Chiral Magnesium(II)-Catalyzed Asymmetric Ring-Opening of *meso*-Aziridines with Primary Alcohols.

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Supporting information

Contents:

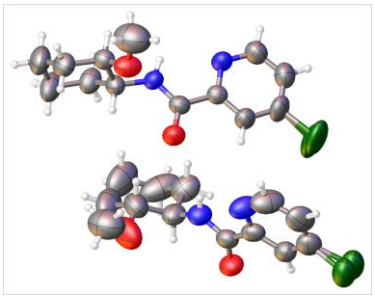
1. General remarks

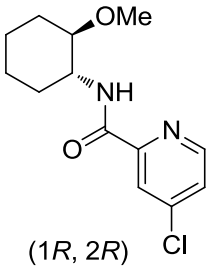
Commercial reagents were used as received with the following exceptions. CH_2Cl_2 was dried over powdered CaH_2 and distilled under nitrogen just before use. CH_3CCl_3, CH_2ClCH_2Cl, $CHCl_3$, $CHCl_2CHCl_2$, Et_2O, $PhCH_3$ and PhCl were directly distilled before use. Enantiomeric excesses (*ee*) were determined by HPLC analysis using the corresponding commercial chiral column as stated in the experimental procedures at 23 ℃ with UV detector at 254 nm. Optical rotations were reported as follows: $[\alpha]^{20}_{D}$ (c g/100 mL, in solvent). ^{1}H NMR spectra were recorded on commercial instruments (400 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26). Spectra were reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration and assignment. ^{13}C NMR spectra were collected on commercial instruments (100 MHz) with complete proton decoupling. Chemical shifts are

reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0). HRMS was recorded on a commercial apparatus (ESI Source).

2. Determination of the absolute configuration of 3b by X-ray crystallography

The absolute configuration of the optically active product **3b** was determined by X-ray chromatography analysis.





Single crystal of **3b** [$C_{14}H_{18}ClNO_2$] was obtained by recrystallization in petroleum ether/CH_2Cl_2. The absolute configuration of **3b** is (1*R*, 2*R*). CCDC 991793 contains the supplementary crystallographic data which can be obtained free of charge from The Cambrige Crystallographic Data Centere via www.ccdc.cam.ac.uk/data_request/cif.

3. General procedures for chiral *N,N'*-dioxide preparation

The *N,N'*-dioxide ligands **L1**–**L8** were synthesized by the same procedure in the literature[1].

4. Preparation of the racemic 3a–3v

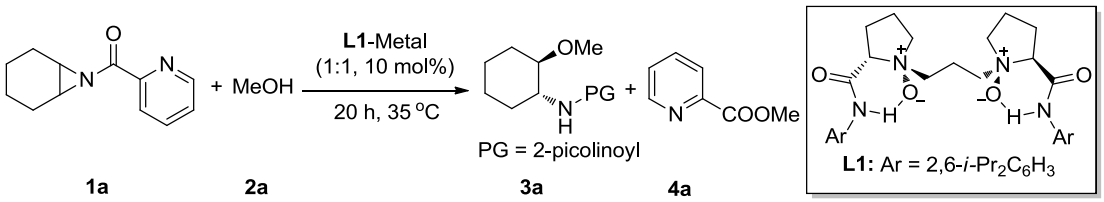
A reaction tube was charged with aziridine **1** (0.1 mmol), alcohol (0.2 mL). Then, CH_2Cl_2 (0.2 mL) and $BF_3 \cdot Et_2O$ (10 mol %) was added. After stirring at 35 ℃ for 4 h, the pure racemic product **3** was obtained directly by silica gel chromatography (Eluent: petroleum ether/AcOEt 4:1 to pure AcOEt).

5. General procedures for the catalytic asymmetric reaction

General procedure for the catalytic asymmetric reaction: A dry reaction tube was charged with **L3**-$Mg(OTf)_2$ (1:1, 10–30 mol% catalyst loading) and **1** (0.1 mmol) under N_2 atmosphere. Then, *p*-xylene (0.5 or 0.4 or 0.2 mL) was added and the mixture was stirred at 35 ℃ for 20 minutes. Finally, alcohol (0.5 – 2.5 mmol) was added under stirring at the indicated temperature (35 ℃, 50 ℃). The reaction mixture was stirred at the indicated temperature for 1–5 days. The residue was purified by flash chromatography (Eluent: petroleum ether/AcOEt 4:1, pure AcOEt) on silica gel to afford the products. The enantiomeric excess (*ee*) was determined by high-performance liquid chromatography (HPLC) with Chiralcel OD-H, Chiralcel IC, Chiralcel IA, Chiralcel AS-H, Chiralcel Lux 5u Cellulose-2 or Chiralcel IE.

6. Extra optimization of the reaction conditions

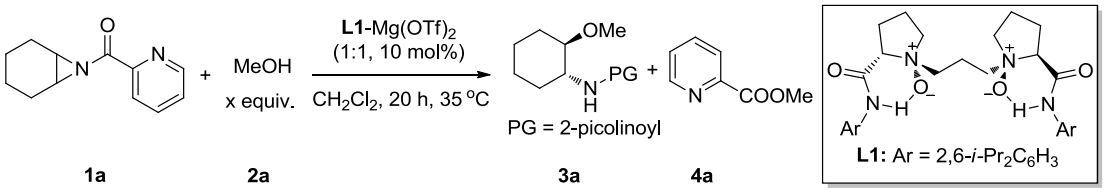
(1) Screen of other Lewis acids



Entry[a]	Metal	Yield[b] (%)	Ee[c] (%)
1	$Cu(OTf)_2$	30	21
2	$Mg(OTf)_2$	24	45
3	$Sn(OTf)_2$	90	0
4	$Ni(ClO_4)_2$ $6H_2O$	25	7
5	$Gd(OTf)_3$	27	5
6	$Zn(NTf_2)_2$	<5	10
7	$Ni(OTf)_2$	60	11
8	$Mg(ClO_4)_2$	34	35
9	$Ca(OTf)_2$	27	35
10	$Ba(OTf)_2$	9	0

[a] Unless otherwise noted, all reactions were performed with **L1**–Metal (1:1, 10 mol%), **1a** (0.1 mmol, PG = 2-picolinoyl), in MeOH (0.2 mL) under N_2 at 35 ℃ for 20 h. [b] Isolated yield of **3a**, **1a** was completely consumed. [c] Determined by HPLC analysis (Chiralcel OD-H).

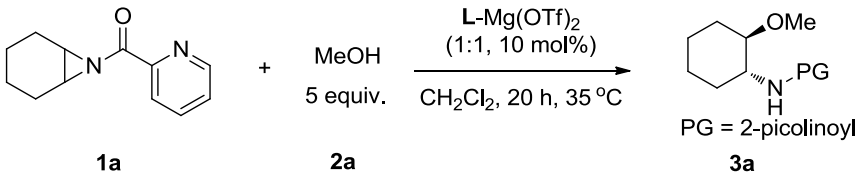
(2) Surry the amount of methanol

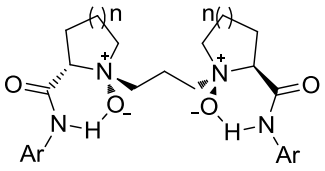


Entry[a]	x equiv.	Yield[b] (%)	Ee[c] (%)
1	1.0	6	68
2	2.0	38	68
3	3.0	63	68
4	4.0	76	68
5[d]	5.0	78	68

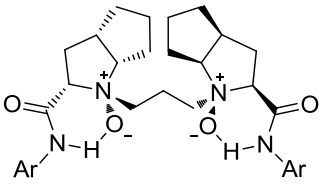
[a] Unless otherwise noted, all reactions were performed with **L1**–$Mg(OTf)_2$ (1:1, 10 mol%),**1a** (0.1 mmol), MeOH (x equiv.) in CH_2Cl_2 (0.2 mL) under N_2 at 35 ℃ for 20 h. [b] Isolated yield. [c] Determined by HPLC analysis (Chiralcel OD-H). [d] **1a** was completely consumed.

(3) Screen of *N,N'*-dioxide ligands





L1: Ar = 2,6-*i*-$Pr_2C_6H_3$, n = 1
L2: Ar = 2,6-*i*-$Pr_2C_6H_3$, n = 2
L4: Ar = 2,6-$Et_2C_6H_3$, n = 2
L5: Ar = 2,6-$Me_2C_6H_3$, n = 2
L6: Ar = Ph, n = 2
L7: Ar = 2,4,6-*i*-$Pr_3C_6H_2$, n = 2

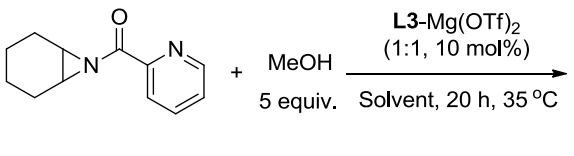


L3: Ar = 2,6-*i*-$Pr_2C_6H_3$
L8: Ar = 2,4,6-*i*-$Pr_3C_6H_2$

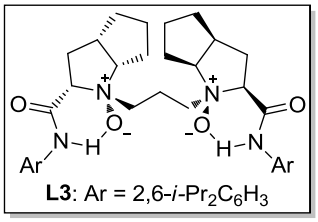
Entry[a]	Ligand	Yield[b] (%)	Ee[c] (%)
1	**L1**	78	68
2	**L2**	64	56
3	**L3**	88	78
4	**L4**	44	35
5	**L5**	28	23
6	**L6**	21	–10
7	**L7**	65	28
8	**L8**	56	56

[a] Unless otherwise noted, all reactions were performed with **L**–$Mg(OTf)_2$ (1:1, 10 mol%), **1a** (0.1 mmol), MeOH (0.5 mmol) in CH_2Cl_2 (0.2 mL) under N_2 at 35 ℃ for 20 h. [b] Isolated yield. [c] Determined by HPLC analysis (Chiralcel OD-H).

(4) Screen of solvent effects

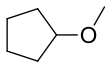


1a **2a** **3a**



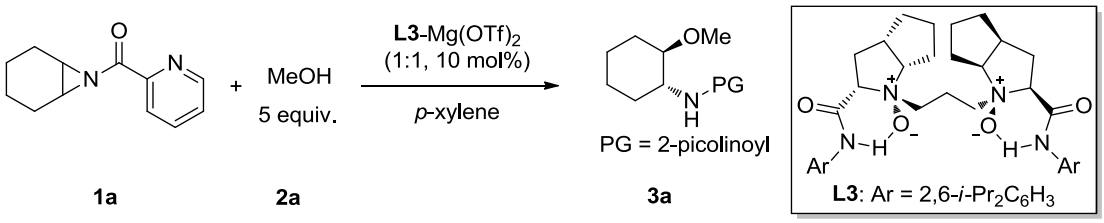
L3: Ar = 2,6-*i*-$Pr_2C_6H_3$

Entry[a]	Solvent	Yield[b] (%)	Ee[c] (%)
1	CH_2Cl_2	88	78
2	Cl_3CCH_3	82	72
3	CH_2ClCH_2Cl	83	79
4	$CHCl_3$	66	76
5	PhCl	99	77
6	$CHCl_2CHCl_2$	75	69
7	$CHCl_2CHCl$	90	77
8	EtOAc	91	73

9	THF	99	78
10	Et_2O	99	81
11	^{t}BuOMe	99	78
12	PhOMe	98	72
13	2-Me-THF	91	71
14	1,4-dioxane	20	72
15		93	80
16	Toluene	99	79
17	$PhCF_3$	99	78
18	PhF	96	70
19	mesitylene	99	77
20[d]	Et_2O	99	90
21[d]	benzene	78	81
22[d]	*o*-xylene	92	90
23[d]	*m*-xylene	89	92
24[d]	*p*-xylene	96	92
25[d,e]	*p*-xylene	88	94

[a] Unless otherwise noted, all reactions were performed with **L3**–$Mg(OTf)_2$ (1:1, 10 mol%), **1a** (0.1 mmol), MeOH (0.5 mmol) in solvent (0.2 mL) under N_2 at 35 ℃ for 20 h. [b] Isolated yield. [c] Determined by HPLC analysis (Chiralcel OD-H). [d] In solvent (0.5 mL) for 21 hours. [e] H_2O (0.1 mmol) was added.

(5) Screen of the reaction temperature



Entry[a]	Temperature (℃)	Time (h)	Yield[b] (%)	Ee[c] (%)
1	50	8.5	92	91
2	35	21	96	92
3	20	26	93	82

[a] Unless otherwise noted, all reactions were performed with **L3**–$Mg(OTf)_2$ (1:1, 10 mol%), **1a** (0.1 mmol), MeOH (0.5 mmol) in *p*-xylene (0.5 mL) under N_2 at the indicated temperature for the indicated time. [b] Isolated yield. [c] Determined by HPLC analysis (Chiralcel OD-H).

(6) Screen of the protecting groups

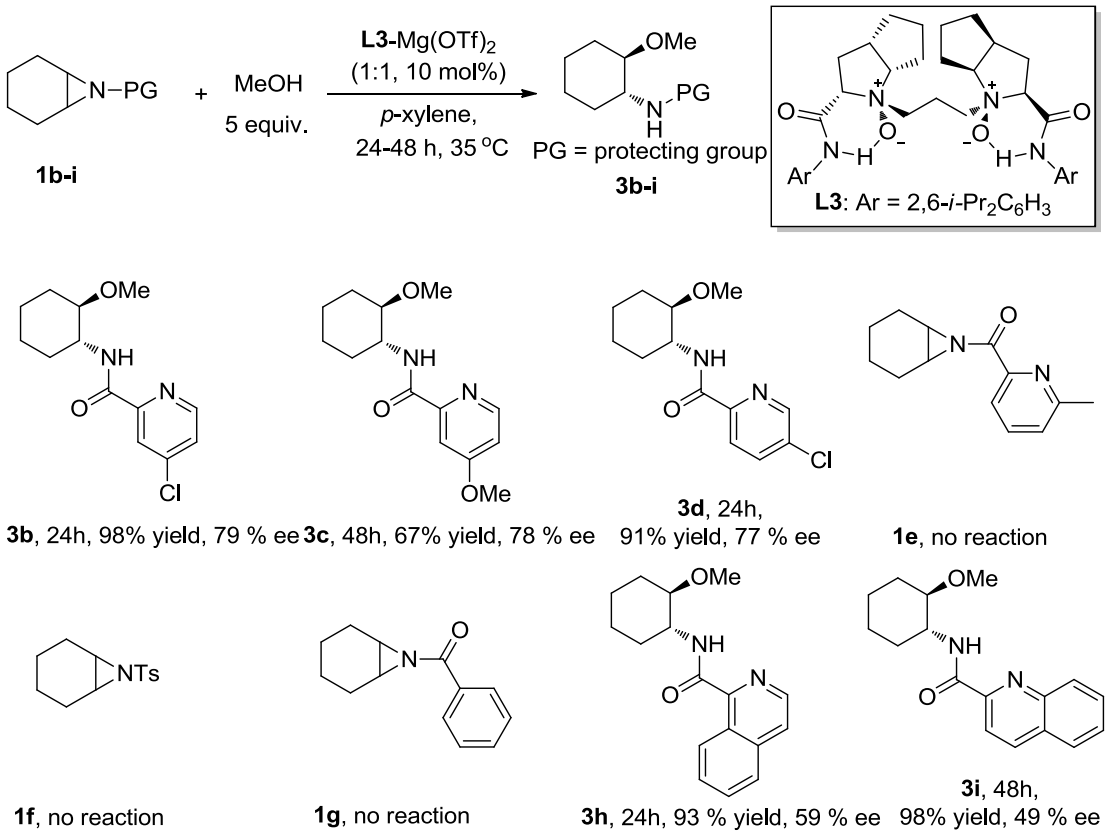


Fig. 1 Unless otherwise noted, all reactions were performed with **L3**–$Mg(OTf)_2$ (1:1, 10 mol%), **1** (0.1 mmol), MeOH (0.5 mmol) in *p*-xylene (0.5 mL) under N_2 at 35 ℃ for the indicated time.

(7) Substrate scope of the other unsuccessful alcohols [a]

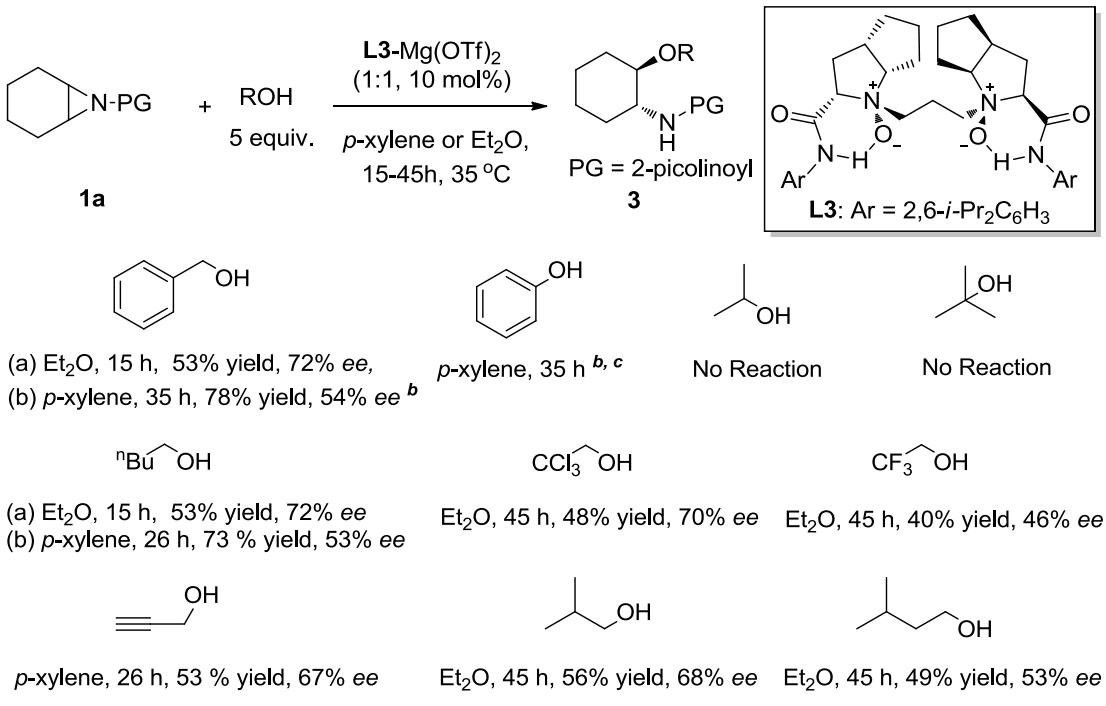
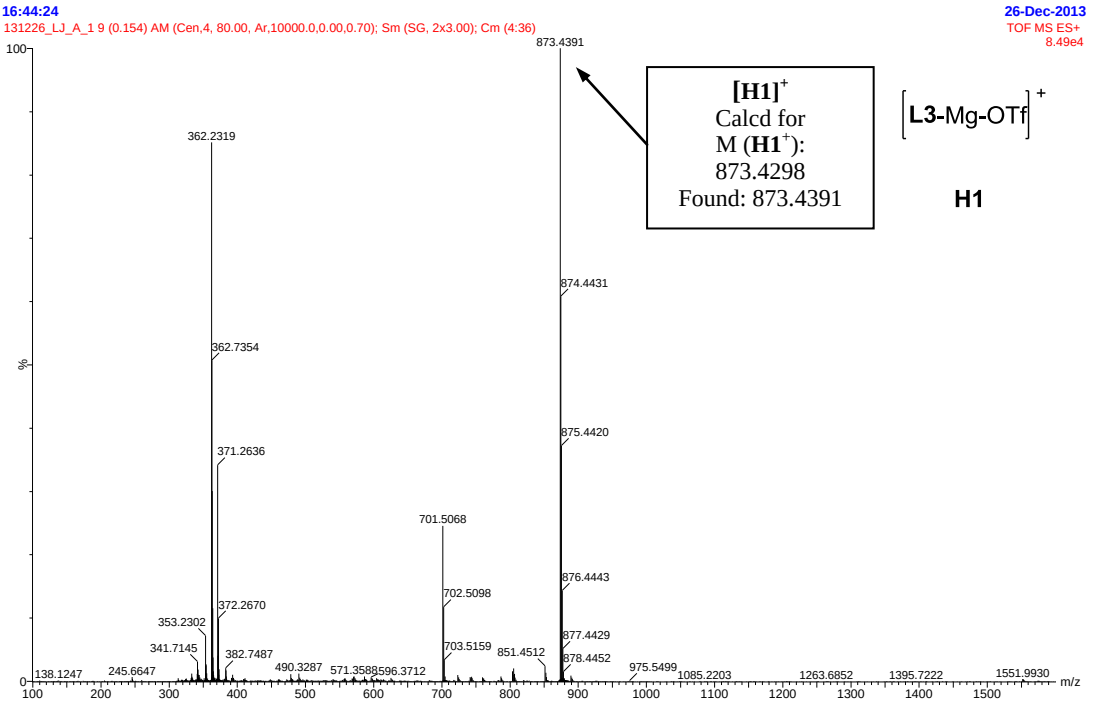


Fig. 2 [a] Unless otherwise noted, all reactions were performed with **L3**–$Mg(OTf)_2$ (1:1, 10 mol%), **1a** (0.1 mmol),

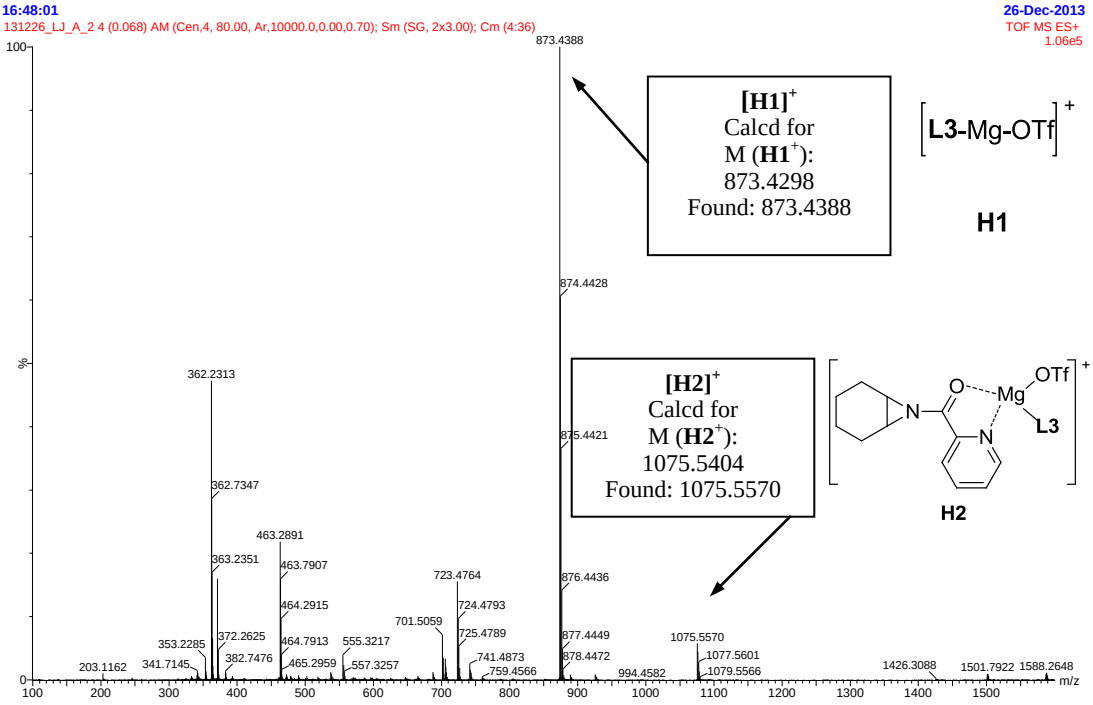
alcohol (0.5 mmol) in *p*-xylene or Et_2O (0.5 mL) under N_2 at 35 ℃ for the indicated time. [b] At 50 ℃. [c] No amino ether product was obtained but phenyl picolinate (14% yield) was obtained.

7. HRMS analysis

a) The mixture of **L3** and $Mg(OTf)_2$ (1:1)

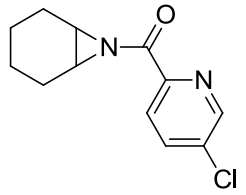


b) The mixture of **L3**, $Mg(OTf)_2$ and **1a** (1:1:1)



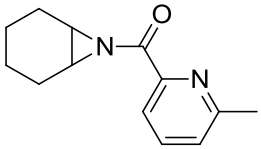
8. Characterization of the new substrates and products

7-azabicyclo[4.1.0]heptan-7-yl(5-chloropyridin-2-yl)methanone (1d)



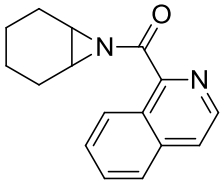
White solid, mp 75 – 76 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.64 (d, *J* = 2.3 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.79 (dd, *J* = 8.4, 2.4 Hz, 1H), 2.92 – 2.82 (m, 2H), 2.25 – 2.12 (m, 2H), 1.97 – 1.84 (m, 2H), 1.60 – 1.47 (m, 2H), 1.42 – 1.29 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 176.6, 149.1, 148.3, 136.4, 135.1, 124.8, 37.5, 23.7, 20.1.

7-azabicyclo[4.1.0]heptan-7-yl(6-methylpyridin-2-yl)methanone (1e)



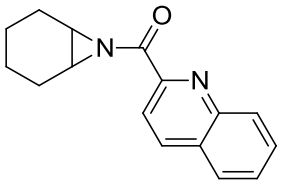
White solid, mp 43 – 44 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.89 (d, *J* = 7.7 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.1 Hz, 1H), 2.88 – 2.79 (m, 2H), 2.62 (s, 3H), 2.28 – 2.16 (m, 2H), 1.97 – 1.86 (m, 2H), 1.61 – 1.47 (m, 2H), 1.40 – 1.30 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 178.1, 158.2, 150.3, 136.9, 126.0, 121.1, 37.3, 24.6, 23.8, 20.1.

7-azabicyclo[4.1.0]heptan-7-yl(isoquinolin-1-yl)methanone (1h)



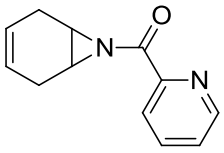
White solid, mp 59 – 60 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.82 (d, *J* = 8.6 Hz, 1H), 8.58 (d, *J* = 5.6 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 5.6 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.68 – 7.63 (m, 1H), 3.05 – 2.95 (m, 2H), 2.11 – 2.00 (m, 2H), 1.92 – 1.80 (m, 2H), 1.61 – 1.49 (m, 2H), 1.38 – 1.25 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 178.5, 152.6, 141.6, 136.8, 130.4, 128.3, 127.0, 126.9, 126.3, 123.1, 37.4, 23.7, 20.0.

7-azabicyclo[4.1.0]heptan-7-yl(quinolin-2-yl)methanone (1i)



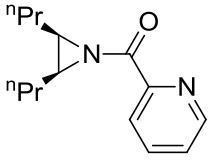
White solid, mp 74 – 75 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 8.5 Hz, 1H), 8.19 (t, *J* = 7.9 Hz, 2H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.81 – 7.73 (m, 1H), 7.66 – 7.60 (m, 1H), 3.02 – 2.86 (m, 2H), 2.42 – 2.29 (m, 2H), 2.04 – 1.91 (m, 2H), 1.67 – 1.54 (m, 2H), 1.46 – 1.33 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 177.8, 150.7, 147.4, 136.8, 130.8, 129.9, 129.2, 128.2, 127.6, 120.3, 37.5, 23.9, 20.2.

7-azabicyclo[4.1.0]hept-3-en-7-yl(pyridin-2-yl)methanone (1n)



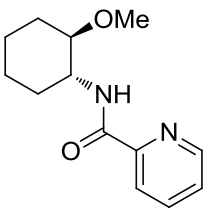
White solid, mp 60 – 61 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.3 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.42 (dd, *J* = 7.3, 4.9 Hz, 1H), 5.53 (s, 2H), 3.02 (s, 2H), 2.83 (d, *J* = 18.1 Hz, 2H), 2.48 (d, *J* = 18.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 177.1, 151.0, 149.2, 136.7, 126.3, 123.8, 122.4, 36.4, 24.0.

((*cis*)-2,3-dipropylaziridin-1-yl)(pyridin-2-yl)methanone (1s)



Colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.70 (d, *J* = 3.8 Hz, 1H), 8.08 (d, *J* = 7.7 Hz, 1H), 7.87 – 7.70 (m, 1H), 7.53 – 7.35 (m, 1H), 2.65 (s, 2H), 1.87 (s, 2H), 1.67 – 1.45 (m, 6H), 1.11 – 0.88 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 178.2, 151.0, 149.1, 136.7, 126.3, 123.9, 42.5, 29.8, 20.6, 14.0.

***N*-((1*R*,2*R*)-2-methoxycyclohexyl)picolinamide (3a)**

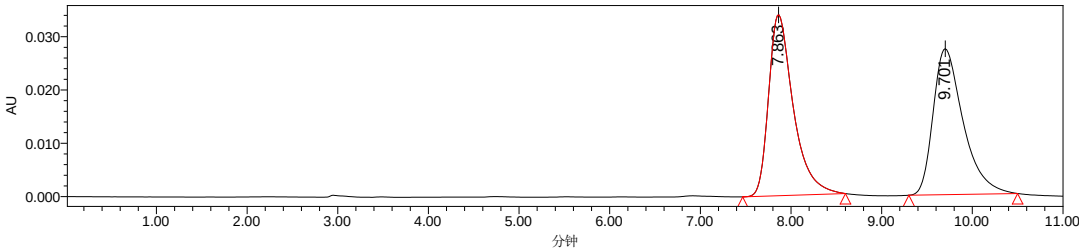


21h, yield 22.5 mg, 96%; white solid, mp 94 – 95 ℃; HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 7.68 min, t_r (minor) = 9.58 min, *ee* = 92%. $[\alpha]^{20}_D$ = −35.6 (*c* =0.45, in CH_2Cl_2).

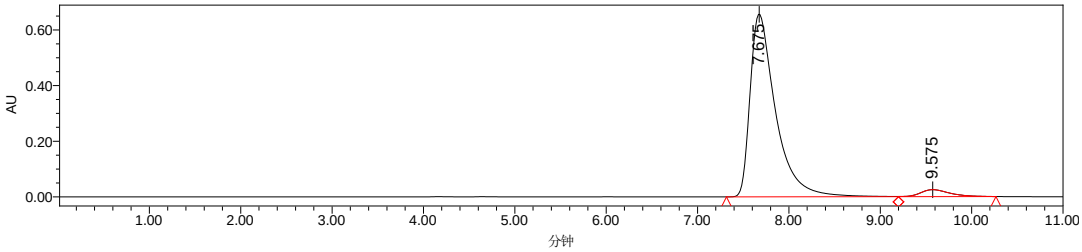
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 3.4 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 4.3 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.49 – 7.35 (m, 1H), 4.06 – 3.92 (m, 1H), 3.38 (d, *J* = 0.7 Hz, 3H), 3.29 – 3.16 (m, 1H), 2.20 (d, *J* = 11.5 Hz, 1H), 2.11 (d, *J* = 9.7 Hz, 1H), 1.84 – 1.74 (m, 1H), 1.72 – 1.65 (m, 1H), 1.47 – 1.28 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 150.2, 148.0, 137.3, 126.0, 122.2, 81.1, 56.1, 52.1, 30.9, 29.2, 23.9, 23.5.

HRMS (ESI-TOF) calcd for $C_{13}H_{18}N_2NaO_2^+$ ([M]+Na^+) = 257.1266, Found 257.1260.

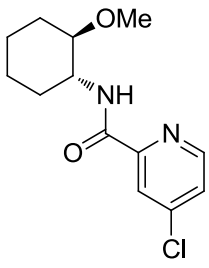


Peak	Retention Time	Area	% Area	Height
1	7.863	641629	50.53	33970
2	9.701	628206	49.47	27375



Peak	Retention Time	Area	% Area	Height
1	7.675	12714712	95.81	658450
2	9.575	556091	4.19	25119

4-chloro-*N*-((1*R*,2*R*)-2-methoxycyclohexyl)picolinamide (3b)

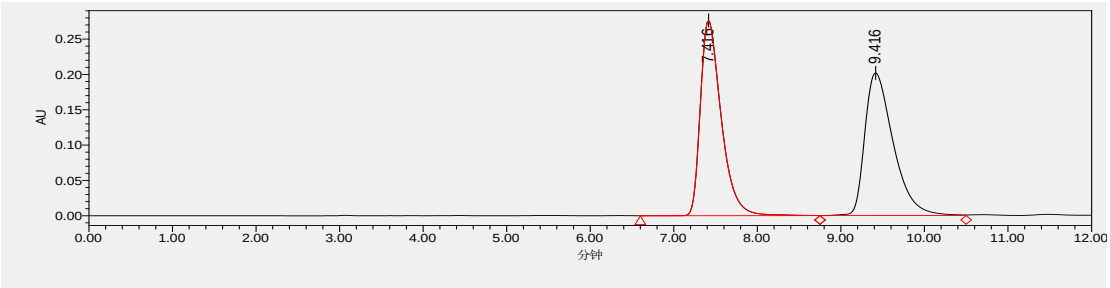


24h, yield 26.3 mg, 98%; white solid, mp 68 – 69 ℃; HPLC (Chiralcel AS-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 7.41 min, t_r (minor) = 9.49 min, *ee* = 79%. $[\alpha]^{20}_D$ = −29.3 (*c* =0.80, in CH_2Cl_2, 96 % *ee*).

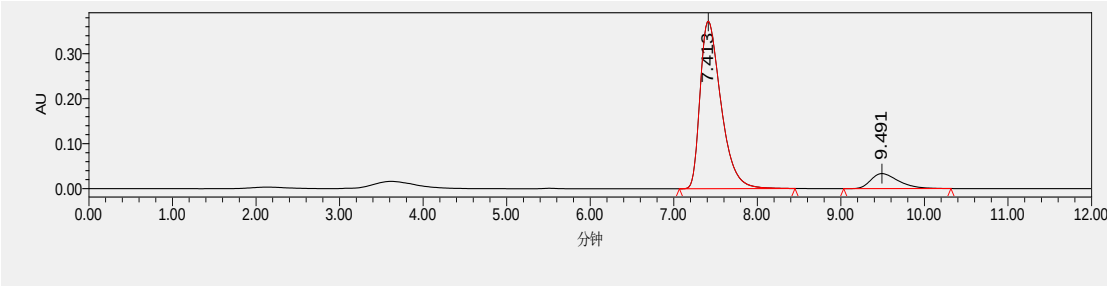
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.45 (d, *J* = 5.2 Hz, 1H), 8.21 (d, *J* = 1.8 Hz, 1H), 8.01 (d, *J* = 6.9 Hz, 1H), 7.50 – 7.36 (m, 1H), 4.07 – 3.86 (m, 1H), 3.37 (s, 3H), 3.27 – 3.12 (m, 1H), 2.28 – 2.16 (m, 1H), 2.16 – 2.06 (m, 1H), 1.86 – 1.74 (m, 1H), 1.73 – 1.63 (m, 1H), 1.48 – 1.22 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.8, 151.7, 148.9, 145.8, 126.2, 122.9, 81.1, 56.1, 52.5, 30.9, 29.3, 24.0, 23.6.

