Supporting Information

Pd(II)-catalyzed Enantioselective Arylation of Unbiased Methylene C(sp^3)–H Bonds Enabled by 3,3'-F_2-BINOL Ligand

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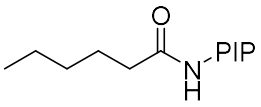
1. General Information

All the materials and solvent were purchased from commercial suppliers and used without additional purification. $Pd(OAc)_2$, $PdBr_2$ was purchased from Laajoo (China), PdI_2 and $Pd(hfac)_2$ was purchased form Strem. (S)-BIONL and derivatives were purchased from Laajoo (China) and Daicel (China). NMR spectra were recorded on a Bruke Avance operating for ^1H NMR at 400 MHz, ^{13}C NMR at 100 MHz, ^{19}F NMR at 376 MHz using TMS as internal standard. The peaks were internally referenced to residual undeuterated chloroform in $CDCl_3$ (δ H = 7.26 ppm, δ C = 77.16 ppm). The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, brs = broad singlet. Mass spectroscopy data of the products were collected on an HRMS-TOF instrument The ee value was determined on Shimadzu HPLC using CHIRALPAK column with hexane and 2-propanol as eluent, Wavelength = 254 nm.

2. Experiment Details and Characterization Data

2.1 Preparation of Substrates.



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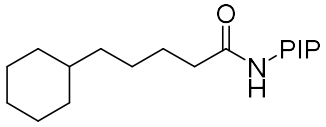

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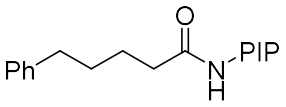

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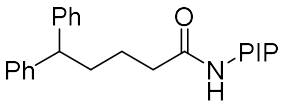

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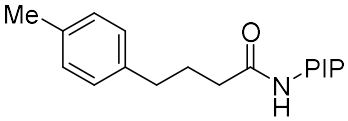

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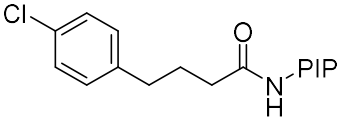

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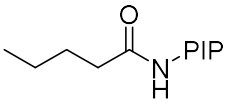

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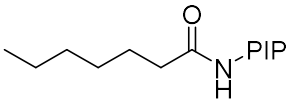

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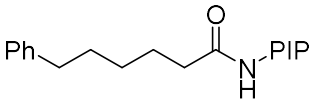

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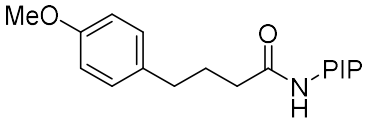

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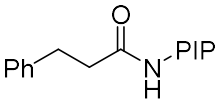

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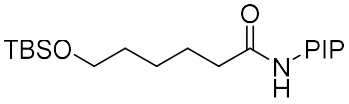
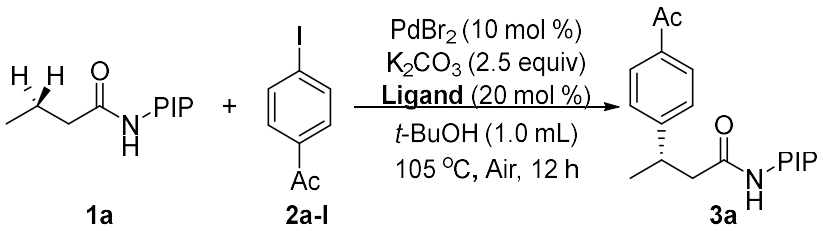


1m

All the aliphatic amides were known compounds and prepared according to the literature procedures.[1,2]

2.2 Optimization of Reaction Conditions

Table S1. Screening of Ligands[a]



entry	Ligand	yield %[b]	ee %[b]
1	**L1**	55	85
2	**L2**	52	78
3	**L3**	52	79
4	**L4**	24	70
5	**L5**	14	54
6	**L6**	37	36
7	**L7**	23	80
8	**L8**	48	85

[a]Reaction conditions: **1a** (0.10 mmol), **2a** (2.0 equiv), $PdBr_2$ (10 mol %), K_2CO_3 (2.5 equiv), **Ligand** (20 mol %), *t*-BuOH (1.0 mL), 12 h, 105 °C, air atmosphere, unless noted otherwise. [a] ^1H NMR yield using 1,3,5-Trimethoxybenzene as internal standard. The ee value was determined by chiral HPLC.

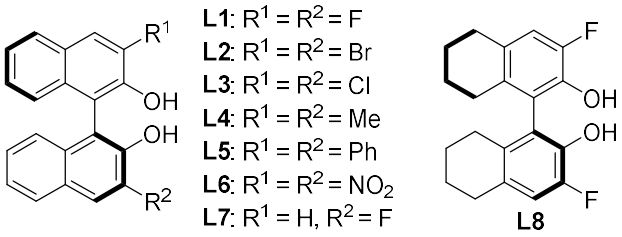
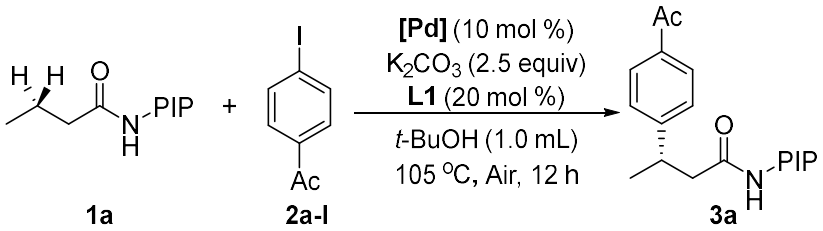


Table S2. Screening of Pd catalysts[a]

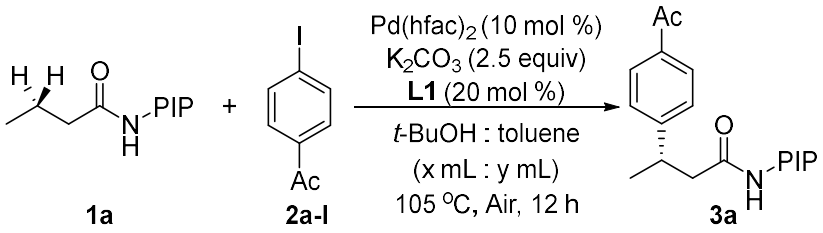


1a **2a-I** **3a**

entry	**[Pd]**	yield %[b]	ee %[b]
1	PdI_2	57	82
2	$PdBr_2$	55	85
3	$Pd(hfac)_2$	59	86
4	$Pd(TFA)_2$	55	83
5	$Pd(OAc)_2$	58	80
6	$Pd(dba)_2$	53	80

[a]Reaction conditions: **1a** (0.10 mmol), **2a** (2.0 equiv), **[Pd]** (10 mol %), K_2CO_3 (2.5 equiv), **L1** (20 mol %), *t*-BuOH (1.0 mL), 12 h, 105 °C, air atmosphere, unless noted otherwise. [b] ^1H NMR yield using 1,3,5-Trimethoxybenzene as internal standard. [b] The ee value was determined by chiral HPLC.

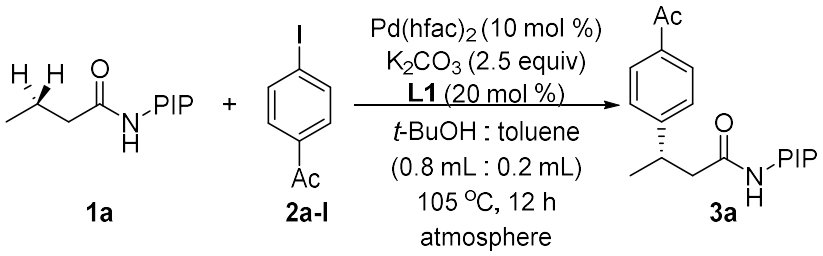
Table S3. Screening of solvents[a]



entry	*t*-BuOH : toluene (mL : mL)	yield (%)[b]	Ee[b]
1	0: 1.0	43	77
2	0.1: 0.9	53	83
3	0.2: 0.8	60	84
4	0.3: 0.7	66	83
5	0.4: 0.6	65	86
6	0.5: 0.5	54	82
7	0.6: 0.4	68	84
8	0.7: 0.3	68	86
9	0.8: 0.2	70	89
10	0.9: 0.1	66	84
11	1.0: 0	59	86

[a]Reaction conditions: **1a** (0.10 mmol), **2a** (2.0 equiv), $Pd(hfac)_2$ (10 mol %), K_2CO_3 (2.5 equiv), **L1** (20 mol%), *t*-BuOH : toluene (1.0 mL), 12 h, 105 °C, air atmosphere, unless noted otherwise. [b]^{1}H NMR yield using 1,3,5-Trimethoxybenzene as internal standard. The ee value was determined by chiral HPLC.

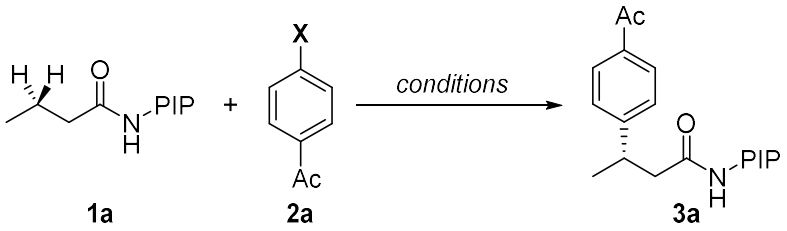
Table S4. Screening of reaction atmosphere[a]



Entry	Atmosphere	Yield (%)[b]	Ee[b]
1	air	70	89
2	O_2	70	89
3	N_2	71 (70)[c]	91

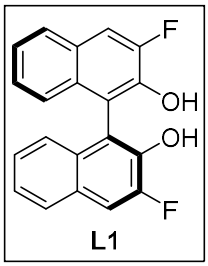
[a]Reaction conditions: **1a** (0.10 mmol), **2a** (2.0 equiv), Pd(hfac)$_2$ (10 mol %), K_2CO_3 (2.5 equiv), L1 (20 mol %), *t*-BuOH : toluene (0.8 mL : 0.2 mL), 12 h, 105 °C, unless noted otherwise. [b]^{1}H NMR yield using 1,3,5-Trimethoxybenzene as internal standard. The ee value was determined by chiral HPLC. [c]Isolated yield.

Table S5 Control experiments

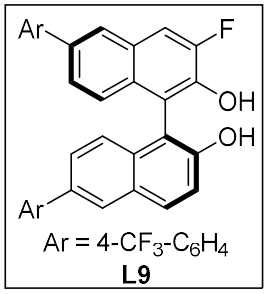


1a 2a 3a

Optimized Conditions	***Optimized Conditions***	***Previous Conditions***[1]
2a-I (2.0 equiv)	**2a-Br** (2.0 equiv)	**2a-Br** (2.0 equiv)
$Pd(hfac)_2$ (10 mol%)	$Pd(hfac)_2$ (10 mol%)	$PdCl_2$ (6 mol%)
K_2CO_3 (2.5 equiv)	K_2CO_3 (2.5 equiv)	K_2CO_3 (1.5 equiv)
L1 (20 mol%)	**L1** (20 mol%)	**L9** (6 mol%)
t-BuOH : toluene	*t*-BuOH : toluene	*t*-BuOH (1.0 mL)
(0.8 mL : 0.2 mL)	(0.8 mL : 0.2 mL)	125 °C, N_2, 24 h
105 °C, N_2, 12 h	105 °C, N_2, 12 h	88% yield, 3% ee
71% yield,91% ee	38% yield,79% ee	



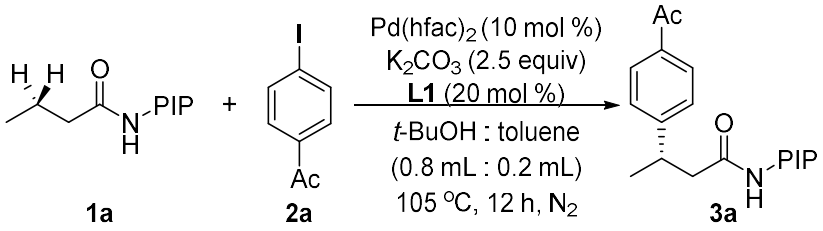
L1



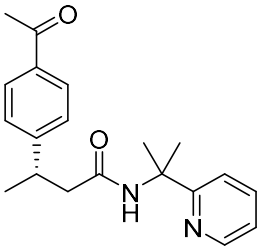
Ar = 4-CF_3-C_6H_4

L9

2.3 General Procedure for the Enantioselective Methylene C(sp^3)–H Arylation.



To a 50 mL Schlenk tube was added aliphatic amide **1a** (0.10 mmol), *p*-acetyliodobenzene **2a** (0.20 mmol), **L1** (6.4 mg, 20 mmol%), K_2CO_3 (34.5 mg, 0.250 mmol), $Pd(hfac)_2$ (5.2 mg, 20 mol%) and *t*-BuOH : toluene (0.8 mL : 0.2 mL). The vial stirred at 105 °C in oil bath for 12 h under N_2 atmosphere. After cooling to room temperature, the mixture was diluted with ethyl acetate, filtrated through celite. After concentration, the resulting residue was purified by preparative TLC using hexane/EtOAc as the eluent to afford the desired product **3a**.



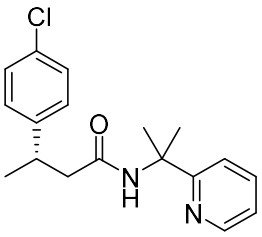
(*S*)-3-(4-acetylphenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 3a:

A purification by flash chromatography in petroleum ether : ethyl acetate = 1 : 1 to give **3a** as pale yellow oil (22.6 mg, 70%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 6.8 min (major), 6.1 min (minor): 91% ee.

3a is a known compound and the absolute stereochemistry was referred to literature report.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.8 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.69 – 7.64 (m, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.16 (dd, *J* = 7.2, 4.8 Hz, 1H), 3.47 – 3.35 (m, 1H), 2.58 – 2.45 (m, 2H), 2.25 (s, 3H), 1.67 (s, 3H), 1.60 (s, 1H), 1.33 (d, *J* = 6.8 Hz, 3H).

HRMS (ESI) calcd for $C_{20}H_{23}N_2O_2$, $(M+H)^+$: 325.1910, found: 325.1911.



(*S*)-3-(4-chlorophenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 3b:

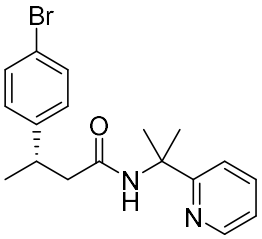
A purification by flash chromatography in dichloromethane : ethyl acetate = 4 : 1 to give **3b** as brown oil (24.3 mg, 77%). The ee value was determined by HPLC analysis on a Chiralcel OD-H column (hexane/isopropanol = 90/10, flow = 1.0 mL/min) with tr = 6.8 min (major), 6.5 min (minor): 92% ee.

The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (ddd, J = 4.8, 2.0, 0.8 Hz, 1H), 7.67 (td, J = 7.6, 2.0 Hz, 1H), 7.57 (s, 1H), 7.29 – 7.28 (m, 1H), 7.26 – 7.22 (m, 2H), 7.21 – 7.15 (m,3 H), 3.37 – 3.26 (m, 1H), 2.57 – 2.43 (m, 2H), 1.68 (s, 3H), 1.62 (s, 3H), 1.30 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 164.5, 147.6, 144.8, 137.3, 131.9, 128.6, 128.5, 122.0, 119.6, 56.6, 46.7, 36.6, 27.6, 27.4, 21.7.

HRMS (ESI) calcd for $C_{18}H_{21}ClN_2OH$, $(M+H)^+$: 317.1418, found: 317.1415.



(*S*)-3-(4-bromophenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 3c:

A purification by flash chromatography in dichloromethane : ethyl acetate = 8 : 1 to give **3c** as pale yellow solid (25.2 mg, 70%). The ee value was determined by HPLC analysis on a Chiralcel OJ-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 4.6 min (major), 6.0 min (minor): 94% ee.

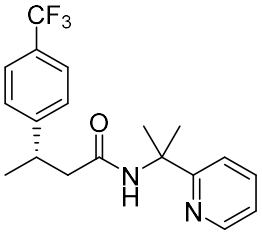
The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (dt, *J* = 4.8, 2.0, 0.8 Hz, 1H), 7.67 (td, *J* = 7.6, 2.0 Hz, 1H), 7.58 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.17 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.14 (d,

J = 8.4 Hz, 2H), 3.39 – 3.21 (m, 1H), 2.54 – 2.40 (m, 2H), 1.67 (s, 3H), 1.62 (s, 3H), 1.29 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) 170.5, 164.4, 147.6, 145.3, 137.2, 131.6, 128.9, 122.0, 120.0, 119.5, 56.6, 46.6, 36.6, 27.6, 27.4, 21.6.

HRMS (ESI) calcd for $C_{18}H_{21}BrN_2OH$, $(M+H)^+$: 361.0911, found: 361.0910.



(*S*)-*N*-(2-(pyridin-2-yl)propan-2-yl)-3-(4-(trifluoromethyl)phenyl)butanamide 3d:

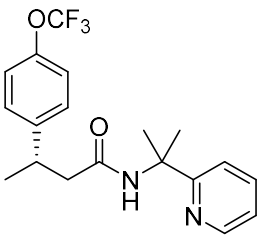
A purification by flash chromatography in dichloromethane : ethyl acetate = 8 : 1 to give **3d** as white solid (19.3 mg, 55%). The ee value was determined by HPLC analysis on a Chiralcel OJ-H column (hexane/isopropanol = 90/10, flow = 1.0 mL/min) with tr = 4.6 min (major), 5.8 min (minor): 92% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (ddd, *J* = 4.8, 1.6, 1.2 Hz, 1H), 7.67 (td, *J* = 8.0, 1.6 Hz, 1H), 7.63 (s, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.17 (ddd, *J* = 7.2, 4.8, 1.2 Hz, 1H), 3.47 – 3.35 (m, 1H), 2.57 – 2.45 (m, 2H), 1.68 (s, 3H), 1.61 (s, 3H), 1.34 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) 170.2, 164.2, 150.3, 147.5, 137.1, 128.5 (q, $^{2}J_{C\text{-}F}$ = 32.2 Hz), 127.4, 125.3 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 124.3 (q, $^{1}J_{C\text{-}F}$ = 271.9 Hz), 121.9, 119.4, 56.4, 46.3, 36.9, 27.4, 27.3, 21.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.31.

HRMS (ESI) calcd for $C_{19}H_{21}F_3N_2OH$, $(M+H)^+$: 351.1680, found: 351.1679.



(*S*)-*N*-(2-(pyridin-2-yl)propan-2-yl)-3-(4-(trifluoromethoxy)phenyl)butanamide 3e:

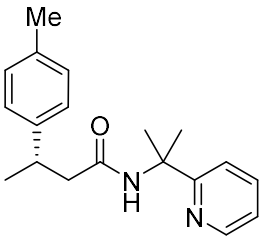
A purification by flash chromatography in dichloromethane : ethyl acetate = 8 : 1 to give **3e** as white flocculent (21.9 mg, 60%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 80/20, flow = 1.0 mL/min) with tr = 4.8 min (major), 4.6 min (minor): 91% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H), 7.66 (td, *J* = 8.0, 1.6 Hz, 1H), 7.59 (s, 1H), 7.31 – 7.26 (m, 3H), 7.16 (ddd, *J* = 7.2, 4.8, 1.2 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 3.42 – 3.30 (m, 1H), 2.53 – 2.42 (m, 2H), 1.67 (s, 3H), 1.59 (s, 3H), 1.32 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 164.4, 147.6, 145.0, 137.2, 128.4, 121.9, 121.1, 119.5, 56.5, 46.8, 36.6, 27.5, 27.4, 21.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.94.

HRMS (ESI) calcd for $C_{19}H_{21}F_3N_2O_2H$, $(M+H)^+$: 367.1629, found: 367.1628.



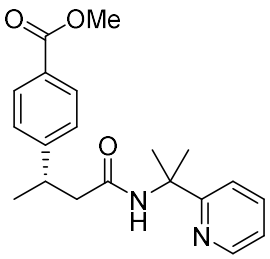
(*S*)-*N*-(2-(pyridin-2-yl)propan-2-yl)-3-(p-tolyl)butanamide 3f:

A purification by flash chromatography in dichloromethane : ethyl acetate = 8 : 1 to give **3f** as light yellow oil (24.2 mg, 82%). The ee value was determined by HPLC analysis on a Chiralcel OJ-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 4.4 min (major), 5.9 min (minor): 92% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (ddd, *J* = 4.8, 2.0, 1.2 Hz, 1H), 7.65 (td, *J* = 8.0, 1.6 Hz, 1H), 7.46 (s, 1H), 7.28 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.18 – 7.14 (m, 3H), 7.10 (s, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 3.34 – 3.24 (m, 1H), 2.52 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.43 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.30 (s, 3H), 1.68 (s, 3H), 1.64 (s, 3H), 1.30 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 164.6, 147.7, 143.3, 137.1, 135.8, 129.2, 126.9, 121.8, 119.5, 56.6, 46.9, 36.8, 27.6, 27.5, 21.8, 21.1.

HRMS (ESI) m/z: calcd for $C_{19}H_{24}N_2OH$, : 297.1962, found: 297.1961.



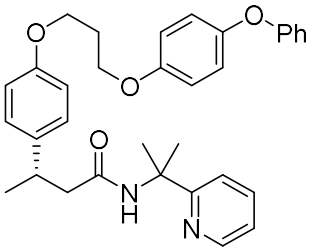
methyl (*S*)-4-(4-oxo-4-((2-(pyridin-2-yl)propan-2-yl)amino)butan-2-yl)benzoate 3g:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **3g** as yellow oil (23.1 mg, 68%). The ee value was determined by HPLC analysis on a Chiralcel OJ-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 5.3 min (major), 6.8 min (minor): 90% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (dt, *J* = 4.8, 1.6, 1.2 Hz, 1H), 7.95 (t, *J* = 1.6 Hz, 1H), 7.85 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.66 (td, *J* = 8.0, 2.0 Hz, 1H), 7.63 (s, 1H), 7.46 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.16 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 3.90 (s, 3H), 3.48 – 3.34 (m, 1H), 2.60 – 2.45 (m, 2H), 1.67 (s, 3H), 1.60 (s, 3H), 1.34 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 167.4, 164.4, 147.6, 146.7, 137.2, 132.2, 130.4, 128.6, 128.0, 127.7, 121.9, 119.5, 56.5, 52.2, 46.6, 37.0, 27.5, 27.4, 21.6.

HRMS (ESI) calcd for $C_{20}H_{24}N_2O_3H$, $(M+H)^+$: 341.1861, found: 341.1860.



(3*S*)-*N*-(1-iodo-2l1-diphosphaneyl)-3-(4-(3-(4-phenoxyphenoxy)propoxy)phenyl)butanamide 3h:

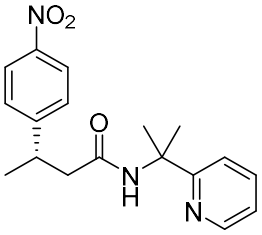
A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **3h** as pale yellow solid (26.7 mg, 45%). The ee value was determined by HPLC analysis on a Chiralcel IB N-5 column (hexane/isopropanol = 85/15, flow = 1.0 mL/min) with tr = 14.8 min (major), 12.2 min (minor): 96% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (ddd, *J* = 4.8, 1.6, 1.2 Hz, 1H), 7.65 (ddd, *J* = 8.0, 7.6, 1.6 Hz, 1H), 7.48 (s, 1H), 7.32 – 7.26 (m, 3H), 7.20 – 7.12 (m, 3H), 7.07 – 7.01 (m, 1H), 7.00 – 6.91 (m, 4H), 6.91 –

6.81 (m, 4H), 4.13 (td, *J* = 6.0, 1.2 Hz, 4H), 3.33 – 3.22 (m 1H), 2.50 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.42 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.27 – 2.19 (m, 2H), 1.68 (s, 6H), 1.63 (s, 6H), 1.29 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 164.6, 158.6, 157.4, 155.3, 150.2, 147.6, 138.6, 137.2, 129.7, 128.0, 122.5, 121.9, 121.0, 119.6, 117.7, 115.6, 114.5, 65.0, 64.5, 56.5, 47.0, 36.4, 29.5, 27.6, 27.5, 21.9.

HRMS (ESI) calcd for $C_{33}H_{36}N_2O_4H$, $(M+H)^+$: 525.2751, found: 525.2748.



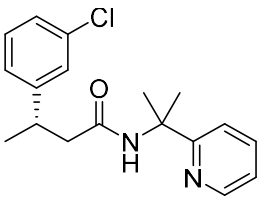
(S)-3-(4-nitrophenyl)-N-(2-(pyridin-2-yl)propan-2-yl)butanamide 3i:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **3i** as pale yellow solid (18.6 mg, 57%). The ee value was determined by HPLC analysis on a Chiralcel AS-H column (hexane/isopropanol = 95/5, flow = 1.0 mL/min) with tr = 21.5 min (major), 26.5 min (minor): 90% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.8 Hz, 1H), 8.13 (d, *J* = 8.8 Hz, 2H), 7.76 (s, 1H), 7.69 (td, *J* = 7.6, 1.6 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.19 (ddd, *J* = 7.6, 4.6, 0.8 Hz, 1H), 3.54 – 3.42 (m, 1H), 2.60 – 2.48 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.35 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 164.3, 154.1, 147.5, 146.6, 137.4, 128.1, 123.8, 122.1, 119.6, 56.5, 46.1, 37.1, 27.5, 27.4, 21.4.

HRMS (ESI) calcd for $C_{18}H_{21}N_3OH$, $(M+H)^+$: 328.1657, found: 328.1656.



(*S*)-3-(3-chlorophenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 3j:

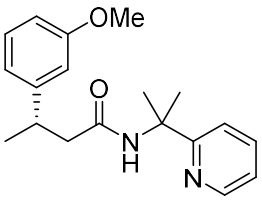
A purification by flash chromatography in dichloromethane : ethyl acetate = 8 : 1 to give **3j** as pale yellow oil (14.2 mg, 45%). The ee value was determined by HPLC analysis on a Chiralcel OJ-H column (hexane/isopropanol = 70/30, flow = 0.8 mL/min) with tr = 12.9 min (major), 11.3 min (minor): 92% ee.

The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (ddd, *J* = 4.8, 1.6, 1.2 Hz, 1H), 7.68 (td, *J* = 7.6, 1.6 Hz, 1H), 7.60 (s, 1H), 7.29 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.25-7.24 (m, 1H), 7.22 – 7.12 (m, 4H), 3.36 – 3.26 (m, 1H), 2.53 – 2.41 (m, 2H), 1.68 (s, 4H), 1.62 (s, 3H), 1.31 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 164.4, 148.4, 147.6, 137.2, 134.3, 129.8, 127.3, 126.5, 125.5, 121.9, 119.5, 56.6, 46.6, 37.0, 27.5, 27.5, 21.6.

HRMS (ESI) calcd for $C_{18}H_{21}ClN_2OH$, $(M+H)^+$: 317.1416, found: 317.1415.



(*S*)-3-(3-methoxyphenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 3k:

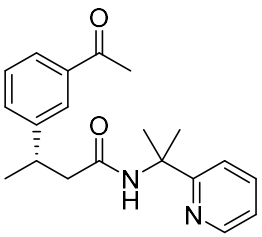
A purification by flash chromatography in petroleum ether : ethyl acetate = 1 : 1 to give **3k** as pale yellow oil (25.8 mg, 83%). The ee value was determined by HPLC analysis on a Chiralcel AS-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 4.1 min (major), 4.5 min (minor): 92% ee.

The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.4 Hz, 1H), 7.66 (td, *J* = 7.6, 2.0 Hz, 1H), 7.50 (s, 1H), 7.27 (d, *J* = 9.6 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 7.2, 5.2 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.81 (t, *J* = 2.0 Hz, 1H), 6.72 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.78 (s, 3H), 3.37 – 3.23 (m, 1H), 2.53 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.43 (dd, *J* = 14.0, 8.0 Hz, 1H), 1.68 (s, 3H), 1.62 (s, 3H), 1.31 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 164.5, 159.8, 148.1, 147.6, 137.1, 129.5, 121.9, 119.5, 119.4, 112.9, 111.6, 56.6, 55.3, 46.8, 37.3, 27.6, 27.5, 21.7.

HRMS (ESI) calcd for $C_{19}H_{24}N_2O_2H$, $(M+H)^+$: 313.1912, found: 313.1911.



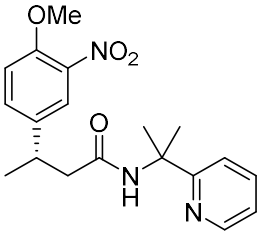
(*S*)-3-(3-acetylphenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 3l:

A purification by flash chromatography in dichloromethane : ethyl acetate = 8 : 1 to give **3l** as pale yellow oil (26.5 mg, 82%). The ee value was determined by HPLC analysis on a Chiralcel OJ-H column (hexane/isopropanol = 70/30, flow = 0.8 mL/min) with tr = 7.3 min (major), 9.4 min (minor): 91% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H), 7.86 (t, *J* = 1.6 Hz, 1H), 7.76 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.69 (td, *J* = 7.6, 2.0 Hz, 1H), 7.48 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.18 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 3.46 – 3.35 (m, 1H), 2.58 (s, 3H), 2.56 – 2.48 m, 2H), 1.67 (s, 3H), 1.59 (s, 3H), 1.35 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 98.5, 170.5, 164.3, 147.5, 146.9, 137.3, 137.3, 132.3, 128.8, 126.8, 126.6, 122.0, 119.5, 56.5, 46.5, 37.1, 27.5, 27.4, 26.9, 21.7.

HRMS (ESI) calcd for $C_{20}H_{24}N_2O_2H$, $(M+H)^+$: 325.1910, found: 325.1911.



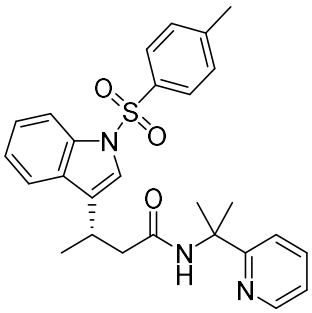
(*S*)-3-(4-methoxy-3-nitrophenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 3m:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **3m** as light yellow oil (19.3 mg, 54%). The ee value was determined by HPLC analysis on a Chiralcel OJ-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 12.5 min (major), 21.2 min (minor): 93% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (dt, *J* = 4.8, 1.6 Hz, 1H), 7.76 (d, J = 2.4 Hz, 1H), 7.73 (s, 1H), 7.68 (td, J = 7.6, 1.6 Hz, 1H), 7.45 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.18 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 3.90 (s, 3H), 3.44 – 3.30 (m, 1H), 2.48 (d, *J* = 7.2 Hz, 2H), 1.68 (s, 6H), 1.61 (s, 1H), 1.33 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 164.3, 151.6, 147.6, 139.5, 138.8, 137.2, 133.5, 123.9, 122.0, 119.5, 113.6, 56.7, 56.5, 46.5, 36.0, 27.4, 21.6.

HRMS (ESI) calcd for $C_{19}H_{23}N_3O_4H$, $(M+H)^+$: 358.1763, found: 358.1761.



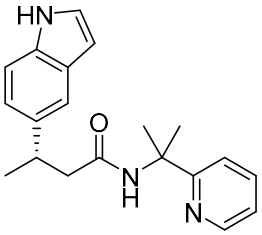
(*S*)-*N*-(2-(pyridin-2-yl)propan-2-yl)-3-(1-tosyl-1H-indol-3-yl)butanamide 3n:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **3n** as pale yellow oil (34.6 mg, 73%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 5.5 min (major), 6.9 min (minor): 92% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.76 (s, 1H), 7.71 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.67 (td, J = 7.6, 2.0 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.36 (s, 1H), 7.33 – 7.26 (m, 2H), 7.22 (td, *J* = 7.6, 1.1 Hz, 1H), 7.18 – 7.12 (m, 3H), 3.61 – 3.50 (m, 1H), 2.71 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.44 (dd, *J* = 14.0, 8.4 Hz, 1H), 2.30 (s, 1H), 1.69 (s, 3H), 1.62 (s, 3H), 1.38 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 164.4, 147.7, 144.8, 137.2, 135.6, 135.5, 130.2, 129.9, 127.9, 126.8, 124.7, 123.1, 122.0, 121.9, 120.2, 119.5, 113.8, 56.6, 45.1, 28.1, 27.53, 27.46, 21.6, 20.4.

HRMS (ESI) calcd for $C_{23}H_{38}N_2OSi$, $(M+H)^+$: 476.2004, found: 476.2002.



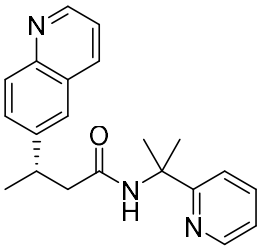
(*S*)-3-(1H-indol-5-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 3o:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **3o** as dark brown oil (11.2 mg, 34%). The ee value was determined by HPLC analysis on a Chiralcel OD-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 5.2 min (major), 7.1 min (minor): 92% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.8 Hz, 0H), 8.20 (s, 1H), 7.55 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.52 (s, 1H), 7.34 (s, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.20 – 7.15 (m, 2H), 7.14 – 7.08 (m, 2H), 6.49 (s, 1H), 3.47 – 3.34 (m, 1H), 2.61 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.50 (dd, *J* = 14.0, 7.8 Hz, 1H), 1.64 (s, 3H), 1.60 (s, 3H), 1.38 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 164.6, 147.6, 137.8, 137.1, 134.8, 128.2, 124.5, 121.8, 121.6, 119.6, 118.6, 111.1, 102.6, 56.6, 47.5, 37.4, 27.7, 27.5, 22.4.

HRMS (ESI) calcd for $C_{20}H_{23}N_3OH$, $(M+H)^+$: 322.1915, found: 322.1914.



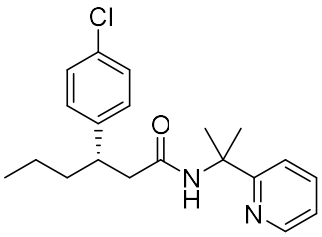
(*S*)-*N*-(2-(pyridin-2-yl)propan-2-yl)-3-(quinolin-6-yl)butanamide 3p:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **3p** as pale yellow oil (19.1 mg, 57%). The ee value was determined by HPLC analysis on a Chiralcel OJ-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 5.4 min (major), 10.1 min (minor): 92% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.35 (ddd, *J* = 4.8, 1.6, 1.2 Hz, 1H), 8.08 (ddd, *J* = 8.4, 1.6, 0.8 Hz, 1H), 8.05 –7.99 (m, 1H), 7.70 – 7.63 (m, 2H), 7.61 – 7.52 (m, 2H), 7.35 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.20 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.10 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 3.61 – 3.48 (m, 1H), 2.67 – 2.52 (m, 2H), 1.65 (s, 3H), 1.56 (s, 3H), 1.42 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 164.3, 149.9, 147.5, 147.4, 144.6, 137.1, 135.9, 129.6, 129.3, 128.4, 125.3, 121.9, 121.2, 119.4, 56.5, 46.6, 37.1, 27.6, 27.3, 21.7.

HRMS (ESI) calcd for $C_{21}H_{23}N_3OH$, $(M+H)^+$: 334.1914, found: 334.1914.



(*S*)-3-(4-chlorophenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)hexanamide 4a:

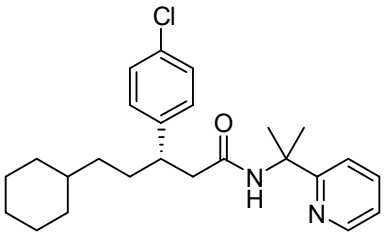
A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **4a** as white foam (24.7 mg, 72%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 85/15, flow = 1.0 mL/min) with tr = 6 min (major), 7.2 min (minor): 91% ee.

The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (ddd, *J* = 5.2, 1.6, 0.8 Hz, 1H), 7.65 (td, *J* = 7.6, 1.6 Hz, 1H), 7.44 (s, 1H), 7.24 – 7.20 (m, 3H), 7.18 – 7.14 (m, 3H), 3.18 – 3.09 (m, 1H), 2.55 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.41 (dd, *J* = 14.0, 8.8 Hz, 1H), 1.80 – 1.65 (m, 1H), 1.64 (s, 3H), 1.62 – 1.57 (m, 1H), 1.56 (s, 3H), 1.23 – 1.13 (m, 2H), 0.84 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 164.4, 147.6, 143.2, 137.1, 131.8, 129.2, 128.5, 121.9, 119.5, 56.5, 45.5, 42.2, 38.4, 27.6, 27.4, 20.6, 14.1.

HRMS (ESI) calcd for $C_{20}H_{25}ClN_2OH$, $(M+H)^+$: 345.1731, found: 345.1728.



(*S*)-3-(4-chlorophenyl)-5-cyclohexyl-*N*-(2-(pyridin-2-yl)propan-2-yl)pentanamide 4b:

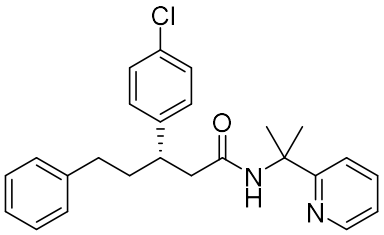
A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **4b** as white solid (26.8 mg, 65%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr =10.1 min (major), 9 min (minor): 94% ee.

The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (ddd, *J* = 4.8, 2.0, 1.2 Hz, 1H), 7.64 (td, *J* = 7.6, 1.6 Hz, 1H), 7.43 (s, 1H), 7.24 – 7.19 (m, 3H), 7.18 – 7.12 (m, 3H), 3.11 – 3.01 (m, 1H), 2.54 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.39 (dd, *J* = 14.0, 8.8 Hz, 1H), 1.73 – 1.63 (m, 2H), 1.63 (s, 3H), 1.61 – 1.56 (m, 5H), 1.55 (s, 3H), 1.35 – 0.99 (m, 5H), 0.99 – 0.89 (m, 1H), 0.85 – 0.68 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 164.4, 147.6, 143.3, 137.2, 131.8, 129.2, 128.5, 121.9, 119.5, 56.5, 45.6, 42.7, 37.7, 35.2, 33.5, 33.4, 33.2, 27.6, 27.4, 26.8, 26.5, 26.4.

HRMS (ESI) calcd for $C_{25}H_{33}ClN_2OH$, $(M+H)^+$: 413.2358, found: 413.2354.



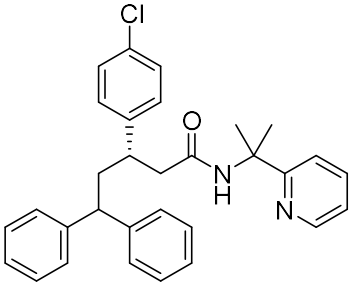
(*S*)-3-(4-chlorophenyl)-5-phenyl-*N*-(2-(pyridin-2-yl)propan-2-yl)pentanamide 4c:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **4c** as yellow solid (28.4 mg, 70%). The ee value was determined by HPLC analysis on a Chiralcel OD-H column (hexane/isopropanol = 90/10, flow = 1.0 mL/min) with tr = 10.9 min (major), 9.5 min (minor): 92% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (ddd, *J* = 12.0, 4.8, 0.8 Hz, 1H), 7.65 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.47 (s, 1H), 7.28 (d, *J* = 2.0 Hz, 1H), 7.25 – 7.19 (m, 5H), 7.19 – 7.13 (m, 3H), 7.10 – 7.05 (m, 2H), 3.25 – 3.13 (m, 1H), 2.58 (dd, *J* = 14.0, 6.8 Hz, 1H), 2.51 – 2.39 (m, 3H), 2.10 – 1.99 (m, 1H), 1.97 – 1.85 (m, 1H), 1.63 (s, 3H), 1.55 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 164.3, 147.6, 142.6, 142.0, 137.2, 132.1, 129.3, 128.7, 128.5, 125.9, 121.9, 119.5, 56.5, 45.5, 42.1, 37.8, 33.7, 27.5, 27.4.

HRMS (ESI) calcd for $C_{25}H_{27}ClN_2OH$, $(M+H)^+$: 407.1885, found: 407.1885.



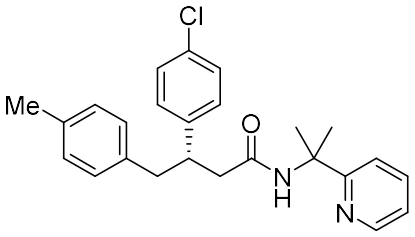
(S)-3-(4-chlorophenyl)-5,5-diphenyl-N-(2-(pyridin-2-yl)propan-2-yl)pentanamide 4d

A purification by flash chromatography in petroleum ether : acetone = 6 : 1 to give **4d** as white flocculent (25.8 mg, 53%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 85/15, flow = 1.0 mL/min) with tr = 7.2 min (major), 6.0 min (minor): 96% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (ddd, *J* = 4.8, 1.6, 1.2 Hz, 1H), 7.64 (td, *J* = 7.6, 1.6 Hz, 1H), 7.38 (s, 1H), 7.27 (dt, *J* = 6.8, 1.6 Hz, 2H), 7.26 – 7.20 (m, 4H), 7.19 (s, 1H), 7.18 – 7.10 (m, 7H), 7.06 (dt, *J* = 8.8, 1.6 Hz, 2H), 3.63 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.09 – 3.00 (m, 1H), 2.63 – 2.52 (m, 2H), 2.44 (dd, *J* = 14.0, 8.8 Hz, 1H), 2.26 (ddd, *J* = 13.6, 10.8, 4.4 Hz, 1H), 1.63 (s, 3H), 1.54 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 164.3, 147.6, 145.5, 143.1, 142.1, 137.1, 132.2, 129.5, 128.7, 128.5, 128.4, 127.6, 126.5, 126.2, 121.9, 119.4, 56.5, 48.6, 45.9, 41.7, 40.3, 27.5, 27.3.

HRMS (ESI) calcd for $C_{32}H_{33}ClN_2OH$, $(M+H)^+$: 483.2204, found: 483.2198.



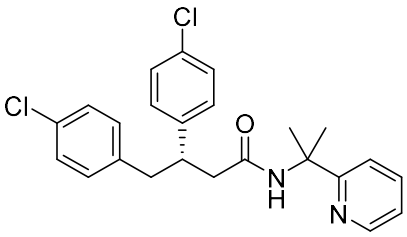
(*S*)-3-(4-chlorophenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)-4-(p-tolyl)butanamide 4e:

A purification by flash chromatography in dichloromethane : ethyl acetate = 10 : 1 to give **4e** as white solid (22.3 mg, 55%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 90/10, flow = 1.0 mL/min) with tr = 9.6 min (major), 11.4 min (minor): 94% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (ddd, *J* = 4.8, 2.0, 1.2 Hz, 1H), 7.65 (td, *J* = 7.6, 2.0 Hz, 1H), 7.49 (s, 1H), 7.23 – 7.14 (m, 4H), 7.10 (dt, *J* = 8.4, 2.4 Hz, 2H), 7.00 (d, *J* = 7.6 Hz, 2H), 6.91 (dd, *J* = 8.0, 1.6 Hz, 2H), 3.48 – 3.39 (m, 1H), 2.93 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.84 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.61 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.46 (dd, *J* = 14.0, 9.2 Hz, 1H), 2.27 (s, 3H), 1.62 (s, 3H), 1.55 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 164.3, 147.5, 142.4, 137.3, 136.4, 135.7, 132.0, 129.3, 129.2, 129.0, 128.4, 121.9, 119.5, 56.5, 44.1, 43.9, 42.3, 27.6, 27.3, 21.1.

HRMS (ESI) calcd for $C_{25}H_{27}ClN_2OH$, $(M+H)^+$: 407.1885, found: 407.1885.



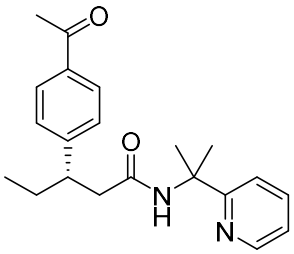
(*S*)-3,4-bis(4-chlorophenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 4f:

A purification by flash chromatography in petroleum ether : ethyl acetate = 8 : 1 to give **4f** as white solid (20.8 mg, 49%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 90/10, flow = 1.0 mL/min) with tr = 13.9 min (major), 18.4 min (minor): 91% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H), 7.65 (ddd, *J* = 8.0, 7.6, 1.6 Hz, 1H), 7.57 (s, 1H), 7.23 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.21 – 7.11 (m, 5H), 7.05 (dt, *J* = 8.8, 2.4 Hz, 2H), 6.92 (dt, *J* = 8.8, 2.4 Hz, 2H), 3.47 – 3.37 (m, 1H), 2.97 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.81 (dd, *J* = 13.6, 8.8 Hz, 1H), 2.60 (dd, *J* = 14.4, 6.8 Hz, 1H), 2.48 (dd, *J* = 14.4, 8.4 Hz, 1H), 1.64 (s, 3H), 1.56 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 164.3, 147.6, 141.8, 138.0, 137.2, 132.2, 132.0, 130.7, 129.3, 128.6, 128.4, 122.0, 119.5, 56.6, 44.0, 43.9, 41.9, 27.6, 27.4.

HRMS (ESI) calcd for $C_{24}H_{24}Cl_2N_2OH$, $(M+H)^+$: 427.1343, found: 427.1338.



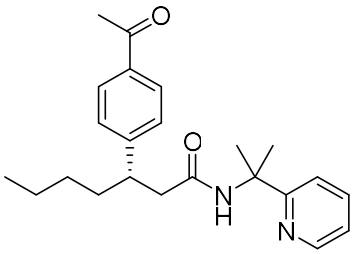
(*S*)-3-(4-acetylphenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)pentanamide 4g:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **4g** as pale yellow oil (28.3 mg, 84%). The ee value was determined by HPLC analysis on a Chiralcel AS-H column (hexane/isopropanol = 80/20, flow = 1.0 mL/min) with tr = 7.5 min (major), 9.5 min (minor): 91% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (ddd, *J* = 4.8, 1.6, 1.2 Hz, 1H), 7.87 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.65 (ddd, *J* = 8.0, 7.6, 1.6 Hz, 1H), 7.62 (s, 1H), 7.32 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.24 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.16 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 3.19 – 3.07 (m, 1H), 2.61 (dd, *J* = 14.0, 6.8 Hz, 1H), 2.56 (s, 3H), 2.48 (dd, *J* = 14.0, 8.8 Hz, 1H), 1.82 – 1.74 (m, 1H), 1.71 – 1.63 (m, 1H), 1.63 (s, 3H), 1.53 (s, 3H), 0.80 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.2, 170.6, 164.3, 150.4, 147.5, 137.2, 135.5, 128.7, 128.1, 121.9, 119.5, 56.5, 44.9, 44.7, 29.0, 27.5, 27.3, 26.7, 12.1.

HRMS (ESI) calcd for $C_{21}H_{26}N_2OH$, $(M+H)^+$: 339.2067, found: 339.2067.



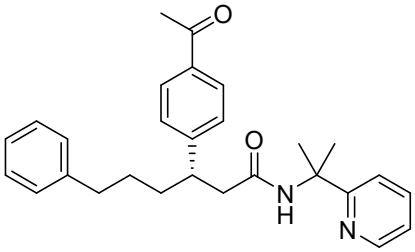
(*S*)-3-(4-acetylphenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)heptanamide 4h:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **4h** as yellow solid (23.1 mg, 63%). The ee value was determined by HPLC analysis on a Chiralcel AS-H column (hexane/isopropanol = 80/20, flow = 1.0 mL/min) with tr = 6.5 min (major), 8.3 min (minor): 92% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H), 7.86 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.64 (td, *J* = 7.6, 1.6 Hz, 1H), 7.57 (s, 1H), 7.31 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.23 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.15 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 3.25 – 3.15 (m, 1H), 2.58 (dd, *J* = 14.0, 6.8 Hz, 1H), 2.55 (s, 3H), 2.46 (dd, *J* = 14.0, 8.4 Hz, 1H), 1.77 – 1.63 (m, 2H), 1.62 (s, 3H), 1.52 (s, 3H), 1.37 – 1.25 (m, 2H), 1.20 – 1.13 (m, 1H), 1.12 – 1.00 (m, 1H), 0.81 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.1, 170.5, 164.3, 150.7, 147.5, 137.3, 135.5, 128.7, 128.1, 122.0, 119.6, 56.5, 45.2, 43.0, 35.7, 29.7, 27.5, 27.4, 26.7, 22.7, 14.0.

