Enantioselective Construction of *cis*-Hydroindole Scaffolds via Asymmetric Inverse-Electron-Demand Diels–Alder Reaction: Application to the Formal Total Synthesis of (+)-Minovincine

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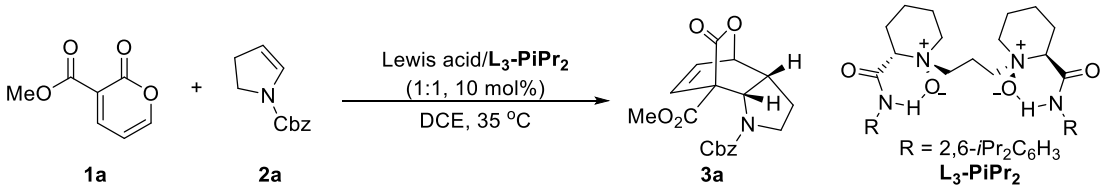
1. General Information

All manipulations were maintained under an atmosphere of argon unless otherwise stated. All solvents were dried and distilled according to general practice prior to use. All reagents were purchased from commercial sources and used without further purification unless specified otherwise. Solvents for flash column chromatography were technical grade and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed using Huanghai silica gel plates with HSGF 254. Visualization of the developed chromatogram was performed by UV absorbance (254 nm) and appropriate stains. Flash column chromatography was performed using silica gel (300-400 mesh) from Leyan.com with the indicated solvent system according to standard techniques. $CDCl_3$ was bought from Leyan.com. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker NMR 400 or Bruker NMR 500. Multiplicities are described as: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); and coupling constants (J) are reported in Hertz (Hz). ^{13}C NMR spectra were recorded with total proton decoupling. Chiral HPLC was recorded on a Shimadzu LC-20A spectrometer using Daicel Chiralcel IA, OJ, ID, AD, OD columns. HRMS (ESI) analysis was performed by the Analytical Instrumentation Center at Peking University Shenzhen Graduate School and (HRMS) data were reported with ion mass/charge (m/z) ratios as values in atomic mass units.

2. Optimization of Reaction Conditions

Table S1. Investigation of Lewis Acids.

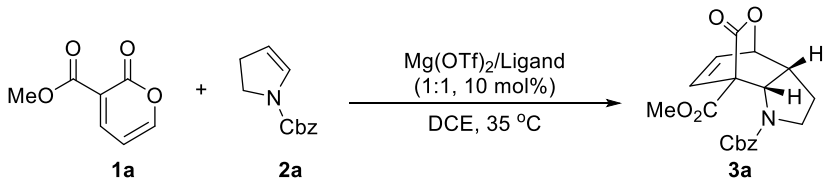


1a 2a 3a

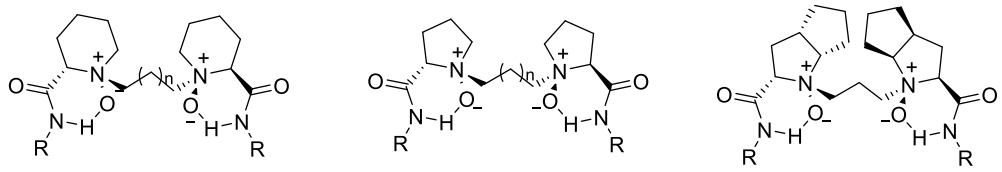
Entry[a]	Lewis acid	Time (h)	Yield (%)[b]	ee (%)[c]
1	$Fe(OTf)_3$	24	trace	--
2	$In(OTf)_3$	24	trace	--
3	$Sc(OTf)_3$	24	trace	--
4	$Zn(OTf)_2$	3	91	-18
5	$Ni(OTf)_2$	3	86	37
6	$Yb(OTf)_3$	3	92	13
7	$La(OTf)_3$	7	91	4
8	$Co(BF_4)_2{\cdot}6H_2O$	3	62	79
9	$Gd(OTf)_3$	3	50	2
10	$Mg(OTf)_2$	3	73	78
11	$Ca(OTf)_2$	12	trace	--
12	$Cu(OTf)_2$	8	66	42
13	$Dy(OTf)_3$	10	74	71

[a] Reaction conditions: **1a** (0.10 mmol), **2a** (0.15 mmol, 1.5 equiv.), Lewis acid (10 mol%), **L_3-PiPr$_2$** (10 mol%), DCE (0.5 mL), rt. [b] NMR yield detected by using CH_2Br_2 as an internal standard. [c] Enantiomeric excess determined by HPLC analysis on a chiral stationary phase. DCE = 1,2-dichloroethane.

Table S2. Investigation of Ligands.



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



L_3-PiPr$_2$: R = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 1
L_2-PiPr$_2$: R = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 0
L_3-PiAd: R =1-adamantyl, n = 1
L_3-PiEt$_2$: R = 2,6-Et$_2$C$_6$H$_3$, n = 1
L_3-PiMe$_2$: R = 2,6-Me$_2$C$_6$H$_3$, n = 1

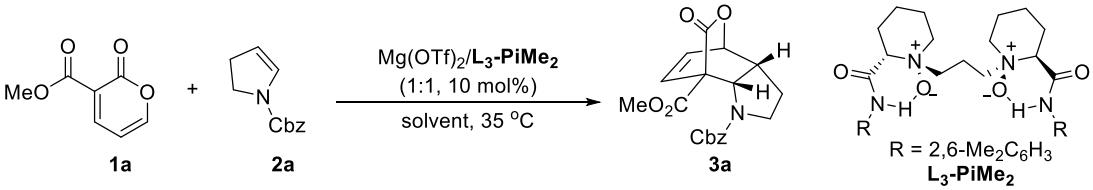
L_3-PrPr$_2$: R = 2,6-*i*Pr$_2$C$_6$H$_3$, n=1
L_2-PrPr$_2$: R = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 0
L_3-PrAd: R =1-adamantyl, n = 1
L_3-PrPh$_2$: R = C$_6$H$_5$, n = 1
L_3-PrCHPh$_2$: R = CH(C$_6$H$_5$)$_2$, n = 1
L_3-PrMe$_2$: R = 2,6-Me$_2$C$_6$H$_3$, n = 1

L_3-RaPr$_2$: R = 2,6-*i*Pr$_2$C$_6$H$_3$

Entry[a]	Ligand.	Time (h)	Yield (%)[b]	ee (%)[c]
1	**L_3-PiPr$_2$**	3	80	79
2	**L_2-PiPr$_2$**	12	99	68
3	**L_3-PrPr$_2$**	12	97	69
4	**L_2-PrPr$_2$**	17	97	67
5	**L_3-RaPr$_2$**	12	99	79
6	**L_3-PiMe$_2$**	3	97	88
7	**L_3-PiAd**	17	91	12
8	**L_3-PiEt$_2$**	6	95	82
9	**L_3-PrMe$_2$**	17	93	43
10	**L_3-PrPh**	12	99	2
11	**L_3-PrAd**	3	96	20
12	**L_3-PrCHPh$_2$**	6	99	6

[a] Reaction conditions: **1a** (0.10 mmol), **2a** (0.15 mmol, 1.5 equiv.), Mg(OTf)$_2$ (10 mol%), ligand (10 mol%), DCE (0.5 mL), rt,. [b] NMR yield detected by using CH_2Br_2 as an internal standard. [c] Enantiomeric excess determined by HPLC analysis on a chiral stationary phase. DCE = 1,2-dichloroethane.

Table S3. Investigation of Solvents.

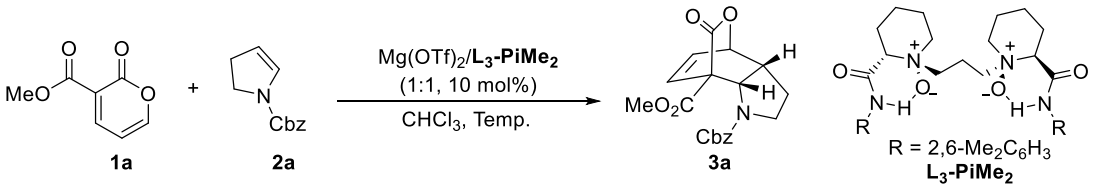


1a 2a 3a

Entry[a]	Solvent	Time (h)	Yield (%)[b]	ee (%)[c]
1	DCE	3	93	88
2	DCM	3	99	91
3	$CHCl_3$	3	99	95
4	Tol	12	86	64
5	PhCl	12	97	85
6	THF	12	96	64
7	Et_2O	12	99	77
8	EA	12	60	85
9	MeCN	12	99	88
10	MeOH	12	68	28

[a] Reaction conditions: **1a** (0.10 mmol), **2a** (0.15 mmol, 1.5 equiv.), $Mg(OTf)_2$ (10 mol %), **L_3-PiMe$_2$** (10 mol %), solvent (0.5 mL), 35 °C. [b] NMR yield detected by using CH_2Br_2 as an internal standard. [c] Enantiomeric excess determined by HPLC analysis on a chiral stationary phase.

Table S4. Investigation of Temperature.

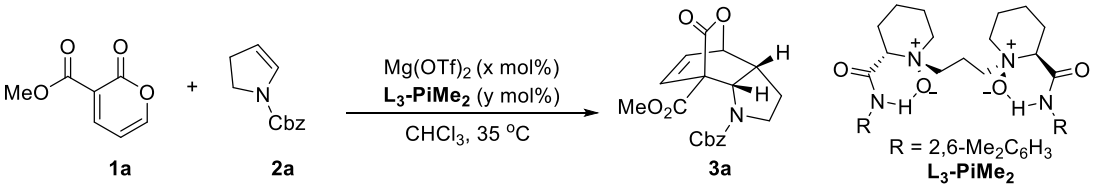


1a 2a 3a

Entry[a]	Temp. (°C)	Time (h)	Yield (%)[b]	ee (%)[c]
1	35	3	>99	95
2	45	3	99	88
3	25	4	>99	94
5	15	12	>99	95
6	5	12	59	93
7	-20	36	trace	--

[a] Reaction conditions: **1a** (0.10 mmol), **2a** (0.15 mmol, 1.5 equiv.), $Mg(OTf)_2$ (10 mol %), **L_3-PiMe$_2$** (10 mol %), $CHCl_3$ (0.5 mL), at indicated temperature. [b] NMR yield detected by using CH_2Br_2 as an internal standard. [c] Enantiomeric excess determined by HPLC analysis on a chiral stationary phase.

Table S5. Investigation of the Loading and Ratio of Catalyst.



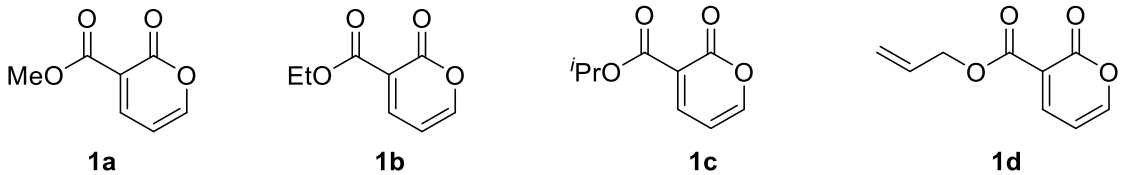
1a 2a 3a

Entry[a]	x	y	Time (h)	Yield (%)[b]	ee (%)[c]
1	10	10	3	99	95
2	5	5	3	99	95
3	2	2	12	99	93
4	10	11	12	89	95
5	10	9	12	90	87

[a] Reaction conditions: **1** (0.10 mmol), **2a** (0.15 mmol, 1.5 equiv.), $Mg(OTf)_2$ (x mol %), **L_3-PiMe$_2$** (y mol %), $CHCl_3$ (0.5 mL), 35 °C. [b] NMR yield detected by using CH_2Br_2 as an internal standard. [c] Enantiomeric excess determined by HPLC analysis on a chiral stationary phase.

3. Preparation of Substrates

Table S6. Structures of Substituted 2-pyrones.

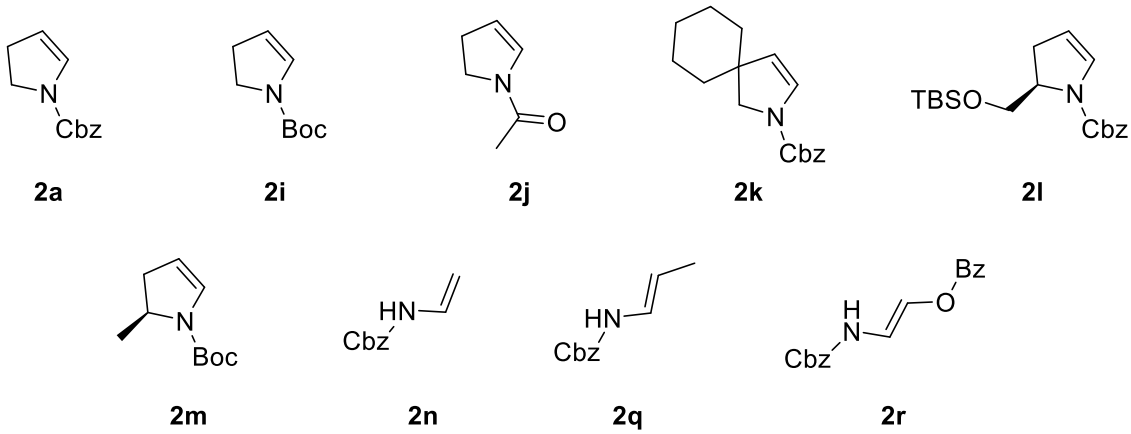


1a 1b 1c 1d

1e 1f 1g 1h

All 2-pyrones were prepared according to the literature.[1]

Table S7. Structures of Substituted Enamines.

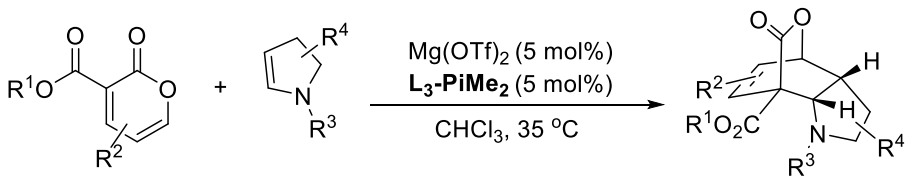


2a **2i** **2j** **2k** **2l**

2m **2n** **2q** **2r**

All enamines were prepared according to the literature.[2-8]

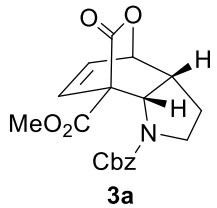
4. General Procedure for the Catalytic Asymmetric Reaction



1 **2** **3**

After stirring a mixture of $Mg(OTf)_2$ (0.005 mmol, 5 mol %) and **L_3-PiMe$_2$** (0.005 mmol, 5 mol %) in dry $CHCl_3$ (0.5 mL) at 35 °C for 1 h under argon atmosphere, substrate **1** (0.10 mmol) and substrate **2** (0.15 mmol) were added, and then the reaction mixture was stirring at 35 °C. After the disappearance of substrate **1** (monitored by TLC), the crude product was purified by silica gel flash chromatography (EtOAc: petroleum ether 1: 3) to afford the desired product **3**.

1-benzyl 7-methyl (3a*R*,4*R*,7*S*,7a*S*)-8-oxo-2,3,3a,7a-tetrahydro-1*H*-4,7-(epoxymethano)indole-1,7(4*H*)-dicarboxylate

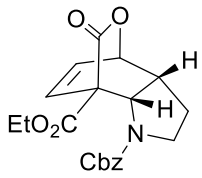


3a

Following the general procedure, reaction time 3 h. Product **3a** was obtained as a white solid (35 mg, 99% yield, 95% ee). The enantiomeric excess was determined by CHIRALPAK AD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t

(minor) = 21.59 min, t (major) = 24.89 min. $[\alpha]^{25}D$ = –81.0 (*c* = 0.23, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.31 (m, 5H), 7.02 (d, *J* = 7.7 Hz, 1H), 6.60 (dd, *J* = 7.8, 5.0 Hz, 1H), 5.25 – 4.98 (m, 3H), 4.92 (d, *J* = 7.7 Hz, 1H), 4.12 – 3.50 (m, 4H), 3.27 (dd, *J* = 11.6, 5.0 Hz, 1H), 3.14 (td, *J* = 11.0, 7.5 Hz, 1H), 2.12 (dd, *J* = 13.6, 10.4 Hz, 1H), 1.81 – 1.55 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 167.3, 154.4, 136.2, 133.0, 130.0, 128.5, 128.2, 128.0, 75.7, 67.4, 60.5, 59.5, 53.0, 48.0, 44.9, 25.9; HRMS (ESI): exact mass calculated for: $C_{19}H_{19}O_6NNa$ $[M+Na]^+$: 380.1105, found: 380.1103.

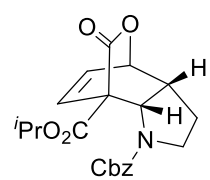
1-benzyl 7-ethyl (3a*R*,4*R*,7*S*,7a*S*)-8-oxo-2,3,3a,7a-tetrahydro-1*H*-4,7-(epoxymethano)indole-1,7(4*H*)-dicarboxylate



3b

Following the general procedure, reaction time 12 h. Product **3b** was obtained as a white solid (32 mg, 86% yield, 88% ee). The enantiomeric excess was determined by CHIRALPAK AD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 17.36 min, t (major) = 14.98 min. $[\alpha]^{25}D$ = –85.7 (*c* = 0.14, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.30 (m, 5H), 7.00 (d, *J* = 7.7 Hz, 1H), 6.58 (d, *J* = 7.8 Hz, 1H), 5.41 – 5.09 (m, 1H), 5.03 (d, *J* = 12.1 Hz, 1H), 4.93 (d, *J* = 7.6 Hz, 1H), 4.60 – 3.97 (m, 2H), 3.74 (t, *J* = 10.0 Hz, 1H), 3.34 – 3.20 (m, 1H), 3.13 (td, *J* = 11.0, 7.4 Hz, 1H), 2.09 (tt, *J* = 10.2, 8.1 Hz, 1H), 1.64 (dd, *J* = 13.7, 7.4 Hz, 1H), 1.47 – 1.16 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 166.7, 154.4, 136.3, 133.1, 130.0, 128.5, 128.2, 128.0, 75.7, 67.3, 62.2, 60.4, 59.6, 48.1, 45.0, 25.8, 14.0. HRMS (ESI): exact mass calculated for: $C_{20}H_{21}O_6NNa$ $[M+Na]^+$: 394.1261, found: 394.1260.

1-benzyl 7-isopropyl (3a*R*,4*R*,7*S*,7a*S*)-8-oxo-2,3,3a,7a-tetrahydro-1*H*-4,7-(epoxymethano)indole-1,7(4*H*)-dicarboxylate

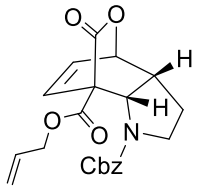


3c

Following the general procedure, reaction time 12 h. Product **3c** was obtained as a white solid (27 mg, 70% yield, 92% *ee*). The enantiomeric excess was determined by CHIRALPAK OJ-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 25.29 min, t (major) = 19.05 min. $[\alpha]^{25}D$ = –71.4 (*c* = 0.17, in CH_2Cl_2). ^1H

NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 5H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.57 (dd, *J* = 7.8, 5.0 Hz, 1H), 5.27 – 5.09 (m, 3H), 5.05 (d, *J* = 12.2 Hz, 1H), 4.92 (d, *J* = 7.6 Hz, 1H), 3.73 (t, *J* = 10.2 Hz, 1H), 3.30 – 3.19 (m, 1H), 3.13 (td, *J* = 11.0, 7.4 Hz, 1H), 2.16 – 1.99 (m, 1H), 1.64 (dd, *J* = 13.7, 7.3 Hz, 1H), 1.46 – 1.30 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 166.1, 154.4, 136.4, 133.2, 129.9, 128.5, 128.1, 128.0, 75.6, 70.0, 67.2, 60.2, 59.7, 48.0, 45.0, 25.9, 21.6. HRMS (ESI): exact mass calculated for: $C_{21}H_{23}O_6NNa$ $[M+Na]^+$: 408.1457, found: 408.1450.

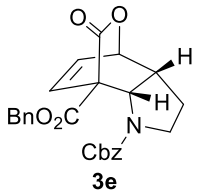
7-allyl 1-benzyl (3a*R*,4*R*,7*S*,7a*S*)-8-oxo-2,3,3a,7a-tetrahydro-1*H*-4,7-(epoxymethano)indole-1,7(4*H*)-dicarboxylate



3d

Following the general procedure, reaction time 12 h. Product **3d** was obtained as a white solid (22 mg, 60% yield, 89% ee). The enantiomeric excess was determined by CHIRALPAK AD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 17.14 min, t (major) = 18.84 min. $[\alpha]^{25}D$ = –55.6 (*c* = 0.14, in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.58 (dd, *J* = 7.8, 5.0 Hz, 1H), 6.01 (s, 1H), 5.43 (d, *J* = 16.9 Hz, 1H), 5.25 (d, *J* = 10.4 Hz, 1H), 5.18 – 5.07 (m, 2H), 5.02 (d, *J* = 11.9 Hz, 1H), 4.96 – 4.80 (m, 2H), 4.79 – 4.31 (m, 1H), 3.72 (s, 1H), 3.36 – 3.18 (m, 1H), 3.11 (td, *J* = 11.0, 7.4 Hz, 1H), 2.08 (tt, *J* = 10.2, 6.0 Hz, 1H), 1.63 (dd, *J* = 13.8, 7.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 166.7, 154.4, 136.3, 132.9, 132.1, 130.1, 128.5, 128.2, 128.0, 118.2, 75.7, 67.3, 66.7, 60.5, 59.6, 48.0, 44.9, 25.8. HRMS (ESI): exact mass calculated for: $C_{21}H_{21}O_6NNa$ $[M+Na]^+$: 406.1261, found: 406.1267.

Dibenzyl (3a*R*,4*R*,7*S*,7a*S*)-8-oxo-2,3,3a,7a-tetrahydro-1*H*-4,7-(epoxymethano)indole-1,7(4*H*)-dicarboxylate

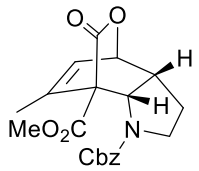


3e

Following the general procedure, reaction time 12 h. Product **3e** was obtained as a colorless oil (35 mg, 80% yield, 86% *ee*). The enantiomeric excess was determined by CHIRALPAK AD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20 1.0 mL/min, λ = 210 nm, t

(minor) = 23.63 min, t (major) = 32.80 min. $[\alpha]^{25}D$ = –44.4 (*c* = 0.32, in CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (s, 2H), 7.31 – 7.18 (m, 8H), 6.92 (d, J = 7.5 Hz, 1H), 6.47 (dd, J = 7.8, 5.0 Hz, 1H), 5.33 (s, 1H), 5.01 (dt, J = 22.8, 9.8 Hz, 4H), 4.84 (d, J = 7.6 Hz, 1H), 3.62 (s, 1H), 3.14 (s, 1H), 3.09 – 2.96 (m, 1H), 2.07 – 1.88 (m, 1H), 1.53 (dd, J = 13.8, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 166.8, 154.5, 136.4, 135.9, 132.9, 130.2, 128.6, 128.5, 128.2, 128.2, 128.1, 75.8, 67.9, 67.4, 60.7, 59.7, 48.1, 45.0, 25.8. HRMS (ESI): exact mass calculated for: $C_{25}H_{23}O_6NNa$ $[M+Na]^+$: 456.1423, found: 456.1418.

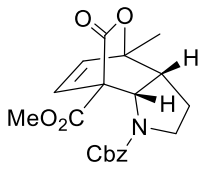
Benzyl (3a*R*,4*R*,7*S*,7a*S*)-6-methyl-7-((methylperoxy)-λ^2-methyl)-8-oxo-2,3,3a,4,7,7a-hexahydro-1*H*-4,7-(epoxymethano)indole-1-carboxylate



3f

Following the general procedure, reaction time 12 h. Product **3f** was obtained as a white solid (34 mg, 90% yield, 89% ee). The enantiomeric excess was determined by CHIRALPAK AD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 18.71 min, t (major) = 15.46 min. $[\alpha]^{25}D$ = –90.7 (*c* = 0.19, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H), 6.57 – 5.83 (m, 1H), 5.19 (d, *J* = 12.4 Hz, 1H), 5.08 – 4.92 (m, 3H), 3.83 (s, 3H), 3.70 (t, *J* = 10.2 Hz, 1H), 3.25 – 3.12 (m, 1H), 3.07 (td, *J* = 10.9, 7.4 Hz, 1H), 2.15 – 2.03 (m, 4H), 1.65 (dd, *J* = 13.7, 7.4 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 167.5, 154.4, 143.4, 136.3, 128.5, 128.2, 128.0, 124.5, 75.1, 67.3, 61.9, 60.8, 52.3, 48.0, 44.9, 25.8, 20.3. HRMS (ESI): exact mass calculated for: $C_{20}H_{21}O_6NNa$ $[M+Na]^+$: 394.1261, found: 394.1263.

1-benzyl 7-methyl (3a*R*,4*R*,7*S*,7a*S*)-4-methyl-8-oxo-2,3,3a,7a-tetrahydro-1*H*-4,7-(epoxymethano)indole-1,7(4*H*)-dicarboxylate

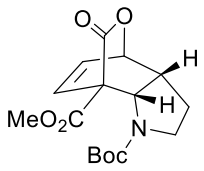


3g

Following the general procedure, reaction time 12 h. Product **3g** was obtained as a white solid (32 mg, 86% yield, 94% ee). The enantiomeric excess was determined by CHIRALPAK AD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 32.09 min, t (major) = 25.16 min. $[\alpha]^{25}D$ = –114.6 (*c* = 0.27, in CH_2Cl_2). ^1H

NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.27 (m, 5H), 6.92 (d, *J* = 7.8 Hz, 1H), 6.30 (d, *J* = 7.9 Hz, 1H), 5.07 (dd, *J* = 40.5, 12.3 Hz, 2H), 4.93 (d, *J* = 7.7 Hz, 1H), 3.86 (d, *J* = 23.9 Hz, 3H), 3.70 (t, *J* = 10.2 Hz, 1H), 3.11 (td, *J* = 10.9, 7.3 Hz, 1H), 3.03 – 2.89 (m, 1H), 2.04 (dq, *J* = 13.8, 10.2 Hz, 1H), 1.70 (s, 3H), 1.64 (dd, *J* = 13.8, 7.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 167.4, 154.5, 136.3, 134.4, 131.9, 128.5, 128.2, 128.0, 82.7, 67.4, 61.98, 59.5, 53.0, 50.7, 47.9, 26.1, 20.9. HRMS (ESI): exact mass calculated for: $C_{20}H_{21}O_6NNa$ $[M+Na]^+$: 394.1261, found: 394.1261.

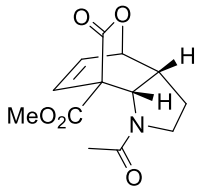
1-(tert-butyl) 7-methyl (3a*R*,4*R*,7*S*,7a*S*)-8-oxo-2,3,3a,7a-tetrahydro-1*H*-4,7-(epoxymethano)indole-1,7(4*H*)-dicarboxylate



3i

Following the general procedure, reaction time 24 h. Product **3i** was obtained as a white solid (26 mg, 80% yield, 94% *ee*). The enantiomeric excess was determined by CHIRALPAK OD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 7.23 min, t (major) = 6.04 min. $[\alpha]^{25}D$ = –121.8 (*c* = 0.11, in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (d, J = 7.5 Hz, 1H), 6.55 (dd, J = 7.9, 5.0 Hz, 1H), 5.15 – 5.08 (m, 1H), 4.84 (d, J = 7.7 Hz, 1H), 3.90 (s, 3H), 3.59 (s, 1H), 3.26 – 3.19 (m, 1H), 3.03 (td, J = 11.0, 7.4 Hz, 1H), 2.06 (m, J = 13.5, 10.3, 2.6 Hz, 1H), 1.58 (dd, J = 13.7, 7.4 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 167.3, 153.9, 133.1, 130.1, 80.5, 75.8, 60.3, 59.5, 53.2, 47.9, 44.5, 28.3, 26.1. HRMS (ESI): exact mass calculated for: $C_{16}H_{21}O_6NNa$ $[M+Na]^+$: 346.1261, found: 346.1260.

Methyl (3a*R*,4*R*,7*S*,7a*S*)-1-acetyl-8-oxo-1,2,3,3a,4,7a-hexahydro-7*H*-4,7-(epoxymethano)indole-7-carboxylate

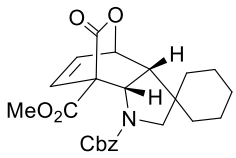


3j

Following the general procedure, $Mg(OTf)_2$ (10 mol%), **L$_3$-PiMe$_2$** (10 mol%), **1a** (0.1 mmol) and **2j** (0.15 mmol) reacted for 24 h. Product **3j** was obtained as a white solid (25 mg, 92% yield, 87% *ee*). The enantiomeric excess was determined by CHIRALPAK OD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 12.39 min, t (major) = 10.29 min. $[\alpha]^{25}D$ = –136.4 (*c* = 0.11, in CH_2Cl_2). ^{1}H NMR (400 MHz,

$CDCl_3$) δ 6.98 (d, J = 7.7 Hz, 1H), 6.57 (d, J = 2.7 Hz, 1H), 5.12 (s, 1H), 4.96 (d, J = 7.6 Hz, 1H), 3.93 (s, 3H), 3.50 (t, J = 10.0 Hz, 1H), 3.24 (dd, J = 17.9, 10.3 Hz, 2H), 2.15 (dq, J = 20.6, 10.2 Hz, 1H), 1.96 (s, 3H), 1.71 (dd, J = 13.7, 7.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 167.8, 167.6, 133.4, 129.9, 75.6, 59.7, 59.1, 53.2, 49.0, 44.3, 26.1, 23.3. HRMS (ESI): exact mass calculated for: $C_{13}H_{15}O_5NNa$ $[M+Na]^+$: 288.0842, found: 288.0842.

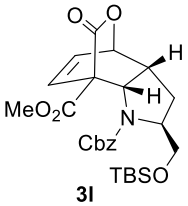
1'-benzyl 7'-methyl (3a'*R*,4'*R*,7'*S*,7a'*S*)-8'-oxo-3a',7a'-dihydrospiro[cyclohexane-1,3'-[4,7](epoxymethano)indole]-1',7'(2'*H*,4'*H*)-dicarboxylate



3k

Following the general procedure, $Mg(OTf)_2$ (10 mol%), **L$_3$-PiMe$_2$** (10 mol%), **1a** (0.1 mmol) and **2k** (0.15 mmol) reacted for 36 h. Product **3k** was obtained as a white solid (34 mg, 79% yield, 85% *ee*). The enantiomeric excess was determined by CHIRALPAK OD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 16.42 min, t (major) = 9.15 min. $[\alpha]^{25}D$ = –85.0 (*c* = 0.11, in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 5H), 6.99 (d, J = 7.5 Hz, 1H), 6.57 (d, J = 4.7 Hz, 1H), 5.45 – 4.86 (m, 4H), 3.90 (d, J = 74.1 Hz, 3H), 3.64 (d, J = 10.7 Hz, 1H), 3.55 (s, 1H), 2.87 (d, J = 4.4 Hz, 1H), 2.81 (d, J = 11.2 Hz, 1H), 1.47 (dd, J = 76.4, 28.8 Hz, 10H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 167.6, 155.1, 136.6, 132.8, 130.0, 128.7, 128.4, 127.8, 74.3, 67.4, 60.4, 59.4, 57.7, 54.7, 53.3, 42.5, 37.2, 32.0, 25.9, 23.6, 22.3. HRMS (ESI): exact mass calculated for: $C_{24}H_{27}O_6NNa$ $[M+Na]^+$: 448.1731, found: 448.1731.

1-benzyl 7-methyl (2*R*,3a*R*,4*R*,7*S*,7a*S*)-2-(((tert-butyldimethylsilyl)oxy)methyl)-8-oxo-2,3,3a,7a-tetrahydro-1*H*-4,7-(epoxymethano)indole-1,7(4*H*)-dicarboxylate

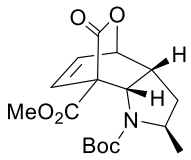


3l

Following the general procedure, reaction time 24 h. Product **3l** was obtained as a colorless oil (44 mg, 88% yield, dr > 20:1). $[\alpha]^{25}D$ = –89.1 (*c* = 0.12, in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 5H), 6.84 (d, J = 7.6 Hz, 1H), 6.47 (dd, J = 7.8, 5.0 Hz, 1H), 5.20 – 4.90 (m, 3H), 4.69 (d, J = 8.0 Hz, 1H), 4.12 – 4.03 (m, 1H), 3.90 (s, 3H), 3.63 (s, 1H), 3.48 (dd, J = 10.2, 2.6 Hz, 1H), 3.24 – 3.15 (m, 1H), 2.09 – 1.98 (m, 1H), 1.48 (ddd, J

= 13.3, 8.8, 7.4 Hz, 1H), 0.85 (s, 9H), -0.03 (d, J = 2.2 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 168.1, 153.7, 136.4, 132.6, 128.8, 128.6, 128.3, 128.3, 75.6, 67.2, 65.3, 61.5, 60.8, 60.0, 52.7, 45.4, 28.1, 26.0, 18.3, -5.4, -5.5. HRMS (ESI): exact mass calculated for: $C_{26}H_{35}O_7NSiNa$ $[M+Na]^+$: 524.2075, found: 524.2076.

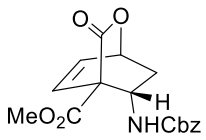
1-(tert-butyl) 7-methyl (2*S*,3a*R*,4*R*,7*S*,7a*S*)-2-methyl-8-oxo-2,3,3a,7a-tetrahydro-1*H*-4,7-(epoxymethano)indole-1,7(4*H*)-dicarboxylate



3m

Following the general procedure, reaction time 36 h. Product **3m** was obtained as a white solid (29 mg, 86% yield, dr > 20:1). $[\alpha]^{25}D$ = –92.5 (*c* = 0.12, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 – 6.80 (m, 1H), 6.46 (dd, J = 7.8, 5.0 Hz, 1H), 5.02 (ddd, J = 5.1, 3.5, 1.8 Hz, 1H), 4.62 (d, J = 7.9 Hz, 1H), 3.87 (s, 3H), 3.86 – 3.79 (m, 1H), 3.16 – 3.05 (m, 1H), 1.73 – 1.57 (m, 2H), 1.37 (s, 9H), 1.10 (d, J = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 167.7, 153.6, 132.9, 128.8, 80.2, 75.5, 60.2, 58.8, 55.6, 52.7, 43.6, 33.3, 28.3, 21.3. HRMS (ESI): exact mass calculated for: $C_{17}H_{23}O_6NNa$ $[M+Na]^+$: 360.1418, found: 360.1418.

Methyl (1*S*,4*S*,8*S*)-8-(((benzyloxy)carbonyl)amino)-3-oxo-2-oxabicyclo [2.2.2]oct-5-ene-4-carboxylate

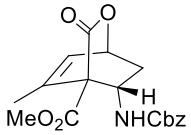


3n

Following the general procedure, $Mg(OTf)_2$ (10 mol%), **L_3-PiMe$_2$** (10 mol%), **1a** (0.1 mmol) and **2n** (0.15 mmol) reacted for 24 h. Product **3n** was obtained as a colorless oil (27 mg, 80% yield, 92% *ee*). The enantiomeric excess was determined by CHIRALPAK ID (0.46 cm × 25 cm), hexanes/*i*PrOH = 70/30, 1.0 mL/min, λ = 210 nm, t (minor) = 69.45 min, t (major) = 28.27 min. $[\alpha]^{25}D$ = –25.5 (*c* = 0.44, in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 11.8 Hz, 5H), 6.90 – 6.79 (m, 1H), 6.73 (dd, *J* = 7.8, 5.1 Hz, 1H), 5.25 (d, *J* = 1.6 Hz, 1H), 5.06 (s, 2H), 4.93 – 4.77 (m, 1H), 4.63 (d, *J* = 9.9 Hz, 1H), 3.83 (s, 3H), 2.86 (d, *J* = 10.0 Hz, 1H), 1.55 (dd, *J* = 14.4, 2.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 167.1, 155.0, 135.9, 133.6, 129.6, 128.7, 128.6, 128.5, 128.3,

73.7, 67.3, 59.7, 53.3, 46.7, 36.9. HRMS (ESI): exact mass calculated for: $C_{17}H_{17}O_6NNa$ $[M+Na]^+$: 354.0954, found: 354.0948.

