# Supplementary Information

## Asymmetric Dearomative Reductive Arylallylation of Indoles with Trifluoromethyl Alkenes by Nickel Catalysis

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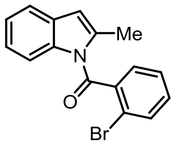
# 1. General Information

Unless otherwise stated, all manipulations were carried out under an atmosphere of nitrogen using standard Schlenk or glove box techniques. Anhydrous Toluene (Na), DMSO ($CaH_2$), NMP ($CaH_2$), DMF ($CaH_2$) were distilled and transferred under nitrogen. Deuterated solvents were used as received ($CDCl_3$ from Adamas-beta, China). Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Indole derivatives were synthesized according to literature[1-2]. Trifluoromethyl alkenes were synthesized according to literature [3-8].

For chromatographic purification, 200-300 mesh silica gel (Leyan, China) was employed. For thin layer chromatography (TLC) analysis, High efficiency thin layer chromatography silica gel plates (HPTLC Silica Gel 60 GF254, 2.5*5.0 cm) were used. $^1H$-NMR and $^{13}C$-NMR spectra were recorded at room temperature using a Bruker Avance-500 instruments. The $^1H$ NMR (500 MHz) chemical shifts were measured relative to tetramethylsilane as an internal standard (TMS: $\delta = 0$ ppm). The $^{13}C$ NMR (126 MHz) chemical shifts were given using $CDCl_3$ as the internal standard ($CDCl_3$: $\delta = 77.16$ ppm). Gas chromatograph (GC) were performed using SHIMADZU Nexis GC-2030 coupled to a DM-5MS gas chromatography column. High-resolution mass spectra (HRMS) was performed using a 1290 Agilent HPLC system coupled to an Agilent quadrupole time of flight (QTQF, 6530) mass spectrometer and TOF MS ESI+ Mass spectrometer. X-Ray singlecrystal diffraction data was collected on a Bruker SMART APEX diffractometer. Optical rotation was measured on a WZZ-2B automatic polarimeter (Shanghai INESA, China). Enantiomeric excess was determined by a SHIMADZU Prominence LC-20A, using chiralpak AS-H column, chiralpak AD-H column or chiralpak ID column with hexane and *i*-PrOH as solvents.

# 2. Synthesis of Substrates

## 2.1 Synthesis of *N*-(2-Bromobenzoyl)indoles



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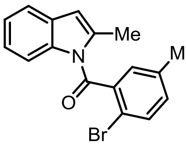

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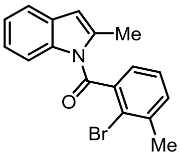

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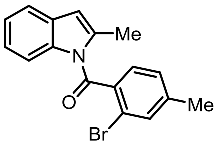

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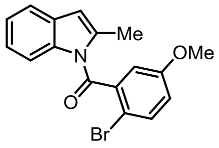

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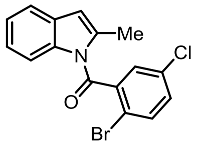

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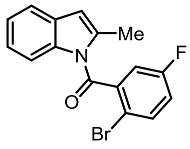

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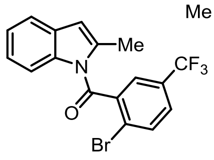

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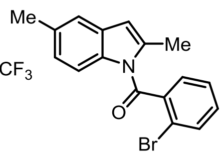

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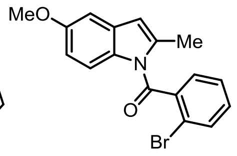

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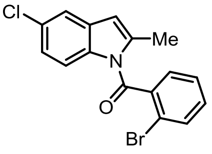

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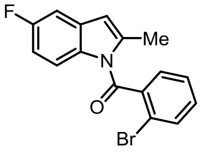

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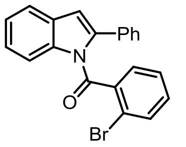

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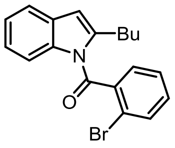

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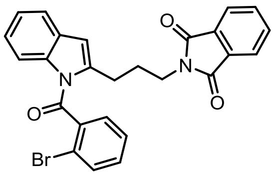
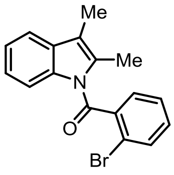


**1n**

***Unsuccessful substrates in the reductive cross-coupling catalytic system***



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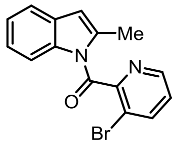

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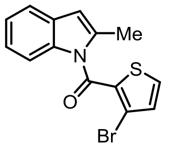

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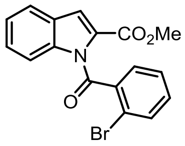
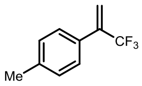


**1r**

As shown above, substrates **1**[1], **1a-l**[1], **1n**[1], **1o-r**[1] and **1m**[2] were prepared according to literature.

## 2.2 Synthesis of Trifluoromethyl Alkenes



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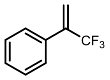

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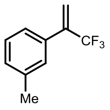

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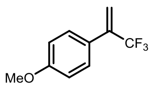

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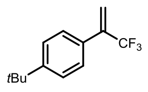

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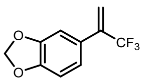

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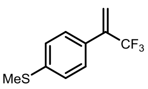

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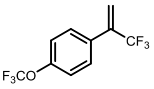

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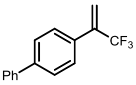

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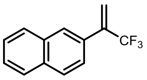

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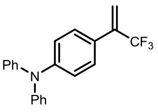

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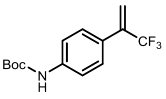

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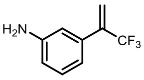

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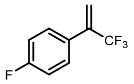

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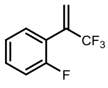

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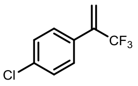

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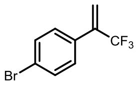

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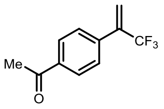

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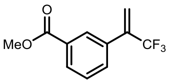

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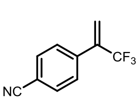

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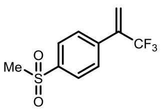

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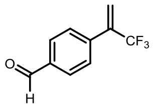

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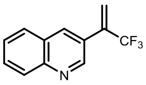

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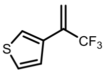

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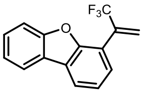

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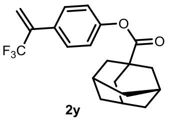

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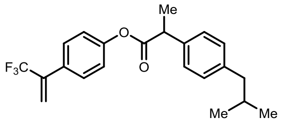

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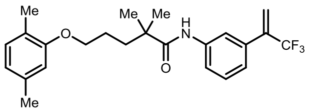

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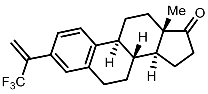

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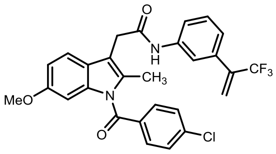

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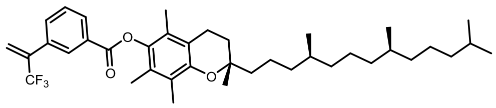

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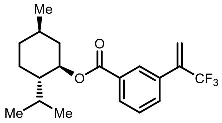

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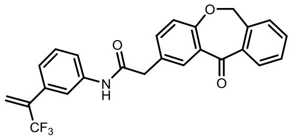

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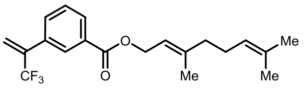

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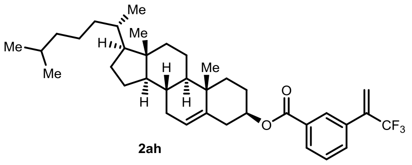
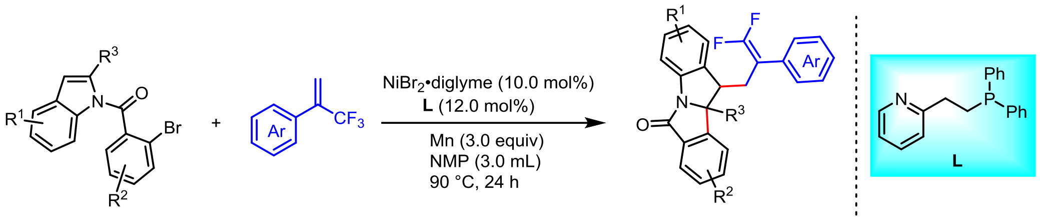


**2ah**

As shown above, compounds **2**[3], **2a-b**[4], **2c**[3], **2e-j**[3], **2k-p**[4], **2q-u**[3], **2v-x**[4], **2y-z**[3], **2aa-ac**[4], **2ae**[5], **2af**[6], **2ag**[7] **and 2ah**[8] were synthesized following the reported procedures.

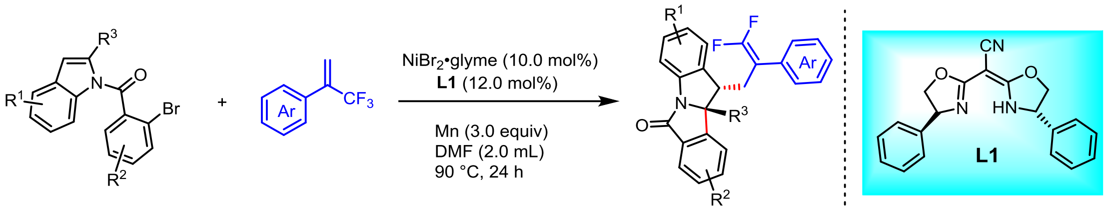
# 3. Experimental Procedures

## 3.1 General Procedure for Nickel-Catalyzed Dearomative Reductive Arylallylation of Indoles with Trifluoromethyl Alkenes (racemic)



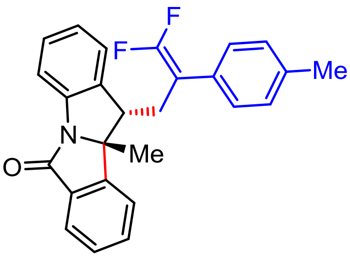
An oven-dried Schlenk tube (20.0 mL) was charged with NiBr$_2$•diglyme (0.02 mmol, 7.1 mg, 10.0 mol%), **L** (0.024 mmol, 6.6 mg, 12.0 mol%), Mn dust (0.6 mmol, 33.0 mg, 3.0 equiv), *N*-(2-bromobenzoyl)indoles (0.2 mmol, 1.0 equiv), trifluoromethyl alkenes (0.4 mmol, 2.0 equiv) and NMP (3.0 mL). The reaction mixture was allowed to stir under N$_2$ atmosphere at 90 ℃ (oil bath) for 24 h. After this time, the tube was cooled to room temperature then the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~10 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Petroleum ether/Ethyl acetate) to afford the desired products.

### 3.2 General Procedure for the Enantioselective Nickel-Catalyzed Dearomative Reductive Arylallylation of Indoles with Trifluoromethyl Alkenes



An oven-dried Schlenk tube (20.0 mL) was charged with NiBr$_2$•glyme (0.02 mmol, 6.2 mg, 10.0 mol%), **L1** (0.024 mmol, 8.0 mg, 12.0 mol%), Mn dust (0.6 mmol, 33.0 mg, 3.0 equiv), *N*-(2-bromobenzoyl)indoles (0.2 mmol, 1.0 equiv), trifluoromethyl alkenes (0.4 mmol, 2.0 equiv) and DMF (2.0 mL). The reaction mixture was allowed to stir under N$_2$ atmosphere at 90 □ (oil bath) for 24 h. After this time, the tube was cooled to room temperature then the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~10 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. Subsequently, the ratio of dr was determined by crude $^1$H NMR. The crude mixture was then purified by column chromatography on silica gel (Petroleum ether/Ethyl acetate) to afford the desired products. Enantiomeric excess was determined by HPLC analysis with a chiral column.

## 4. Characterization Data and HPLC Spectra of Chiral Products



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 3**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **3** as a yellow solid (53.3 mg, 0.133 mmol, 66% yield). **m.p.** 42.6 – 45.8 □.

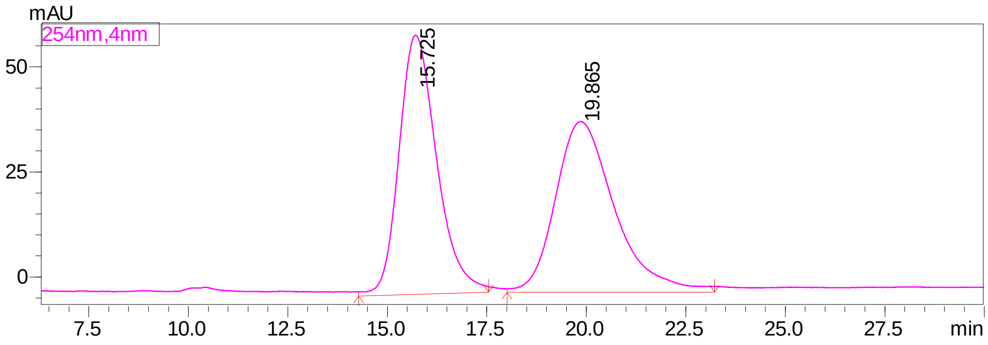
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 (td, *J* = 7.5, 1.0 Hz, 1H), 7.55 (td, *J* = 7.5, 1.0 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.36 (td, *J* = 7.5, 1.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.20 – 7.17 (m, 3H), 7.10 (td, *J* = 7.5, 1.0 Hz, 1H), 3.06 (dd, *J* = 10.5, 4.5 Hz, 1H), 2.39 (s, 3H), 2.23 – 2.18 (m, 1H), 1.65 – 1.60 (m, 1H), 1.49 (s, 3H) ppm.

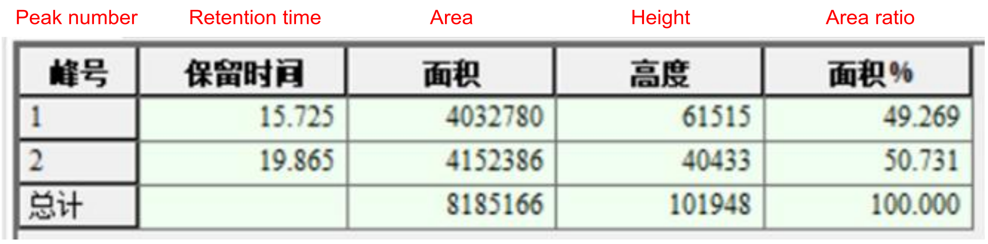
**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.0 (dd, *J* = 291.8, 289.0 Hz), 147.8, 138.5, 137.7, 137.5, 133.8, 132.5, 129.73 (t, *J* = 3.7 Hz), 129.67, 129.0, 128.7, 128.0 (t, *J* = 3.3 Hz), 126.0, 125.1, 124.4, 123.0, 117.4, 88.7 (dd, *J* = 20.9, 14.2 Hz), 75.0, 47.2, 31.6, 27.0, 21.3 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.1 (d, *J* = 37.7 Hz), -90.1 (dd, *J* = 37.7, 4.7 Hz ) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+H]$^+$ calcd for $C_{26}H_{22}F_2NO^+$ 402.1664, found 402.1664.

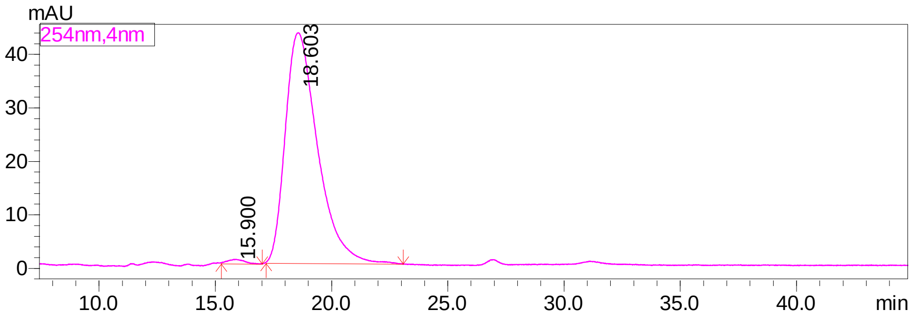
$[\alpha]^{25}_{D}$ = 104.0°(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 99.2:0.8 (Chiralpak AS-H, *i*-propanol/hexane = 1/99, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 18.603 min, $t_{minor}$ = 15.900 min.





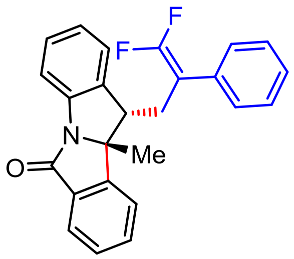
| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 15.725 | 4032780 | 61515 | 49.269 |
| 2 | 19.865 | 4152386 | 40433 | 50.731 |
| 总计 |  | 8185166 | 101948 | 100.000 |

**Figure S1.** HPLC chromatography of the racemic product **3**



| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 15.900 | 33097 | 753 | 0.790 |
| 2 | 18.603 | 4157940 | 43205 | 99.210 |
| 总计 |  | 4191037 | 43957 | 100.000 |

**Figure S2.** HPLC chromatography of chiral product **3**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-phenylallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 4**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **4** as colorless oil (40.7 mg, 0.105 mmol, 53% yield).

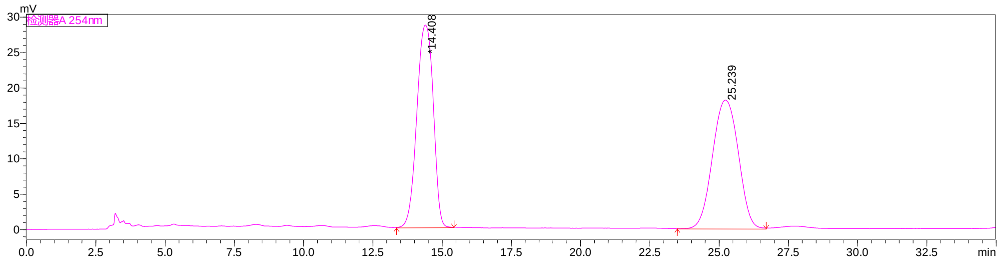
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.37 – 7.32 (m, 2H), 7.28 (d, *J* = 7.5 Hz, 2H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 3.07 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.25 – 2.20 (m, 1H), 1.68 – 1.62 (m, 1H), 1.49 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.1 (dd, *J* = 292.4, 289.9 Hz), 147.8, 138.4, 137.8, 133.9, 132.9 (t, *J* = 3.9 Hz), 132.5, 129.05, 128.96, 128.7, 128.1 (t, *J* = 3.3 Hz), 127.7, 126.0, 125.1, 124.4, 123.0, 117.4, 89.0 (dd, *J* = 21.0, 14.0 Hz), 75.0, 47.3, 31.6, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.5 (d, *J* = 36.3 Hz), -89.2 (d, *J* = 36.7 Hz ) ppm.

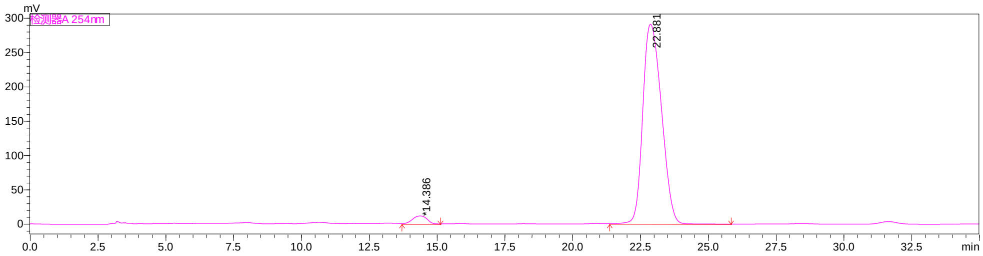
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{25}H_{19}F_2NNaO^+$ 410.1327, found 410.1325.

$[\alpha]^{25}_{D}$ = 118.0 °(c = 0.40 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 96.9:3.1 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 22.881 min, $t_{minor}$ = 14.386 min.



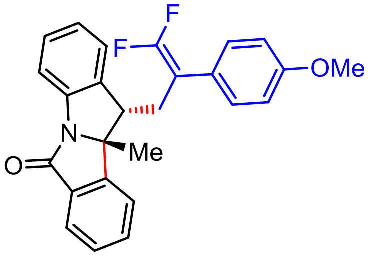
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 14.408 | 1174756 | 28535 | 50.027 |
| 2 | 25.239 | 1173496 | 18135 | 49.973 |
| 总计 | | 2348252 | 46669 | 100.000 |

**Figure S3.** HPLC chromatography of the racemic product **4**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 14.386 | 451238 | 11789 | 3.127 |
| 2 | 22.881 | 13980699 | 291164 | 96.873 |
| 总计 |  | 14431938 | 302953 | 100.000 |

**Figure S4.** HPLC chromatography of chiral product **4**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-methoxyphenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 5**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 6/1, v/v) afforded **5** as a white solid (41.6 mg, 0.100 mmol, 50% yield). **m.p.** 99.4 – 101.5 □.

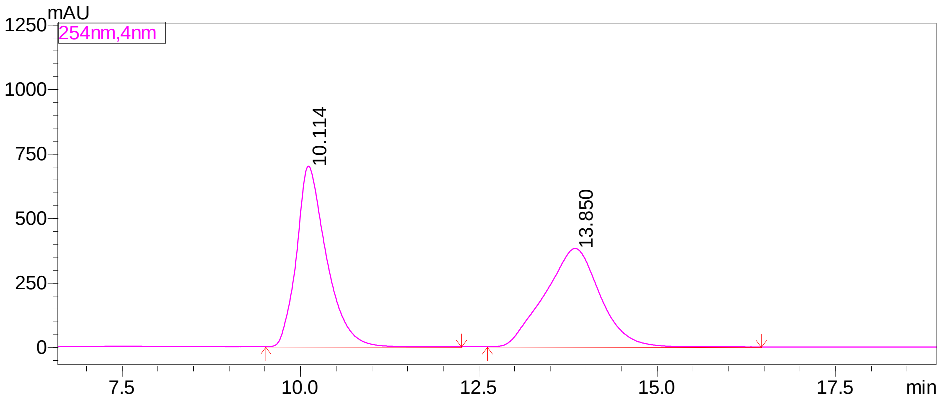
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.67 (td, *J* = 7.5, 1.0 Hz, 1H), 7.55 (td, *J* = 7.5, 1.0 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.35 (td, *J* = 7.5, 1.0 Hz, 1H), 7.20 (d, *J* = 7.5 Hz, 2H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 6.95 (d, *J* = 8.5 Hz, 2H), 3.84 (s, 3H), 3.07 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.21 – 2.16 (m, 1H), 1.64 – 1.59 (m, 1H), 1.49 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 158.9, 153.9 (dd, *J* = 291.2, 289.0 Hz), 147.8, 138.5, 137.8, 133.8, 132.5, 129.2 (t, *J* = 3.4 Hz), 129.0, 128.7, 126.0, 125.1, 124.9 (t, *J* = 3.7 Hz), 124.4, 123.0, 117.4, 114.4, 88.4 (dd, *J* = 21.2, 14.5 Hz), 75.0, 55.4, 47.3, 31.7, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.7 (d, *J* = 39.6 Hz), -90.7 (dd, *J* = 39.6, 4.2 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: $[M+H]^+$ calcd for $C_{26}H_{22}F_2NO_2^+$ 418.1613, found 418.1614.

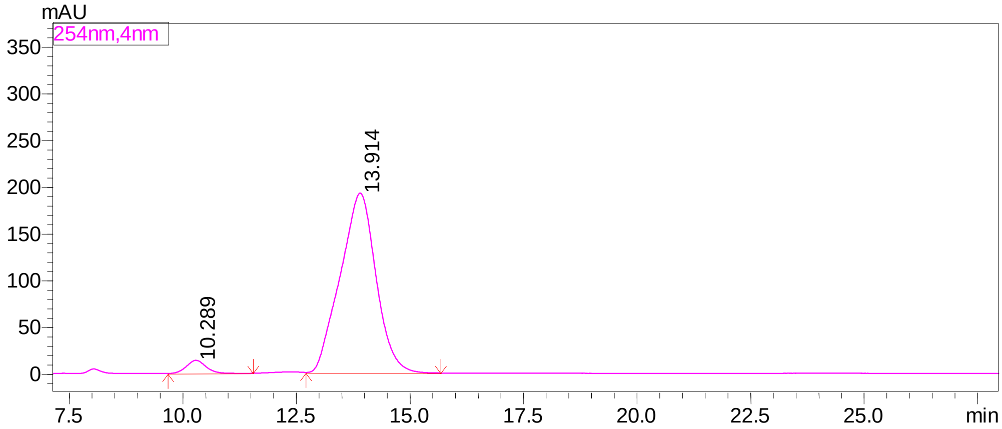
$[\alpha]^{25}_{D}$ = 264.0°(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 96.2:3.8 (Chiralpak AD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 13.914 min, $t_{minor}$ = 10.289 min.



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 10.114 | 20358022 | 702077 | 49.883 |
| 2 | 13.850 | 20453898 | 381916 | 50.117 |
| 总计 |  | 40811920 | 1083993 | 100.000 |

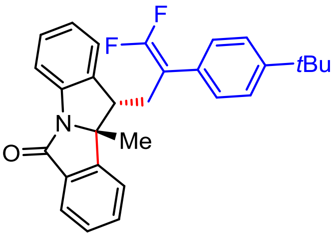
**Figure S5.** HPLC chromatography of the racemic product **5**



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 10.289 | 412640 | 14063 | 3.768 |
| 2 | 13.914 | 10539012 | 192933 | 96.232 |
| 总计 |  | 10951653 | 206997 | 100.000 |

**Figure S6.** HPLC chromatography of chiral product **5**



### (10b*R*,11*S*)-11-(2-(4-(*tert*-Butyl)phenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 6

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **6** as colorless oil (45.7 mg, 0.103 mmol, 52% yield).

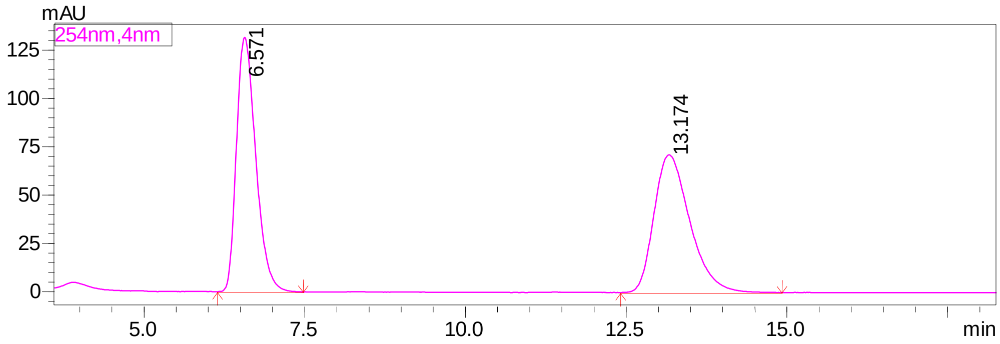
**$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.94 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 (td, *J* = 7.5, 1.5 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.35 (td, *J* = 7.5, 1.5 Hz, 1H), 7.21 (dd, *J* = 8.5, 1.5 Hz, 2H), 7.18 (d, *J* = 7.0 Hz, 1H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 3.10 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.25 – 2.21 (m, 1H), 1.65 – 1.59 (m, 1H), 1.50 (s, 3H), 1.35 (s, 9H) ppm.