HRMS (ESI-TOF) calcd for $C_{13}H_{17}Cl^{34.9689}N_2NaO_2^+$ ([M]+Na^+) = 291.0876, Found 291.0878.

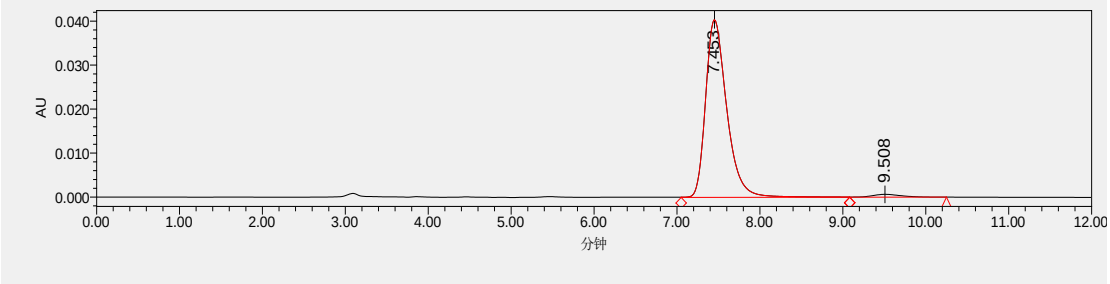


Peak	Retention Time	Area	% Area	Height
1	7.416	4783757	50.03	276240
2	9.416	4778283	49.97	201931



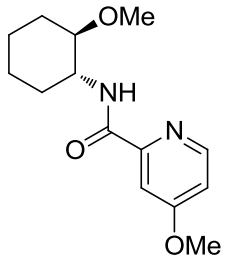
Peak	Retention Time	Area	% Area	Height
1	7.413	6460704	89.34	372537
2	9.491	770623	10.66	33515

After single recrystallization, 96 % *ee* was obtained.



Peak	Retention Time	Area	% Area	Height
1	7.453	715047	97.86	40428
2	9.508	15603	2.14	644

trans-4-methoxy-_N_-(2-methoxycyclohexyl)picolinamide (3c)

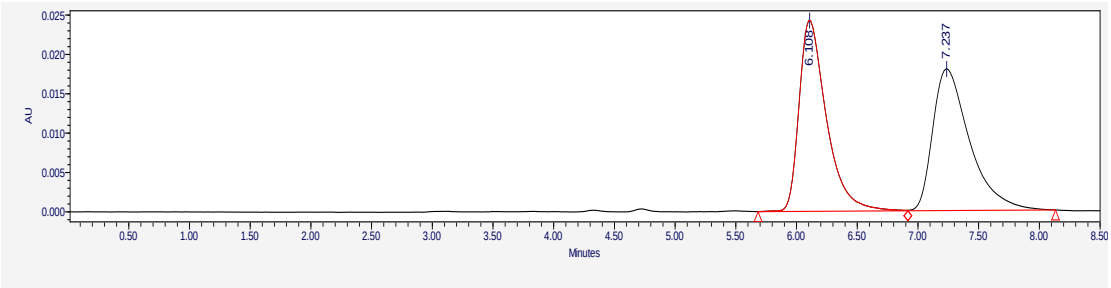


48h, yield 17.7 mg, 67 %; colorless oil, HPLC (Chiralcel AS-H, hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 6.02 min, t_r (minor) = 7.24 min, *ee* = 78%. $[\alpha]^{20}_D = -21.8$ (*c* =0.35, in CH_2Cl_2)

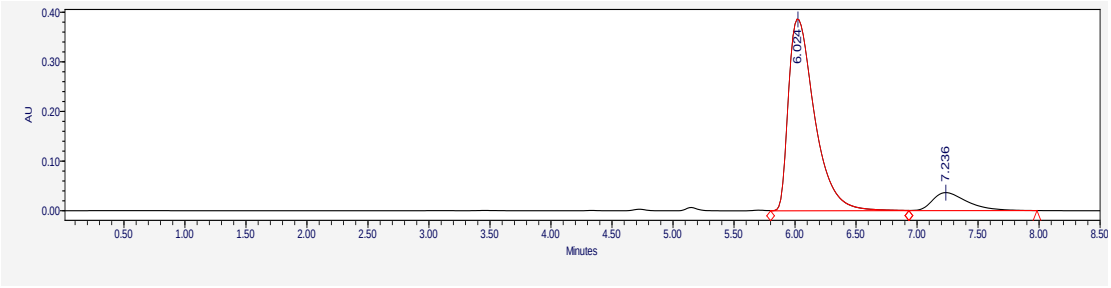
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 5.6 Hz, 1H), 8.11 (d, *J* = 7.4 Hz, 1H), 7.75 (d, *J* = 2.6 Hz, 1H), 6.91 (dd, *J* = 5.6, 2.6 Hz, 1H), 4.02 – 3.93 (m, 1H), 3.91 (s, 3H), 3.37 (s, 3H), 3.26 – 3.16 (m, 1H), 2.24 – 2.16 (m, 1H), 2.14 – 2.06 (m, 1H), 1.83 – 1.74 (m, 1H), 1.72 – 1.65 (m, 1H), 1.48 – 1.27 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.9, 163.9, 152.3, 149.1, 112.9, 107.3, 81.1, 56.2, 55.5, 52.2, 30.9, 29.2, 23.9, 23.5.

HRMS (ESI-TOF) calcd for $C_{14}H_{20}N_2NaO_3^+$ ([M]+Na^+) = 287.1372, Found 287.1375.

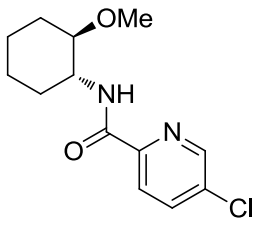


Peak	Retention Time	Area	% Area	Height
1	6.108	379995	50.00	24348
2	7.237	380017	50.00	18020



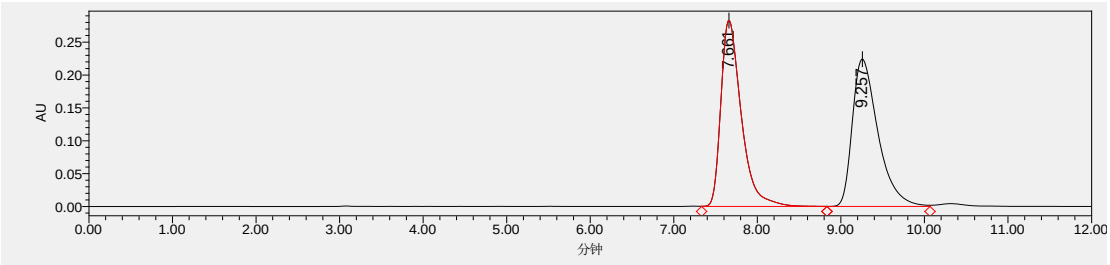
Peak	Retention Time	Area	% Area	Height
1	6.024	5759461	88.92	387421
2	7.236	717984	11.08	36437

trans-5-chloro-_N_-(2-methoxycyclohexyl)picolinamide (3d)

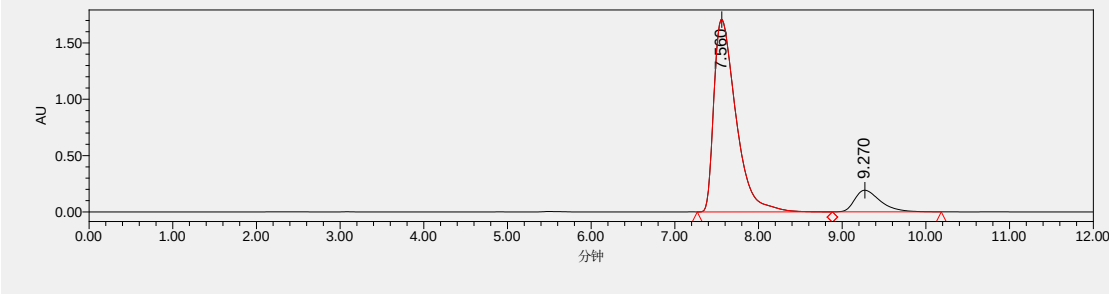


24h, yield 24.4 mg, 91%; colorless oil, HPLC (Chiralcel AS-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 7.56 min, t_r (minor) = 9.27 min, *ee* = 77%. $[\alpha]^{20}_D$ = −24.4 (*c* =0.49, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.0 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 6.7 Hz, 1H), 7.81 (dd, *J* = 8.4, 2.1 Hz, 1H), 4.06 – 3.86 (m, 1H), 3.37 (s, 3H), 3.26 – 3.15 (m, 1H), 2.29 – 2.17 (m, 1H), 2.17 – 2.09 (m, 1H), 1.87 – 1.76 (m, 1H), 1.74 – 1.63 (m, 1H), 1.48 – 1.26 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.1, 148.4, 147.0, 137.0, 134.8, 123.3, 81.1, 56.1, 52.4, 31.0, 29.2, 24.0, 23.6.

HRMS (ESI-TOF) calcd for $C_{13}H_{17}Cl^{34.9689}N_2NaO_2^+$ ([M]+Na^+) = 291.0876, Found 291.0878.

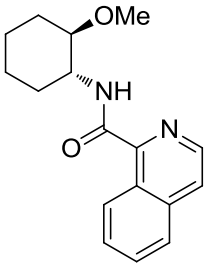


Peak	Retention Time	Area	% Area	Height
1	7.661	4795028	50.07	283345
2	9.257	4780796	49.93	224318



Peak	Retention Time	Area	% Area	Height
1	7.560	31311272	88.41	1709321
2	9.270	4104090	11.59	192223

***trans*-*N*-(2-methoxycyclohexyl)isoquinoline-1-carboxamide (3h)**

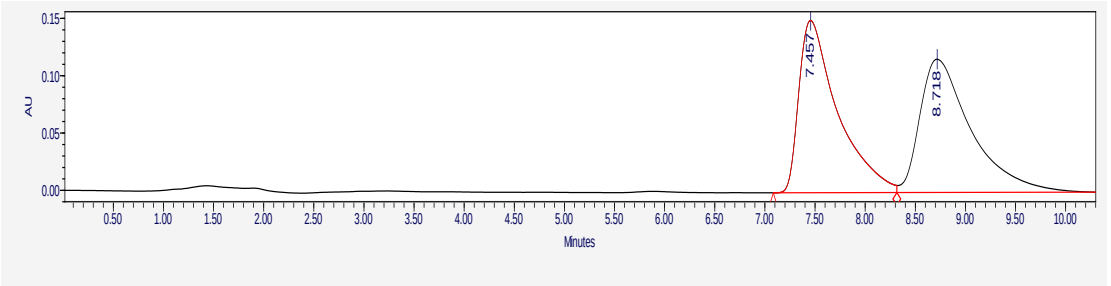


24h, yield 26.3 mg, 93%; colorless oil, HPLC (Chiralcel AS-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 7.48 min, t_r (minor) = 8.89 min, *ee* = 59%. $[\alpha]^{20}_D$ = −17.5 (*c* =0.53, in CH_2Cl_2).

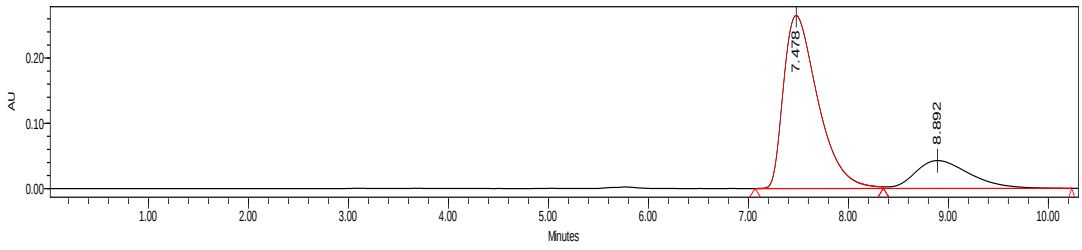
^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.63 (d, *J* = 8.4 Hz, 1H), 8.46 (d, *J* = 5.5 Hz, 1H), 8.27 (d, *J* = 7.2 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 5.5 Hz, 1H), 7.74 – 7.61 (m, 2H), 4.12 – 3.97 (m, 1H), 3.40 (s, 3H), 3.31 – 3.21 (m, 1H), 2.35 – 2.20 (m, 1H), 2.18 – 2.09 (m, 1H), 1.86 – 1.76 (m, 1H), 1.76 – 1.67 (m, 1H), 1.52 – 1.29 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.8, 148.6, 140.2, 137.4, 130.4, 128.5, 128.1, 127.1, 126.7, 124.2, 81.2, 56.2, 52.2, 30.9, 29.3, 24.1, 23.6.

HRMS (ESI-TOF) calcd for $C_{17}H_{20}N_2NaO_2^+$ ([M]+Na^+) = 307.1422, Found 307.1425.

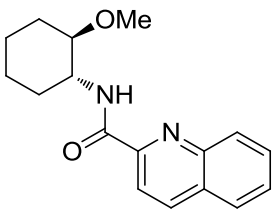


Peak	Retention Time	Area	% Area	Height
1	7.457	4038587	49.43	150480
2	8.718	4131585	50.57	116326



Peak	Retention Time	Area	% Area	Height
1	7.478	6324654	79.61	265193
2	8.892	1620308	20.39	42716

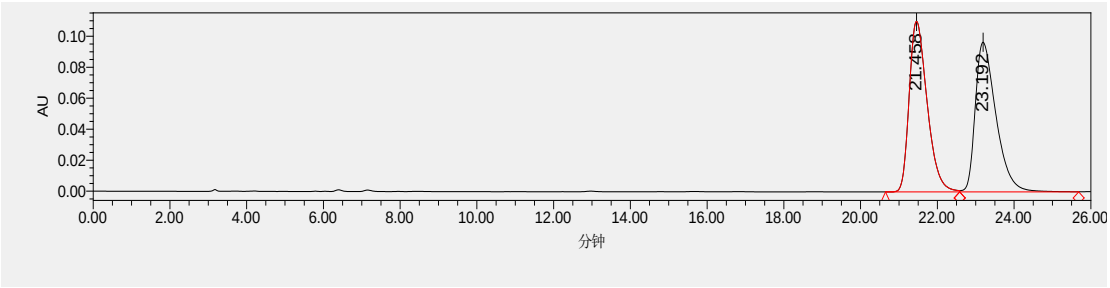
***trans*-*N*-(2-methoxycyclohexyl)quinoline-2-carboxamide (3i)**



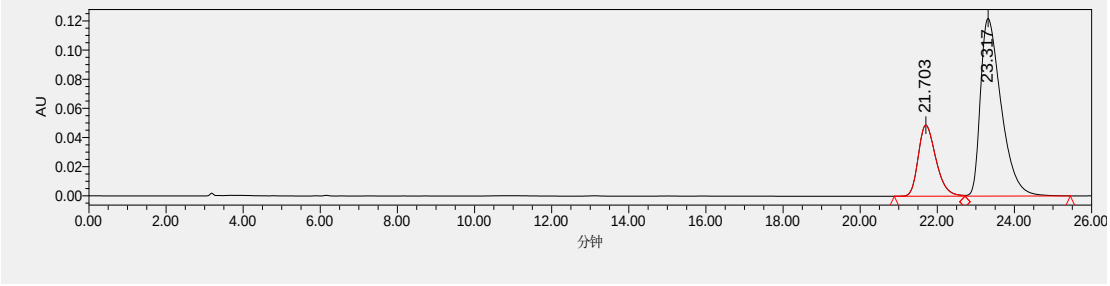
48h, yield 27.7 mg, 98%; colorless oil, HPLC (Chiralcel IE, hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 23.32 min, t_r (minor) = 21.70 min, *ee* = 49%. $[\alpha]^{20}_D$ = −17.5 (*c* =0.53, in CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.43 – 8.25 (m, 3H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.82 – 7.72 (m, 1H), 7.67 – 7.57 (m, 1H), 4.15 – 3.97 (m, 1H), 3.40 (s, 3H), 3.37 – 3.27 (m, 1H), 2.33 – 2.20 (m, 1H), 2.19 – 2.10 (m, 1H), 1.87 – 1.77 (m, 1H), 1.77 – 1.67 (m, 1H), 1.52 – 1.31 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.2, 150.1, 146.4, 137.4, 130.0, 129.8, 129.3, 127.8, 119.0, 81.2, 56.2, 52.4, 31.0, 29.4, 24.1, 23.7.

HRMS (ESI-TOF) calcd for $C_{17}H_{20}N_2NaO_2^+$ ([M]+Na^+) = 307.1422, Found 307.1428.

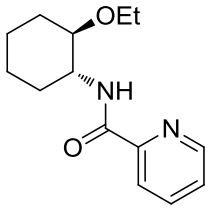


Peak	Retention Time	Area	% Area	Height
1	21.458	3574279	49.69	110113
2	23.192	3618909	50.31	96636



Peak	Retention Time	Area	% Area	Height
1	21.703	1552034	25.47	48769
2	23.317	4541749	74.53	121818

***N*-((1*R*,2*R*)-2-ethoxycyclohexyl)picolinamide (3j)**

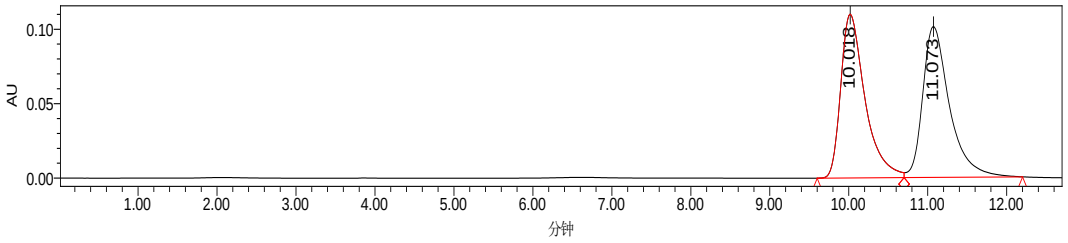


24h, yield 21.4 mg, 87%; yellow oil; HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 95/5, flow rate 0.8 mL/min, λ = 254 nm) t_r (major) = 10.04 min, t_r (minor) = 11.15 min, *ee* = 87%. $[\alpha]^{20}_D$ = −49.5 (*c* =0.43, in CH_2Cl_2).

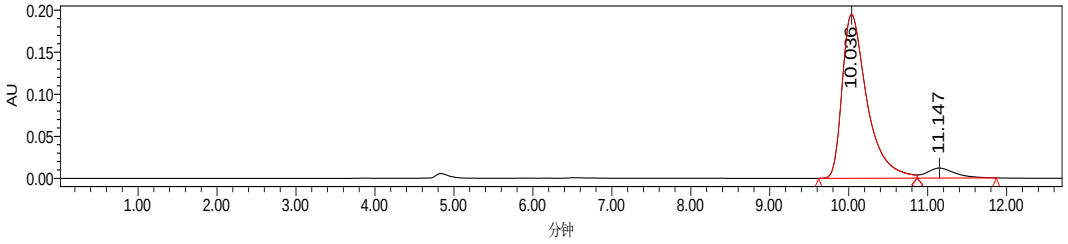
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 4.3 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 8.12 (d, *J* = 5.5 Hz, 1H), 7.84 (td, *J* = 7.7, 1.2 Hz, 1H), 7.46 – 7.37 (m, 1H), 4.03 – 3.88 (m, 1H), 3.72 – 3.60 (m, 1H), 3.55 – 3.43 (m, 1H), 3.31 (td, *J* = 9.1, 3.9 Hz, 1H), 2.24 (d, *J* = 10.8 Hz, 1H), 2.10 – 2.00 (m, 1H), 1.84 – 1.73 (m, 1H), 1.73 – 1.62 (m, 1H), 1.50 – 1.28 (m, 4H), 1.14 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.9, 150.3, 148.0, 137.3, 125.9, 122.1, 79.5, 64.0, 52.5, 30.8, 30.2, 23.9, 23.7, 15.7.

HRMS (ESI-TOF) calcd for $C_{14}H_{20}N_2NaO_2^+$ ([M]+Na^+) = 271.1422, Found 271.1419.

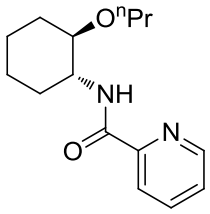


Peak	Retention Time	Area	% Area	Height
1	10.018	2344362	49.56	110049
2	11.073	2386145	50.44	101430



Peak	Retention Time	Area	% Area	Height
1	10.036	4253900	93.57	194963
2	11.147	292268	6.43	11873

_N_-((1_R_,2_R_)-2-propoxycyclohexyl)picolinamide (3k)

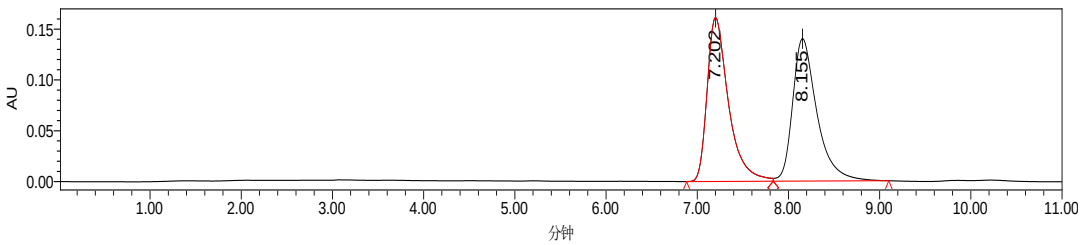


35h, yield 23.6 mg, 90%; colorless oil; HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 7.19 min, t_r (minor) = 8.16 min, *ee* = 88%. $[\alpha]^{20}_D$ = −47.5 (*c* =0.47, in CH_2Cl_2).

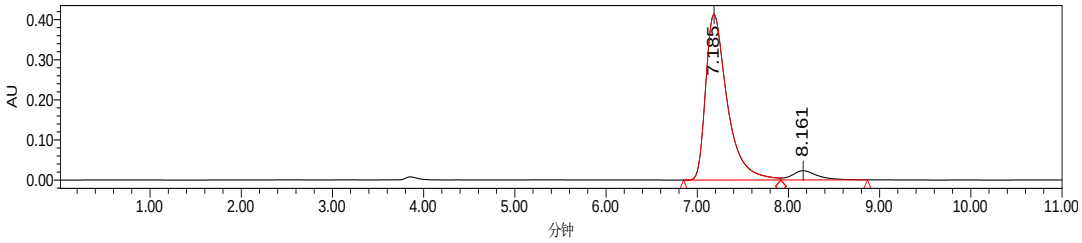
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.54 (d, *J* = 4.5 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 8.14 (d, *J* = 5.0 Hz, 1H), 7.88 – 7.77 (m, 1H), 7.46 – 7.34 (m, 1H), 4.01 – 3.87 (m, 1H), 3.63 – 3.51 (m, 1H), 3.40 – 3.22 (m, 2H), 2.30 – 2.16 (m, 1H), 2.13 – 2.00 (m, 1H), 1.84 – 1.73 (m, 1H), 1.72 – 1.61 (m, 1H), 1.58 – 1.49 (m, 2H), 1.46 – 1.25 (m, 4H), 0.84 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 150.30, 147.9, 137.3, 125.9, 122.1, 79.8, 70.4, 52.5, 30.8, 30.1, 23.9, 23.7, 23.3, 10.6.

HRMS (ESI-TOF) calcd for $C_{15}H_{22}N_2NaO_2^+$ ([M]+Na^+) = 285.1579, Found 285.1578.

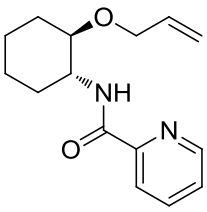


Peak	Retention Time	Area	% Area	Height
1	7.202	2622920	50.31	161505
2	8.155	2590435	49.69	140340



Peak	Retention Time	Area	% Area	Height
1	7.185	6788363	93.90	413966
2	8.161	441291	6.10	23020

_N_-((1_R_,2_R_)-2-(allyloxy)cyclohexyl)picolinamide (3l)

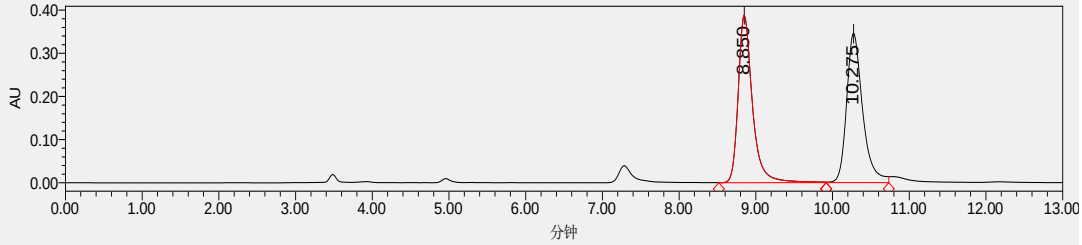


16h, yield 23.2 mg, 89%; colorless oil; HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 10.30 min, t_r (minor) = 8.91 min, *ee* = 92%. $[\alpha]^{20}_D = -37.3$ (*c* =0.46, in CH_2Cl_2).

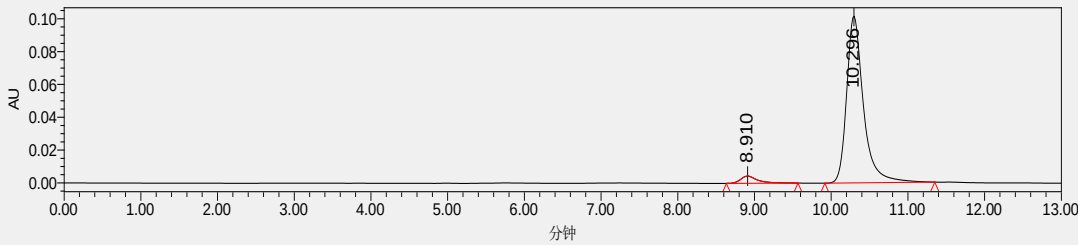
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 4.4 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 8.12 (d, *J* = 6.1 Hz, 1H), 7.83 (t, *J* = 7.5 Hz, 1H), 7.41 (dd, *J* = 6.5, 5.3 Hz, 1H), 5.87 (ddd, *J* = 22.2, 10.6, 5.4 Hz, 1H), 5.24 (d, *J* = 17.2 Hz, 1H), 5.10 (d, *J* = 10.3 Hz, 1H), 4.20 – 4.18 (m, 1H), 4.05 – 3.90 (m, 2H), 3.36 (td, *J* = 9.0, 3.8 Hz, 1H), 2.30 – 2.18 (m, 1H), 2.12 – 1.98 (m, 1H), 1.86 – 1.73 (m, 1H), 1.72 – 1.60 (d, *J* = 12.0 Hz, 1H), 1.51 – 1.27 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.9, 150.3, 147.9, 137.3, 135.4, 126.0, 122.2, 116.5, 79.0, 69.6, 52.3, 30.8, 30.0, 23.8, 23.6.

HRMS (ESI-TOF) calcd for $C_{15}H_{20}N_2NaO_2^+$ ([M]+Na^+) = 283.1422, Found 283.1423.

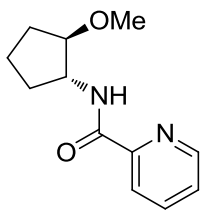


Peak	Retention Time	Area	% Area	Height
1	8.850	5029939	50.04	388961
2	10.275	5021779	49.96	346617



Peak	RetTime	Area	% Area	Height
1	8.910	67498	4.19	4400
2	10.296	1542129	95.81	101613

***trans*-_N_-(2-methoxycyclopentyl)picolinamide (3m)**



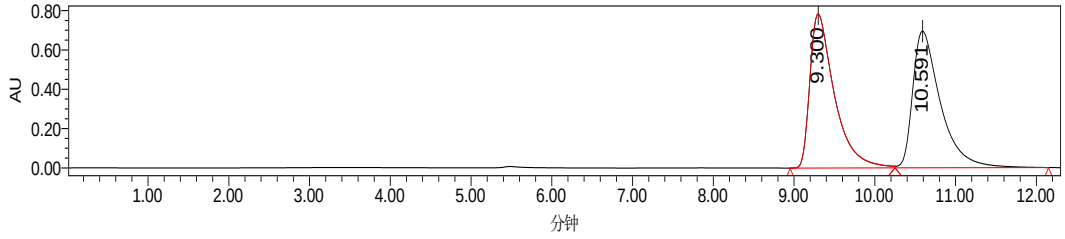
48h, yield 17.8 mg, 81%; colorless oil; HPLC (Chiralcel OD-H, hexane/*i*-PrOH =

95/5, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 9.32 min, t_r (minor) = 10.69 min, *ee* = 91%. $[\alpha]^{20}_D$ = −12.9 (*c* =0.36, in CH_2Cl_2).

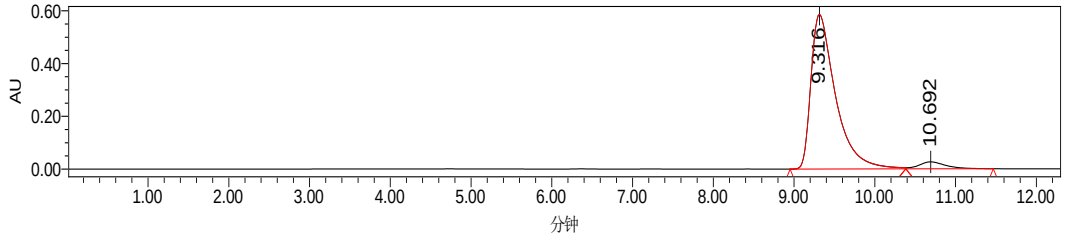
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.54 (d, *J* = 3.7 Hz, 1H), 8.20 (d, *J* = 7.7 Hz, 1H), 8.00 (s, 1H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.47 – 7.37 (m, 1H), 4.38 (s, 1H), 3.76 (s, 1H), 3.43 (s, 3H), 2.29 – 2.16 (m, 1H), 2.01 – 1.92 (m, 1H), 1.88 – 1.68 (m, 3H), 1.66 – 1.53 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.8, 149.0, 148.0, 137.4, 126.1, 122.1, 87.1, 57.0, 55.3, 30.8, 30.5, 21.8.

HRMS (ESI-TOF) calcd for $C_{12}H_{17}N_2O_2^+$ ([M]+H^+) = 221.1290, Found 221.1287.

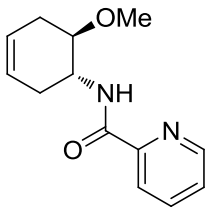


Peak	Retention Time	Area	% Area	Height
1	9.300	16487159	49.88	784469
2	10.591	16564707	50.12	696154



Peak	Retention Time	Area	% Area	Height
1	9.316	12392393	95.31	586390
2	10.692	609321	4.69	26358

_N_-((1_R_,6_R_)-6-methoxycyclohex-3-en-1-yl)picolinamide (3n)

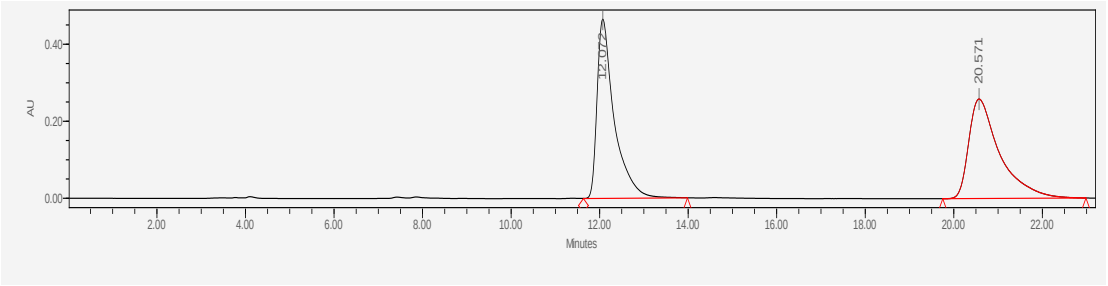


75h, yield 20.4 mg, 88%; colorless oil; HPLC (Chiralcel IC, hexane/*i*-PrOH = 70/30, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 12.13 min, t_r (minor) = 20.17 min, *ee* = 83%. $[\alpha]^{20}_D$ = −77.0 (*c* =0.41, in CH_2Cl_2).

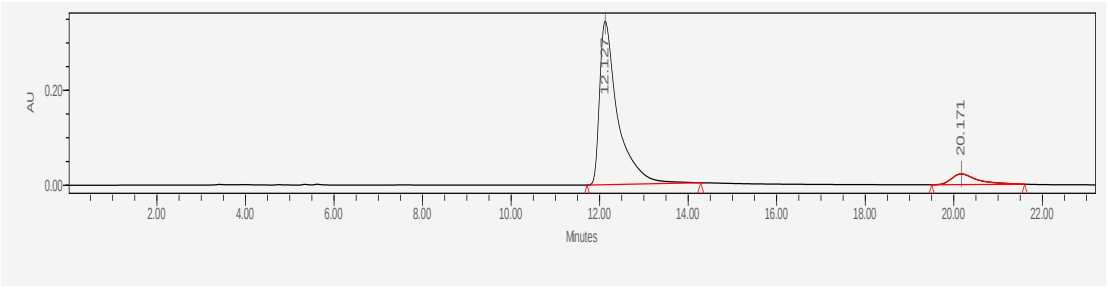
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 4.2 Hz, 1H), 8.27 – 8.11 (m, 2H), 7.85 (t, *J* = 7.7 Hz, 1H), 7.48 – 7.37 (m, 1H), 5.78 – 5.59 (m, 2H), 4.47 – 4.34 (m, 1H), 3.63 (dd, *J* = 12.0, 5.3 Hz, 1H), 3.45 (s, 3H), 2.80 – 2.68 (m, 1H), 2.54 – 2.41 (m, 1H), 2.26 – 2.16 (m, 1H), 2.13 – 2.03 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.2, 150.0, 148.1, 137.3, 126.1, 124.3, 124.2, 122.2, 76.1, 56.6, 46.8, 28.9, 28.3.

HRMS (ESI-TOF) calcd for $C_{13}H_{17}N_2O_2^+$ ([M]+H^+) = 233.1290, Found 233.1286.