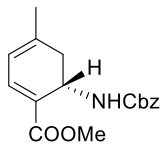
Benzyl ((1*S*,4*S*,5*S*)-8-methyl-4-((methylperoxy)-λ²-methyl)-3-oxo-2-oxabicyclo[2.2.2]oct-7-en-5-yl)carbamate



3o

Following the general procedure, $Mg(OTf)_2$ (10 mol%), **L3-PiMe2** (10 mol%), **1f** (0.1 mmol) and **2n** (0.15 mmol) reacted for 36 h. Product **3o** was obtained as a colorless oil (28 mg, 82% yield, 90% *ee*). The enantiomeric excess was determined by CHIRALPAK OD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 6.84 min, t (major) = 7.40 min. $[\alpha]^{25}D$ = –20.3 (*c* = 1.8, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 1.8 Hz, 5H), 6.30 (d, J = 3.6 Hz, 1H), 5.17 – 4.96 (m, 3H), 4.91 – 4.78 (m, 1H), 4.64 (d, J = 9.4 Hz, 1H), 3.80 (s, 3H), 2.81 – 2.63 (m, 1H), 2.08 (d, J = 1.5 Hz, 3H), 1.55 (d, J = 14.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 166.8, 155.3, 139.1, 136.1, 128.6, 128.4, 128.3, 127.5, 72.8, 67.3, 62.7, 52.8, 46.9, 36.8, 20.8. HRMS (ESI): exact mass calculated for: $C_{18}H_{19}O_6NNa$ $[M+Na]^+$: 368.1105, found: 368.1103.

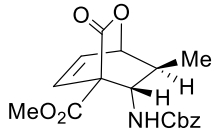
Benzyl (*S*)-(5-methyl-2-((methylperoxy)-λ²-methyl)cyclohexa-2,4-dien-1-yl)carbamate



3p

Following the general procedure, $Mg(OTf)_2$ (10 mol%), **L3-PiMe2** (10 mol%), **1g** (0.1 mmol) and **2n** (0.15 mmol) reacted for 36 h at 35°C. After that, evaporate the solvent and add PhCl (1 mL) to the residue, then heat to 110 °C and stir for 2 h. Product **3p** was obtained as a colorless oil (25 mg, 83% yield, 92% *ee*). The enantiomeric excess was determined by CHIRALPAK OD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 15.27 min, t (major) = 13.37 min. $[\alpha]^{25}D$ = –96.3 (*c* = 0.13, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.24 (m, 5H), 7.14 (d, J = 5.8 Hz, 1H), 5.91 (dd, J = 4.5, 1.3 Hz, 1H), 5.07 (s, 2H), 4.81 (d, J = 6.6 Hz, 2H), 3.73 (s, 3H), 2.52 (d, J = 8.6 Hz, 2H), 1.88 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 155.4, 144.5, 136.8, 128.6, 128.2, 123.6, 118.6, 66.8, 51.9, 42.7, 36.8, 24.1. HRMS (ESI): exact mass calculated for: $C_{17}H_{19}O_4NNa$ $[M+Na]^+$: 324.1206, found: 324.1208.

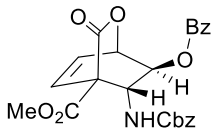
Methyl (1*R*,4*S*,7*S*,8*S*)-8-(((benzyloxy)carbonyl)amino)-7-methyl-3-oxo-2-oxabicyclo[2.2.2]oct-5-ene-4-carboxylate



3q

Following the general procedure, using $Mg(OTf)_2$ (5 mol%), **L3-PiMe2** (5 mol%), **1a** (0.2 mmol), benzyl (*E*)-prop-1-en-1-ylcarbamate (0.4 mmol), reaction time 24 h. Product **3q** was obtained as a colorless oil (56 mg, 82% yield, 86% *ee*). The enantiomeric excess was determined by CHIRALPAK AD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 14.94 min, t (major) = 10.81 min. $[\alpha]^{25}D$ = –44.7 (*c* = 1.13, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 5H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.75 (dd, *J* = 8.0, 4.9 Hz, 1H), 5.17 – 5.01 (m, 2H), 4.92 (d, *J* = 5.0 Hz, 1H), 4.72 (d, *J* = 10.0 Hz, 1H), 4.30 (d, *J* = 10.0 Hz, 1H), 3.81 (s, 3H), 1.83 – 1.77 (m, 1H), 1.38 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 167.2, 155.3, 136.0, 134.4, 128.7, 128.5, 128.3, 78.9, 67.3, 59.9, 54.1, 53.2, 43.7, 17.0. HRMS (ESI): exact mass calculated for: $C_{18}H_{19}O_6NNa$ $[M+Na]^+$: 368.1105, found: 368.1100.

Methyl (1*R*,4*S*,7*S*,8*R*)-7-(benzoyloxy)-8-(((benzyloxy)carbonyl)amino)-3-oxo-2-oxabicyclo[2.2.2]oct-5-ene-4-carboxylate

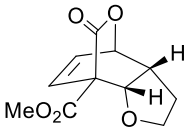


3r

Following the general procedure, $Mg(OTf)_2$ (10 mol%), **L3-PiMe2** (10 mol%), **1a** (0.2 mmol) and benzyl (*E*)-prop-1-en-1- ylcarbamate (0.3 mmol) reacted for 48 h. Product **3r** was obtained as a yellow solid (36 mg, 40% yield, 92% *ee*). The enantiomeric excess was determined by CHIRALPAK OD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 8.17 min, t (major) = 9.15 min. $[\alpha]^{25}D$ = +83.92 (*c* = 0.37, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.3 Hz, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.29 (d, J = 8.3 Hz, 4H), 7.15 (d, J = 6.1 Hz, 1H), 7.08 (d, J = 7.6 Hz, 1H), 6.76 (dd, J = 7.7, 5.1 Hz, 1H), 5.73 (dd, J = 7.6, 3.6 Hz, 1H), 5.46 (s, 1H), 5.30 – 5.11 (m, 1H), 4.98 (s, 2H), 4.67 (d, J = 10.8 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 166.2, 164.6, 155.2, 135.6, 134.0, 131.6, 131.5, 129.7, 128.7,

128.5, 128.3, 128.1, 72.8, 68.2, 67.5, 59.2, 53.5, 50.2. HRMS (ESI): exact mass calculated for: $C_{24}H_{22}O_8N$ $[M+H]^+$: 452.1340, found: 452.1340.

Methyl (3a*S*,4*R*,7*S*,7a*S*)-8-oxo-2,3,3a,7a-tetrahydro-4,7-(epoxymethano)benzo furan-7(4*H*)-carboxylate

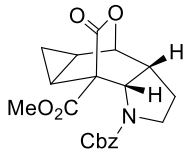


3s

Following the general procedure, $Mg(OTf)_2$ (10 mol%), **L3-PiMe2** (10 mol%), **1a** (0.1 mmol) and 2,3-dihydrofuran (0.2 mmol) were reacted for 36 h. Product **3s** was obtained as a colorless oil (21 mg, 94% yield, 70% *ee*). The enantiomeric excess was determined by CHIRALPAK OD-H (0.46 cm × 25 cm), hexanes/ethanol = 90/10, 1.0 mL/min, λ = 210 nm, t (minor) = 14.25 min, t (major) = 16.09 min. $[\alpha]^{25}D$ = +40.0 (*c* = 0.42, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 6.84 – 6.76 (m, 1H), 6.55 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.26 – 5.22 (m, 1H), 4.86 (d, *J* = 7.8, 1H), 3.93 (s, 3H), 3.92 – 3.86 (m, 1H), 3.79 – 3.73 (m, 1H), 3.22 – 3.15 (m, 1H), 2.17 – 2.08 (m, 1H), 1.57 – 1.49 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 167.5, 131.7, 129.7, 78.6, 76.5, 70.8, 61.7, 53.4, 45.3, 28.2. HRMS (ESI): exact mass calculated for: $C_{11}H_{12}O_5Na$ $[M+Na]^+$: 247.0577, found: 247.0575.

5. Procedure for Transformation of Product

1-benzyl 6-methyl (3a*R*,4*R*,4a*S*,5a*R*,6*S*,6a*S*)-7-oxooctahydro-4,6-(epoxymethano)cyclopropa[f]indole-1,6-dicarboxylate

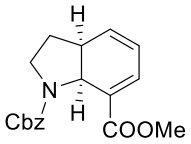


3t

3a (21.4 mg, 0.06 mmol) and palladium acetate (20 mol%) were dissolved in DCM (5 mL), an excess of ethereal diazomethane (~ 10 equiv.) was added slowly at 0 °C. The solution was stirred at rt for 16 h until the yellow color disappeared. The solvent was removed under reduced pressure and the residue was purified by flash chromatography directly on silica gel (petroleum ether: ethyl acetate = 2:1) to obtain **3t** as a white solid (15 mg, 68% yield, 96% *ee*). The enantiomeric excess was determined by CHIRALPAK OD-H (0.46 cm × 25 cm), hexanes/ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 14.58 min, t (major) =18.78 min. $[\alpha]^{25}D$ = –110.0 (*c*=0.10, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$)

δ 7.48 – 7.28 (m, 5H), 5.09 (d, J = 47.8 Hz, 2H), 4.76 (d, J = 8.6 Hz, 1H), 4.68 (s, 1H), 3.87 (d, J = 76.9 Hz, 4H), 3.45 (td, J = 11.2, 7.3 Hz, 1H), 3.14 – 2.99 (m, 1H), 2.14 (m, J = 21.1, 10.4 Hz, 1H), 1.78 (m, J = 21.7, 10.9, 5.6 Hz, 2H), 1.34 (td, J = 7.8, 3.9 Hz, 1H), 0.79 (q, J = 7.8 Hz, 1H), 0.54 (dt, J = 7.2, 3.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 167.7, 154.6, 136.3, 128.6, 128.0, 74.3, 67.5, 60.0, 57.3, 52.9, 48.2, 43.6, 25.4, 10.2, 7.7, 3.0. HRMS (ESI): exact mass calculated for: $C_{20}H_{21}O_6NNa$ $[M+Na]^+$: 394.1261, found: 394.1262.

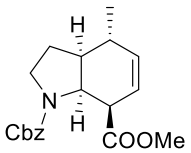
1-benzyl 7-methyl (3a*S*,7a*S*)-2,3,3a,7a-tetrahydro-1*H*-indole-1,7-dicarboxylate



3u

3a (35.7 mg, 0.1 mmol) was dissolved in chlorobenzene (1.0 mL), then warmed to 130 °C and stirred for 12 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography directly on silica gel (petroleum ether: ethyl acetate = 6:1) to obtain **3u** as a colorless oil (24 mg, 74% yield, 96% *ee*). The enantiomeric excess was determined by CHIRALPAK OD-H (0.46 cm × 25 cm), hexanes/ ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 6.09 min, t (major) = 5.52 min. $[\alpha]^{25}D$ = –29.0 (*c*=1.2, in CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO) δ 7.42 – 7.14 (m, 5H), 6.81 (d, J = 5.0 Hz, 1H), 6.18 – 6.07 (m, 1H), 5.90 (d, J = 9.1 Hz, 1H), 4.92 (s, 2H), 4.49 (d, J = 6.8 Hz, 1H), 3.52 (dd, J = 37.2, 27.9 Hz, 4H), 3.08 (s, 1H), 2.98 (d, J = 6.4 Hz, 1H), 2.27 – 2.11 (m, 1H), 2.07 (dd, J = 12.0, 6.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 167.7, 154.0, 137.5, 136.0, 131.9, 128.8, 128.2, 128.0, 127.9, 124.1, 66.2, 52.2, 51.8, 46.6, 39.5, 30.2. HRMS (ESI): exact mass calculated for: $C_{18}H_{19}O_4NNa$ $[M+Na]^+$: 336.1212, found: 336.1204.

1-benzyl 7-methyl (3a*S*,4*R*,7*R*,7a*S*)-4-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-indole-1,7-dicarboxylate



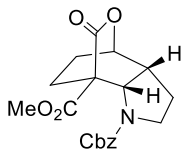
3v

To a stirred suspension of CuI (152 mg, 0.8 mmol) in dry Et_2O (2 mL) was added MeLi (1.6 M in Et_2O, 0.88 mL, 1.4 mmol) dropwise at 0 °C. After stirring at this temperature for 10 min, TMSI (112 mg, 0.8 mmol) and **3u** (31.3 mg, 0.1 mmol) was added dropwise at –78 °C. The reaction

mixture was stirred at this temperature for 90 min. After the reaction was completed, $NH_3 \cdot H_2O$ (25%, w/w, 2mL) was slowly added. Then the mixture was warmed to rt and extracted with ethyl acetate (3 × 10 mL). The organic phase was washed with brine (10 mL) and dried over sodium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography (petroleum ether: ethyl acetate = 8:1). Product **3v** was obtained as a colorless oil (18 mg, 56% yield, 97% *ee*). The enantiomeric excess was determined by CHIRALPAK AD-H (0.46 cm × 25 cm), hexanes/ ethanol = 90/10, 1.0 mL/min, λ = 210 nm, t (minor) = 9.37 min, t (major) = 10.98 min. $[\alpha]^{25}D$ = –16.0 (*c*=0.10, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.26 (m, 5H), 5.75 (s, 1H), 5.49 (dd, J = 36.4, 9.5 Hz, 1H), 5.06 (dt, J = 19.9, 15.7 Hz, 2H), 4.36 (d, J = 24.8 Hz, 1H), 3.68 (s, 1H), 3.50 – 3.36 (m, 2H), 3.31 (s, 2H), 3.04 (d, J = 49.7 Hz, 1H), 2.31 – 2.01 (m, 2H), 1.94 (s, 1H), 1.71 (d, J = 11.0 Hz, 1H), 1.12 (d, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.4, 174.1, 155.1, 154.9, 133.0, 132.5, 128.5, 128.3, 128.0, 127.9, 127.8, 121.1, 120.9, 67.1, 66.6, 55.1, 53.9, 52.4, 51.9, 46.7, 45.3, 45.0, 44.7, 43.5, 42.6, 31.3, 31.0, 29.7, 29.6, 28.7, 22.4. HRMS (ESI): exact mass calculated for: $C_{19}H_{23}O_4NNa$ $[M+Na]^+$: 352.1519, found: 352.1522.

6. Asymmetric Formal Total Synthesis of (+)-Minovincine

1-benzyl 7-methyl (3a*R*,4*R*,7*S*,7a*S*)-8-oxohexahydro-1*H*-4,7-(epoxymethano) indole-1,7(4*H*)-dicarboxylate

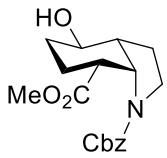


4

3a (857 mg, 2.4 mmol) and $[Ir(cod)(PCy_3)(Py)]PF_6$ (Crabtree's catalyst, 96.2 mg, 0.12 mmol) were dissolved in THF (20 mL), then the mixture was stirred at rt for 4 h under H_2 atmosphere. The solvent was removed under reduced pressure and the residue was purified by flash chromatography directly on silica gel (petroleum ether: ethyl acetate = 3:1) to obtain product **4** as a white solid (790 mg, 92% yield, 97% *ee*). The enantiomeric excess was determined by CHIRALPAK IA-H (0.46 cm × 25 cm), hexanes/ ethanol = 80/20, 1.0 mL/min, λ = 210 nm, t (minor) = 16.37 min, t (major) = 25.58 min. $[\alpha]^{25}D$ = –74.8

(c=0.5, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 5.24 – 4.95 (m, 2H), 4.80 (dd, J = 9.3, 1.6 Hz, 1H), 4.56 – 4.52 (m, 1H), 4.00 – 3.90 (m, 1H), 3.76 (s, 3H), 3.48 – 3.40 (m, 1H), 3.06 – 2.98 (m, 1H), 2.30 – 2.22 (m, 1H), 2.20 – 2.10 (m, 1H), 2.09 – 1.96 (m, 2H), 1.85 – 1.78 (m, 1H), 1.69 – 1.63 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 169.4, 154.8, 136.3, 128.6, 128.3, 128.0, 77.4, 67.5, 58.9, 53.3, 52.7, 47.7, 42.2, 25.0, 21.2, 19.6. HRMS (ESI): exact mass calculated for: $C_{19}H_{21}O_6NNa$ $[M+Na]^+$: 382.1267, found: 382.1261.

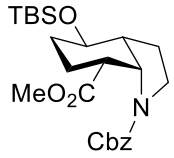
1-benzyl 7-methyl (3a*R*,4*R*,7*R*,7a*S*)-4-hydroxyoctahydro-1*H*-indole-1,7-dicarboxylate



5

A solution of KOH (985.6 mg, 17.6 mmol) in MeOH (10 mL) was added dropwise into **4** (790 mg, 2.2 mmol) in THF (10 mL) at rt. The mixture was stirred at 40 °C for 24 h. After that, the pH was adjusted to 4 by $KHSO_4$ solution (1 M) at 0 °C, then the mixture was extracted by ethyl acetate (3 × 30 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The obtained intermediate then was dissolved in a mixture solvent of Et_2O and MeOH (4:1, a total of 20 mL). Next, trimethylsilyldiazomethane (2 mol/L in hexane, 2.2 mL, 4.4 mmol) was added to the solution and the mixture was stirred at rt for 2 h. Then the mixture was concentrated and the residue was purified by flash column chromatography (silica gel, petroleum ether: ethyl acetate = 1:1) to afford **5** as a white solid (670 mg, 91% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.17 (m, 5H), 5.08 (dd, J = 56.6, 46.0 Hz, 2H), 4.32 (s, 1H), 3.97 (d, J = 51.1 Hz, 1H), 3.67 – 3.21 (m, 5H), 2.46 (d, J = 108.1 Hz, 2H), 2.19 – 1.87 (m, 3H), 1.79 (s, 1H), 1.70 – 1.44 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 155.1, 137.2, 136.6, 128.5, 128.1, 128.0, 127.9, 67.7, 67.5, 67.2, 66.7, 57.1, 56.4, 52.1, 51.6, 45.8, 45.1, 44.7, 44.4, 28.1, 27.6, 26.6, 25.6, 21.2. HRMS (ESI): exact mass calculated for: $C_{18}H_{23}NO_5Na$ $[M+Na]^+$: 356.1468, found: 356.1468.

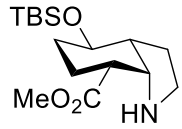
1-benzyl 7-methyl (3a*R*,4*R*,7*R*,7a*S*)-4-((tert-butyldimethylsilyl)oxy)octahydro-1*H*-indole-1,7-dicarboxylate



6

To a solution of **5** (670 mg, 2 mmol) and imidazole (1.36 g, 20 mmol) in dry DCM were added tert-butyldimethylsilyl chloride (3.01 g, 20 mmol) slowly at 0 °C. Then the reaction mixture was warmed to rt and stirred for 2 h until the reaction was complete (monitored by TLC). The reaction mixture was diluted with DCM and washed with saturated $NaHCO_3$ solution. Then the mixture was concentrated under reduced pressure and purified by flash column chromatography (silica gel, petroleum ether: ethyl acetate 10:1) to afford **6** as a colorless oil (0.90 g, 99% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.21 (m, 5H), 5.25 – 4.90 (m, 2H), 4.26 (dd, J = 9.5, 6.7 Hz, 1H), 3.92 (d, J = 17.2 Hz, 1H), 3.64 – 3.25 (m, 5H), 2.48 – 2.14 (m, 2H), 2.05 (d, J = 9.9 Hz, 1H), 1.86 (s, 1H), 1.73 (dd, J = 19.9, 10.0 Hz, 1H), 1.58 – 1.42 (m, 3H), 0.87 (s, 9H), 0.02 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.0, 174.7, 155.1, 154.9, 137.2, 136.8, 128.4, 127.9, 67.9, 66.9, 66.5, 57.1, 56.6, 52.0, 51.4, 46.7, 45.8, 45.0, 44.6, 28.2, 27.8, 26.3, 25.8, 25.3, 21.3, 21.0, 18.1, -4.7, -4.9. HRMS (ESI): exact mass calculated for: $C_{24}H_{37}NO_5SiNa$ [M+Na]$^+$: 470.2333, found: 470.2332.

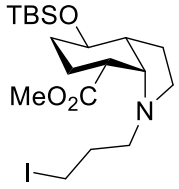
Methyl (3a*R*,4*R*,7*R*,7a*S*)-4-((tert-butyldimethylsilyl)oxy)octahydro-1*H*-indole-7-carboxylate



7

A mixture of **6** (0.90 g, 2 mmol) and Pd/C (40% wt, 0.36 g) in EtOH (20 mL) was stirred under H_2 atmosphere (1 atm) at rt for 2 h, and then filtered through a short pad of celite. The mixture was concentrated under reduced pressure and purified by flash column chromatography (silica gel, DCM: MeOH = 15:1) to afford **7** as a colorless oil (0.55 g, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 (d, J = 3.3 Hz, 1H), 3.73 (s, 3H), 3.69 – 3.60 (m, 1H), 3.27 (s, 1H), 3.18 – 3.01 (m, 2H), 2.40 (dd, J = 13.3, 6.0 Hz, 1H), 2.30 – 2.16 (m, 1H), 1.99 – 1.84 (m, 2H), 1.80 – 1.70 (m, 1H), 1.59 (ddt, J = 13.9, 9.3, 7.6 Hz, 3H), 0.90 (s, 9H), 0.06 (d, J = 5.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4, 68.7, 57.3, 51.9, 46.6, 43.7, 43.2, 28.9, 27.1, 25.8, 21.7, 18.1, -4.6, -4.9. HRMS (ESI): exact mass calculated for: $C_{16}H_{31}NO_3SiNa$ [M+Na]$^+$: 336.1965, found: 336.1963.

methyl (3a*R*,4*R*,7*R*,7a*S*)-4-((tert-butyldimethylsilyl)oxy)-1-(3-iodopropyl) octahydro-1*H*-indole-7-carboxylate



8

To a solution of **7** (0.55 g, 1.75 mmol) in DMF (5 mL) was added $NaHCO_3$ (1.47 g, 17.5 mmol) followed by 1,3-diiodopropane (5.18 g, 17.5 mmol). The reaction mixture was heated to 35 °C for 3 h until the reaction was complete. The mixture was diluted with water and extracted with ethyl acetate (3 × 30 mL). The organic layer was washed with saturated NaCl solution (3 × 30 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether: ethyl acetate = 10: 1) to afford **8** as a colorless oil (0.44 g, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 – 3.56 (m, 4H), 3.21 (td, J = 6.3, 3.8 Hz, 2H), 3.15 – 3.00 (m, 2H), 2.75 (dd, J = 7.1, 4.6 Hz, 1H), 2.57 (d, J = 5.2 Hz, 1H), 2.36 – 2.21 (m, 2H), 2.12 – 2.01 (m, 1H), 1.96 – 1.83 (m, 3H), 1.82 – 1.74 (m, 1H), 1.74 – 1.58 (m, 3H), 1.47 – 1.33 (m, 1H), 0.86 (s, 9H), 0.02 (d, J = 5.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5, 70.7, 64.2, 55.0, 51.8, 51.6, 45.3, 42.3, 32.3, 30.5, 26.6, 25.9, 22.3, 18.1, 5.2, -4.1, -4.6. HRMS (ESI): exact mass calculated for: $C_{19}H_{37}INO_3Si$ $[M+H]^+$: 482.1582, found: 482.1583.

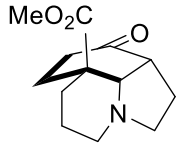
(3^1*S*,6a*S*,9*R*,9a*R*)-9-((tert-butyldimethylsilyl)oxy)octahydro-4*H*-pyrrolo[3,2,1-ij]quinoline-6a(3^1*H*)-carboxylate

9

To a solution of **8** (0.44 g, 0.91 mmol) in THF (5 mL) was added LDA (1.82 mL, 1.82 mmol) slowly at -78 °C under N_2 atmosphere. Then the reaction mixture was stirred at -78 °C for 2 h and then heated to 0 °C for another 2 h. The reaction was quenched with saturated NH_4Cl solution, extracted with ethyl acetate and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether: ethyl acetate = 10: 1) to afford **9** as a colorless oil (0.28 g, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 3H), 3.48 (ddd, J = 11.4, 9.1, 4.4 Hz, 1H), 3.08 (d, J = 3.4 Hz, 1H), 2.96 (d, J = 10.7 Hz, 1H), 2.36 (d, J = 4.6 Hz, 1H), 2.13 – 1.89 (m, 3H), 1.83 – 1.70 (m, 5H), 1.70 – 1.61 (m, 2H), 1.55 – 1.44 (m, 1H), 1.44 – 1.33 (m, 1H), 1.22 – 1.11 (m,

1H), 0.83 (s, 9H), 0.01 (d, J = 7.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.1, 73.9, 66.7, 53.0, 52.9, 51.9, 46.0, 44.9, 33.1, 33.1, 26.2, 25.9, 25.7, 21.8, 18.0, -3.8, -4.4. HRMS (ESI): exact mass calculated for: $C_{19}H_{36}NO_3Si$ $[M+H]^+$: 354.2459, found: 354.2458.

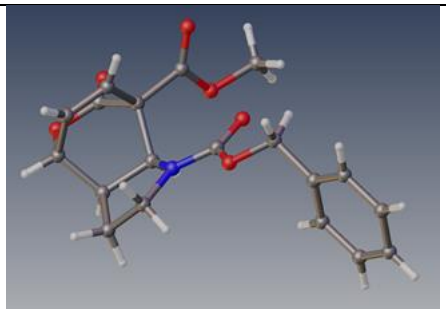
methyl (3^1*S*,6a*S*,9a*R*)-9-oxooctahydro-4*H*-pyrrolo[3,2,1-ij]quinoline-6a(3^1*H*)-carboxylate

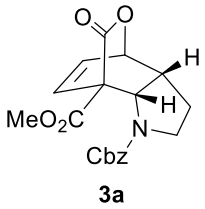


10

To a solution of **9** (0.28 g, 0.79 mmol) in THF (5 mL) was added HCl solution (1 M, 4 mL, 4 mmol). The reaction mixture was stirred at rt for 4 h until the reaction was complete. The pH of the mixture was adjusted to 8 by saturated $NaHCO_3$ solution, then the mixture was extracted with ethyl acetate, dried over Na_2SO_4 and concentrated under reduced pressure to obtain a white solid. Next, the white solid and Et_3N (0.48 g, 4.8 mmol) were dissolved in a mixed solvent of DCM and DMSO (1:2, a total of 6 mL). then a solution of $PySO_3$ (4.0 mmol) in DMSO (2 mL) was added to the mixture at rt. The reaction was stirred at rt overnight, then quenched with saturated $NaHCO_3$ solution. The mixture was extracted with ethyl acetate, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether: ethyl acetate = 5: 1) to afford **10** as a yellow oil (0.13 g, 70% yield over two steps). $[\alpha]^{25}D = -27.8$ (*c* = 1.0, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 3.07 – 2.97 (m, 2H), 2.92 – 2.84 (m, 1H), 2.62 (d, J = 5.1 Hz, 1H), 2.43 (ddd, J = 30.1, 17.4, 10.4 Hz, 3H), 2.25 (td, J = 14.7, 5.3 Hz, 1H), 2.08 – 1.97 (m, 2H), 1.96 – 1.85 (m, 2H), 1.82 – 1.65 (m, 2H), 1.63 – 1.51 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.2, 176.4, 67.9, 52.6, 52.5, 52.2, 49.3, 45.8, 38.5, 32.5, 27.2, 21.2, 21.1. HRMS (ESI): exact mass calculated for: $C_{13}H_{20}NO_3$ $[M+H]^+$: 238.1438, found: 238.1438.

7. X-ray Crystallographic Data of 3a





3a

Table S8. Crystal Data and Structure Refinement for 3a.

Information	**3a**	
Identification code	mjr18224_0m	
Empirical formula	$C_{25}H_{19}BrN_4O_2$	
Formula weight	487.35	
Temperature	173(2) K	
Wavelength	1.34139 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.6491(4) Å	α = 90°.
	b = 13.5692(7) Å	β = 90°.
	c = 23.9241(13) Å	γ = 90°.
Volume	2158.5(2) $Å^3$	
Z	4	
Density (calculated)	1.500 Mg/m^3	
Absorption coefficient	1.873 mm^{-1}	
F(000)	992	
Crystal size	0.170 x 0.140 x 0.100 mm^3	
Theta range for data collection	5.673 to 54.994°.	
Index ranges	-7<=h<=8, -16<=k<=14, -27<=l<=29	
Reflections collected	13564	
Independent reflections	3900 [R(int) = 0.0462]	
Completeness to theta = 53.594°	94.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.4677	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3900 / 0 / 290
Goodness-of-fit on F^2	1.045
Final R indices [I>2sigma(I)]	R1 = 0.0269, wR2 = 0.0663
R indices (all data)	R1 = 0.0274, wR2 = 0.0667
Absolute structure parameter	0.097(7)
Extinction coefficient	0.0147(16)
Largest diff. peak and hole	0.278 and -0.473 e.$Å^{-3}$
CCDC number	2158164

8. Reference

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5. E. M. Boyd and J. Sperry, *Tetrahedron Lett.*, 2012, **53**, 3623–3626.
6. T. Yokoi, Y. Nakagawa and H. Miyagawa, *Pest Manag Sci*, 2019, **75**, 115–124.
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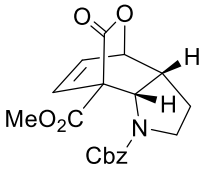
9. Chromatographic Data for Chiral Products

Compound 3a



HPLC Conditions

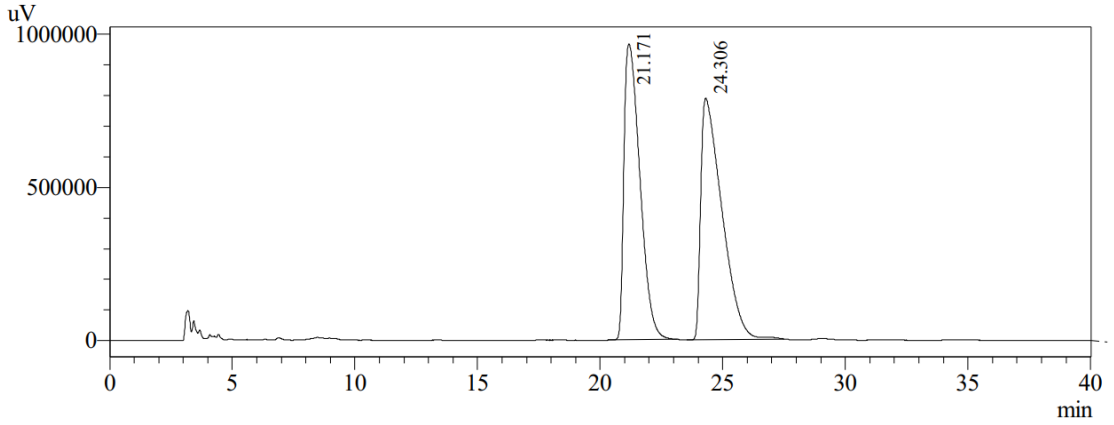
Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

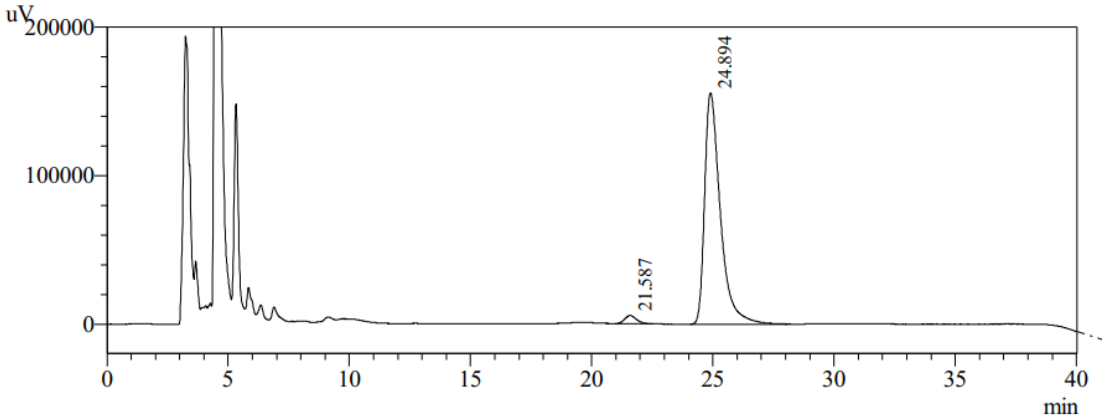
Detection: UV 210 nm

Racemic



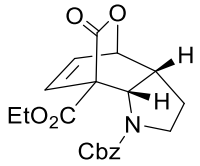
Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.171	43905539	967122	48.185	55.093
2	24.306	47213950	788309	51.815	44.907
Total		91119488	1755431	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.587	189378	5533	2.623	3.426
2	24.894	7031675	155974	97.377	96.574
Total		7221054	161507	100.000	100.000

Compound 3b



HPLC Conditions

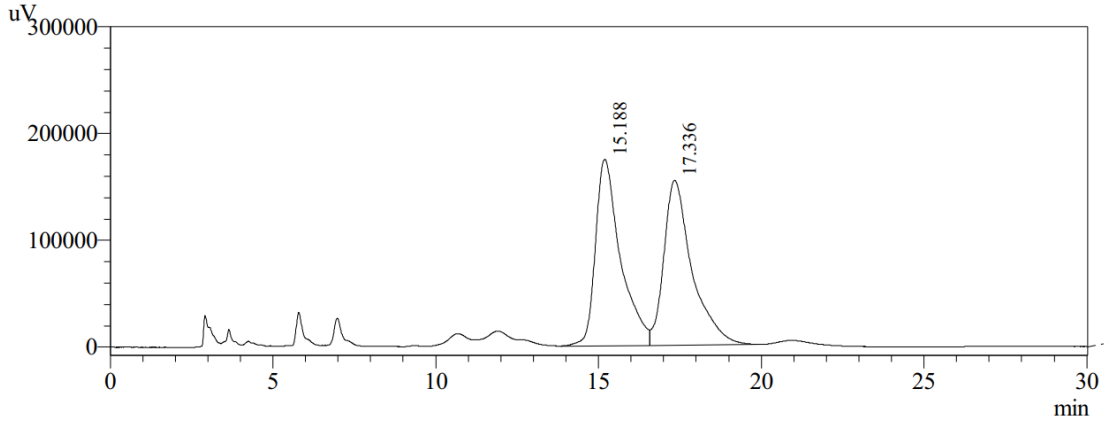
Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

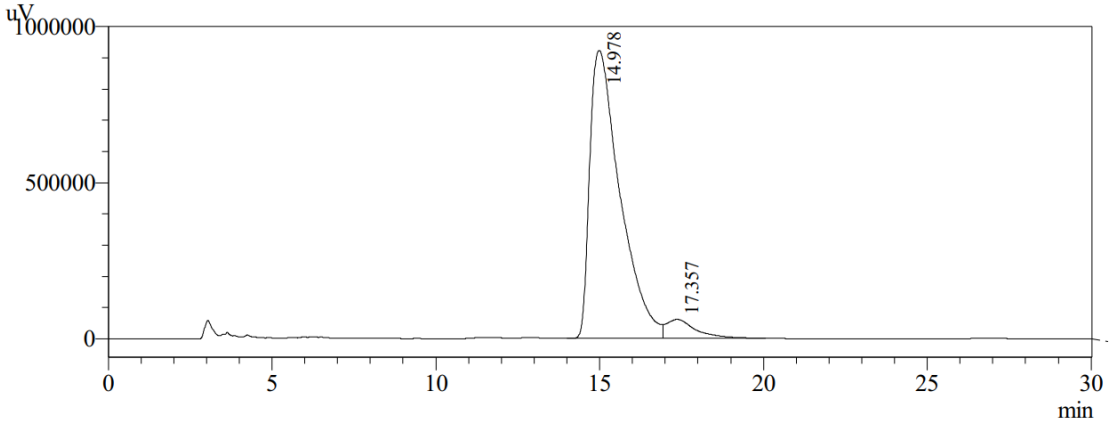
Detection: UV 210 nm

Racemic



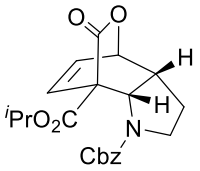
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.188	9345107	174644	50.153	53.104
2	17.336	9288049	154231	49.847	46.896
Total		18633156	328875	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.978	59374578	922980	93.922	93.824
2	17.357	3842659	60760	6.078	6.176
Total		63217238	983740	100.000	100.000