**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 167.3, 154.1 (dd, *J* = 292.7, 289.0 Hz), 150.6, 147.8, 138.5, 137.8, 133.9, 132.5, 129.7 (t, *J* = 3.9 Hz), 129.0, 128.7, 127.7 (t, *J* = 3.3 Hz), 126.1, 125.9, 125.1, 124.4, 123.1, 117.4, 88.7 (dd, *J* = 20.9, 14.0 Hz), 75.0, 47.3, 34.7, 31.5 (d, *J* = 1.9 Hz), 31.4, 27.0 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -88.8 (d, *J* = 37.7 Hz), -89.9 (dd, *J* = 37.7, 3.8 Hz) ppm.

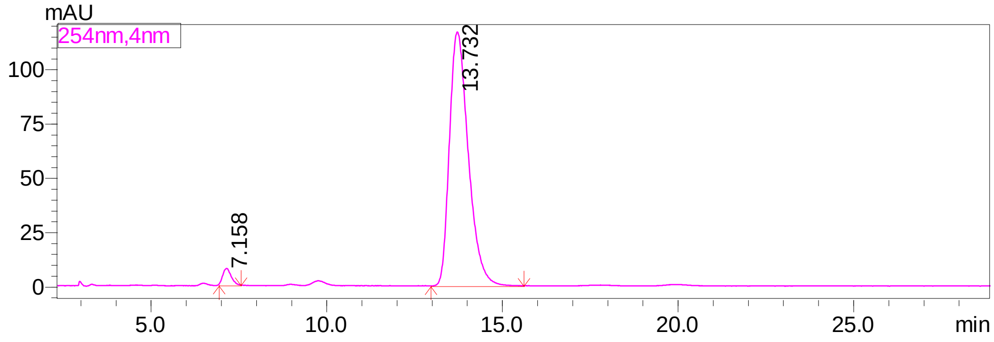
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for: $C_{29}H_{27}F_2NNaO^+$ 466.1953, found 466.1953.

$[\alpha]^{25}_{D}$ = 84.0° (c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.1:2.9 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 13.732 min, $t_{minor}$ = 7.158 min.



| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 6.571 | 2771086 | 132227 | 49.999 |
| 2 | 13.174 | 2771145 | 71648 | 50.001 |
| 总计 |  | 5542230 | 203875 | 100.000 |

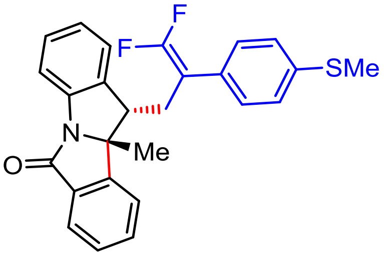
**Figure S7.** HPLC chromatography of the racemic product **6**



Peak number | Retention time | Area | Height | Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 7.158 | 131166 | 7797 | 2.910 |
| 2 | 13.732 | 4376714 | 117440 | 97.090 |
| 总计 | | 4507880 | 125236 | 100.000 |

**Figure S8.** HPLC chromatography of chiral product **6**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-(methylthio)phenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 7**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **7** as a white solid (40.8 mg, 0.094 mmol, 47% yield). **m.p.** 120.1 – 122.5 □.

**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.68 (td, *J* = 7.5, 1.0 Hz, 1H), 7.55 (td, *J* = 7.5, 1.0 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.35 (td, *J* = 7.5, 1.5 Hz, 1H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.18 (dd, *J* = 8.5, 1.5 Hz, 2H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 3.07 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.52 (s, 3H), 2.23 – 2.17 (m, 1H), 1.65 – 1.59 (m, 1H), 1.50 (s, 3H) ppm.

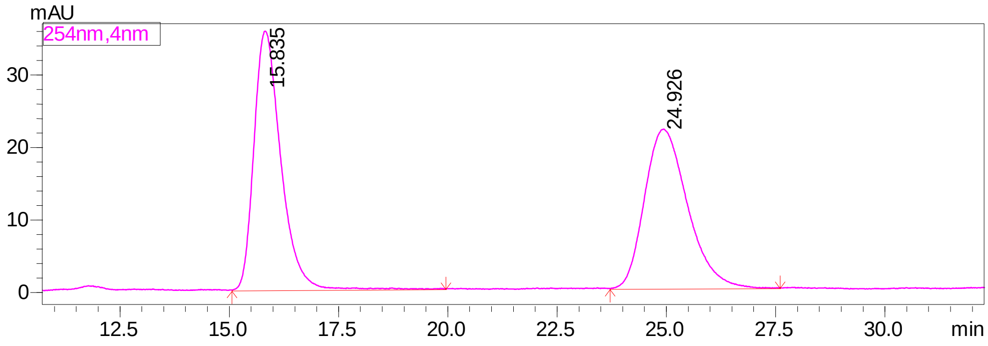
**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.1 (dd, *J* = 292.8, 289.8 Hz), 147.7, 138.4, 138.2, 137.8, 133.9, 132.5, 129.3 (t, *J* = 3.9 Hz), 129.1, 128.8, 128.4 (t, *J* = 3.3 Hz), 126.7, 125.9, 125.2, 124.4, 123.0, 117.4, 88.6 (dd, *J* = 21.5, 14.0 Hz), 75.0, 47.3, 31.5, 27.0, 15.6 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.4 (d, *J* = 36.3 Hz), -89.4 (dd, *J* = 36.7, 3.8 Hz)

ppm.

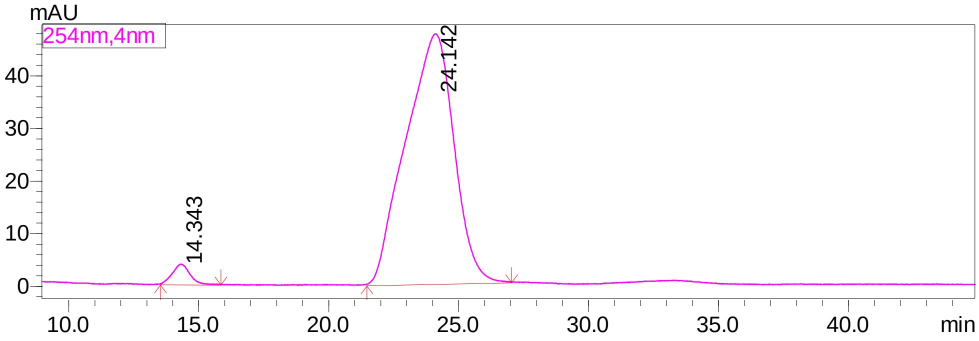
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{21}F_2NNaOS^+$ 456.1204, found 456.1205.

$[\alpha]^{25}_{D}$ = 113.6° (c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.2:2.8 (Chiralpak AD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 24.142 min, $t_{minor}$ = 14.343 min.



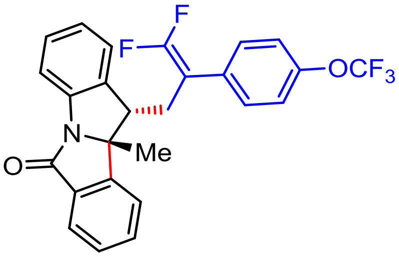
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 15.835 | 1506048 | 35436 | 50.350 |
| 2 | 24.926 | 1485083 | 21747 | 49.650 |
| 总计 | | 2991131 | 57183 | 100.000 |

**Figure S9.** HPLC chromatography of the racemic product **7**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 14.343 | 174778 | 3799 | 2.790 |
| 2 | 24.142 | 6089882 | 47290 | 97.210 |
| 总计 | | 6264660 | 51089 | 100.000 |

**Figure S10.** HPLC chromatography of chiral product **7**



### (10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-(trifluoromethoxy)phenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 8

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **8** as a white solid (66.3 mg, 0.141 mmol, 70% yield). **m.p.** 44.6 – 45.2 □.

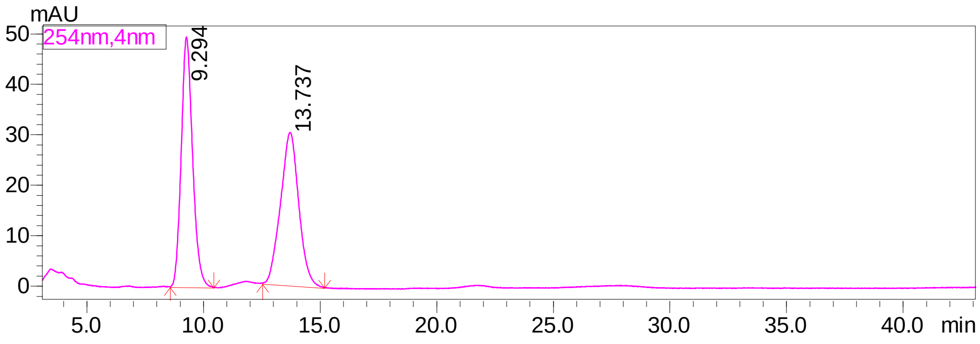
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.0 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.23 (s, 4H), 7.13 (d, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 3.09 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.26 – 2.21 (m, 1H), 1.67 – 1.62 (m, 1H), 1.52 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.2, 154.3 (dd, *J* = 293.3, 290.4 Hz), 148.3, 147.6, 138.1, 137.8, 133.9, 132.6, 131.6 (t, *J* = 4.0 Hz), 129.5 (t, *J* = 3.4 Hz), 129.1, 128.9, 126.0, 125.2, 124.4, 123.0, 121.6 (t, *J* = 257.9 Hz), 121.3, 120.5 (q, *J* = 257.9 Hz), 117.5, 88.3 (dd, *J* = 21.8, 13.5 Hz), 75.0, 47.5 (t, *J* = 2.5 Hz), 31.5, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -57.8 (s) , -87.4 (d, *J* = 34.9 Hz), -88.8 (dd, *J* = 35.8, 4.2 Hz) ppm.

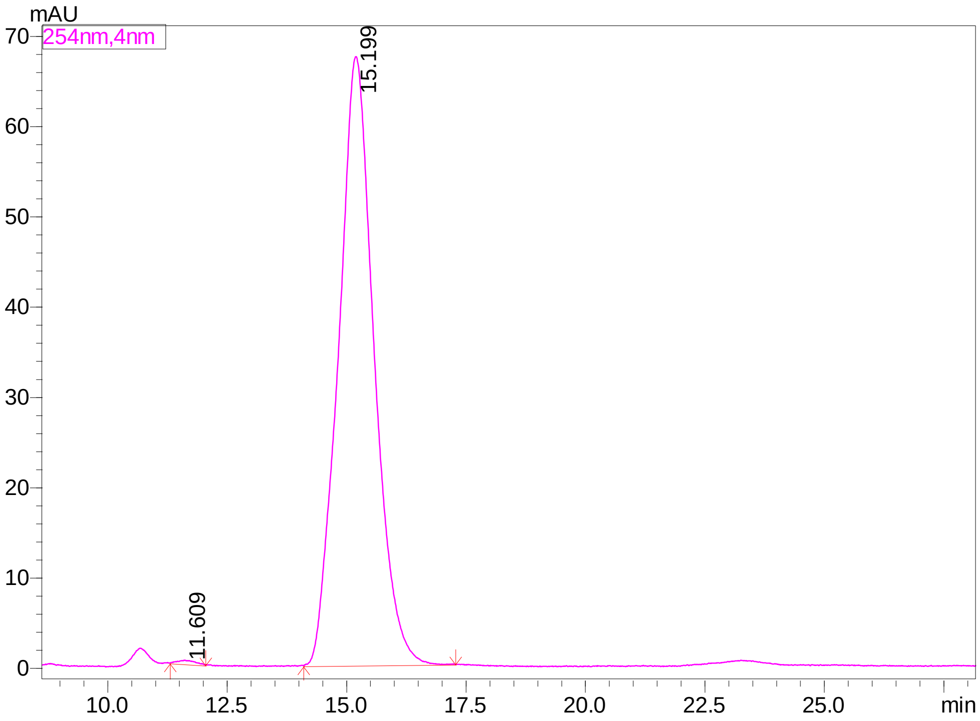
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{18}F_5NNaO_2^+$ 494.1150, found 494.1152.

$[\alpha]^{25}_{D}$ = 220.0°(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 99.7:0.3 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 15.199 min, $t_{minor}$ = 11.609 min.



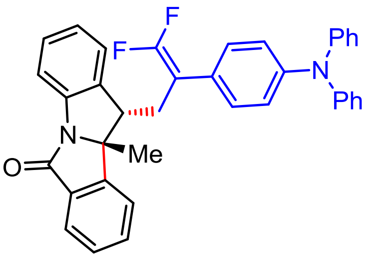
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.294 | 1685460 | 49745 | 50.489 |
| 2 | 13.737 | 1652835 | 30454 | 49.511 |
| 总计 | | 3338295 | 80199 | 100.000 |

**Figure S11.** HPLC chromatography of the racemic product **8**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 11.609 | 10984 | 421 | 0.313 |
| 2 | 15.199 | 3496496 | 67699 | 99.687 |
| 总计 | | 3507481 | 68119 | 100.000 |

**Figure S12.** HPLC chromatography of chiral product **8**



**(10b*R*,11*R*)-11-(2-(4-(Diphenylamino)phenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 9**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 6/1, v/v) afforded **9** as a white solid (67.6 mg, 0.122 mmol, 61% yield). **m.p.** 74.6 – 75.9 □.

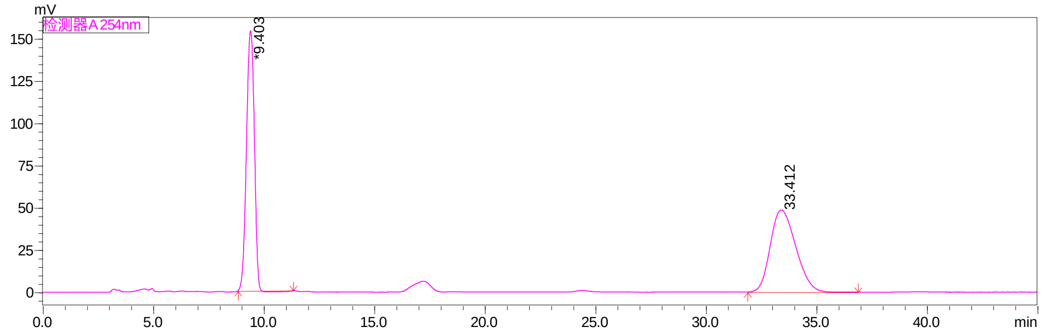
**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 4H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 4H), 7.10 – 7.04 (m, 7H), 3.16 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.23 – 2.18 (m, 1H), 1.62 – 1.57 (m, 1H), 1.53 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.1 (dd, *J* = 292.4, 289.3 Hz), 147.8, 147.4, 147.1, 138.4, 137.8, 133.8, 132.5, 129.5, 129.0, 128.7, 128.6 (t, *J* = 3.7 Hz), 126.1, 125.9 (t, *J* = 3.7 Hz), 125.1, 124.9, 124.3, 123.4, 123.0, 122.9, 117.4, 88.6 (dd, *J* = 21.2, 13.9 Hz), 75.0, 47.5, 31.4, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.8 (d, *J* = 38.2 Hz), -89.8 (dd, *J* = 38.2, 4.2 Hz) ppm.

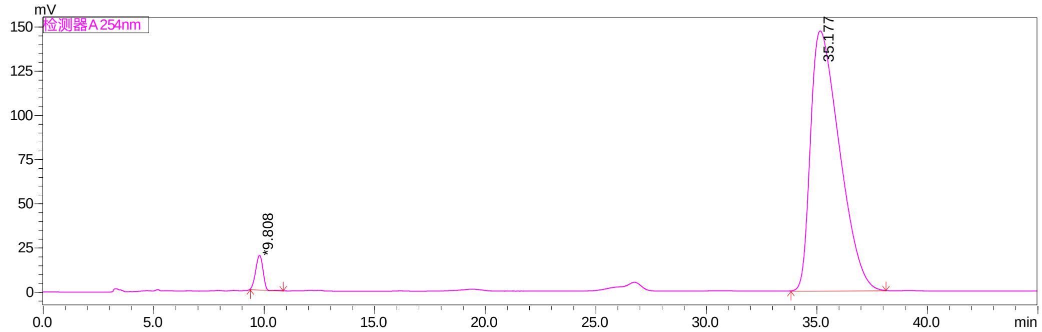
**HRMS (ESI$^+$):** *m/z*: $[M+H]^+$ calcd for :$C_{37}H_{29}F_2N_2O^+$ 555.2242, found 555.2242.

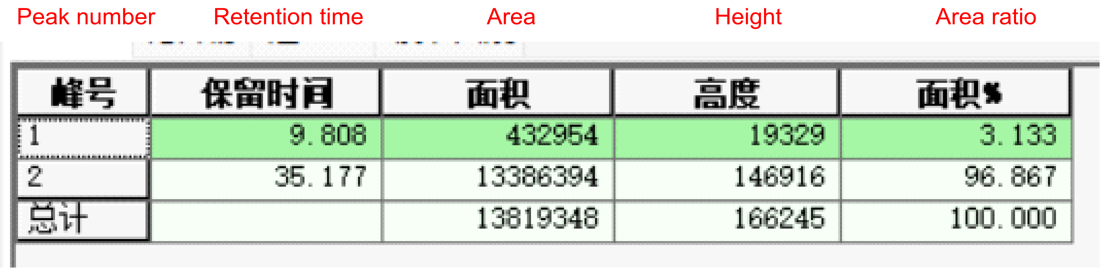
$[\alpha]^{25}_{D}$ = 32.0°(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 96.9:3.1 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 35.177 min, $t_{minor}$ = 9.808 min.



| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 9.403 | 3762231 | 153810 | 49.240 |
| 2 | 33.412 | 3878345 | 48512 | 50.760 |
| 总计 |  | 7640576 | 202322 | 100.000 |

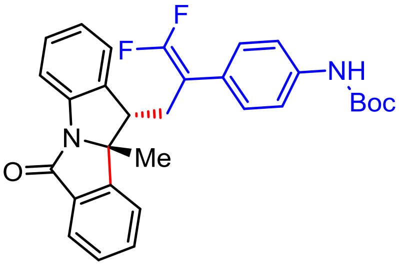
**Figure S13.** HPLC chromatography of the racemic product **9**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.808 | 432954 | 19329 | 3.133 |
| 2 | 35.177 | 13386394 | 146916 | 96.867 |
| 总计 |  | 13819348 | 166245 | 100.000 |

**Figure S14.** HPLC chromatography of chiral product **9**



***tert*-Butyl (4-(1,1-difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl)carbamate, 10**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1, v/v) afforded **10** as a white solid (43.9 mg, 0.087 mmol, 44% yield). **m.p.** 42.5 – 44.2 □.

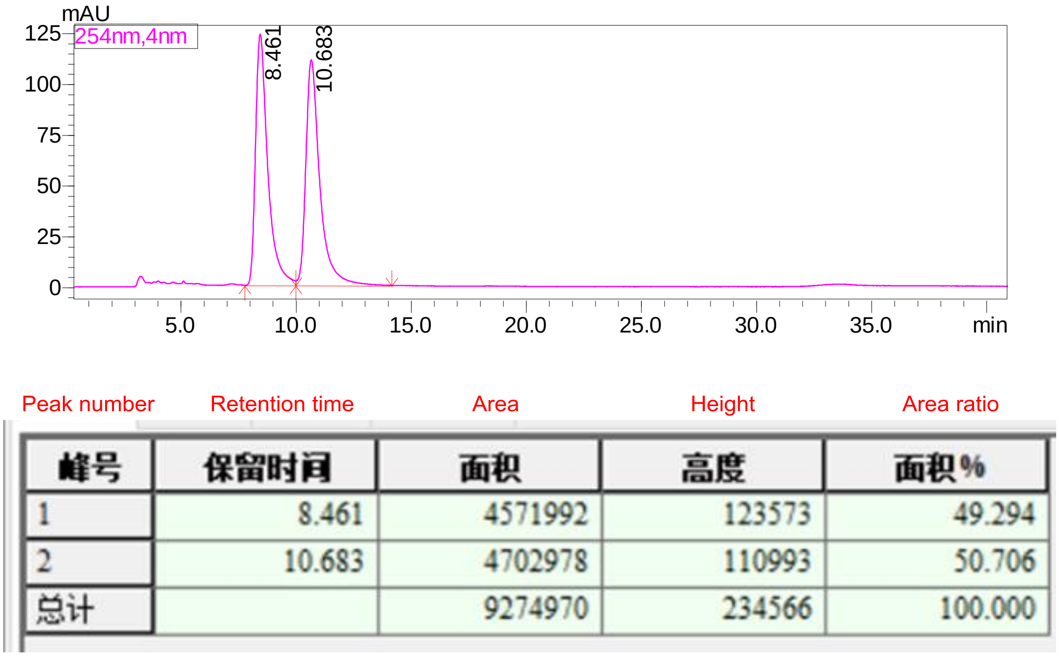
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 (td, *J* = 7.5, 1.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.35 (td, *J* = 7.5, 1.5 Hz, 1H), 7.22 (d, *J* = 7.5 Hz, 2H), 7.15 (d, *J* = 6.0 Hz, 1H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 6.70 (s, 1H), 3.04 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.21 – 2.15 (m, 1H), 1.65 – 1.59 (m, 1H), 1.54 (s, 9H), 1.48 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.0 (dd, *J* = 291.7, 289.2 Hz), 152.9, 147.8, 138.5, 137.81, 137.75, 133.8, 132.5, 129.0, 128.73 (t, *J* = 3.3 Hz), 128.71, 127.2 (t, *J* = 4.0 Hz), 125.9, 125.1, 124.5, 123.0, 118.9, 117.4, 88.5 (dd, *J* = 21.3, 14.1 Hz), 81.0, 75.0, 47.2, 31.5, 28.4, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.1 (d, *J* = 38.2 Hz), -90.1 (d, *J* = 38.2 Hz) ppm.

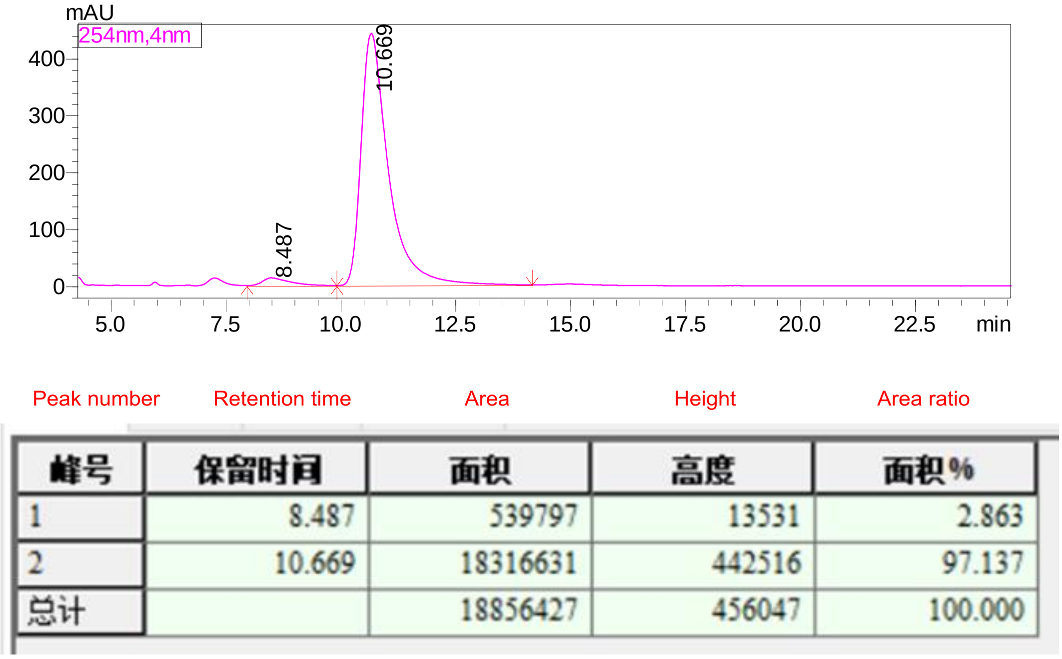
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{30}H_{28}F_2N_2NaO_3^+$ 525.1960, found 525.1960.

$[\alpha]^{25}_{D}$ = 82.4°(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.1:2.9 (Chiralpak AD-H, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 10.669 min, $t_{minor}$ = 8.487 min.



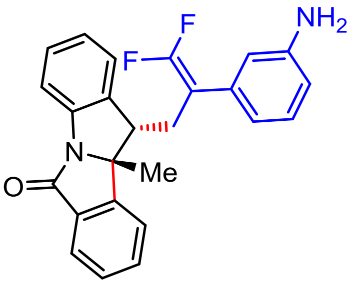
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 8.461 | 4571992 | 123573 | 49.294 |
| 2 | 10.683 | 4702978 | 110993 | 50.706 |
| 总计 |  | 9274970 | 234566 | 100.000 |

**Figure S15.** HPLC chromatography of the racemic product **10**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 8.487 | 539797 | 13531 | 2.863 |
| 2 | 10.669 | 18316631 | 442516 | 97.137 |
| 总计 |  | 18856427 | 456047 | 100.000 |

**Figure S16.** HPLC chromatography of chiral product **10**



**(10b*R*,11*S*)-11-(2-(3-Aminophenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 11**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1 to 2/1, v/v) afforded **11** as a white solid (27.0 mg, 0.067 mmol, 34% yield). **m.p.** 58.0 – 58.8 □.

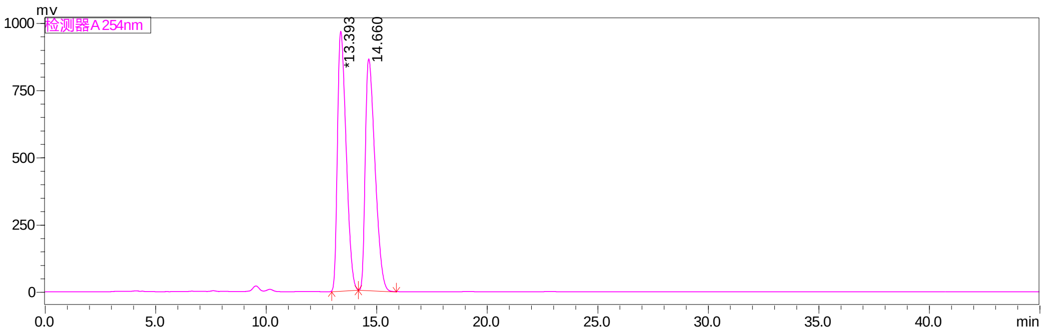
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 7.0 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.36 (td, *J* = 7.5, 1.5 Hz, 1H), 7.21 – 7.18 (m, 2H), 7.10 (t, *J* = 7.0 Hz, 1H), 6.66 (dd, *J* = 14.0, 7.5 Hz, 2H), 6.57 (s, 1H), 3.67 (br, 2H), 3.10 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.19 – 2.14 (m, 1H), 1.63 – 1.57 (m, 1H), 1.50 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.0 (dd, *J* = 292.7, 289.5 Hz), 147.8, 146.9, 138.6, 137.8, 133.93 (t, *J* = 3.5 Hz), 133.87, 132.5, 129.8, 129.0, 128.7, 126.1, 125.1, 124.4, 123.1, 118.2 (t, *J* = 2.6 Hz), 117.4, 114.8 (t, *J* = 3.5 Hz), 114.5, 89.0 (dd, *J* = 20.9, 13.6 Hz), 75.0, 47.3, 31.7, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.8 (d, *J* = 36.7 Hz), -89.2 (d, *J* = 36.7 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+H]$^+$ calcd for $C_{25}H_{21}F_2N_2O^+$ 403.1616, found 403.1617.

