Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Nickel(II)-Catalyzed Enantioselective All-Carbon-Based Inverse-Electron-Demand Diels–Alder Reaction of 2-Pyrones with Indenes

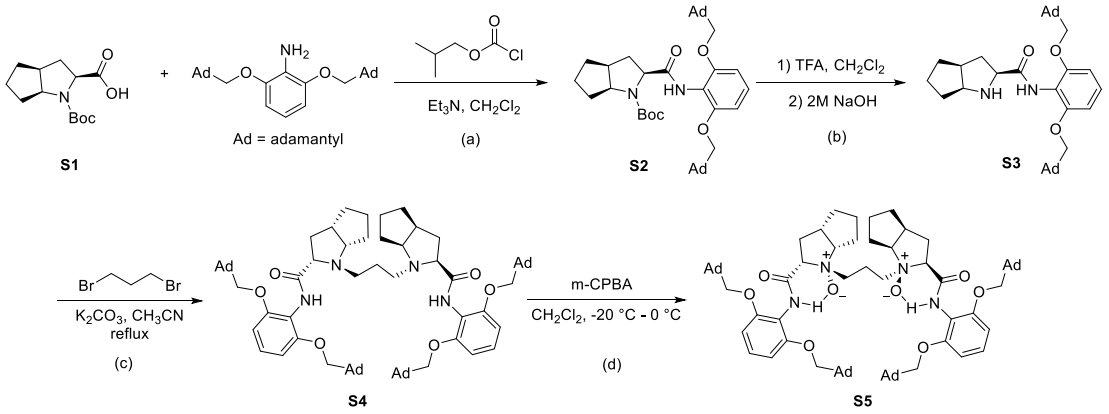
Fangqing Zhang,‡ Bing-Tao Ren,‡ Yangbin Liu* and Xiaoming Feng*

1. General Information

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 Bruker NMR 400 MHz or 500 MHz. Melting points were recorded on a Shanghai Jingke SGWX-4B melting-point Meter and are uncorrected. Chiral HPLC was recorded on a Shimadzu LC-20AD spectrometer using Daicel Chiralcel AD column. HRMS (ESI) analysis was performed by the Analytical Instrumentation Center at Peking University Shenzhen Graduate School and (HRMS) datas were reported with ion mass/charge (m/z) ratios as values in atomic mass units.

2. Preparation of Ligand and Substrates

Ligand synthesis



Ligand **L_3-Ra(OCH_2Ad)$_2$** (**S5**) was prepared according to our reported procedure.[1]

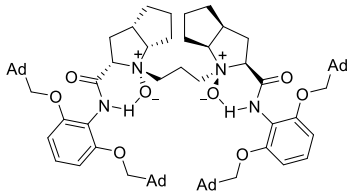
(a) To a stirred solution of (tert-butoxycarbonyl)-L-ramipril-2-carboxylic acid (**S1**, 4.5 mmol) in CH_2Cl_2 (20 mL) was added with Et_3N (4.5 mmol) and isobutyl carbonochloridate (4.5 mmol) at 0 ^oC. After 30 min, the amine (4 mmol) was added, and the reaction was allowed to warm to ambient temperature for 24 hours. The mixture was washed with 1 M $KHSO_4$, saturated $NaHCO_3$, brine, dried over anhydrous Na_2SO_4, concentrated and washed with hexane.

(b) To the residue (**S2**) in CH_2Cl_2 (10 mL) was added with TFA (10 mL) and stirred before the reaction was finished. Then, the solvent was evaporated, and the pH value of the mixture was brought into the range of 8-10 by the addition of 2M NaOH. The aqueous phase was extracted with CH_2Cl_2 (5×20 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 and evaporated in vacuo. The residue purified by silica gel column chromatography to give a white product **S3**.

(c) To a solution of **S3** (1 equiv.) in CH_3CN (12 mL) was added K_2CO_3 (5 equiv.) and 1,3-dibromopropane (0.5 equiv.) under stirring. It was kept at 80 ^oC, and monitored by TLC. Then, K_2CO_3 was removed by filtration. The residue was concentrated and purified by silica gel column chromatography to give a white product **S4**.

(d) To a solution of **S4** (1 equiv.) in CH_2Cl_2 (10 mL) was added *m*-CPBA (2.5 equiv.) at −20 °C under stirring. Two hours later, the mixture was concentrated and purified by silica gel column chromatography to give a white powder **S5** (0.59 g, 25% yield for 4 steps).

L_3-Ra(OCH_2Ad)$_2$ (S5)



S5 was obtained as a white solid (0.59 g, 25% yield).

TLC: R_f = 0.3 (ethyl acetate/Petroleum ether 2:1).

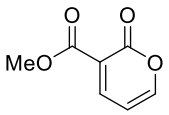
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.60 (s, 2H), 7.08 (t, *J* = 8.4 Hz, 2H), 6.50 (d, *J* = 8.4 Hz, 4H), 4.04–3.92 (m, 2H), 3.91–3.73 (m, 4H), 3.50–3.39 (m, 10H), 2.76 (dt, *J* = 14.4, 6.5 Hz, 4H), 2.65–2.44 (m, 6H), 2.02 (d, *J* = 14.8 Hz, 4H), 1.95 (t, *J* = 3.3 Hz, 12H), 1.69 (d, *J* = 12.5 Hz, 16H), 1.62–1.53 (m, 40H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 155.2, 127.0, 114.0, 104.3, 83.2, 80.9, 78.5, 66.6, 42.4, 39.4, 37.2, 35.1, 33.8, 32.3, 28.2, 28.0, 27.2, 20.1.

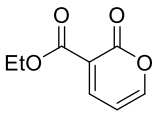
m.p. 160–161 °C.

[α]$^{25}_D$ = +34.8 (*c* = 1.00, CH_2Cl_2).

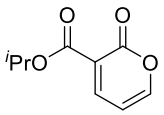
Table S1. Structures of 2-pyrones



1a



1b



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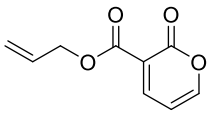
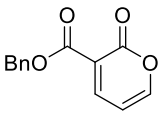
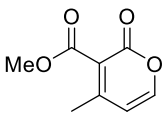


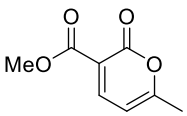
1d



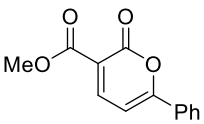
1e



1f



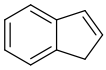
1g



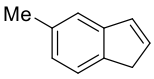
1h

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

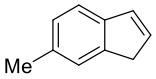
Table S2. Structures of indenes



2a



2b



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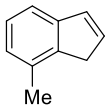
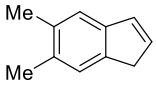
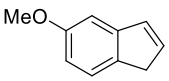


2d



2e



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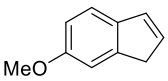
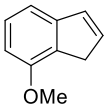
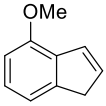


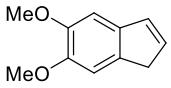
2g



2h



2i



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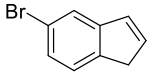
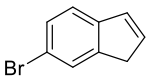
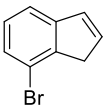


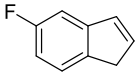
2k



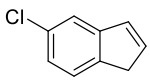
2l



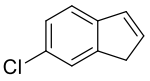
2m



2n



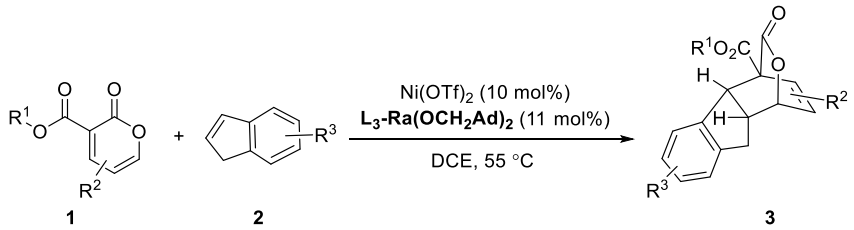
2o



2p

Indenes **2a**, **2o** and **2p** were purchased from Bidepharm and used without further purification. Indenes **2b**-**2n** were prepared according to the literature.[3]

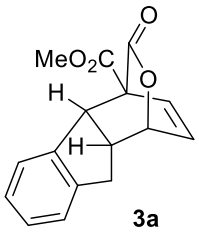
3. General Procedure for the Catalytic Asymmetric Reaction



1 2 3

After stirring a mixture of $Ni(OTf)_2$ (0.01 mmol, 10 mol%) and **L_3-Ra(OCH_2Ad)$_2$** (0.011 mmol, 11 mol %) in dry DCE (1.0 mL) at 35 °C for 1.0 h under argon atmosphere, 2-pyrones **1** (0.1 mmol) and indenes **2** (0.2 mmol) were added, and the reaction mixture was stirring at 55 °C. After the disappearance of 2-pyrones (monitored by TLC), the crude product was purified by silica gel flash chromatography (petroleum ether/ethyl acetate 6:1) to afford the desired product **3**.

Methyl (4*S*,4a*S*,9a*R*)-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano) fluorene-4-carboxylate (3a)



3a

Following the general procedure, reaction time 40 h. Product **3a** was obtained as a white solid (23.1 mg, 85% yield, 87% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 7.4 Hz, 1H), 7.07 – 6.98 (m, 2H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.47 – 6.40 (m, 1H), 6.31 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.21 (td, *J* = 4.7, 1.9 Hz, 1H), 4.28 (d, *J* = 8.9 Hz, 1H), 3.95 (s, 3H), 3.35 (ddt, *J* = 10.4, 8.7, 4.2 Hz, 1H), 3.09 (dd, *J* = 17.2, 10.5 Hz, 1H), 2.47 (dd, *J* = 17.2, 3.9 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 168.5, 143.3, 140.0, 132.7, 129.1, 128.4, 127.3, 125.0, 124.2, 77.1, 59.9, 53.2, 48.3, 41.9, 34.0.

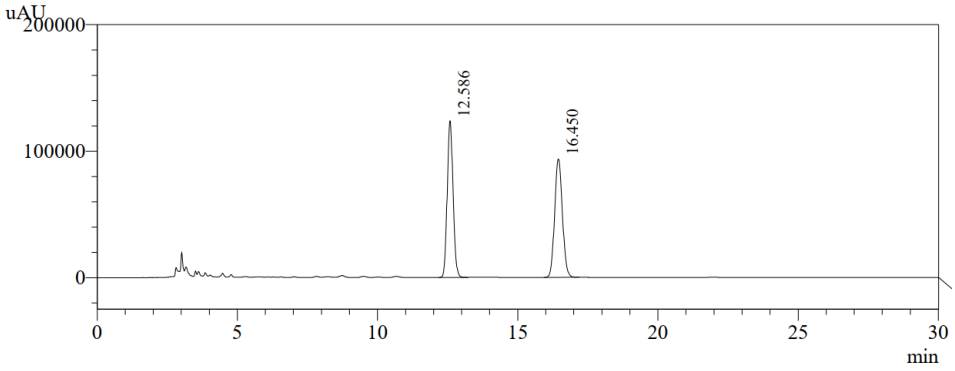
HPLC: 87% *ee*, chiral stationary column: AD, mobile phase: hexane/*i*-PrOH = 90/10, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 12.7 min, t_R (minor) = 16.6 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{14}NaO_4$: 293.0784; found: 293.0785.

m.p. 132–133 °C.

[α]$^{25}_D$ = +14.5 (*c* = 1.00, $CHCl_3$).

***rac*-3a:**



PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.586	1799891	123674	49.992	56.930
2	16.450	1800493	93564	50.008	43.070
Total		3600384	217238	100.000	100.000

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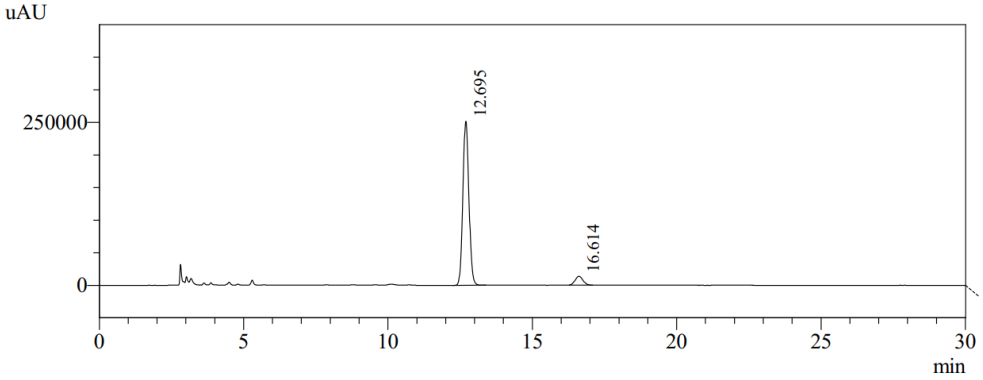

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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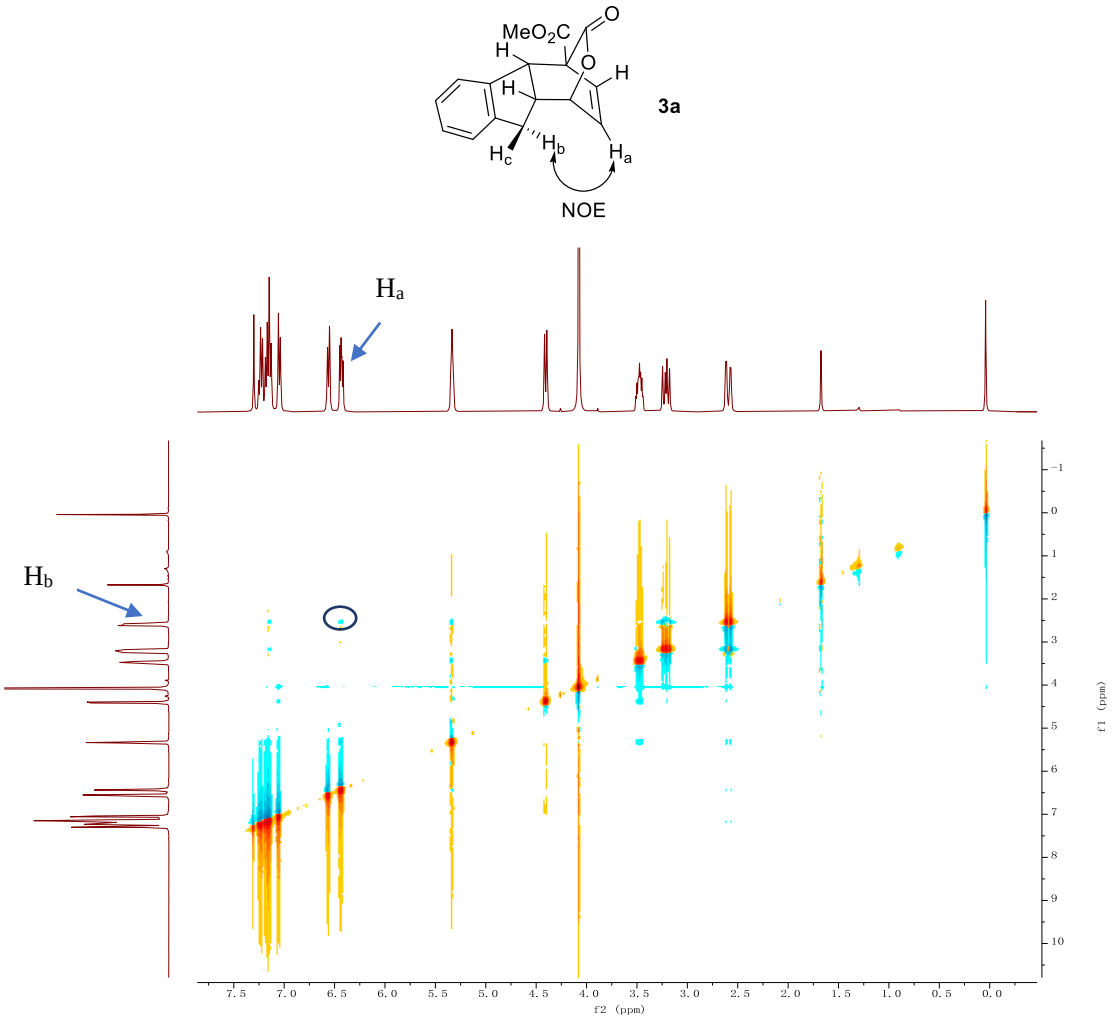
2	16.614	252303	13406	6.411	5.057
Total		3935601	265078	100.000	100.000

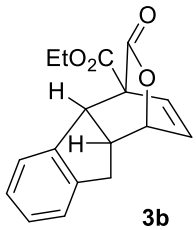
Determination of the relative and absolute confirguration of product 3a:

The Diels–Alder reaction is mechanistically considered a concerted pericyclic reaction. Generally, the predominant product is the kinetically favourable *endo*-cycloadduct. For the racemic version of this IEDDA reaction catalysed by $Cu(OTf)_2$ or $Ni(OTf)_2$, only one diastereomeric isomer of product (dr = 20:1) was detected, which was consistent with the previous work reported by Cai group (*Angew. Chem. Int. Ed.*, 2021, 60, 26610–26615). They also found that $Cu(OTf)_2$ could promote IEDDA reaction of 2-pyrone and indene smoothly to generate the desired adduct with excellent yield and diastereomeric ratio. The relative configuration of one representative D-A product was determined to be *endo* by X-ray crystallography analysis in Cai's work. Thus, we presumed that the relative configuration of product **3** in our work was also *endo*, which was also confirmed by NOESY NMR of product **3a**.

The absolute configuration of product **3a** was found to be opposite to that reported by the Cai group through the comparison of optical rotation. Cai's method was used to prepare **3a** in 94% ee, and the optical rotation of this sample was measured as $[\alpha]^{25}_D = -14.02$ (*c* = 1.00, $CHCl_3$). In our work, a sample of **3a** was prepared in 87% ee and the optical rotation was measured as $[\alpha]^{25}_D = +14.5$ (c = 1.00, $CHCl_3$).


MeO2C
O
H
O
H
H
Hc
Hb
Ha
NOE
3a
Ha
Hb
f2 (ppm)
f1 (ppm)

Ethyl (4*S*,4a*S*,9a*R*)-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3b)



3b

Following the general procedure, reaction time 40 h. Product **3b** was obtained as a white solid (23 mg, 80% yield, 90% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, *J* = 7.3 Hz, 1H), 7.14 (dq, *J* = 13.9, 7.5 Hz, 3H), 6.56 (d, *J* = 7.7 Hz, 1H), 6.42 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.32 (dt, *J* = 4.7, 2.4 Hz, 1H), 4.61 – 4.48 (m, 2H), 4.42 (d, *J* = 8.8 Hz, 1H), 3.47 (ddt, *J* = 13.2, 8.7, 4.2 Hz, 1H), 3.21 (dd, *J* = 17.2, 10.5 Hz, 1H), 2.59 (dd, *J* = 17.2, 3.7 Hz, 1H), 1.48 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 168.0, 143.2, 140.1, 132.8, 128.9, 128.3, 127.2, 124.9, 124.2, 77.0, 62.3, 59.8, 48.1, 41.8, 33.9, 14.2.

HPLC: 90% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 16.0 min, t_R (minor) = 31.3 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{16}NaO_4$: 307.0941; found: 307.0940.

m.p. 142–143 °C.

[α]$^{25}_D$ = +27.0 (*c* = 0.25, CH_2Cl_2).

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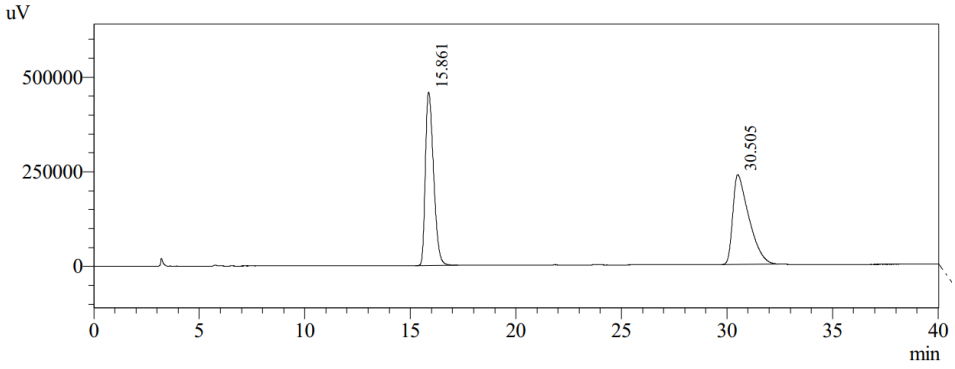

Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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2	30.505	12640625	237547	50.566	34.150
Total		24998038	695599	100.000	100.000

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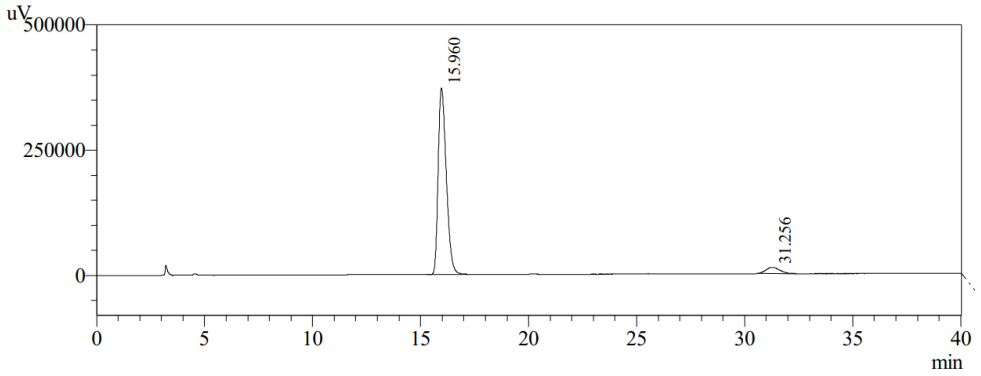
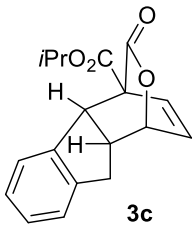


Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.960	9744621	372166	94.632	96.775
2	31.256	552770	12403	5.368	3.225
Total		10297391	384570	100.000	100.000

Isopropyl (4*S*,4a*S*,9a*R*)-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano) fluorene-4-carboxylate (3c)



3c

Following the general procedure, reaction time 40 h. Product **3c** was obtained as a white solid (20 mg, 70% yield, 93% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 5.0, 2.6 Hz, 1H), 7.20 – 7.07 (m, 3H), 6.55 (d, *J* = 7.8 Hz, 1H), 6.47 – 6.35 (m, 1H), 5.48 – 5.37 (m, 1H), 5.30 (td, *J* = 4.6, 1.7 Hz, 1H), 4.41 (d, *J* = 8.8 Hz, 1H), 3.45 (dd, *J* = 9.7, 5.1 Hz, 1H), 3.21 (dd, *J* = 17.2, 10.5 Hz, 1H), 2.59 (dd, *J* = 17.2, 3.8 Hz, 1H), 1.47 (dd, *J* = 10.2, 6.3 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 167.4, 143.2, 140.2, 133.0, 128.7, 128.2, 127.1, 124.8, 124.3, 76.9, 70.3, 59.7, 48.0, 41.8, 33.9, 21.9, 21.8.

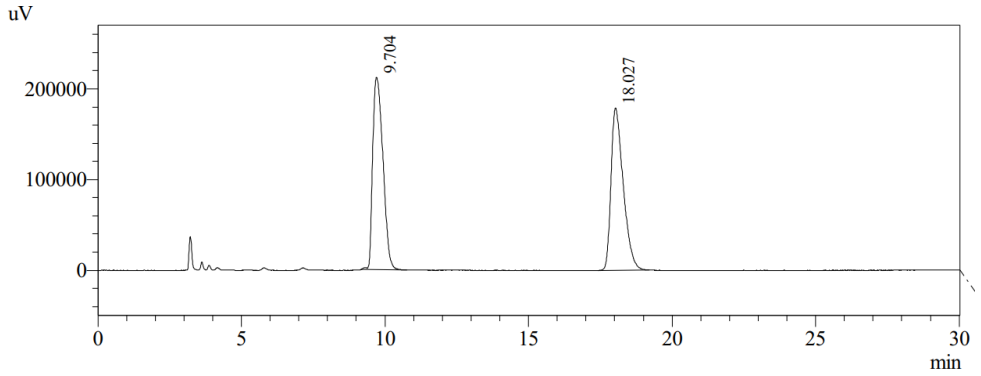
HPLC: 93% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 93/7, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 9.9 min, t_R (minor) = 18.6 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{18}H_{18}NaO_4$: 321.1097; found: 321.1096.

m.p. 111–112 °C.

[α]$^{25}_D$ = +32.7 (*c* = 0.22, CH_2Cl_2).

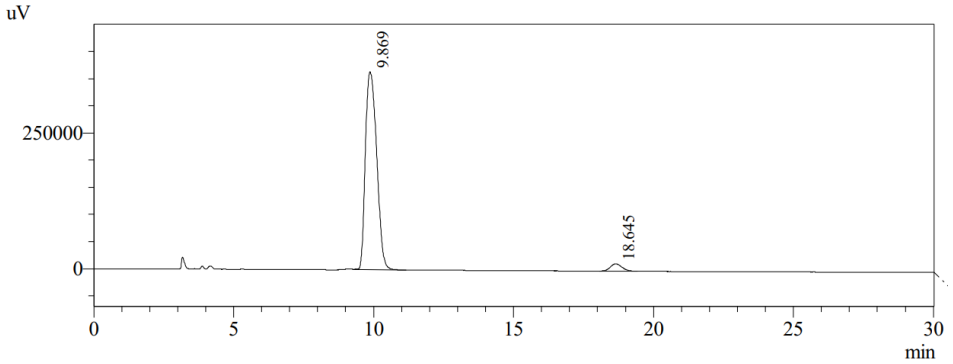
***rac*-3c:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.704	5270722	211997	49.922	54.196
2	18.027	5287160	179169	50.078	45.804
Total		10557882	391166	100.000	100.000

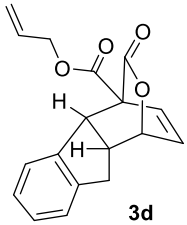
***cat*-3c:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.869	10205060	364038	96.318	96.420
2	18.645	390105	13516	3.682	3.580
Total		10595166	377554	100.000	100.000

Allyl (4a*S*,9a*R*)-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3d)



3d

Following the general procedure, reaction time 40 h. Product **3d** was obtained as a white solid (24 mg, 81% yield, 90% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 7.2 Hz, 1H), 7.17 (dq, *J* = 14.8, 7.5 Hz, 3H), 6.60 (d, *J* = 7.8 Hz, 1H), 6.46 (dd, *J* = 7.9, 5.0 Hz, 1H), 6.21 – 6.05 (m, 1H), 5.62 – 5.48 (m, 1H), 5.46 – 5.37 (m, 1H), 5.36 (td, *J* = 4.6, 1.9 Hz, 1H), 5.02 (hept, *J* = 7.3, 6.5 Hz, 2H), 4.46 (d, *J* = 8.8 Hz, 1H), 3.50 (ddt, *J* = 10.2, 8.7, 4.2 Hz, 1H), 3.24 (dd, *J* = 17.2, 10.5 Hz, 1H), 2.62 (dd, *J* = 17.2, 3.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 167.7, 143.2, 140.0, 132.6, 131.4, 129.0, 128.3, 127.2, 124.9, 124.3, 119.4, 77.0, 66.8, 59.9, 48.2, 41.8, 34.0.