Compound 3c



HPLC Conditions

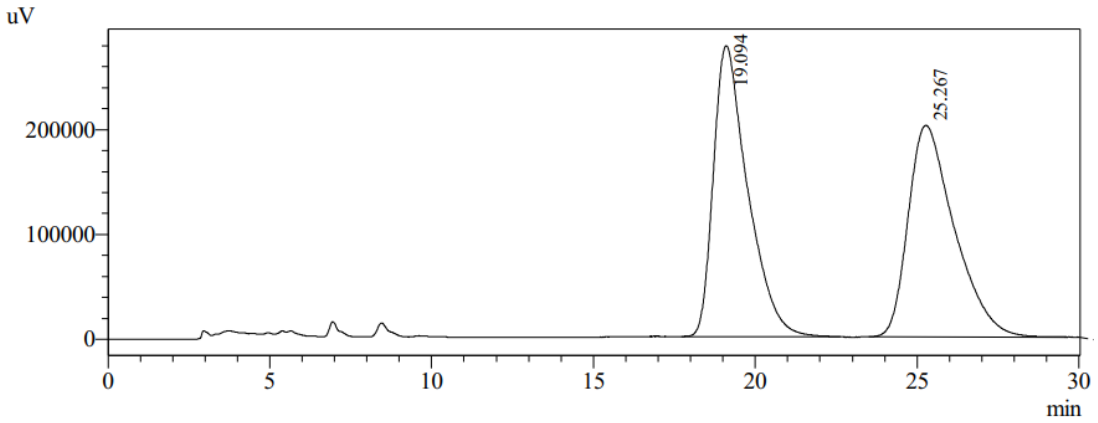
Column: Chiralcel OJ-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

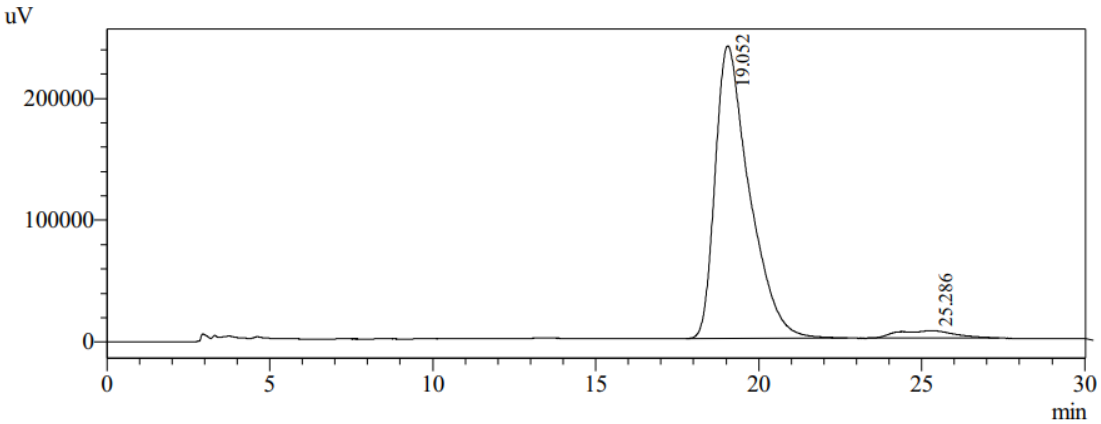
Detection: UV 210 nm

Racemic



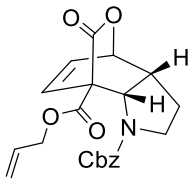
Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.094	20497645	277275	50.582	57.898
2	25.267	20025690	201631	49.418	42.102
Total		40523335	478906	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.052	17585864	240463	95.899	97.493
2	25.286	752074	6182	4.101	2.507
Total		18337939	246646	100.000	100.000

Compound 3d



HPLC Conditions

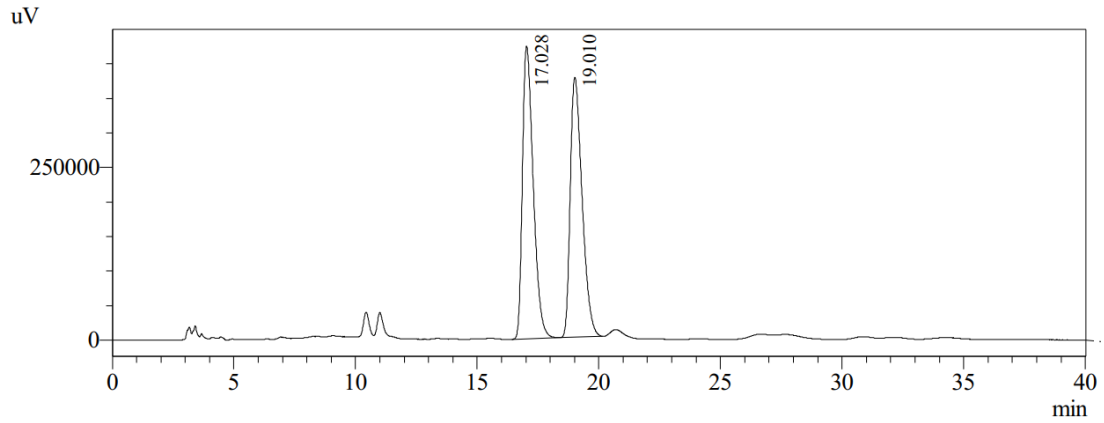
Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

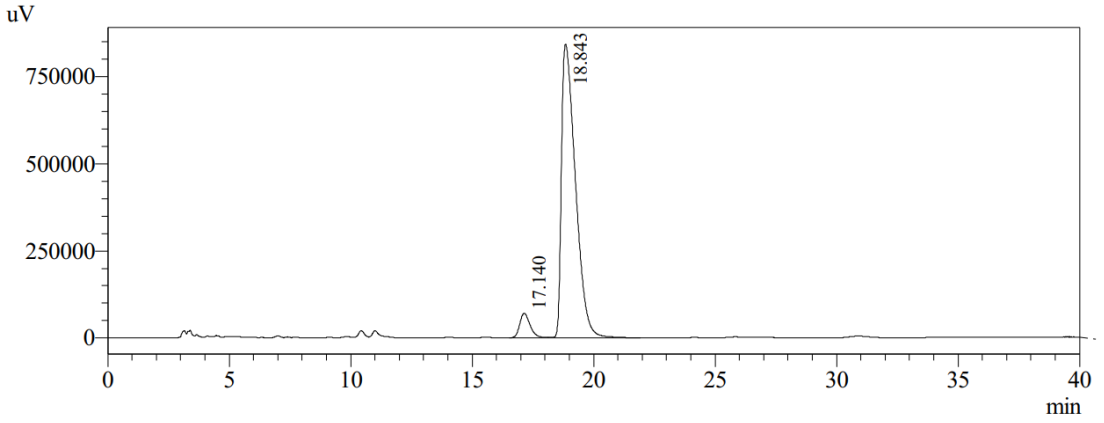
Detection: UV 210 nm

Racemic



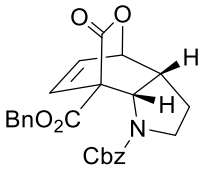
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.028	13130151	423857	50.669	52.961
2	19.010	12783329	376465	49.331	47.039
Total		25913480	800322	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.140	2079915	70092	5.796	7.675
2	18.843	33802914	843124	94.204	92.325
Total		35882828	913217	100.000	100.000

Compound 3e



HPLC Conditions

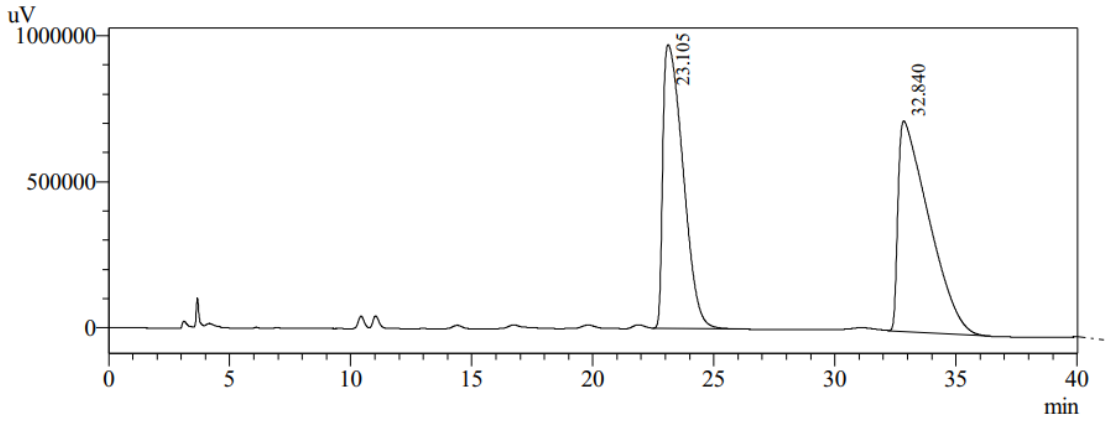
Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

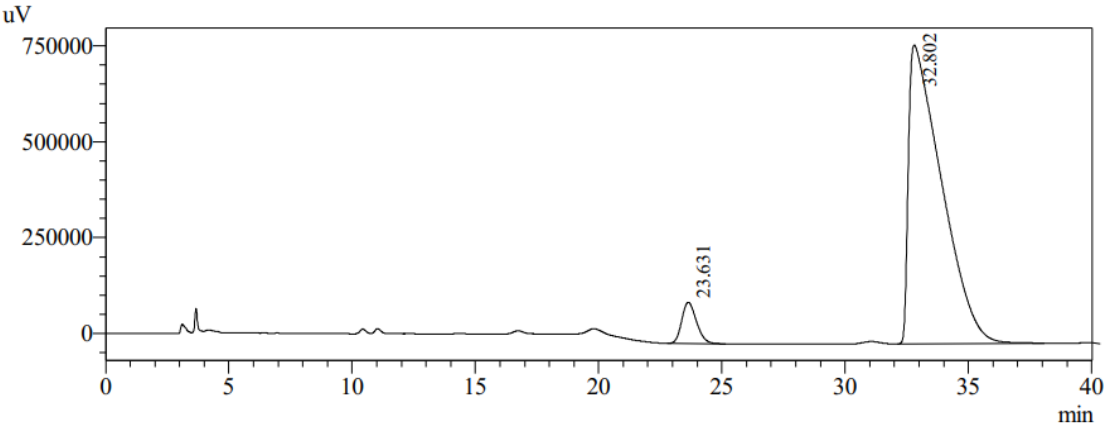
Detection: UV 210 nm

Racemic



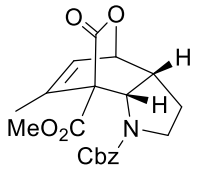
Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.105	56222157	971982	46.872	57.411
2	32.840	63725302	721031	53.128	42.589
Total		119947459	1693013	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.631	4464223	107426	5.782	12.109
2	32.802	72738116	779763	94.218	87.891
Total		77202339	887188	100.000	100.000

Compound 3f



HPLC Conditions

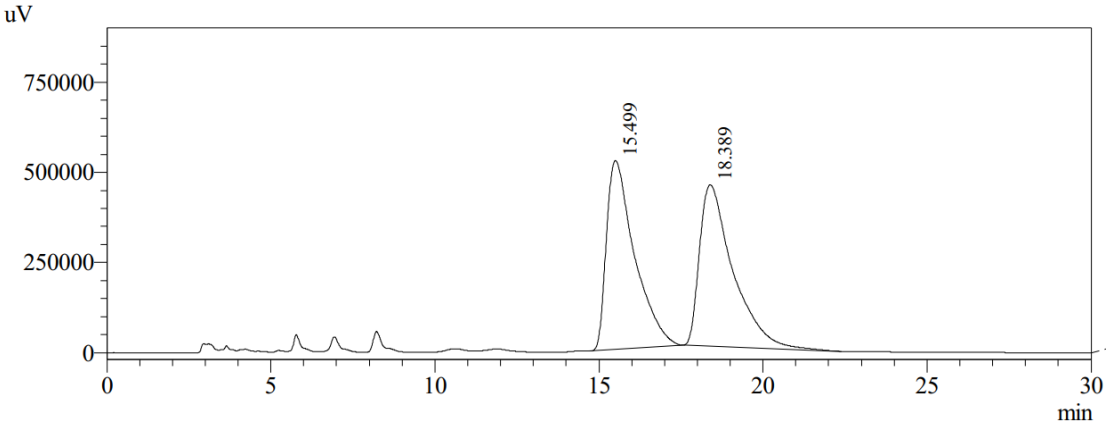
Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

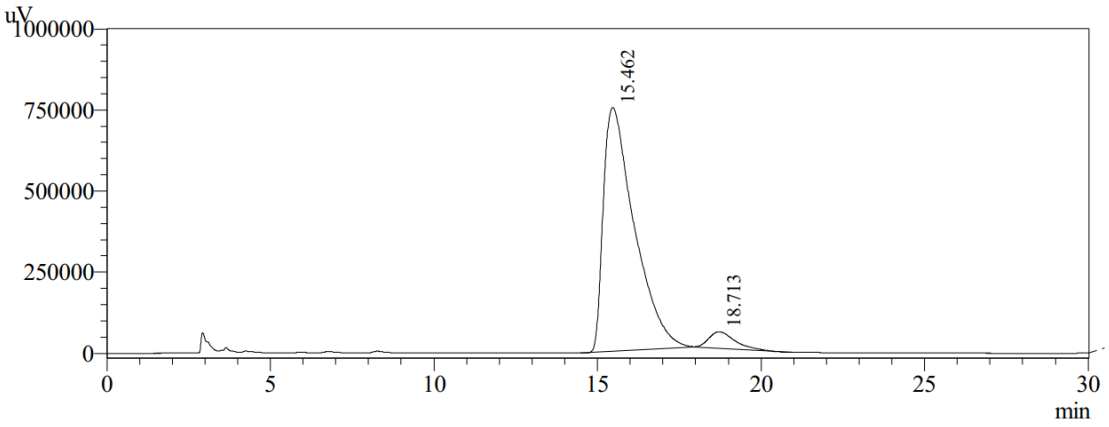
Detection: UV 210 nm

Racemic



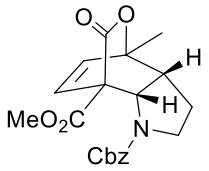
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.499	31273527	523477	49.577	53.903
2	18.389	31807636	447664	50.423	46.097
Total		63081163	971141	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.462	49628398	751080	94.624	93.681
2	18.713	2819853	50663	5.376	6.319
Total		52448251	801743	100.000	100.000

Compound 3g



HPLC Conditions

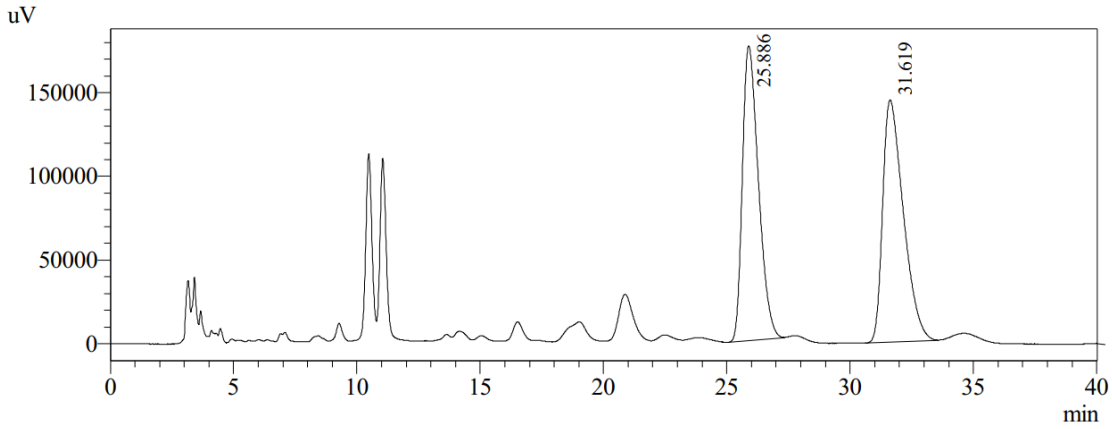
Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

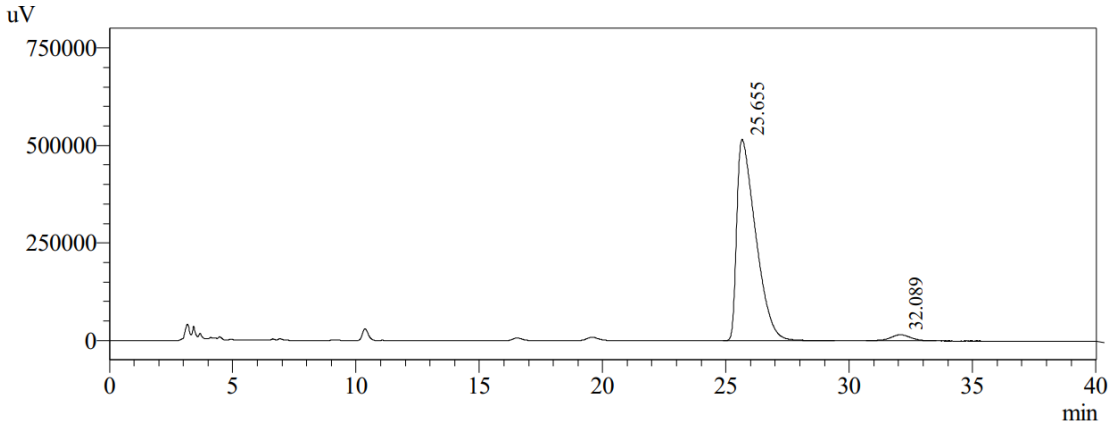
Detection: UV 210 nm

Racemic



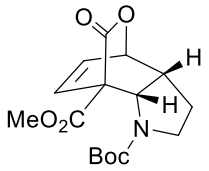
Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.886	7968330	176039	48.570	54.898
2	31.619	8437395	144625	51.430	45.102
Total		16405725	320664	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.655	27643708	516246	96.876	97.077
2	32.089	891336	15544	3.124	2.923
Total		28535044	531790	100.000	100.000

Compound 3i



HPLC Conditions

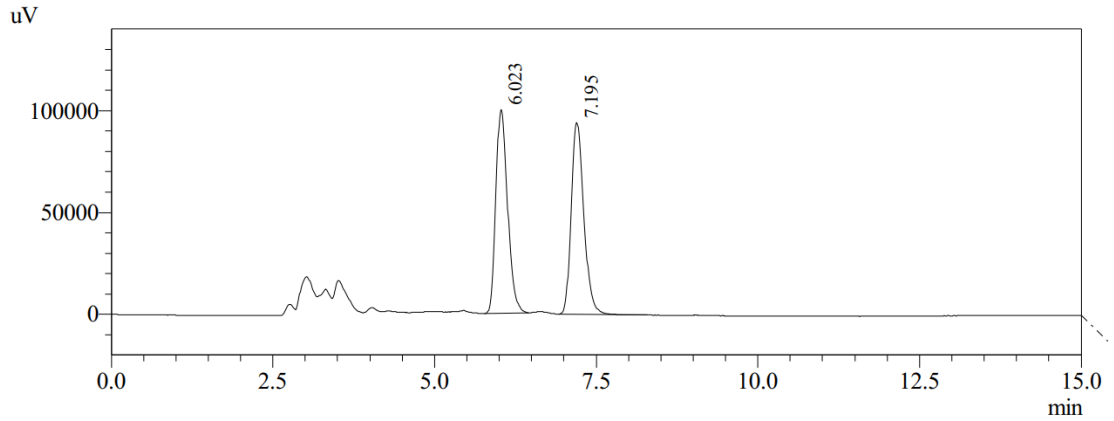
Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

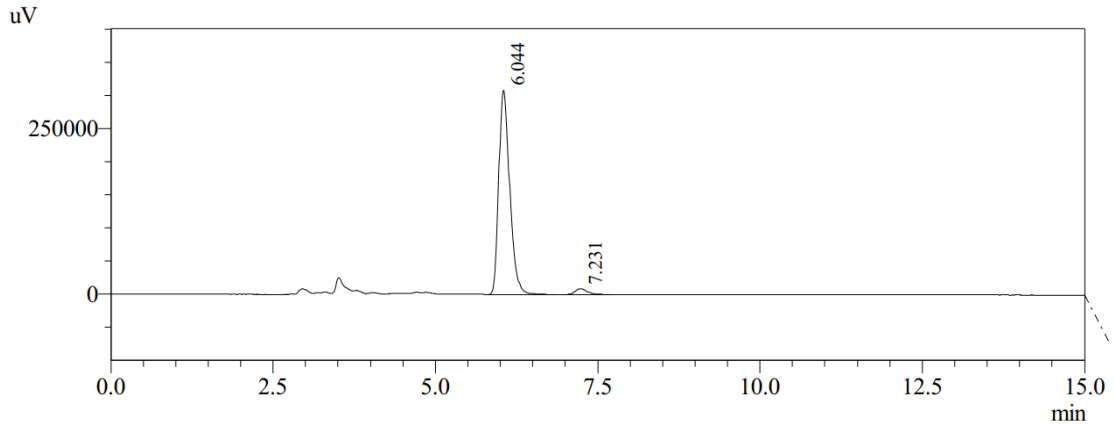
Detection: UV 210 nm

Racemic



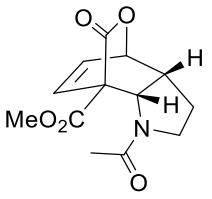
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.023	1269405	99893	49.756	51.473
2	7.195	1281857	94174	50.244	48.527
Total		2551262	194068	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.044	3625454	308196	96.990	97.267
2	7.231	112497	8659	3.010	2.733
Total		3737951	316855	100.000	100.000

Compound 3j



HPLC Conditions

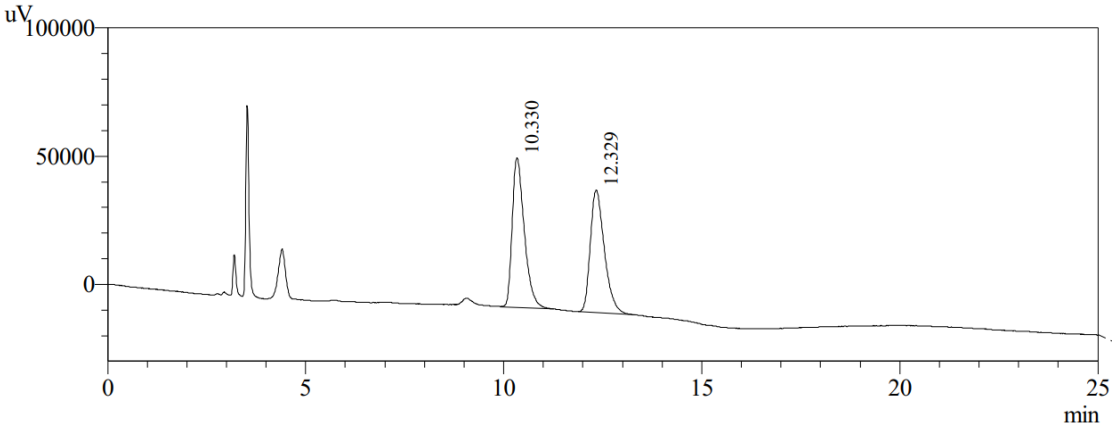
Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

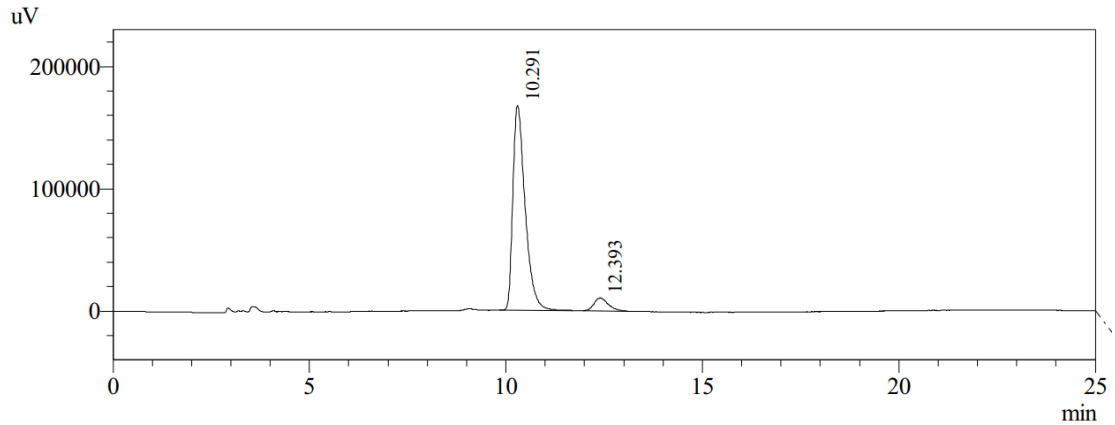
Detection: UV 210 nm

Racemic



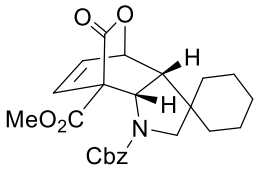
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.330	1239124	58244	51.061	54.906
2	12.329	1187620	47835	48.939	45.094
Total		2426743	106079	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.291	3633763	167668	93.277	94.078
2	12.393	261904	10553	6.723	5.922
Total		3895666	178221	100.000	100.000

Compound 3k



HPLC Conditions

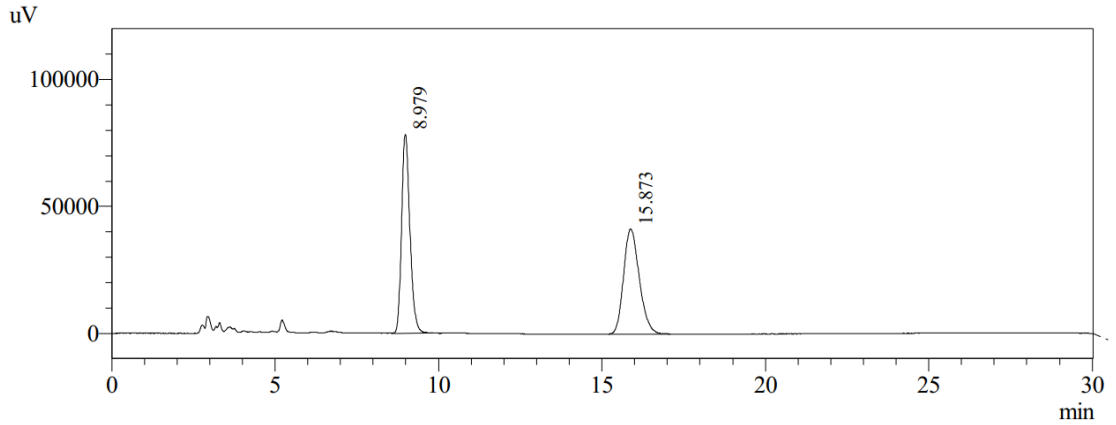
Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

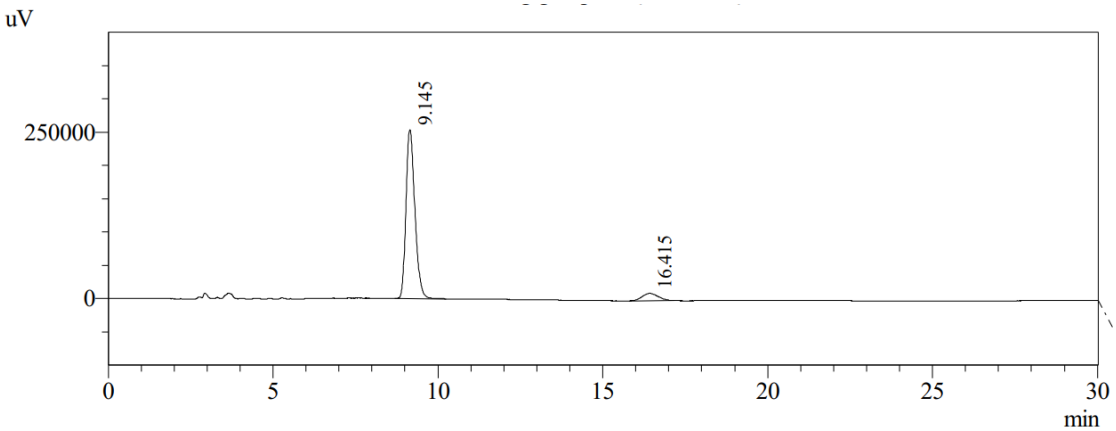
Detection: UV 210 nm

Racemic



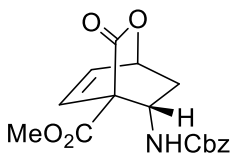
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.979	1390548	78396	50.068	65.405
2	15.873	1386796	41466	49.932	34.595
Total		2777344	119862	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.145	4761460	254035	92.772	95.860
2	16.415	370994	10970	7.228	4.140
Total		5132455	265005	100.000	100.000

Compound 3n



HPLC Conditions

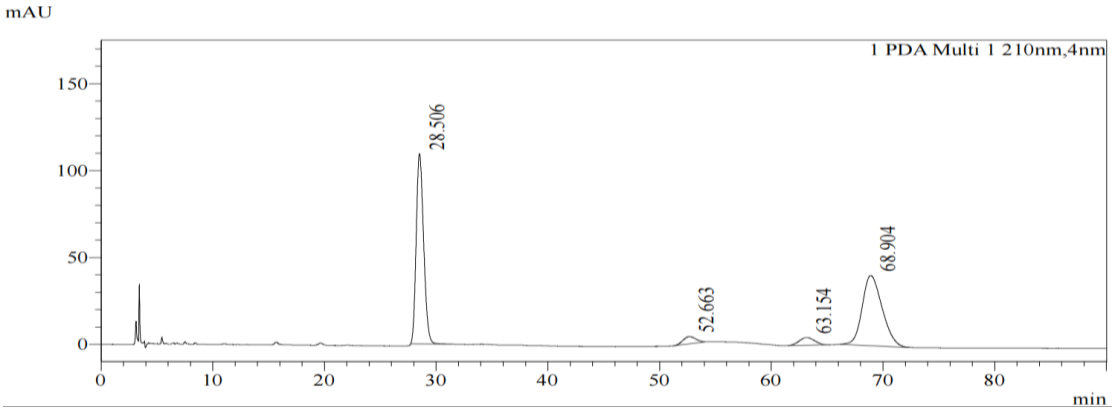
Column: Chiralcel ID, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ *i*PrOH (70:30)

Flow rate: 1.0 mL/min

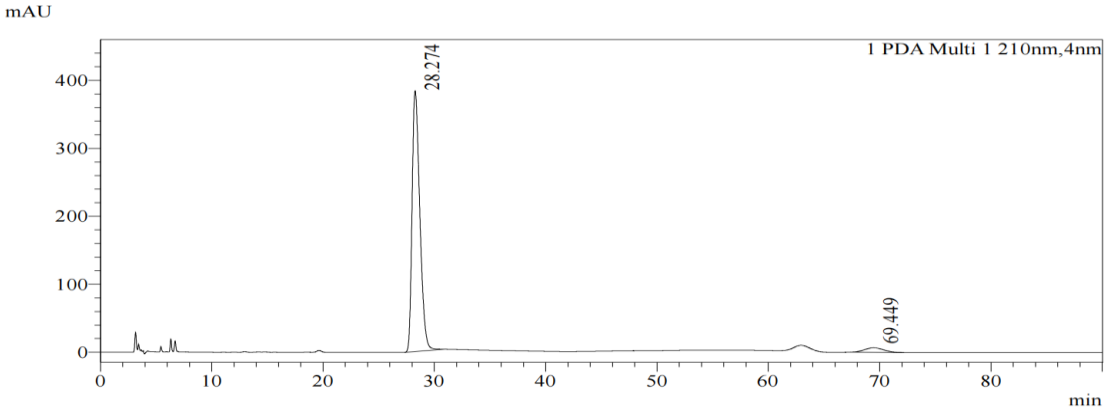
Detection: UV 210 nm

Racemic



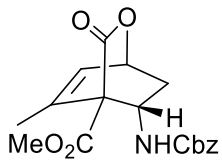
Peak#	Ret. Time	Area	Height	Area%	Height%
1	28.506	5061418	109442	46.740	69.069
2	52.663	336757	4202	3.110	2.652
3	63.154	422496	4407	3.902	2.781
4	68.904	5008279	40401	46.249	25.497
Total		10828950	158453	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area%	Height%
1	28.274	18569446	383735	95.895	98.291
2	69.449	794871	6670	4.105	1.709
Total		19364317	390405	100.000	100.000

Compound 3o



HPLC Conditions

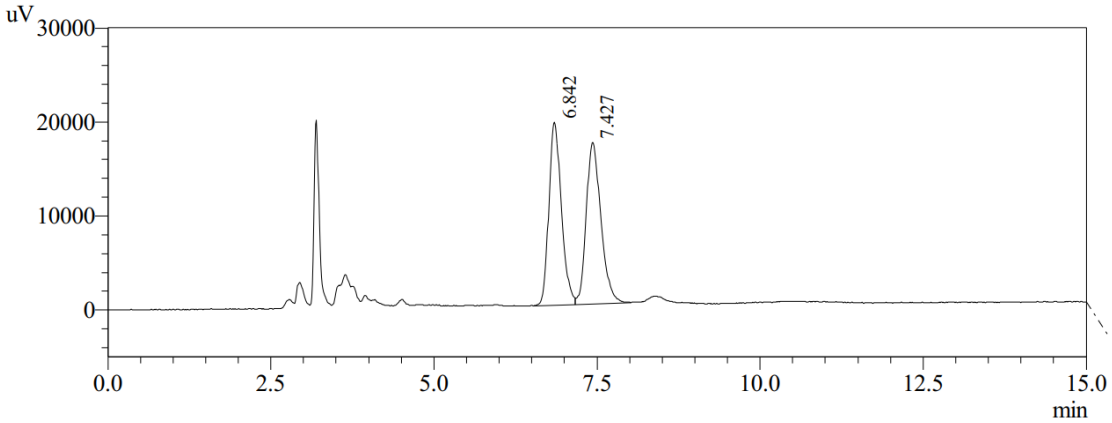
Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

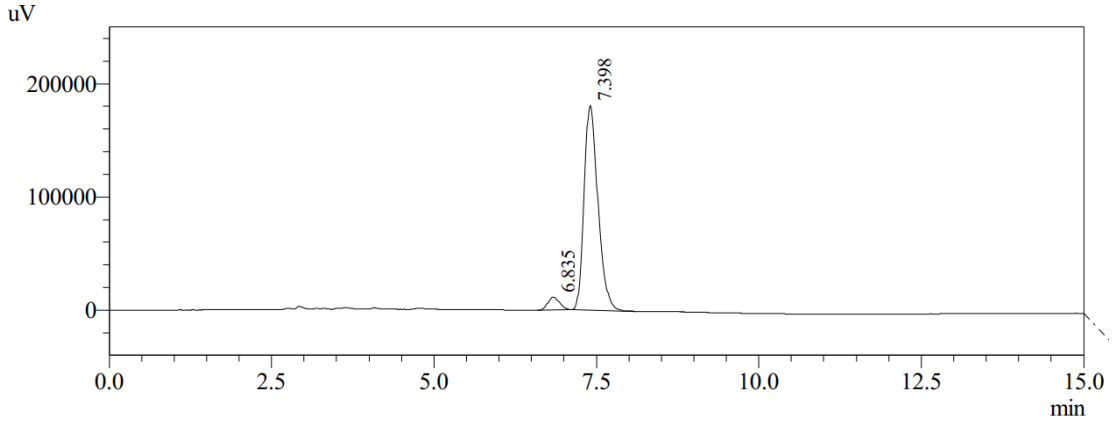
Detection: UV 210 nm

Racemic



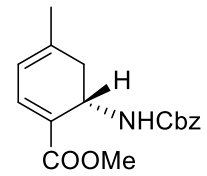
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.842	261236	19486	49.222	53.197
2	7.427	269490	17144	50.778	46.803
Total		530726	36630	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.835	142987	11291	5.044	5.884
2	7.398	2691580	180583	94.956	94.116
Total		2834567	191873	100.000	100.000

