Chiral Chemistry https://doi.org/10.70401/cc.2025.0010

Supplementary information

Development of a scalable iridium-catalyzed asymmetric hydrogenation process for synthesis of chiral 2-methyl-1,2,3,4-tetrahydroquinoline

Huan Jing, Chang-Bin Yu, Yong-Gui Zhou

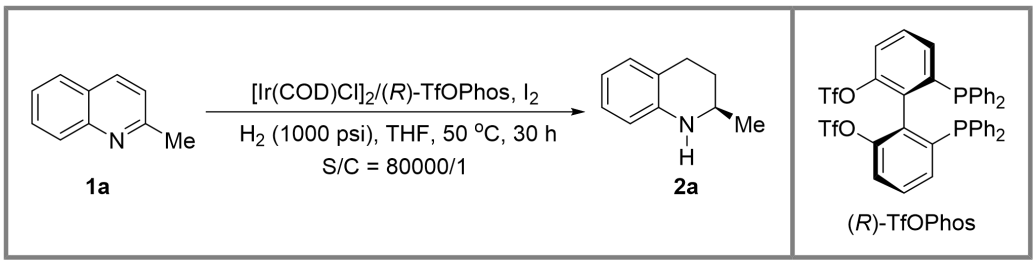
Table of Contents

1.General and Materials

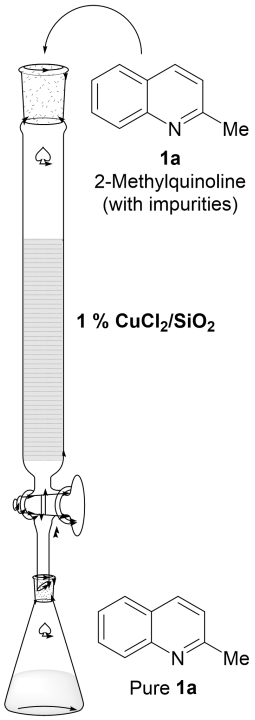
General: All reactions were carried out under an atmosphere of nitrogen using the standard Schlenk techniques, unless otherwise noted. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at room temperature in $CDCl_3$ on 400 MHz instrument with tetramethylsilane (TMS) as internal standard. Flash column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by TLC analysis. The optical rotations were measured by polarimeter. Enantiomeric excess was determined by HPLC analysis using chiral column described below in detail.

Materials: Commercially available solvents and reagents were used as received. 2-Methylquinoline could be suitable after adsorption purification through a silica gel column doped with 1% copper chloride. The ligand (*R*)-TfOPhos was synthesized according to the known procedure.[1]

2.Iridium-Catalyzed Asymmetric Hydrogenation



2.1 Iridium-catalyzed asymmetric hydrogenation of 2-methylquinoline

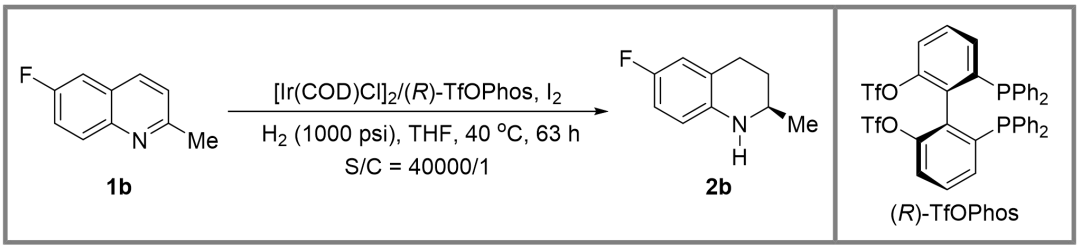


The Purification of 2-Methylquinoline 1a. Copper(II) chloride was added to the weighed silica gel (note: the mass ratio is at 1%, 300 mesh) and mechanically stirred for 5-10 minutes until mixed uniformly. Then, the mixture was packed into the chromatography column as the stationary phase and fully saturated with hexanes. Then, commercially available 2-methylquinoline with trace amount of impurities was purified through the above chromatography column with hexanes/ethyl acetate = 10/1 as the eluent. The solvents were removed under the reduced pressure, and the resulting residue **1a** could be directly used for next asymmetric hydrogenation with good repeatability.

Ir-Catalyzed Asymmetric Hydrogenation of 2-Methylquinoline 1a. In a nitrogen-filled glovebox, a mixture of $[Ir(COD)Cl]_2$ (14.7 mg, 21.9 μmol) and chiral ligand (*R*)-6,6'-bis(diphenylphosphino)-1,1'-biphenyl-2,2'-diylbis(trifluoromethylsulfonate) ((*R*)-TfOPhos 43.0 mg, 52.5 μmol) in tetrahydrofuran (THF, 24 mL) was stirred at room temperature for 30 minutes to give the chiral catalyst solution. Then, the above solution was transferred to a 2 L autoclave in which the additive iodine (1.110 g, 4.38 mmol), tetrahydrofuran (560 mL) and 2-methylquinoline **1a** (250.3 g, 1.75 mol) have been added. Then charged with hydrogen gas (1000 psi) and stirred at 50 ºC for 30 hours (Note: hydrogen gas was continuously supplemented to keep the pressure at 1000 psi). After carefully releasing the hydrogen gas, the mixture was concentrated under the reduced pressure. The crude residue was washed with sodium thiosulfate solution (3.0 M, 100 mL) and extracted

three times with ethyl acetate (100 mL x 3). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated under the reduced pressure to afford 256.1 g of chiral reductive product (*R*)-**2a** in 99% yield with 91.4% ee.
The optical purity was determined by HPLC analysis using the chiral column (OJ-H).

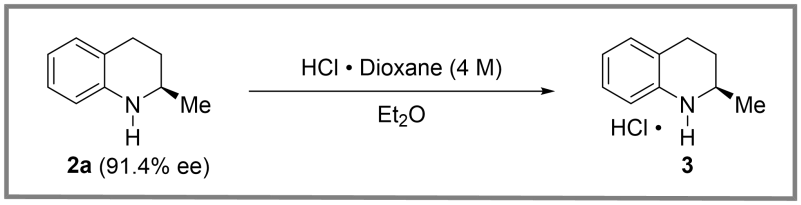
(*R*)-2-Methyl-1,2,3,4-tetrahydroquinoline (2a):
Known compound,[2] R_f = 0.75 (hexanes/ethyl acetate = 5/1), 91.4% ee. [>99% ee, $[\alpha]^{20}_D$ = + 91.4 (*c* 2.00, $CHCl_3$)], [lit.[2]: 99% ee, $[\alpha]^{RT}_D$ = + 84.3 (*c* 0.20, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99-6.93 (m, 2H), 6.64-6.56 (t, *J* = 7.3 Hz, 1H), 6.50-6.43 (d, *J* = 8.4 Hz, 1H), 3.69 (brs, 1H), 3.44-3.35 (m, 1H), 2.88-2.79 (m, 1H), 2.76-2.68 (m, 1H), 1.96-1.89 (m, 1H), 1.64-1.53 (m, 1H), 1.20 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 129.3, 126.7, 121.1, 117.0, 114.0, 47.2, 30.2, 26.6, 22.7. HPLC: Chiracel OJ-H column, 254 nm, 30 °C, *n*-Hexane/*i*-PrOH = 95/5, flow = 1.0 mL/min, retention time 10.9 min and 11.9 min (major).



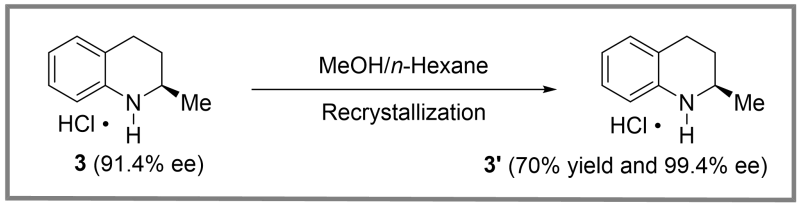
2.2 Iridium-catalyzed asymmetric hydrogenation of 6-fluoro-2-methylquinoline 1b
In a nitrogen-filled glovebox, a mixture of $[Ir(COD)Cl]_2$ (2.0 mg, 3.0 μmol) and chiral bisphosphine ligand (*R*)-6,6'-bis(diphenylphosphino)-1,1'-biphenyl-2,2'-diylbis(trifluoromethylsulfonate) ((*R*)-TfOPhos, 5.9 mg, 7.2 μmol) in tetrahydrofuran (4 mL) was stirred at room temperature for 30 minutes to give the chiral catalyst solution. Then, the above solution was transferred to a 300 mL autoclave in which additive iodine (152.0 mg, 0.6 mmol), tetrahydrofuran (36 mL) and 6-fluoro-2-methylquinoline **1b** (19.34 g, 0.12 mol) have been added. Then charged with hydrogen gas (1000 psi) and stirred at 40 ºC for 63 hours (Note: hydrogen gas was continuously supplemented to keep the reaction pressure at 1000 psi). After carefully releasing hydrogen gas, the mixture was concentrated under the reduced pressure. The crude residue was washed with sodium thiosulfate solution (3.0 M, 10 mL) and extracted three times with ethyl acetate (30 mL x 3). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated under the reduced pressure to give 19.71 g of chiral reductive product (*R*)-**2b** in 99% yield and 91.4% ee.