HRMS (ESI) calcd for $C_{23}H_{30}N_2O_2H$, $(M+H)^+$: 367.2380, found: 367.2380.



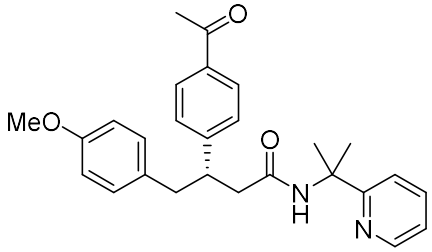
(*S*)-3-(4-acetylphenyl)-6-phenyl-*N*-(2-(pyridin-2-yl)propan-2-yl)hexanamide 4i:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **4i** as pale yellow flocculent (23.1 mg, 54%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 20 min (major), 17.2 min (minor): 91% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (ddd, *J* = 4.8, 1.6, 1.2 Hz, 1H), 7.86 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.64 (td, *J* = 7.6, 1.6 Hz, 1H), 7.57 (s, 1H), 7.30 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.26 – 7.18 (m, 3H), 7.18 – 7.10 (m, 2H), 7.09 – 7.05 (m, 2H), 3.31 – 3.21 (m, 1H), 2.64 – 2.56 (m, 2H), 2.55 (s, 3H), 2.54 – 2.43 (m, 2H), 1.83 – 1.69 (m, 2H), 1.62 (s, 3H), 1.53 (s, 3H), 1.52 – 1.32 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.1, 170.3, 164.4, 150.4, 147.6, 142.3, 137.2, 135.5, 128.7, 128.5, 128.4, 128.1, 125.8, 121.9, 119.5, 56.5, 45.2, 42.9, 35.8, 35.4, 29.2, 27.5, 27.4, 26.7.

HRMS (ESI) calcd for $C_{28}H_{32}N_2O_2H$, $(M+H)^+$: 429.2538, found: 429.2537.



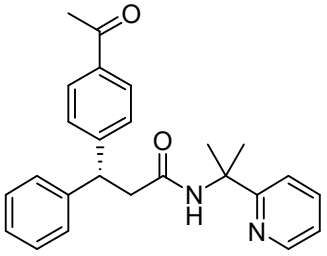
(*S*)-3-(4-acetylphenyl)-4-(4-methoxyphenyl)-*N*-(2-(pyridin-2-yl)propan-2-yl)butanamide 4j:

A purification by flash chromatography in dichloromethane : ethyl acetate = 6 : 1 to give **4j** as yellow solid (20.2 mg, 47%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 80/20, flow = 1.0 mL/min) with tr = 10.7 min (major), 9.9 min (minor): 92% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (ddd, *J* = 4.8, 1.6, 1.2 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.63 (td, *J* = 7.6, 1.6 Hz, 1H), 7.59 (s, 1H), 7.25 – 7.20 (m, 3H), 7.15 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 6.93 (dt, *J* = 8.4, 2.4 Hz, 1H), 6.72 (dt, *J* = 8.8, 2.4 Hz, 1H), 3.74 (s, 3H), 3.57 – 3.45 (m, 1H), 2.96 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.86 (dd, *J* = 13.6, 8.4 Hz, 1H), 2.65 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.57 –2.49 (dd, *J* = 14.4, 8.0 Hz, 1H), 2.53 (s, 3H), 1.62 (s, 3H), 1.53 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ δ 198.1, 170.2, 164.4, 158.1, 149.8, 147.5, 137.2, 135.5, 131.4, 130.3, 128.5, 128.2, 122.0, 119.5, 113.7, 56.5, 55.3, 44.9, 43.6, 41.7, 27.5, 27.4, 26.7.

HRMS (ESI) calcd for $C_{27}H_{30}N_2O_3H$, $(M+H)^+$: 431.2332, found: 431.2329.



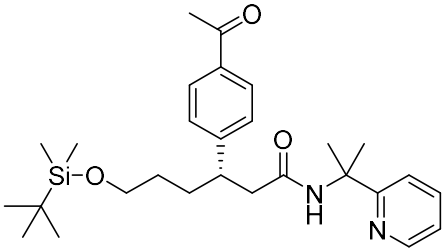
(*R*)-3-(4-acetylphenyl)-3-phenyl-*N*-(2-(pyridin-2-yl)propan-2-yl)propanamide 4k:

A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 to give **4k** as pale yellow oil (27.0 mg, 70%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 7.6 min (major), 8.8 min (minor): 90% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.9 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.70 (s, 1H), 7.64 (td, *J* = 7.6, 1.6 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.26 (s, 2H), 7.22 – 7.13 (m, 5H), 4.67 (d, *J* = 7.8 Hz, 1H), 3.00 (d, *J* = 7.6 Hz, 2H), 2.54 (s, 3H), 1.56 (s, 3H), 1.54 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.0, 169.7, 164.2, 149.7, 147.5, 143.1, 137.2, 135.4, 128.8, 128.7, 128.3, 128.0, 126.8, 122.0, 119.5, 56.6, 47.5, 43.8, 27.4, 26.7.

HRMS (ESI) calcd for $C_{25}H_{26}N_2O_2H$, $(M+H)^+$: 387.2067, found: 387.2067.



(*S*)-3-(4-acetylphenyl)-6-((tert-butyldimethylsilyl)oxy)-*N*-(2-(pyridin-2-yl)propan-2-yl)hexanamide 4l:

A purification by flash chromatography in petroleum ether : ethyl acetate = 1 : 1 to give **4l** as yellow oil (40.0 mg, 83%). The ee value was determined by HPLC analysis on a Chiralcel AD-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min) with tr = 4.2 min (major), 3.9 min (minor): 89% ee. The absolute stereochemistry was assigned by analogy to compound **3a**.

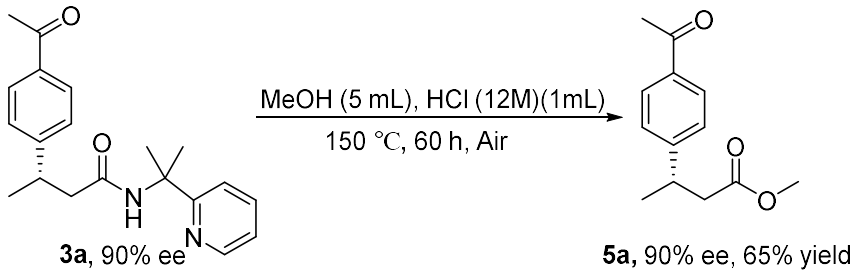
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (ddd, *J* = 5.2, 2.0 1.2 Hz, 1H), 7.85 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.63 (td, *J* = 7.6, 1.6 Hz, 1H), 7.59 (s, 1H), 7.31 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.22 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.14 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 3.53 (t, *J* = 6.4 Hz, 2H), 3.26 – 3.16 (m, 1H), 2.59 (dd, *J* = 14.0, 6.4 Hz,

1H), 2.54 (s, 3H), 2.47 (dd, J = 14.0, 8.8 Hz, 1H), 1.83 – 1.74 (m, 1H), 1.73 – 1.64 (m, 1H), 1.61 (s, 3H), 1.52 (s, 3H), 1.49 – 1.39 (m, 1H), 1.33 – 1.25 (m, 1H), 0.84 (s, 9H), -0.02 (s, 3H), -0.03 (s, 3H).

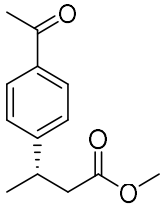
^{13}C NMR (101 MHz, $CDCl_3$) δ 198.2, 170.4, 164.3, 150.4, 147.5, 137.2, 135.5, 128.7, 128.1, 121.9, 119.5, 63.0, 56.5, 45.3, 42.9, 32.3, 30.8, 27.5, 27.3, 26.7, 26.1, 18.4, -5.2.

HRMS (ESI) calcd for $C_{28}H_{42}N_2O_3SiH$, $(M+H)^+$: 483.3039, found: 483.3037.

2.4 Cleavage of Directing Group



To a 25 mL flask was added aliphatic amide **3a** (0.10 mmol) and MeOH (5.0 mL) and HCl (12 M) (1.0 mL). The reaction was stirred in 150 °C for 60 h. The reaction mixture was alkalize to pH 12 with aq. NaOH (3 M), and extracted with EtOAc (10 mL x 3). The organic layers were combined，washed with brine，dried over anhydrous Na_2SO_4, Purification by flash chromatography gave compound **5a** as a white solid (16.2 mg, 65% yield, 90% ee).



methyl (*S*)-3-(4-acetylphenyl)butanoate 5a:

A purification by flash chromatography in petroleum ether : ethyl acetate= 2 : 1 to give **5a** as white solid (16.2 mg, 65%). The ee value was determined by HPLC analysis on a Chiralcel OJ-H column (hexane/isopropanol = 70/30, flow = 1.0 mL/min, 254 nm) with tr = 10.5 min (minor), 9.4 min (major): 90% ee.

The absolute stereochemistry was assigned by analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 2H), 3.61 (d, *J* = 1.6 Hz, 3H), 3.40 – 3.29 (m, 1H), 2.69 – 2.54 (m, 5H), 1.60 (s, 1H), 1.31 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 172.6, 151.4, 135.7, 128.9, 127.1, 53.6, 51.8, 42.3, 36.6, 26.7, 21.8.

HRMS (ESI) calcd for $C_{13}H_{16}O_3$, $(M+H)^+$: 221.1170, found: 221.1170.

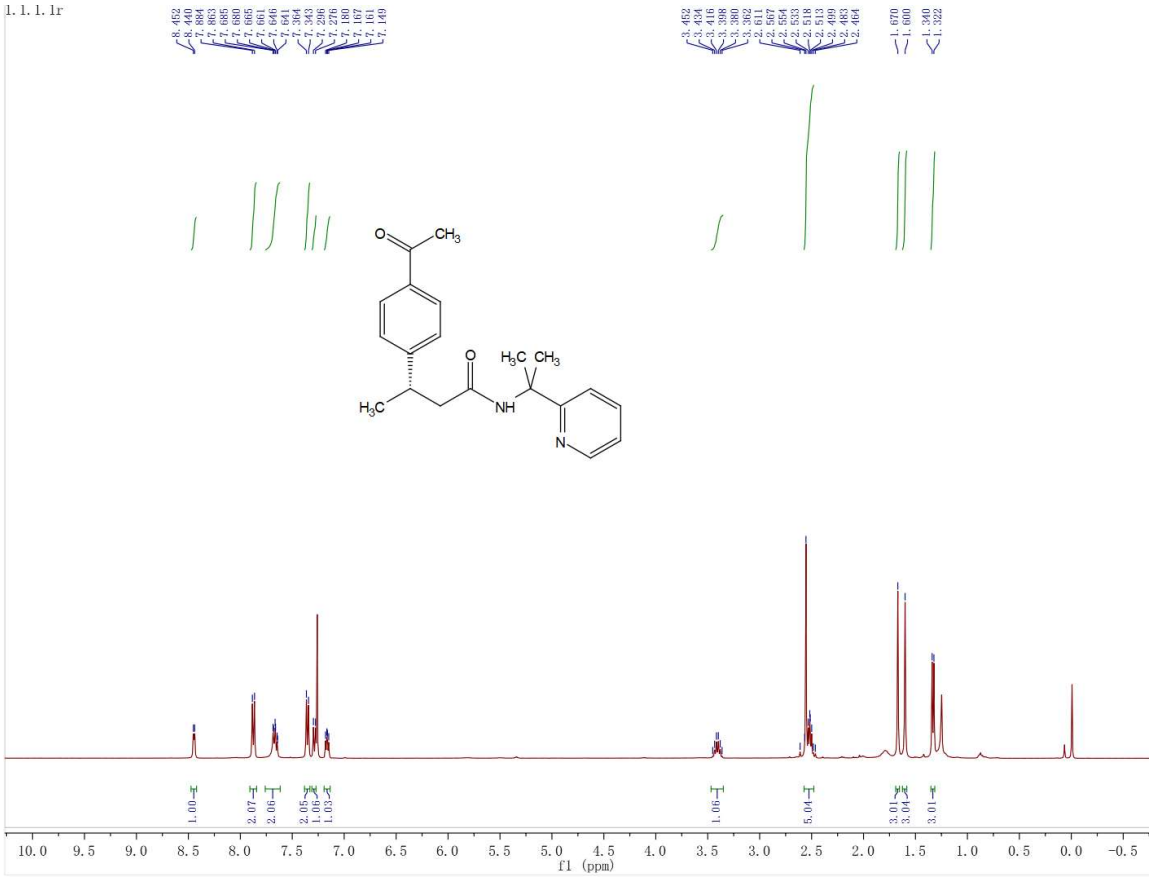
3. References

[1] S.-Y. Yan, Y.-Q. Han, Q.-J. Yao, X.-L. Nie, L. Liu, B.-F. Shi, Palladium(II)-catalyzed enantioselective arylation of unbiased methylene C(sp^3)–H bonds enabled by a 2-pyridinylisopropyl auxiliary and chiral phosphoric acids. *Angew. Chem. Int. Ed*. 2018, **57**, 9093.

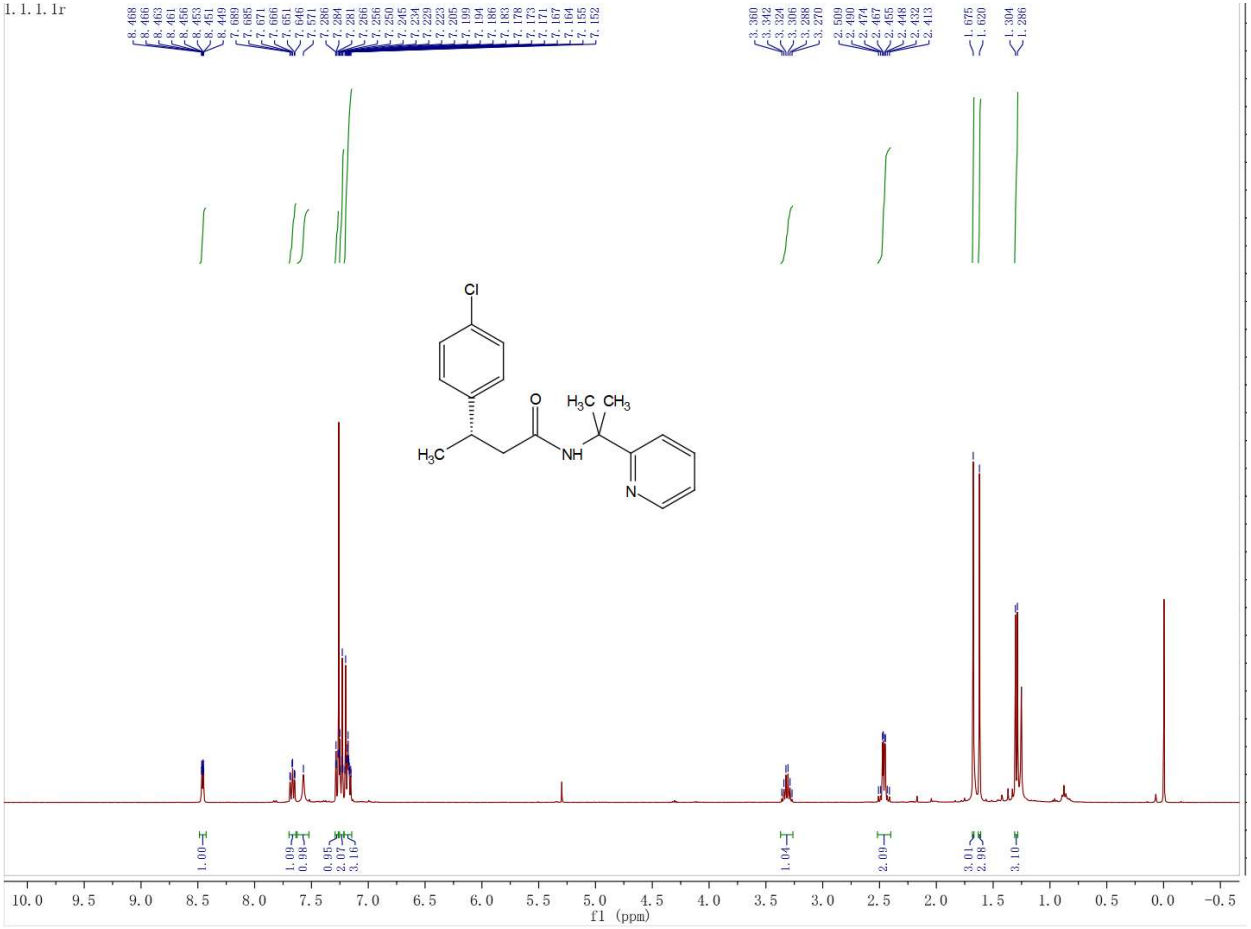
[2] F.-J. Chen, S. Zhao, F. Hu, K. Chen, Q. Zhang, S.-Q. Zhang, B.-F. Shi, Pd(II)-catalyzed alkoxylation of unactivated C(sp^3)–H and C(sp^2)–H bonds using a removable directing group: efficient synthesis of alkyl ethers. *Chem. Sci*. 2013, **4**, 418