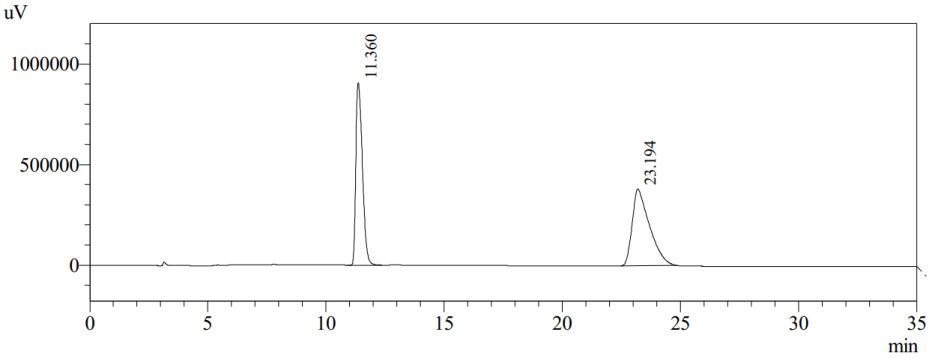
HPLC: 90% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 88/12, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 11.4 min, t_R (minor) = 23.7 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{18}H_{16}NaO_4$: 319.0941; found: 319.0940.

m.p. 64–65 °C.

[α]$^{25}_D$ = +33.0 (*c* = 0.23, CH_2Cl_2).

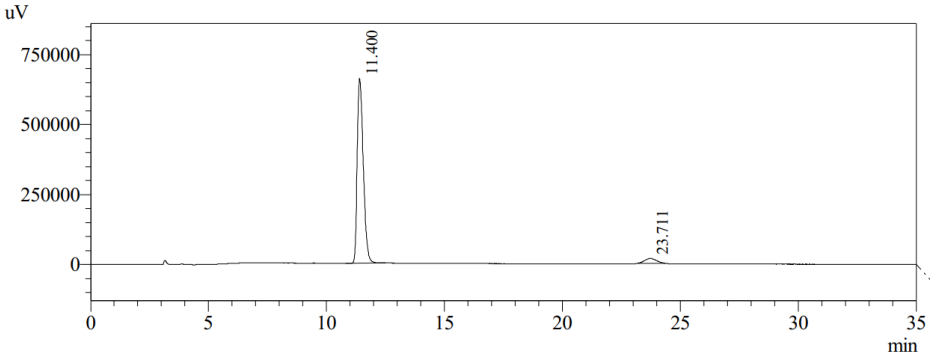
***rac*-3d:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.360	17543041	905777	47.444	70.315
2	23.194	19433292	382399	52.556	29.685
Total		36976333	1288177	100.000	100.000

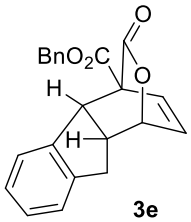
***cat*-3d:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.400	11843849	658947	95.031	97.419
2	23.711	619230	17460	4.969	2.581
Total		12463079	676407	100.000	100.000

Benzyl (4*S*,4a*S*,9a*R*)-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano) fluorene-4-carboxylate (3e)



3e

Following the general procedure, reaction time 40 h. Product **3e** was obtained as a white solid (30 mg, 83% yield, 89% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.45 (m, 2H), 7.39 (q, *J* = 7.5, 6.8 Hz, 3H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 6.53 (d, *J* = 7.3 Hz, 1H), 6.37 (dd, *J* = 7.9, 4.9 Hz, 1H), 5.48 (s, 2H), 5.27 (td, *J* = 4.7, 1.9 Hz, 1H), 4.38 (d, *J* = 8.8 Hz, 1H), 3.48 – 3.34 (m, 1H), 3.15 (dd, *J* = 17.2, 10.5 Hz, 1H), 2.53 (dd, *J* = 17.2, 3.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 167.8, 143.1, 139.9, 135.1, 132.7, 128.9, 128.8, 128.7, 128.6, 128.2, 127.2, 124.8, 124.2, 77.0, 68.0, 59.8, 48.3, 41.7, 33.9.

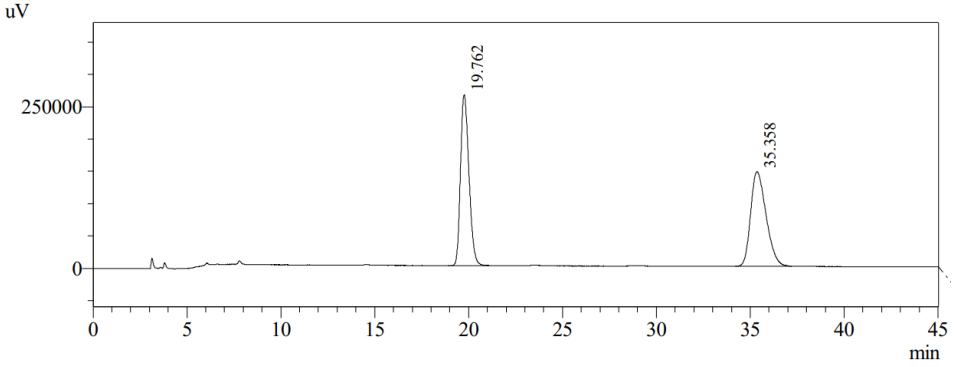
HPLC: 89% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 88/12, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 19.8 min, t_R (minor) = 35.9 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{22}H_{18}NaO_4$: 369.1097; found: 369.1096.

m.p. 56–57 °C.

[α]$^{25}_D$ = +44.5 (*c* = 0.21, CH_2Cl_2).

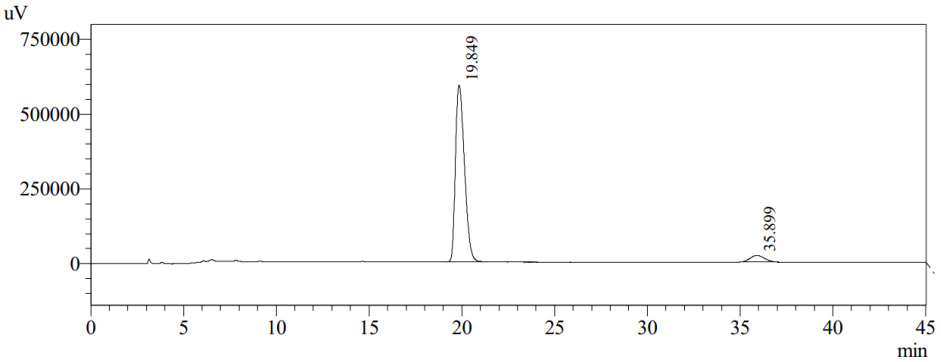
***rac*-3e:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.762	8256037	264205	49.689	64.341
2	35.358	8359324	146426	50.311	35.659
Total		16615362	410631	100.000	100.000

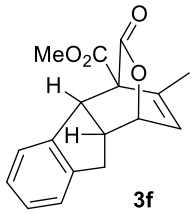
***cat*-3e:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.849	19972032	592056	94.637	96.504
2	35.899	1131860	21446	5.363	3.496
Total		21103892	613502	100.000	100.000

Methyl (4*R*,4a*S*,9a*R*)-3-methyl-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3f)



3f

Following the general procedure, reaction time 60 h. Product **3f** was obtained as a white solid (15 mg, 53% yield, 88% *ee*).

TLC: R_f = 0.5 (Petroleum ether /ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.03 (m, 4H), 5.97 (dq, *J* = 5.3, 1.7 Hz, 1H), 5.09 (dd, *J* = 5.1, 3.9 Hz, 1H), 4.45 (d, *J* = 8.4 Hz, 1H), 4.01 (s, 3H), 3.29 (ddt, *J* = 10.4, 8.0, 3.7 Hz, 1H), 3.15 (dd, *J* = 17.1, 10.4 Hz, 1H), 2.52 (dd, *J* = 17.1, 3.5 Hz, 1H), 1.56 (d, *J* = 1.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 168.5, 143.4, 142.3, 139.9, 128.2, 126.9, 124.9, 124.8, 123.2, 76.3, 63.4, 52.8, 48.1, 41.8, 34.1, 20.2.

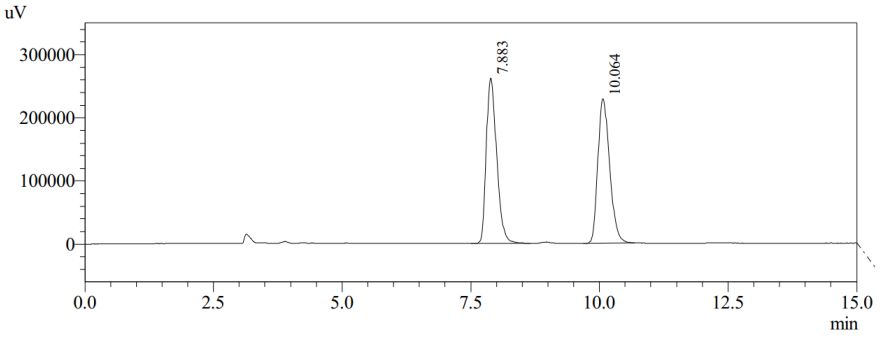
HPLC: 88% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 90/10, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 7.9 min, t_R (minor) = 10.1 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{16}NaO_4$: 307.0941; found: 307.0941.

m.p. 119–120 °C.

[α]$^{25}_D$ = +4.6 (*c* = 0.35, $CHCl_3$).

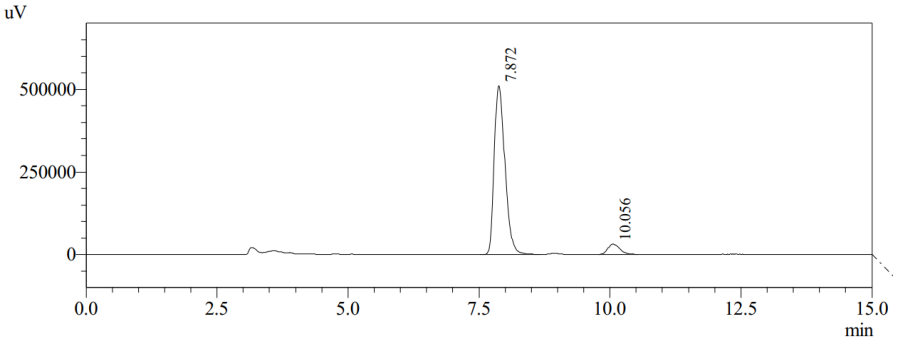
***rac*-3f:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.883	3682499	261054	50.195	53.278
2	10.064	3653889	228927	49.805	46.722
Total		7336388	489982	100.000	100.000

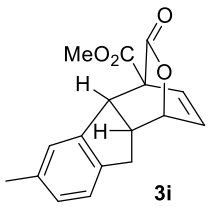
***cat*-3f:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.872	7305908	509828	93.803	94.272
2	10.056	482684	30975	6.197	5.728
Total		7788592	540803	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-6-methyl-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3i)



3i

Following the general procedure, reaction time 60 h. Product **3i** was obtained as a white solid (28 mg, 98% yield, 86% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (q, *J* = 7.8 Hz, 2H), 6.71 (s, 1H), 6.49 – 6.41 (m, 1H), 6.30 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.20 (td, *J* = 4.7, 1.9 Hz, 1H), 4.22 (d, *J* = 8.8 Hz, 1H), 3.95 (s, 3H), 3.33 (ddd, *J* = 8.9, 6.1, 4.5 Hz, 1H), 3.08 – 2.95 (m, 1H), 2.41 (dd, *J* = 17.0, 3.8 Hz, 1H), 2.19 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 168.5, 140.2, 140.0, 136.8, 132.5, 129.3, 129.0, 124.6, 77.1, 59.8, 53.1, 48.1, 42.1, 33.5, 21.5.

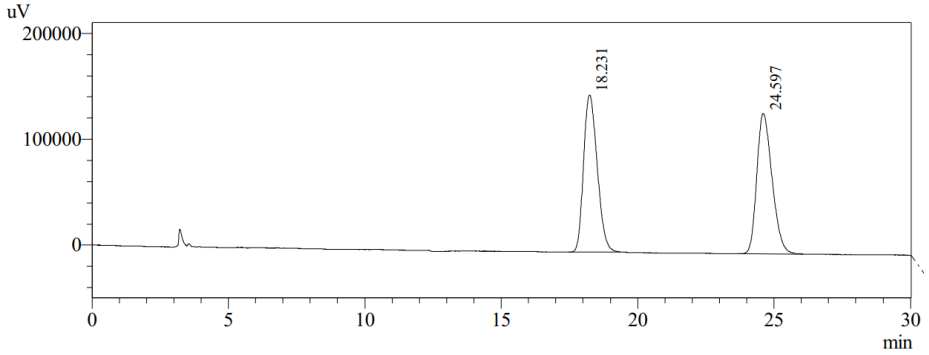
HPLC: 86% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 18.4 min, t_R (minor) = 24.8 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{16}NaO_4$: 307.0941; found: 307.0941.

m.p. 128–129 °C.

[α]$^{25}_D$ = –6.9 (*c* = 0.23, CH_2Cl_2).

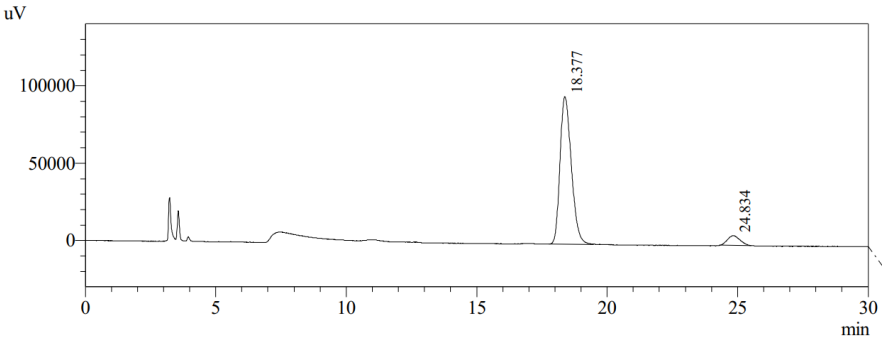
***rac*-3i:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.231	5164390	148272	50.002	52.787
2	24.597	5164045	132614	49.998	47.213
Total		10328434	280886	100.000	100.000

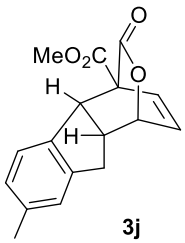
***cat*-3i:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.377	2881400	95385	93.189	93.780
2	24.834	210607	6326	6.811	6.220
Total		3092007	101711	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-7-methyl-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3j)



3j

Following the general procedure, the reaction was stirred at 35 °C for 40 h. Product **3j** was obtained as a white solid (26 mg, 91% yield, 89% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 – 6.81 (m, 3H), 6.60 – 6.46 (m, 1H), 6.38 (dd, *J* = 7.9, 4.9 Hz, 1H), 5.28 (td, *J* = 4.6, 1.9 Hz, 1H), 4.31 (d, *J* = 8.8 Hz, 1H), 4.02 (s, 3H), 3.42 (ddt, *J* = 10.2, 8.6, 4.2 Hz, 1H), 3.12 (dd, *J* = 17.2, 10.5 Hz, 1H), 2.50 (dd, *J* = 17.2, 4.1 Hz, 1H), 2.28 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 168.5, 143.3, 138.2, 136.9, 132.6, 128.9, 128.2, 125.5, 123.8, 77.0, 59.8, 53.1, 47.9, 42.0, 33.8, 21.3.

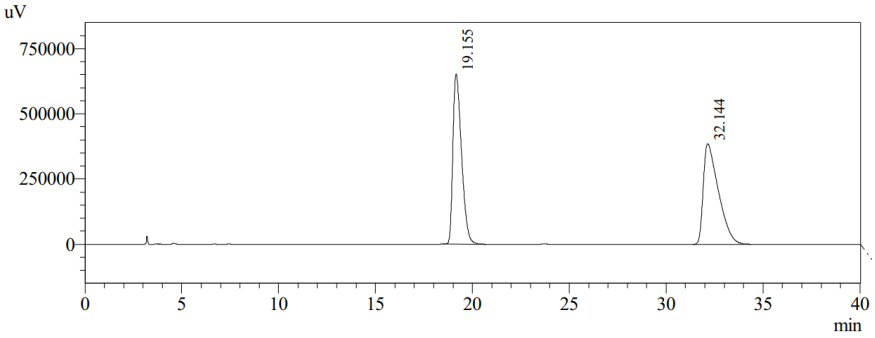
HPLC: 89% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 19.2 min, t_R (minor) = 32.7 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{16}NaO_4$: 307.0941; found: 307.0941.

m.p. 117–118 °C.

[α]$^{25}_D$ = +18.3 (*c* = 0.23, CH_2Cl_2).

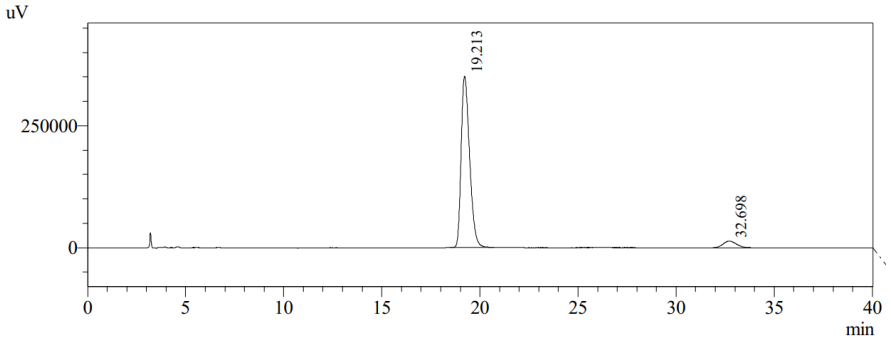
***rac*-3j:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.155	20237006	652125	49.163	62.793
2	32.144	20926161	386401	50.837	37.207
Total		41163167	1038526	100.000	100.000

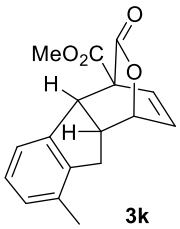
***cat*-3j:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.213	10516786	351050	94.327	96.265
2	32.698	632542	13622	5.673	3.735
Total		11149328	364672	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-8-methyl-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3k)



3k

Following the general procedure, reaction time 40 h. Product **3k** was obtained as a white solid (27 mg, 94% yield, 87% *ee*).

TLC: R_f = 0.5 (Petroleum ether /ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 – 6.97 (m, 2H), 6.83 (d, *J* = 7.5 Hz, 1H), 6.53 (dt, *J* = 7.9, 1.5 Hz, 1H), 6.38 (dd, *J* = 8.0, 4.9 Hz, 1H), 5.30 (td, *J* = 4.6, 1.9 Hz, 1H), 4.35 (d, *J* = 8.9 Hz, 1H), 4.03 (s, 3H), 3.43 (ddt, *J* = 10.4, 8.7, 4.2 Hz, 1H), 3.04 (dd, *J* = 17.2, 10.4 Hz, 1H), 2.43 (dd, *J* = 17.3, 4.1 Hz, 1H), 2.16 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 168.4, 142.2, 139.6, 134.4, 132.7, 129.0, 129.0, 127.6, 121.3, 77.0, 59.8, 53.1, 48.5, 41.6, 33.0, 19.1.

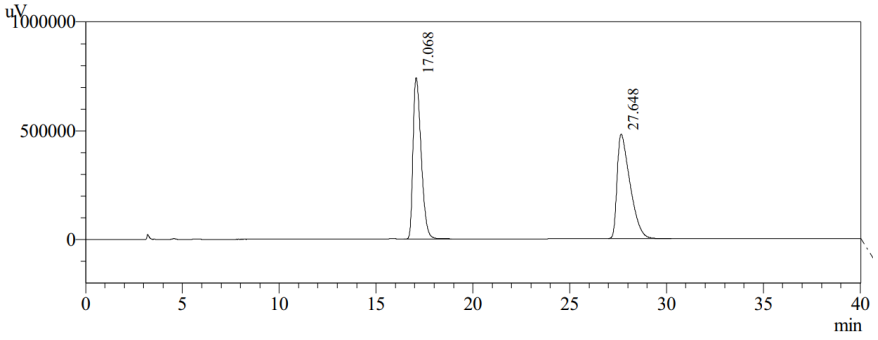
HPLC: 87% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 17.2 min, t_R (minor) = 28.2 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{16}NaO_4$: 307.0941; found: 307.0942.

m.p. 138–139 °C.

[α]$^{25}_D$ = +21.4 (*c* = 0.24, CH_2Cl_2).

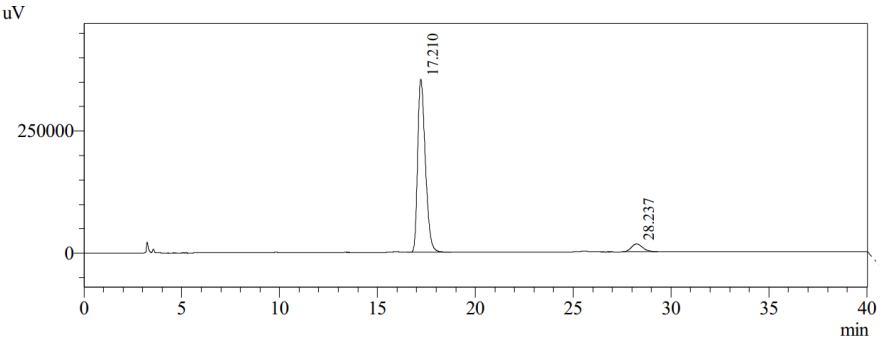
***rac*-3k:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.068	21563992	740635	49.419	60.724
2	27.648	22070660	479046	50.581	39.276
Total		43634652	1219680	100.000	100.000

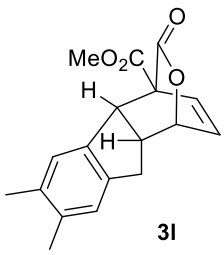
***cat*-3k:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.210	9676483	354670	93.676	95.638
2	28.237	653221	16175	6.324	4.362
Total		10329704	370844	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-6,7-dimethyl-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3l)



3l

Following the general procedure, the reaction was stirred at 35 °C for 72 h. Product **3l** was obtained as a white solid (28 mg, 93% yield, 85% *ee*).

TLC: R_f = 0.5 (Petroleum ether /ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (s, 1H), 6.79 (s, 1H), 6.58 (d, *J* = 7.8 Hz, 1H), 6.42 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.31 (td, *J* = 4.6, 1.7 Hz, 1H), 4.32 (d, *J* = 8.8 Hz, 1H), 4.08 (s, 3H), 3.44 (tt, *J* = 8.7, 4.2 Hz, 1H), 3.13 (dd, *J* = 17.0, 10.5 Hz, 1H), 2.51 (dd, *J* = 17.0, 3.7 Hz, 1H), 2.22 (d, *J* = 4.3 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 168.5, 140.7, 137.4, 137.0, 135.6, 132.6, 128.9, 125.8, 124.9, 77.1, 59.8, 53.0, 48.0, 42.1, 33.6, 20.1, 19.9.

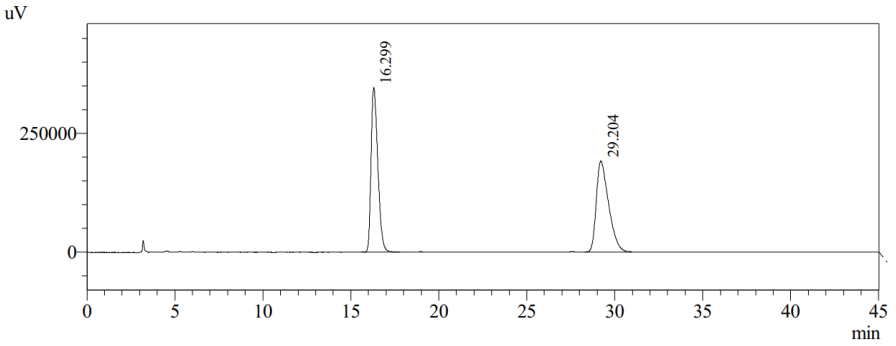
HPLC: 85% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 16.3 min, t_R (minor) = 29.5 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{18}H_{18}NaO_4$: 321.1097; found: 321.1098.

m.p. 134–135 °C.

[α]$^{25}_D$ = –4.3 (*c* = 0.23, CH_2Cl_2).

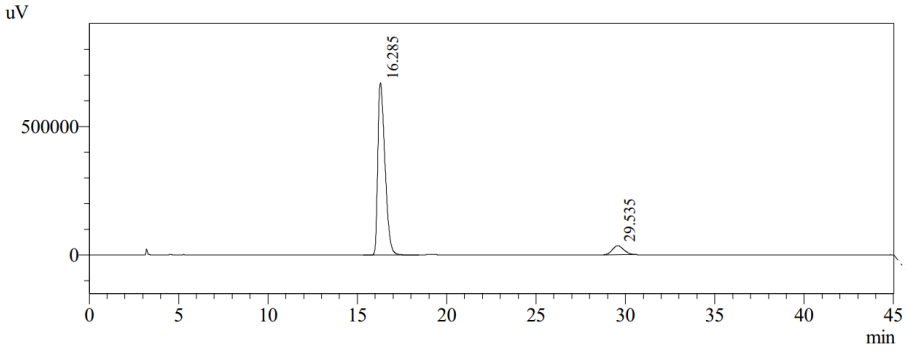
***rac*-3l:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.299	9269150	346323	49.881	64.410
2	29.204	9313548	191363	50.119	35.590
Total		18582699	537686	100.000	100.000

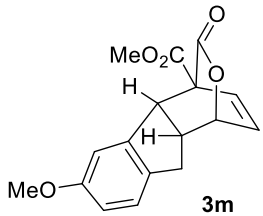
***cat*-3l:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.285	18652395	668455	92.298	95.003
2	29.535	1556498	35161	7.702	4.997
Total		20208893	703616	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-6-methoxy-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3m)



3m

Following the general procedure, the reaction was stirred at 35 °C for 40 h. Product **3m** was obtained as a white solid (22 mg, 73% yield, 84% *ee*).

TLC: R_f = 0.4 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, *J* = 8.4 Hz, 1H), 6.78 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.61 – 6.53 (m, 2H), 6.43 (dd, *J* = 7.9, 4.9 Hz, 1H), 5.31 (td, *J* = 4.7, 1.9 Hz, 1H), 4.34 (d, *J* = 8.8 Hz, 1H), 4.06 (s, 3H), 3.76 (s, 3H), 3.53 – 3.40 (m, 1H), 3.12 (dd, *J* = 16.7, 10.5 Hz, 1H), 2.50 (dd, *J* = 16.8, 3.9 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 168.5, 159.1, 141.3, 135.0, 132.4, 129.1, 125.4, 114.6, 109.1, 77.0, 59.7, 55.3, 53.1, 48.2, 42.4, 33.1.

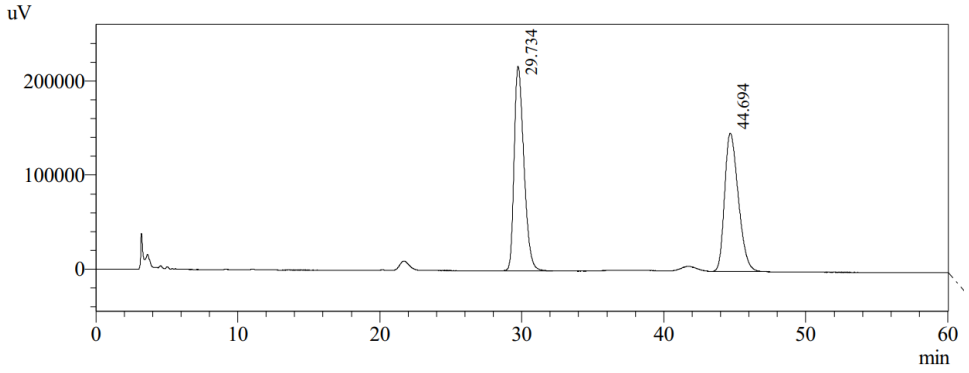
HPLC: 84% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 29.1 min, t_R (minor) = 43.9 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{16}NaO_5$: 323.0890; found: 323.0889.

m.p. 115–116 °C.

