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

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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**

![Chemical structures](image)

Ligand $L_3$-$Ra$($\text{OCH}_2\text{Ad}$)$_2$ ($S5$) 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 °C. 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$_2$SO$_4$, 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$_2$SO$_4$ 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 °C, 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 $S4$.  

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¹ Reference is needed for the procedure.
(d) To a solution of S4 (1 equiv.) in CH$_2$Cl$_2$ (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$_2$Ad)$_2$ (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$_3$) $\delta$ 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$_3$) $\delta$ 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.

$[\alpha]_{D}^{25} = +34.8$ (c = 1.00, CH$_2$Cl$_2$).
Table S1. Structures of 2-pyrones

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

Table S2. Structures of indenes

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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

After stirring a mixture of Ni(OTf)$_2$ (0.01 mmol, 10 mol%) and L$_3$-Ra(OCH$_2$Ad)$_2$ (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$S$,4$a$S,9$a$R)-10-oxo-1,4$a$,9,9$a$-tetrahydro-4$H$-1,4-(epoxymethano)fluorene-4-carboxylate (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]$^+$ calcld for C$_{16}$H$_{14}$NaO$_4$: 293.0784; found: 293.0785.

m.p. 132–133 °C.

$[\alpha]_{D}^{25}$ = +14.5 (c = 1.00, CHCl$_3$).
**rac-3a:**

![Chart for rac-3a](chart1.png)

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**cat-3a:**

![Chart for cat-3a](chart2.png)

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Determination of the relative and absolute configuration 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$_3$).
9
Ethyl (4S,4aS,9aR)-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-(epoxymethano)fluorene-4-carboxylate (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$_3$) $\delta$ 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$_3$) $\delta$ 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.

$[\alpha]^{25}_D = +27.0$ (c = 0.25, CH$_2$Cl$_2$).
**rac-3b:**

![Graph and Table](image1)

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**cat-3b:**

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

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

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

\[ 3c \]

\[ ^1H \text{NMR} \ (400 \text{ MHz}, \text{CDCl}_3) \delta 7.22 \ (dd, \ J = 5.0, 2.6 \text{ Hz}, 1\text{H}), \ 7.20 - 7.07 \ (m, 3\text{H}), \ 6.55 \ (d, \ J = 7.8 \text{ Hz}, 1\text{H}), \ 6.47 - 6.35 \ (m, 1\text{H}), \ 5.48 - 5.37 \ (m, 1\text{H}), \ 5.30 \ (td, \ J = 4.6, 1.7 \text{ Hz}, 1\text{H}), \ 4.41 \ (d, \ J = 8.8 \text{ Hz}, 1\text{H}), \ 3.45 \ (dd, \ J = 9.7, 5.1 \text{ Hz}, 1\text{H}), \ 3.21 \ (dd, \ J = 17.2, 10.5 \text{ Hz}, 1\text{H}), \ 2.59 \ (dd, \ J = 17.2, 3.8 \text{ Hz}, 1\text{H}), \ 1.47 \ (dd, \ J = 10.2, 6.3 \text{ Hz}, 6\text{H}). \]

\[ ^{13}C \text{NMR} \ (101 \text{ MHz}, \text{CDCl}_3) \delta 170.2, 167.4, 143.2, 140.2, 133.0, 128.7, 128.2, 127.1, 124.8, 124.3, 76.9, 70.3, 59.7, 48.0, 41.8, 33.9, 21.9, 21.8. \]

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

[\alpha]^{25}_D = +32.7 \ (c = 0.22, \text{CH}_2\text{Cl}_2).
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![Graph of rac-3c](image1)

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**cat-3c:**

![Graph of cat-3c](image2)

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Allyl (4aS,9aR)-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-(epoxymethano)fluorene-4-carboxylate (3d)

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

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

**1H NMR** (400 MHz, CDCl₃) 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).

**13C NMR** (101 MHz, CDCl₃) 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, tᵣ (major) = 11.4 min, tᵣ (minor) = 23.7 min.

