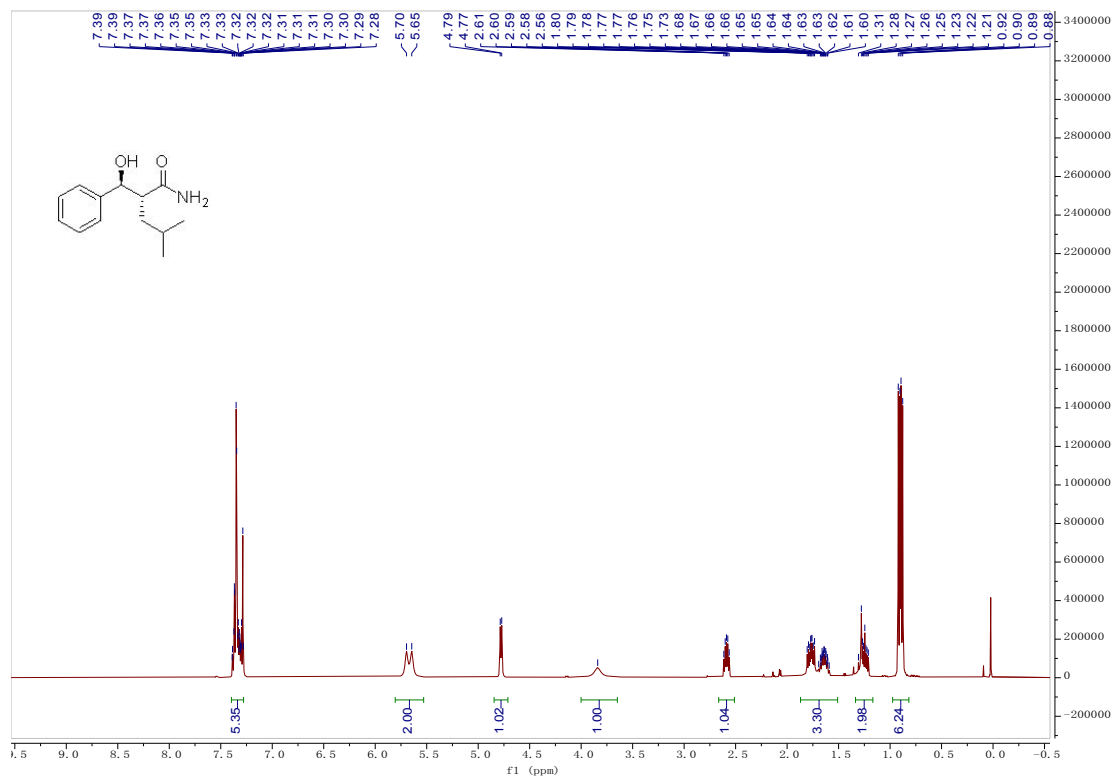
¹H NMR of 2z (400 MHz, Chloroform-*d*)



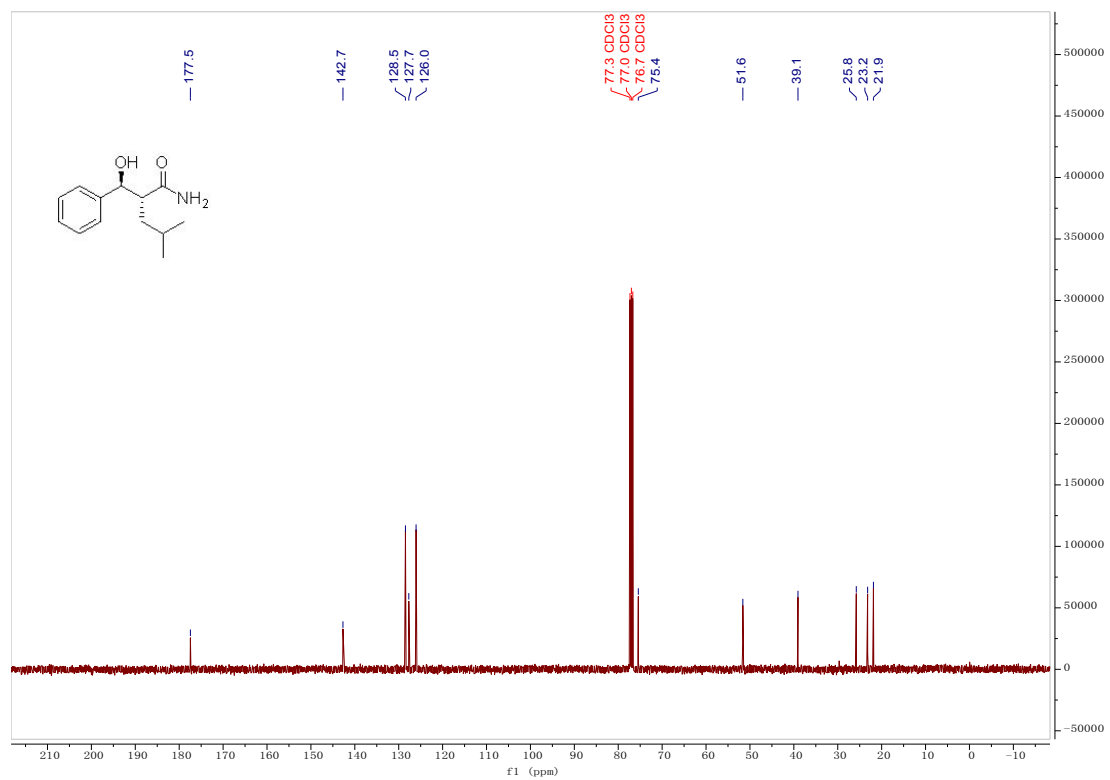
¹³C NMR of 2z (101 MHz, Chloroform-*d*)



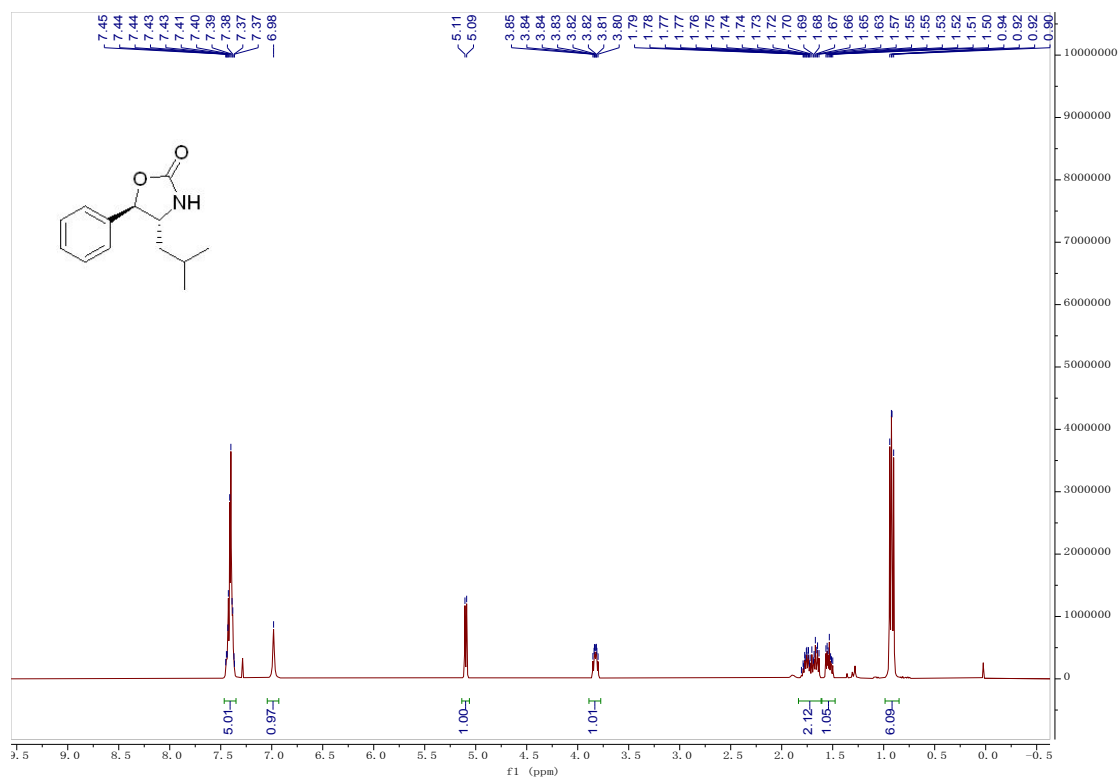
¹H NMR of 3d (400 MHz, Chloroform-*d*)



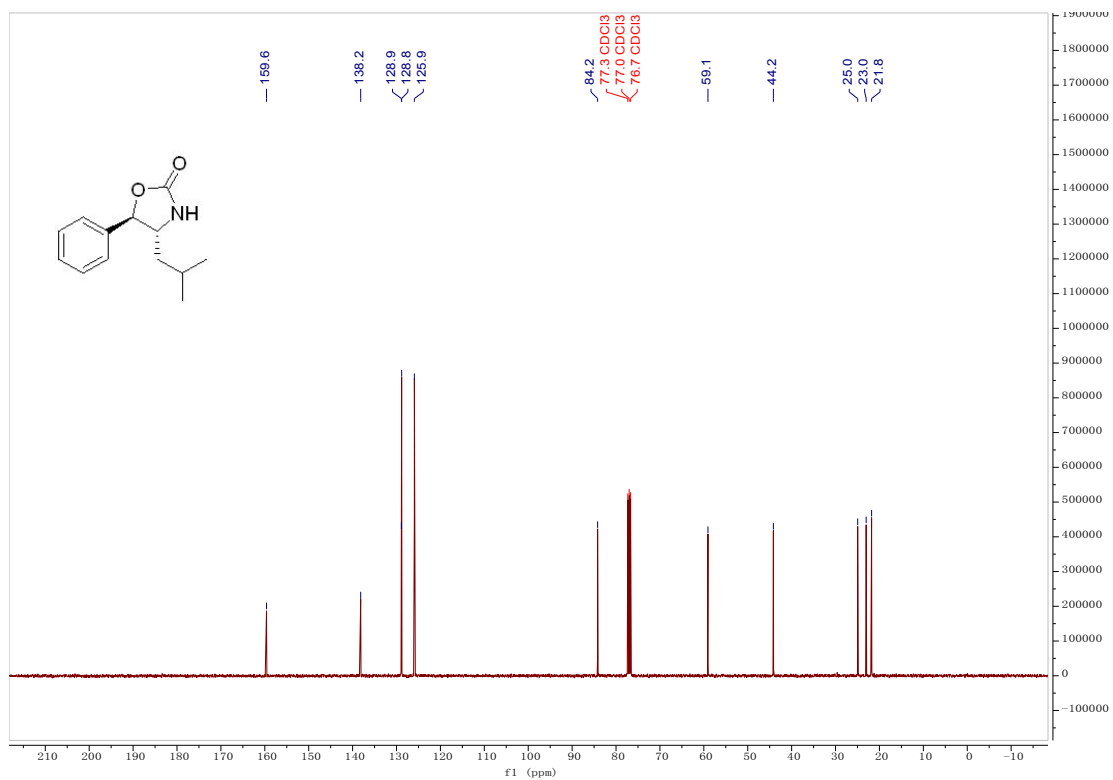
¹³C NMR of 3d (101 MHz, Chloroform-*d*)



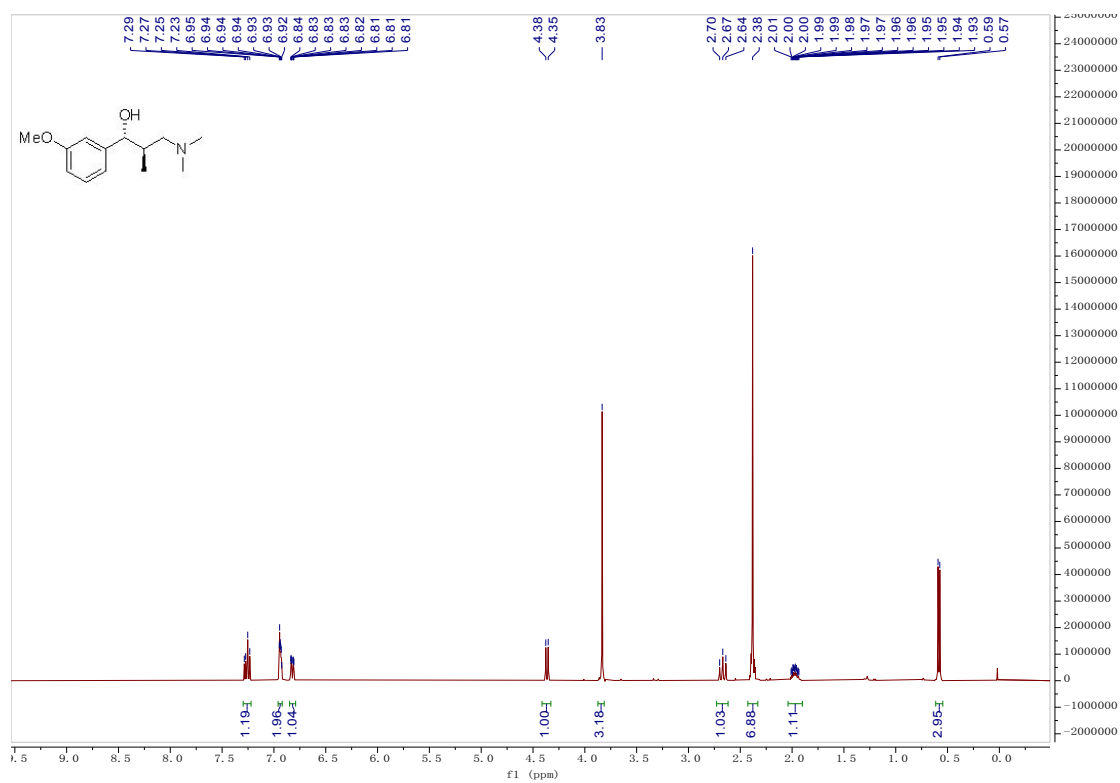
¹H NMR of 4d (400 MHz, Chloroform-*d*)



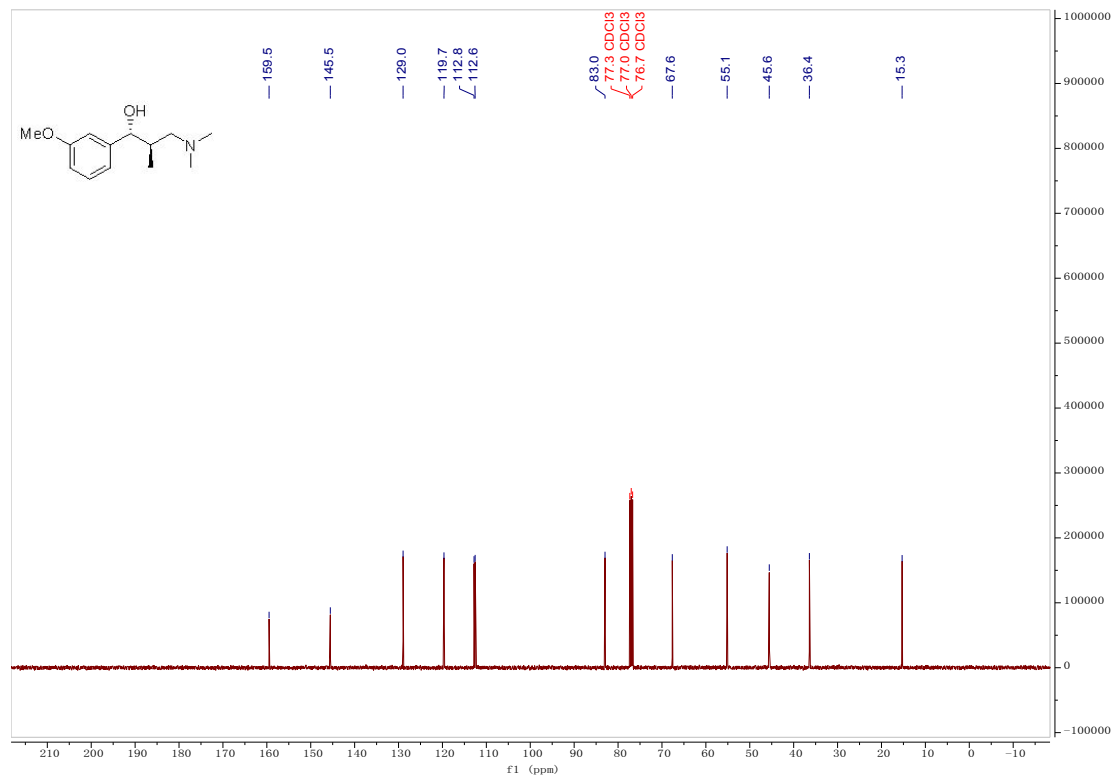
¹³C NMR of 4d (101 MHz, Chloroform-*d*)



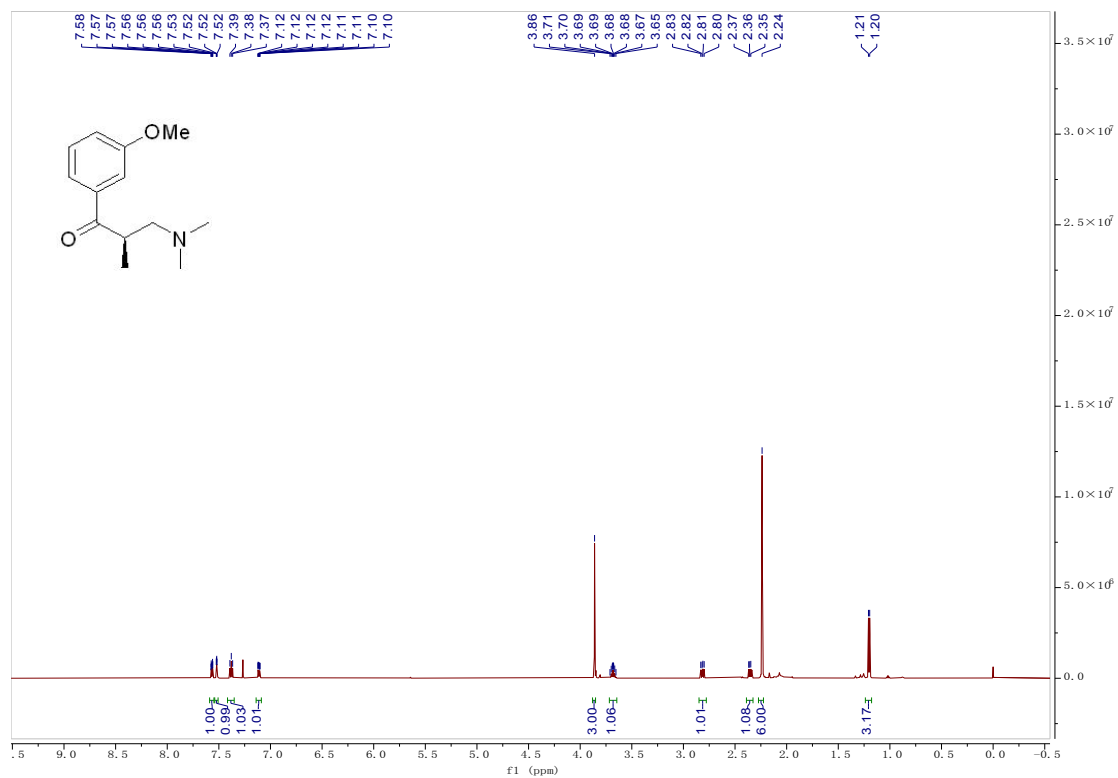
¹H NMR of 5o (400 MHz, Chloroform-d)



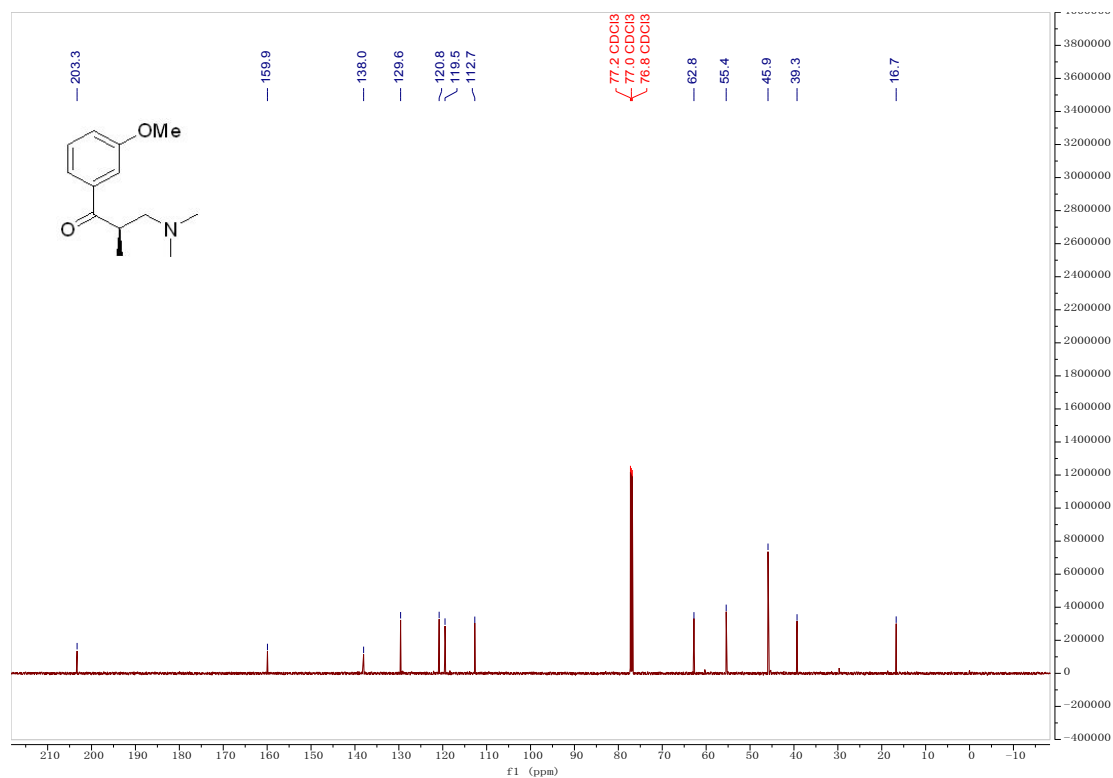
¹³C NMR of 5o (101 MHz, Chloroform-d)



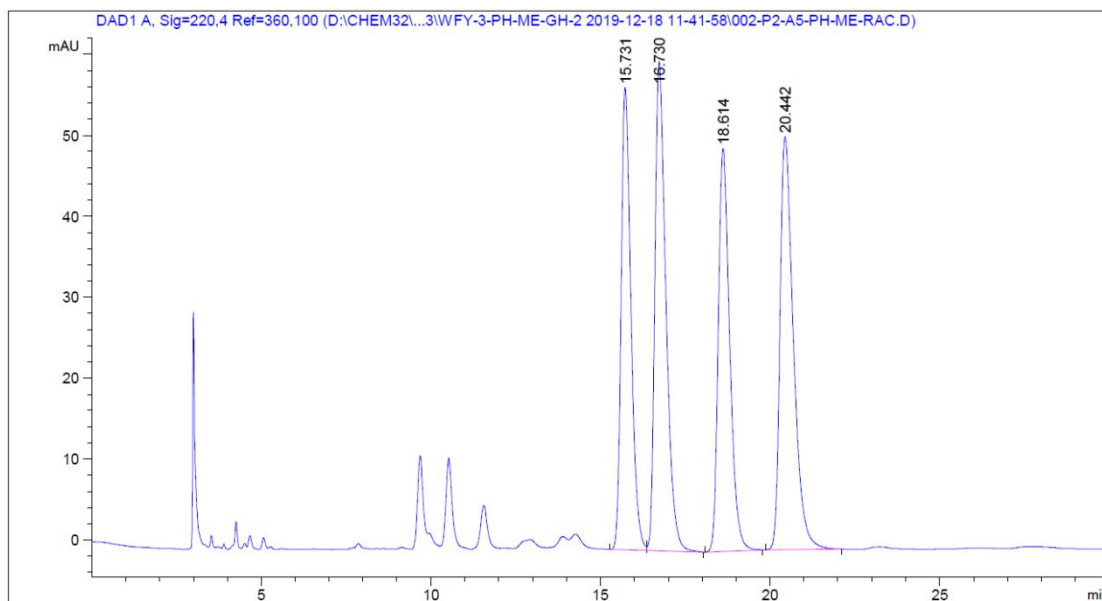
¹H NMR of 6o (400 MHz, Chloroform-d)