(*R*)-6-Fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (2b):
Known compound,[2] R_f = 0.75 (hexanes/ethyl acetate = 5/1), 91.4% ee. $[\alpha]^{20}_D$ = + 81.8 (*c* 2.00, $CHCl_3$), [lit.[2]: 98% ee, $[\alpha]^{RT}_D$ = + 80.3 (*c* 0.19, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75-6.61 (m, 2H), 6.46-6.34 (m, 1H), 3.56 (d, *J* = 59.2 Hz, 1H), 3.40-3.29 (m, 1H), 2.89-2.75 (m, 1H), 2.73-2.66 (m, 1H), 1.96-1.87 (m, 1H), 1.62-1.49 (m, 1H), 1.23-1.18 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 156.7, 154.4, 141.0, 122.5, 122.4, 115.5, 115.3, 114.8, 114.7, 113.3, 113.0, 47.3, 29.9, 26.7, 22.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -128.34. HPLC: Chiralcel OJ-H, 254 nm, 30 °C, *n*-Hexane/*i*-PrOH = 98.5/1.5, flow = 1.0 mL/min, retention time 11.1 min (minor) and 11.6 min (major).

3.Recrystallization of 2-Methyl-1,2,3,4-tetrahydroquinoline

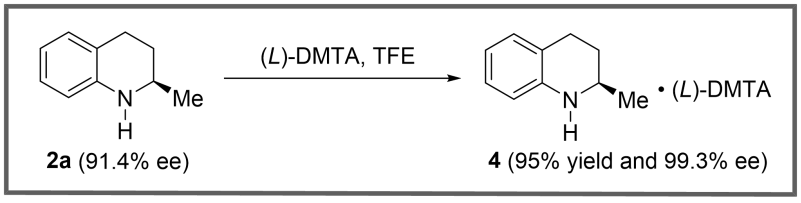


Under the ice bath, 2-methyl-1,2,3,4-tetrahydroquinoline **2a** (80.0 g, 0.544 mol, 91.4% ee) and diethyl ether (400 mL) were added to a 1000 mL of round-bottomed flask, equipped with a mechanical stirring bar. Hydrogen chloride in 1,4-dioxane solution (4.0 M, 136 mL, 0.544 mol) was added dropwise, and the mixture was stirred for 1.5 hours. Then, the crude mixture was filtered over Buchner funnel, and washed with cold ethyl ether three times (50 mL×3). The residue was collected and dried under vacuum to afford 99.9 gram of white solid 2-methyl-1,2,3,4-tetrahydroquinoline hydrochloride **3** in quantitative yield.



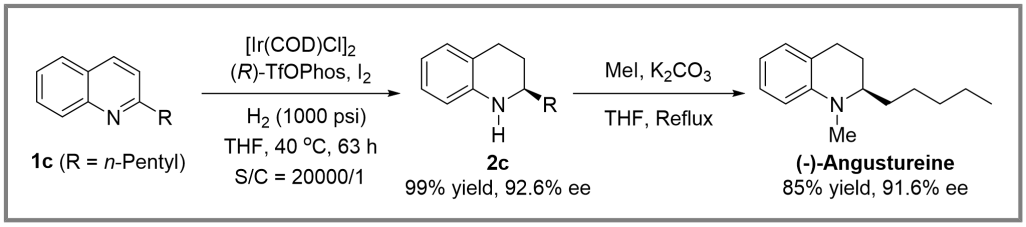
To a 500 mL round-bottom flask was charged 99.9 g of the 2-methyl-1,2,3,4-tetrahydroquino-line hydrochloride **3** and 120 mL of methanol. An additional 24 mL of methanol was added drop-wise under reflux until complete dissolution. Subsequently, *n*-hexane (20 mL) was introduced at reflux. Heating was stopped, and the mixture was allowed to cool naturally to room temperature and stand overnight. The precipitated solid was collected by the filtration, washed with chilled methanol, and dried under vacuum to afford 70.1 g of white solid **3'** with 70% yield and 99.4% ee. (Note: the optical purity was determined by the analysis of 2-methyl-1,2,3,4-tetrahydroquino-line after neutralization with sodium carbonate)

4.Resolution of 2-Methyl-1,2,3,4-tetrahydroquinoline with (*L*)-DMTA



The (*L*)-DMTA (653.9 g, 1.563 mol) and solvent trifluoroethanol (TFE, 2.67 L) were added to a round-bottom flask and stirred for 10 minutes. Then, a solution of 2-methyl-1,2,3,4-tetrahydroquinoline **2a** (230.1 g, 1.563 mol, 91.4% ee) in trifluoroethanol (382 mL) was added dropwise under reflux. After the addition was completed, the mixture was stirred for 5 hours. Heating was stopped, and the solution was allowed to cool naturally to room temperature with continued stirring for 12-15 hours. The resulting mixture was filtered, and the solid was washed with the cold trifluoroethanol (2×100 mL) and dried under vacuum to afford 842.2 g of powdered solid product **4** in 95% yield and 99.3% ee. (Note: the optical purity was determined by the HPLC analysis of 2-methyl-1,2,3,4-tetrahydroquinoline after neutralization with sodium carbonate)

5.Enantioselective Synthesis of Alkaloid (-)-Angustureine



In a nitrogen-filled glovebox, a mixture of $[Ir(COD)Cl]_2$ (2.0 mg, 3.0 μmol) and (*R*)-TfOPhos, (5.9 mg, 7.2 μmol) in tetrahydrofuran (2 mL) was stirred at room temperature for 30 minutes to give the chiral catalyst solution. Then, the above solution was transferred to a 300 mL autoclave in which additive iodine (152.0 mg, 0.6 mmol), tetrahydrofuran (20 mL) and 2-*n*-pentylquinoline (11.96 g, 60 mmol) have been added. Then charged with hydrogen gas (1000 psi) and stirred at 40 ºC for 63 hours. After carefully releasing hydrogen gas, the mixture was concentrated under the reduced pressure. The crude residue was washed with sodium thiosulfate solution (3.0 M, 10 mL) and extracted three times with ethyl acetate (15 mL x 3). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated under the reduced pressure to give 12.11 g of chiral product (*R*)-2-*n*-pentyl-1,2,3,4-tetrahydroquinoline in 99% yield and 92.6% ee.

(*R*)-2-*n*-Pentyl-1,2,3,4-tetrahydroquinoline (2c):

Known compound,[3] R_f = 0.70 (hexanes/ethyl acetate = 20/1), 92.6% ee. $[\alpha]^{20}_D$ = +72.6 (*c* 1.05, $CHCl_3$), [lit.[3]: 94% ee, $[\alpha]^{25}_D$ = +74.4 (*c* 1.03, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (d, *J* = 7.5 Hz, 2H), 6.60 (t, *J* = 7.4 Hz, 1H), 6.51-6.46 (m, 1H), 3.90 (s, 1H), 3.28-3.18 (m, 1H), 2.86-2.66 (m, 2H), 2.00-1.91 (m, 1H), 1.65-1.26 (m, 9H), 0.94-0.87 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 144.5, 129.3, 126.7, 121.6, 117.1, 114.2, 51.7, 36.6, 32.0, 28.1, 26.4, 25.5, 22.7, 14.1. HPLC: Chiralcel OJ-H, 254 nm, 30 ºC, *n*-Hexane/*i*-PrOH = 95/5, flow = 0.5 mL/min, retention time 13.0 min (minor) and 14.0 min (major).

To a solution of (+)-**2c** (11.93 g, 59 mmol) and K_2CO_3 (32.60 g, 236 mmol) in THF (400 mL) was added MeI (21.00 g, 148 mmol) under nitrogen. After the mixture was refluxed for 10 h, the reaction was quenched by water. The mixture was extracted with dichloromethane (20 mL x 3) and the combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was purified by column chromatography on silica gel to afford (-)-Angustureine (10.87 g) as pale-yellow oil with 85% yield and 91.6% ee.

(*R*)-2-*n*-Pentyl-2,3,4-tetrahydro-1-methylquinoline ((-)-Angustureine):

Known compound,[3] R_f = 0.75 (hexanes/ethyl acetate = 20/1), 91.6% ee. $[\alpha]^{20}_D$ = -7.16 (*c* 1.69, $CHCl_3$), [lit.[3]: 94% ee, $[\alpha]^{15}_D$ = -6.70 (*c* 1.00, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (t, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 7.0 Hz, 1H), 6.64-6.47 (m, 2H), 3.27-3.18 (m, 1H), 2.92 (s, 3H), 2.85-2.73 (m, 1H), 2.70-2.59 (m, 1H), 1.93-1.85 (m, 2H), 1.65-1.55 (m, 1H), 1.49-1.14 (m, 7H), 0.89 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 145.4, 128.7, 127.1, 121.8, 115.2, 110.4, 59.0, 38.0, 32.1, 31.2, 25.8, 24.4, 23.6, 22.7, 14.1. HPLC: Chiralcel OJ-H, 254 nm, 30 ºC, *n*-Hexane/*i*-PrOH = 95/5, flow = 0.5 mL/ min, retention time 8.4 min (major) and 9.2 min (minor).