[α]$^{25}_D$ = +1.5 (*c* = 0.23, CH_2Cl_2).

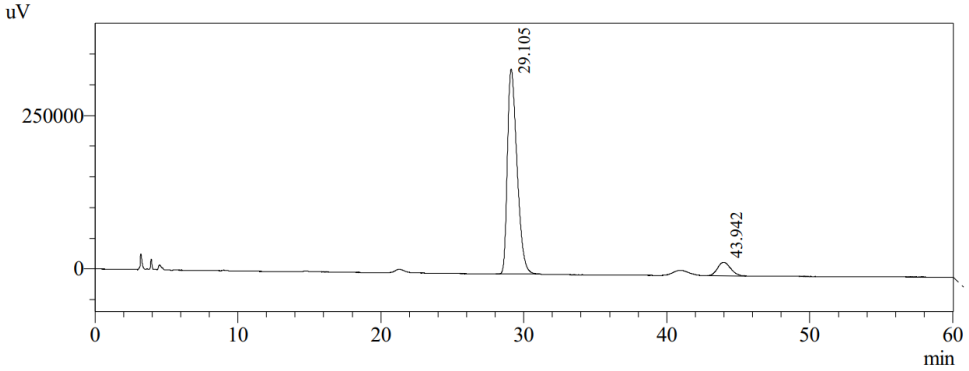
***rac*-3m:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.734	10355700	217435	51.290	59.662
2	44.694	9834816	147008	48.710	40.338
Total		20190516	364443	100.000	100.000

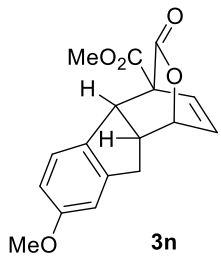
***cat*-3m:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.105	15630696	333995	91.860	93.827
2	43.942	1385052	21976	8.140	6.173
Total		17015749	355971	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-7-methoxy-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3n)



3n

Following the general procedure, the reaction was stirred at 35 °C for 40 h. Product **3n** was obtained as a white solid (26 mg, 86% yield, 87% *ee*).

TLC: R_f = 0.4 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, *J* = 8.5 Hz, 1H), 6.75 – 6.67 (m, 1H), 6.64 (s, 1H), 6.56 (d, *J* = 7.9 Hz, 1H), 6.42 (dd, *J* = 7.7, 5.0 Hz, 1H), 5.31 (t, *J* = 4.5 Hz, 1H), 4.31 (d, *J* = 8.8 Hz, 1H), 4.05 (s, 3H), 3.78 (s, 3H), 3.46 (dq, *J* = 8.9, 4.4 Hz, 1H), 3.16 (dd, *J* = 17.3, 10.5 Hz, 1H), 2.54 (dd, *J* = 17.3, 3.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 168.5, 160.0, 144.8, 132.6, 131.9, 128.8, 124.7, 113.6, 109.5, 77.0, 59.9, 55.3, 53.1, 47.5, 42.3, 34.0.

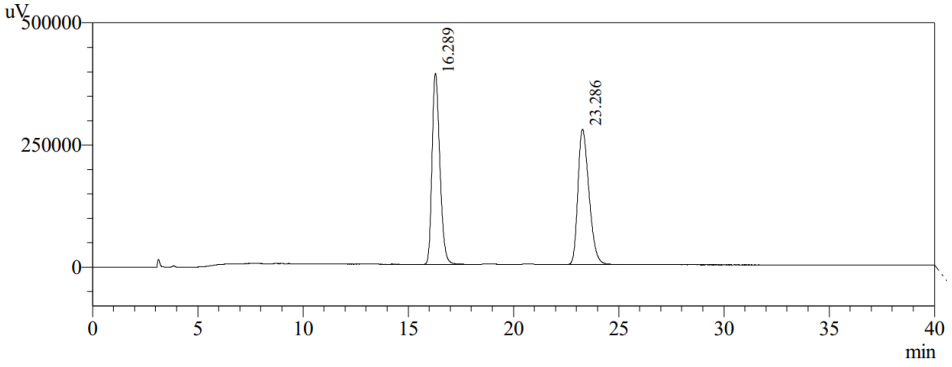
HPLC: 87% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 88/12, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 16.5 min, t_R (minor) = 23.7 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{16}NaO_5$: 323.0890; found: 323.0890.

m.p. 141–142 °C.

[α]$^{25}_D$ = +16.7 (*c* = 0.20, CH_2Cl_2).

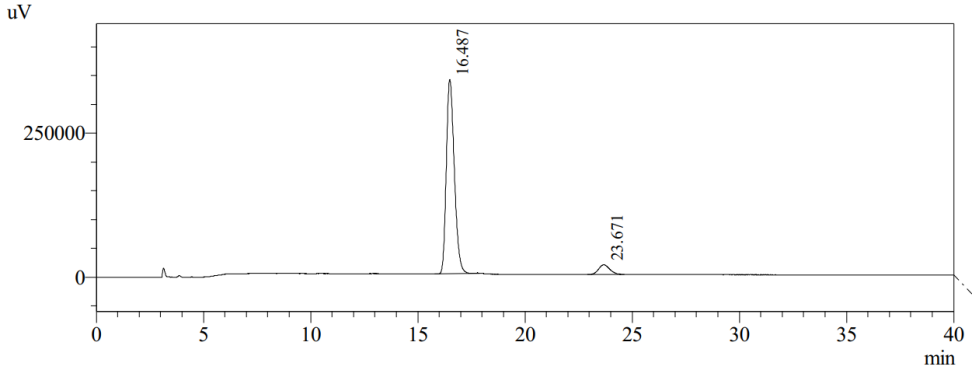
***rac*-3n:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.289	10114844	391677	49.891	58.559
2	23.286	10158885	277186	50.109	41.441
Total		20273730	668863	100.000	100.000

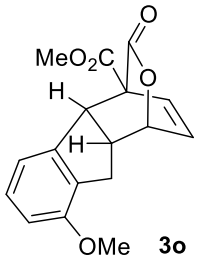
***cat*-3n:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.487	8783036	337813	93.571	95.265
2	23.671	603457	16790	6.429	4.735
Total		9386493	354603	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-8-methoxy-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3o)



3o

Following the general procedure, the reaction was stirred at 35 °C for 72 h. Product **3o** was obtained as a white solid (18 mg, 60% yield, 90% *ee*).

TLC: R_f = 0.4 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (t, *J* = 7.9 Hz, 1H), 6.60 (d, *J* = 8.1 Hz, 1H), 6.52 (s, 1H), 6.45 (d, *J* = 7.1 Hz, 1H), 6.31 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.20 (td, *J* = 4.7, 1.8 Hz, 1H), 4.27 (d, *J* = 8.8 Hz, 1H), 3.94 (s, 3H), 3.70 (s, 3H), 3.35 (ddd, *J* = 13.2, 8.7, 4.2 Hz, 1H), 2.95 (dd, *J* = 17.5, 10.4 Hz, 1H), 2.37 (dd, *J* = 17.5, 3.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 168.4, 155.9, 141.7, 132.5, 131.1, 129.1, 129.0, 116.0, 109.2, 77.0, 59.6, 55.1, 53.1, 48.6, 42.0, 31.0.

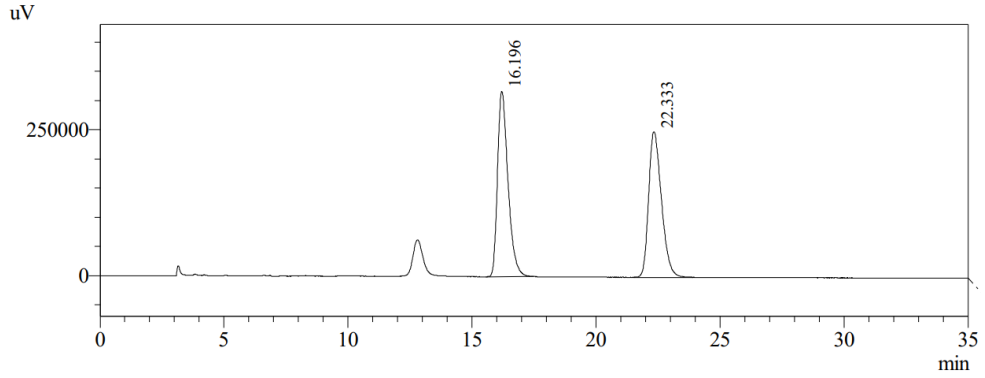
HPLC: 90% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 90/10, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 16.1 min, t_R (minor) = 22.3 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{16}NaO_5$: 323.0890; found: 323.0891.

m.p. 117–118 °C.

[α]$^{25}_D$ = +16.1 (*c* = 0.19, CH_2Cl_2).

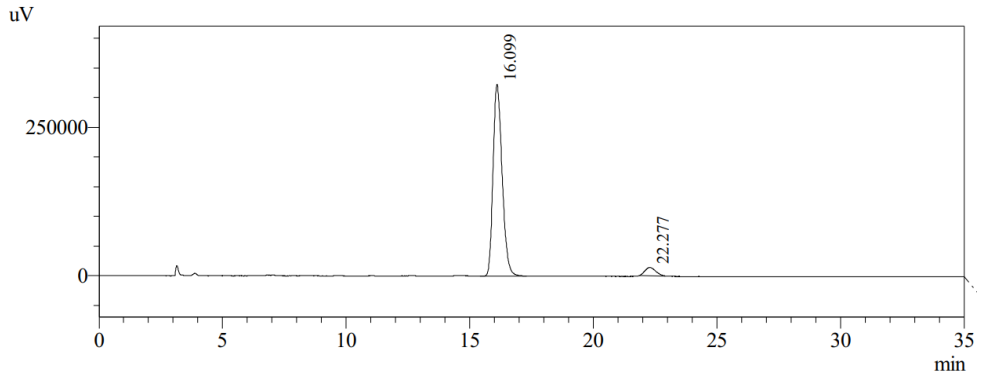
***rac*-3o:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.196	9338696	317409	51.050	55.983
2	22.333	8954414	249562	48.950	44.017
Total		18293110	566971	100.000	100.000

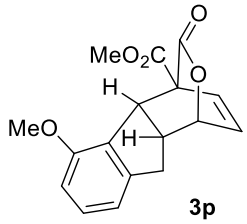
***cat*-3o:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.099	8242872	322669	95.167	95.863
2	22.277	418647	13924	4.833	4.137
Total		8661519	336593	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-5-methoxy-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3p)



3p

Following the general procedure, the reaction was stirred at 35 °C for 72 h. Product **3p** was obtained as a white solid (26 mg, 86% yield, 70% *ee*).

TLC: R_f = 0.4 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 7.8 Hz, 1H), 6.68 (t, *J* = 8.5 Hz, 2H), 6.61 (d, *J* = 8.1 Hz, 1H), 6.32 (dd, *J* = 7.8, 4.9 Hz, 1H), 5.16 (s, 1H), 4.45 (d, *J* = 8.2 Hz, 1H), 4.00 (s, 3H), 3.73 (s, 3H), 3.32 (ddd, *J* = 10.9, 7.9, 3.7 Hz, 1H), 3.18 (dd, *J* = 17.1, 10.4 Hz, 1H), 2.62 – 2.49 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 168.5, 156.4, 145.3, 133.8, 130.0, 128.0, 127.2, 116.9, 108.6, 76.6, 58.7, 55.4, 52.5, 48.0, 42.3, 34.3.

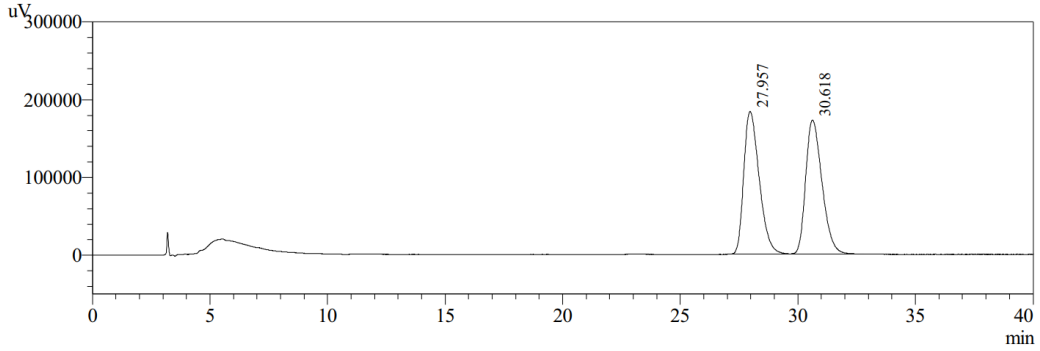
HPLC: 70% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 27.6 min, t_R (minor) = 30.5 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{17}H_{16}NaO_5$: 323.0890; found: 323.0890.

m.p. 148–149 °C.

[α]$^{25}_D$ = –34.0 (*c* = 0.20, CH_2Cl_2).

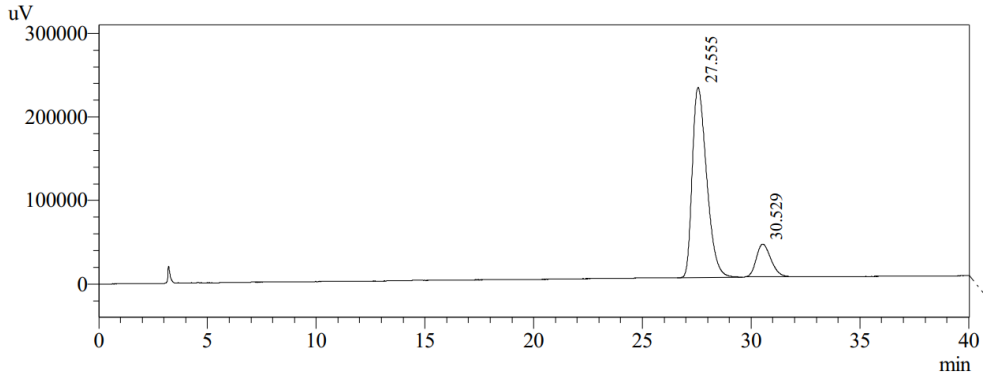
***rac*-3p:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.957	8368658	183657	50.266	51.600
2	30.618	8280006	172266	49.734	48.400
Total		16648664	355923	100.000	100.000

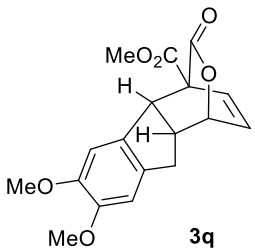
***cat*-3p:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.555	10423152	227689	85.196	85.343
2	30.529	1811132	39103	14.804	14.657
Total		12234285	266792	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-6,7-dimethoxy-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3q)



3q

Following the general procedure, the reaction was stirred at 10 °C for 64 h. Product **3q** was obtained as a white solid (30 mg, 90% yield, 71% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.47 (s, 1H), 6.42 (d, *J* = 4.1 Hz, 2H), 6.29 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.18 (td, *J* = 4.7, 1.9 Hz, 1H), 4.17 (d, *J* = 8.7 Hz, 1H), 3.91 (s, 3H), 3.70 (d, *J* = 11.8 Hz, 6H), 3.38 – 3.28 (m, 1H), 2.98 (dd, *J* = 16.7, 10.4 Hz, 1H), 2.36 (dd, *J* = 16.7, 3.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 168.6, 149.6, 148.5, 134.9, 132.3, 131.3, 129.0, 107.1, 106.5, 77.0, 59.9, 55.9, 55.8, 53.1, 48.4, 42.3, 33.9.

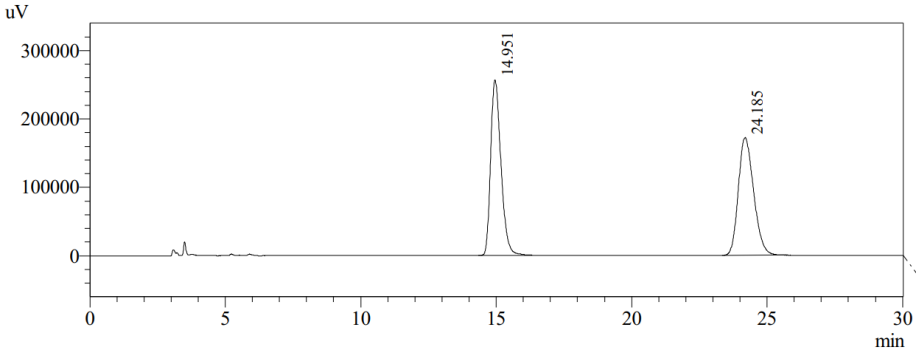
HPLC: 71% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 80/20, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 15.0 min, t_R (minor) = 24.3 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{18}H_{18}NaO_6$: 353.0996; found: 353.0995.

m.p. 100–101 °C.

[α]$^{25}_D$ = +10.4 (*c* = 0.24, CH_2Cl_2).

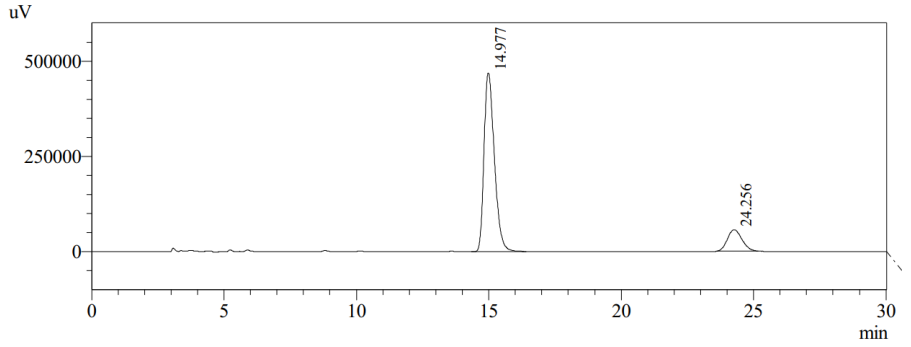
***rac*-3q:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.951	6780117	256842	49.968	59.860
2	24.185	6788724	172233	50.032	40.140
Total		13568841	429075	100.000	100.000

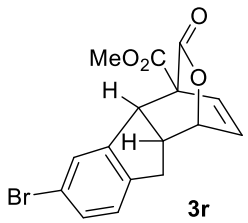
***cat*-3q:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.977	12725585	468684	85.680	89.304
2	24.256	2126810	56136	14.320	10.696
Total		14852394	524820	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-6-bromo-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3r)



3r

Following the general procedure, reaction time 90 h. Product **3r** was obtained as a white solid (25 mg, 71% yield, 82% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.15 (s, 1H), 6.97 (d, *J* = 8.1 Hz, 1H), 6.57 – 6.51 (m, 1H), 6.41 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.29 (td, *J* = 4.7, 1.9 Hz, 1H), 4.33 (d, *J* = 8.9 Hz, 1H), 4.04 (s, 3H), 3.45 (ddt, *J* = 10.4, 8.7, 4.2 Hz, 1H), 3.11 (dd, *J* = 17.4, 10.5 Hz, 1H), 2.49 (dd, *J* = 17.4, 4.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 168.2, 142.3, 142.2, 132.6, 131.5, 129.2, 127.5, 126.3, 120.9, 76.8, 59.7, 53.3, 47.9, 42.1, 33.6.

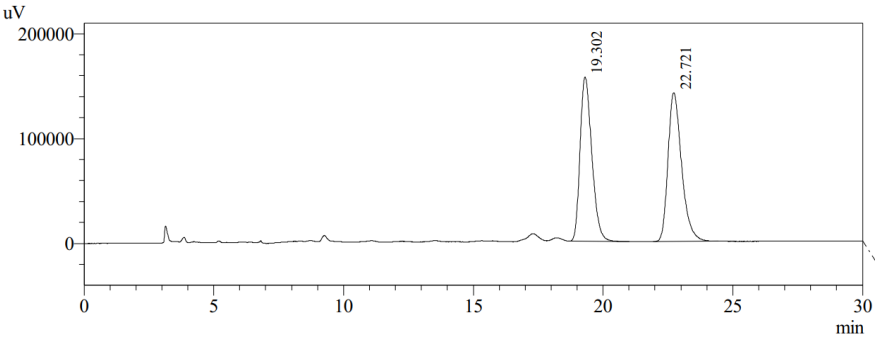
HPLC: 82% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 90/10, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 19.2 min, t_R (minor) = 22.7 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{13}NaO_4Br$: 370.9889, 372.9869; found: 370.9890, 372.9868.

m.p. 136–137 °C.

[α]$^{25}_D$ = –15.5 (*c* = 0.22, CH_2Cl_2).

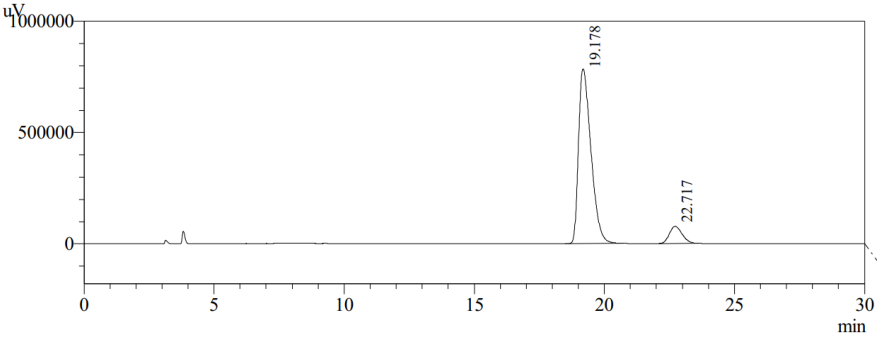
***rac*-3r:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.302	4944710	156797	48.840	52.510
2	22.721	5179679	141806	51.160	47.490
Total		10124389	298603	100.000	100.000

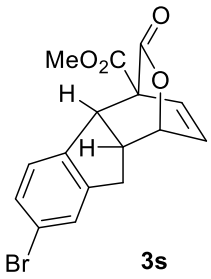
***cat*-3r:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.178	26075608	784304	90.814	91.027
2	22.717	2637571	77309	9.186	8.973
Total		28713179	861613	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-7-bromo-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3s)



3s

Following the general procedure, reaction time 72 h. Product **3s** was obtained as a white solid (26 mg, 75% yield, 81% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 7.6 Hz, 2H), 6.89 (d, *J* = 8.1 Hz, 1H), 6.51 (ddd, *J* = 7.9, 2.0, 0.9 Hz, 1H), 6.41 (dd, *J* = 7.9, 4.9 Hz, 1H), 5.29 (ddd, *J* = 6.7, 4.9, 2.6 Hz, 1H), 4.30 (d, *J* = 8.8 Hz, 1H), 4.02 (s, 3H), 3.49 – 3.40 (m, 1H), 3.15 (dd, *J* = 17.5, 10.5 Hz, 1H), 2.53 (dd, *J* = 17.5, 4.1 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 168.3, 145.6, 139.1, 132.7, 130.5, 129.2, 128.1, 125.7, 122.4, 76.8, 59.7, 53.3, 47.7, 42.0, 33.8.

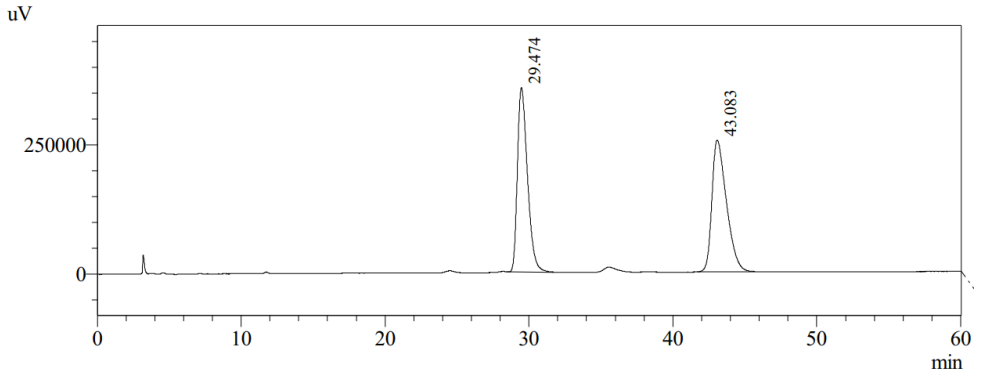
HPLC: 81% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 29.2 min, t_R (minor) = 43.0 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{13}NaO_4Br$: 370.9889, 372.9869; found: 370.9889, 372.9868.

m.p. 146–147 °C.

[α]$^{25}_D$ = +24.7 (*c* = 0.23, CH_2Cl_2).

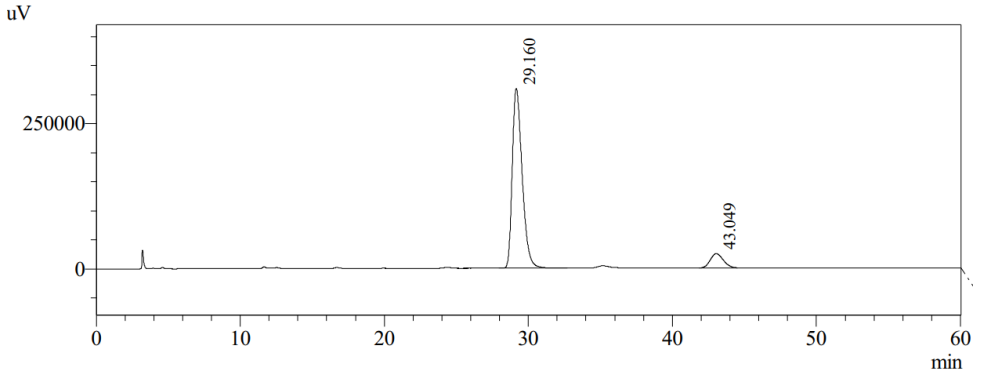
***rac*-3s:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.474	17247619	355516	49.125	58.282
2	43.083	17861797	254473	50.875	41.718
Total		35109416	609989	100.000	100.000

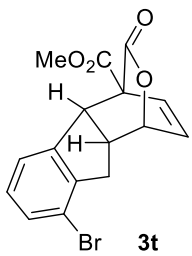
***cat*-3s:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.160	14763040	309781	90.474	92.627
2	43.049	1554339	24656	9.526	7.373
Total		16317379	334438	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-8-bromo-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3t)



3t

Following the general procedure, reaction time 6 d. Product **3t** was obtained as a white solid (24 mg, 68% yield, 82% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.7 Hz, 1H), 7.05 (t, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.57 (d, *J* = 7.1 Hz, 1H), 6.48 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.35 (dt, *J* = 4.6, 2.4 Hz, 1H), 4.47 (d, *J* = 8.9 Hz, 1H), 4.06 (s, 3H), 3.55 – 3.41 (m, 1H), 3.18 (dd, *J* = 17.8, 10.5 Hz, 1H), 2.57 (dd, *J* = 17.8, 3.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 168.2, 143.6, 141.7, 132.6, 131.4, 129.2, 129.1, 123.0, 120.2, 76.7, 59.7, 53.2, 49.1, 40.8, 35.9.

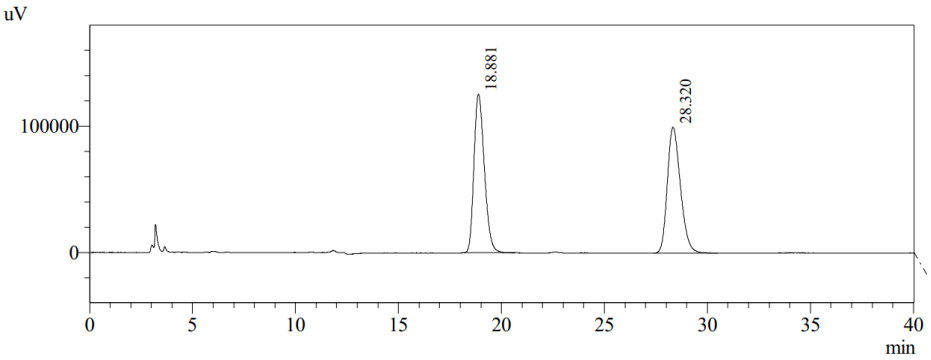
HPLC: 82% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 18.8 min, t_R (minor) = 28.1 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{13}NaO_4Br$: 370.9889, 372.9869; found: 370.9890, 372.9869.

m.p. 140–141 °C.