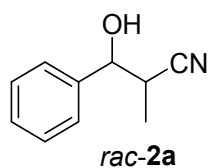
¹³C NMR of 6o (101 MHz, Chloroform-*d*)



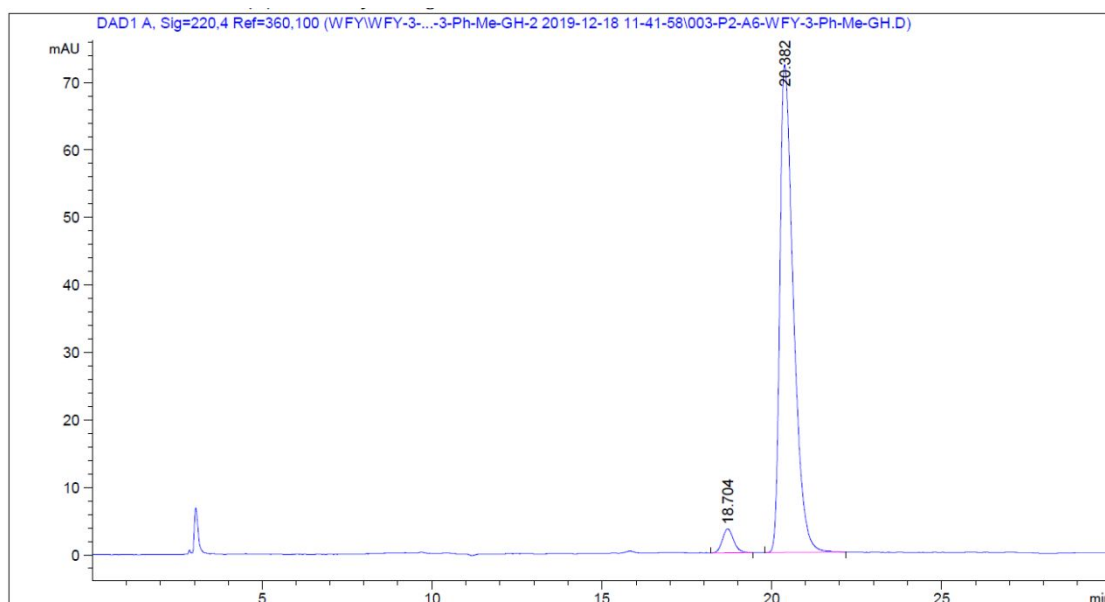
9. HPLC Spectra of the Products



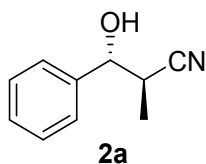
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



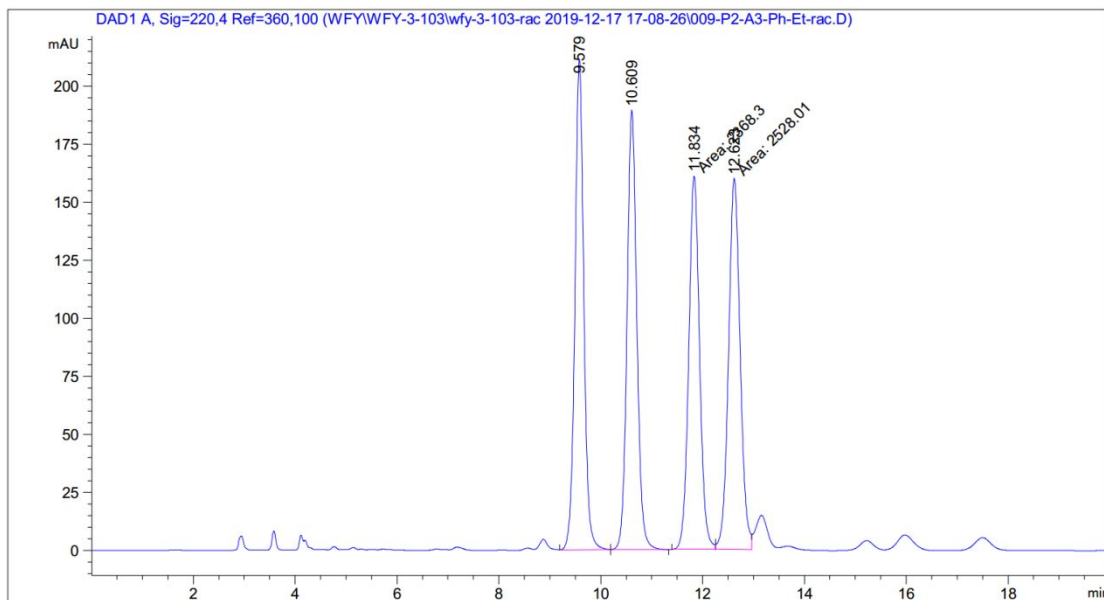
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.731	BV	0.3079	1145.29163	57.12619	22.5809
2	16.730	VB	0.3435	1365.03845	60.43626	26.9134
3	18.614	BB	0.3582	1161.72754	49.79366	22.9049
4	20.442	BB	0.4140	1399.89929	51.03371	27.6008



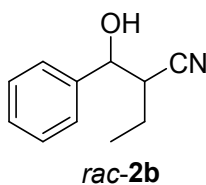
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



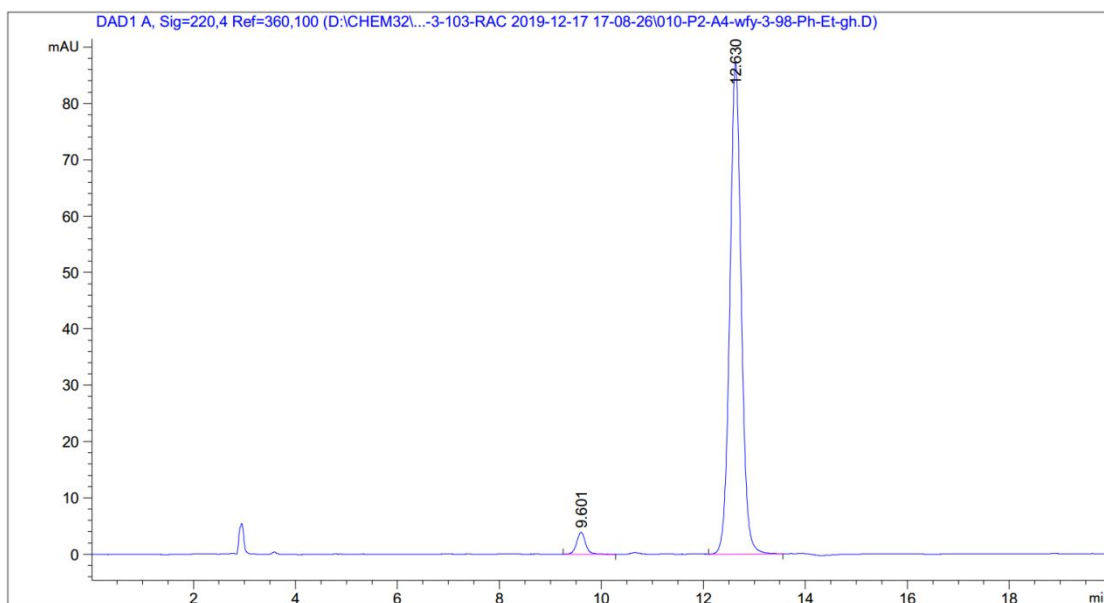
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.704	BB	0.3400	82.19085	3.57836	3.9347
2	20.382	BB	0.4176	2006.66602	72.35162	96.0653



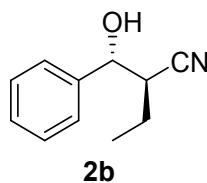
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



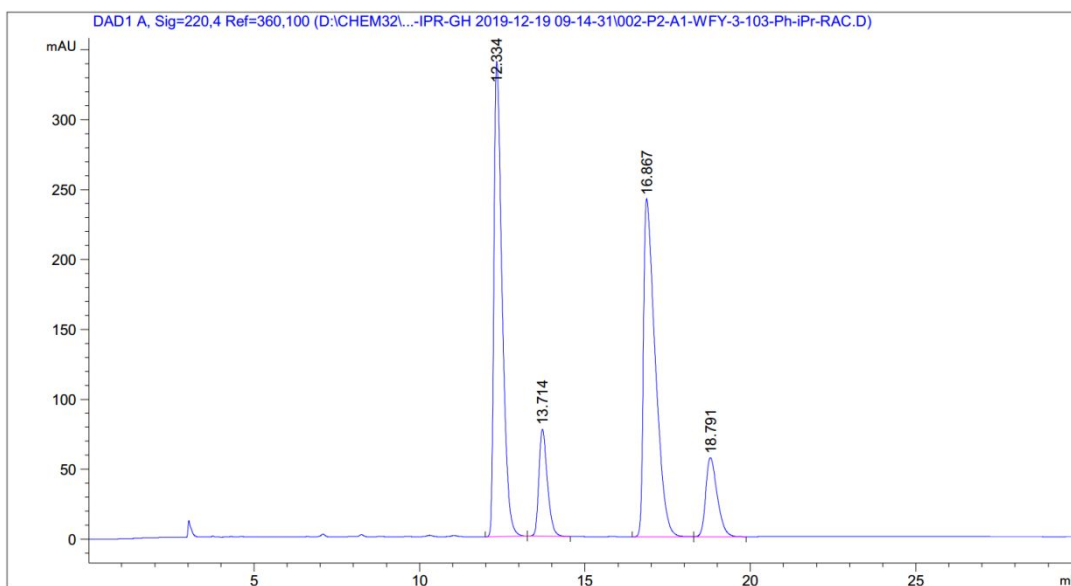
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.579	VB	0.1854	2557.42505	211.06950	25.6237
2	10.609	BB	0.2057	2526.95093	189.32288	25.3184
3	11.834	MF	0.2454	2368.29712	160.83191	23.7288
4	12.623	MF	0.2637	2528.00952	159.79291	25.3290



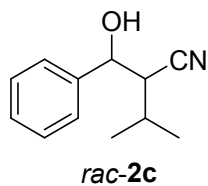
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



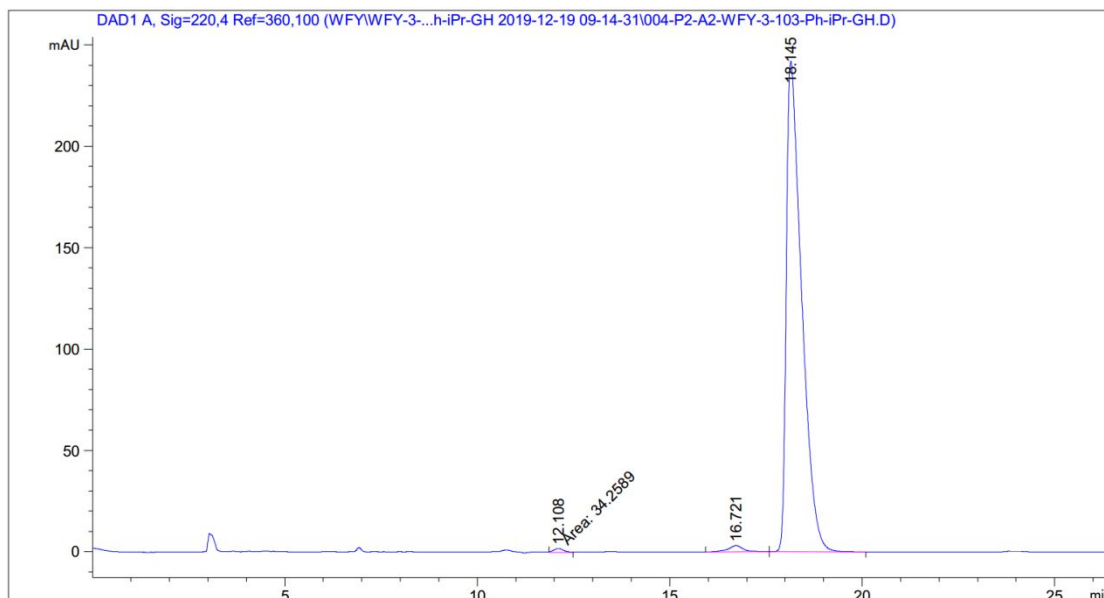
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.601	BB	0.1857	47.53036	3.91227	3.3995
2	12.630	BB	0.2389	1350.63159	87.11134	96.6005



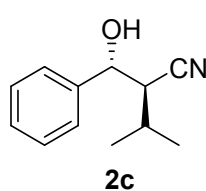
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



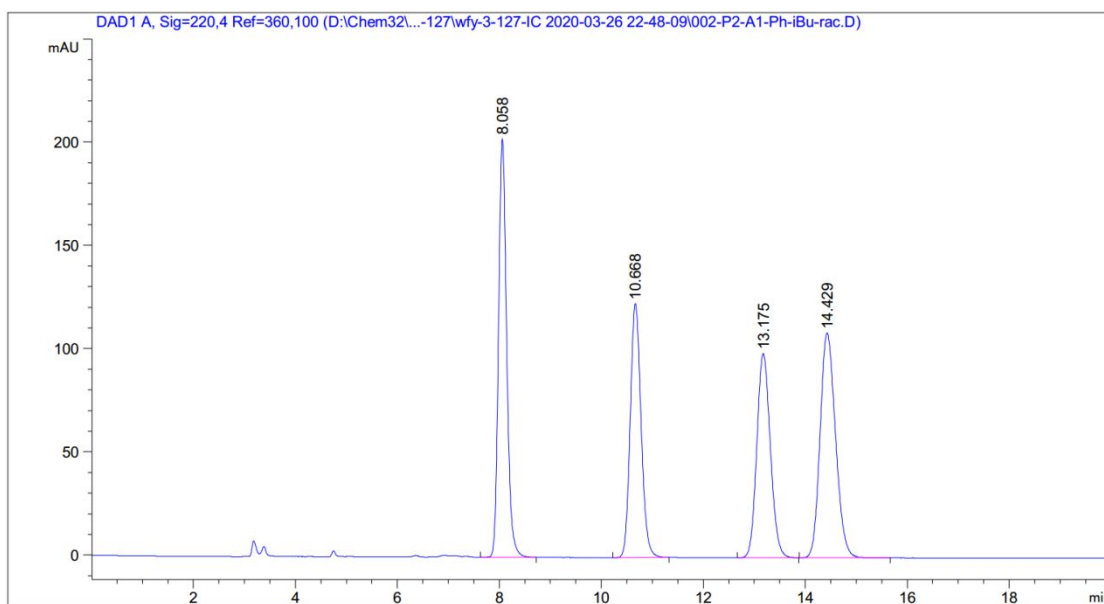
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.334	BB	0.2597	5818.49023	339.94931	40.0401
2	13.714	BB	0.2713	1362.35803	76.66584	9.3751
3	16.867	BB	0.3669	5985.54590	241.71751	41.1897
4	18.791	BB	0.3695	1365.25842	56.58040	9.3951



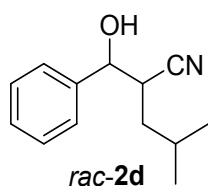
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



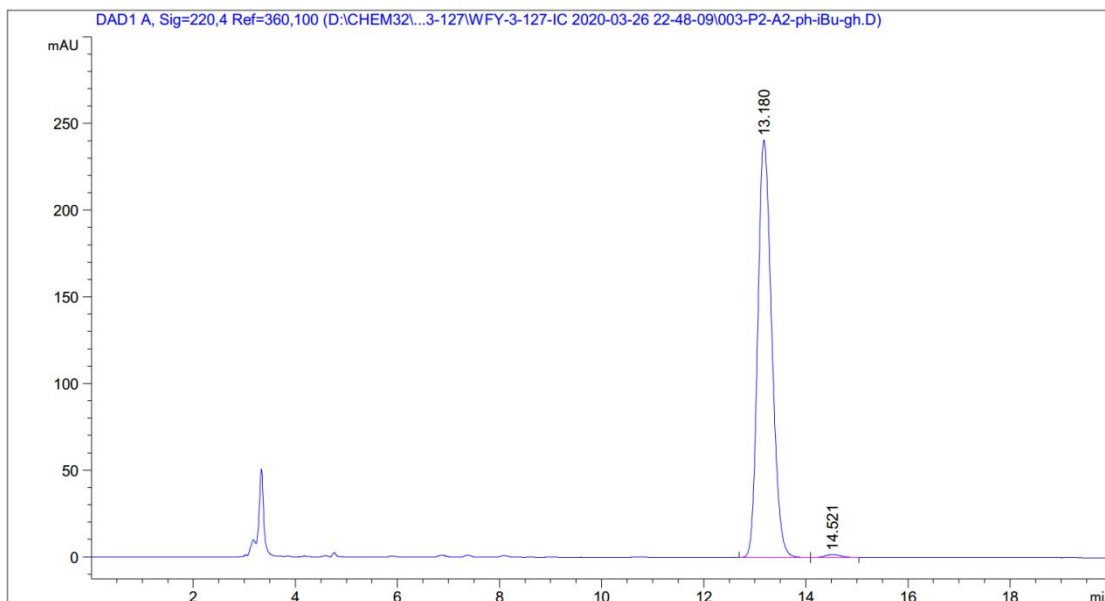
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.108	MM	0.3007	34.25894	1.89907	0.5043
2	16.721	BB	0.3852	80.72643	3.04639	1.1883
3	18.145	BB	0.4101	6678.21973	241.92043	98.3073



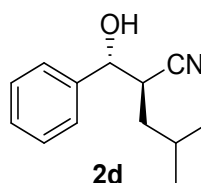
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



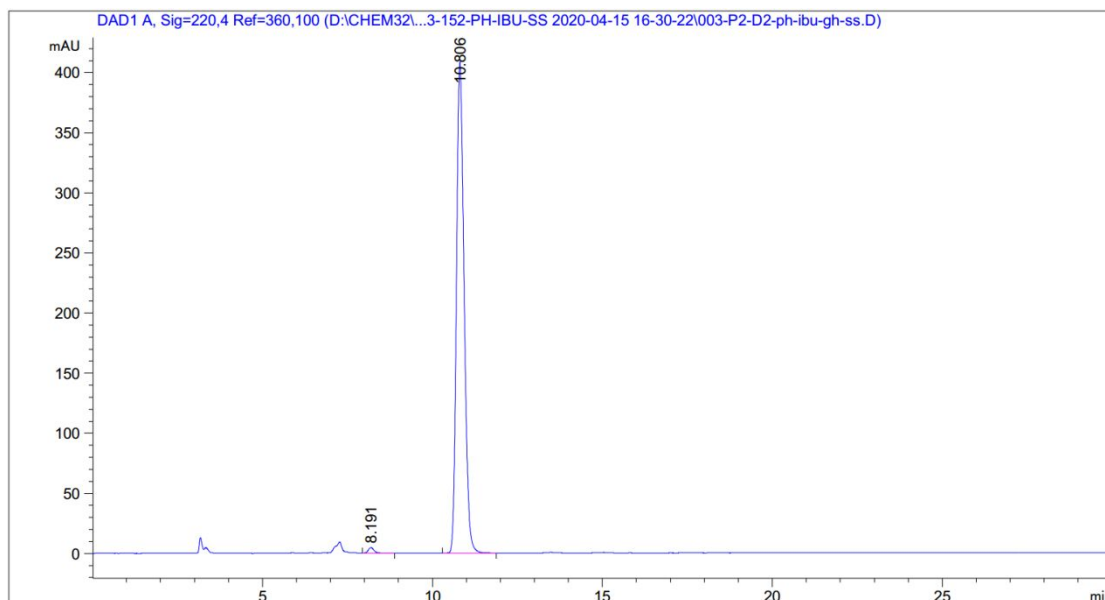
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.058	BB	0.1715	2246.27783	202.40559	27.4718
2	10.668	BB	0.2281	1813.80139	122.97688	22.1827
3	13.175	BB	0.2872	1824.44727	98.91670	22.3129
4	14.429	BB	0.3277	2292.13672	108.82095	28.0327



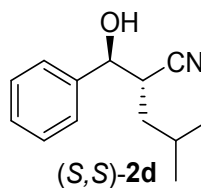
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



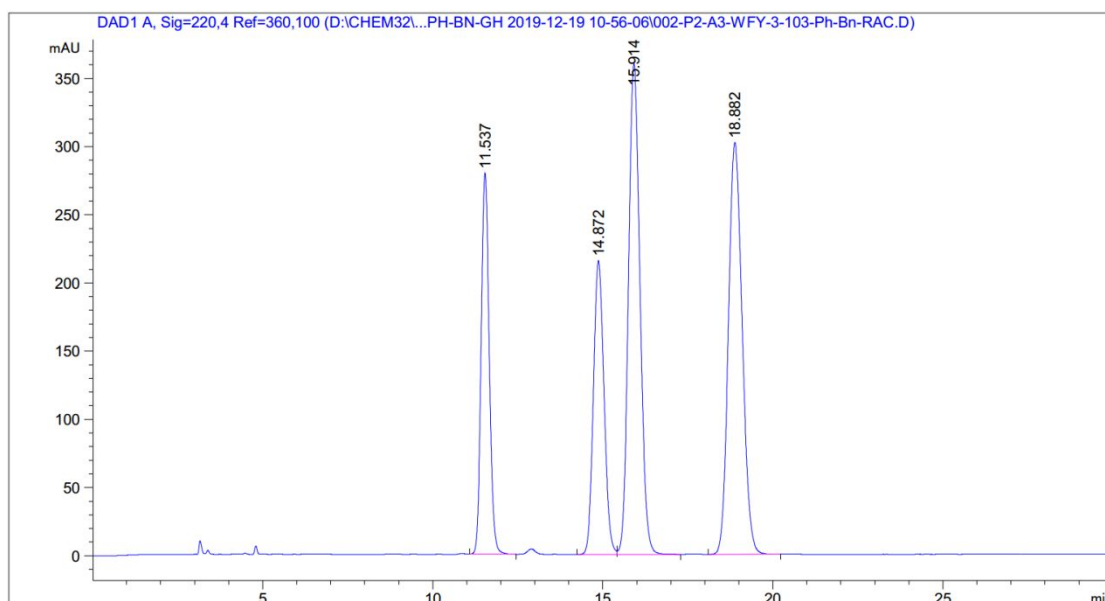
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.180	BB	0.2953	4566.75293	240.78107	99.2367
2	14.521	BB	0.3115	35.12726	1.72535	0.7633



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

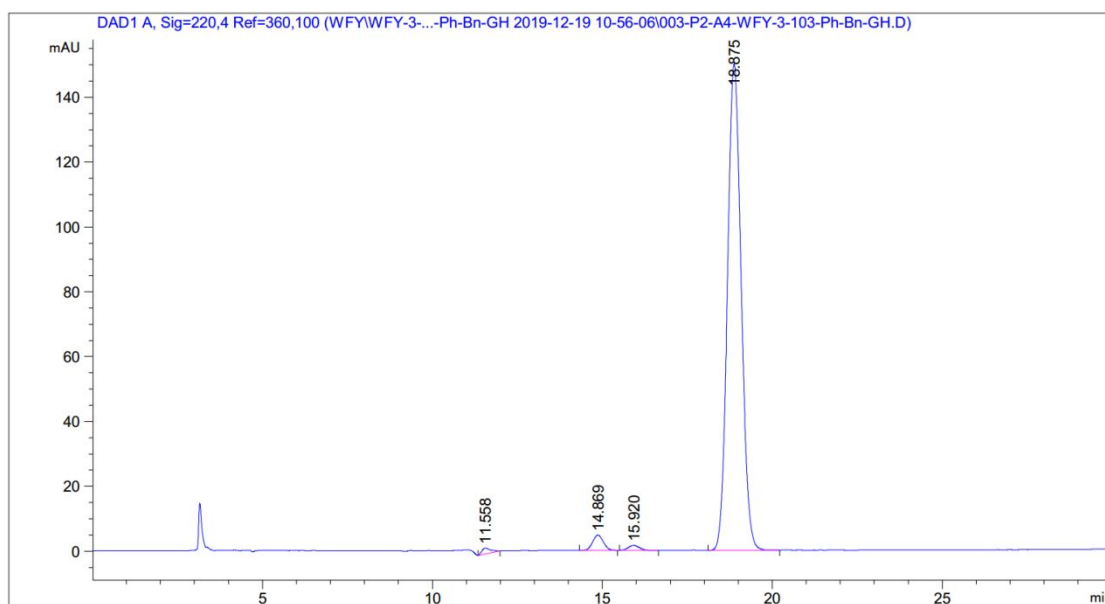
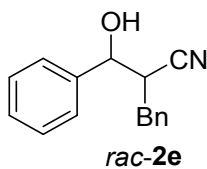