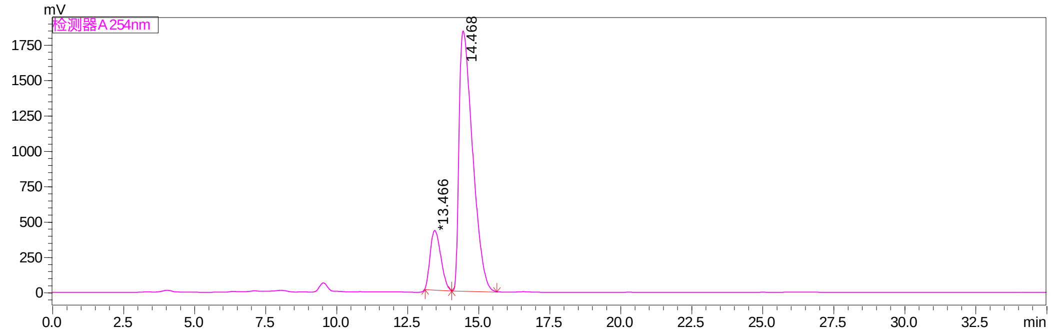
$[\alpha]^{25}_{D}$ = 109.6°(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 84.8:15.2 (Chiralpak AD-H, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 14.468 min, $t_{minor}$ = 13.466 min.



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 13.393 | 26288775 | 965260 | 50.045 |
| 2 | 14.660 | 26241574 | 860567 | 49.955 |
| 总计 | | 52530348 | 1825826 | 100.000 |

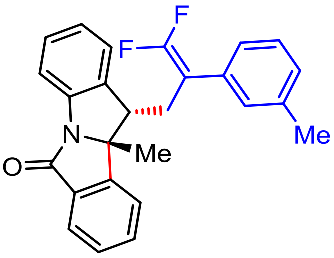
**Figure S17.** HPLC chromatography of the racemic product **11**



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 13.466 | 10889111 | 419062 | 15.163 |
| 2 | 14.468 | 60923437 | 1836778 | 84.837 |
| 总计 | | 71812549 | 2255839 | 100.000 |

**Figure S18.** HPLC chromatography of chiral product **11**



### (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*m*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 12

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **12** as yellow oil (35.0 mg, 0.087 mmol, 44% yield).

**$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.68 (td, *J* = 7.5, 1.0 Hz, 1H), 7.55 (td, *J* = 7.5, 1.0 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.36 (td, *J* = 8.0, 1.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* =

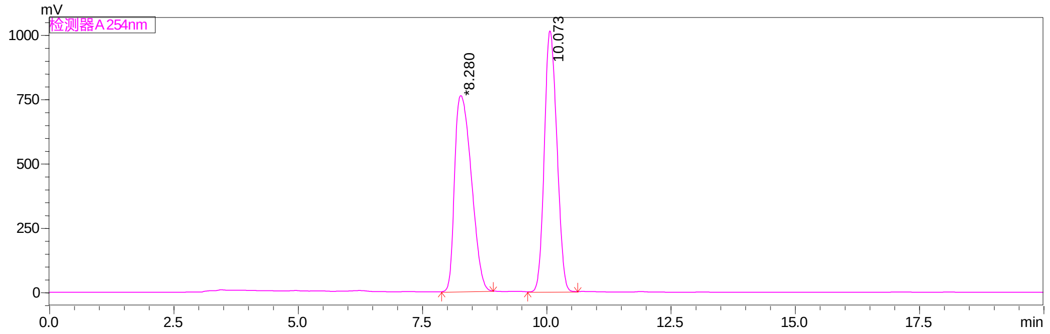
8.0 Hz, 1H), 7.12 – 7.05 (m, 3H), 3.07 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.40 (s, 3H), 2.23 – 2.18 (m, 1H), 1.66 – 1.61 (m, 1H), 1.50 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.1 (dd, *J* = 292.4, 289.5 Hz), 147.8, 138.6, 138.5, 137.8, 133.9, 132.8 (t, *J* = 3.8 Hz), 132.5, 129.0, 128.9 (t, *J* = 3.3 Hz), 128.8, 128.7, 128.5, 126.0, 125.14, 125.12, 124.4, 123.0, 117.4, 89.0 (dd, *J* = 20.8, 14.1 Hz), 75.0, 47.4 (t, *J* = 2.4 Hz), 31.7 (d, *J* = 1.9 Hz), 27.0, 21.7 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.7 (d, *J* = 37.2 Hz), -89.7 (dd, *J* = 37.2, 4.2 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{21}F_2NNaO^+$ 424.1483, found 424.1484.

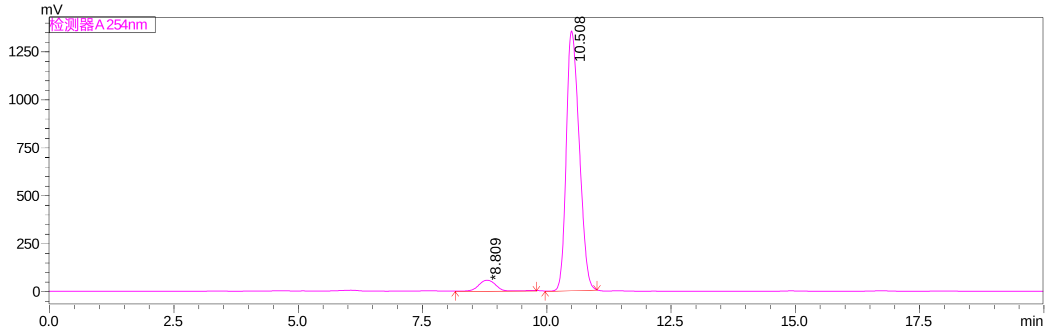
$[\alpha]^{25}_{D}$ = 48.0°(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 95.2:4.8 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 10.508 min, $t_{minor}$ = 8.809 min.

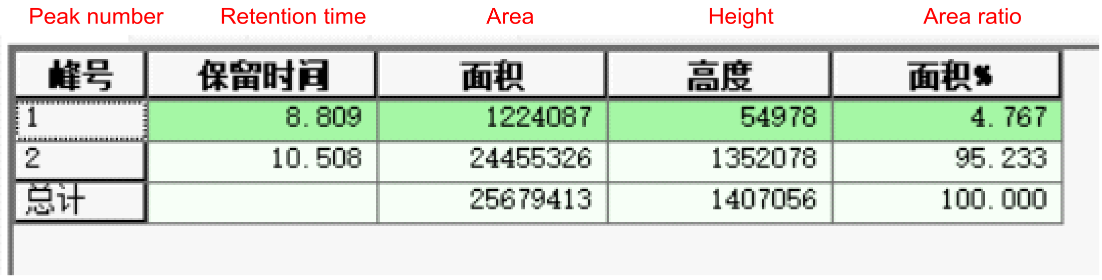


Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 8.280 | 17826554 | 760963 | 50.096 |
| 2 | 10.073 | 17758159 | 1013706 | 49.904 |
| 总计 |  | 35584714 | 1774669 | 100.000 |

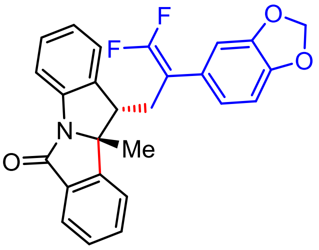
**Figure S19.** HPLC chromatography of the racemic product **12**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 8.809 | 1224087 | 54978 | 4.767 |
| 2 | 10.508 | 24455326 | 1352078 | 95.233 |
| 总计 |  | 25679413 | 1407056 | 100.000 |

**Figure S20.** HPLC chromatography of chiral product **12**



**(10b*R*,11*S*)-11-(2-(Benzo[*d*][1,3]dioxol-5-yl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 13**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1, v/v) afforded **13** as a yellow solid (37.8 mg, 0.088 mmol, 44% yield). **m.p.** 45.3 – 46.0 □.

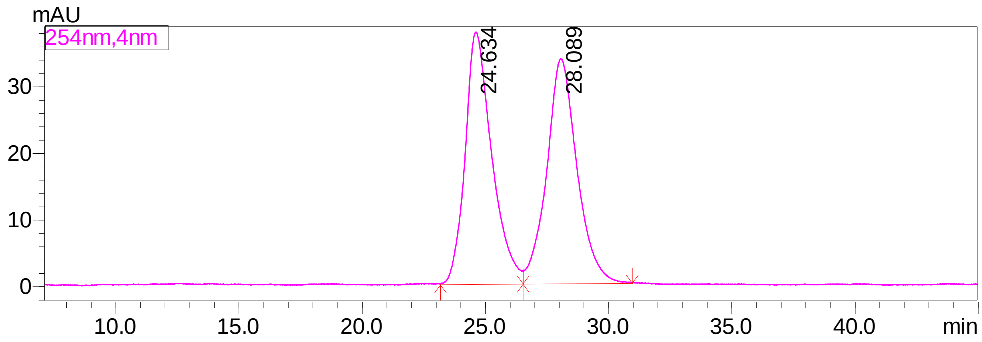
**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.68 (td, *J* = 7.5, 1.0 Hz, 1H), 7.55 (td, *J* = 7.5, 1.0 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.36 (td, *J* = 7.5, 1.5 Hz, 1H), 7.17 (d, *J* = 7.0 Hz, 1H), 7.10 (td, *J* = 7.5, 1.5 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.77 – 6.73 (m, 2H), 6.02 (q, *J* = 1.5 Hz, 2H), 3.07 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.17 – 2.11 (m, 1H), 1.63 – 1.58 (m, 1H), 1.51 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.0 (dd, *J* = 291.6, 289.4 Hz), 148.2, 147.7, 147.0, 138.4, 137.8, 133.8, 132.5, 129.0, 128.7, 126.4 (t, *J* = 3.8 Hz), 125.9, 125.1, 124.4, 123.0, 121.7 (t, *J* = 3.2 Hz), 117.4, 108.7, 108.5 (t, *J* = 3.4 Hz), 101.4, 88.7 (dd, *J* = 21.8, 14.1 Hz), 74.9, 47.2, 31.9, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.3 (d, *J* = 38.2 Hz), -89.9 (dd, *J* = 38.6, 4.2 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{19}F_2NNaO_3^+$ 454.1225, found 454.1240.

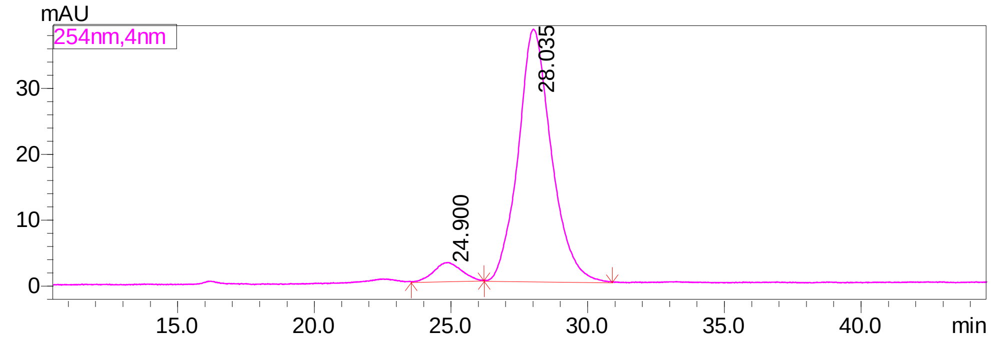
$[\alpha]^{25}_{D}$ = 236.8 °(c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 94.3:5.7 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 28.035 min, $t_{minor}$ = 24.900 min.



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 24.634 | 2847669 | 37876 | 49.685 |
| 2 | 28.089 | 2883757 | 33736 | 50.315 |
| 总计 | | 5731425 | 71611 | 100.000 |

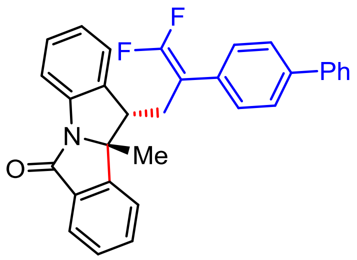
**Figure S21.** HPLC chromatography of the racemic product **13**



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 24.900 | 194581 | 2847 | 5.679 |
| 2 | 28.035 | 3231990 | 38296 | 94.321 |
| 总计 | | 3426572 | 41143 | 100.000 |

**Figure S22.** HPLC chromatography of chiral product **13**



**(10b*R*,11*S*)-11-(2-([1,1'-Biphenyl]-4-yl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 14**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **14** as a white solid (64.8 mg, 0.140 mmol, 70% yield). **m.p.** 56.4 – 58.5 □.

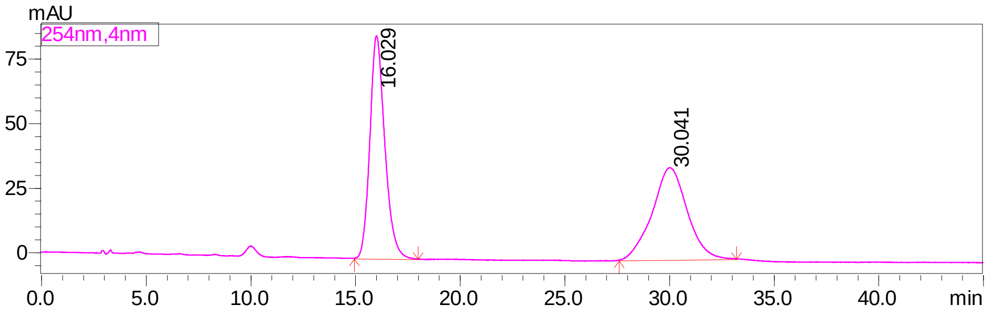
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.69 (td, *J* = 7.5, 1.5 Hz, 1H), 7.63 (t, *J* = 8.5 Hz, 4H), 7.57 – 7.53 (m, 2H), 7.46 (t, *J* = 7.0 Hz, 2H), 7.38 – 7.34 (m, 4H), 7.20 (d, *J* = 7.0 Hz, 1H), 7.10 (td, *J* = 7.5, 1.5 Hz, 1H), 3.13 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.30 – 2.24 (m, 1H), 1.70 – 1.65 (m, 1H), 1.51 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.2 (dd, *J* = 293.1, 289.9 Hz), 147.7, 140.39, 140.35, 138.4, 137.8, 133.9, 132.5, 131.7 (t, *J* = 3.9 Hz), 129.1, 129.0, 128.7, 128.4 (t, *J* = 3.4 Hz), 127.7, 127.6, 127.1, 126.0, 125.1, 124.4, 123.0, 117.4, 88.8 (dd, *J* = 21.2, 13.7 Hz), 75.0, 47.4 (t, *J* = 2.5 Hz), 31.5, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -87.9 (d, *J* = 35.8 Hz), -89.1 (dd, *J* = 35.8, 4.2 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+H]$^+$ calcd for $C_{31}H_{24}F_2NO^+$ 464.1820, found 464.1818.

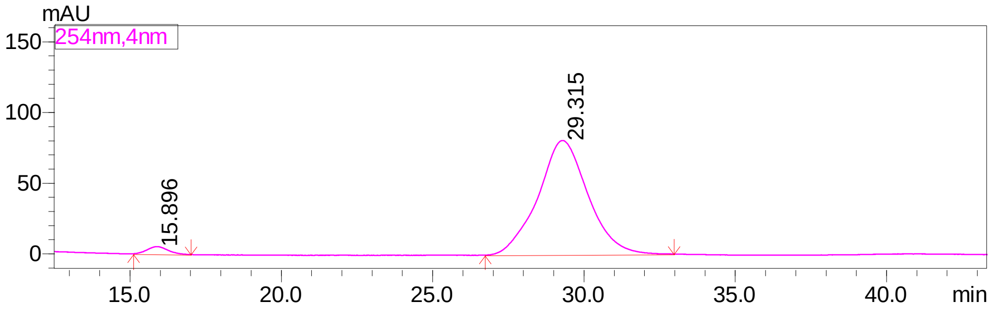
$[\alpha]^{25}_{D}$ = 196.0˚(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.3:2.7 (Chiralpak AD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); t$_{major}$ = 29.315 min, t$_{minor}$ = 15.896 min.



Peak number Retention time Area Height Area ratio

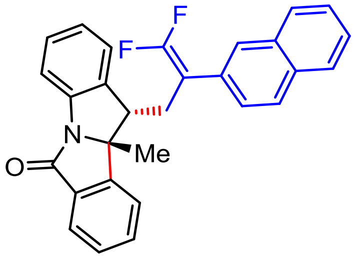
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 16.029 | 4272941 | 86024 | 50.926 |
| 2 | 30.041 | 4117509 | 35504 | 49.074 |
| 总计 | | 8390449 | 121528 | 100.000 |

**Figure S23.** HPLC chromatography of the racemic product **14**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 15.896 | 255548 | 5305 | 2.688 |
| 2 | 29.315 | 9251604 | 80534 | 97.312 |
| 总计 |  | 9507152 | 85839 | 100.000 |

**Figure S24.** HPLC chromatography of chiral product **14**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(naphthalen-2-yl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 15**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **15** as a white solid (42.3 mg, 0.097 mmol, 48% yield). **m.p.** 47.1 – 49.4 □.

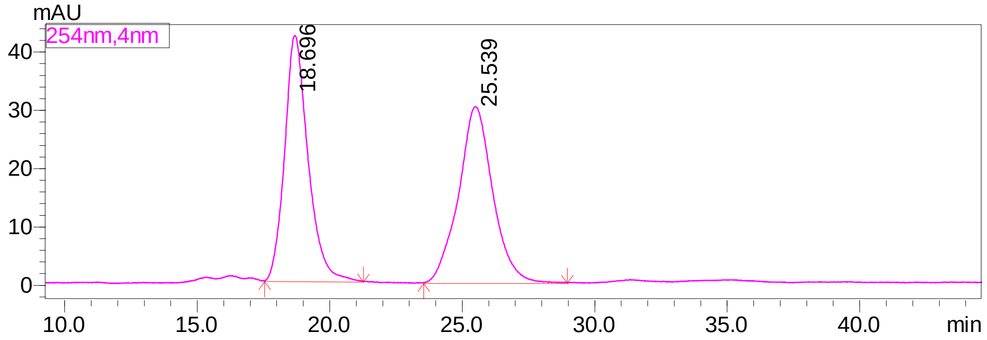
**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.90 – 7.84 (m, 3H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.71 – 7.69 (m, 2H), 7.57 – 7.51 (m, 4H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 9.0 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 3.10 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.36 – 2.31 (m, 1H), 1.77 – 1.72 (m, 1H), 1.47 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.3 (dd, *J* = 292.8, 289.8 Hz), 147.7, 138.5, 137.8, 133.9, 133.4, 132.6, 132.5, 130.3 (t, *J* = 3.8 Hz), 129.1, 128.8, 128.7, 128.1, 127.7, 127.4 (t, *J* = 3.3 Hz), 126.7, 126.6, 126.0, 125.7 (t, *J* = 3.2 Hz), 125.2, 124.5, 123.0, 117.4, 89.2 (dd, *J* = 21.4, 14.1 Hz), 75.0, 47.4, 31.8, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -87.9 (d, *J* = 36.3 Hz), -89.3 (dd, *J* = 36.3, 4.2 Hz) ppm.

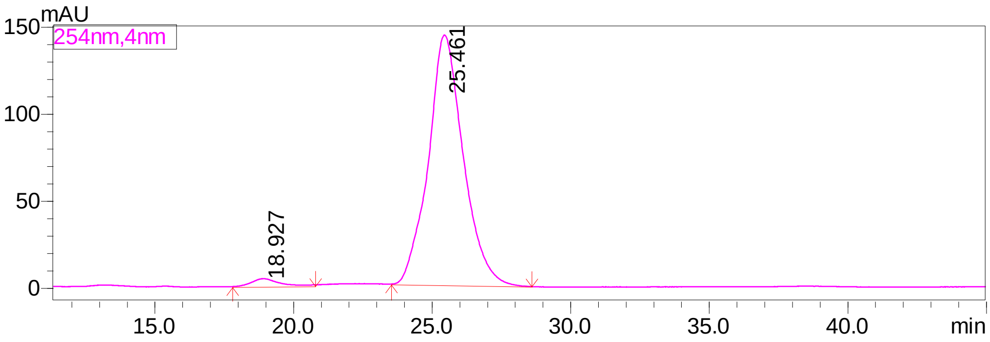
**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{29}H_{21}F_2NNaO^+$ 460.1483, found 460.1485.

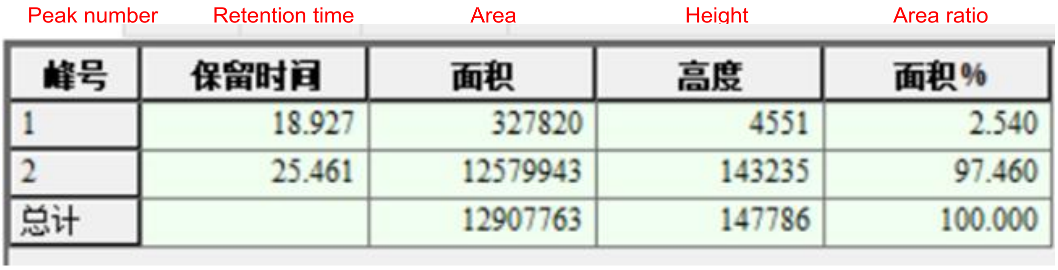
$[\alpha]^{25}_{D}$ = 19.2° (c = 0.25 in $CHCl_3$). The enantiomeric excess was analysed by HPLC: e.r. = 97.5:2.5 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 25.461 min, $t_{minor}$ = 18.927 min.



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 18.696 | 2582575 | 41989 | 48.926 |
| 2 | 25.539 | 2695943 | 30116 | 51.074 |
| 总计 | | 5278518 | 72104 | 100.000 |

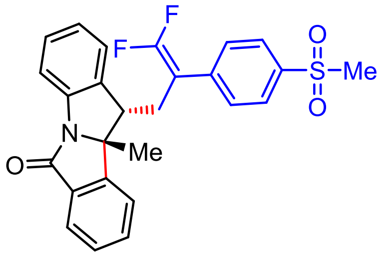
**Figure S25.** HPLC chromatography of the racemic product **15**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 18.927 | 327820 | 4551 | 2.540 |
| 2 | 25.461 | 12579943 | 143235 | 97.460 |
| 总计 | | 12907763 | 147786 | 100.000 |

**Figure S26.** HPLC chromatography of chiral product **15**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-(methylsulfonyl)phenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 16**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1 to 2/1, v/v) afforded **16** a white solid (78.0 mg, 0.168 mmol, 84% yield). **m.p.** 158.9 – 160.5 □.

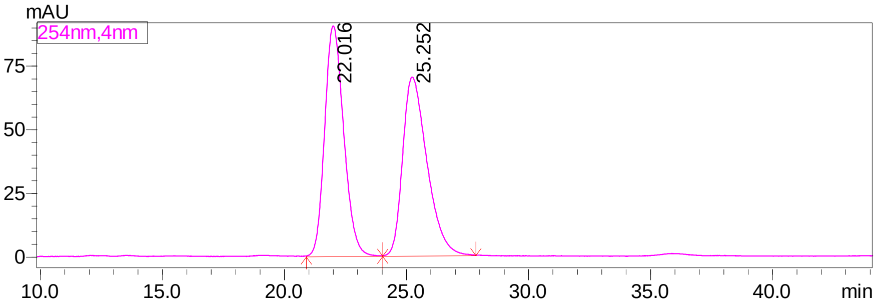
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 8.5 Hz, 3H), 7.73 – 7.69 (m, 2H), 7.57 (td, *J* = 7.5, 1.0 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.38 – 7.34 (m, 3H), 7.11 (d, *J* = 8.0 Hz, 1H), 7.06 (td, *J* = 7.5, 1.0 Hz, 1H), 3.11 – 3.08 (m, 4H), 2.34 – 2.29 (m, 1H), 1.71 – 1.66 (m, 1H), 1.53 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.1, 154.6 (dd, *J* = 295.7, 292.3 Hz), 147.4, 139.3, 138.9 (t, *J* = 4.4 Hz), 137.8, 137.7, 133.8, 132.6, 129.2, 128.93, 128.86 (t, *J* = 3.7 Hz), 127.9, 125.9, 125.2, 124.4, 122.9, 117.5, 88.5 (dd, *J* = 22.3, 13.0 Hz), 74.9, 47.4, 44.5, 31.2, 26.9 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -84.6 (d, *J* = 29.2 Hz), -86.5 (dd, *J* = 29.2, 3.8 Hz) ppm.

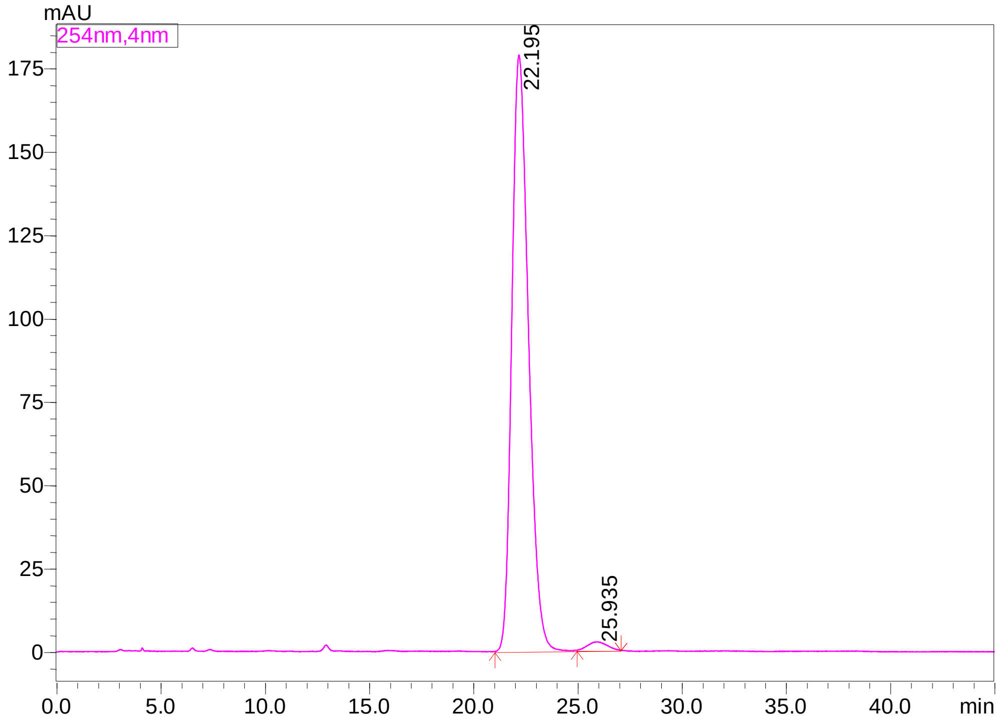
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{21}F_2NNaO_3S^+$ 488.1102, found 488.1105.