Compound 3p



HPLC Conditions

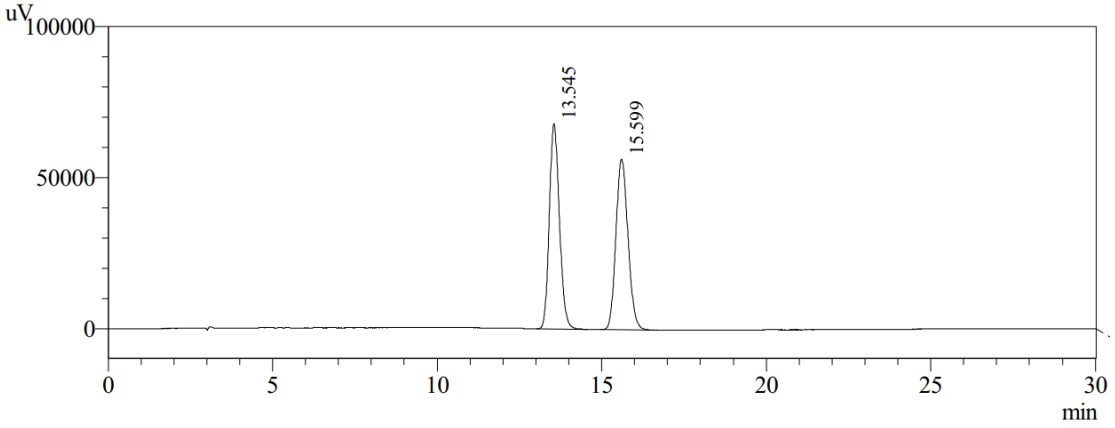
Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

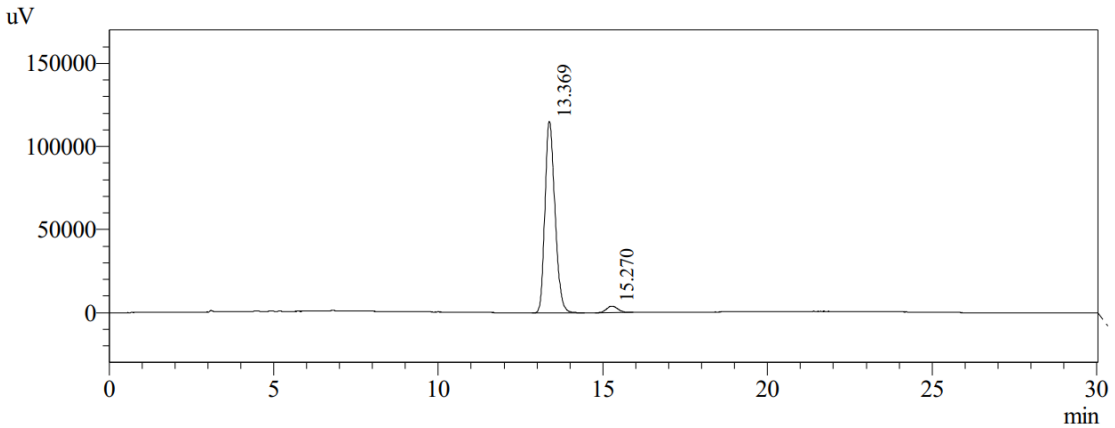
Detection: UV 210 nm

Racemic



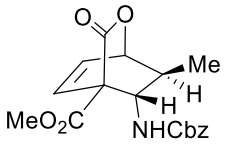
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.545	1453937	68046	50.096	54.568
2	15.599	1448391	56653	49.904	45.432
Total		2902328	124699	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.369	2442771	115177	96.166	96.673
2	15.270	97391	3964	3.834	3.327
Total		2540162	119141	100.000	100.000

Compound 3q



HPLC Conditions

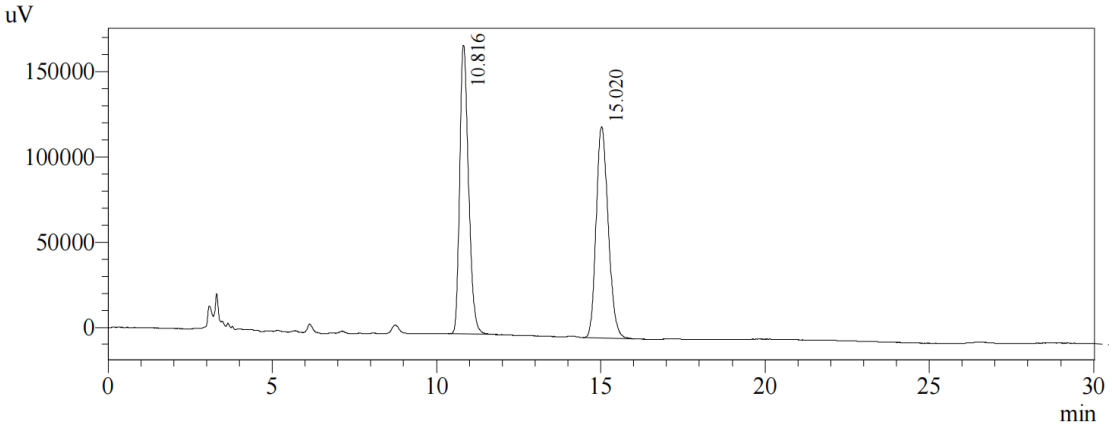
Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/EtOH (80:20)

Flow rate: 1.0 mL/min

Detection: UV 210 nm

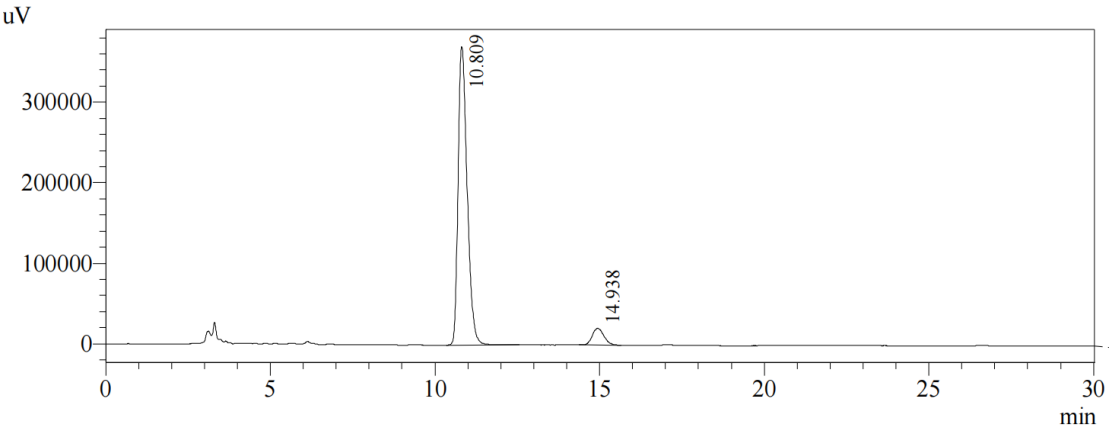
Racemic



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	10.816	3179813	50.125
2	15.020	3163912	49.875
Total		6343724	100.000

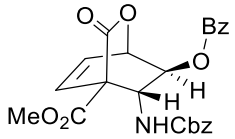
Chiral



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	10.809	7113824	93.282
2	14.938	512354	6.718
Total		7626178	100.000

Compound 3r



HPLC Conditions

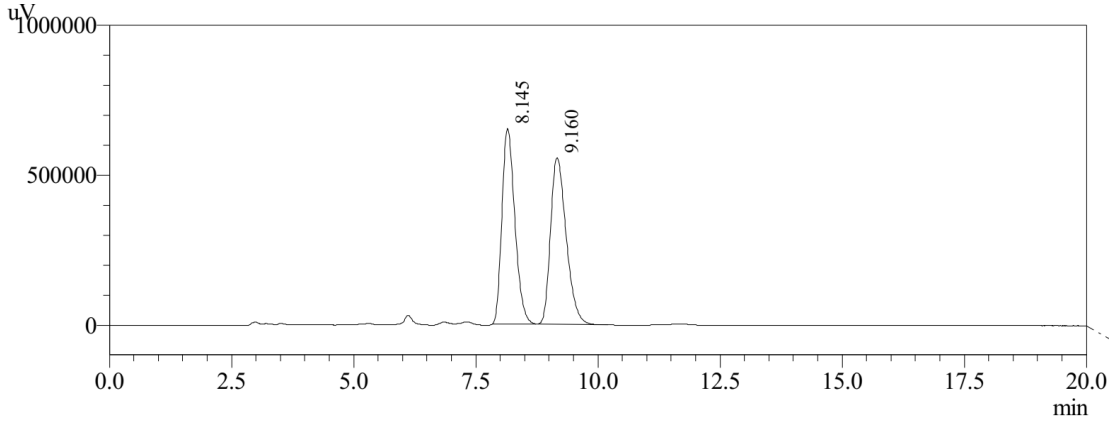
Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/EtOH (80:20)

Flow rate: 1.0 mL/min

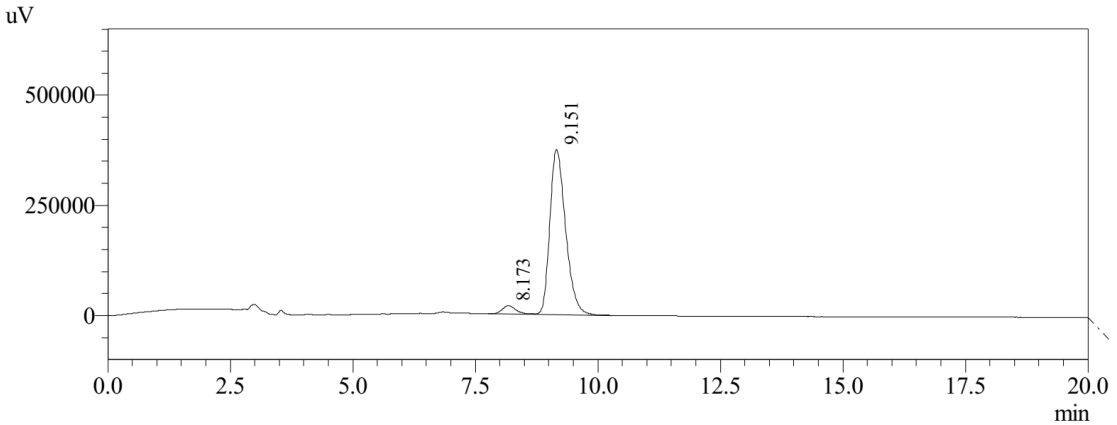
Detection: UV 210 nm

Racemic



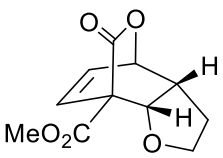
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.145	12016389	652847	49.197	53.977
2	9.160	12408738	556642	50.803	46.023
Total		24425127	1209489	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.173	362320	18742	4.150	4.769
2	9.151	8369041	374285	95.850	95.231
Total		8731361	393027	100.000	100.000

Compound 3s



HPLC Conditions

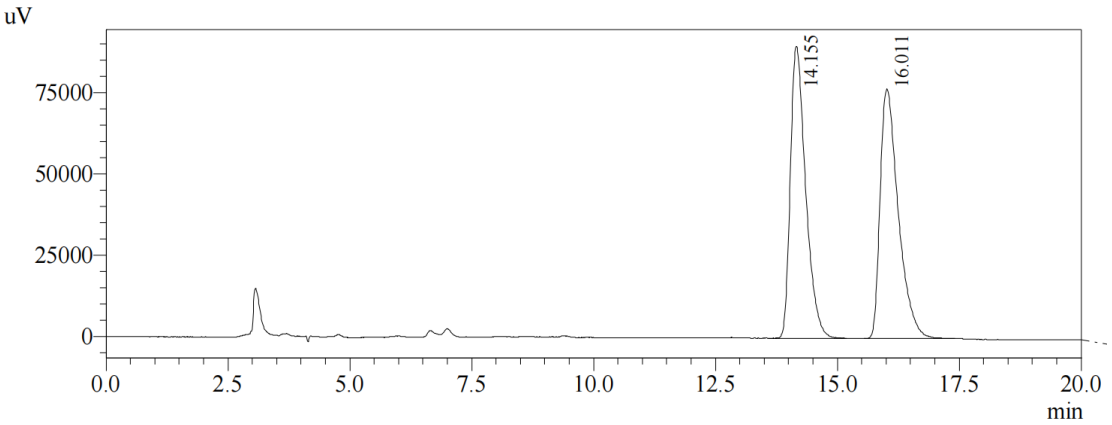
Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/EtOH (90:10)

Flow rate: 1.0 mL/min

Detection: UV 210 nm

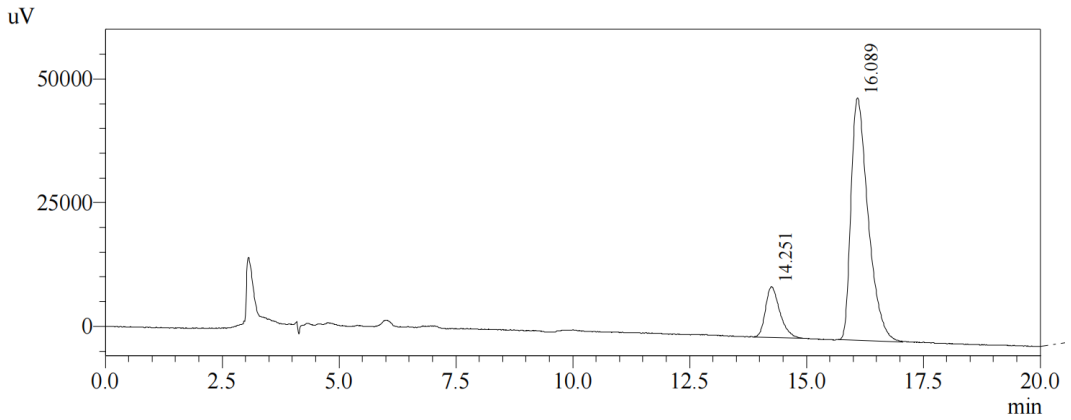
Racemic



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	14.155	1970125	49.738
2	16.011	1990848	50.262
Total		3960973	100.000

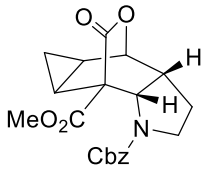
Chiral



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	14.251	219698	14.925
2	16.089	1252273	85.075
Total		1471971	100.000

Compound 3t



HPLC Conditions

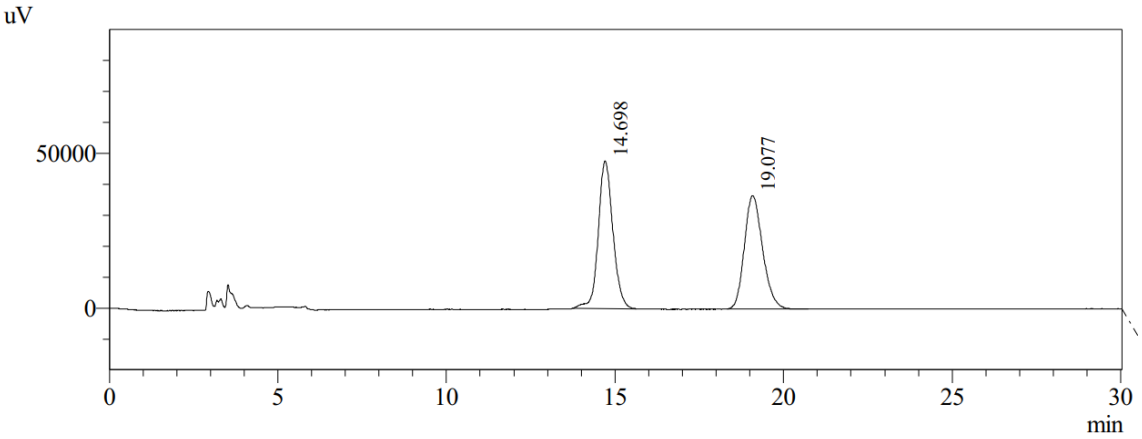
Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

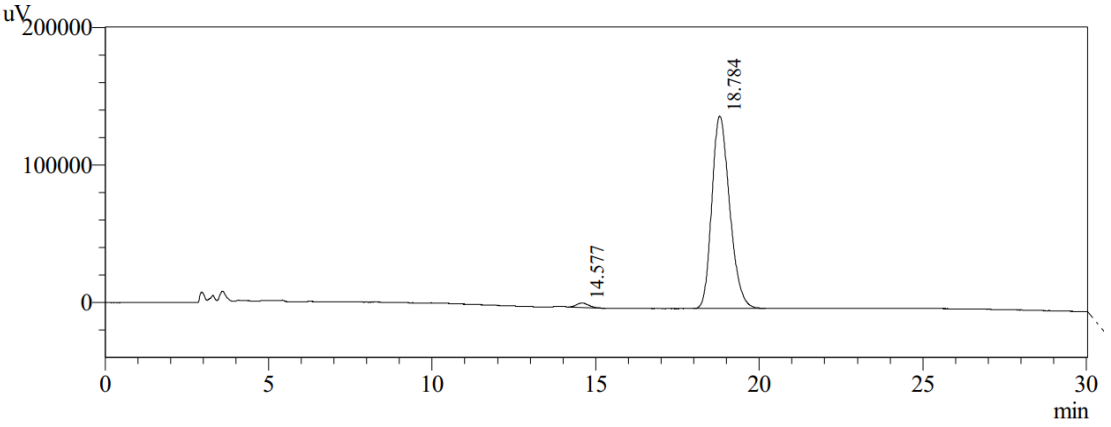
Detection: UV 210 nm

Racemic



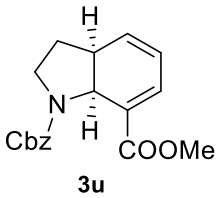
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.698	1445197	47776	50.995	56.542
2	19.077	1388825	36721	49.005	43.458
Total		2834022	84496	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.577	84391	3167	1.564	2.217
2	18.784	5312263	139715	98.436	97.783
Total		5396654	142882	100.000	100.000

Compound 3u



3u

HPLC Conditions

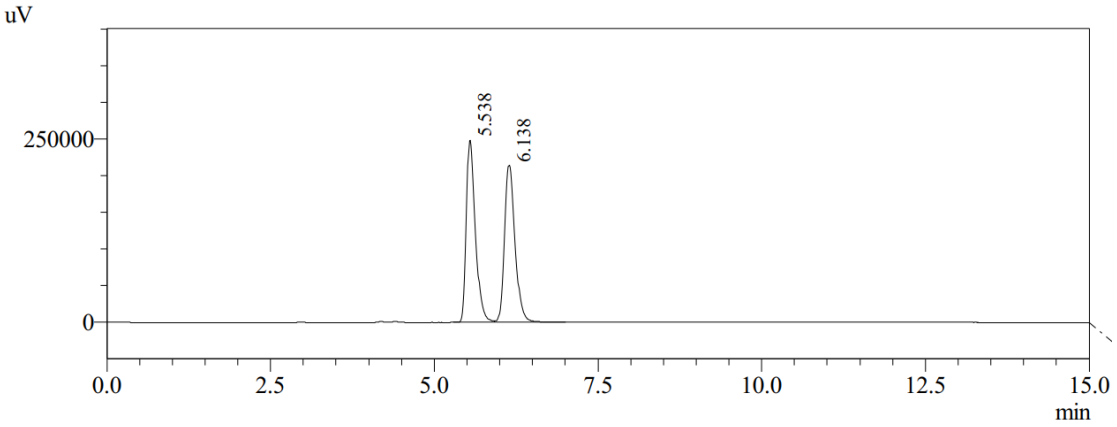
Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

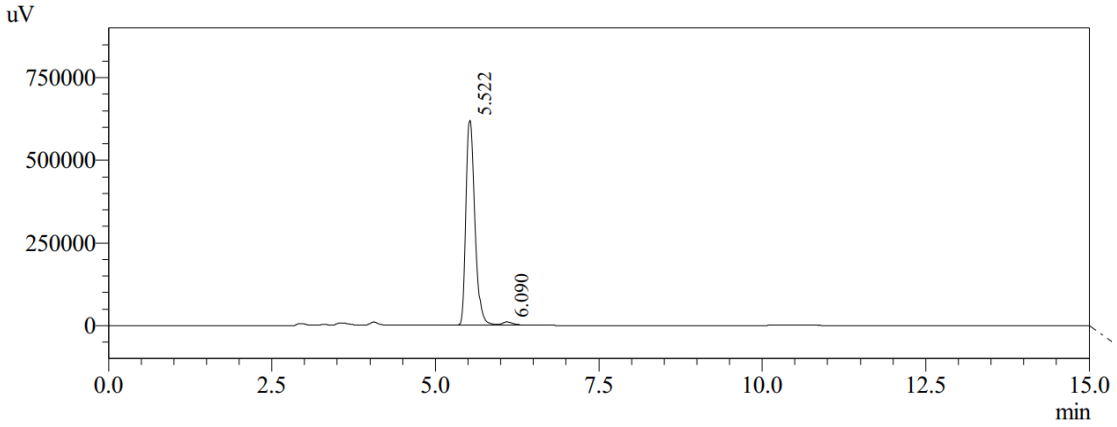
Detection: UV 210 nm

Racemic



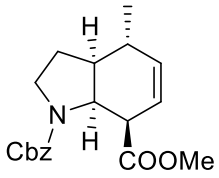
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.538	2402141	248549	50.123	53.694
2	6.138	2390393	214354	49.877	46.306
Total		4792534	462904	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.522	5902774	620835	97.834	98.360
2	6.090	130670	10349	2.166	1.640
Total		6033444	631183	100.000	100.000

Compound 3v



3v

HPLC Conditions

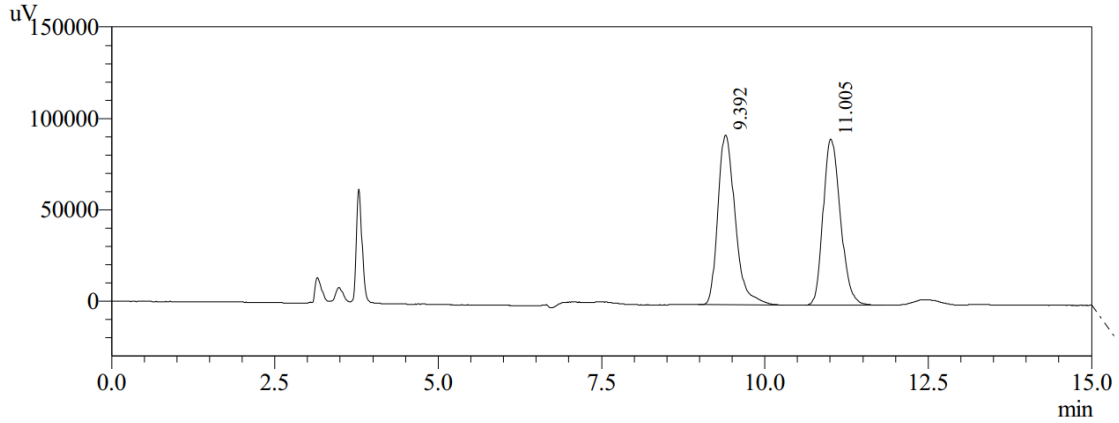
Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (90:10)

Flow rate: 1.0 mL/min

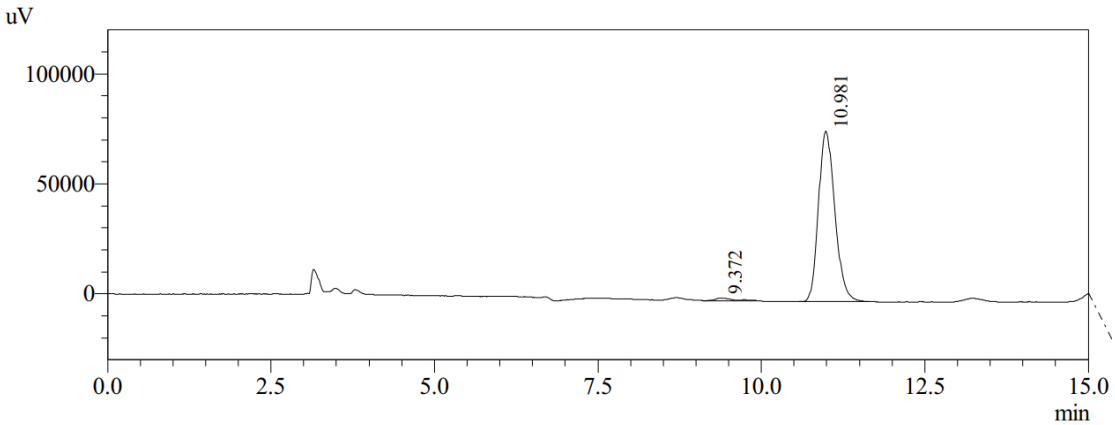
Detection: UV 210 nm

Racemic



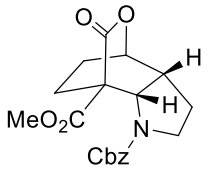
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.392	1716399	92787	50.534	50.518
2	11.005	1680142	90884	49.466	49.482
Total		3396541	183671	100.000	100.000

Chiral



Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.372	20378	1196	1.480	1.520
2	10.981	1356342	77471	98.520	98.480
Total		1376720	78666	100.000	100.000

Compound 4



HPLC Conditions

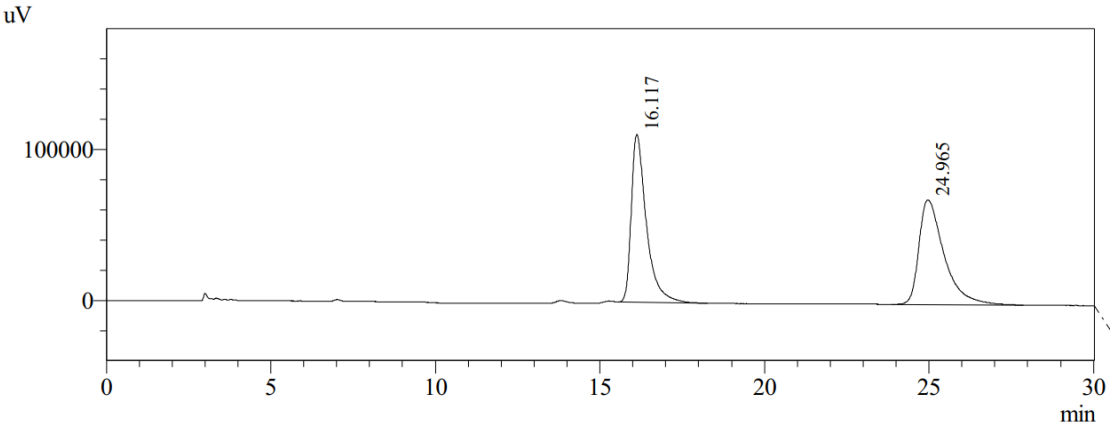
Column: Chiralcel IA-H, Daicel Chemical Industries, Ltd.

Eluent: hexanes/ethanol (80:20)

Flow rate: 1.0 mL/min

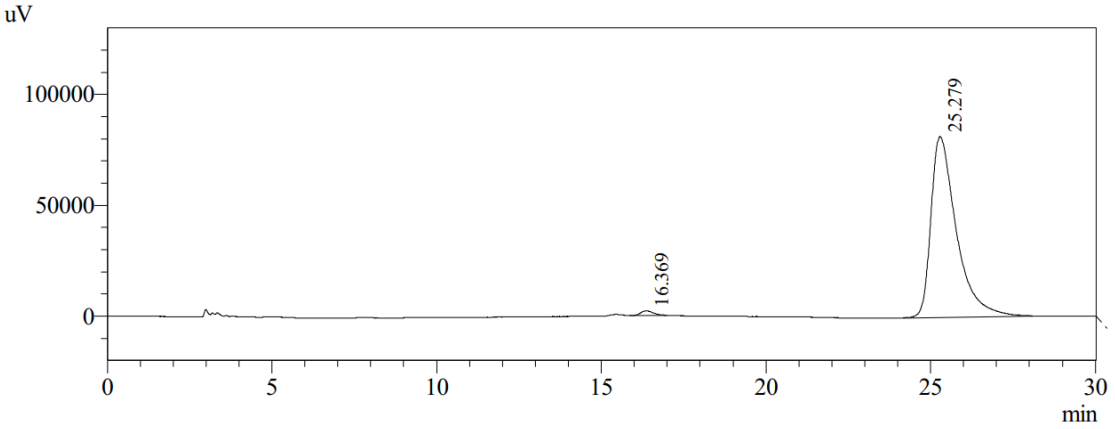
Detection: UV 210 nm

Racemic



Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.117	3559033	111235	48.984	61.532
2	24.965	3706643	69541	51.016	38.468
Total		7265676	180777	100.000	100.000

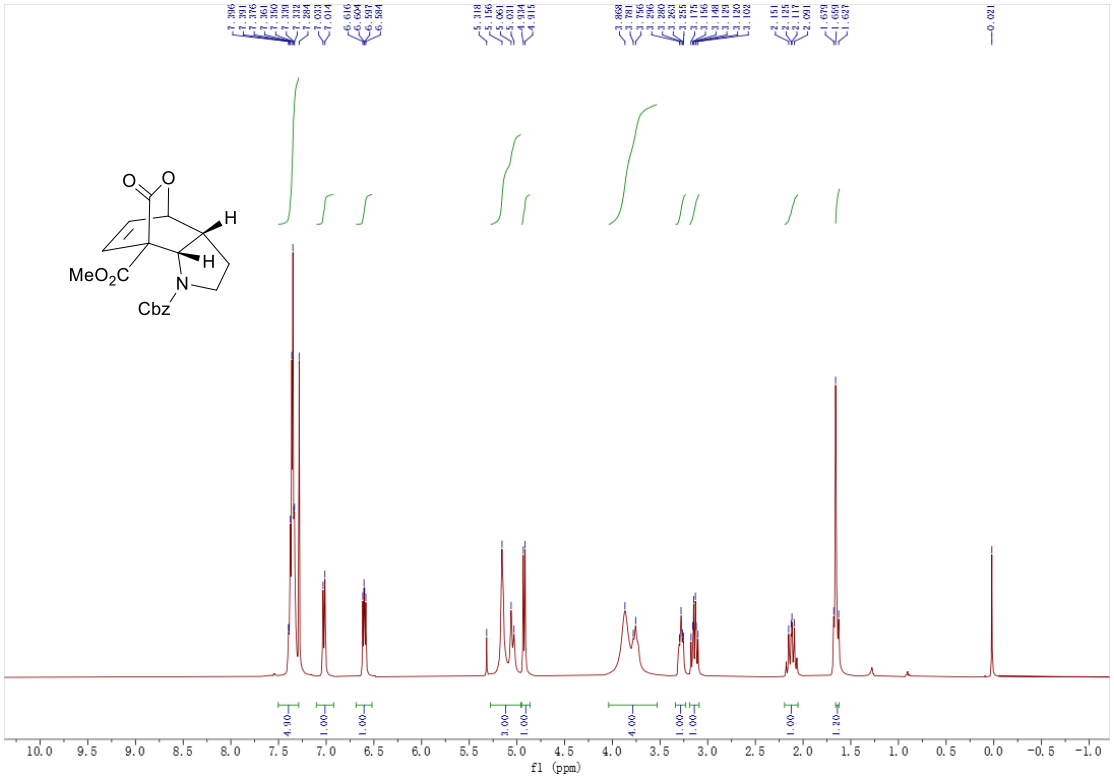
Chiral



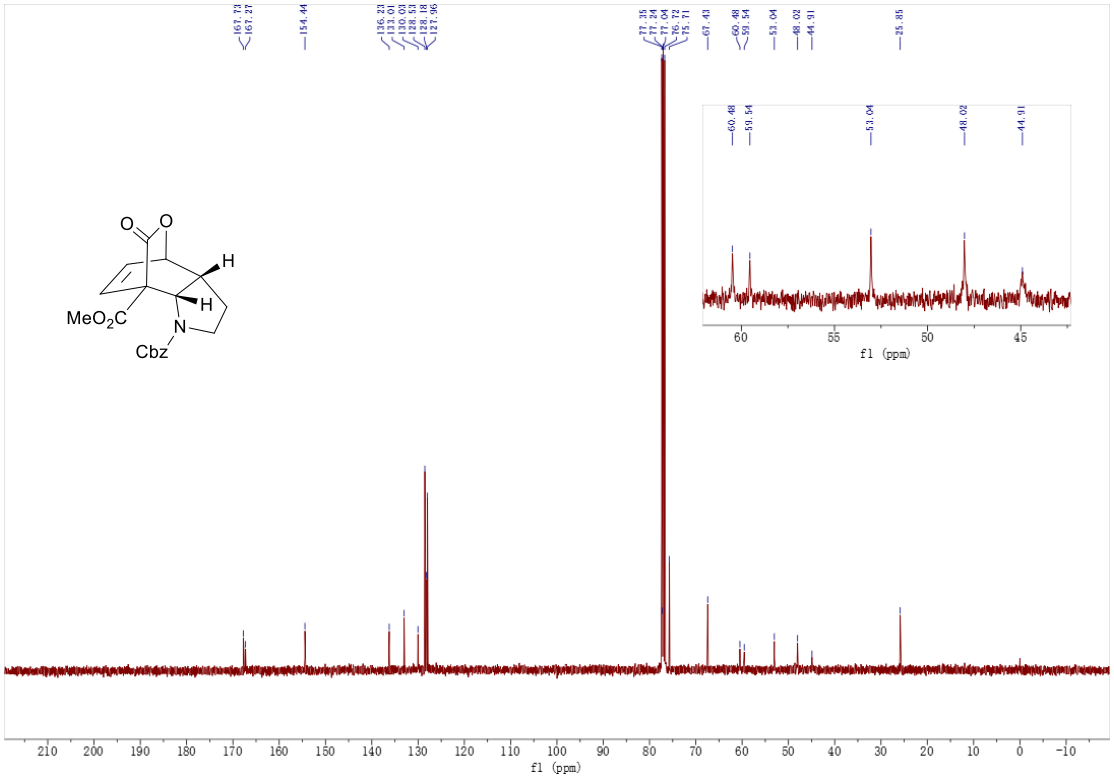
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.369	59367	2132	1.338	2.547
2	25.279	4378507	81577	98.662	97.453
Total		4437874	83709	100.000	100.000