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.191	BB	0.1749	53.10488	4.66295	0.8258
2	10.806	BB	0.2441	6377.93945	408.59674	99.1742



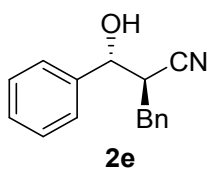
Signal 1: DAD1 A, Sig=220,4 Ref=360,100

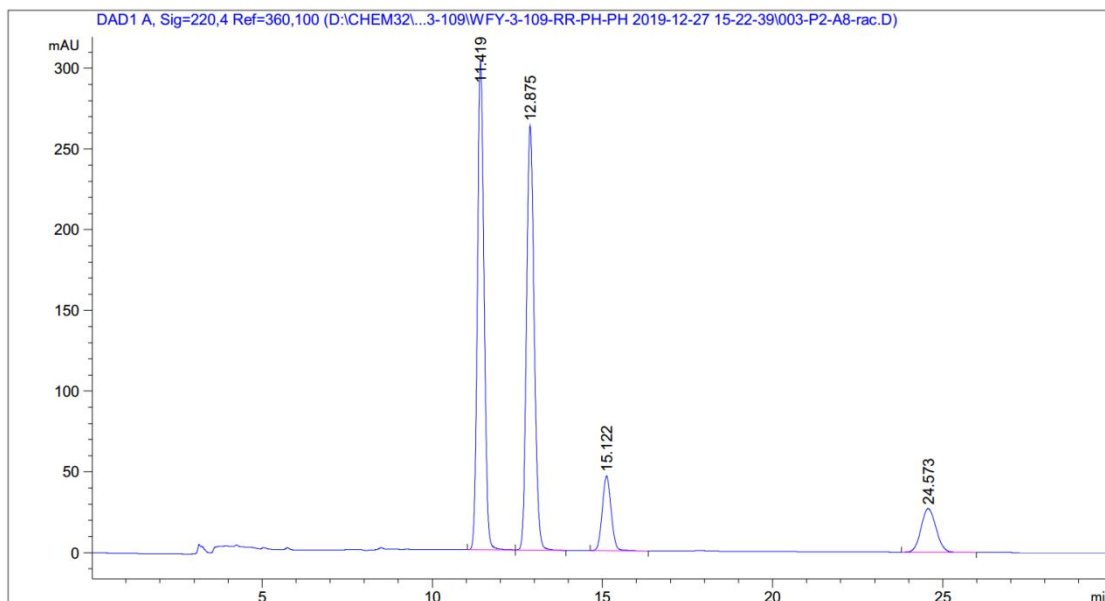
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.537	BB	0.2583	4603.34619	279.25366	17.5640
2	14.872	BV	0.3362	4659.10010	215.56697	17.7767
3	15.914	VB	0.3681	8451.85254	359.73685	32.2479
4	18.882	BB	0.4401	8494.70117	302.04135	32.4114



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

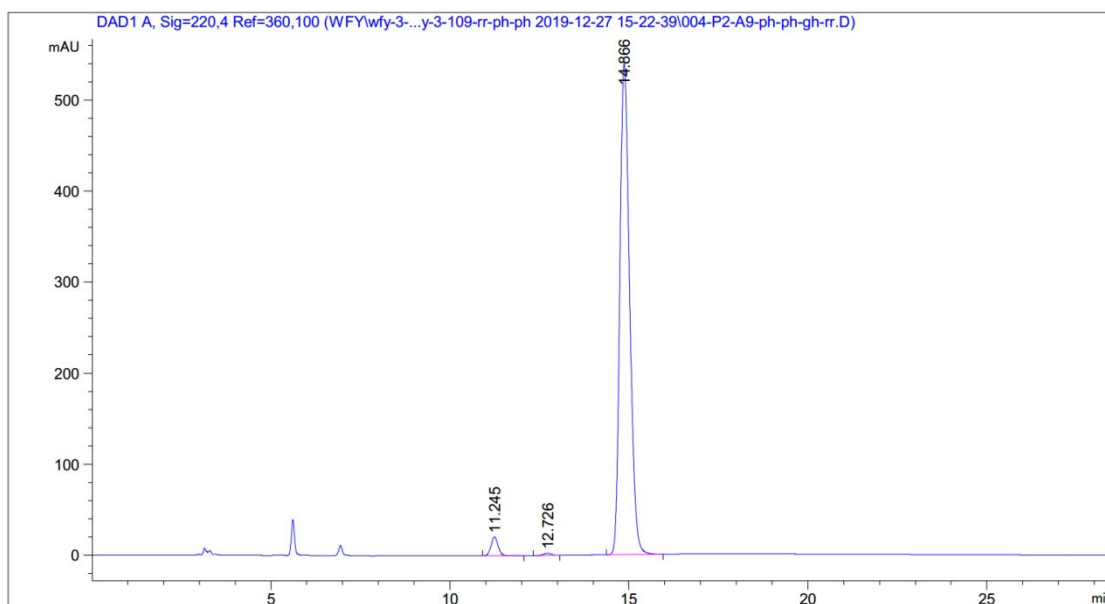
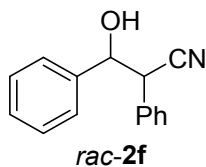
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.558	BB	0.2604	30.50459	1.75828	0.6980
2	14.869	BB	0.3364	102.40769	4.73421	2.3433
3	15.920	BB	0.3201	34.12290	1.50765	0.7808
4	18.875	BB	0.4369	4203.23535	150.01447	96.1779





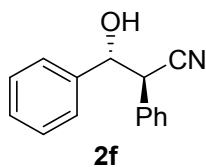
Signal 1: DAD1 A, Sig=220,4 Ref=360,100

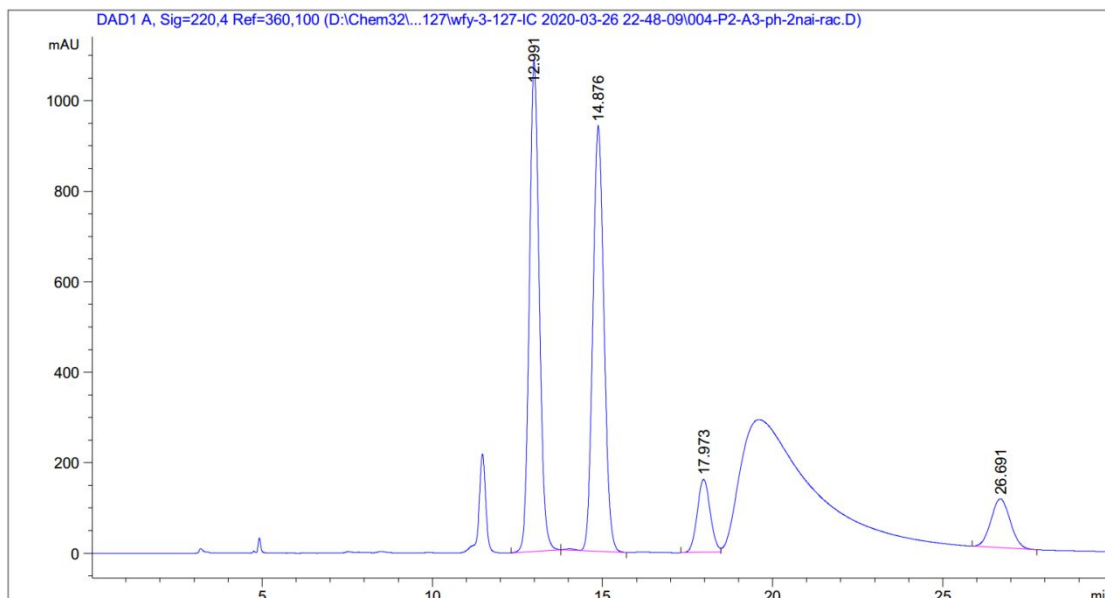
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.419	BB	0.2118	4091.59668	302.56561	41.4906
2	12.875	BB	0.2421	4103.66406	262.98245	41.6130
3	15.122	BB	0.2827	834.58087	46.21941	8.4630
4	24.573	BB	0.4792	831.65771	27.16036	8.4334



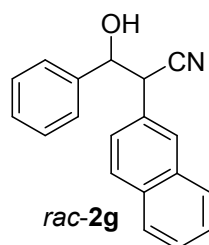
Signal 1: DAD1 A, Sig=220,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.245	BB	0.2122	286.65045	20.87524	2.7226
2	12.726	BB	0.2389	37.41732	2.43966	0.3554
3	14.866	BB	0.2926	1.02046e4	539.79620	96.9220

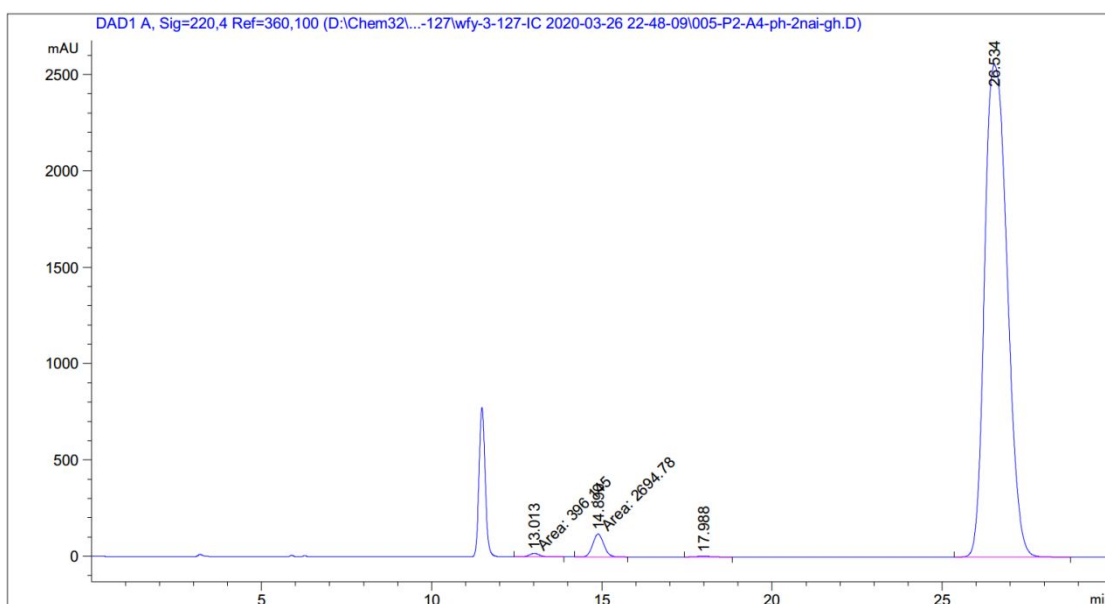




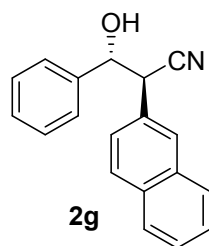
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



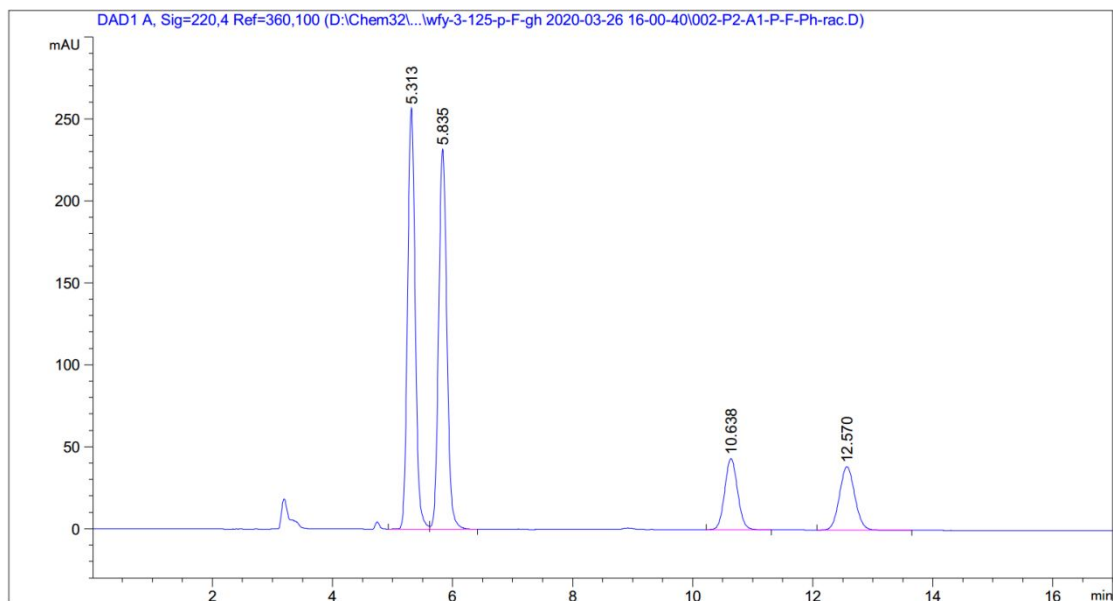
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.991	BB	0.3131	2.18268e4	1083.35278	42.2539
2	14.876	VB R	0.3542	2.13362e4	939.96118	41.3041
3	17.973	BV	0.4125	4254.04590	160.90092	8.2353
4	26.691	BBA	0.6141	4239.25928	107.95382	8.2067



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

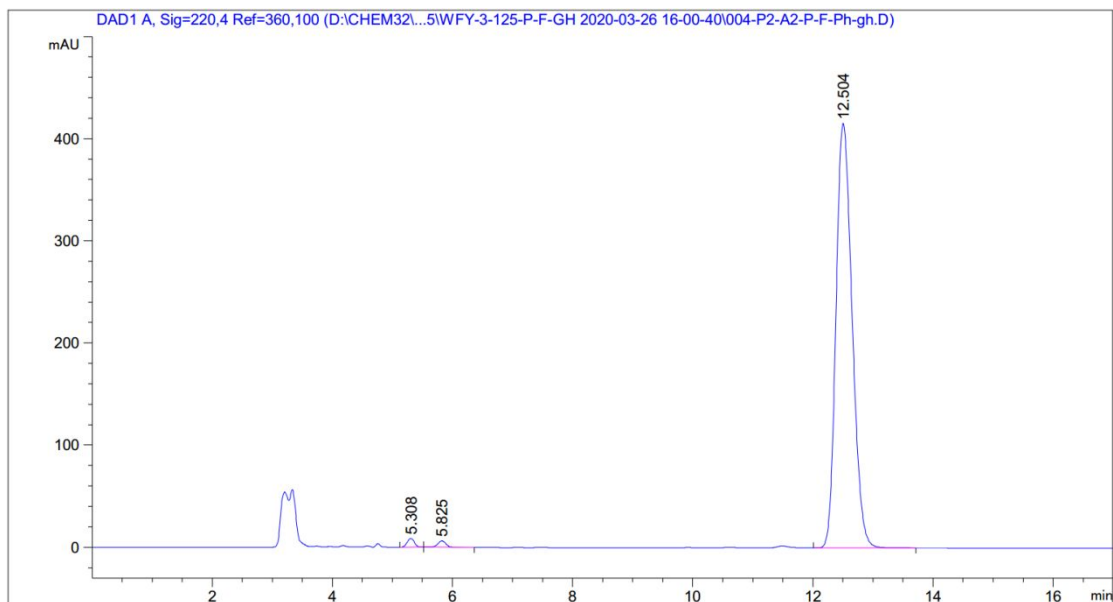
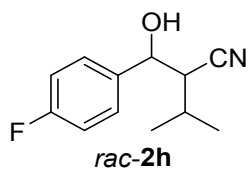


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.013	MM	0.3447	396.14542	19.15421	0.3280
2	14.890	MM	0.3771	2694.77539	119.09927	2.2314
3	17.988	BB	0.4185	112.86046	4.13392	0.0935
4	26.534	BB	0.7331	1.17564e5	2553.61279	97.3471

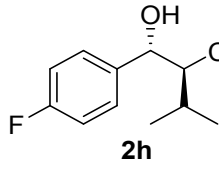


Signal 1: DAD1 A, Sig=220,4 Ref=360,100

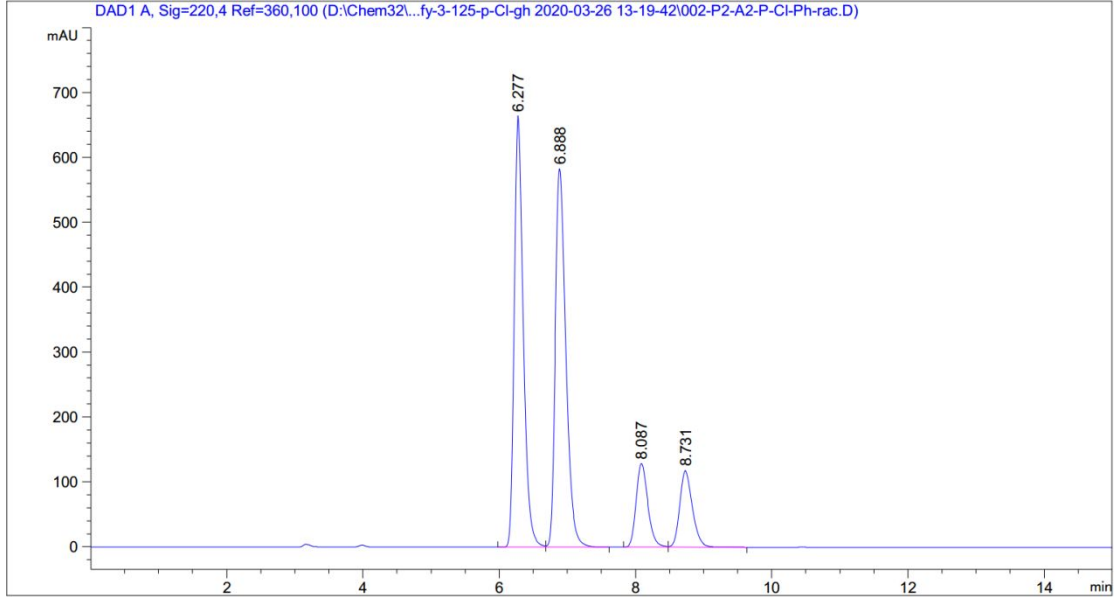
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.313	BV	0.1368	2262.32690	256.73651	39.0514
2	5.835	VB	0.1486	2198.22900	231.79065	37.9450
3	10.638	BB	0.2318	646.10577	43.36775	11.1528
4	12.570	BB	0.2752	686.53595	38.65216	11.8507



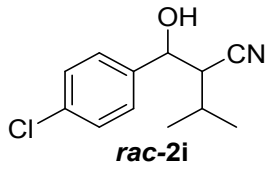
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



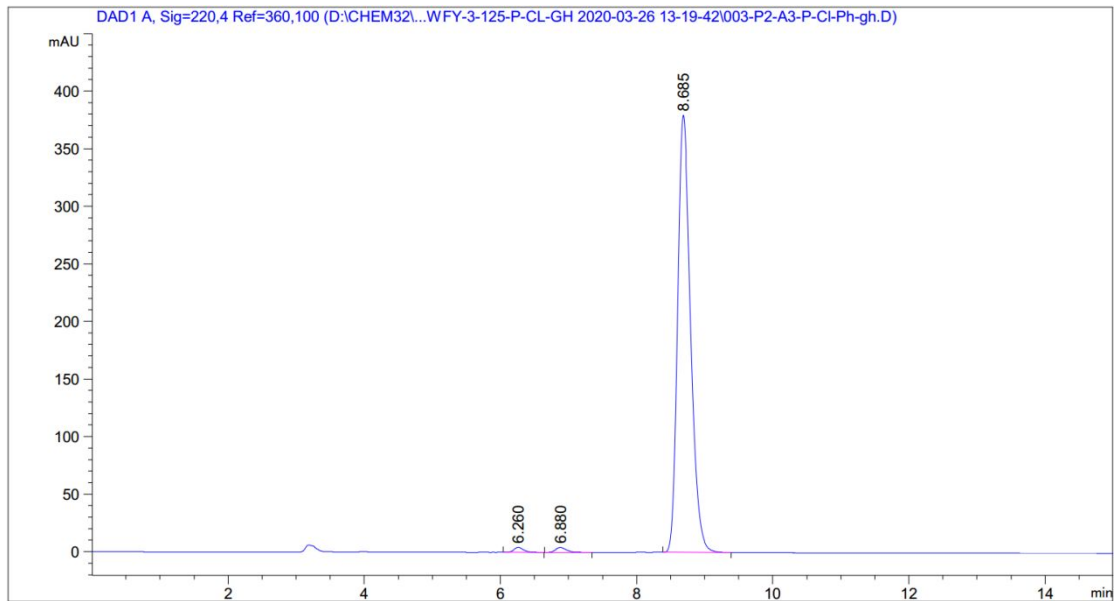
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.308	BB	0.1311	72.36233	8.69673	0.9207
2	5.825	BB	0.1492	60.45570	6.23175	0.7692
3	12.504	BB	0.2928	7726.95703	415.76404	98.3102



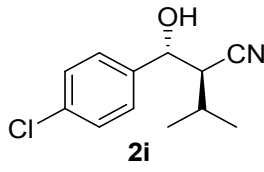
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



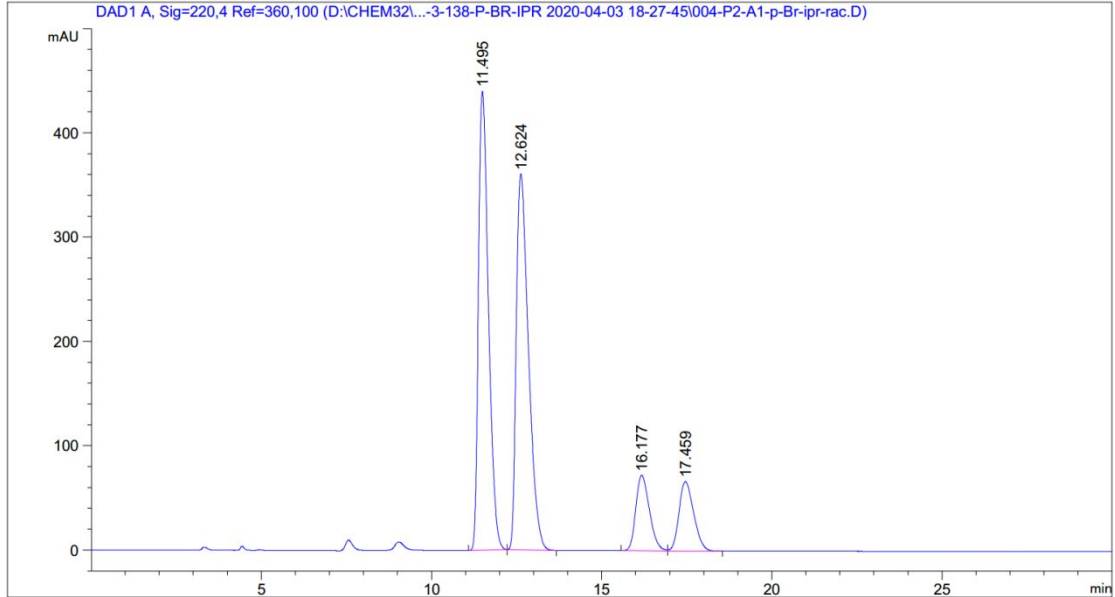
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.277	BV	0.1436	6238.18506	664.27386	40.1052
2	6.888	VB	0.1652	6261.91846	583.40918	40.2578
3	8.087	BV	0.1822	1524.20667	128.63445	9.7991
4	8.731	VB	0.1993	1530.24524	117.95774	9.8379



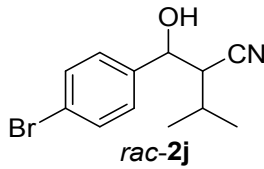
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