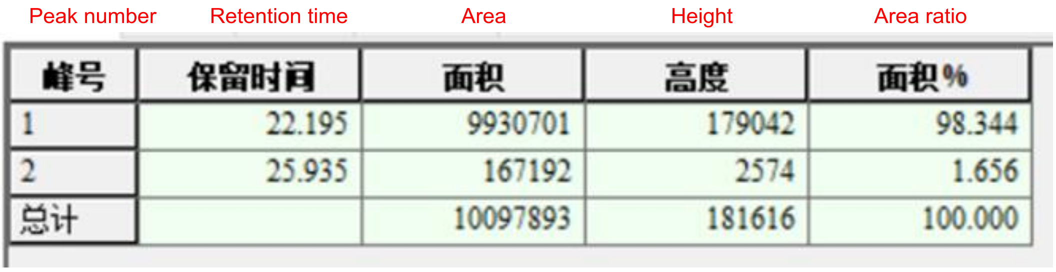
$[\alpha]^{25}_{D}$ = 41.6° (c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 98.3:1.7 (Chiralpak AD-H, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 22.195 min, $t_{minor}$ = 25.935 min.



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 22.016 | 4896287 | 90467 | 50.252 |
| 2 | 25.252 | 4847229 | 70121 | 49.748 |
| 总计 |  | 9743516 | 160588 | 100.000 |

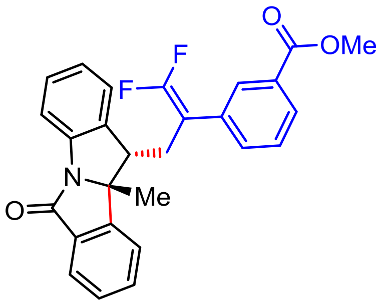
**Figure S27.** HPLC chromatography of the racemic product **16**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 22.195 | 9930701 | 179042 | 98.344 |
| 2 | 25.935 | 167192 | 2574 | 1.656 |
| 总计 |  | 10097893 | 181616 | 100.000 |

**Figure S28.** HPLC chromatography of chiral product **16**



**Methyl 3-(1,1-difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzoate, 17**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1, v/v) afforded **17** as colorless oil (58.8 mg, 0.132 mmol, 66% yield).

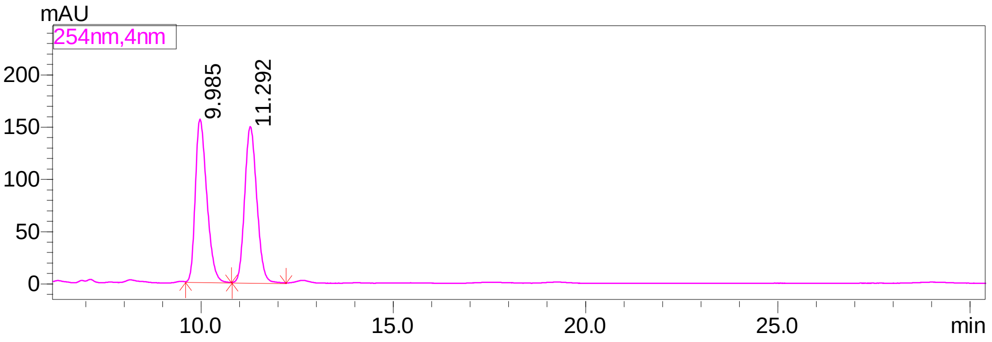
**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 8.00 – 7.94 (m, 3H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.70 (td, *J* = 7.5, 1.0 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.50 – 7.44 (m, 2H), 7.36 (td, *J* = 7.5, 1.5 Hz, 1H), 7.16 (d, *J* = 7.0 Hz, 1H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 3.98 (s, 3H), 3.06 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.30 – 2.25 (m, 1H), 1.73 – 1.67 (m, 1H), 1.50 (s, 3H) ppm.

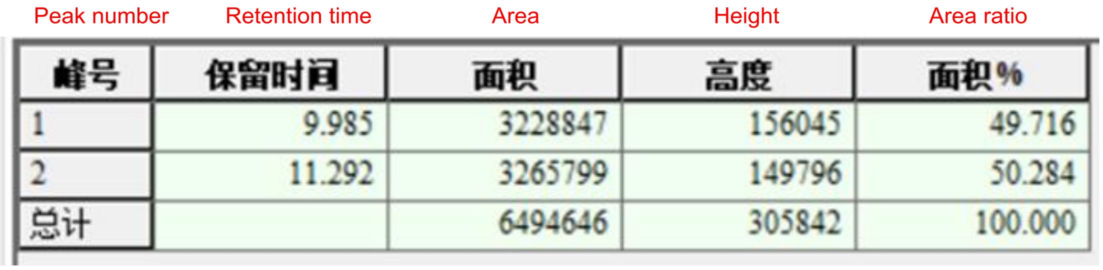
**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.2, 166.8, 154.3 (dd, *J* = 293.7, 290.6 Hz), 147.6, 138.2, 137.8, 133.8, 133.3 (t, *J* = 4.2 Hz), 132.6, 132.5 (dd, *J* = 4.4, 3.0 Hz), 130.8, 129.1, 129.05, 129.02, 128.8, 128.7, 125.9, 125.1, 124.5, 123.0, 117.5, 88.6 (dd, *J* = 21.9, 13.7 Hz), 75.0, 52.5, 47.4 (t, *J* = 2.1 Hz), 31.4, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -87.1 (d, *J* = 33.9 Hz), -88.4 (dd, *J* = 34.4, 4.2 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{27}H_{21}F_2NNaO_3^+$ 468.1382, found 468.1383.

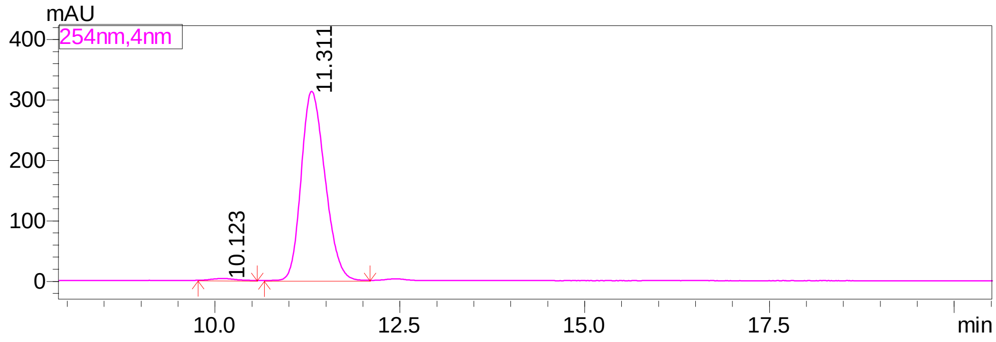
$[\alpha]^{25}_{D}$ = 152.8° (c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 99.0:0.9 (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 11.311 min, $t_{minor}$ = 10.123 min.





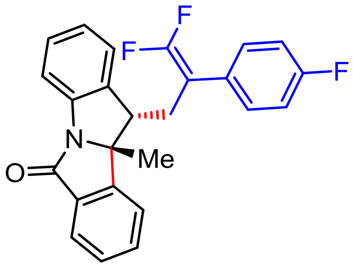
| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 9.985 | 3228847 | 156045 | 49.716 |
| 2 | 11.292 | 3265799 | 149796 | 50.284 |
| 总计 | | 6494646 | 305842 | 100.000 |

**Figure S29.** HPLC chromatography of the racemic product **17**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 10.123 | 61604 | 3026 | 0.869 |
| 2 | 11.311 | 7028977 | 313824 | 99.131 |
| 总计 | | 7090581 | 316850 | 100.000 |

**Figure S30.** HPLC chromatography of chiral product **17**



### (10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-fluorophenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 18

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **18** as a white solid (49.2 mg, 0.121 mmol, 61% yield). **m.p.** 97.9 – 99.0 □.

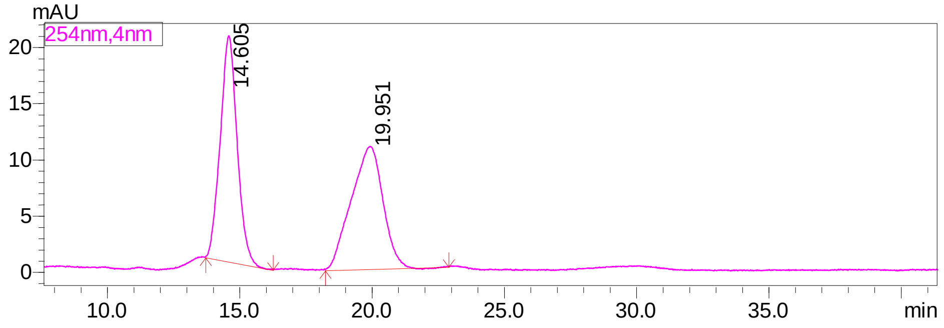
**$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.22 – 7.20 (m, 2H), 7.14 (d, *J* = 7.5 Hz, 1H), 7.11 – 7.07 (m, 3H), 3.07 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.23 – 2.18 (m, 1H), 1.66 – 1.60 (m, 1H), 1.51 (s, 3H) ppm.

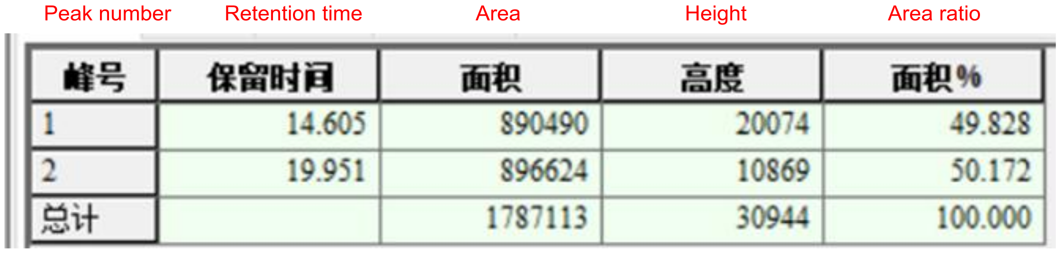
**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 167.2, 162.0 (d, *J* = 248.3 Hz), 154.1 (dd, *J* = 291.6, 290.1 Hz), 147.6, 138.2, 137.8, 133.8, 132.5, 129.84 – 129.72 (m, 2C), 129.1, 128.8, 125.9, 125.2, 124.4, 123.0, 117.5, 115.9 (d, *J* = 21.5 Hz), 88.3 (dd, *J* = 21.7, 14.2 Hz), 75.0, 47.3 (t, *J* = 2.6 Hz), 31.8, 27.0 ppm.

**$^{19}F$ NMR (471 MHz, $CDCl_3$):** δ -88.5 (d, *J* = 37.2 Hz), -89.7 (dd, *J* = 37.2, 4.2 Hz), -113.9 (m) ppm.

**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{25}H_{18}F_3NNaO^+$ 428.1233, found 428.1230.

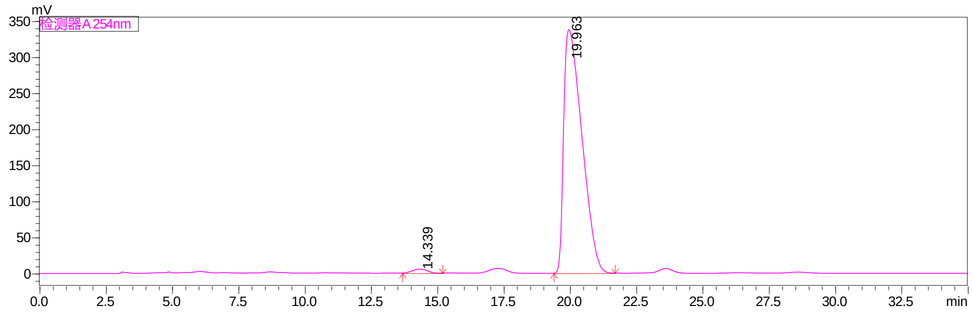
$[\alpha]^{25}_D$ = 114.8°(c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 98.8:1.2 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 19.963 min, $t_{minor}$ = 14.339 min.

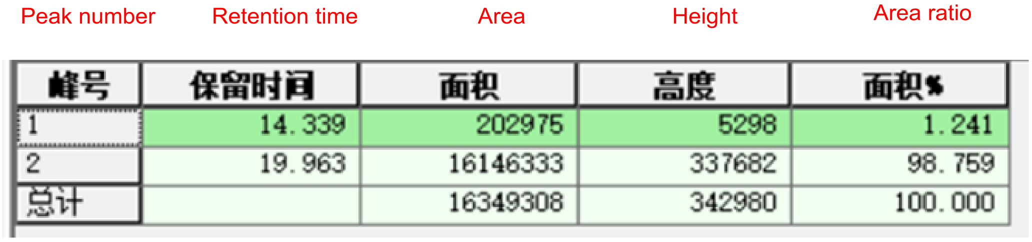




| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 14.605 | 890490 | 20074 | 49.828 |
| 2 | 19.951 | 896624 | 10869 | 50.172 |
| 总计 |  | 1787113 | 30944 | 100.000 |

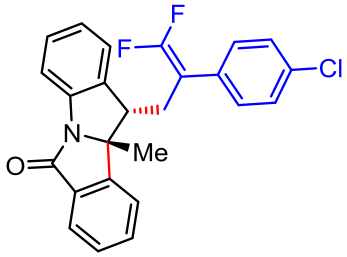
**Figure S31.** HPLC chromatography of the racemic product **18**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 14. 339 | 202975 | 5298 | 1. 241 |
| 2 | 19. 963 | 16146333 | 337682 | 98. 759 |
| 总计 |  | 16349308 | 342980 | 100. 000 |

**Figure S32.** HPLC chromatography of chiral product **18**



### (10b*R*,11*S*)-11-(2-(4-Chlorophenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 19

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **19** as yellow oil (53.2 mg, 0.126 mmol, 63% yield).

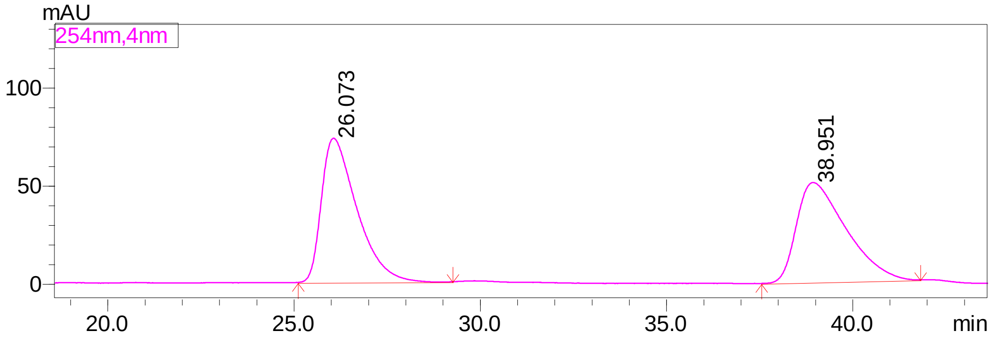
**$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.68 (td, *J* = 7.5, 1.0 Hz, 1H), 7.55 (td, *J* = 7.5, 1.0 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.38 – 7.34 (m, 3H), 7.17 (dd, *J* = 8.5, 1.5 Hz, 2H), 7.13 (d, *J* = 6.0 Hz, 1H), 7.08 (td, *J* = 7.5, 1.0 Hz, 1H), 3.06 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.23 – 2.18 (m, 1H), 1.65 – 1.60 (m, 1H), 1.50 (s, 3H) ppm.

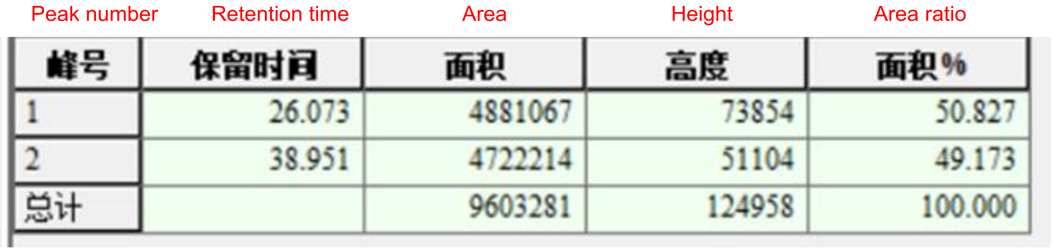
**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 167.2, 154.1 (dd, *J* = 293.2, 290.2 Hz), 147.6, 138.1, 137.8, 133.8, 133.4, 132.5, 131.3 (t, *J* = 4.2 Hz), 129.4 (t, *J* = 3.5 Hz), 129.14, 129.10, 128.8, 125.9, 125.2, 124.4, 123.0, 117.5, 88.3 (dd, *J* = 21.8, 13.7 Hz), 74.9, 47.4 (t, *J* = 2.1 Hz), 31.5, 27.0 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -87.5 (d, *J* = 35.3 Hz), -88.8 (dd, *J* = 34.9, 3.8 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: $[M+H]^+$ calcd for $C_{25}H_{19}ClF_2NO^+$ 422.1118, found 422.1121.

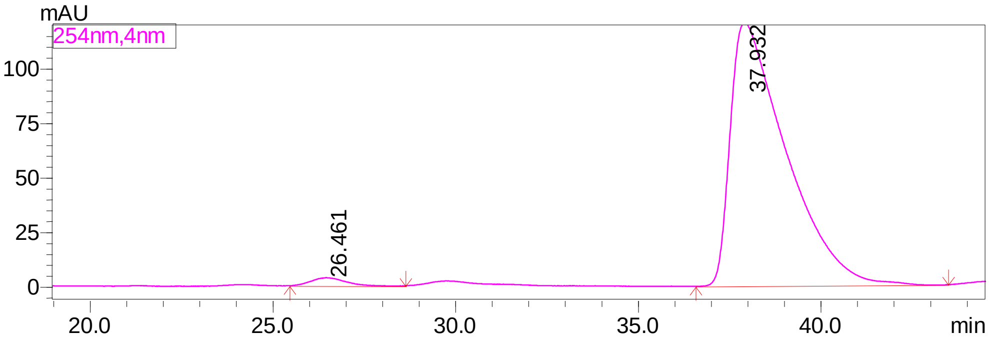
$[\alpha]^{25}_{D}$ = 189.6 ° (c = 0.50 in $CHCl_3$). The enantiomeric excess was determined analysed by HPLC: e.r. = 98.2:1.8 (Chiralpak ID *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 37.932 min, $t_{minor}$ = 26.461 min.





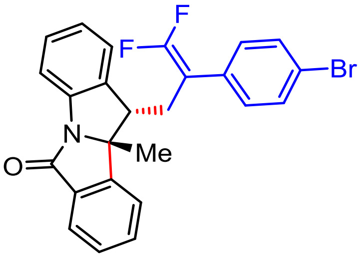
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 26.073 | 4881067 | 73854 | 50.827 |
| 2 | 38.951 | 4722214 | 51104 | 49.173 |
| 总计 |  | 9603281 | 124958 | 100.000 |

**Figure S33.** HPLC chromatography of the racemic product **19**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 26.461 | 236388 | 3734 | 1.806 |
| 2 | 37.932 | 12849970 | 121402 | 98.194 |
| 总计 |  | 13086358 | 125136 | 100.000 |

**Figure S34.** HPLC chromatography of chiral product **19**



**(10b*R*,11*S*)-11-(2-(4-Bromophenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 20**

This compound was prepared according to the general procedure **3.2**, but the reaction was run on 100 °C for 36 h. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **20** as colorless oil (41.0 mg, 0.088 mmol, 44% yield).

**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.68

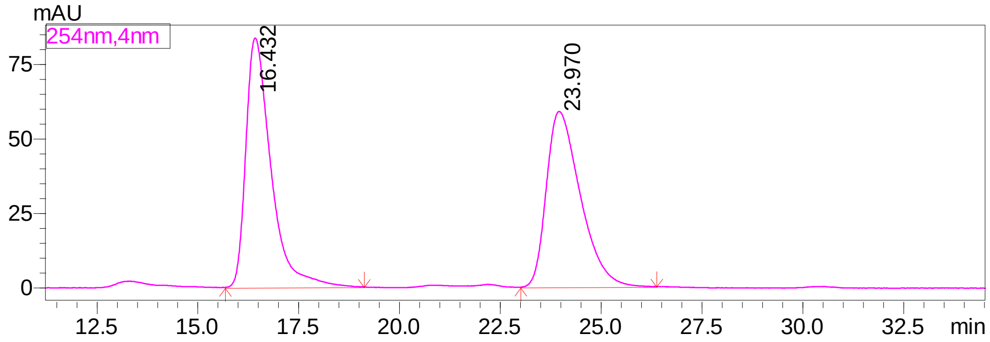
(td, *J* = 7.5, 1.0 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 8.5 Hz, 2H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.36 (td, *J* = 7.5, 1.5 Hz, 1H), 7.13 – 7.07 (m, 4H), 3.05 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.23 – 2.17 (m, 1H), 1.65 – 1.59 (m, 1H), 1.51 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.2, 154.1 (dd, *J* = 293.6, 290.7 Hz), 147.6, 138.2, 137.8, 133.9, 132.6, 132.1, 131.9 (t, *J* = 4.2 Hz), 129.7 (t, *J* = 3.4 Hz), 129.1, 128.9, 125.9, 125.2, 124.5, 123.0, 121.6, 117.5, 88.4 (dd, *J* = 21.9, 13.7 Hz), 75.0, 47.4 (t, *J* = 2.5 Hz), 31.5, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -87.3 (d, *J* = 33.9 Hz), -88.6 (dd, *J* = 34.9, 4.2 Hz) ppm.

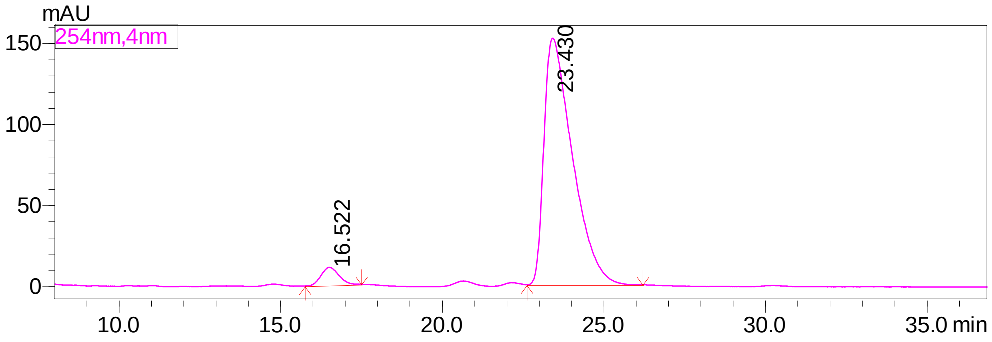
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{25}H_{18}BrF_2NNaO^+$ 488.0432, found 488.0430.

$[\alpha]^{25}_{D}$ = 174.4°(c = 0.25 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 95.7:4.3 (Chiralpak AD-H, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ= 254 nm); t$_{major}$ = 23.430 min, t$_{minor}$ = 16.522 min.



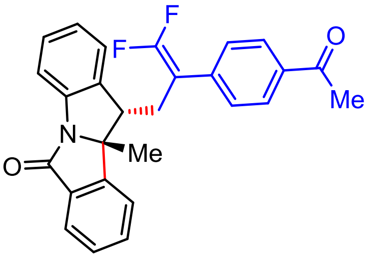
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 16.432 | 3645945 | 84187 | 51.256 |
| 2 | 23.970 | 3467257 | 59214 | 48.744 |
| 总计 | | 7113202 | 143401 | 100.000 |

**Figure S35.** HPLC chromatography of the racemic product **20**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 16.522 | 420858 | 11086 | 4.303 |
| 2 | 23.430 | 9359107 | 152918 | 95.697 |
| 总计 | | 9779966 | 164003 | 100.000 |

**Figure S36.** HPLC chromatography of chiral product **20**



**(10b*R*,11*S*)-11-(2-(4-Acetylphenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 21**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1, v/v) afforded **21** as a white solid (68.9 mg, 0.160 mmol, 80% yield). **m.p.** 47.5 – 48.7 □.

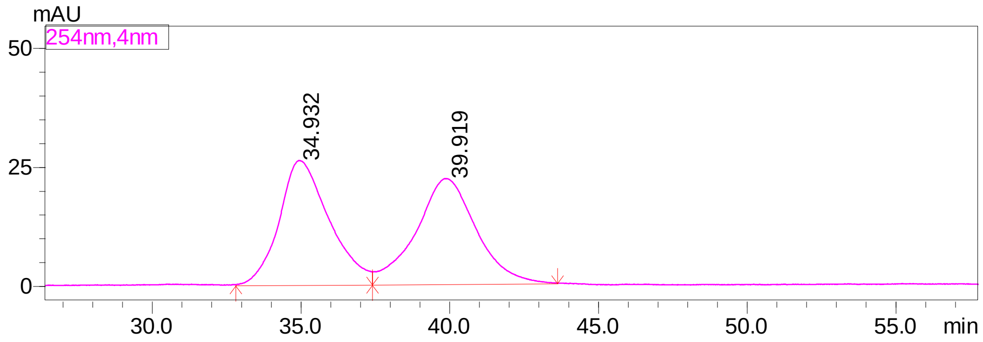
**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 7.99 (d, *J* = 8.5 Hz, 2H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.34 (m, 3H), 7.13 (d, *J* = 7.0 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 3.07 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.63 (s, 3H), 2.31– 2.26 (m, 1H), 1.70 – 1.65 (m, 1H), 1.51 (s, 3H) ppm.

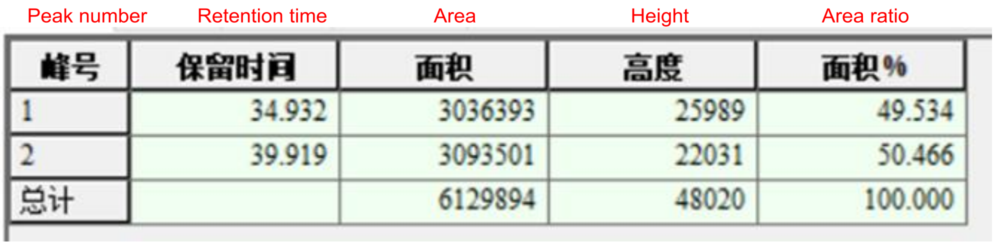
**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 197.4, 167.2, 154.4 (dd, *J* = 295.2, 291.3 Hz), 147.5, 138.0, 137.8 (t, *J* = 4.3 Hz), 137.7, 136.0, 133.8, 132.6, 129.1, 128.85, 128.83, 128.1 (t, *J* = 3.7 Hz), 125.9, 125.1, 124.4, 122.9, 117.5, 88.9 (dd, *J* = 21.9, 13.2 Hz), 74.9, 47.4, 31.2, 26.9, 26.7 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -85.7 (d, *J* = 30.6 Hz), -87.1 (dd, *J* = 30.6, 3.8 Hz) ppm.

**HRMS (ESI$^{+}$):** *m/z*: [M+Na]$^{+}$ calcd for $C_{27}H_{21}F_{2}NNaO_{2}^{+}$ 452.1433, found 452.1435.

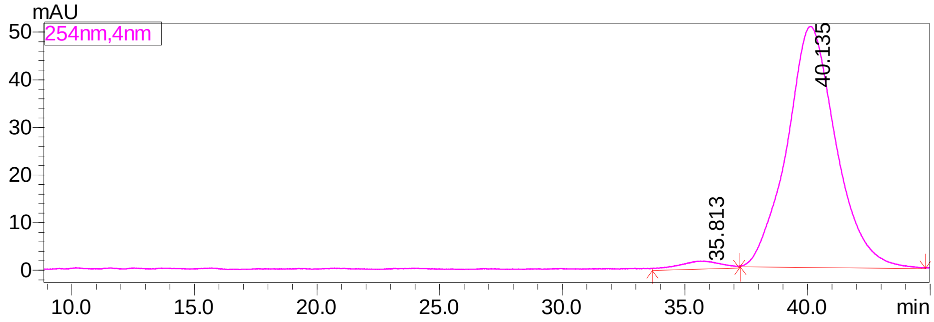
$[\alpha]^{25}_{D}$ = 141.6°(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.5:2.5 (Chiralpak AD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 40.135 min, $t_{minor}$ = 35.813 min.