10. NMR Spectra of New Compounds

Compound **3a**

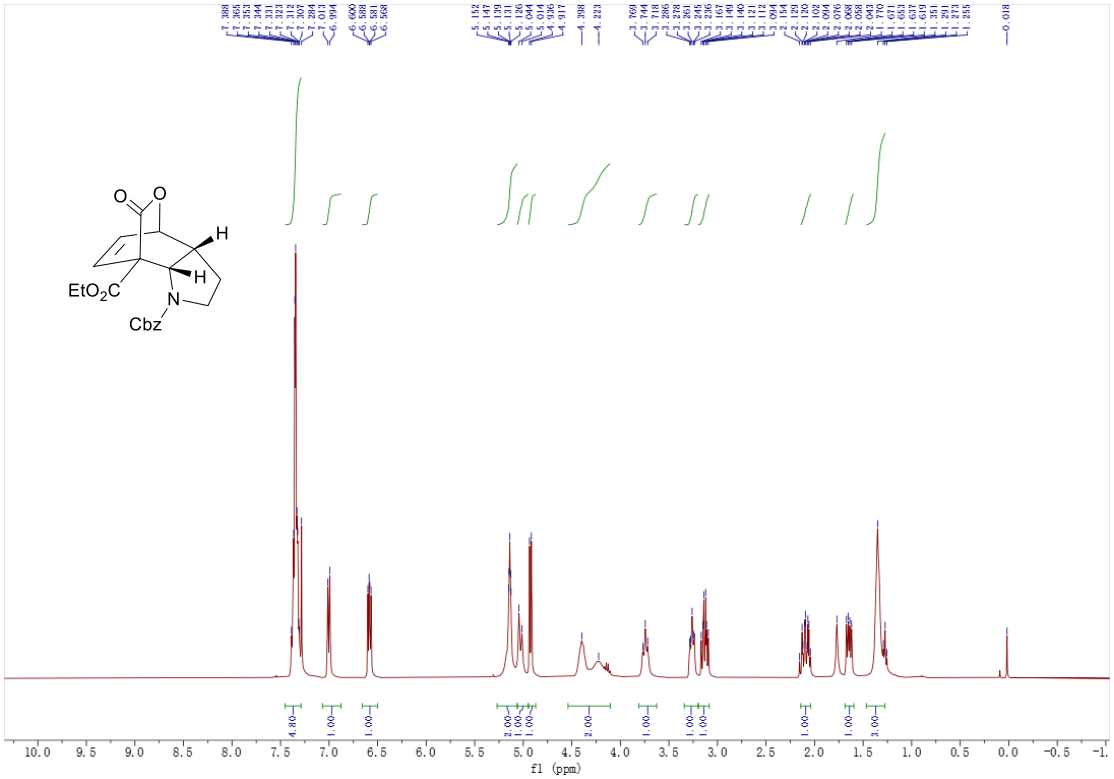


^{1}H NMR of Compound **3a**

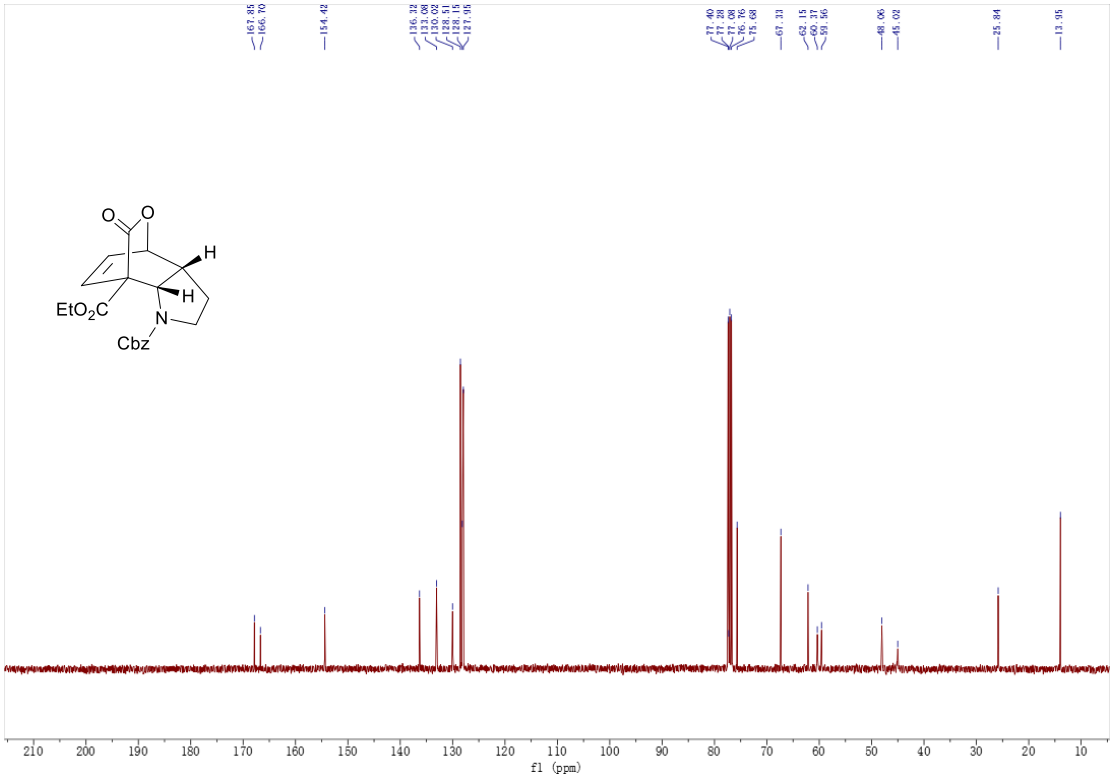


^{13}C NMR of Compound **3a**

Compound **3b**

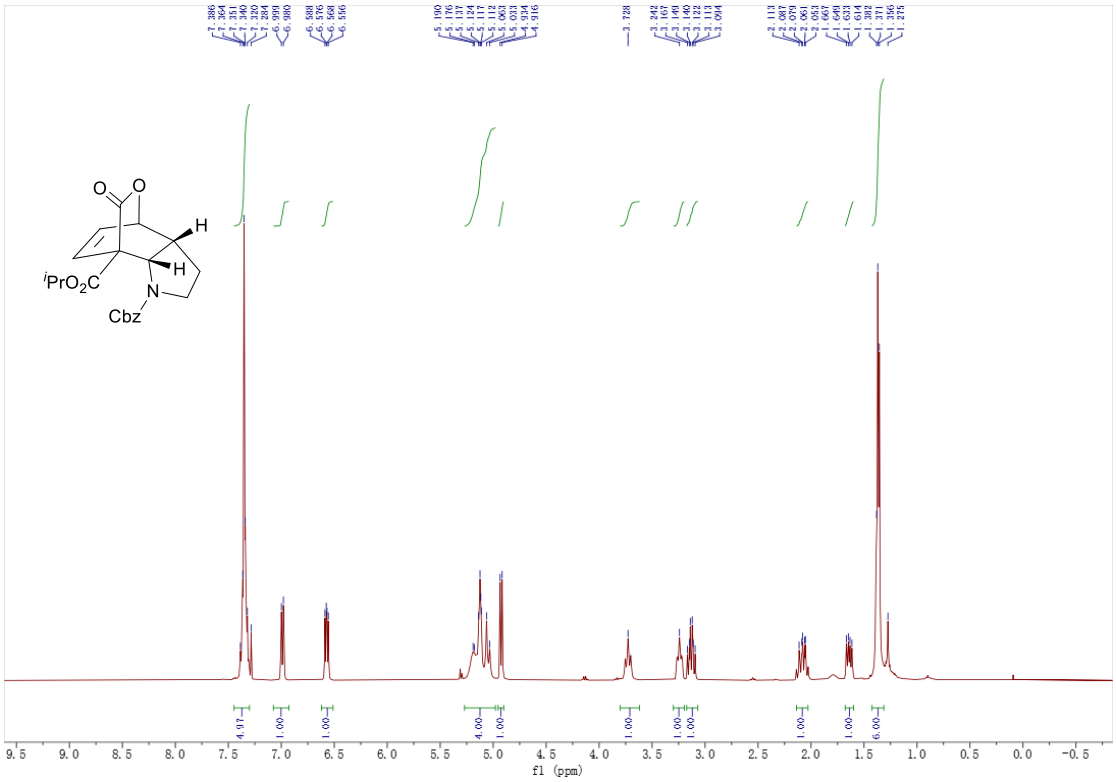


^{1}H NMR of Compound **3b**

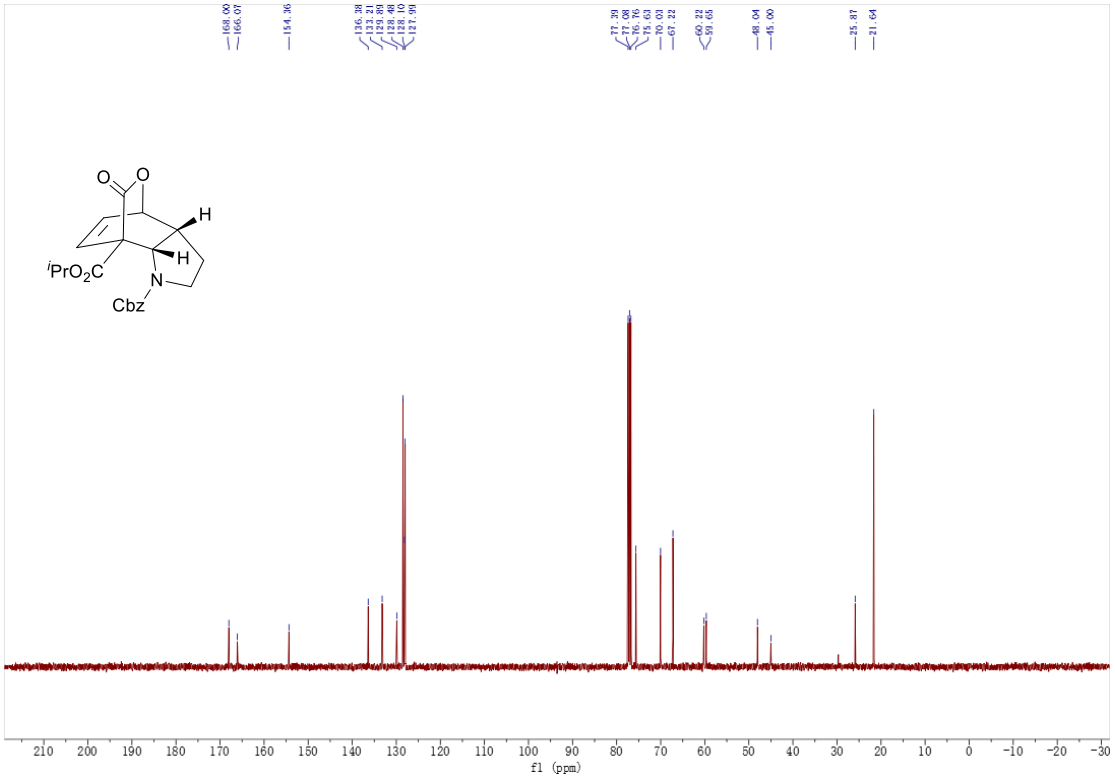


^{13}C NMR of Compound **3b**

Compound **3c**

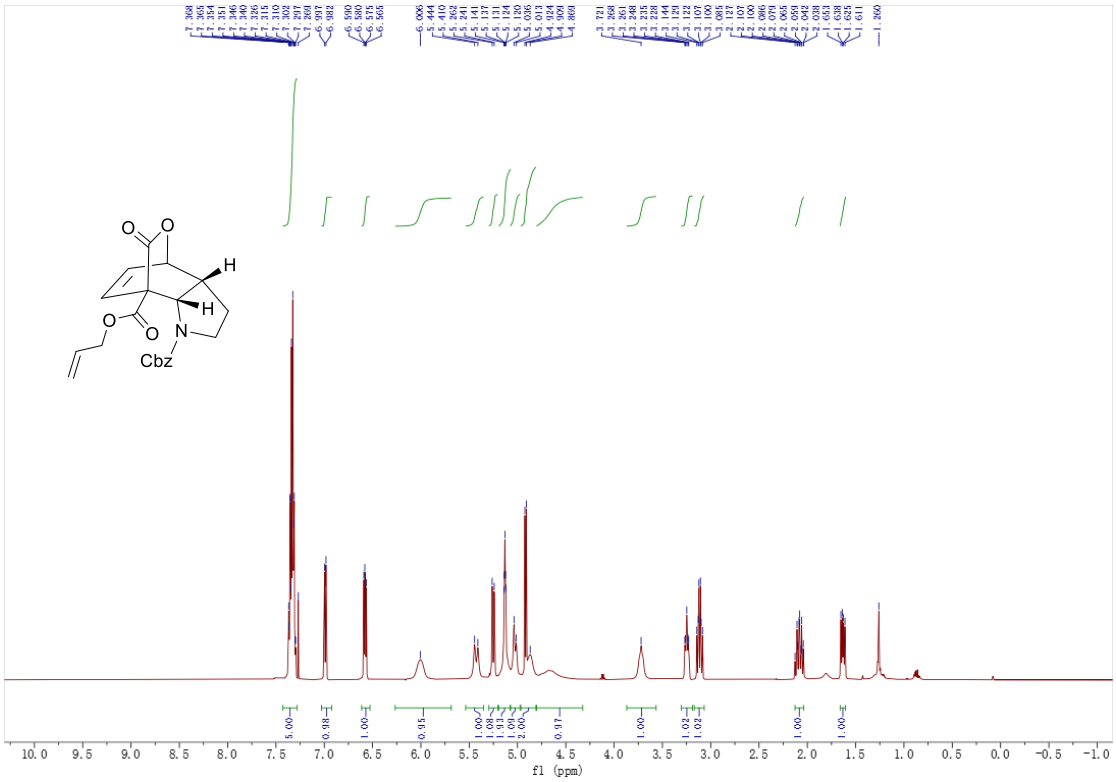


^{1}H NMR of Compound **3c**

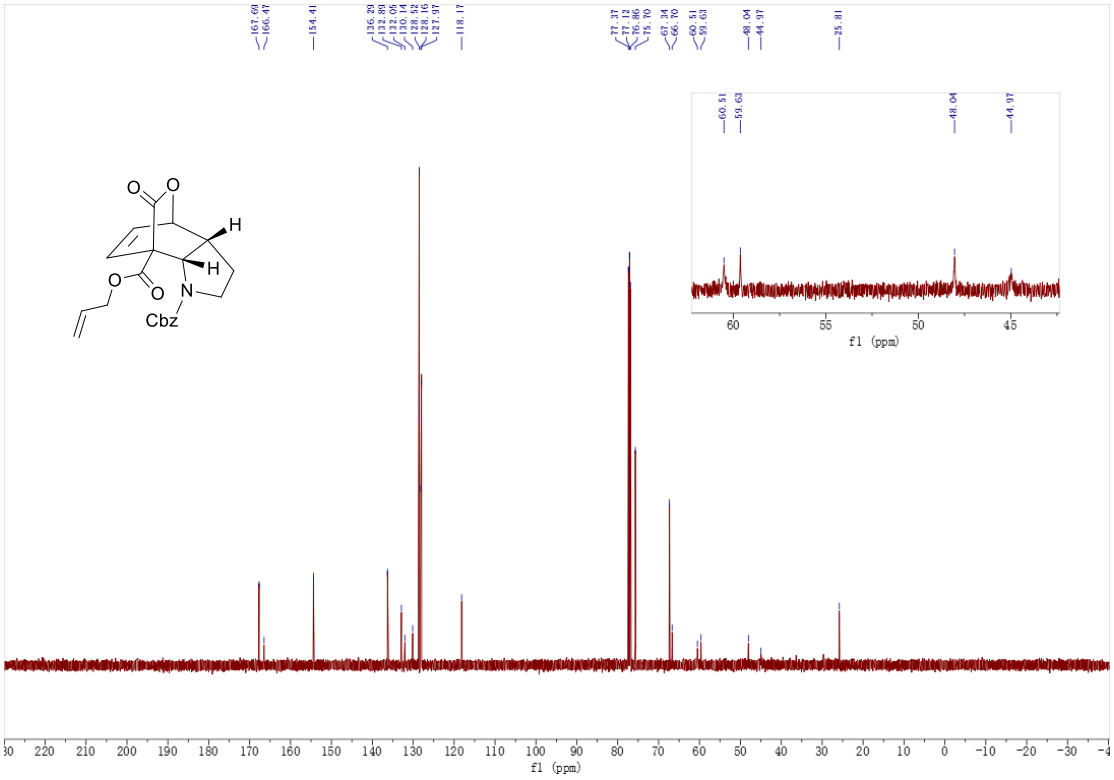


^{13}C NMR of Compound **3c**

Compound **3d**

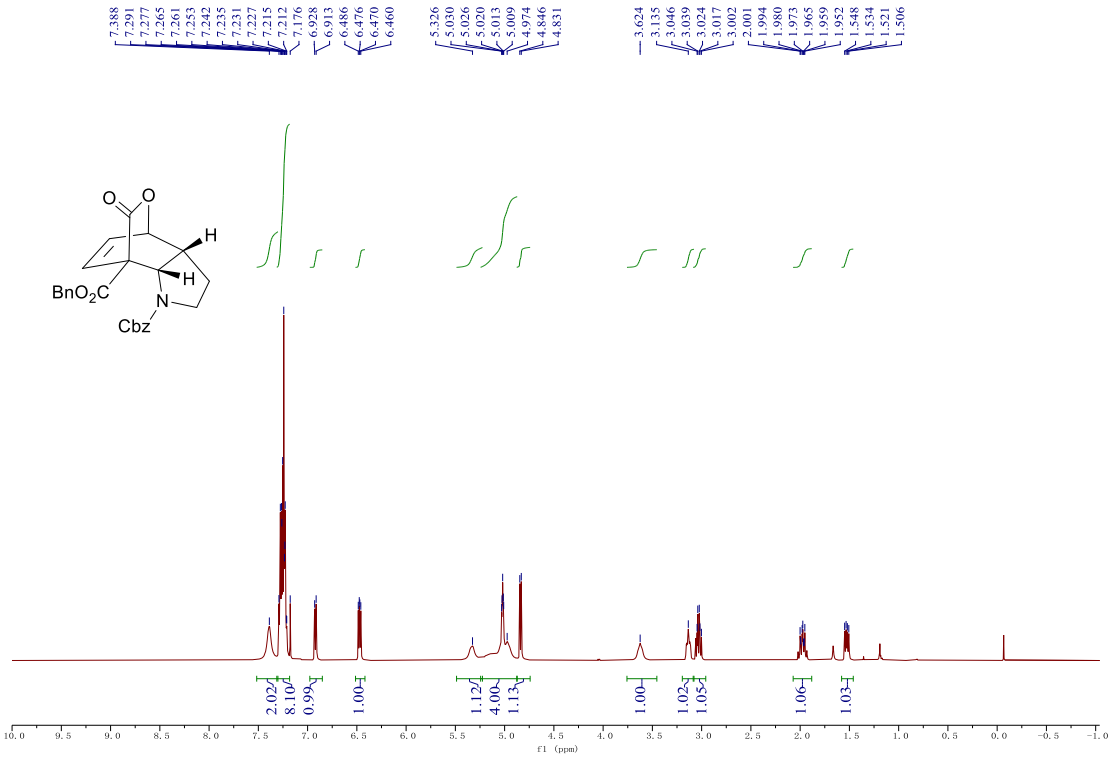


^{1}H NMR of Compound **3d**

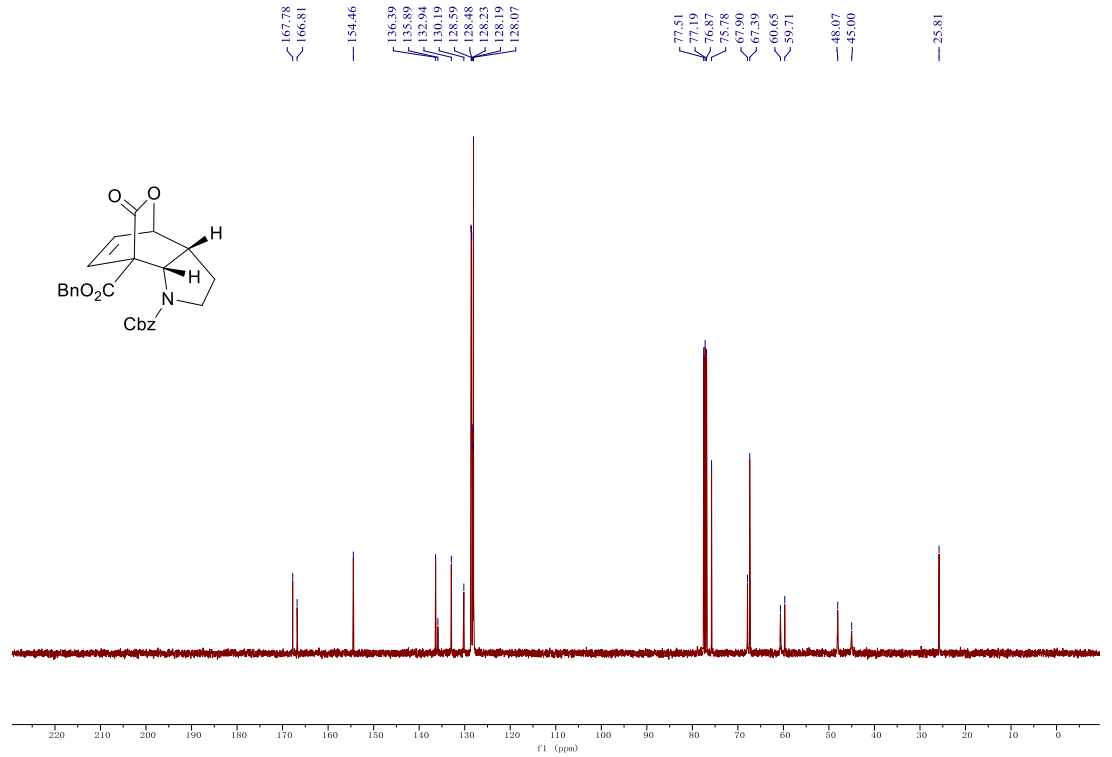


^{13}C NMR of Compound **3d**

Compound **3e**

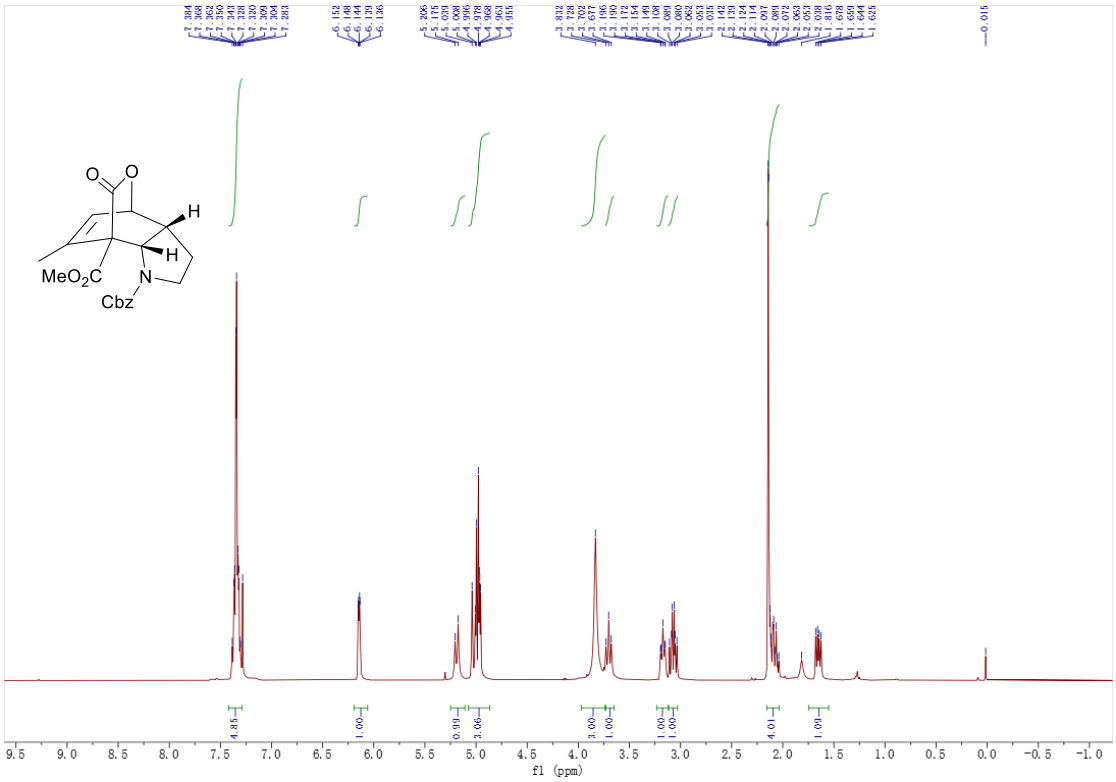


^{1}H NMR of Compound **3e**

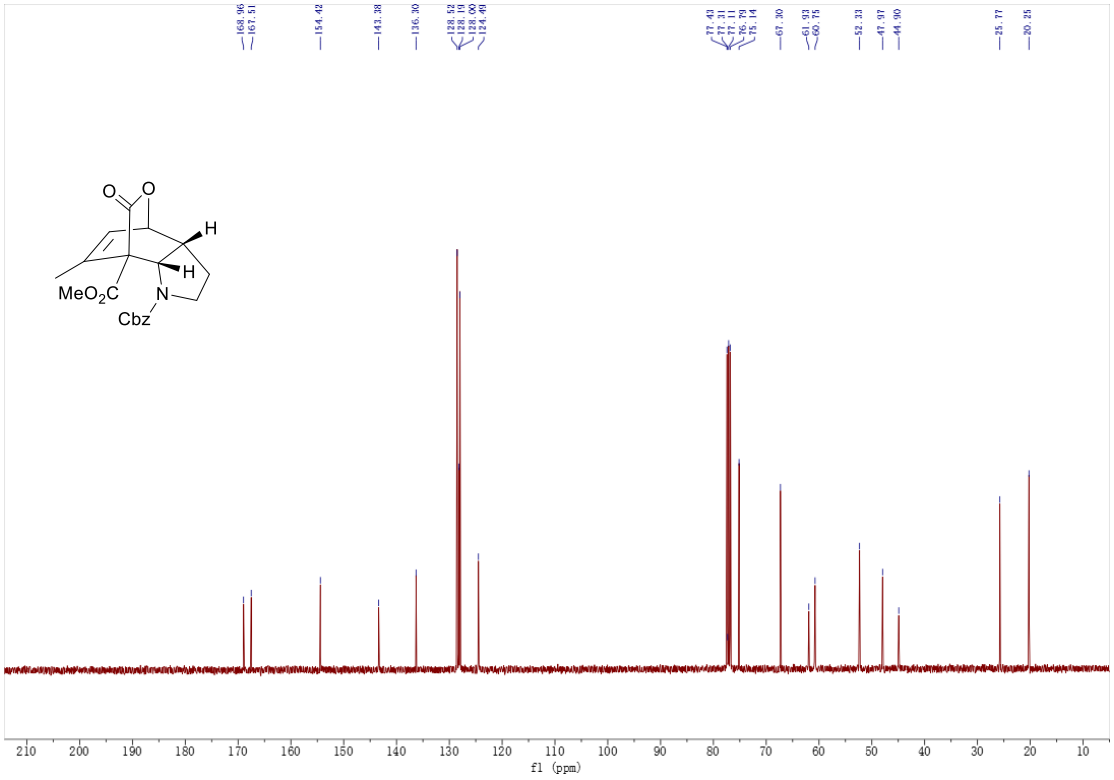


^{13}C NMR of Compound **3e**

Compound **3f**

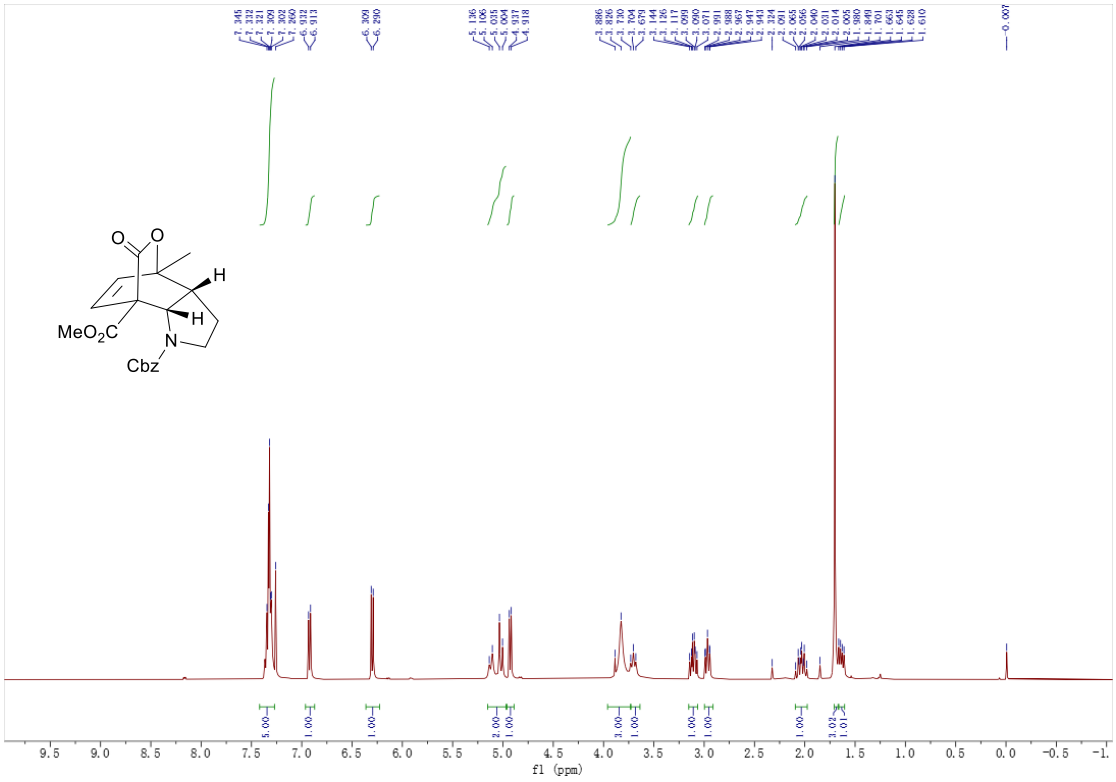


^{1}H NMR of Compound **3f**

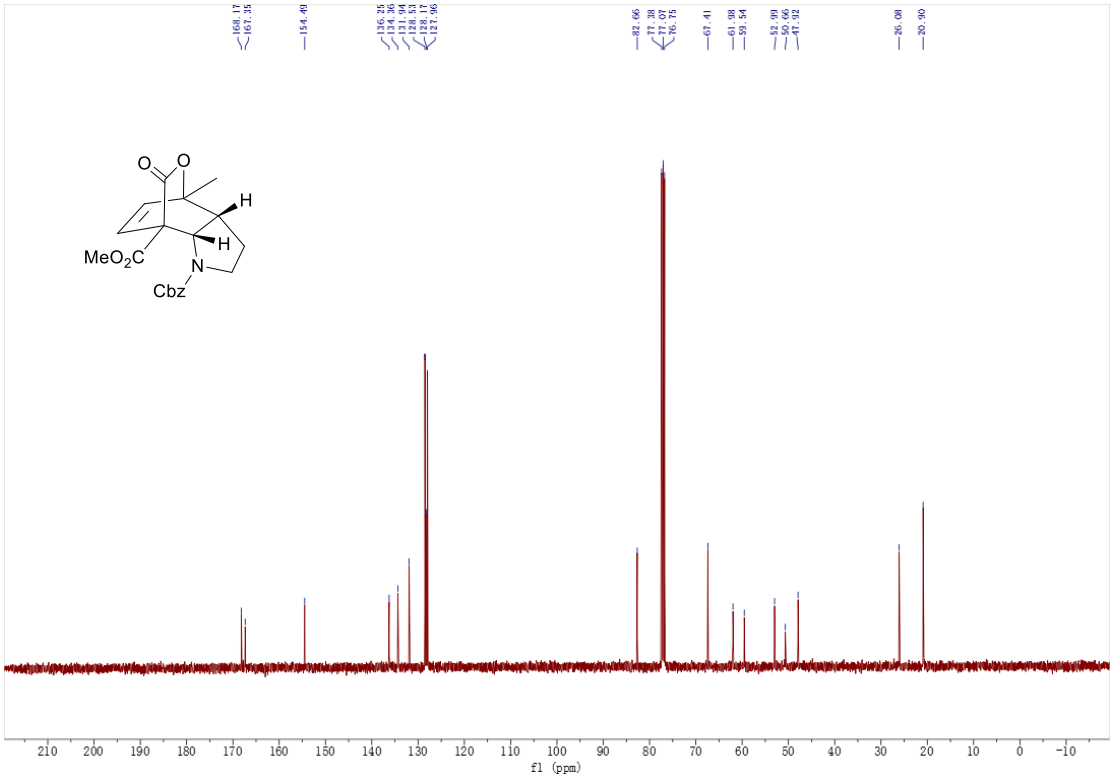


^{13}C NMR of Compound **3f**

Compound **3g**

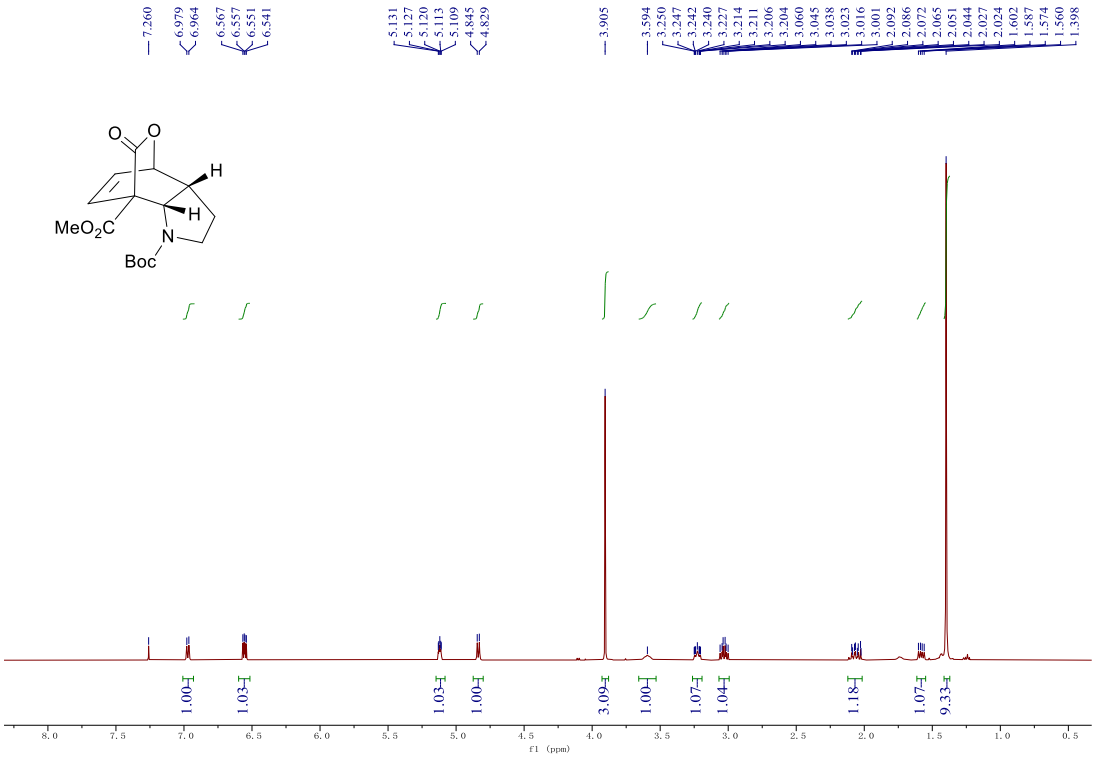


^{1}H NMR of Compound **3g**

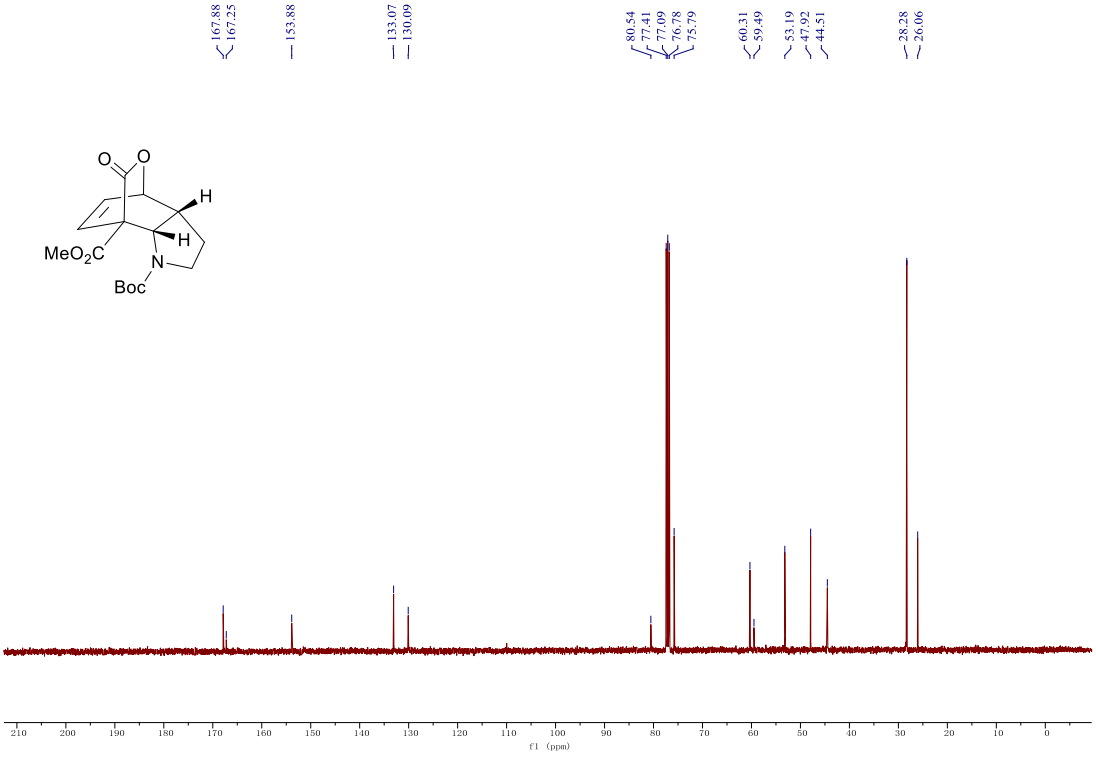