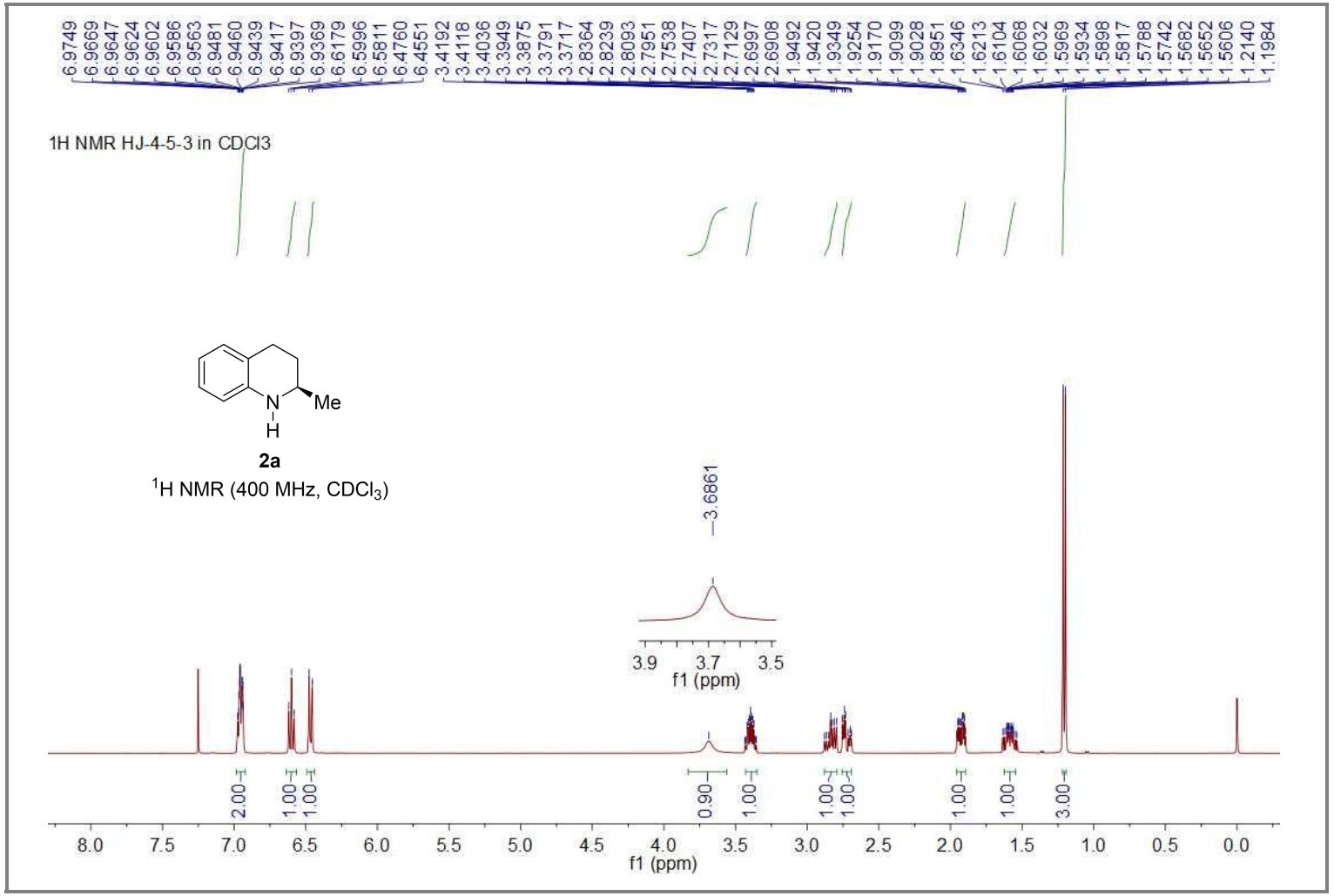
6.References

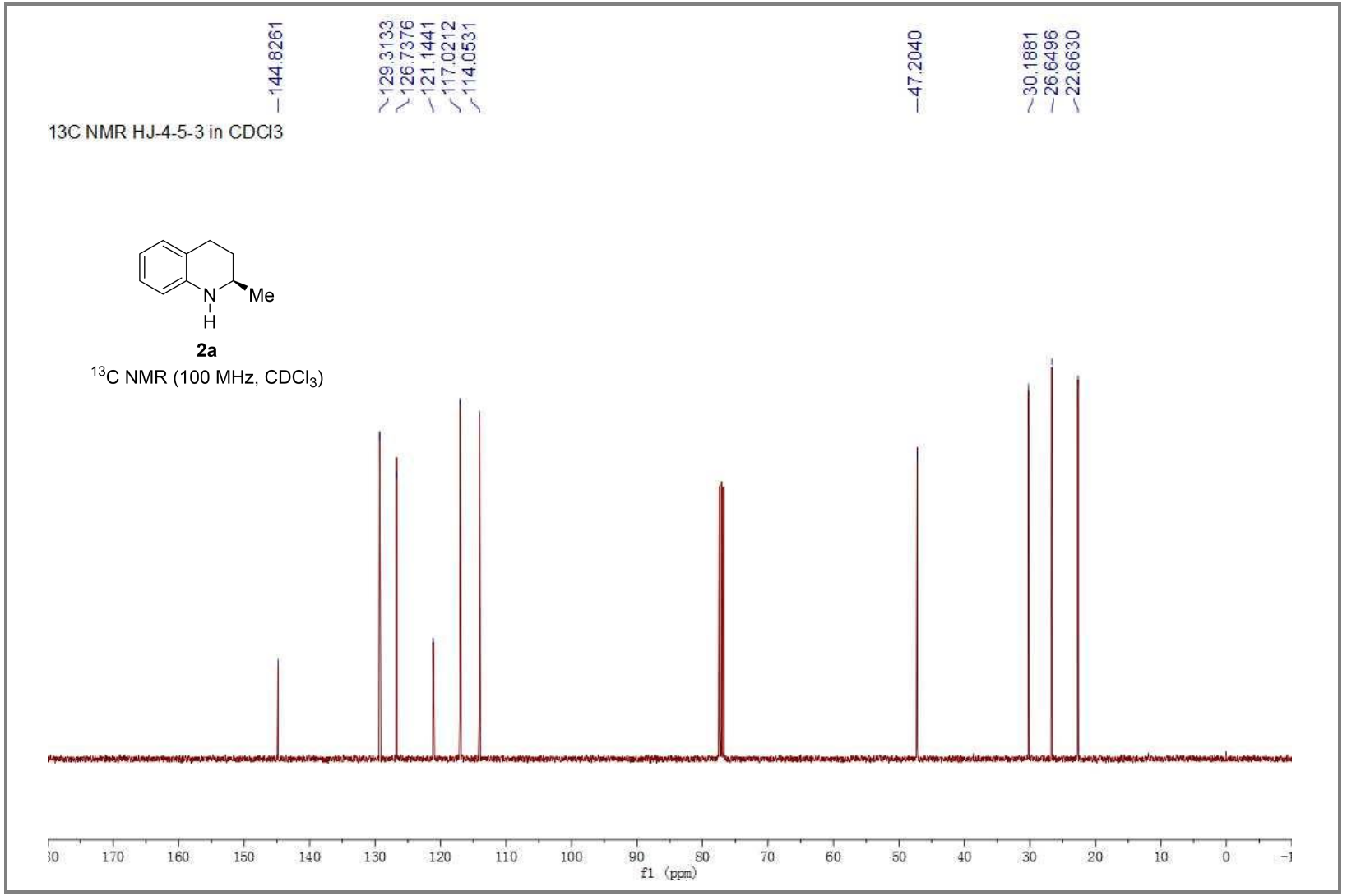
1.Zhang DY, Wang DS, Wang MC, Yu CB, Gao K, Zhou YG. Synthesis of electronically deficient atropisomeric bisphosphine ligands and their application in asymmetric hydrogenation of quinolines. Synthesis. 2011;2011(17):2796-2802. [DOI:10.1055/s-0030-1260129]

2.Wang T, Zhuo LG, Li Z, Chen F, Ding Z, He Y, et al. Highly enantioselective hydrogenation of quinolines using phosphine-free chiral cationic ruthenium catalysts: Scope, mechanism, and origin of enantioselectivity. J Am Chem Soc. 2011;133(25):9878-9891. [DOI:10.1021/ja2023042]

3.Wang WB, Lu SM, Yang PY, Han XW, Zhou YG. Highly enantioselective iridium-catalyzed hydrogenation of heteroaromatic compounds, quinolines. J Am Chem Soc. 2003;125(35):10536-10537. [DOI:10.1021/ja0353762]