4. NMR Spectra

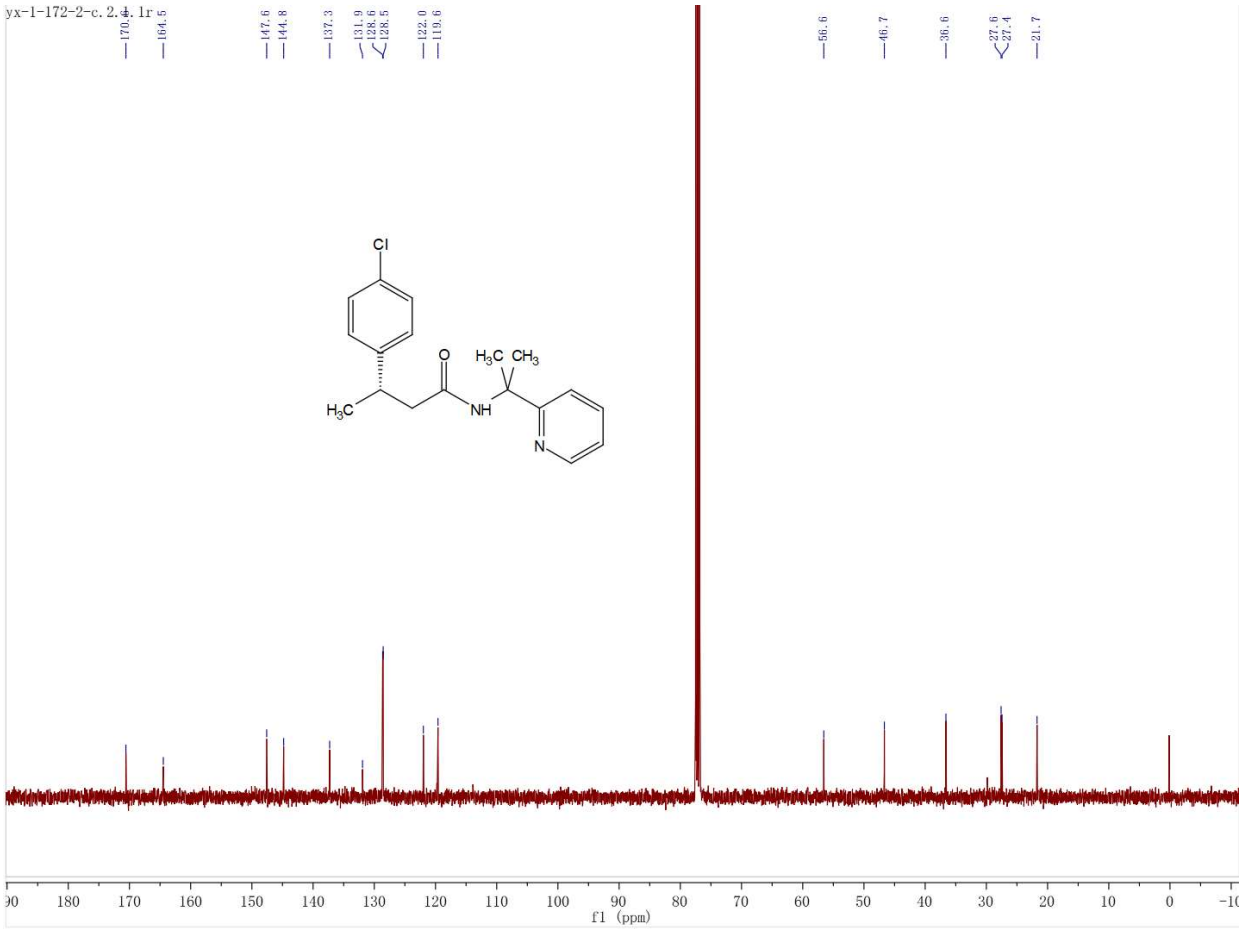
3a, ^{1}H NMR, 400 MHz, $CDCl_3$



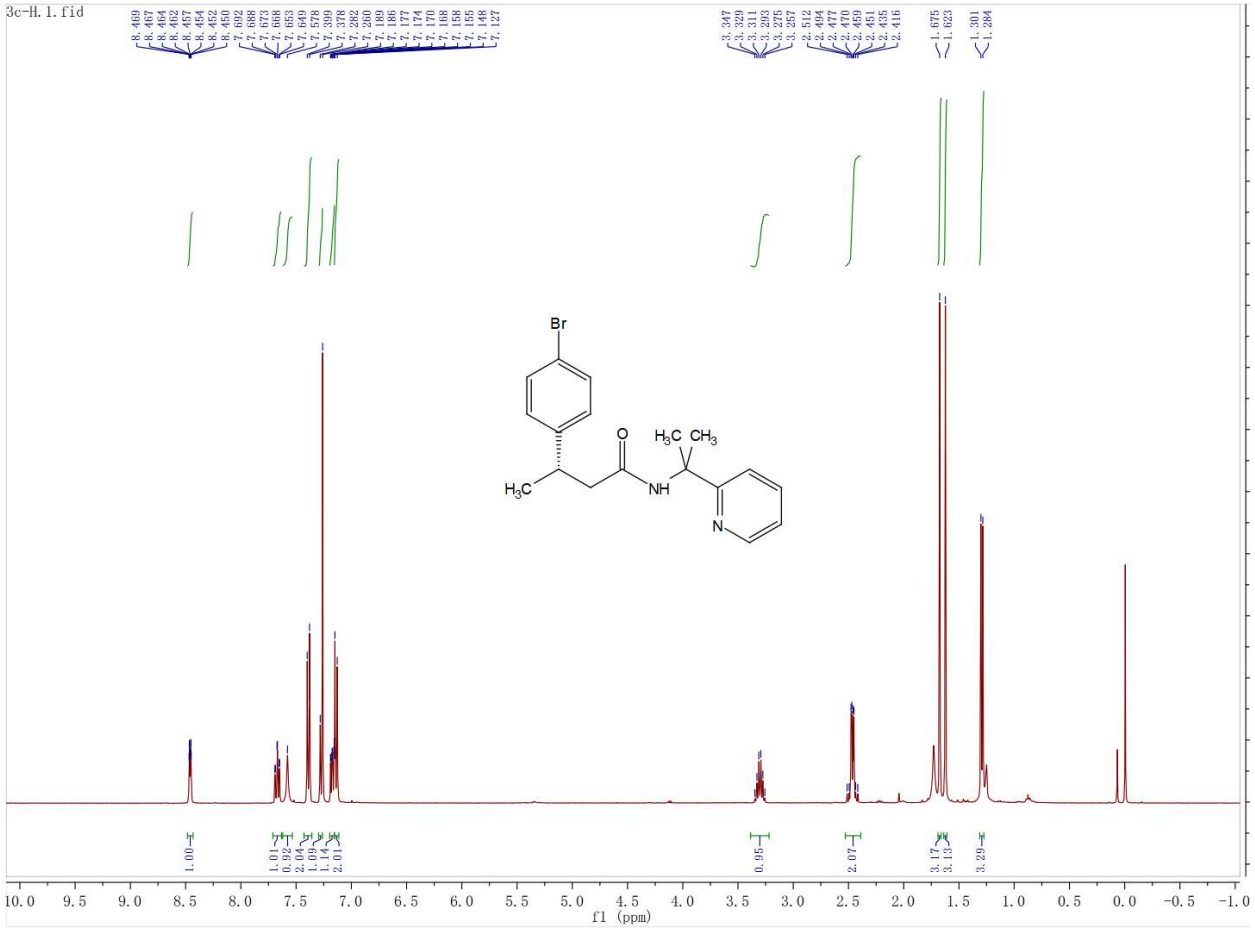
3b, ^{1}H NMR, 400 MHz, $CDCl_3$



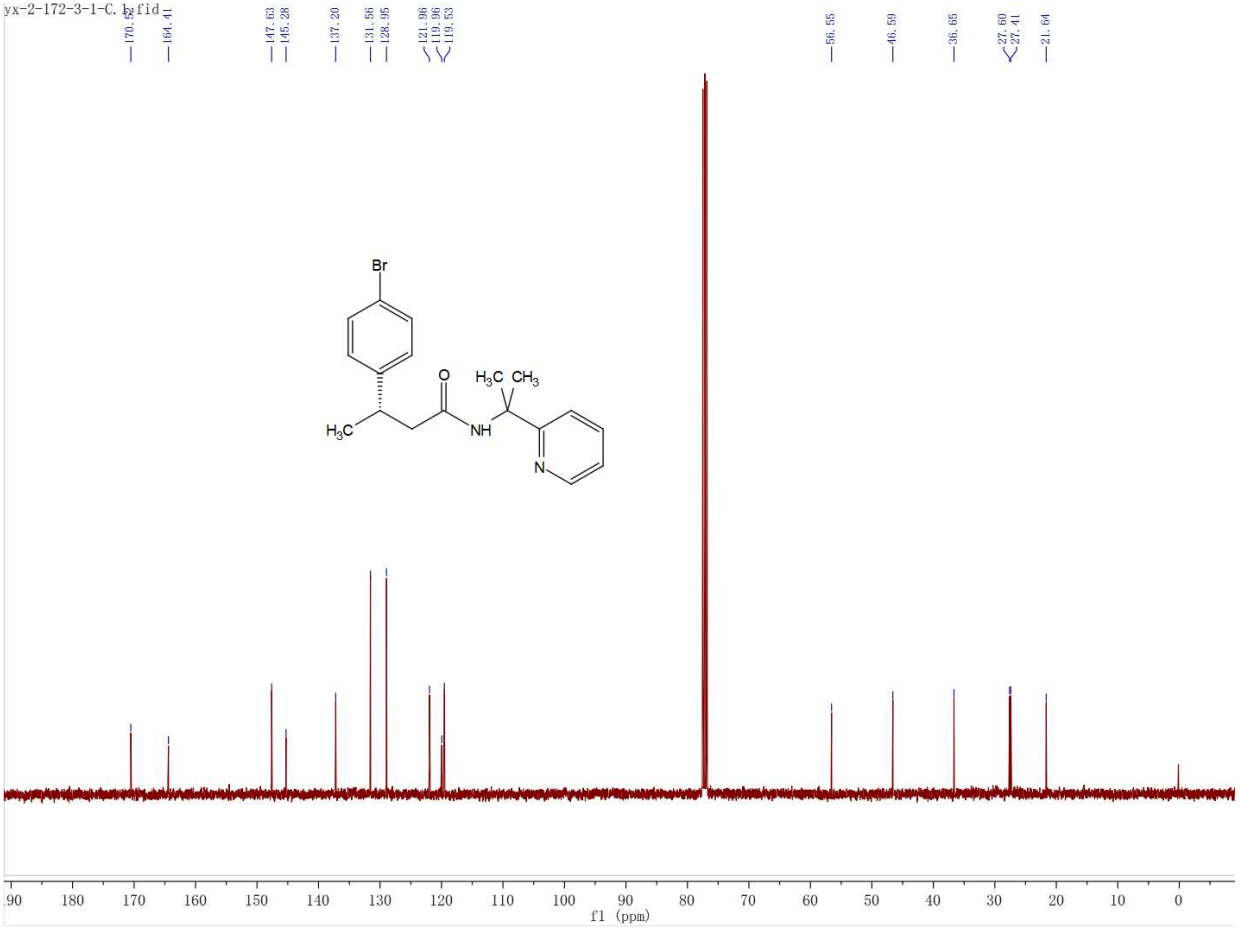
3b,^{13}C NMR, 101 MHz, $CDCl_3$



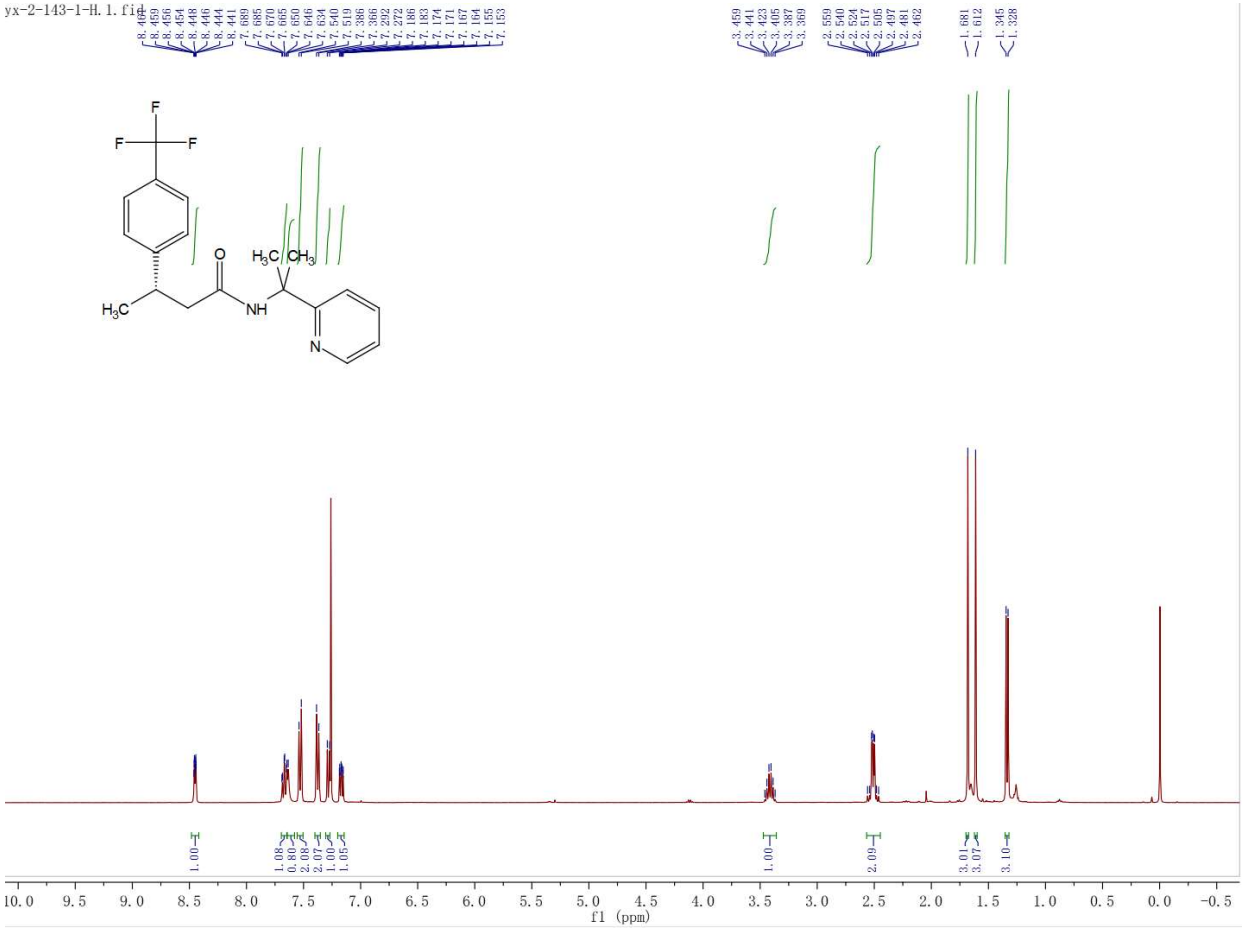
3c, ^{1}H NMR, 400 MHz, $CDCl_3$



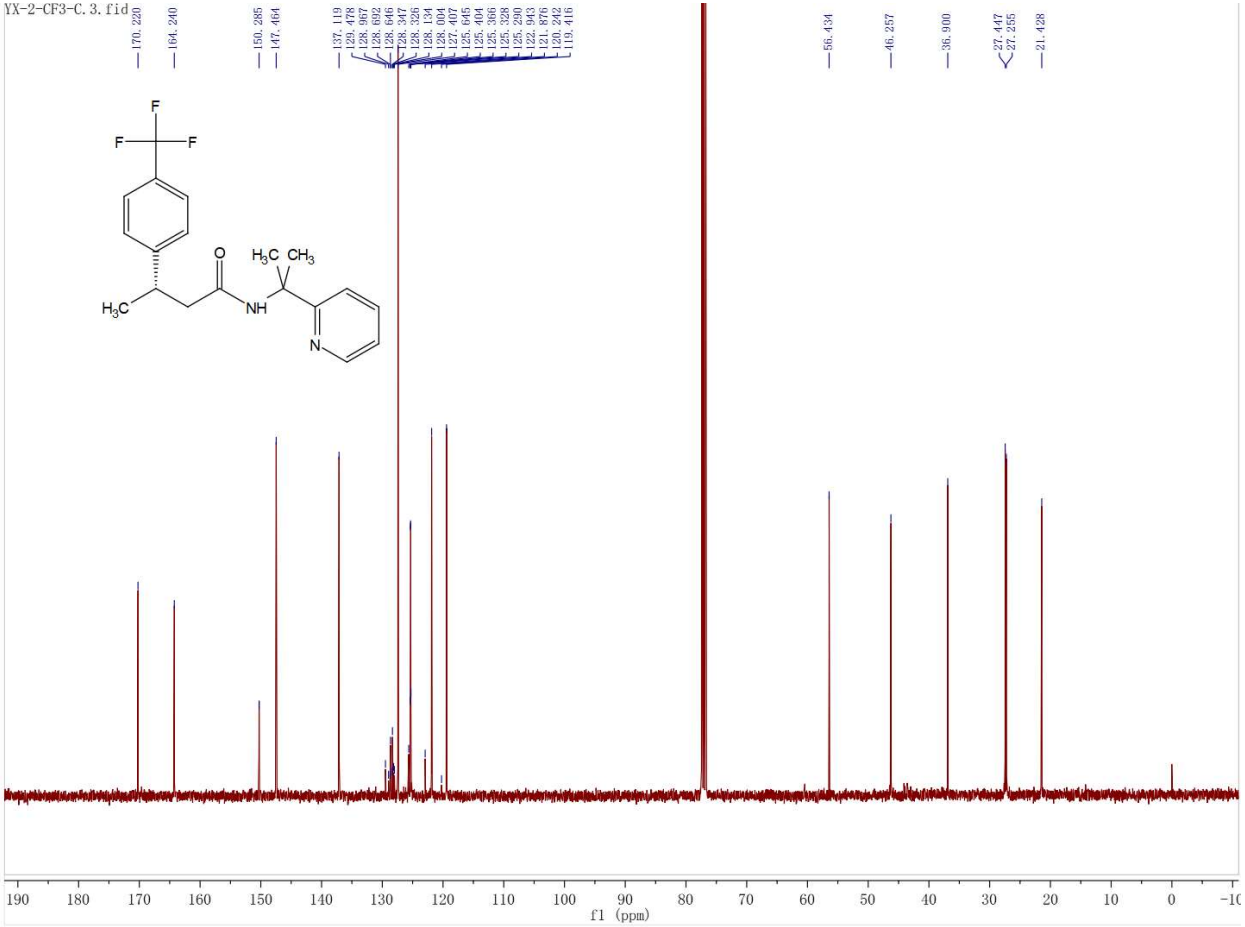
3c,^{13}C NMR, 101 MHz, $CDCl_3$



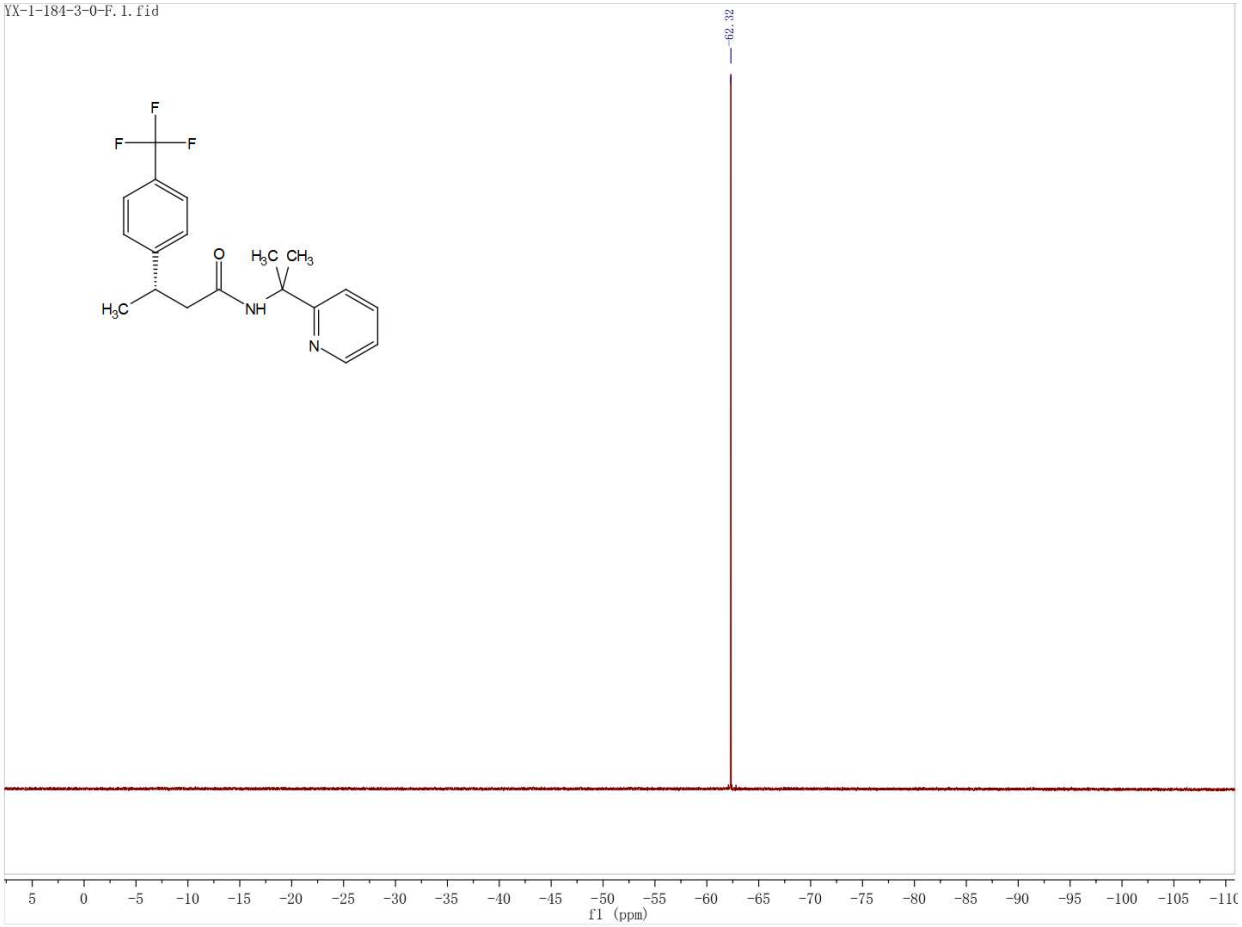
3d, ^{1}H NMR, 400 MHz, $CDCl_3$



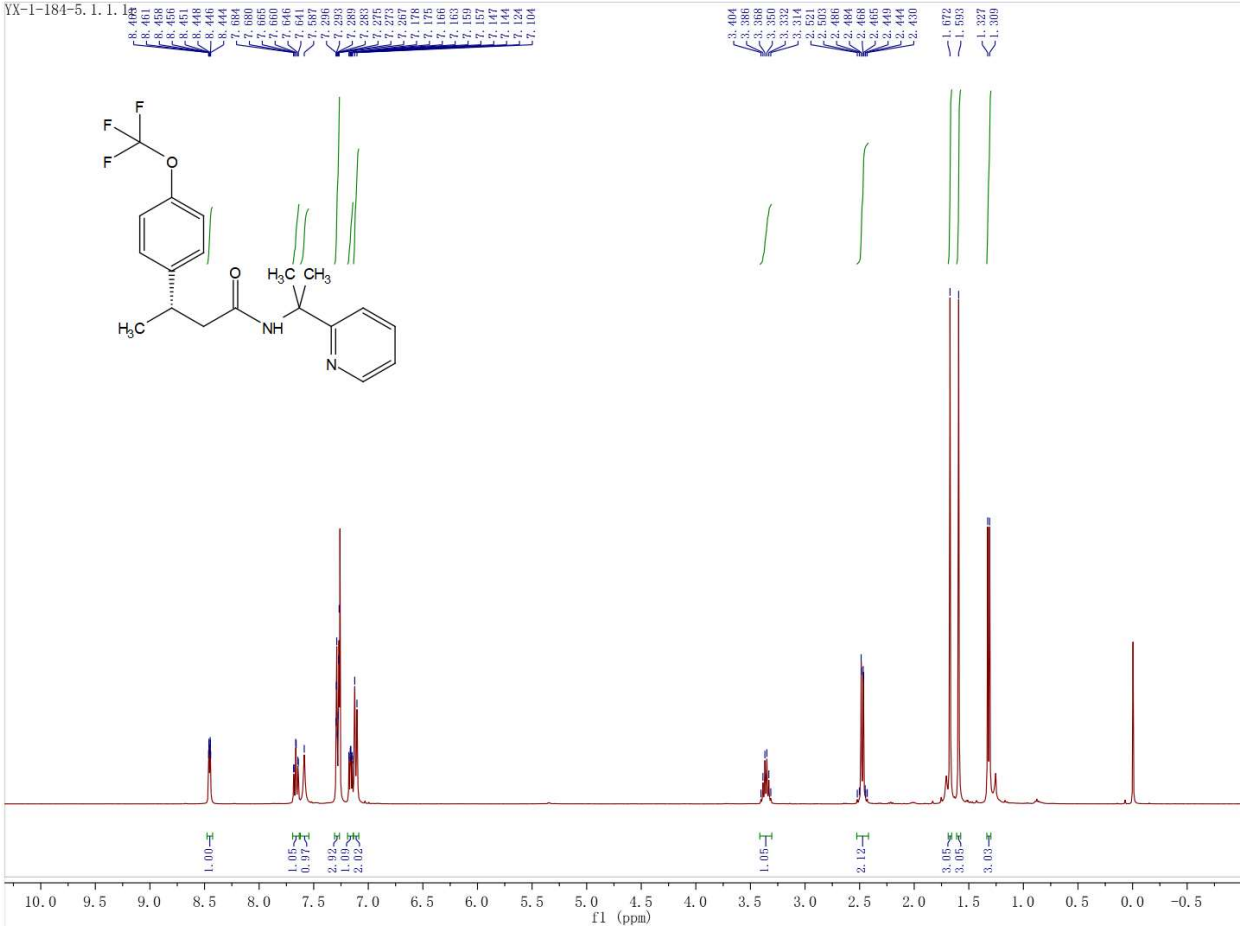
3d,^{13}C NMR, 101 MHz, $CDCl_3$



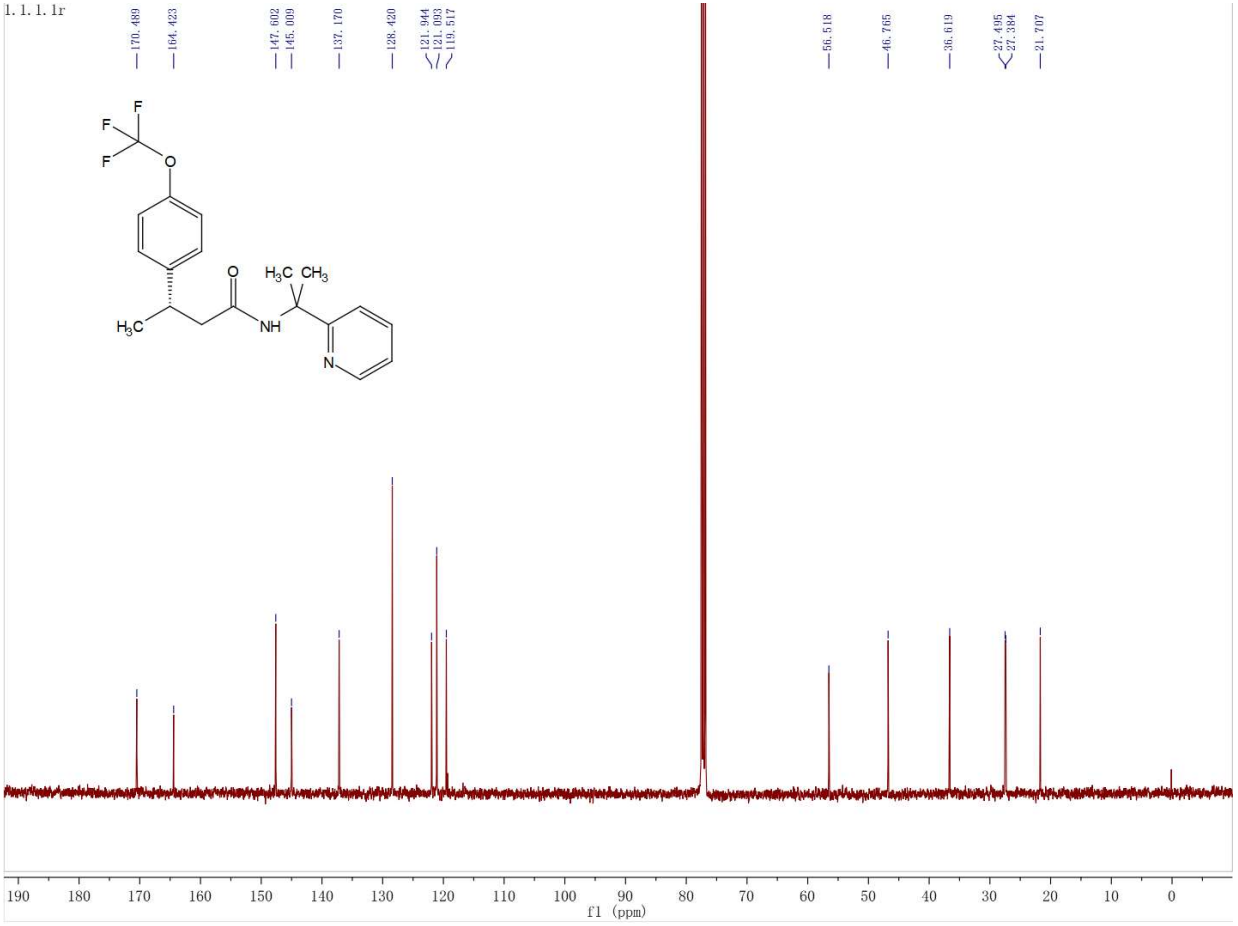
3d,^{19}F NMR, 400 MHz, $CDCl_3$



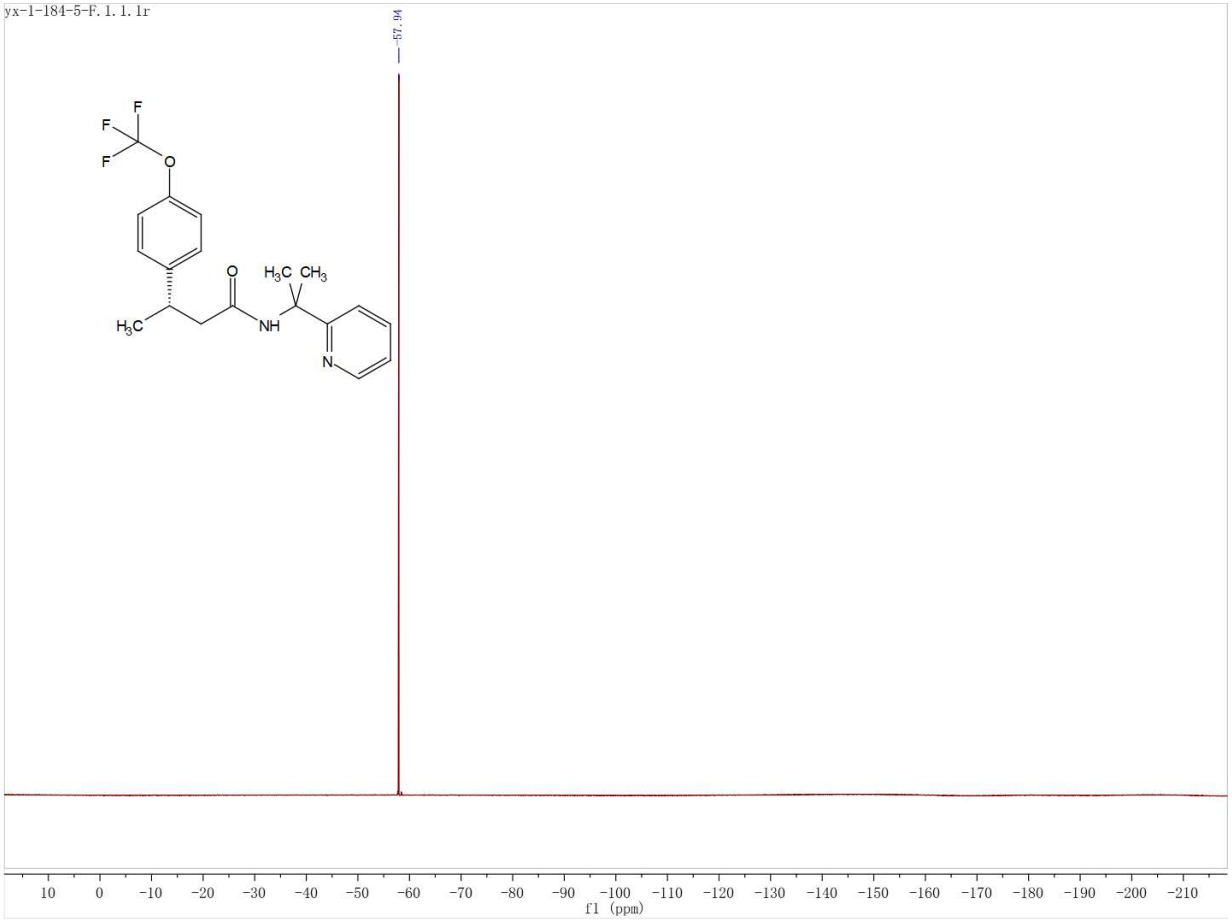
3e, ^{1}H NMR, 400 MHz, $CDCl_3$



3e,^{13}C NMR, 101 MHz, $CDCl_3$



3e,^{19}F NMR, 400 MHz, $CDCl_3$



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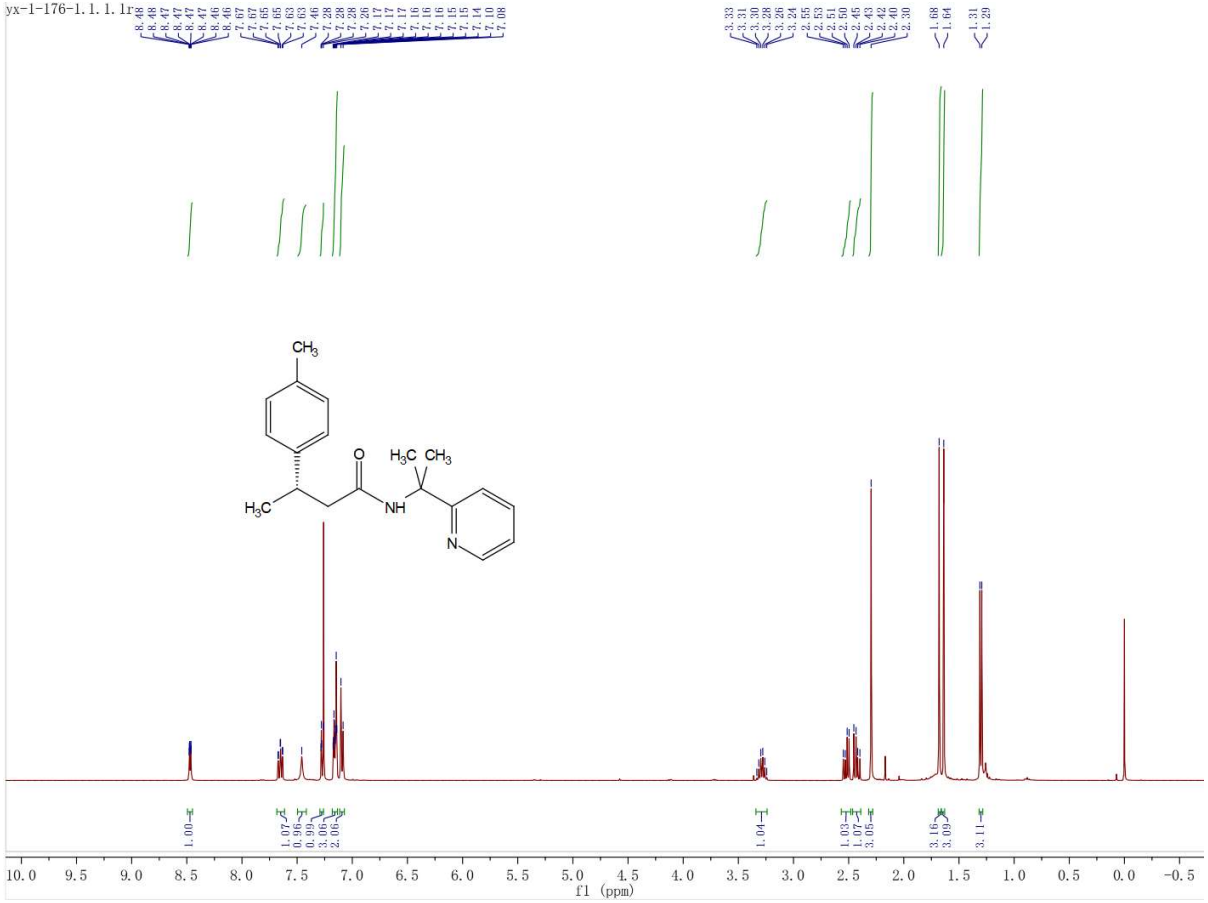
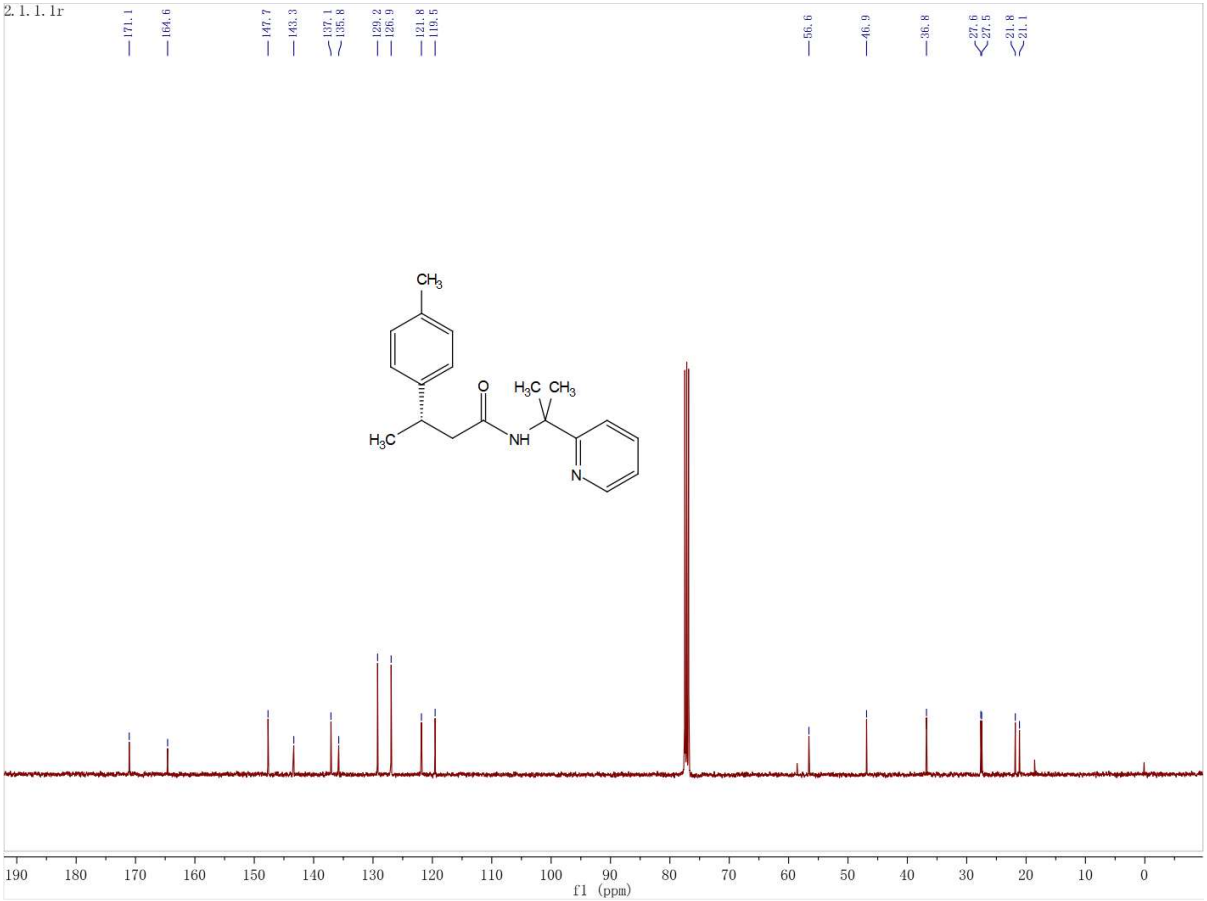
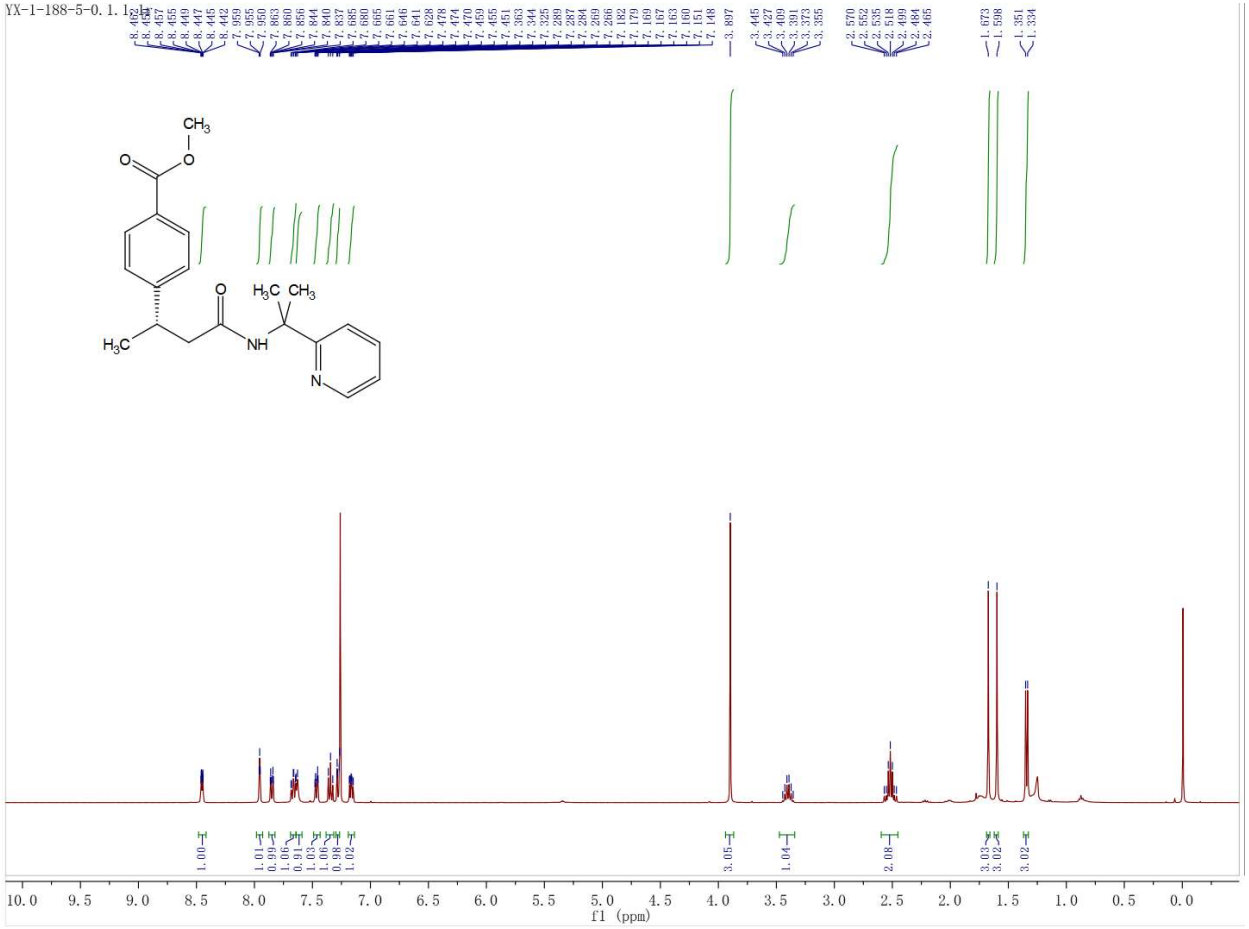


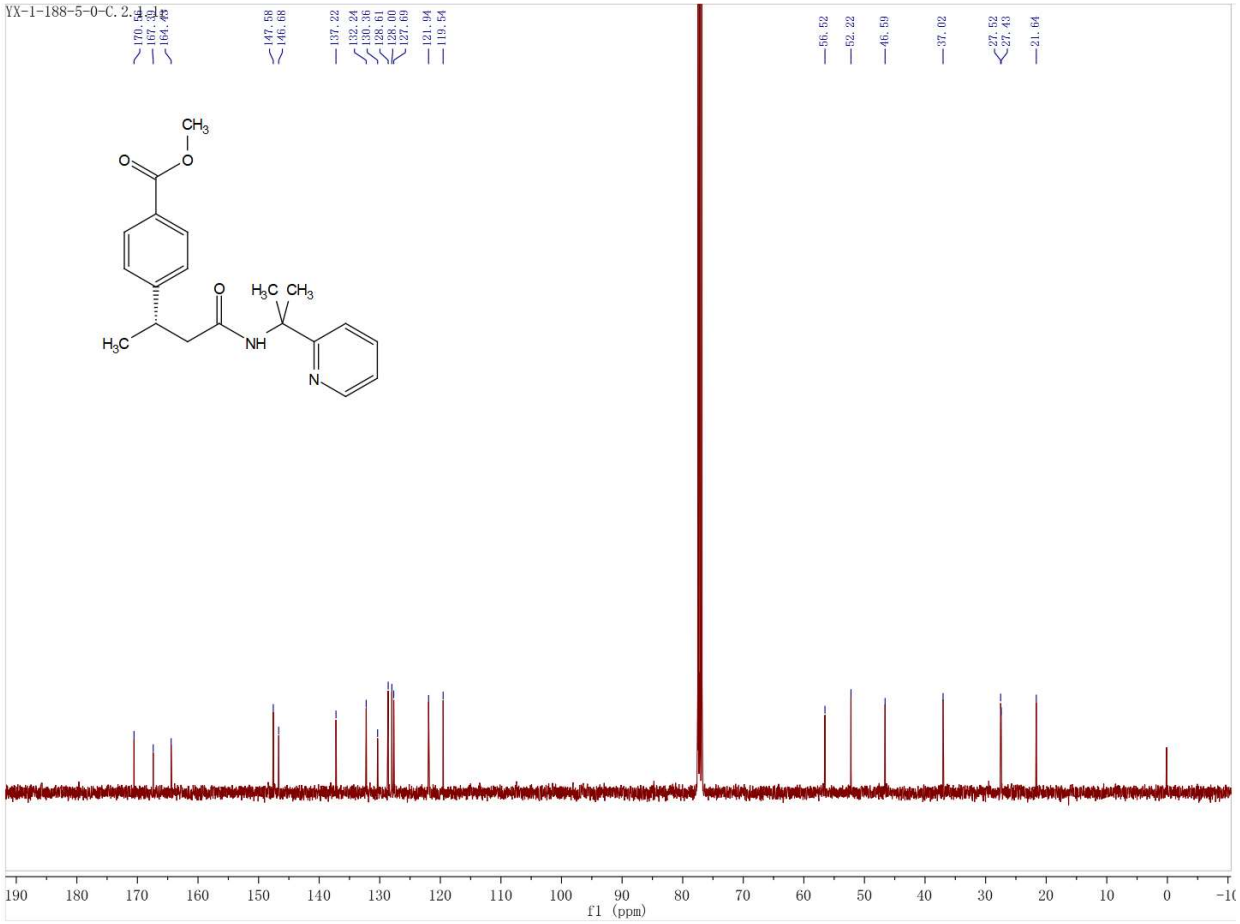
3f, ^{13}C NMR, 400 MHz, $CDCl_3$



3g, ^{1}H NMR, 400 MHz, $CDCl_3$



3g,^{13}C NMR, 101 MHz, $CDCl_3$



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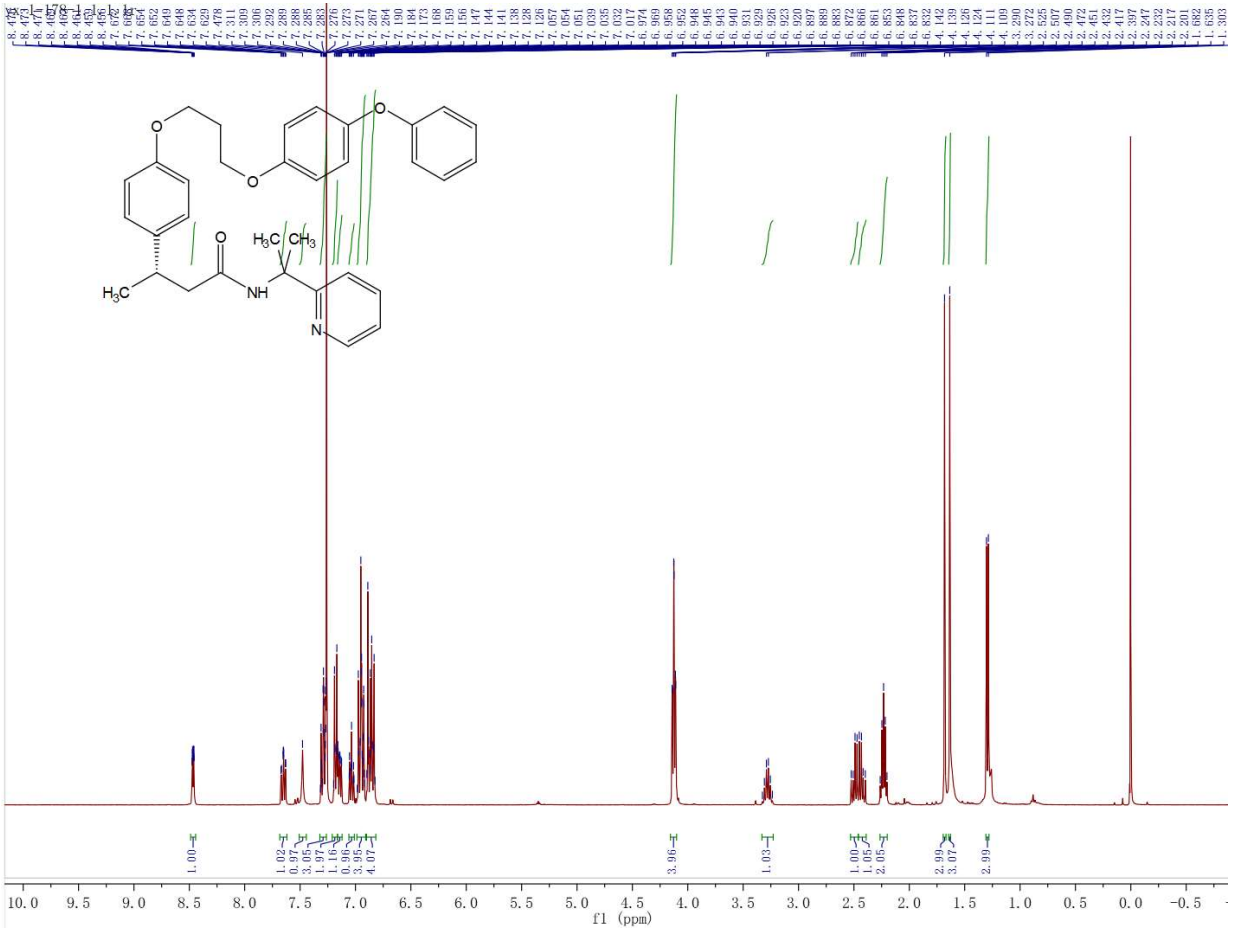

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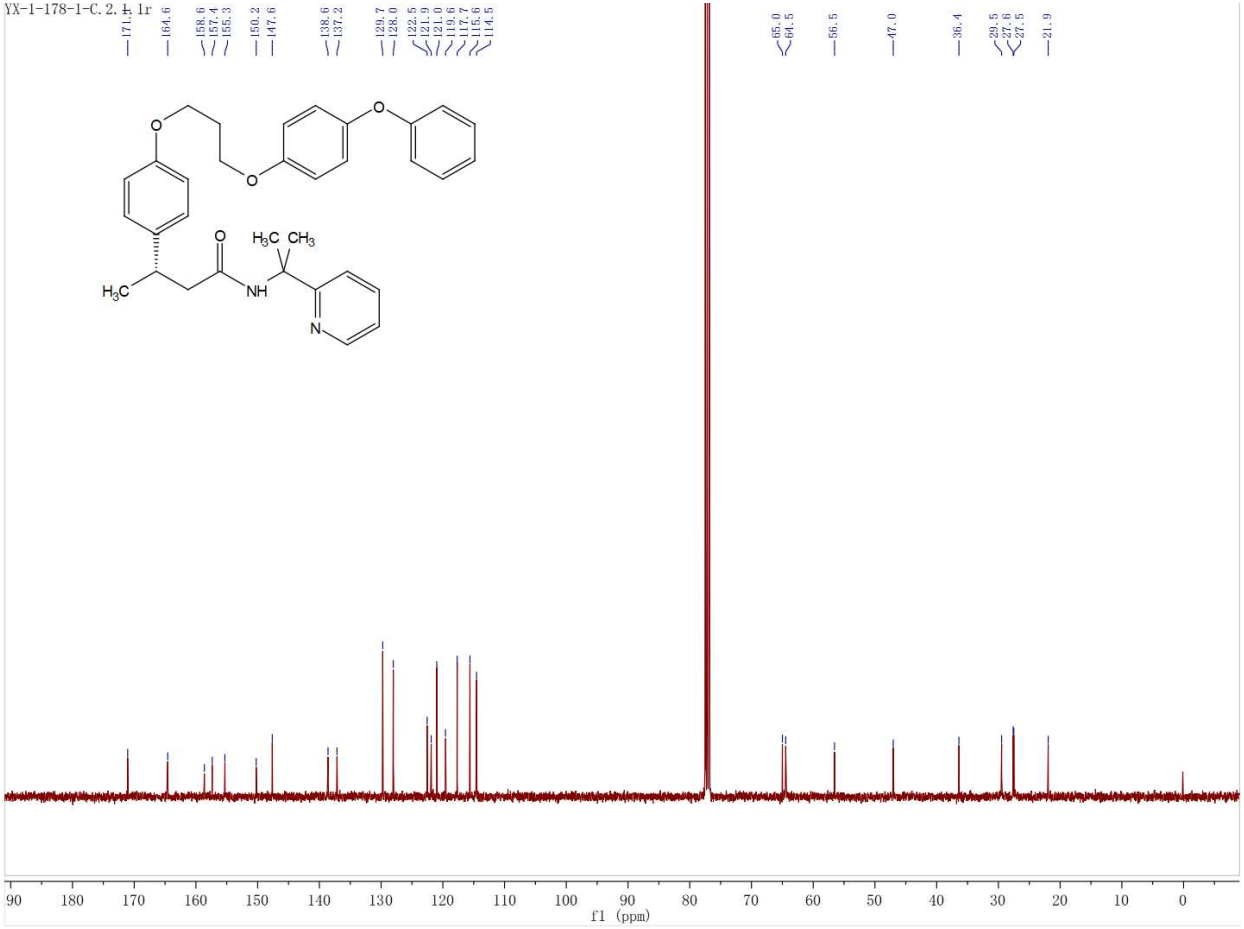
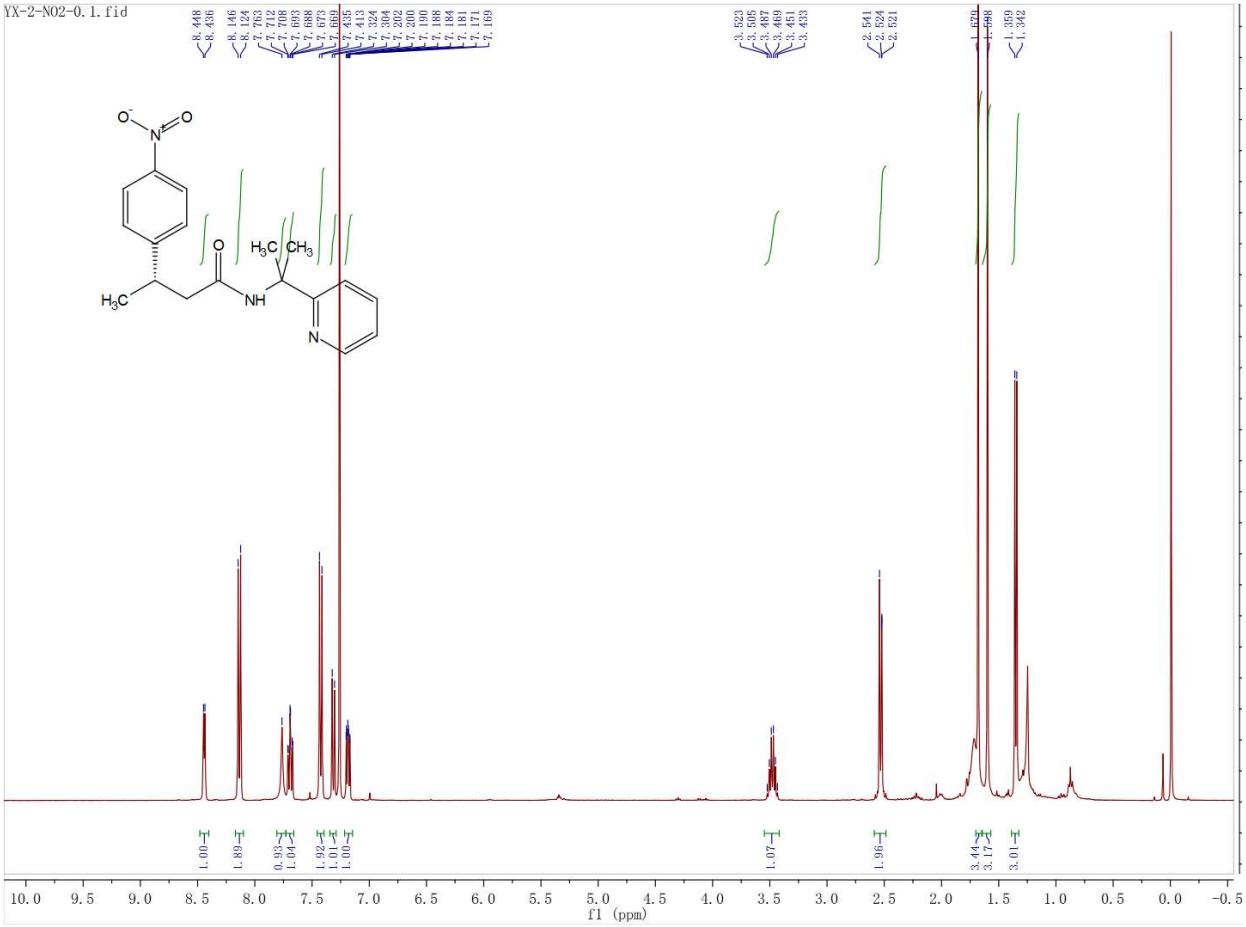
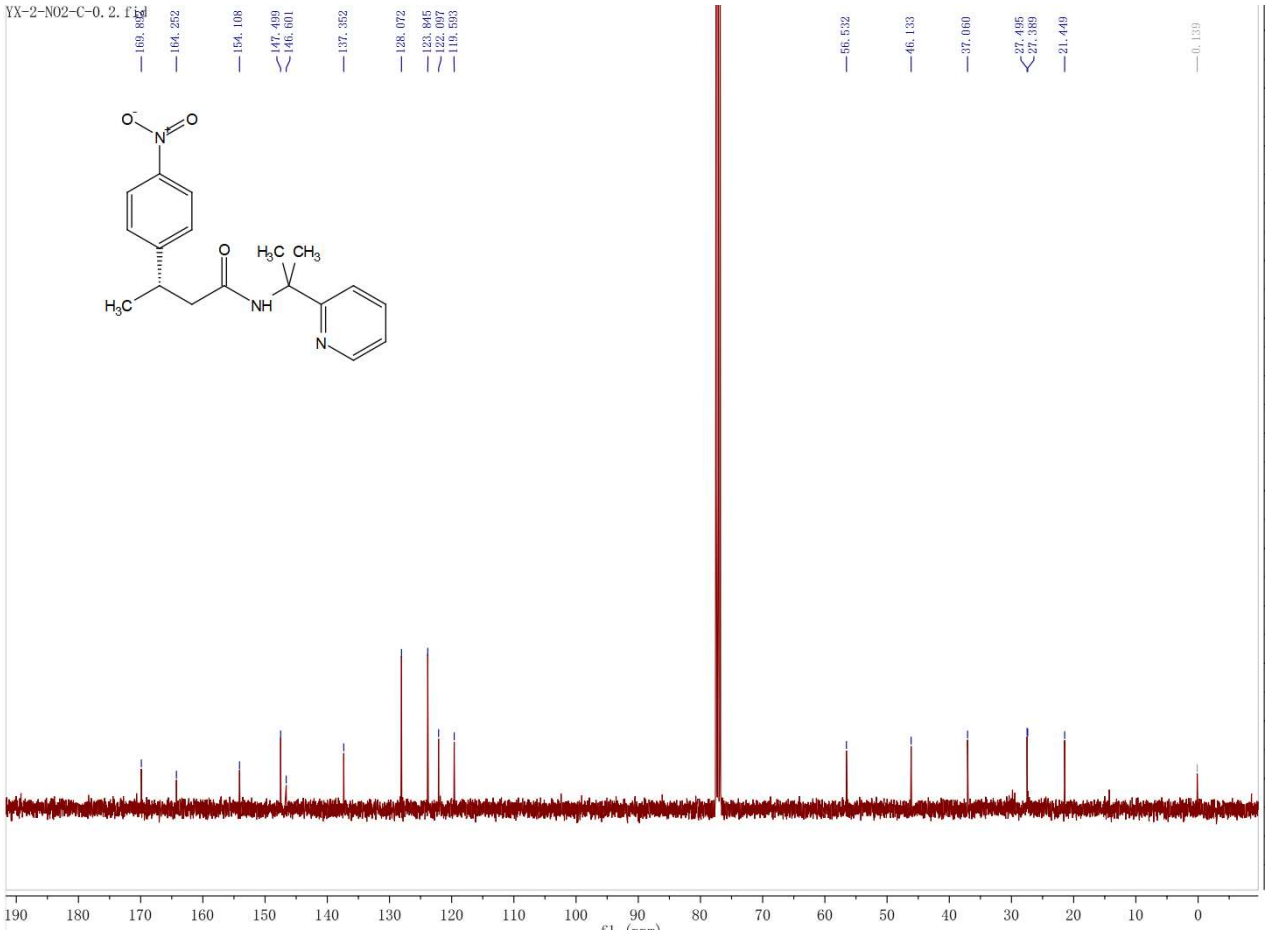


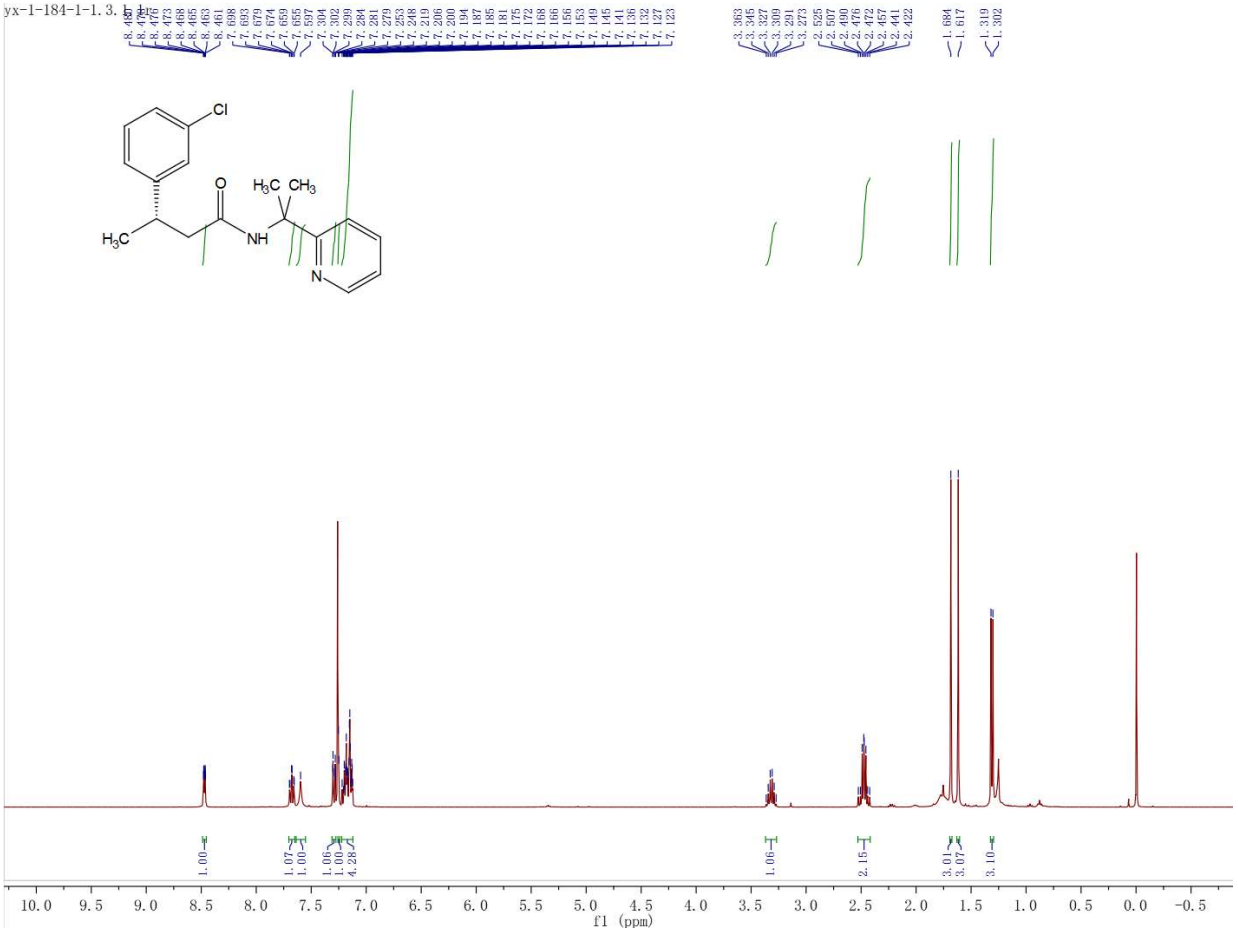
3i, ^{1}H NMR, 400 MHz, $CDCl_3$



3i,^{13}C NMR, 101 MHz, $CDCl_3$



3j, ^{1}H NMR, 400 MHz, $CDCl_3$



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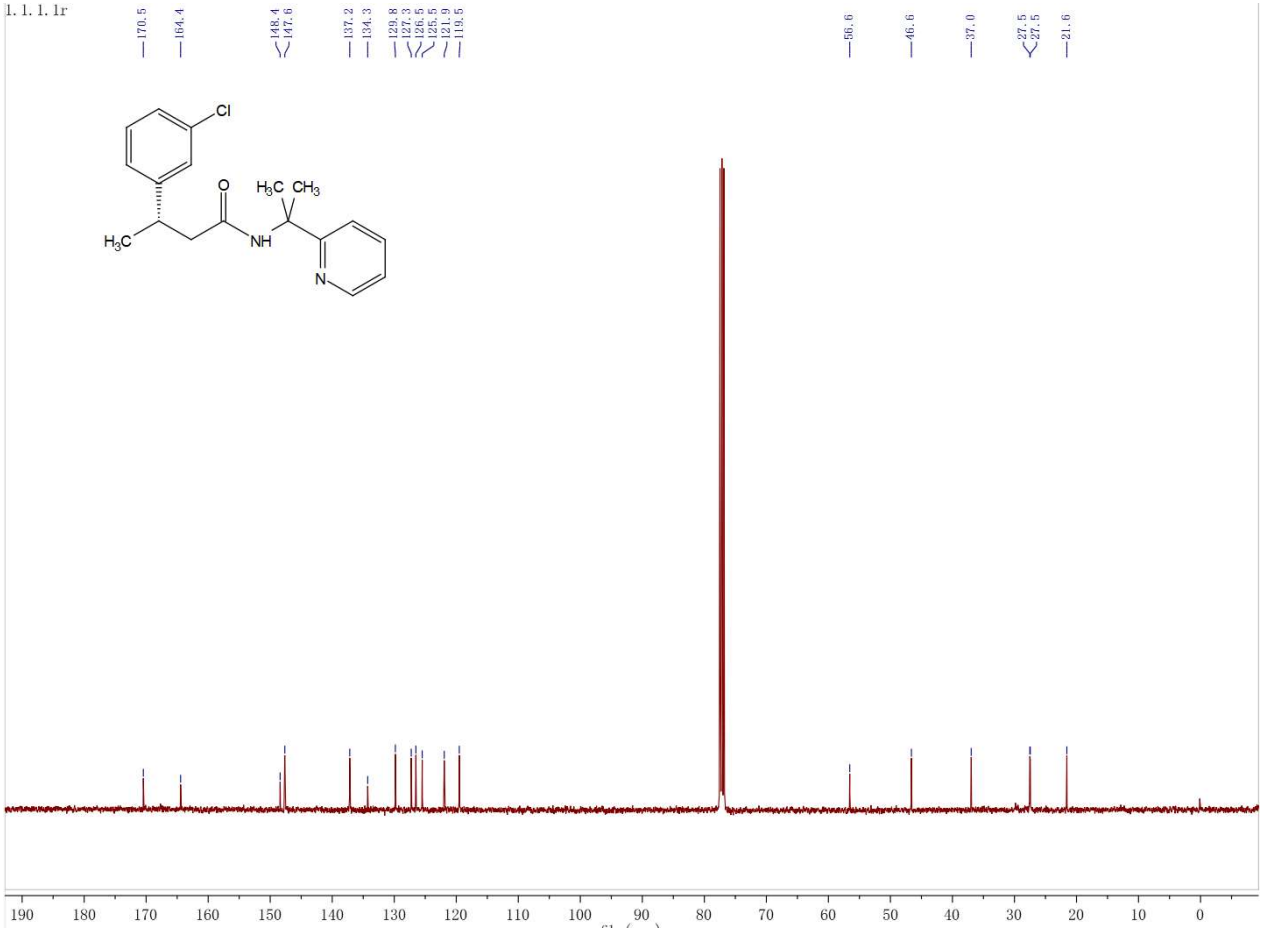
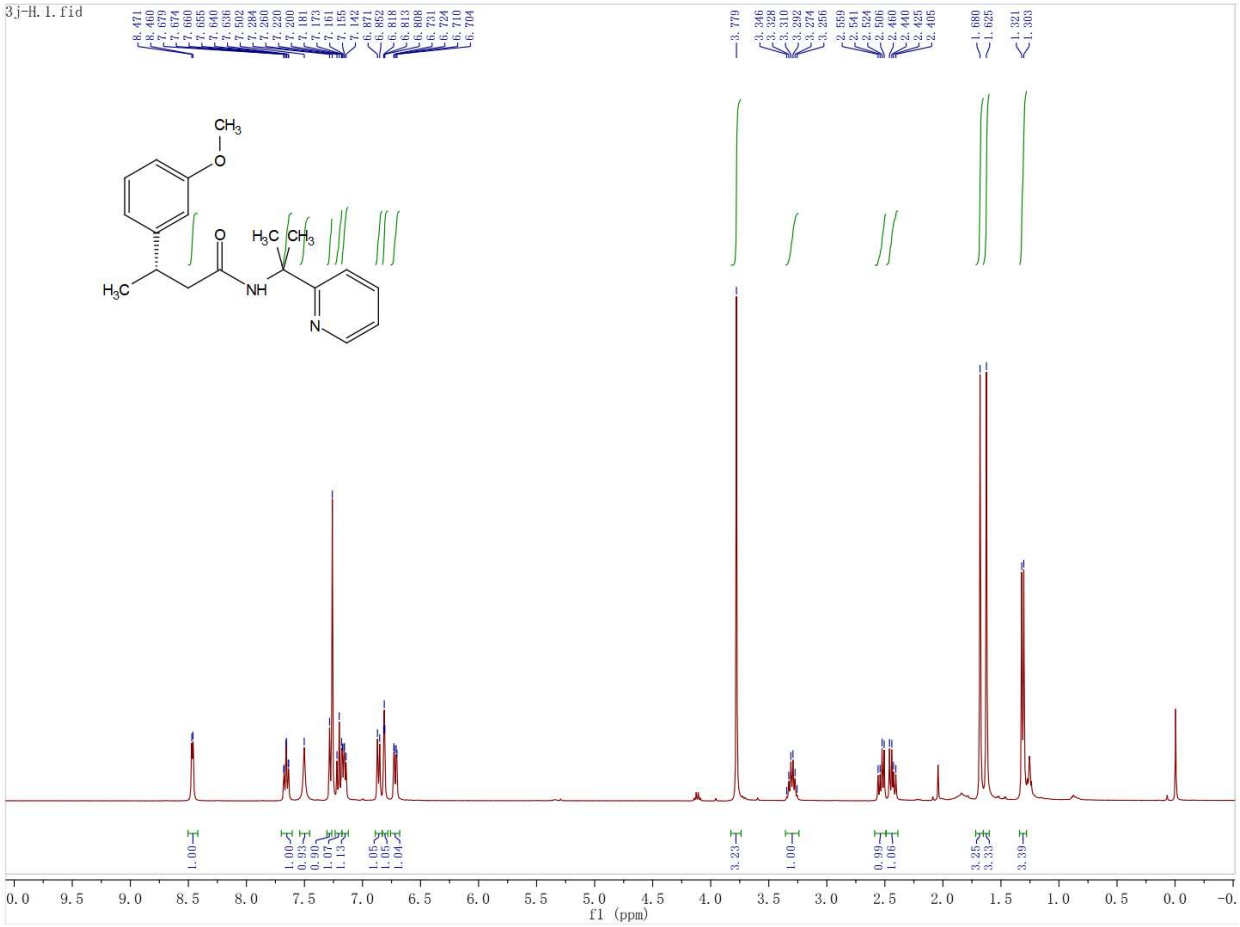