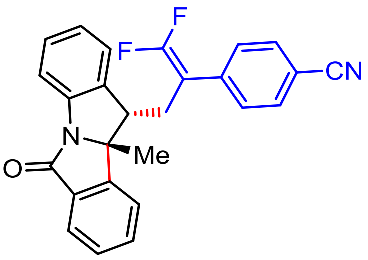
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 34.932 | 3036393 | 25989 | 49.534 |
| 2 | 39.919 | 3093501 | 22031 | 50.466 |
| 总计 |  | 6129894 | 48020 | 100.000 |

**Figure S37.** HPLC chromatography of the racemic product **21**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 35.813 | 177099 | 1516 | 2.476 |
| 2 | 40.135 | 6974206 | 50276 | 97.524 |
| 总计 |  | 7151305 | 51792 | 100.000 |

**Figure S38.** HPLC chromatography of chiral product **21**



**4-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-**

**isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzonitrile, 22**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1 v/v) afforded **22** as a white solid (60.8 mg, 0.147 mmol, 74% yield). **m.p.** 137.7 – 139.9 □.

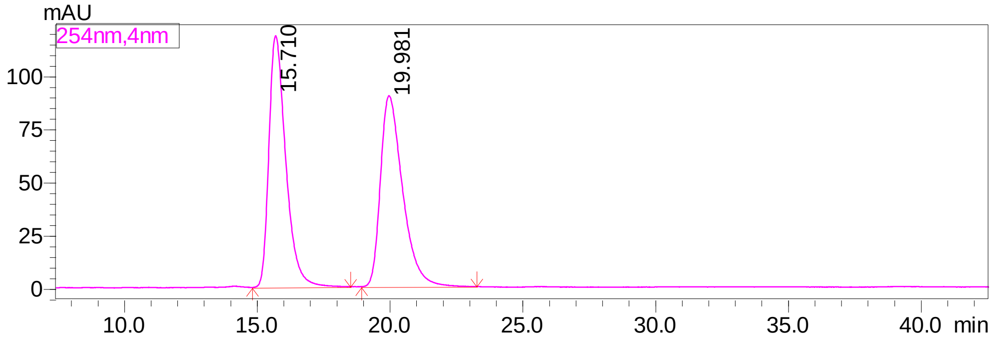
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 – 7.68 (m, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.35 (td, *J* = 7.0, 1.5 Hz, 1H), 7.28 (d, *J* = 7.0 Hz, 2H), 7.09 – 7.03 (m, 2H), 3.10 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.31 – 2.26 (m, 1H), 1.68 – 1.63 (m, 1H), 1.53 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.1, 154.6 (dd, *J* = 296.1, 292.1 Hz), 147.4, 137.9 (t, *J* = 4.5 Hz), 137.8, 137.7, 133.8, 132.6, 132.5, 129.2, 129.0, 128.6 (t, *J* = 3.9 Hz), 125.9, 125.2, 124.4, 122.9, 118.5, 117.5, 111.1, 88.7 (dd, *J* = 22.2, 12.6 Hz), 74.9, 47.5, 31.0, 26.9 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -84.3 (d, *J* = 27.8 Hz), -86.1 (dd, *J* = 28.7, 3.3 Hz) ppm.

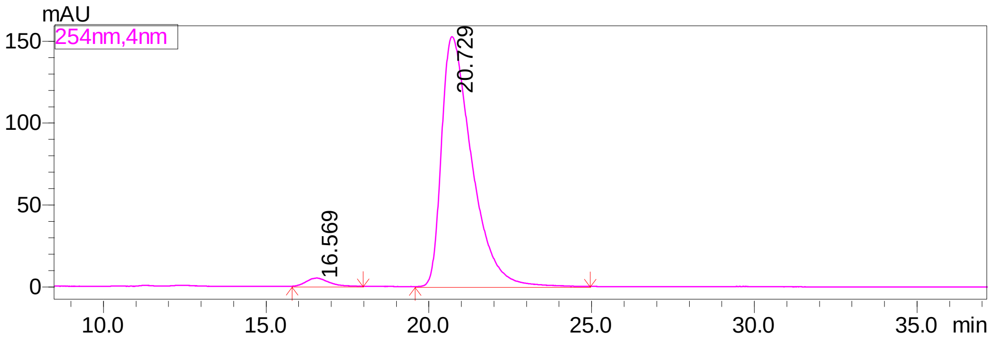
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{18}F_2N_2NaO^+$ 435.1279, found 435.1278.

$[\alpha]^{25}_{D}$ = 221.6˚(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.6:2.4 (Chiralpak ID, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 20.729 min, $t_{minor}$ = 16.569 min.



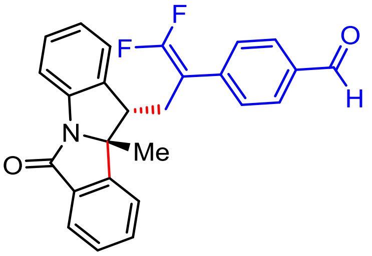
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 15.710 | 5219807 | 118196 | 50.037 |
| 2 | 19.981 | 5212084 | 89762 | 49.963 |
| 总计 |  | 10431891 | 207958 | 100.000 |

**Figure S39.** HPLC chromatography of the racemic product **22**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 16.569 | 242345 | 5058 | 2.401 |
| 2 | 20.729 | 9852135 | 152369 | 97.599 |
| 总计 |  | 10094479 | 157427 | 100.000 |

**Figure S40.** HPLC chromatography of chiral product **22**



### 4-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzaldehyde, 23

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1, v/v) afforded **23** as a white solid (66.7 mg, 0.160 mmol, 80% yield). **m.p.** 57.1 – 59.3 □.

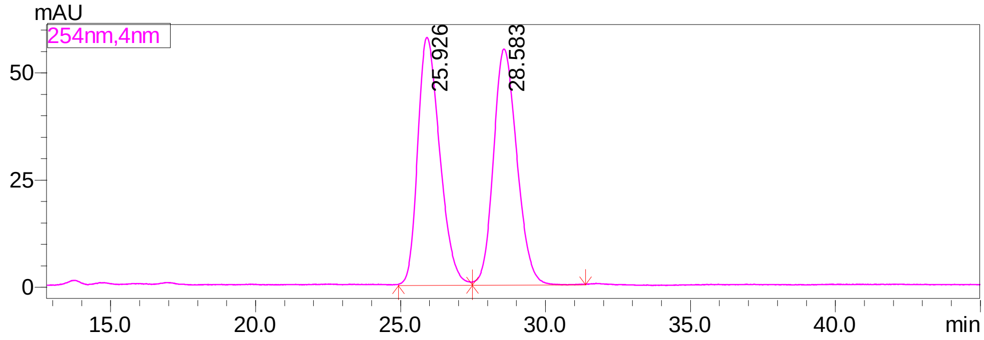
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 10.02 (s, 1H), 7.95 (d, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.70 (td, *J* = 7.5, 1.0 Hz, 1H), 7.57 (td, *J* = 7.5, 1.0 Hz, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.40 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.35 (td, *J* = 7.5, 1.0 Hz, 1H), 7.12 (d, *J* = 6.5 Hz, 1H), 7.07 (td, *J* = 7.5, 1.0 Hz, 1H), 3.09 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.33 – 2.28 (m, 1H), 1.71 – 1.66 (m, 1H), 1.52 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 191.5, 167.2, 154.5 (dd, *J* = 296.0, 291.9 Hz), 147.5, 139.4 (t, *J* = 4.4 Hz), 137.9, 137.8, 135.3, 133.8, 132.6, 130.1, 129.2, 128.9, 128.6 (t, *J* = 3.4 Hz), 125.9, 125.2, 124.4, 123.0, 117.5, 89.0 (dd, *J* = 21.9, 12.9 Hz), 74.9, 47.5, 31.2, 26.9 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -84.9 (d, *J* = 29.2 Hz), -86.5 (dd, *J* = 29.2, 3.8 Hz) ppm.

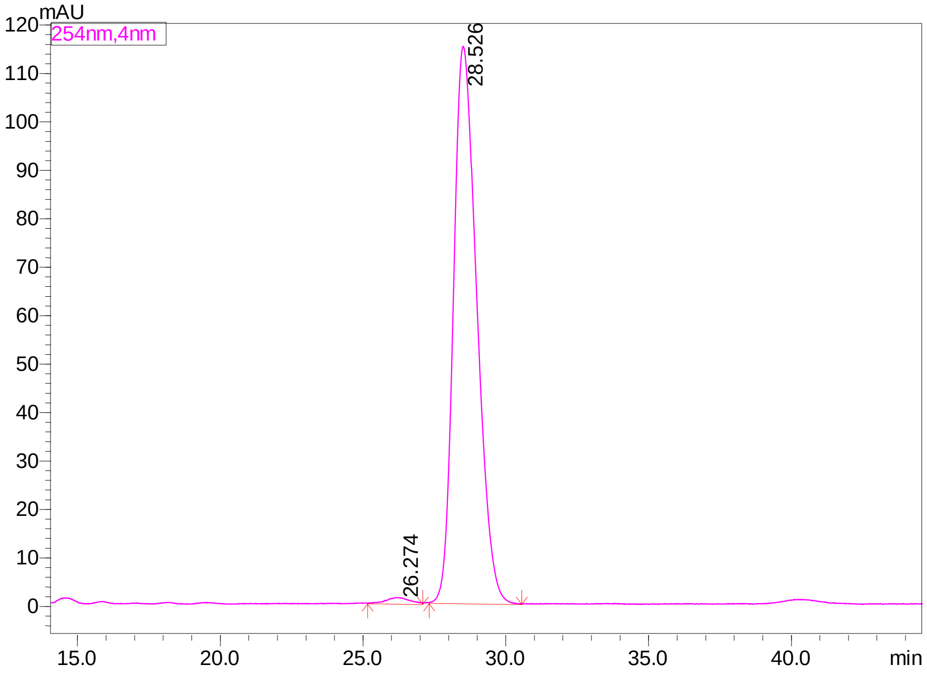
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for: $C_{26}H_{19}F_2NNaO_2^+$ 438.1276, found 438.1274.

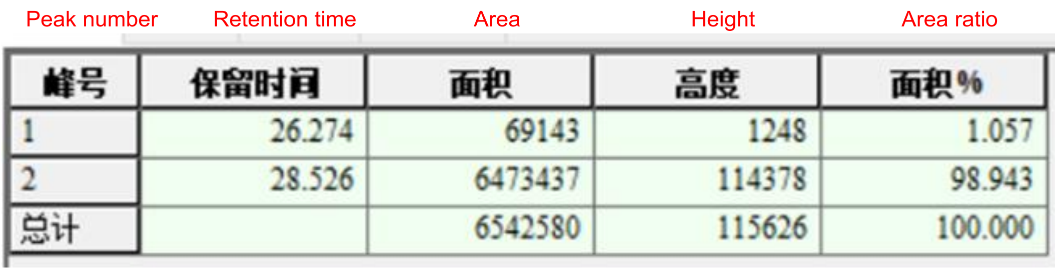
$[\alpha]^{25}_{D}$ = 136.0 ° (c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 98.9:1.1 (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ= 254 nm); t$_{major}$ = 28.526 min, t$_{minor}$ = 26.274 min.



| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 25.926 | 3029096 | 57456 | 49.792 |
| 2 | 28.583 | 3054454 | 54689 | 50.208 |
| 总计 |  | 6083550 | 112146 | 100.000 |

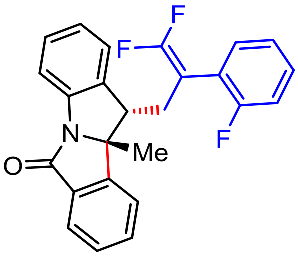
**Figure S41.** HPLC chromatography of the racemic product **23**





| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 26.274 | 69143 | 1248 | 1.057 |
| 2 | 28.526 | 6473437 | 114378 | 98.943 |
| 总计 |  | 6542580 | 115626 | 100.000 |

**Figure S42.** HPLC chromatography of chiral product **23**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(2-fluorophenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 24**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1, v/v) afforded **24** as colorless oil (33.7 mg, 0.083 mmol, 42% yield).

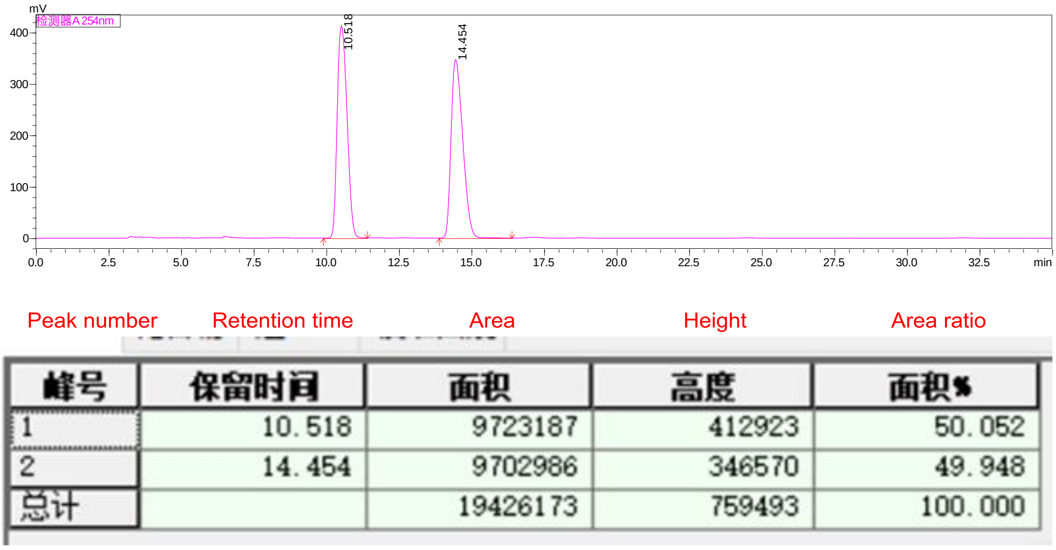
**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.22 – 7.14 (m, 3H), 7.11 (t, *J* = 7.5 Hz, 1H), 2.97 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.23 – 2.18 (m, 1H), 1.72 – 1.67 (m, 1H), 1.48 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 160.3 (d, *J* = 248.5 Hz), 153.7 (t, *J* = 291.3 Hz), 147.7, 138.5, 137.7, 133.8, 132.5, 130.6, 130.0 (d, *J* = 8.3 Hz), 129.0, 128.7, 125.9 (d, *J* = 2.8 Hz), 125.0, 124.7 (d, *J* = 3.5 Hz), 124.6, 123.2, 120.6 (*J* = 14.1 Hz), 117.3, 116.4 (d, *J* = 22.7 Hz), 84.1 (dd, *J* = 24.4, 17.0 Hz), 75.0, 47.6, 32.3, 27.1 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -85.8 (dd, *J* = 31.6, 15.5 Hz), -88.6 (d, *J* = 31.6 Hz), -112.7 (m) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{25}H_{18}F_3NNaO^+$ 428.1233, found 428.1233.

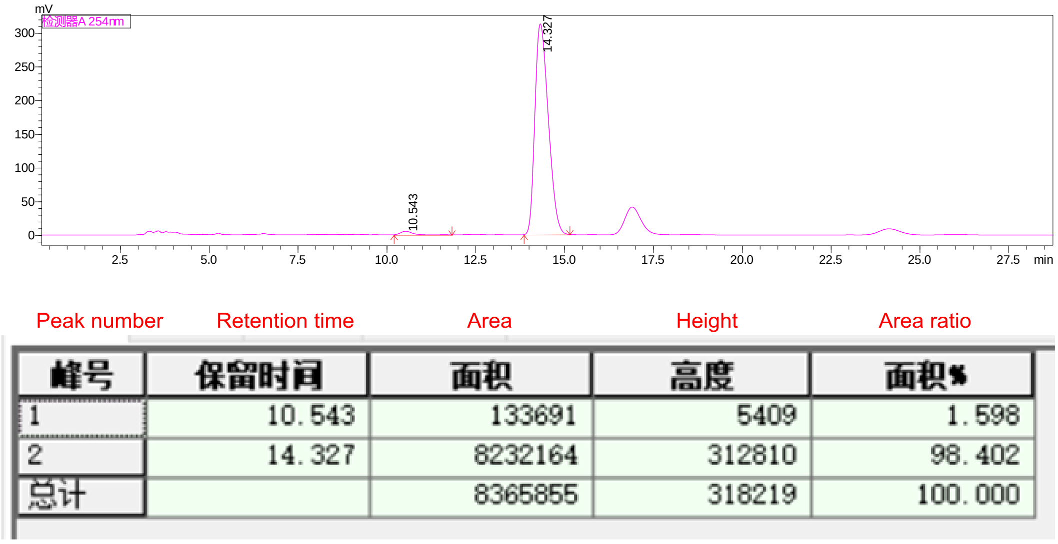
$[\alpha]^{25}_{D}$ = 88.8 (c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 98.4:1.6 (Chiralpak ID, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 14.327 min, $t_{minor}$ = 10.543 min.



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 10. 518 | 9723187 | 412923 | 50. 052 |
| 2 | 14. 454 | 9702986 | 346570 | 49. 948 |
| 总计 | | 19426173 | 759493 | 100. 000 |

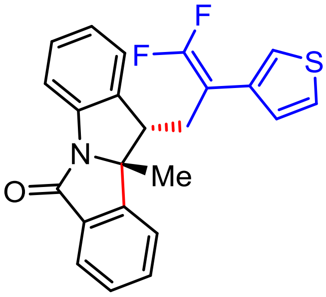
**Figure S43.** HPLC chromatography of the racemic product **24**



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 10. 543 | 133691 | 5409 | 1. 598 |
| 2 | 14. 327 | 8232164 | 312810 | 98. 402 |
| 总计 | | 8365855 | 318219 | 100. 000 |

**Figure S44.** HPLC chromatography of chiral product **24**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(thiophen-3-yl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 25**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **25** as a white solid (41.2 mg, 0.105 mmol, 52% yield). **m.p.** 57.0 – 59.0 □.

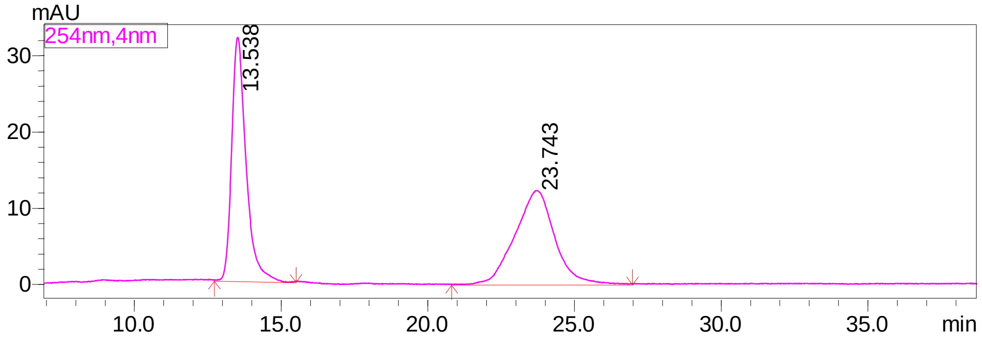
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.57 – 7.53 (m, 2H), 7.36 – 7.33 (m, 2H), 7.07 – 7.03 (m, 4H), 3.22 (dd, *J* = 11.0, 4.5 Hz, 1H), 2.23 – 2.18 (m, 1H), 1.57 – 1.56 (m, 4H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.5 (dd, *J* = 294.3, 289.2 Hz), 147.8, 138.2, 137.8, 133.9, 133.2 (t, *J* = 4.0 Hz), 132.6, 129.1, 128.8, 126.7 (dd, *J* = 5.9, 2.0 Hz), 126.22, 126.16, 125.2, 124.4, 123.0, 122.1 (t, *J* = 5.0 Hz), 117.4, 85.6 (dd, *J* = 23.6, 14.1 Hz), 75.1, 47.8, 31.3, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -86.0 (d, *J* = 34.9 Hz), -89.4 (d, *J* = 35.3 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{23}H_{17}F_2NNaOS^+$ 416.0891, found 416.0889.

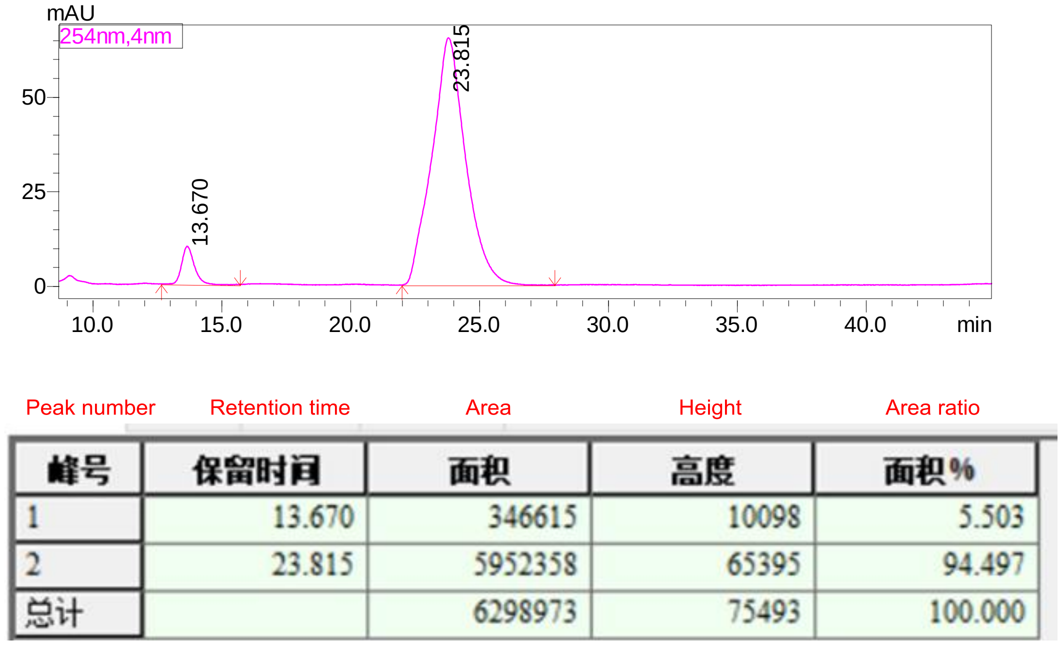
$[\alpha]^{25}_{D}$ = 169.6 ° (c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 94.5:5.5 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); t$_{major}$ = 23.815 min, t$_{minor}$ = 13.670 min.



Peak number Retention time Area Height Area ratio

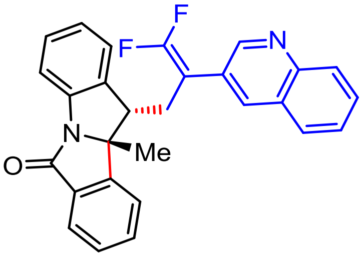
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 13.538 | 1084851 | 31948 | 48.353 |
| 2 | 23.743 | 1158740 | 12317 | 51.647 |
| 总计 | | 2243590 | 44266 | 100.000 |

**Figure S45.** HPLC chromatography of the racemic product **25**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 13.670 | 346615 | 10098 | 5.503 |
| 2 | 23.815 | 5952358 | 65395 | 94.497 |
| 总计 | | 6298973 | 75493 | 100.000 |

**Figure S46.** HPLC chromatography of chiral product **25**



### (10b*R*,11*S*)-11-(3,3-Difluoro-2-(quinolin-3-yl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 26

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1 to 3/1, v/v) afforded **26** as a white solid (49.1 mg, 0.112 mmol, 56% yield). **m.p.** 57.7 – 58.3 □.

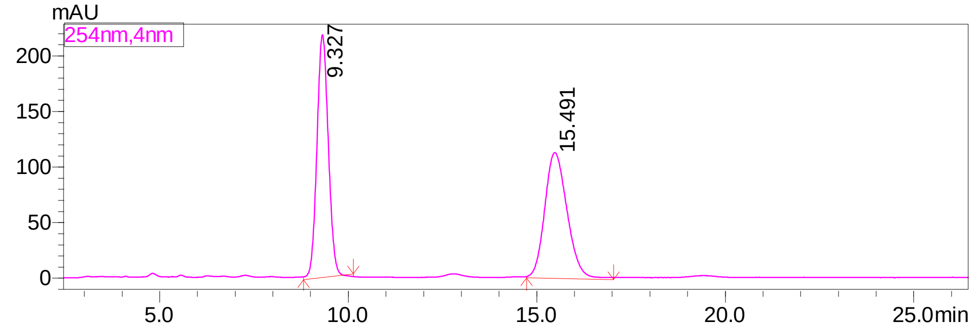
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 8.85 (t, *J* = 2.0 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 1H), 7.82 – 7.79 (m, 2H), 7.76 – 7.74 (m, 2H), 7.70 (t, *J* = 7.5, 1.5 Hz, 1H), 7.61 – 7.53 (m, 3H), 7.34 (td, *J* = 7.5, 1.0 Hz, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 3.15 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.42 – 2.37 (m, 1H), 1.79 – 1.74 (m, 1H), 1.52 (s, 3H) ppm.

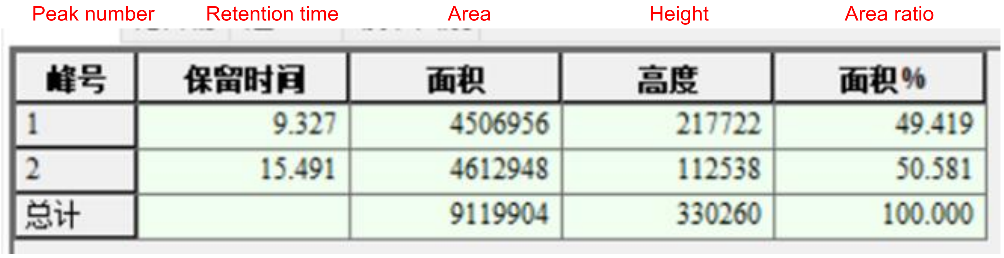
**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.2, 154.7 (dd, *J* = 294.5, 292.4 Hz), 149.6, 147.5, 147.1, 138.0, 137.9, 134.9 (t, *J* = 2.9 Hz), 133.8, 132.7, 130.1, 129.3, 129.2, 129.0, 128.0, 127.7, 127.4, 126.2 (t, *J* = 4.0 Hz), 125.9, 125.2, 124.5, 123.0, 117.6, 86.9 (dd, *J* = 22.6, 14.0 Hz), 75.0, 47.6, 31.4, 26.9 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -85.7 (d, *J* = 32.0 Hz), -87.7 (dd, *J* = 32.0, 1.4 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+H]$^+$ calcd for $C_{28}H_{21}F_2N_2O^+$ 439.1616, found 439.1614.