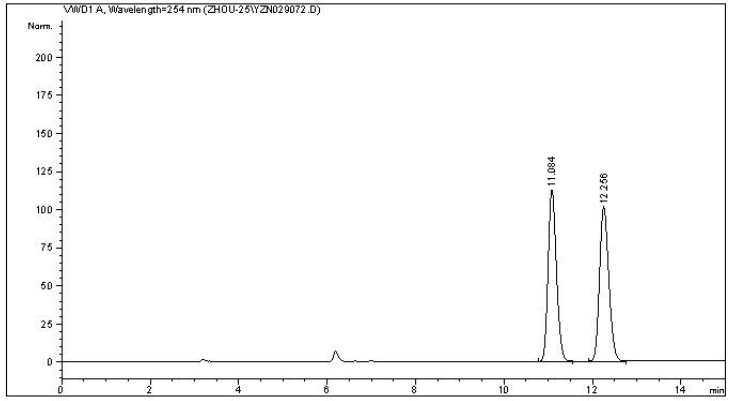
7. Copy of NMR and HPLC Data



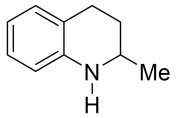

144.8261
129.3133
126.7376
121.1441
117.0212
114.0531
47.2040
30.1881
26.6496
22.6630
13C NMR HJ-4-5-3 in CDCl3
N
H
Me
2a
13C NMR (100 MHz, CDCl3)
f1 (ppm)

Data File C:\CHEM32\1\DATA\ZHOU-25\YZN029072.D
Sample Name: HJ-4-5 (+-)

```
Acq. Operator   :
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 5/29/2025 4:16:16 AM
Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
Last changed    : 5/29/2025 4:08:15 AM
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF_LC.M
Last changed    : 5/29/2025 4:38:09 AM
                  (modified after loading)
Sample Info     : OJ-H, n-Hexane/i-PrOH = 95/5, 1.0 mL/min, 30 oC, 254 nm
                  .
```



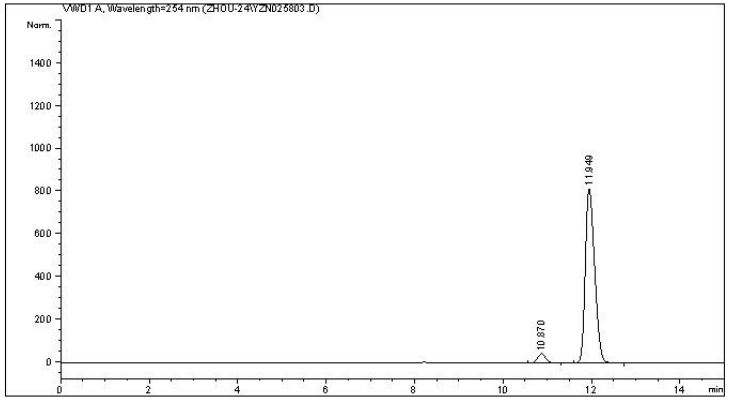

```
Area Percent Report

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|------|----|------|---------|---------|-------|
   1  11.084 BB    0.2036 1468.45581  112.20956  50.0216
   2  12.256 BB    0.2244 1467.18738  101.25979  49.9784

Totals :                 2935.64319  213.46935

*** End of Report ***
```



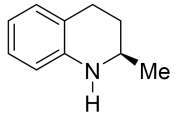
(+/-)-**2a**

Data File C:\CHEM32\1\DATA\ZHOU-24\YZN025803.D
Sample Name: HJ-4-5

```
Acq. Operator   :
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 5/9/2024 3:09:56 AM
Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
Last changed    : 5/9/2024 3:06:40 AM
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF_LC.M
Last changed    : 5/29/2025 3:37:07 AM
                  (modified after loading)
Sample Info     : OJ-H, Hexane/iPrOH = 95/5, 1.0 mL/ min, 30 oC, 254 nm.
```



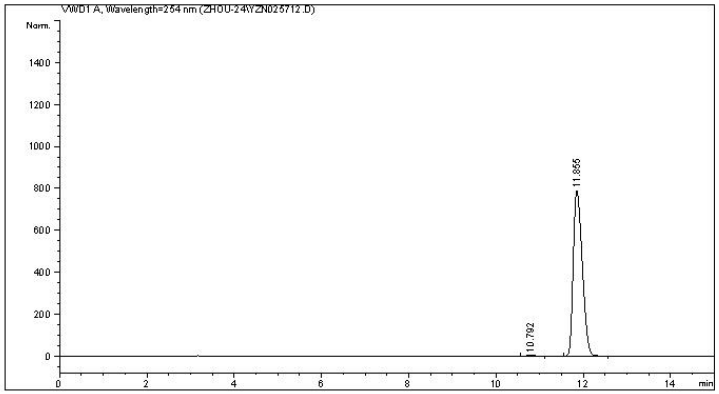

```
Area Percent Report

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Sample Amount:                :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|------|----|------|---------|---------|-------|
   1  10.870 BB    0.1906  535.39185   43.36814   4.2987
   2  11.949 BB    0.2284 1.19192e4   817.21271  95.7013

Totals :                 1.24546e4   860.58085

*** End of Report ***
```



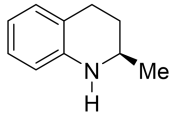
2a

Data File C:\CHEM32\1\DATA\ZHOU-24\YZN025712.D
Sample Name: HJ-3-91

```
Acq. Operator   :
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 4/23/2024 10:52:49 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
Last changed    : 4/23/2024 10:50:06 PM
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF_LC.M
Last changed    : 5/29/2025 3:46:41 AM
                  (modified after loading)
Sample Info     : OJ-H, Hexane/iPrOH = 95/5, 1.0 mL/min, 30 oC, 254 nm
```



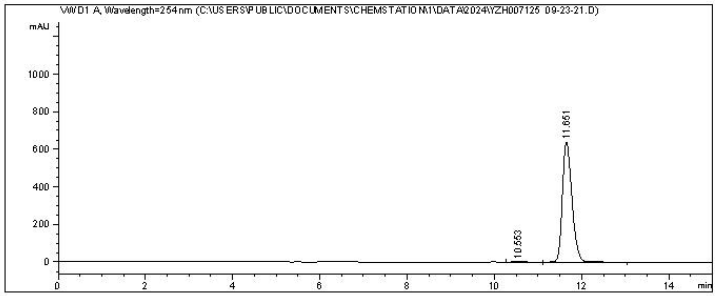

```
                          Area Percent Report

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Sample Amount:               :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|---------|---------|--------|
   1  10.792 BB    0.1910   31.56655    2.57659   0.2786
   2  11.855 BB    0.2271 1.12980e4   787.23285  99.7214

Totals :                  1.13296e4   789.80944

                        *** End of Report ***
```



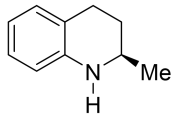
(Recrystalization)

Data File C:\USERS\PUBLIC\DOCUMENTS\CHEMSTATION\1\DATA\2024\YZH007125 09-23-21.D
Sample Name: HJ-4-22

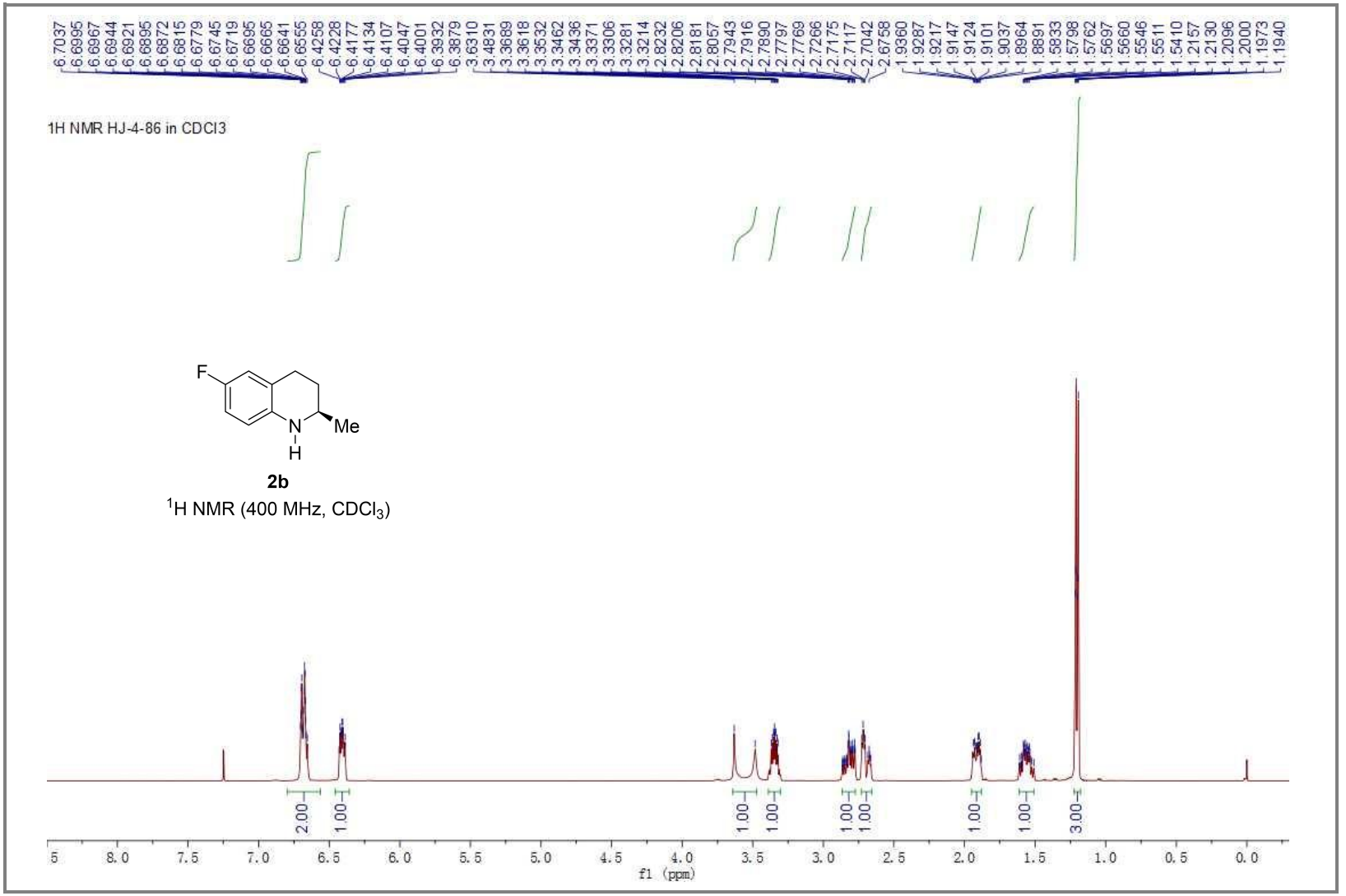
```
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : HPLC1260 II                     Location :   1
Injection Date  : 5/30/2024 9:23:21 AM                 Inj :   1
                                                  Inj Volume : No inj
Acq. Method     : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed    : 5/30/2024 8:50:25 AM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed    : 5/28/2025 4:24:57 PM by SYSTEM
                  (modified after loading)
Sample Info     : OJ-H,  n-Hexane/i-PrOH = 95/5, 1.0 mL/min, 30 oC, 254 nm
```