3k, ^{1}H NMR, 400 MHz, $CDCl_3$



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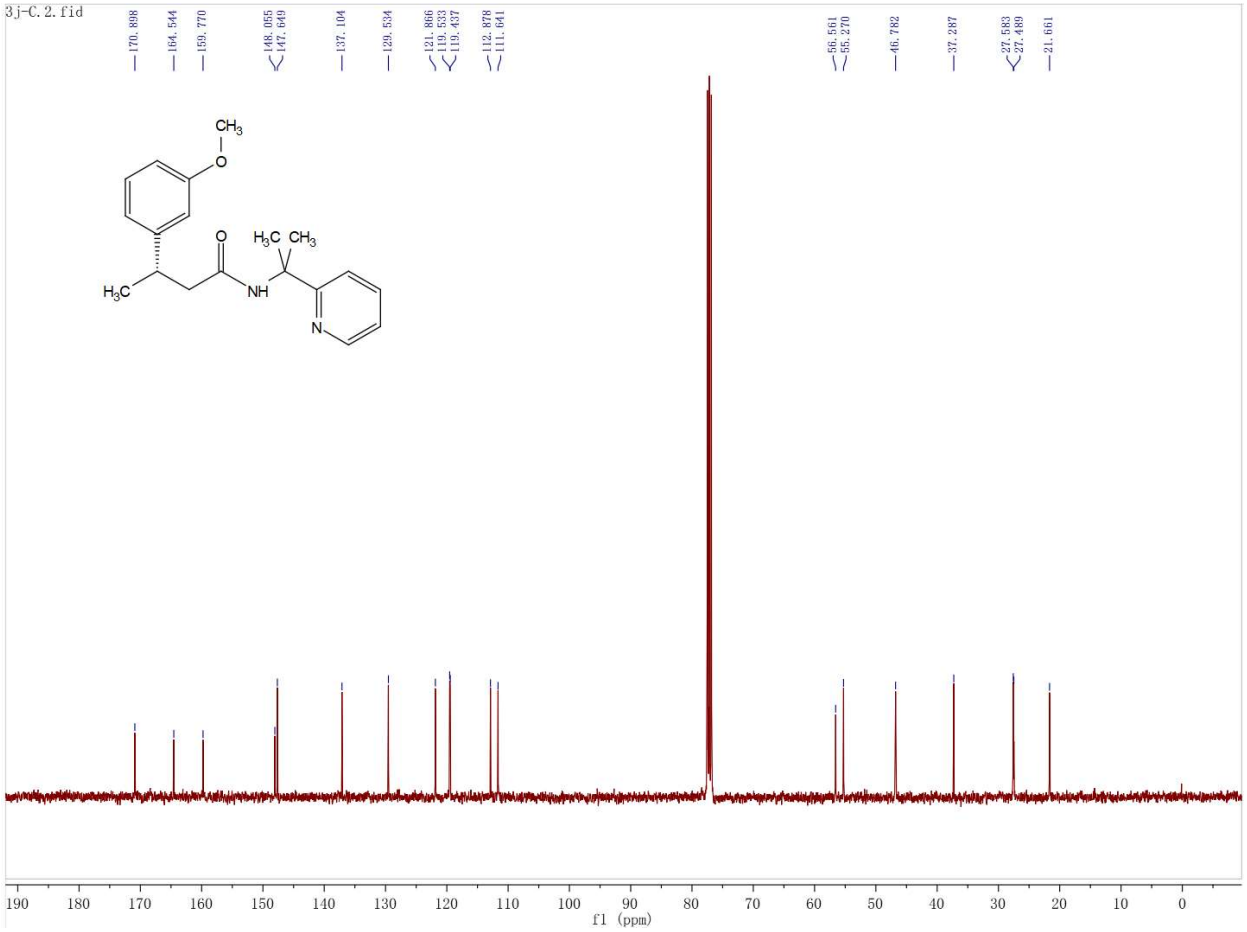
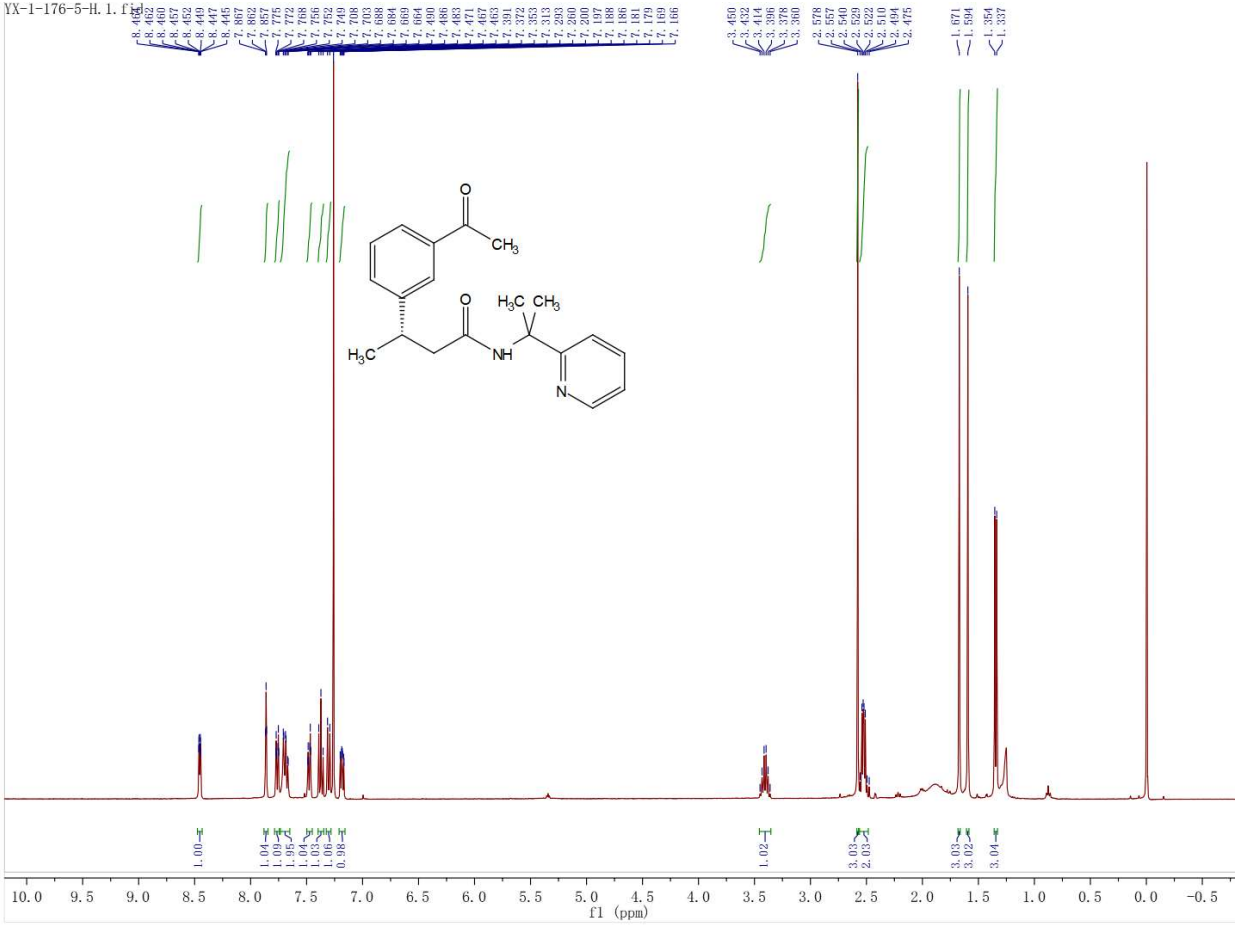


3l, ^{1}H NMR, 400 MHz, $CDCl_3$



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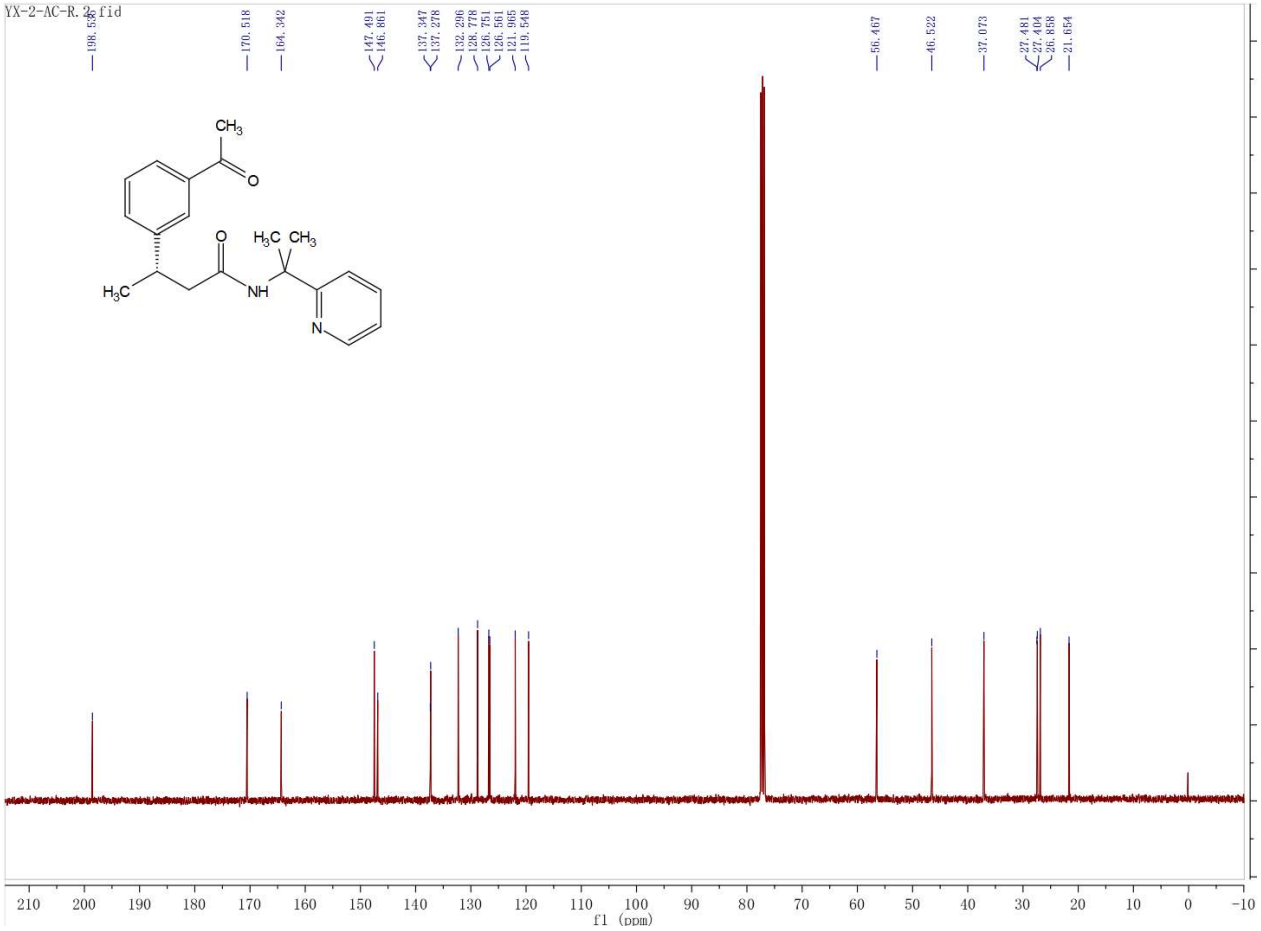
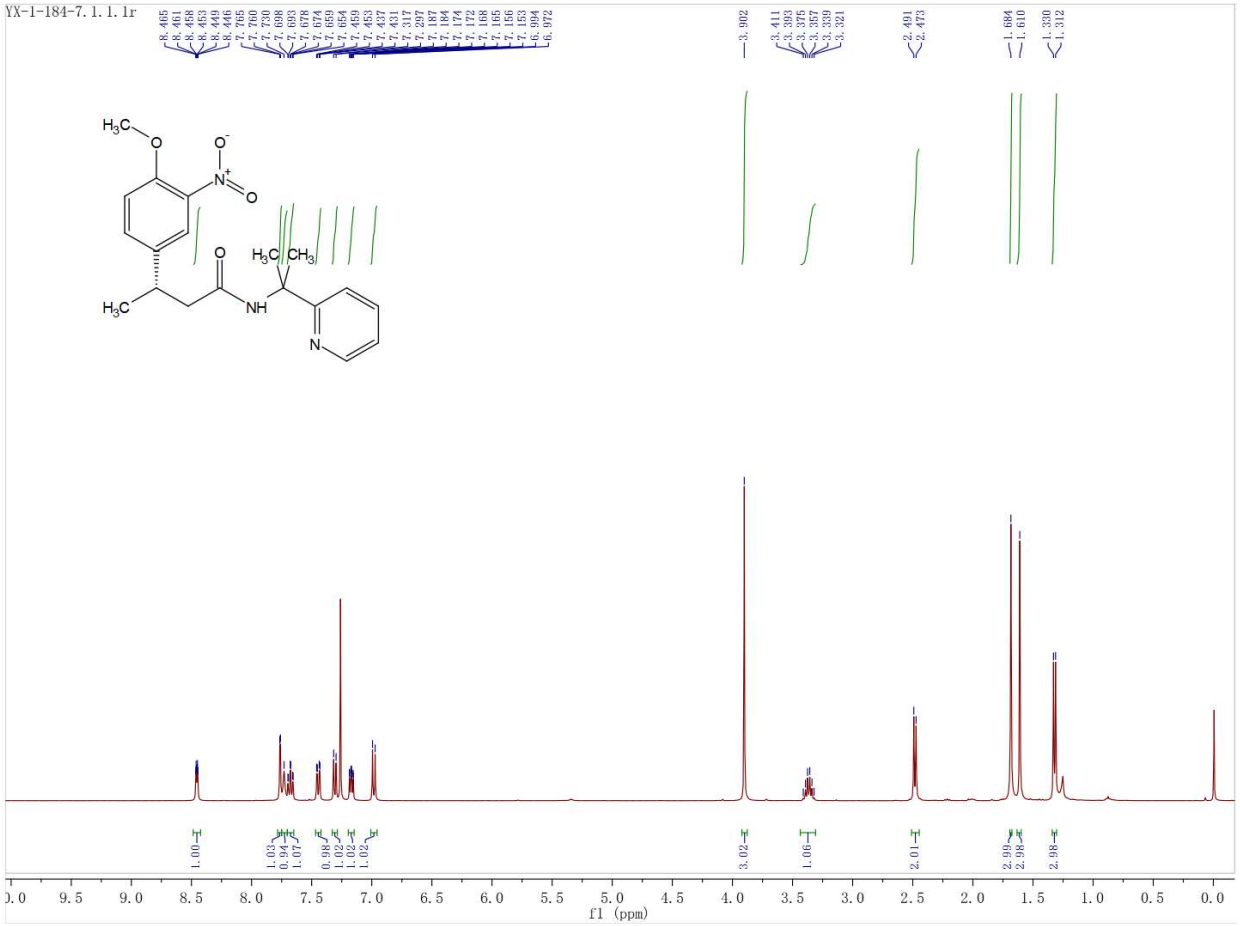
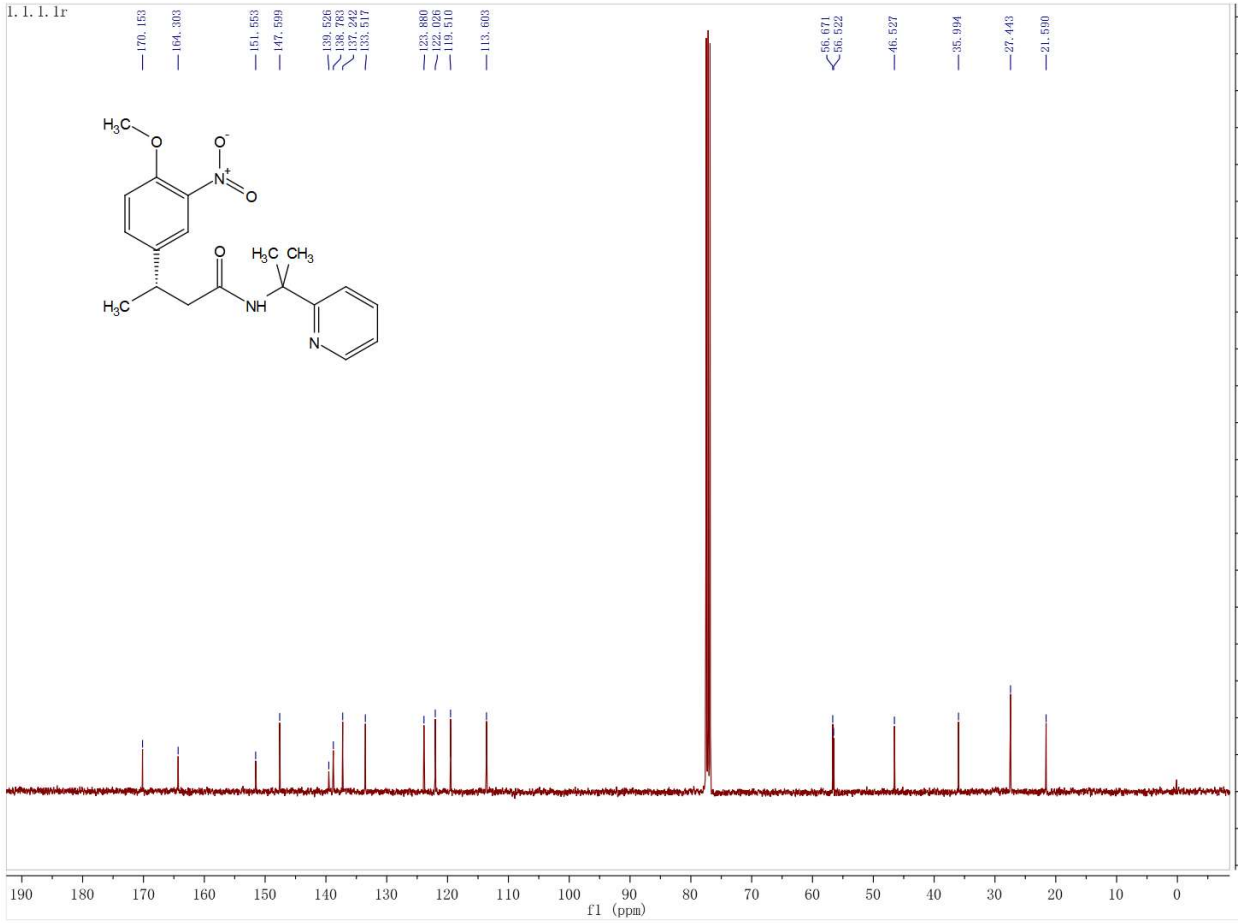


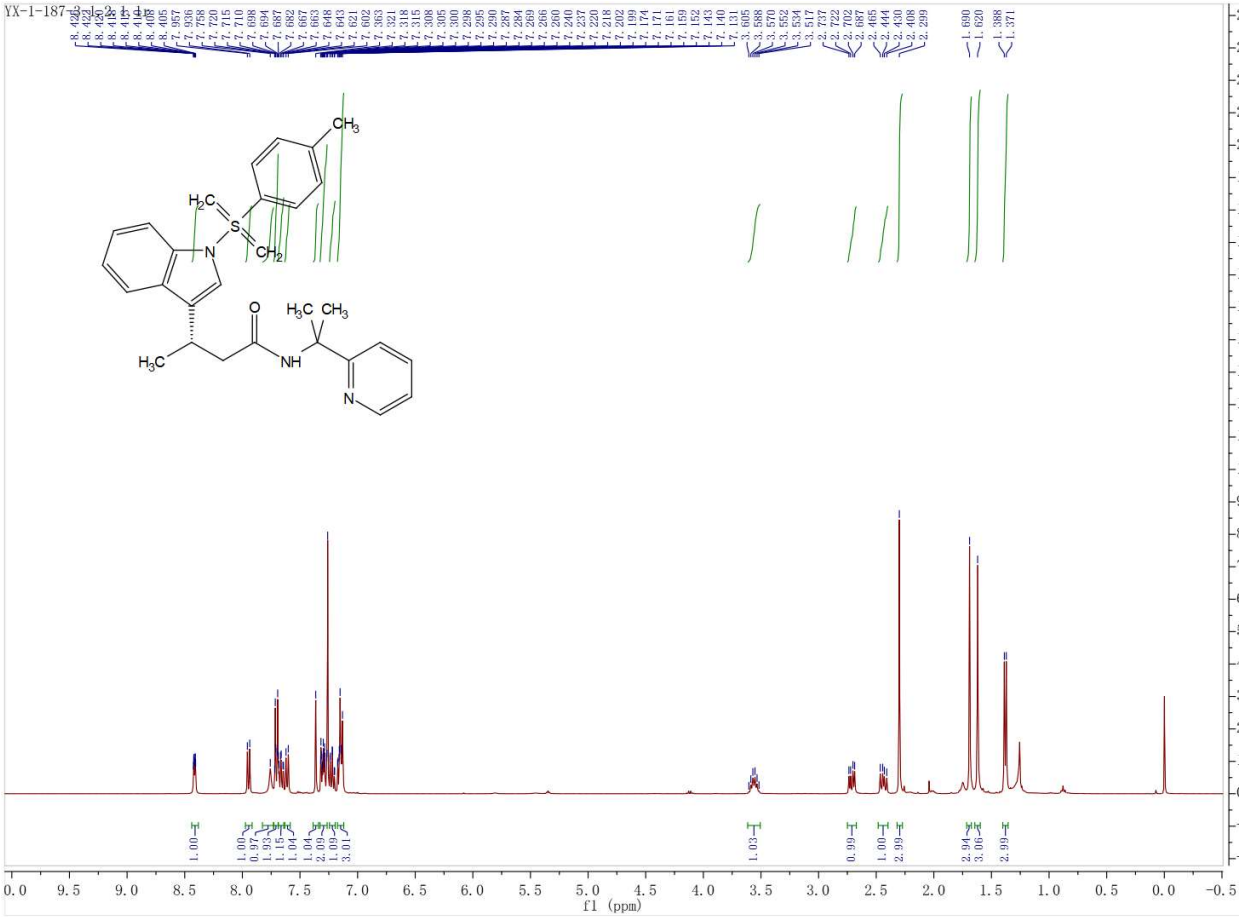
3m, ^{1}H NMR, 400 MHz, $CDCl_3$



3m,^{13}C NMR, 101 MHz, $CDCl_3$



3n, ^{1}H NMR, 400 MHz, $CDCl_3$



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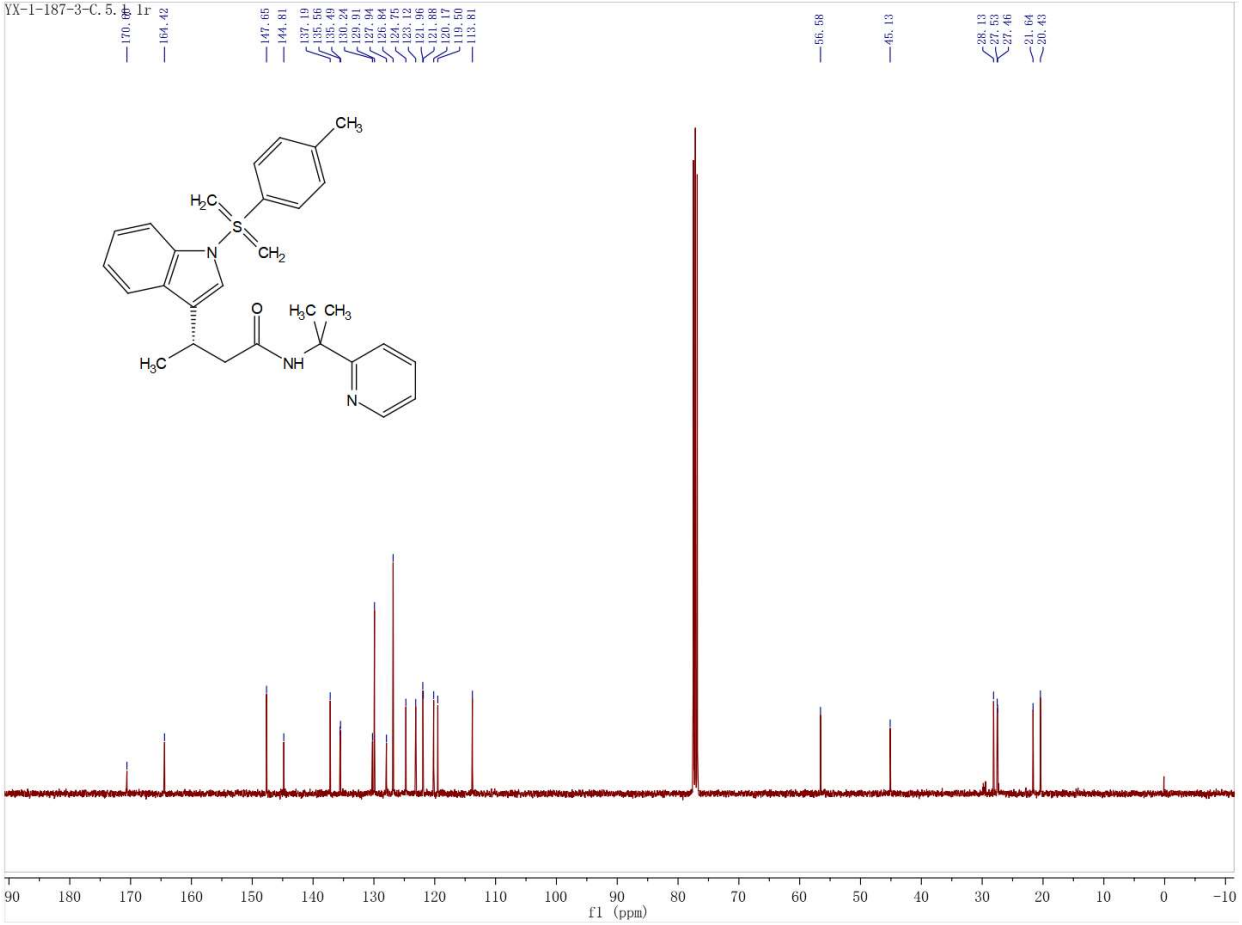
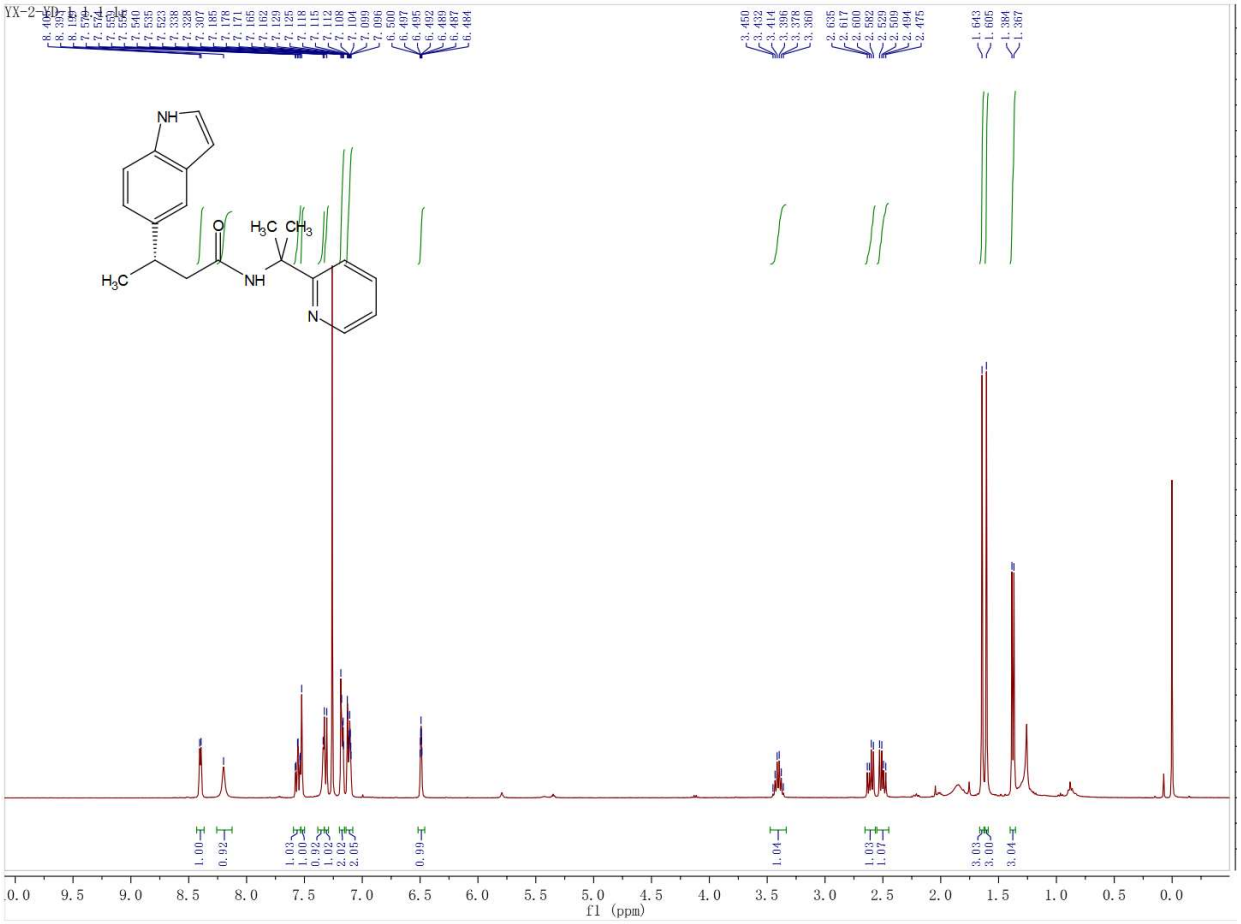
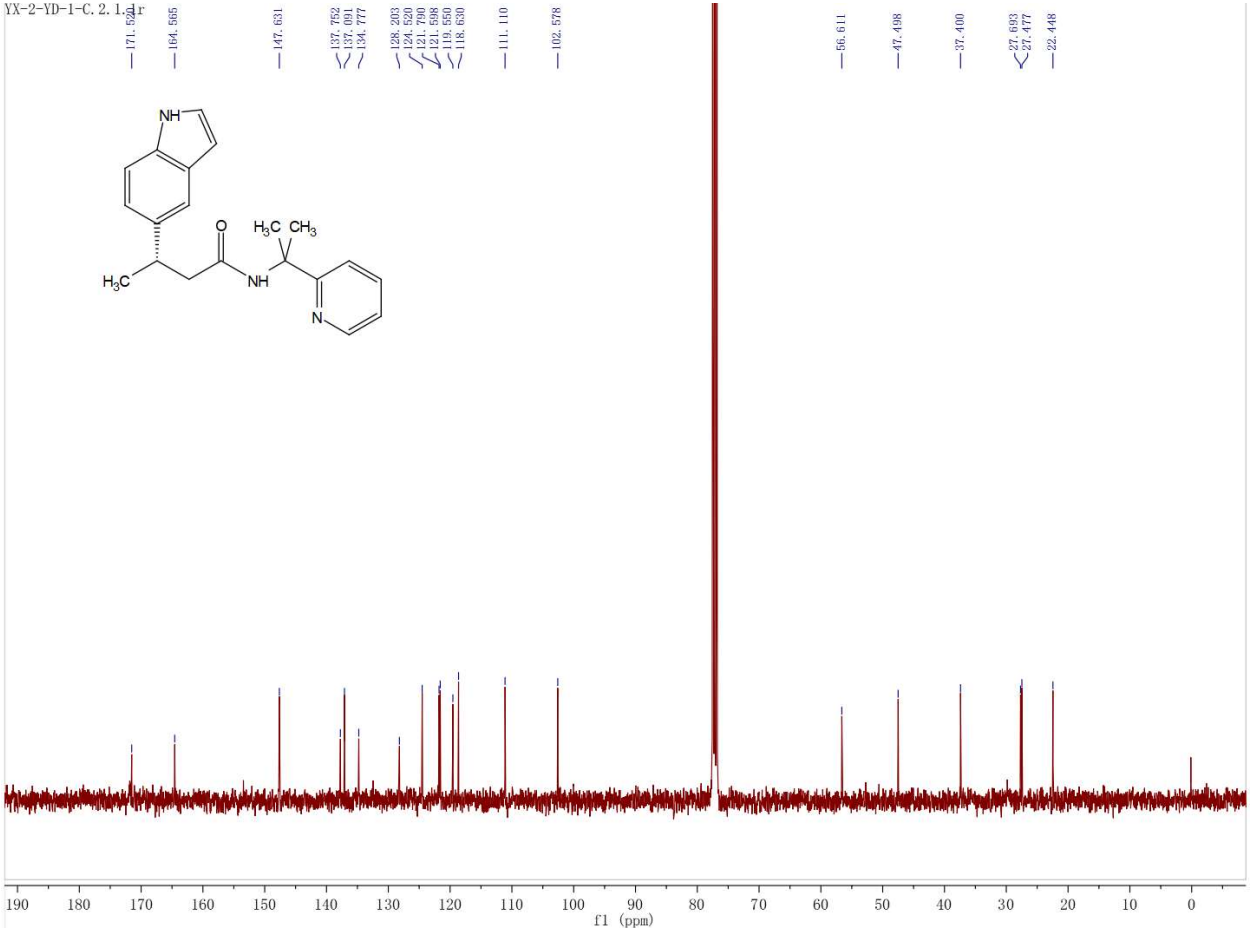


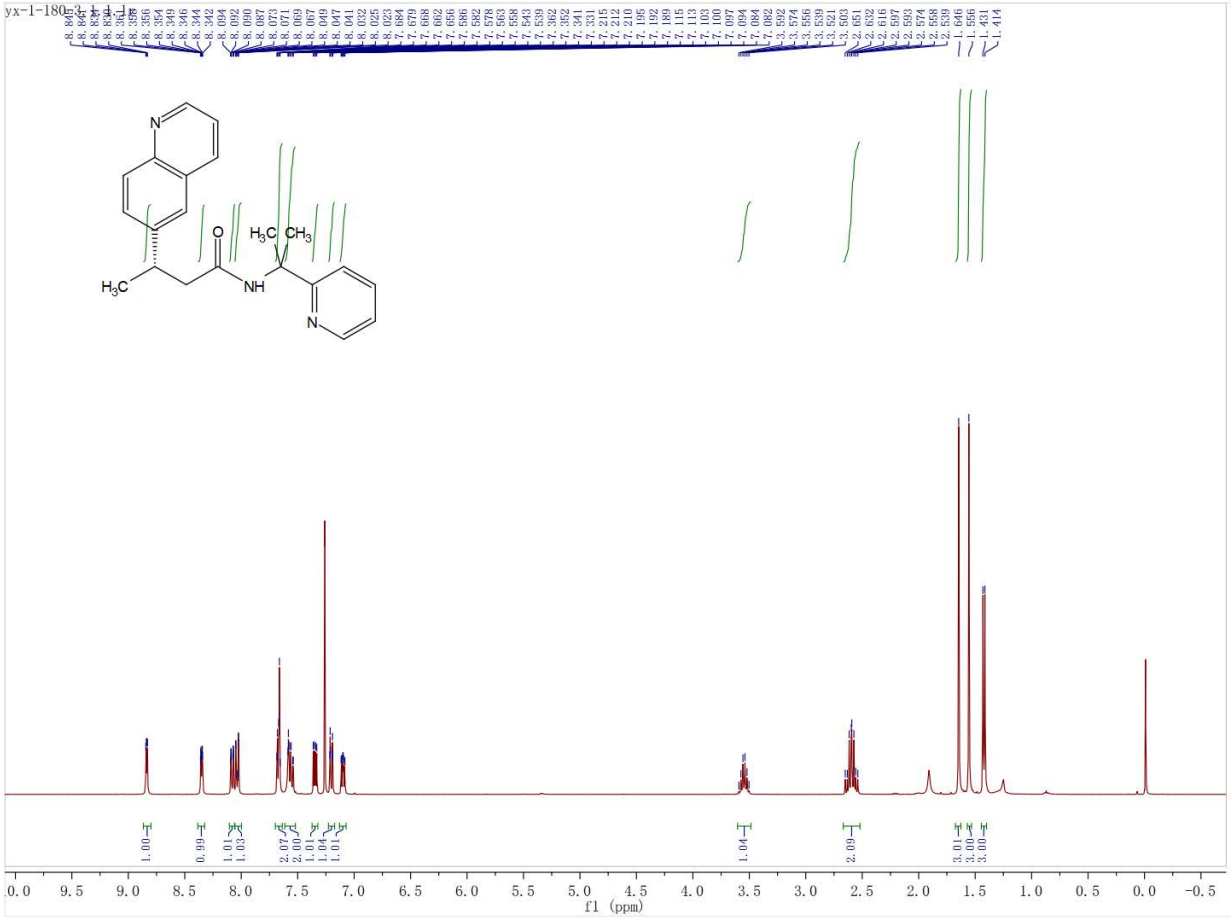
3o, ^{1}H NMR, 400 MHz, $CDCl_3$



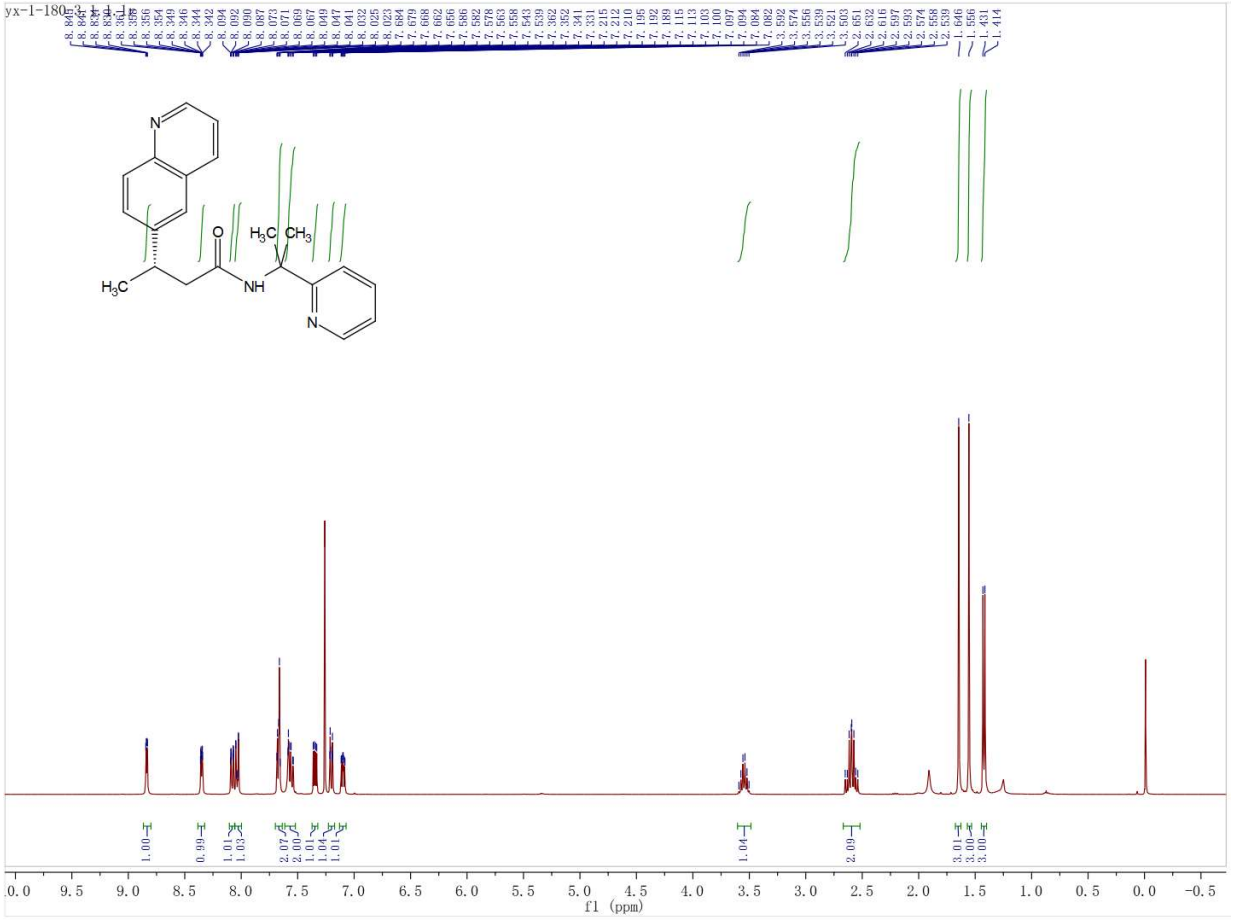
3o,^{13}C NMR, 101 MHz, $CDCl_3$



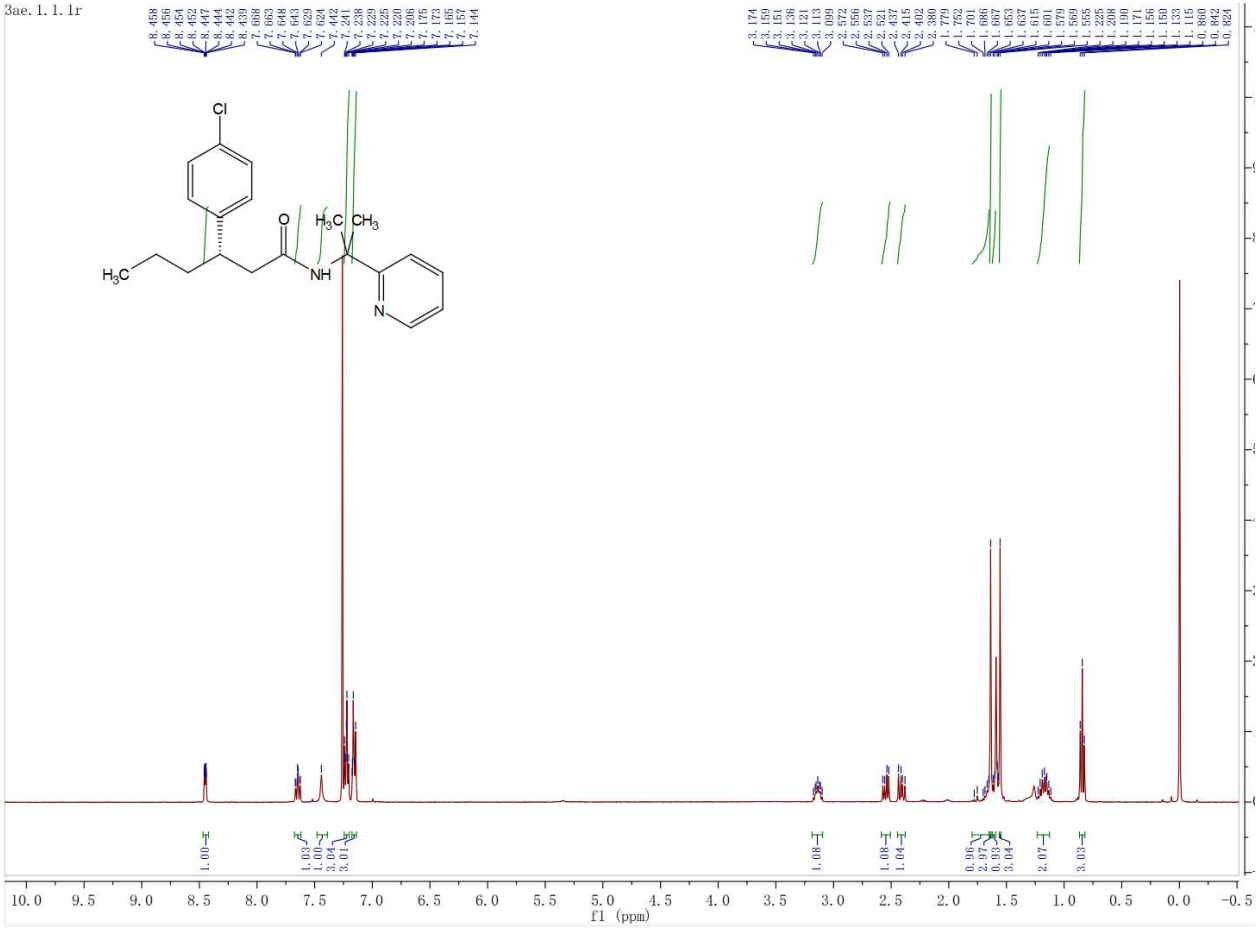
3p, ^{1}H NMR, 400 MHz, $CDCl_3$



3p,^{13}C NMR, 101 MHz, $CDCl_3$



4a, ^{1}H NMR, 400 MHz, $CDCl_3$



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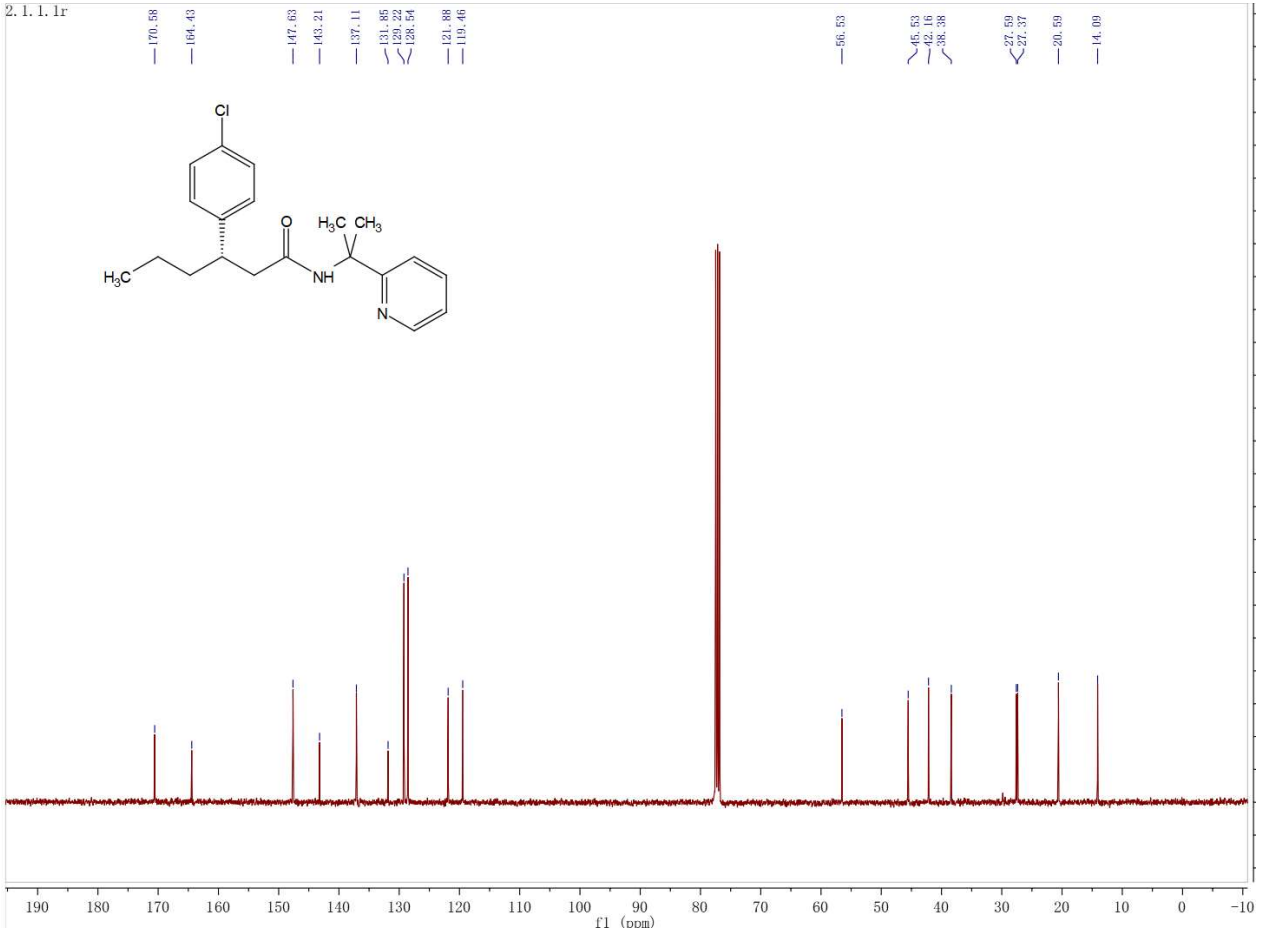

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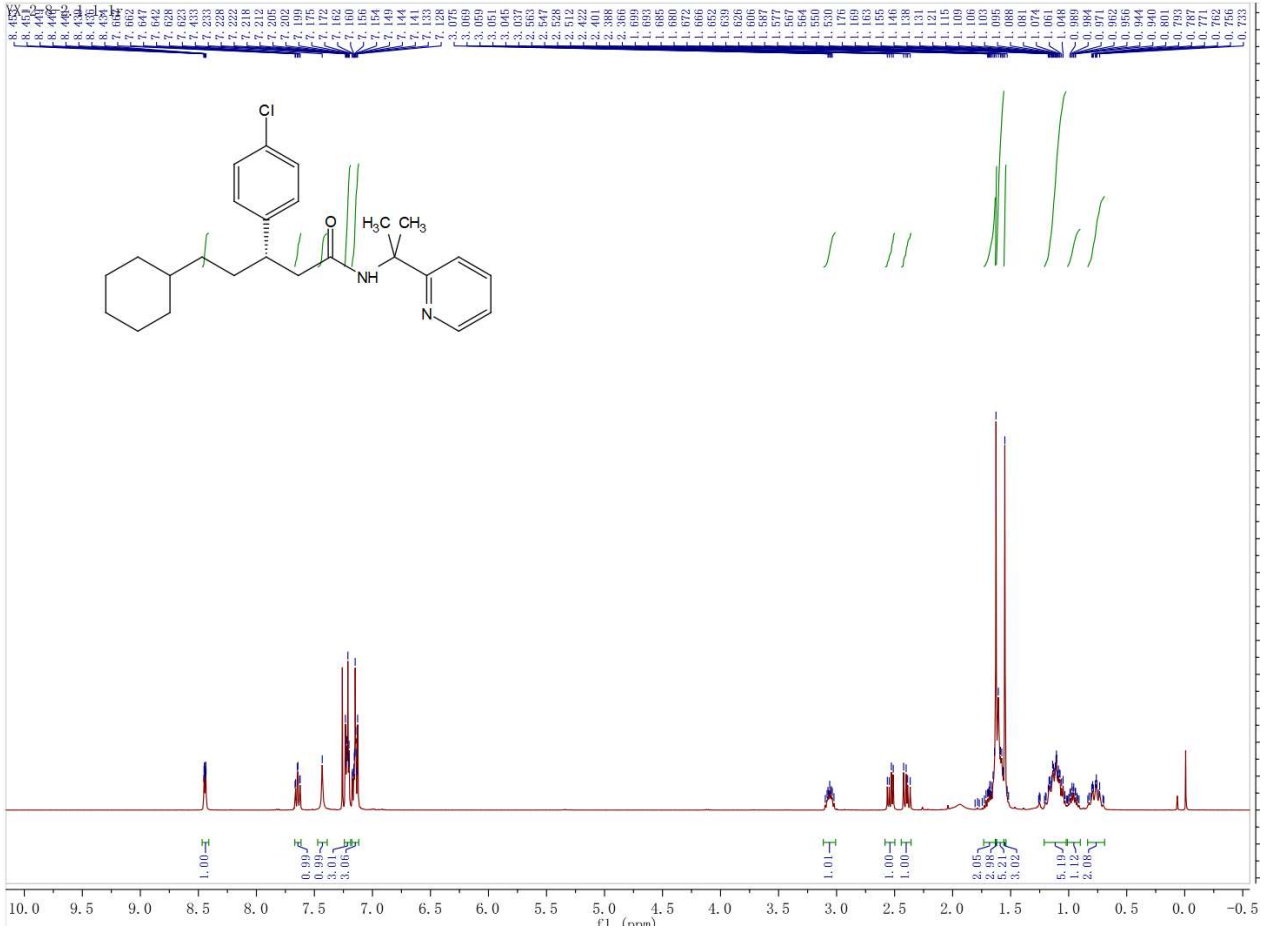