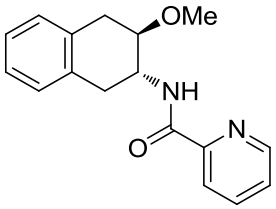


Peak	Retention Time	Area	% Area	Height
1	12.072	12483600	49.92	465978
2	20.571	12522676	50.08	258336



Peak	Retention Time	Area	% Area	Height
1	12.127	9773915	91.38	344921
2	20.171	921703	8.62	22575

_N_-((2_R_,3_R_)-3-methoxy-1,2,3,4-tetrahydronaphthalen-2-yl)picolinamide (3o)

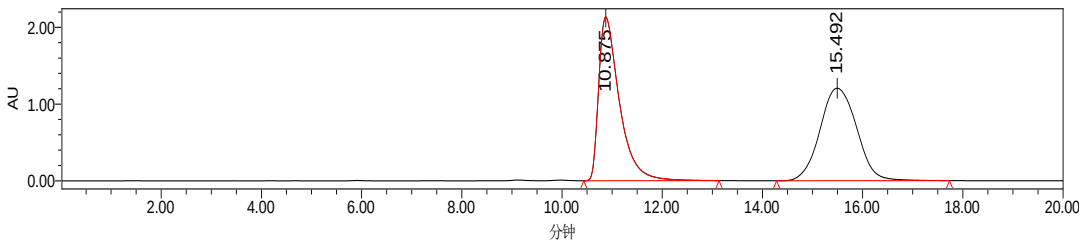


93h, yield 24.3 mg, 86%; colorless oil; HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 15.41 min, t_r (minor) = 11.13 min, *ee* = 76%. $[\alpha]^{20}_D$ = −57.8 (*c* =0.49, in CH_2Cl_2).

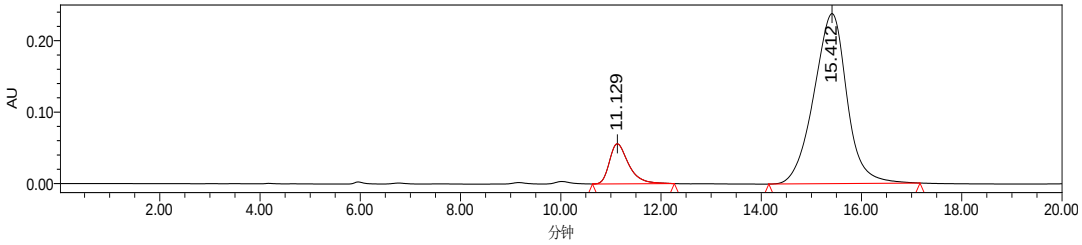
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.46 (d, *J* = 4.7 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 2H), 7.79 (td, *J* = 7.7, 1.6 Hz, 1H), 7.42 – 7.31 (m, 1H), 7.19 – 7.04 (m, 4H), 4.56 (dt, *J* = 13.2, 6.6 Hz, 1H), 3.81 (dd, *J* = 11.5, 6.1 Hz, 1H), 3.51 – 3.40 (m, 4H), 3.18 (dd, *J* = 17.0, 4.7 Hz, 1H), 2.92 (dd, *J* = 17.0, 6.0 Hz, 1H), 2.81 (dd, *J* = 16.8, 6.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.3, 149.8, 148.1, 137.3, 133.4, 133.3, 129.3, 129.2, 126.4, 126.3, 126.2, 122.2, 76.9, 56.6, 48.0, 32.6, 31.9.

HRMS (ESI-TOF) calcd for $C_{17}H_{18}N_2NaO_2^+$ ([M]+Na^+) = 305.1266, Found 305.1263.

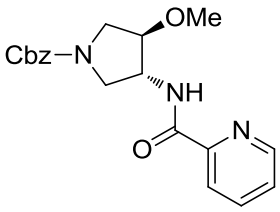


Peak	Retention Time	Area	% Area	Height
1	10.875	61229742	49.92	2136044
2	15.492	61428813	50.08	1205860



Peak	Retention Time	Area	% Area	Height
1	11.129	1491198	12.04	56104
2	15.412	10895701	87.96	238000

***trans*-Benzyl 3-methoxy-4-(picolinamido)pyrrolidine-1-carboxylate (3p)**

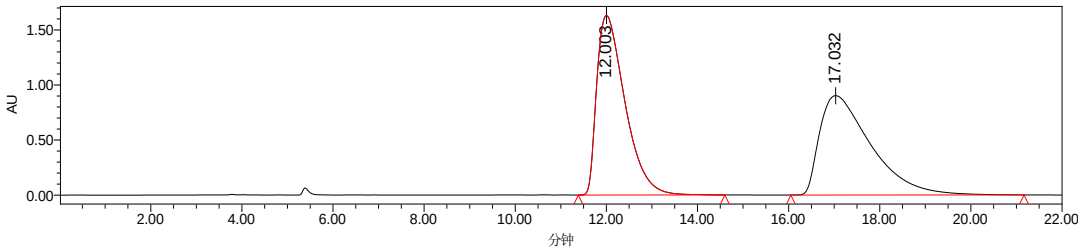


49h, yield 26.6 mg, 75%; colorless oil; HPLC (Chiralcel AS-H, hexane/*i*-PrOH = 70/30, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 12.41 min, t_r (minor) = 18.10 min, *ee* = 80%. $[\alpha]^{20}_D$ = + 22.4 (*c* =0.53, in CH_2Cl_2).

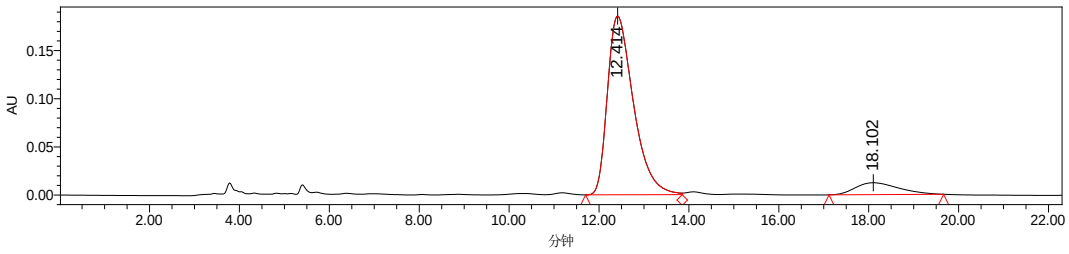
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 3.6 Hz, 1H), 8.27 – 8.08 (m, 2H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.45 – 7.38 (m, 1H), 7.38 – 7.21 (m, 5H), 5.15 (s, 2H), 4.60 (s, 1H), 3.95 (d, *J* = 11.1 Hz, 1H), 3.85 (dd, *J* = 10.9, 5.5 Hz, 1H), 3.74 – 3. 51 (m, 3H), 3.45 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.3/164.2 (rotamer), 154.91/154.89 (rotamer), 149.1, 148.1, 137.4, 136.60/136.57 (rotamer), 128.4, 128.0, 127.9, 126.5, 122.1, 83.1/82.2 (rotamer), 66.9, 57.1, 53.1/52.2 (rotamer), 49.71/49.68 (rotamer), 49.5/49.4 (rotamer).

HRMS (ESI-TOF) calcd for $C_{19}H_{22}N_3O_4^+$ ([M]+H^+) = 356.1610, Found 356.1607.

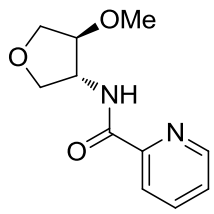


Peak	Retention Time	Area	% Area	Height
1	12.003	70232625	49.88	1630908
2	17.032	70564884	50.12	902317



Peak	Retention Time	Area	% Area	Height
1	12.414	7464001	90.01	185584
2	18.102	828419	9.99	12381

***trans*-*N*-(4-methoxytetrahydrofuran-3-yl)picolinamide (3q)**

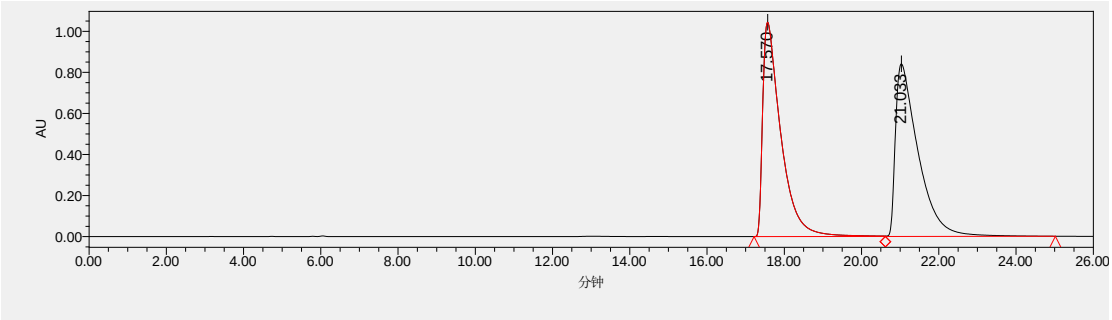


118h, yield 14.6 mg, 66%; colorless oil; HPLC (Chiralcel IE, hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 21.56 min, t_r (minor) = 18.63 min, *ee* = 78%. $[\alpha]^{20}_D$ = + 7.2 (*c* =0. 29, in CH_2Cl_2).

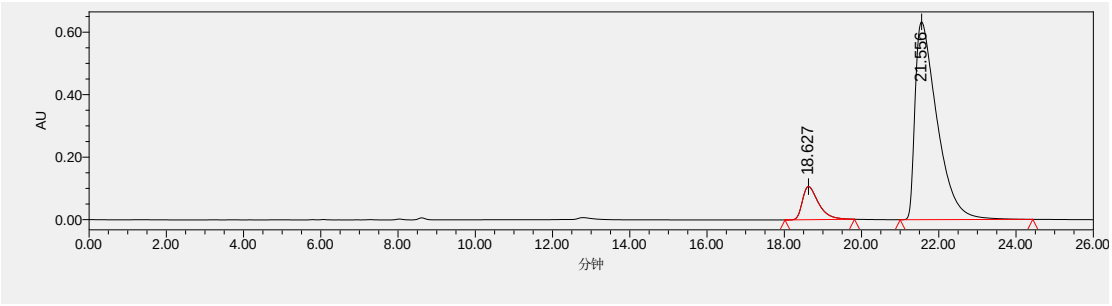
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 4.7 Hz, 1H), 8.29 – 8.08 (m, 2H), 7.87 (td, *J* = 7.7, 1.4 Hz, 1H), 7.45 (dd, *J* = 7.5, 4.8 Hz, 1H), 4.68 – 4.54 (m, 1H), 4.14 (dd, *J* = 10.2, 5.2 Hz, 1H), 4.08 (dd, *J* = 9.6, 4.9 Hz, 1H), 3.97 – 3.92 (m, 1H), 3.90 – 3.84 (m, 1H), 3.76 (dd, *J* = 10.2, 2.2 Hz, 1H), 3.53 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 149.3, 148.1, 137.4, 126.4, 122.1, 86.1, 72.3, 71.4, 57.5, 54.5.

HRMS (ESI-TOF) calcd for $C_{11}H_{14}N_2NaO_3^+$ ([M]+Na^+) = 245.0902, Found 245.0901.

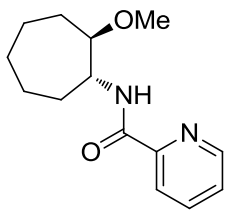


Peak	Retention Time	Area	% Area	Height
1	17.570	34111336	49.92	1044797
2	21.033	34217544	50.08	840941



Peak	Retention Time	Area	% Area	Height
1	18.627	3078943	10.96	106155
2	21.556	25013888	89.04	633373

trans-*N*-(2-methoxycycloheptyl)picolinamide (3r)

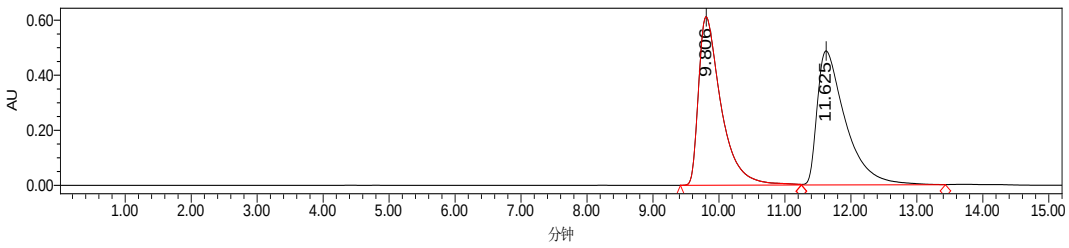


118h, yield 15.4 mg, 62%; colorless oil; HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 9.91 min, t_r (minor) = 11.97 min, *ee* = 75%. $[\alpha]^{20}_D$ = −16.6 (*c* =0.31, in CH_2Cl_2).

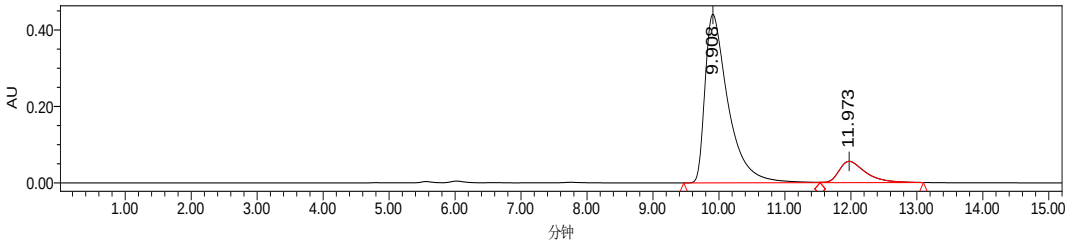
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 3.1 Hz, 1H), 8.20 (d, *J* = 7.0 Hz, 2H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.49 – 7.36 (m, 1H), 4.28 – 4.09 (m, 1H), 3.45 – 3.30 (m, 4H), 2.04 – 1.93 (m, 1H), 1.87 –1.78 (m, 2H), 1.77 – 1.60 (m, 5H), 1.59 – 1.42(m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.6, 150.2, 148.0, 137.3, 126.0, 122.2, 84.4, 56.5, 54.4, 30.55, 29.2, 28.5, 23.9, 22.3.

HRMS (ESI-TOF) calcd for $C_{14}H_{21}N_2O_2^+$ ([M]+H^+) = 249.1603, Found 249.1603.

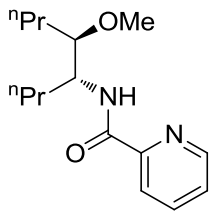


Peak	Retention Time	Area	% Area	Height
1	9.806	14537834	50.09	612967
2	11.625	14483800	49.91	487622



Peak	Retention Time	Area	% Area	Height
1	9.908	10728615	87.35	441874
2	11.973	1553952	12.65	55774

***trans*-*N*-(5-methoxyoctan-4-yl)picolinamide (3s)**

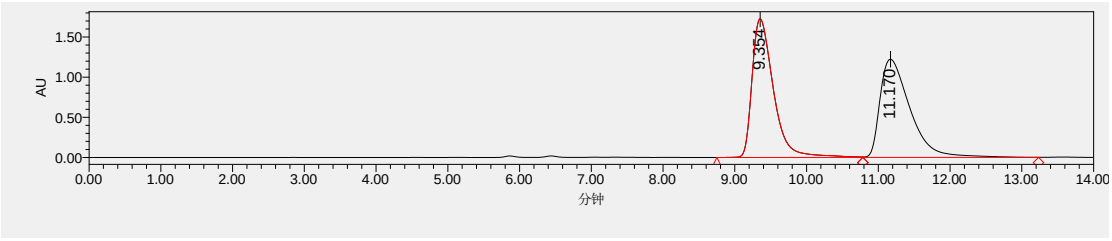


65h, yield 23.1 mg, 88%; colorless oil; HPLC (Chiralcel Lux 5u Cellulose-2, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 10.64 min, t_r (minor) = 9.51min, *ee* = 84%. $[\alpha]^{20}_D = -1.3$ (*c* =0.47, in CH_2Cl_2).

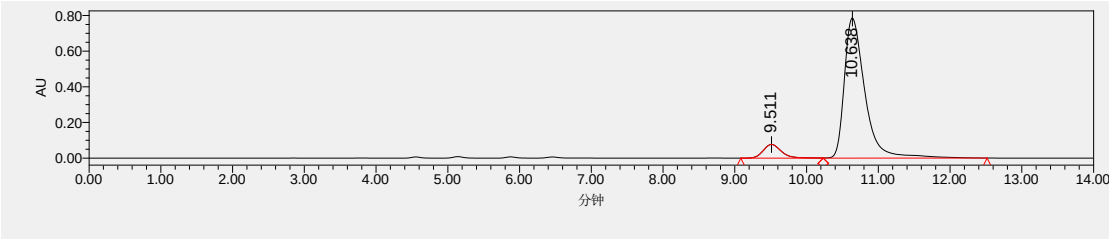
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.47 (d, *J* = 4.2 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 8.04 (d, *J* = 9.5 Hz, 1H), 7.81 – 7.66 (m, 1H), 7.31 (dd, *J* = 6.7, 5.4 Hz, 1H), 4.14 (dd, *J* = 14.7, 7.9 Hz, 1H), 3.38 (s, 3H), 3.25 – 3.09 (m, 1H), 1.64 – 1.52 (m, 2H), 1.50 – 1.41 (m, 1H), 1.38 – 1.23 (m, 5H), 0.91 – 0.74 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.1, 145.0, 148.1, 137.1, 125.9, 122.2, 82.5, 58.6, 51.0, 34.6, 33.0, 19.6, 19.1, 14.2, 14.0.

HRMS (ESI-TOF) calcd for $C_{15}H_{25}N_2O_2^+$ ([M]+H^+) = 265.1916, Found 265.1915.

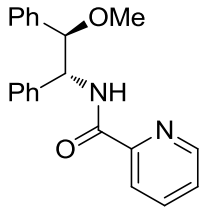


Peak	Retention Time	Area	% Area	Height
1	9.354	35731478	50.16	1728407
2	11.170	35503105	49.84	1223519



Peak	Retention Time	Area	% Area	Height
1	9.511	1348352	7.95	76947
2	10.638	15616576	92.05	786706

***trans*-*N*-(2-methoxy-1,2-diphenylethyl)picolinamide (3t)**

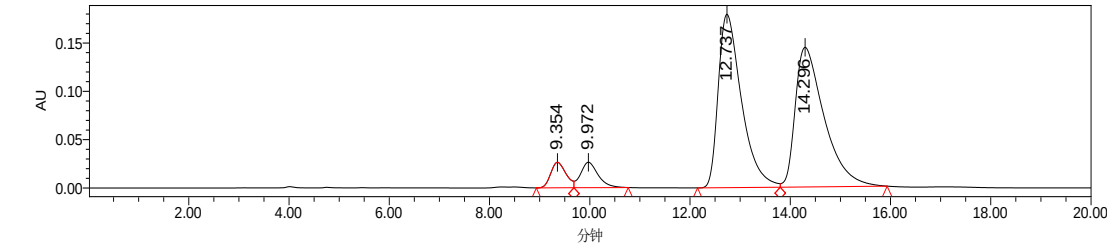


118h, yield 22.7 mg, 68%, dr = 99/1; white solid; mp 102 – 103 ℃; HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 12.86 min, t_r (minor) = 14.60 min, *ee* = 57%. $[\alpha]^{20}_D$ = −22.0 (*c* =0.45, in CH_2Cl_2).

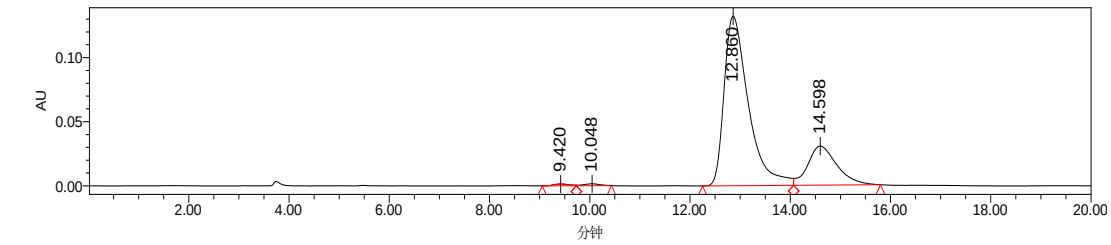
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.92 (d, *J* = 8.3 Hz, 1H), 8.55 (d, *J* = 4.4 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.71 (td, *J* = 7.7, 1.6 Hz, 1H), 7.37 – 7.31 (m, 1H), 7.30 – 7.25 (d, *J* = 7.1 Hz, 2H), 7.23 – 7.13 (m, 8H), 5.21 (dd, *J* = 8.5, 4.1 Hz, 1H), 4.49 (d, *J* = 4.1 Hz, 1H), 3.21 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.8, 149.9, 148.2, 140.3, 138.7, 137.2, 128.3, 128.2, 127.9, 127.34, 127.32, 127.1, 126.1, 122.3, 86.0, 58.8, 57.5.

HRMS (ESI-TOF) calcd for $C_{21}H_{21}N_2O_2^+$ ([M]+H$^+$) = 333.1603, Found 333.1608.



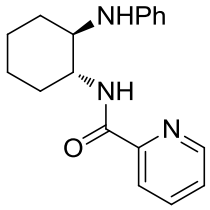
Peak	Retention Time	Area	% Area	Height
1	9.354	554567	4.34	26396
2	9.972	637584	4.99	26348
3	12.737	5787280	45.31	179442
4	14.296	5794162	45.36	144450



Peak	Retention Time	Area	% Area	Height
1	9.420	29465	0.51	1403
2	10.048	33656	0.59	1471
3	12.860	4447720	77.49	132225

4	14.598	1229126	21.41	30489

***trans*-*N*-(2-(phenylamino)cyclohexyl)picolinamide (3u)**

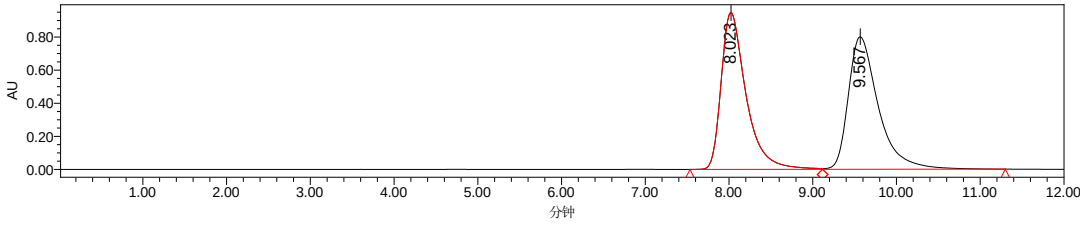


Reacted in 0.5 mL *p*-xylene for 18h, yield 28.7 mg, 97%; light yellow solid; mp 100 – 101 ℃; HPLC (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 9.70 min, t_r (minor) = 8.16 min, *ee* = 95%. $[\alpha]^{20}_D$ = −5.6 (*c* =0.57 , in CH_2Cl_2).

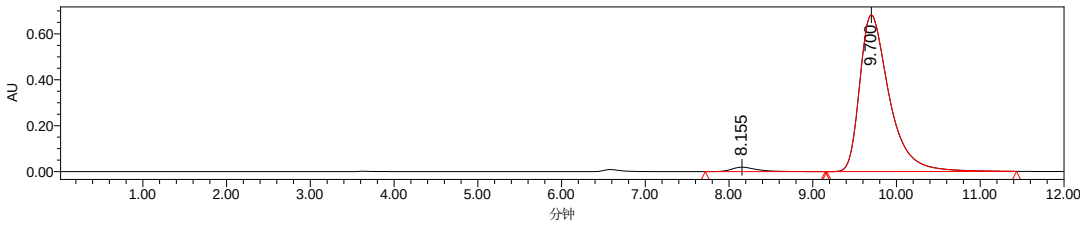
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.46 (d, *J* = 3.9 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.46 – 7.30 (m, 1H), 7.07 (t, *J* = 7.4 Hz, 2H), 6.63 – 6.46 (m, 3H), 4.40 (s, 1H), 4.14 – 3.91 (m, 1H), 3.33 – 3.12 (m, 1H), 2.33 (d, *J* = 12.4 Hz, 1H), 2.21 – 2.07 (m, 1H), 1.89 – 1.69 (m, 2H), 1.56 – 1.31 (m, 3H), 1.30 –1.17 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.0, 149.6, 148.0, 147.7, 137.3, 129.2, 126.2, 122.3, 116.5, 112.7, 58.4, 52.8, 32.6, 32.4, 25.0, 24.4.

HRMS (ESI-TOF) calcd for $C_{18}H_{22}N_3O^+$ ([M]+H^+) = 296.1763, Found 296.1757.

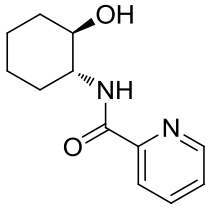


Peak	Retention Time	Area	% Area	Height
1	8.023	19526622	49.52	948078
2	9.567	19902133	50.48	800881



Peak	Retention Time	Area	% Area	Height
1	8.155	407723	2.39	19356
2	9.700	16678054	97.61	682750

***N*-((1*R*,2*R*)-2-hydroxycyclohexyl)picolinamide (3v**, 92 % *ee*)

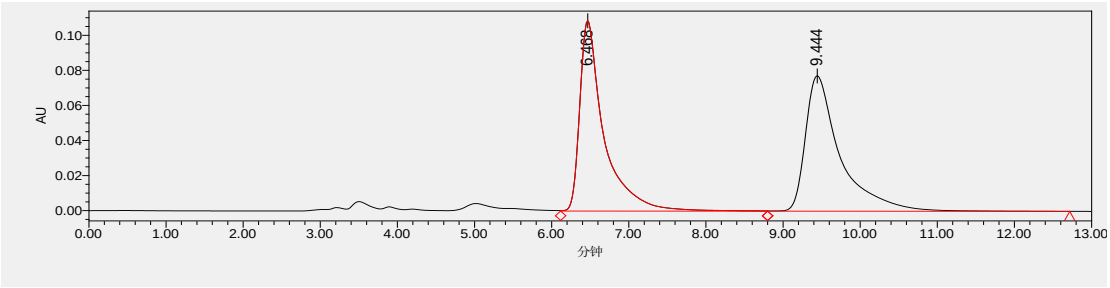


Reacted in 0.2 mL *p*-xylene for 118h, yield 11.0 mg, 50 %; white solid; mp 116 – 117 ℃; HPLC (Chiralcel AS-H, hexane/*i*-PrOH = 70/30, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 9.47 min, t_r (minor) = 6.50 min, *ee* = 92%. $[\alpha]^{20}_D$ = + 1.9 (*c* =0.22 , in CH_2Cl_2).

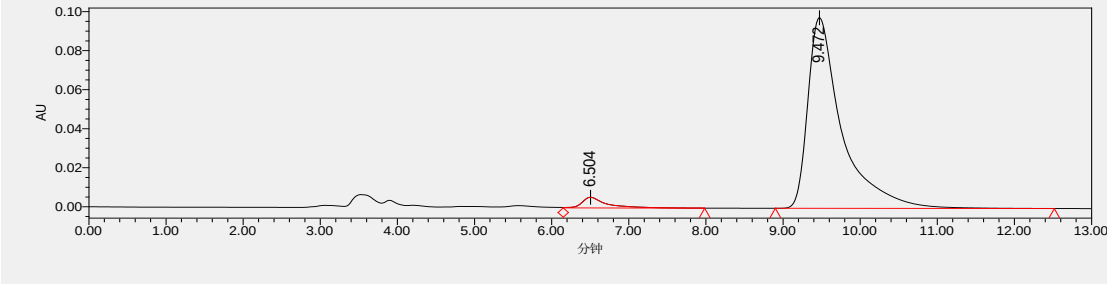
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.53 (d, *J* = 4.0 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 4.6 Hz, 1H), 7.84 (t, *J* = 7.7 Hz, 1H), 7.50 – 7.36 (m, 1H), 3.96 – 3.79 (m, 1H), 3.72 (s, 1H), 3.58 – 3.45 (m, 1H), 2.16 – 2.04 (m, 2H), 1.76 (s, 2H), 1.49 – 1.28 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.6, 149.5, 148.0, 137.4, 126.3, 122.5, 75.2, 55.8, 34.3, 31.5, 24.6, 24.1.

HRMS (ESI-TOF) calcd for $C_{12}H_{16}N_2NaO_2^+$ ([M]+Na^+) = 243.1109, Found 243.1108.



Peak	Retention Time	Area	% Area	Height
1	6.468	2363505	49.44	108597
2	9.444	2416589	50.56	77208

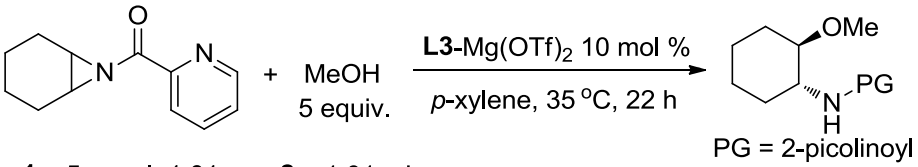


Peak	Retention Time	Area	% Area	Height
1	6.504	120698	3.88	5469
2	9.472	2988210	96.12	97780

9. References

[1] (a) Y. H. Wen, X. Huang, J. L. Huang, Y. Xiong, B. Qin, X. M. Feng, *Synlett.*, 2005, 2445; (b) D. J. Shang, J. G. Xin, Y. L. Liu, X. Zhou, X. H. Liu and X. M. Feng, *J. Org. Chem.*, 2008, **73**, 630; (c) X. Li, X. H. Liu, Y. Z. Fu, L. j. Wang, L. Zhou and X. M. Feng, *Chem.–Eur. J.*, 2008, **14**, 4796.

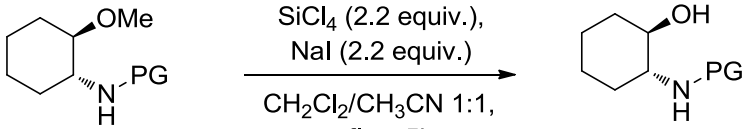
10. Experimental procedure for the scale-up reaction and transformations of the product.



1a, 5 mmol, 1.01 g **2a**, 1.01 mL **3a**

A 50 mL round-bottom flask was charged with $Mg(OTf)_2$ (0. 5 mmol, 160 mg), **L3** (0. 5 mmol, 350 mg) and **1a** (5.0 mmol, 1.01g) under N_2 atmosphere. Then, *p*-xylene (25 mL) was added and the mixture was stirred at 35 ℃ for 20 minutes. Finally, methanol (25.0 mmol, 1.01 mL) were added under stirring at 35 ℃. The reaction mixture was stirred at 35 ℃ for 22 hours. The residue was purified by flash chromatography (Eluent: petroleum ether/AcOEt 2:1) on silica gel to afford the desired product **3a** (1.12 g, 96% yield, 90% *ee*). And the optical pure product **3a** (57 %

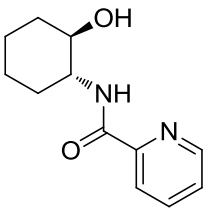
yield, >99% *ee*) was obtained through single recrystallization.



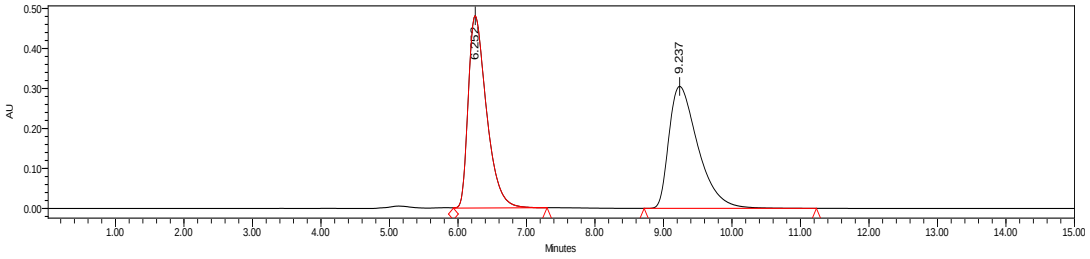
3a, > 99% *ee* PG = 2-picolinoyl **3v**, 93% yiled, > 99% *ee*

3a (46.8 mg, 0.20 mmol) and sodium iodide (66.0 mg, 0.44 mmol) was dissolved in CH_2Cl_2/CH_3CN (1:1, 0.2 mL). Silicon tetrachloride (50 uL, 0.44 mmol) was added and heated under reflux for 5 hours. The mixture is then hydrolyzed by adding 10% sodium hydroxide solution (1 mL) and extracted with CH_2Cl_2 (3×5 mL). The solvent was evaporated and the residue was purified by column chromatography (Eluent: ethyl acetate) on silica gel to give product **3v** (40.9 mg, 93% yield, >99% *ee*).

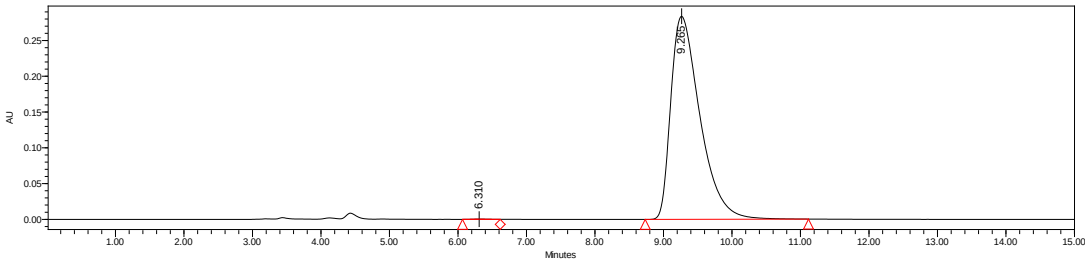
***N*-((1*R*,2*R*)-2-hydroxycyclohexyl)picolinamide (3v, > 99% *ee*)**



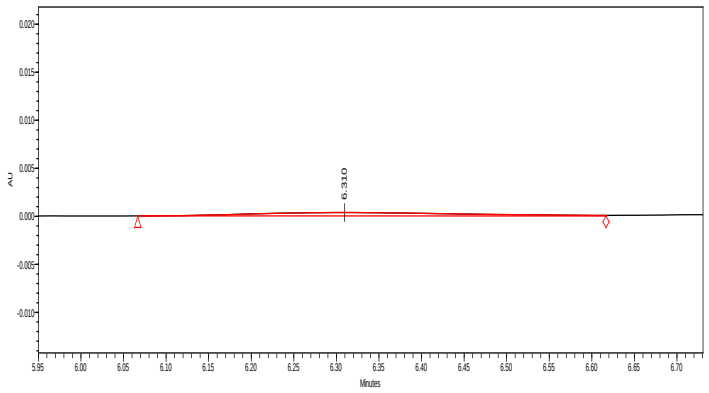
5h, yield 40.9 mg, 93%; white solid; HPLC (Chiralcel AS-H, hexane/*i*-PrOH = 70/30, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 9.27 min, t_r (minor) = 6.31 min, *ee* > 99%. $[\alpha]^{20}_D$ = + 18.1 (*c* =0.43 , in CH_2Cl_2).