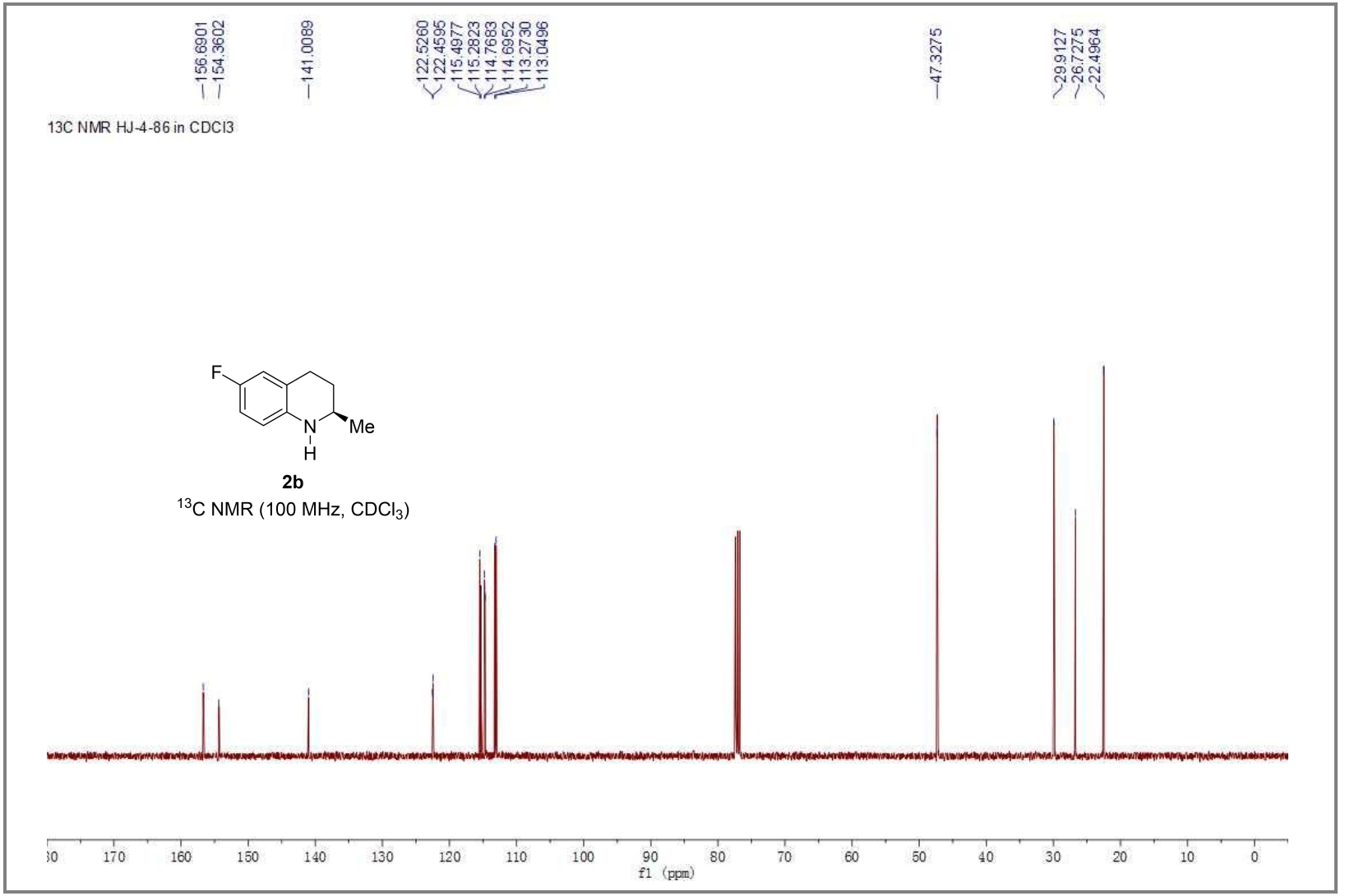


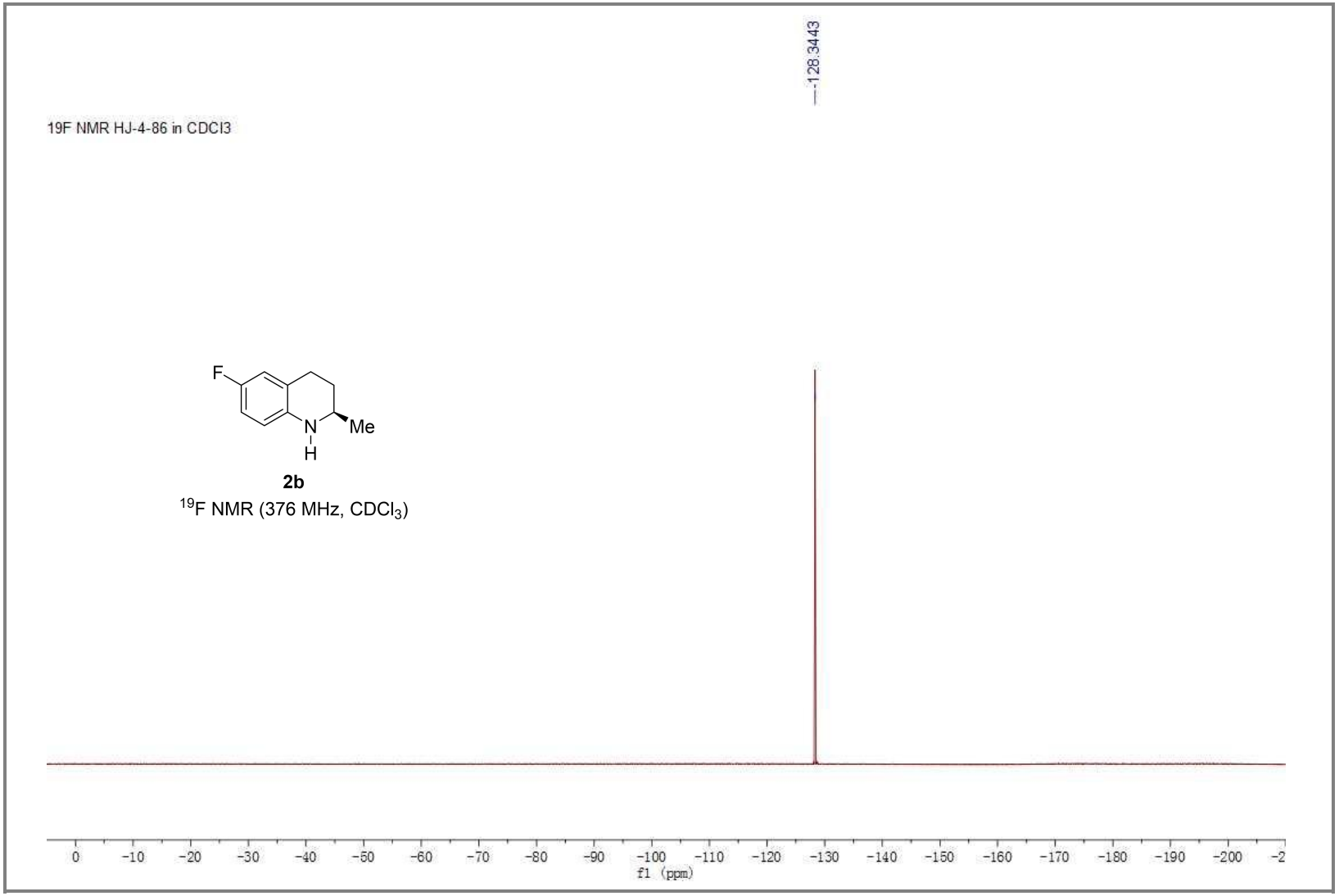

```
                          Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:        :      1.00000  [ng/ul]   (not used in calc.)
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.553 BB    0.1643   33.10708    3.13275   0.3408
   2  11.651 BB    0.2322 9682.25781  640.93048  99.6592

Totals :                  9715.36489  644.06323

                        *** End of Report ***
```