[α]$^{25}_D$ = +38.5 (*c* = 0.22, CH_2Cl_2).

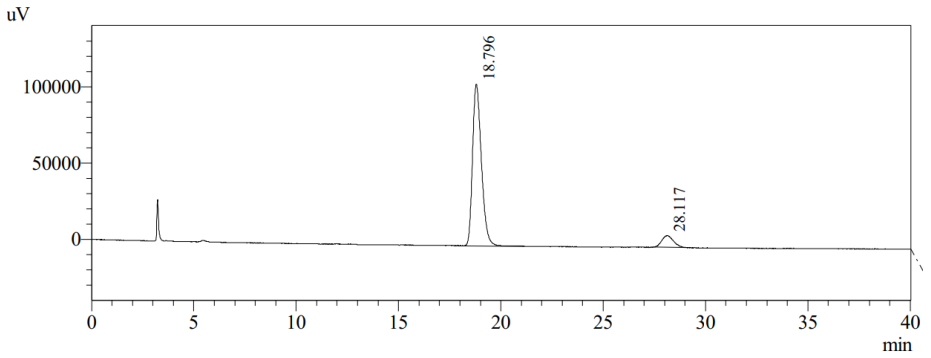
***rac*-3t:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.881	4418614	125816	49.970	55.745
2	28.320	4423905	99881	50.030	44.255
Total		8842519	225697	100.000	100.000

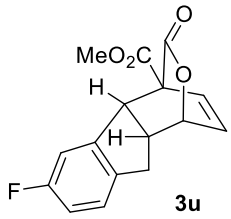
***cat*-3t:**



PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.796	3192023	105781	91.157	93.171
2	28.117	309650	7754	8.843	6.829
Total		3501673	113534	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-6-fluoro-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3u)



3u

Following the general procedure, reaction time 96 h. Product **3u** was obtained as a white solid (18 mg, 62% yield, 83% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (dd, *J* = 8.2, 5.3 Hz, 1H), 6.92 (td, *J* = 8.6, 2.3 Hz, 1H), 6.74 (dd, *J* = 9.1, 2.1 Hz, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 6.45 (dd, *J* = 7.9, 5.0 Hz, 1H), 5.32 (td, *J* = 4.6, 1.8 Hz, 1H), 4.36 (d, *J* = 8.9 Hz, 1H), 4.07 (s, 3H), 3.51 (ddd, *J* = 13.3, 8.7, 4.2 Hz, 1H), 3.16 (dd, *J* = 17.0, 10.5 Hz, 1H), 2.54 (dd, *J* = 17.0, 3.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 168.3, 163.4, 161.0, 141.9 (d, *J* = 7.1 Hz), 138.6 (d, *J* = 2.0 Hz), 132.4, 129.2, 125.9 (d, *J* = 9.1 Hz), 115.6 (d, *J* = 22.2 Hz), 111.2 (d, *J* = 23.2 Hz), 76.8, 59.7, 53.3, 48.0, 48.0, 42.4, 33.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -115.35.

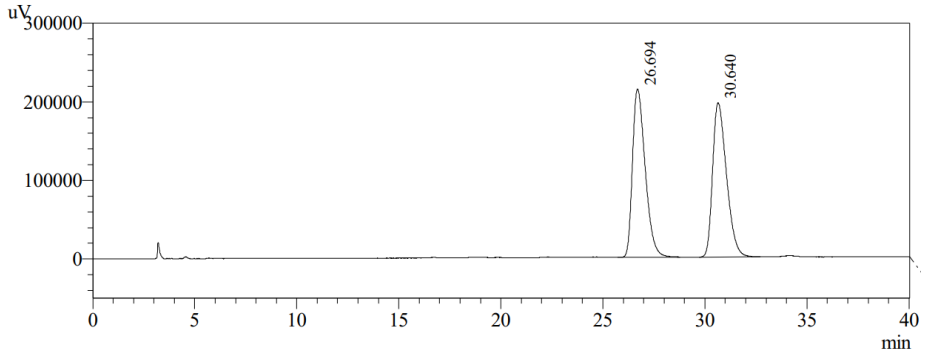
HPLC: 83% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 26.8 min, t_R (minor) = 30.9 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{13}NaO_4F$: 311.0690; found: 311.0691.

m.p. 135–136 °C.

[α]$^{25}_D$ = +25.8 (*c* = 0.24, CH_2Cl_2).

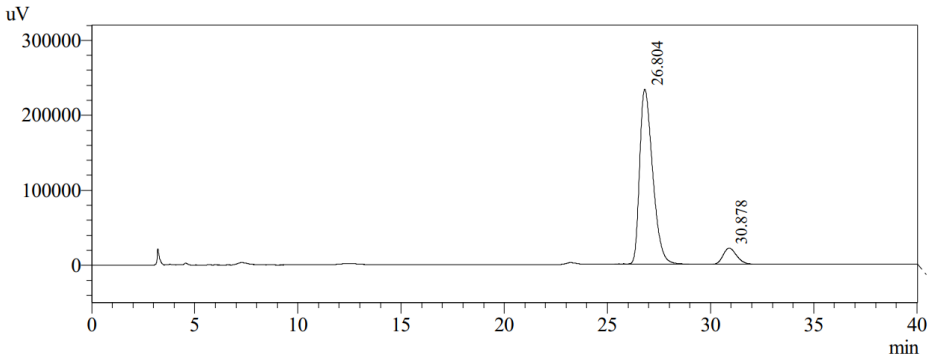
***rac*-3u:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.694	9296120	214485	49.984	52.213
2	30.640	9302091	196304	50.016	47.787
Total		18598212	410789	100.000	100.000

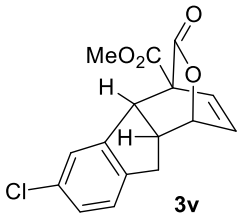
***cat*-3u:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.804	10227653	233272	91.435	91.633
2	30.878	958057	21300	8.565	8.367
Total		11185710	254572	100.000	100.000

Methyl (4*S*,4a*S*,9a*R*)-6-chloro-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3v)



3v

Following the general procedure, reaction time 72 h. Product **3v** was obtained as a white solid (26 mg, 85% yield, 84% *ee*).

TLC: R_f = 0.5 (Petroleum ether /ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.09 – 6.99 (m, 2H), 6.57 (dd, *J* = 7.8, 2.1 Hz, 1H), 6.45 (dt, *J* = 7.8, 3.3 Hz, 1H), 5.41 – 5.26 (m, 1H), 4.36 (d, *J* = 8.9 Hz, 1H), 4.08 (d, *J* = 1.5 Hz, 3H), 3.57 – 3.41 (m, 1H), 3.17 (dd, *J* = 17.4, 10.5 Hz, 1H), 2.55 (dd, *J* = 17.4, 4.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 168.2, 141.6, 133.0, 132.6, 129.2, 128.6, 125.9, 124.5, 76.8, 59.7, 53.3, 47.9, 42.2, 33.5.

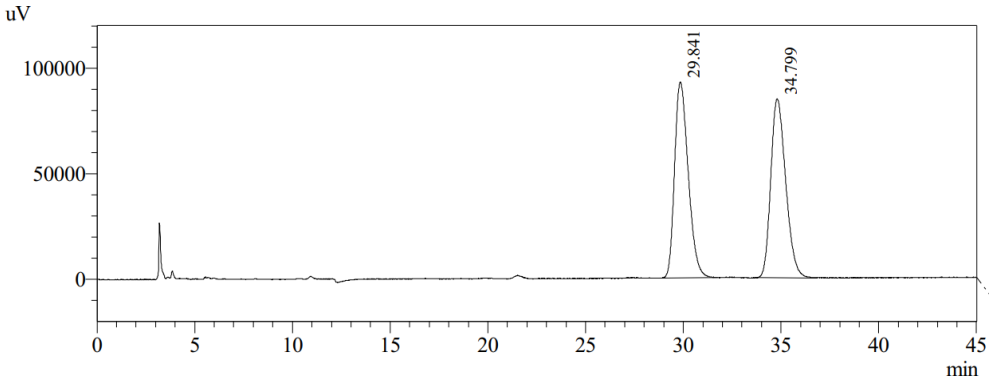
HPLC: 84% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 29.8 min, t_R (minor) = 34.9 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{13}NaO_4Cl$: 327.0395, 329.0365; found: 327.0394, 329.0364.

m.p. 150–151 °C.

[α]$^{25}_D$ = +25.3 (*c* = 0.23, CH_2Cl_2).

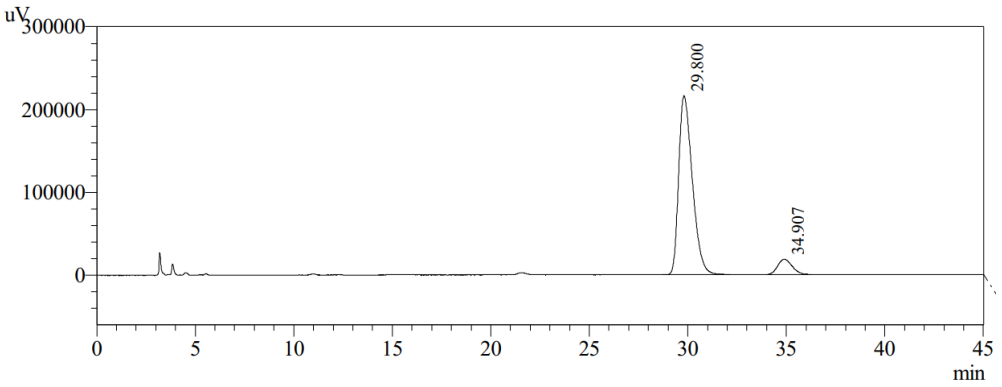
***rac*-3v:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.841	4500607	92783	49.983	52.279
2	34.799	4503692	84694	50.017	47.721
Total		9004298	177477	100.000	100.000

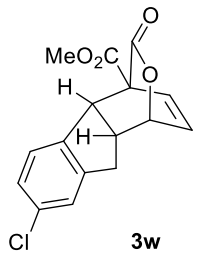
***cat*-3v:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.800	10392494	215946	91.711	92.122
2	34.907	939339	18467	8.289	7.878
Total		11331834	234413	100.000	100.000

methyl (4*S*,4a*S*,9a*R*)-7-chloro-10-oxo-1,4a,9,9a-tetrahydro-4*H*-1,4-(epoxymethano)fluorene-4-carboxylate (3w)



3w

Following the general procedure, reaction time 72 h. Product **3x** was obtained as a white solid (26 mg, 85% yield, 83% *ee*).

TLC: R_f = 0.5 (Petroleum ether/ethyl acetate 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 – 7.03 (m, 2H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.56 – 6.45 (m, 1H), 6.41 (dd, *J* = 7.9, 4.9 Hz, 1H), 5.28 (td, *J* = 4.6, 1.8 Hz, 1H), 4.31 (d, *J* = 8.9 Hz, 1H), 4.02 (s, 3H), 3.54 – 3.38 (m, 1H), 3.15 (dd, *J* = 17.5, 10.5 Hz, 1H), 2.53 (dd, *J* = 17.5, 3.9 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 168.3, 145.2, 138.5, 134.2, 132.6, 129.1, 127.5, 125.2, 125.0, 76.7, 59.7, 53.2, 47.5, 42.0, 33.8.

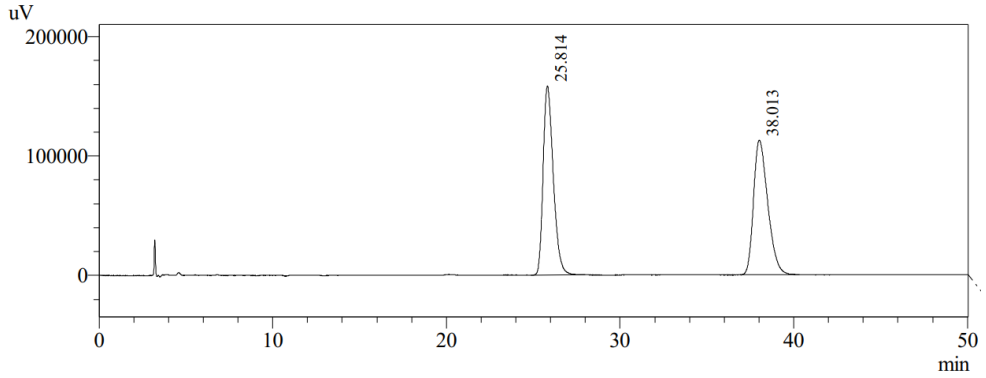
HPLC: 83% *ee*, chiral stationary column: AD, mobile phase: hexane/EtOH = 95/5, 1.0 mL/min, 210 nm, 30 °C, t_R (major) = 25.8 min, t_R (minor) = 38.2 min.

HRMS: m/z $[M+Na]^+$ calcd for $C_{16}H_{13}NaO_4Cl$: 327.0395, 329.0365; found: 327.0396, 329.0364.

m.p. 135–136 °C.

[α]$^{25}_D$ = –8.8 (*c* = 0.23, CH_2Cl_2).

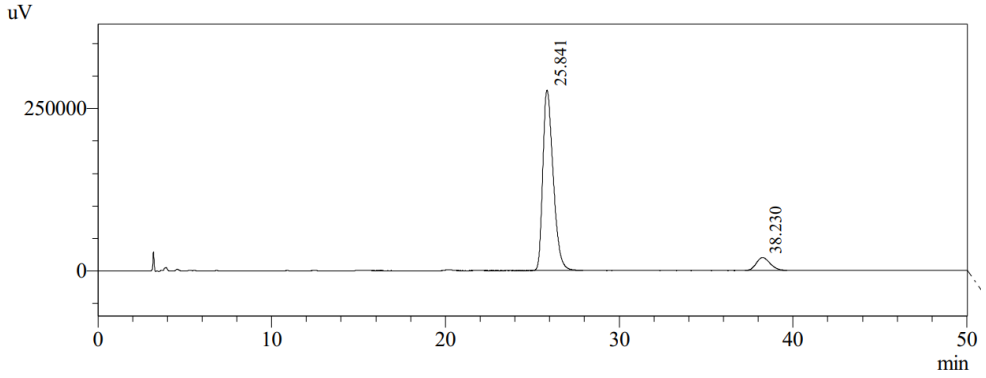
***rac*-3w:**



Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.814	6423332	158265	50.001	58.443
2	38.013	6423097	112539	49.999	41.557
Total		12846429	270804	100.000	100.000

***cat*-3w:**



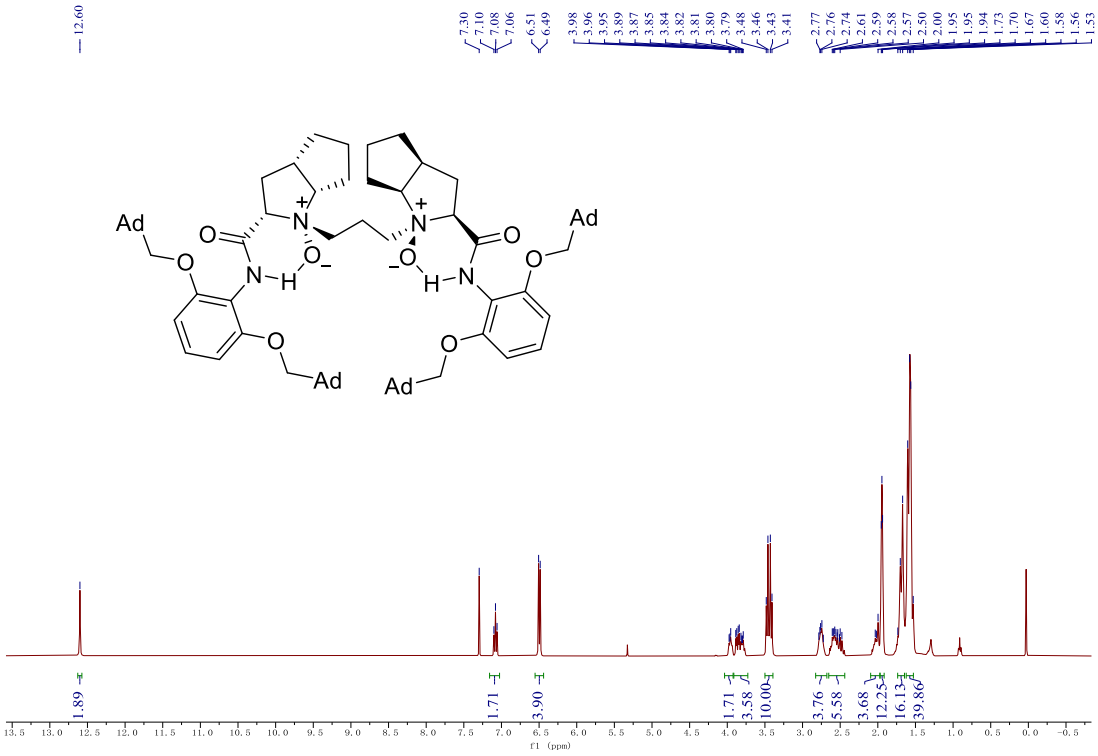
Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.841	11535635	278117	91.320	93.315
2	38.230	1096444	19923	8.680	6.685
Total		12632078	298040	100.000	100.000

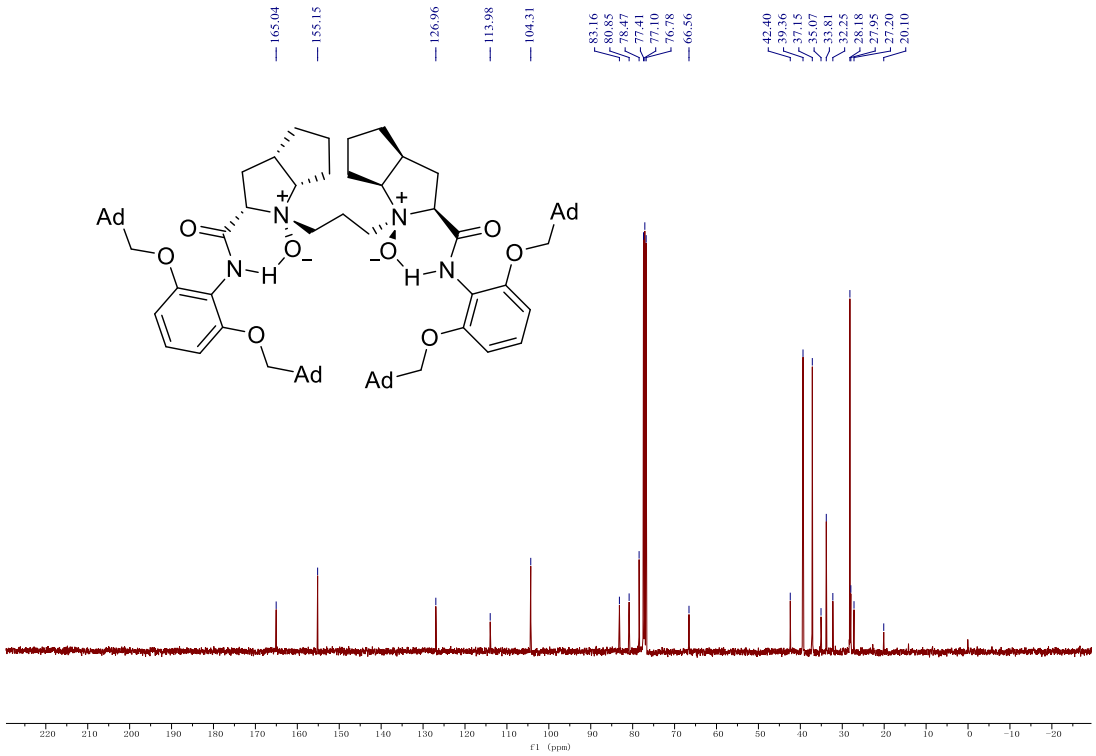
4. References

1. J. Huang, X. Liu, Y. Wen, B. Qin and X. Feng, *J. Org. Chem.*, 2007, **72**, 204-208.
2. X.-W. Liang, Y. Zhao, X.-G. Si, M.-M. Xu, J.-H. Tan, Z.-M. Zhang, C.-G. Zheng, C. Zheng and Q. Cai, *Angew. Chem. Int. Ed.*, 2019, **58**, 14562-14567.
3. Y. Lu, M.-M. Xu, Z.-M. Zhang, J. Zhang and Q. Cai, *Angew. Chem. Int. Ed.*, 2021, **60**, 26610-26615.