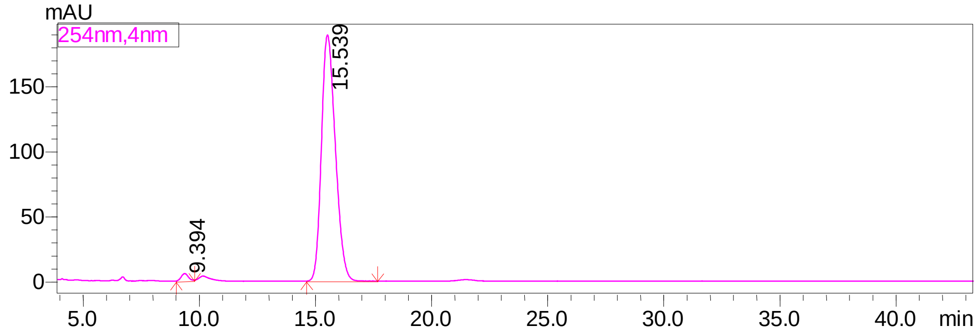
$[\alpha]^{25}_{D}$ = 64.0 ° (c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 98.4:1.6 (Chiralpak AD-H, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 15.539 min, $t_{minor}$ = 9.394 min.

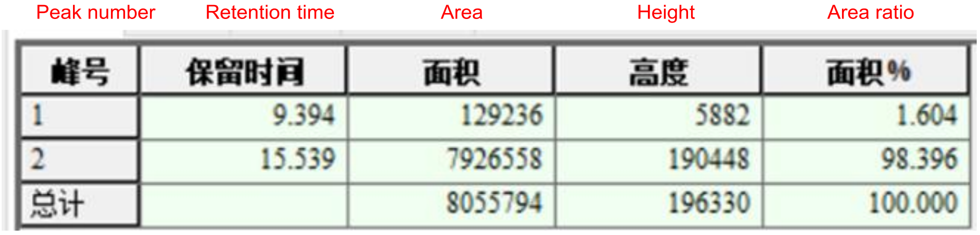




| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.327 | 4506956 | 217722 | 49.419 |
| 2 | 15.491 | 4612948 | 112538 | 50.581 |
| 总计 | | 9119904 | 330260 | 100.000 |

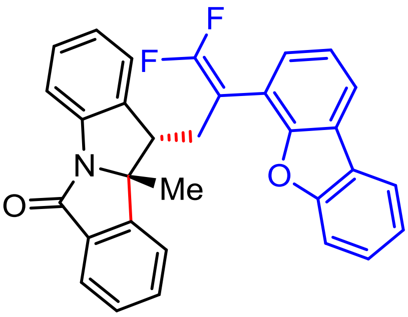
**Figure S47.** HPLC chromatography of the racemic product **26**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.394 | 129236 | 5882 | 1.604 |
| 2 | 15.539 | 7926558 | 190448 | 98.396 |
| 总计 | | 8055794 | 196330 | 100.000 |

**Figure S48.** HPLC chromatography of chiral product **26**



### (10b*R*,11*S*)-11-(2-(Dibenzo[*b*,*d*]furan-4-yl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 27

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **27** as a white solid (50.3 mg, 0.105 mmol, 53% yield). **m.p.** 63.8 – 65.7 □.

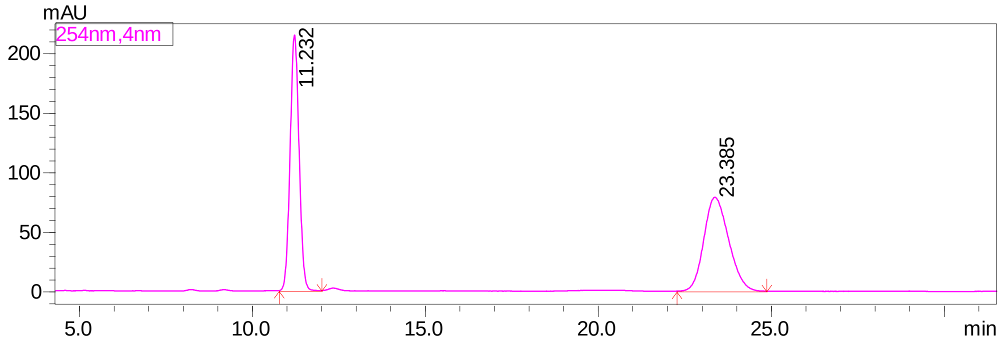
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 8.02 – 7.95 (m, 3H), 7.74 – 7.66 (m, 3H), 7.57 – 7.50 (m, 3H), 7.44 – 7.40 (m, 2H), 7.37 – 7.33 (m, 3H), 7.11 (t, *J* = 7.5 Hz, 1H), 2.95 (dd, *J* = 10.0, 5.0 Hz, 1H), 2.61 – 2.56 (m, 1H), 1.95 – 1.90 (m, 1H), 1.40 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.4, 156.0, 154.0 (dd, *J* = 291.6, 289.7 Hz), 153.8 (t, *J* = 1.1 Hz), 147.8, 138.7, 137.8, 133.8, 132.4, 129.0, 128.6, 127.8, 127.7, 126.0, 125.1, 124.5, 124.1, 123.35, 123.29, 123.2, 121.0, 120.6, 117.46 – 117.40 (m, 1C), 117.3, 111.7, 85.5 (dd, *J* = 24.3, 16.0 Hz), 75.0, 47.7, 31.7, 27.1 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -85.9 (dd, *J* = 31.6, 3.8 Hz), -88.6 (d, *J* = 31.6 Hz) ppm.

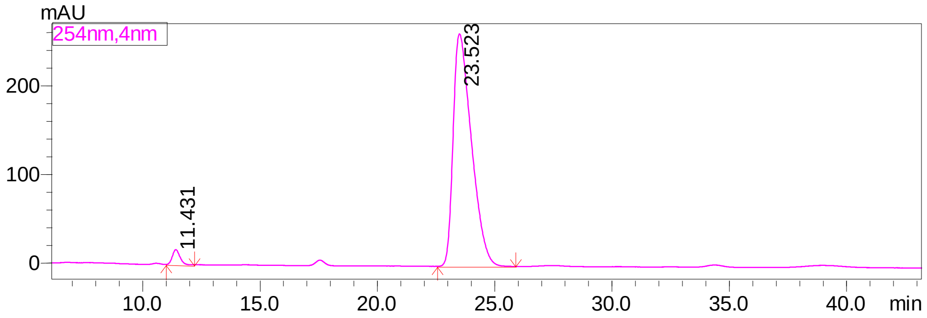
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{31}H_{21}F_2NNaO_2^+$ 500.1433, found 500.1436.

$[\alpha]^{25}_{D}$ = 89.6 °(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.2:2.8 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); t$_{major}$ = 23.523 min, t$_{minor}$ = 11.431 min.



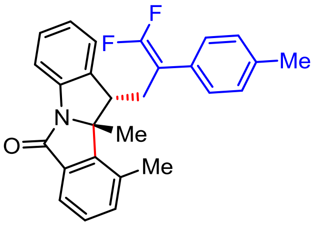
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 11.232 | 3900317 | 215878 | 49.673 |
| 2 | 23.385 | 3951597 | 79251 | 50.327 |
| 总计 | | 7851914 | 295129 | 100.000 |

**Figure S49.** HPLC chromatography of the racemic product **27**



| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 11.431 | 418832 | 17548 | 2.846 |
| 2 | 23.523 | 14298153 | 263868 | 97.154 |
| 总计 | | 14716985 | 281416 | 100.000 |

**Figure S50.** HPLC chromatography of chiral product **27**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-10,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 28**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **28** as a yellow solid (41.2 mg, 0.099 mmol, 50% yield). **m.p.** 42.4 – 43.3 □.

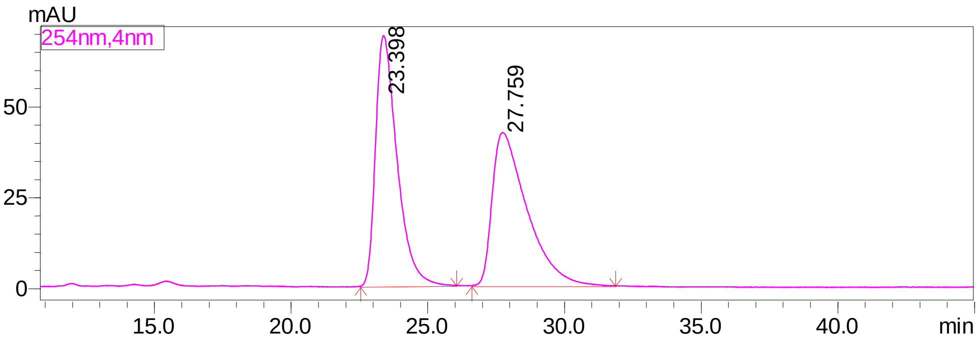
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.79 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.35 (td, *J* = 7.5, 1.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.19 – 7.16 (m, 3H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 3.11 (dd, *J* = 12.0, 3.5 Hz, 1H), 2.49 (s, 3H), 2.37 (s, 3H), 2.17 – 2.12 (m, 1H), 1.62 – 1.56 (m, 1H), 1.51 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 166.6, 154.2 (dd, *J* = 291.9, 289.2 Hz), 145.6, 138.1, 137.5, 137.2, 134.4, 134.3, 132.6, 129.9 (t, *J* = 3.8 Hz), 129.6, 129.3, 128.7, 128.1 (t, *J* = 3.2 Hz), 126.1, 124.2, 122.8, 117.2, 88.7 (dd, *J* = 21.3, 14.6 Hz), 75.3, 46.8 (t, *J* = 2.4 Hz), 31.3, 24.8, 21.3, 19.0 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -89.3 (d, *J* = 38.2 Hz), -90.4 (dd, *J* = 38.2, 5.2 Hz) ppm.

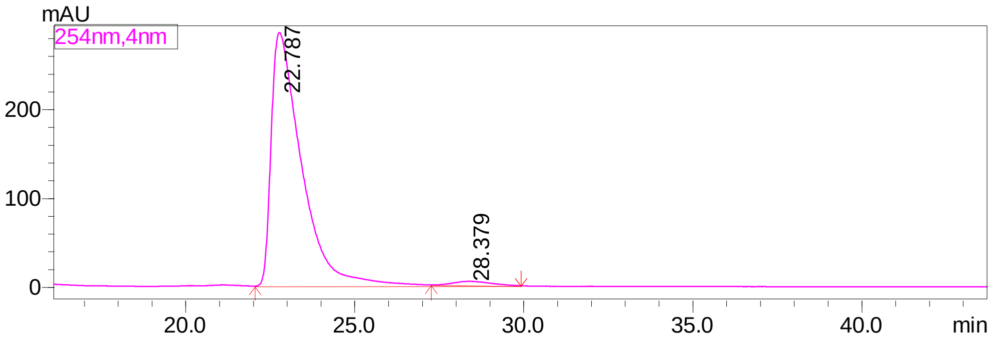
**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{23}F_2NNaO^+$ 438.1640, found 438.1640.

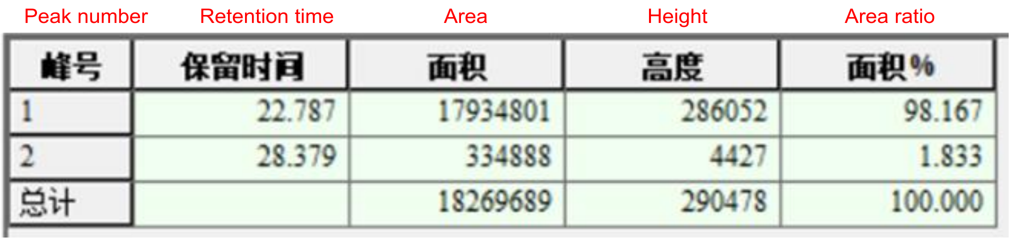
$[\alpha]^{25}_{D}$ = 105.6° (c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 98.0:1.8 (Chiralpak ID, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 22.787 min, $t_{minor}$ = 28.379 min



| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 23.398 | 3785170 | 69101 | 50.297 |
| 2 | 27.759 | 3740511 | 42274 | 49.703 |
| 总计 |  | 7525681 | 111375 | 100.000 |

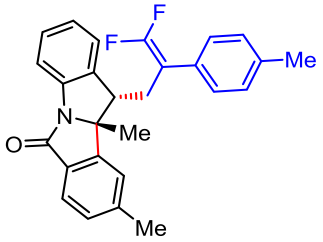
**Figure S51.** HPLC chromatography of the racemic product **28**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 22.787 | 17934801 | 286052 | 98.167 |
| 2 | 28.379 | 334888 | 4427 | 1.833 |
| 总计 | | 18269689 | 290478 | 100.000 |

**Figure S52.** HPLC chromatography of chiral product **28**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-9,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 29**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **29** as a yellow solid (46.3 mg, 0.111 mmol, 56% yield). **m.p.** 42.4 – 43.3 □.

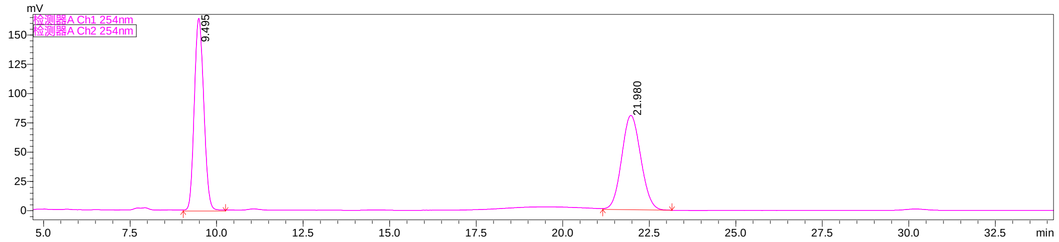
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.81 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.29 (s, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.19 – 7.15 (m, 3H), 7.07 (td, *J* = 7.5, 1.0 Hz, 1H), 3.05 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.55 (s, 3H), 2.38 (s, 3H), 2.25 – 2.19 (m, 1H), 1.68 – 1.63 (m, 1H), 1.46 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.5, 154.0 (dd, *J* = 291.7, 289.2 Hz), 148.1, 143.3, 138.4, 137.9, 137.5, 131.3, 130.1, 129.8 (t, *J* = 3.8 Hz), 129.7, 128.6, 128.0 (t, *J* = 3.3 Hz), 125.9, 124.9, 124.3, 123.5, 117.3, 88.8 (dd, *J* = 21.0, 14.2 Hz), 74.8, 47.2, 31.6, 27.0, 22.2, 21.3 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.1 (d, *J* = 38.2 Hz), -90.2 (d, *J* = 37.7 Hz) ppm.

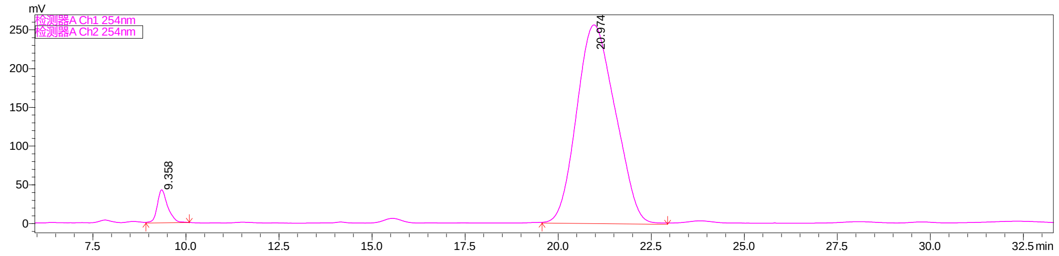
**HRMS (ESI$^+$):** *m/z*: $[M+H]^+$ calcd for $C_{27}H_{24}F_2NO^+$ 416.1820, found 416.1826.

$[\alpha]^{25}_{D}$ = 63.2 ° (c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 95.9:4.1 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 20.974 min, $t_{minor}$ = 9.358 min.



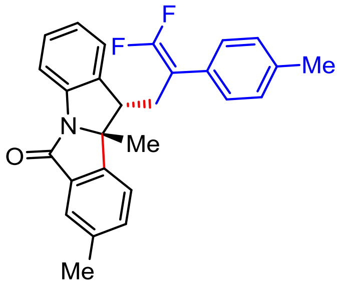
| 峰号 | 保留时间 | 面积 | 面积% | 高度 |
|---|---|---|---|---|
| 1 | 9.495 | 3141372 | 50.635 | 164145 |
| 2 | 21.980 | 3062521 | 49.365 | 80248 |
| 总计 | | 6203893 | 100.000 | 244393 |

**Figure S53.** HPLC chromatography of the racemic product **29**



| 峰号 | 保留时间 | 面积 | 面积% | 高度 |
|---|---|---|---|---|
| 1 | 9.358 | 796511 | 4.144 | 41977 |
| 2 | 20.974 | 18424862 | 95.856 | 255885 |
| 总计 | | 19221374 | 100.000 | 297862 |

**Figure S54.** HPLC chromatography of chiral product **29**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-8,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 30**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **30** as a yellow solid (49.3 mg, 0.119 mmol, 59% yield). **m.p.** 81.3 – 85.5 □.

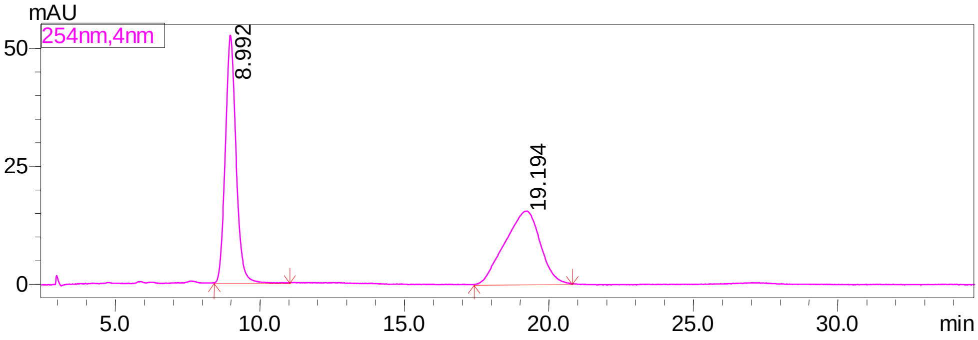
**$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.35 – 7.32 (m, 2H), 7.29 (s, 1H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.19 – 7.15 (m, 3H), 7.08 (td, *J* = 7.0, 1.0 Hz, 1H), 3.05 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.55 (s, 3H), 2.39 (s, 3H), 2.25 – 2.19 (m, 1H), 1.68 – 1.63 (m, 1H), 1.47 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 167.5, 154.0 (dd, *J* = 292.1, 289.2 Hz), 148.2, 143.3, 138.4, 138.0, 137.5, 131.3, 130.0, 129.8 (t, *J* = 3.9 Hz), 129.7, 128.6, 128.0 (t, *J* = 3.4 Hz), 125.9, 124.8, 124.2, 123.6, 117.3, 88.8 (dd, *J* = 21.0, 14.1 Hz), 74.7, 47.2, 31.6, 27.0, 22.2, 21.3 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -89.1 (d, *J* = 37.7 Hz), -90.2 (dd, *J* = 38.2, 3.8 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{27}H_{23}F_2NNaO^+$ 438.1640, found 438.1648.

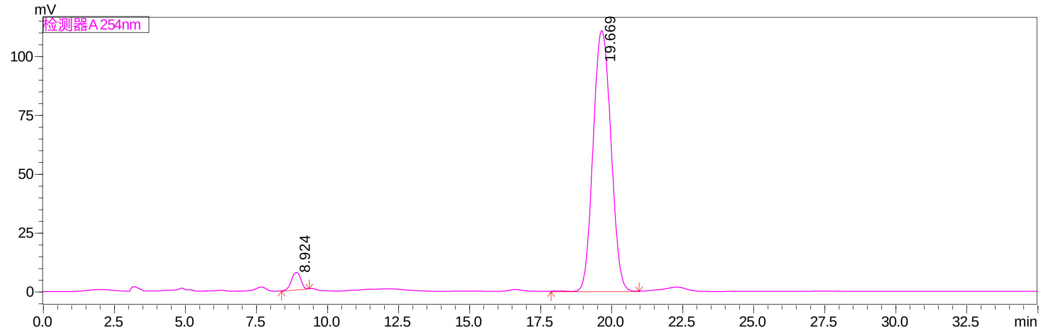
$[\alpha]^{25}_{D}$ = 180.0˚(c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 96.7:3.3 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 19.669 min, $t_{minor}$ = 8.924 min.



Peak number Retention time Area Height Area ratio

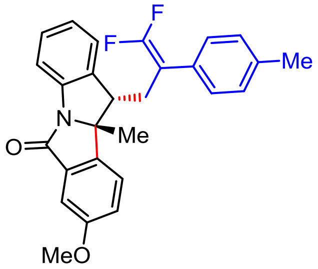
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 8.992 | 1353201 | 52580 | 50.643 |
| 2 | 19.194 | 1318833 | 15508 | 49.357 |
| 总计 | | 2672034 | 68088 | 100.000 |

**Figure S55.** HPLC chromatography of the racemic product **30**



| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 8.924 | 163617 | 7264 | 3.283 |
| 2 | 19.669 | 4819731 | 110660 | 96.717 |
| 总计 | | 4983348 | 117924 | 100.000 |

**Figure S56.** HPLC chromatography of chiral product **30**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-8-methoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 31**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 6/1, v/v) afforded **31** as a yellow solid (48.1 mg, 0.111 mmol, 56% yield). **m.p.** 54.4 – 56.2 □.

**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.72 (d, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 2.5 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 1H), 7.35 (td, *J* = 7.5, 1.0 Hz, 1H), 7.24 – 7.22 (m, 3H), 7.19 – 7.16 (m, 3H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 3.89 (s, 3H), 3.02 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.38 (s, 3H), 2.22 – 2.17 (m, 1H), 1.66 – 1.61 (m, 1H), 1.46 (s, 3H) ppm.

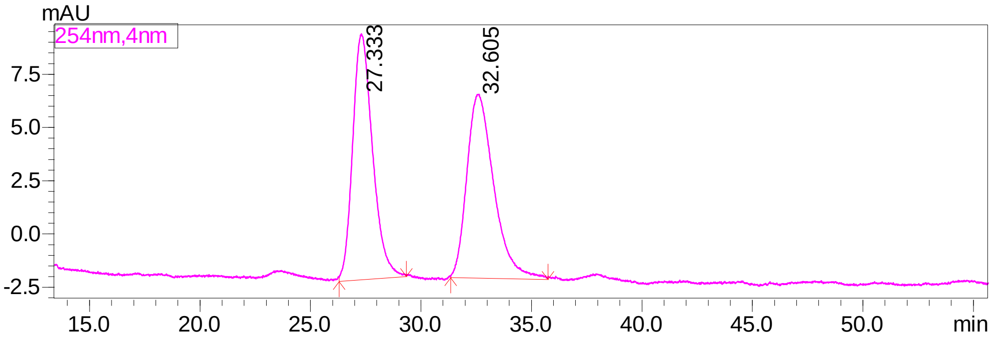
**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 160.6, 154.0 (dd, *J* = 292.1, 289.2 Hz), 140.0, 138.7, 137.8, 137.5, 135.2, 129.8 (t, *J* = 3.8 Hz), 129.6, 128.6, 128.0 (t, *J* = 3.3 Hz), 126.0, 124.4, 123.8, 120.9, 117.3, 107.5, 88.8 (dd, *J* = 21.0, 14.0 Hz), 74.6, 55.8, 47.3 (t, *J* = 2.6 Hz), 31.7, 27.0, 21.3 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.2 (d, *J* = 38.2 Hz), -90.2 (dd, *J* = 37.7, 3.8 Hz)

ppm.

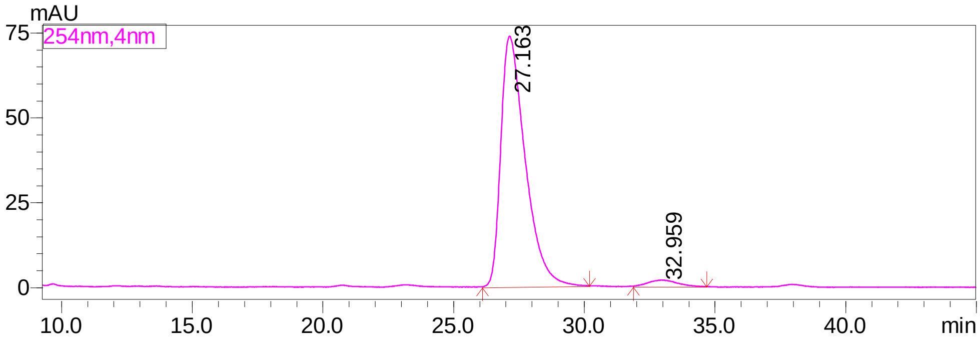
**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{23}F_2NaNO_2^+$ 454.1589, found 454.1589.

$[\alpha]^{25}_{D}$ = 208.8 °(c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.1:2.9 (Chiralpak ID, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 27.163 min, $t_{minor}$ = 32.959 min.



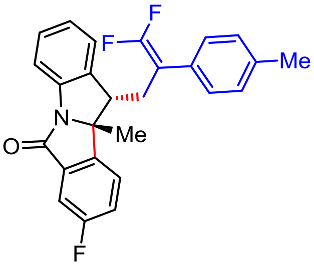
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 27.333 | 717451 | 11523 | 49.842 |
| 2 | 32.605 | 721992 | 8601 | 50.158 |
| 总计 |  | 1439443 | 20124 | 100.000 |

**Figure S57.** HPLC chromatography of the racemic product **31**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 27.163 | 4787652 | 73906 | 97.059 |
| 2 | 32.959 | 145088 | 1935 | 2.941 |
| 总计 |  | 4932741 | 75841 | 100.000 |

**Figure S58.** HPLC chromatography of chiral product **31**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-8-fluoro-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 32**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 10/1, v/v) afforded **32** as yellow oil (52.3 mg, 0.125 mmol, 62% yield).

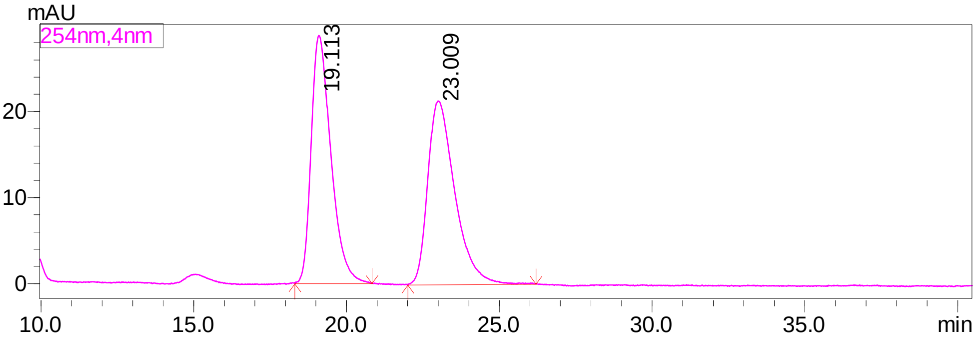
**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 7.72 (d, *J* = 8.0 Hz, 1H), 7.60 (dd, *J* = 7.5, 2.5 Hz, 1H), 7.46 (dd, *J* = 8.5, 4.5 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.19 – 7.17 (m, 3H), 7.11 (td, *J* = 7.5, 1.5 Hz, 1H), 3.06 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.39 (s, 3H), 2.20 – 2.15 (m, 1H), 1.69 – 1.63 (m, 1H), 1.48 (s, 3H) ppm.

