Electronic Supplementary Information

Asymmetric Ring Opening Reactions of Azabenzonorbornadienes through Transfer Hydrogenation using Secondary Amines as Hydrogen Sources: Tuning of Absolute Configuration by Acids

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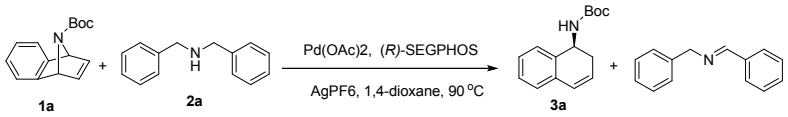
Contents

1. General methods and General procedure

General Methods. The reactions and manipulations were performed under an atmosphere of argon by using standard Schlenk techniques and Drybox (Mikrouna, Supper 1220/750). All solvents were purified and dried by using standard methods prior to use and stored under argon. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-Avance 400 MHz spectrometer. Chemical shifts (δ) were reported in ppm with tetramethylsilane as internal standard, and *J* values were given in Hz. ^{1}H NMR spectra were recorded in $CDCl_3$ and the chemical shifts were referenced to $CDCl_3$ (δ 7.27) and that of ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.00). The enantioselective excesses were determined by Agilent 1260 Series HPLC using Daicel AD-H, AS-H, OJ-H and OD-H chiral columns eluted with a mixture of isopropyl alcohol and hexane. Melting points were measured on X-4 melting point apparatus and uncorrected. Column chromatography was performed with silica gel (200-300 mesh) with petroleum ether and ethyl acetate as eluents.

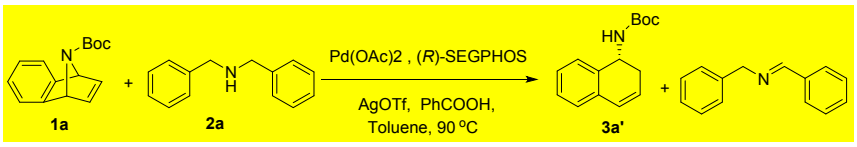
Experimental Procedures

(a) Typical procedure for the asymmetric transfer hydrogenation reaction of azabenzonorbornadienes:



1. $Pd(OAc)_2$ (2.3 mg, 0.01 mmol), (*R*)-SEGPHOS (7.3 mg, 0.012 mmol) and 1.0 mL 1,4-dioxane were added to a Schlenk tube under argon atmosphere. The resulting solution was stirred at room temperature for 30 min, then $AgPF_6$ (5.1 mg, 0.02 mmol) was added and stirred for an additional 10 min, then a solution of *N*-Boc-azabenzonorbornadiene **1a** (48.6 mg, 0.2 mmol) in 1,4-dioxane (1.0 mL) was added, and the mixture was stirred for additional 10 min. After the addition of dibenzylamine **2a** (115μL, 0.6 mmol), the mixture was stirred at 90 °C under argon atmosphere with TLC monitoring until the complete consumption of **1a**. The residue was purified by chromatography on a silica gel column to afford the desired product **3a**. The absolute configuration of the products were determined by comparing the characterization data such as ^{1}H NMR and HPLC of the products with the one reported earlier.[1]

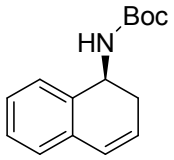
(b) Typical procedure for the asymmetric transfer hydrogenation reaction of azabenzonorbornadienes in presence of benzoic acid:



$Pd(OAc)_2$ (2.3 mg, 0.01 mmol), (*R*)-SEGPHOS (7.8 mg, 0.012 mmol) and 1.0 mL toluene were added to a Schlenk tube under argon atmosphere. The resulting solution was stirred at room temperature for 30 min, then AgOTf (5.1 mg, 0.02 mmol) was added and stirred for an additional 10 min, then a solution of *N*-Boc-azabenzonorbornadiene **1a** (48.6 mg, 0.2 mmol) in toluene (1.0 mL) was added, and the mixture was stirred for additional 10 min, then benzoic acid (48.8 mg, 0.2 mmol) was added and stirred for an additional 10 minutes. After the addition of dibenzylamine **2a** (115μL, 0.6 mmol), the mixture was stirred at 90 °C under argon atmosphere with TLC monitoring until the complete consumption of **1a**. The residue was purified by chromatography on a silica gel column to afford the desired product **3a´**.

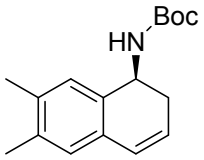
2. Characterization Data of the products

(*S*)-*tert*-butyl (1,2-dihydronaphthalen-1-yl)carbamate (3a)



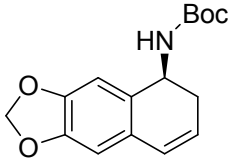
Colorless oil, 91% yield, 93% *ee*. $[\alpha]_D^{20}$ = -46.3 (c = 0.54, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.24 (m, 1H), 7.19-7.11 (m, 2H), 7.00 (dd*, J* = 7.2, 1.7 Hz, 1H), 6.44 (d, *J* = 9.6 Hz, 1H), 5.91-5.87 (m, 1H), 4.83-4.65 (m, 2H), 2.52-2.37 (m, 2H), 1.36 (s, 9H). The *ee* of **3a** was determined by HPLC analysis using Daicel Chiralcel OJ-H column (25 cm × 0.46 cm ID), conditions: n-hexane/i-PrOH = 98/2, 0.8 mL/min, 254 nm; t_{minor} = 8.1 min, t_{major} = 9.2 min.

(*S*)-*tert*-butyl (6,7-dimethyl-1,2-dihydronaphthalen-1-yl) carbamate (3b)



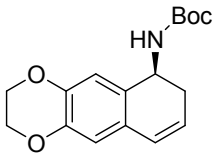
Colorless oil, 96% yield, 90% *ee*. $[\alpha]_D^{24}$= -22.8 (c = 0.78, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (s,1H), 6.87 (s, 1H), 6.47 (d, *J* = 9.5 Hz, 1H), 5.89 (t, *J* = 4.8 Hz1H), 4.84-4.59 (m, 2H), 2.57-2.44 (m, 2H), 2.24 (d, *J* = 6.2 Hz,6H), 1.44(s, 9H).The *ee* of **3b** was determined by HPLC analysis using Daicel Chiralcel AD-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 98/2, 0.3 mL/min, 254 nm; t_{minor} =15.7 min, t_{major} = 16.9 min.

(*S*)-*tert*-butyl (5,6-dihydronaphtho[2,3-*d*][1,3]dioxol-5-yl) carbamate (3c)



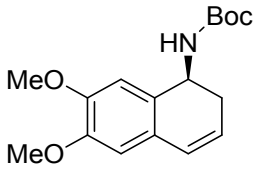
Colorless oil, 92% yield, 94% *ee*. $[\alpha]_D^{24}$ = -38.3 (c = 0.72, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s,1H), 6.57 (s, 1H), 6.39 (d, *J* = 9.6 Hz, 1H), 5.92 (d, *J* = 2.2 Hz, 2H), 5.87-5.83 (m, 1H), 4.87 (d, *J* = 8.4 Hz, 1H), 4.78-4.62 (m, 1H), 2.55-2.40 (m, 2H), 1.43 (s, 9H).The *ee* of **3c** was determined by HPLC analysis using Daicel Chiralcel AS-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 95/5, 0.5 mL/min, 254 nm; t_{major} = 13.8 min, t_{minor} = 14.9 min.

(*S*)-tert-butyl(2,3,6,7-tetrahydronaphtho[2,3-*b*][1,4]dioxin-6-yl) carbamate (3d)



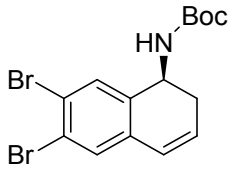
Colorless oil, 95% yield, 96% *ee*.$[\alpha]_D^{24}$ = -20.0 (c = 0.74, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s,1H), 6.59 (s, 1H), 6.38 (d, *J* = 9.7 Hz, 1H), 5.87-5.82 (m,1H), 4.84(d, *J* = 8.7 Hz, 1H), 4.79-4.61 (m,1H), 4.23 (s, 4H), 2.54-2.37 (m, 2H), 1.43(s, 9H).The *ee* of **3d** was determined by HPLC analysis using Daicel Chiralcel AS-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 98/2, 0.8mL/min, 254 nm; t_{major}=22.7min, t_{minor} = 25.3 min.