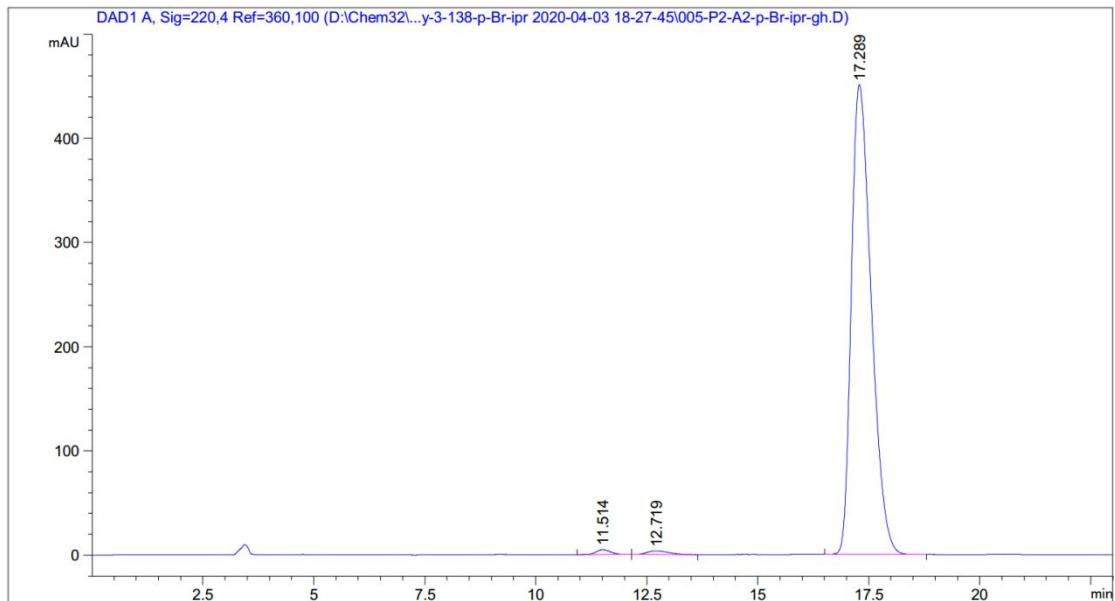
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.260	BB	0.1491	42.70802	4.40583	0.8394
2	6.880	BB	0.1718	48.47708	4.29161	0.9528
3	8.685	BB	0.2015	4996.67480	379.66565	98.2078



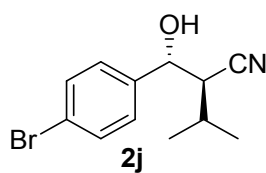
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



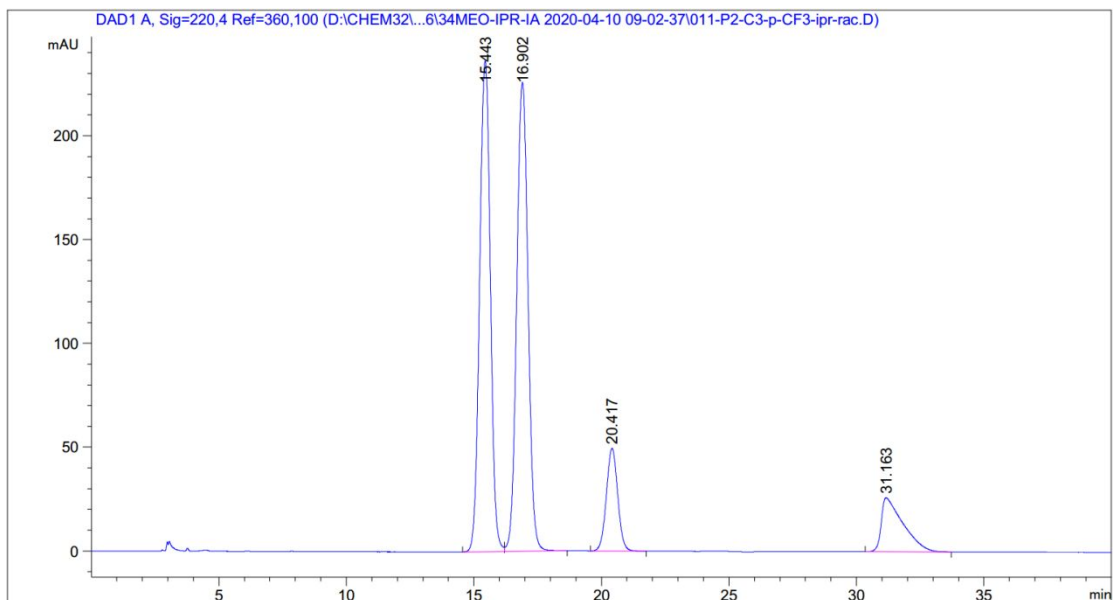
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.495	BB	0.3157	8967.84180	440.18137	40.8856
2	12.624	BB	0.3842	8970.76855	360.67764	40.8989
3	16.177	BV	0.4288	2002.16211	72.35490	9.1281
4	17.459	VB	0.4661	1993.22327	66.42188	9.0874



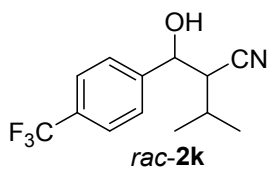
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



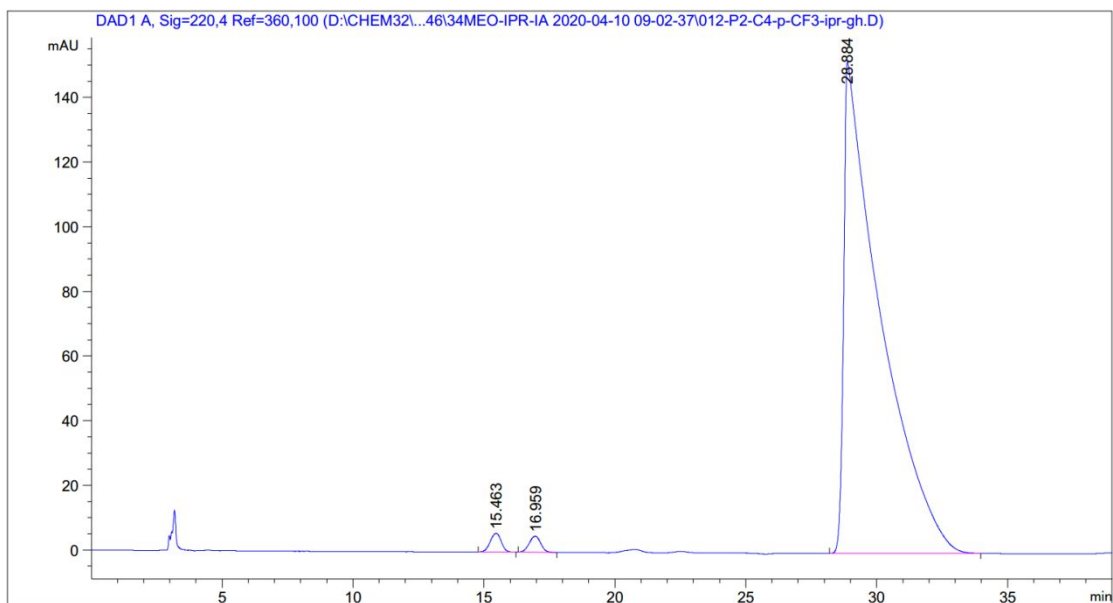
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.514	BB	0.3498	106.58302	4.64356	0.7468
2	12.719	BB	0.4468	119.38648	3.54566	0.8366
3	17.289	BB	0.4836	1.40451e4	450.71274	98.4166



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

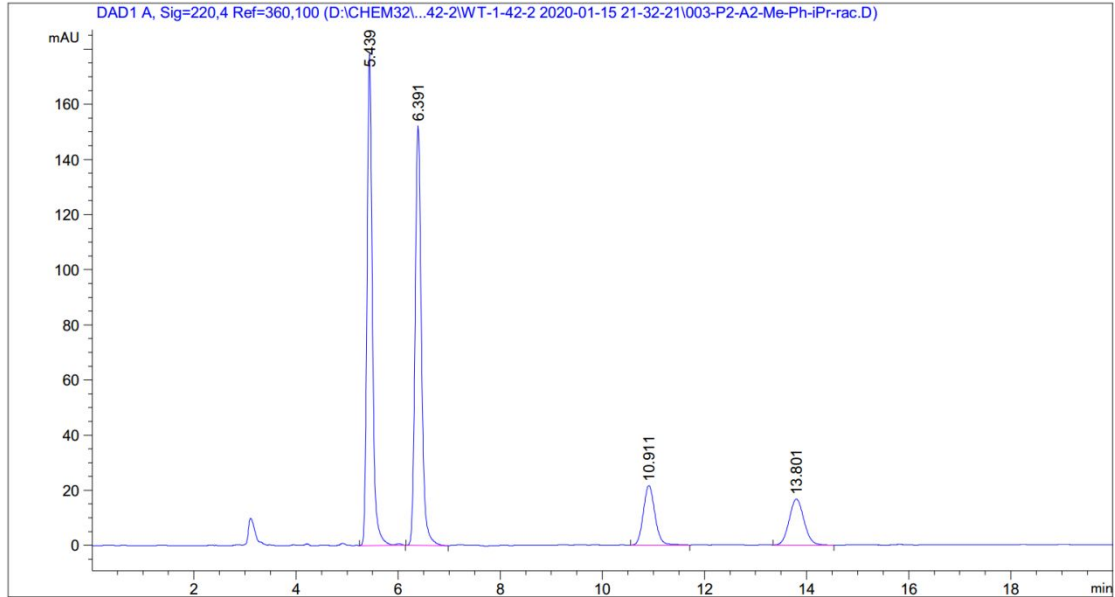
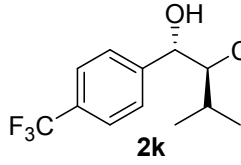


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.443	BV	0.4677	6922.04834	236.36053	40.8411
2	16.902	VB	0.4875	6961.53223	225.92717	41.0741
3	20.417	BB	0.4803	1529.25085	49.51363	9.0228
4	31.163	BB	0.7682	1535.89575	26.03856	9.0620



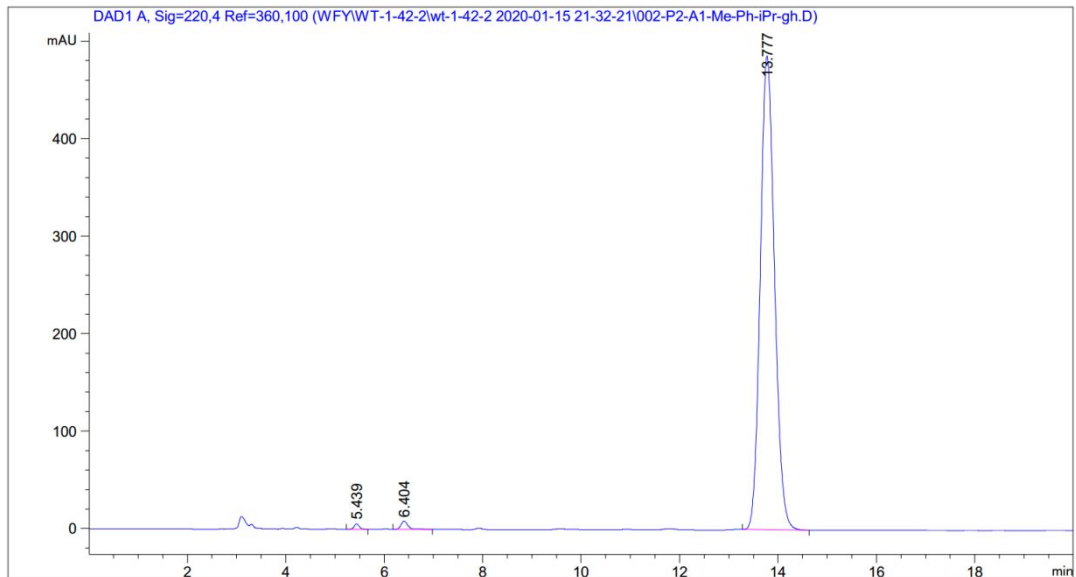
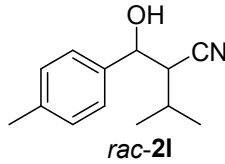
Signal 1: DAD1 A, Sig=220,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.463	BB	0.4391	167.71164	5.76951	1.1140
2	16.959	BB	0.4548	150.04596	4.93426	0.9967
3	28.884	BB	1.2048	1.47366e4	152.03629	97.8893

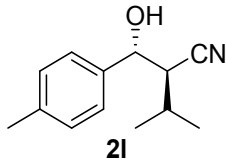


Signal 1: DAD1 A, Sig=220,4 Ref=360,100

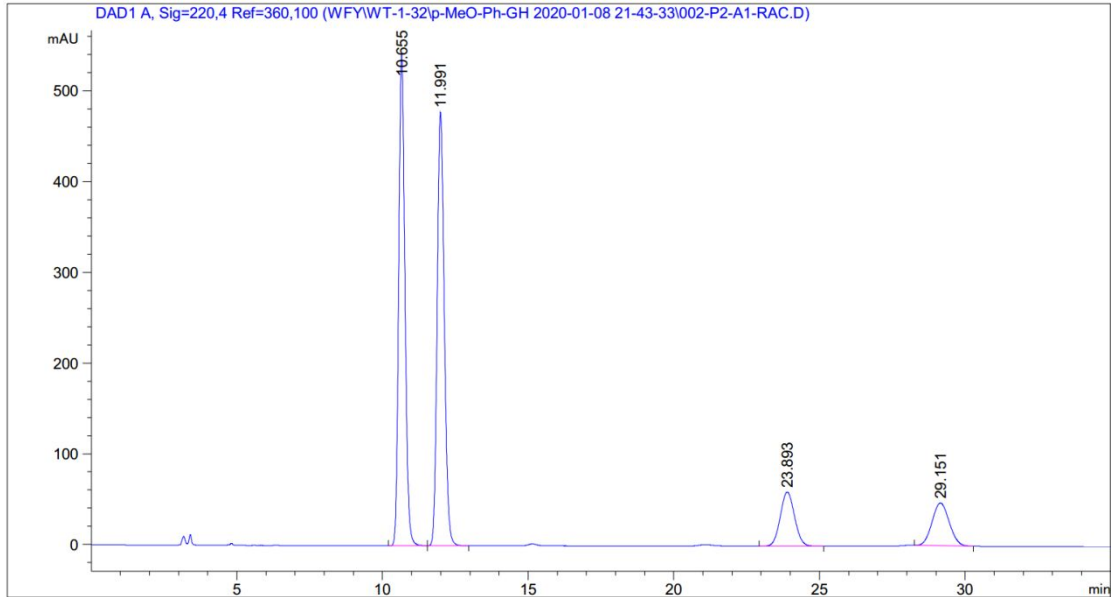
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.439	BV R	0.1112	1301.81860	178.26654	39.6570
2	6.391	BB	0.1316	1301.72913	152.40450	39.6542
3	10.911	BB	0.2439	340.89539	21.62929	10.3846
4	13.801	BB	0.3139	338.25549	16.72901	10.3042



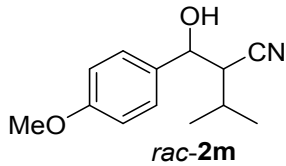
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



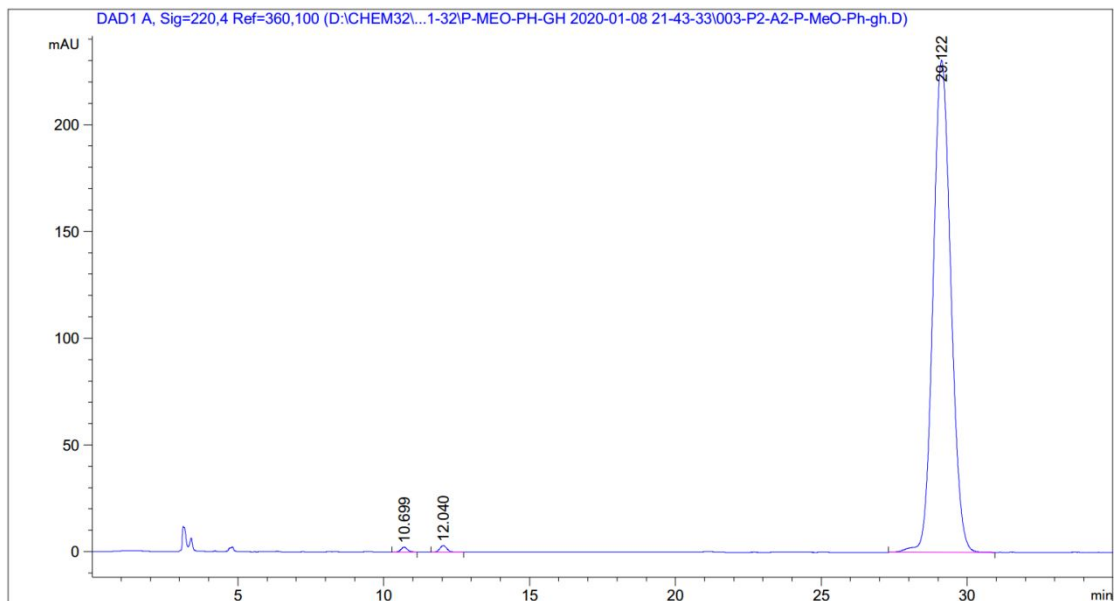
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.439	BB	0.1083	38.31833	5.42966	0.3878
2	6.404	BV R	0.1509	84.04675	8.39009	0.8506
3	13.777	BB	0.3124	9758.14844	485.65204	98.7616



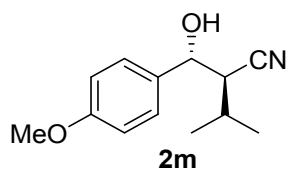
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



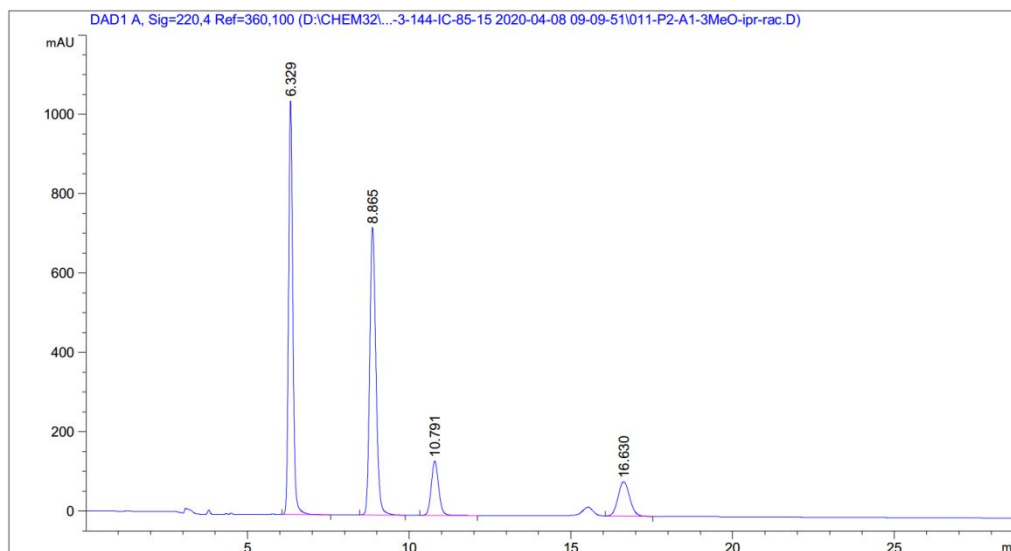
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.655	BB	0.2293	8040.62256	541.26685	40.1140
2	11.991	BB	0.2624	8042.65869	477.83093	40.1242
3	23.893	BB	0.5288	2031.00696	59.72286	10.1325
4	29.151	BB	0.6385	1930.12415	47.05499	9.6292



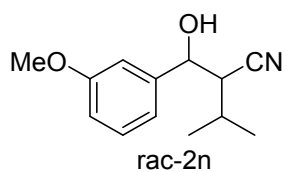
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



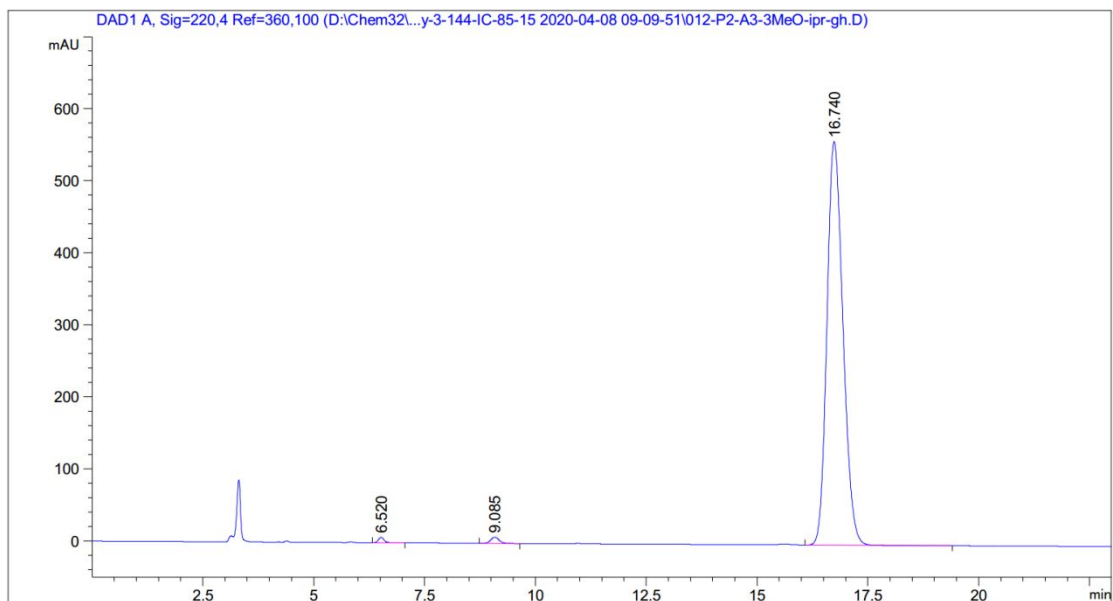
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.699	BB	0.2314	34.99600	2.30113	0.3550
2	12.040	BB	0.2662	54.13079	3.12301	0.5491
3	29.122	BB	0.6585	9769.68066	230.50720	99.0960



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

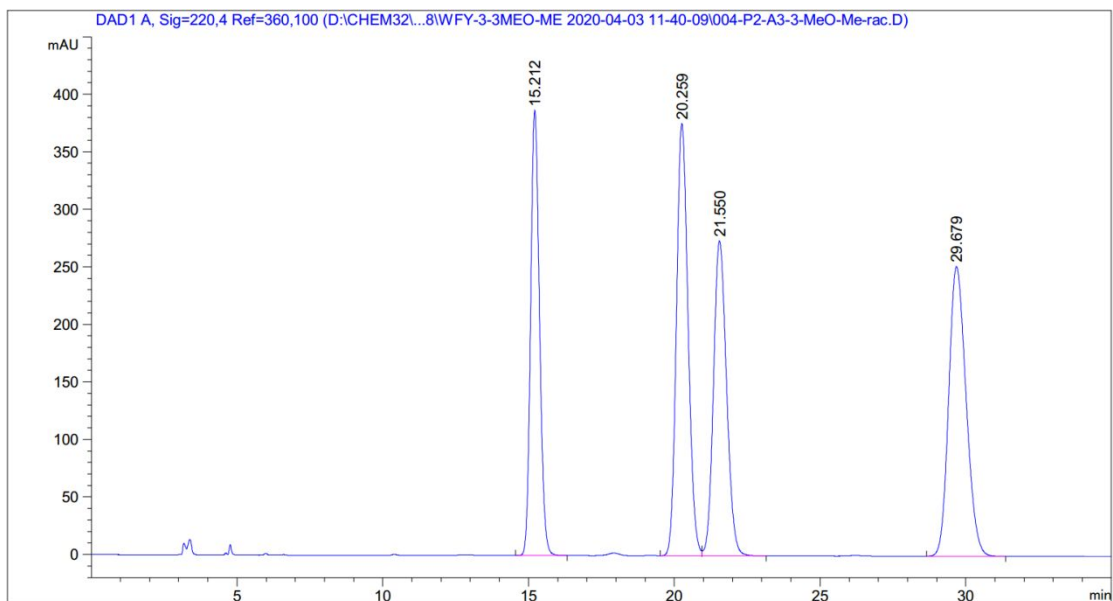
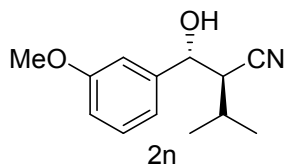