^{13}C NMR of Compound **3g**

Compound **3i**

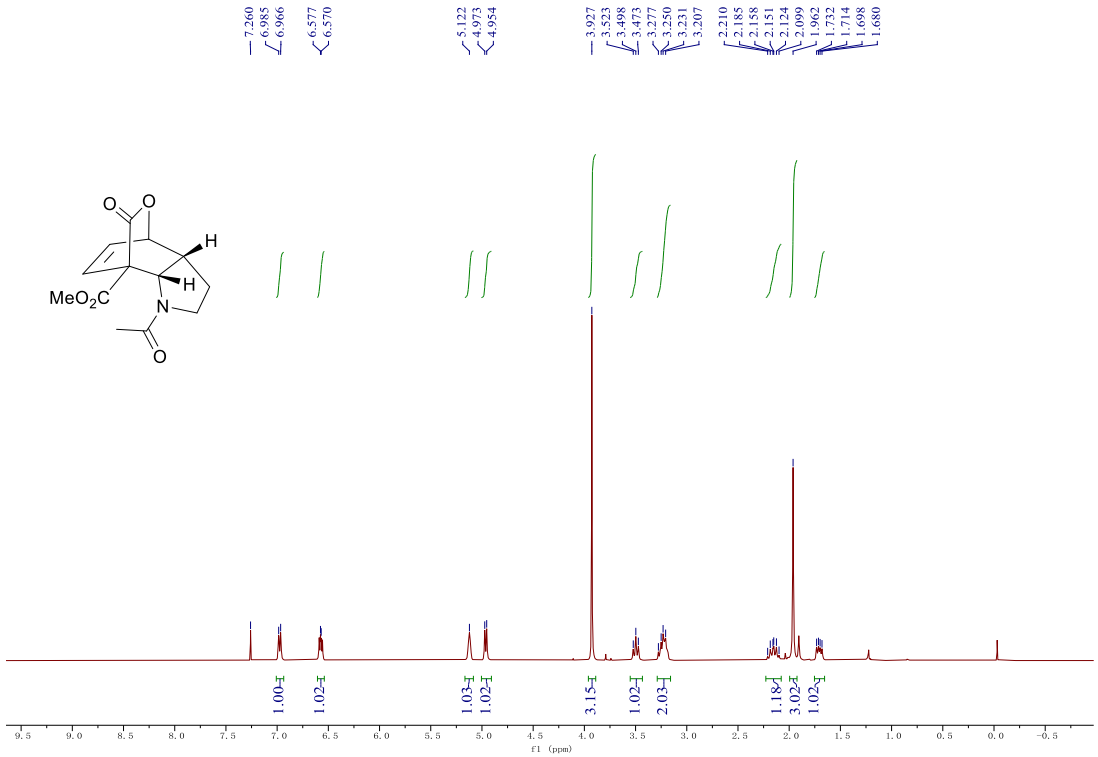


^{1}H NMR of Compound **3i**

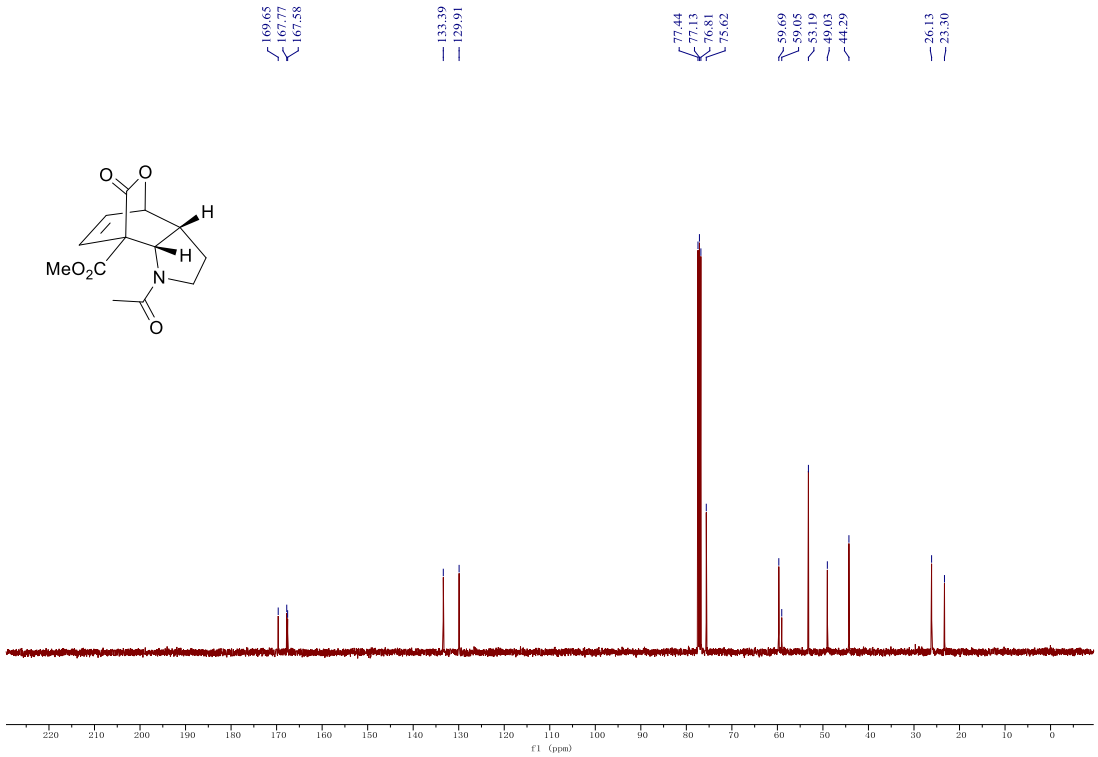


^{13}C NMR of Compound **3i**

Compound **3j**

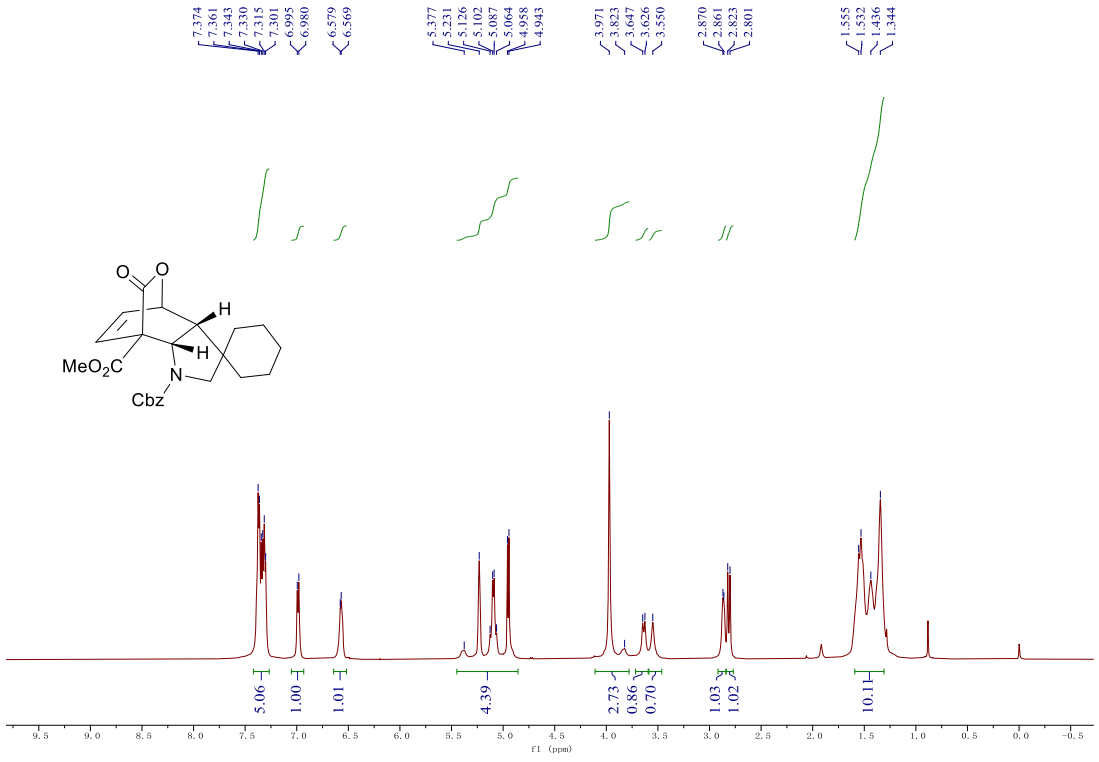


^{1}H NMR of Compound **3j**

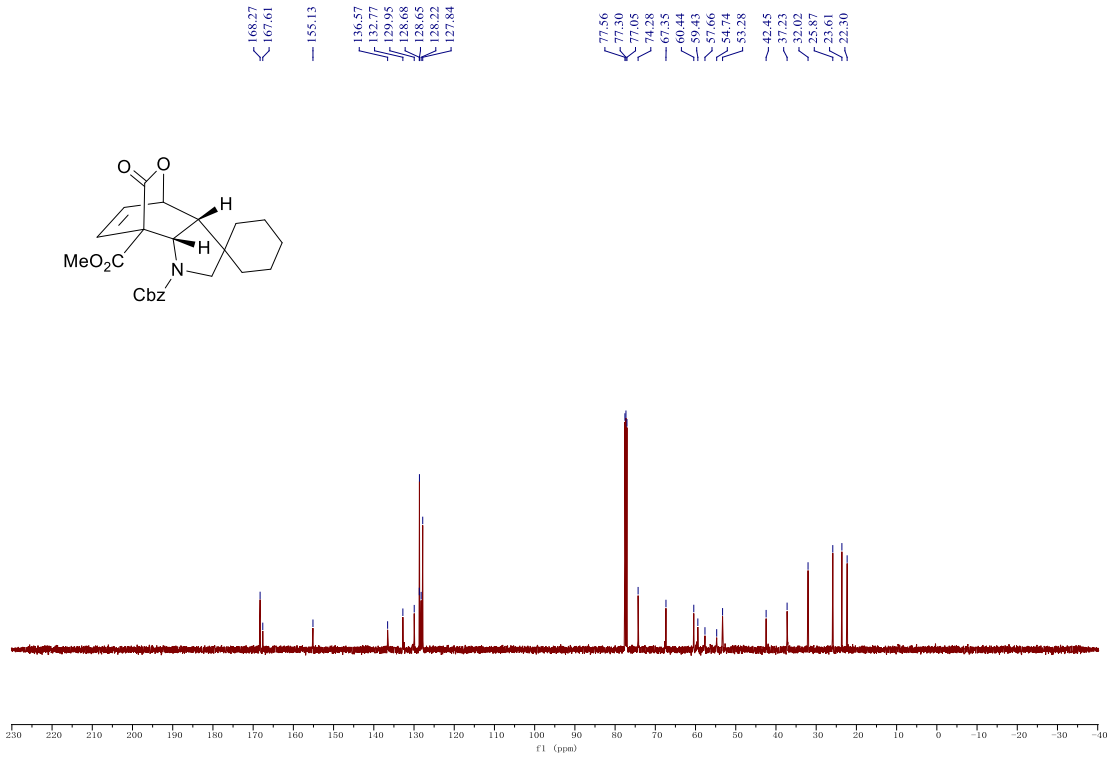


^{13}C NMR of Compound **3j**

Compound **3k**

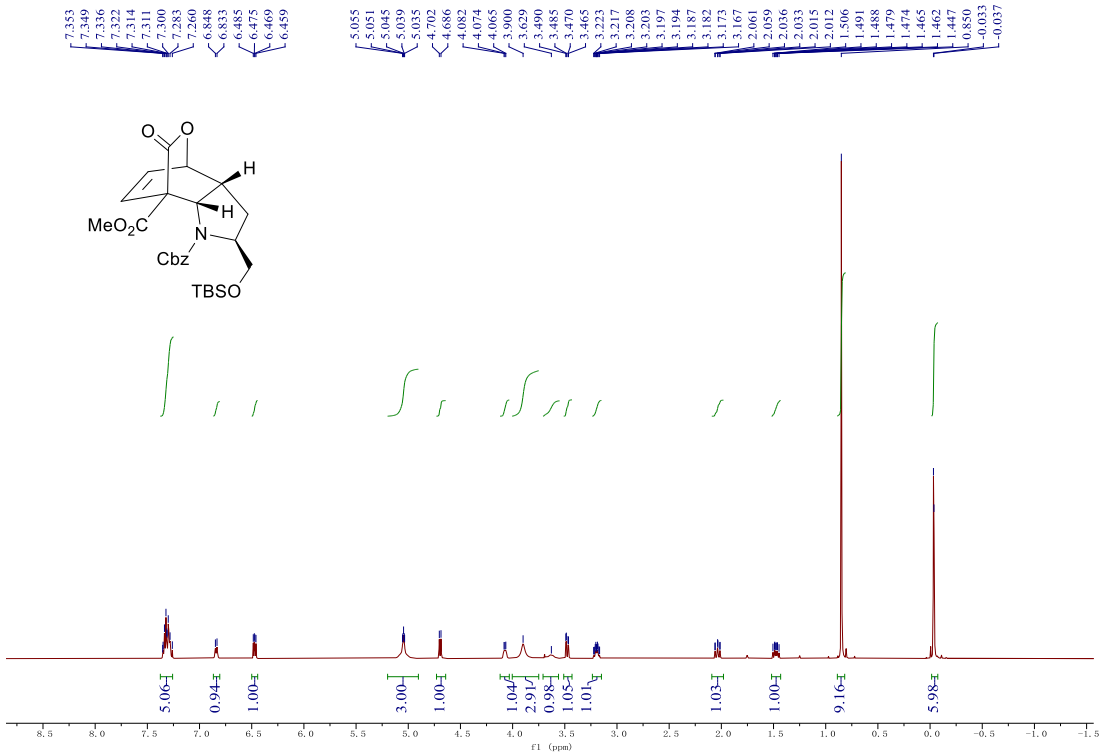


^{1}H NMR of Compound **3k**

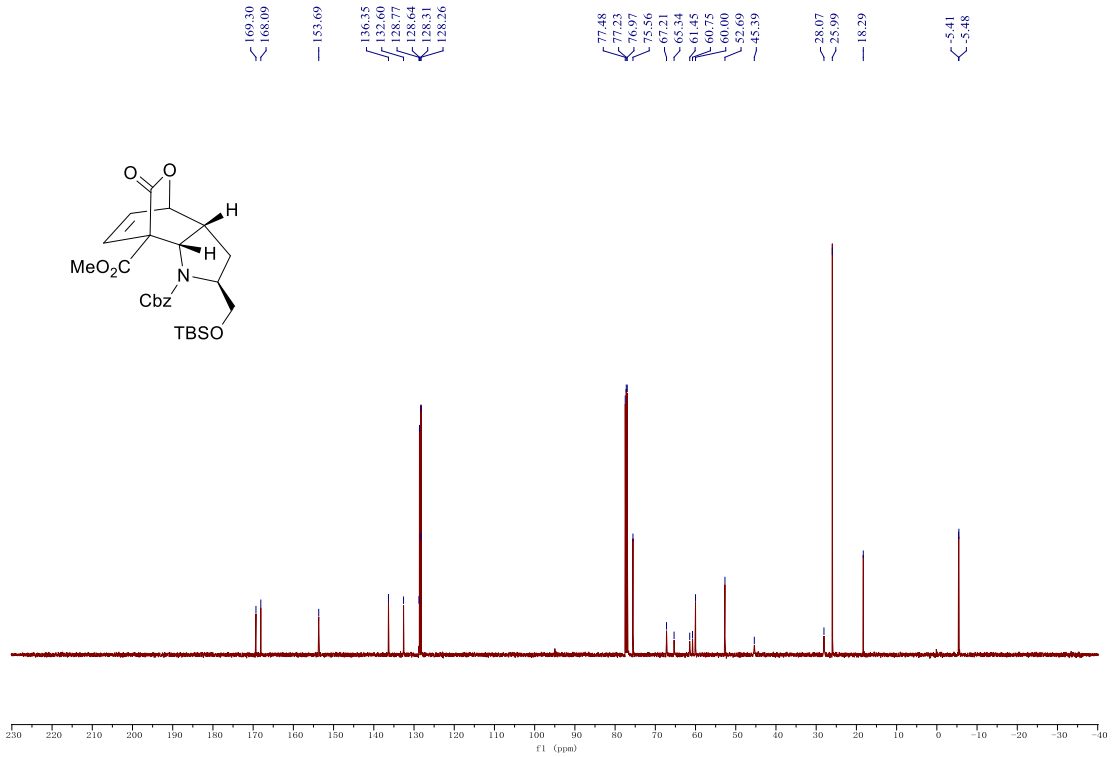


^{13}C NMR of Compound **3k**

Compound **3l**

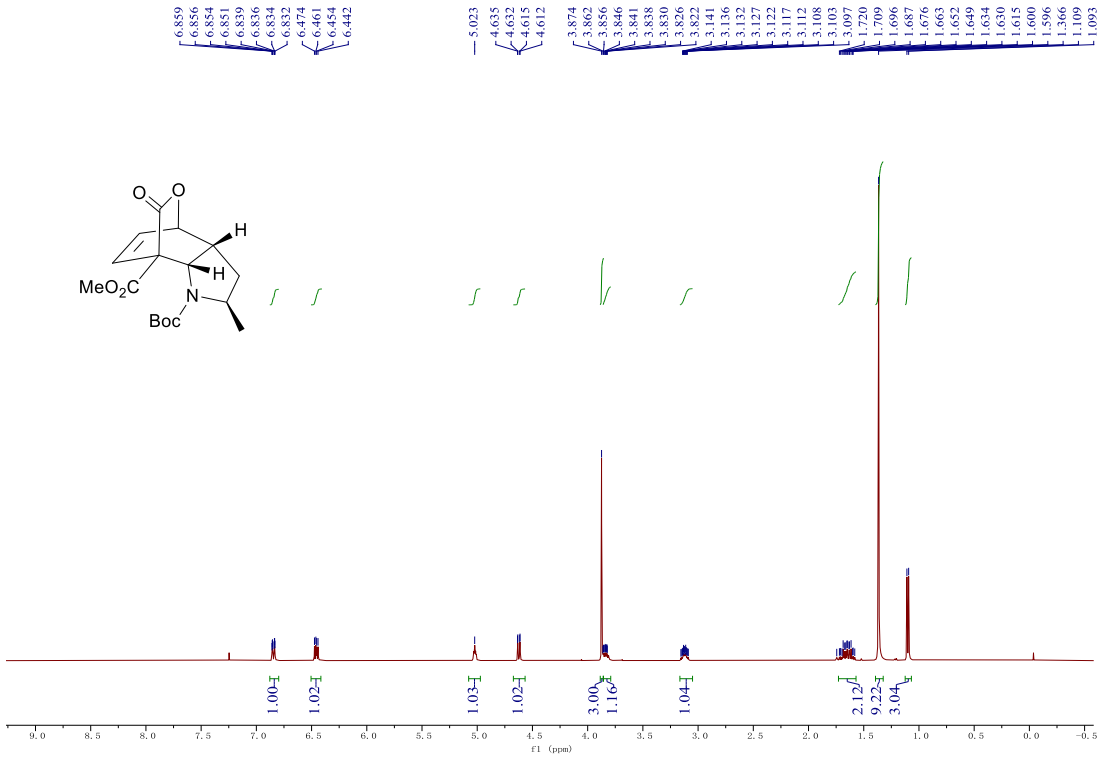


^{1}H NMR of Compound **3l**

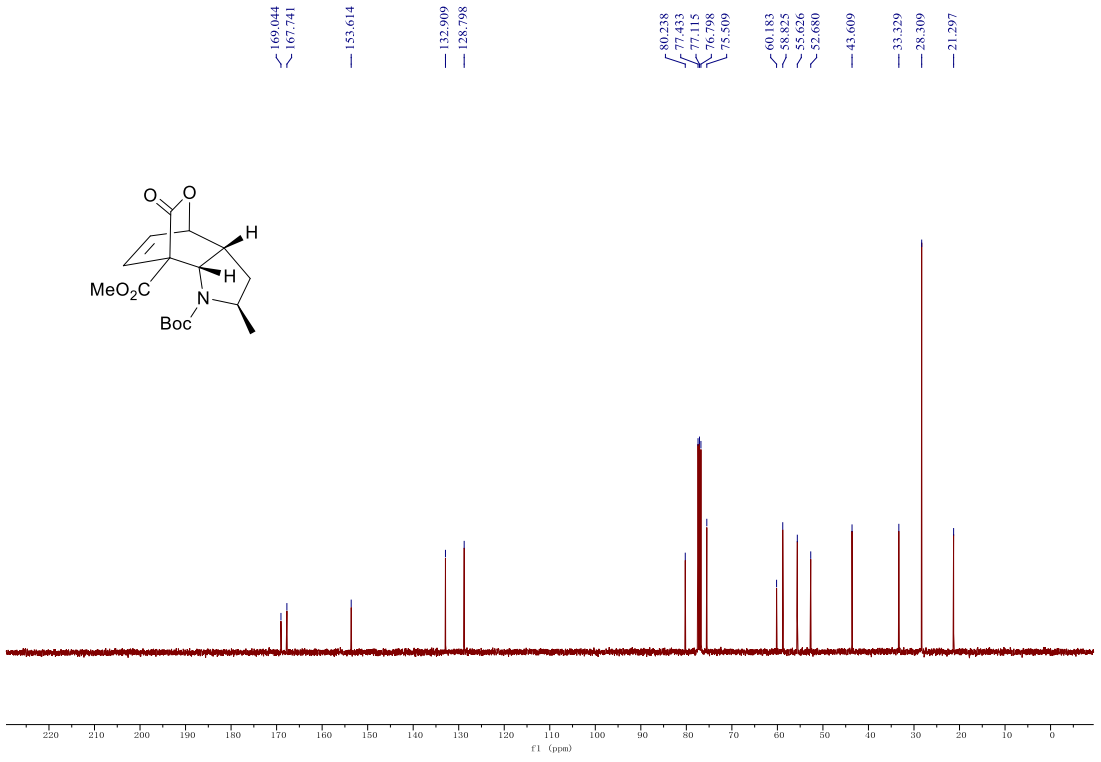


^{13}C NMR of Compound **3l**

Compound **3m**

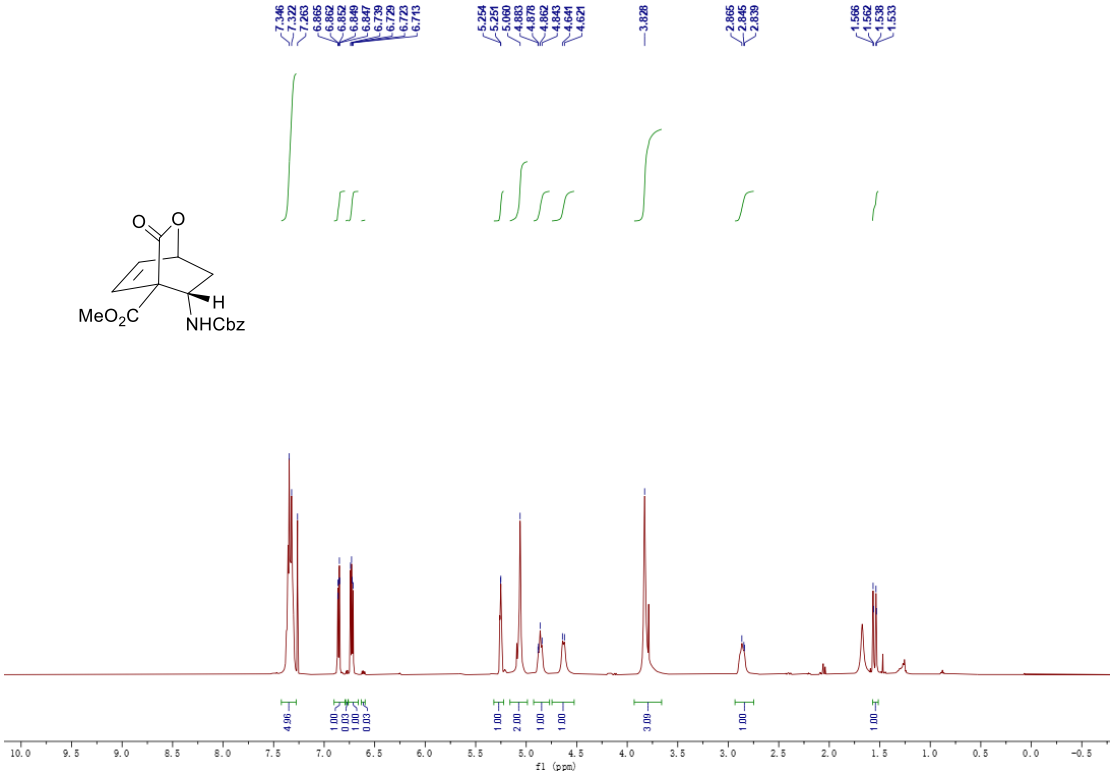


^{1}H NMR of Compound **3m**

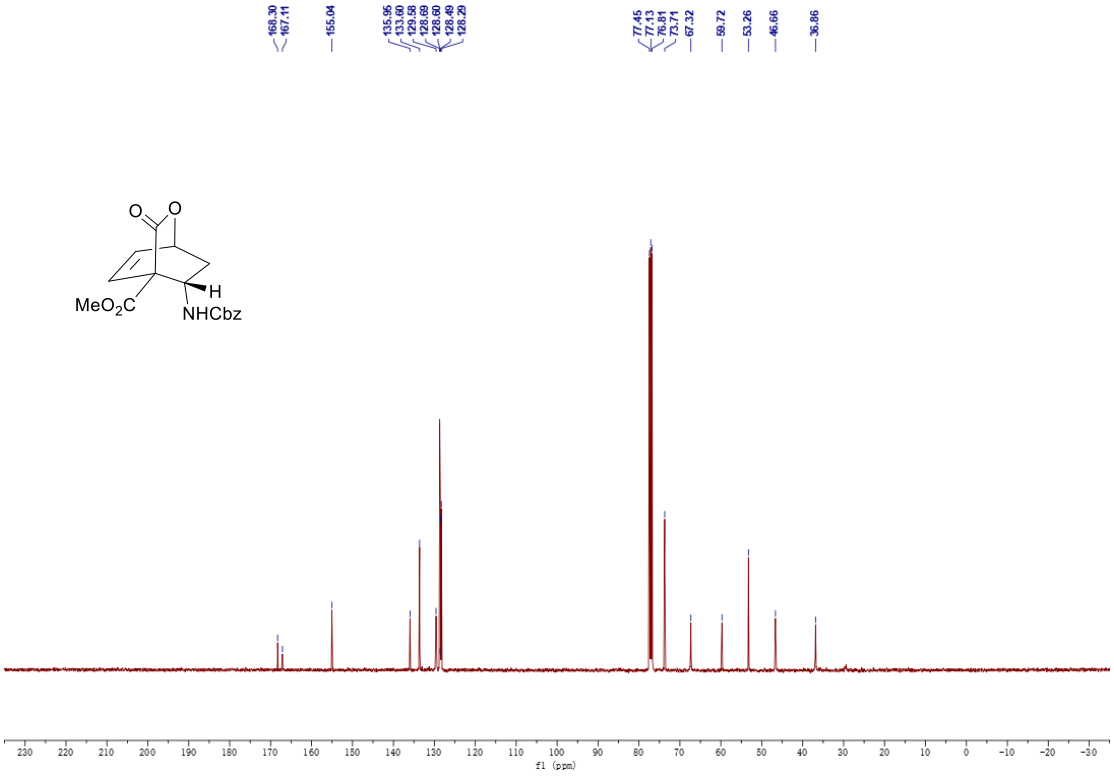


^{13}C NMR of Compound **3m**

Compound **3n**

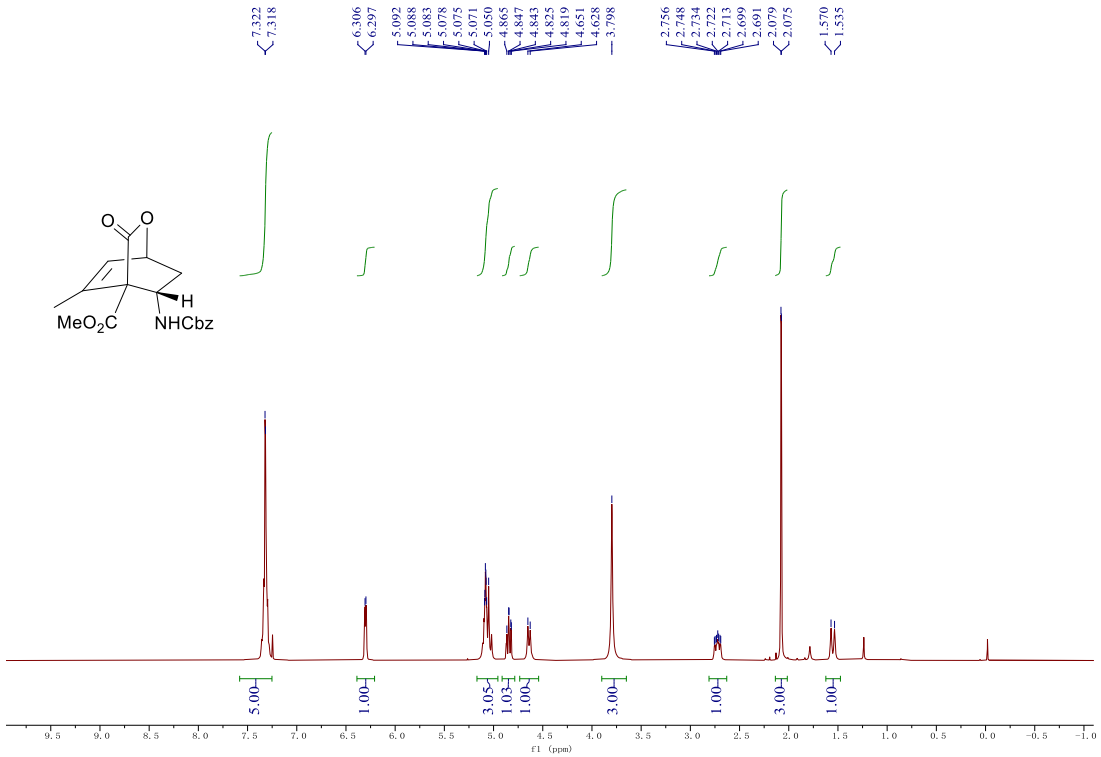


^{1}H NMR of Compound **3n**

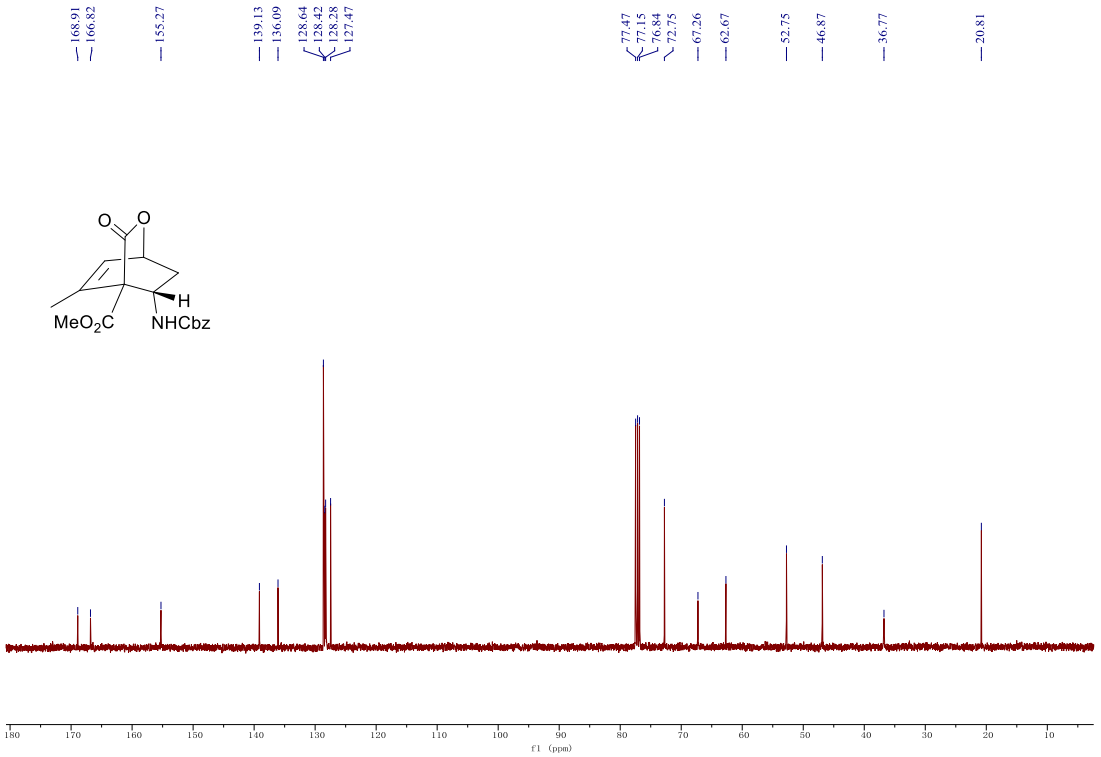


^{13}C NMR of Compound **3n**

Compound **3o**

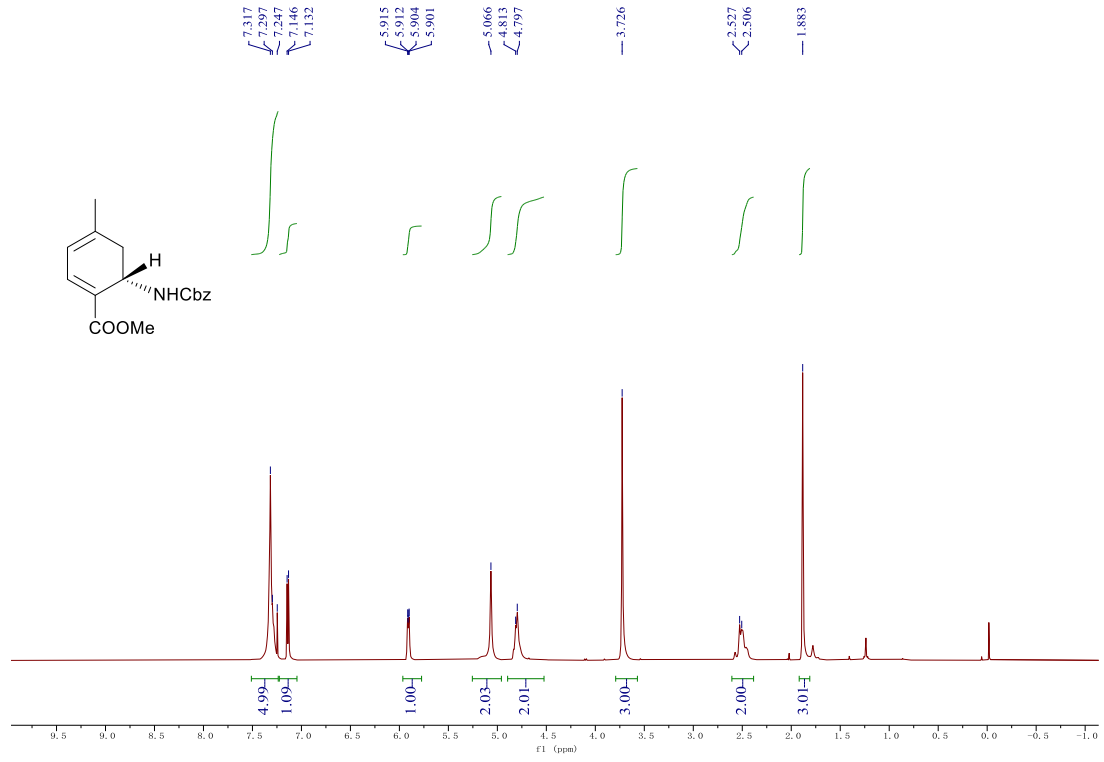


^{1}H NMR of Compound **3o**