Peak	Retention Time	Area	% Area	Height
1	6.252	8899959	49.74	481014
2	9.237	8991826	50.26	305240

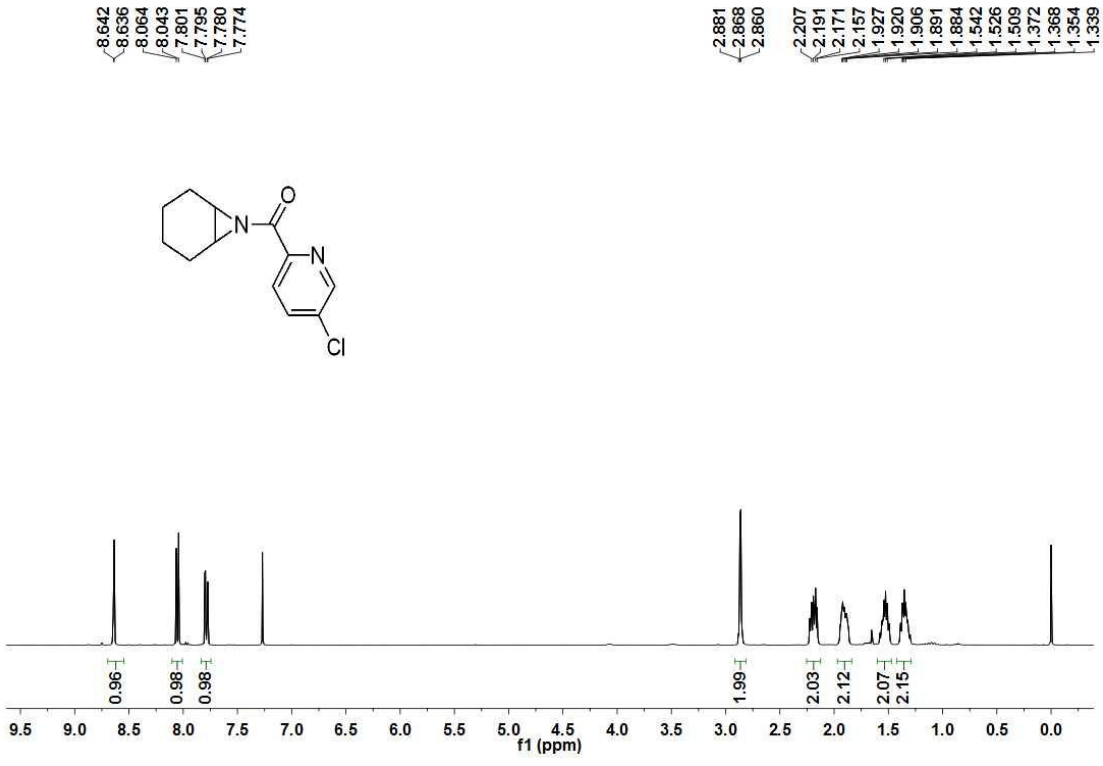


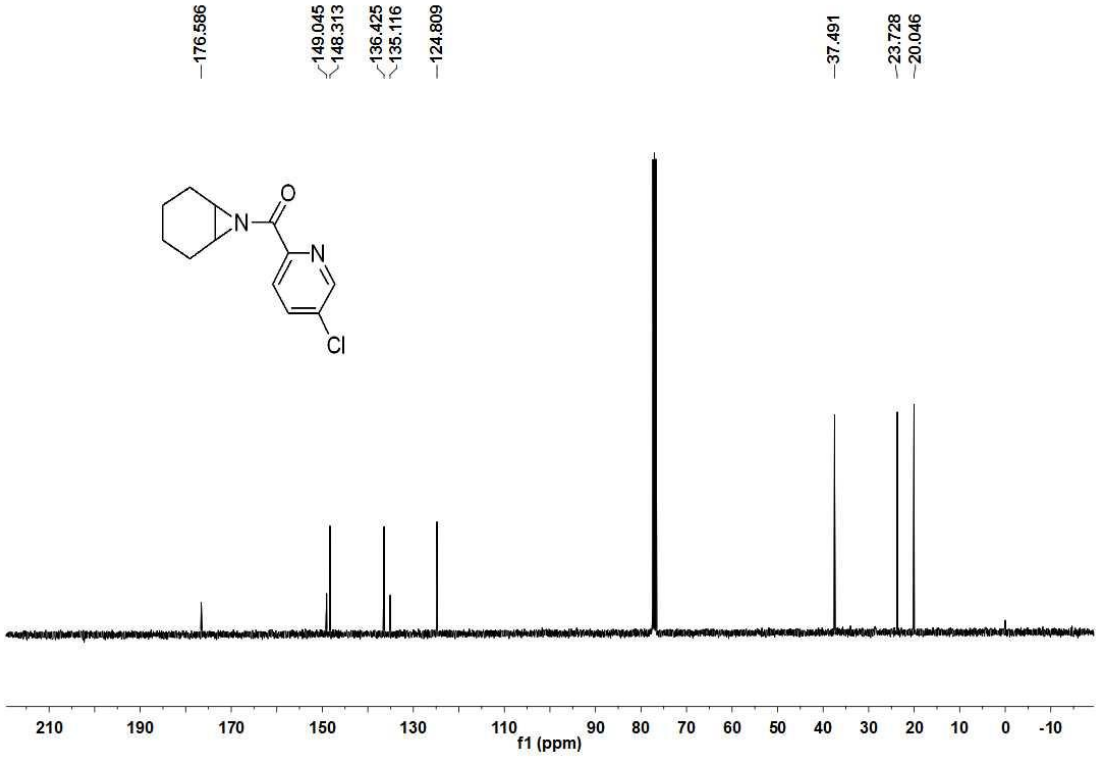
Peak	Retention Time	Area	% Area	Height
1	6.310	6239	0.07	357
2	9.265	8380531	99.93	283802



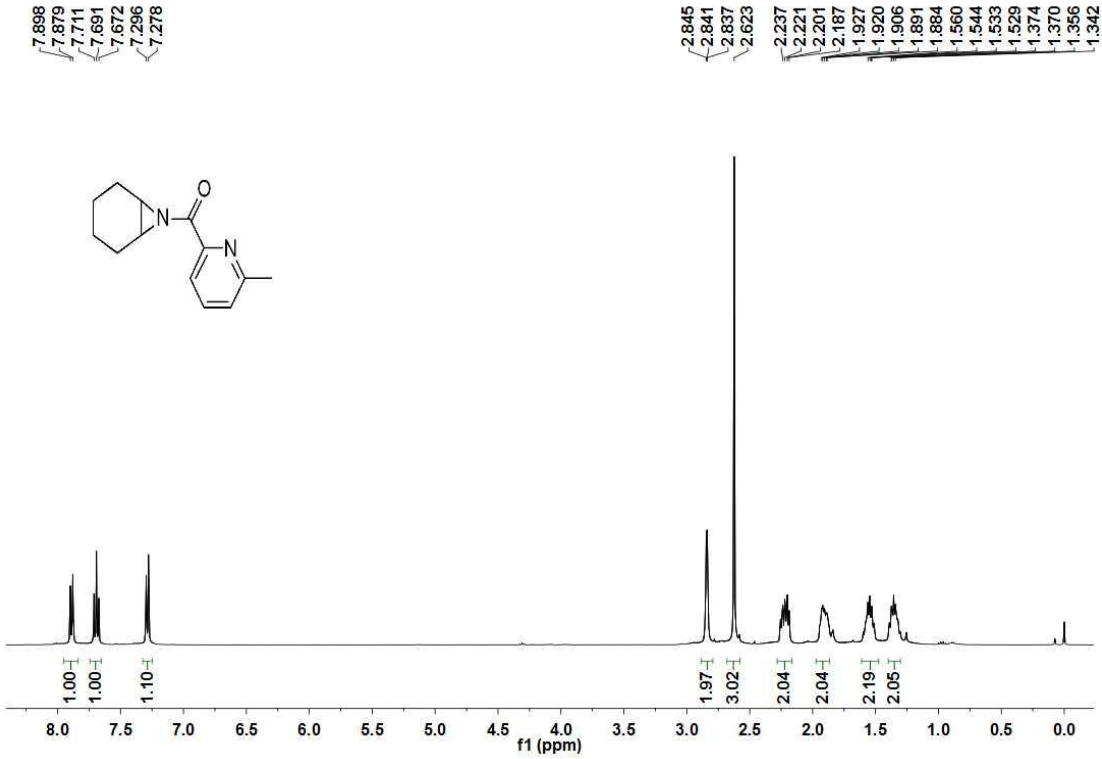
11. Copy of ^{1}H NMR and ^{13}C NMR spectra

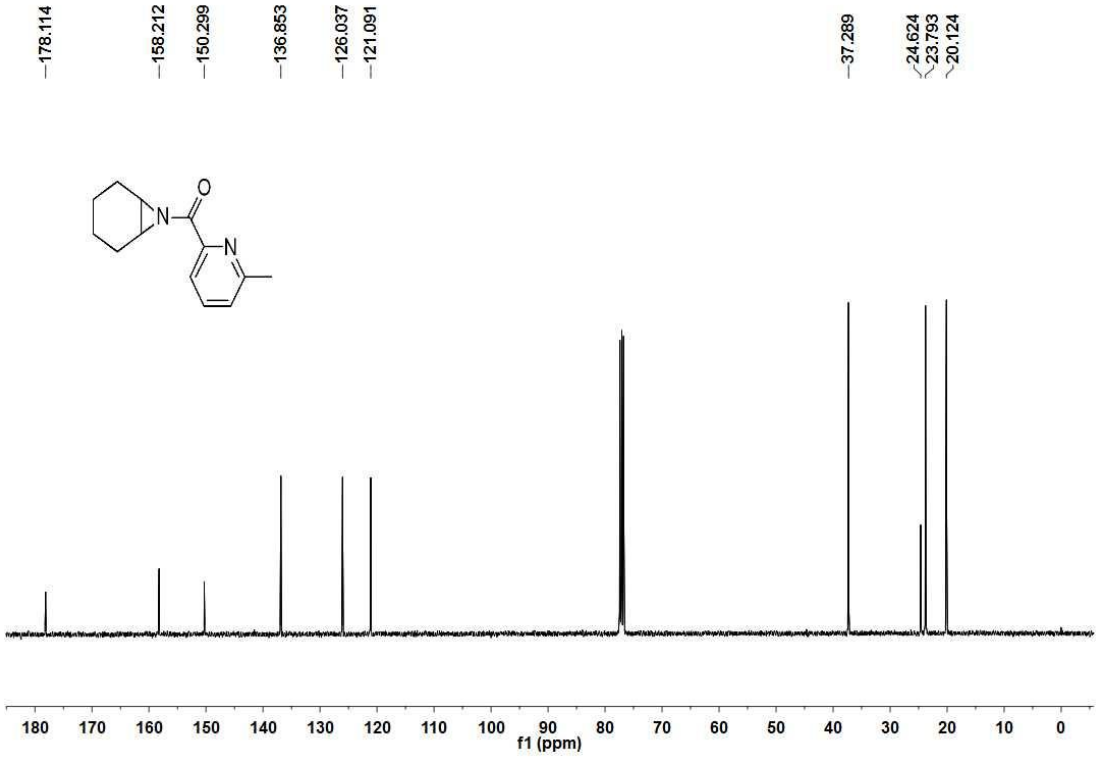
1d



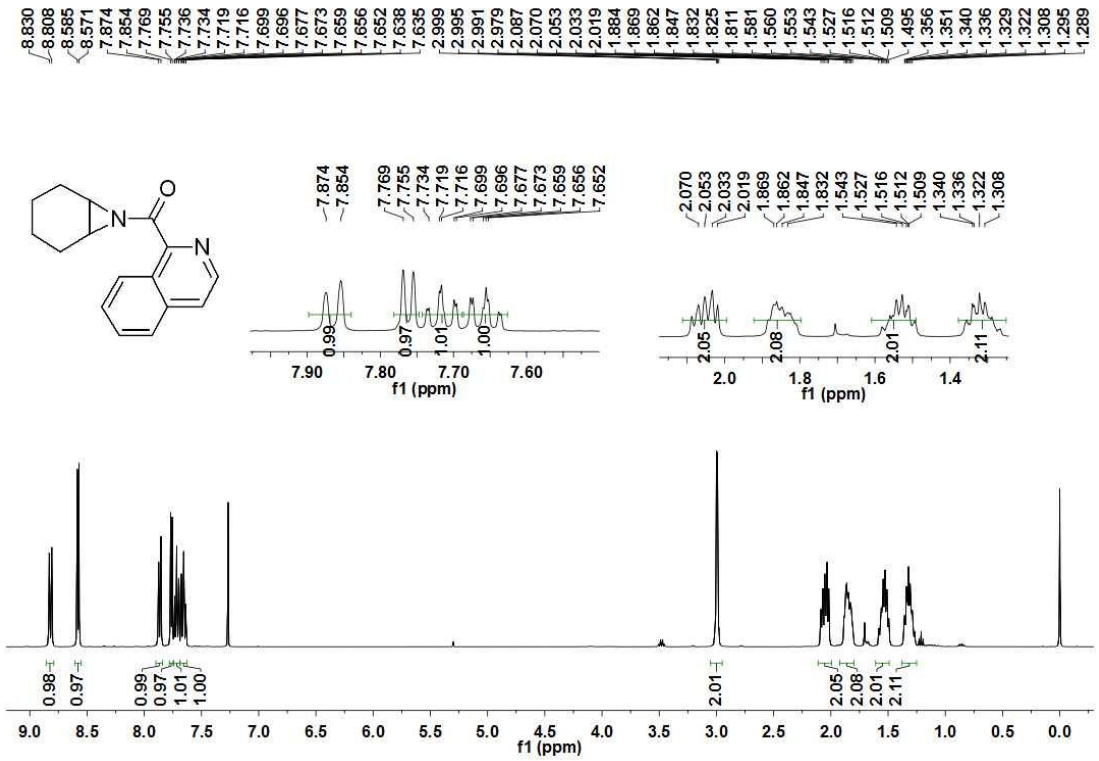

176.586
149.045
148.313
136.425
135.116
124.809
37.491
23.728
20.046
O
N
N
Cl
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

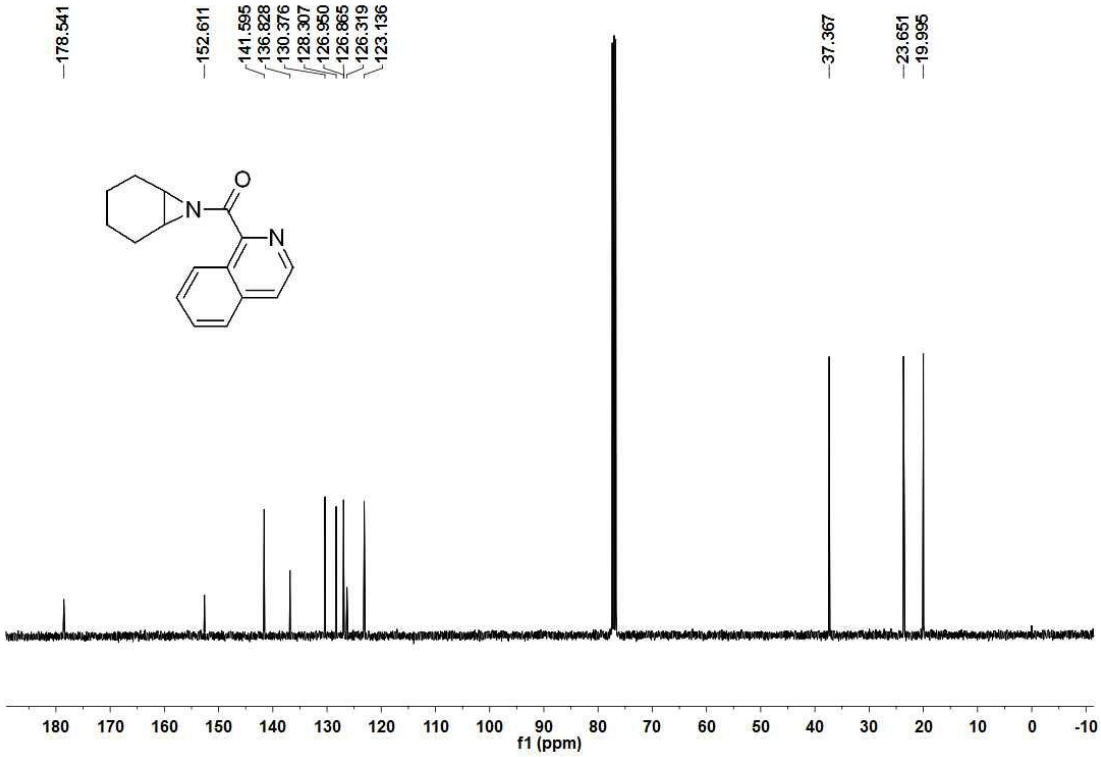
1e


7.898
7.879
7.711
7.691
7.672
7.296
7.278
2.845
2.841
2.837
2.623
2.237
2.221
2.201
2.187
1.927
1.920
1.906
1.891
1.884
1.560
1.544
1.533
1.529
1.374
1.370
1.356
1.342
O
N
N
1.00
1.00
1.10
1.97
3.02
2.04
2.04
2.19
2.05
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)

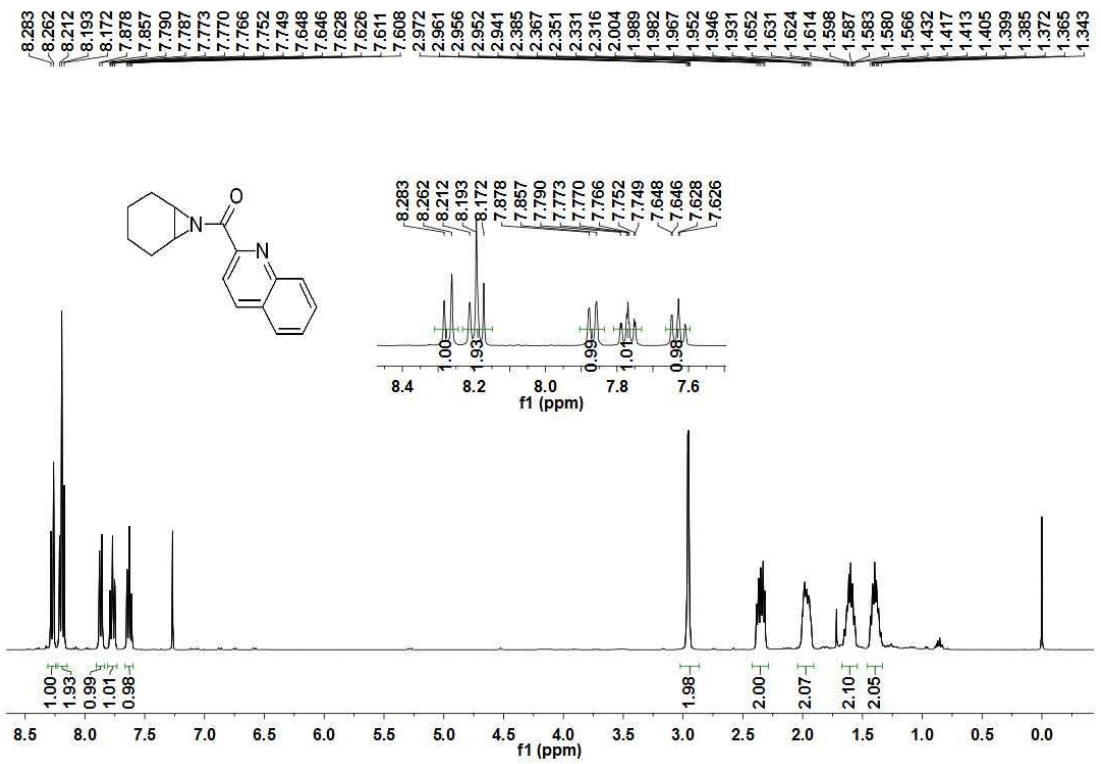

178.114
158.212
150.299
136.853
126.037
121.091
37.289
24.624
23.793
20.124
O
N
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

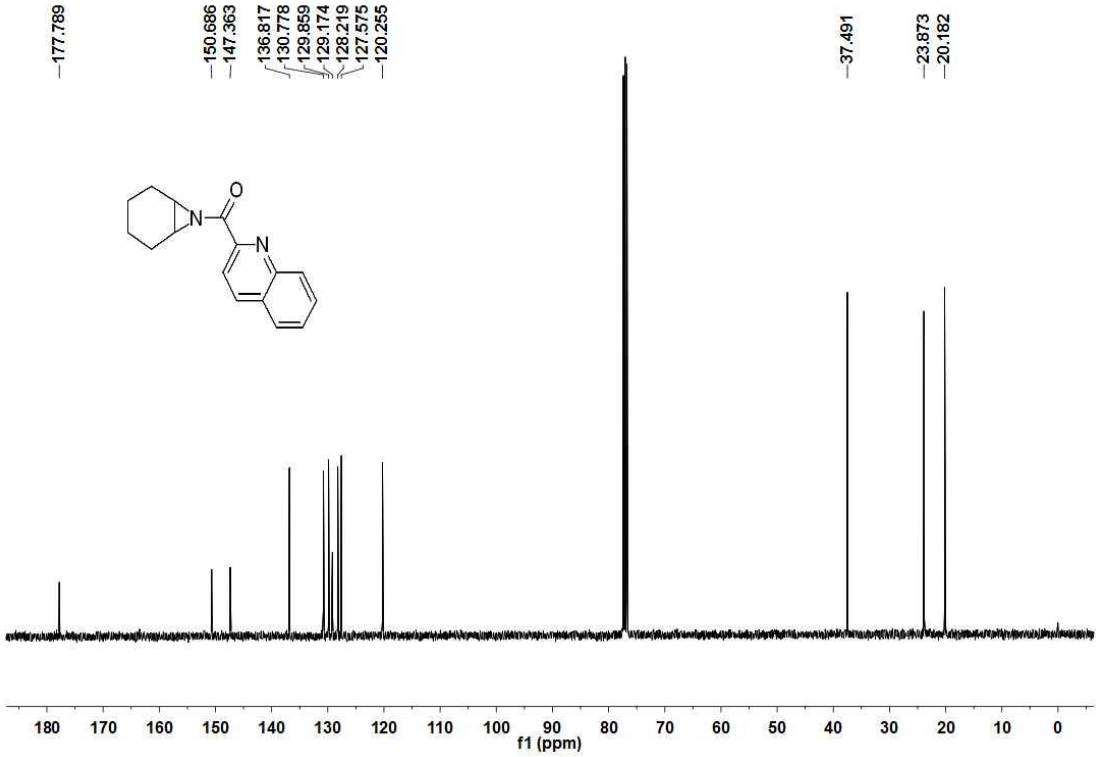
1h


8.830
8.808
8.585
8.571
7.874
7.854
7.769
7.755
7.736
7.734
7.719
7.716
7.699
7.696
7.677
7.673
7.659
7.656
7.652
7.638
7.635
2.999
2.995
2.991
2.979
2.087
2.070
2.053
2.033
2.019
1.884
1.869
1.862
1.847
1.832
1.825
1.811
1.581
1.560
1.553
1.543
1.527
1.516
1.512
1.509
1.495
1.356
1.351
1.340
1.336
1.329
1.322
1.308
1.295
1.289
O
N
N
0.99
0.97
1.01
1.00
7.90 7.80 7.70 7.60
f1 (ppm)
2.05
2.08
2.01
2.11
2.0 1.8 1.6 1.4
f1 (ppm)
0.98
0.97
0.99
0.97
1.01
1.00
2.01
2.05
2.08
2.01
2.11
9.0 8.5 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)

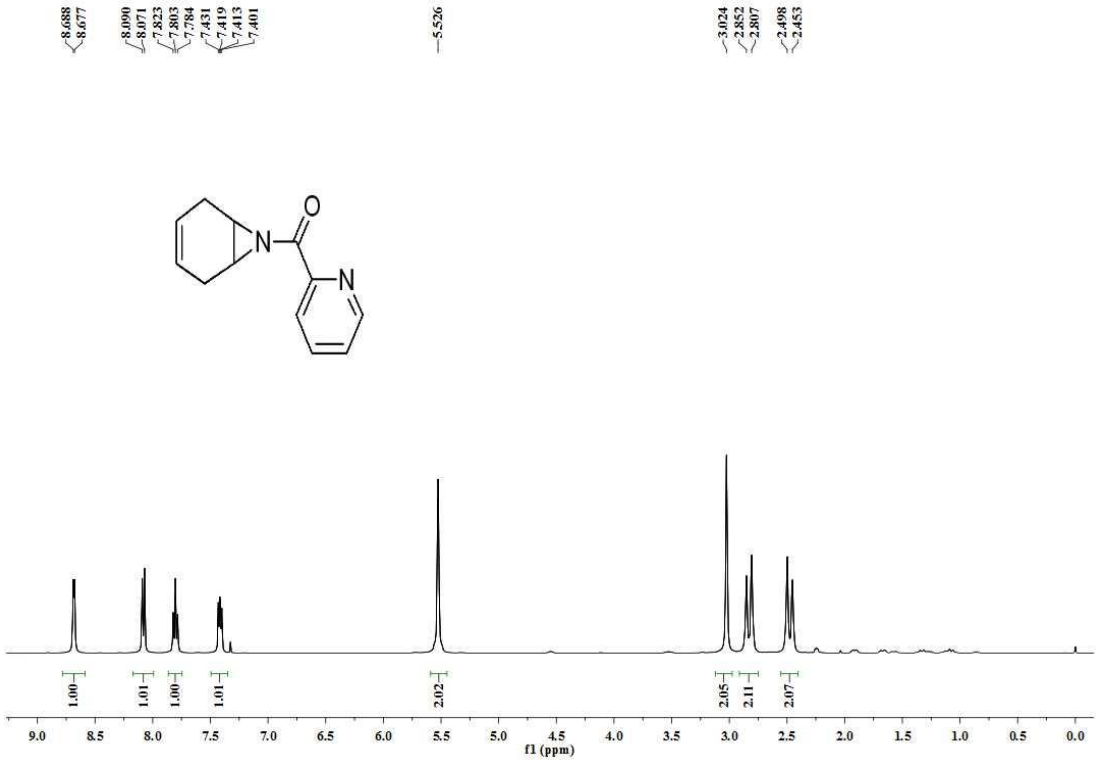

178.541
152.611
141.595
136.828
130.376
128.307
126.950
126.865
126.319
123.136
37.367
23.651
19.995
O
N
N
f1 (ppm)

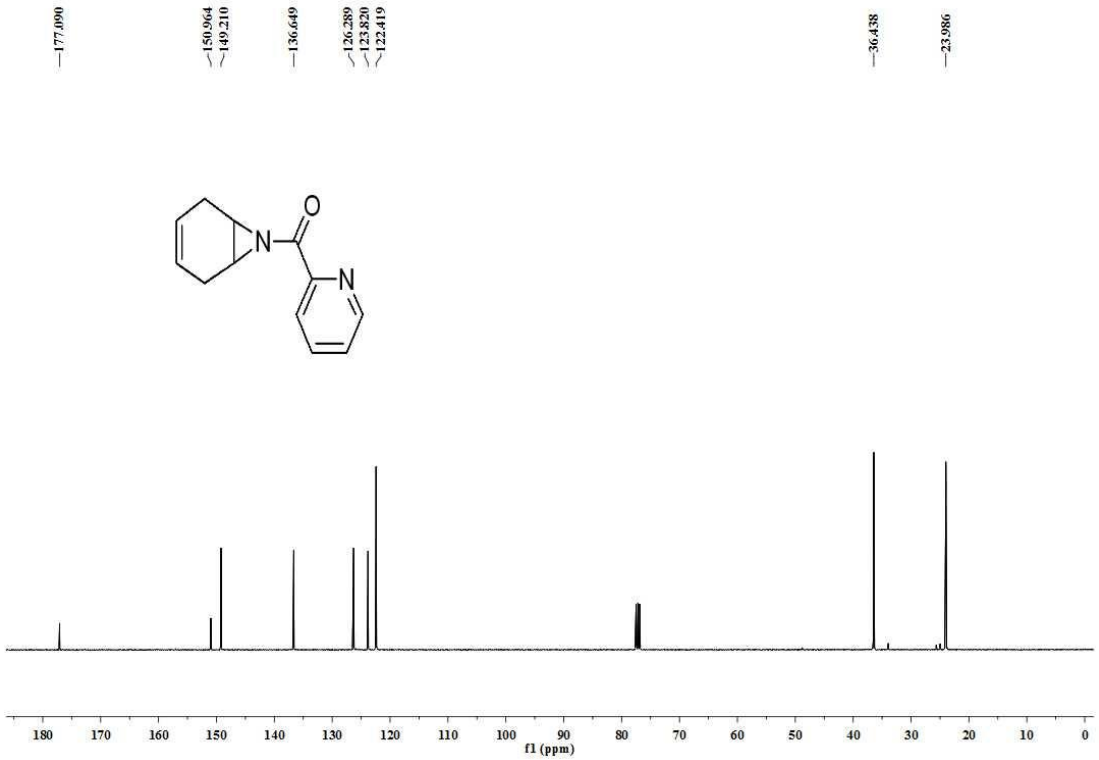
1i


8.283
8.262
8.212
8.193
8.172
7.878
7.857
7.790
7.787
7.773
7.770
7.766
7.752
7.749
7.648
7.646
7.628
7.626
7.611
7.608
2.972
2.961
2.956
2.952
2.941
2.385
2.367
2.351
2.331
2.316
2.004
1.989
1.982
1.967
1.952
1.946
1.931
1.652
1.631
1.624
1.614
1.598
1.587
1.583
1.580
1.566
1.432
1.417
1.413
1.405
1.399
1.385
1.372
1.365
1.343
O
N
N
1.00
1.93
0.99
1.01
0.98
1.98
2.00
2.07
2.10
2.05
f1 (ppm)

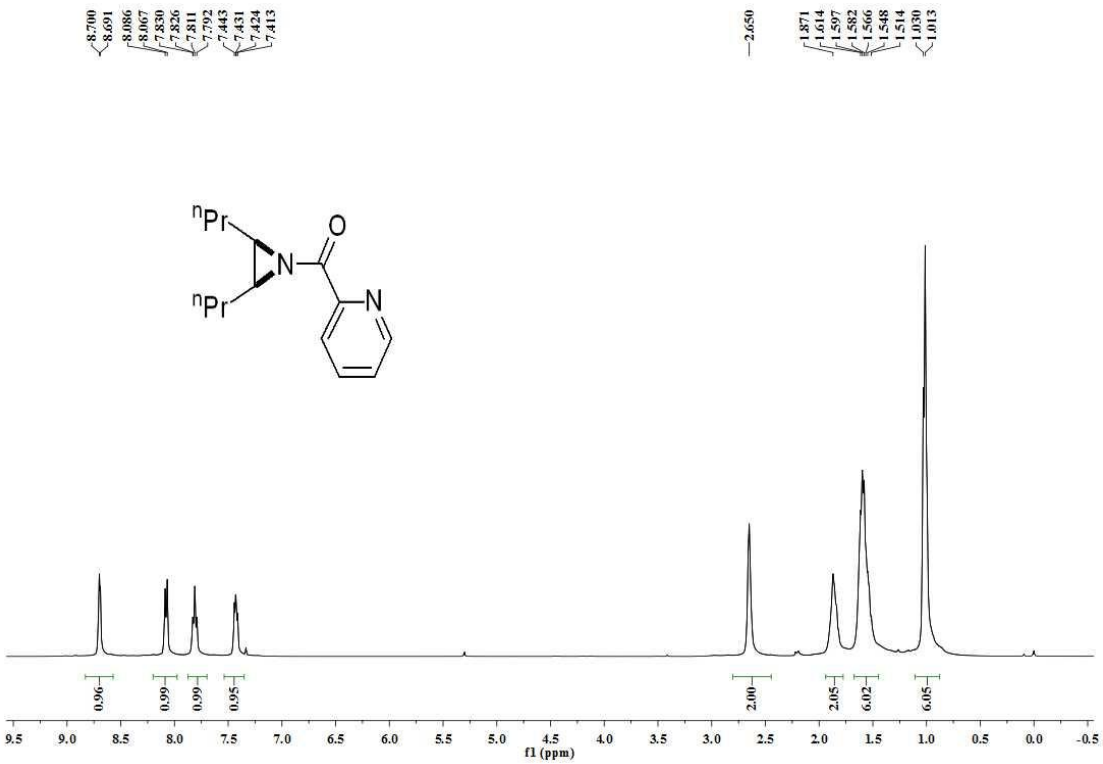

177.789
150.686
147.363
136.817
130.778
129.859
129.174
128.219
127.575
120.255
37.491
23.873
20.182
O
N
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

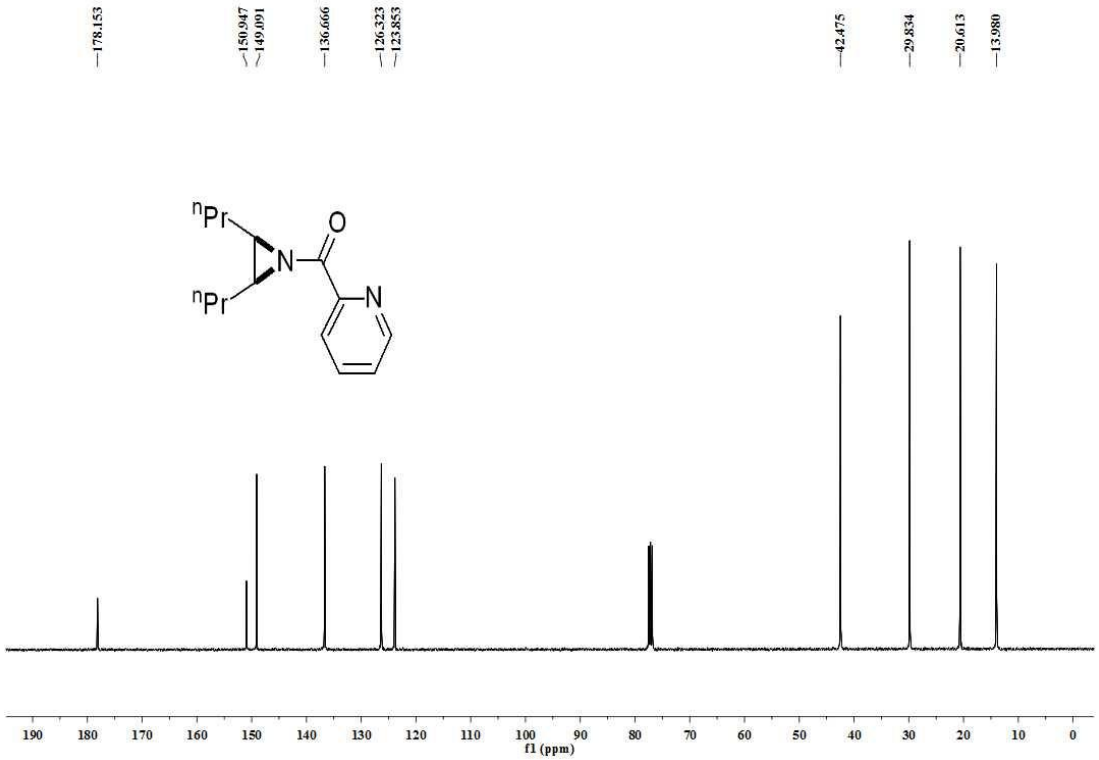
1n


8.688
8.677
8.090
8.071
7.823
7.803
7.784
7.431
7.419
7.413
7.401
5.526
3.024
2.852
2.807
2.498
2.453
O
N
N
1.00
1.01
1.00
1.01
2.02
2.05
2.11
2.07
9.0 8.5 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)