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.329	BB	0.1421	9664.85547	1043.45007	40.7994
2	8.865	BB	0.2061	9698.44043	724.63324	40.9412
3	10.791	BB	0.2483	2174.72412	136.19897	9.1804
4	16.630	BB	0.3861	2150.69092	86.49084	9.0790



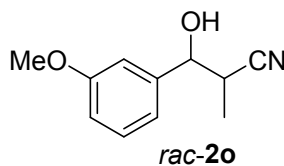
Signal 1: DAD1 A, Sig=220,4 Ref=360,100

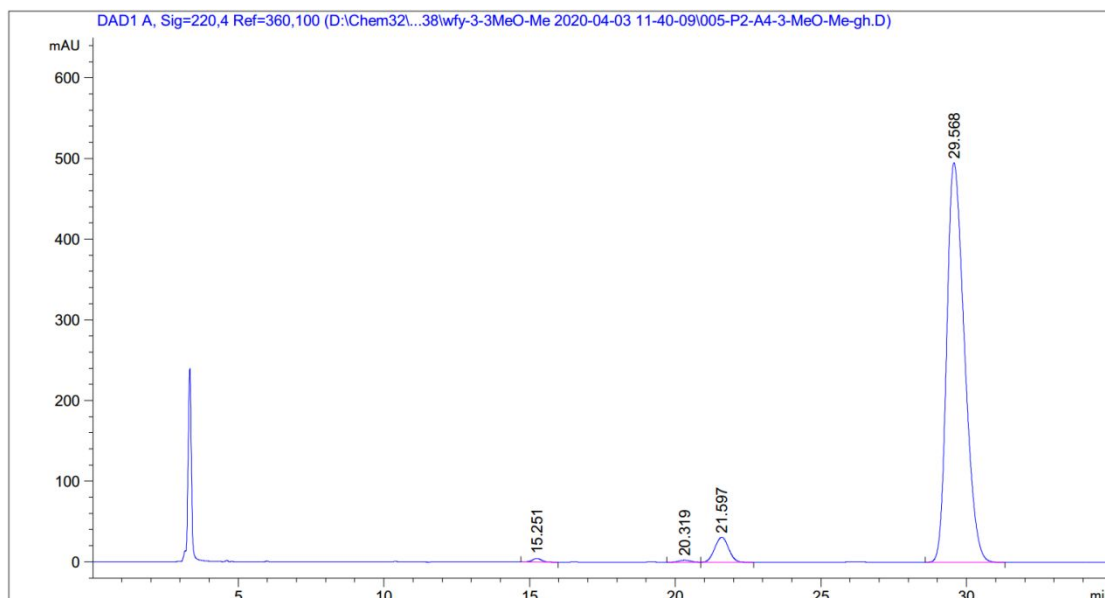
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.520	BB	0.1381	66.87336	7.49793	0.4700
2	9.085	BB	0.2009	114.76154	8.75934	0.8065
3	16.740	BB	0.3904	1.40472e4	560.47455	98.7235



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

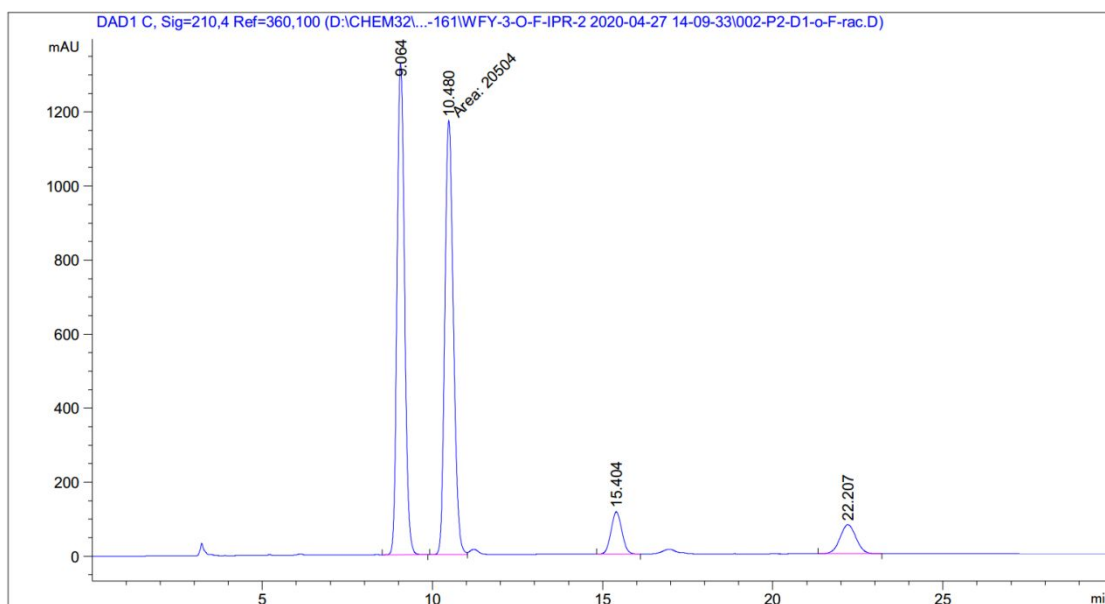
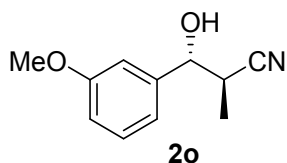
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.212	BB	0.3286	8178.73438	386.88409	21.8069
2	20.259	BV	0.4288	1.03999e4	375.90005	27.7293
3	21.550	VB	0.4808	8511.24902	273.66748	22.6935
4	29.679	BB	0.6446	1.04153e4	251.77489	27.7702





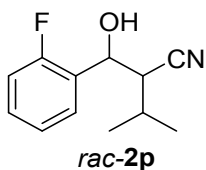
Signal 1: DAD1 A, Sig=220,4 Ref=360,100

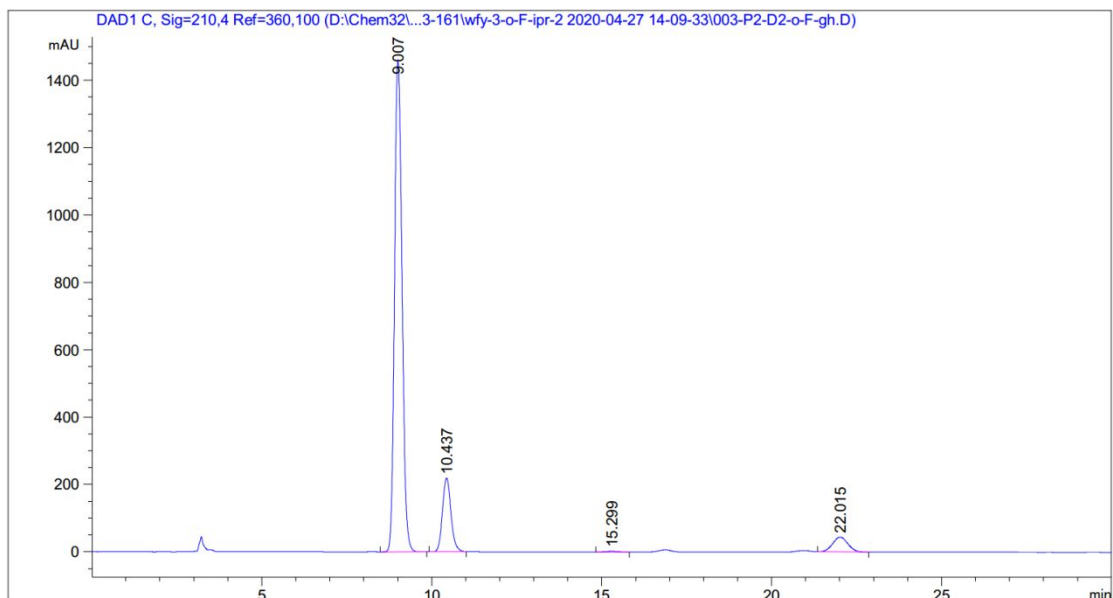
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.251	BB	0.3405	103.28951	4.62576	0.4684
2	20.319	BB	0.3832	66.03498	2.44445	0.2995
3	21.597	BB	0.5173	1021.89075	30.94227	4.6341
4	29.568	BB	0.6512	2.08602e4	495.46228	94.5980



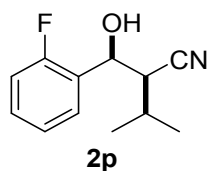
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.064	BB	0.2401	2.02769e4	1327.95178	44.2037
2	10.480	MF	0.2915	2.05040e4	1172.18066	44.6989
3	15.404	BB	0.3433	2520.09692	114.26657	5.4938
4	22.207	BB	0.5105	2570.42969	78.39901	5.6036

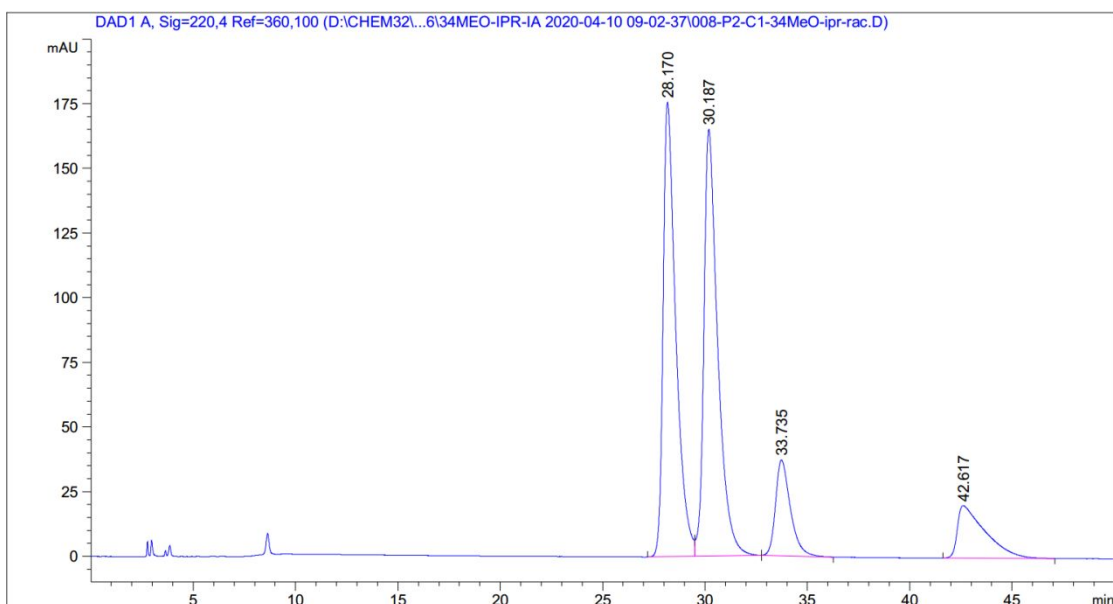




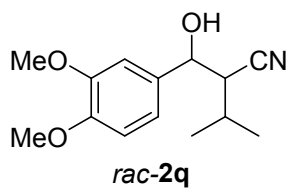
Signal 1: DAD1 C, Sig=210,4 Ref=360,100



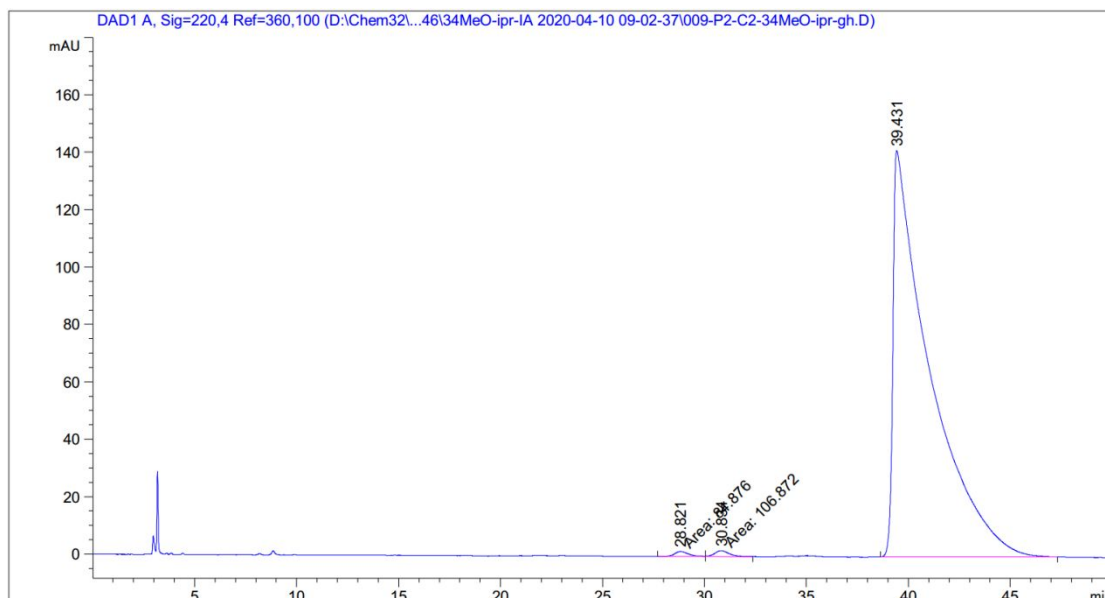
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.007	BB	0.2410	2.23563e4	1457.16895	81.0743
2	10.437	BB	0.2712	3799.98022	218.13766	13.7805
3	15.299	BB	0.2894	47.78440	2.14945	0.1733
4	22.015	BB	0.4854	1371.02393	44.01171	4.9720



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

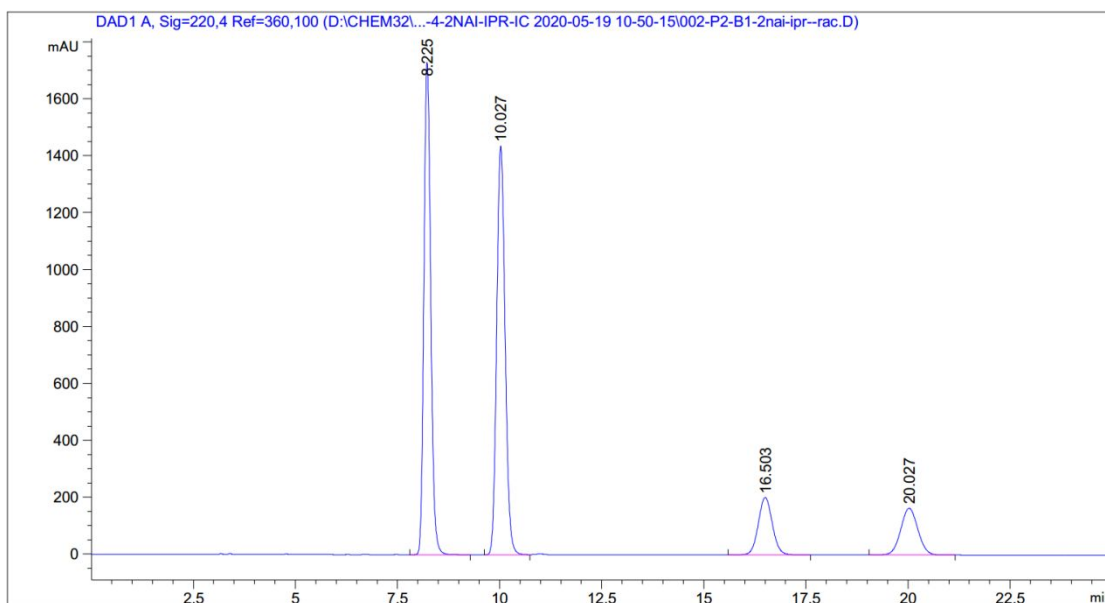
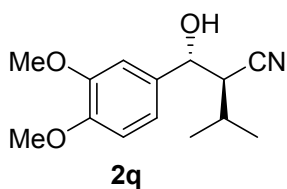


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.170	BV	0.6345	7562.81836	175.58913	39.6231
2	30.187	VB	0.6875	7742.40039	164.97217	40.5640
3	33.735	BB	0.7559	1864.88452	37.00548	9.7705
4	42.617	BB	1.2378	1916.77527	20.33390	10.0424



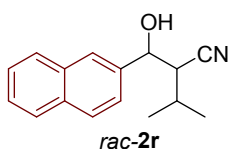
Signal 1: DAD1 A, Sig=220,4 Ref=360,100

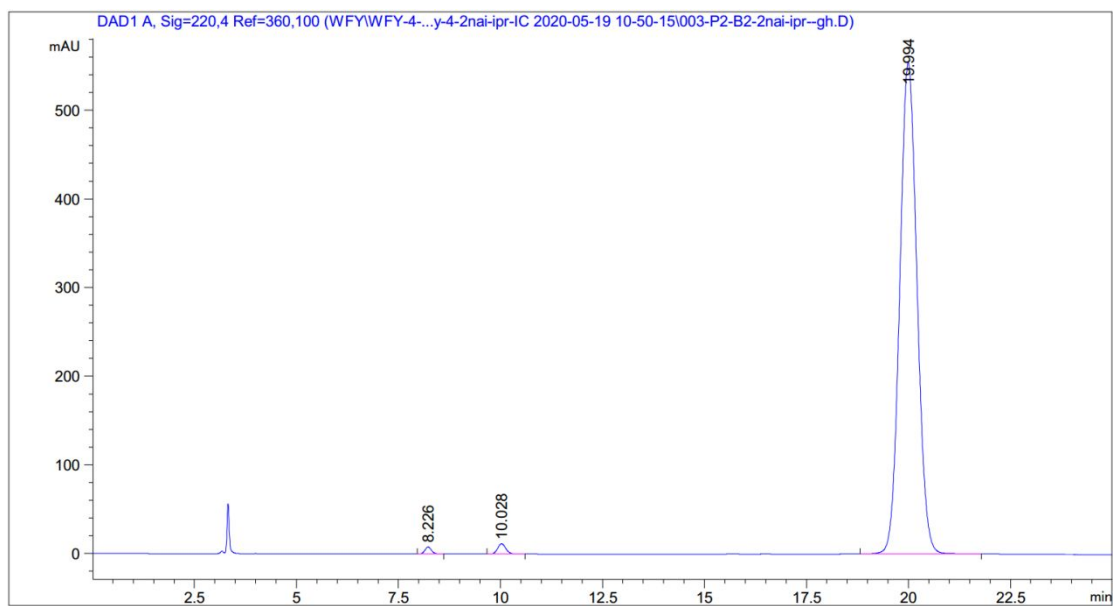
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.821	MF	0.8000	84.87601	1.76833	0.4777
2	30.834	FM	0.8544	106.87153	2.08463	0.6015
3	39.431	BB	1.5787	1.75765e4	141.54314	98.9208



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

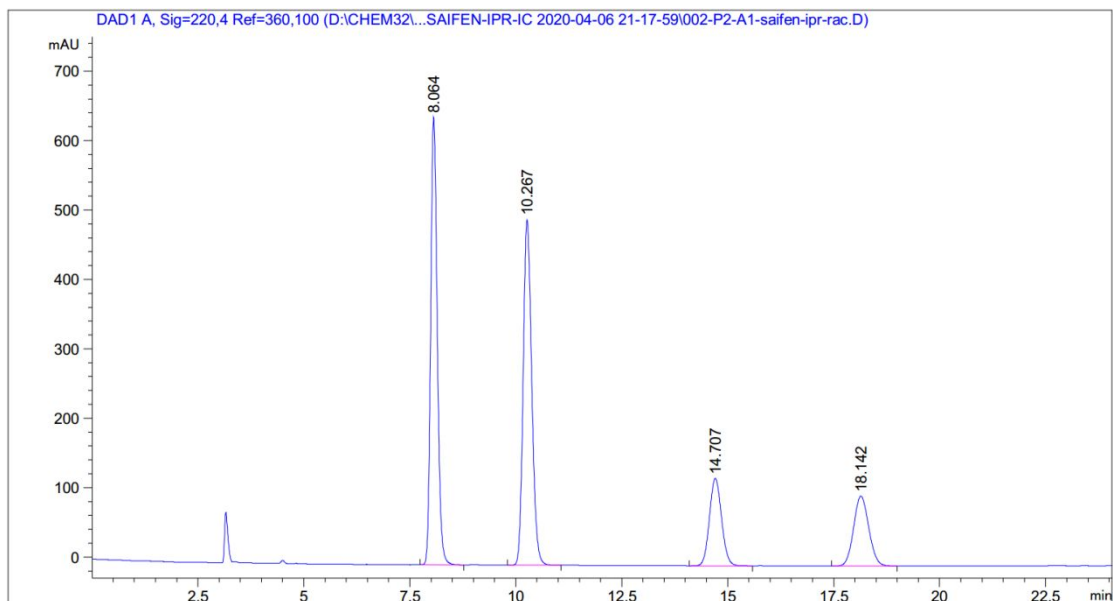
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.225	BB	0.1817	2.00924e4	1727.65234	39.9902
2	10.027	BB	0.2226	2.05040e4	1436.21814	40.8092
3	16.503	BB	0.3719	4848.21973	202.10570	9.6495
4	20.027	BB	0.4529	4798.82959	164.24512	9.5512



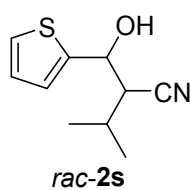


Signal 1: DAD1 A, Sig=220,4 Ref=360,100

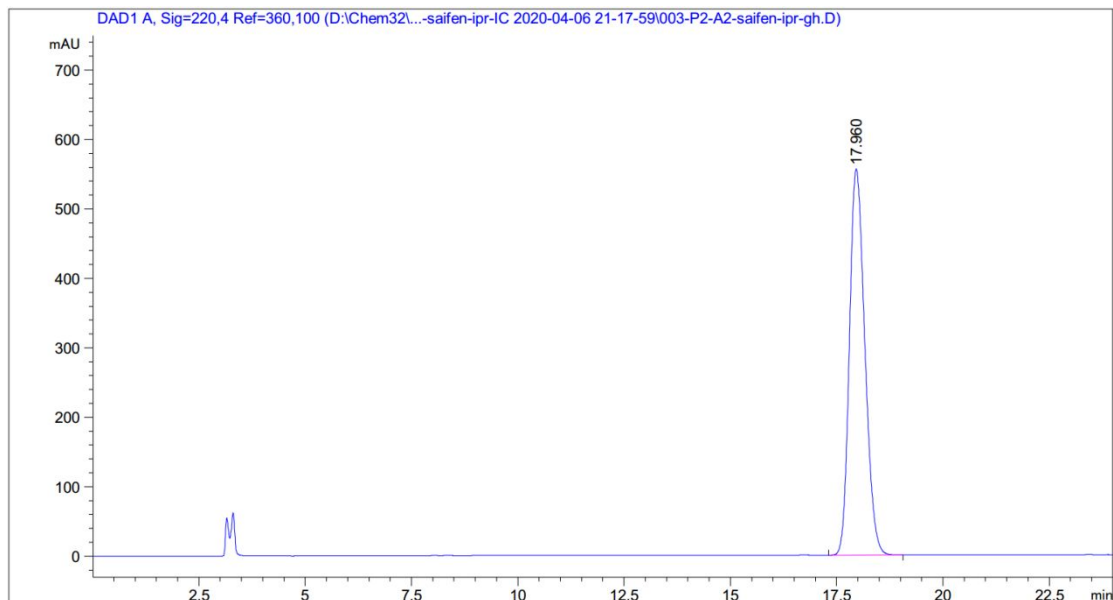
	Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
<p>2r</p>	1	8.226	BB	0.1682	85.53915	7.78632	0.5178
	2	10.028	BB	0.2169	161.65442	11.57545	0.9785
	3	19.994	BB	0.4587	1.62735e4	554.03052	98.5037



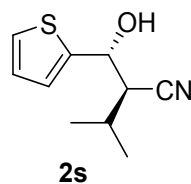
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