**HRMS:** m/z [M+Na]^+ calcd for C₁₈H₁₆NaO₄: 319.0941; found: 319.0940.

**m.p.** 64–65 °C.

[α]²⁵_D = +33.0 (c = 0.23, CH₂Cl₂).
**rac-3d:**

![Graph of rac-3d data]

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

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

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

1H NMR (400 MHz, CDCl3) 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).

13C NMR (101 MHz, CDCl3) 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, tR (major) = 19.8 min, tR (minor) = 35.9 min.


m.p. 56–57 °C.

[α]D25 = +44.5 (c = 0.21, CH2Cl2).
**rac-3e:**

![Graph showing peaks and retention times for rac-3e.]

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**cat-3e:**

![Graph showing peaks and retention times for cat-3e.]

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

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

\textbf{TLC:} Rf = 0.5 (Petroleum ether /ethyl acetate 2:1).

\textbf{\textsuperscript{1}H NMR} (400 MHz, CDCl\textsubscript{3}) \(\delta 7.25 – 7.03\) (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).

\textbf{\textsuperscript{13}C NMR} (101 MHz, CDCl\textsubscript{3}) \(\delta 170.7, 168.5, 143.4, 142.3, 139.9, 128.2, 126.9, 124.9, 124.8, 123.2, 76.3, 63.4, 52.8, 48.1, 41.8, 34.1, 20.2\).

\textbf{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.

\textbf{HRMS:} m/z [M+Na]\textsuperscript{+} calcd for C\textsubscript{17}H\textsubscript{16}NaO\textsubscript{4}: 307.0941; found: 307.0941.

\textbf{m.p.} 119–120 °C.

\([\alpha]\)\textsuperscript{25}D = +4.6 (c = 0.35, CHCl\textsubscript{3}).
**rac-3f:**

![Graph for rac-3f](image)

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**cat-3f:**

![Graph for cat-3f](image)

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

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

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

**1H NMR** (500 MHz, CDCl₃) 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).

**13C NMR** (101 MHz, CDCl₃) 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, CH₂Cl₂).
**rac-3i:**

![Graph and Table]

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**cat-3i:**

![Graph and Table]

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Methyl (4S,4aS,9aR)-7-methyl-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-(epoxymethano)fluorene-4-carboxylate (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:** Rf = 0.5 (Petroleum ether/ethyl acetate 2:1).

**1H NMR** (400 MHz, CDCl₃) 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).

**13C NMR** (101 MHz, CDCl₃) 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, tᵣ (major) = 19.2 min, tᵣ (minor) = 32.7 min.

**HRMS:** m/z [M+Na]+ calcd for C₁₇H₁₆NaO₄: 307.0941; found: 307.0941.

**m.p.** 117–118 °C.

\[ \alpha \] = +18.3 (c = 0.23, CH₂Cl₂).
**rac-3j:**

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**cat-3j:**

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

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

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

**¹H NMR** (400 MHz, CDCl₃) 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).

**¹³C NMR** (101 MHz, CDCl₃) 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, tₘ (major) = 17.2 min, tₘ (minor) = 28.2 min.

**HRMS:** m/z [M+Na]⁺ calcd for C₁₇H₁₆NaO₄: 307.0941; found: 307.0942.

**m.p.** 138–139 °C.

[α]₂⁵ₒ = +21.4 (c = 0.24, CH₂Cl₂).
**rac-3k:**

![Graph](image1)

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**cat-3k:**

![Graph](image2)

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

Following the general procedure, the reaction was stirred at 35 °C for 72 h. Product 3I 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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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.