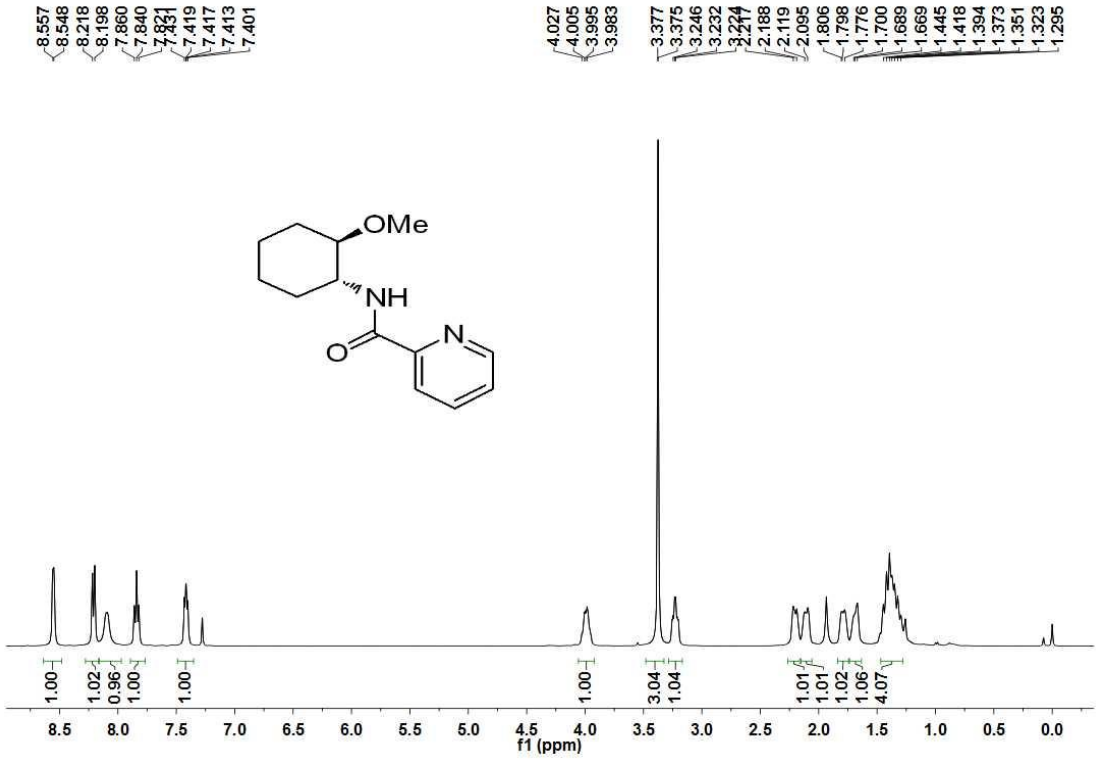

177.090
150.964
149.210
136.649
126.289
123.820
122.419
36.438
23.986
O
N
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

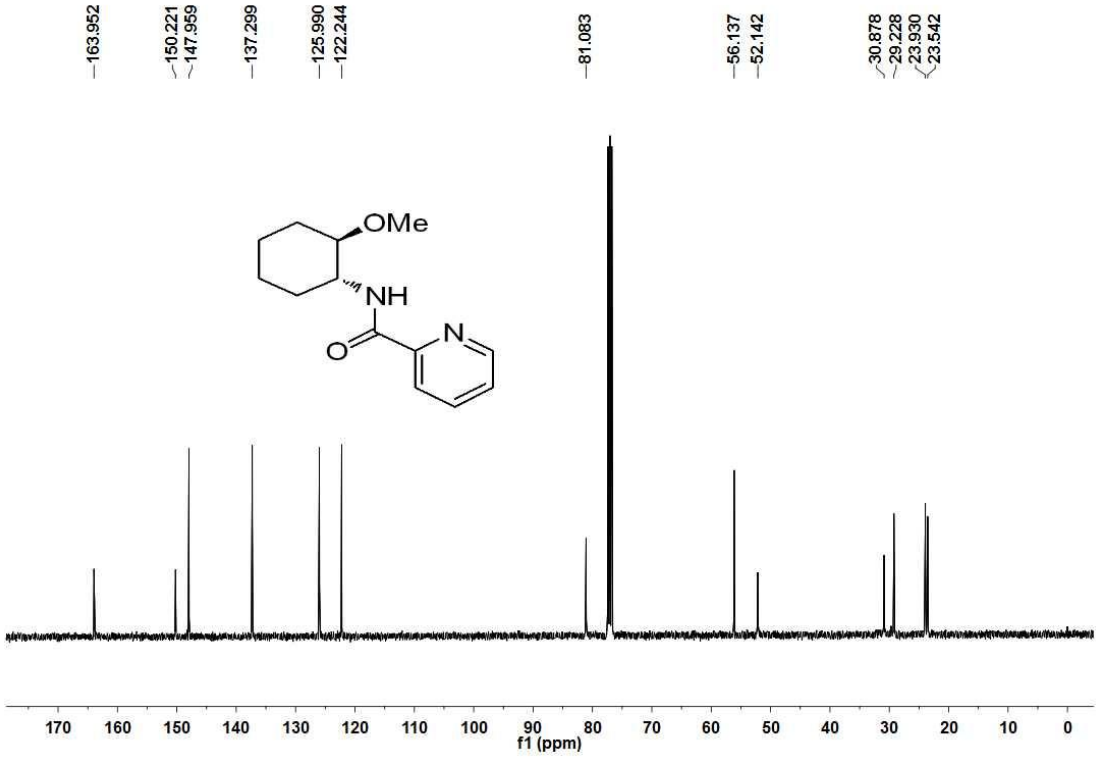
1s


8.700
8.691
8.086
8.067
7.830
7.826
7.811
7.792
7.443
7.431
7.424
7.413
2.650
1.871
1.614
1.597
1.582
1.566
1.548
1.514
1.030
1.013
nPr
nPr
O
N
N
0.96
0.99
0.99
0.95
2.00
2.05
6.02
6.05
9.5 9.0 8.5 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 -0.5
f1 (ppm)

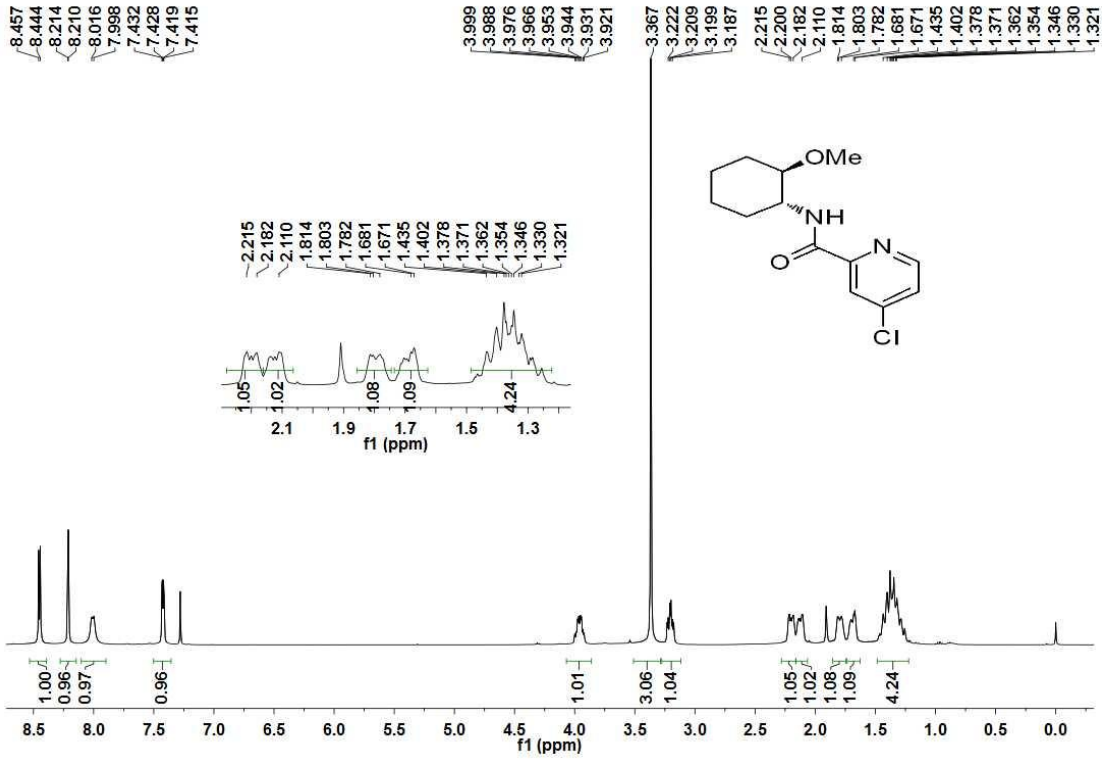

178.153
150.947
149.091
136.666
126.323
123.853
42.475
29.834
20.613
13.980
nPr
nPr
O
N
N
f1 (ppm)

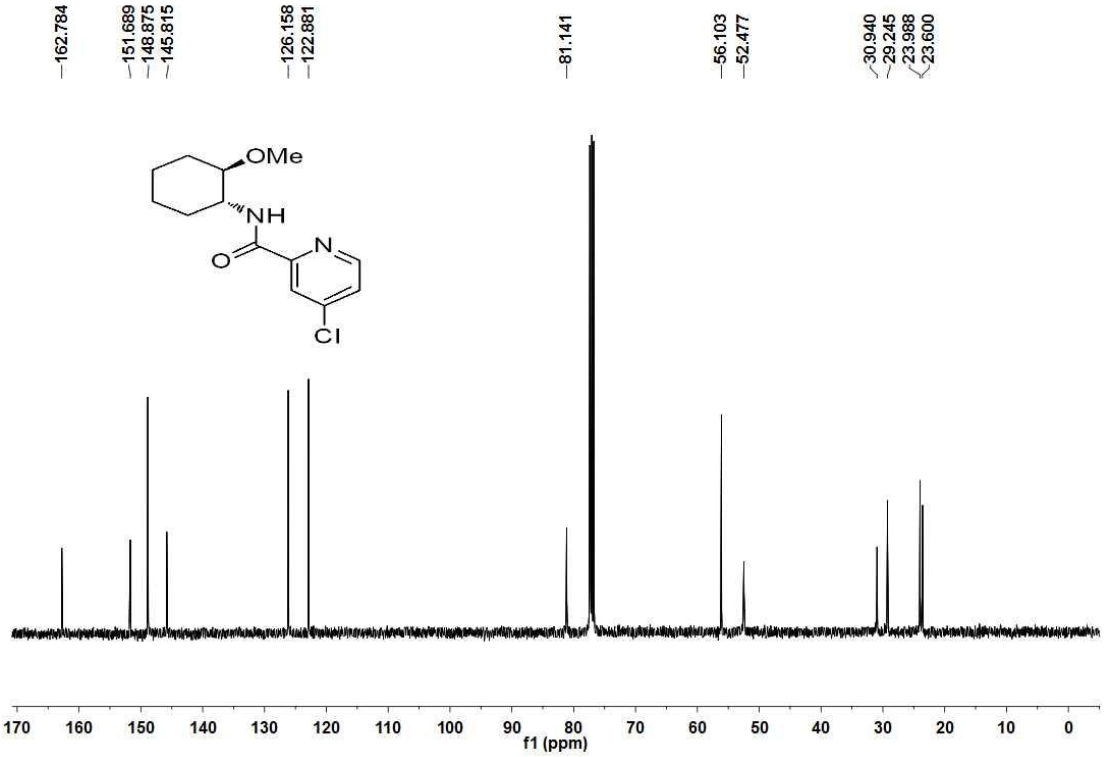
3a


8.557
8.548
8.218
8.198
7.860
7.840
7.821
7.431
7.419
7.417
7.413
7.401
4.027
4.005
3.995
3.983
3.377
3.375
3.246
3.232
2.188
2.119
2.095
1.806
1.798
1.776
1.700
1.689
1.669
1.445
1.418
1.394
1.373
1.351
1.323
1.295
OMe
NH
O
N
1.00
1.02
0.96
1.00
1.00
1.00
3.04
1.04
1.01
1.01
1.02
1.06
4.07
f1 (ppm)

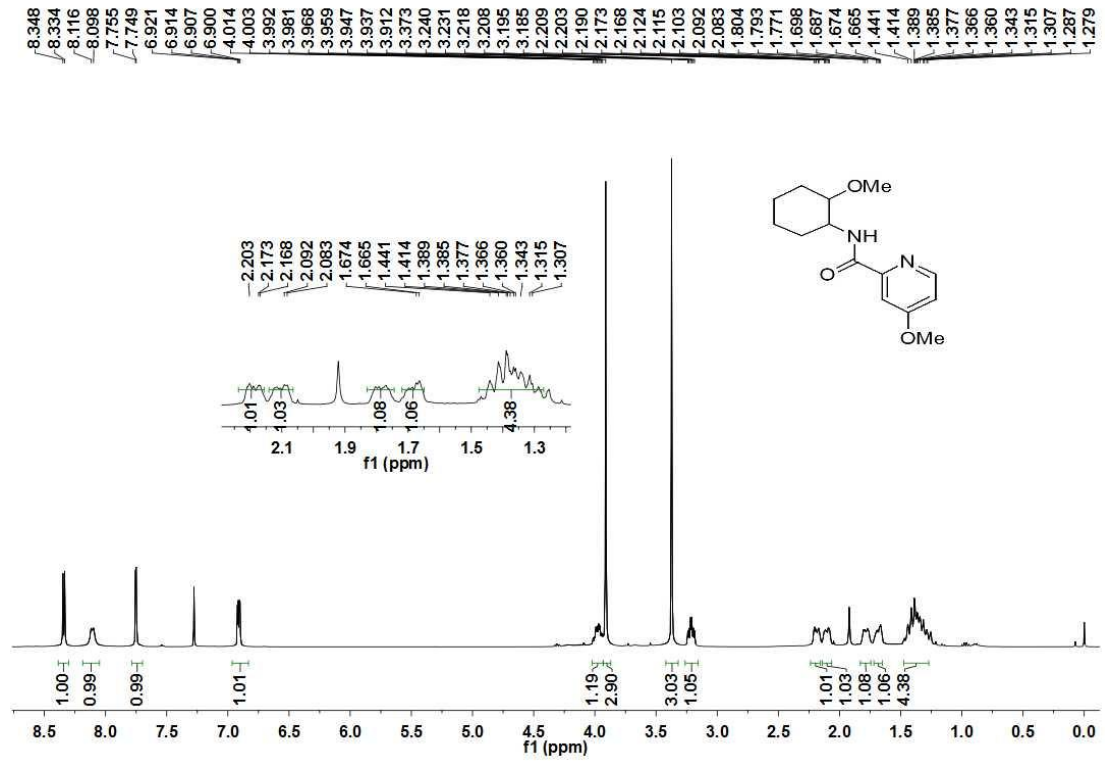

163.952
150.221
147.959
137.299
125.990
122.244
81.083
56.137
52.142
30.878
29.228
23.930
23.542
OMe
NH
O
N
f1 (ppm)

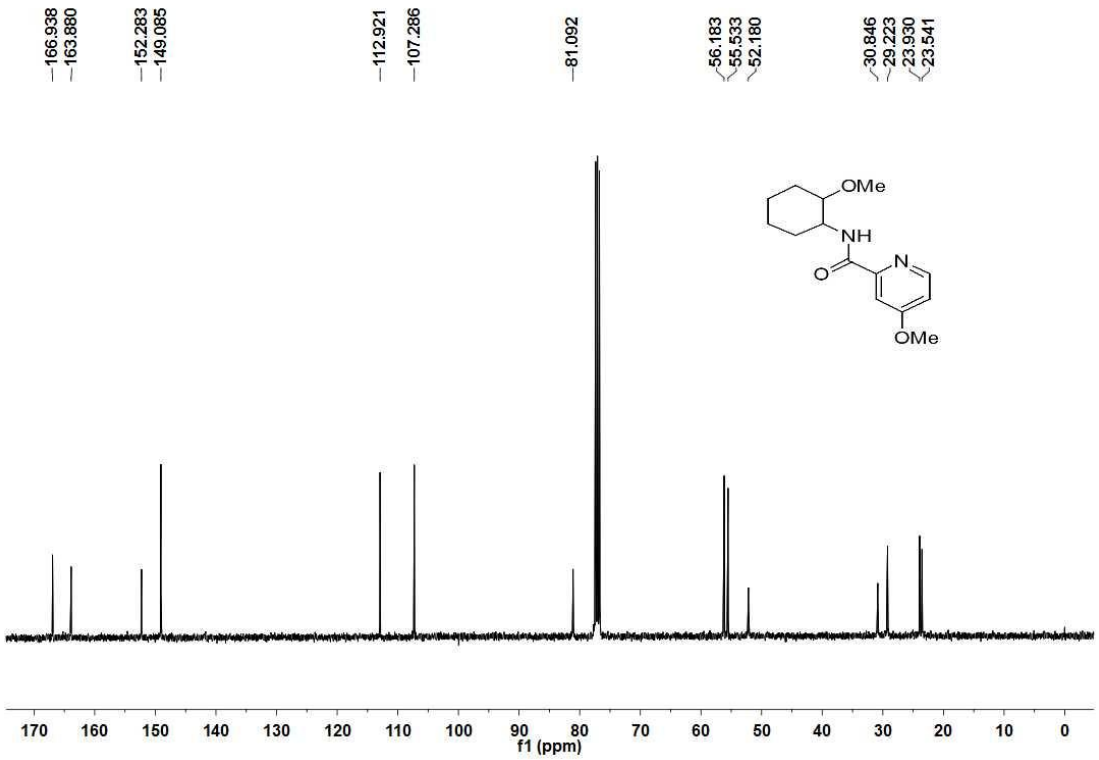
3b


8.457
8.444
8.214
8.210
8.016
7.998
7.432
7.428
7.419
7.415
3.999
3.988
3.976
3.966
3.953
3.944
3.931
3.921
3.367
3.222
3.209
3.199
3.187
2.215
2.200
2.182
2.110
1.814
1.803
1.782
1.681
1.671
1.435
1.402
1.378
1.371
1.362
1.354
1.346
1.330
1.321
OMe
NH
O
N
Cl
1.05
1.02
1.08
1.09
4.24
f1 (ppm)
1.00
0.96
0.97
0.96
1.01
3.06
1.04
1.05
1.02
1.08
1.09
4.24
f1 (ppm)

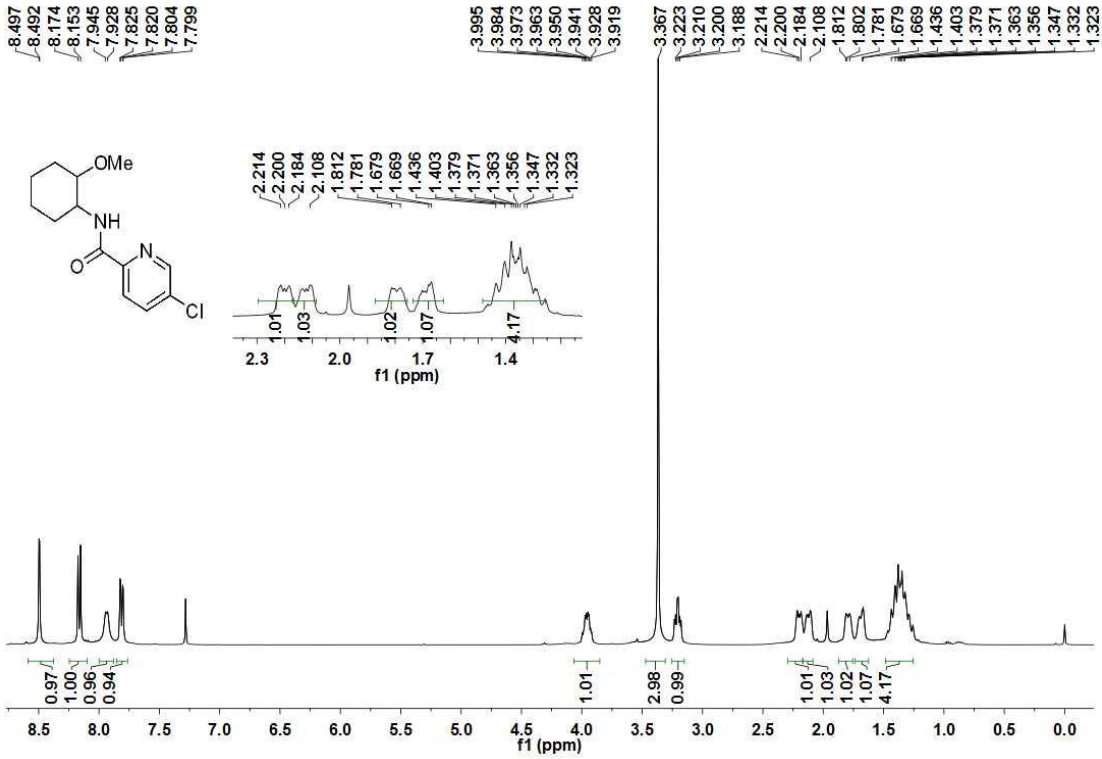

162.784
151.689
148.875
145.815
126.158
122.881
81.141
56.103
52.477
30.940
29.245
23.988
23.600
OMe
NH
O
N
Cl
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

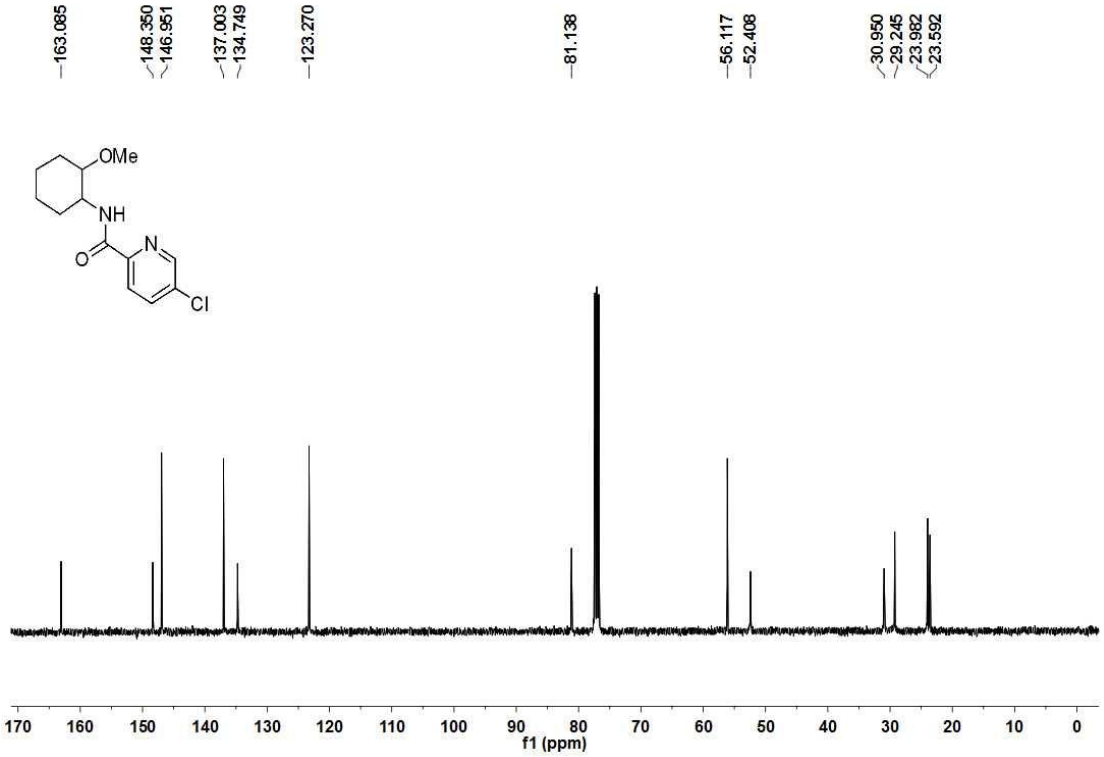
3c


8.348
8.334
8.116
8.098
7.755
7.749
6.921
6.914
6.907
6.900
4.014
4.003
3.992
3.981
3.968
3.959
3.947
3.937
3.912
3.373
3.240
3.231
3.218
3.208
3.195
3.185
2.209
2.203
2.190
2.173
2.168
2.124
2.115
2.103
2.092
2.083
1.804
1.793
1.771
1.698
1.687
1.674
1.665
1.441
1.414
1.389
1.385
1.377
1.366
1.360
1.343
1.315
1.307
1.287
1.279
OMe
NH
O
N
OMe
1.01
1.03
1.08
1.06
4.38
2.1 1.9 1.7 1.5 1.3
f1 (ppm)
1.00
0.99
0.99
1.01
1.19
2.90
3.03
1.05
1.01
1.03
1.08
1.06
4.38
8.5 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)

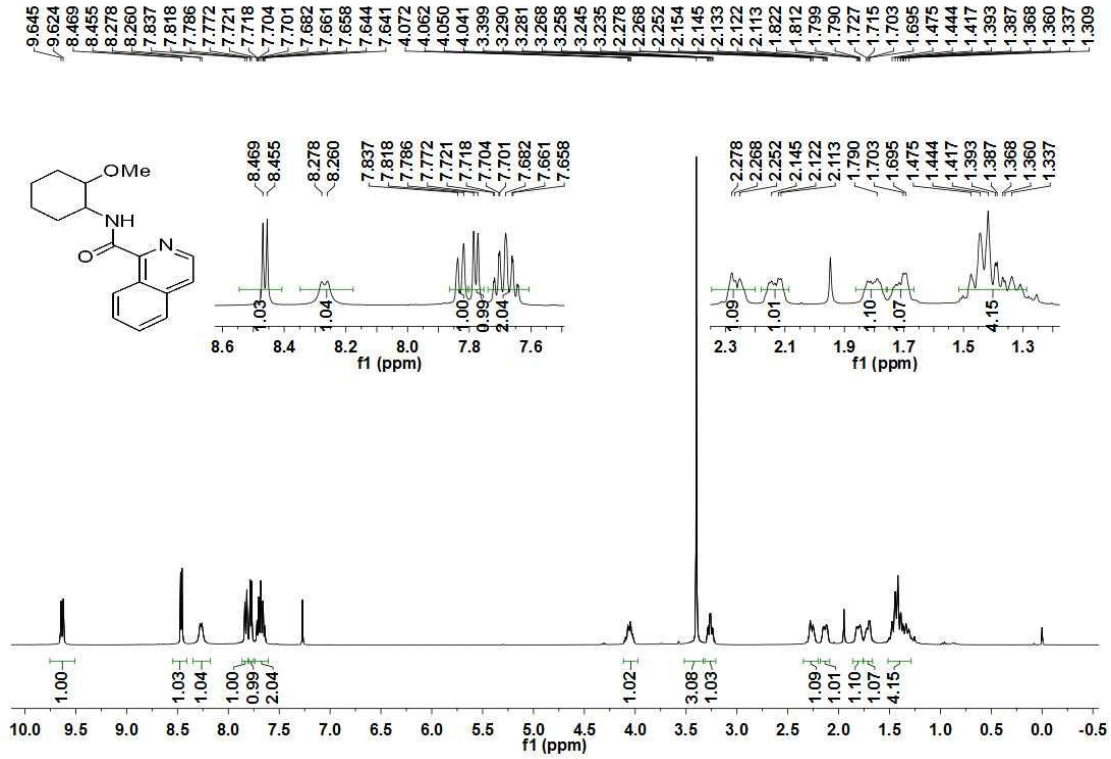

166.938
163.880
152.283
149.085
112.921
107.286
81.092
56.183
55.533
52.180
30.846
29.223
23.930
23.541
OMe
NH
O
N
OMe
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

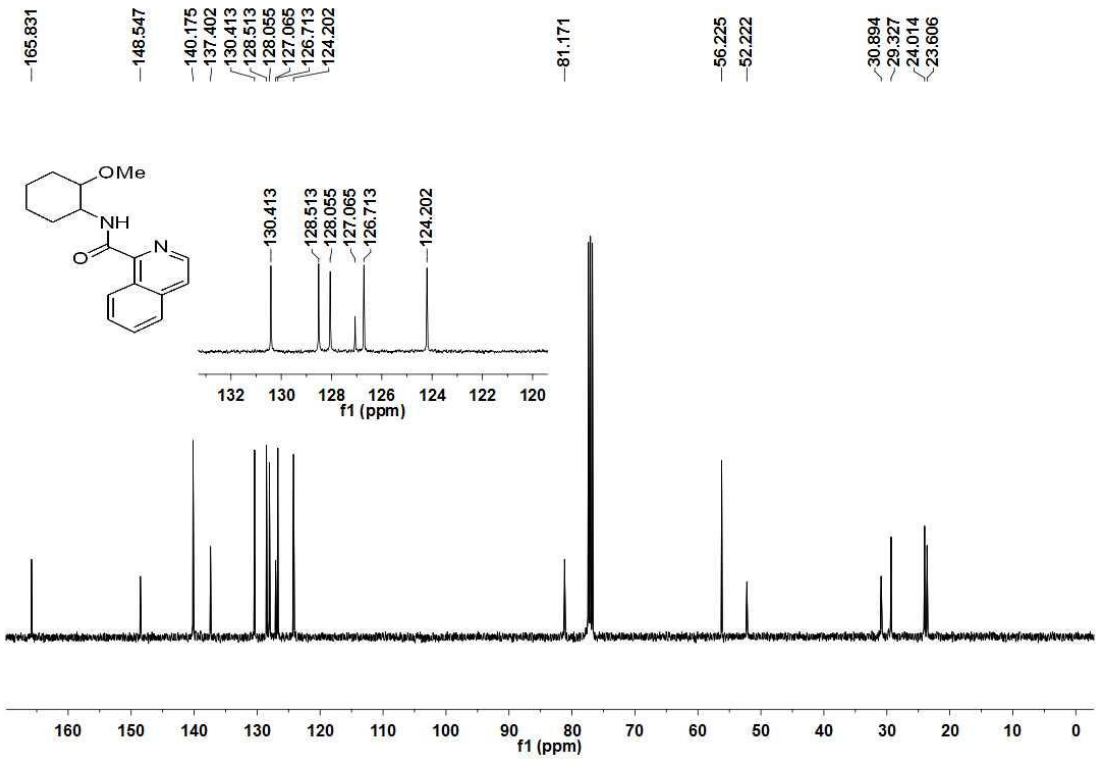
3d


8.497
8.492
8.174
8.153
7.945
7.928
7.825
7.820
7.804
7.799
3.995
3.984
3.973
3.963
3.950
3.941
3.928
3.919
3.367
3.223
3.210
3.200
3.188
2.214
2.200
2.184
2.108
1.812
1.802
1.781
1.679
1.669
1.436
1.403
1.379
1.371
1.363
1.356
1.347
1.332
1.323
OMe
NH
O
N
Cl
1.01
1.03
1.02
1.07
4.17
2.3 2.0 1.7 1.4
f1 (ppm)
0.97
1.00
0.96
0.94
1.01
2.98
0.99
1.01
1.03
1.02
1.07
4.17
8.5 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)

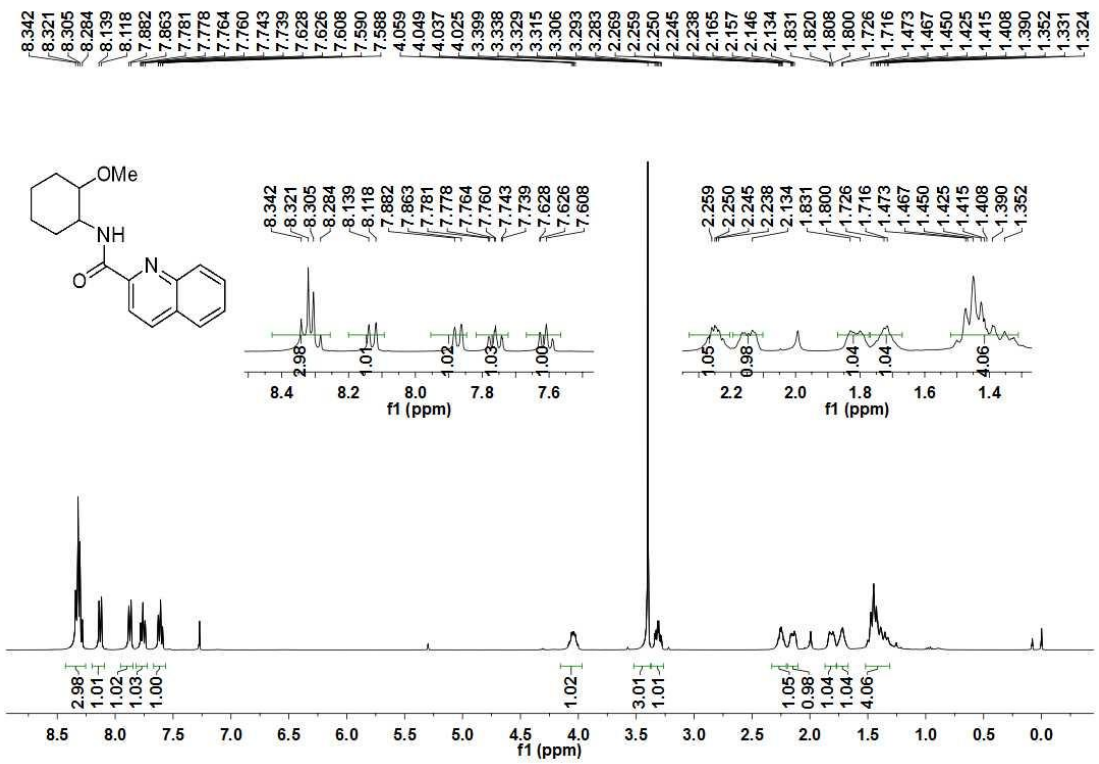

163.085
148.350
146.951
137.003
134.749
123.270
81.138
56.117
52.408
30.950
29.245
23.982
23.592
OMe
NH
O
N
Cl
f1 (ppm)