(*S*)-*tert*-butyl (6,7-dimethoxy-1,2-dihydronaphthalen-1-yl) carbamate (3e)



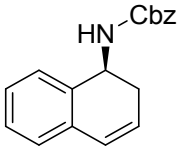
Colorless oil, 78% yield, 94% *ee*.$[\alpha]_D^{25}$ = -43.1 (c = 0.64, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (s,1H), 6.60 (s, 1H), 6.42 (d, *J* = 9.6 Hz, 1H), 5.86-5.82 (m,1H), 4.89 (d, *J* = 8.8 Hz, 1H), 4.79-4.63 (m, 1H), 3.86 (d, *J* = 6.6Hz,6H), 2.57-2.42 (m, 2H), 1.41 (s, 9H).The *ee* of **3e** was determined by HPLC analysis using Daicel Chiralcel OD-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 90/10, 0.5 mL/min, 254 nm; t_{minor} = 10.7 min, t_{major} =11.8 min.

***S*)-*tert*-butyl (6,7-dibromo-1,2-dihydronaphthalen-1-yl) carbamate (3f)**



Colorless oil, 37% yield, 73% *ee*.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s,1H), 7.30 (s, 1H), 6.40 (d, *J* = 9.6 Hz, 1H), 6.05-6.03 (m,1H), 4.87-4.71 (m, 2H), 2.56-2.39 (m, 2H), 1.44 (s,9H).The *ee* of **3f** was determined by HPLC analysis using Daicel Chiralcel AS-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 98/2, 0.2mL/min, 254 nm; t_{minor} = 15.3 min, t_{major} = 16.3 min.

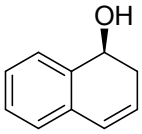
(*S*)-benzyl (1,2-dihydronaphthalen-1-yl)carbamate (3g)



Colorless oil, 87% yield, 88% *ee*.$[\alpha]_D^{25}$ = -31.7 (c = 0.64, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.23 (m, 8H), 7.12 (d, *J* = 7.2 Hz, 1H), 6.56 (d, *J* = 9.6 Hz, 1H), 6.02-5.98 (m,1H), 5.21-5.09 (m, 3H), 4.98 (dd, *J* = 14.4 Hz, 6.0 Hz, 1H), 2.66-2.51 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.54, 135.34, 133.48, 132.00, 127.49, 127.17, 127.11, 126.83, 126.70, 126.11, 125.51,

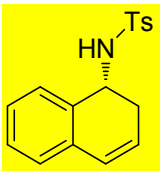
124.57, 65.71, 47.08, 29.38. The *ee* of **3g** was determined by HPLC analysis using Daicel Chiralcel OJ-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 90/10, 1.2mL/min, 254 nm; t_{minor} = 14.9 min, t_{major} = 17.8min.

(*S*)-1,2-dihydronaphthalen-1-ol（3h）



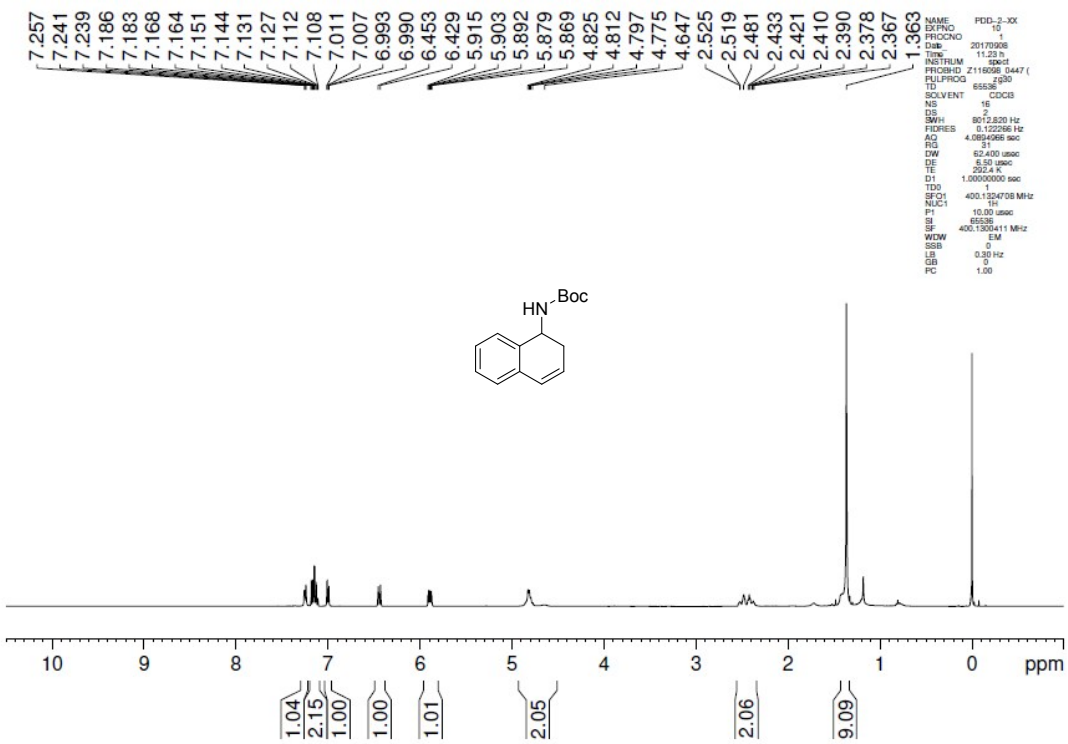
Colorless oil, 40% yield, 66% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 7.2, 0.7 Hz, 1H), 7.24-7.15 (m, 2H), 7.05 (dd, *J* = 8.0, 1.3 Hz, 1H),6.48 (d, *J* = 9.6 Hz,1H), 5.94-5.90 (m, 1H), 4.71 (t, *J* = 5.3 Hz, 1H), 2.55-2.51 (m, 2H). The *ee* of **3h** was determined by HPLC analysis using Daicel Chiralcel OD-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, 254 nm; t_{minor} = 9.8 min, t_{major} =8.9min.

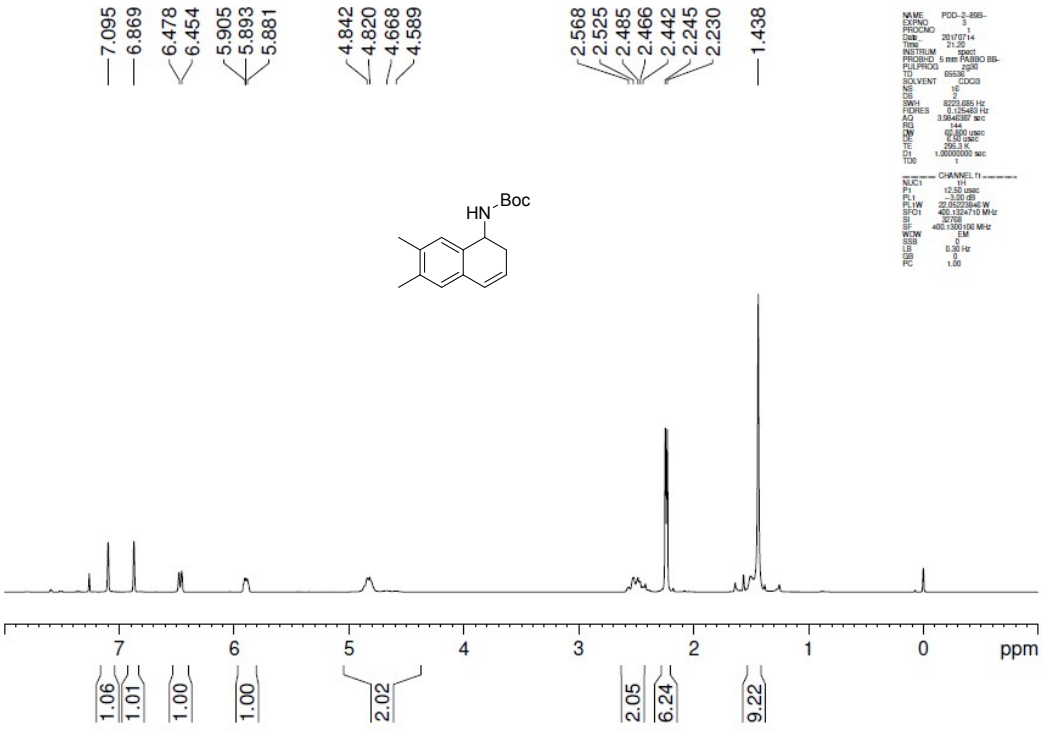
(*R*)-*N*-(1,2-dihydronaphthalen-1-yl)-4-methylbenzenesulfonamide (3i)