\([\alpha]^{25}_D = -4.3\) (c = 0.23, CH\(_2\)Cl\(_2\)).
**rac-3l:**

![Graph of rac-3l](image1)

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**cat-3l:**

![Graph of cat-3l](image2)

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Methyl (4S,4aS,9aR)-6-methoxy-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-(epoxymethano)fluorene-4-carboxylate (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: Rf = 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]$^+$ calcld 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$_2$Cl$_2$).
**rac-3m:**

![Graph and Table]

**cat-3m:**

![Graph and Table]
**Methyl (4S,4aS,9aR)-7-methoxy-10-oxo-1,4a,9,9a-tetrahydro-4H,1,4-(epoxymethano)fluorene-4-carboxylate (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**: Rf = 0.4 (Petroleum ether/ethyl acetate 2:1).

**1H NMR** (400 MHz, CDCl3) 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).

**13C NMR** (101 MHz, CDCl3) 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, tR (major) = 16.5 min, tR (minor) = 23.7 min.

**HRMS**: m/z [M+Na]+ calcd for C17H16NaO5: 323.0890; found: 323.0890.

**m.p.** 141–142 °C.

[α]25D = +16.7 (c = 0.20, CH2Cl2).
**rac-3n:**

![Graph of rac-3n](image1)

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**cat-3n:**

![Graph of cat-3n](image2)

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Methyl (4S,4aS,9aR)-8-methoxy-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-(epoxymethano)fluorene-4-carboxylate (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$_3$) $\delta$ 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$_3$) $\delta$ 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.

$[\alpha]^{25}_D = +16.1$ (c = 0.19, CH$_2$Cl$_2$).
**rac-3o:**

![Graph of rac-3o](image)

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**cat-3o:**

![Graph of cat-3o](image)

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Methyl (4S,4aS,9aR)-5-methoxy-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-(epoxymethano)fluorene-4-carboxylate (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: Rf = 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.

$[\alpha]_{D}^{25} = -34.0$ (c = 0.20, CH$_2$Cl$_2$).
rac-3p:

![Graph of rac-3p with peak details and a table showing peak numbers, retention times, areas, heights, area percentages, and height percentages.]

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cat-3p:

![Graph of cat-3p with peak details and a table showing peak numbers, retention times, areas, heights, area percentages, and height percentages.]

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Methyl (4S,4aS,9aR)-6,7-dimethoxy-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-(epoxymethano)fluorene-4-carboxylate (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**: Rf = 0.5 (Petroleum ether/ethyl acetate 1:1).

**1H NMR** (500 MHz, CDCl3) 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).

**13C NMR** (101 MHz, CDCl3) 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, tR (major) = 15.0 min, tR (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.

\([\alpha]_{D}^{25} = +10.4\) (c = 0.24, CH₂Cl₂).
**rac-3q:**

![Graph of rac-3q](image)

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**cat-3q:**

![Graph of cat-3q](image)

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Methyl (4S,4aS,9aR)-6-bromo-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-(epoxymethano)fluorene-4-carboxylate (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).

**1H 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).

**13C 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:**

![Graph](image)

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**cat-3r:**

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

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

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

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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.


m.p. 146–147 °C.

\([\alpha]\)\(^{25}\) = +24.7 (c = 0.23, CH\(_2\)Cl\(_2\)).
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Methyl (4S,4aS,9aR)-8-bromo-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-(epoxymethano)fluorene-4-carboxylate (3t)

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

TLC: Rf = 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.


m.p. 140–141 °C.

$[\alpha]^{25}_D$ = +38.5 (c = 0.22, CH$_2$Cl$_2$).
**rac-3t:**

![Graph showing rac-3t chromatogram with peak areas and heights.]

### PDA Ch1 210nm 4nm

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**cat-3t:**

![Graph showing cat-3t chromatogram with peak areas and heights.]

### PDA Ch1 210nm 4nm

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

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

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

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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$_3$) $\delta$ -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$_4$F: 311.0690; found: 311.0691.

m.p. 135–136 °C.

$[\alpha]^{25}_D = +25.8$ (c = 0.24, CH$_2$Cl$_2$).
**rac-3u:**

![Graph for rac-3u](image1)

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**cat-3u:**

![Graph for cat-3u](image2)

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Methyl (4S,4aS,9aR)-6-chloro-10-oxo-1,4a,9,9a-tetrahydro-4H-1,4-
(epoxymethano)fluorene-4-carboxylate (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).