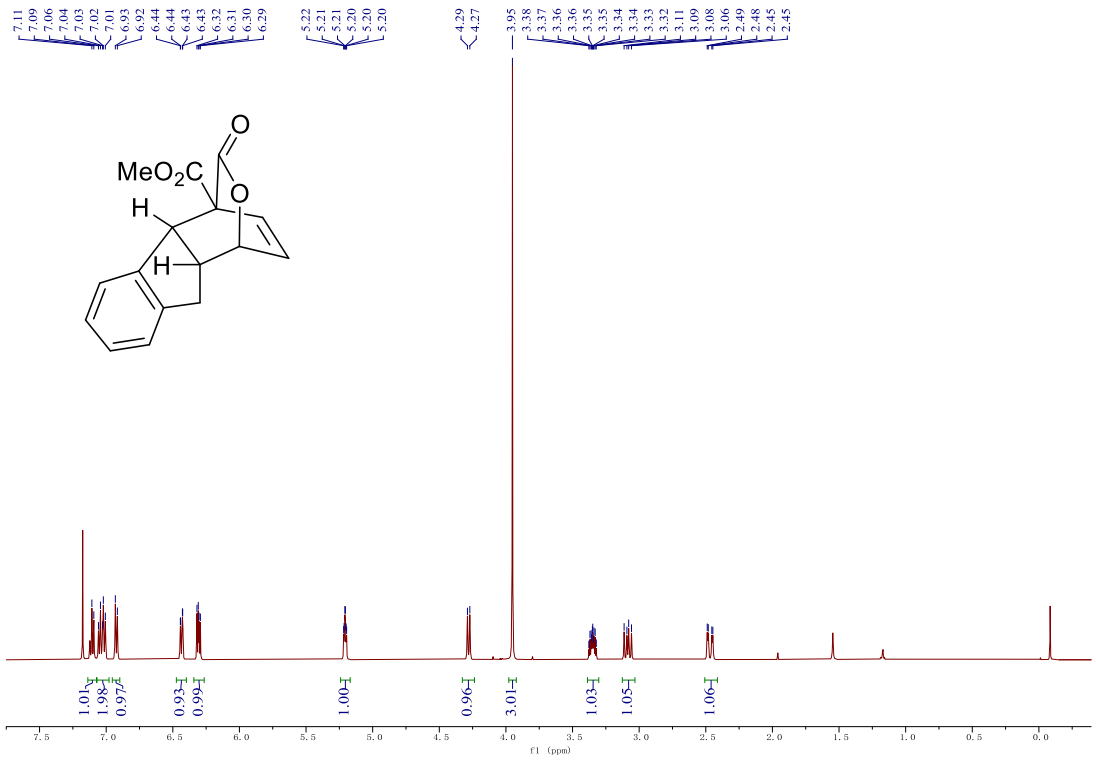
5. NMR Spectra



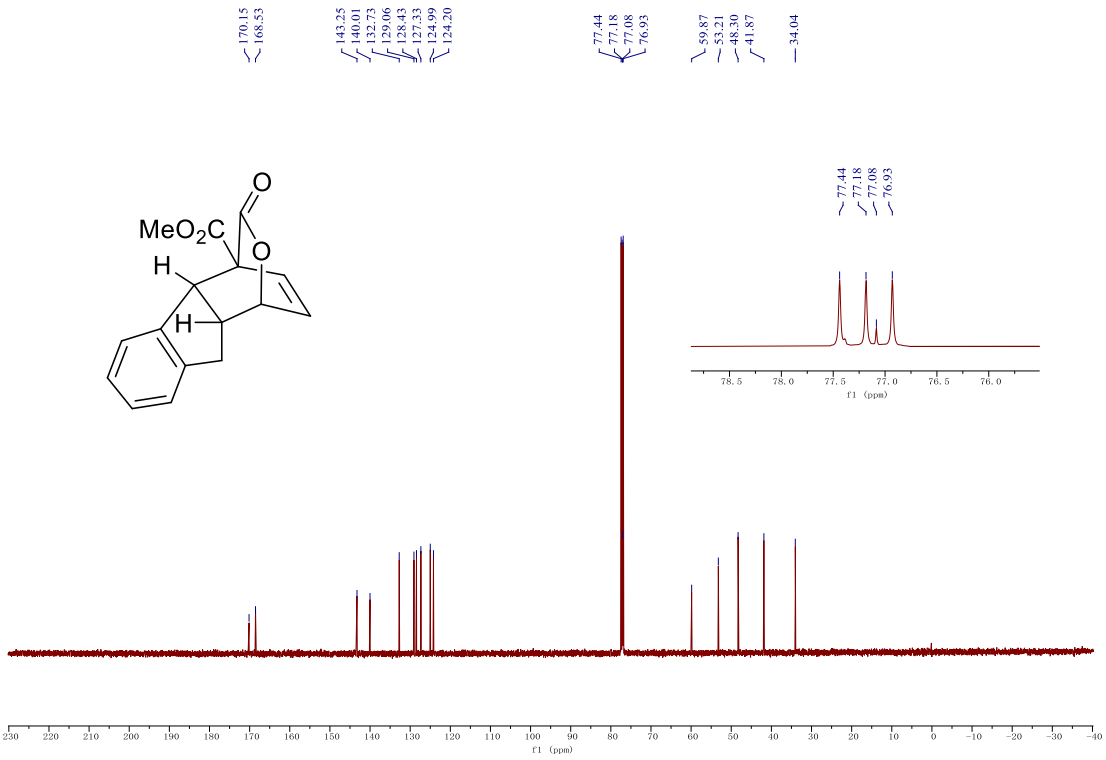
^{1}H NMR of **L_3-Ra(OCH_2Ad)$_2$**



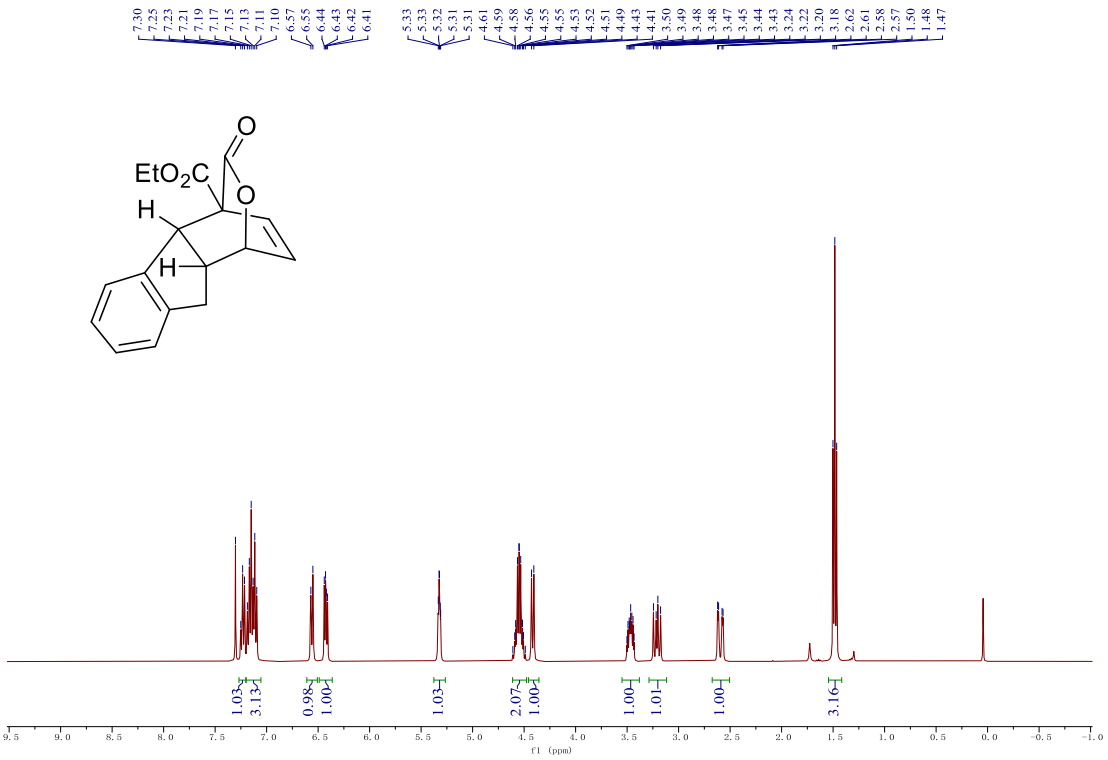
^{13}C NMR of **L_3-Ra(OCH_2Ad)$_2$**



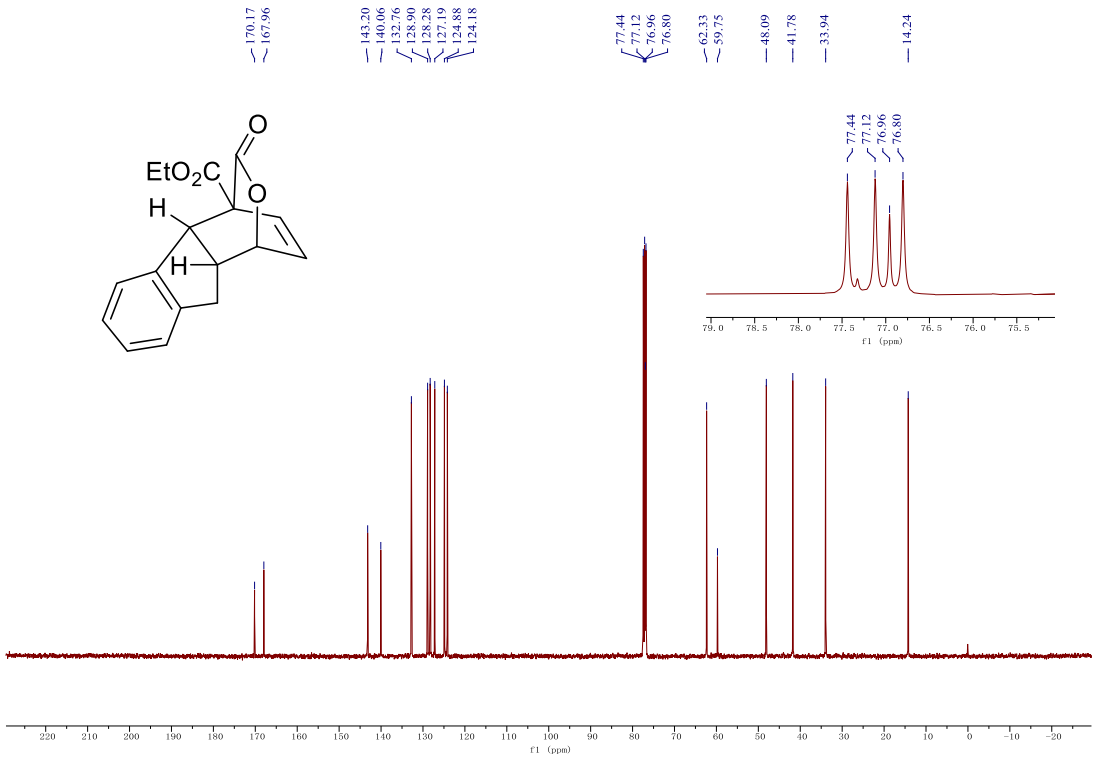
^{1}H NMR of Compound **3a**



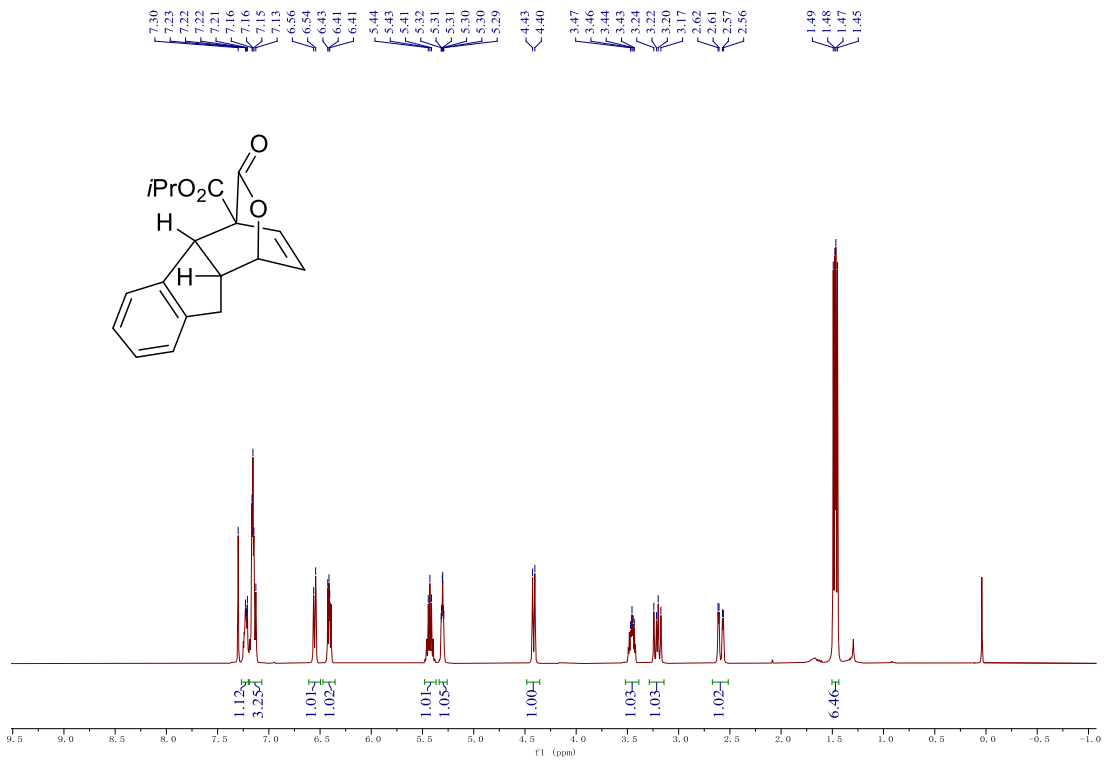
^{13}C NMR of Compound **3a**



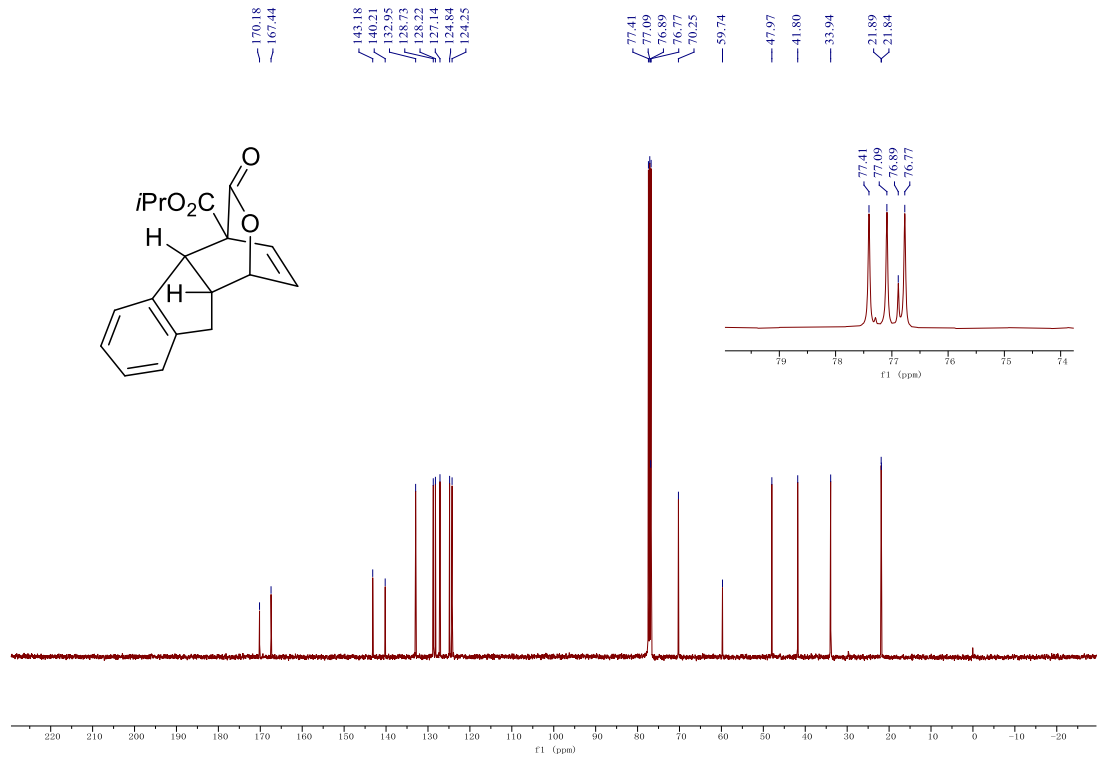
^{1}H NMR of Compound **3b**



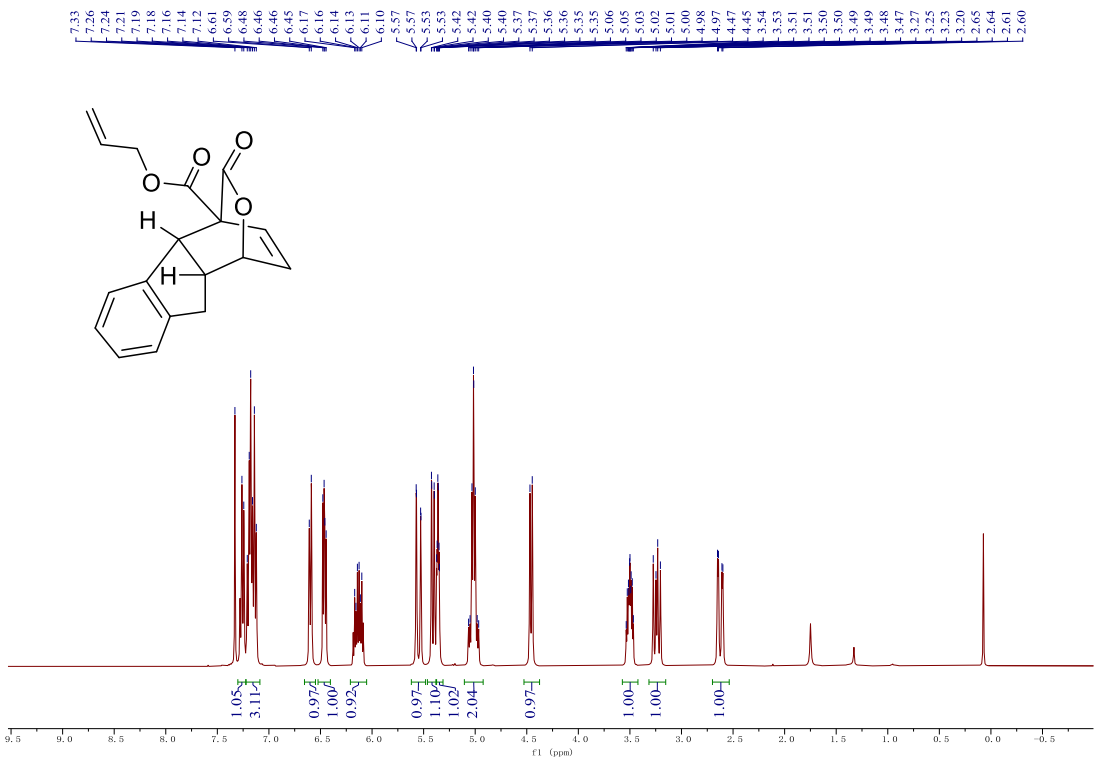
^{13}C NMR of Compound **3b**



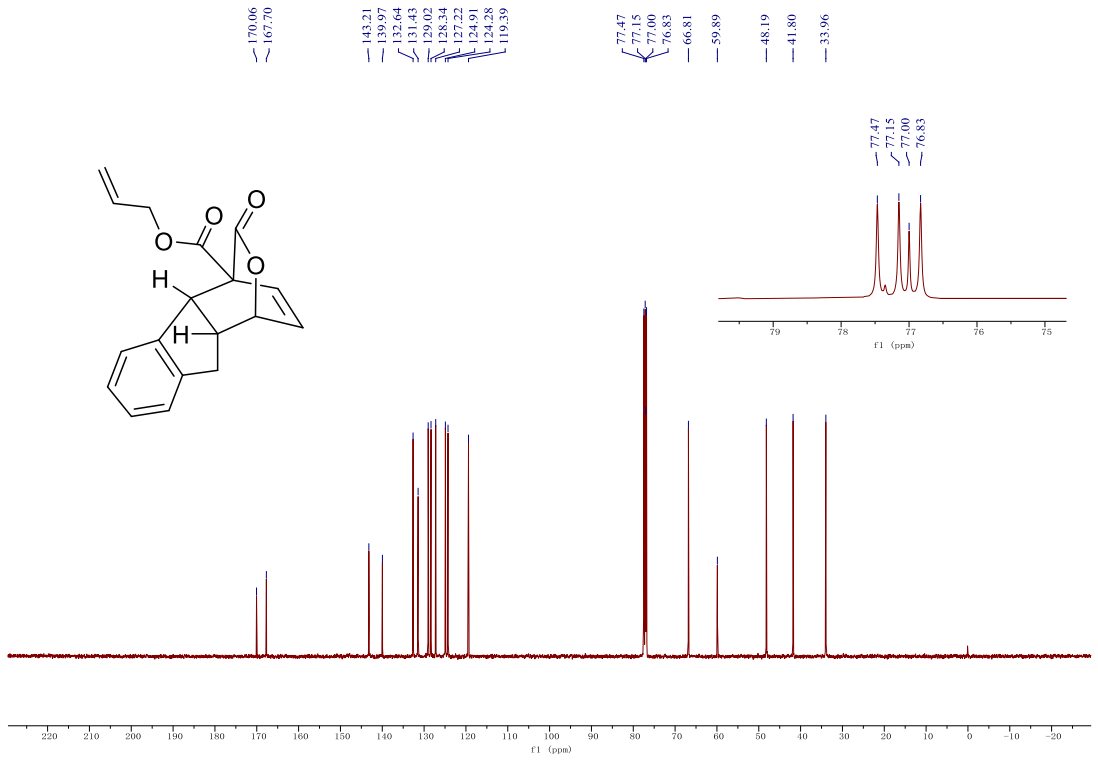
^{1}H NMR of Compound **3c**



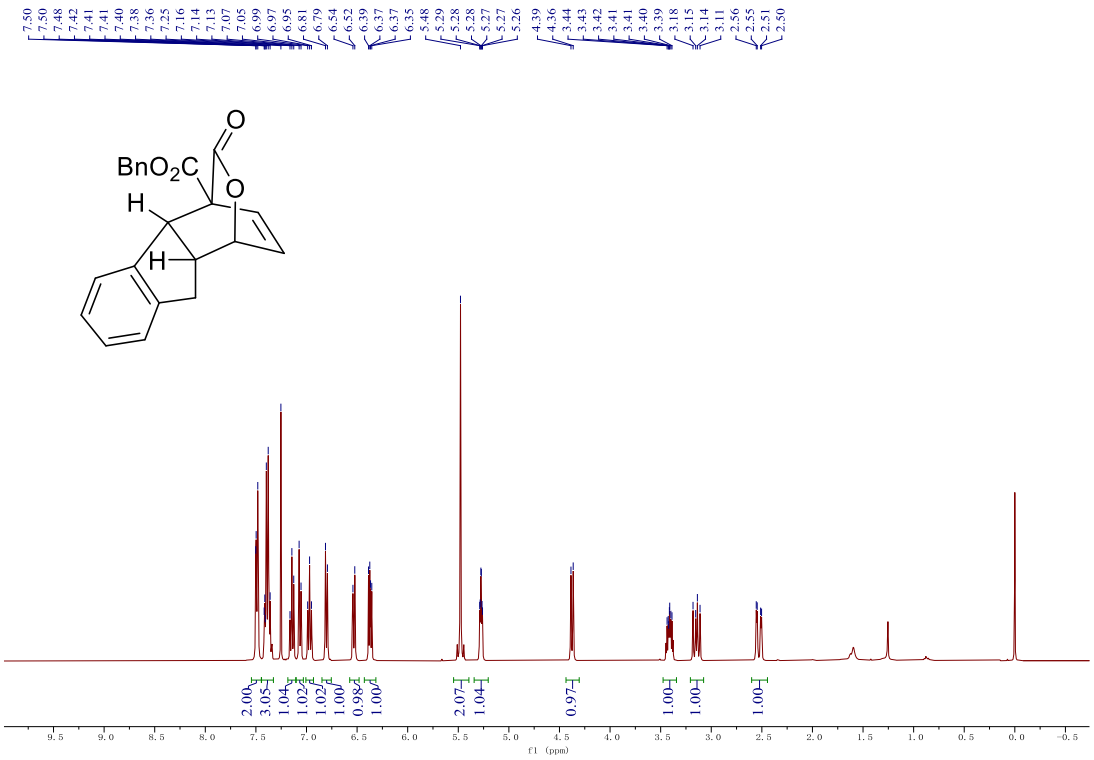
^{13}C NMR of Compound **3c**



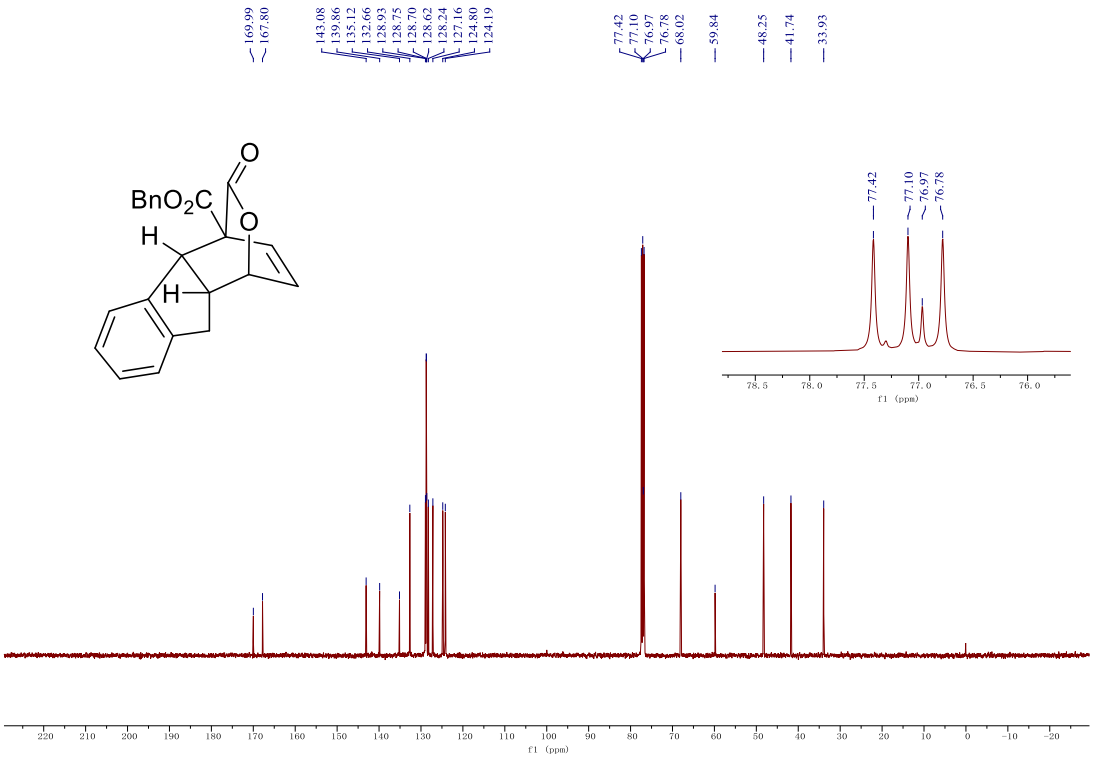
^{1}H NMR of Compound **3d**



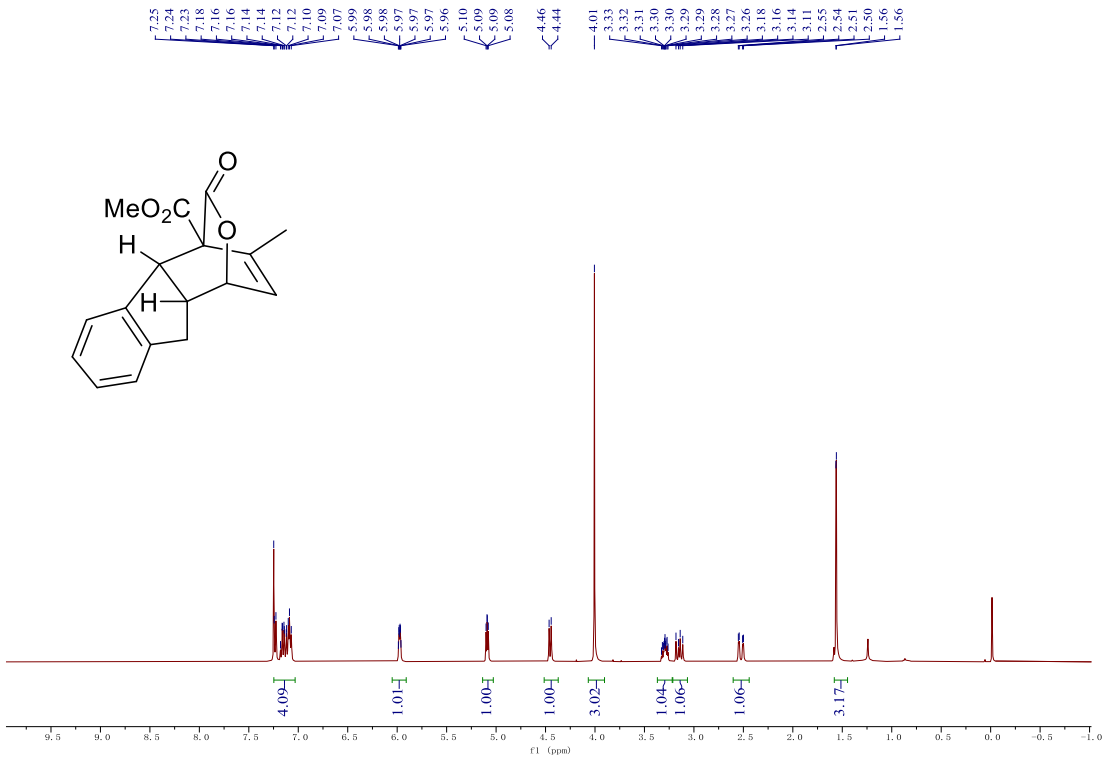
^{13}C NMR of Compound **3d**



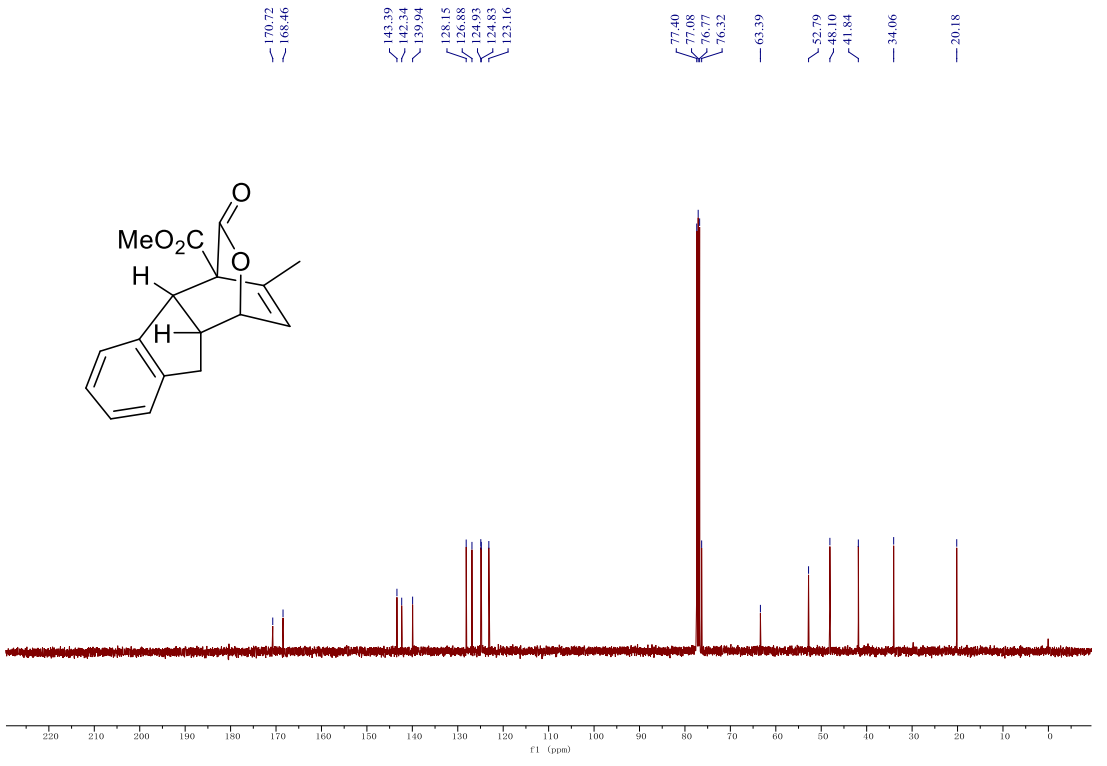