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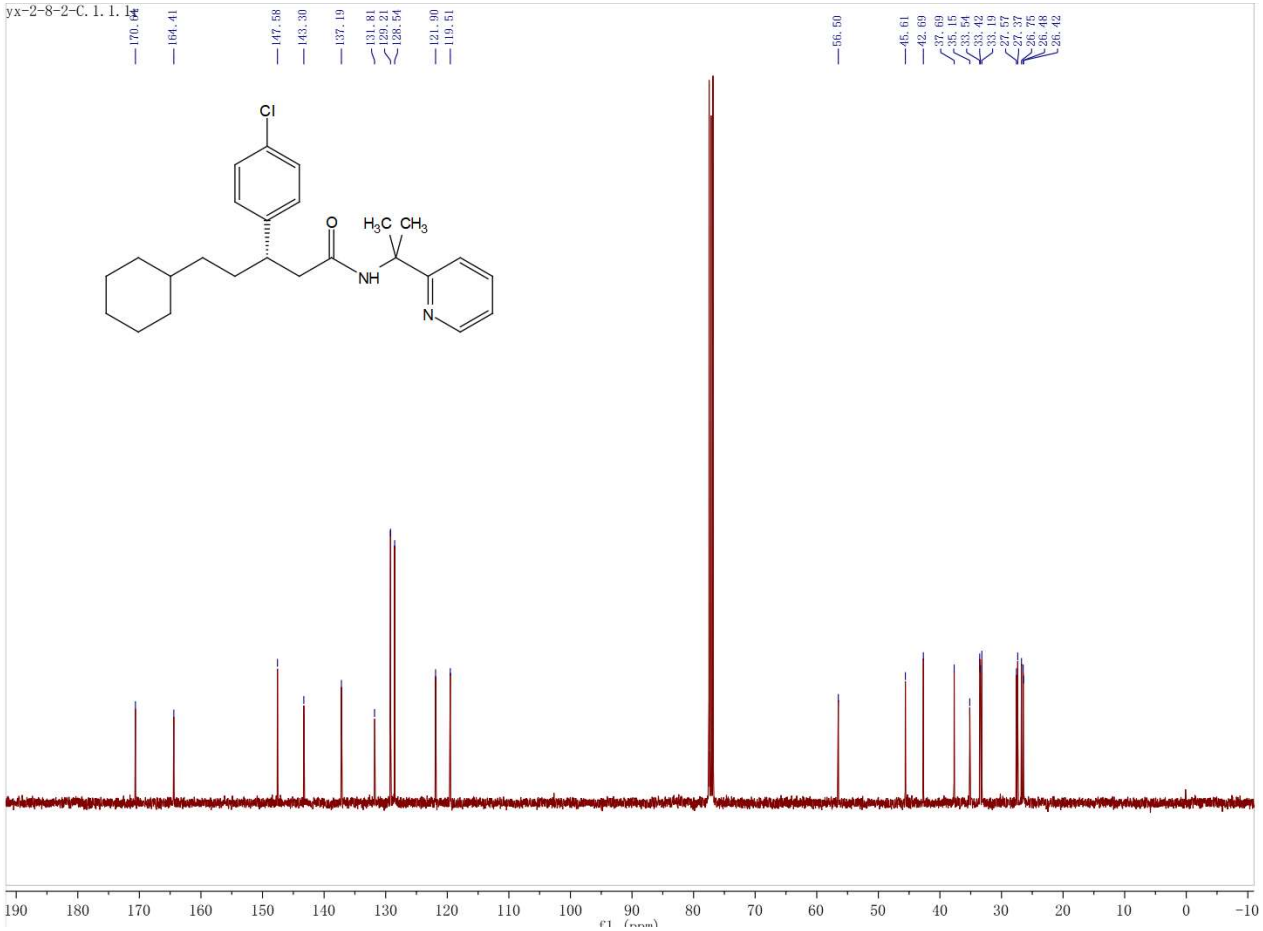

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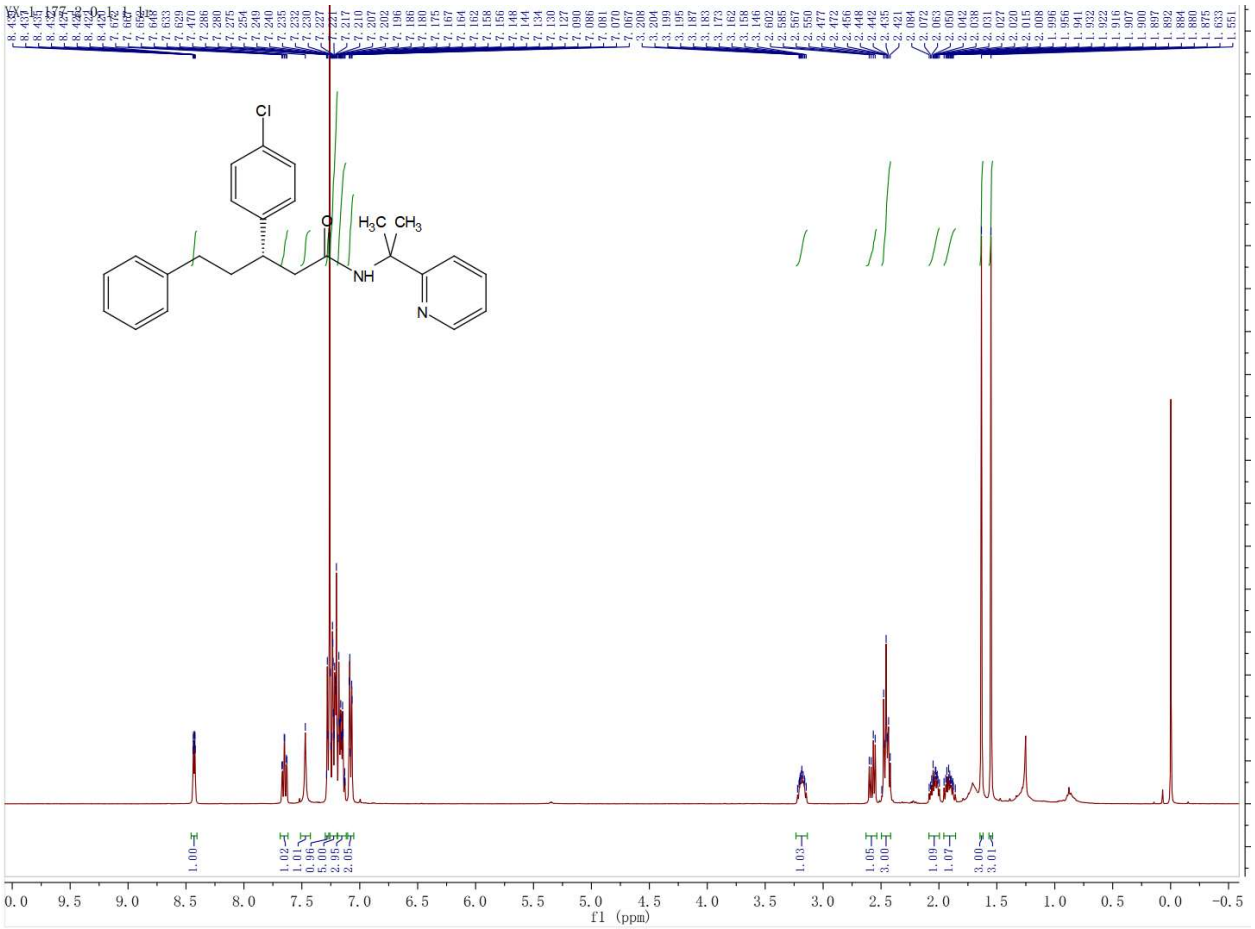

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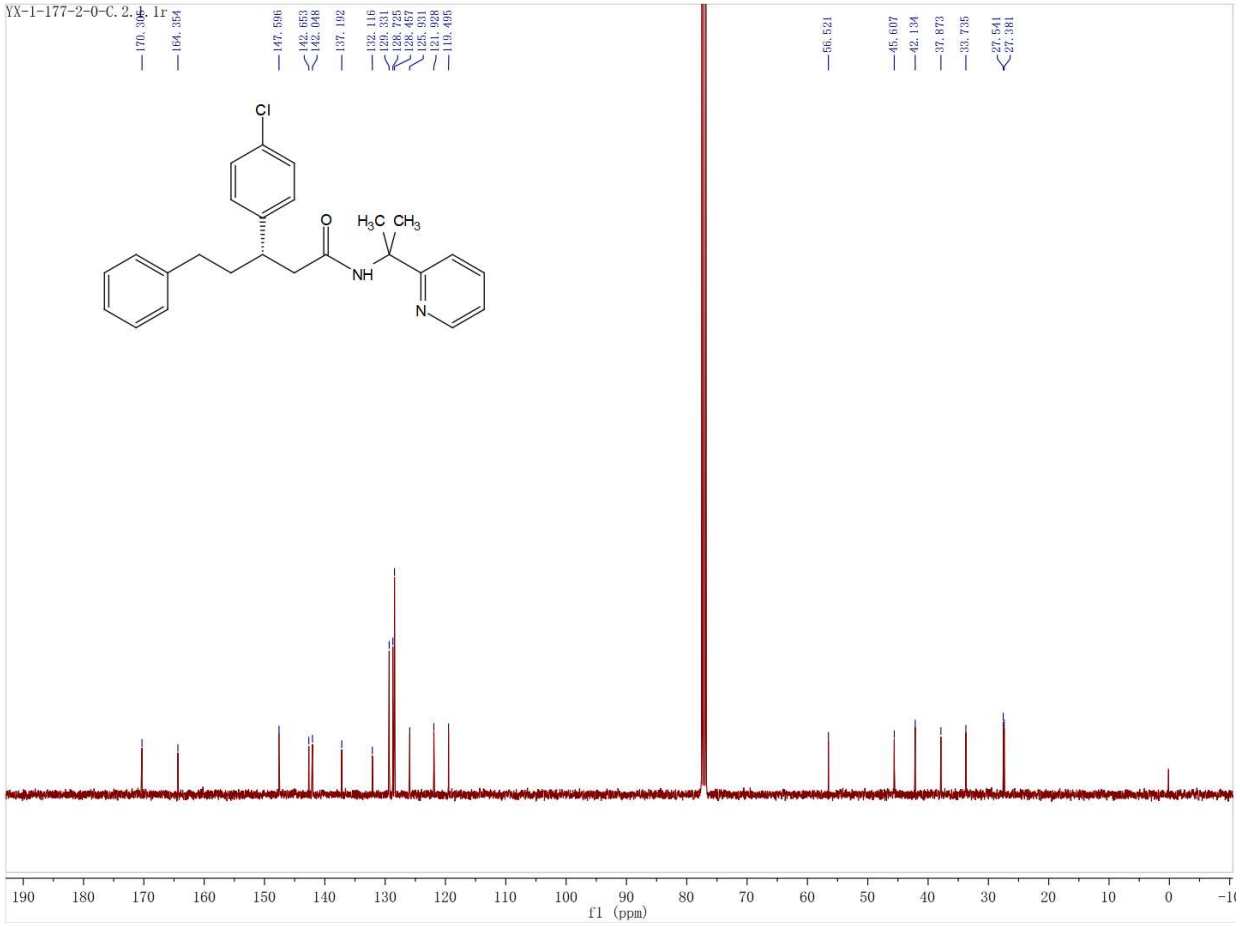
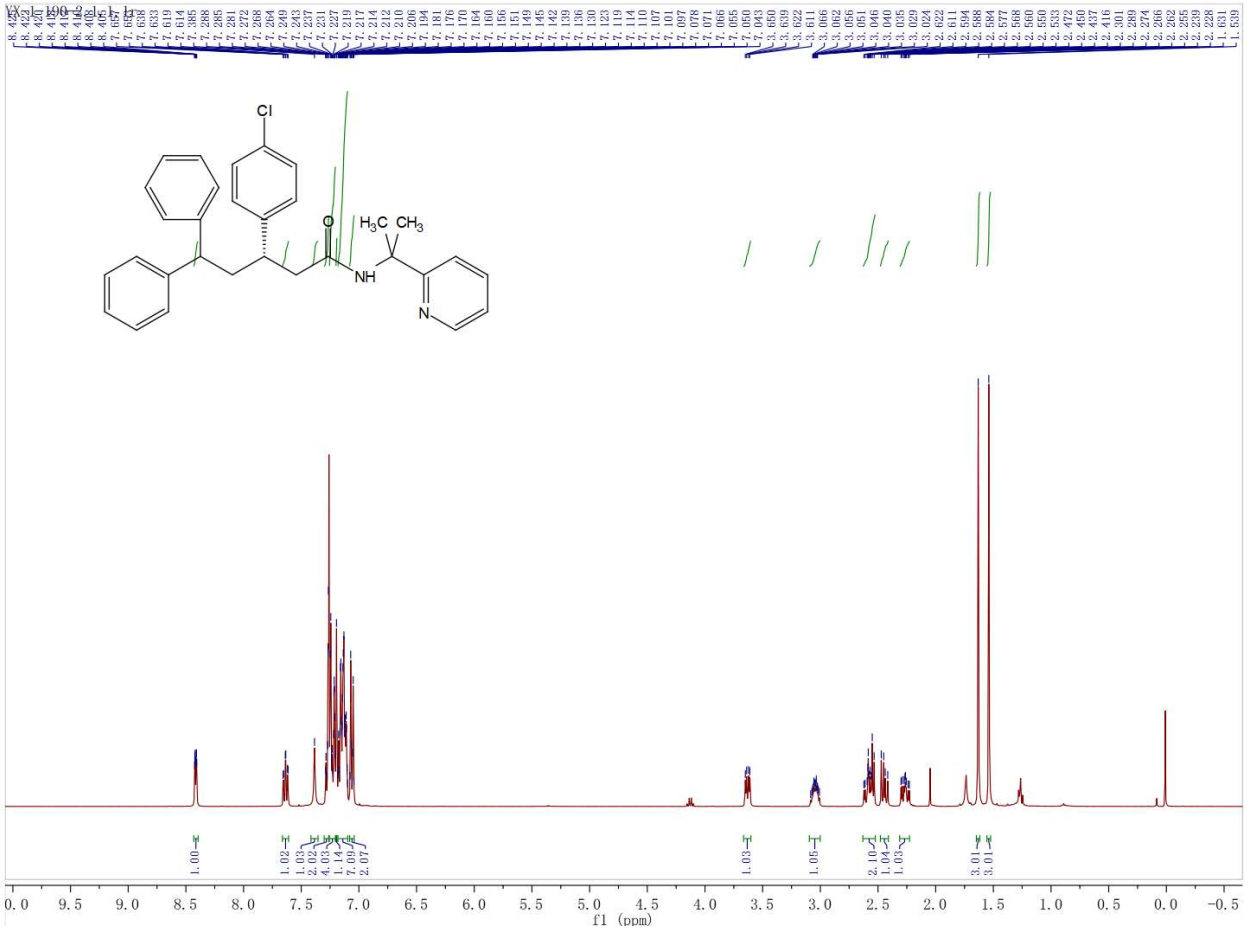


4d, ^{1}H NMR, 400 MHz, $CDCl_3$



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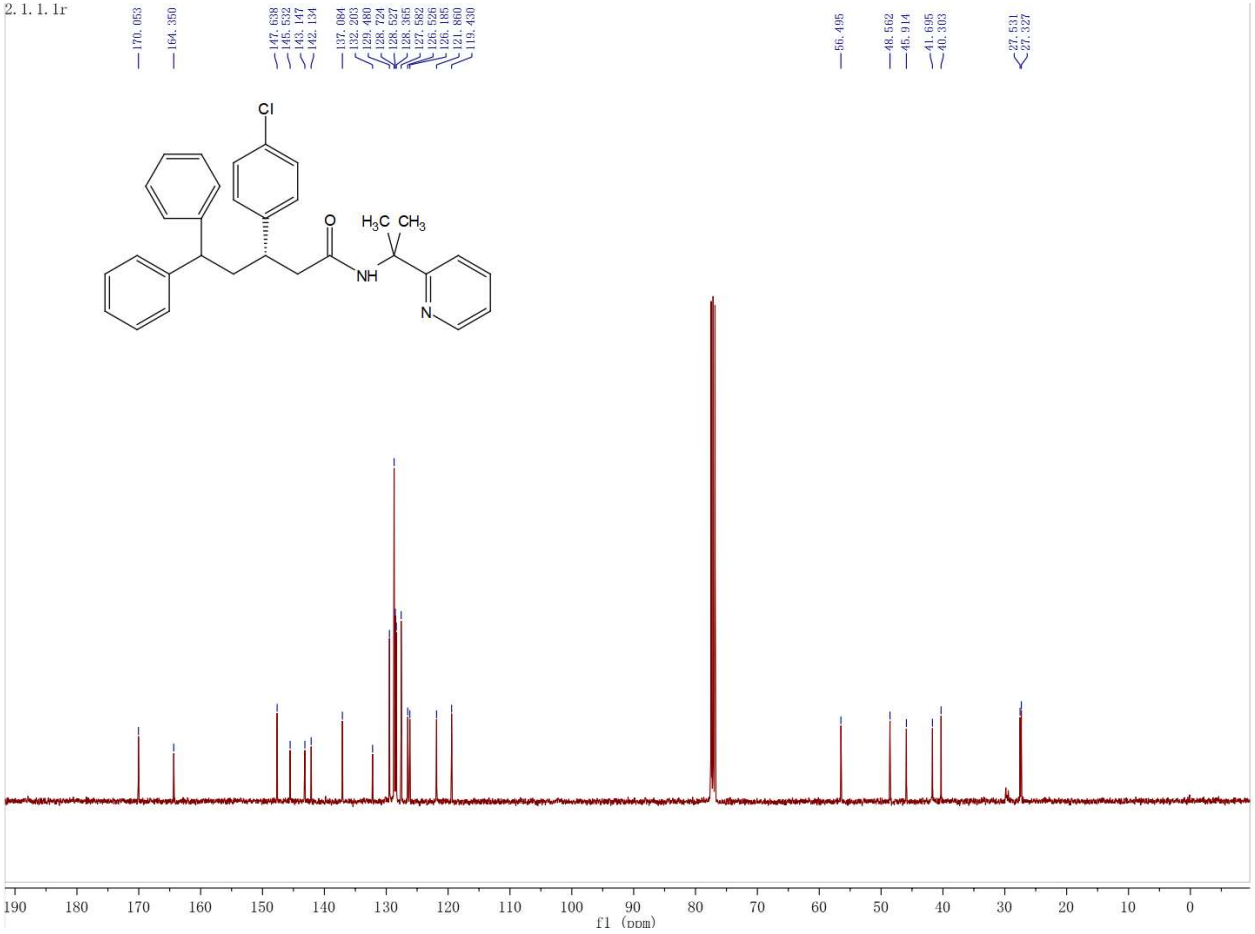
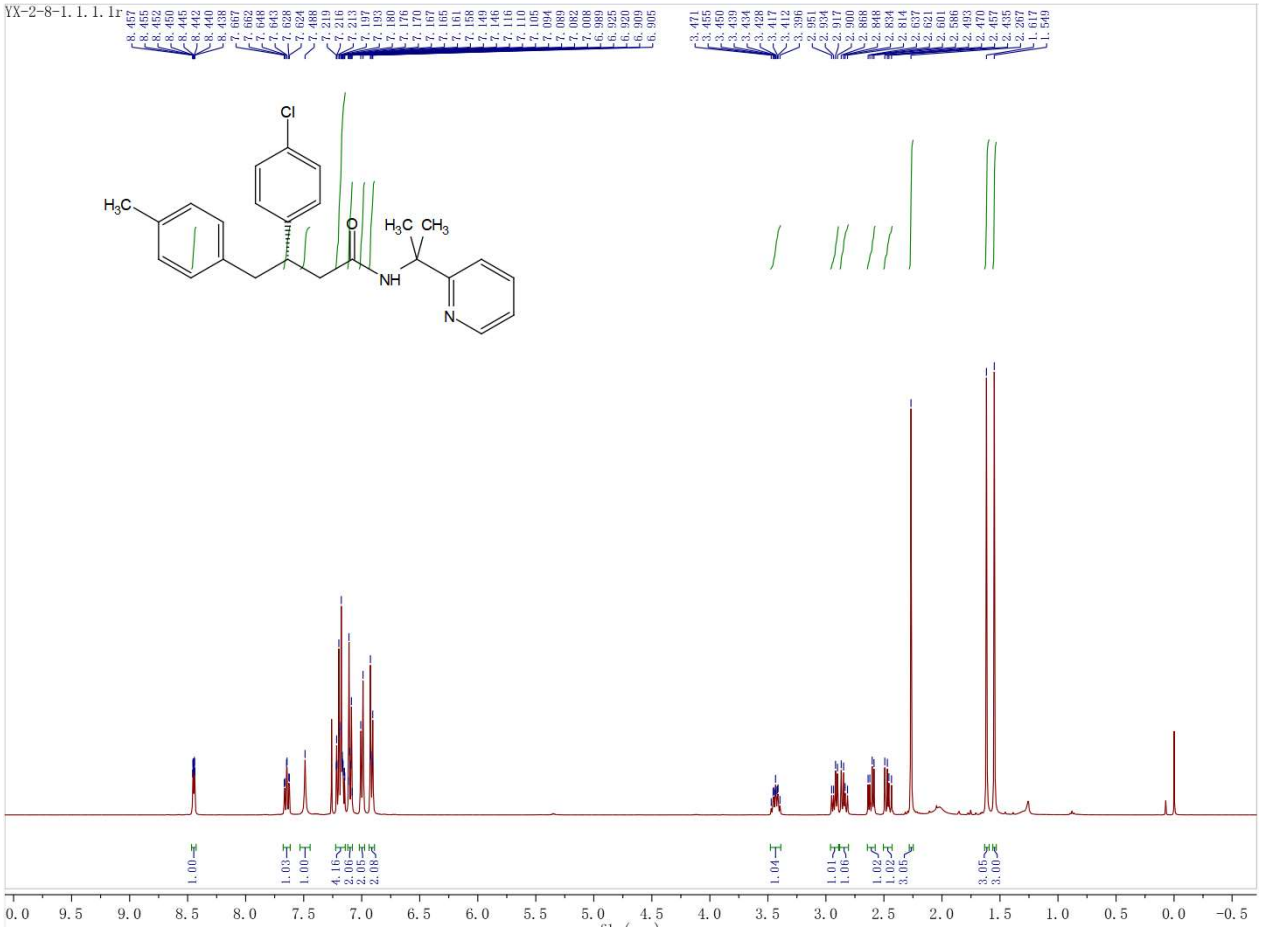


4e, ^{1}H NMR, 400 MHz, $CDCl_3$



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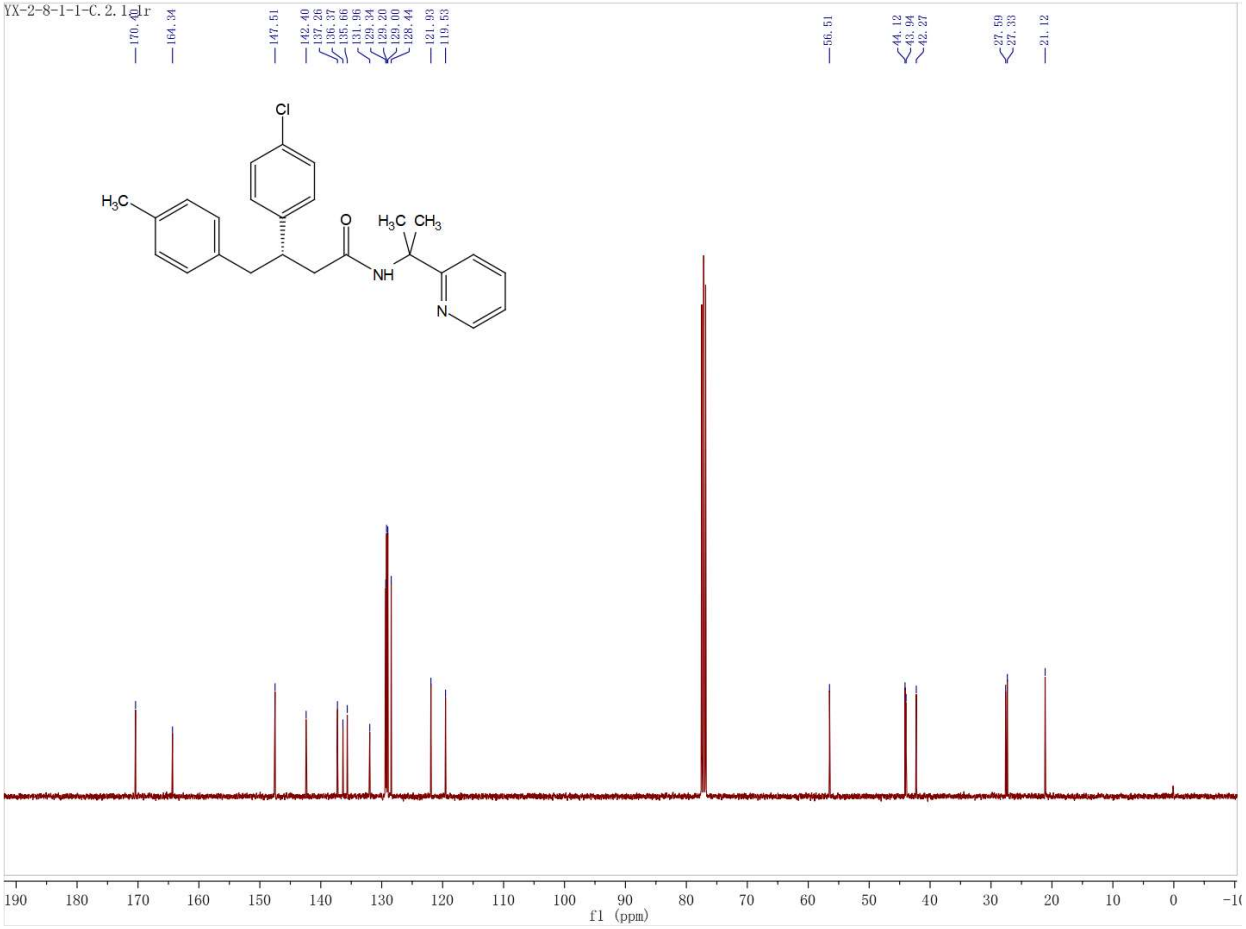
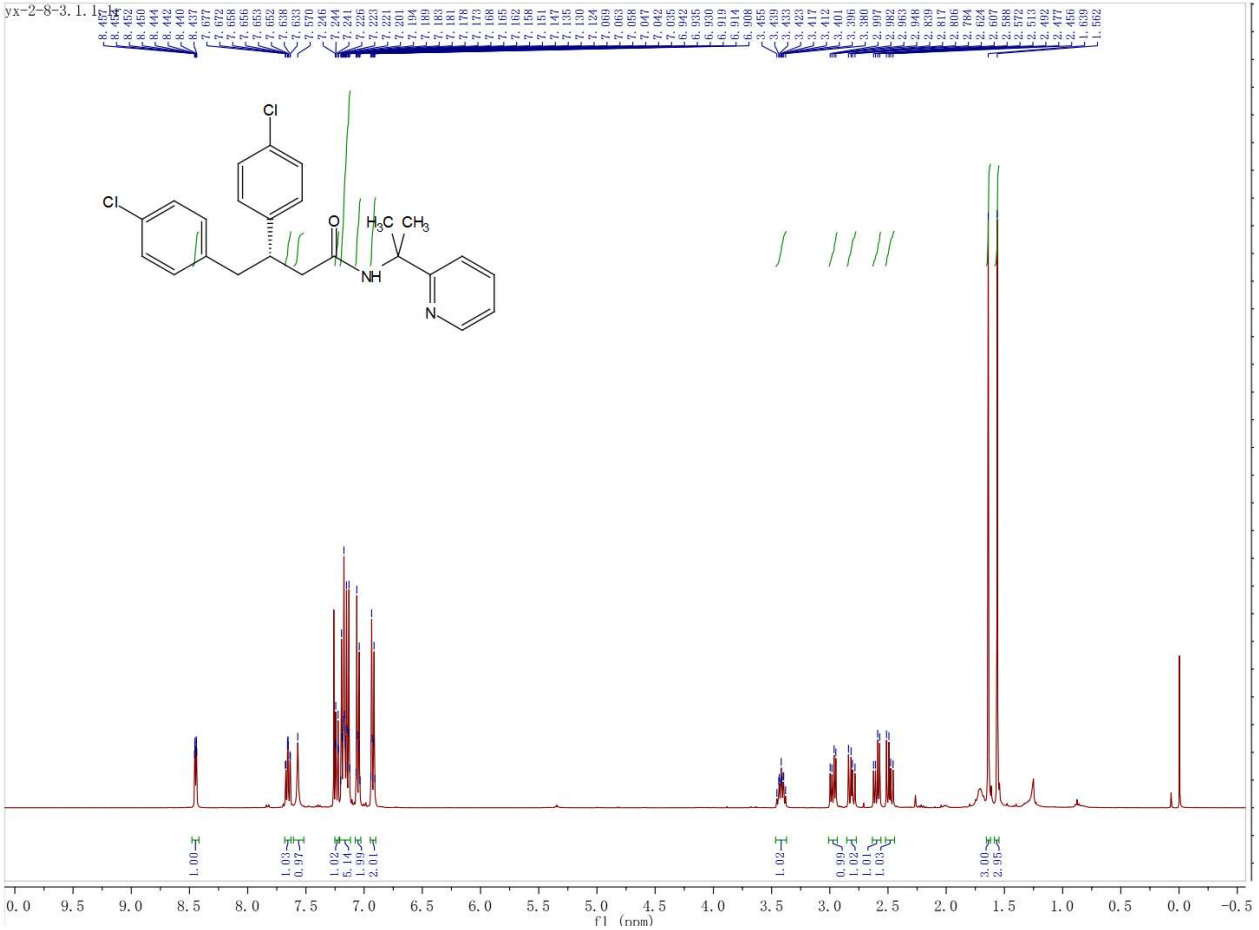
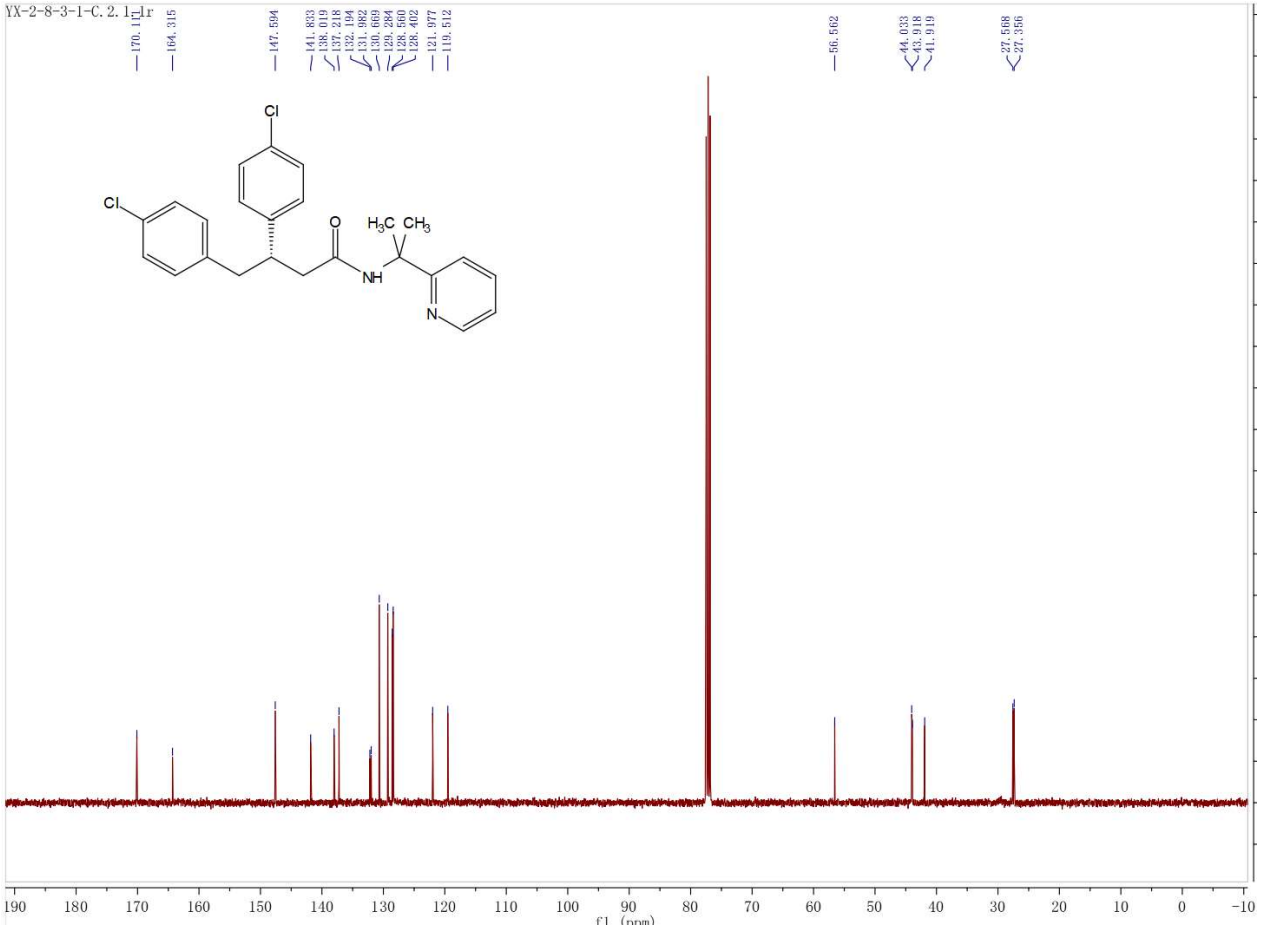


4f, ^{1}H NMR, 400 MHz, $CDCl_3$



4f,^{13}C NMR, 101 MHz, $CDCl_3$



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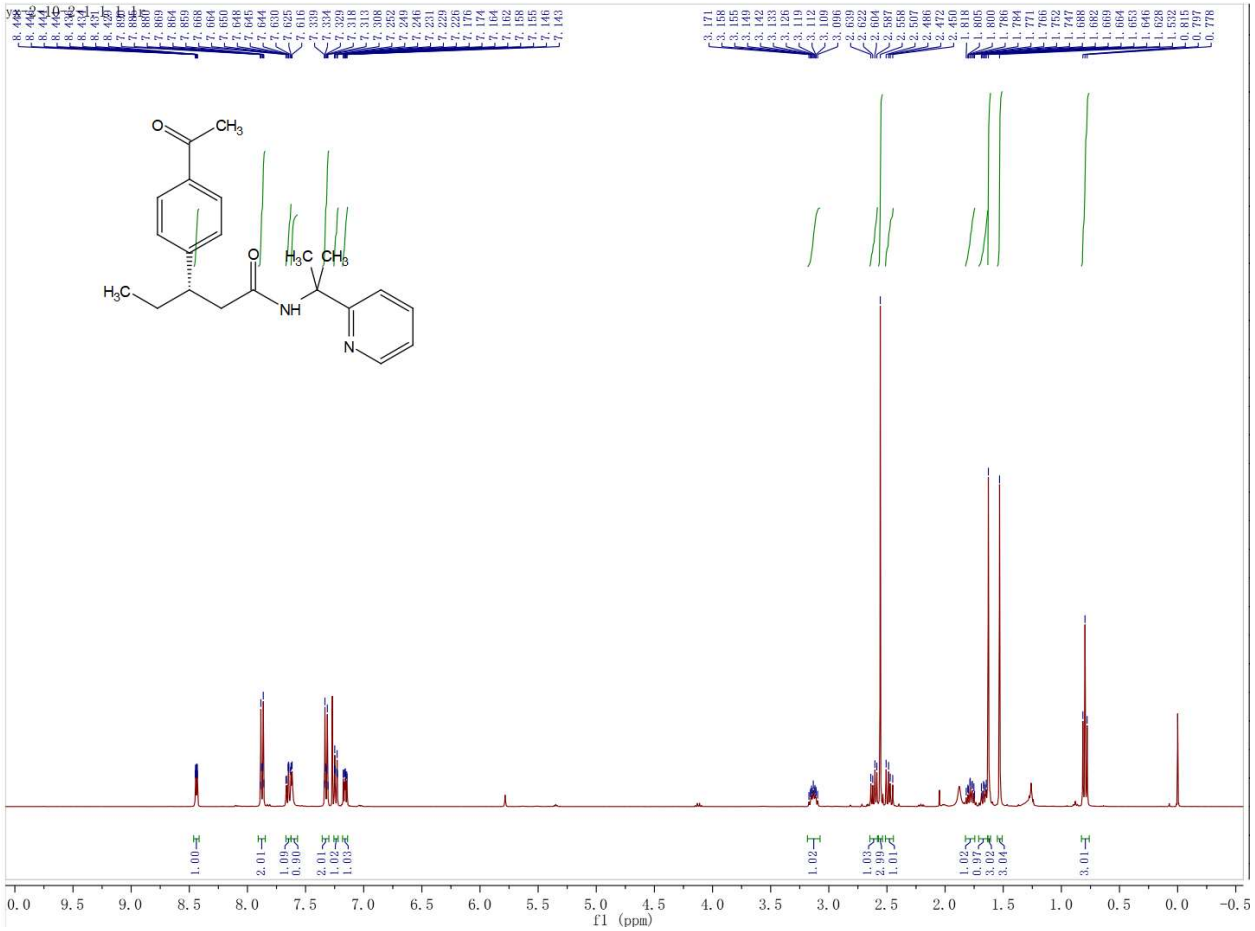
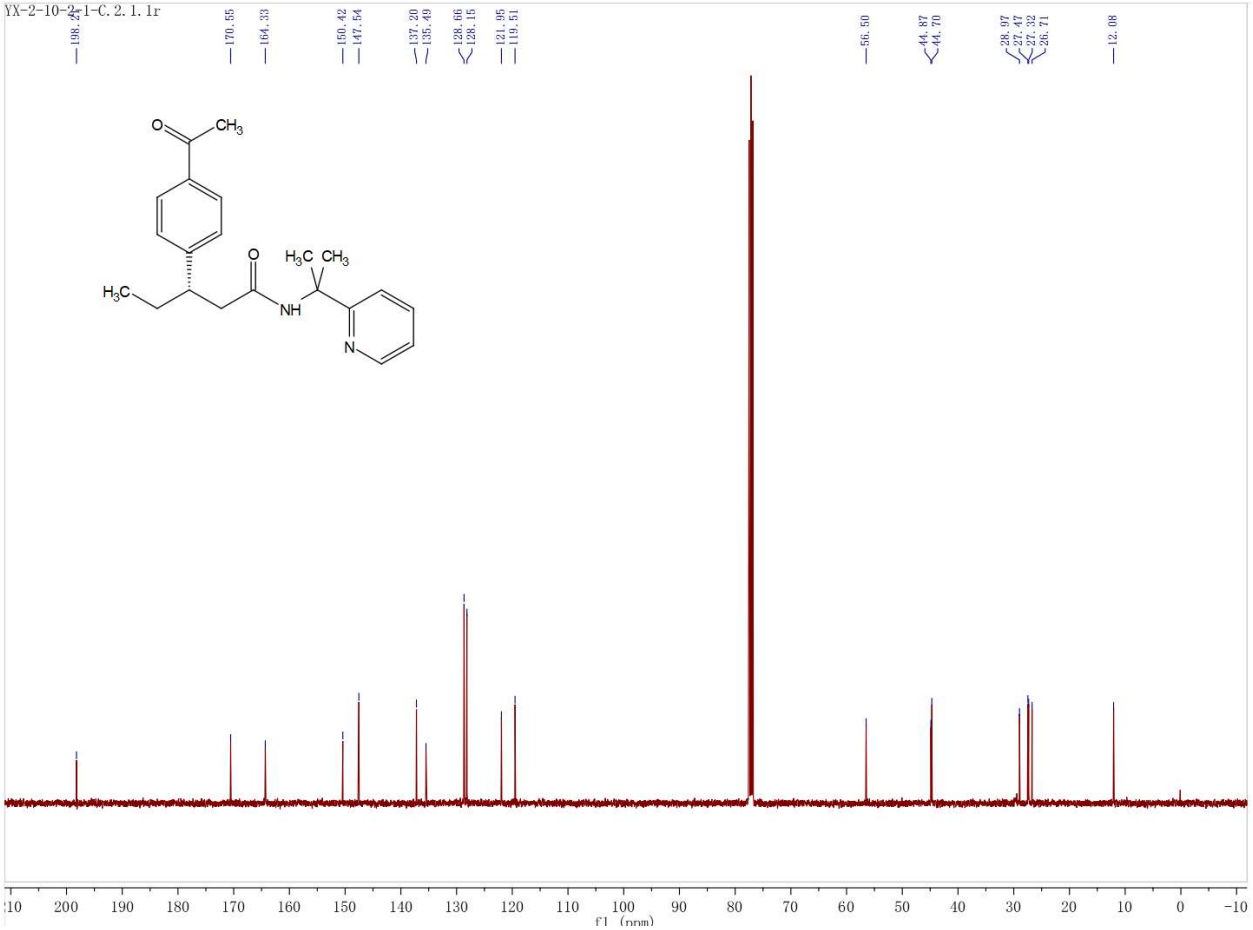


4g, ^{13}C NMR, 101 MHz, $CDCl_3$



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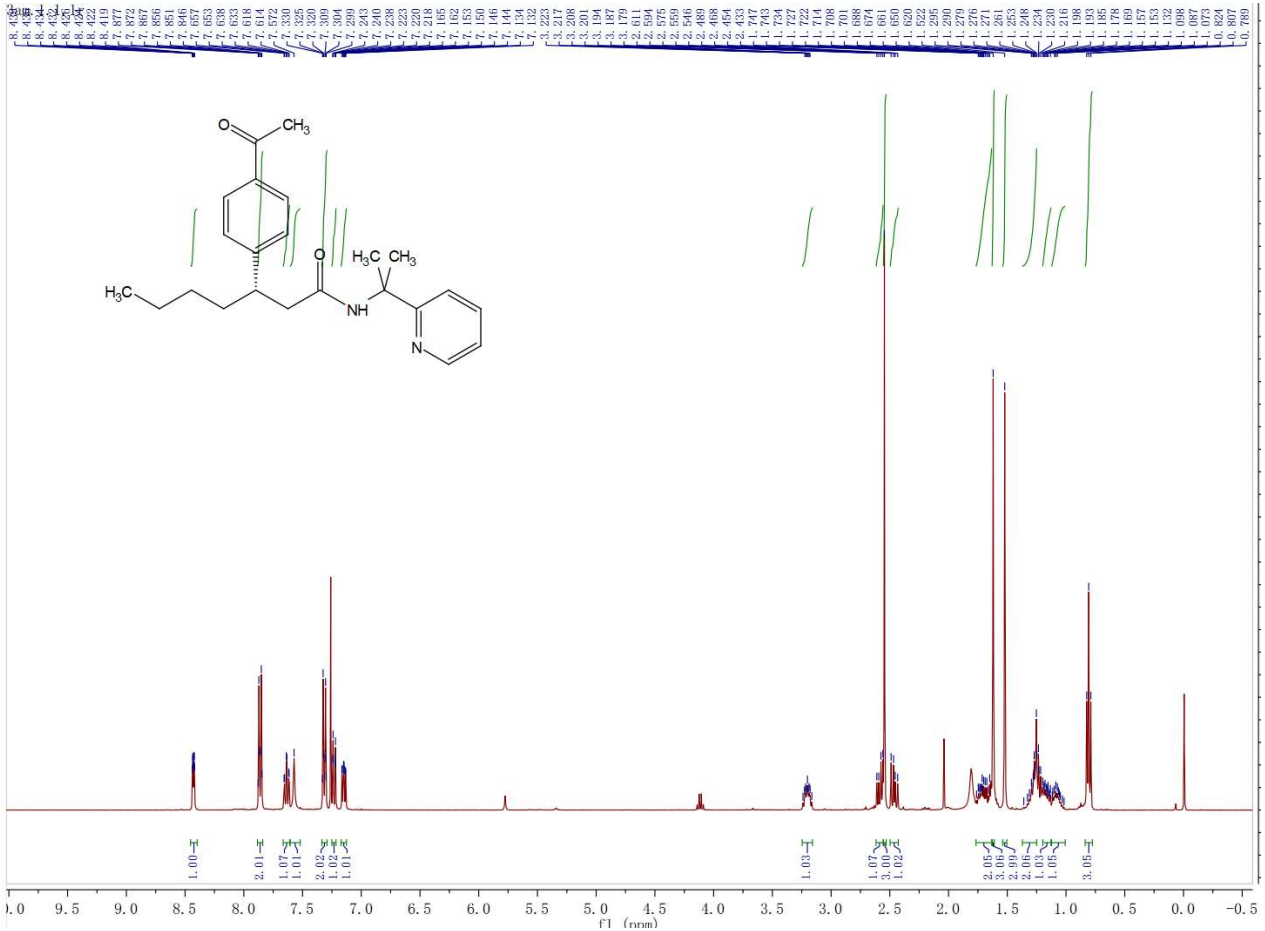
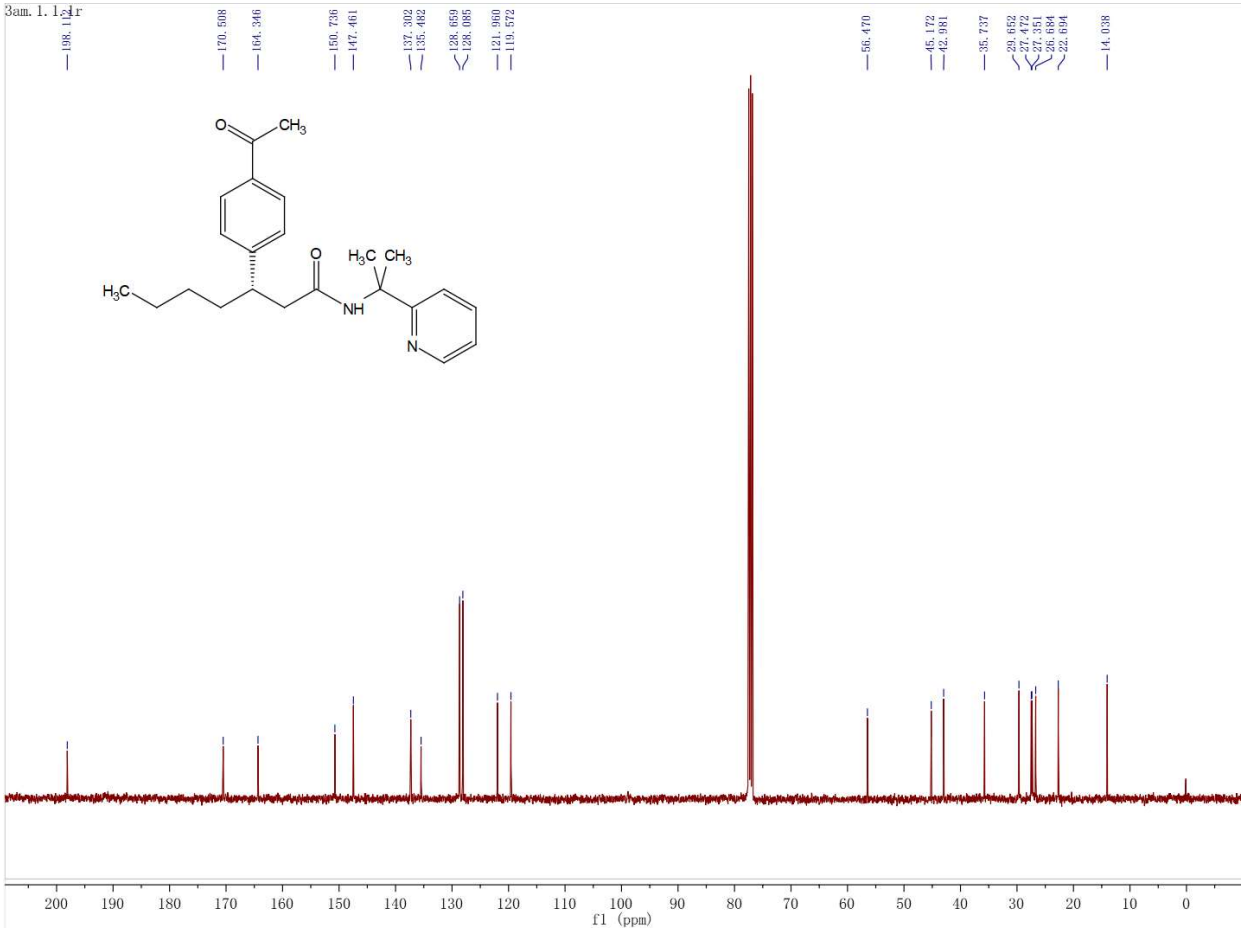
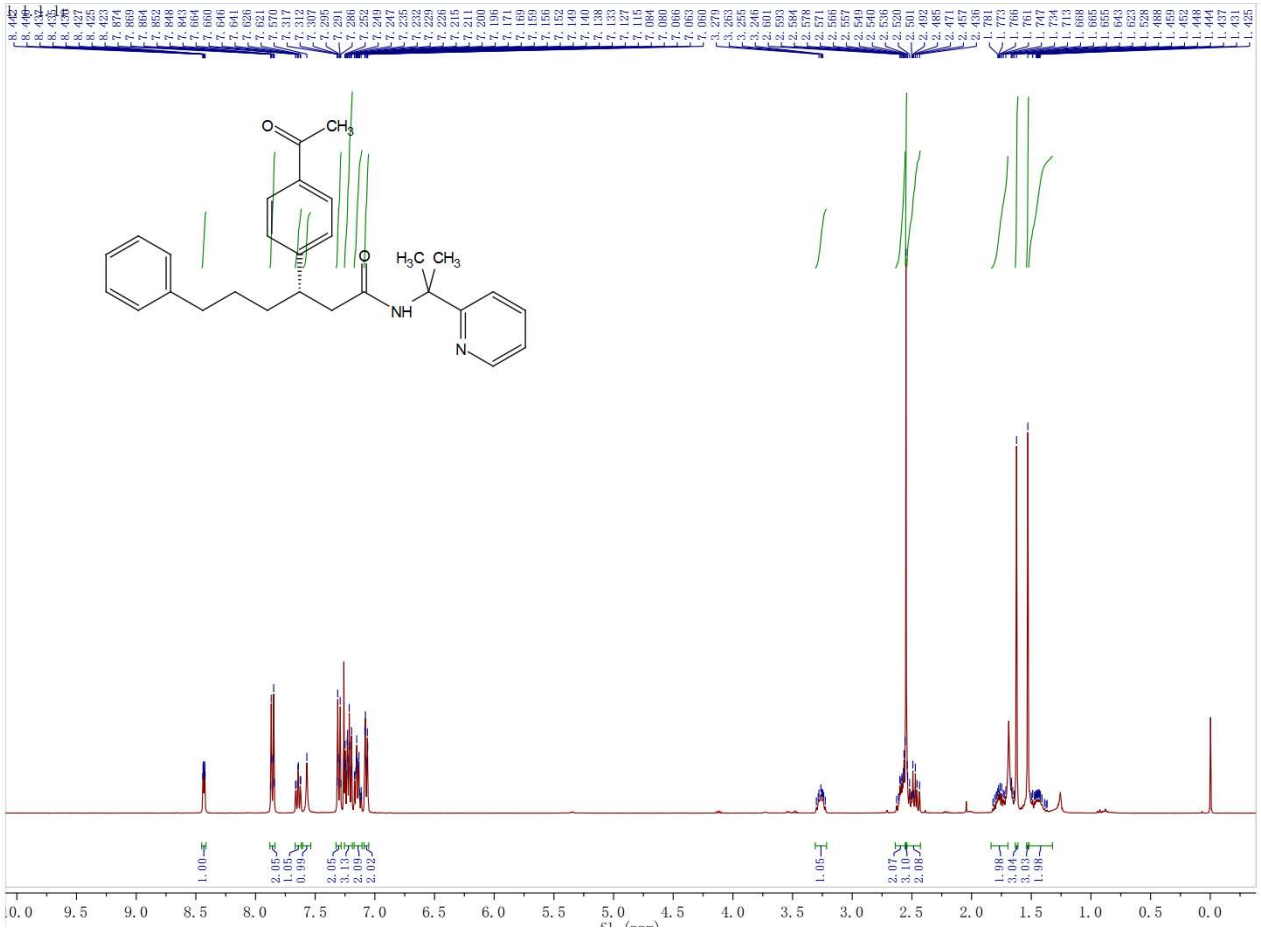