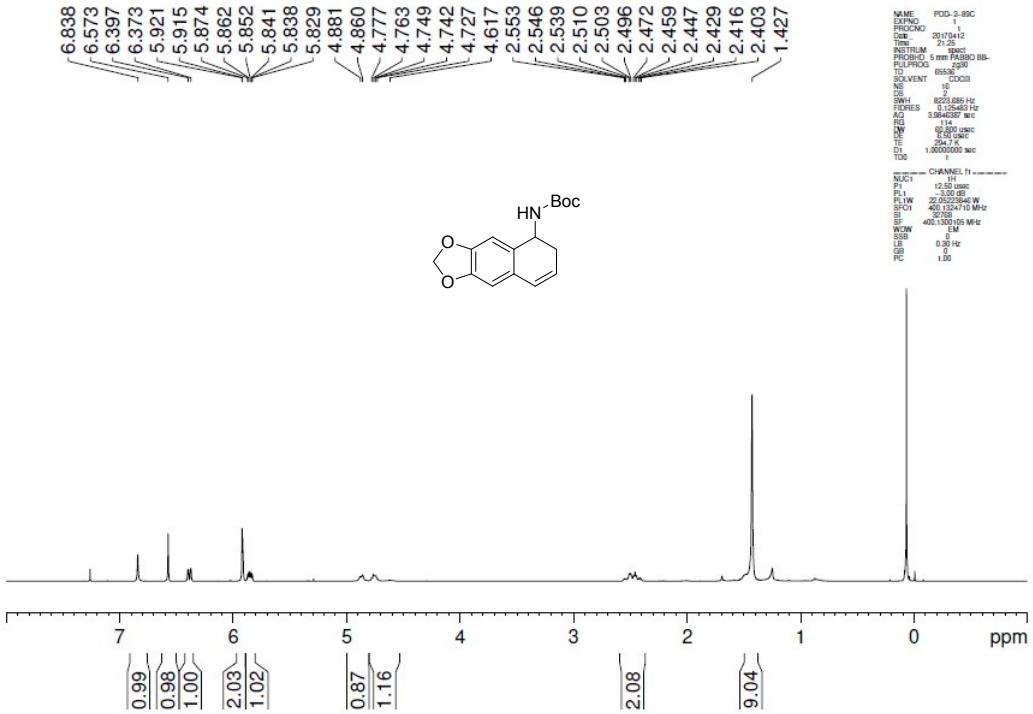


White solid, 42% yield, 98% *ee*. $[\alpha]_D^{25}$=25.7(c = 0.44, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J*=8.4Hz, 2H), 7.28 (t, *J* = 8.4 Hz, 2H), 7.20 (t, *J* = 8.4 Hz, 1H), 7.11-7.04 (m, 2H), 6.91 (d, *J* = 7.6Hz, 1H), 6.51 (d, *J* = 9.6 Hz, 1H), 5.91-5.87(m, 1H), 4.84 (d, *J* = 8.4 Hz, 1H), 4.50-4.45 (m, 1H), 2.52-2.39 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.3, 138.1, 133.4, 133.1, 129.7, 128.5, 127.9, 127.6, 127.1, 126.9, 126.6, 125.3, 50.9, 31.0, 21.6. The *ee* of **3i** was determined by HPLC analysis using Daicel Chiralcel AD-H column (25 cm × 0.46 cm ID), conditions: *n*-hexane/*i*-PrOH = 90/10, 1.0mL/min, 254nm; t_{major} =16.7min, t_{minor} =18.3min.

3. NMR Spectra of products



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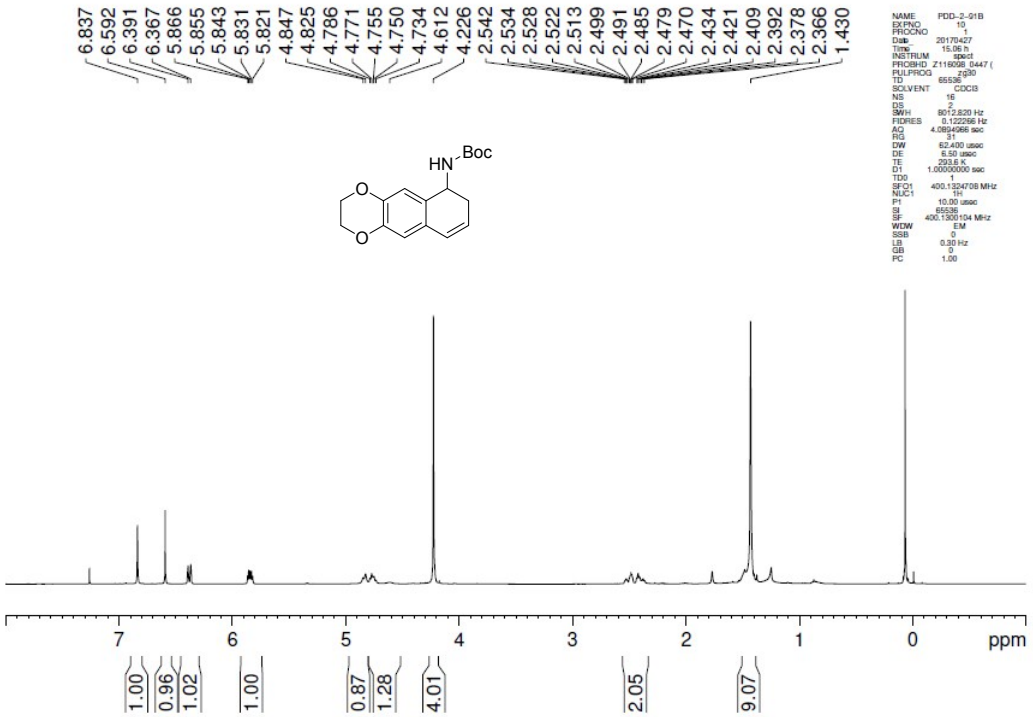
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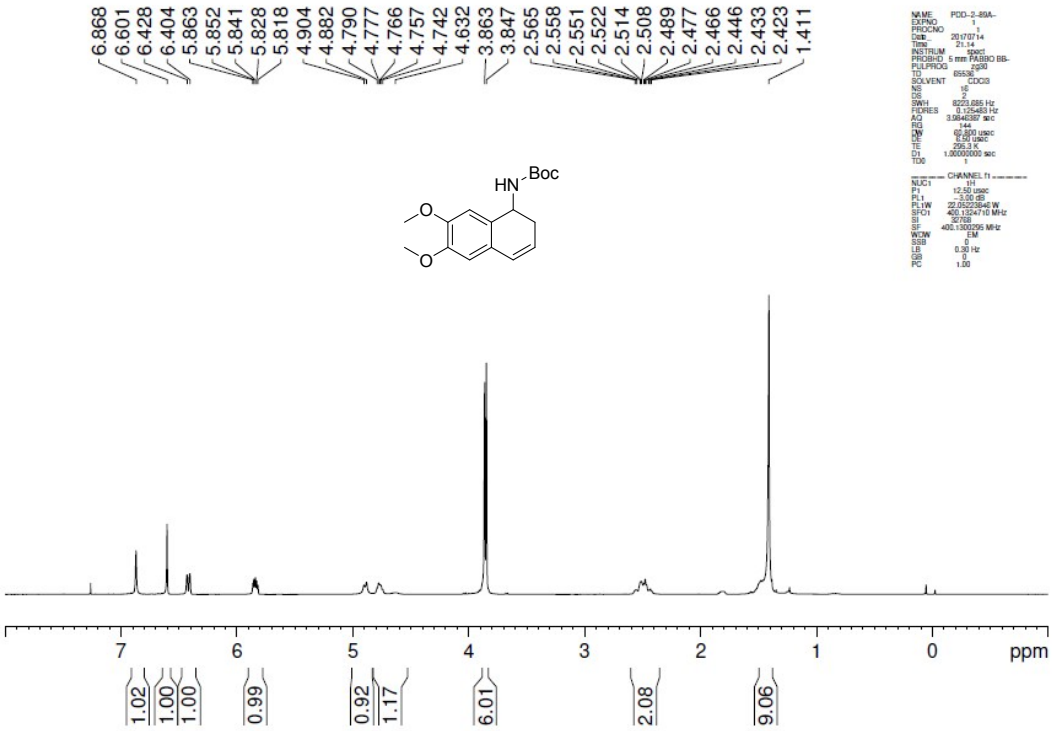
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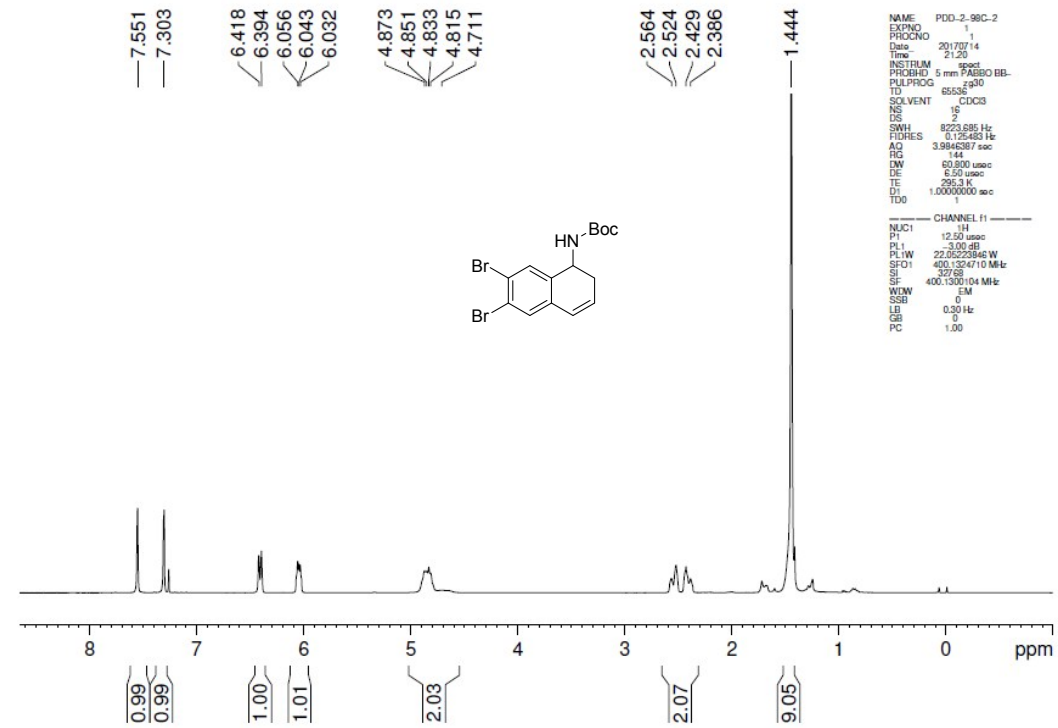
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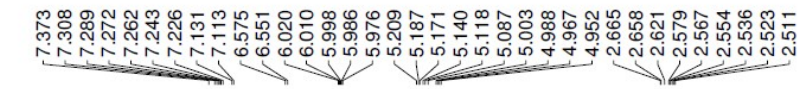
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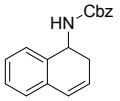
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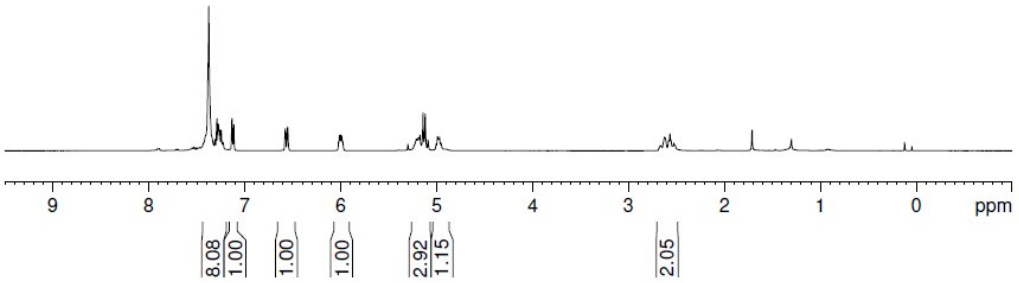
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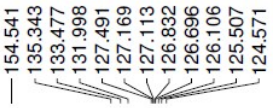
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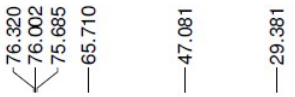
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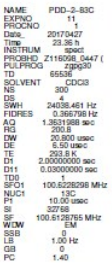
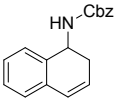
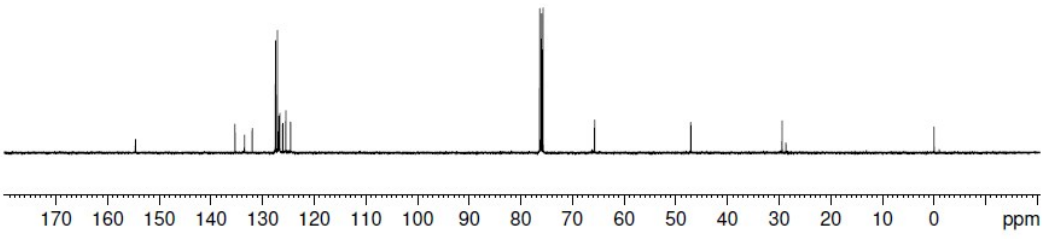