^{1}H NMR of Compound **3e**



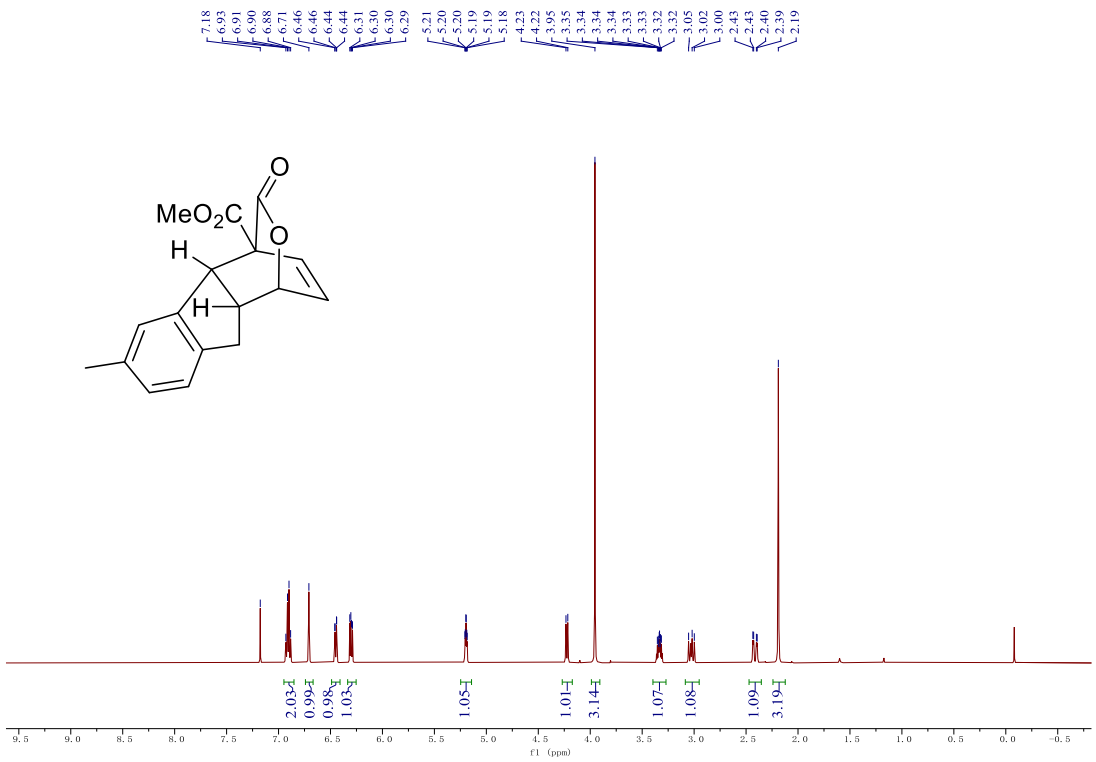
^{13}C NMR of Compound **3e**



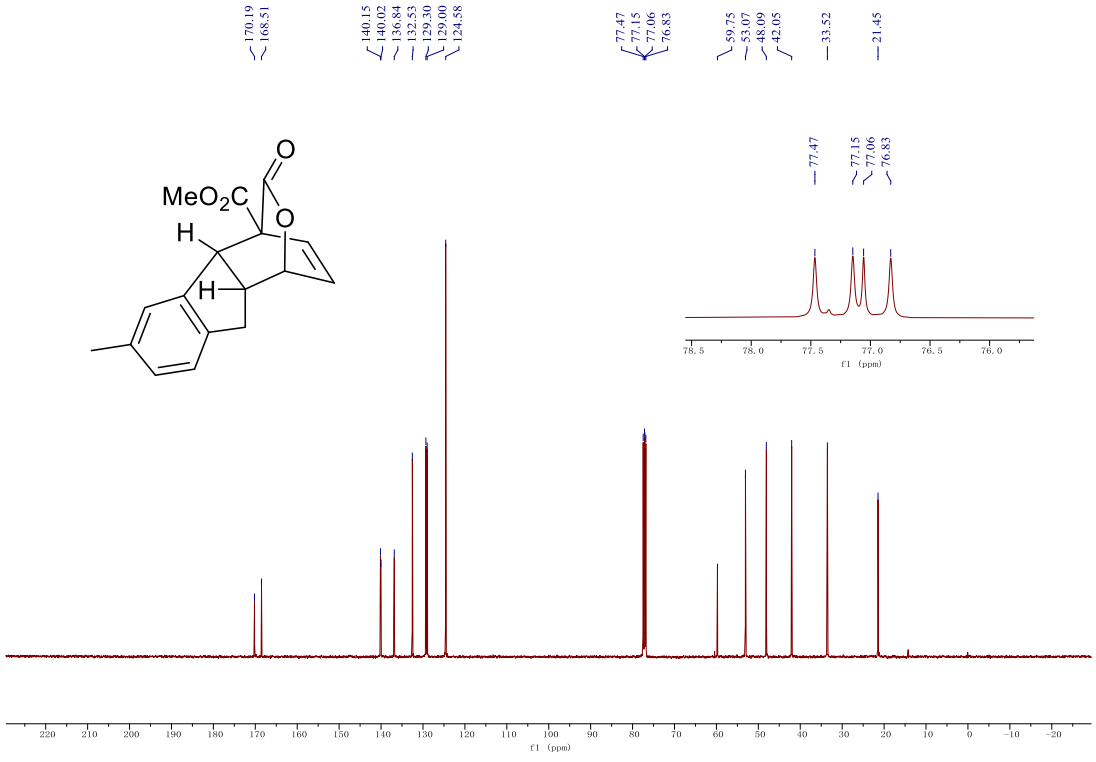
^{1}H NMR of Compound **3f**



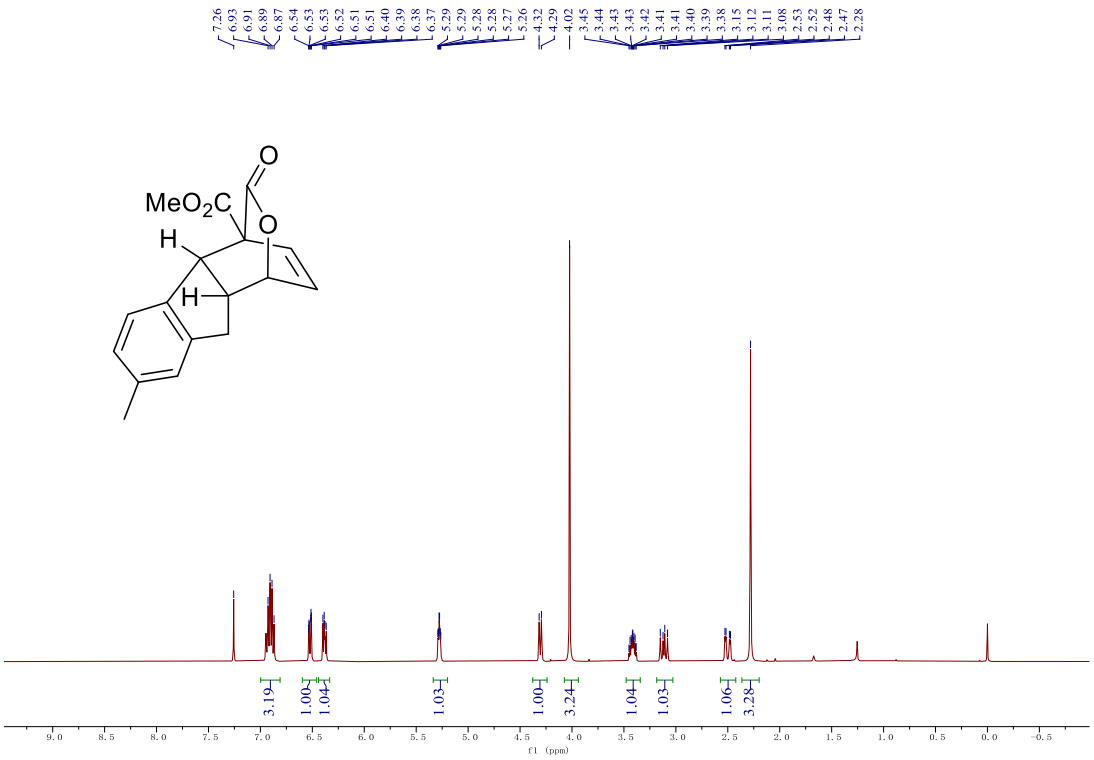
^{13}C NMR of Compound **3f**



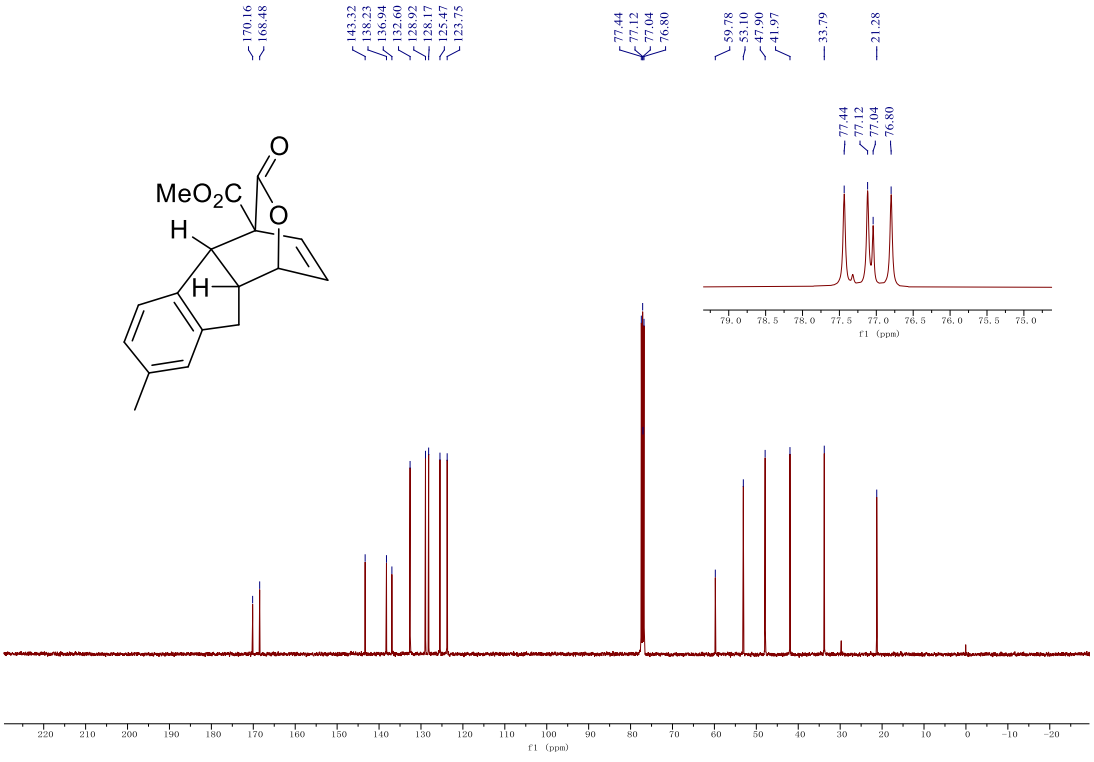
^{1}H NMR of Compound **3i**



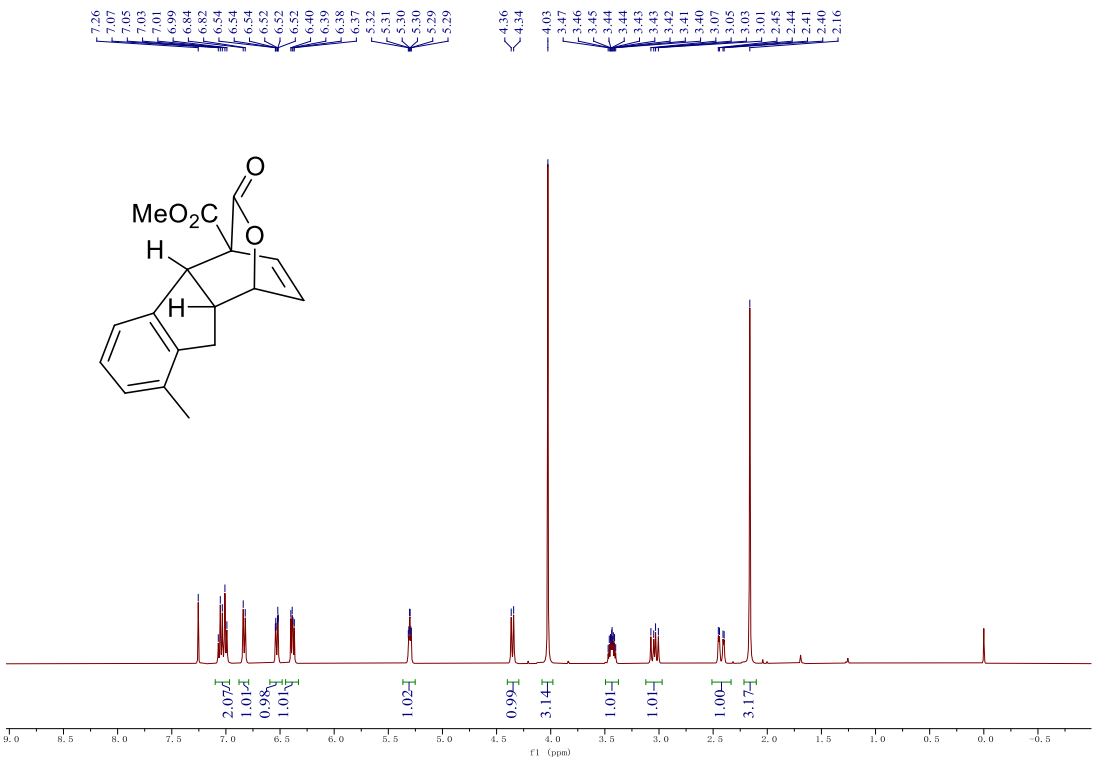
^{13}C NMR of Compound **3i**



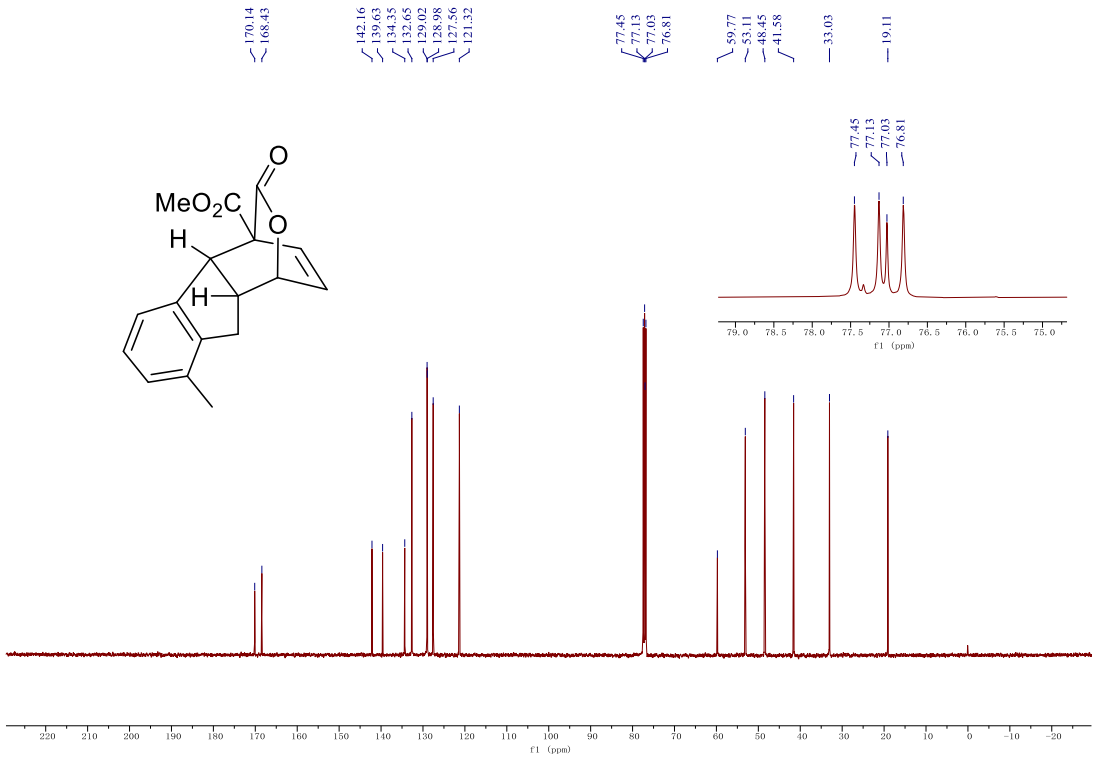
^{1}H NMR of Compound **3j**



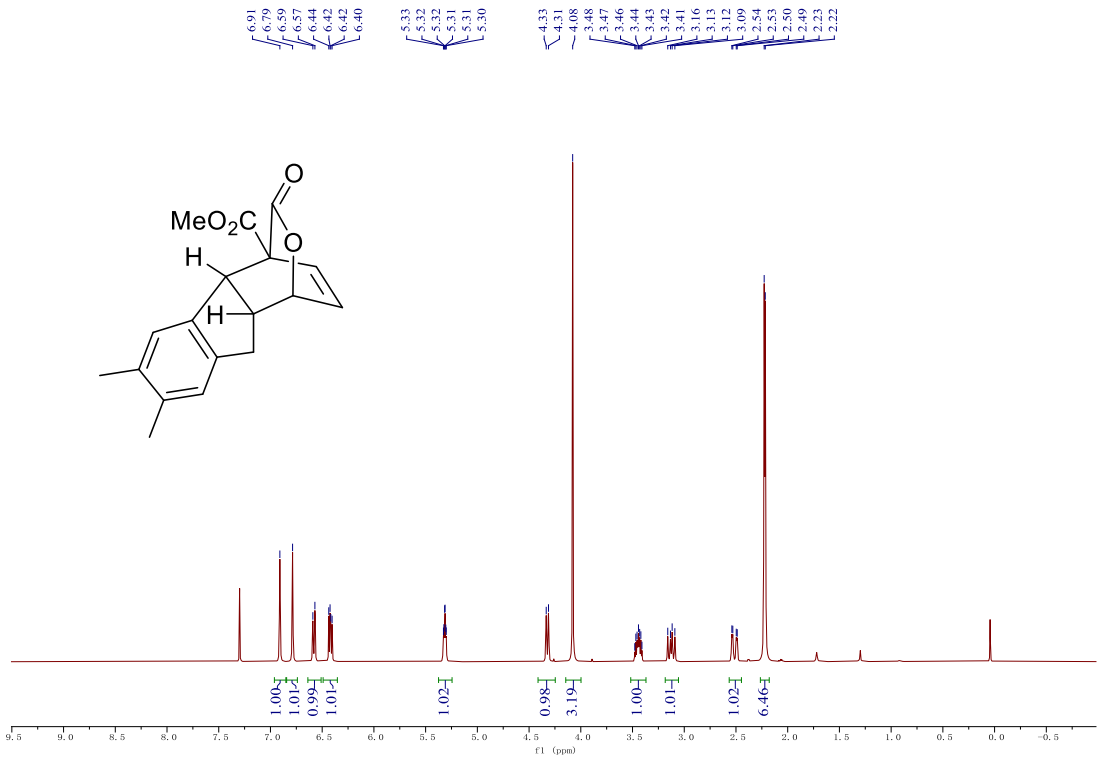
^{13}C NMR of Compound **3j**



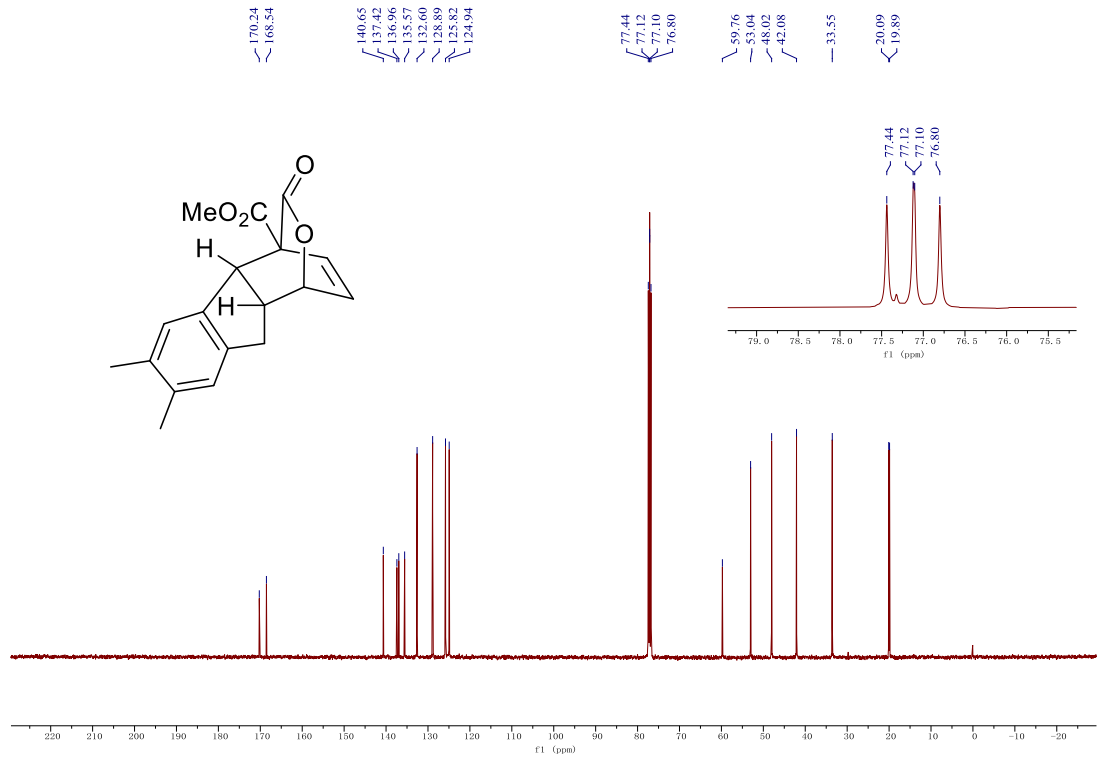
^{1}H NMR of Compound **3k**



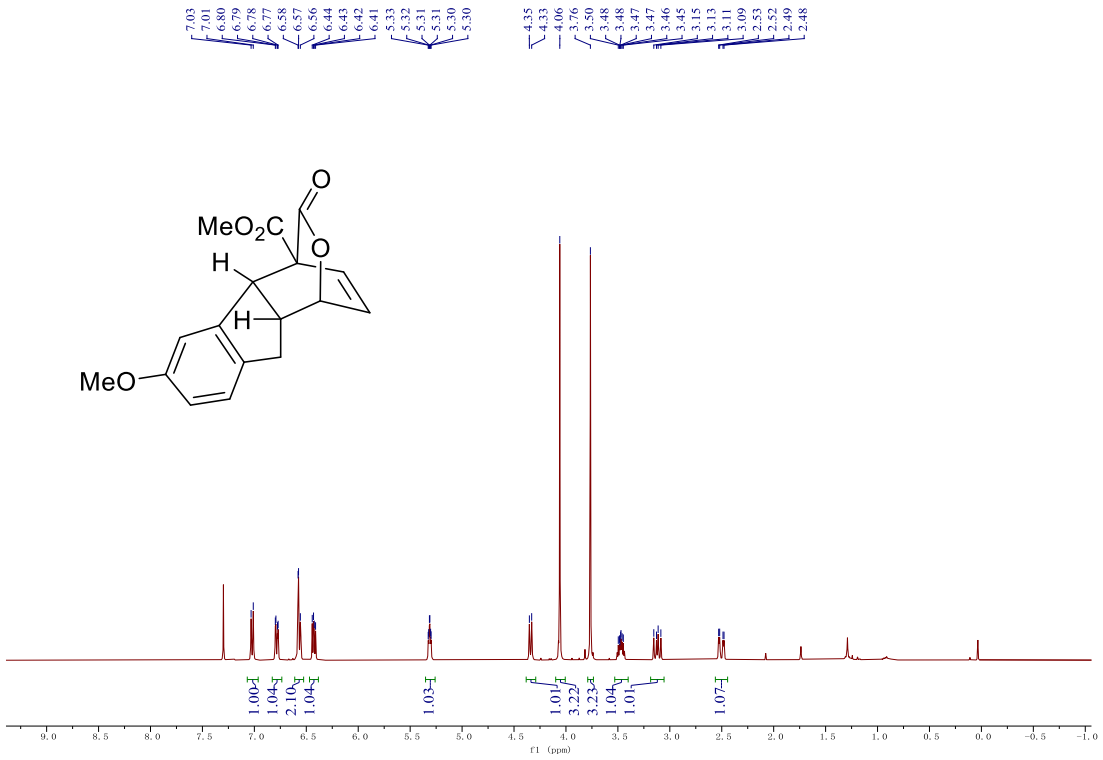
^{13}C NMR of Compound **3k**



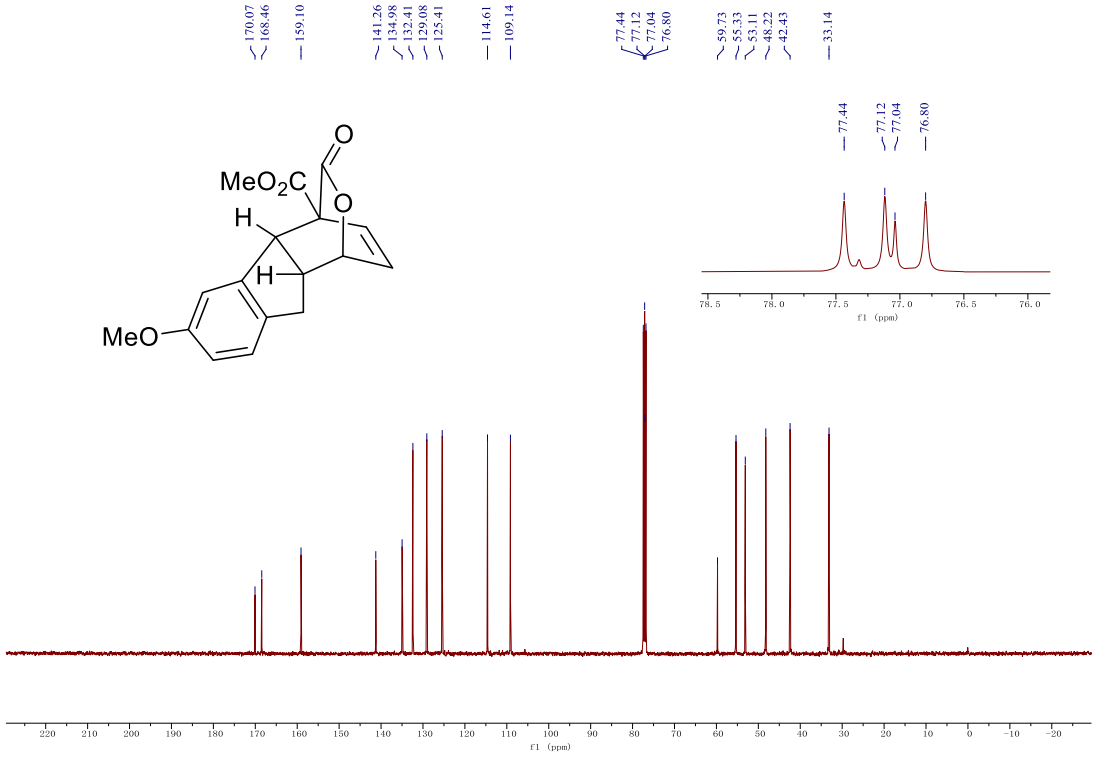
^{1}H NMR of Compound **3l**



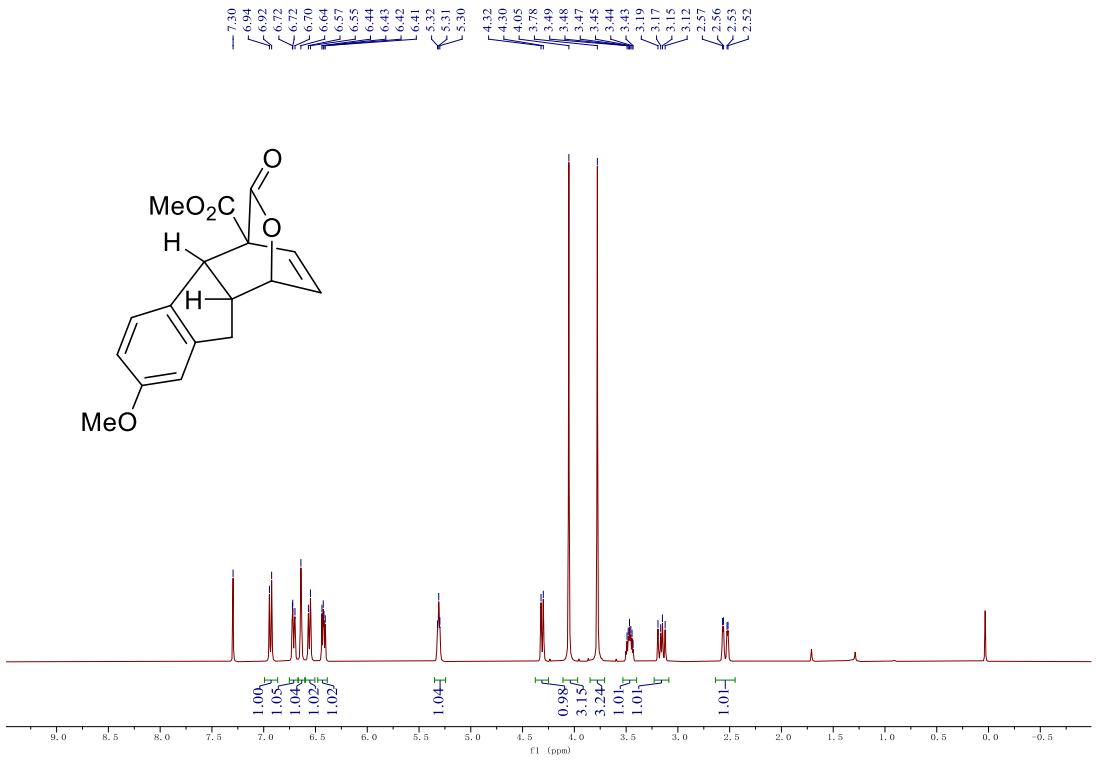