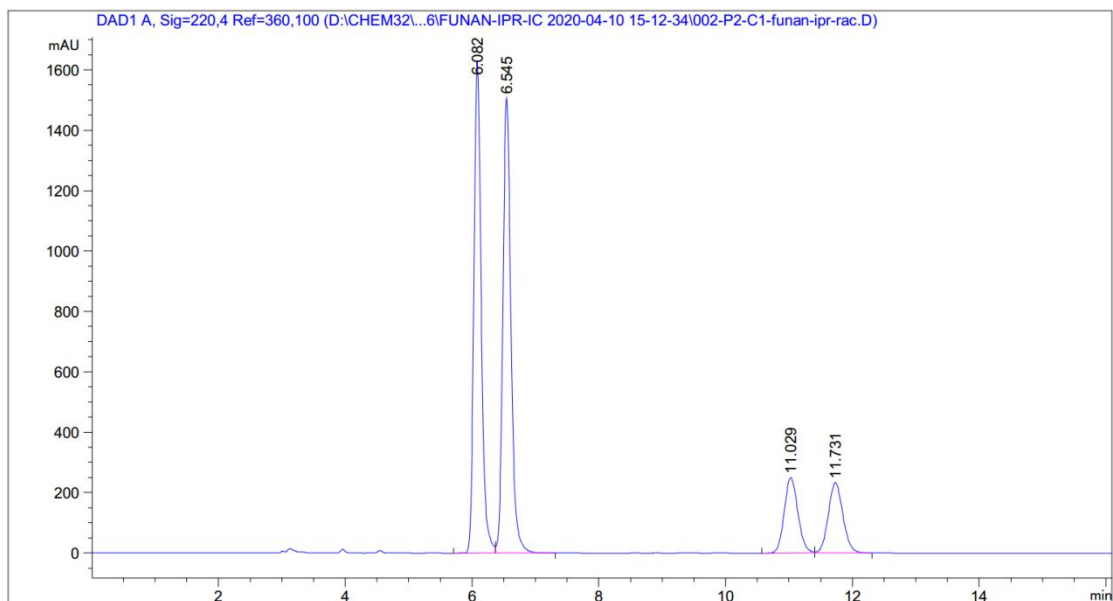
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.064	BB	0.1679	6961.39844	644.96796	36.7072
2	10.267	BB	0.2174	6976.12891	498.06754	36.7848
3	14.707	BB	0.3079	2504.91479	126.03194	13.2083
4	18.142	BB	0.3890	2522.24023	101.13436	13.2997



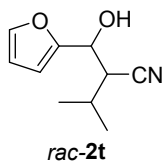
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



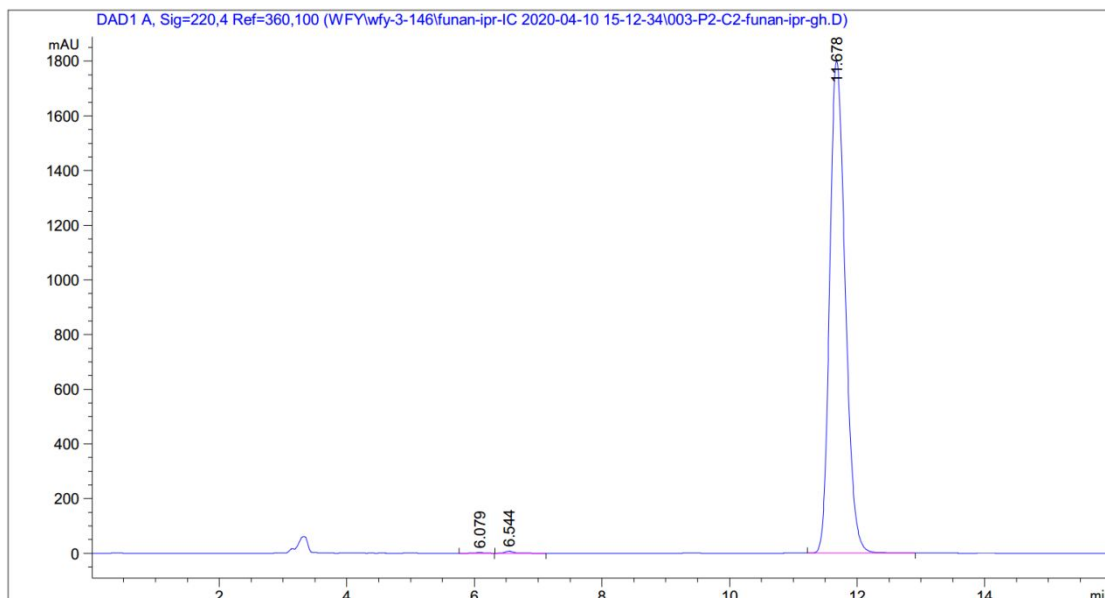
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.960	BB	0.3922	1.40207e4	556.08441	100.0000



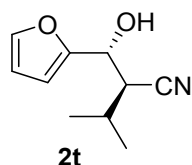
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



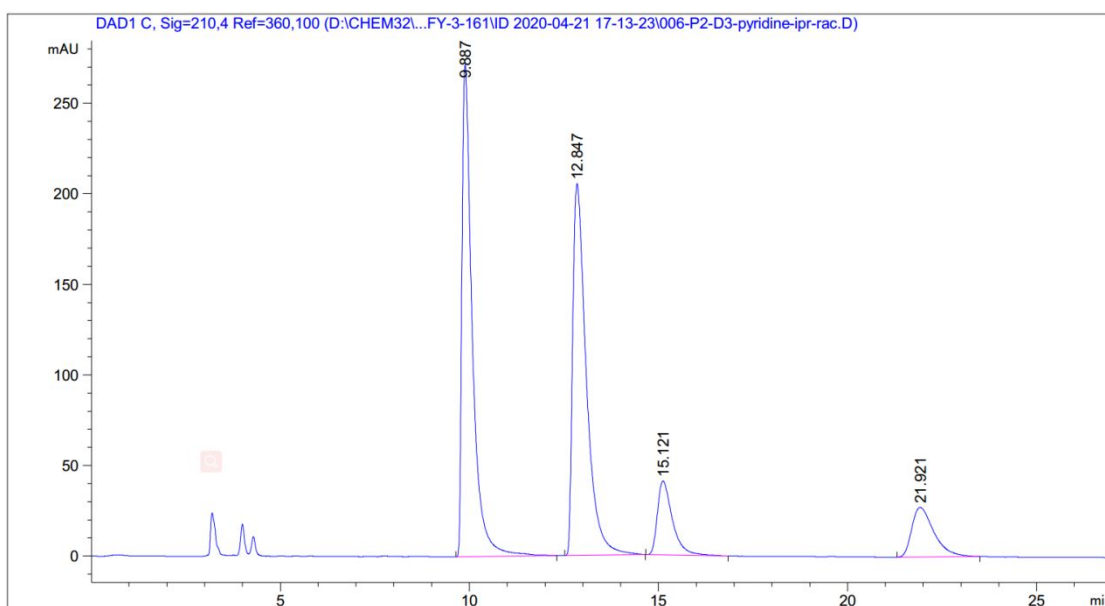
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.082	BV	0.1239	1.31248e4	1629.85120	38.6726
2	6.545	VB	0.1373	1.33320e4	1505.92297	39.2832
3	11.029	BV	0.2308	3742.30273	249.83577	11.0268
4	11.731	VB	0.2496	3739.09009	232.55389	11.0174



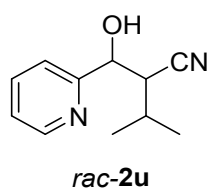
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



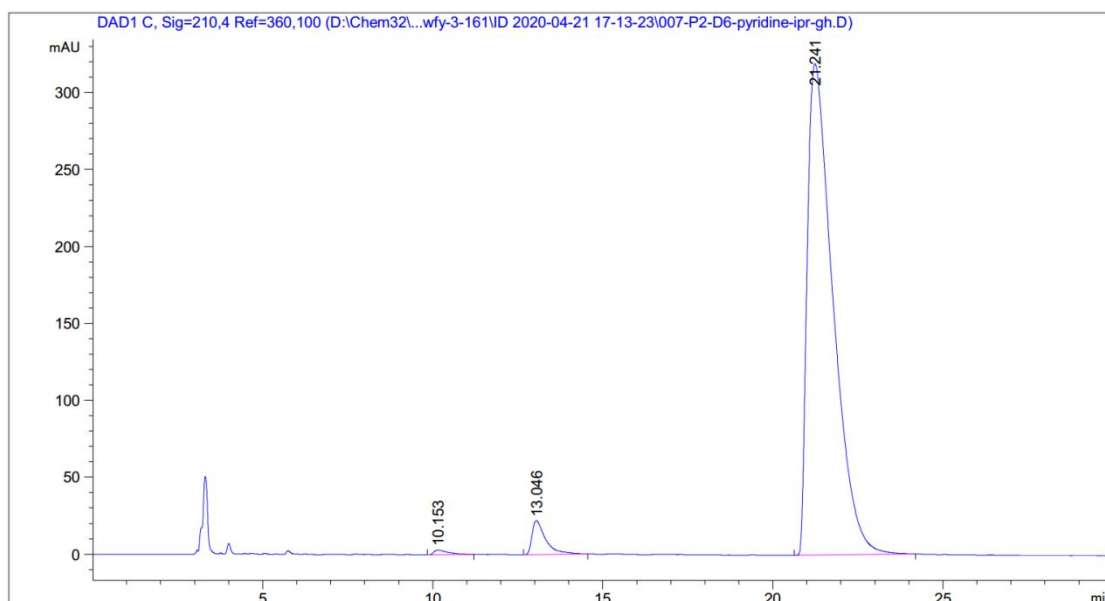
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.079	BB	0.1302	22.42718	2.61248	0.0735
2	6.544	BB	0.1434	67.50278	7.19804	0.2212
3	11.678	BB	0.2632	3.04244e4	1800.02405	99.7053



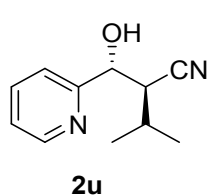
Signal 1: DAD1 C, Sig=210,4 Ref=360,100



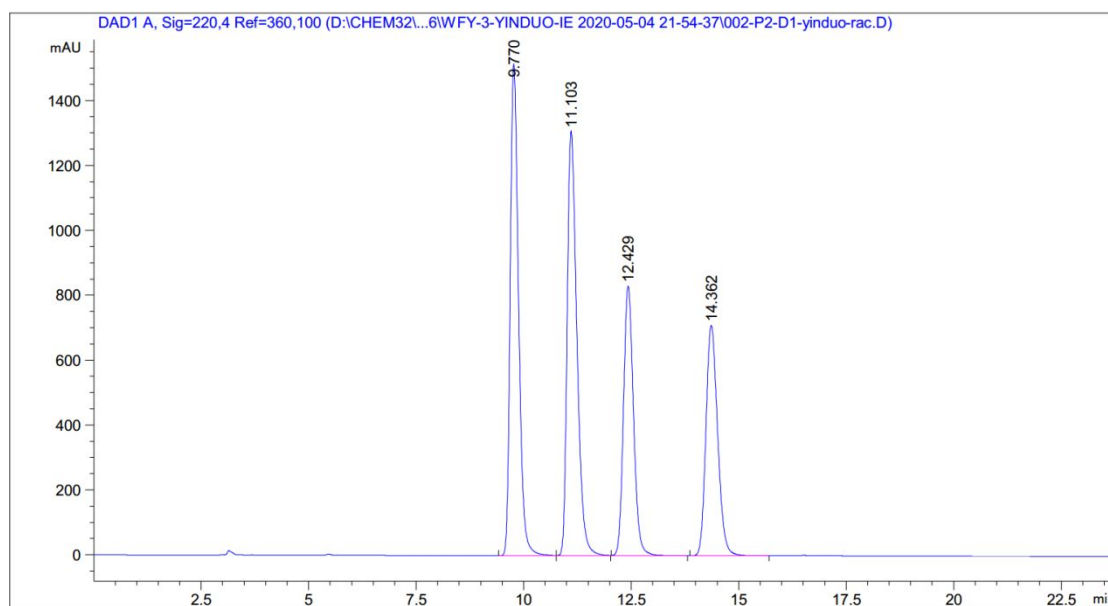
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.887	BB	0.2796	5158.41553	271.56555	41.1046
2	12.847	BB	0.3786	5149.39355	205.29298	41.0327
3	15.121	BB	0.4168	1130.03271	40.83860	9.0046
4	21.921	BB	0.6159	1111.64343	27.36733	8.8581



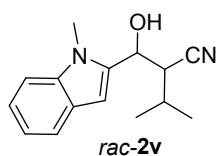
Signal 1: DAD1 C, Sig=210,4 Ref=360,100



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.153	BB	0.3928	88.19749	2.95008	0.5061
2	13.046	BB	0.4056	620.99884	22.11316	3.5633
3	21.241	BB	0.7889	1.67186e4	319.29181	95.9307

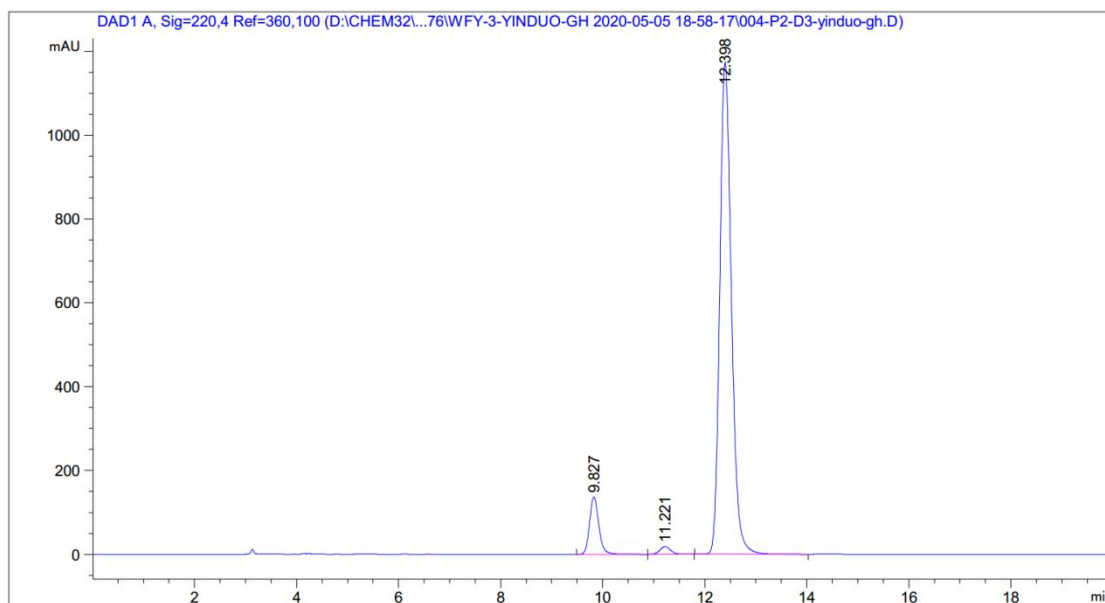


Signal 1: DAD1 A, Sig=220,4 Ref=360,100



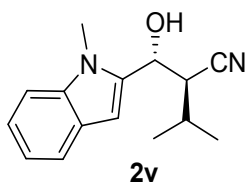
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.770	BB	0.2073	2.04307e4	1515.25439	30.2138
2	11.103	BB	0.2404	2.04278e4	1306.91003	30.2095
3	12.429	BB	0.2500	1.33722e4	829.93390	19.7754
4	14.362	BB	0.2918	1.33897e4	710.56689	19.8013

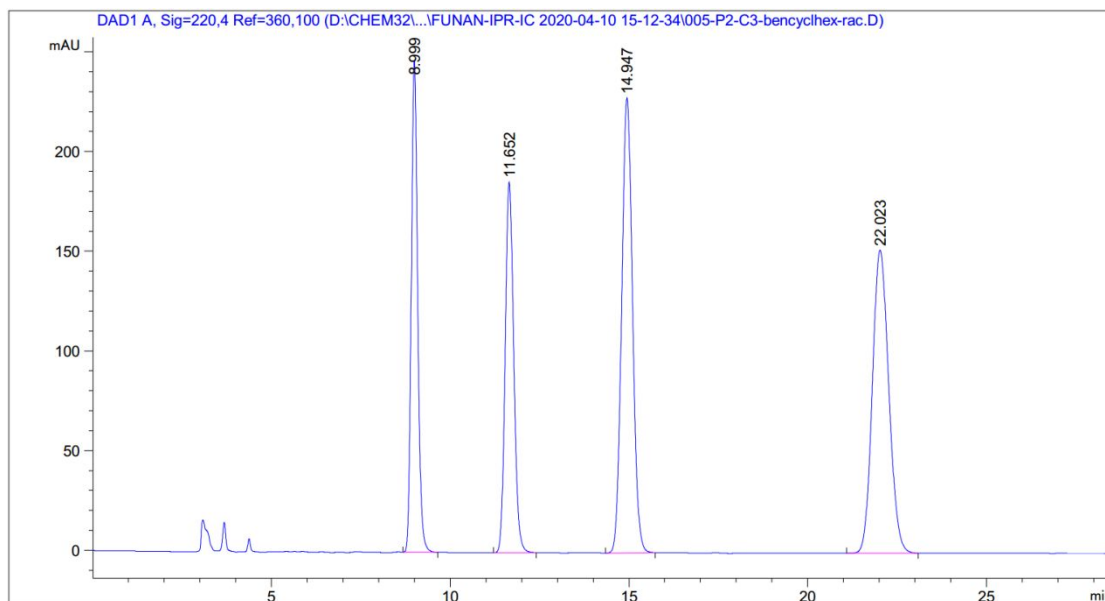
S155



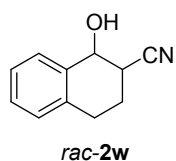
Signal 1: DAD1 A, Sig=220,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.827	BB	0.1928	1718.35608	136.54561	8.3563
2	11.221	BB	0.2262	268.78317	18.42914	1.3071
3	12.398	BB	0.2449	1.85764e4	1172.30872	90.3366

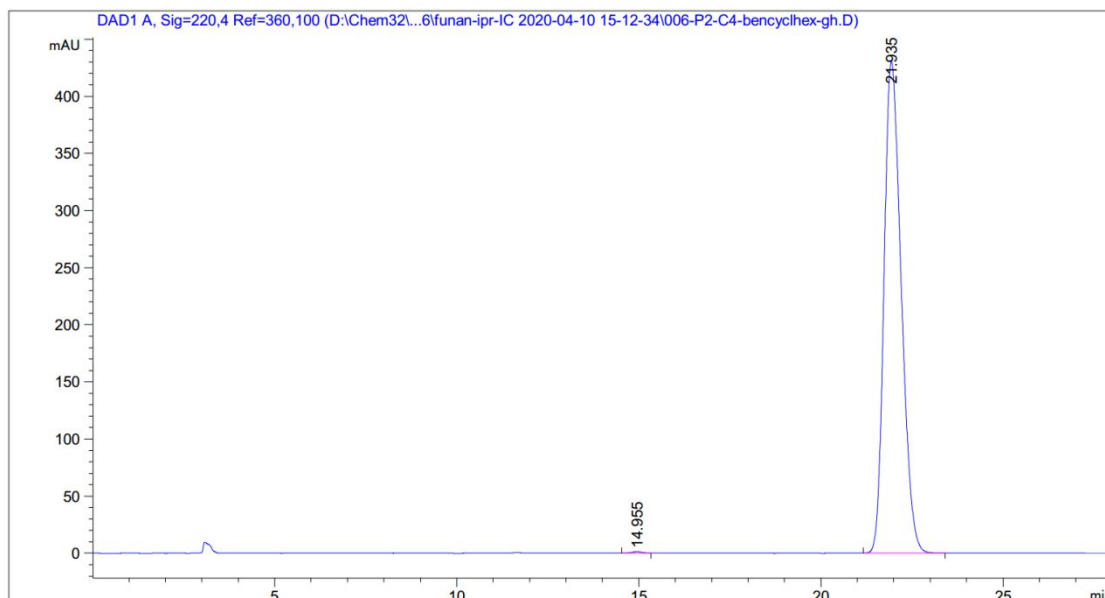




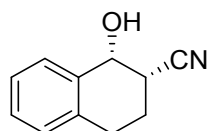
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.999	BB	0.1916	3070.74023	245.97900	19.4299
2	11.652	BB	0.2576	3081.28271	185.72432	19.4967
3	14.947	BB	0.3277	4803.76807	228.07408	30.3956
4	22.023	BB	0.4980	4848.36914	152.03448	30.6778

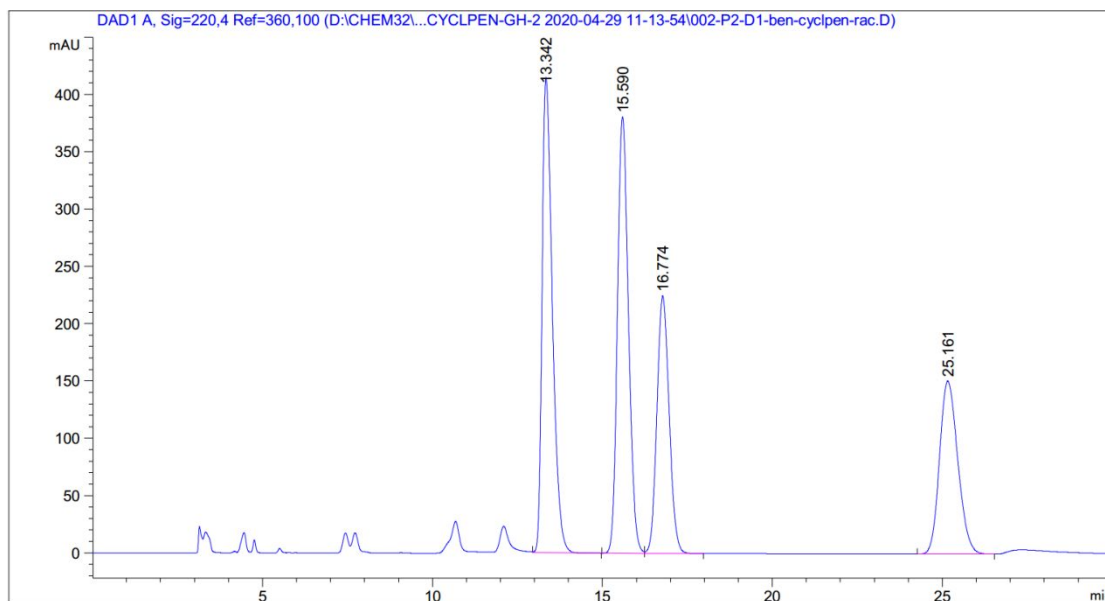


Signal 1: DAD1 A, Sig=220,4 Ref=360,100

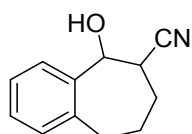


2w

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.955	BB	0.2604	25.32539	1.29339	0.1793
2	21.935	BB	0.5104	1.40977e4	430.13272	99.8207

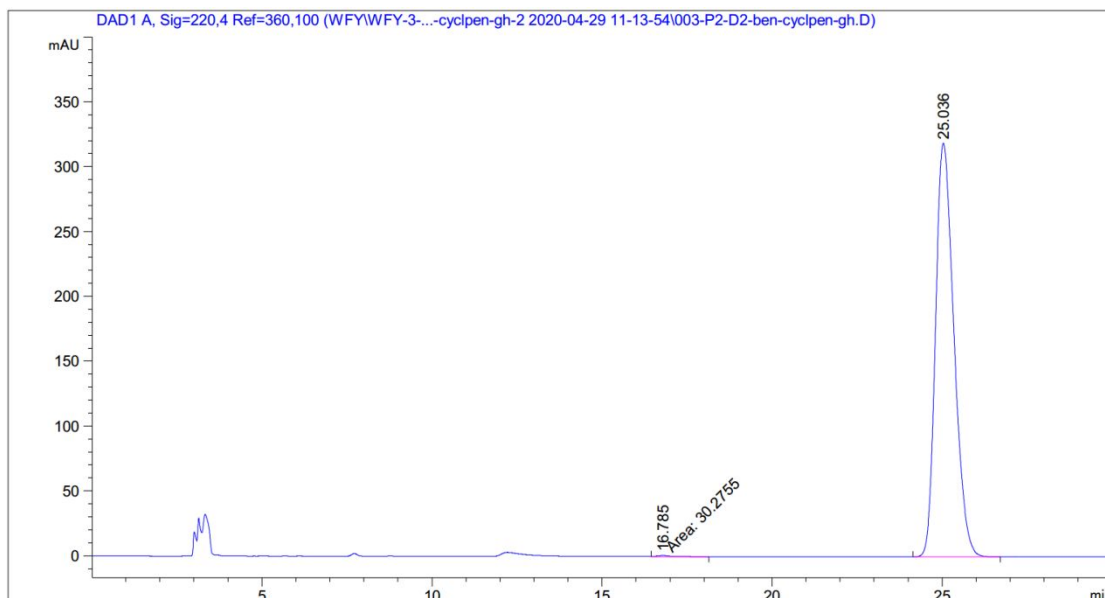


Signal 1: DAD1 A, Sig=220,4 Ref=360,100

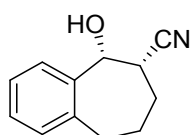


rac-2x

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.342	VB	0.3208	8690.33887	414.22369	30.4958
2	15.590	BV	0.3502	8552.07422	380.58572	30.0107
3	16.774	VB	0.3895	5617.70508	224.83192	19.7135
4	25.161	BB	0.5776	5636.67627	150.96576	19.7800