HN
Cbz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150
140
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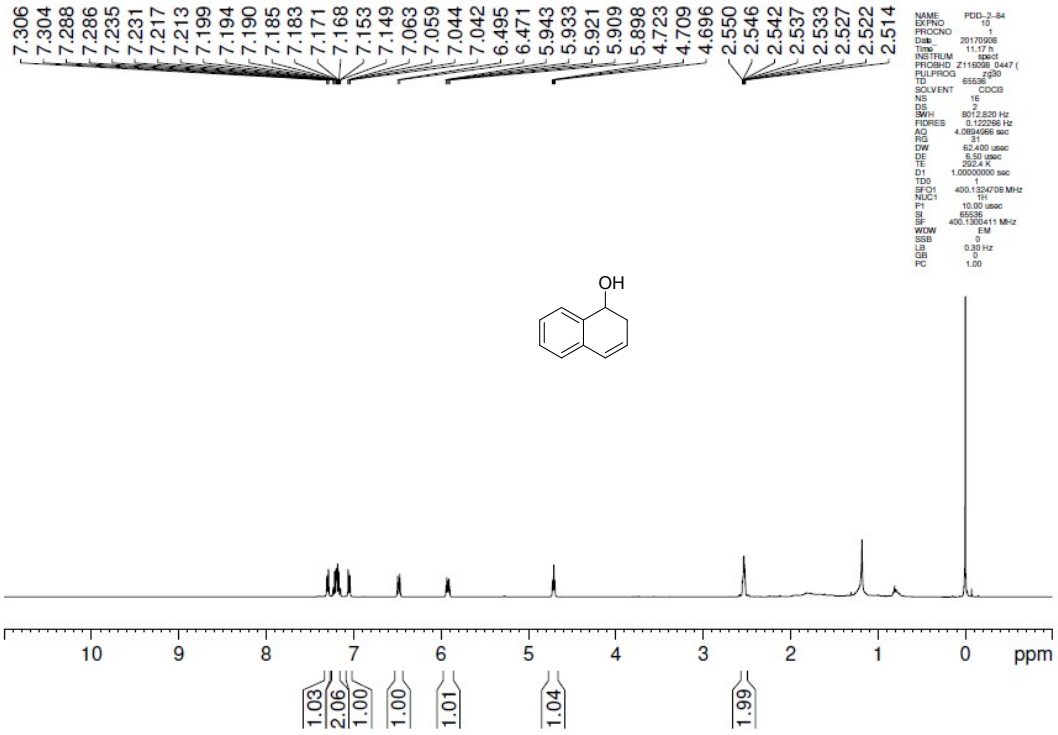
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.304
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7.213
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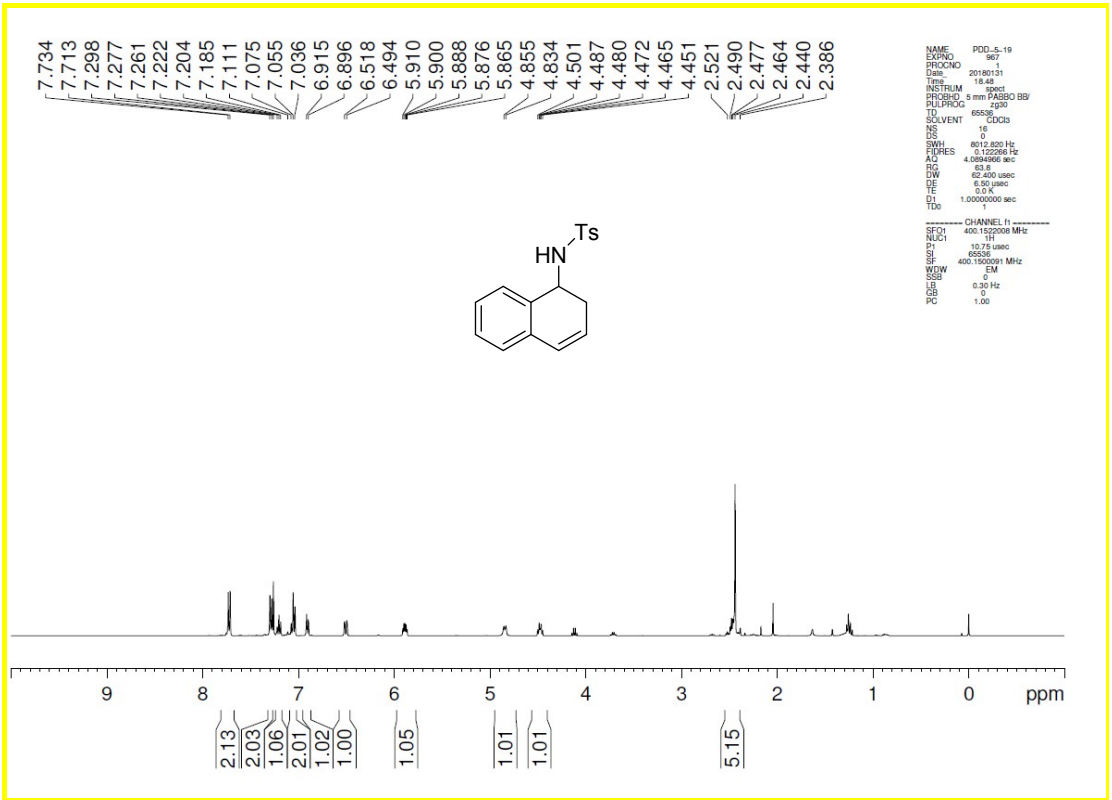
7.194
7.190
7.185
7.183
7.171
7.168
7.153
7.149
7.063
7.059
7.044
7.042
6.495
6.471
5.943
5.933
5.921
5.909
5.898
4.723
4.709
4.696
2.550
2.546
2.542
2.537
2.533
2.527
2.522
2.514
OH
10
9
8
7
6
5
4
3
2
1
0
ppm
1.03
2.06
1.00
1.00
1.01
1.04
1.99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7.075
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7.036
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6.896
6.518
6.494
5.910
5.900
5.888
5.876
5.865
4.855
4.834
4.501
4.487
4.480
4.472
4.465
4.451
2.521
2.490
2.477
2.464
2.440
2.386
Ts
HN
9
8
7
6
5
4
3
2
1
0
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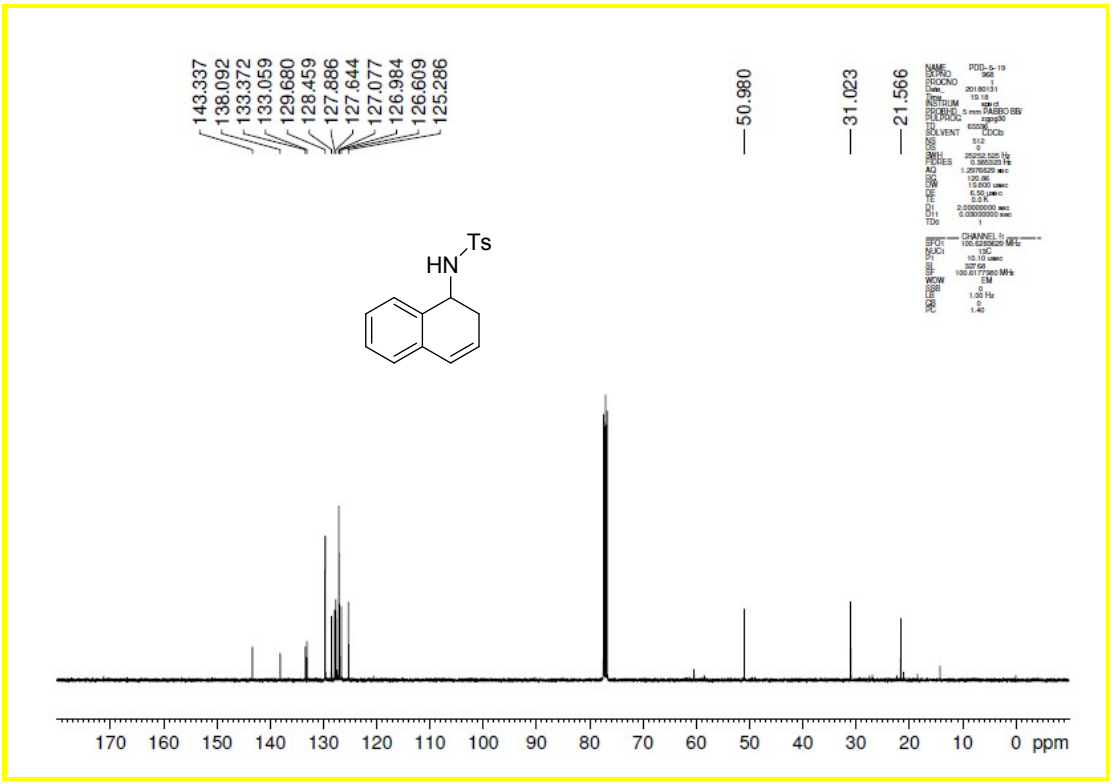
2.03
1.06
2.01
1.02
1.00
1.05
1.01
1.01
5.15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133.059
129.680
128.459
127.886
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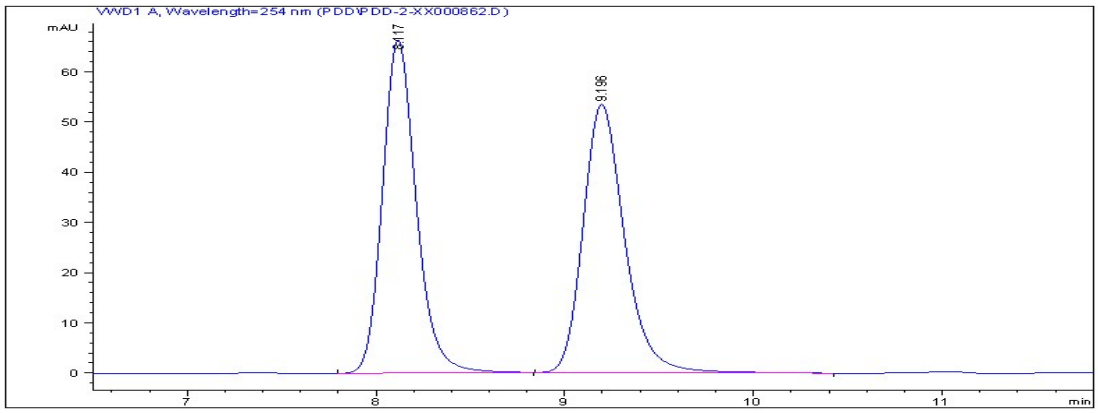
127.077
126.984
126.609
125.286
50.980
31.023
21.566
Ts
HN
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