^{13}C NMR of Compound **3l**



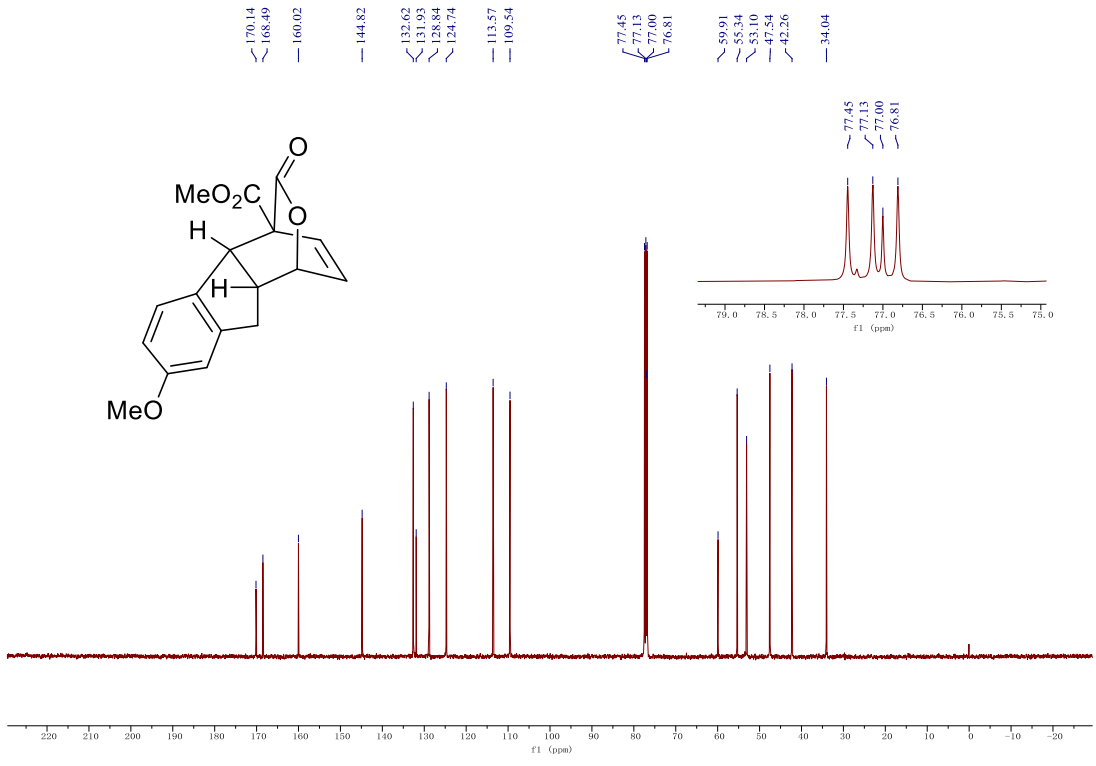
^{1}H NMR of Compound **3m**



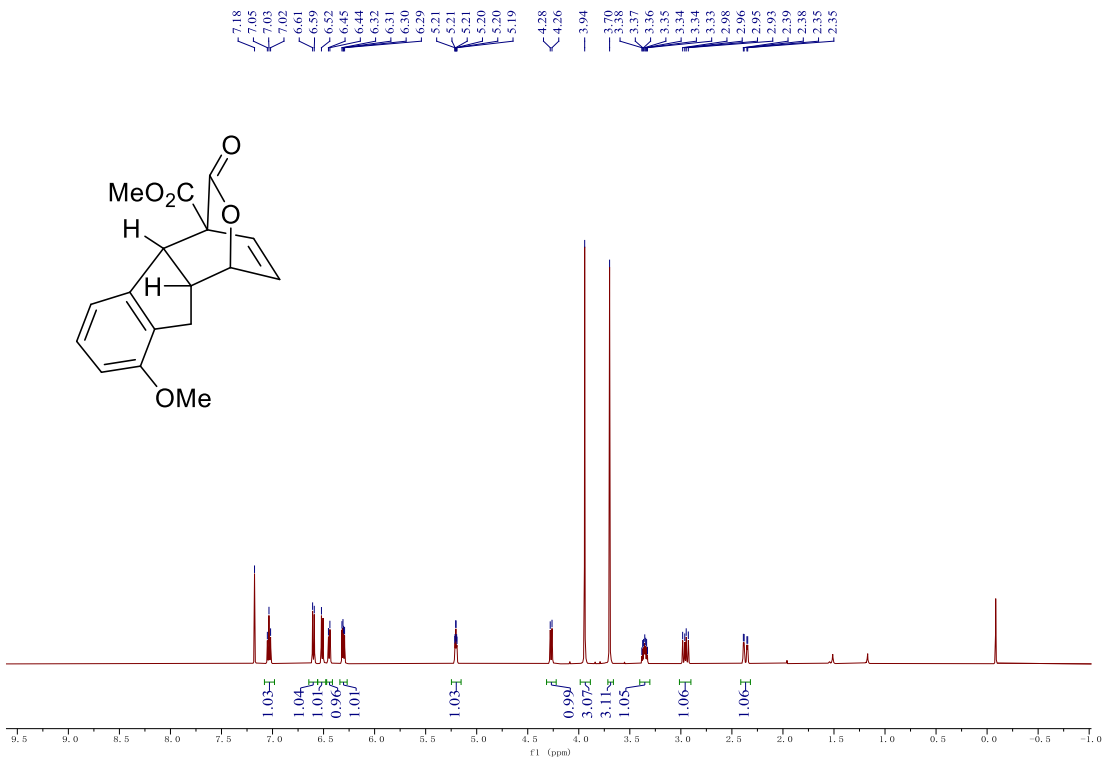
^{13}C NMR of Compound **3m**



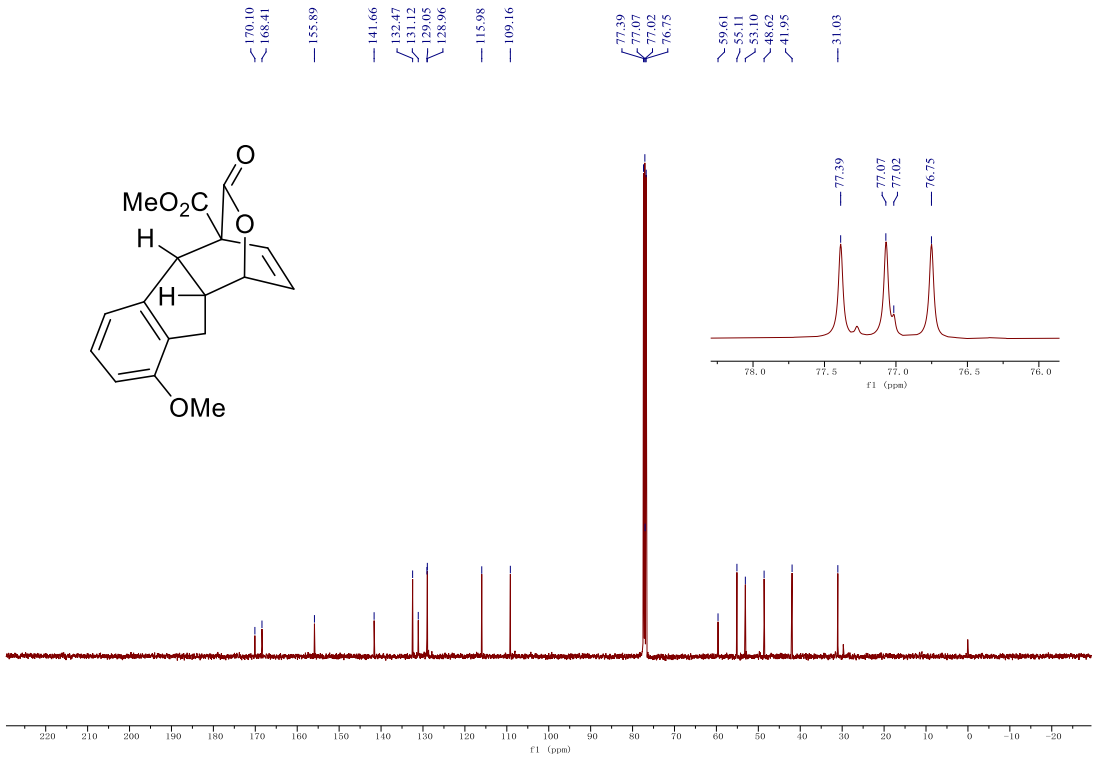
^{1}H NMR of Compound **3n**



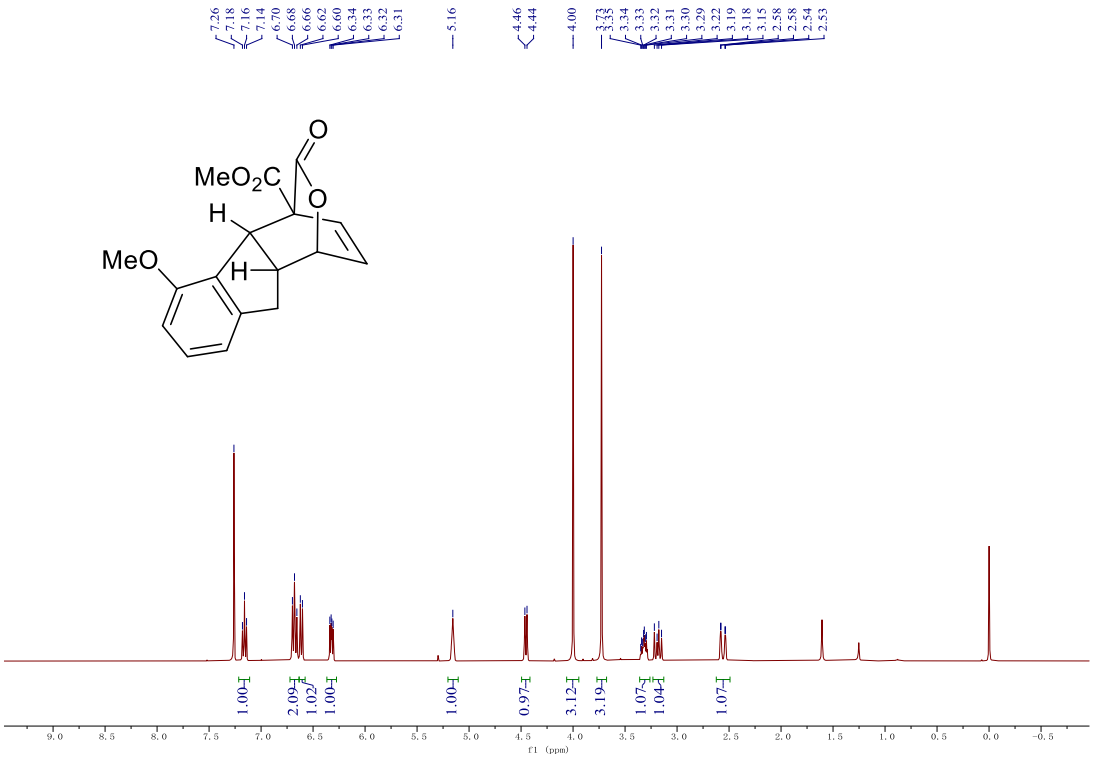
^{13}C NMR of Compound **3n**



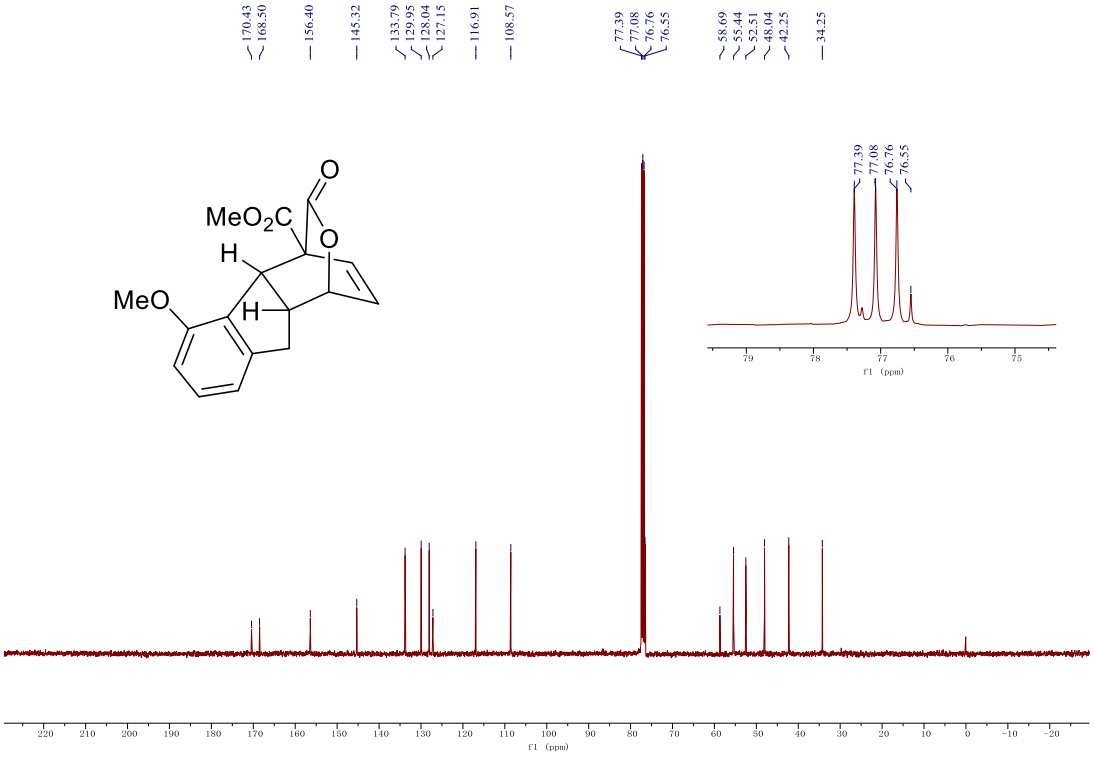
^{1}H NMR of Compound **3o**



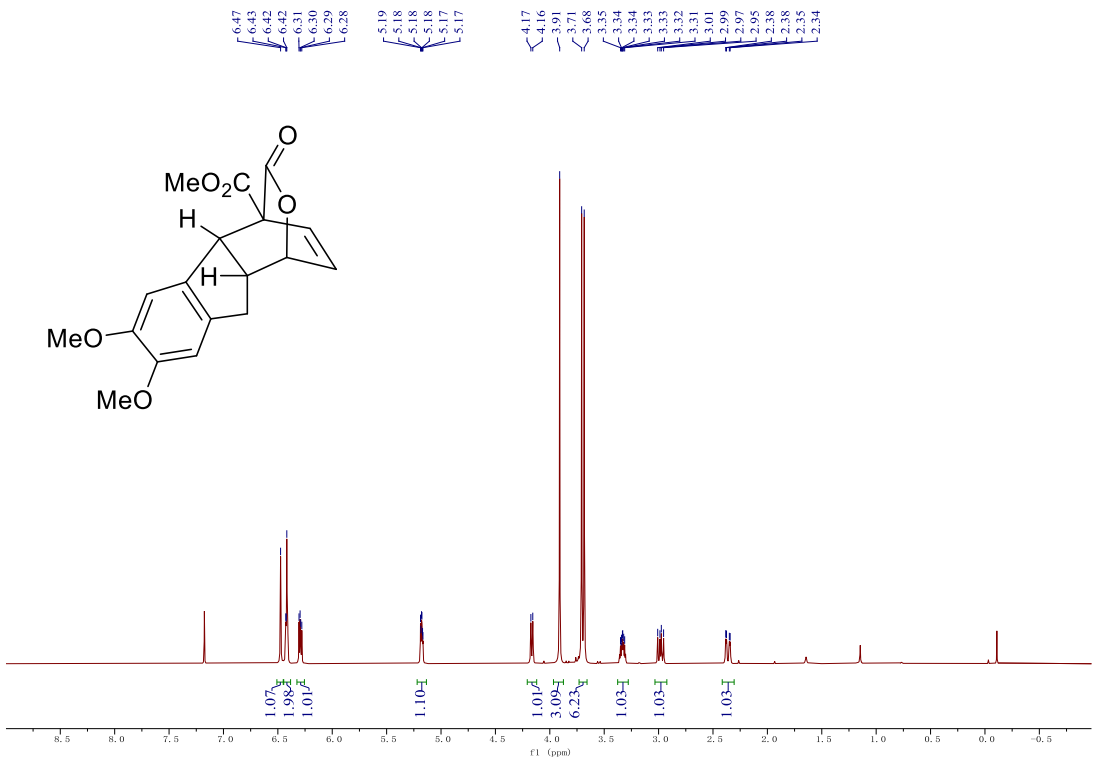
^{13}C NMR of Compound **3o**



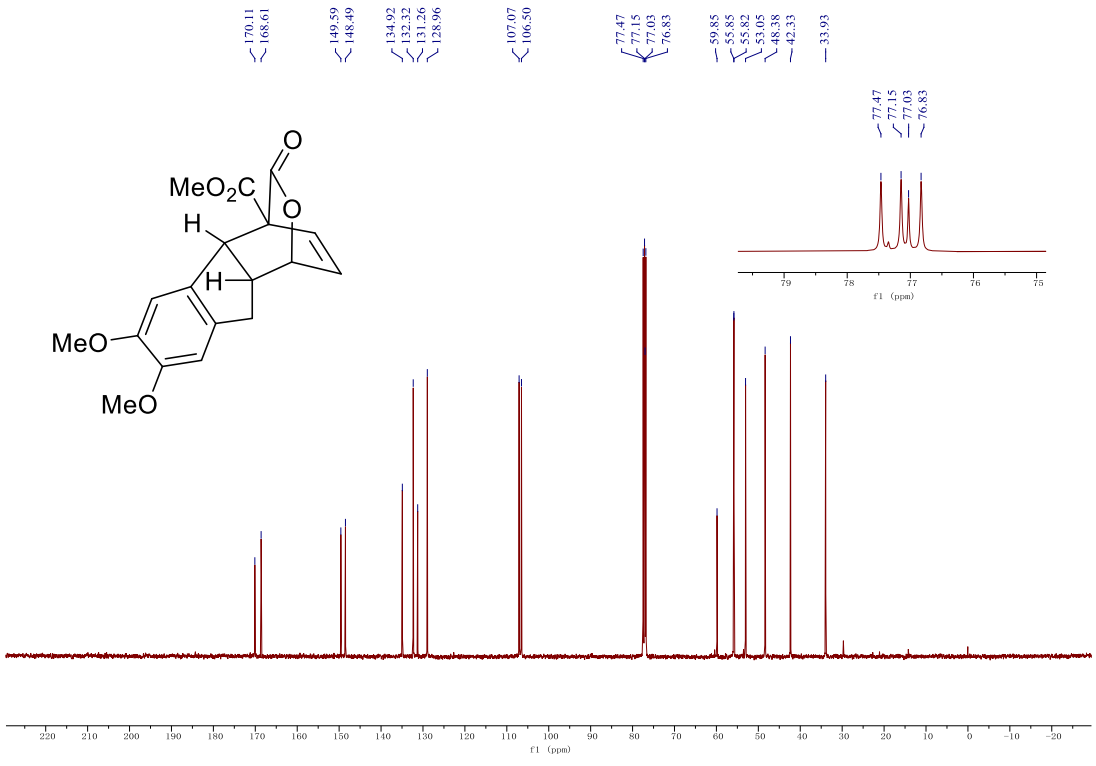
^{1}H NMR of Compound **3p**



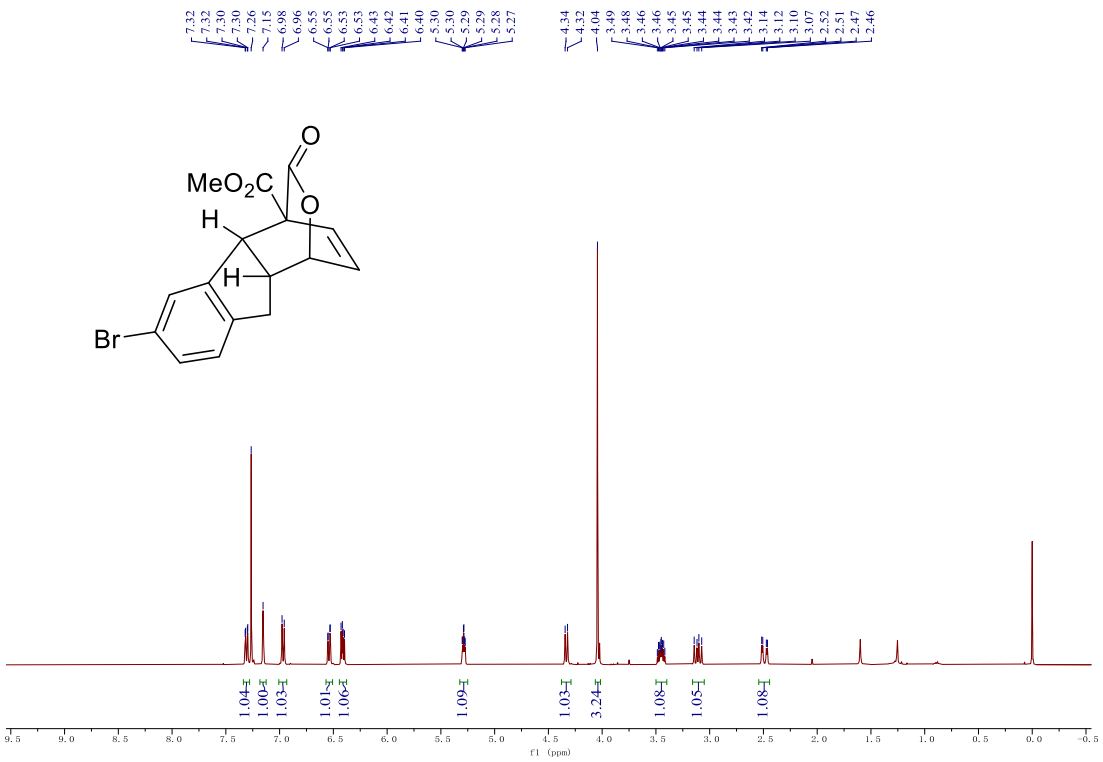
^{13}C NMR of Compound **3p**



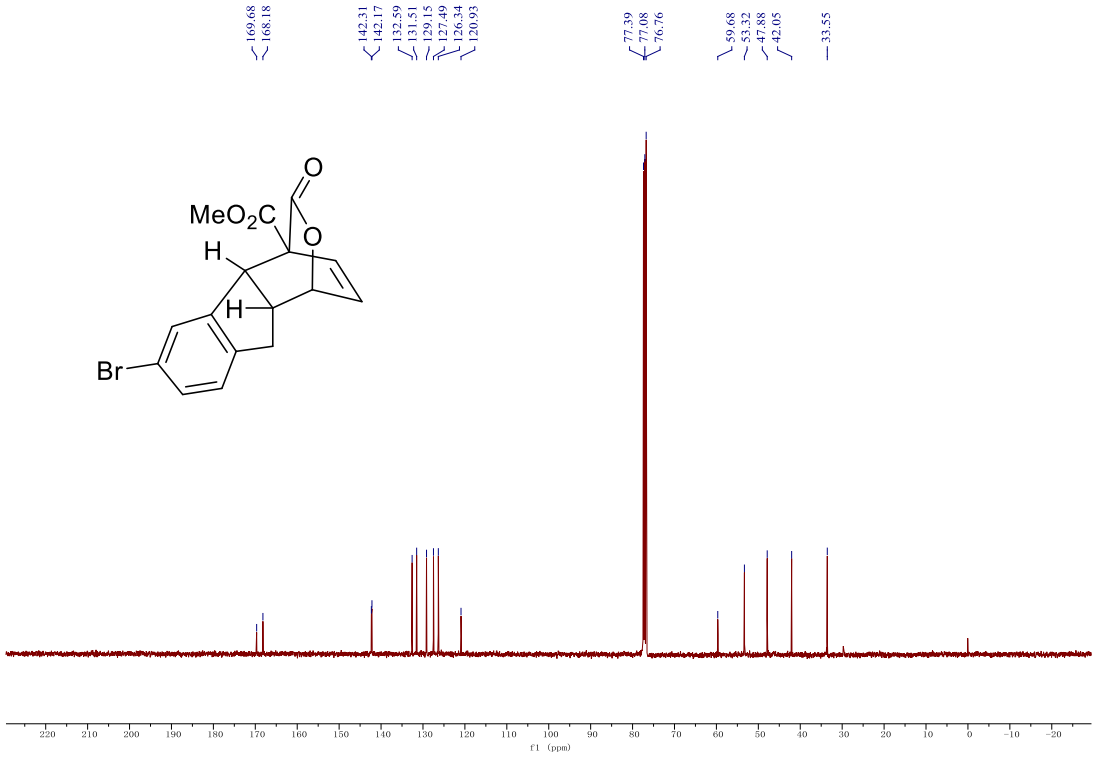
^{1}H NMR of Compound **3q**



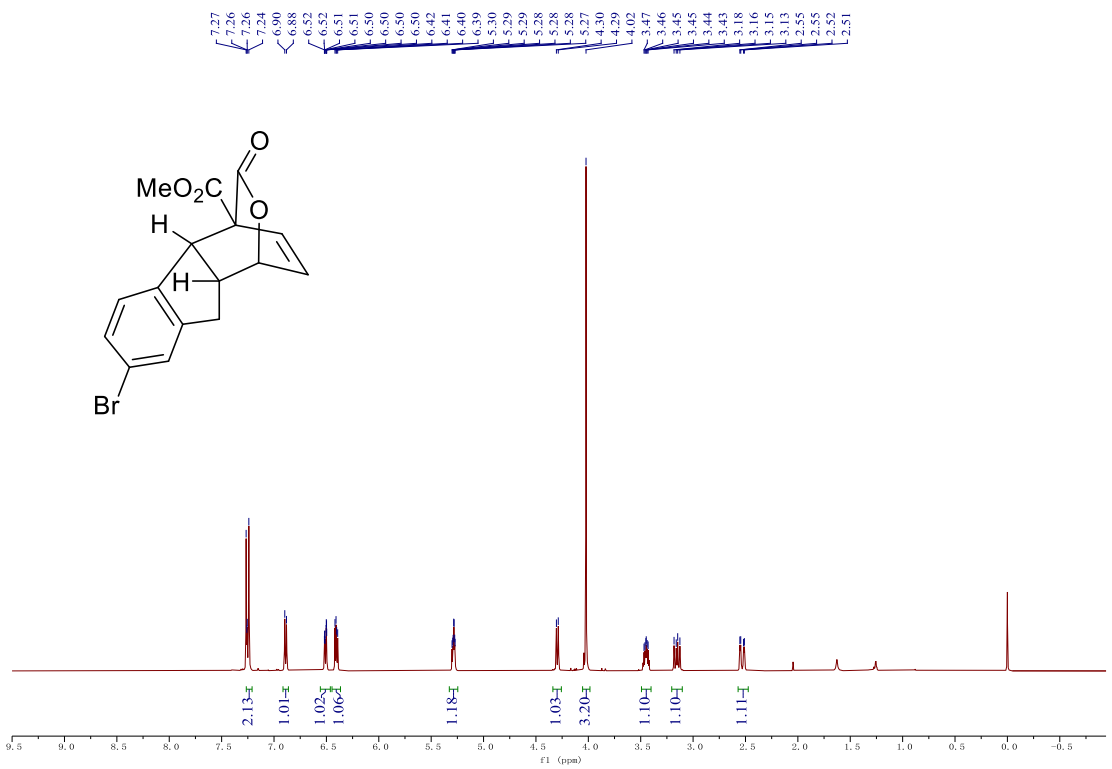
^{13}C NMR of Compound **3q**



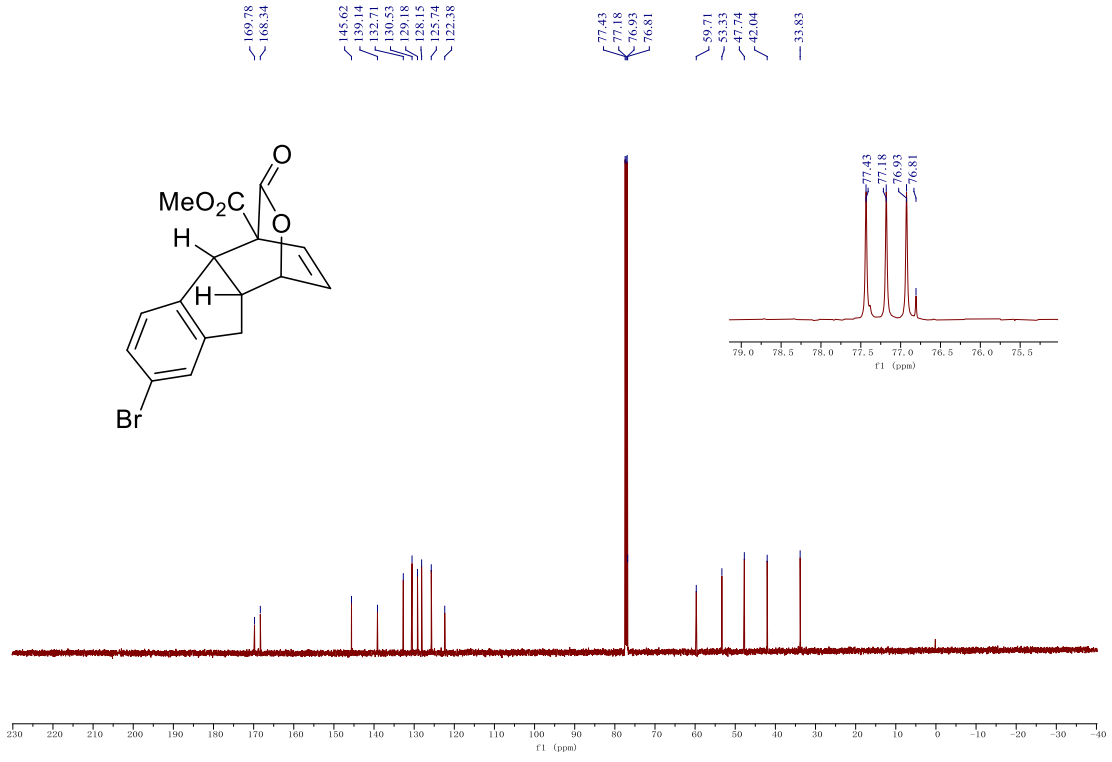
^{1}H NMR of Compound **3r**