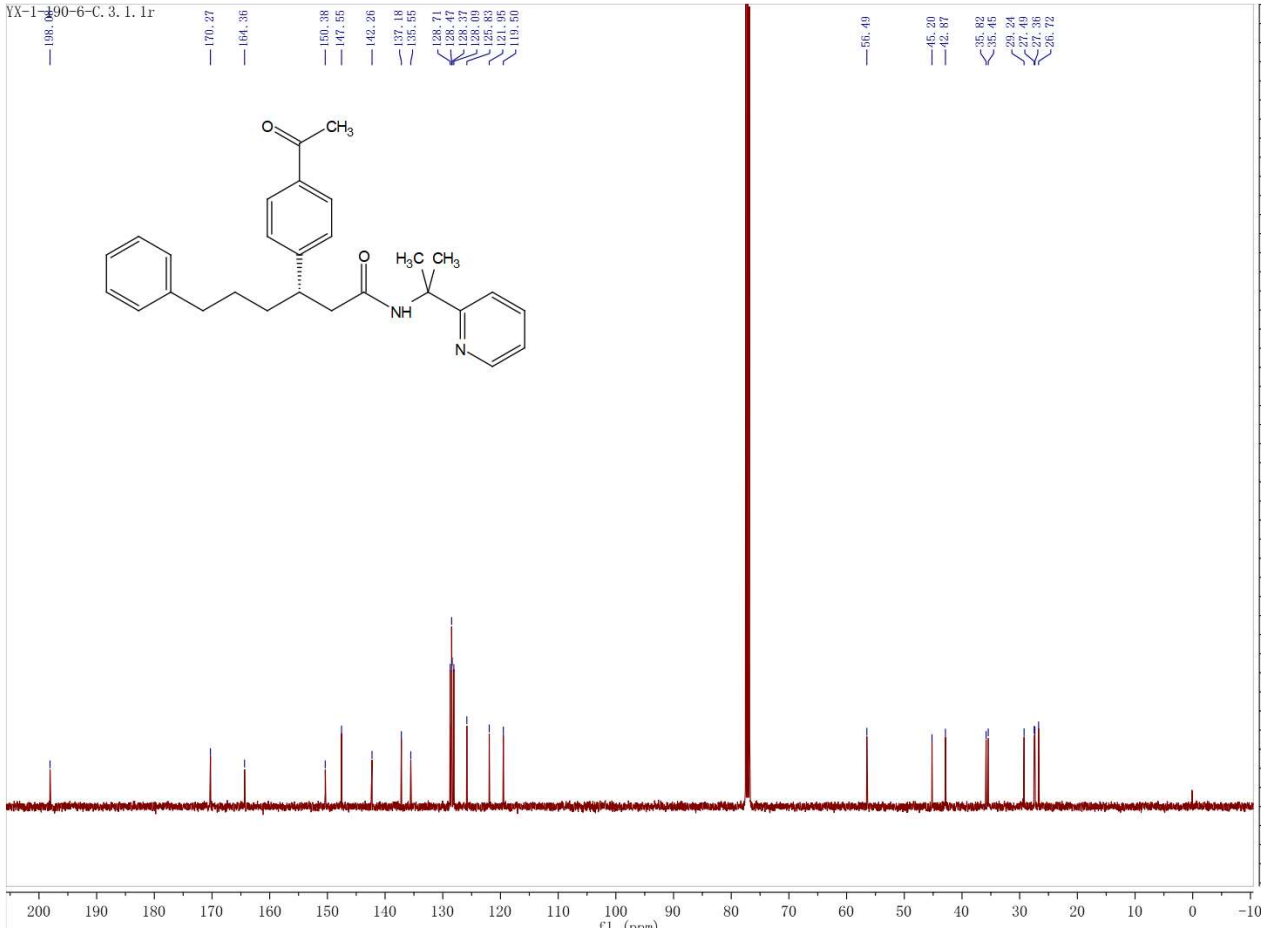
4h,^{13}C NMR, 101 MHz, $CDCl_3$



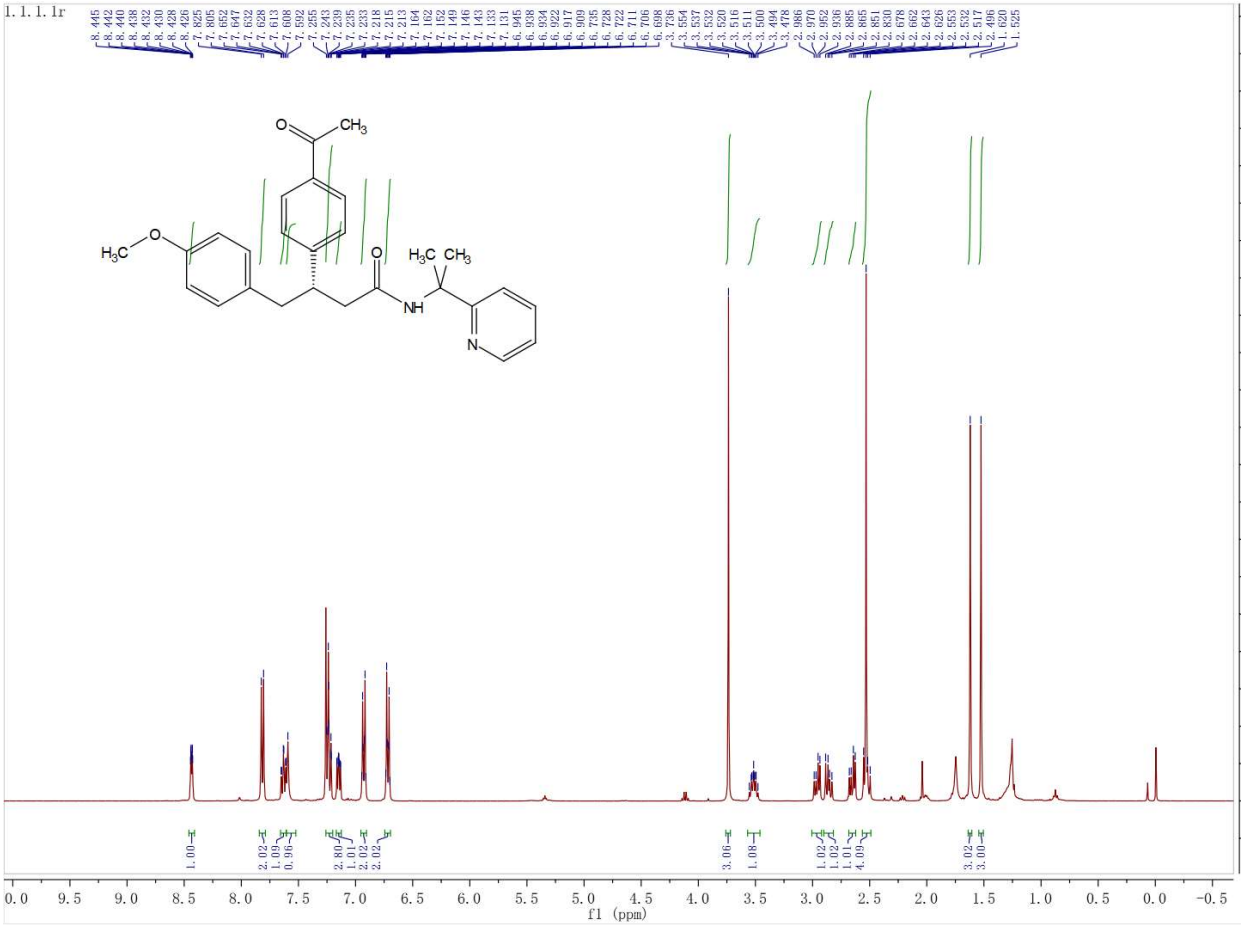
4i, ^{1}H NMR, 400 MHz, $CDCl_3$



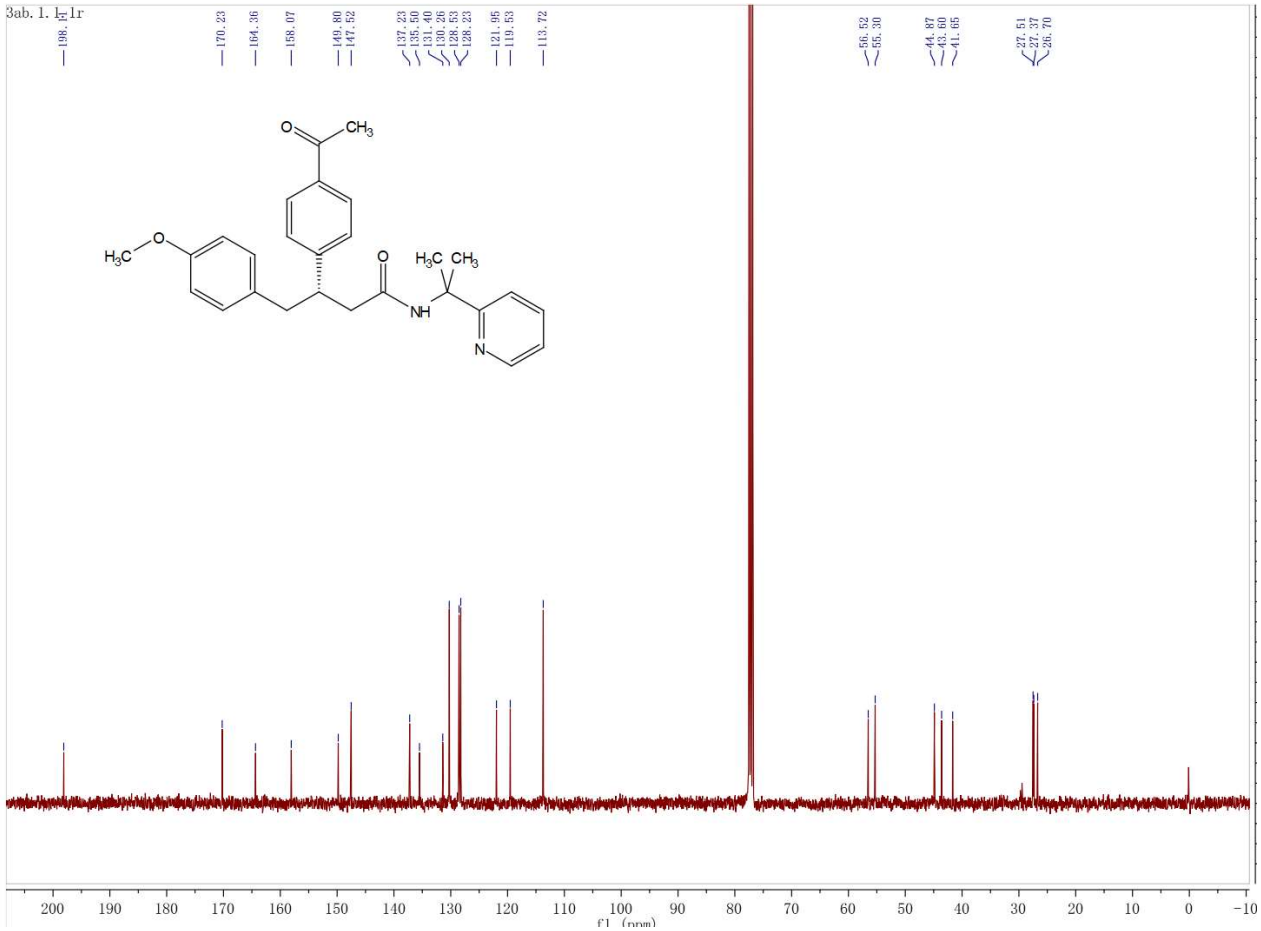
4i,^{13}C NMR, 101 MHz, $CDCl_3$



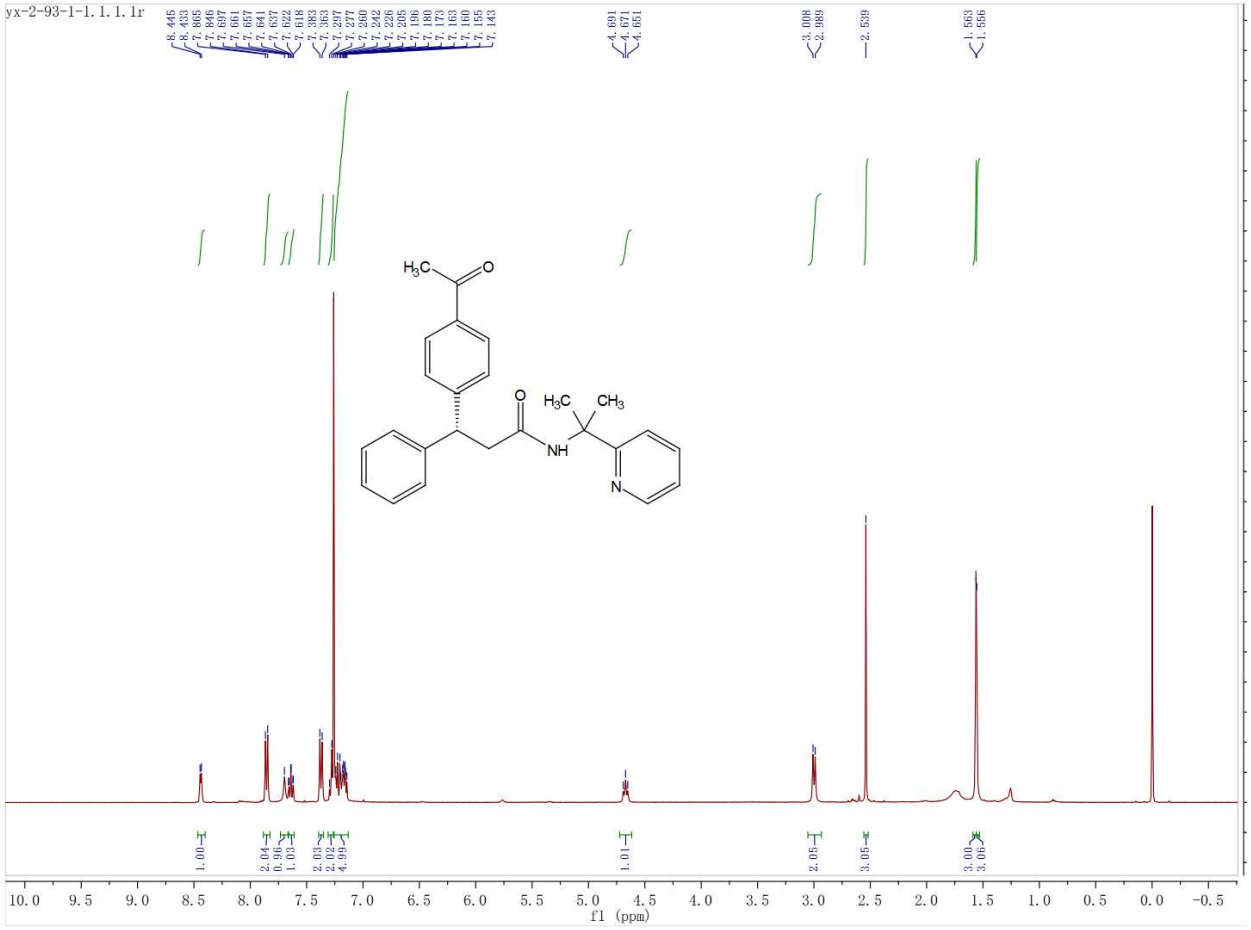
4j, ^{1}H NMR, 400 MHz, $CDCl_3$



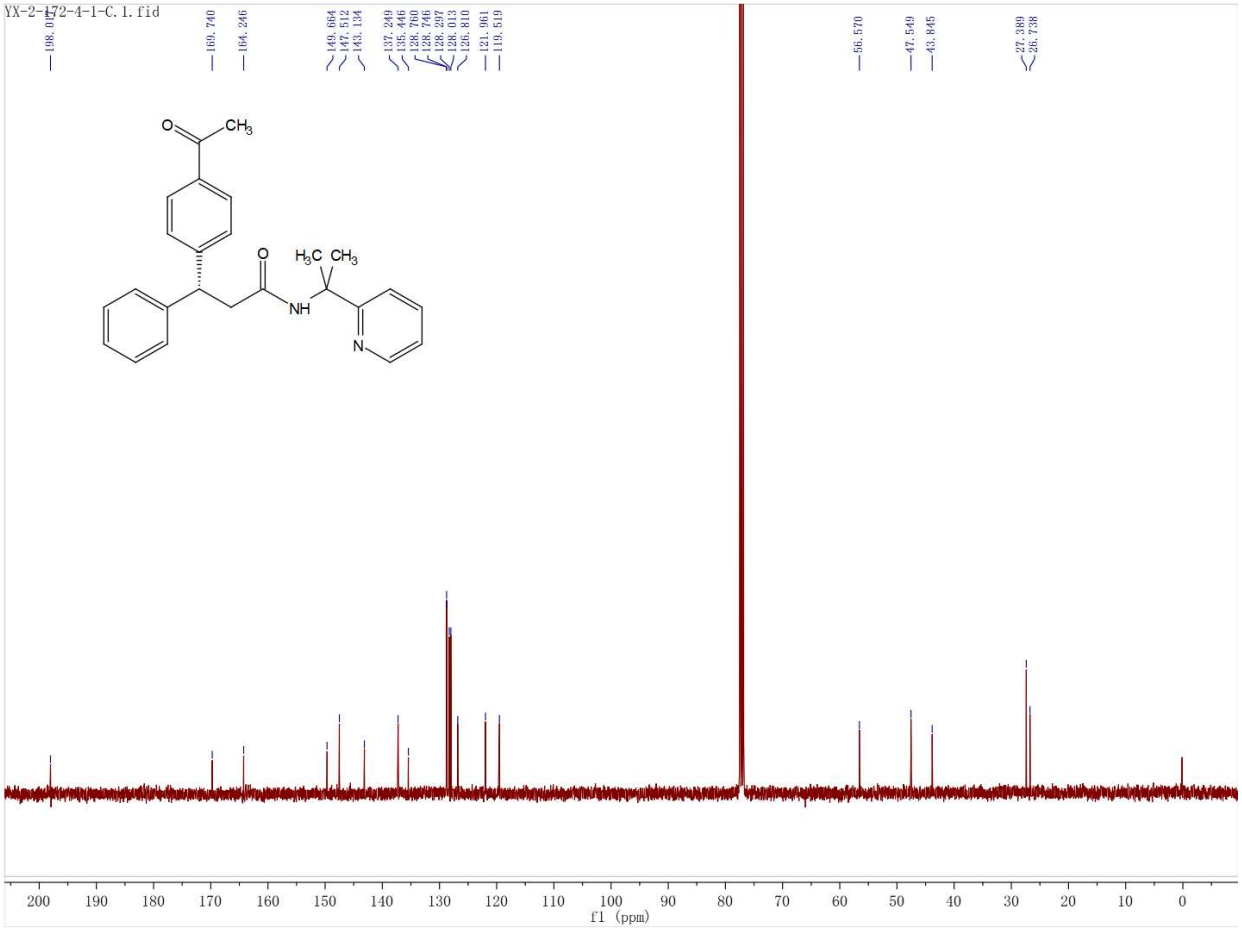
4j,^{13}C NMR, 101 MHz, $CDCl_3$



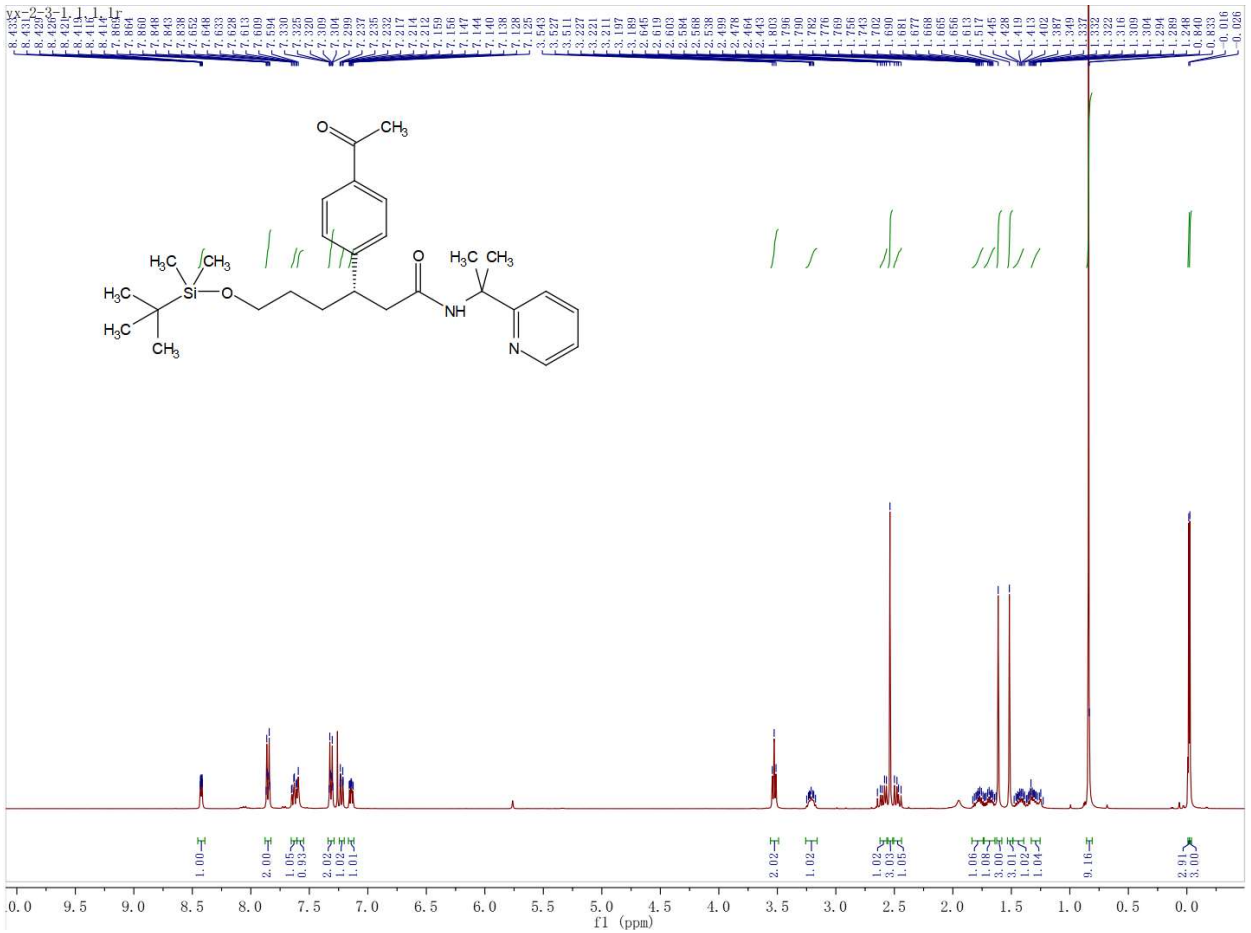
4k, ^{1}H NMR, 400 MHz, $CDCl_3$



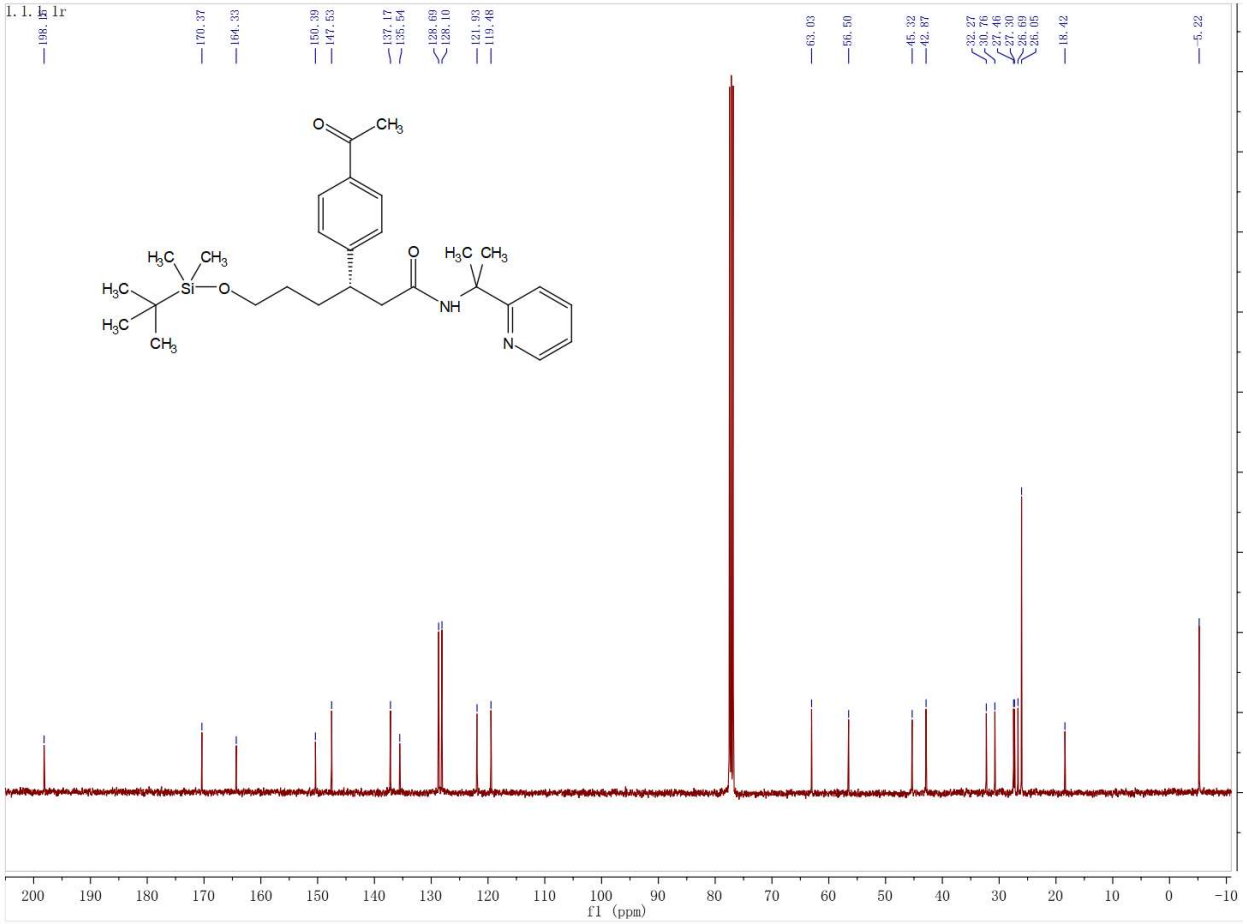
4k,^{13}C NMR, 101 MHz, $CDCl_3$



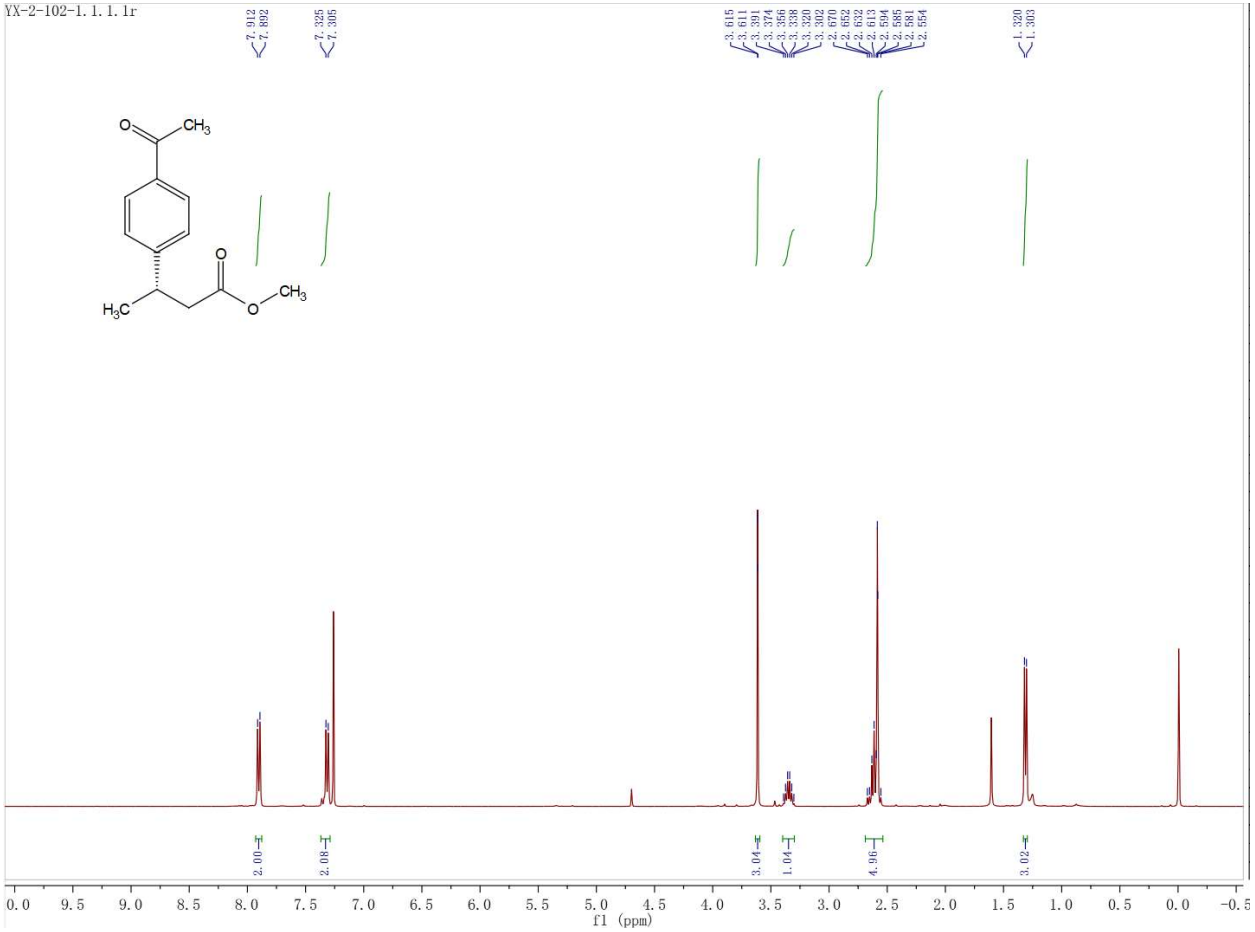
4l, ^{1}H NMR, 400 MHz, $CDCl_3$



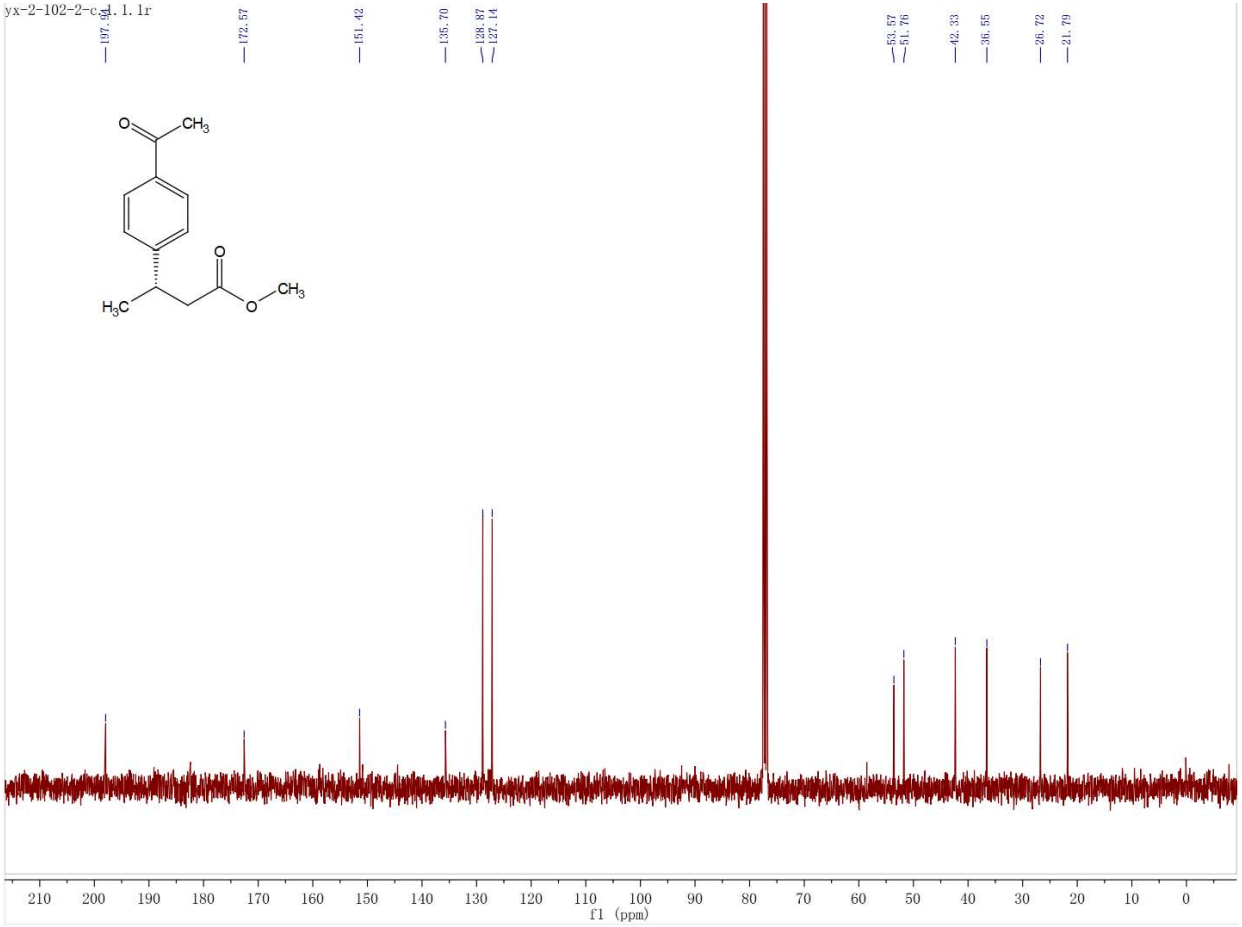
4l,^{13}C NMR, 101 MHz, $CDCl_3$



5a, ^{1}H NMR, 400 MHz, $CDCl_3$



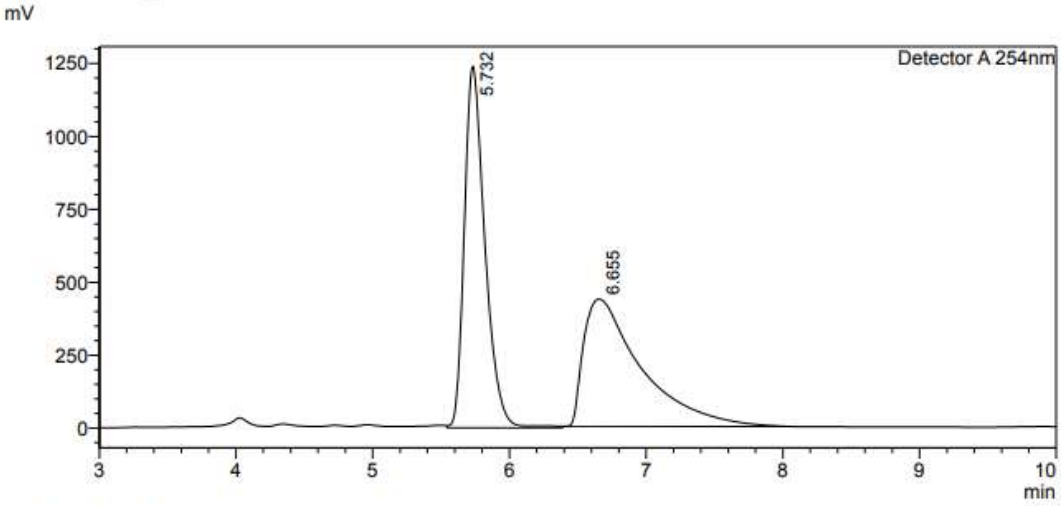
5a,^{13}C NMR, 101 MHz, $CDCl_3$



5. HPLC Charts

3a: OJ-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.732	12997336	1238194	50.468			
2	6.655	12756084	436038	49.532		M	
Total		25753421	1674232				

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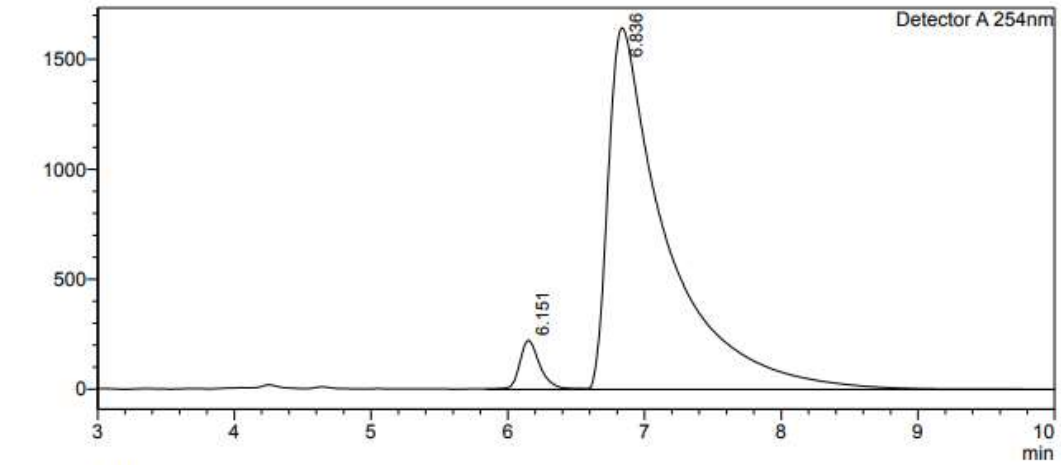

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.151	2306833	222876	4.511			
2	6.836	48835317	1642832	95.489		V	
Total		51142150	1865708				

3b: OD-H, Hexane/iPrOH=90/10, rate=1.0 mL/min, 254 nm

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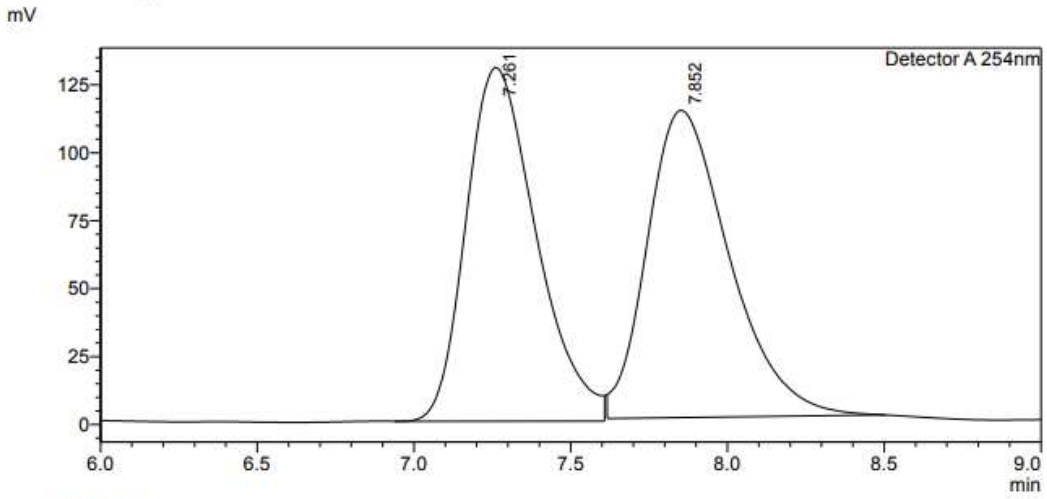
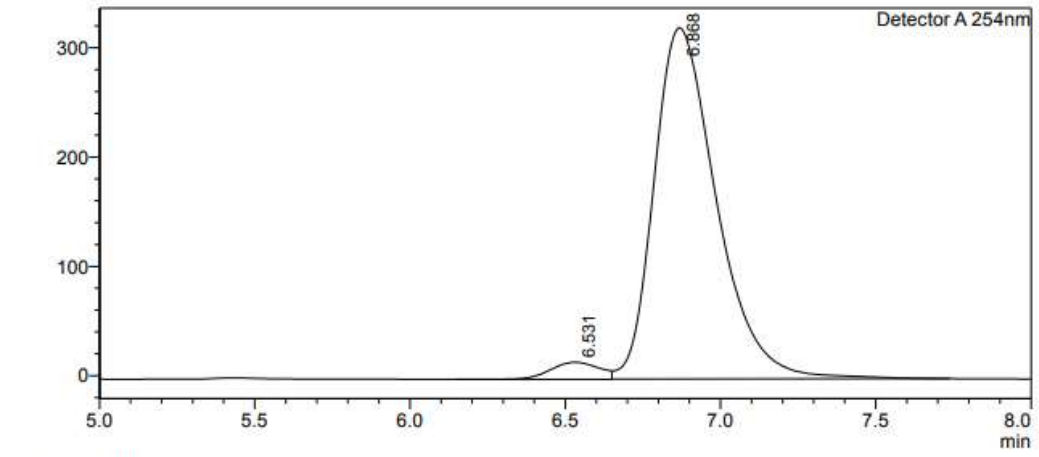


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.261	2028936	130074	49.545		M	
2	7.852	2066206	113031	50.455		M	
Total		4095141	243105				

<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.531	170642	15528	3.661			
2	6.868	4490395	321380	96.339		M	
Total		4661037	336909				