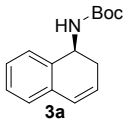
4. HPLC Spectra of Products

Note: All of the racemic products were prepared by using (±)-binap as ligand.

Racemic:

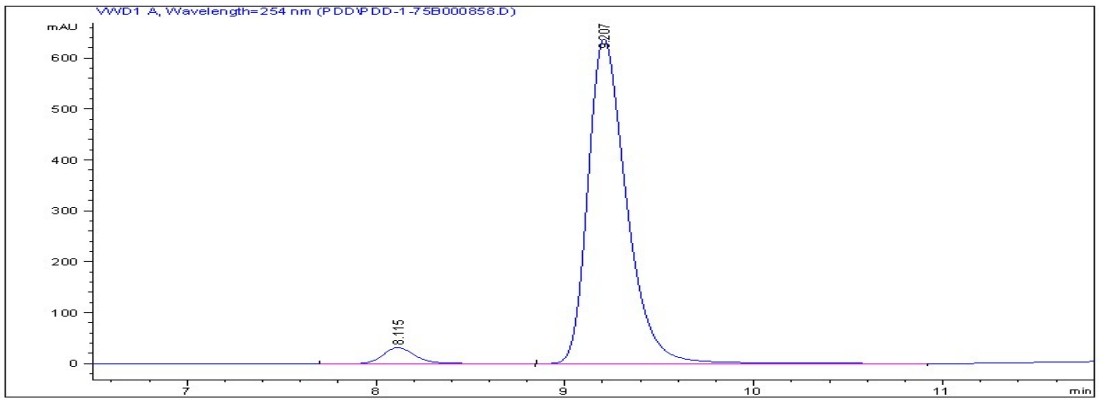


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.117	BB	0.1909	824.81531	66.39390	50.2946
2	9.196	BB	0.2339	815.15289	53.46169	49.7054

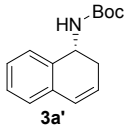


3a

Enantioenriched:

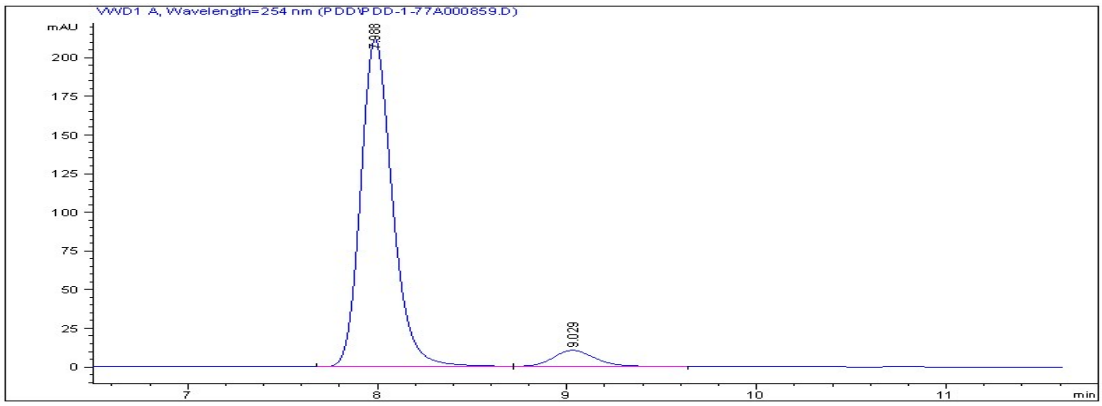


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.115	BB	0.1813	369.46960	31.38863	3.9468
2	9.207	BB	0.2146	8991.88281	637.47467	96.0532