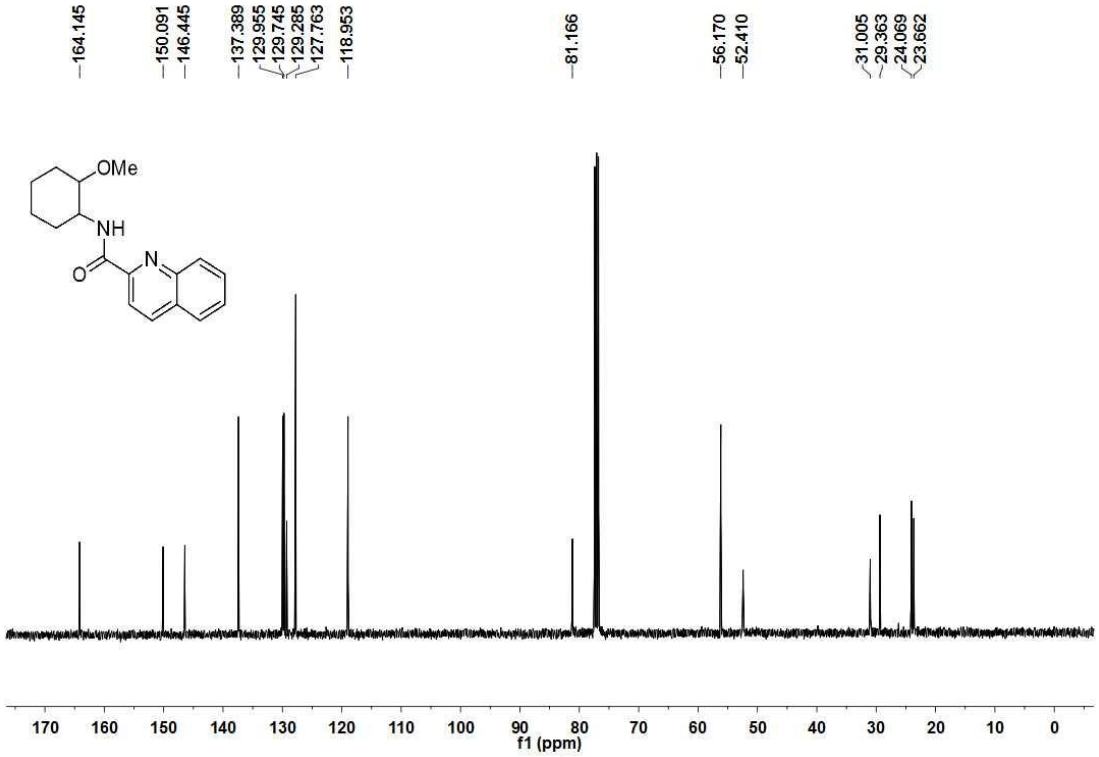
3h


9.645
9.624
8.469
8.455
8.278
8.260
7.837
7.818
7.786
7.772
7.721
7.718
7.704
7.701
7.682
7.661
7.658
7.644
7.641
4.072
4.062
4.050
4.041
3.399
3.290
3.281
3.268
3.258
3.245
3.235
2.278
2.268
2.252
2.154
2.145
2.133
2.122
2.113
1.822
1.812
1.799
1.790
1.727
1.715
1.703
1.695
1.475
1.444
1.417
1.393
1.387
1.368
1.360
1.337
1.309
OMe
NH
O
N
1.03
1.04
1.00
0.99
2.04
1.09
1.01
1.10
1.07
4.15
f1 (ppm)

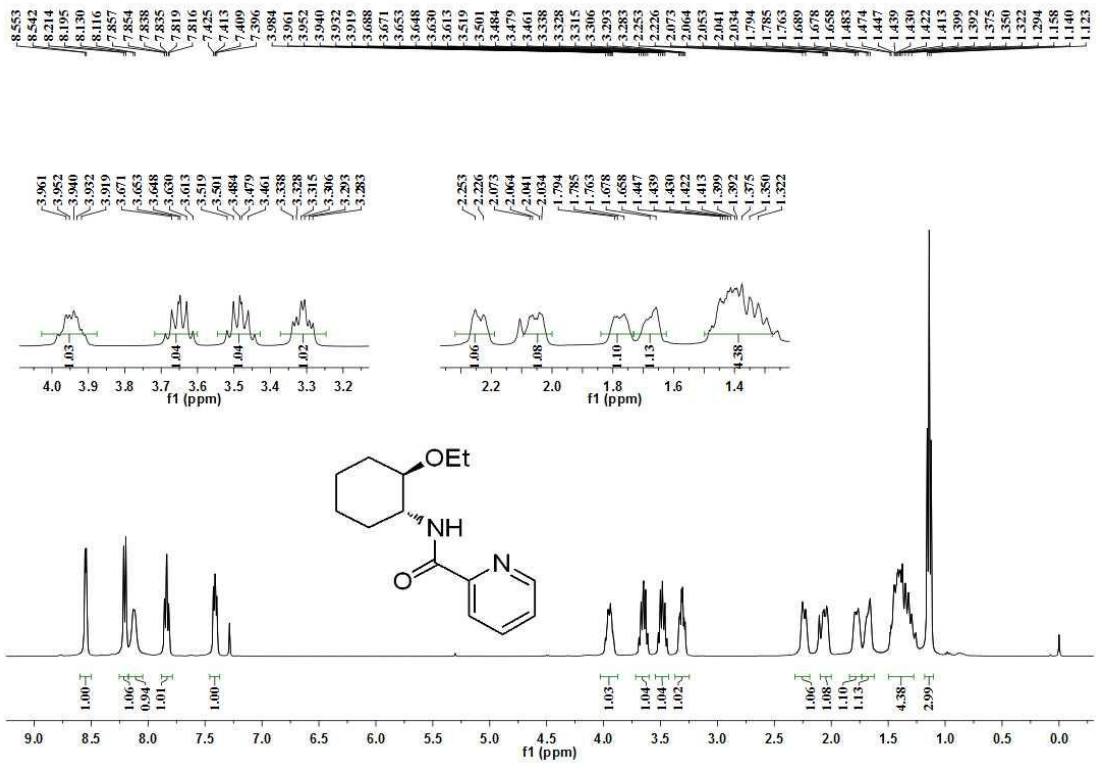

165.831
148.547
140.175
137.402
130.413
128.513
128.055
127.065
126.713
124.202
81.171
56.225
52.222
30.894
29.327
24.014
23.606
OMe
NH
O
N
f1 (ppm)
f1 (ppm)

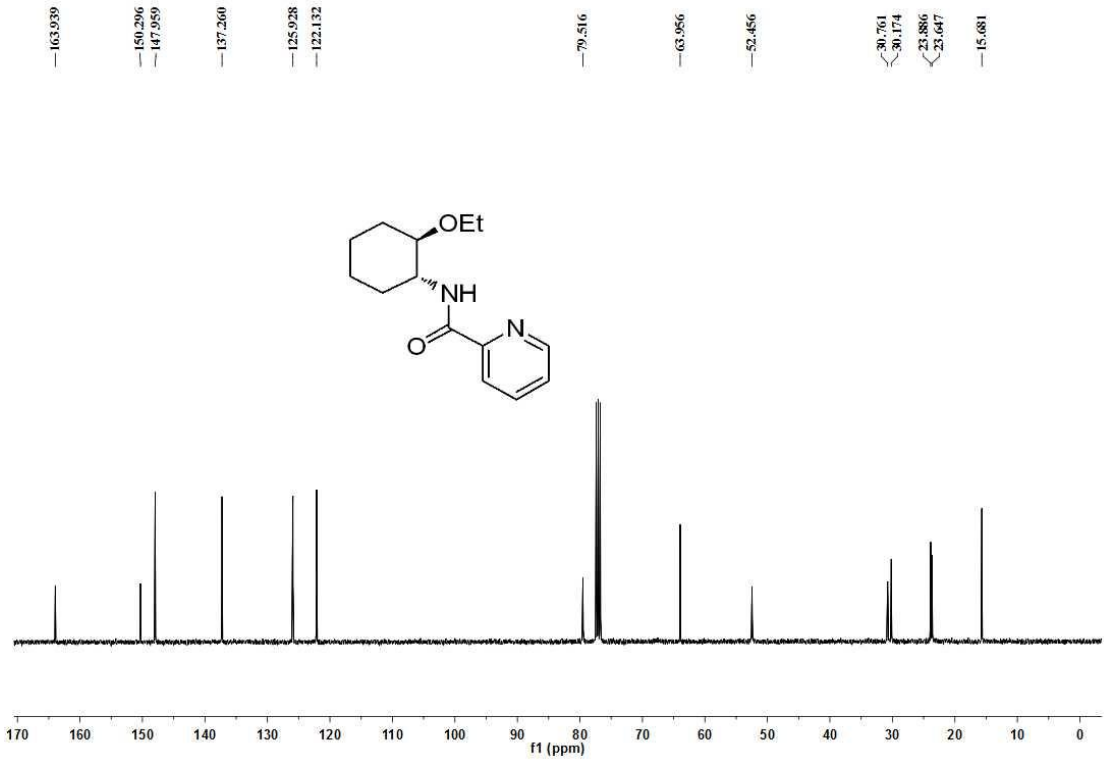
3i


OMe
NH
O
N
f1 (ppm)
f1 (ppm)
f1 (ppm)

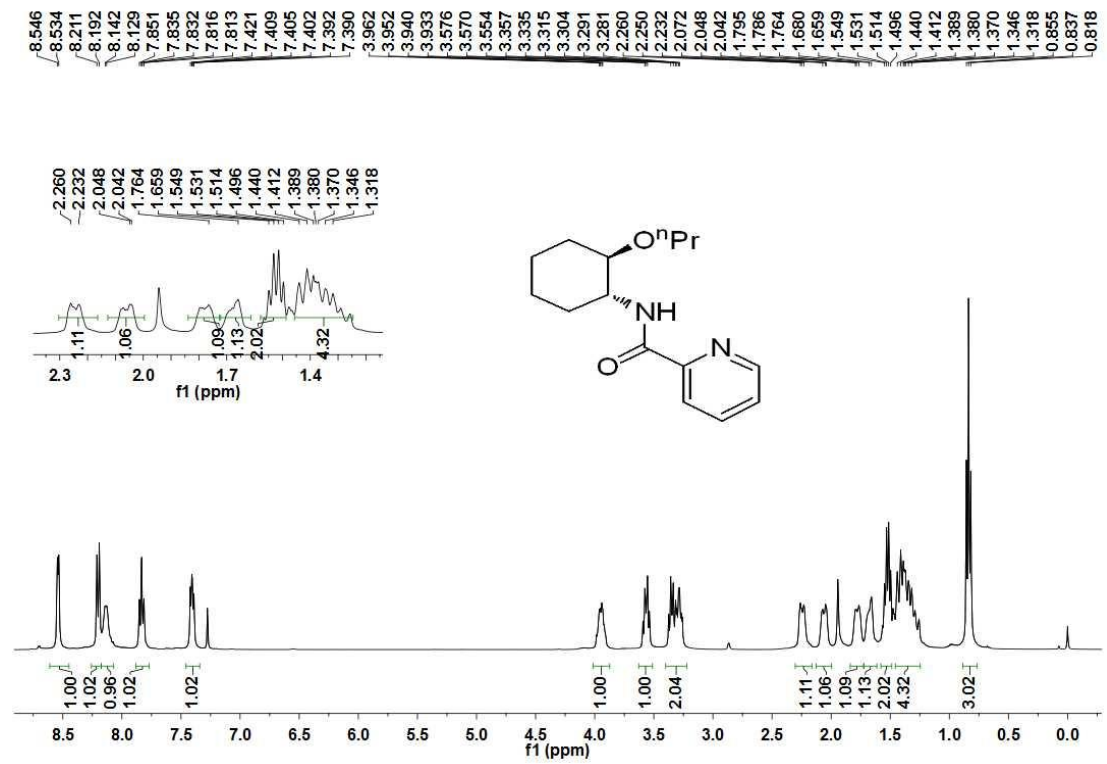

164.145
150.091
146.445
137.389
129.955
129.745
129.285
127.763
118.953
81.166
56.170
52.410
31.005
29.363
24.069
23.662
OMe
NH
O
N
f1 (ppm)

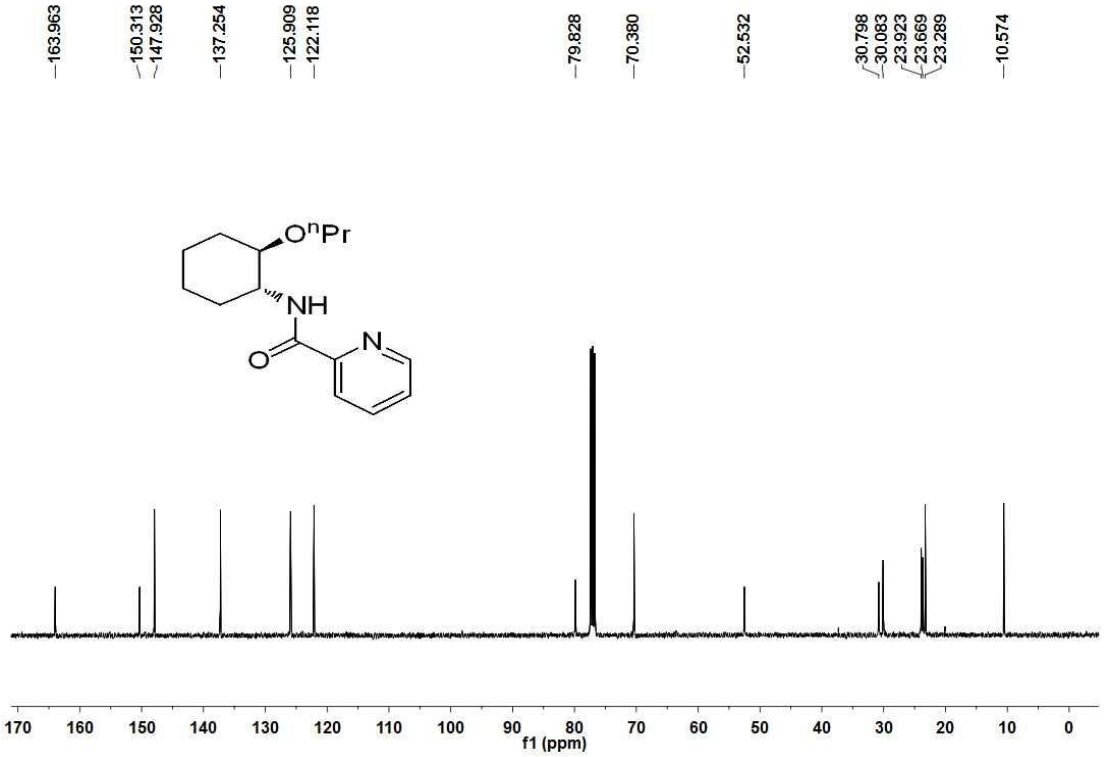
3j


OEt
NH
O
N
f1 (ppm)

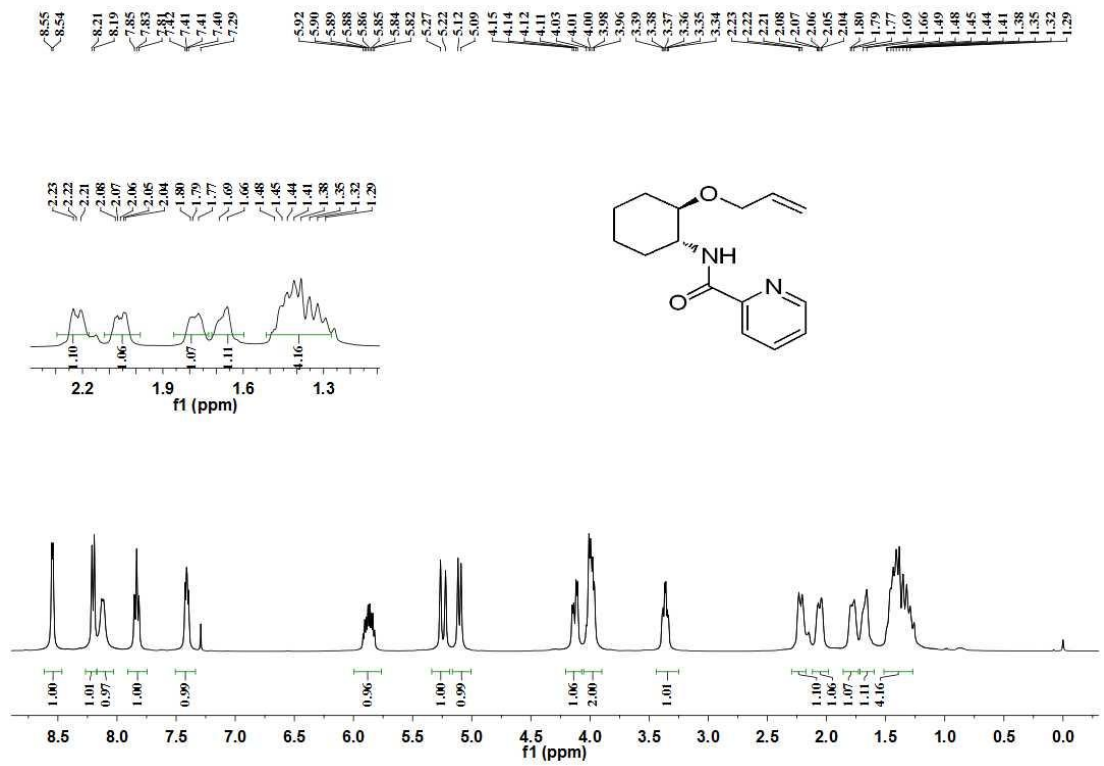

163.939
150.296
147.959
137.260
125.928
122.132
79.516
63.956
52.456
30.761
30.174
23.886
23.647
15.681
OEt
NH
O
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

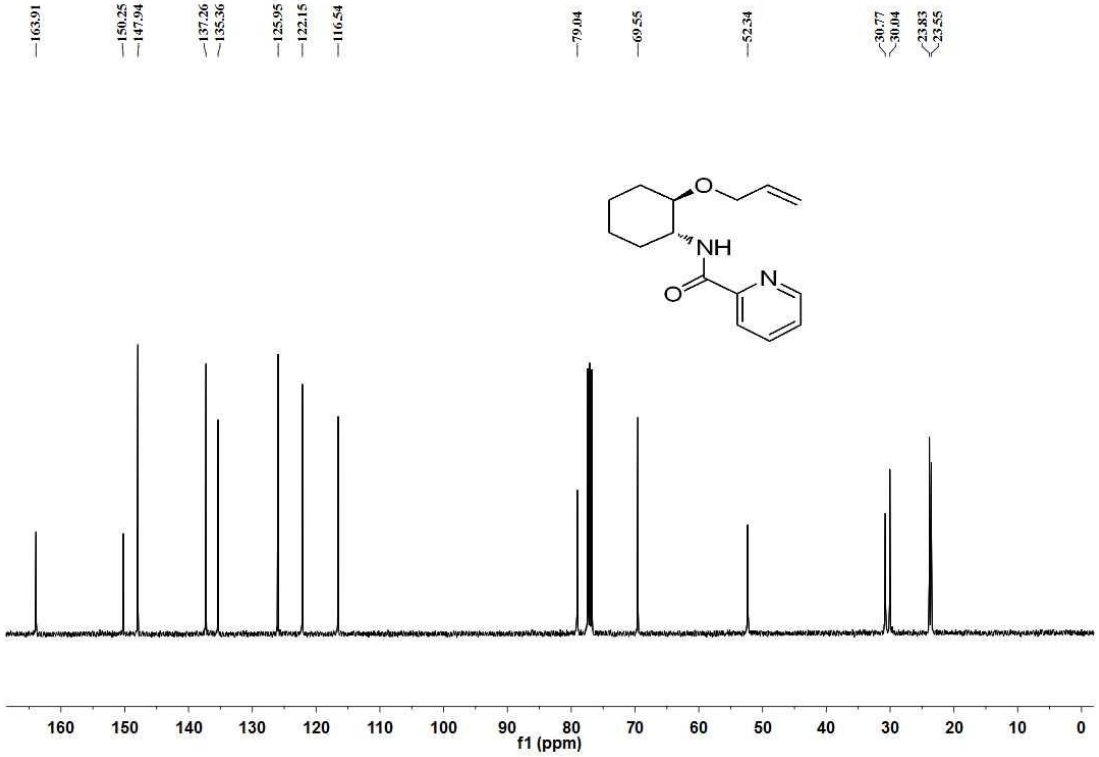
3k


8.546
8.534
8.211
8.192
8.142
8.129
7.851
7.835
7.832
7.816
7.813
7.421
7.409
7.405
7.402
7.392
7.390
3.962
3.952
3.940
3.933
3.576
3.570
3.554
3.357
3.335
3.315
3.304
3.291
3.281
2.260
2.250
2.232
2.072
2.048
2.042
1.795
1.786
1.764
1.680
1.659
1.549
1.531
1.514
1.496
1.440
1.412
1.389
1.380
1.370
1.346
1.318
0.855
0.837
0.818
O^nPr
NH
O
N
1.00
1.02
0.96
1.02
1.02
1.00
1.00
2.04
1.11
1.06
1.09
1.13
2.02
4.32
3.02
8.5 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)
2.3 2.0 1.7 1.4
f1 (ppm)

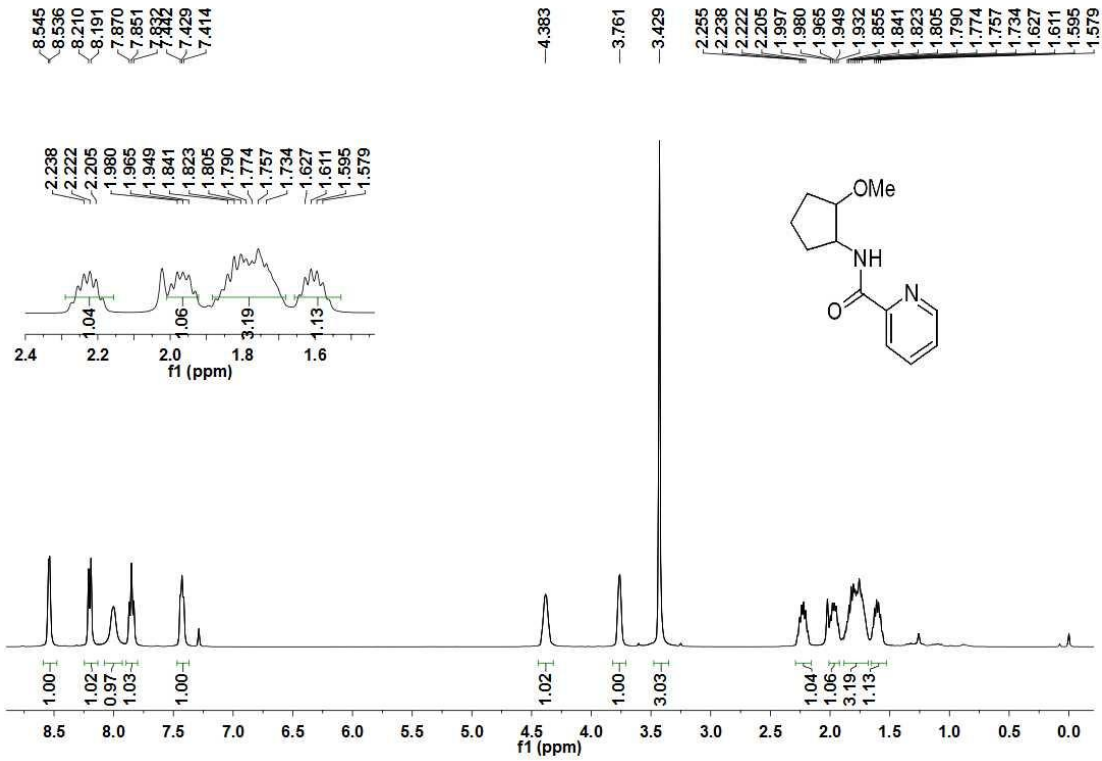

163.963
150.313
147.928
137.254
125.909
122.118
79.828
70.380
52.532
30.798
30.083
23.923
23.669
23.289
10.574
O^nPr
NH
O
N
f1 (ppm)

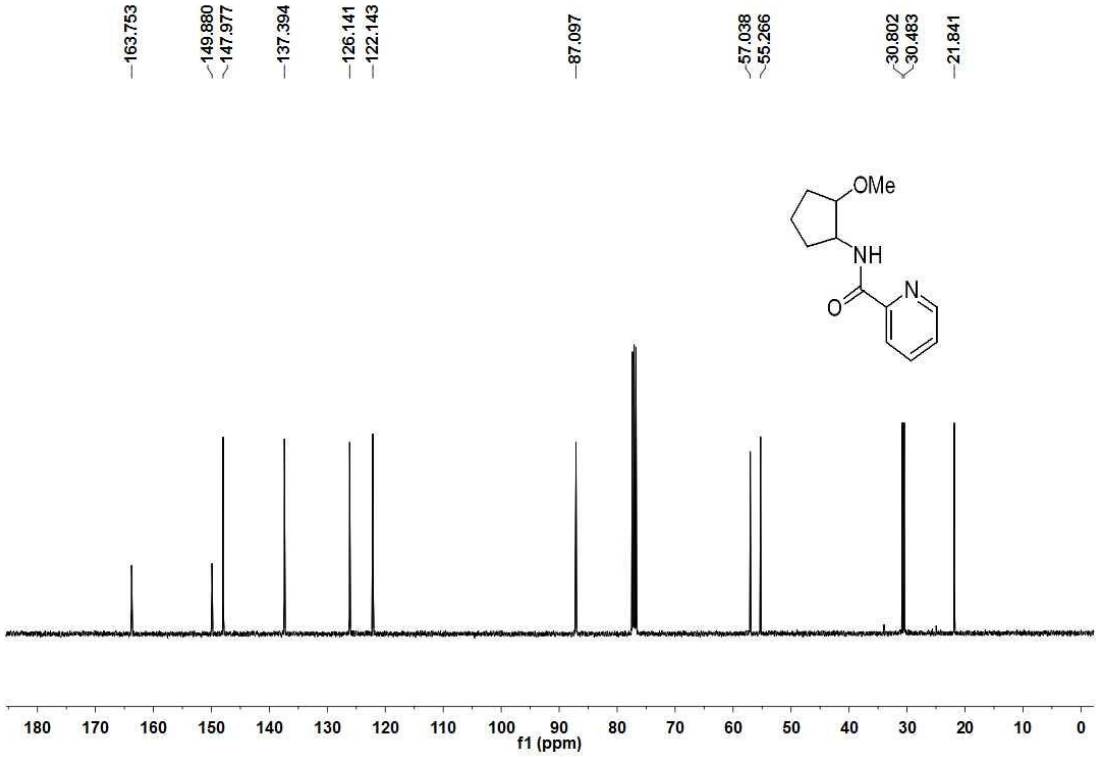
3l


f1 (ppm)
O
NH
O
N
f1 (ppm)

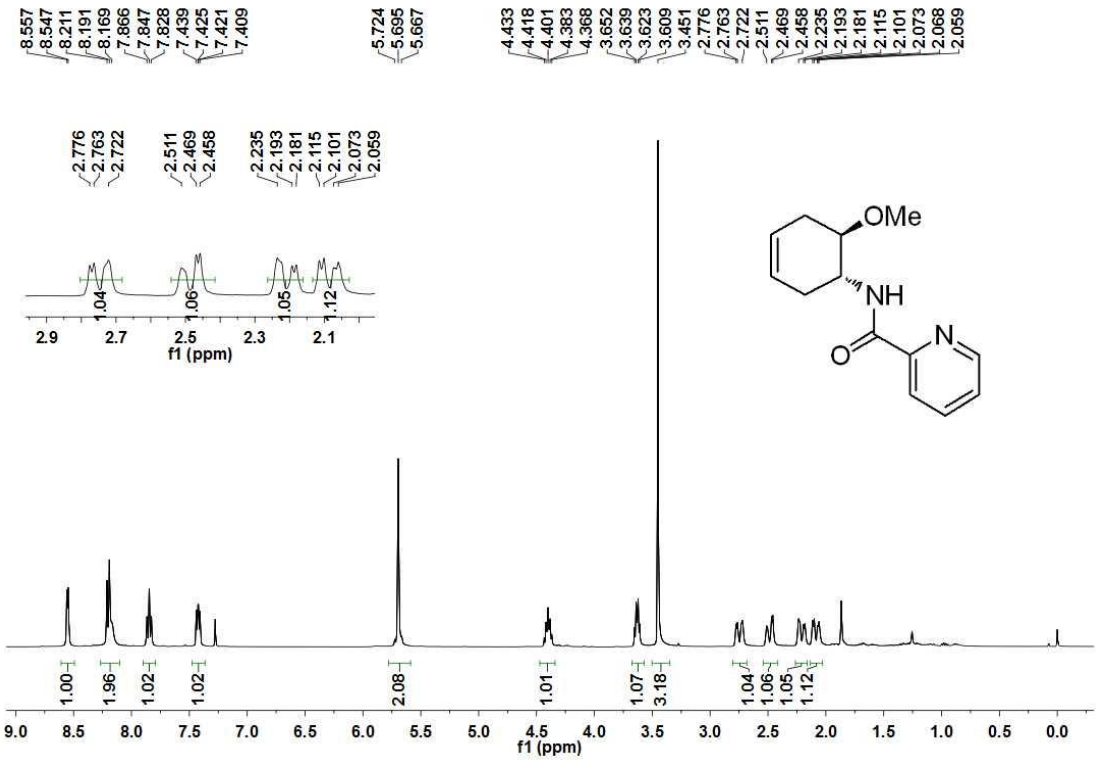

163.91
150.25
147.94
137.26
135.36
125.95
122.15
116.54
79.04
69.55
52.34
30.77
30.04
23.83
23.55
O
NH
N
O
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

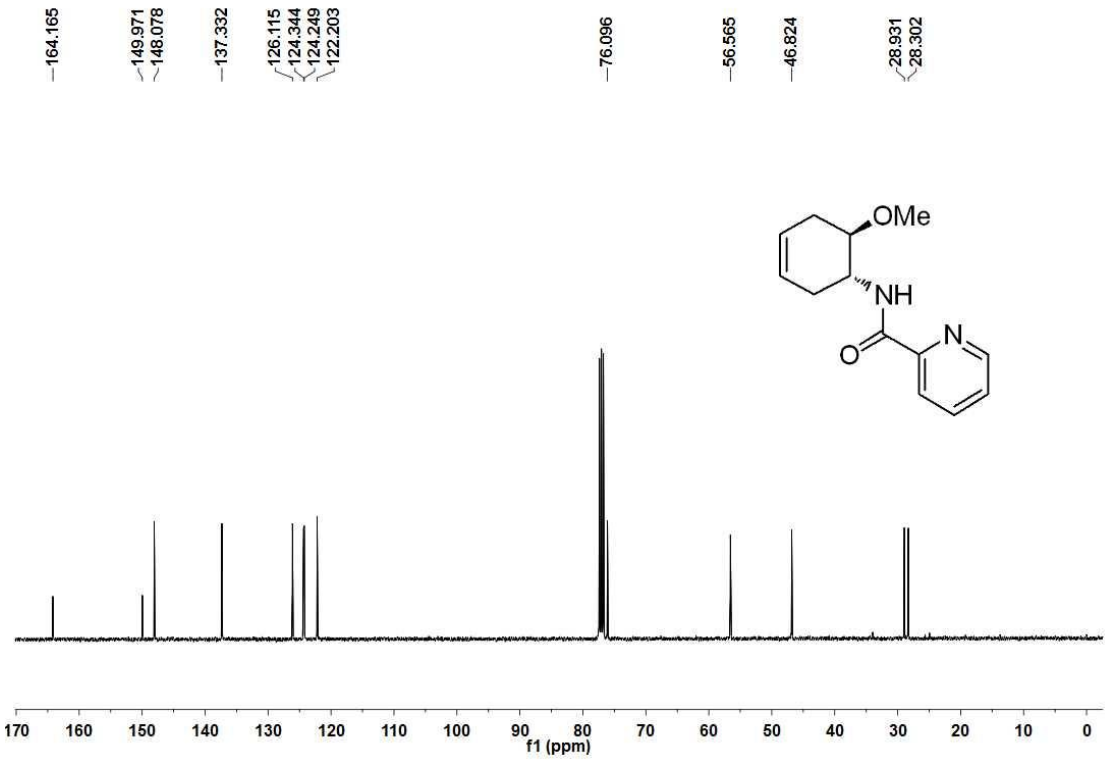
3m


8.545
8.536
8.210
8.191
7.870
7.851
7.832
7.442
7.429
7.414
4.383
3.761
3.429
2.255
2.238
2.222
2.205
1.997
1.980
1.965
1.949
1.932
1.855
1.841
1.823
1.805
1.790
1.774
1.757
1.734
1.627
1.611
1.595
1.579
OMe
NH
N
O
1.04
1.06
3.19
1.13
2.4 2.2 2.0 1.8 1.6
f1 (ppm)
1.00
1.02
0.97
1.03
1.00
1.02
1.00
3.03
1.04
1.06
3.19
1.13
8.5 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)

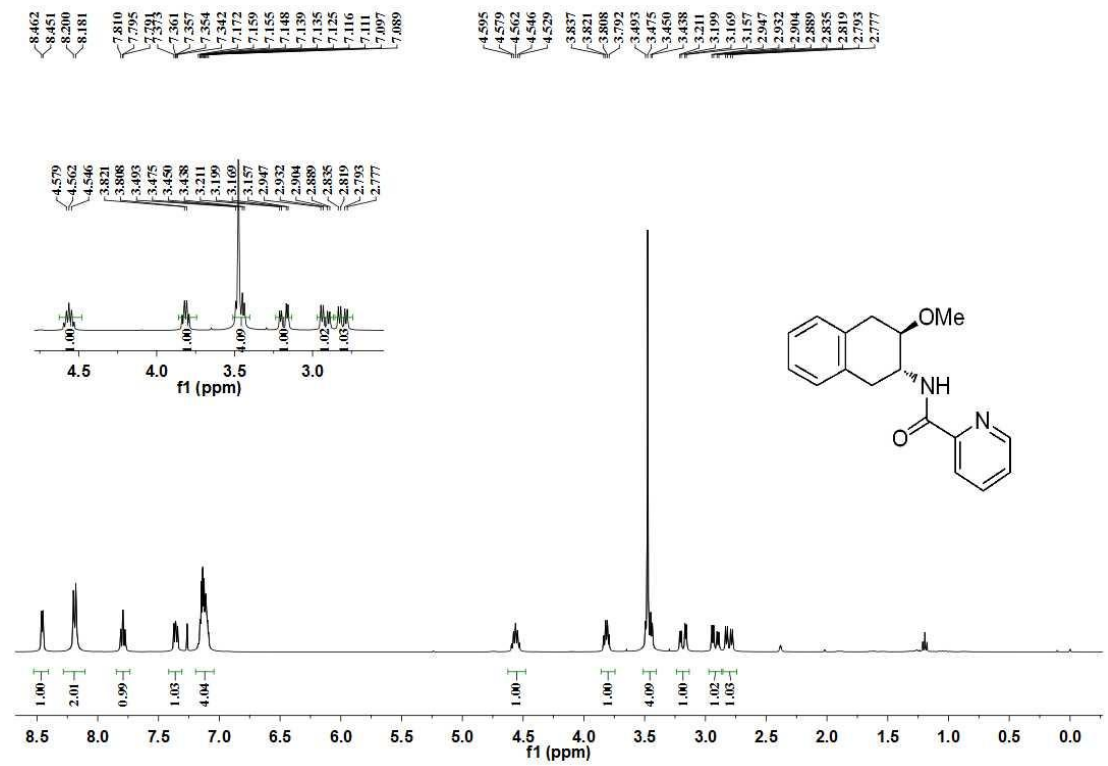

163.753
149.880
147.977
137.394
126.141
122.143
87.097
57.038
55.266
30.802
30.483
21.841
OMe
NH
O
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