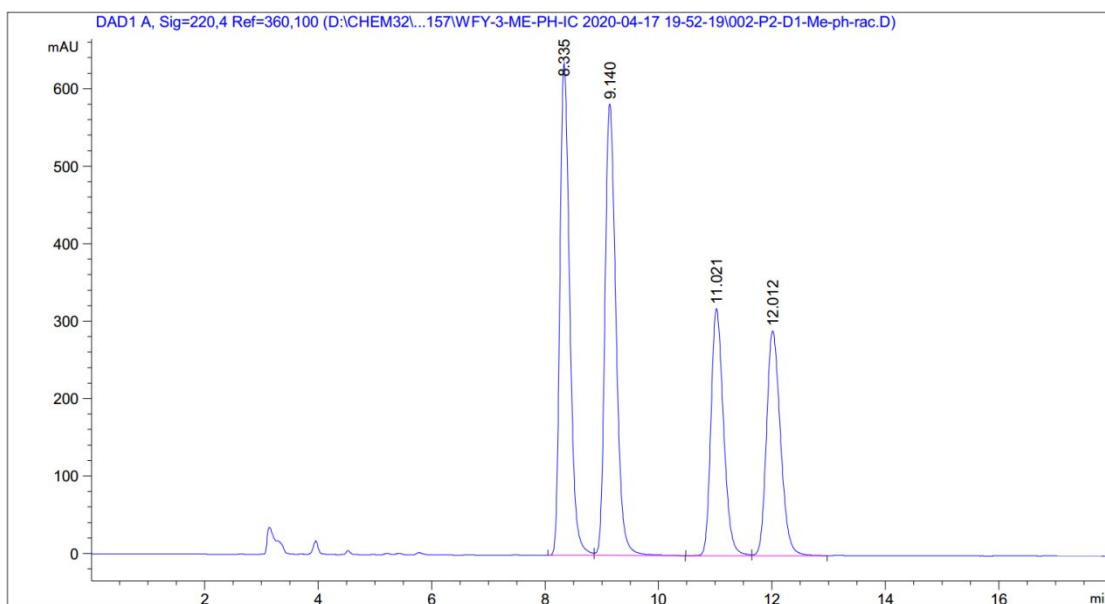


Signal 1: DAD1 A, Sig=220,4 Ref=360,100

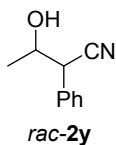


2x

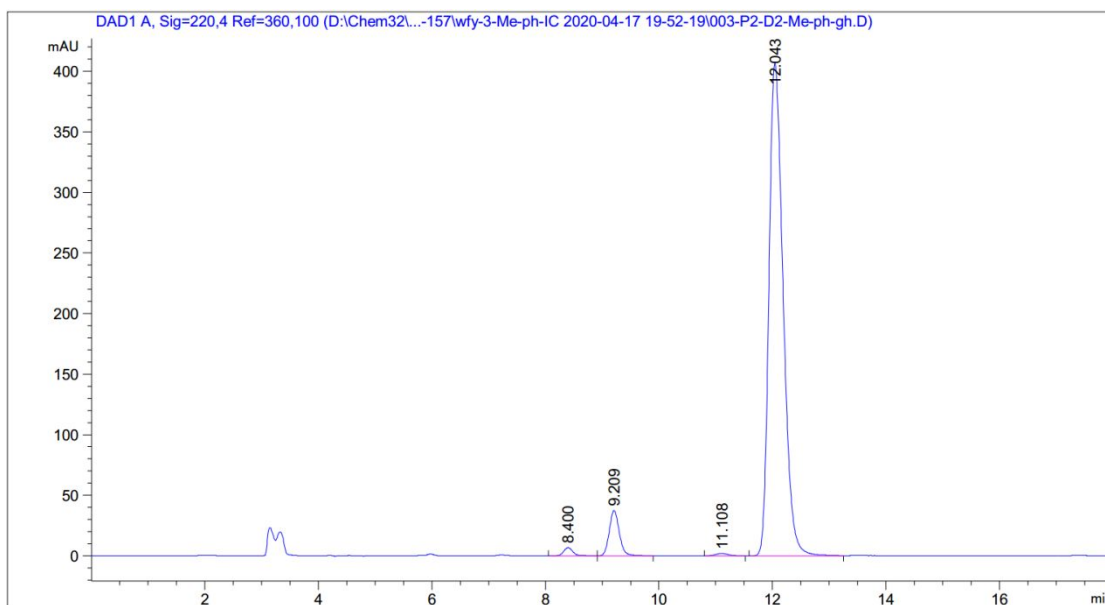
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.785	MM	0.5542	30.27547	9.10512e-1	0.2525
2	25.036	BB	0.5836	1.19590e4	318.80624	99.7475



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

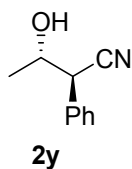


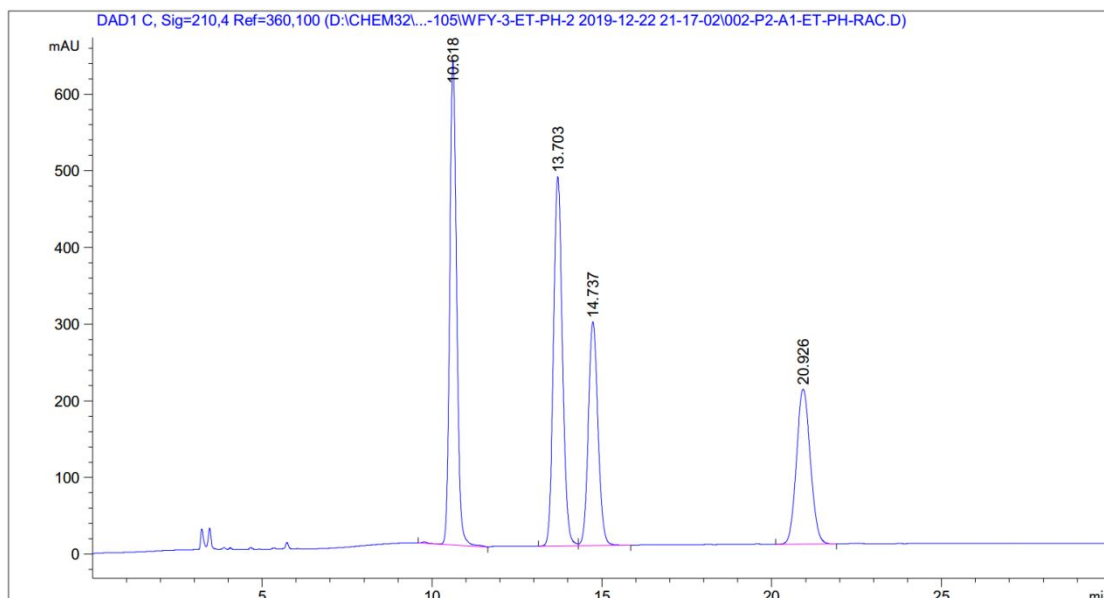
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.335	BV	0.1882	7635.12012	635.41748	30.1394
2	9.140	VB	0.2091	7852.36914	583.09247	30.9970
3	11.021	BV	0.2393	4899.50146	318.87286	19.3406
4	12.012	VB	0.2647	4945.70752	290.39880	19.5230



Signal 1: DAD1 A, Sig=220,4 Ref=360,100

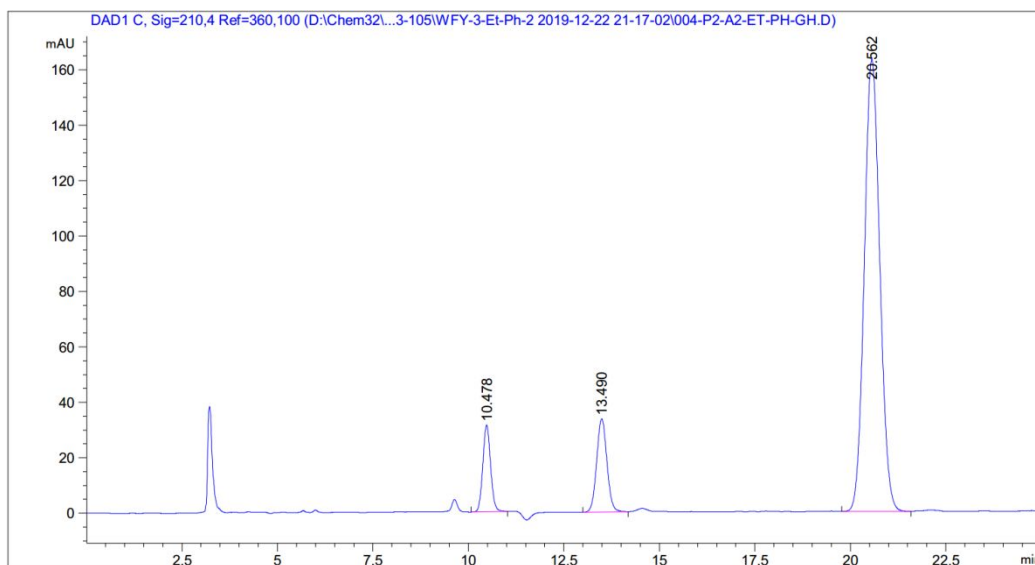
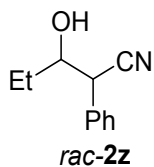
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.400	BB	0.1723	76.85056	6.77885	1.0094
2	9.209	BB	0.1897	459.63934	37.30819	6.0371
3	11.108	BB	0.2383	30.45492	1.99315	0.4000
4	12.043	BB	0.2701	7046.66113	406.83102	92.5535





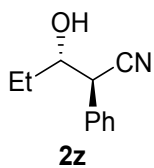
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

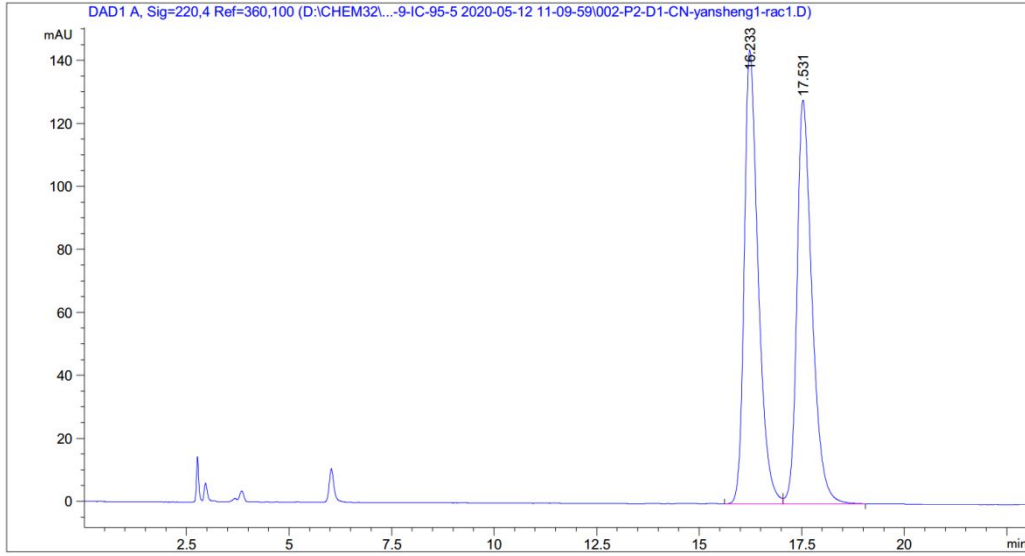
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.618	VB R	0.2164	8907.22168	630.19586	30.4836
2	13.703	BV	0.2841	8837.02832	481.55527	30.2434
3	14.737	VB	0.3059	5747.90088	291.67786	19.6713
4	20.926	BB	0.4406	5727.51855	202.10811	19.6016



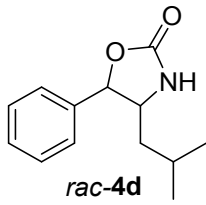
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.478	BB	0.2194	443.20517	31.26807	7.8148
2	13.490	BB	0.2895	627.30200	33.64384	11.0609
3	20.562	BB	0.4409	4600.82275	163.21222	81.1242

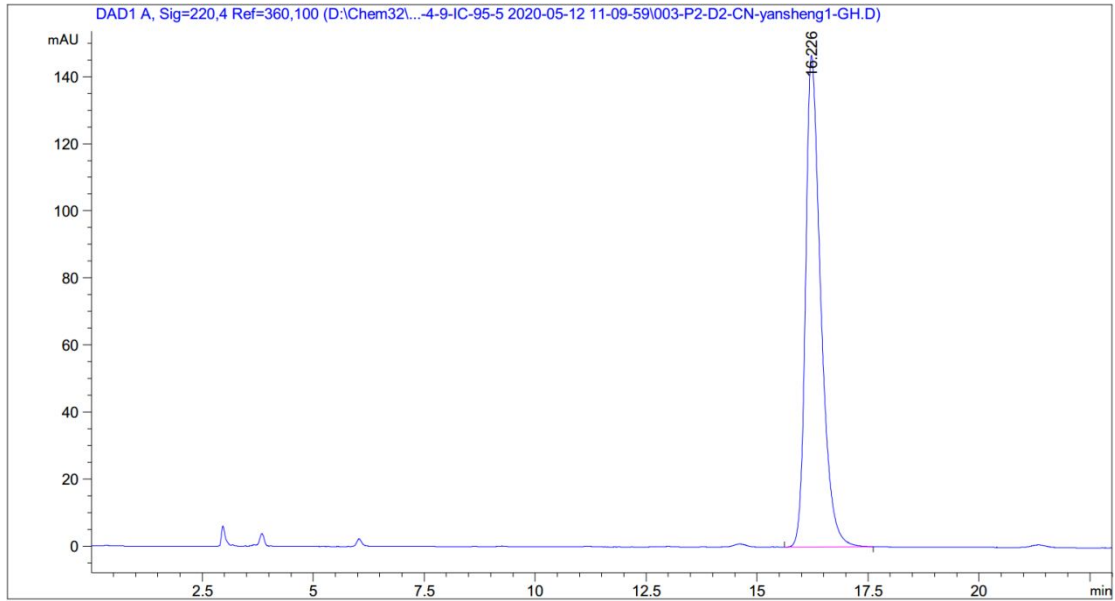




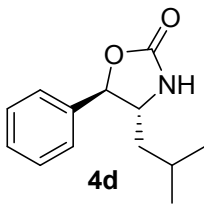
Signal 1: DAD1 A, Sig=220,4 Ref=360,100



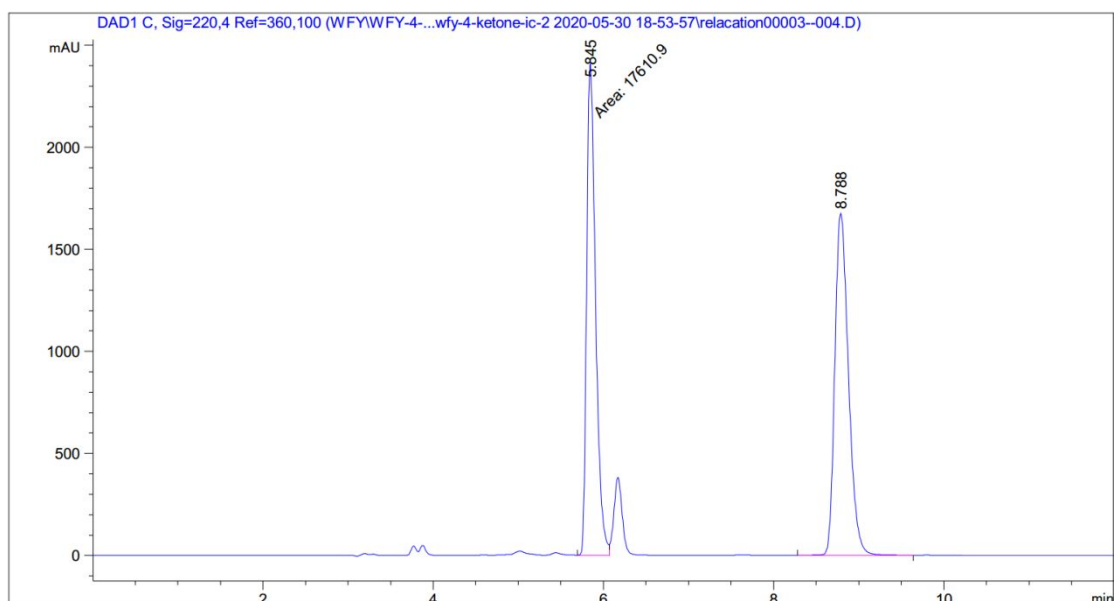
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.233	BV	0.3534	3400.99731	144.08339	50.8713
2	17.531	VB	0.3849	3284.50098	128.18715	49.1287



Signal 1: DAD1 A, Sig=220,4 Ref=360,100



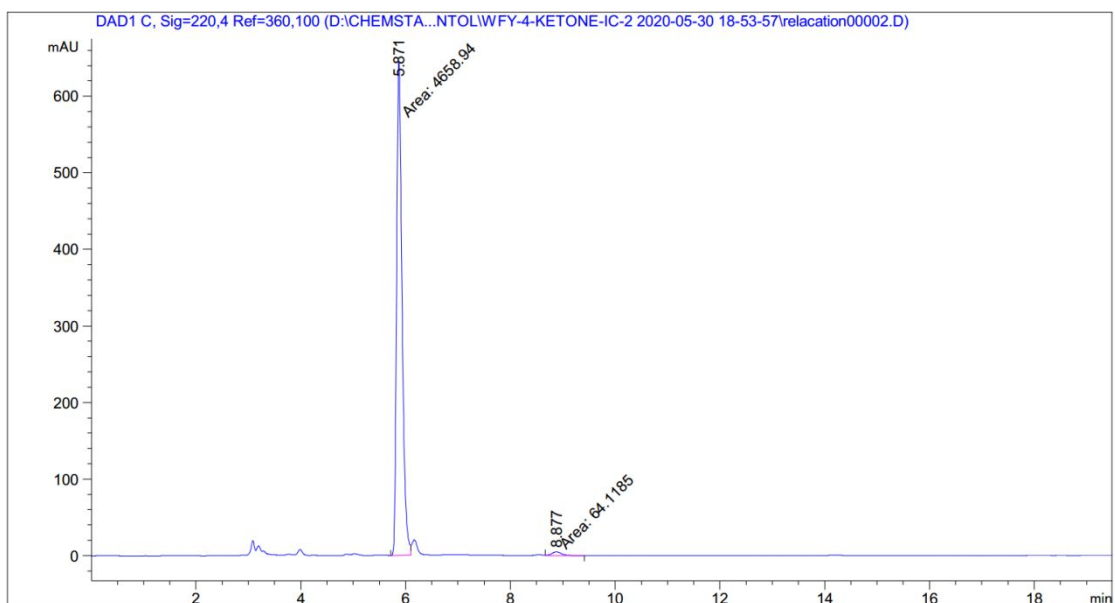
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.226	BB	0.3577	3489.90430	146.61394	100.0000



Signal 1: DAD1 C, Sig=220,4 Ref=360,100

COc1ccc(cc1)C(=O)C(C)CN(C)C
rac-6o

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.845	MF	0.1217	1.76109e4	2411.45508	48.5819
2	8.788	BB	0.1718	1.86390e4	1675.39746	51.4181



Signal 1: DAD1 C, Sig=220,4 Ref=360,100

COc1ccc(cc1)C(=O)C(C)CN(C)C
6o

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.871	MF	0.1205	4658.94385	644.43915	98.6424
2	8.877	FM	0.2151	64.11850	4.96781	1.3576

10. Crystallographic Information

The crystal data of compound **2y** has been deposited in CCDC with number 2013113.

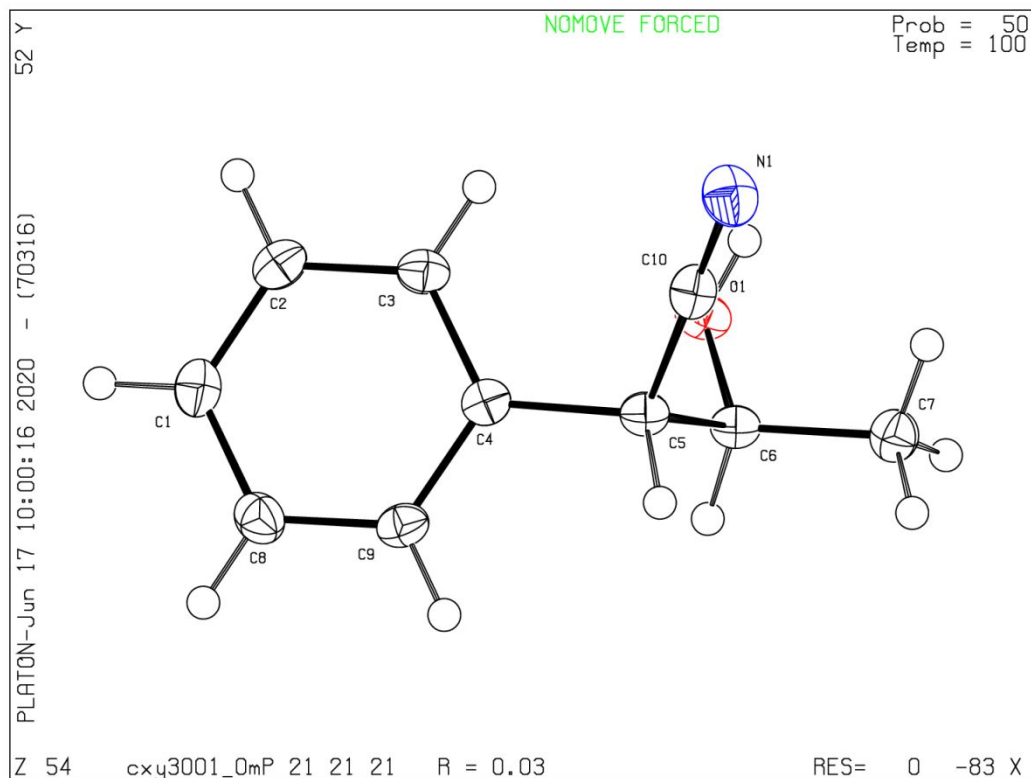


Table S3. Crystal data and structure refinement for cxy3001_0m.