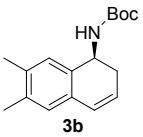


3a'

Enantioenriched:

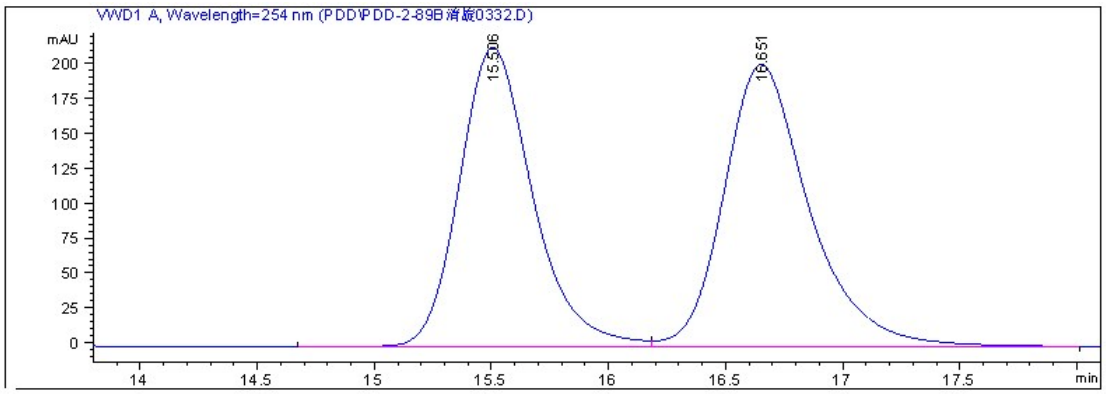


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.988	BV	0.1785	2461.13013	211.89738	93.8529
2	9.029	VB	0.2365	161.19783	10.42110	6.1471



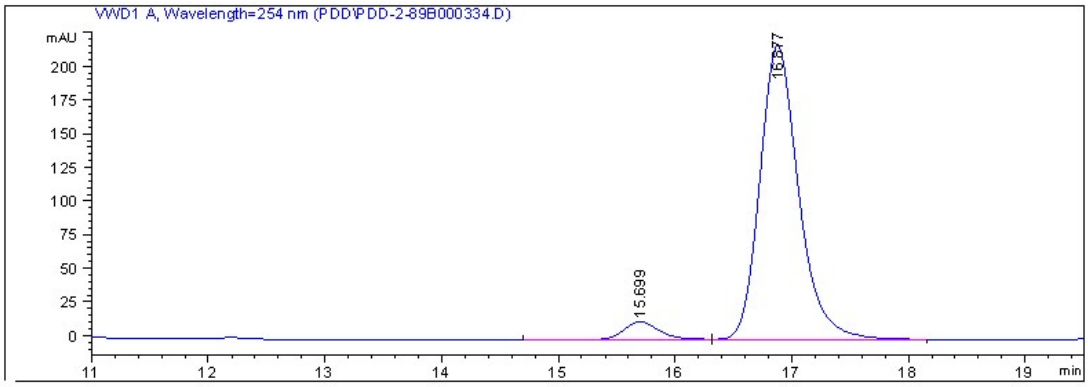
3b

Racemic:

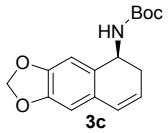


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.506	BV	0.3330	4669.07178	214.47264	47.6808
2	16.651	VB	0.3814	5123.28223	202.36613	52.3192

Enantioenriched:

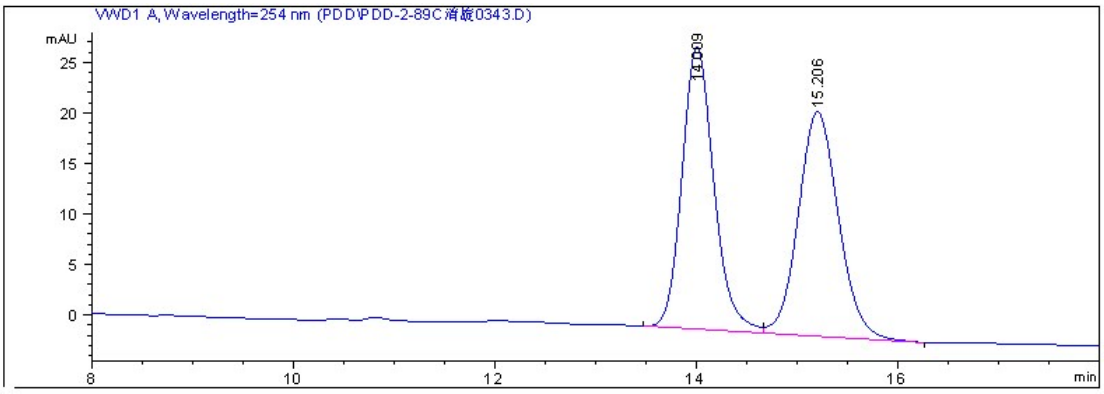


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.699	BB	0.3136	269.16464	13.16284	5.0837
2	16.877	BB	0.3529	5025.48486	218.01230	94.9163



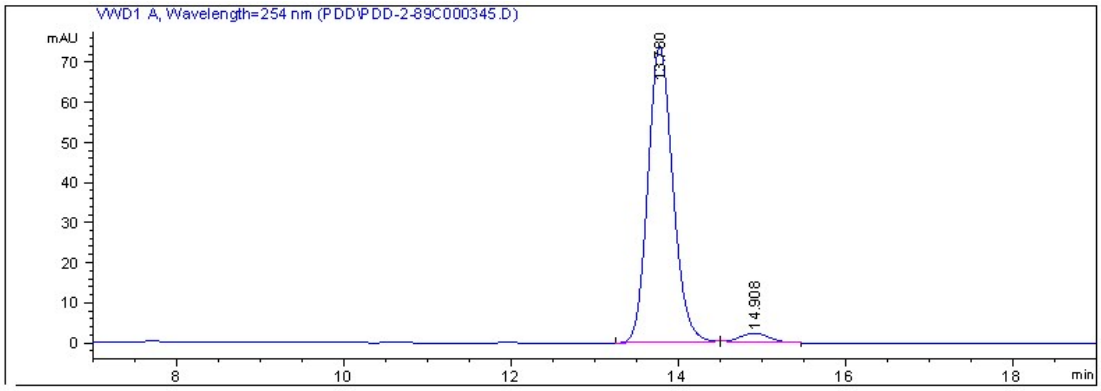
3c

Racemic:

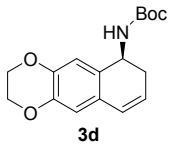


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.009	BV	0.3388	614.28790	27.90339	49.9564
2	15.206	VB	0.4259	615.36017	22.23675	50.0436

Enantioenriched:

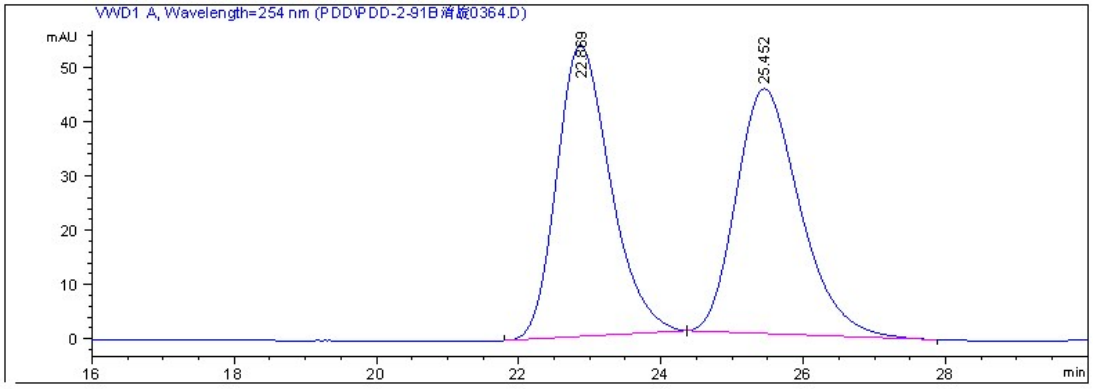


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.780	BB	0.3206	1529.50952	73.84499	96.8246
2	14.908	BB	0.3687	50.16080	2.14595	3.1754