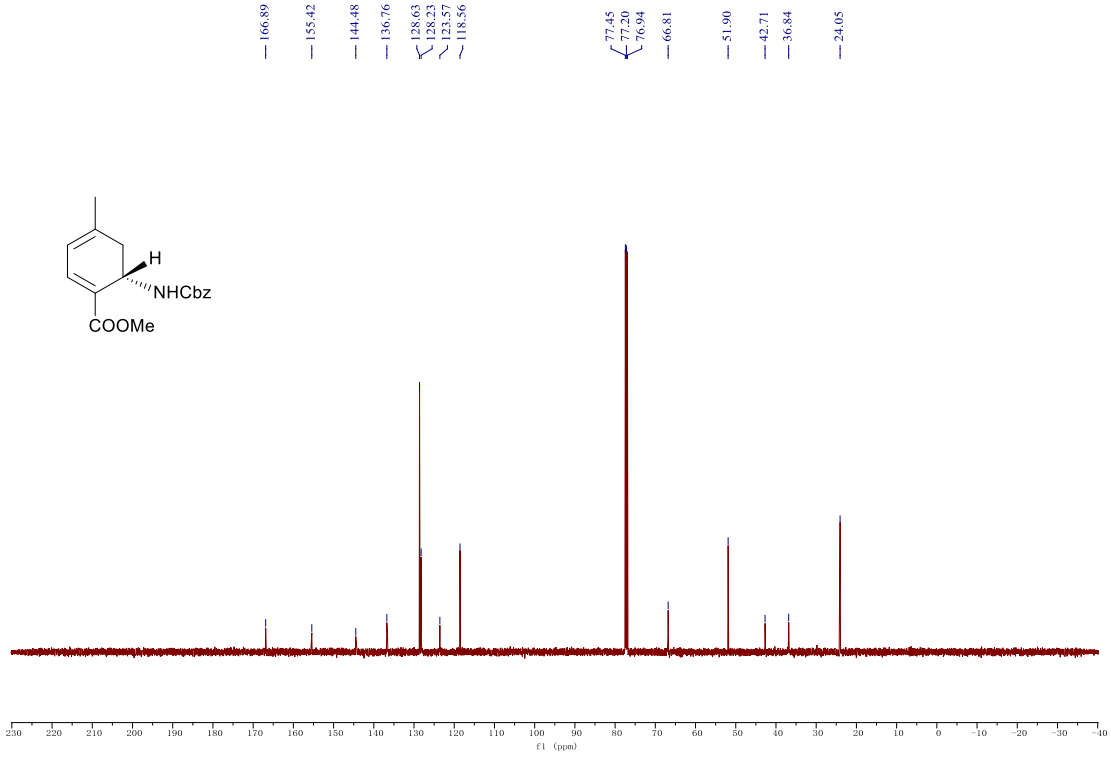


^{13}C NMR of Compound **3o**

Compound **3p**

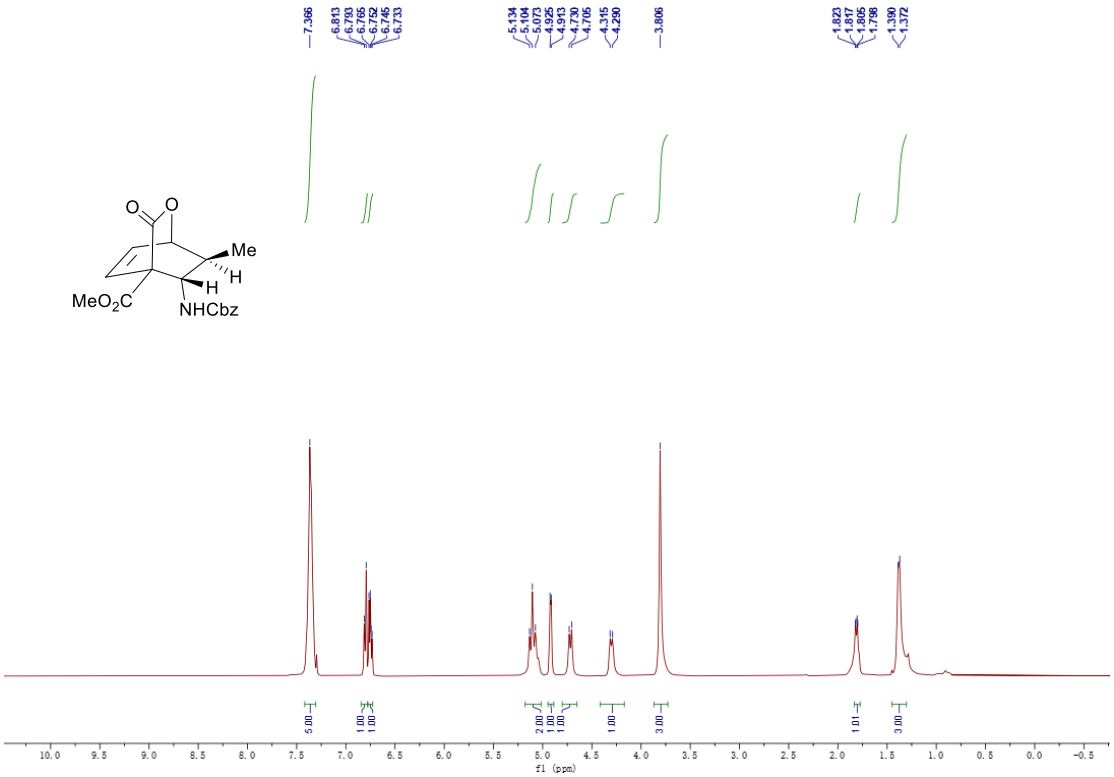


^{1}H NMR of Compound **3p**

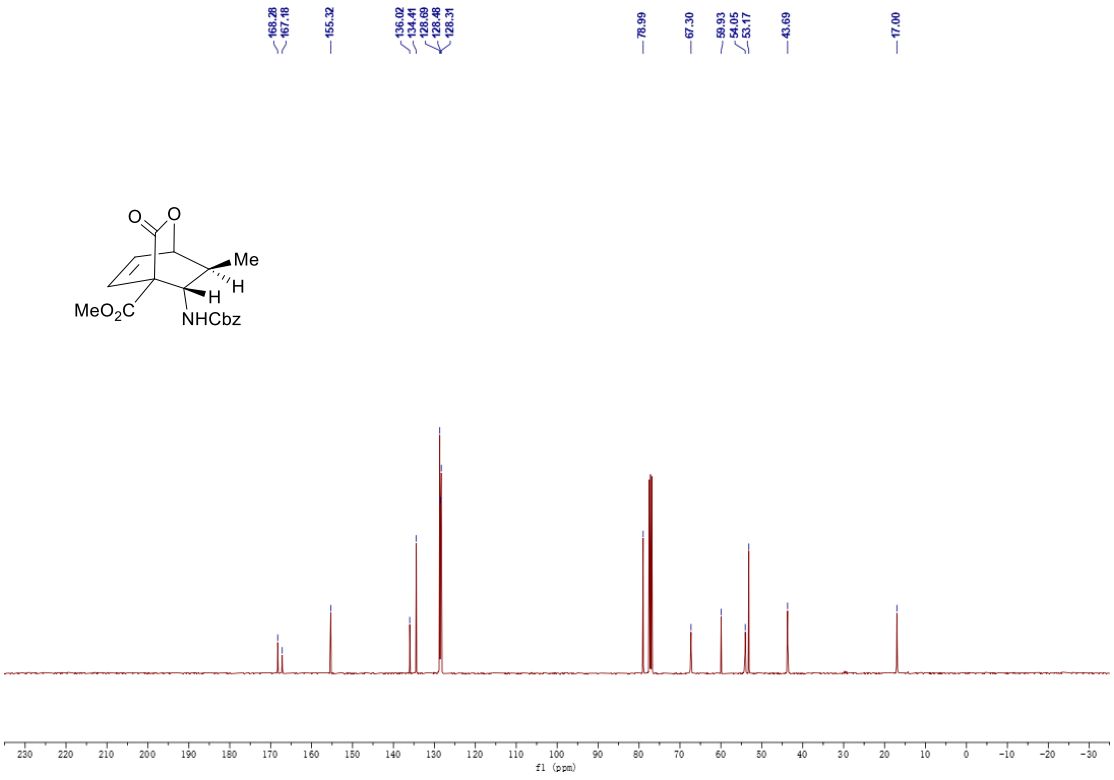


^{13}C NMR of Compound **3p**

Compound **3q**

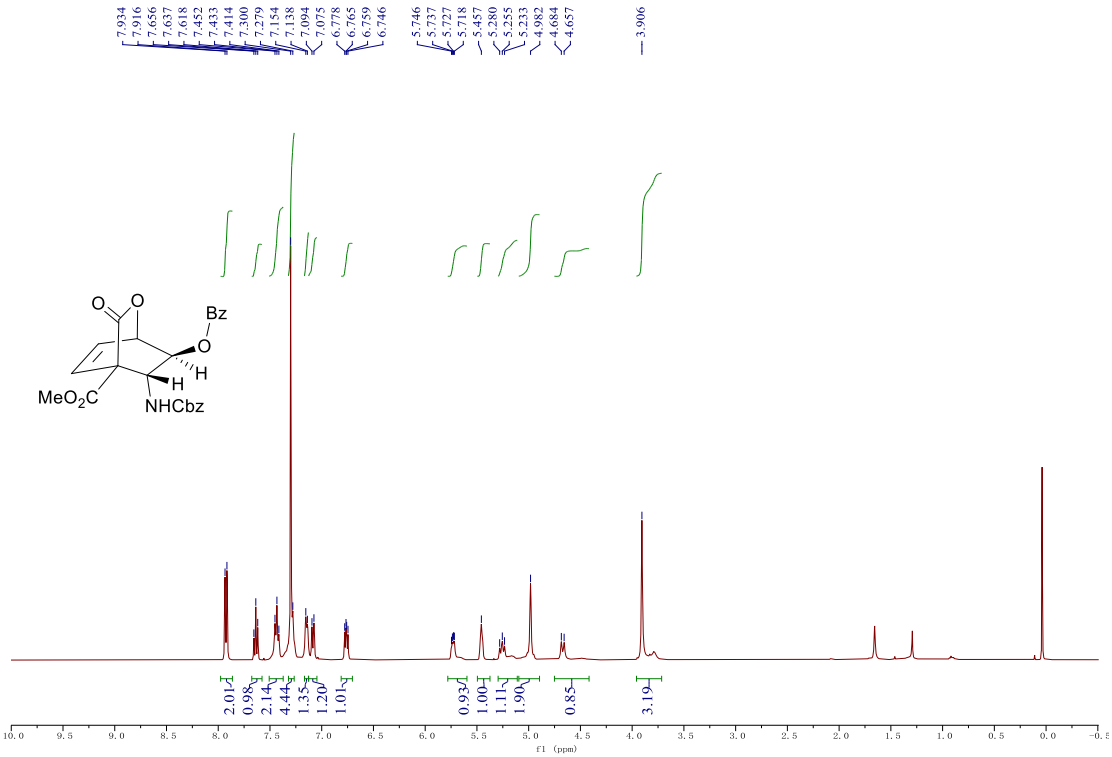


^{1}H NMR of Compound **3q**

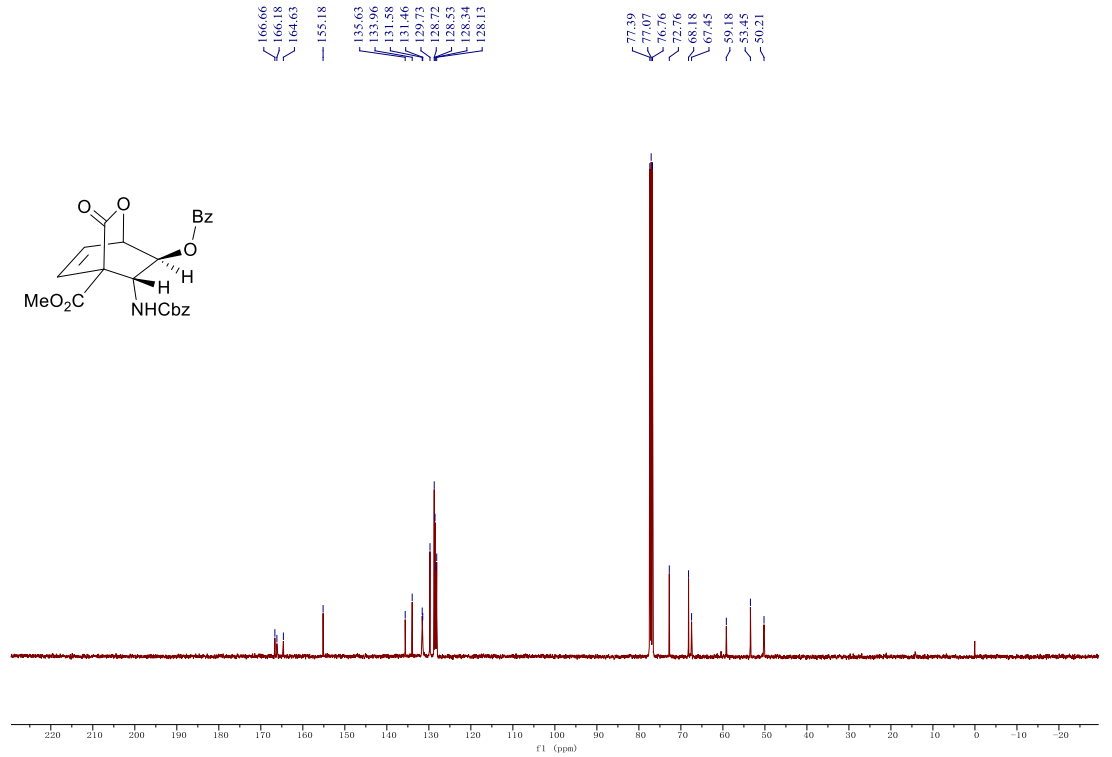


^{13}C NMR of Compound **3q**

Compound **3r**

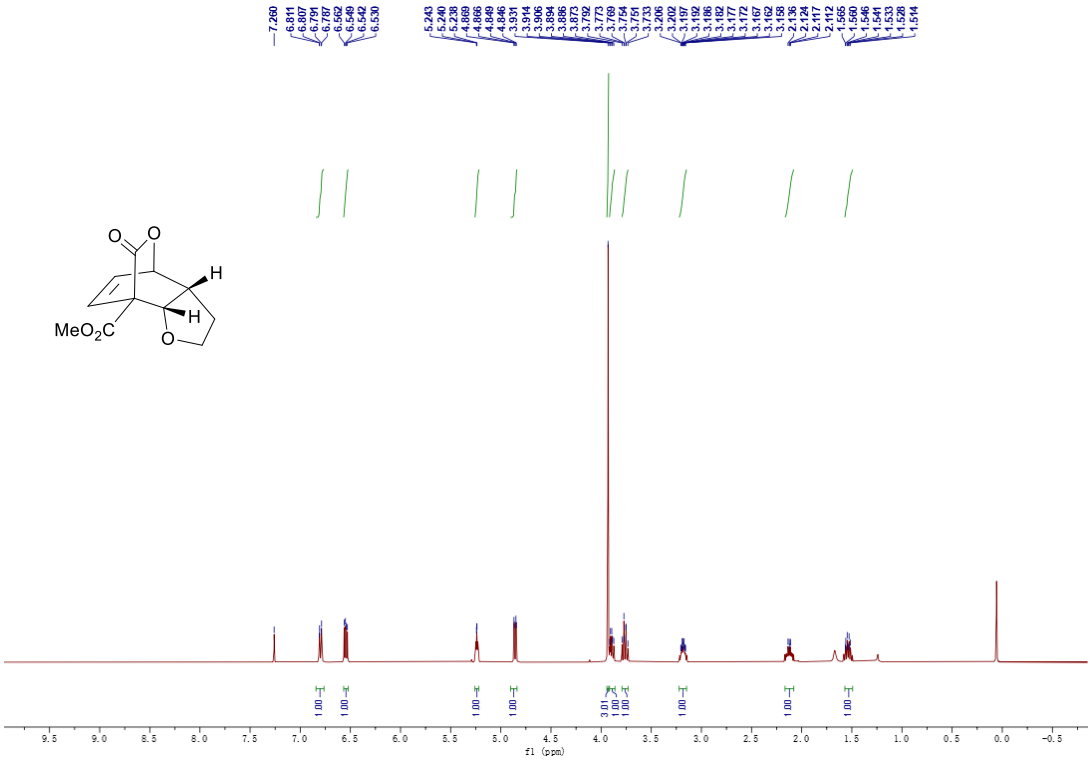


^{1}H NMR of Compound **3r**

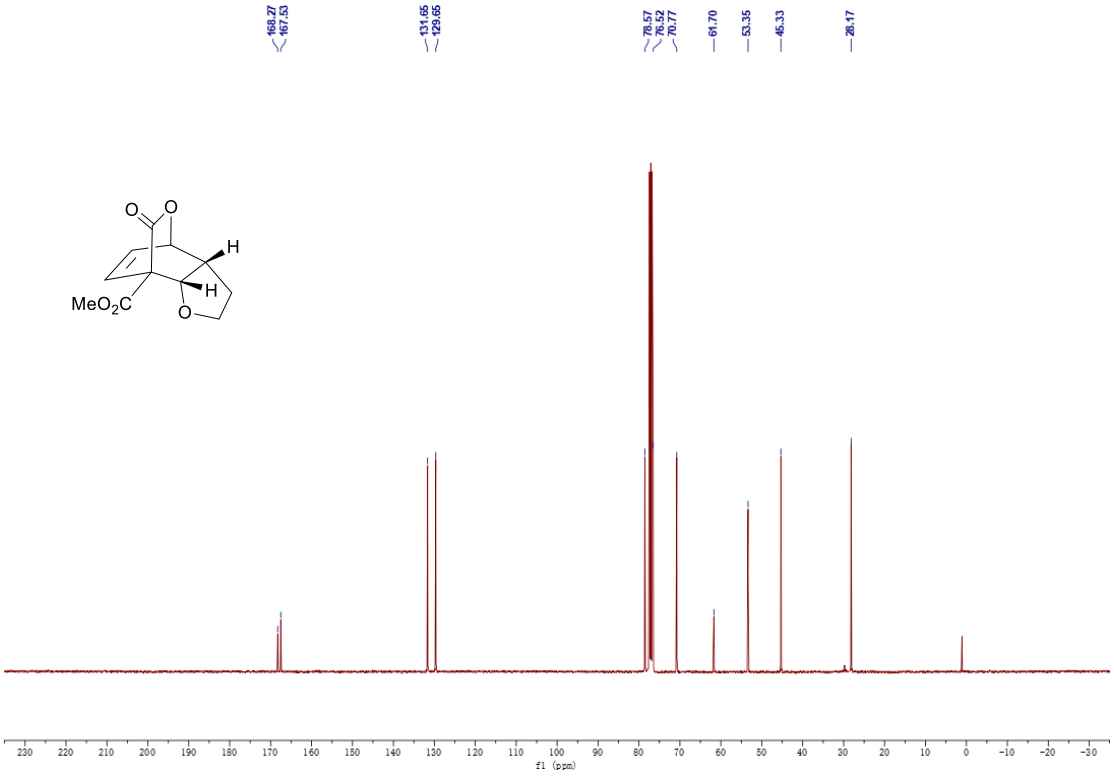


^{13}C NMR of Compound **3r**

Compound **3s**

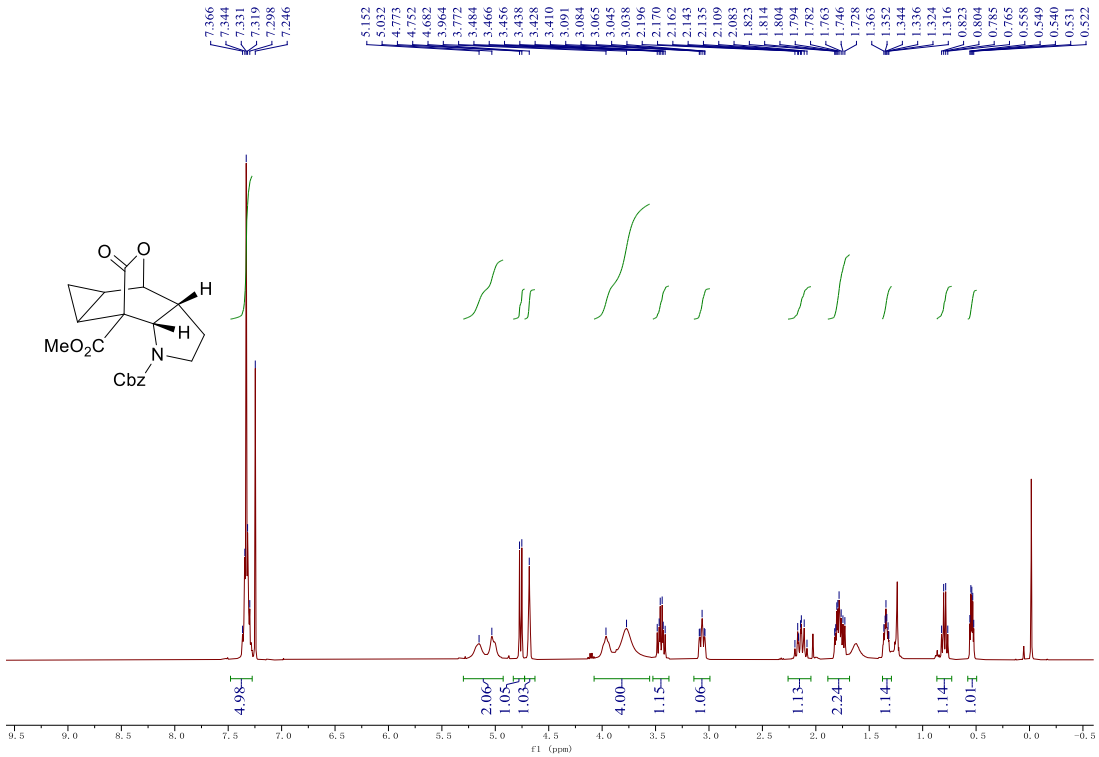


^{1}H NMR of Compound **3s**

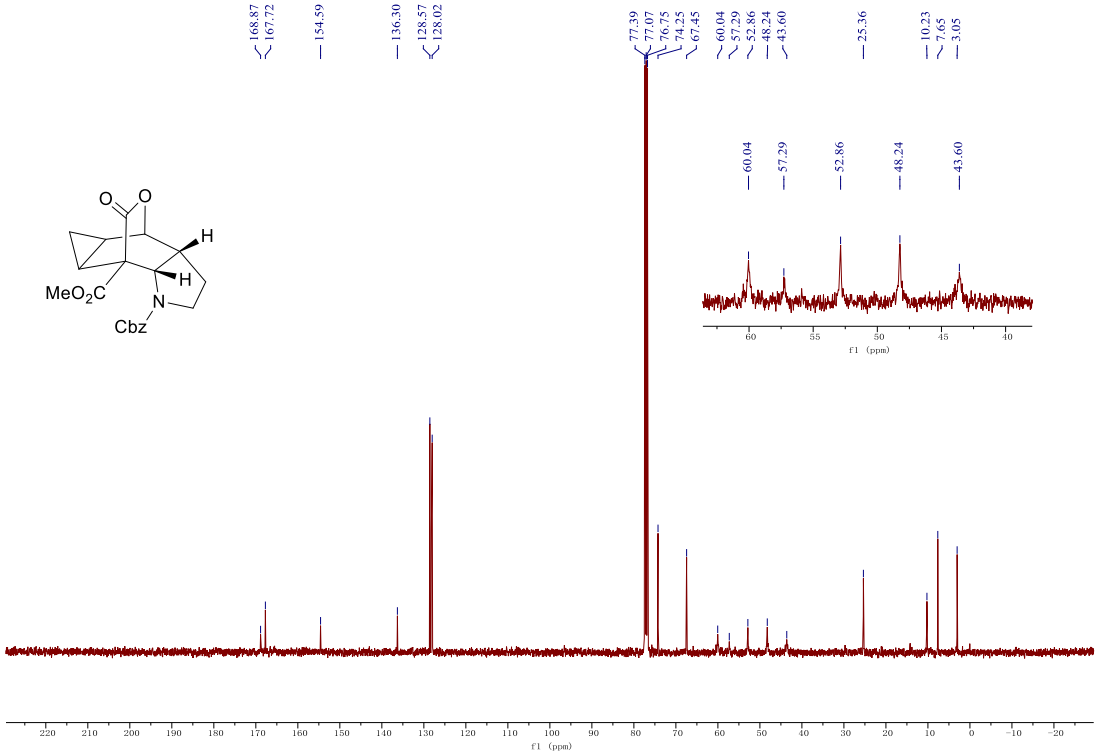


^{13}C NMR of Compound **3s**

Compound **3t**

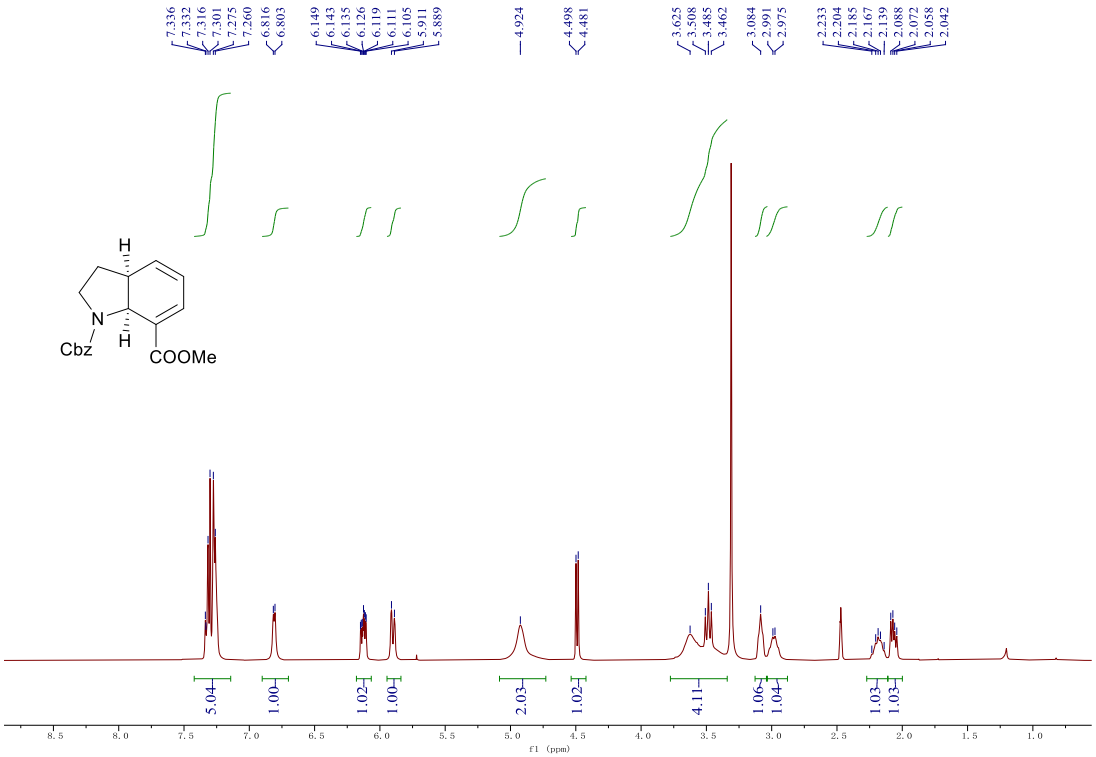


^{1}H NMR of Compound **3t**

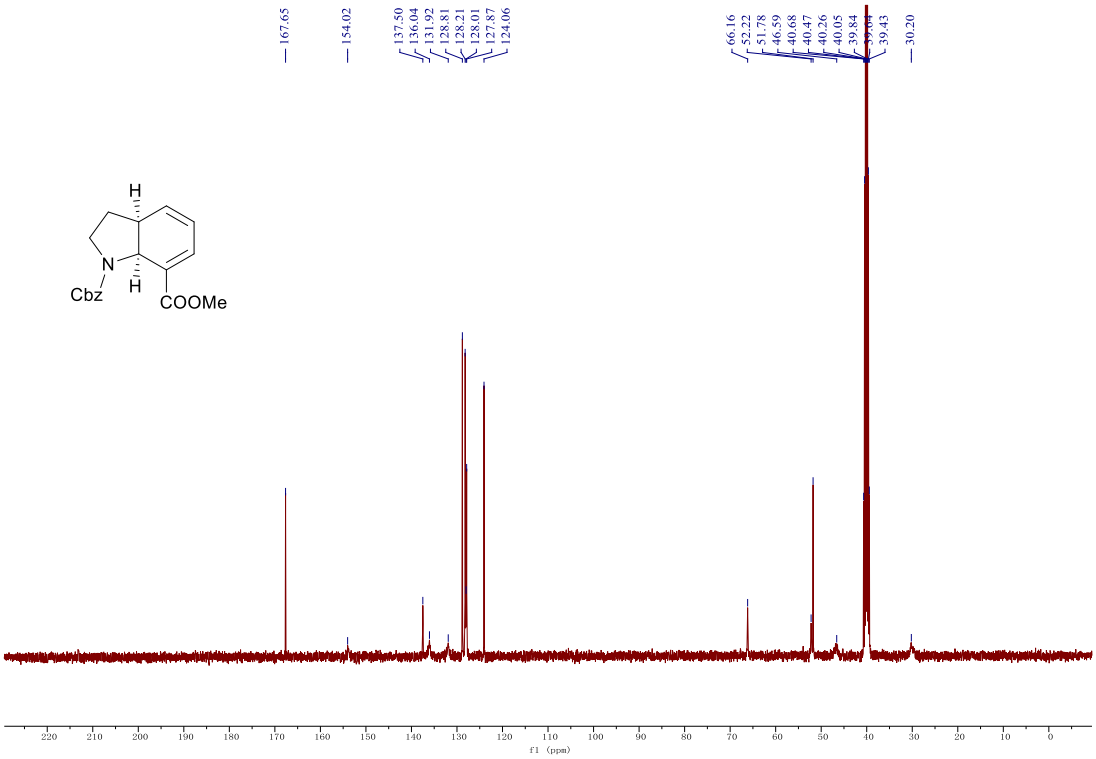


^{13}C NMR of Compound **3t**

Compound **3u**

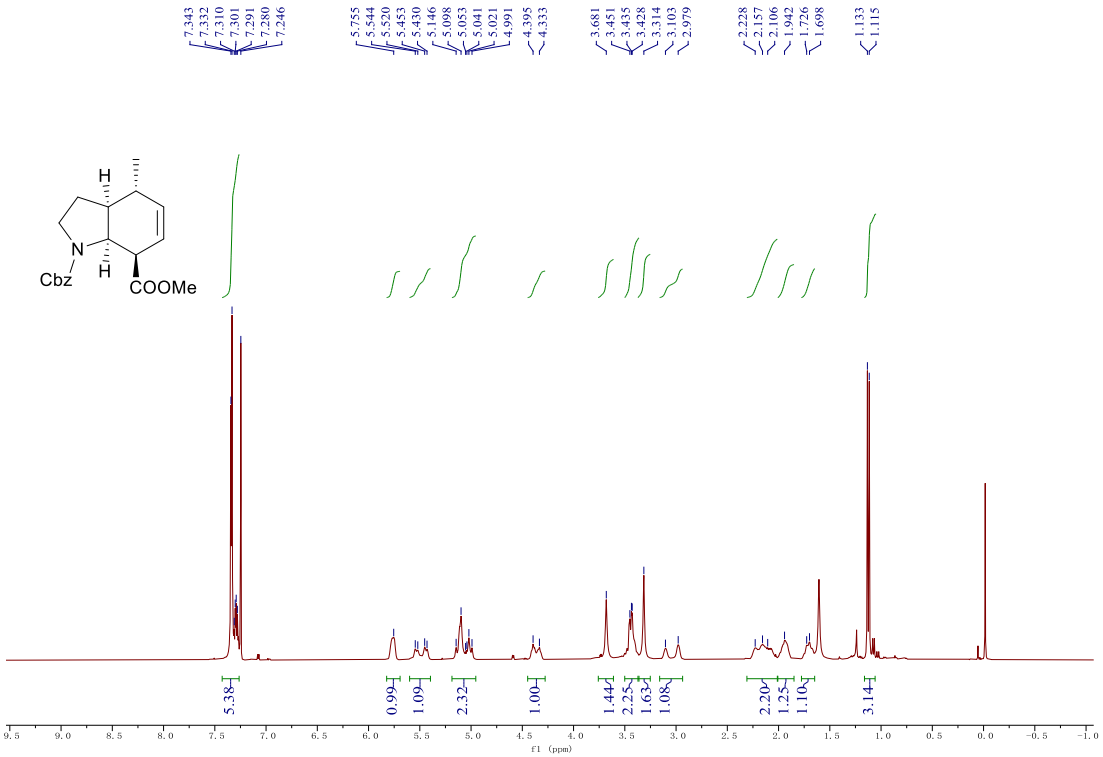


^{1}H NMR of Compound **3u**

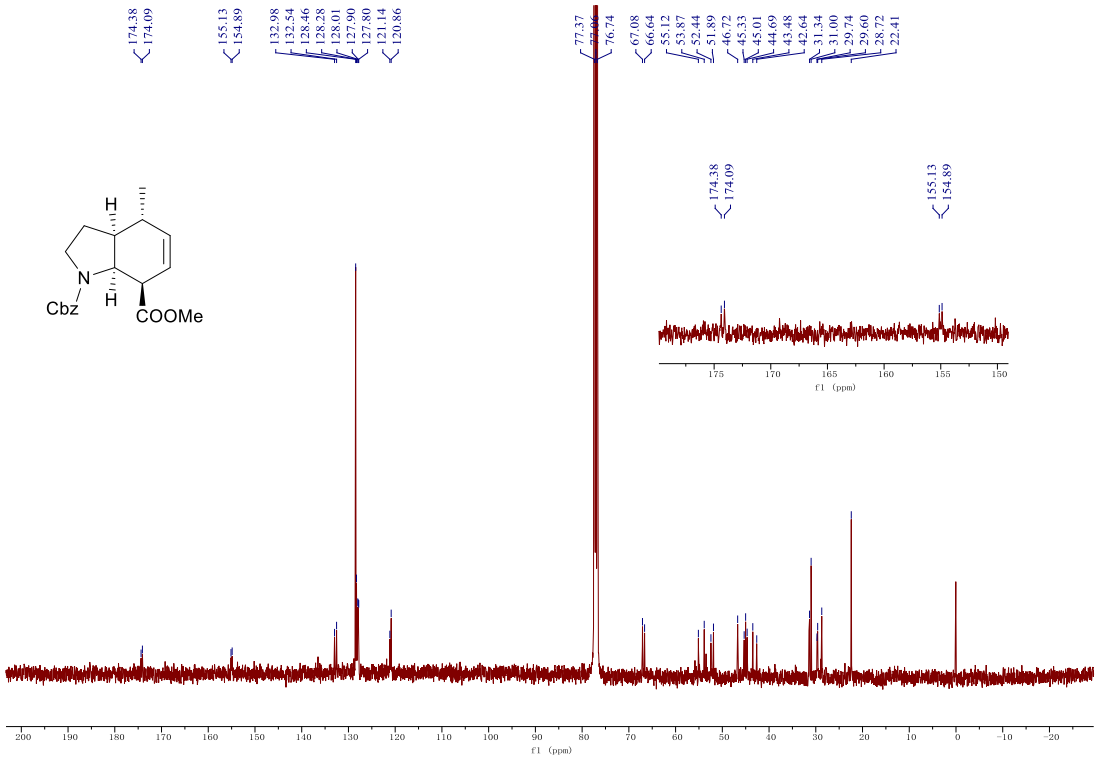


^{13}C NMR of Compound **3u**

Compound **3v**

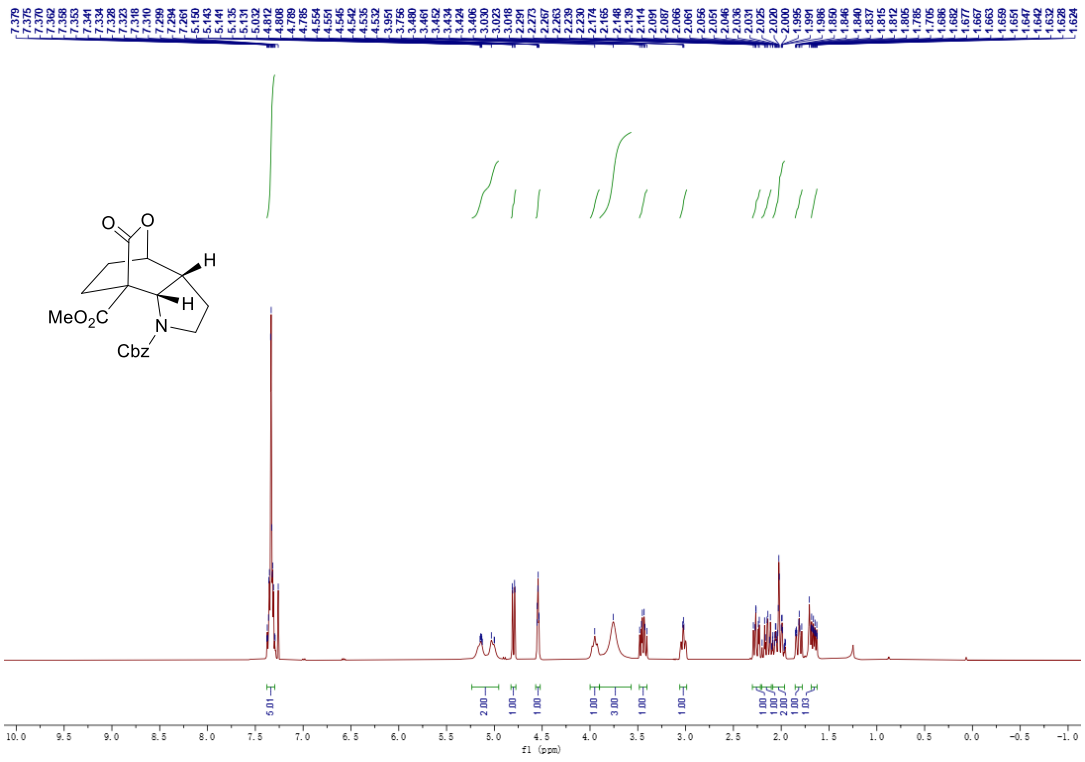


^{1}H NMR of Compound **3v**