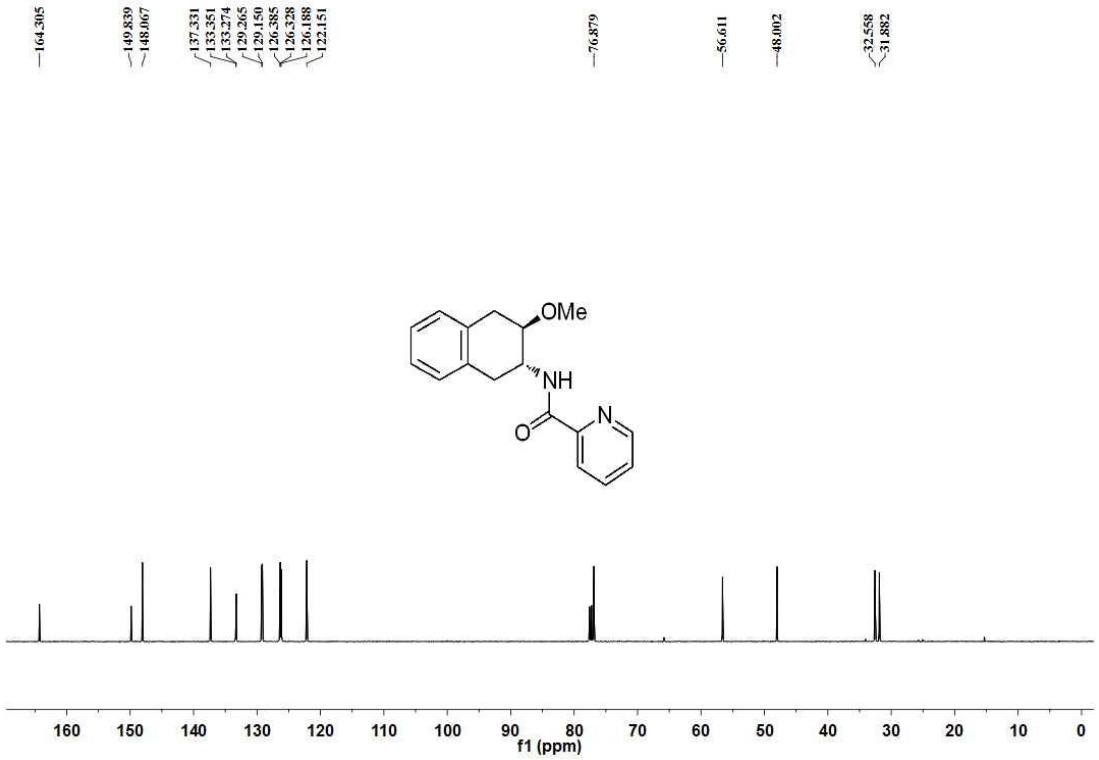
3n


8.557
8.547
8.211
8.191
8.169
7.866
7.847
7.828
7.439
7.425
7.421
7.409
5.724
5.695
5.667
4.433
4.418
4.401
4.383
4.368
3.652
3.639
3.623
3.609
3.451
2.776
2.763
2.722
2.511
2.469
2.458
2.235
2.193
2.181
2.115
2.101
2.073
2.068
2.059
1.04
1.06
1.05
1.12
2.9 2.7 2.5 2.3 2.1
f1 (ppm)
OMe
NH
O
N
1.00
1.96
1.02
1.02
2.08
1.01
1.07
3.18
1.04
1.06
1.05
1.12
9.0 8.5 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)

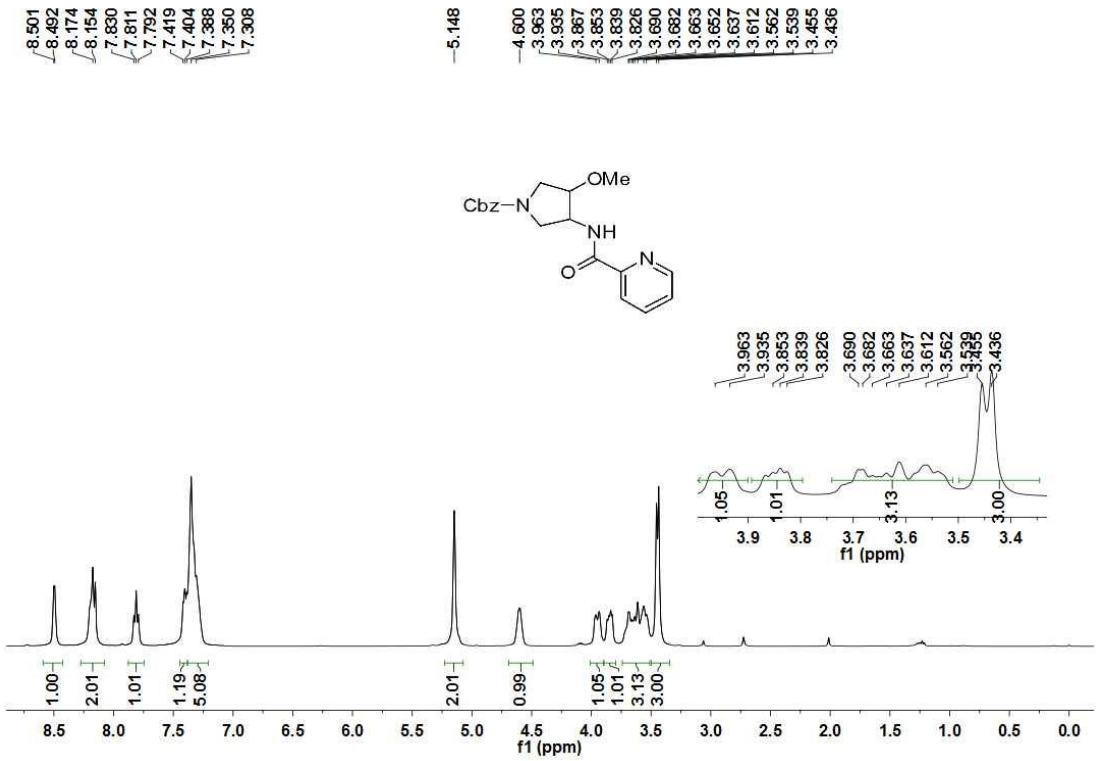

164.165
149.971
148.078
137.332
126.115
124.344
124.249
122.203
76.096
56.565
46.824
28.931
28.302
OMe
NH
O
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

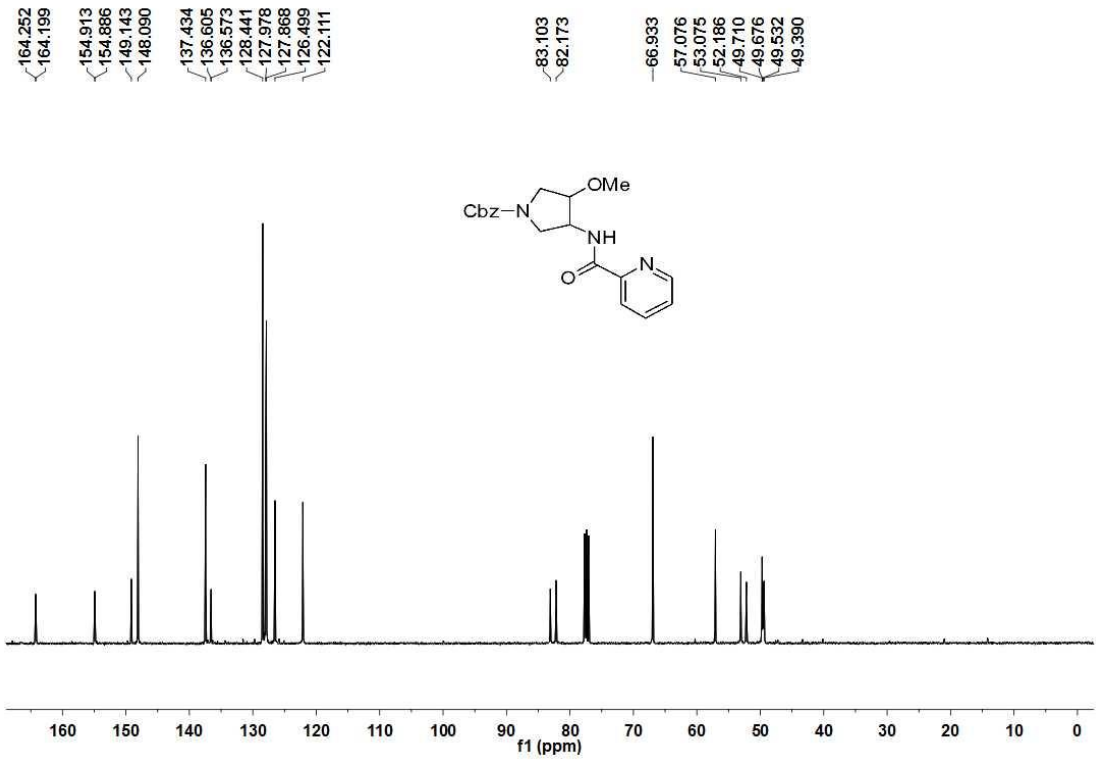
3o


8.462
8.451
8.200
8.181
7.810
7.795
7.791
7.373
7.361
7.357
7.354
7.342
7.172
7.159
7.155
7.148
7.139
7.135
7.125
7.116
7.111
7.097
7.089
4.595
4.579
4.562
4.546
4.529
3.837
3.821
3.808
3.792
3.493
3.475
3.450
3.438
3.211
3.199
3.169
3.157
2.947
2.932
2.904
2.889
2.835
2.819
2.793
2.777
1.00
2.01
0.99
1.03
4.04
1.00
1.00
4.09
1.00
1.02
1.03
OMe
NH
O
N
8.5 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)

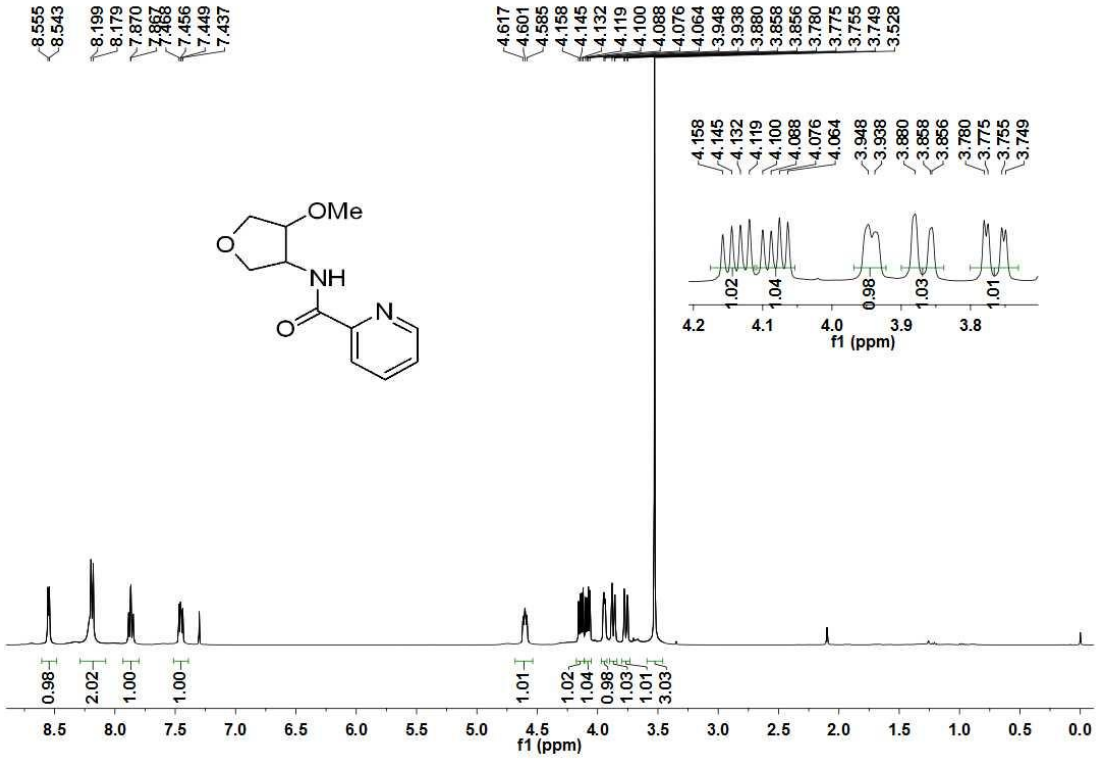

164.305
149.839
148.067
137.331
133.351
133.274
129.265
129.150
126.385
126.328
126.188
122.151
76.879
56.611
48.002
32.558
31.882
OMe
NH
O
N
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

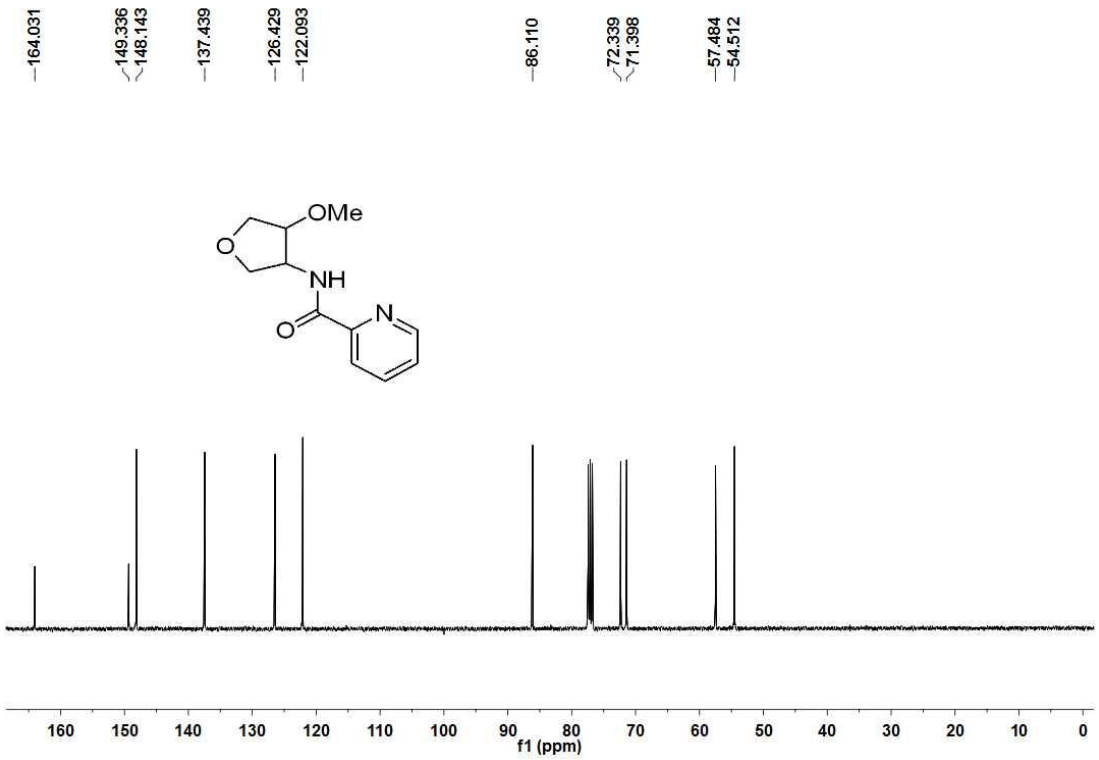
3p


8.501
8.492
8.174
8.154
7.830
7.811
7.792
7.419
7.404
7.388
7.350
7.308
5.148
4.600
3.963
3.935
3.867
3.853
3.839
3.826
3.690
3.682
3.663
3.652
3.637
3.612
3.562
3.539
3.455
3.436
OMe
Cbz–N
NH
O
N
1.00
2.01
1.01
1.19
5.08
2.01
0.99
1.05
1.01
3.13
3.00
8.5
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)
1.05
1.01
3.13
3.00
3.9
3.8
3.7
3.6
3.5
3.4
f1 (ppm)

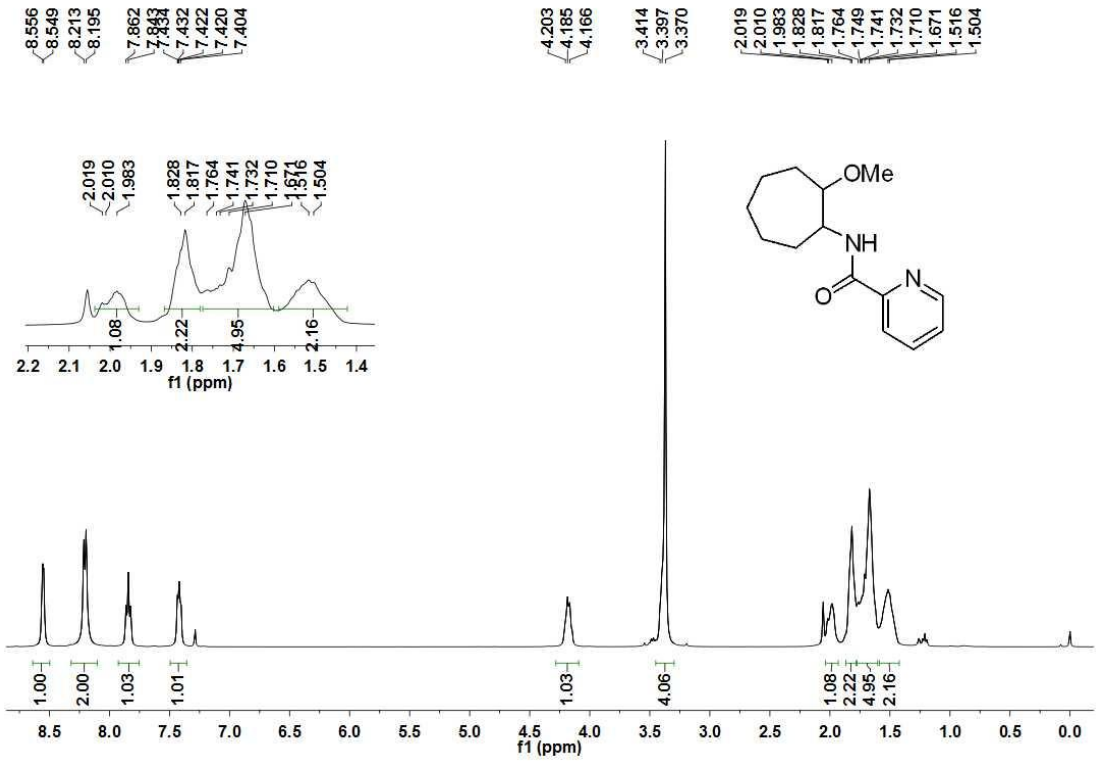

164.252
164.199
154.913
154.886
149.143
148.090
137.434
136.605
136.573
128.441
127.978
127.868
126.499
122.111
83.103
82.173
66.933
57.076
53.075
52.186
49.710
49.676
49.532
49.390
OMe
Cbz—N
NH
O
N
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

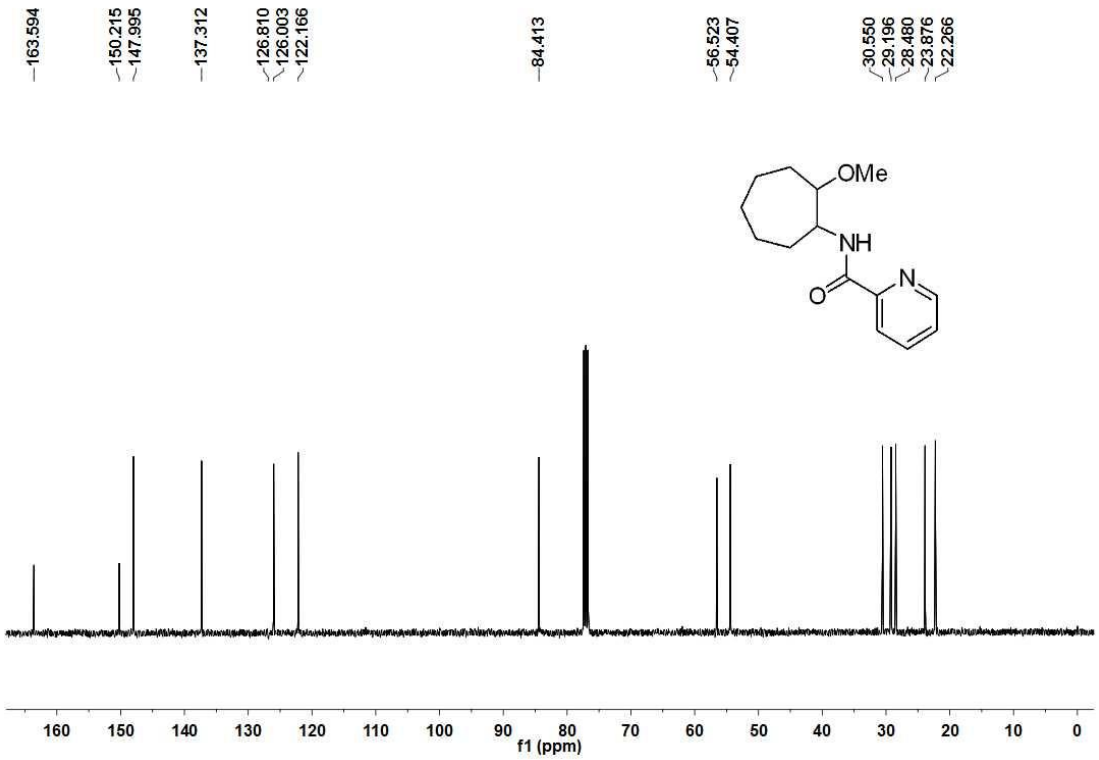
3q


8.555
8.543
8.199
8.179
7.870
7.867
7.468
7.456
7.449
7.437
4.617
4.601
4.585
4.158
4.145
4.132
4.119
4.100
4.088
4.076
4.064
3.948
3.938
3.880
3.858
3.856
3.780
3.775
3.755
3.749
3.528
OMe
O
NH
O
N
1.02
1.04
0.98
1.03
1.01
4.2 4.1 4.0 3.9 3.8
f1 (ppm)
0.98
2.02
1.00
1.00
1.01
1.02
1.04
0.98
1.03
1.01
3.03
8.5 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)

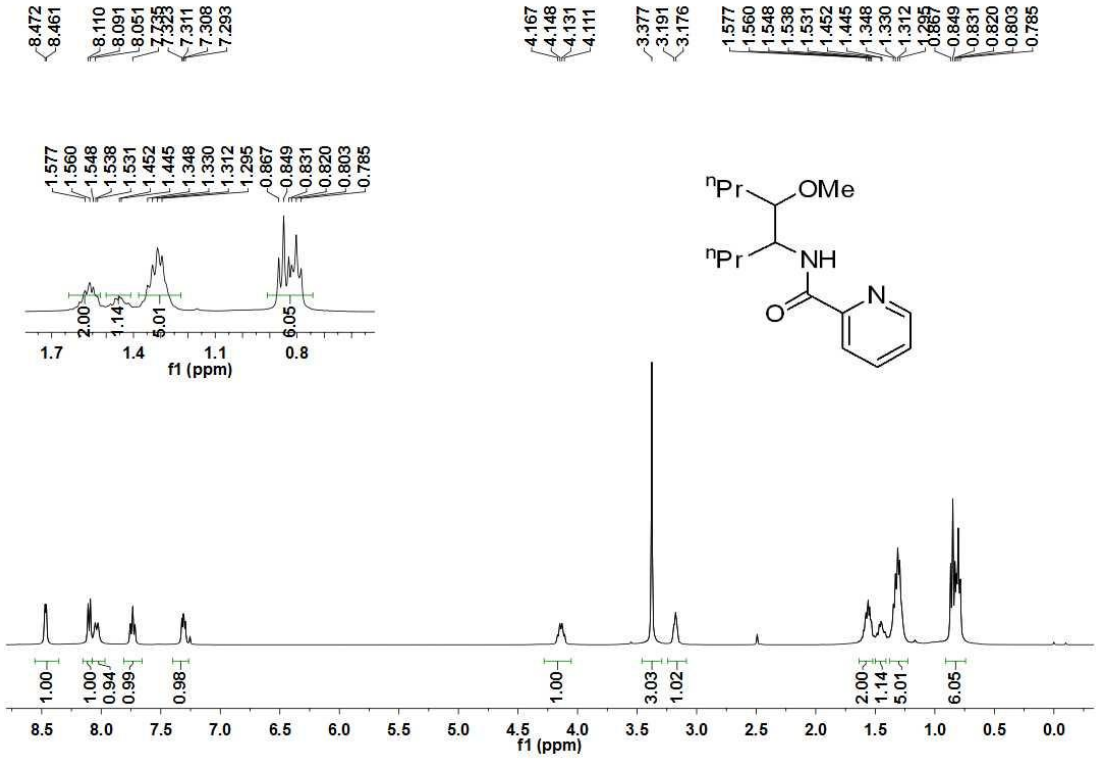

164.031
149.336
148.143
137.439
126.429
122.093
86.110
72.339
71.398
57.484
54.512
OMe
O
NH
O
N
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

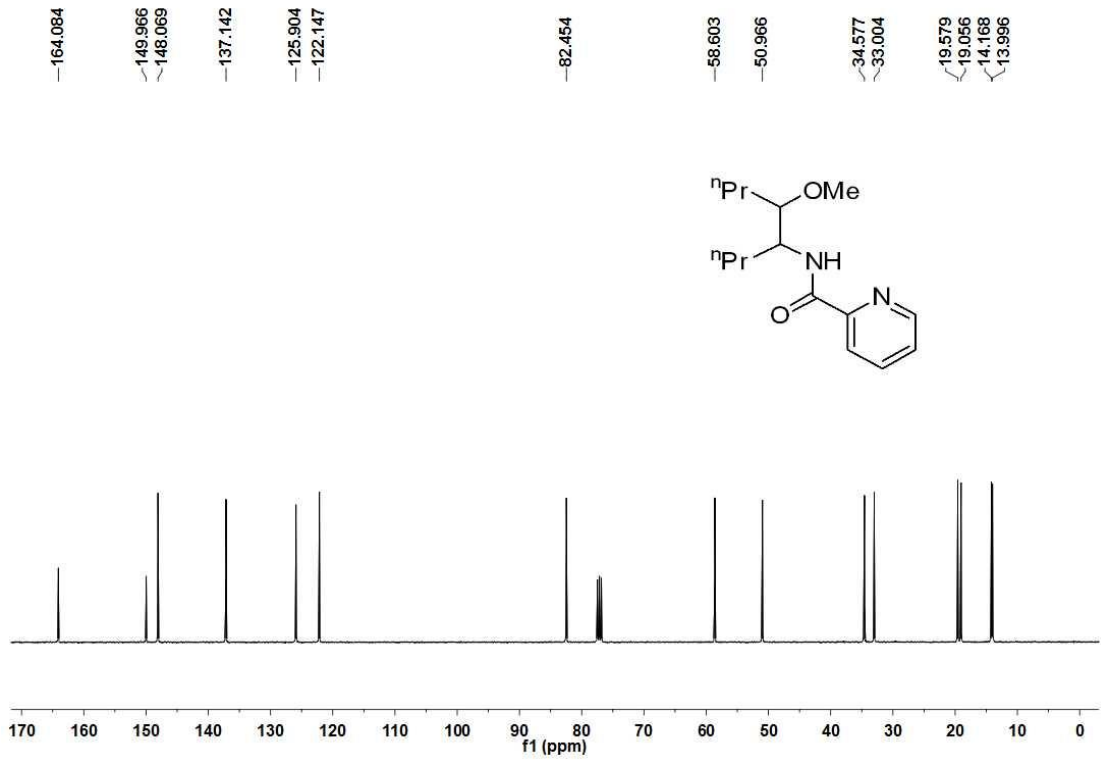
3r


8.556
8.549
8.213
8.195
7.862
7.843
7.434
7.432
7.422
7.420
7.404
4.203
4.185
4.166
3.414
3.397
3.370
2.019
2.010
1.983
1.828
1.817
1.764
1.749
1.741
1.732
1.710
1.671
1.516
1.504
OMe
NH
O
N
1.00
2.00
1.03
1.01
1.03
4.06
1.08
2.22
4.95
2.16
8.5 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)
1.08
2.22
4.95
2.16
2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4
f1 (ppm)

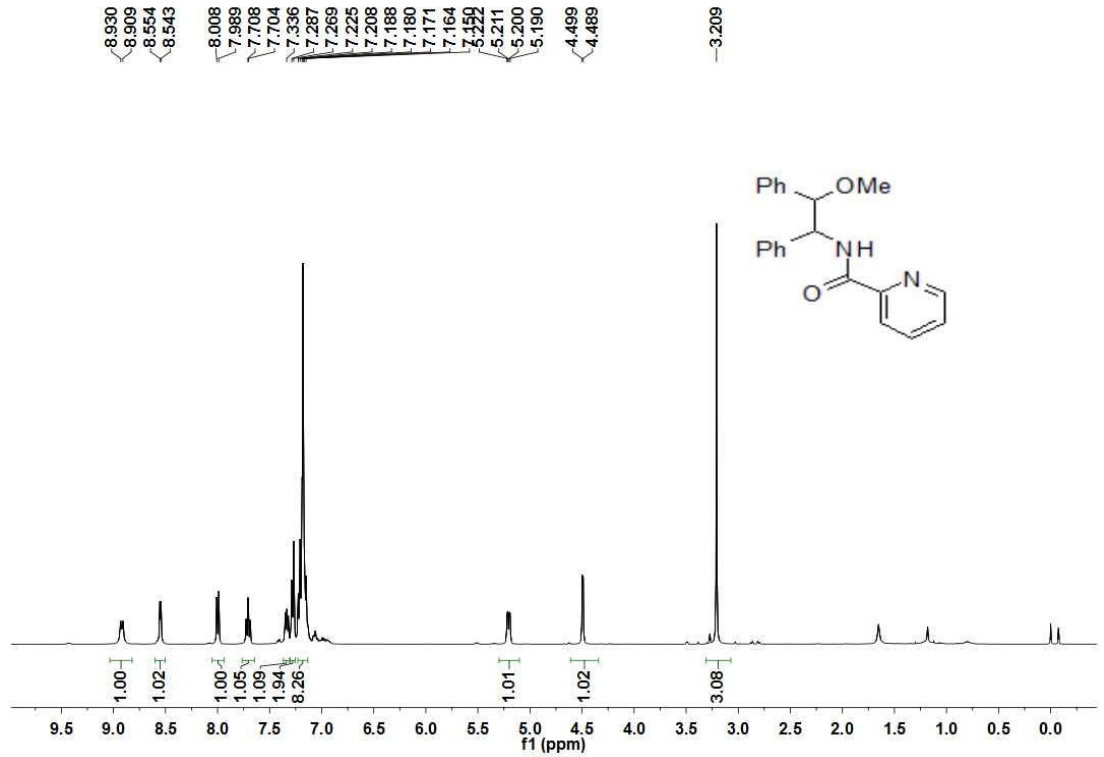

163.594
150.215
147.995
137.312
126.810
126.003
122.166
84.413
56.523
54.407
30.550
29.196
28.480
23.876
22.266
OMe
NH
O
N
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

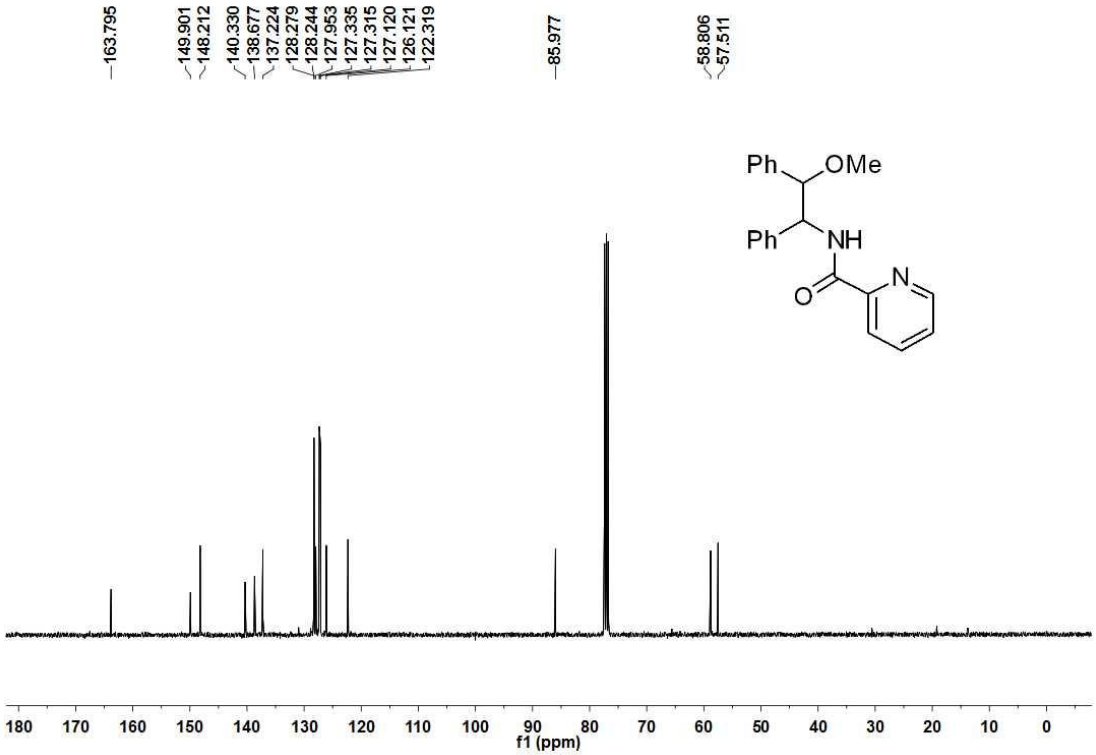
3s


8.472
8.461
8.110
8.091
8.051
7.735
7.323
7.311
7.308
7.293
4.167
4.148
4.131
4.111
3.377
3.191
3.176
1.577
1.560
1.548
1.538
1.531
1.452
1.445
1.348
1.330
1.312
1.295
0.867
0.849
0.831
0.820
0.803
0.785
2.00
1.14
5.01
6.05
1.7 1.4 1.1 0.8
f1 (ppm)
nPr
OMe
nPr
NH
O
N
1.00
1.00
0.94
0.99
0.98
1.00
3.03
1.02
2.00
1.14
5.01
6.05
8.5 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)