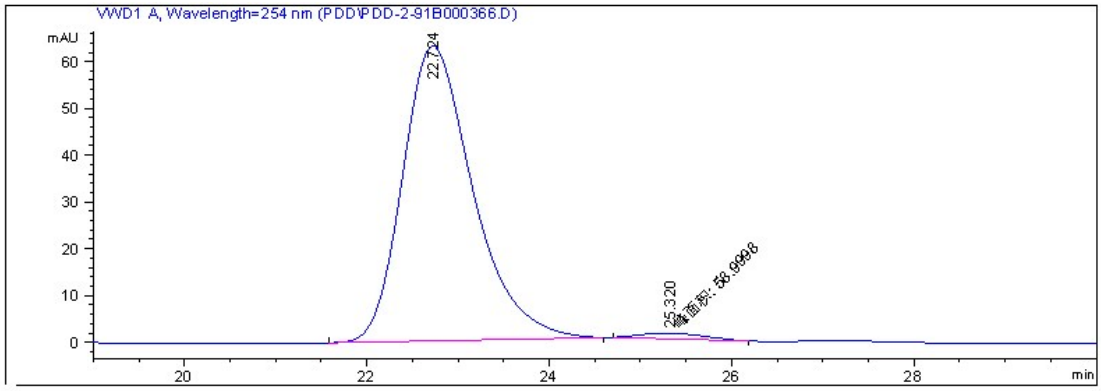
3d

Racemic:

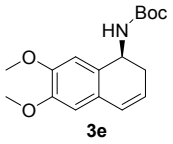


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.869	BB	0.8012	2806.99170	53.66749	49.9802
2	25.452	BB	0.9579	2809.21460	45.08805	50.0198

Enantioenriched:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.724	BB	0.8169	3375.41870	63.01539	98.2821
2	25.320	PP	0.7845	58.99982	1.25344	1.7179



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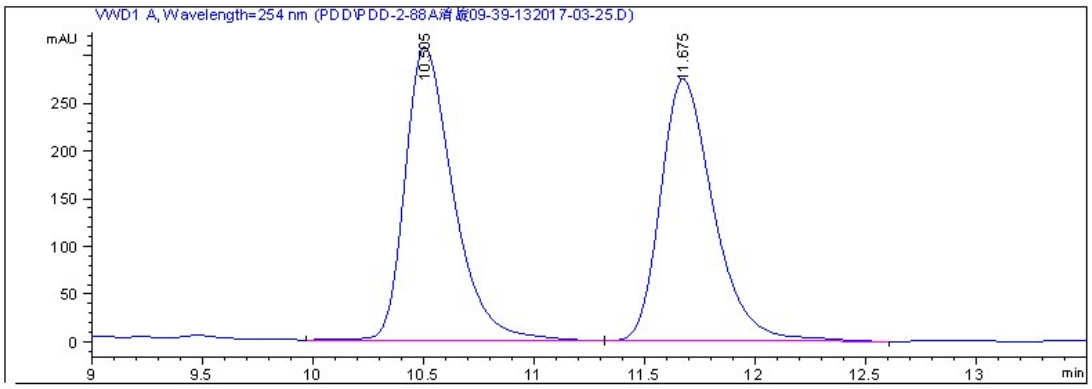
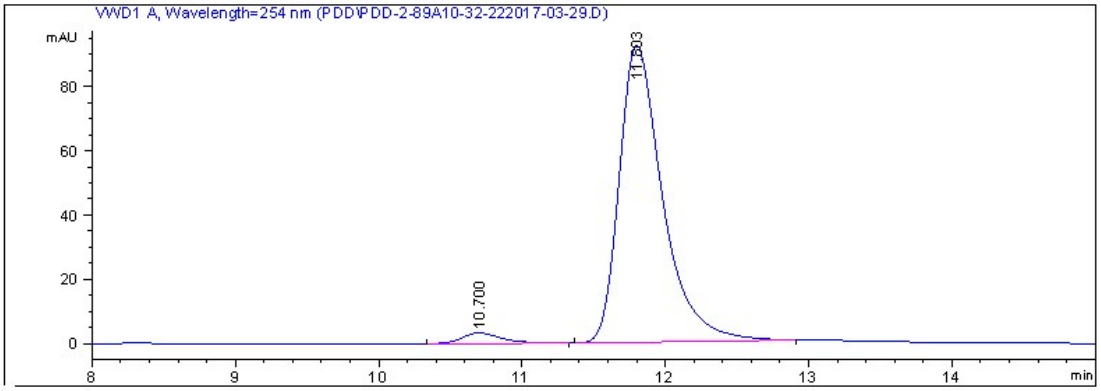
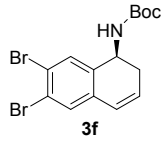


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.505	BB	0.2311	4671.27295	307.69165	50.5051
2	11.675	BB	0.2555	4577.82959	274.61224	49.4949

Enantioenriched:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.700	BB	0.2839	61.12031	3.24248	3.0436
2	11.803	BB	0.3178	1947.04089	92.43177	96.9564



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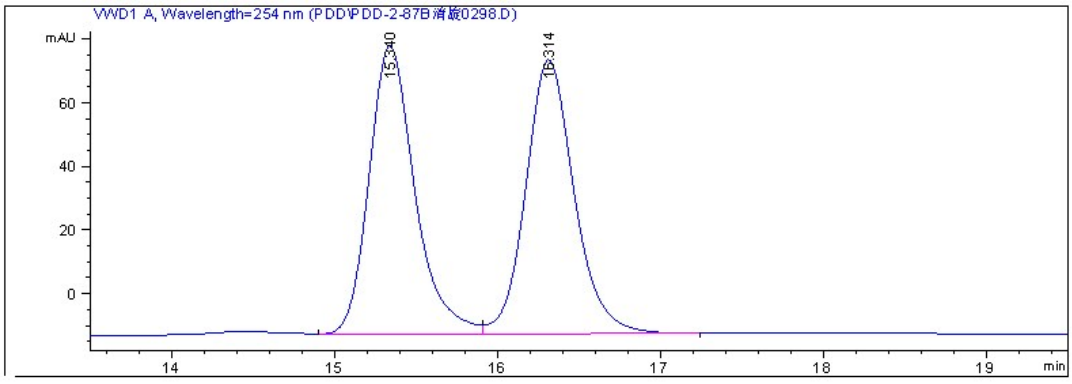
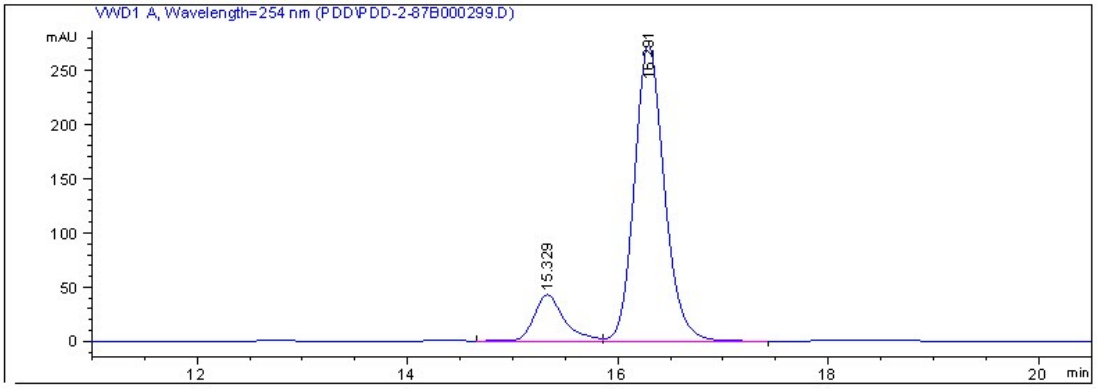
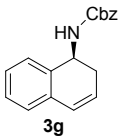


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.340	VV	0.2965	1768.43384	90.66959	49.8797
2	16.314	VB	0.3159	1776.96155	86.06216	50.1203

Enantioenriched:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.329	BV	0.2985	846.28113	42.46787	13.5459
2	16.291	VB	0.3030	5401.23926	272.76181	86.4541