3c: OJ-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

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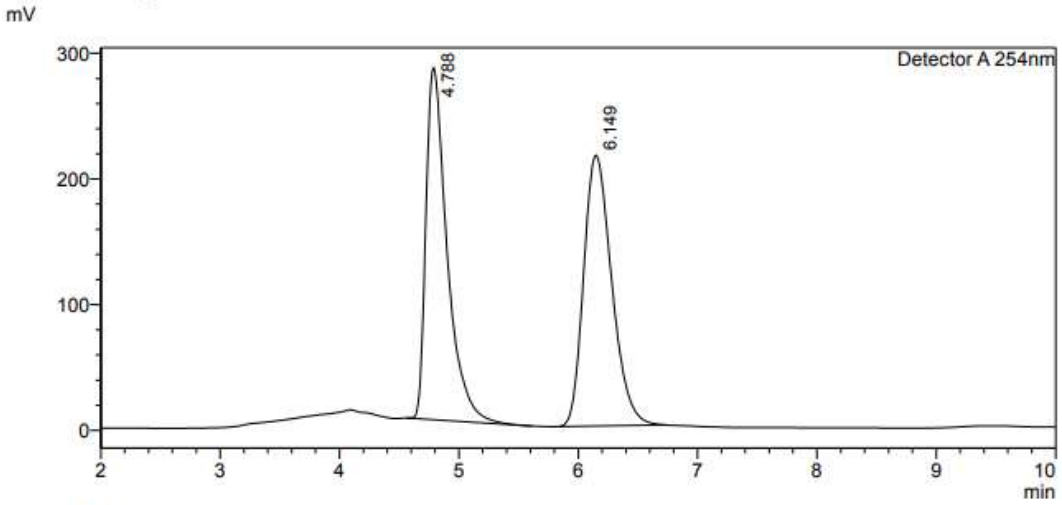
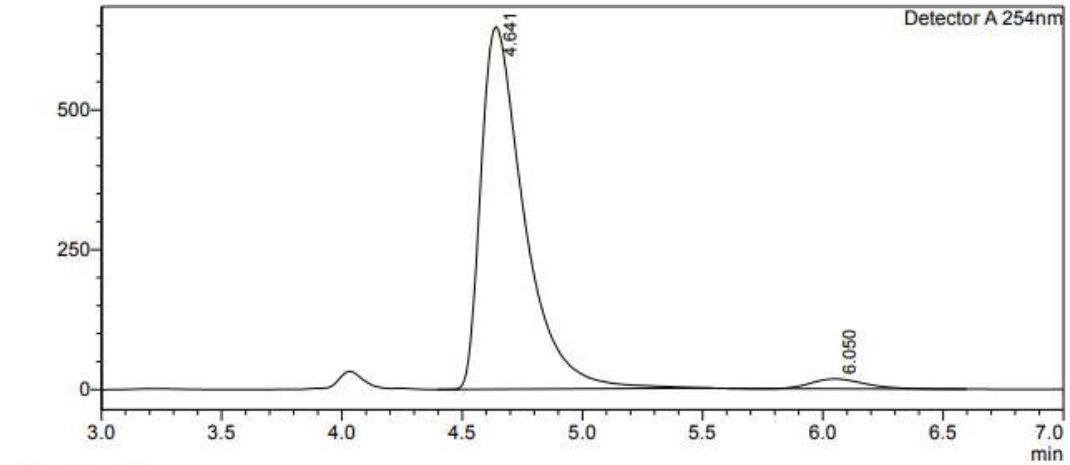


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.788	3447646	279920	49.465		M	
2	6.149	3522239	215356	50.535		M	
Total		6969884	495276				

<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.641	8119139	647969	96.832		M	
2	6.050	265659	17602	3.168		M	
Total		8384798	665571				

3d: OJ-H, Hexane/iPrOH=90/10, rate=1.0 mL/min, 254 nm

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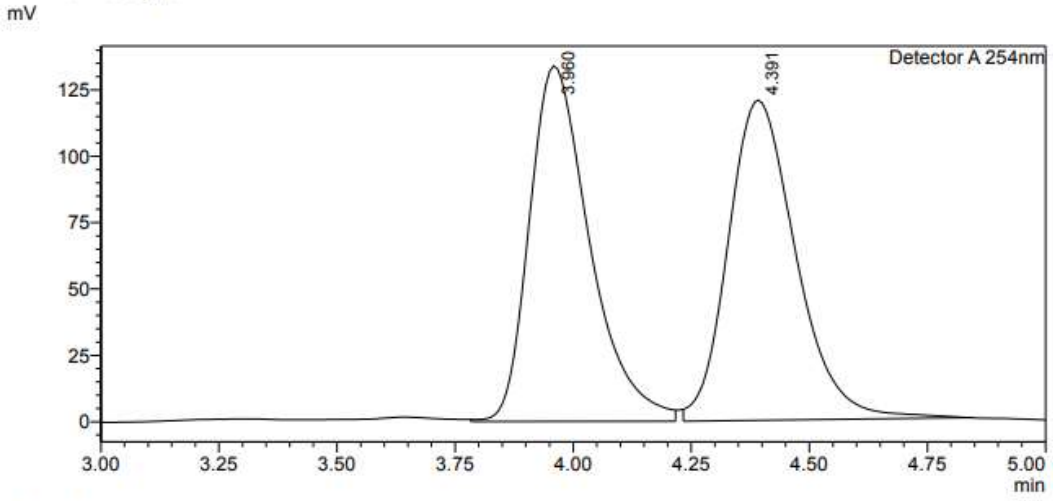
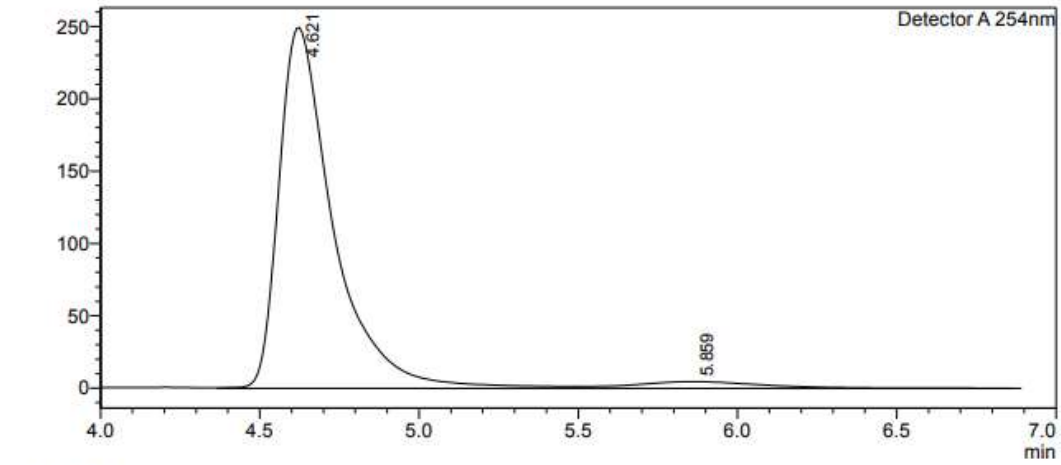


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	3.960	1191348	133947	49.695			
2	4.391	1205981	120658	50.305		M	
Total		2397329	254605				

<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.621	2956415	249051	95.878			
2	5.859	127089	4540	4.122		V	
Total		3083504	253591				

3e: AD-H, Hexane/iPrOH=80/20, rate=0.8 mL/min, 254 nm

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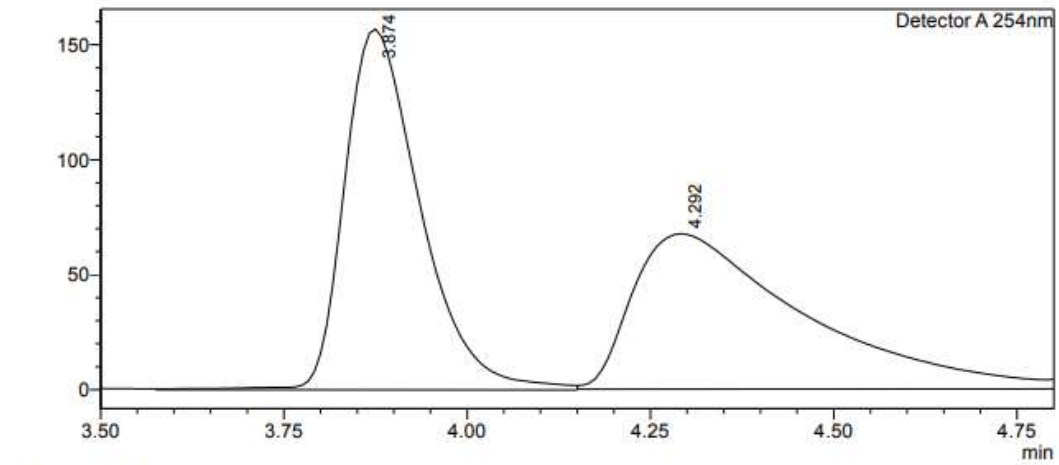
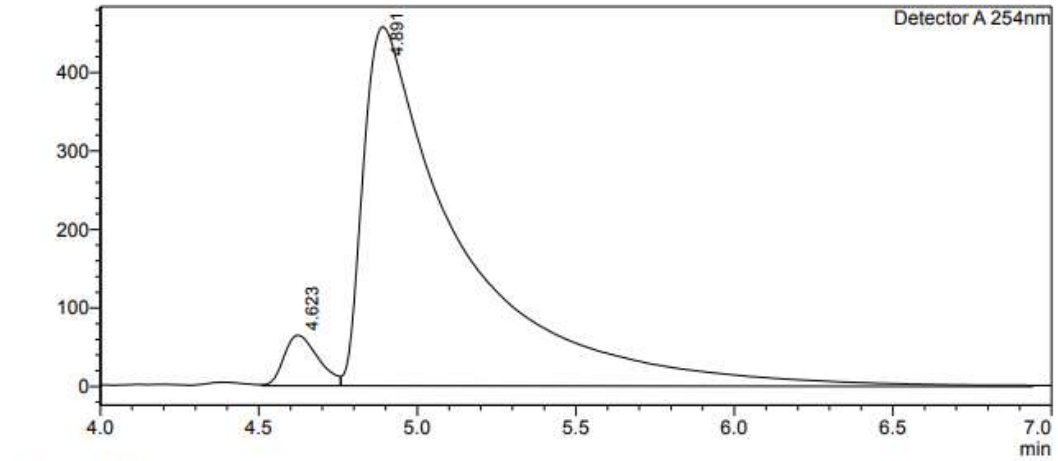


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	3.874	1129791	156871	49.581		M	
2	4.292	1148909	67553	50.419		M	
Total		2278699	224425				

<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.623	486862	64506	4.690			
2	4.891	9894154	457646	95.310		V M	
Total		10381016	522152				

3f: AD-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

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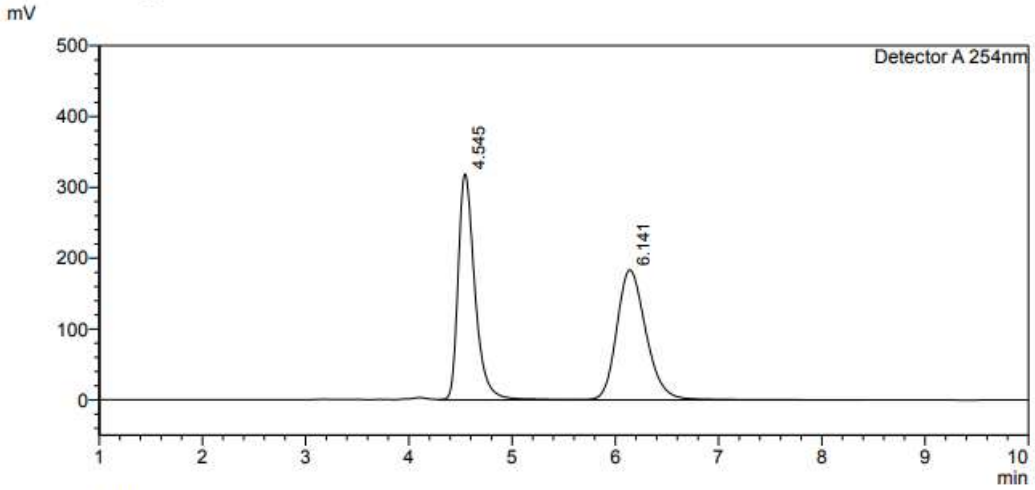

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.545	3597711	318863	49.745			
2	6.141	3634621	183404	50.255		V	
Total		7232333	502267				

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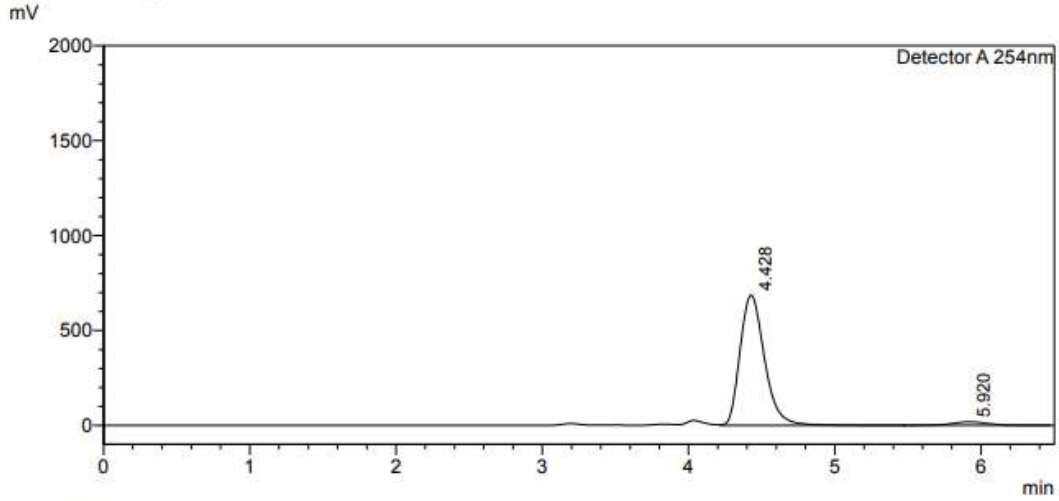

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.428	8010087	685855	96.146			
2	5.920	321080	18561	3.854		V	
Total		8331167	704416				

3g: OJ-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

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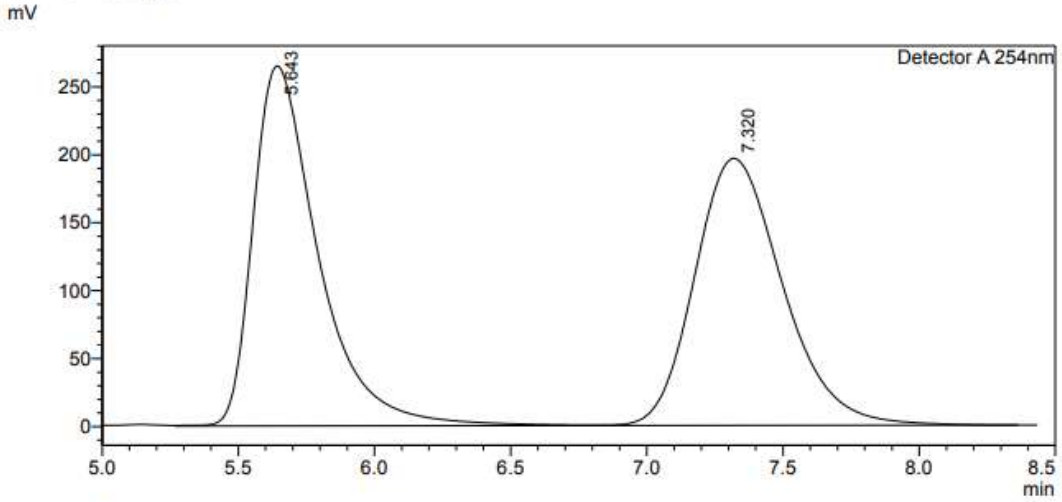

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.643	4413776	265003	49.964			
2	7.320	4420196	196535	50.036		V	
Total		8833972	461539				

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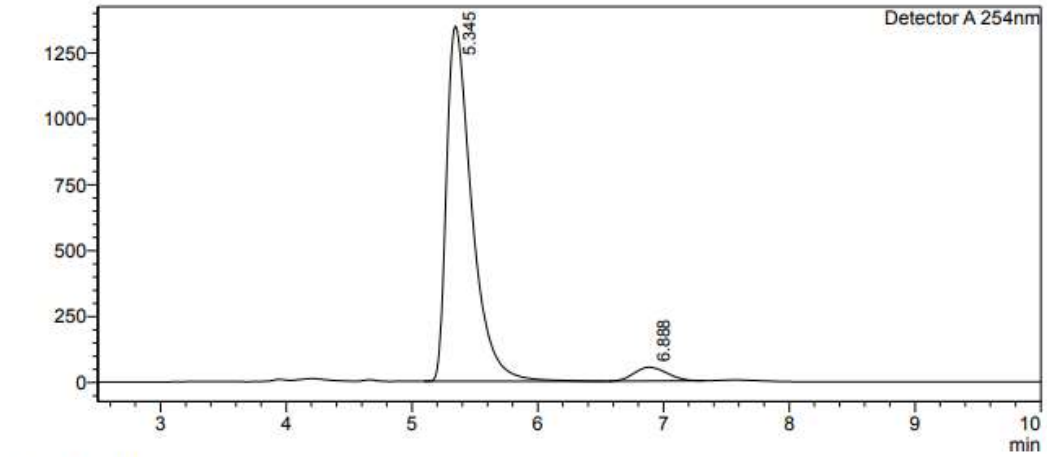

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.345	18828832	1345594	95.189		M	
2	6.888	951668	52203	4.811		M	
Total		19780500	1397797				

3h: IB N-5, Hexane/iPrOH=85/15, rate=1.0 mL/min, 254 nm

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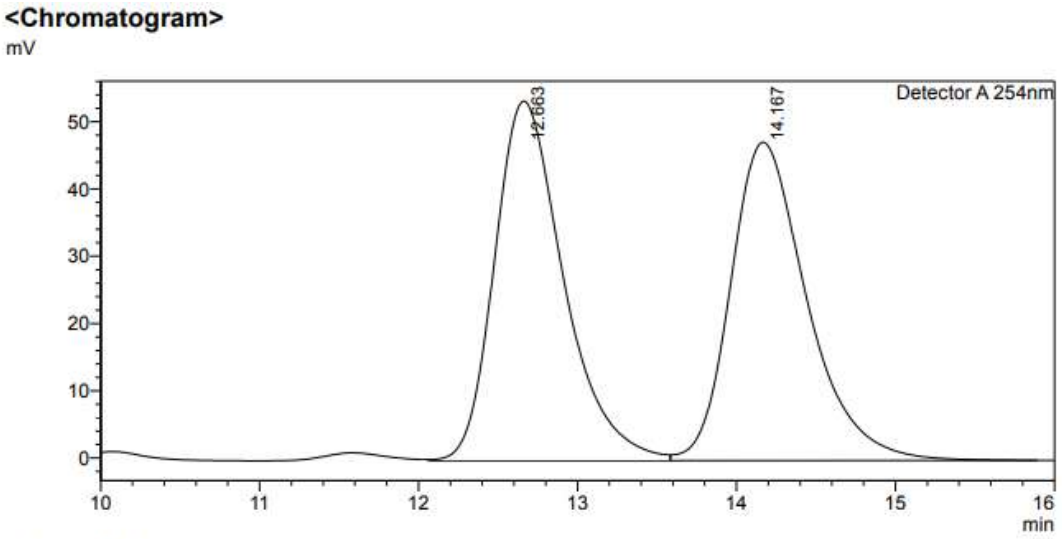

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.663	1614166	53426	50.558			
2	14.167	1578533	47310	49.442		V	
Total		3192699	100736				

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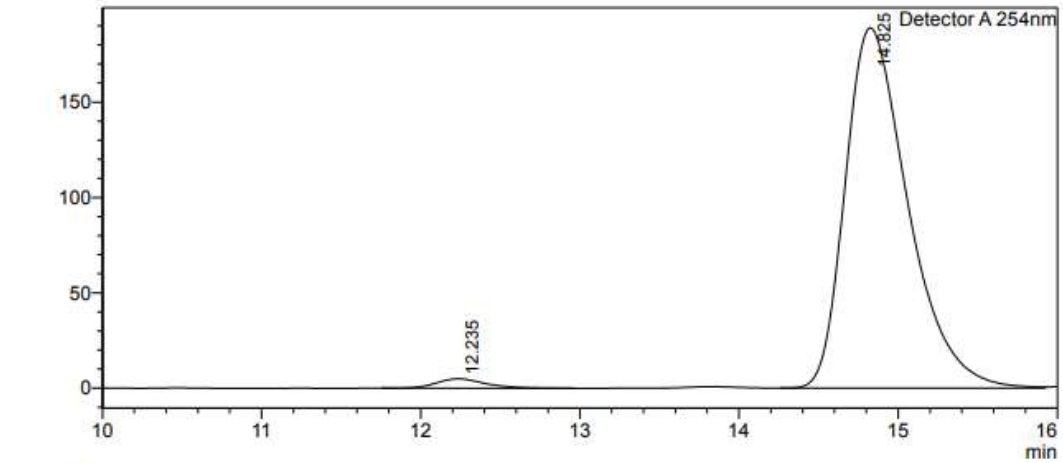

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.235	103833	4869	1.967		M	
2	14.825	5175768	188944	98.033			
Total		5279601	193812				

3i: AS-H, Hexane/iPrOH=95/5, rate=1.0 mL/min, 254 nm

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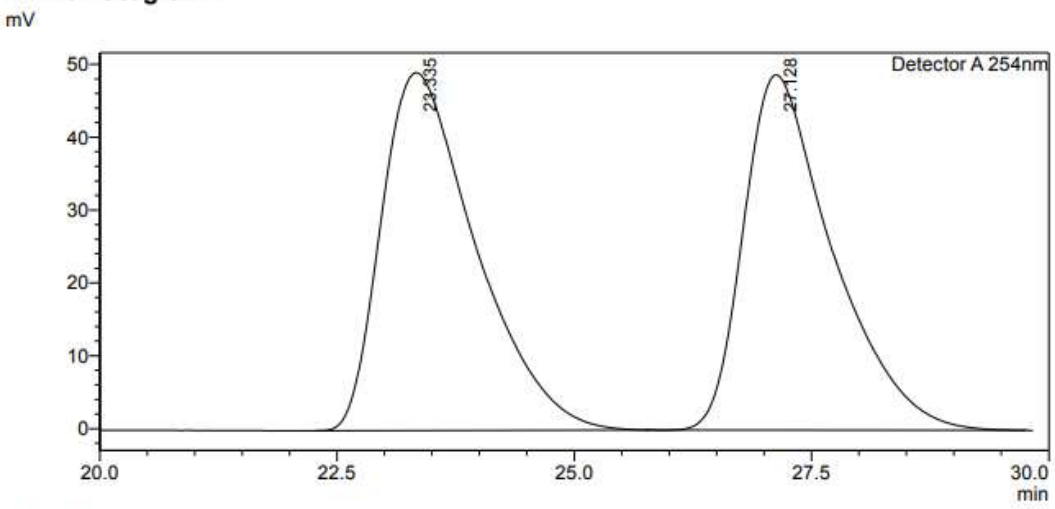

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	23.335	3393672	49104	51.549		M	
2	27.128	3189690	48760	48.451		M	
Total		6583362	97864				

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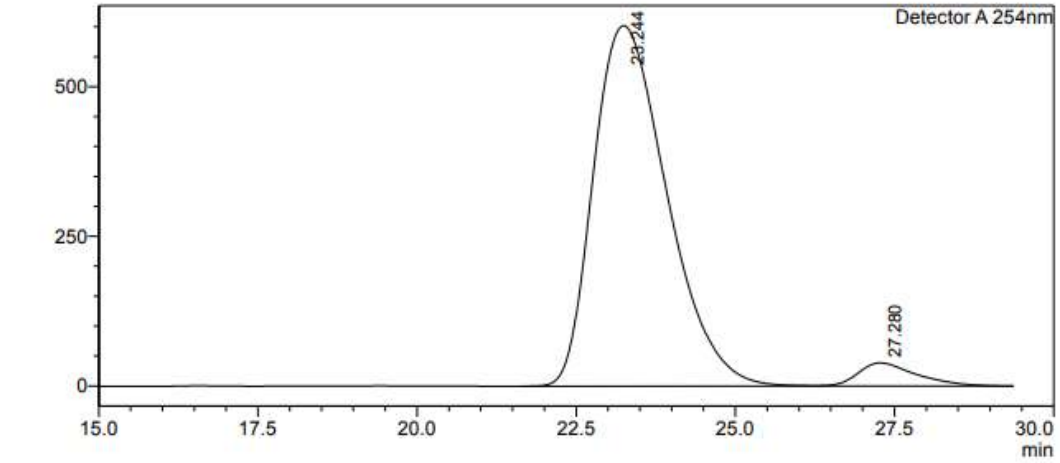

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	23.244	48376268	602249	95.143			
2	27.280	2469801	38798	4.857		V	
Total		50846070	641047				

3j: OJ-H, Hexane/iPrOH=70/30, rate=0.8 mL/min, 254 nm

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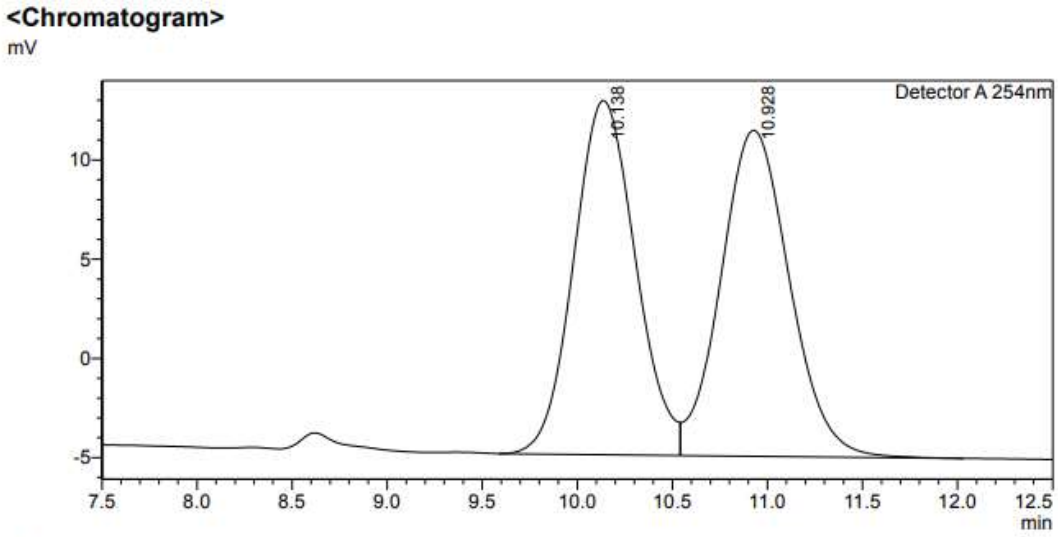
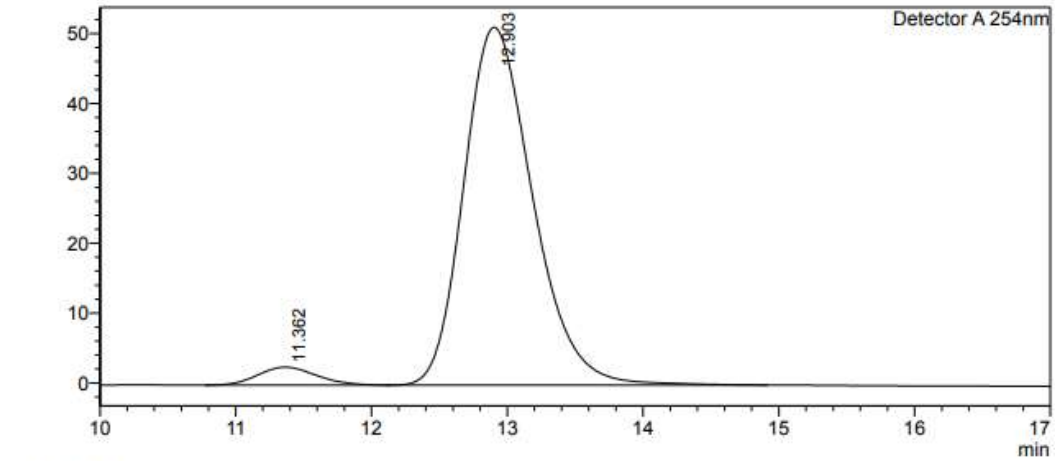


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.138	404110	17840	49.456			
2	10.928	412993	16419	50.544		V	
Total		817103	34259				

<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.362	76980	2566	4.077			
2	12.903	1811266	51209	95.923			
Total		1888247	53776				

3k: AS-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

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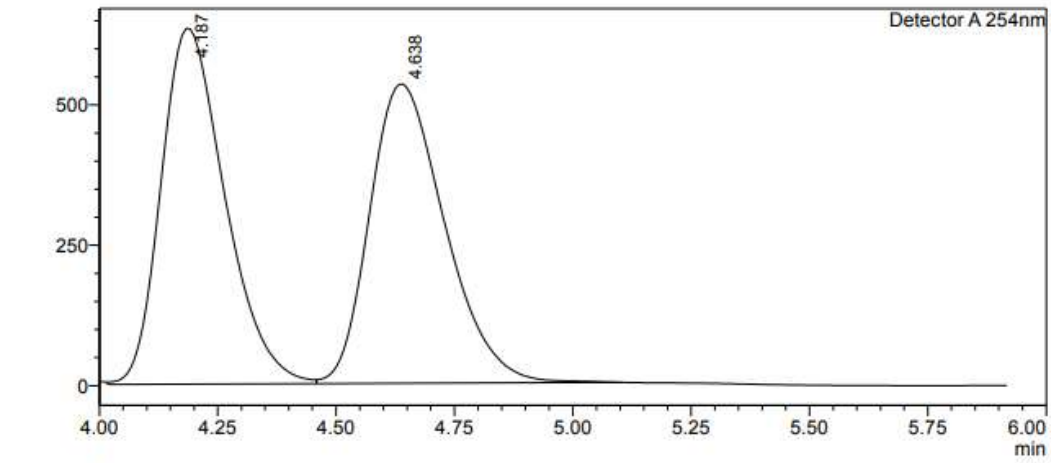
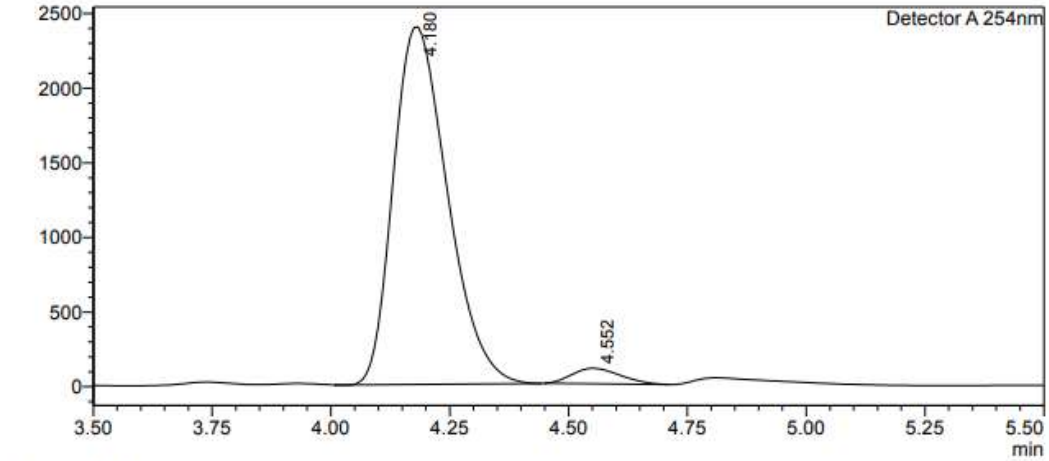


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.187	5948143	633525	50.205		M	
2	4.638	5899527	532472	49.795		V M	
Total		11847670	1165997				

<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.180	18984952	2393390	96.294		M	
2	4.552	730587	103637	3.706		M	
Total		19715538	2497027				

3l: OJ-H, Hexane/iPrOH=70/30, rate=0.8 mL/min, 254 nm

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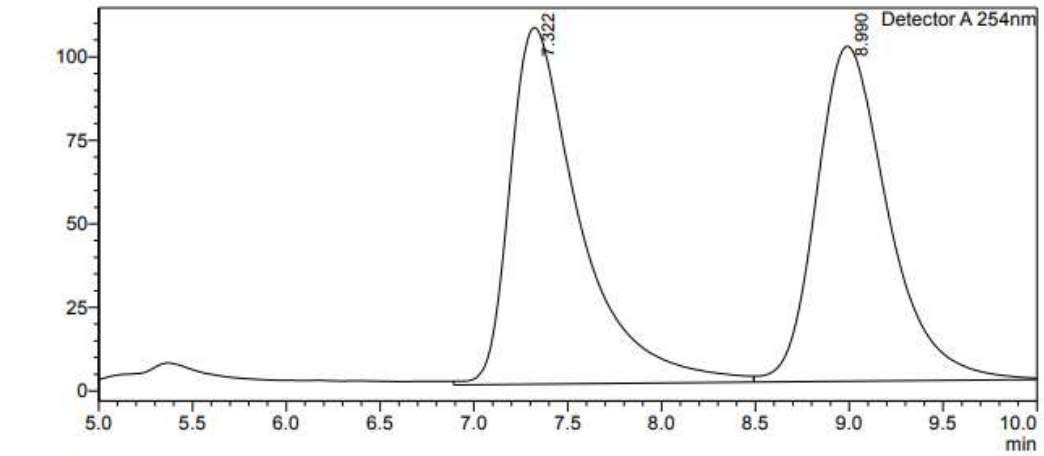
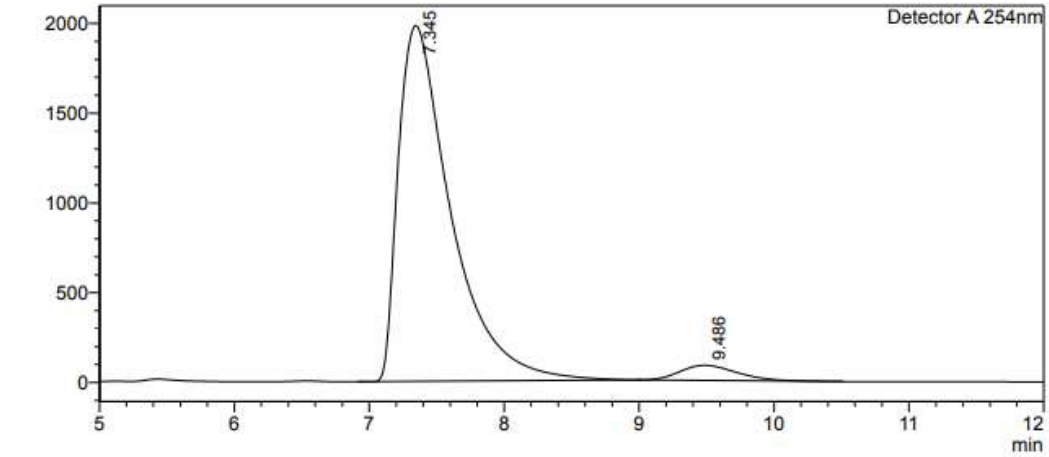


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.322	2770115	106705	50.882			
2	8.990	2674092	100256	49.118		V	
Total		5444208	206962				

<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.345	53810434	1982023	95.540		M	
2	9.486	2511750	84597	4.460			
Total		56322183	2066621				

3m: OJ-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

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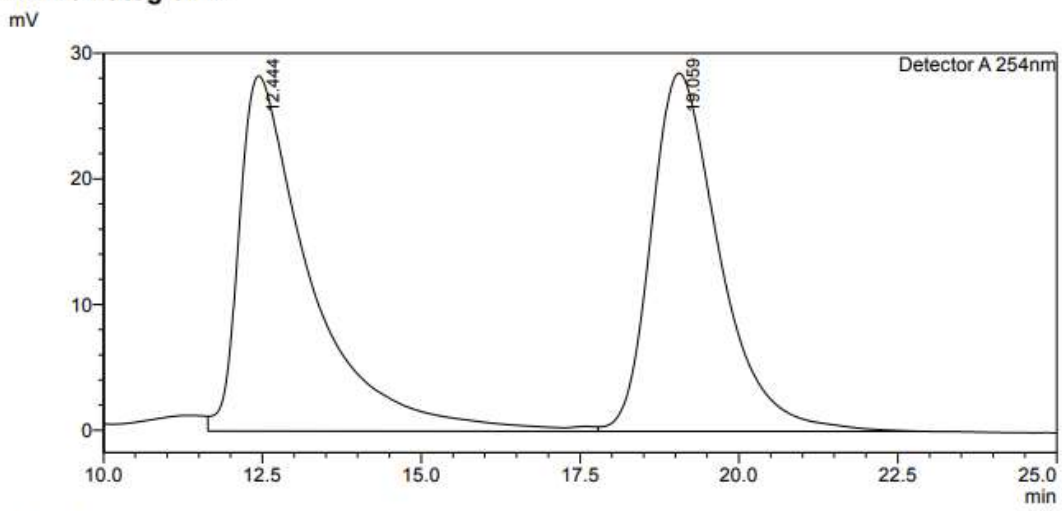
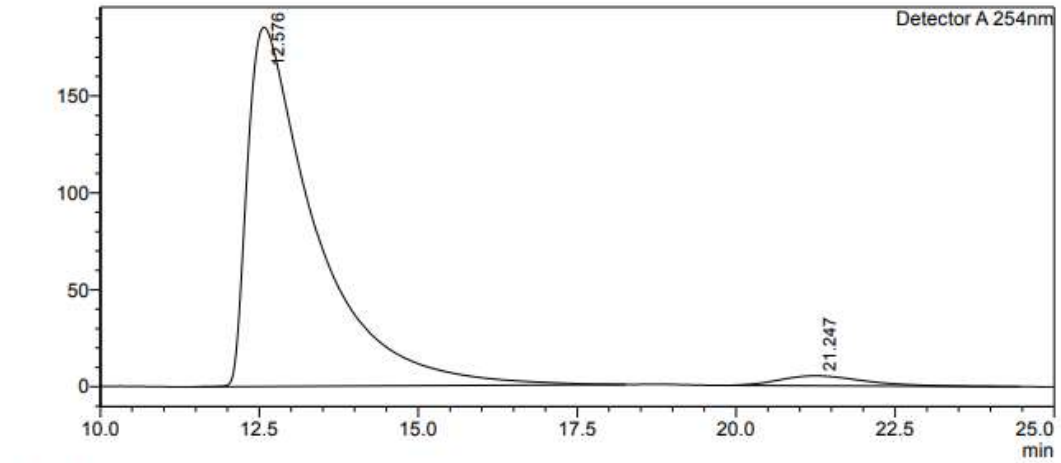


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.444	2210651	28246	50.937		S	
2	19.059	2129341	28480	49.063		V	
Total		4339992	56726				

<Chromatogram>



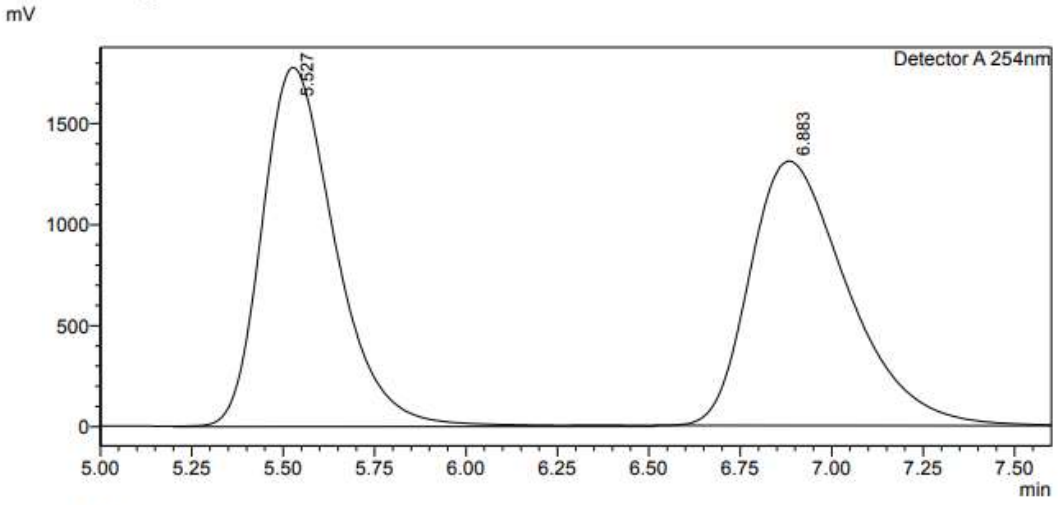
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.576	13795384	185288	96.656		M	
2	21.247	477341	5130	3.344			
Total		14272725	190418				

3n: AD-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

<Chromatogram>

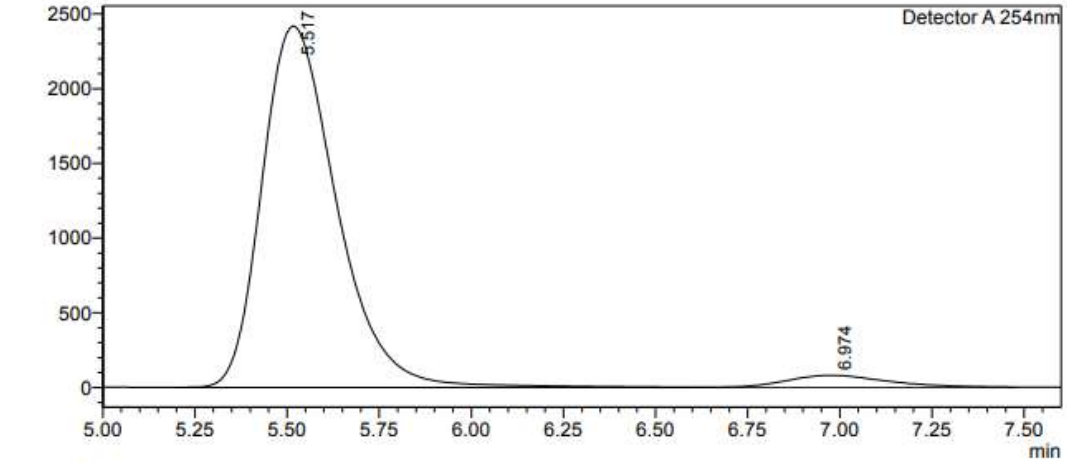


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.527	24836725	1778048	50.347			
2	6.883	24493930	1309695	49.653		M	
Total		49330654	3087743				

<Chromatogram>



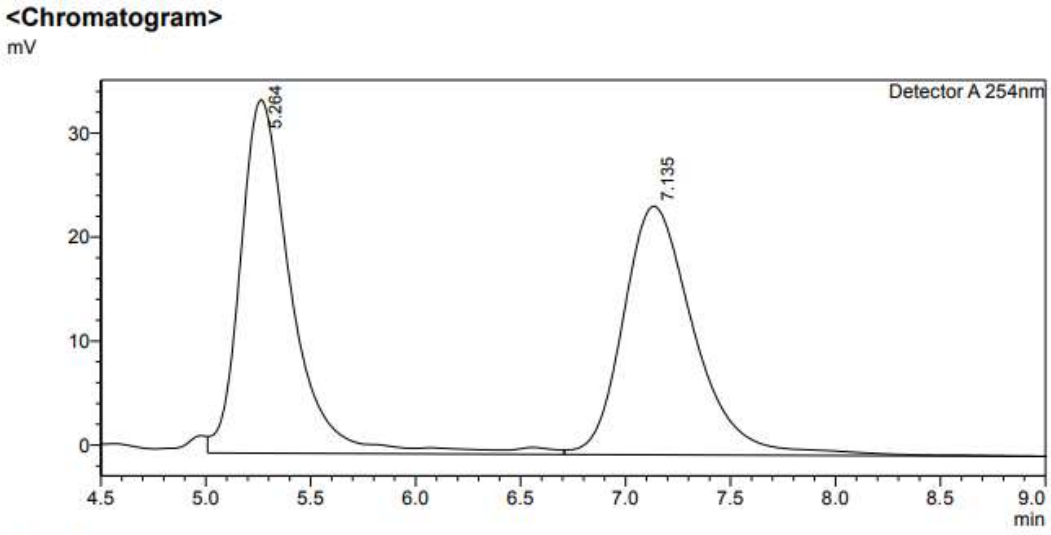
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.517	34116591	2418030	95.915		M	
2	6.974	1453105	78482	4.085		M	
Total		35569696	2496512				

3o: OD-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

<Chromatogram>

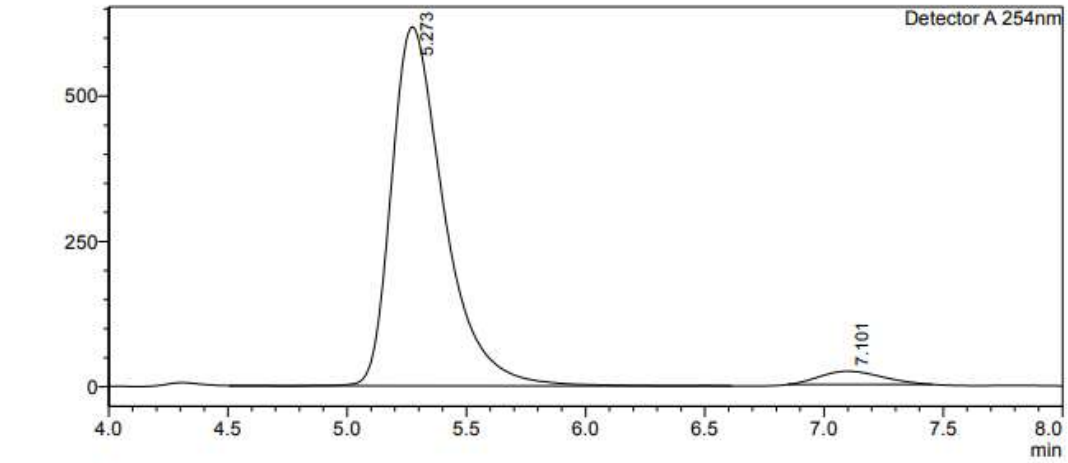


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.264	581039	33956	50.771		S	
2	7.135	563403	23888	49.229		V	
Total		1144442	57844				

<Chromatogram>



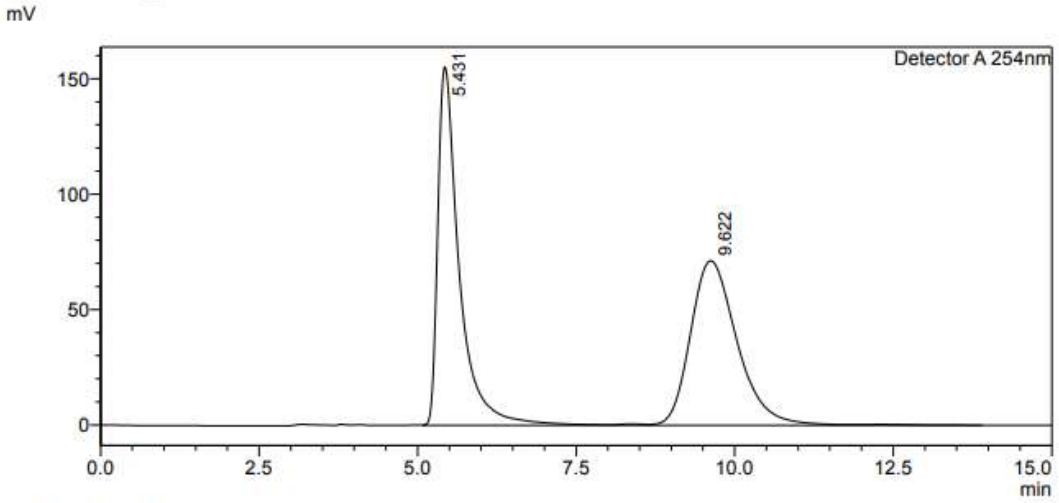
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.273	9486299	617447	95.817		M	
2	7.101	414128	22725	4.183		M	
Total		9900427	640172				

3p: OJ-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

<Chromatogram>

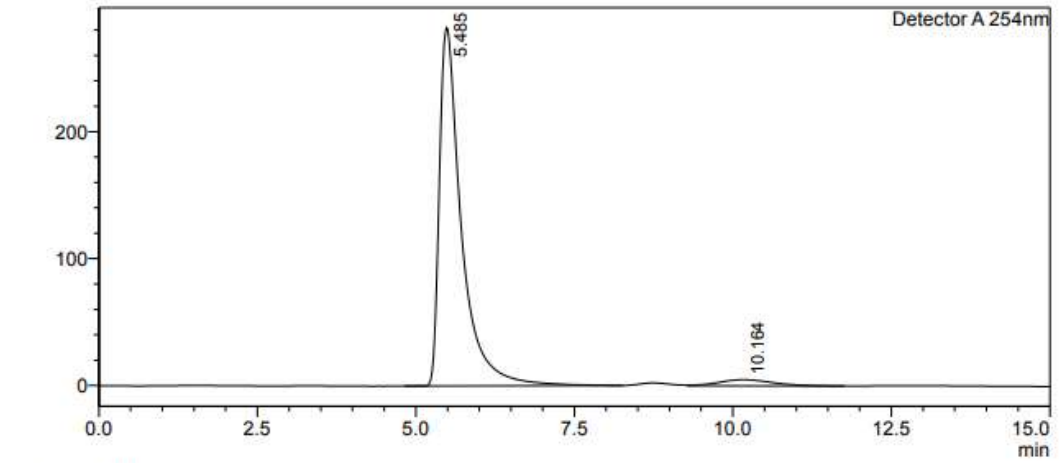


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.431	3649482	155195	49.927			
2	9.622	3660187	71242	50.073		V	
Total		7309669	226436				