(Resolution)


1H NMR HJ-4-86 in CDCl3
F
N
H
Me
2b
1H NMR (400 MHz, CDCl3)
f1 (ppm)


156.6901
154.3602
141.0089
122.5260
122.4595
115.4977
115.2823
114.7683
114.6952
113.2730
113.0496
47.3275
29.9127
26.7275
22.4964
13C NMR HJ-4-86 in CDCl3
F
N
H
Me
2b
13C NMR (100 MHz, CDCl3)
f1 (ppm)

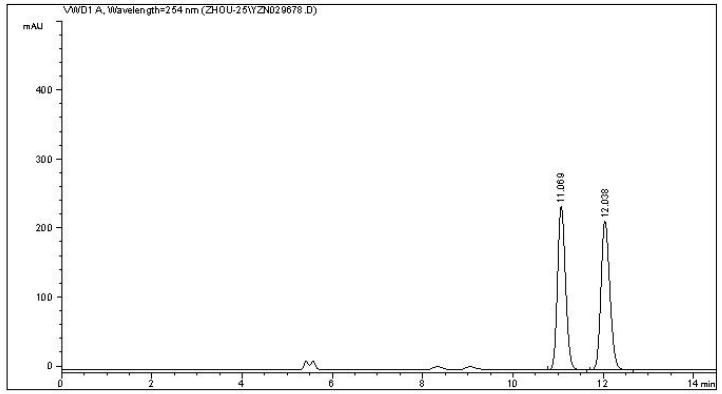


2b

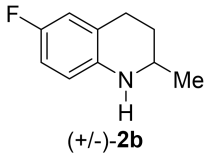
^{19}F NMR (376 MHz, $CDCl_3$)

Data File C:\CHEM32\1\DATA\ZHOU-25\YZN029678.D
Sample Name: HJ-4-86(+/-)

```
Acq. Operator   :
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 7/17/2025 11:31:03 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF_LC.M
Last changed    : 7/17/2025 11:27:47 PM
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF_LC.M
Last changed    : 7/18/2025 1:46:36 AM
                  (modified after loading)
Sample Info     : OJ-H, n-Hexane/i-PrOH = 98.5/1.5, 1.0 mL/min, 30 oC, 25
                  4 nm.
```



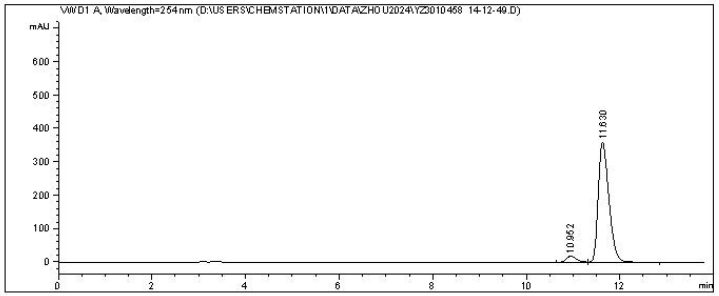

```
                          Area Percent Report

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.069 BB    0.1919 2922.28442  237.03415  49.9396
   2  12.038 BB    0.2127 2929.35352  215.24231  50.0604

Totals :                  5851.63794  452.27646


                          *** End of Report ***
```



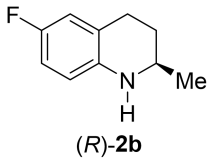
(+/-)-**2b**

Data File D:\USERS\CHEMSTATION\1\DATA\ZHOU2024\YZ3010458 14-12-49.D
Sample Name: HJ-4-86

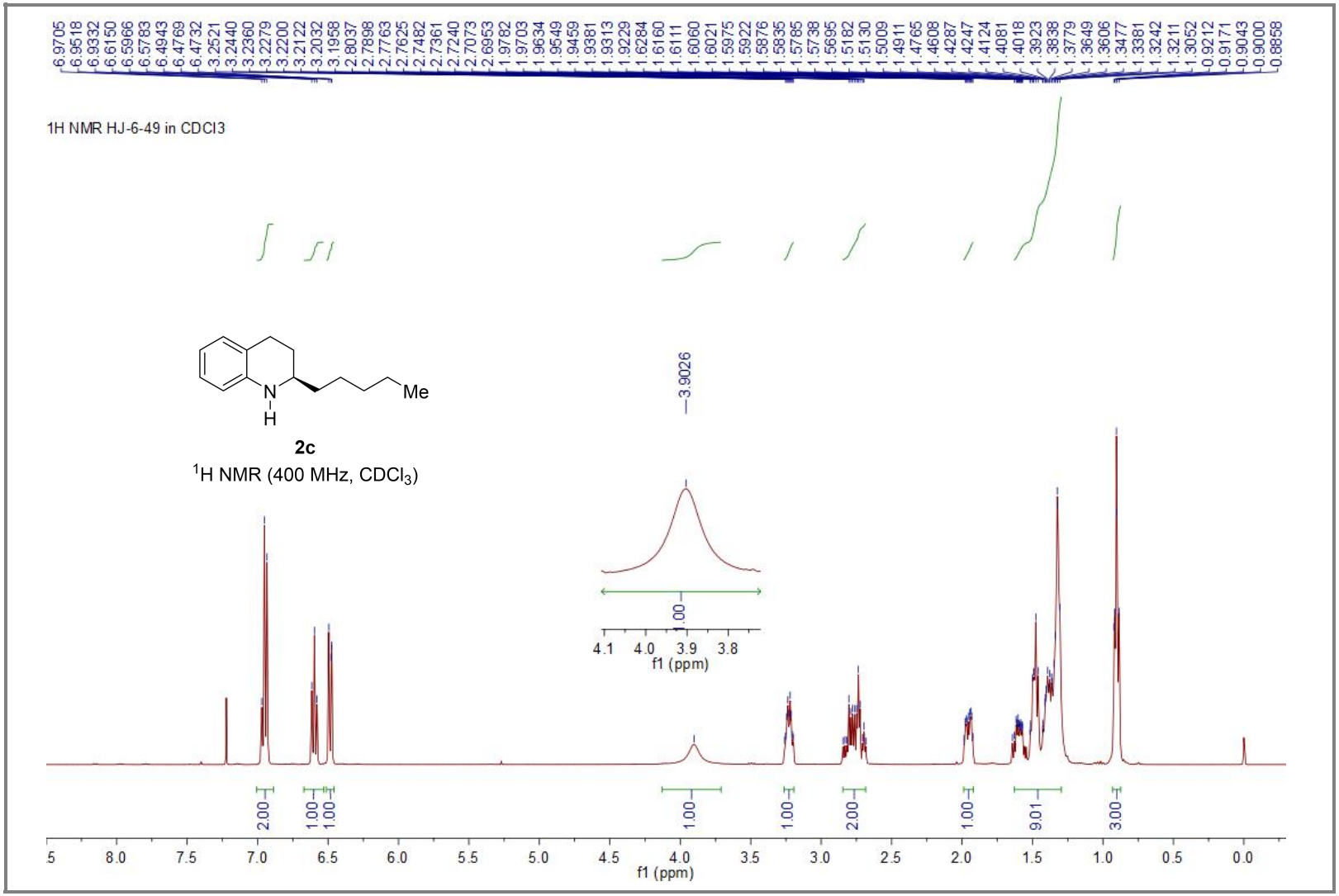
```
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : 1260II                      Location :     -
Injection Date  : 10/24/2024 2:12:49 PM            Inj :   1
                                              Inj Volume : No inj
Acq. Method     : C:\Users\Public\Documents\ChemStation\1\Methods\def_LC.M
Last changed    : 10/24/2024 1:58:47 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\def_LC.M
Last changed    : 7/30/2025 4:25:02 PM by SYSTEM
                  (modified after loading)
Sample Info     : OJ-H, n-Hexane/i-PrOH = 98.5/1.5, 1.0 mL/min, 30 oC, 254 nm
```