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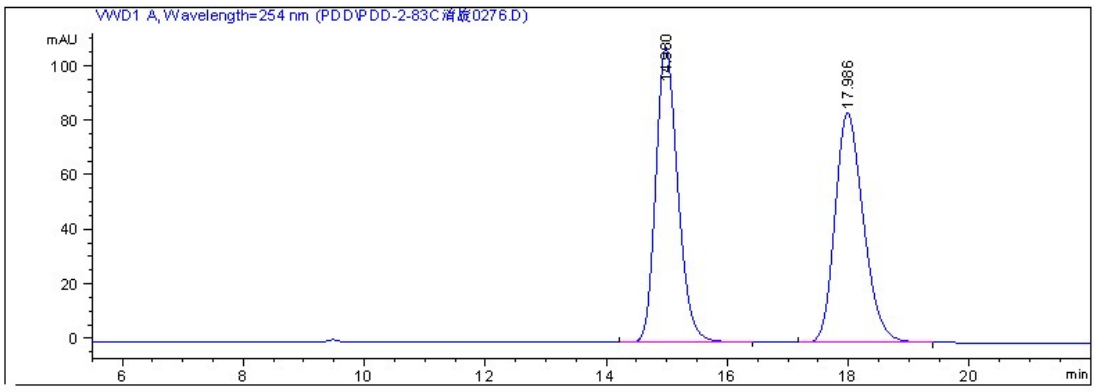
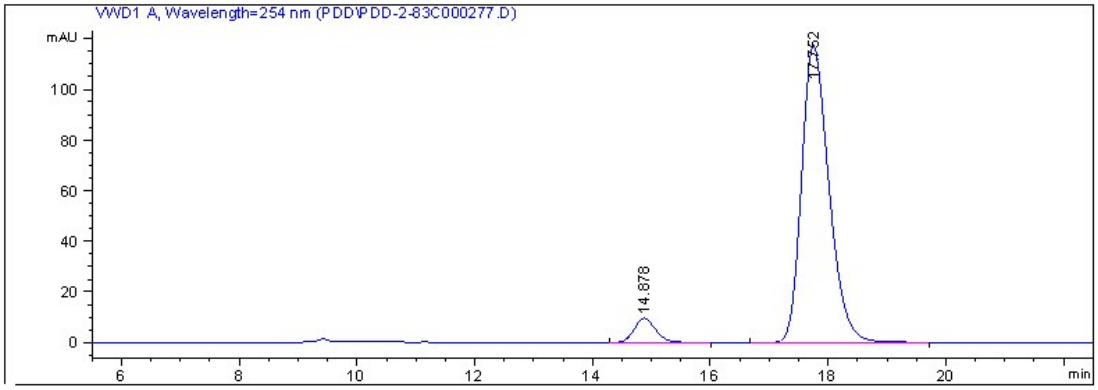
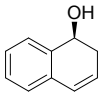


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.980	BB	0.3905	2744.64990	107.99549	49.9880
2	17.986	BB	0.5006	2745.97241	84.16503	50.0120

Enantioenriched:

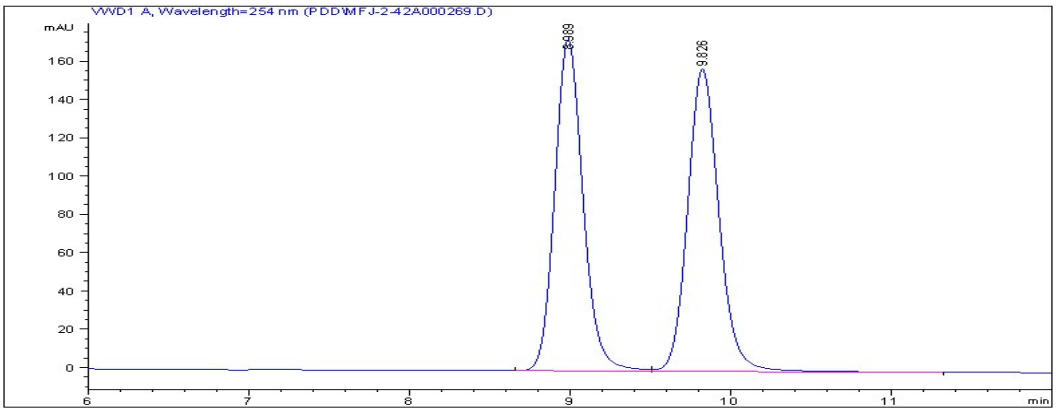


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.878	BB	0.3926	245.56967	9.59412	6.0673
2	17.752	BB	0.4988	3801.82617	117.40385	93.9327



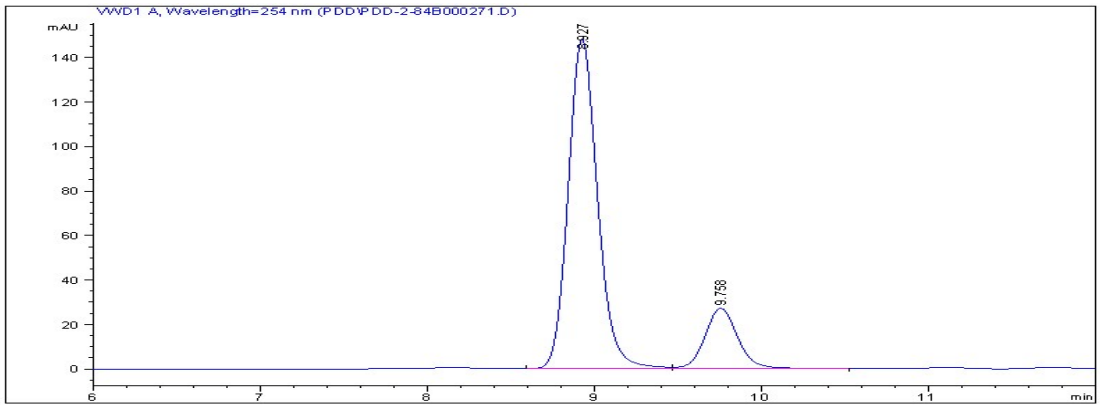
3h

Racemic:

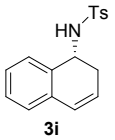


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.989	BV	0.1889	2116.86841	172.88521	49.7181
2	9.826	VB	0.2092	2140.87598	157.89984	50.2819

Enantioenriched:

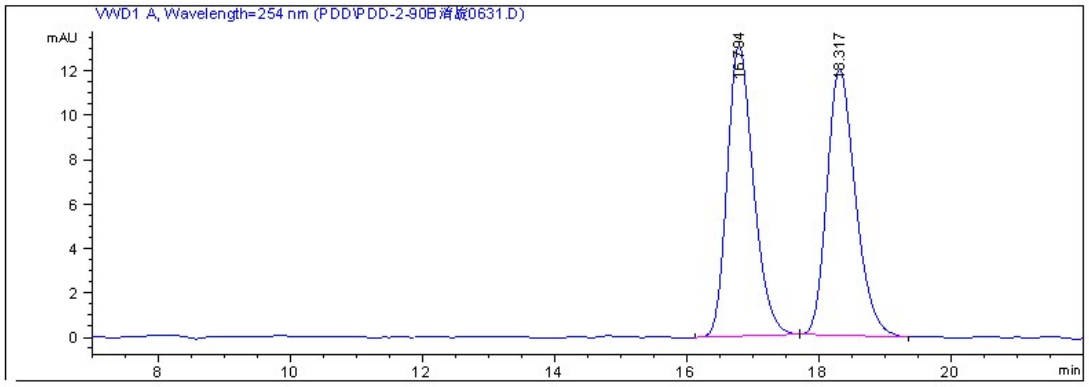


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.927	BV	0.1877	1809.50452	147.97963	82.9939
2	9.758	VB	0.2089	370.78247	27.21755	17.0061



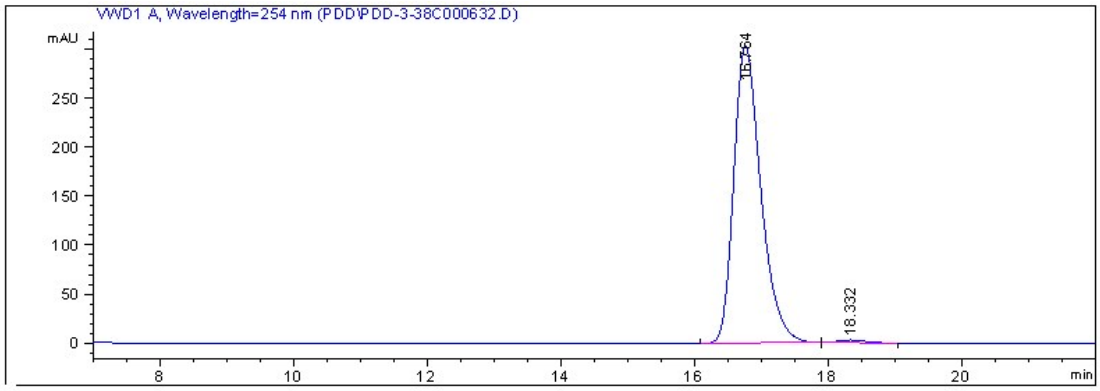
3i

Racemic:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.794	BB	0.4224	361.49081	13.08208	50.1490
2	18.317	BB	0.4583	359.34232	12.00273	49.8510

Enantioenriched:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.764	BB	0.4311	8521.29297	302.05930	99.0965
2	18.332	BB	0.4156	77.69044	2.87204	0.9035

References

1. F. Yang, J. -C. Chen, J. -B. Xu, F. -J. Ma, Y. -Y. Zhou, M. V. Shinde and B.-M. Fan, *Org. Lett.*, 2016, **18**, 4832–4835.