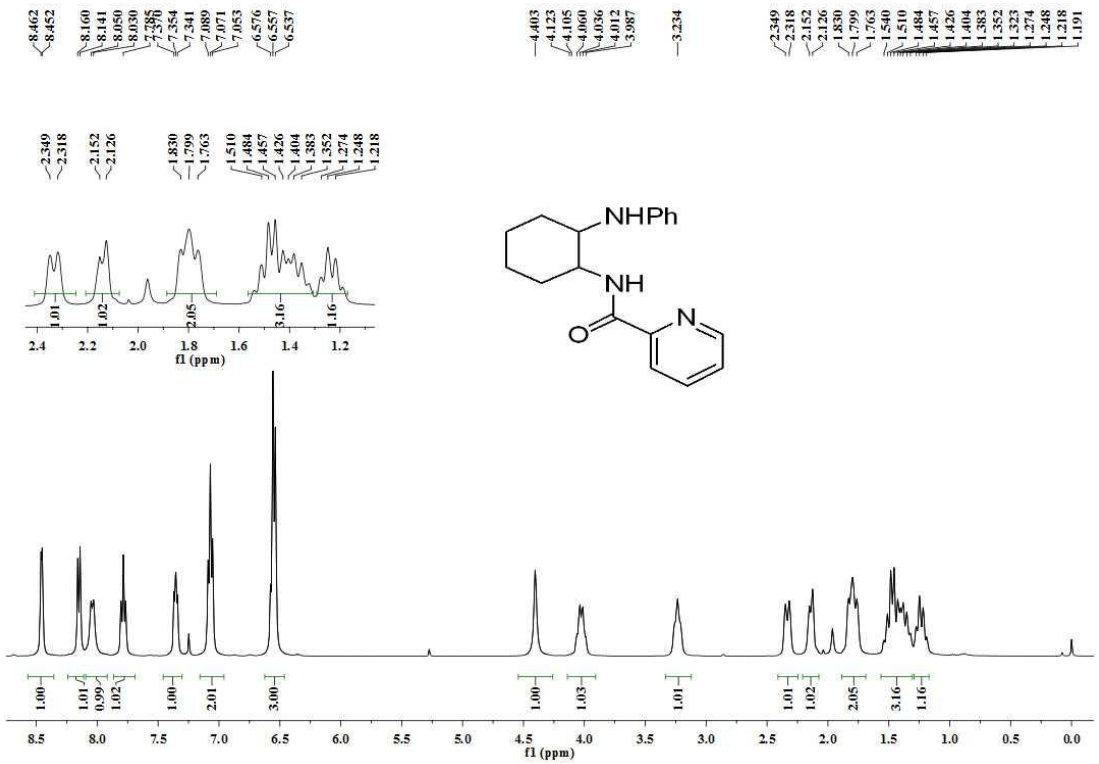

164.084
149.966
148.069
137.142
125.904
122.147
82.454
58.603
50.966
34.577
33.004
19.579
19.056
14.168
13.996
nPr
OMe
nPr
NH
O
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

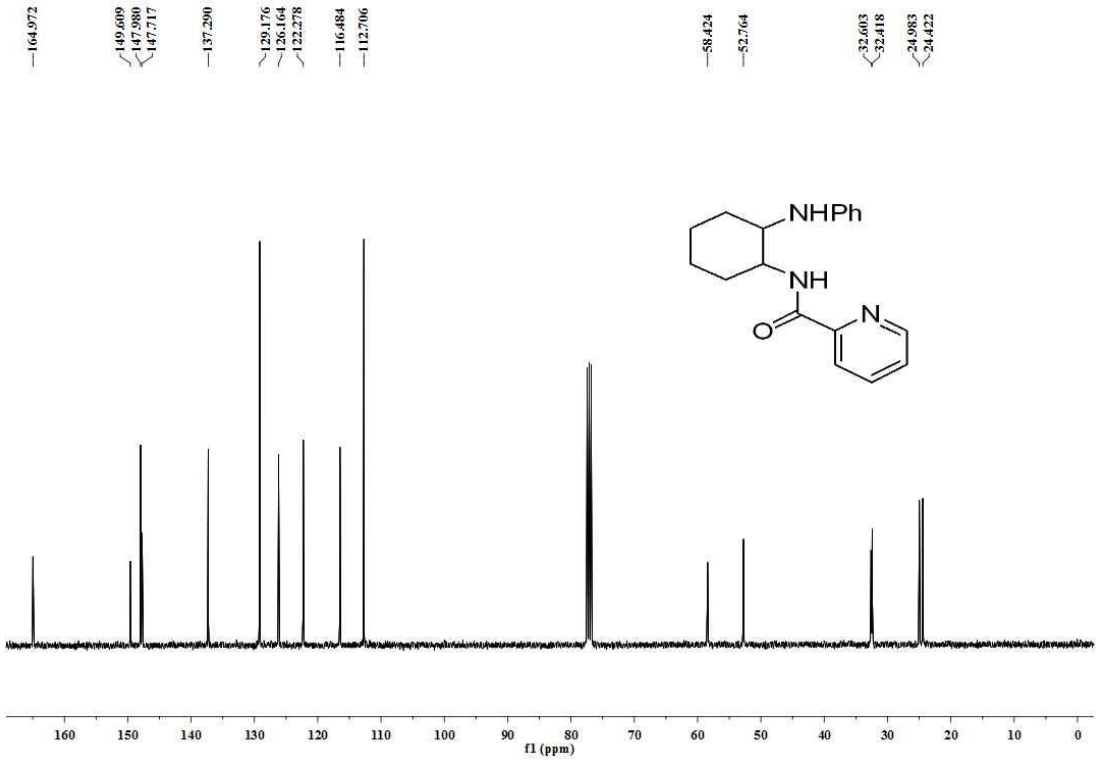
3t


8.930
8.909
8.554
8.543
8.008
7.989
7.708
7.704
7.336
7.287
7.269
7.225
7.208
7.188
7.180
7.171
7.164
5.211
5.200
5.190
4.499
4.489
3.209
Ph
OMe
Ph
NH
O
N
1.00
1.02
1.00
1.05
1.09
1.94
8.26
1.01
1.02
3.08
9.5 9.0 8.5 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)

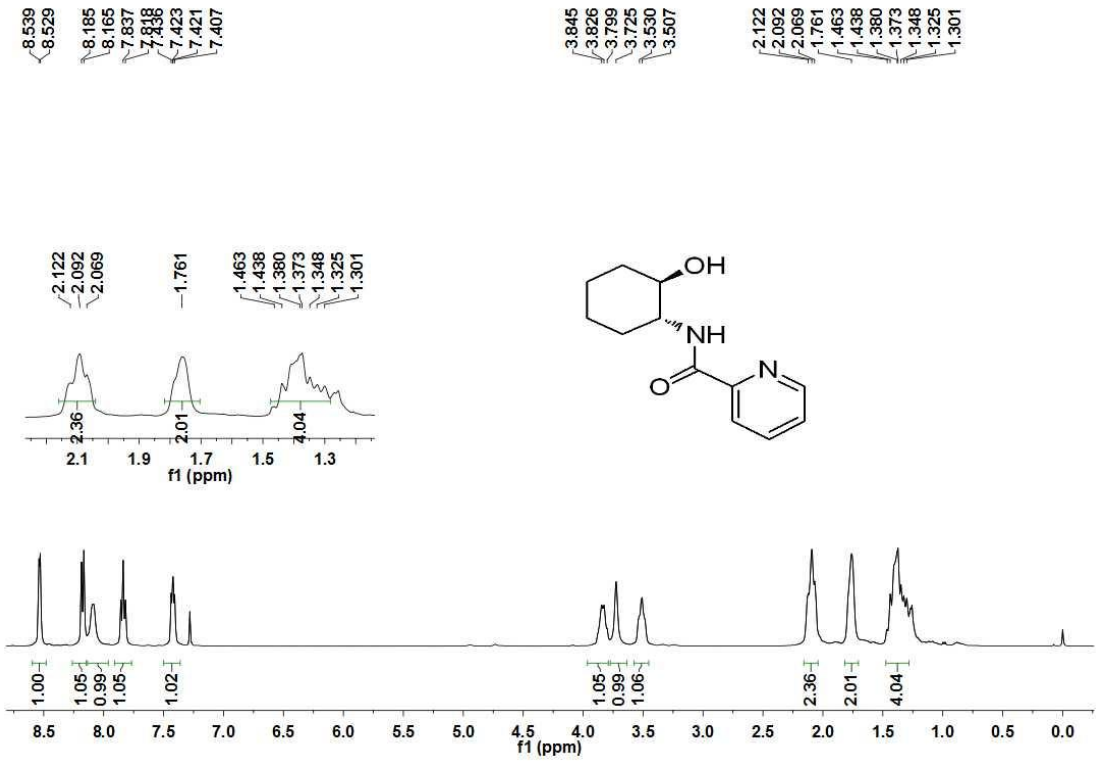

163.795
149.901
148.212
140.330
138.677
137.224
128.279
128.244
127.953
127.335
127.315
127.120
126.121
122.319
85.977
58.806
57.511
Ph
OMe
Ph
NH
O
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

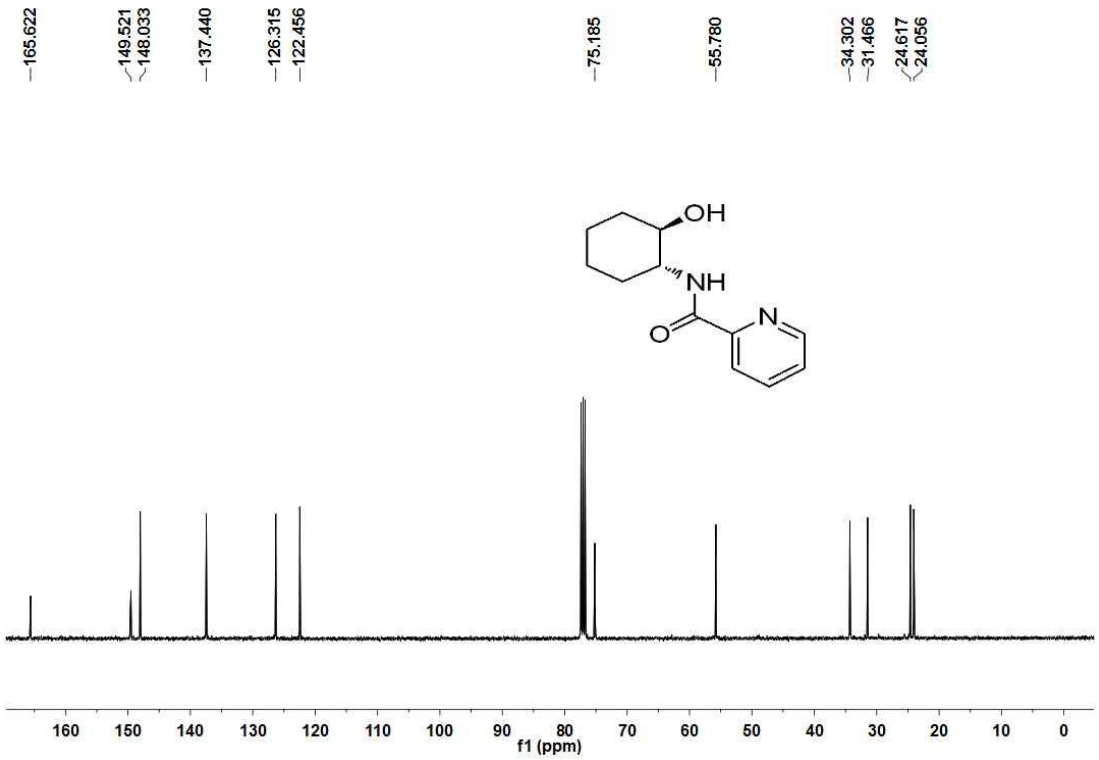
3u


8.462
8.452
8.160
8.141
8.050
8.030
7.396
7.354
7.341
7.089
7.071
7.053
6.576
6.557
6.537
4.403
4.123
4.105
4.060
4.036
4.012
3.987
3.234
2.349
2.318
2.152
2.126
1.830
1.799
1.763
1.540
1.510
1.484
1.457
1.426
1.404
1.383
1.352
1.323
1.274
1.248
1.218
1.191
NHPh
NH
O
N
1.00
1.01
0.99
1.02
1.00
2.01
3.00
1.00
1.03
1.01
1.01
1.02
2.05
3.16
1.16
8.5 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)


164.972
149.609
147.980
147.717
137.290
129.176
126.164
122.278
116.484
112.706
58.424
52.764
32.603
32.418
24.983
24.422
NHPh
NH
O
N
f1 (ppm)

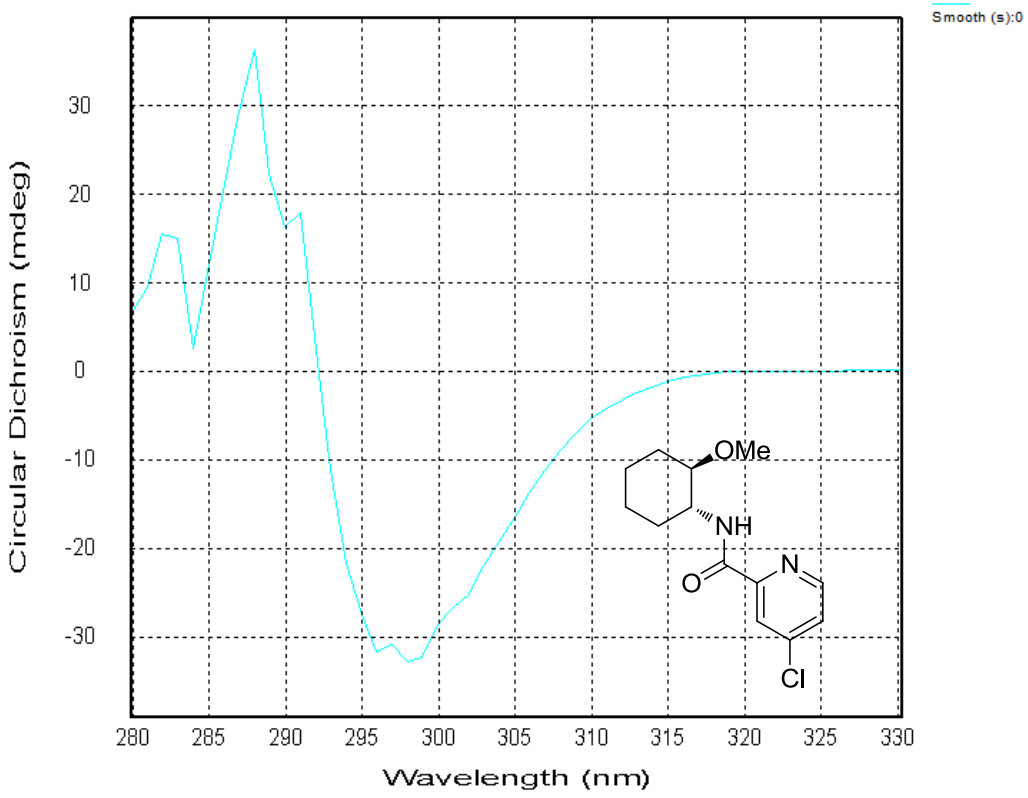
3v


8.539
8.529
8.185
8.165
7.837
7.423
7.421
7.407
3.845
3.826
3.799
3.725
3.530
3.507
2.122
2.092
2.069
1.761
1.463
1.438
1.380
1.373
1.348
1.325
1.301
OH
NH
O
N
2.36
2.01
4.04
f1 (ppm)
1.00
1.05
0.99
1.05
1.02
1.05
0.99
1.06
2.36
2.01
4.04

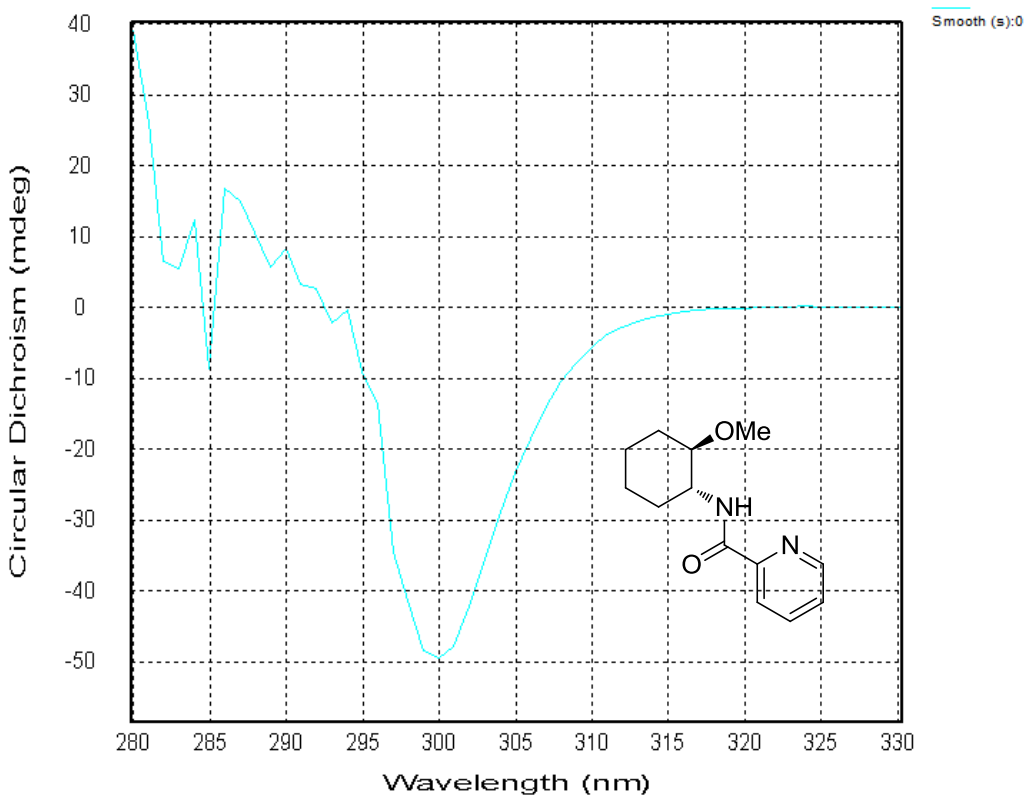


12. Copy of CD spectra in CH_2Cl_2

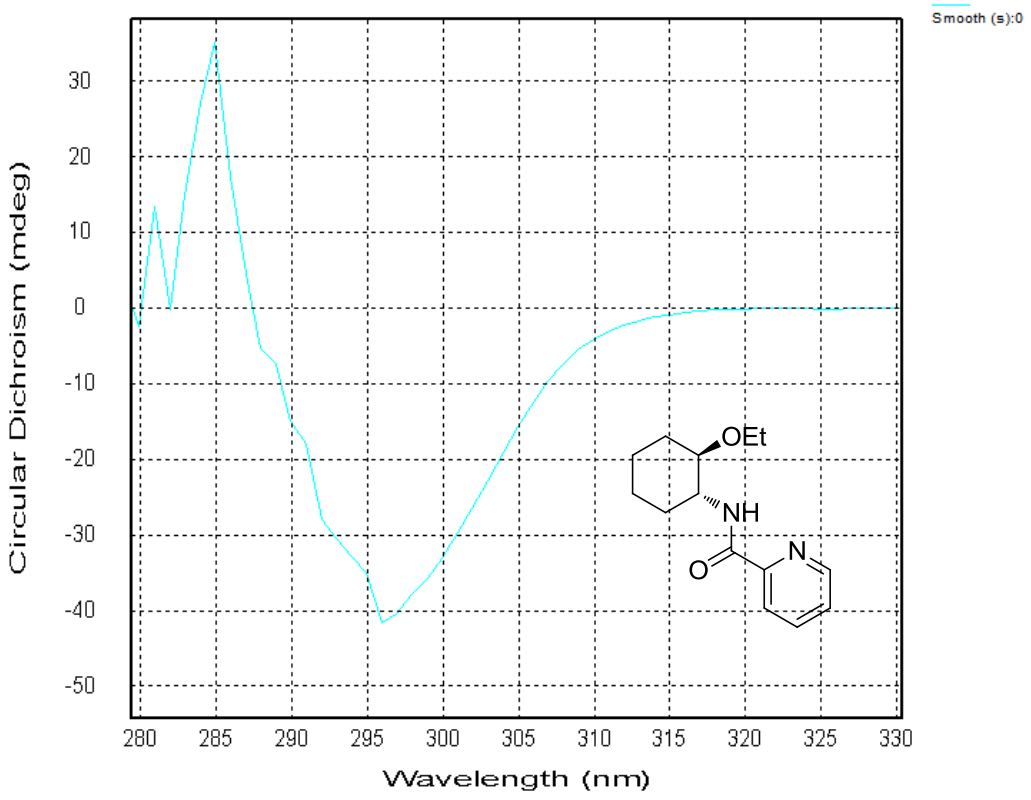
(1*R*,2*R*)-3b (standard)



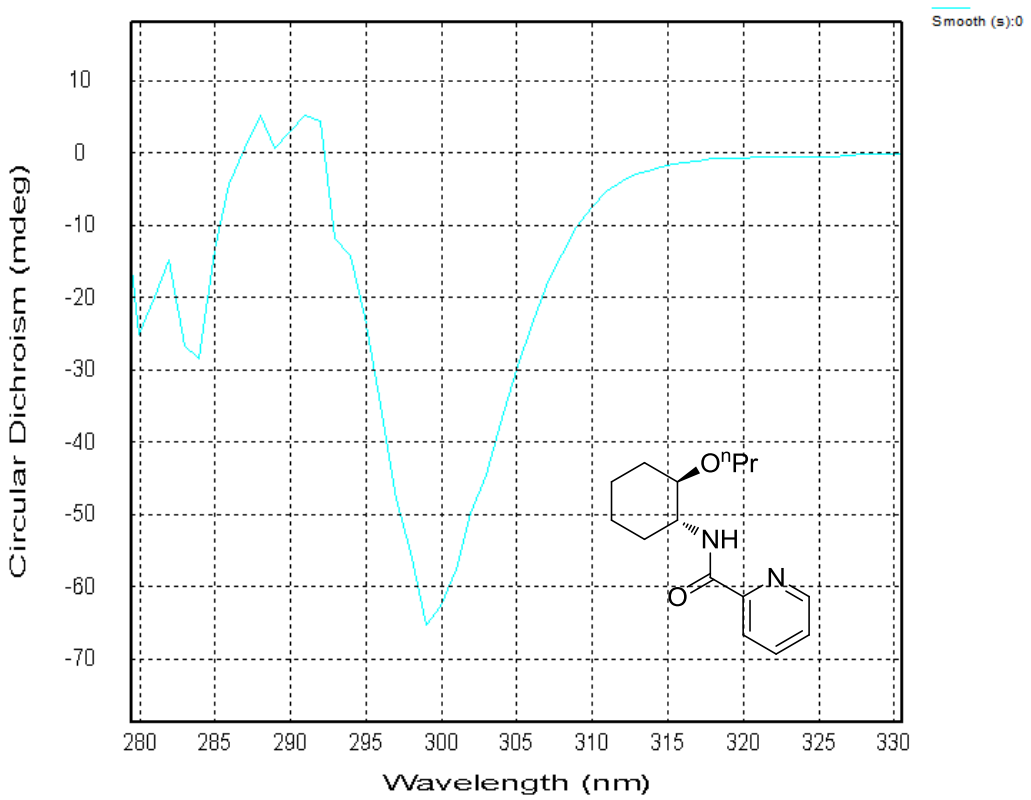
3a


Smooth (s):0
Circular Dichroism (mdeg)
40
30
20
10
0
-10
-20
-30
-40
-50
280
285
290
295
300
305
310
315
320
325
330
Wavelength (nm)
OMe
NH
O
N

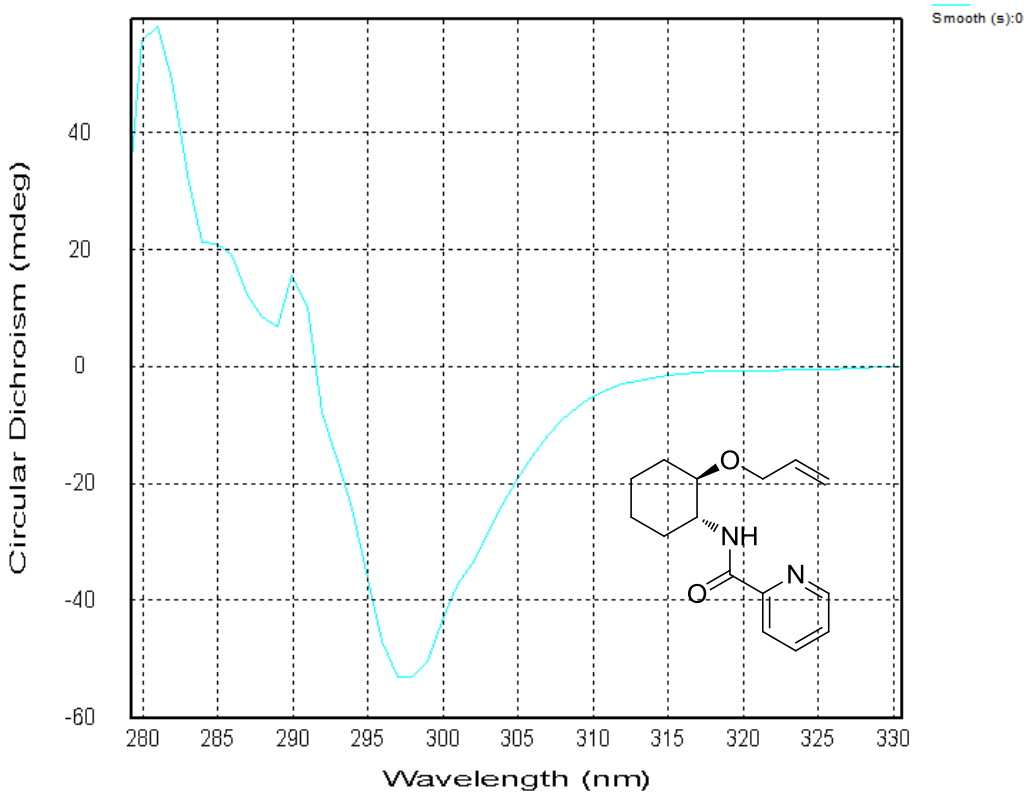
3j


Smooth (s):0
Circular Dichroism (mdeg)
30
20
10
0
-10
-20
-30
-40
-50
280
285
290
295
300
305
310
315
320
325
330
Wavelength (nm)
OEt
NH
O
N

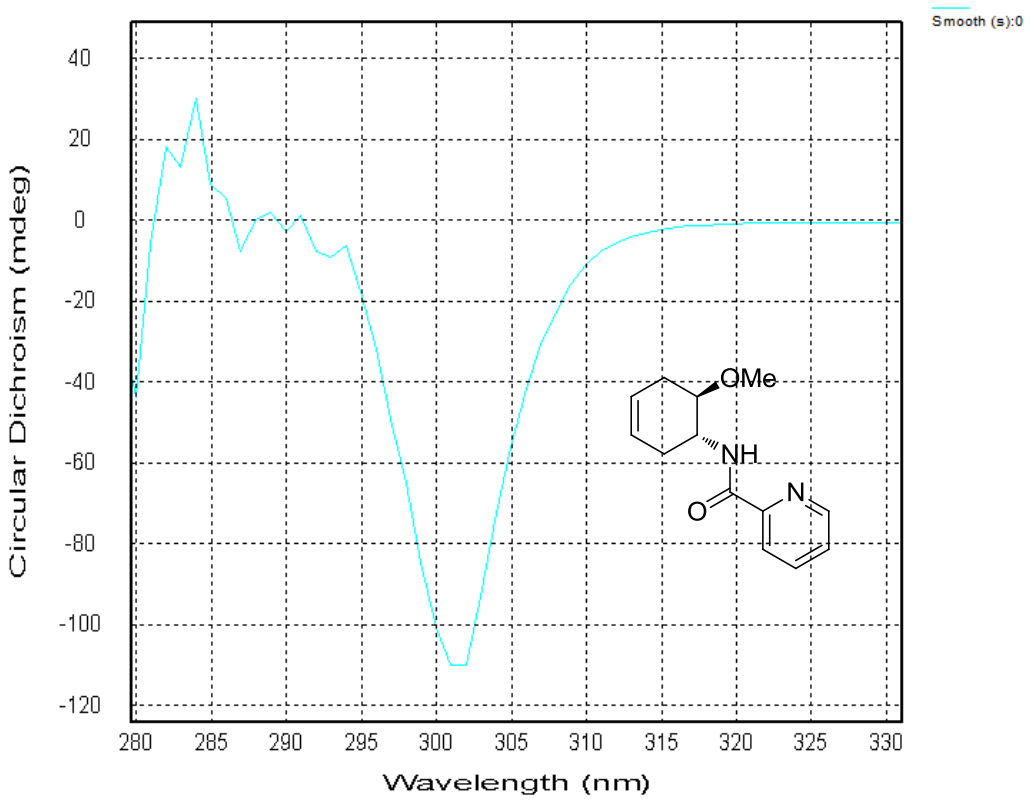
3k


Smooth (s):0
Circular Dichroism (mdeg)
10
0
-10
-20
-30
-40
-50
-60
-70
280
285
290
295
300
305
310
315
320
325
330
Wavelength (nm)
O^nPr
NH
O
N

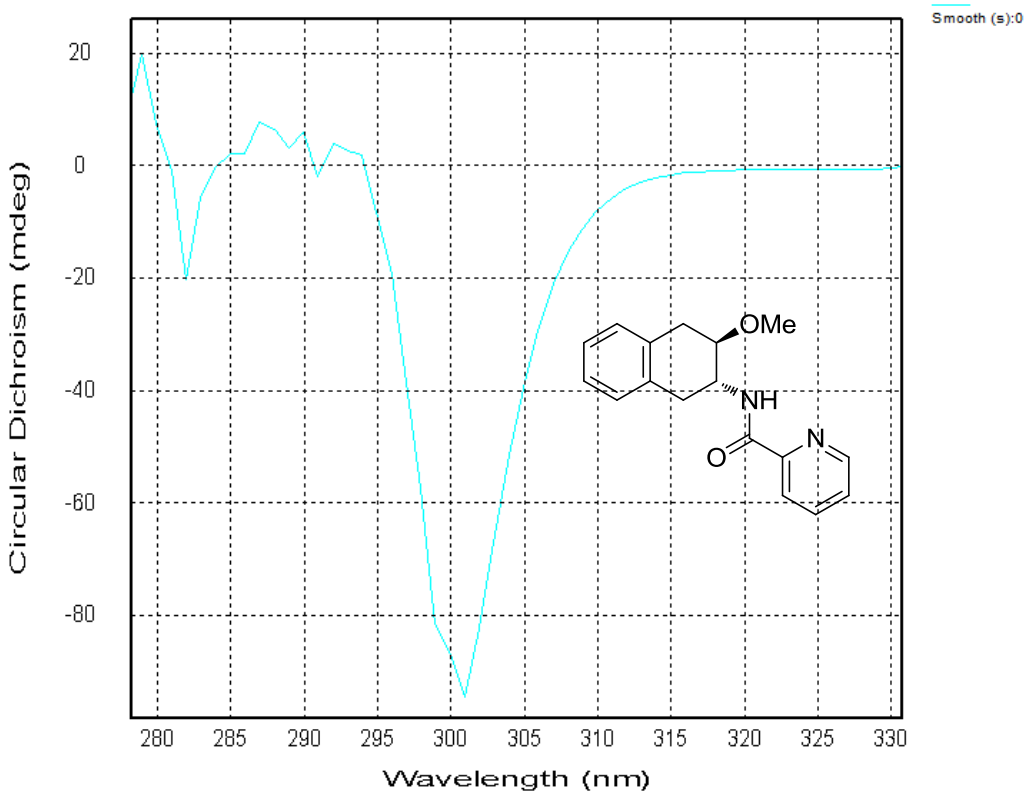
3l


Smooth (s):0
Circular Dichroism (mdeg)
40
20
0
-20
-40
-60
280
285
290
295
300
305
310
315
320
325
330
Wavelength (nm)
O
NH
O
N

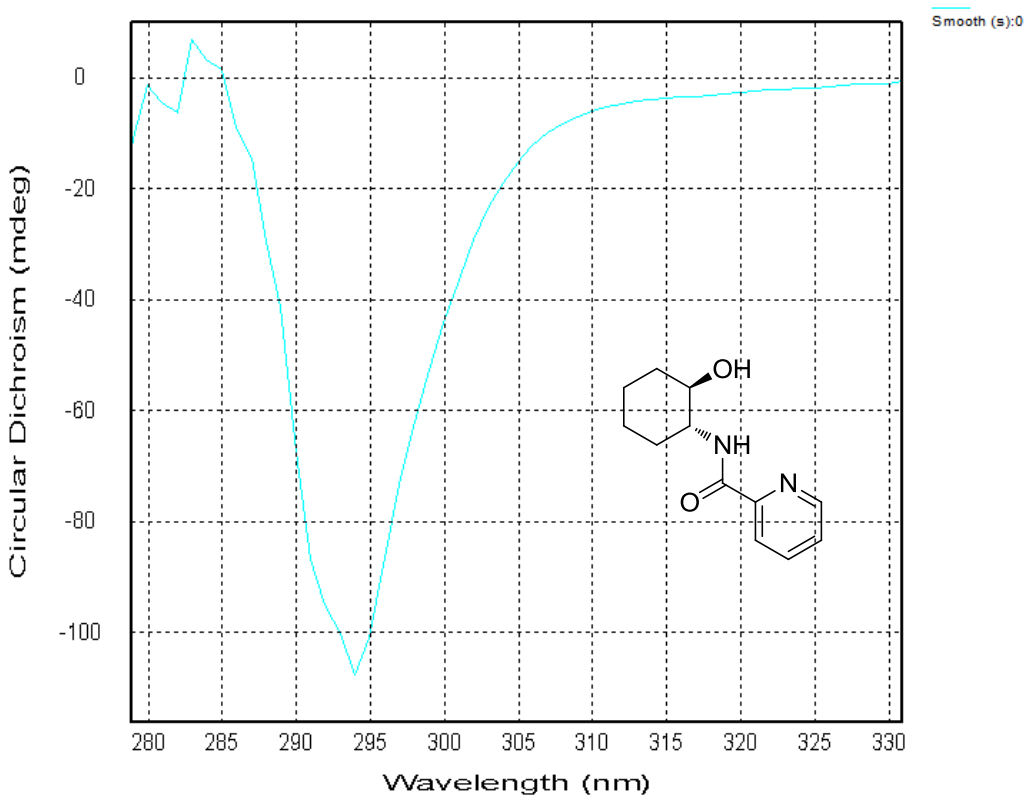
3n


Smooth (s):0
Circular Dichroism (mdeg)
40
20
0
-20
-40
-60
-80
-100
-120
280
285
290
295
300
305
310
315
320
325
330
Wavelength (nm)
OMe
NH
O
N

3o


Smooth (s):0
Circular Dichroism (mdeg)
20
0
-20
-40
-60
-80
280
285
290
295
300
305
310
315
320
325
330
Wavelength (nm)
OMe
NH
O
N

3v


Smooth (s):0
Circular Dichroism (mdeg)
0
-20
-40
-60
-80
-100
280
285
290
295
300
305
310
315
320
325
330
Wavelength (nm)
OH
NH
O
N