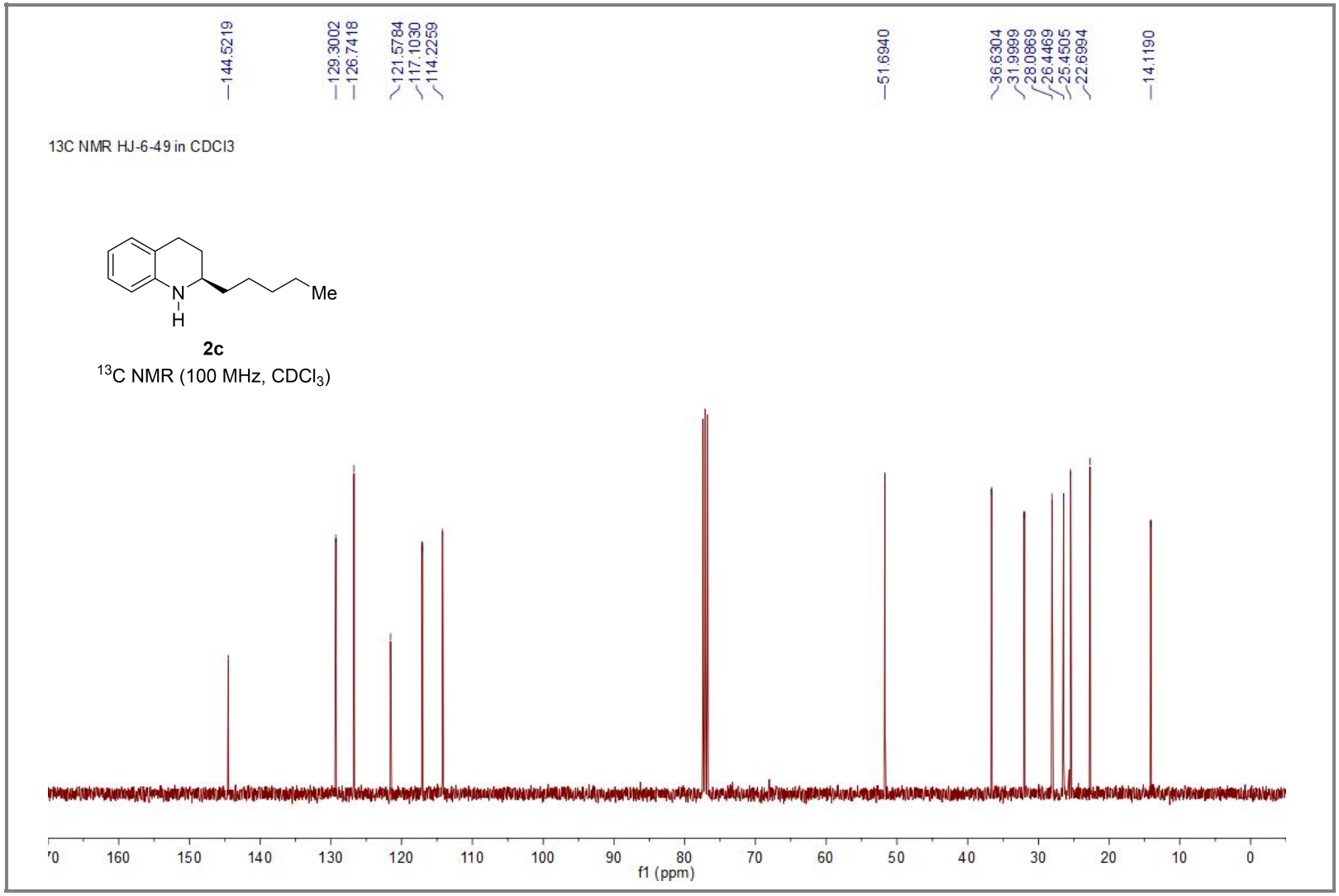



```
                          Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.952 BV    0.2220  255.19766   17.83031   4.3271
   2  11.630 VB    0.2425 5642.44971  358.66989  95.6729

Totals :                  5897.64737  376.50021


                          *** End of Report ***
```



(*R*)-**2b**

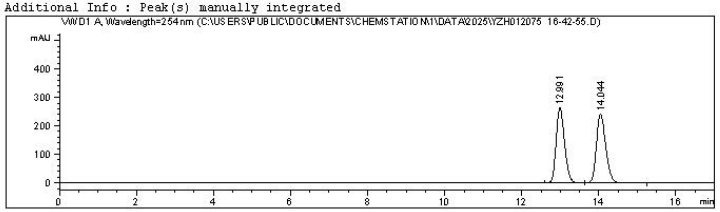

1H NMR HJ-6-49 in CDCl3
Me
2c
1H NMR (400 MHz, CDCl3)
3.9026
1.00
4.1 4.0 3.9 3.8
f1 (ppm)
2.00
1.00
1.00
1.00
1.00
2.00
1.00
9.01
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


144.5219
129.3002
126.7418
121.5784
117.1030
114.2259
51.6940
36.6304
31.9999
28.0869
26.4469
25.4505
22.6994
14.1190
13C NMR HJ-6-49 in CDCl3
N
H
Me
2c
13C NMR (100 MHz, CDCl3)
f1 (ppm)

Data File C:\USERS\PUBLIC\DOCUMENTS\CHEMSTATION\1\DATA\2025\YZH012075 16-42-55.D
Sample Name: HJ-6-49-(+/-)

Acq. Operator : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : HPLC1260 II Location : 1
Injection Date : 11/30/2025 4:42:55 PM Inj : 1
Inj Volume : No inj
Acq. Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed : 11/30/2025 3:12:00 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed : 11/30/2025 5:11:52 PM by SYSTEM
(modified after loading)
Sample Info : OJ-H, n-Hexane/i-PrOH = 95/5, 0.5 mL/min, 30 oC, 254 nm.

Additional Info : Peak(s) manually integrated

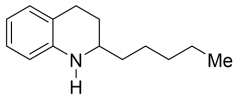


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount: : 1.00000 [ng/ul] (not used in calc.)
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.991	BB	0.2368	3992.90698	263.47165	49.8067
2	14.044	BB	0.2619	4023.89502	242.07472	50.1933
Totals :				8016.80200	505.54637	



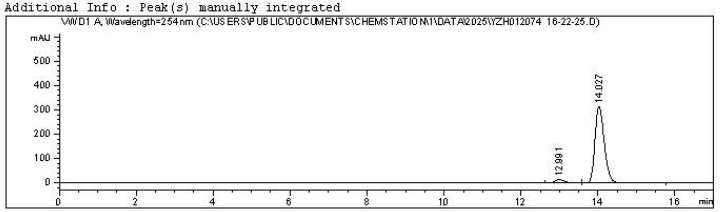
(+/-)-**2c**

*** End of Report ***

Data File C:\USERS\PUBLIC\DOCUMENTS\CHEMSTATION\1\DATA\2025\YZH012074 16-22-25.D
Sample Name: HJ-6-49

Acq. Operator : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : HPLC1260 II Location : 1
Injection Date : 11/30/2025 4:22:25 PM Inj : 1
Inj Volume : No inj
Acq. Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed : 11/30/2025 3:12:00 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed : 11/30/2025 4:46:36 PM by SYSTEM
(modified after loading)
Sample Info : OJ-H, n-Hexane/i-PrOH = 95/5, 0.5 mL/min, 30 oC, 254 nm.

Additional Info : Peak(s) manually integrated

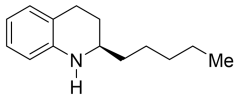


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount: : 1.00000 [ng/ul] (not used in calc.)
Do not use Multiplier & Dilution Factor with ISTDs