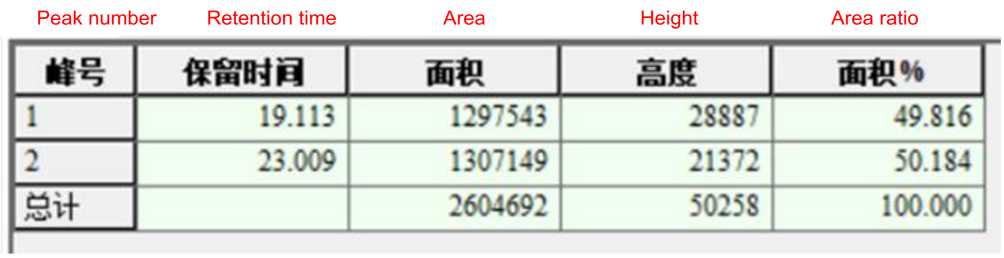
**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 166.0 (d, *J* = 3.3 Hz), 163.4 (d, *J* = 249.4 Hz), 154.0 (dd, *J* = 292.3, 289.5 Hz), 143.3 (d, *J* = 2.6 Hz), 138.5, 137.6, 137.5, 136.1 (d, *J* = 8.4 Hz), 129.7, 128.8, 128.0 (t, *J* = 3.2 Hz), 126.0, 124.7, 124.6 (d, *J* = 8.4 Hz), 120.1, 119.9, 117.4, 111.8 (d, *J* = 23.2 Hz), 88.7 (dd, *J* = 20.9, 14.5 Hz), 74.7, 47.3 (d, *J* = 2.6 Hz), 31.7 (d, *J* = 1.3 Hz), 27.1, 21.3 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.1 (d, *J* = 37.7 Hz), -90.0 (d, *J* = 37.2 Hz), -111.7 (m) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{20}F_3NNaO^+$ 442.1389, found 442.1392.

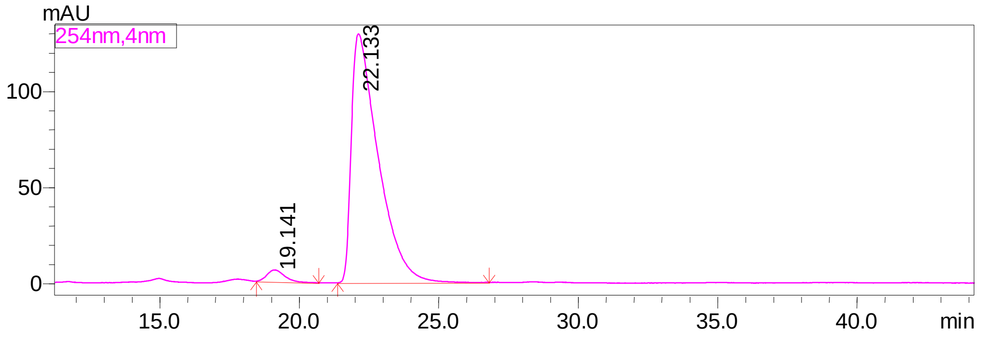
$[\alpha]^{25}_{D}$ = 124.8 °(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.0:3.0 (Chiralpak ID, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); t$_{\text{major}}$ = 22.133 min, t$_{\text{minor}}$ = 19.141 min.

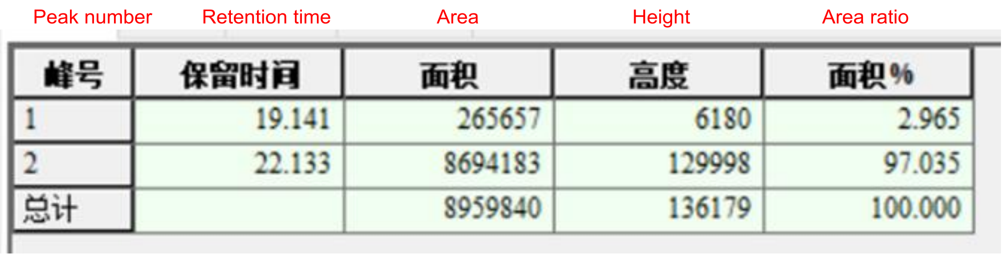




| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 19.113 | 1297543 | 28887 | 49.816 |
| 2 | 23.009 | 1307149 | 21372 | 50.184 |
| 总计 | | 2604692 | 50258 | 100.000 |

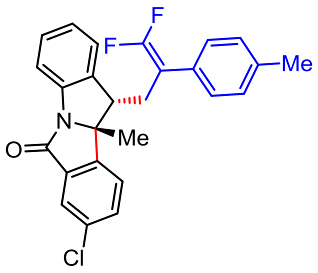
**Figure S59.** HPLC chromatography of the racemic product **32**





| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 19.141 | 265657 | 6180 | 2.965 |
| 2 | 22.133 | 8694183 | 129998 | 97.035 |
| 总计 | | 8959840 | 136179 | 100.000 |

**Figure S60.** HPLC chromatography of chiral product **32**



### (10b*R*,11*S*)-8-Chloro-11-(3,3-difluoro-2-(*p*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 33

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/ Ethyl acetate = 10/1, v/v) afforded **33** as yellow oil (48.7 mg, 0.112 mmol, 56% yield).

**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.90 (d, *J* = 2.0 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 1H), 7.63 (dd, *J* = 8.0, 2.5 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.36 (td, *J* = 8.0, 1.5 Hz, 1H), 7.23

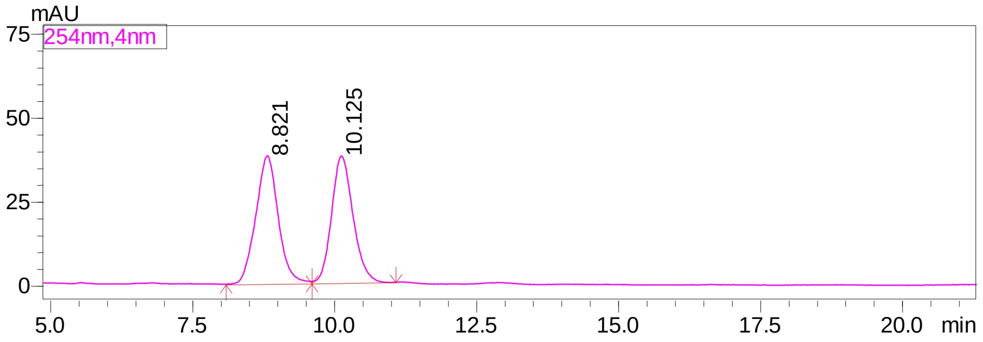
(d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 7.5 Hz, 3H), 7.11 (td, *J* = 7.5, 1.0 Hz, 1H), 3.06 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.39 (s, 3H), 2.20 – 2.15 (m, 1H), 1.68 – 1.63 (m, 1H), 1.47 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 165.8, 154.0 (dd, *J* = 292.1, 289.2 Hz), 145.9, 138.3, 137.6, 137.5, 135.6, 135.4, 132.6, 129.7, 129.6 (t, *J* = 3.9 Hz), 128.8, 127.9 (t, *J* = 3.0 Hz), 126.1, 125.2, 124.7, 124.3, 117.4, 88.7 (dd, *J* = 20.9, 14.5 Hz), 74.8, 47.3, 31.6, 26.9, 21.3 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -89.0 (d, *J* = 37.2 Hz), -89.9 (d, *J* = 38.2 Hz) ppm.

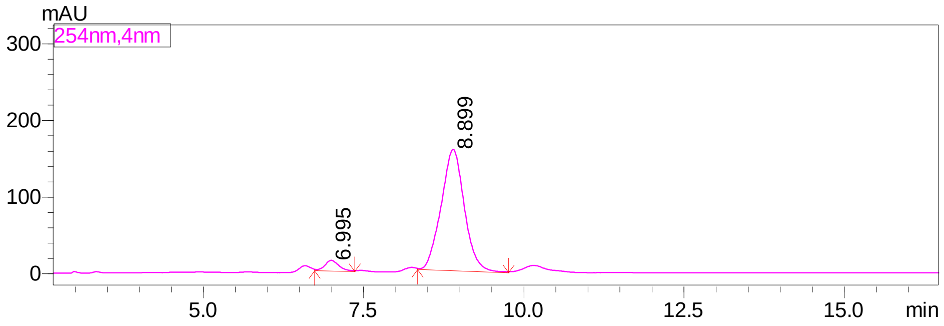
**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{20}ClF_2NNaO^+$ 458.1094, found 458.1095.

$[\alpha]^{25}_{D}$ = 89.6°(c = 0.25 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 95.5:4.5 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 8.899 min, $t_{minor}$ = 6.995 min.



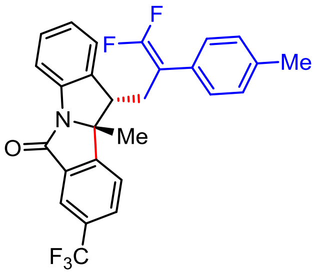
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 8.821 | 1050466 | 38206 | 51.300 |
| 2 | 10.125 | 997206 | 37947 | 48.700 |
| 总计 | | 2047672 | 76153 | 100.000 |

**Figure S61.** HPLC chromatography of the racemic product **33**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 6.995 | 187294 | 13112 | 4.518 |
| 2 | 8.899 | 3958415 | 158323 | 95.482 |
| 总计 | | 4145709 | 171435 | 100.000 |

**Figure S62.** HPLC chromatography of chiral product **33**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-10b-methyl-8-(trifluoromethyl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 34**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **34** as yellow oil (52.9 mg, 0.113 mmol, 56% yield).

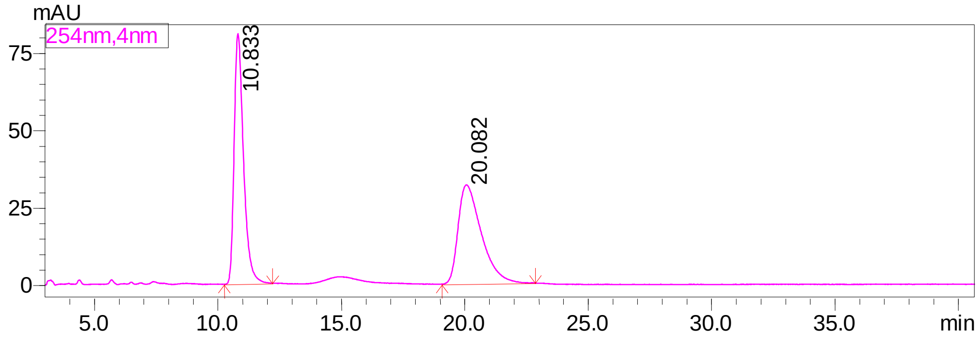
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 8.21 (s, 1H), 7.93 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.38 (td, *J* = 7.5, 1.5 Hz, 1H), 7.24 – 7.20 (m, 3H), 7.17 – 7.12 (m, 3H), 3.13 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.39 (s, 3H), 2.19 – 2.15 (m, 1H), 1.70 –1.65 (m, 1H), 1.51 (s, 3H) ppm.

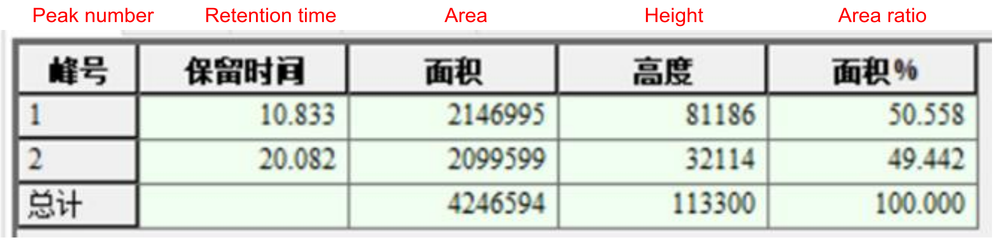
**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 165.6, 154.0 (dd, *J* = 292.6, 289.4 Hz), 151.0, 138.2, 137.7, 137.4, 134.7, 131.8 (q, *J* = 33.0 Hz), 129.7, 129.5 (t, *J* = 3.8 Hz), 129.2 (t, *J* = 3.8 Hz), 128.9, 127.9 (t, *J* = 3.2 Hz), 126.1, 124.9, 123.76 (q, *J* = 273.3 Hz), 123.78, 122.4 (q, *J* = 3.8 Hz), 117.5, 88.6 (dd, *J* = 20.9, 14.5 Hz), 75.2, 47.4 (t, *J* = 2.3 Hz), 31.6, 26.9, 21.3 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -62.3 (s), -89.0 (d, *J* = 37.7 Hz), -89.8 (dd, *J* = 37.7, 3.8 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$calcd for $C_{27}H_{20}F_5NNaO^+$ 492.1357, found 492.1359.

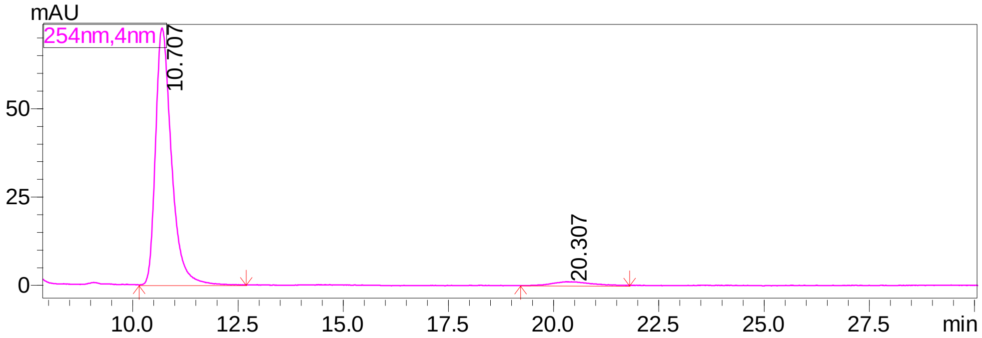
$[\alpha]^{25}_{D}$ = 31.2 °(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 96.7:3.3 (Chiralpak ID, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 10.707 min, $t_{minor}$ = 20.307 min.

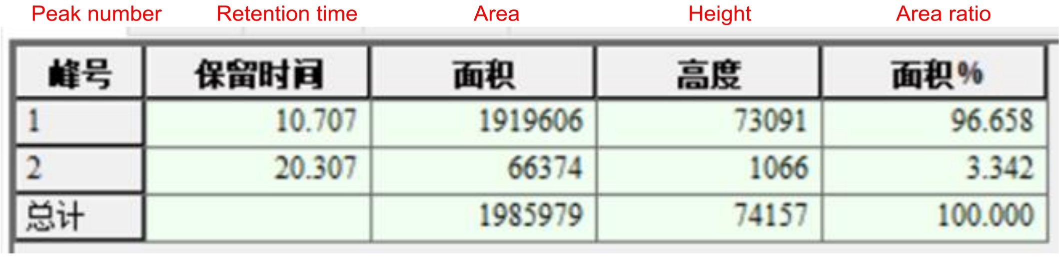




| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 10.833 | 2146995 | 81186 | 50.558 |
| 2 | 20.082 | 2099599 | 32114 | 49.442 |
| 总计 |  | 4246594 | 113300 | 100.000 |

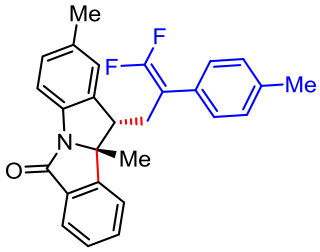
**Figure S63.** HPLC chromatography of the racemic product **34**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 10.707 | 1919606 | 73091 | 96.658 |
| 2 | 20.307 | 66374 | 1066 | 3.342 |
| 总计 |  | 1985979 | 74157 | 100.000 |

**Figure S64.** HPLC chromatography of chiral product **34**



### (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-2,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 35

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **35** as colorless oil (50.9 mg, 0.123 mmol, 61% yield).

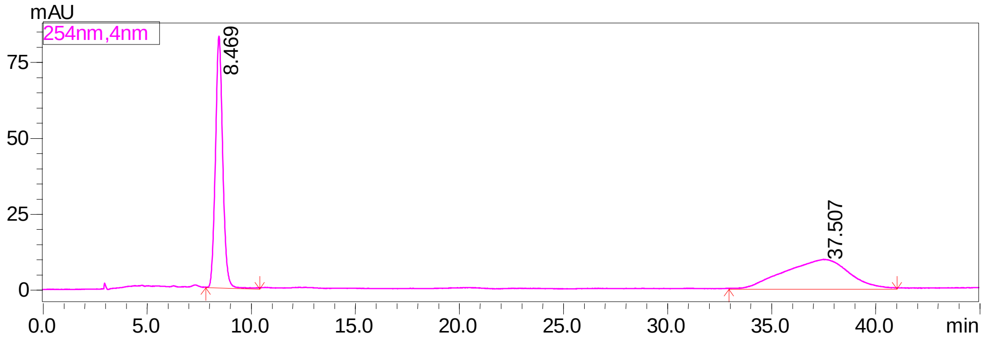
**$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.92 (d, *J* = 7.5 Hz, 1H), 7.66 (t, *J* = 7.0 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 9.5 Hz, 1H), 6.95 (s, 1H), 3.03 (dd, *J* = 10.5, 5.5 Hz, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.21 – 2.15 (m, 1H), 1.68 – 1.62 (m, 1H), 1.47 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 167.2, 154.0 (dd, *J* = 291.9, 289.2 Hz), 147.7, 138.7, 137.4, 135.4, 133.99, 133.98, 132.3, 129.8 (t, *J* = 3.9 Hz), 129.6, 129.0, 128.9, 128.0 (t, *J* = 3.3 Hz), 126.7, 125.0, 123.0, 116.9, 88.9 (dd, *J* = 21.2, 14.4 Hz), 75.1, 47.4 (t, *J* = 2.5 Hz), 31.6, 26.9, 21.4, 21.2 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -89.1 (d, *J* = 38.2 Hz), -90.4 (d, *J* = 38.2 Hz) ppm.

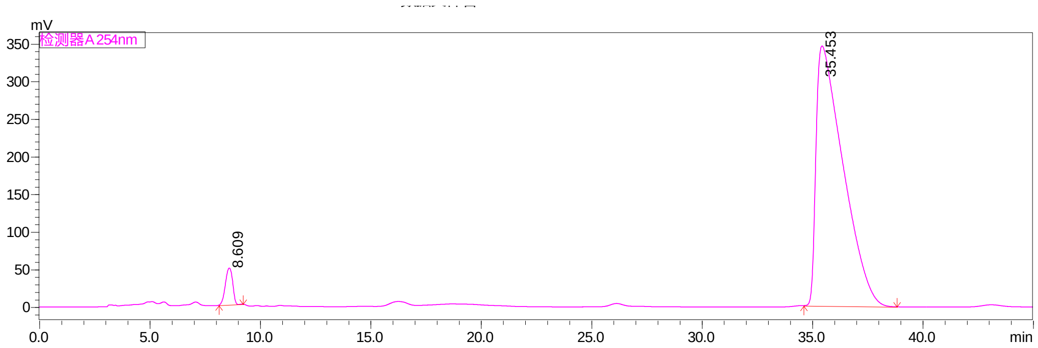
**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{23}F_2NNaO^+$ 438.1640, found 438.1641.

$[\alpha]^{25}_{D}$ = 73.6 ˚(c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 96.4:3.6 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 35.453 min, $t_{minor}$ = 8.609 min.



| 峰号<br>Peak number | 保留时间<br>Retention time | 面积<br>Area | 高度<br>Height | 面积%<br>Area ratio |
|---|---|---|---|---|
| 1 | 8.469 | 2013945 | 83121 | 49.699 |
| 2 | 37.507 | 2038304 | 9619 | 50.301 |
| 总计 |  | 4052250 | 92740 | 100.000 |

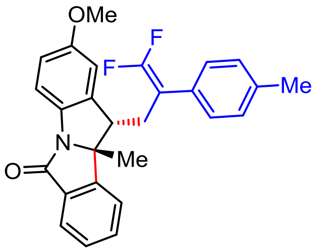
**Figure S65.** HPLC chromatography of the racemic product **35**



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 8.609 | 1110004 | 48694 | 3.640 |
| 2 | 35.453 | 29383070 | 345348 | 96.360 |
| 总计 |  | 30493074 | 394042 | 100.000 |

**Figure S66.** HPLC chromatography of chiral product **35**



### (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-2-methoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 36

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **36** as a yellow solid (56.2 mg, 0.130 mmol, 65% yield). **m.p.** 38.0 – 39.7 □.

**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 7.92 (d, *J* = 7.5 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.87 (dd, *J* = 8.5, 3.0 Hz, 1H), 6.73 (d, *J* = 2.5 Hz, 1H), 3.78 (s, 3H), 3.02 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.38 (s, 3H), 2.22 – 2.17 (m, 1H), 1.69 – 1.63 (m, 1H), 1.47 (s, 3H) ppm.

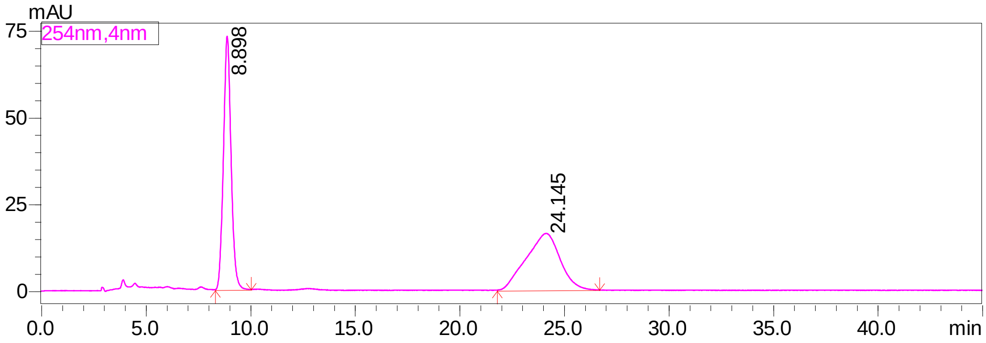
**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.2, 156.9, 154.0 (dd, *J* = 291.8, 289.2 Hz), 147.6, 140.1, 137.5, 133.9, 132.2, 131.4, 129.7, 129.0, 127.9 (t, *J* = 3.4 Hz), 124.9, 122.9, 117.8, 113.2, 112.6, 88.9 (*J* = 20.9, 14.1 Hz), 75.3, 55.8, 47.5 (t, *J* = 2.3 Hz), 31.4, 26.9, 21.2 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.0 (d, *J* = 37.7 Hz), -90.1 (dd, *J* = 38.2, 4.2 Hz)

ppm.

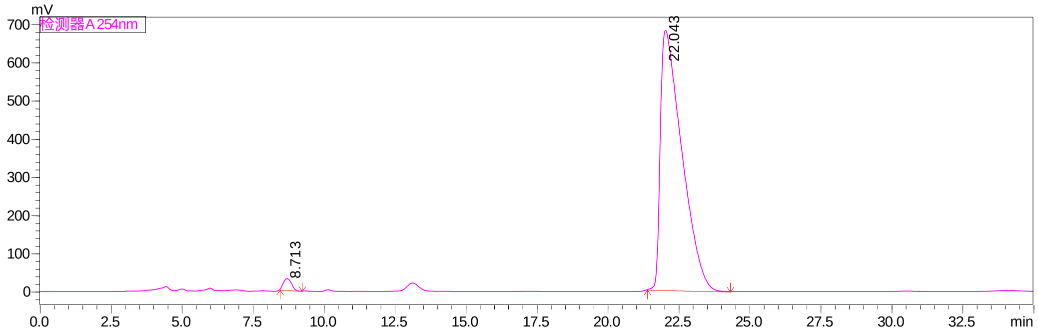
**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{23}F_2NNaO_2^+$ 454.1589, found 454.1587.

$[\alpha]^{25}_{D} = 27.2^{\circ}$ (c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 98.4:1.6 (Chiralpak AD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 22.043 min, $t_{minor}$ = 8.713 min.



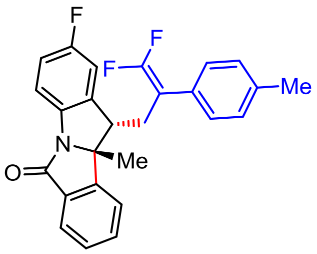
| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 8.898 | 1860092 | 73290 | 50.125 |
| 2 | 24.145 | 1850848 | 16433 | 49.875 |
| 总计 |  | 3710940 | 89723 | 100.000 |

**Figure S67.** HPLC chromatography of the racemic product **36**



| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 8. 713 | 584379 | 29996 | 1. 612 |
| 2 | 22. 043 | 35669400 | 679982 | 98. 388 |
| 总计 |  | 36253779 | 709979 | 100. 000 |

**Figure S68.** HPLC chromatography of chiral product **36**



### (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-2-fluoro-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 37

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 10/1, v/v) afforded **37** as a white solid (53.2 mg, 0.123 mmol, 63% yield). **m.p.** 39.3 – 41.7 □.

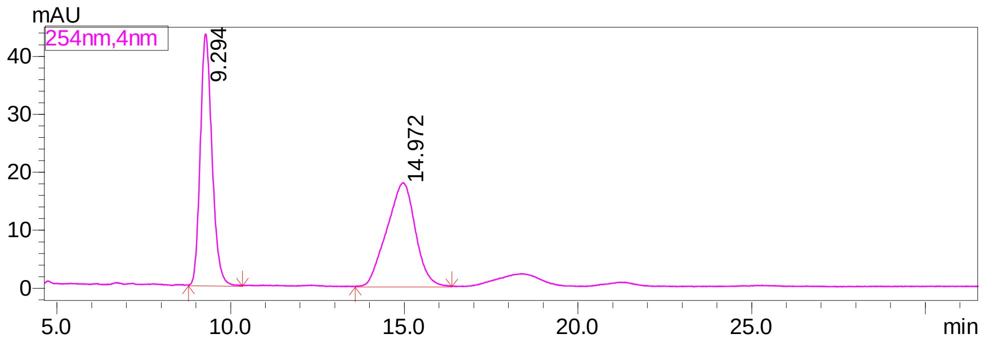
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 7.5 Hz, 2H), 7.05 (td, *J* = 9.0, 2.5 Hz, 1H), 6.87 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.03 (dd, *J* = 10.5, 4.5 Hz, 1H), 2.39 (s, 3H), 2.24 – 2.18 (m, 1H), 1.67 – 1.61 (m, 1H), 1.49 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.4, 160.0 (d, *J* = 243.4 Hz), 154.1 (dd, *J* = 292.3, 289.2 Hz), 147.6, 140.4 (d, *J* = 8.3 Hz), 137.7, 134.0 (d, *J* = 1.8 Hz), 133.7, 132.6, 129.8, 129.5 (t, *J* = 3.4 Hz), 129.2, 127.9 (t, *J* = 3.2 Hz), 125.2, 123.0, 118.1 (d, *J* = 8.8 Hz), 115.2 (d, *J* = 23.6 Hz), 113.5 (d, *J* = 24.3 Hz), 88.6 (dd, *J* = 21.2, 14.6 Hz), 75.4, 47.5, 31.4, 26.9, 21.3 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.9 (d, *J* = 37.2 Hz), -89.7 (dd, *J* = 37.2, 3.8 Hz), -118.0 (m) ppm.