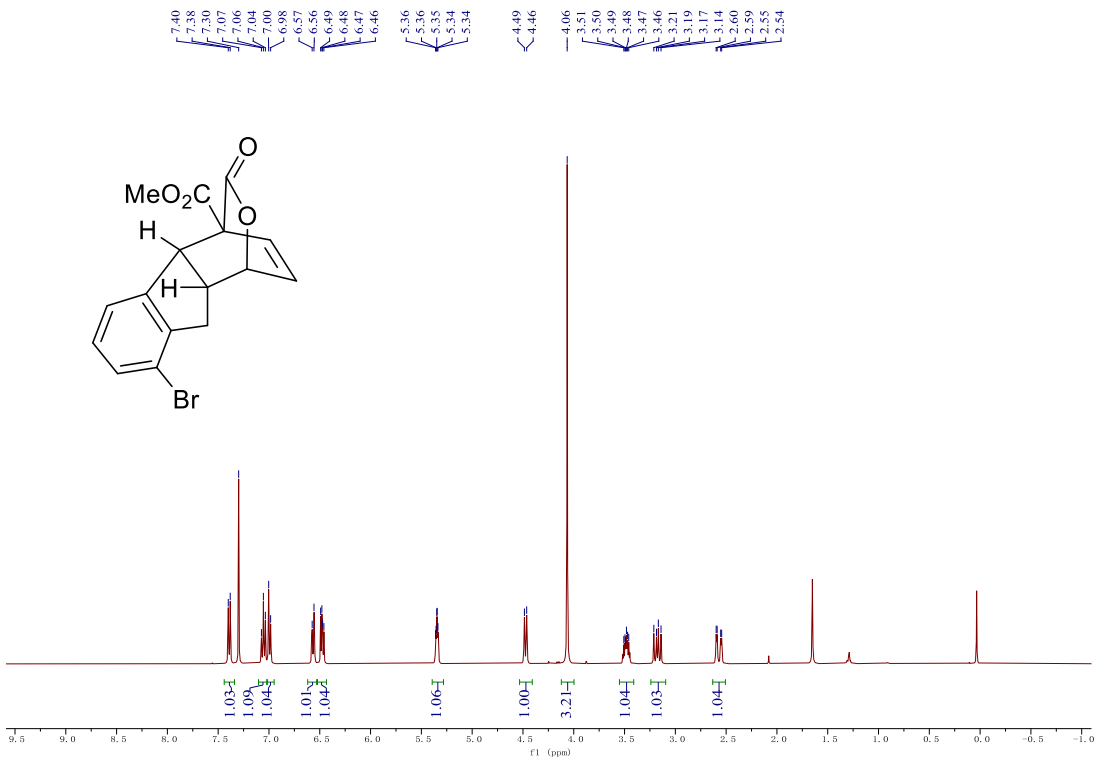
^{13}C NMR of Compound **3r**



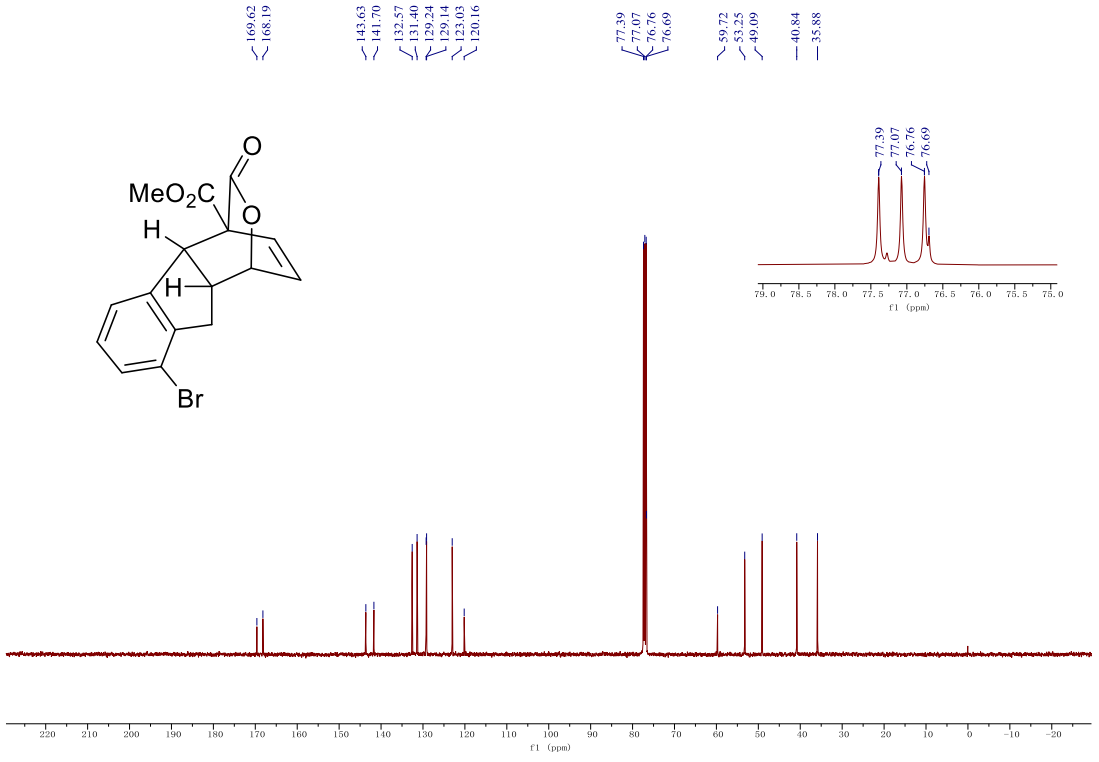
^{1}H NMR of Compound **3s**



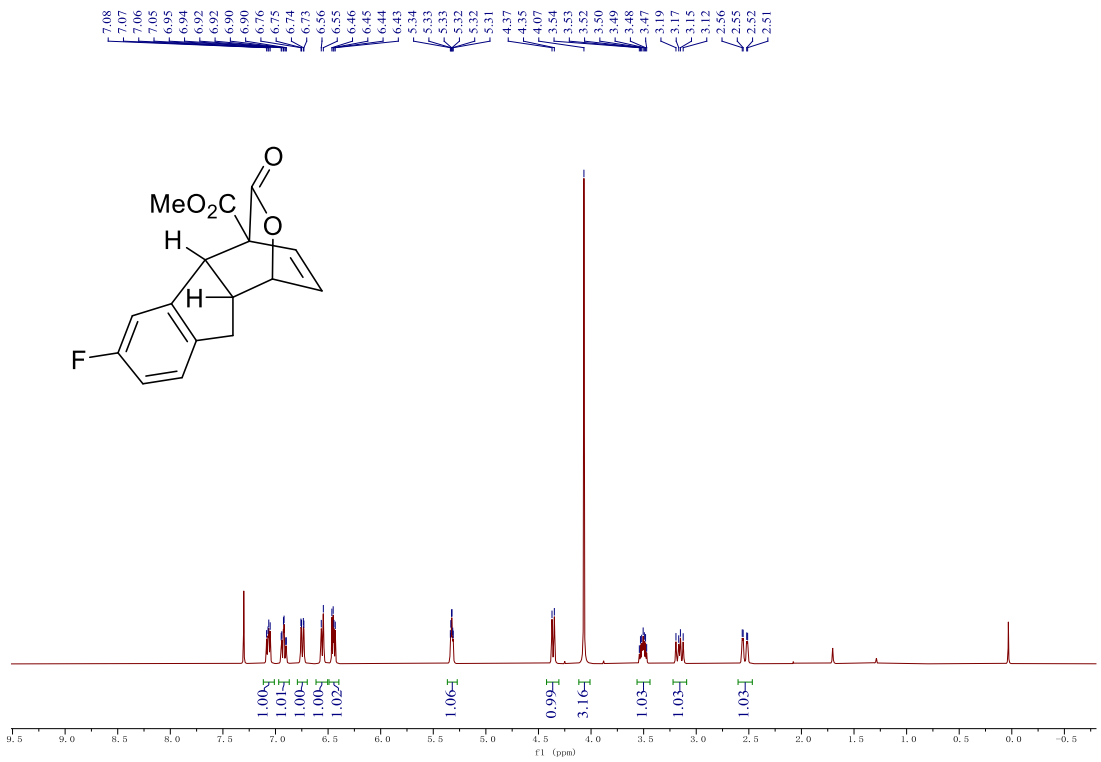
^{13}C NMR of Compound **3s**



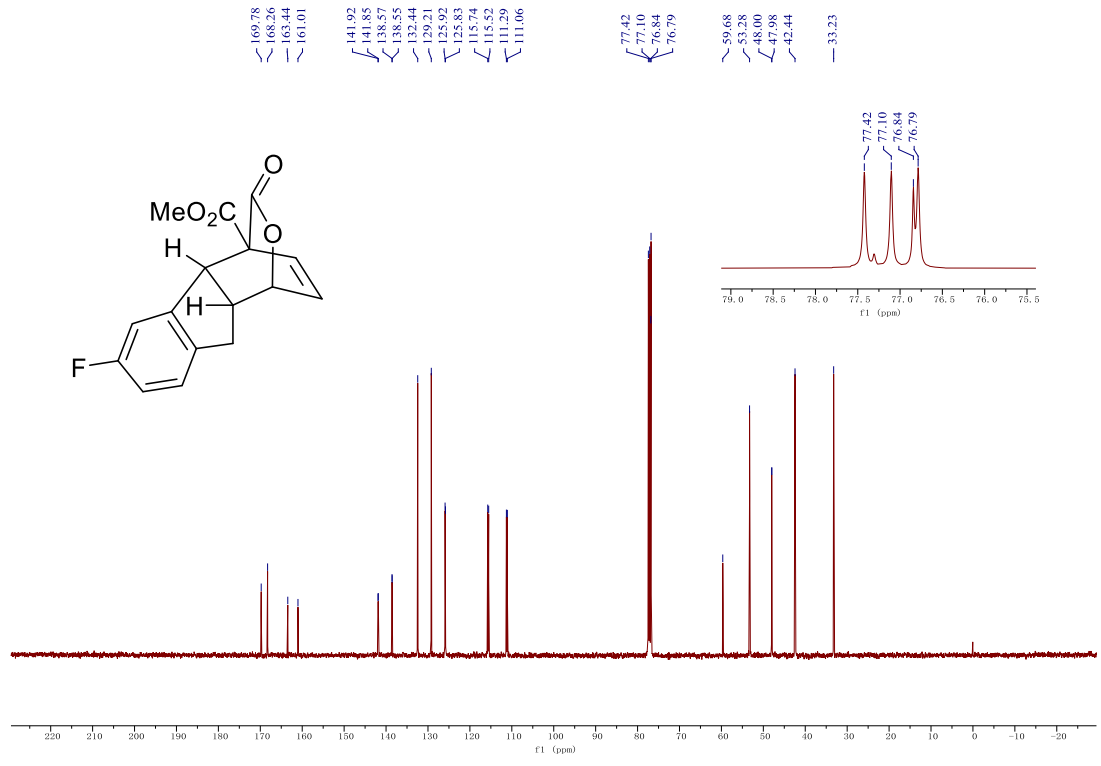
^{1}H NMR of Compound **3t**



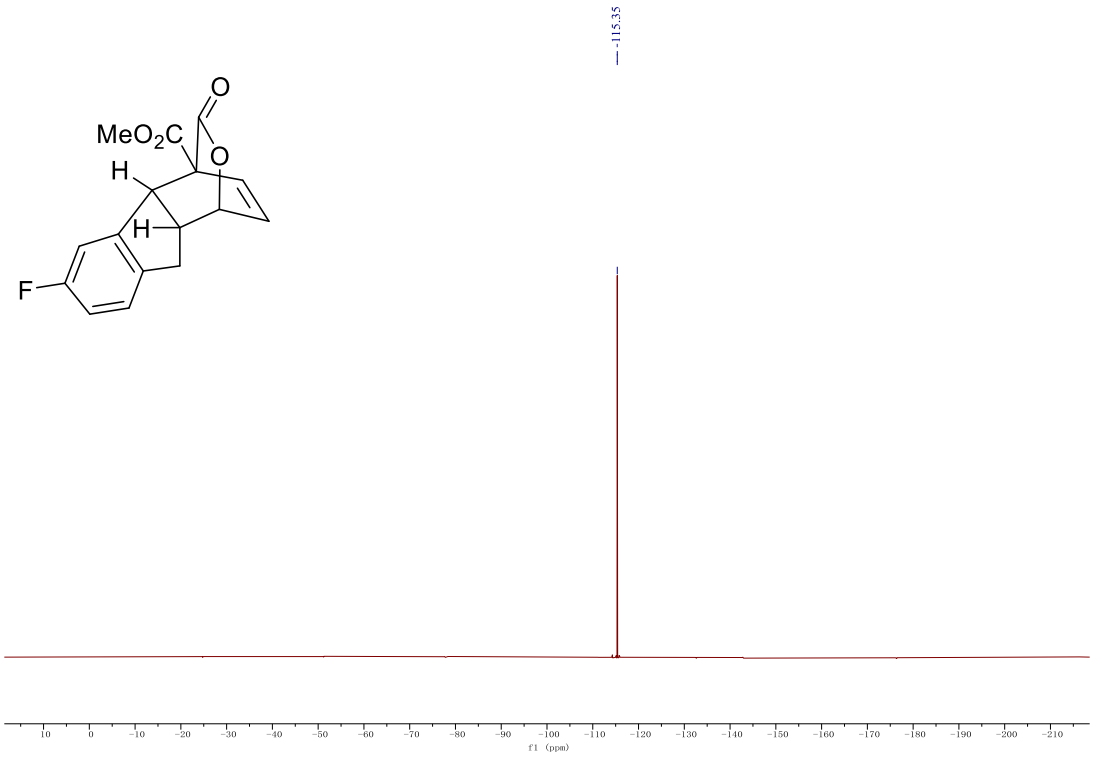
^{13}C NMR of Compound **3t**



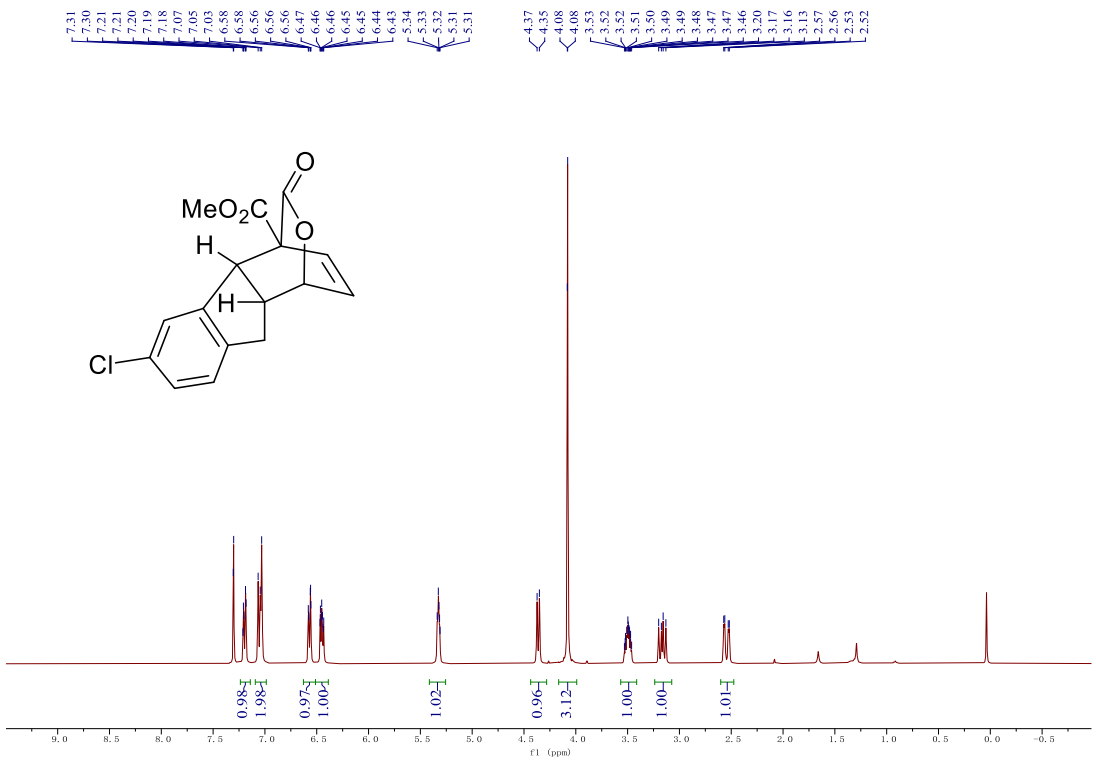
^{1}H NMR of Compound **3u**



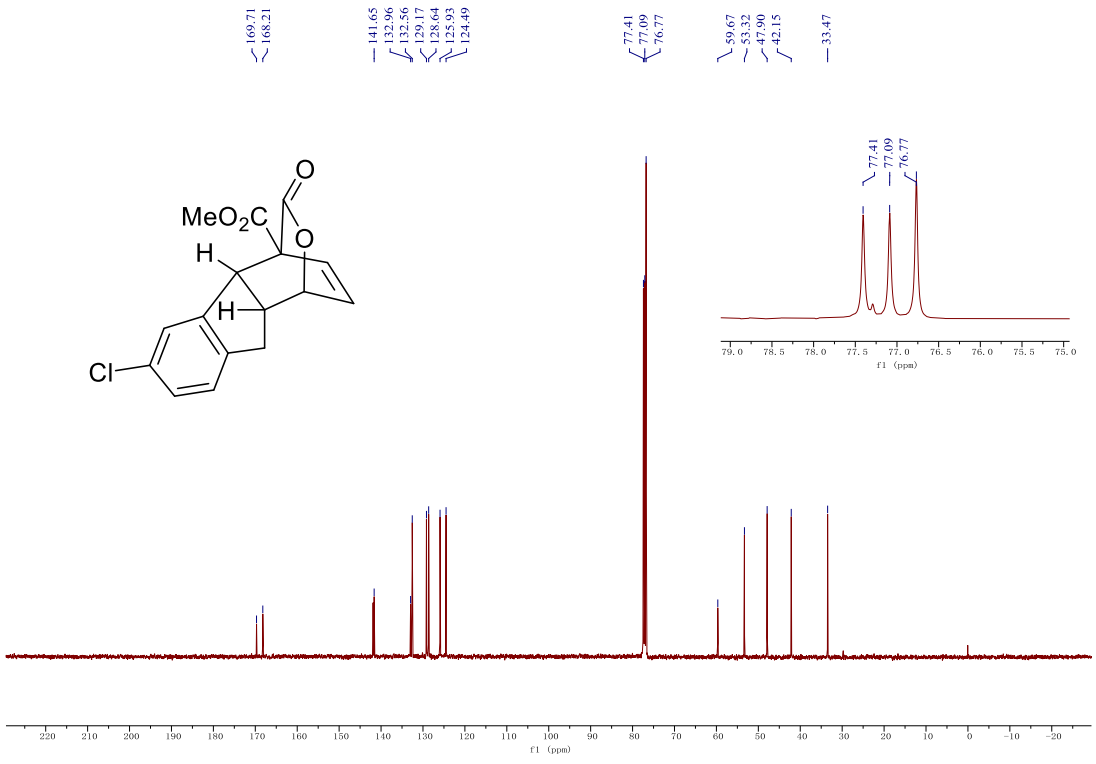
^{13}C NMR of Compound **3u**



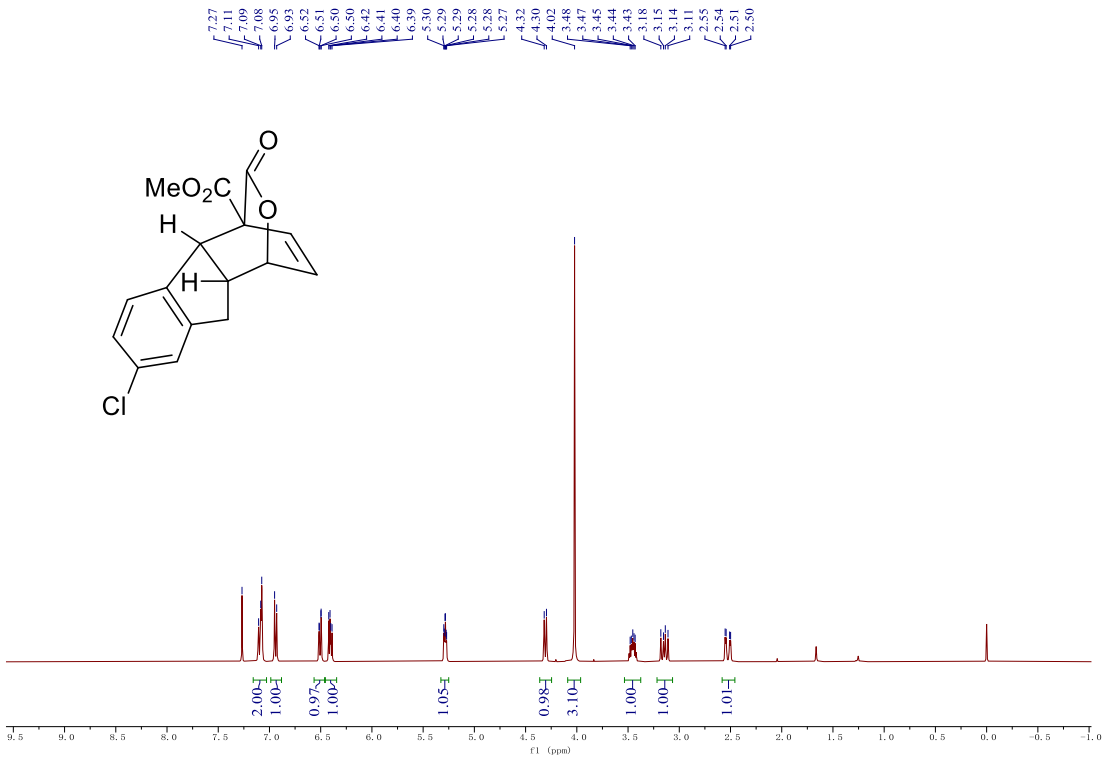
^{19}F NMR of Compound **3u**



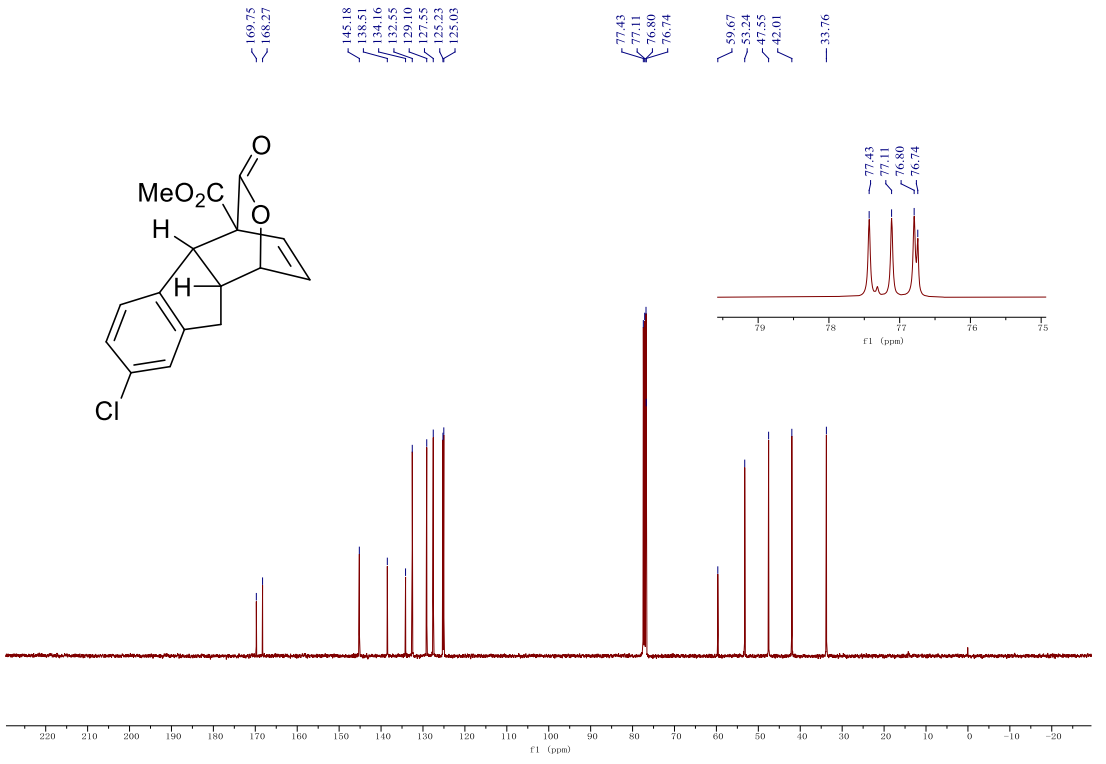
^{1}H NMR of Compound **3v**



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



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



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