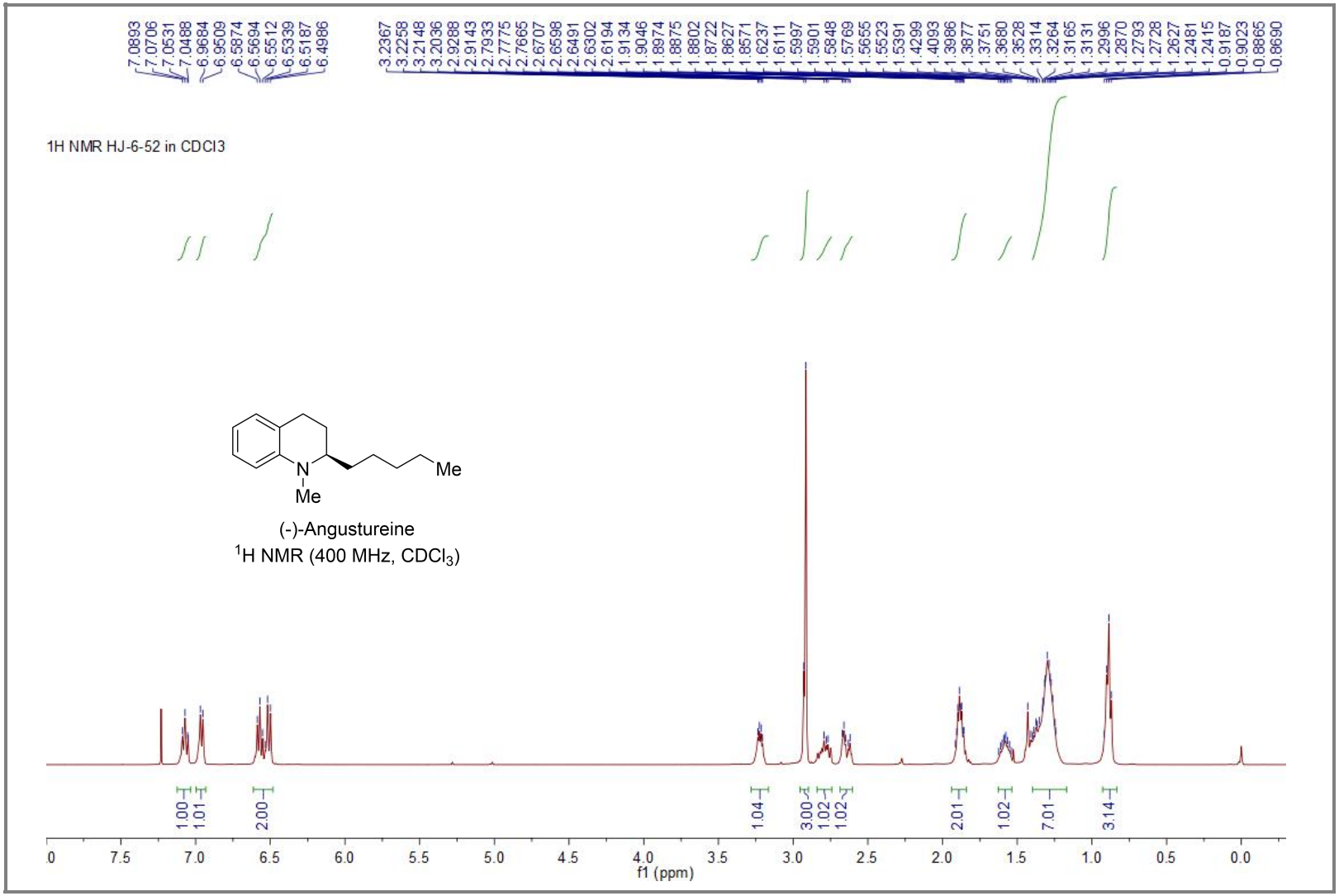
Signal 1: VWD1 A, Wavelength=254 nm

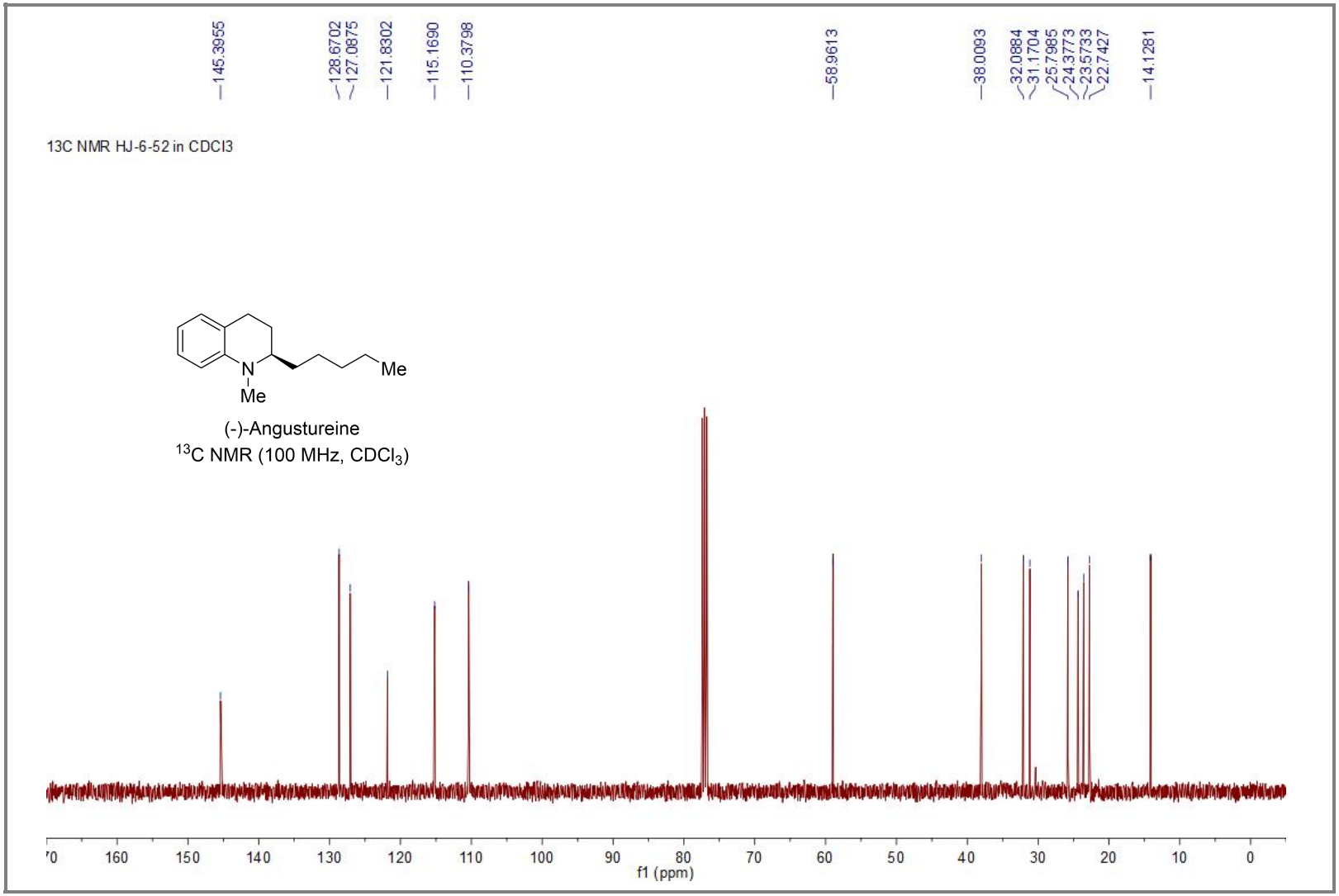
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.991	VB	0.2322	199.97949	13.39006	3.7090
2	14.027	BV	0.2570	5191.69434	313.75299	96.2910
Totals :				5391.67383	327.14305	



(*R*)-**2c**

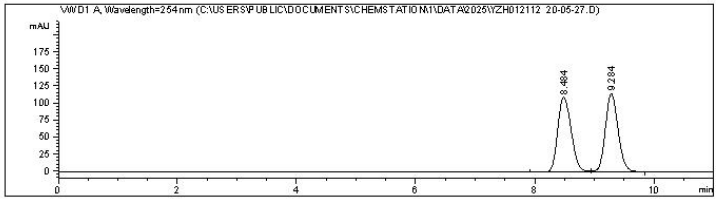
*** End of Report ***


1H NMR HJ-6-52 in CDCl3
Me
N
Me
(-)-Angustureine
1H NMR (400 MHz, CDCl3)
f1 (ppm)


145.3955
128.6702
127.0875
121.8302
115.1690
110.3798
58.9613
38.0093
32.0884
31.1704
25.7985
24.3773
23.5733
22.7427
14.1281
13C NMR HJ-6-52 in CDCl3
N
Me
Me
(-)-Angustureine
13C NMR (100 MHz, CDCl3)
f1 (ppm)

Data File C:\USERS\PUBLIC\DOCUMENTS\CHEMSTATION\1\DATA\2025\YZH012112 20-05-27.D
Sample Name: HJ-6-52(+/-)

Acq. Operator : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : HPLC1260 II Location : 1
Injection Date : 12/2/2025 8:05:27 PM Inj : 1
Inj Volume : No inj
Acq. Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed : 12/2/2025 8:02:21 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed : 12/2/2025 8:33:32 PM by SYSTEM
(modified after loading)
Sample Info : OJ-H, n-Hexane/i-PrOH = 95/5, 0.5 mL/min, 30 oC, 254 nm.

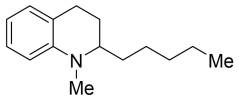


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount: : 1.00000 [ng/ul] (not used in calc.)
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.484	BV	0.2488	1723.68726	109.98250	49.9971
2	9.284	VB	0.2323	1723.88562	115.41101	50.0029
Totals :				3447.57288	225.39351	

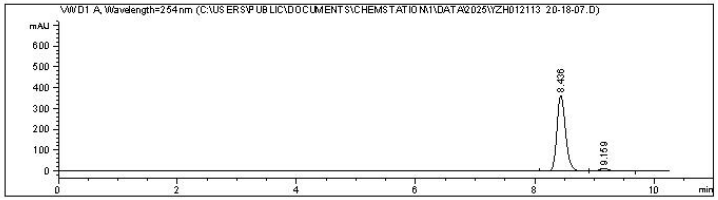


(+/-)-Angustureine

*** End of Report ***

Data File C:\USERS\PUBLIC\DOCUMENTS\CHEMSTATION\1\DATA\2025\YZH012113 20-18-07.D
Sample Name: HJ-6-52

Acq. Operator : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : HPLC1260 II Location : 1
Injection Date : 12/2/2025 8:18:07 PM Inj : 1
Inj Volume : No inj
Acq. Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed : 12/2/2025 8:02:21 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\DEF_LC.M
Last changed : 12/3/2025 3:43:11 PM by SYSTEM
(modified after loading)
Sample Info : OJ-H, n-Hexane/i-PrOH = 95/5, 0.5 mL/min, 30 oC, 254 nm.

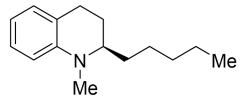


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount: : 1.00000 [ng/ul] (not used in calc.)
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.436	BV	0.1549	3685.02490	364.71320	95.7994
2	9.159	VB	0.1826	161.58066	13.30829	4.2006
Totals :				3846.60556	378.02148	



(-)-Angustureine

*** End of Report ***