**\( ^1H \) NMR** (400 MHz, CDCl\(_3\)) \( \delta \) 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\(_3\)) \( \delta \) 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, \( t_R \) (major) = 29.8 min, \( t_R \) (minor) = 34.9 min.

**HRMS:** m/z [M+Na]\(^+\) calcd for C\(_{16}\)H\(_{13}\)NaO\(_4\)Cl: 327.0395, 329.0365; found: 327.0394, 329.0364.

**m.p.** 150–151 °C.

\([\alpha]^{25}_D = +25.3 \) (c = 0.23, CH\(_2\)Cl\(_2\)).
**rac-3v:**

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**cat-3v:**

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

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

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

**1H NMR** (400 MHz, CDCl₃) 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).

**13C NMR** (101 MHz, CDCl₃) 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, t_R (major) = 25.8 min, t_R (minor) = 38.2 min.

**HRMS:** m/z [M+Na]^+ calcd for C_{16}H_{13}NaO_{4}Cl: 327.0395, 329.0365; found: 327.0396, 329.0364.

**m.p.** 135–136 °C.

[α]^{25}_D = −8.8 (c = 0.23, CH₂Cl₂).
**rac-3w:**

![Graph of rac-3w with data table]

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**cat-3w:**

![Graph of cat-3w with data table]

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4. **References**

5. NMR Spectra

$^1$H NMR of L$_3$-Ra(OCH$_2$Ad)$_2$

$^{13}$C NMR of L$_3$-Ra(OCH$_2$Ad)$_2$
**1H NMR of Compound 3c**

![1H NMR Spectrum](image)

**13C NMR of Compound 3c**

![13C NMR Spectrum](image)
$^1$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
H NMR of Compound 3j

13C NMR of Compound 3j
$^{1}H$ NMR of Compound 3k

$^{13}C$ NMR of Compound 3k
$^1$H NMR of Compound 3I

$^{13}$C NMR of Compound 3I
$^{1}H$ NMR of Compound $3m$

$^{13}C$ NMR of Compound $3m$
$^1$H NMR of Compound 3n

$^{13}$C NMR of Compound 3n
H NMR of Compound 3p

$^1$H NMR of Compound 3p

$^13$C NMR of Compound 3p
\[ ^1H \text{ NMR of Compound 3q} \]

\[ ^{13}C \text{ NMR of Compound 3q} \]
H NMR of Compound 3r

$\text{MeO}_2\text{C}$

O

H

Br

$\text{C}_\text{H}_\text{Br}$

$1^\text{H}$ NMR of Compound 3r

$\text{MeO}_2\text{C}$

O

H

Br

$1^{13}\text{C}$ NMR of Compound 3r
$^1$H NMR of Compound 3s

$^{13}$C NMR of Compound 3s
H NMR of Compound 3u

\[ \text{MeO}_2 \text{C} \]

\[ \text{O} \]

\[ \text{H} \]

\[ \text{H} \]

\[ \text{F} \]

\[ \text{F} \]

\[ \text{H} \]

\[ \text{H} \]

\[ \text{MeO}_2 \text{C} \]

\[ \text{O} \]

\[ \text{H} \]

\[ \text{F} \]

\[ \text{F} \]

\[ \text{H} \]

\[ \text{H} \]

\[ \text{MeO}_2 \text{C} \]

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\[ \text{H} \]

\[ \text{F} \]

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\[ \text{H} \]

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\[ \text{H} \]

\[ \text{F} \]

\[ \text{F} \]

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\[ \text{H} \]

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\[ \text{H} \]

\[ \text{F} \]

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$^{19}$F NMR of Compound 3u
H NMR of Compound 3v

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\[ \text{Cl} \]

\[ \text{O} \]

\[ \text{MeO}_2C \]

\[ \text{H} \]

\[ \text{Cl} \]

\[ \text{O} \]

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