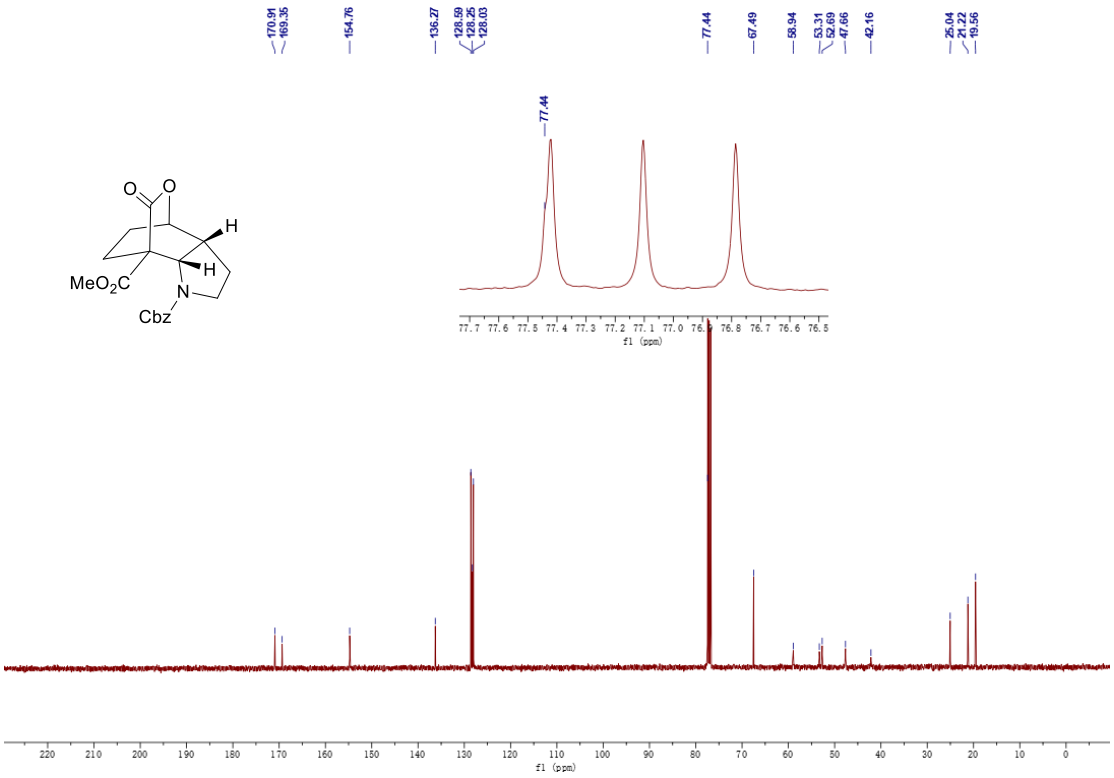


^{13}C NMR of Compound **3v**

Compound **4**

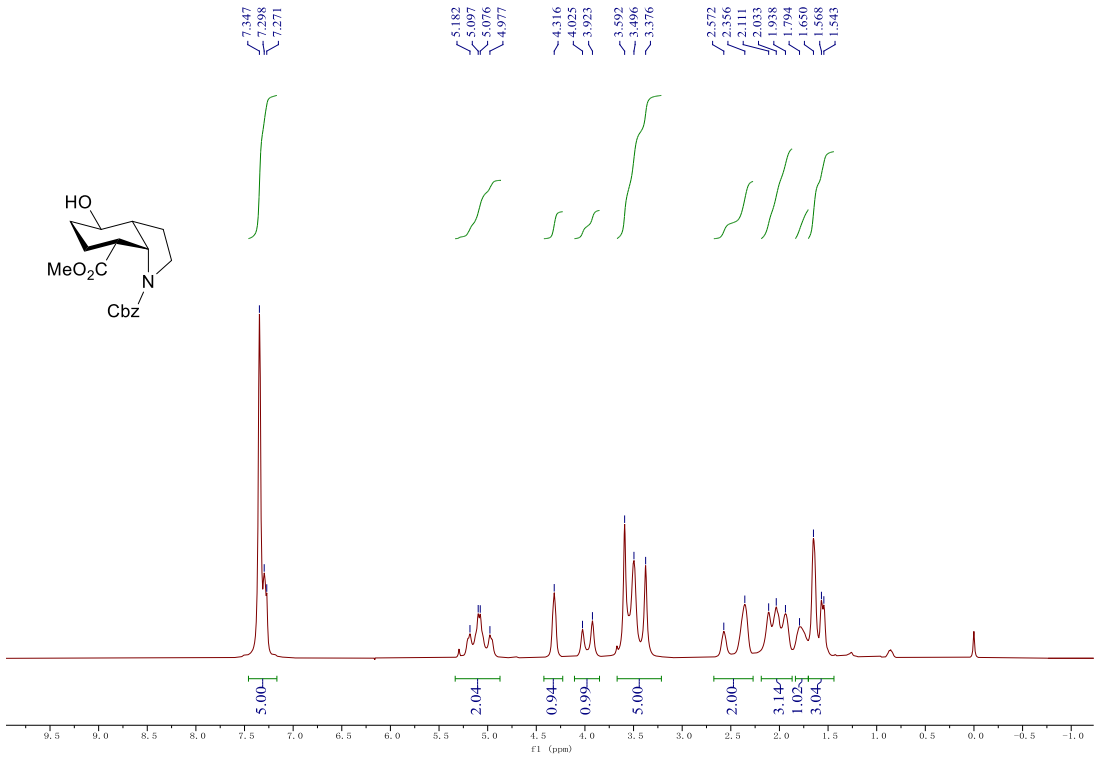


^{1}H NMR of Compound **4**

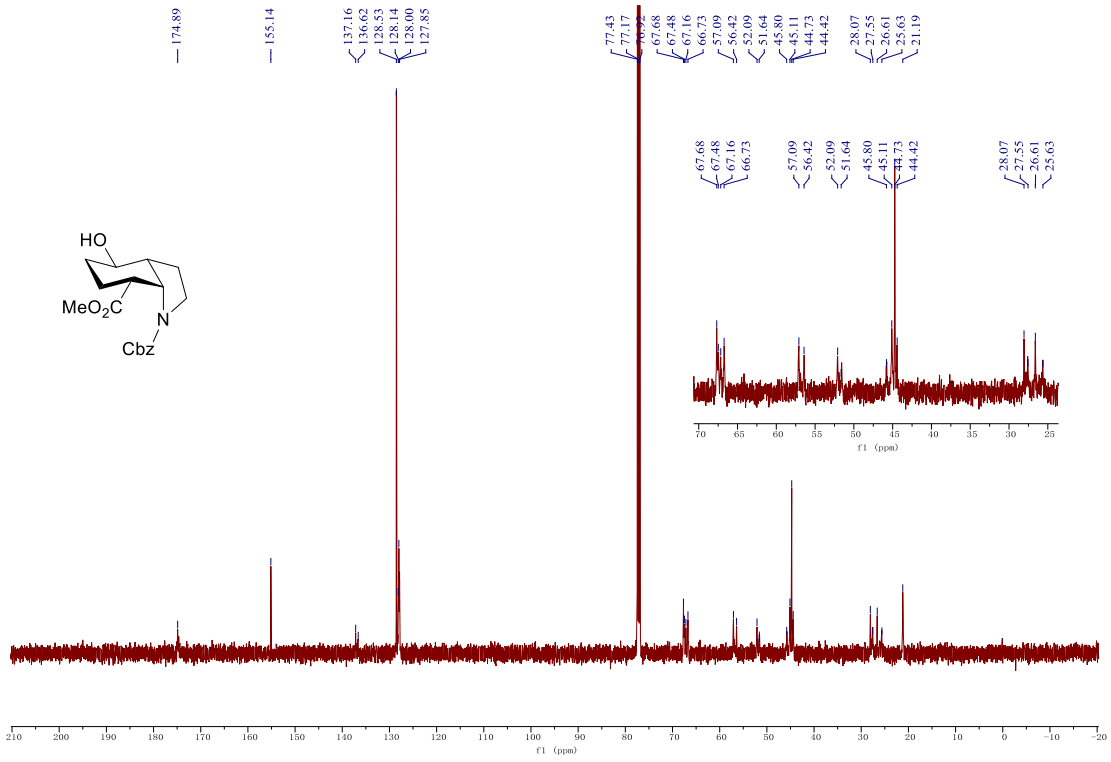


^{13}C NMR of Compound **4**

Compound **5**

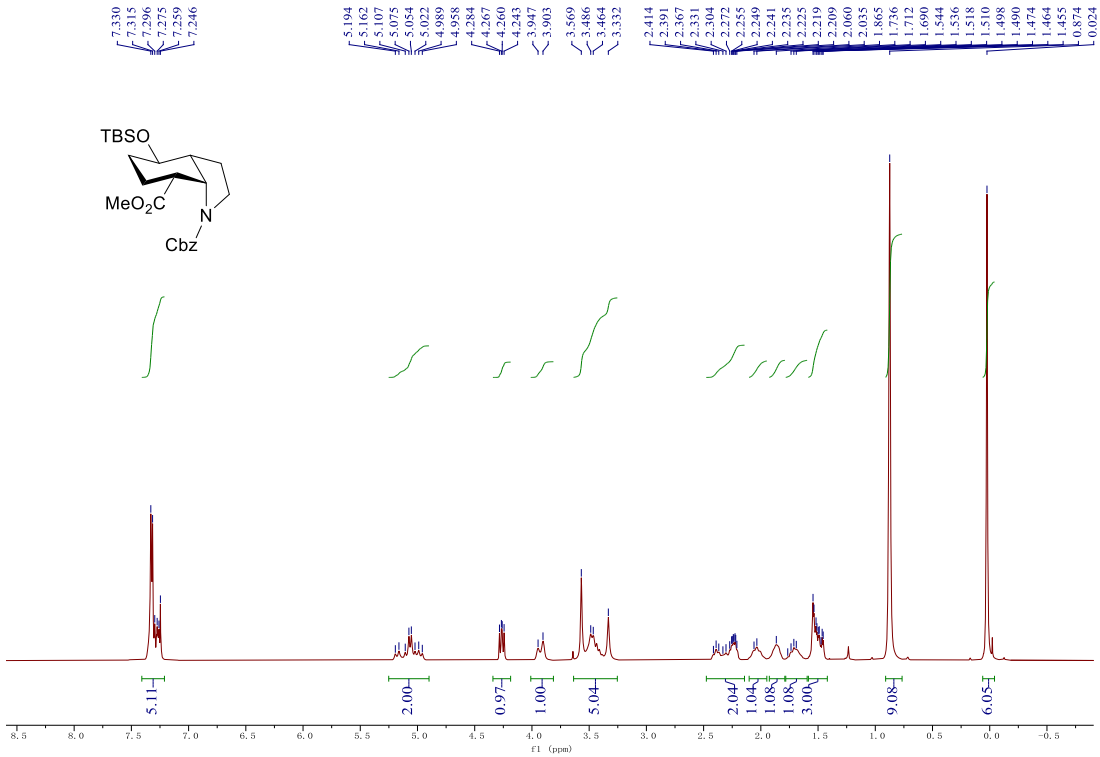


^{1}H NMR of Compound **5**

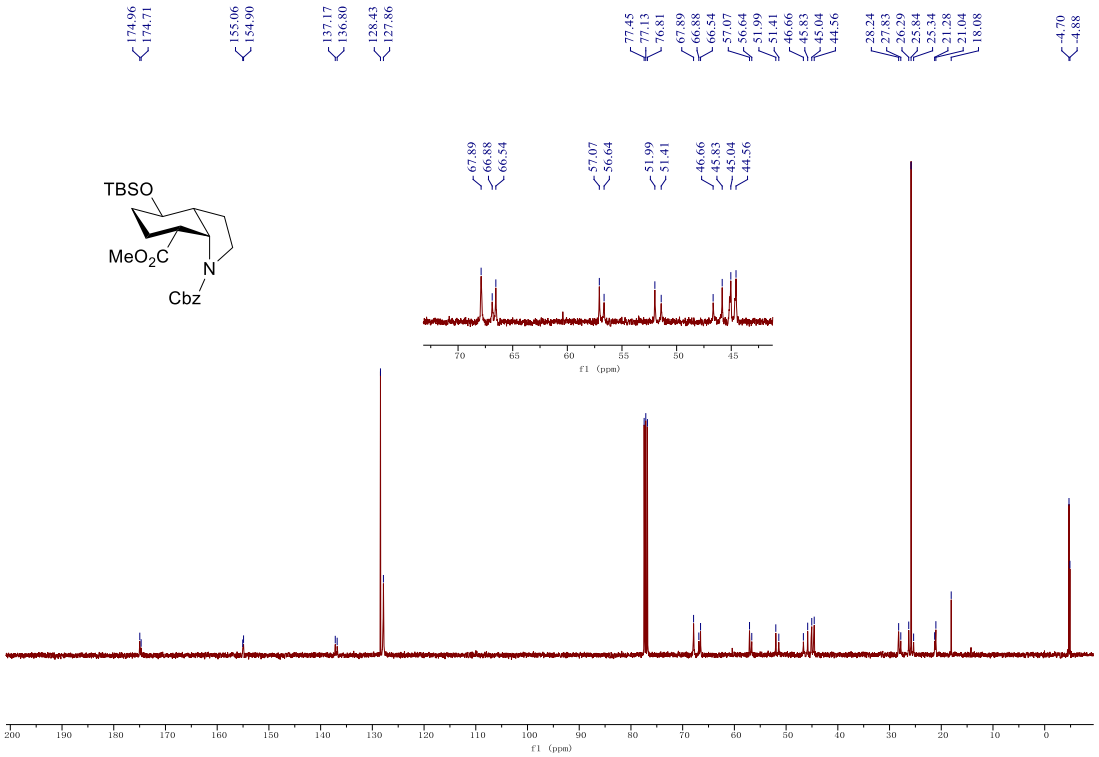


^{13}C NMR of Compound **5**

Compound **6**

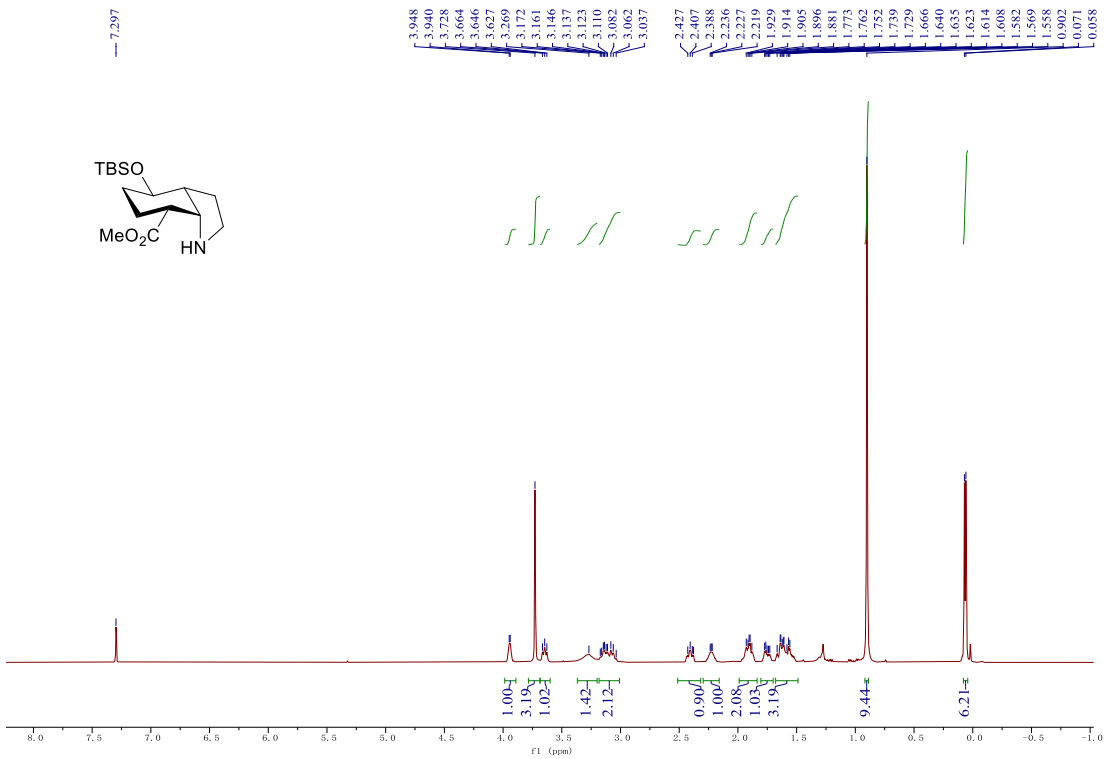


^{1}H NMR of Compound **6**

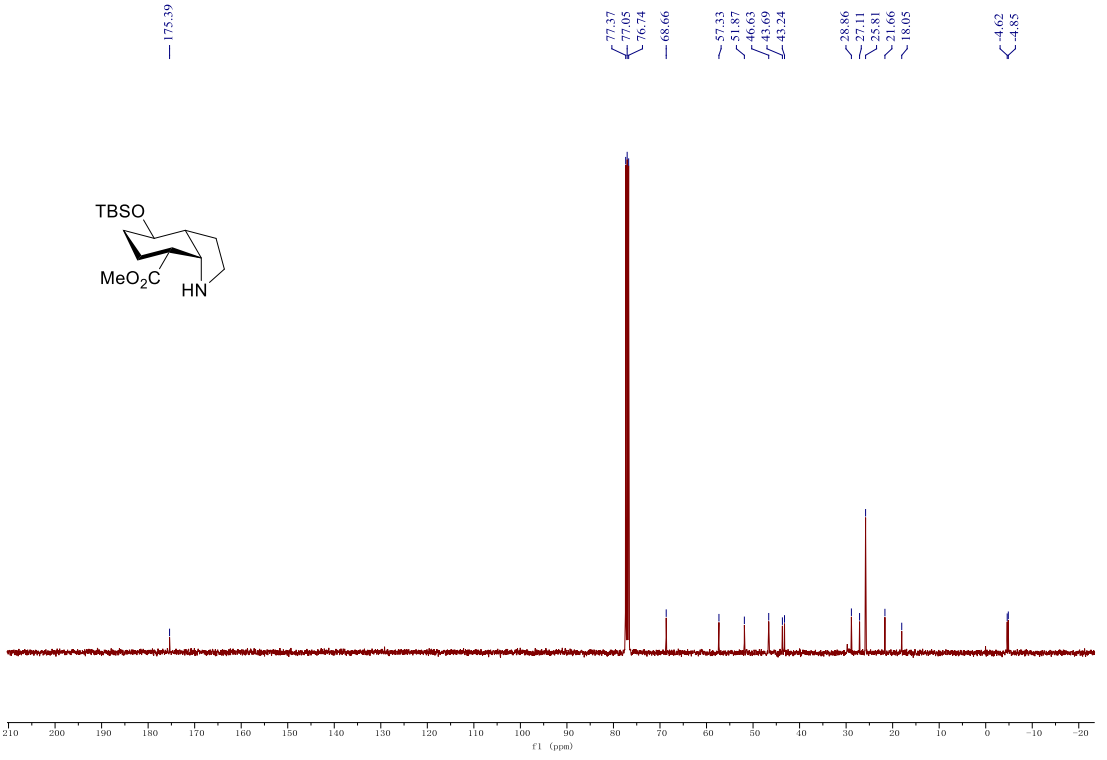


^{13}C NMR of Compound **6**

Compound **7**

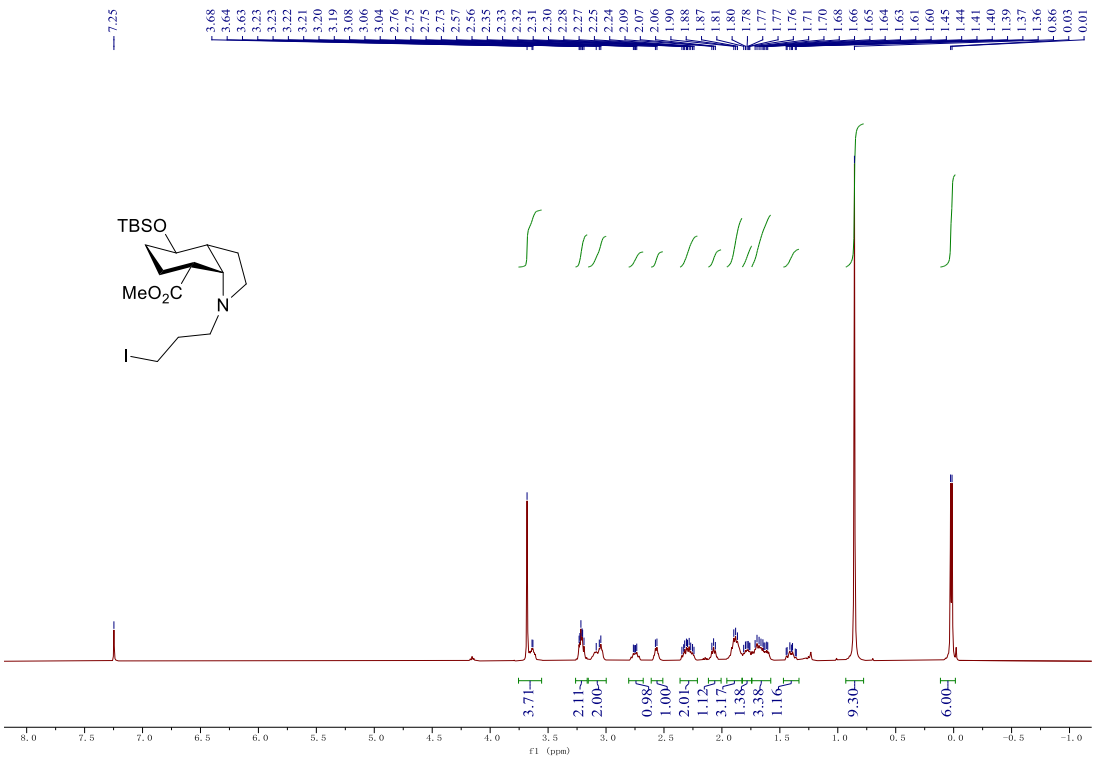


^{1}H NMR of Compound **7**

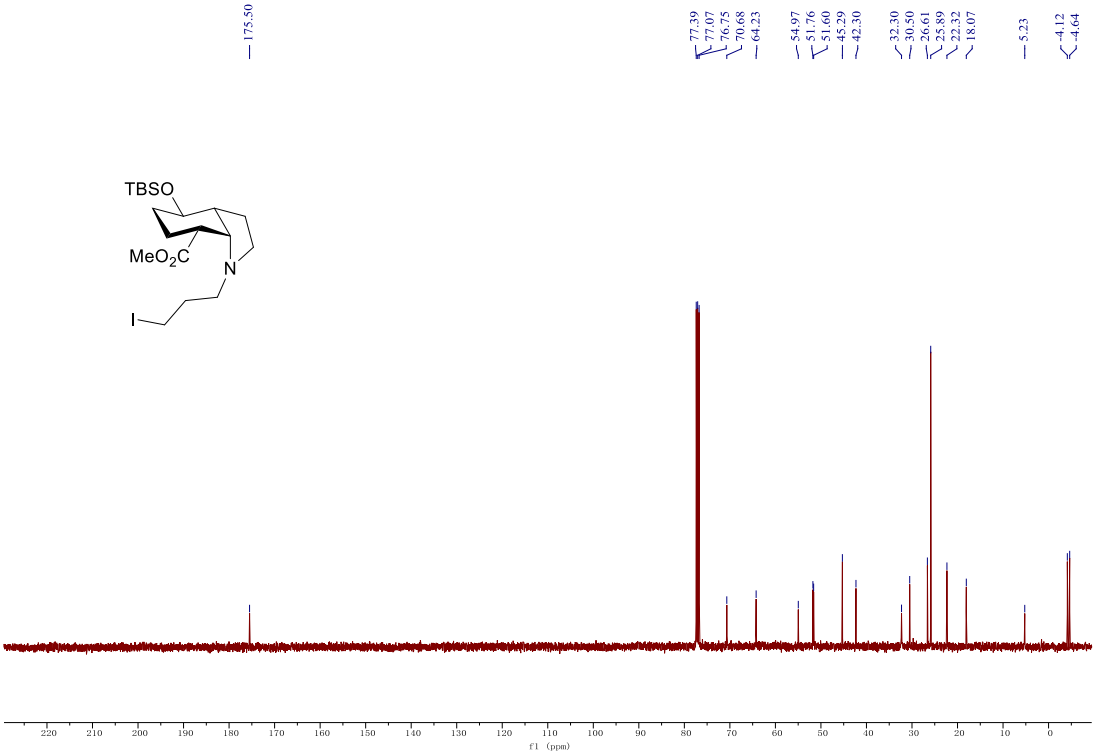


^{13}C NMR of Compound **7**

Compound **8**

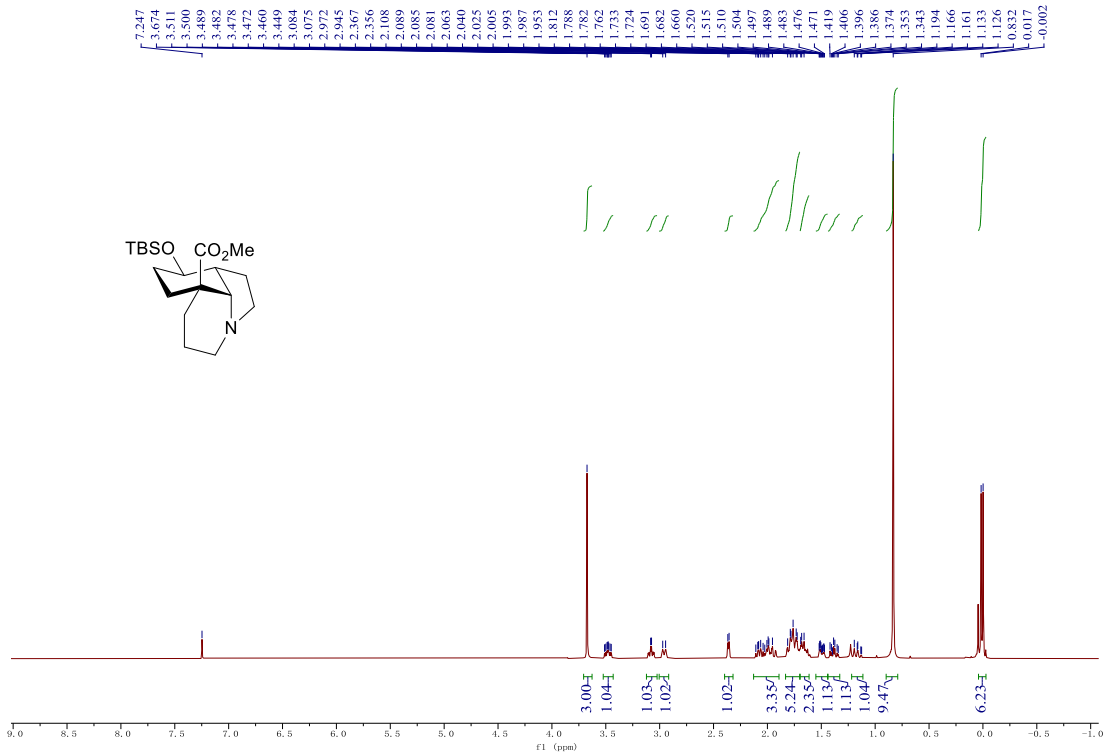


^{1}H NMR of Compound **8**

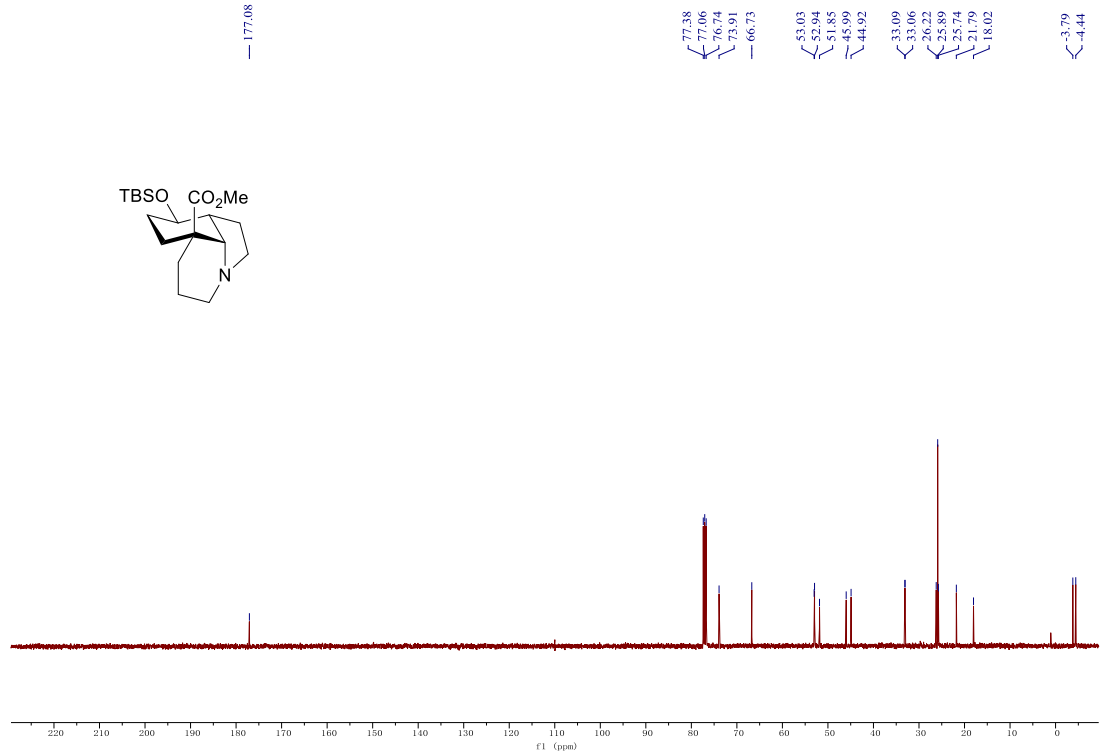


^{13}C NMR of Compound **8**

Compound **9**

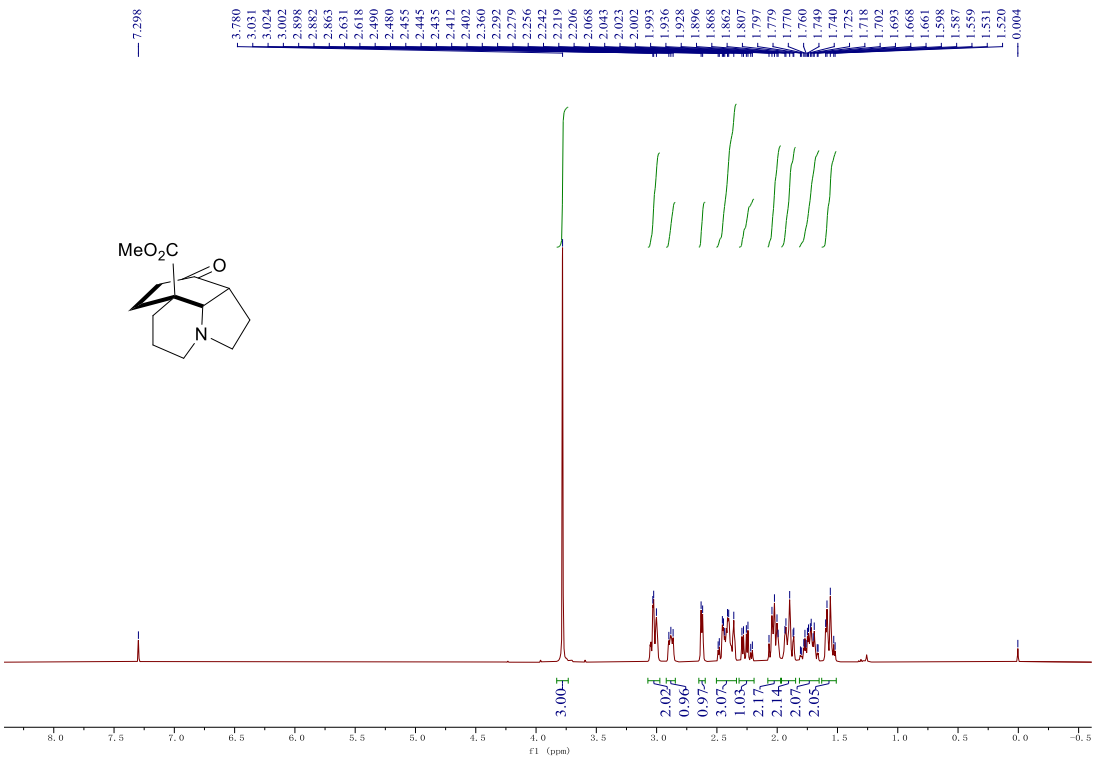


^{1}H NMR of Compound **9**

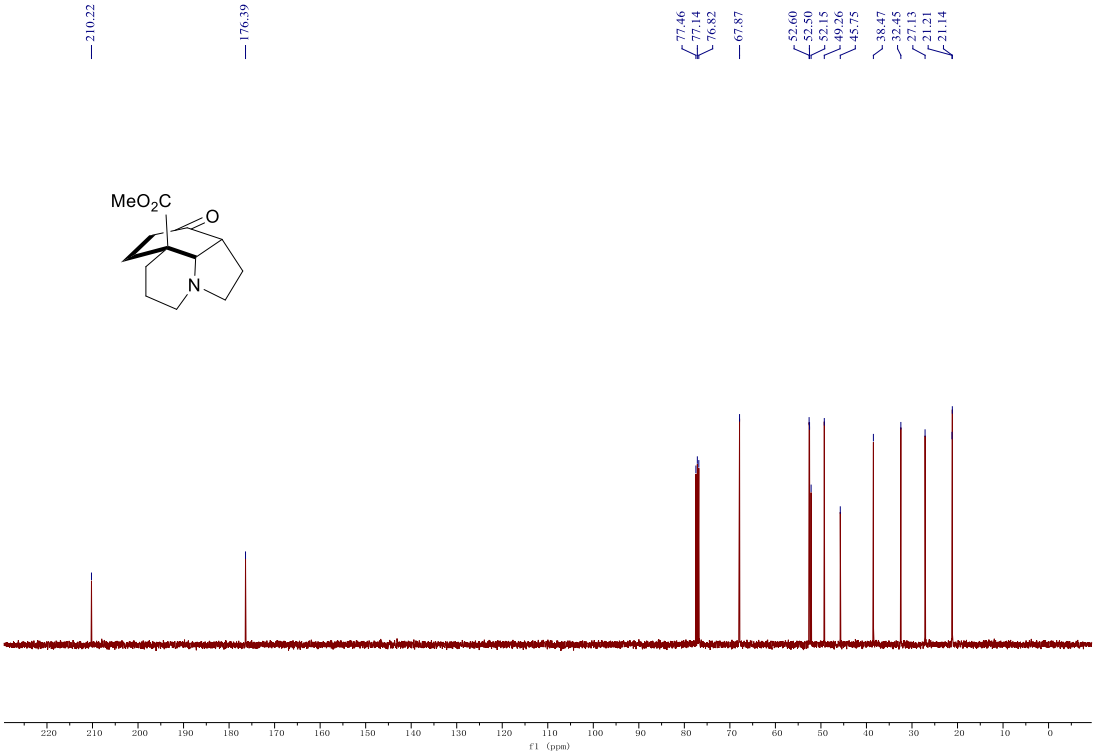


^{13}C NMR of Compound **9**

Compound **10**



^{1}H NMR of Compound **10**



^{13}C NMR of Compound **10**