Identification code	cxy3001_0m
Empirical formula	C ₁₀ H ₁₁ NO
Formula weight	161.20
Temperature/K	100.0
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	5.3129(3)
b/Å	9.1009(5)
c/Å	18.1932(9)
α/°	90
β/°	90
γ/°	90
Volume/Å ³	879.68(8)
Z	4
ρ _{calc} /cm ³	1.217

μ/mm^{-1}	0.629
F(000)	344.0
Crystal size/ mm^3	$0.41 \times 0.31 \times 0.29$
Radiation	CuK α ($\lambda = 1.54178$)
2 Θ range for data collection/	9.722 to 144.17
Index ranges	$-6 \leq h \leq 6, -11 \leq k \leq 11, -20 \leq l \leq 22$
Reflections collected	8067
Independent reflections	1716 [$R_{\text{int}} = 0.0228, R_{\text{sigma}} = 0.0224$]
Data/restraints/parameters	1716/0/112
Goodness-of-fit on F^2	1.113
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0250, wR_2 = 0.0644$
Final R indexes [all data]	$R_1 = 0.0251, wR_2 = 0.0644$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.16/-0.11
Flack parameter	0.02(5)

Table S4. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for cxy3001_0m. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	x	y	z	$U(\text{eq})$
O1	1658.5(17)	4938.0(11)	5773.7(5)	22.5(3)
N1	6162(3)	8150.6(14)	5488.7(7)	29.1(3)
C1	925(3)	7114.0(16)	8251.1(8)	24.3(3)
C2	398(3)	7724.5(16)	7569.7(8)	23.9(3)
C3	1866(3)	7366.7(15)	6963.9(8)	21.0(3)
C4	3885(2)	6400.5(14)	7035.8(7)	18.2(3)
C5	5438(2)	5931.4(14)	6375.0(7)	18.7(3)
C6	4200(2)	4629.2(14)	5953.6(7)	18.7(3)
C7	5711(3)	4171.6(16)	5283.5(7)	22.9(3)
C8	2936(3)	6157.7(15)	8327.2(7)	24.6(3)
C9	4411(3)	5802.4(15)	7723.5(7)	20.9(3)
C10	5866(3)	7180.9(15)	5876.4(7)	21.6(3)

The crystal data of compound **3p** has been deposited in CCDC with number 2013116.

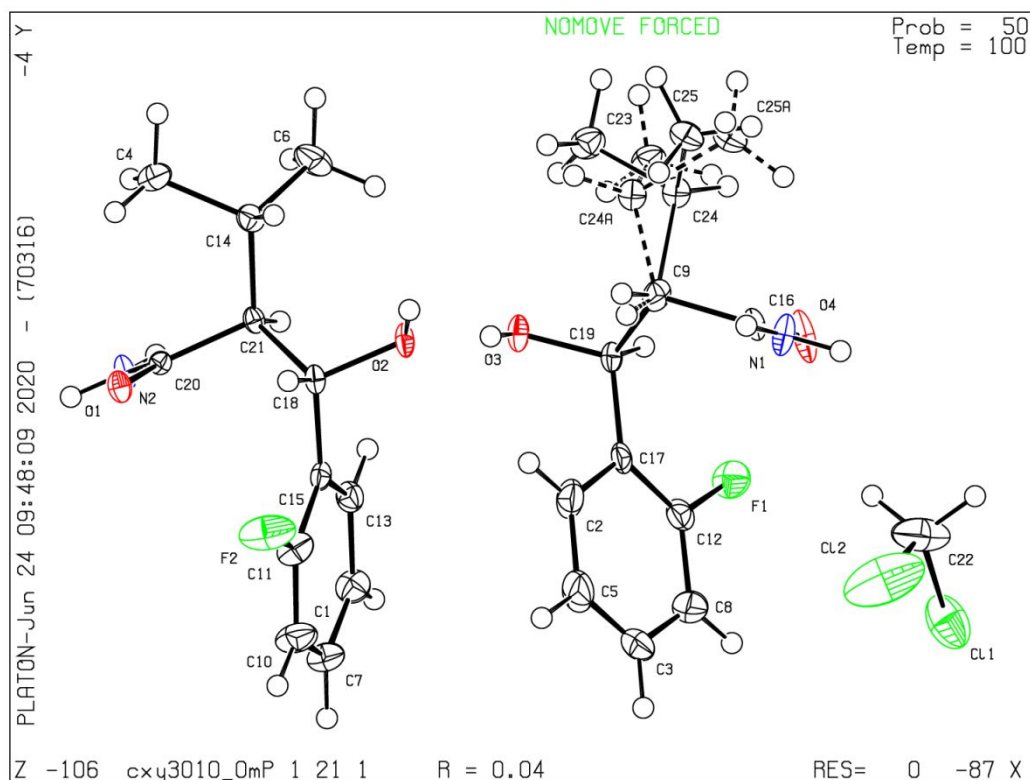


Table S5. Crystal data and structure refinement for cxy3010_0m.

Identification code	cxy3010_0m
Empirical formula	C _{12.5} H ₁₇ ClFNO ₂
Formula weight	267.72
Temperature/K	100.0
Crystal system	monoclinic
Space group	P2 ₁
a/Å	10.8748(3)
b/Å	9.6587(2)
c/Å	12.8523(3)
α/°	90
β/°	101.2930(10)
γ/°	90
Volume/Å ³	1323.82(6)
Z	4
ρ _{calc} /cm ³	1.343
μ/mm ⁻¹	2.615
F(000)	564.0

Crystal size/mm ³	0.32 × 0.26 × 0.25
Radiation	CuKα (λ = 1.54178)
2θ range for data collection/°	7.014 to 144.436
Index ranges	-13 ≤ h ≤ 13, -11 ≤ k ≤ 11, -15 ≤ l ≤ 15
Reflections collected	21243
Independent reflections	5043 [R _{int} = 0.0331, R _{sigma} = 0.0298]
Data/restraints/parameters	5043/5/334
Goodness-of-fit on F ²	1.026
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0417, wR ₂ = 0.1124
Final R indexes [all data]	R ₁ = 0.0420, wR ₂ = 0.1128
Largest diff. peak/hole / e Å ⁻³	0.41/-0.40
Flack parameter	-0.006(17)

Table S6. Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³) for cxy3010_0m. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Atom	x	y	z	U(eq)
Cl1	427.2(11)	3619.1(11)	7949.9(8)	49.7(3)
Cl2	936.4(13)	6465.5(13)	7470.2(17)	81.1(5)
F1	2672.7(17)	2282(2)	5908.5(15)	30.6(4)
O1	4409.8(17)	6437(2)	-531.9(14)	15.7(4)
O2	4754.2(18)	6199(2)	2813.4(14)	17.7(4)
O3	4840.9(19)	3795(2)	4024.2(14)	19.0(4)
F2	2187.4(18)	7693(2)	720(2)	41.4(6)
O4	4484(2)	3991(2)	7239.1(15)	29.0(5)
N2	4706(2)	4125(3)	-513.4(17)	16.9(5)
N1	4418(2)	6317(3)	7100.4(18)	20.9(5)
C1	1546(3)	3641(3)	1365(2)	24.3(6)
C2	2445(3)	5216(4)	4141(2)	30.4(7)
C3	396(3)	4603(5)	4425(3)	40.8(10)
C4	7275(3)	5993(4)	500(2)	26.6(7)
C5	1156(4)	5424(5)	3950(3)	42.8(10)
C6	7383(3)	4978(4)	2300(3)	28.7(7)
C7	566(3)	4469(4)	868(3)	26.7(7)
C8	909(3)	3546(4)	5093(3)	32.6(7)
C9	5159(3)	4986(3)	5743(2)	21.4(6)
C10	796(3)	5846(4)	649(3)	30.8(7)
C11	1997(3)	6354(3)	933(2)	24.0(6)
C12	2195(3)	3345(3)	5263(2)	21.4(6)

C13	2755(3)	4172(3)	1629(2)	19.9(5)
C14	6611(2)	5890(3)	1448(2)	17.0(5)
C15	3009(2)	5554(3)	1420.6(19)	15.1(5)
C16	4652(2)	5068(3)	6759(2)	15.8(5)
C17	2999(3)	4154(3)	4810.5(19)	18.1(5)
C18	4314(2)	6167(3)	1680.4(19)	13.9(5)
C19	4407(2)	3891(3)	5003(2)	15.9(5)
C20	4744(2)	5352(3)	-40.8(19)	12.3(5)
C21	5234(2)	5341(3)	1148.2(18)	12.3(5)
C22	1592(4)	4891(5)	7965(4)	50.8(12)
C23	7363(5)	4181(7)	5415(5)	24.8(8)
C24	6579(5)	4403(6)	6267(4)	17.5(8)
C25	7270(5)	5977(7)	6619(5)	22.5(9)
C24A	6567(5)	4974(6)	5783(5)	17.5(8)
C25A	7226(6)	5448(7)	7082(5)	22.5(9)
C23A	7081(6)	3511(7)	6020(5)	24.8(8)

The crystal data of compound **2b** has been deposited in CCDC with number 2013520.

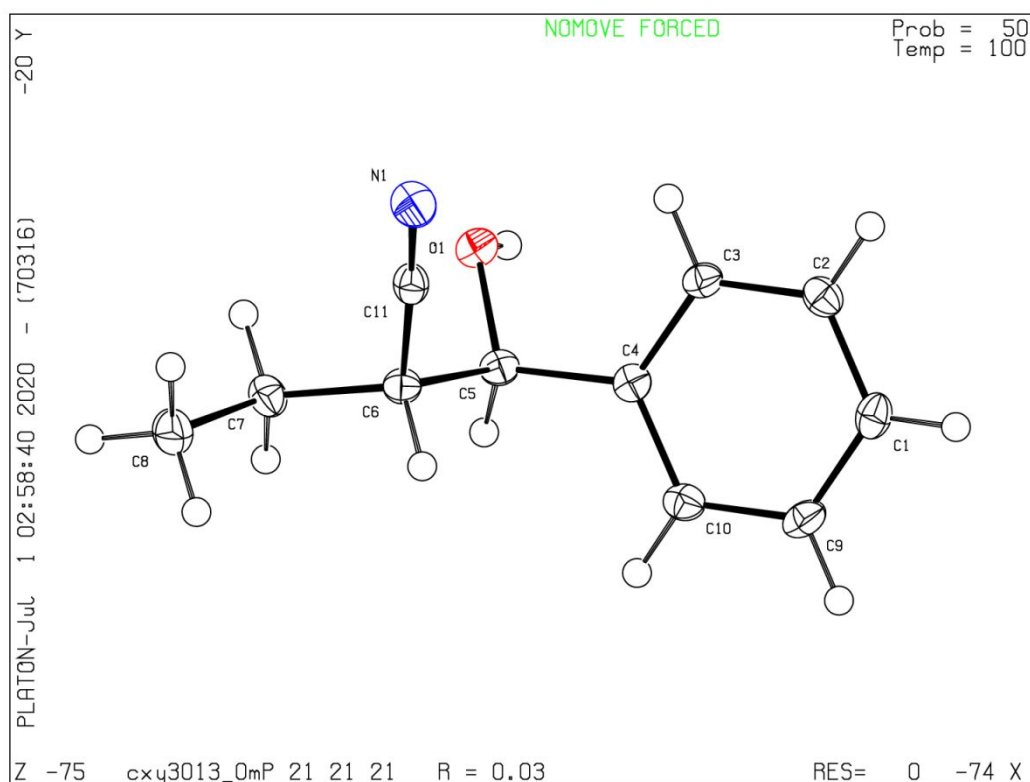


Table S7. Crystal data and structure refinement for cxy3013_0m.

Identification code	cxy3013_0m
Empirical formula	C ₁₁ H ₁₃ NO
Formula weight	175.22
Temperature/K	100.0
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	5.3989(2)
b/Å	12.0855(5)
c/Å	14.8743(6)
α/°	90
β/°	90
γ/°	90
Volume/Å ³	970.52(7)
Z	4
ρ _{calc} /cm ³	1.199
μ/mm ⁻¹	0.608
F(000)	376.0

Crystal size/mm ³	0.34 × 0.31 × 0.28
Radiation	CuKα (λ = 1.54178)
2θ range for data collection/°	9.428 to 144.266
Index ranges	-6 ≤ h ≤ 6, -14 ≤ k ≤ 13, -15 ≤ l ≤ 18
Reflections collected	7903
Independent reflections	1863 [R _{int} = 0.0316, R _{sigma} = 0.0272]
Data/restraints/parameters	1863/0/120
Goodness-of-fit on F ²	1.099
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0279, wR ₂ = 0.0692
Final R indexes [all data]	R ₁ = 0.0280, wR ₂ = 0.0693
Largest diff. peak/hole / e Å ⁻³	0.15/-0.14
Flack parameter	-0.01(6)

Table S8. Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³) for cxy3013_0m. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	U(eq)
O1	9635.6(19)	5771.5(8)	2386.9(7)	17.8(2)
N1	7904(2)	8604.4(10)	2518.5(9)	23.1(3)
C1	7274(3)	6085.4(11)	5666.5(10)	19.3(3)
C2	9208(3)	6518.6(12)	5165.1(10)	18.6(3)
C3	9226(3)	6398.7(12)	4234.2(10)	16.7(3)
C4	7300(3)	5851.5(10)	3797.8(9)	15.0(3)
C5	7237(3)	5746.6(11)	2782.7(9)	15.8(3)
C6	5709(3)	6682.8(11)	2339.0(9)	15.7(3)
C7	5211(3)	6463.6(12)	1334.7(9)	19.5(3)
C8	3423(3)	7289.5(13)	915.2(10)	24.7(4)
C9	5345(3)	5533.6(12)	5236.7(10)	19.9(3)
C10	5362(3)	5420.1(12)	4308.8(10)	18.0(3)
C11	6958(3)	7757.6(12)	2456.5(9)	17.0(3)

The crystal data of compound **4d** has been deposited in CCDC with number 2013878.

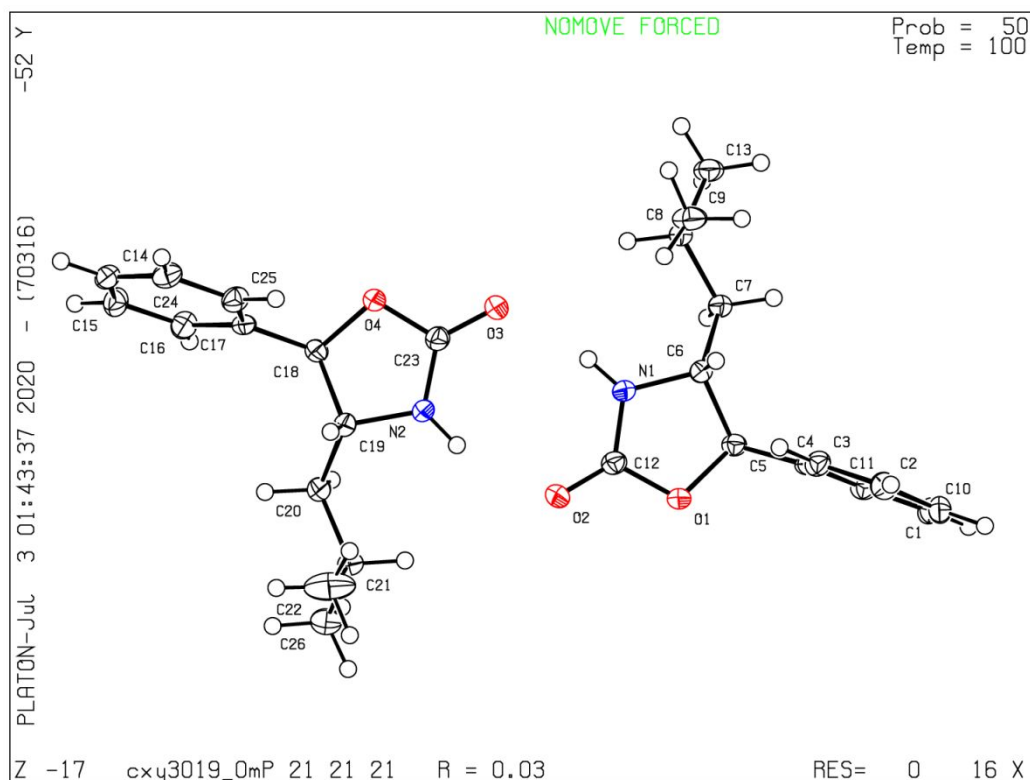


Table S9. Crystal data and structure refinement for cxy3019_0m.

Identification code	cxy3019_0m
Empirical formula	C ₁₃ H ₁₇ NO ₂
Formula weight	219.27
Temperature/K	100.0
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	5.75740(10)
b/Å	19.2528(5)
c/Å	22.0973(5)
α/°	90
β/°	90
γ/°	90
Volume/Å ³	2449.40(9)
Z	8
ρ _{calc} /cm ³	1.189
μ/mm ⁻¹	0.640
F(000)	944.0

Crystal size/mm ³	0.32 × 0.29 × 0.28
Radiation	CuKα (λ = 1.54178)
2θ range for data collection/°	6.088 to 143.97
Index ranges	-7 ≤ h ≤ 6, -23 ≤ k ≤ 23, -25 ≤ l ≤ 26
Reflections collected	33200
Independent reflections	4729 [R _{int} = 0.0315, R _{sigma} = 0.0213]
Data/restraints/parameters	4729/0/294
Goodness-of-fit on F ²	1.075
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0264, wR ₂ = 0.0650
Final R indexes [all data]	R ₁ = 0.0267, wR ₂ = 0.0652
Largest diff. peak/hole / e Å ⁻³	0.18/-0.20
Flack parameter	-0.01(3)

Table S10. Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³) for cxy3019_0m. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Atom	x	y	z	U(eq)
O1	7338.0(19)	4164.5(5)	4188.2(5)	22.1(2)
O2	4569(2)	4715.2(6)	3651.1(5)	26.7(3)
O3	4752(2)	6544.9(6)	4031.3(5)	26.1(3)
O4	2669.8(19)	7182.0(5)	3378.6(5)	21.8(2)
N1	6963(2)	5297.1(7)	4317.9(6)	23.7(3)
N2	2919(2)	6054.9(6)	3203.7(6)	23.0(3)
C1	10454(3)	2753.4(8)	5868.2(8)	26.0(3)
C2	8406(3)	3134.5(8)	5889.4(7)	24.9(3)
C3	8037(3)	3669.2(8)	5480.5(7)	22.4(3)
C4	9716(3)	3830.2(8)	5046.1(7)	18.6(3)
C5	9276(3)	4383.3(8)	4578.7(7)	19.4(3)
C6	8481(3)	5095.3(7)	4814.0(7)	18.6(3)
C7	10402(3)	5614.3(8)	4941.8(7)	19.9(3)
C8	9506(3)	6338.0(8)	5127.9(7)	22.0(3)
C9	7741(3)	6297.6(9)	5640.0(8)	30.6(4)
C10	12140(3)	2914.4(8)	5442.8(8)	26.2(4)
C11	11775(3)	3452.8(8)	5033.9(7)	21.9(3)
C12	6145(3)	4743.7(8)	4020.4(7)	21.4(3)
C13	11532(3)	6805.1(8)	5312.5(8)	26.3(4)
C14	-3595(3)	8515.8(8)	2323.3(8)	24.0(3)

C15	-1807(3)	8388.6(8)	1919.5(7)	26.8(4)
C16	-49(3)	7926.0(8)	2069.3(7)	24.3(3)
C17	-86(3)	7575.6(8)	2619.8(7)	19.1(3)
C18	1823(3)	7073.3(8)	2763.9(6)	19.6(3)
C19	1220(3)	6294.4(8)	2758.9(7)	20.4(3)
C20	1504(3)	5965.4(8)	2139.2(7)	23.2(3)
C21	1124(3)	5178.7(8)	2115.6(8)	28.1(4)
C22	-1310(5)	4967.0(12)	2292.3(12)	56.8(6)
C23	3554(3)	6571.8(8)	3577.4(7)	21.6(3)
C24	-3616(3)	8177.3(8)	2875.7(8)	25.1(3)
C25	-1889(3)	7704.6(8)	3025.0(7)	23.2(3)
C26	1714(4)	4913.0(10)	1484.0(8)	40.6(5)

The crystal data of compound **2o** has been deposited in CCDC with number 2015445.

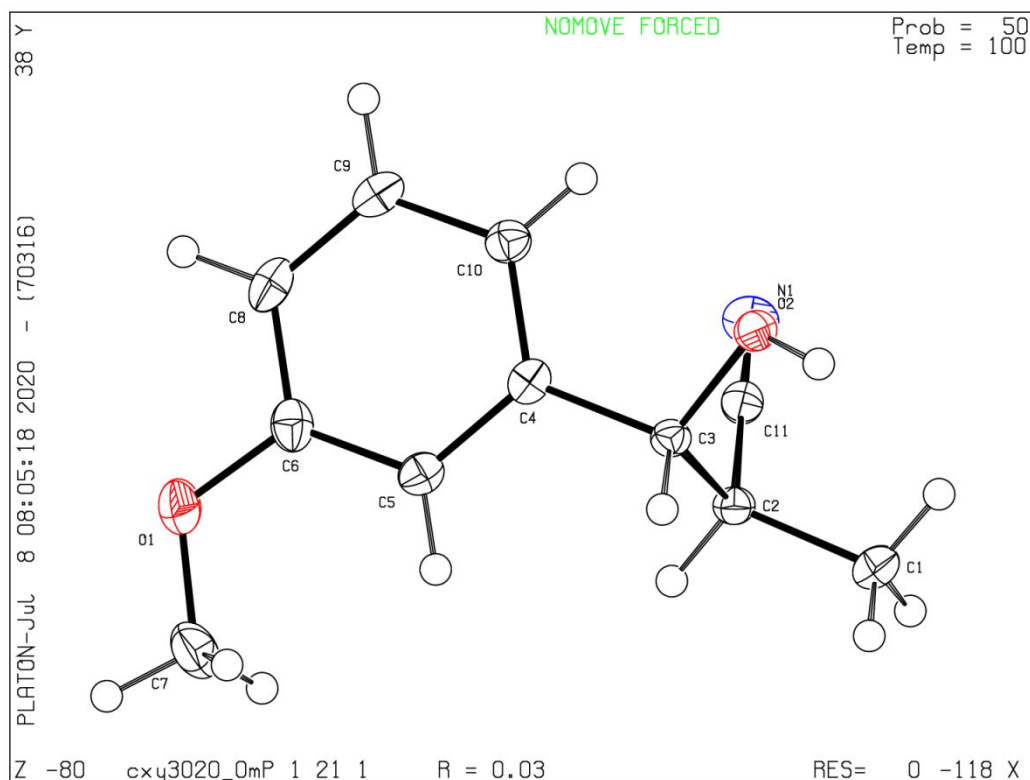


Table S11. Crystal data and structure refinement for cxy3020_0m.

Identification code	cxy3020_0m
Empirical formula	C ₁₁ H ₁₃ NO ₂
Formula weight	191.22
Temperature/K	100.0
Crystal system	monoclinic
Space group	P2 ₁
a/Å	5.6863(2)
b/Å	10.3963(3)
c/Å	8.8733(3)
α /°	90
β /°	100.3130(10)
γ /°	90
Volume/Å ³	516.08(3)
Z	2
ρ_{calc} /cm ³	1.231
μ /mm ⁻¹	0.689
F(000)	204.0

Crystal size/mm ³	0.28 × 0.25 × 0.24
Radiation	CuKα (λ = 1.54178)
2θ range for data collection/°	10.132 to 136.282
Index ranges	-5 ≤ h ≤ 6, -12 ≤ k ≤ 12, -10 ≤ l ≤ 10
Reflections collected	9079
Independent reflections	1836 [R _{int} = 0.0311, R _{sigma} = 0.0245]
Data/restraints/parameters	1836/1/131
Goodness-of-fit on F ²	1.064
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0253, wR ₂ = 0.0655
Final R indexes [all data]	R ₁ = 0.0255, wR ₂ = 0.0656
Largest diff. peak/hole / e Å ⁻³	0.16/-0.12
Flack parameter	0.05(8)

Table S12. Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³) for cxy3020_0m. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Atom	x	y	z	U(eq)
O1	4315(2)	4119.4(14)	3112.8(14)	29.4(3)
O2	11200.2(18)	6083.0(11)	8651.0(13)	18.3(3)
N1	7831(3)	3576.8(16)	10156.2(18)	24.9(4)
C1	7184(3)	6876.1(17)	10180(2)	21.5(4)
C2	7022(3)	5853.7(15)	8921.0(19)	16.8(4)
C3	8825(3)	6093.2(15)	7828.8(17)	15.4(3)
C4	8564(3)	5077.0(15)	6583.6(18)	16.7(4)
C5	6559(3)	5119.7(17)	5413.8(19)	19.0(4)
C6	6201(3)	4160.2(18)	4305(2)	21.4(4)
C7	2657(4)	5161(2)	2967(2)	30.4(4)
C8	7840(3)	3154.7(17)	4365(2)	23.5(4)
C9	9817(3)	3119.2(17)	5521(2)	23.1(4)
C10	10204(3)	4081.5(16)	6636.3(19)	19.3(4)
C11	7452(3)	4567.0(16)	9606.8(19)	17.3(4)