<Chromatogram>



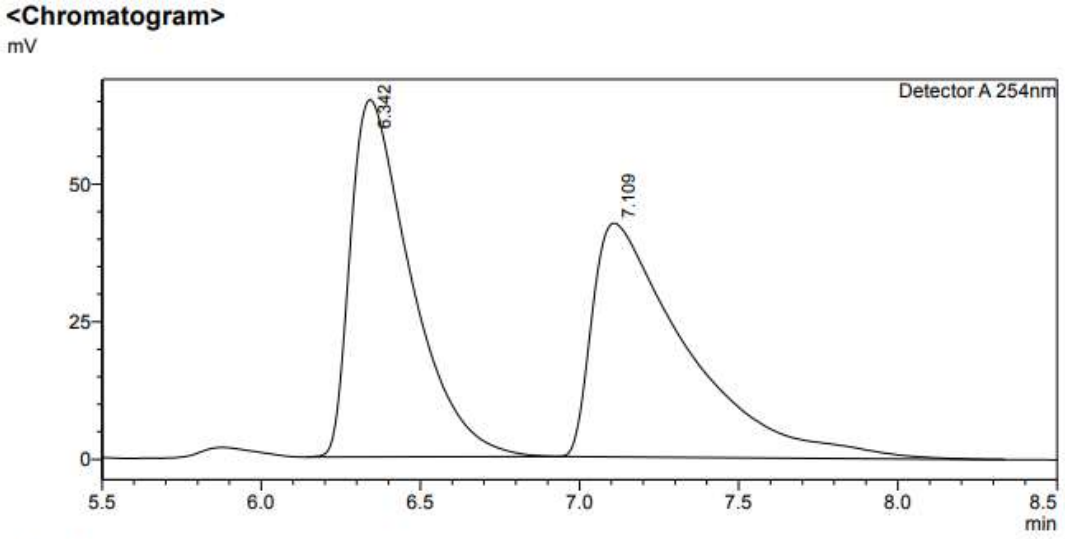
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.485	6797361	282091	96.051		M	
2	10.164	279437	4771	3.949			
Total		7076799	286862				

4a: AD-H, Hexane/iPrOH=85/15, rate=1.0 mL/min, 254 nm

<Chromatogram>

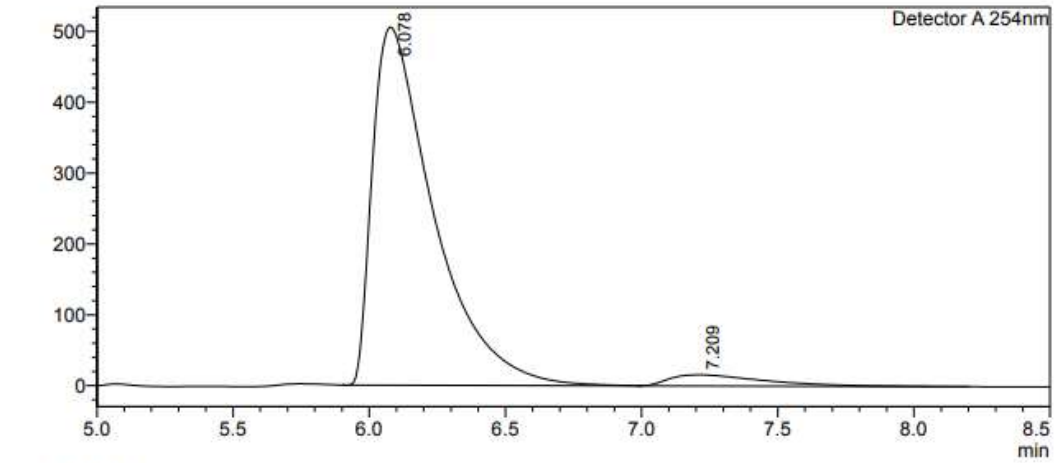


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.342	857719	64910	49.374		M	
2	7.109	879482	42449	50.626		M	
Total		1737201	107358				

<Chromatogram>



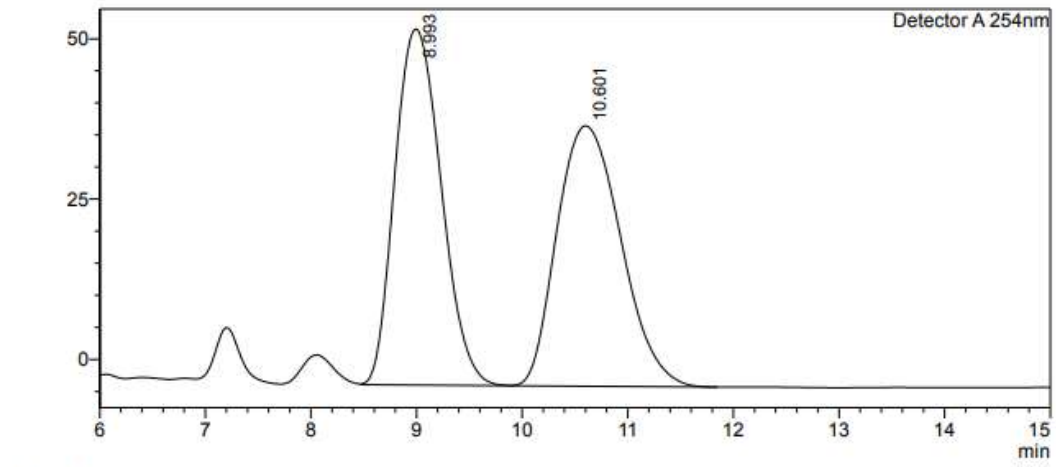
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.078	7894257	505236	95.421		M	
2	7.209	378866	15675	4.579			
Total		8273122	520911				

4b: AD-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

<Chromatogram>

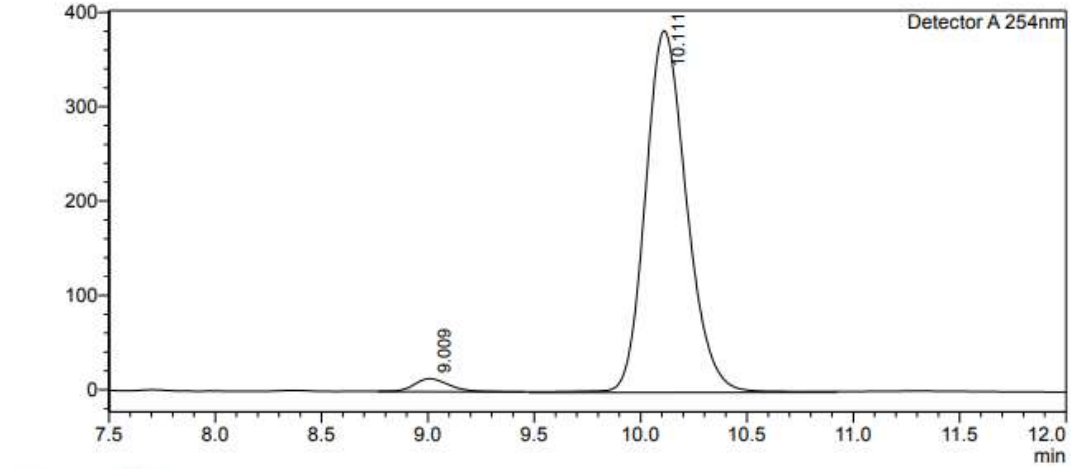


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.993	1695923	55525	49.719			
2	10.601	1715127	40596	50.281			
Total		3411050	96121				

<Chromatogram>



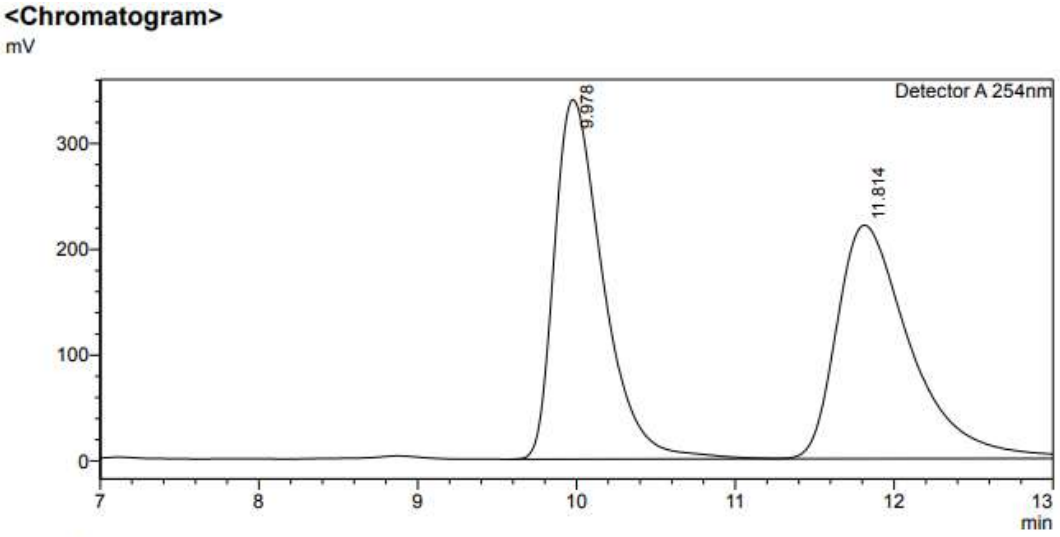
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.009	157264	13770	2.941			
2	10.111	5189605	383327	97.059			
Total		5346870	397096				

4c: OD-H, Hexane/iPrOH=90/10, rate=1.0 mL/min, 254 nm

<Chromatogram>

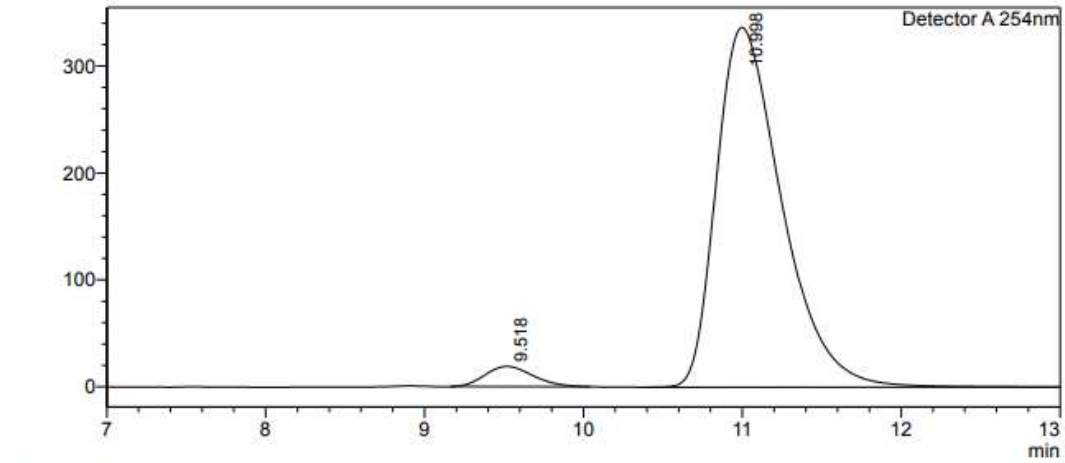


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.978	7236294	339787	50.272			
2	11.814	7157902	220655	49.728		V	
Total		14394196	560442				

<Chromatogram>



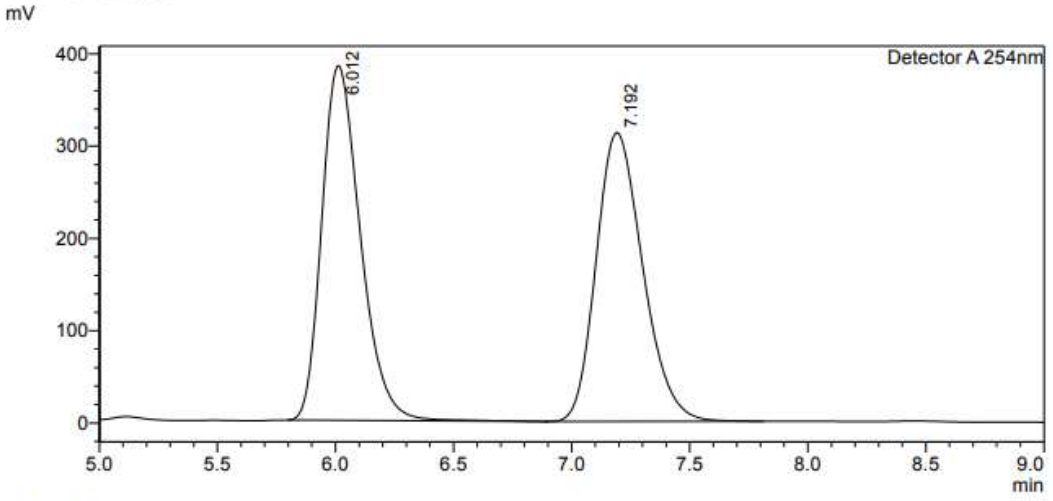
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.518	397131	18901	3.961		M	
2	10.998	9629048	336210	96.039			
Total		10026179	355111				

4d: AD-H, Hexane/iPrOH=85/15, rate=1.0 mL/min, 254 nm

<Chromatogram>

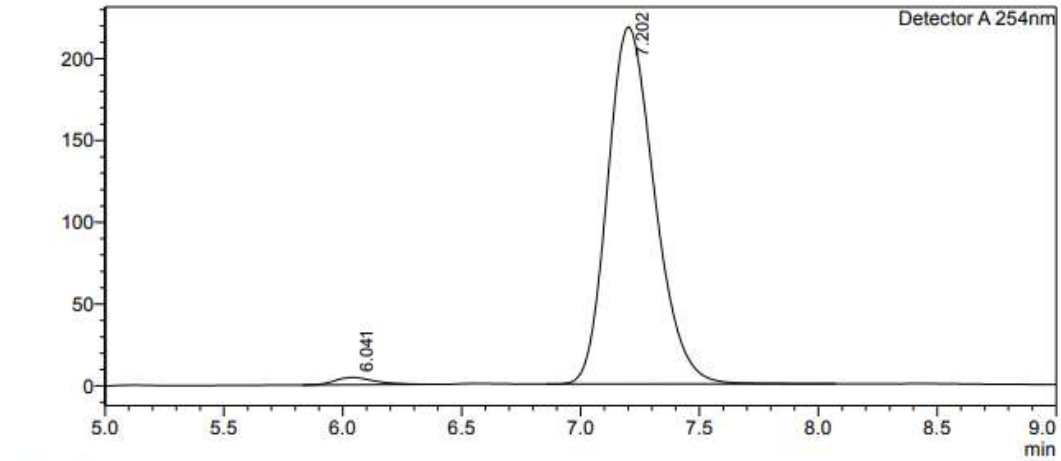


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.012	4369137	384010	50.432		M	
2	7.192	4294320	312978	49.568		M	
Total		8663457	696989				

<Chromatogram>



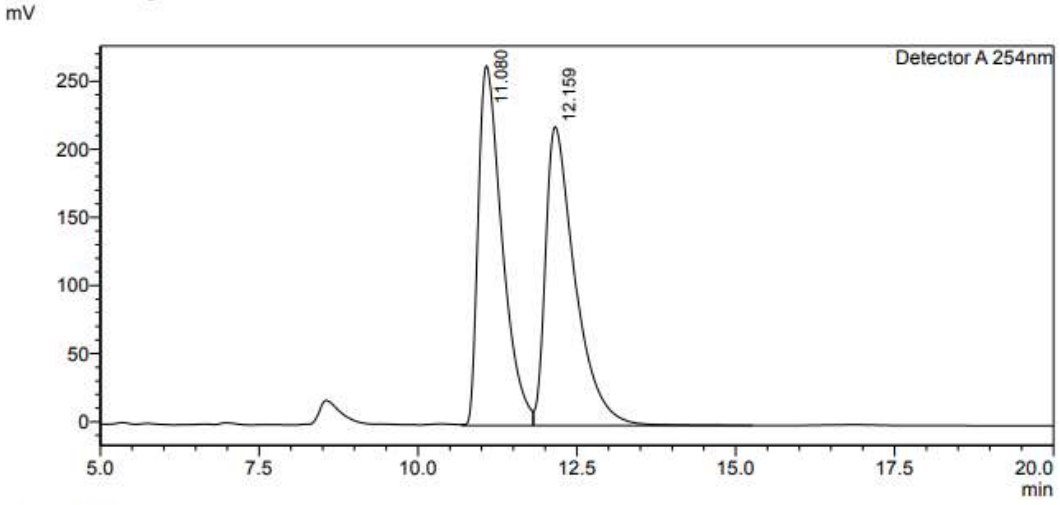
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.041	52495	4495	1.718		M	
2	7.202	3002535	218162	98.282		M	
Total		3055030	222657				

4e: AD-H, Hexane/iPrOH=90/10, rate=1.0 mL/min, 254 nm

<Chromatogram>

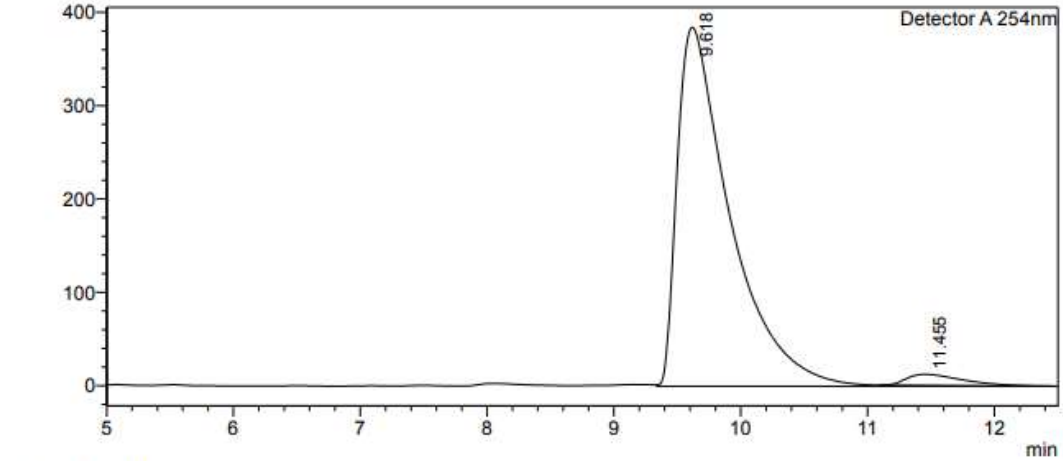


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.080	6897139	263794	49.190			
2	12.159	7124303	219235	50.810		V	
Total		14021441	483029				

<Chromatogram>



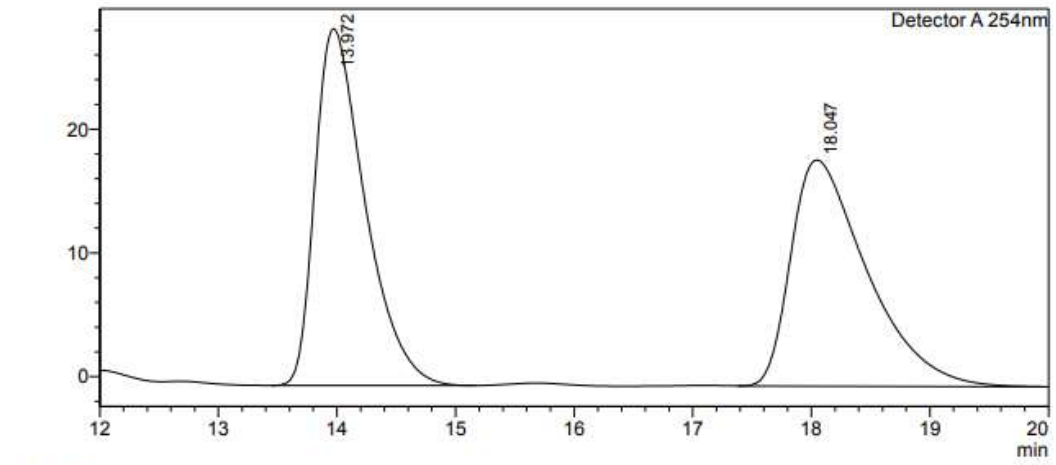
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.618	11148999	384351	96.869		S	
2	11.455	360352	11894	3.131		T	
Total		11509351	396245				

4f: AD-H, Hexane/iPrOH=90/10, rate=1.0 mL/min, 254 nm

<Chromatogram>

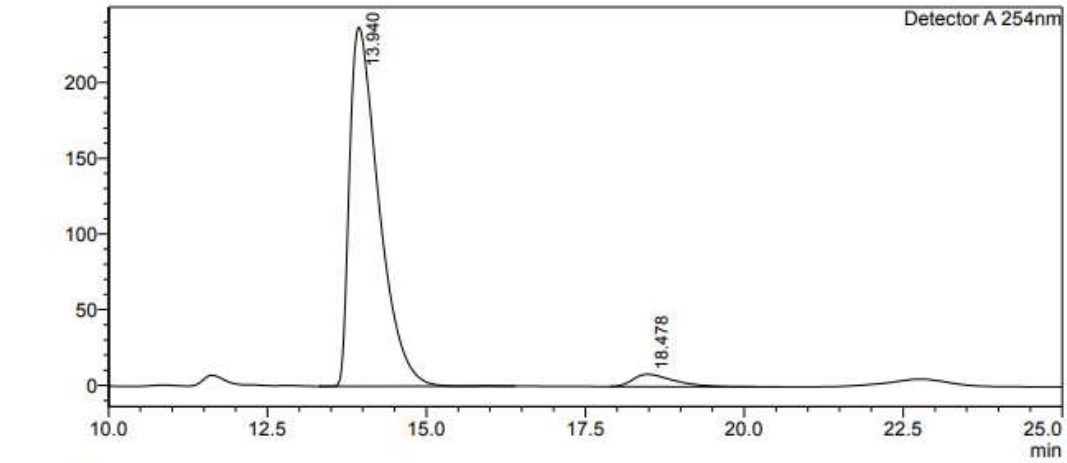


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.972	843790	28833	50.874			
2	18.047	814811	18271	49.126			
Total		1658601	47103				

<Chromatogram>



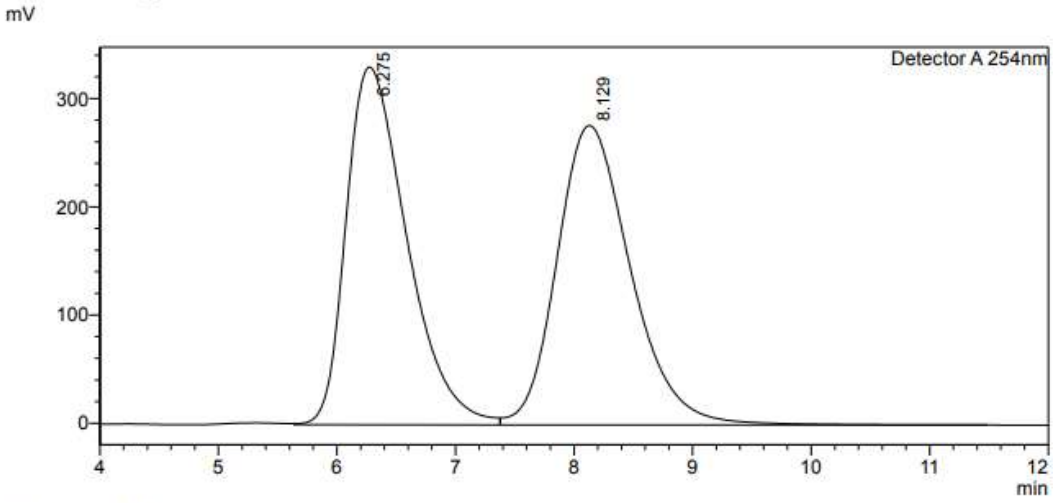
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.940	7592186	237221	95.469			
2	18.478	360314	8135	4.531		M	
Total		7952500	245356				

4g: AS-H, Hexane/iPrOH=80/20, rate=1.0 mL/min, 254 nm

<Chromatogram>

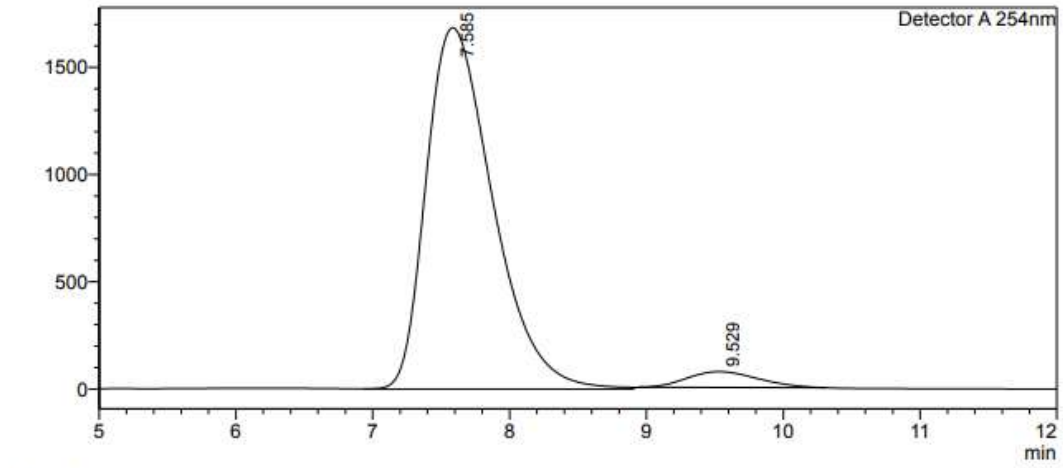


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.275	11754272	330379	49.602			
2	8.129	11943118	276541	50.398		V	
Total		23697390	606920				

<Chromatogram>



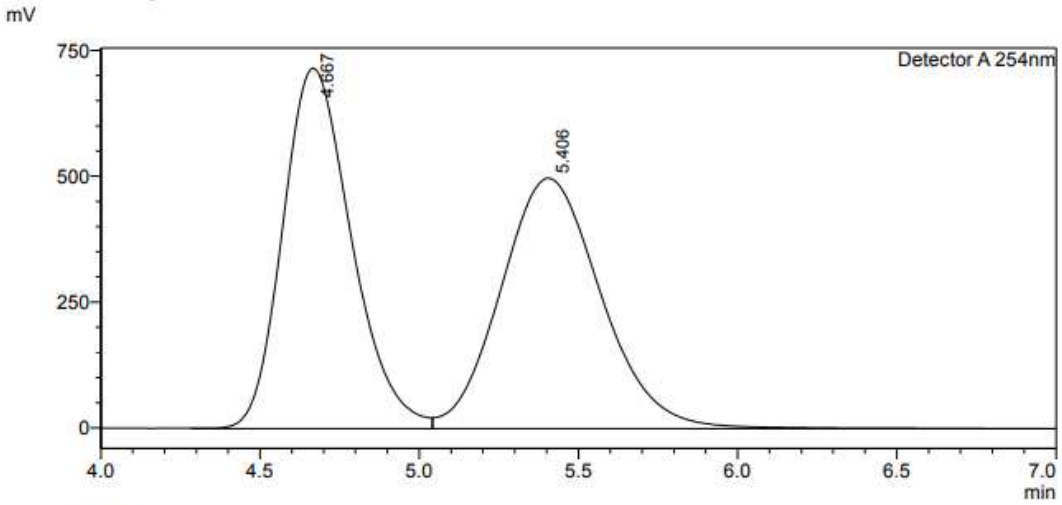
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.585	57008343	1684875	95.521			
2	9.529	2673349	73828	4.479		M	
Total		59681692	1758703				

4h: AS-H, Hexane/iPrOH=80/20, rate=1.0 mL/min, 254 nm

<Chromatogram>

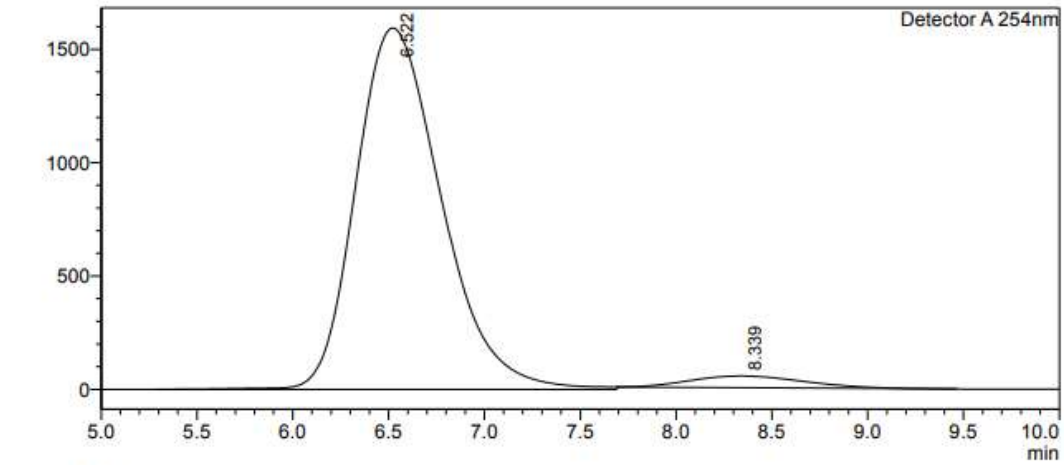


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.667	10755699	716000	49.597			
2	5.406	10930355	497429	50.403		V	
Total		21686053	1213429				

<Chromatogram>



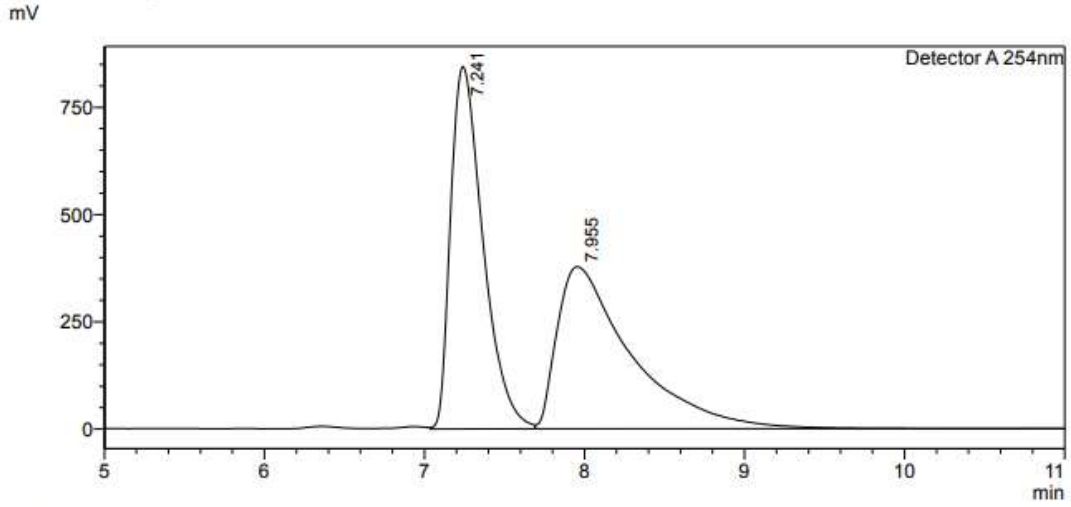
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.522	49574990	1594243	95.855			
2	8.339	2143963	51711	4.145		M	
Total		51718953	1645954				

4i: AD-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

<Chromatogram>

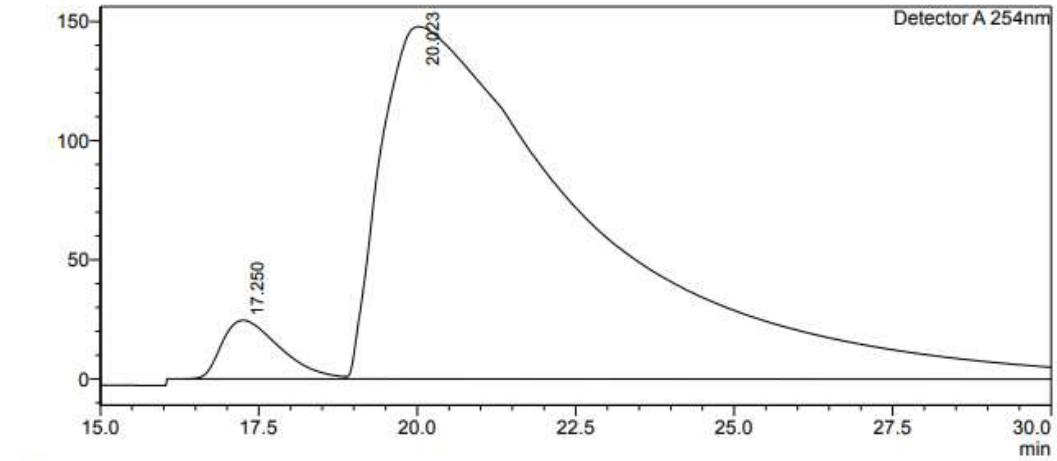


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.241	11885247	844363	49.309			
2	7.955	12218289	377827	50.691		V	
Total		24103536	1222191				

<Chromatogram>



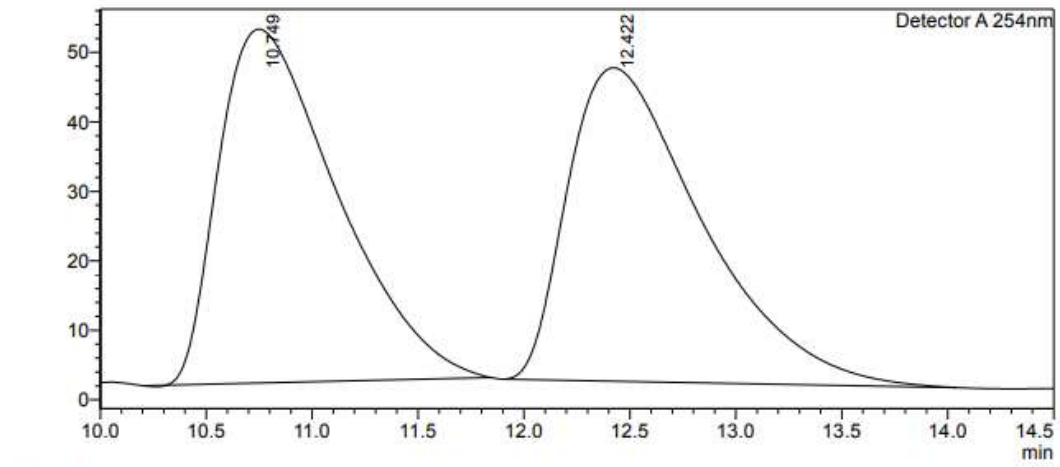
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	17.250	1566979	24599	4.357			
2	20.023	34396592	147824	95.643		V M	
Total		35963571	172423				

4j: AD-H, Hexane/iPrOH=80/20, rate=1.0 mL/min, 254 nm

<Chromatogram>

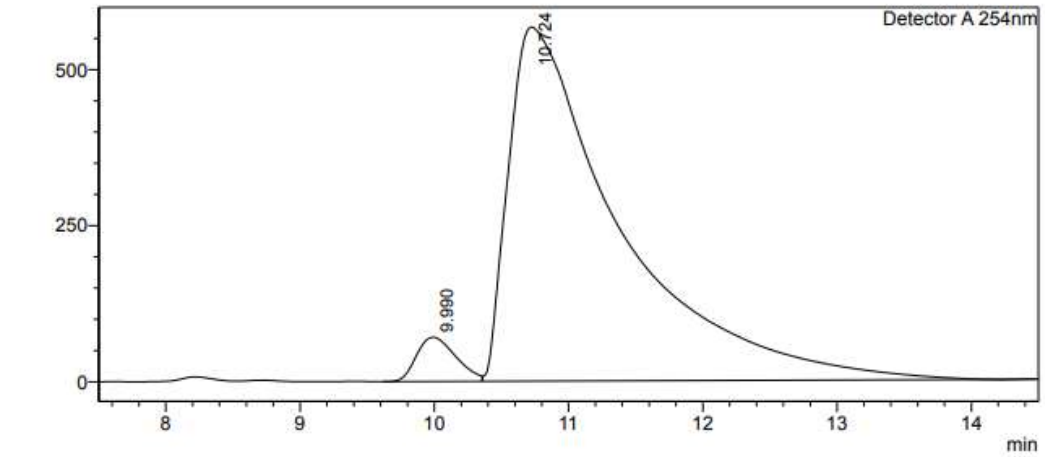


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.749	1977100	50927	49.768		M	
2	12.422	1995571	45105	50.232		M	
Total		3972671	96031				

<Chromatogram>



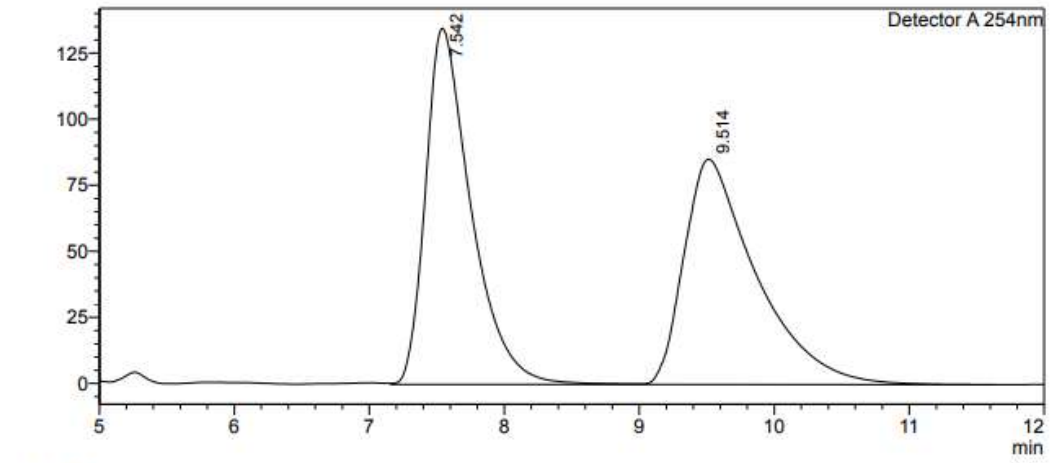
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.990	1445443	70820	4.236			
2	10.724	32674555	566979	95.764		V	
Total		34119998	637799				

4k: AD-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

<Chromatogram>

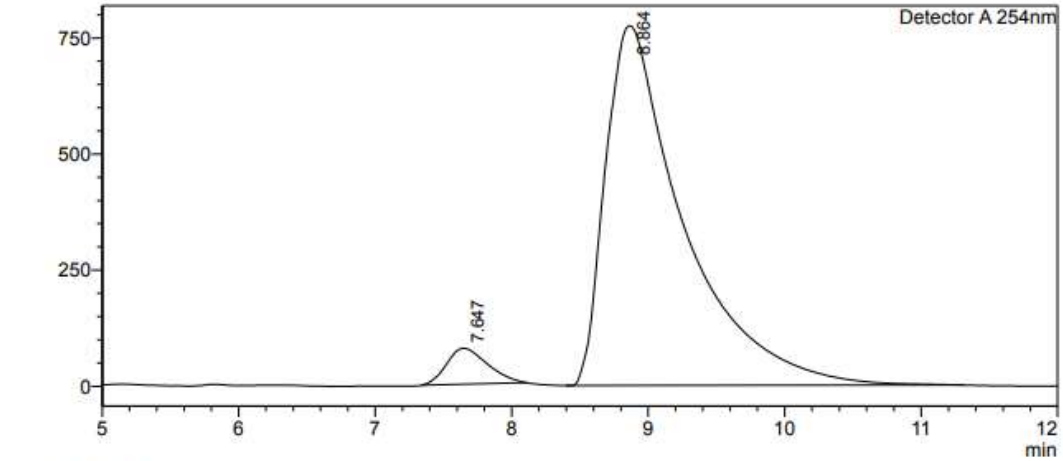


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.542	3166985	134758	49.981			
2	9.514	3169419	85282	50.019		V	
Total		6336404	220040				

<Chromatogram>



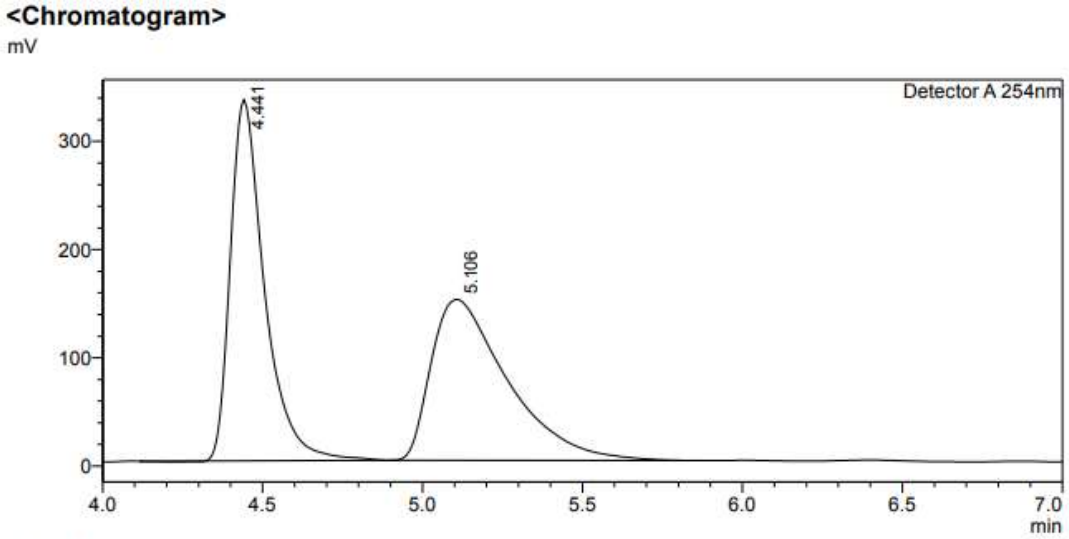
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.647	1601984	77345	4.940		M	
2	8.864	30827791	774774	95.060		M	
Total		32429776	852118				

4l: AD-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

<Chromatogram>

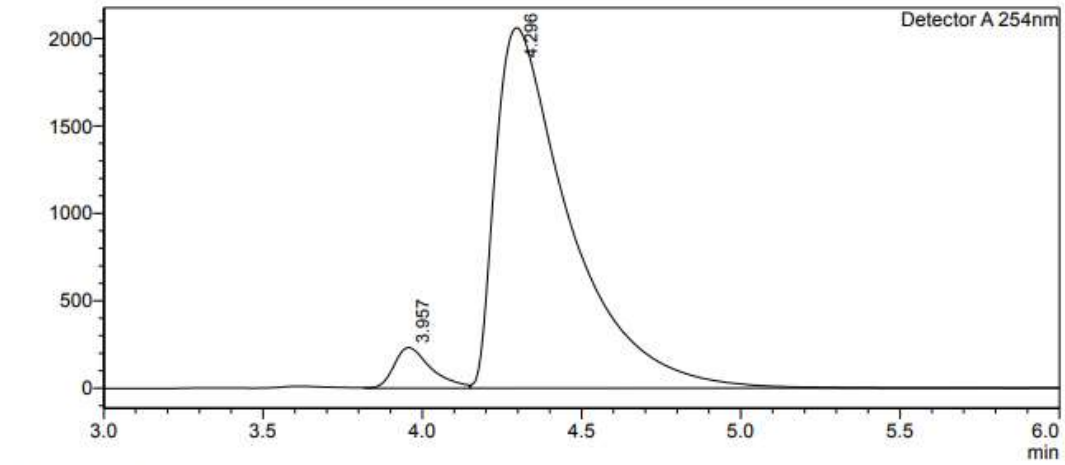


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.441	2474192	333485	50.033		M	
2	5.106	2470973	148746	49.967		M	
Total		4945166	482231				

<Chromatogram>



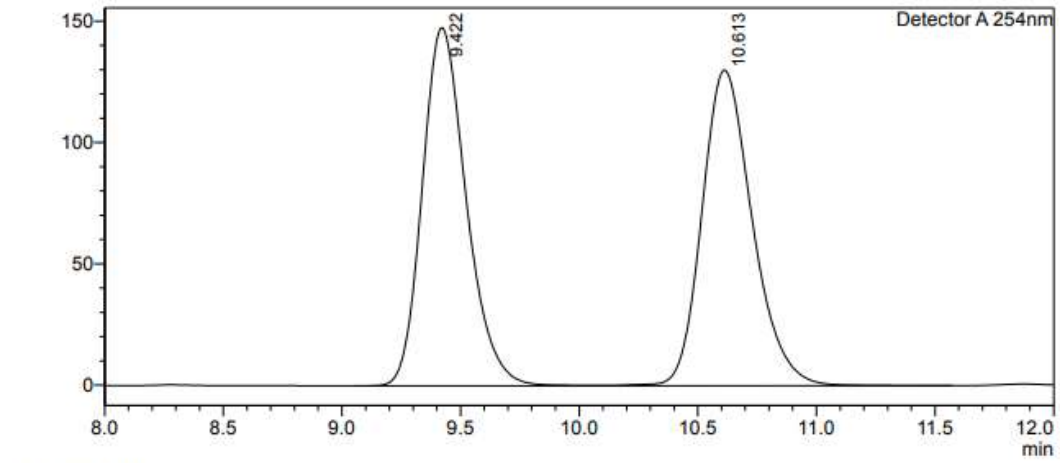
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	3.957	1896027	233518	5.350			
2	4.296	33541939	2060989	94.650		V	
Total		35437966	2294507				

5a: OJ-H, Hexane/iPrOH=70/30, rate=1.0 mL/min, 254 nm

<Chromatogram>

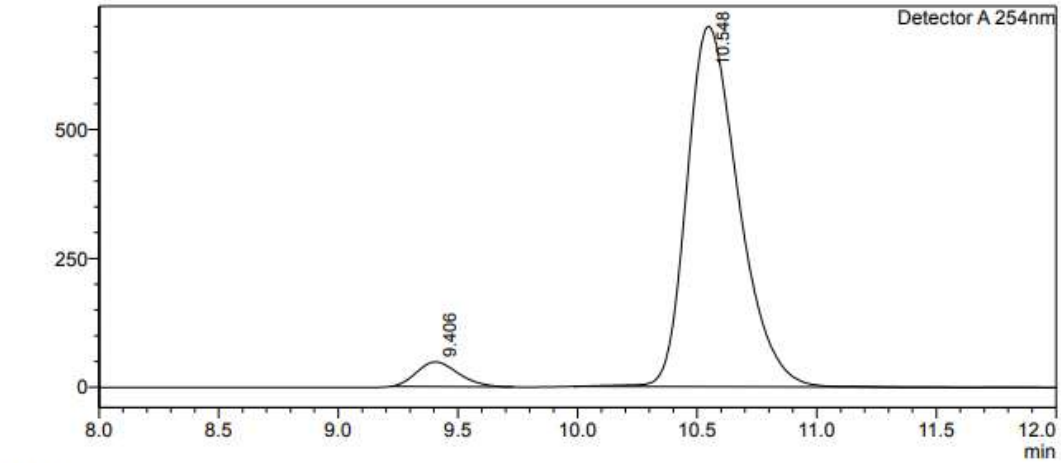


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.422	1903285	147475	49.752			
2	10.613	1922268	130001	50.248		V	
Total		3825552	277475				

<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.406	586395	47964	5.281		M	
2	10.548	10518314	699104	94.719		M	
Total		11104709	747068				