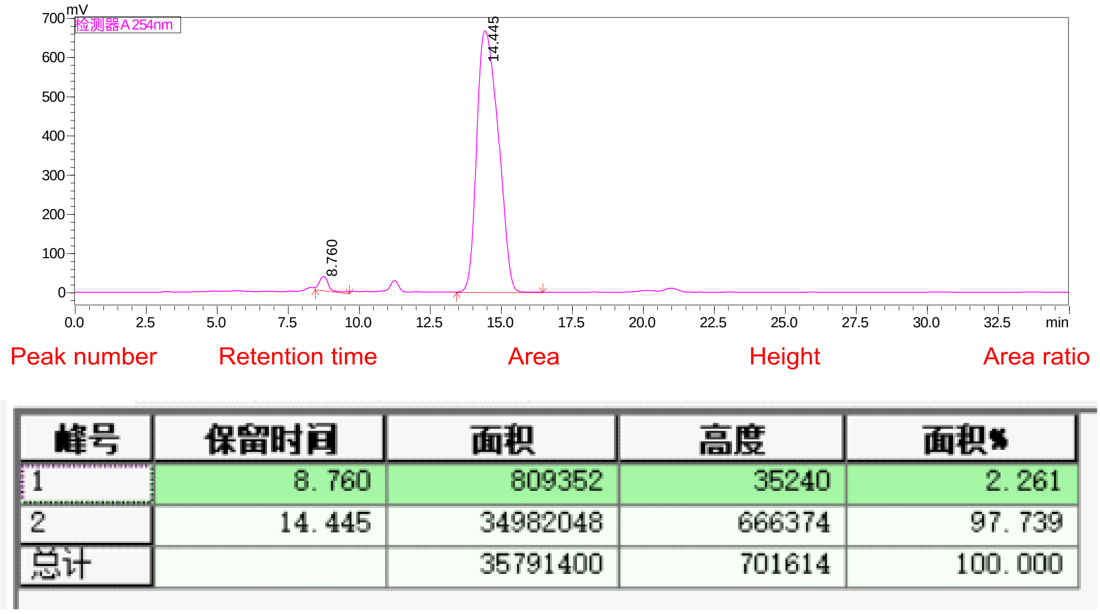
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{20}F_3NNaO^+$ 442.1389, found 442.1389.

$[\alpha]^{25}_{D}$ = 253.6 °(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.7:2.3 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 14.445 min, $t_{minor}$ = 8.760 min.



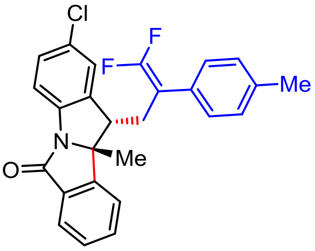
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 9.294 | 1019211 | 43534 | 49.825 |
| 2 | 14.972 | 1026371 | 17952 | 50.175 |
| 总计 | | 2045582 | 61487 | 100.000 |

**Figure S69.** HPLC chromatography of the racemic product **37**



| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 8. 760 | 809352 | 35240 | 2. 261 |
| 2 | 14. 445 | 34982048 | 666374 | 97. 739 |
| 总计 | | 35791400 | 701614 | 100. 000 |

**Figure S70.** HPLC chromatography of chiral product **37**



**(10b*R*,11*S*)-2-Chloro-11-(3,3-difluoro-2-(*p*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 38**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 10/1, v/v) afforded **38** as yellow oil (54.1 mg, 0.124 mmol, 62% yield).

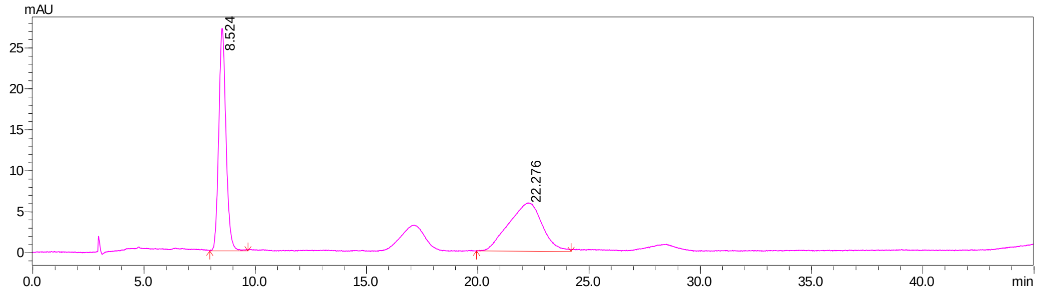
**$^{1}$H NMR (500 MHz, CDCl$_3$):** ) δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.31 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 7.5 Hz, 2H), 7.09 (d, *J* = 1.5 Hz, 1H), 3.05 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.39 (s, 3H), 2.23 – 2.18 (m, 1H), 1.68 – 1.62 (m, 1H), 1.48 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 154.1 (dd, *J* = 292.3, 289.0 Hz), 147.5, 140.3, 137.7, 136.5, 133.6, 132.7, 129.8, 129.6, 129.5 (t, $J$ = 3.5 Hz), 129.2, 128.7, 127.9 (t, $J$ = 3.3 Hz), 126.3, 125.3, 123.1, 118.2, 88.6 (dd, $J$ = 21.0, 14.7 Hz), 75.3, 47.5, 31.4, 27.0, 21.3 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.9 (d, $J$ = 37.2 Hz), -89.8 (dd, $J$ = 37.2, 3.3 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd $C_{26}H_{20}ClF_2NNaO^+$ 458.1094, found 458.1092.

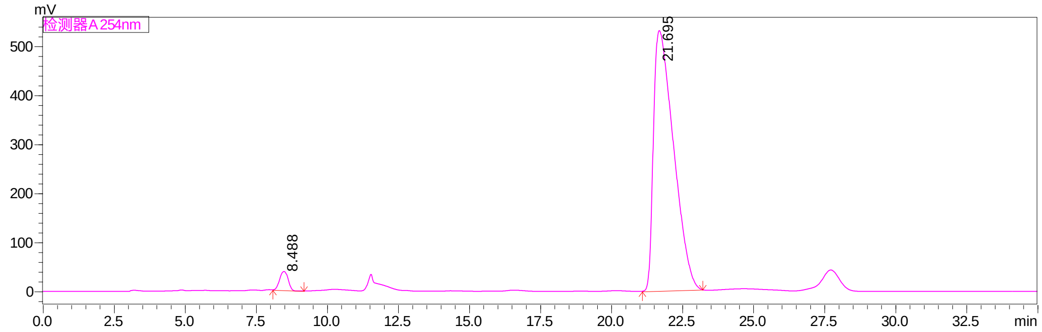
$[\alpha]^{25}_{D}$ = 152.0˚(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.1:2.9 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); t$_{major}$ = 21.695 min, t$_{minor}$ = 8.488 min.



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 8.524 | 610809 | 27188 | 50.013 |
| 2 | 22.276 | 610504 | 5908 | 49.987 |
| 总计 | | 1221313 | 33096 | 100.000 |

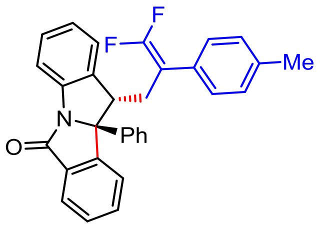
**Figure S71.** HPLC chromatography of the racemic product **38**



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 8.488 | 773273 | 38315 | 2.883 |
| 2 | 21.695 | 26052937 | 530473 | 97.117 |
| 总计 | | 26826211 | 568788 | 100.000 |

**Figure S72.** HPLC chromatography of chiral product **38**



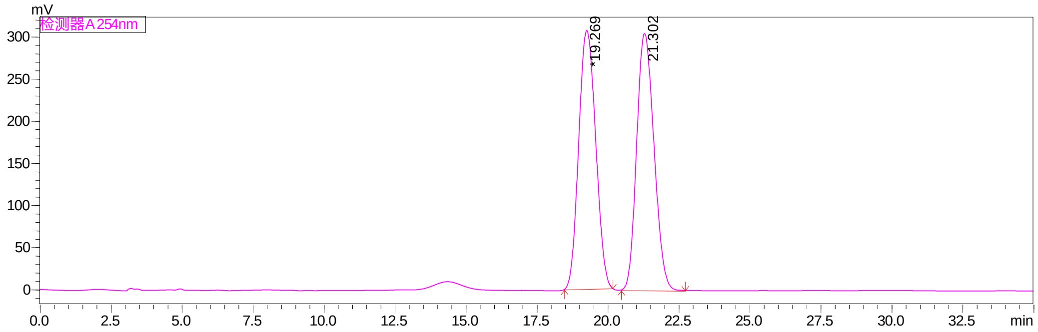
**(10b*S*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-10b-phenyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 39**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **39** as a white solid (33.6 mg, 0.072 mmol, 36% yield). **m.p.** 75.7 – 80.8 □. **$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 4.5 Hz, 2H), 7.51 – 7.48 (m, 1H), 7.39 (d, *J* = 7.5 Hz, 2H), 7.35 – 7.32 (m, 1H), 7.29 –7.26 (m, 4H), 7.20 (t, *J* = 7.5 Hz, 2H), 7.15 (t, *J* = 7.0 Hz, 1H), 7.06 – 7.02 (m, 2H), 3.72 (dd, *J* = 10.5, 5.5 Hz, 1H), 2.50 – 2.45 (m, 1H), 2.41 (s, 3H), 1.90 – 1.85 (m, 1H) ppm.

**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 168.1, 154.1 (dd, *J* = 292.3, 288.9 Hz), 147.0, 142.8, 138.4, 138.3, 137.7, 133.2, 132.7, 129.8, 129.1, 128.9, 128.8, 127.99, 127.98, 127.96, 125.6, 125.2, 124.9, 124.8, 124.1, 117.3, 88.9 (dd, *J* = 20.9, 14.4 Hz), 80.4, 48.7, 32.0, 21.3 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -88.8 (d, *J* = 36.7 Hz), -89.8 (d, *J* = 36.7 Hz) ppm.

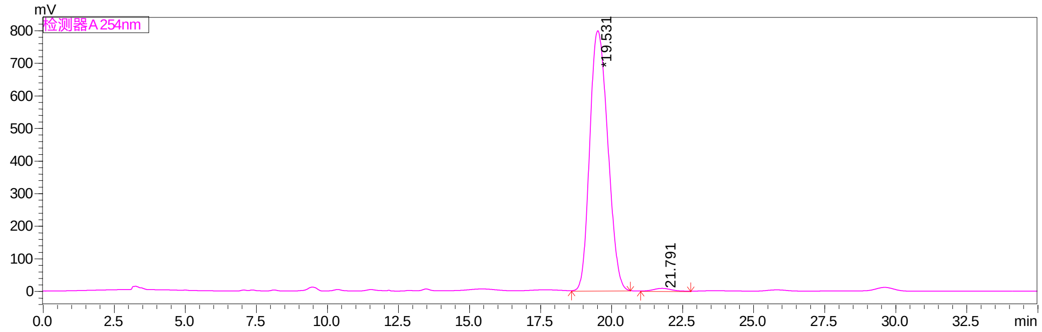
**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{31}H_{23}F_2NNaO^+$ 486.1640, found 486.1641. $[\alpha]^{25}_{D}$ = 174.4 °(c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 99.1:0.9 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 19.531 min, $t_{minor}$ = 21.791 min.



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 19.269 | 12775933 | 306806 | 49.660 |
| 2 | 21.302 | 12951121 | 304678 | 50.340 |
| 总计 | | 25727054 | 611484 | 100.000 |

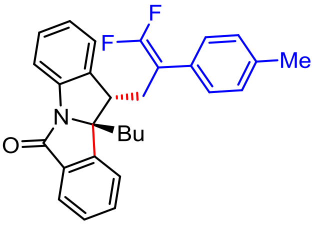
**Figure S73.** HPLC chromatography of the racemic product **39**



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 19.531 | 35181822 | 797274 | 99.066 |
| 2 | 21.791 | 331811 | 8183 | 0.934 |
| 总计 | | 35513632 | 805456 | 100.000 |

**Figure S74.** HPLC chromatography of chiral product **39**



### (10b*R*,11*S*)-10b-Butyl-11-(3,3-difluoro-2-(*p*-tolyl)allyl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 40

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **40** as colorless oil (58.5 mg, 0.132 mmol, 66% yield).

**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 7.0 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.19 – 7.15 (m, 3H), 7.08 (t, *J* = 7.5 Hz, 1H), 3.06

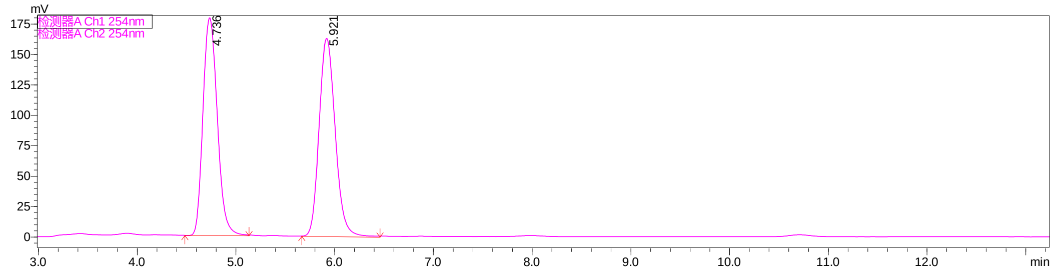
(dd, $J$ = 11.0, 5.0 Hz, 1H), 2.39 (s, 3H), 2.27 – 2.22 (m, 1H), 1.84 – 1.81 (m, 2H), 1.67 – 1.61 (m, 1H), 1.07 – 1.01 (m, 3H), 0.66 (t, $J$ = 7.0 Hz, 3H), 0.61 – 0.55 (m, 1H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 168.0, 154.0 (dd, $J$ = 291.7, 289.2 Hz), 146.4, 139.0, 138.1, 137.5, 134.7, 132.4, 129.8 (t, $J$ = 3.4 Hz), 129.7, 129.0, 128.6, 128.0 (t, $J$ = 3.3 Hz), 125.9, 125.0, 124.4, 123.1, 117.3, 88.8 (dd, $J$ = 21.3, 14.4 Hz), 78.2, 47.2, 38.9, 31.4, 25.2, 22.6, 21.3,13.9 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.1 (d, $J$ = 37.7 Hz), -90.1 (d, $J$ = 38.2, 4.2 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{29}H_{27}F_2NNaO^+$ 466.1953, found 466.1954.

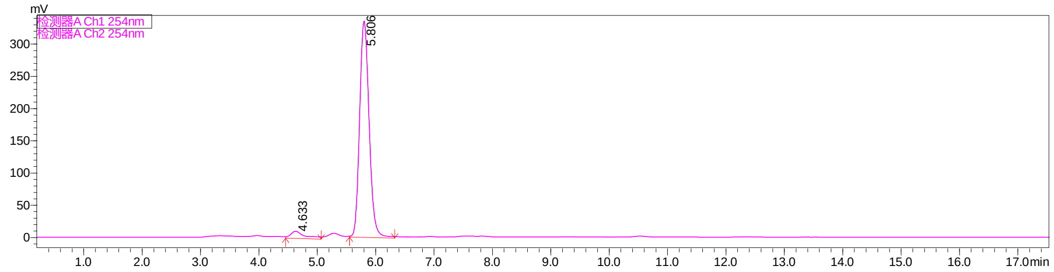
[α]$^{25}$$_{D}$ = 20.8 °(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.8:2.2 (Chiralpak AD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ= 254 nm); t$_{major}$ = 5.806 min, t$_{minor}$ = 4.633 min.



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 4.736 | 1801174 | 178652 | 49.434 |
| 2 | 5.921 | 1842421 | 162531 | 50.566 |
| 总计 |  | 3643594 | 341183 | 100.000 |

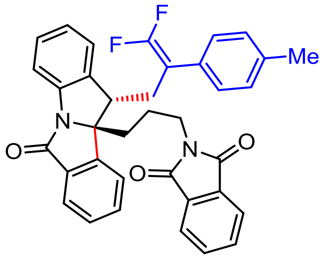
**Figure S75.** HPLC chromatography of the racemic product **40**



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 4.633 | 83537 | 8322 | 2.190 |
| 2 | 5.806 | 3730379 | 333984 | 97.810 |
| 总计 |  | 3813916 | 342307 | 100.000 |

**Figure S76.** HPLC chromatography of chiral product **40**



### 2-(3-((10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-6-oxo-6*H*-isoindolo[2,1-*a*]indol-10b(11H)-yl)propyl)isoindoline-1,3-dione, 41

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1, v/v) afforded **41** as a white solid (48.3 mg, 0.084 mmol, 42% yield). **m.p.** 69.5 – 70.9 □.

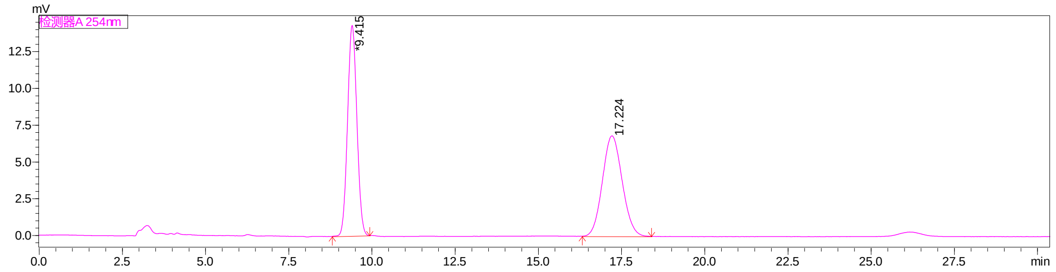
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.83 (d, *J* = 7.5 Hz, 1H), 7.66 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.58 – 7.56 (m, 3H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.09 – 7.05 (m, 3H), 6.99 (t, *J* = 7.0 Hz, 1H), 3.33 (td, *J* = 7.0, 3.0 Hz, 2H), 2.97 (dd, *J* = 10.5, 4.5 Hz, 1H), 2.30 (s, 3H), 2.15 – 2.10 (m, 1H), 1.90 – 1.77 (m, 2H), 1.55 – 1.50 (m, 1H), 1.42 – 1.33 (m, 1H), 0.97 – 0.88 (m, 1H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 168.2, 167.9, 154.0 (dd, *J* = 291.8, 289.4 Hz), 145.7, 138.6, 137.9, 137.5, 134.5, 134.0, 132.7, 132.0, 129.7, 129.6 (t, *J* = 3.5 Hz), 129.2, 128.7, 127.9 (t, *J* = 3.3 Hz), 125.9, 125.1, 124.4, 123.3, 123.0, 117.5, 88.7 (dd, *J* = 21.0, 14.6 Hz), 77.6, 47.2, 37.6, 36.1, 31.4, 22.6, 21.3 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -89.1 (d, *J* = 37.7 Hz), -90.1 (d, *J* = 38.2, 4.2 Hz) ppm.

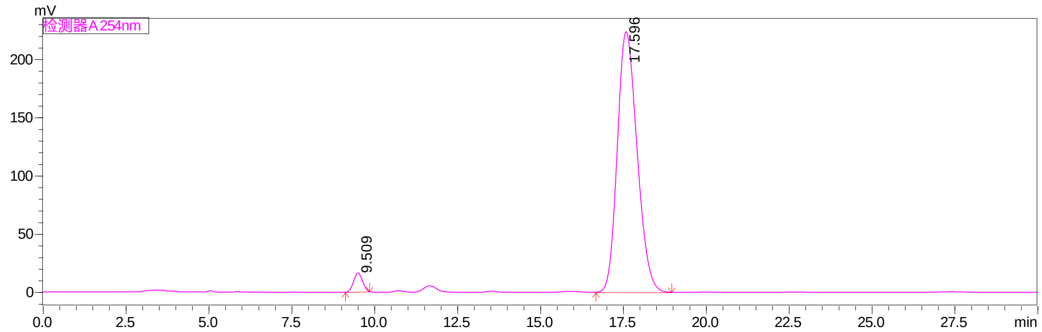
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{36}H_{28}F_2N_2NaO_3^+$ 597.1960, found 597.1960.

$[\alpha]^{25}_{D}$ = 99.2 ° (c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 96.9:3.1 (Chiralpak AD-H, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 17.596 min, $t_{minor}$ = 9.509 min.



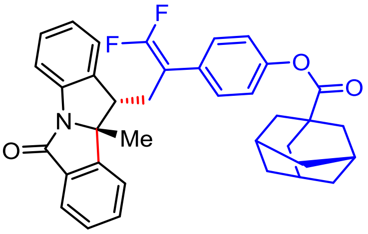
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.415 | 279091 | 14322 | 49.786 |
| 2 | 17.224 | 281487 | 6828 | 50.214 |
| 总计 | | 560579 | 21149 | 100.000 |

**Figure S77.** HPLC chromatography of the racemic product **41**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.509 | 296420 | 16007 | 3.095 |
| 2 | 17.596 | 9280311 | 223812 | 96.905 |
| 总计 | | 9576731 | 239819 | 100.000 |

**Figure S78.** HPLC chromatography of chiral product **41**



### 4-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl adamantane-1-carboxylate, 42

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **42** as a white solid (62.0 mg, 0.110 mmol, 55% yield). **m.p.** 71.2 – 72.5 □.

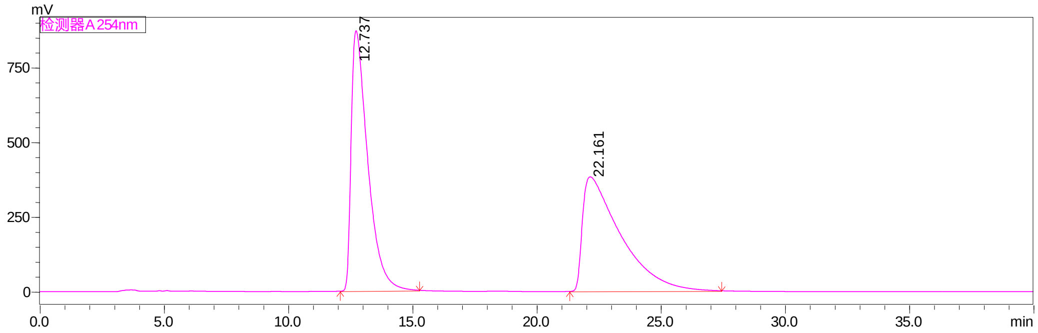
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 7.0 Hz, 2H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.12 – 7.08 (m, 3H), 3.07 (dd, *J* = 10.5, 4.5 Hz, 1H), 2.22 – 2.16 (m, 1H), 2.11 – 2.07 (m, 9H), 1.81 – 1.76 (m, 6H), 1.66 – 1.60 (m, 1H), 1.50 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 176.3, 167.3, 154.2 (dd, *J* = 292.4, 290.2 Hz), 150.4, 147.7, 138.3, 137.8, 133.9, 132.5, 130.1 (t, *J* = 3.5 Hz), 129.11, 129.08, 128.8, 125.9, 125.2, 124.5, 123.0, 122.2, 117.5, 88.4 (dd, *J* = 21.7, 14.1 Hz), 75.0, 47.3, 41.2, 38.9, 36.5, 31.7, 28.0, 27.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.4 (d, *J* = 35.8 Hz), -89.5 (dd, *J* = 36.3, 4.2 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{36}H_{33}F_2NNaO_3^+$ 588.2321, found 588.2320.

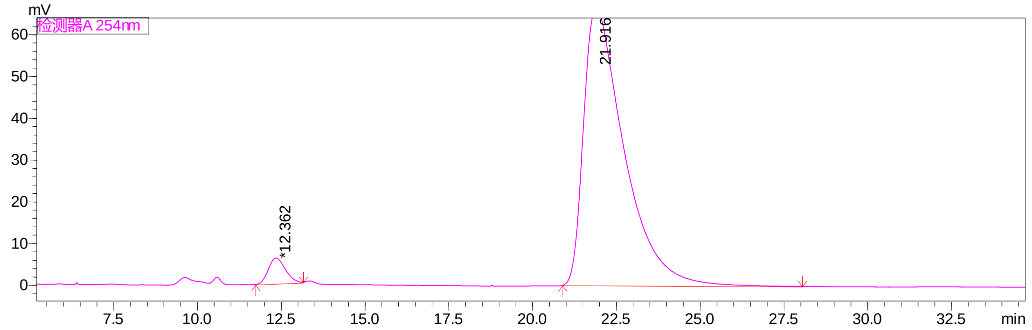
$[\alpha]^{25}_{D}$ = 92.8 °(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 96.3:3.7 (Chiralpak ID, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 21.916 min, $t_{minor}$ = 12.362 min.



Peak number Retention time Area Height Area ratio

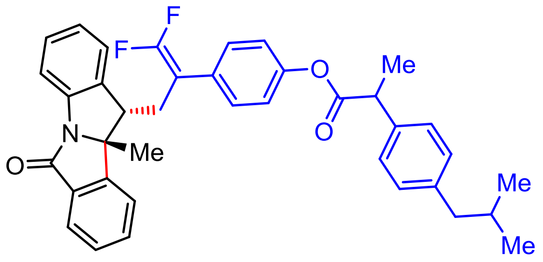
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 12. 737 | 40353679 | 871596 | 49. 727 |
| 2 | 22. 161 | 40796747 | 383209 | 50. 273 |
| 总计 | | 81150426 | 1254805 | 100. 000 |

**Figure S79.** HPLC chromatography of the racemic product **42**



| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 12.362 | 211897 | 6107 | 3.658 |
| 2 | 21.916 | 5580173 | 66539 | 96.342 |
| 总计 |  | 5792070 | 72646 | 100.000 |

**Figure S80.** HPLC chromatography of chiral product **42**



**4-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl 2-(4-isobutylphenyl)propanoate, 43**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **43** as a yellow solid (62.6 mg, 0.106 mmol, 53% yield). **m.p.** 43.3 – 44.0 □.

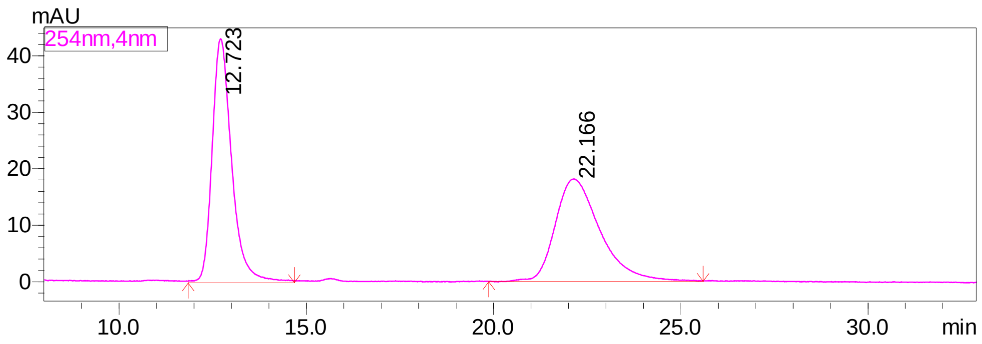
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.36 – 7.31 (m, 3H), 7.25 – 7.23 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 7.0 Hz, 1H), 7.09 – 7.05 (m, 3H), 3.96 (q, *J* = 7.0 Hz, 1H), 3.04 (dd, *J* = 10.5, 3.5 Hz, 1H), 2.48 (d, *J* = 7.5 Hz, 2H), 2.20 – 2.15 (m, 1H), 1.90 – 1.85 (m, 1H), 1.62 (d, *J* = 7.5 Hz, 4H), 1.48 (s, 3H), 0.92 (d, *J* = 6.5 Hz, 6H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 173.3, 167.2, 154.1 (dd, *J* = 293.1, 289.8 Hz), 150.1, 147.6, 141.0, 138.3, 137.7, 137.1, 133.8, 132.5, 130.3 (t, *J* = 4.0 Hz), 129.6, 129.0 (t, *J* = 3.9 Hz), 128.7, 127.3, 125.9, 125.1, 124.4, 123.0, 122.0, 117.4, 88.4 (dd, *J* = 21.9, 14.2 Hz), 75.0, 47.2, 45.3, 45.1, 31.6, 30.3, 26.9, 22.5, 18.6 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.2 (dd, *J* = 35.8, 12.2 Hz), -89.4 (d, *J* = 35.3 Hz) ppm.

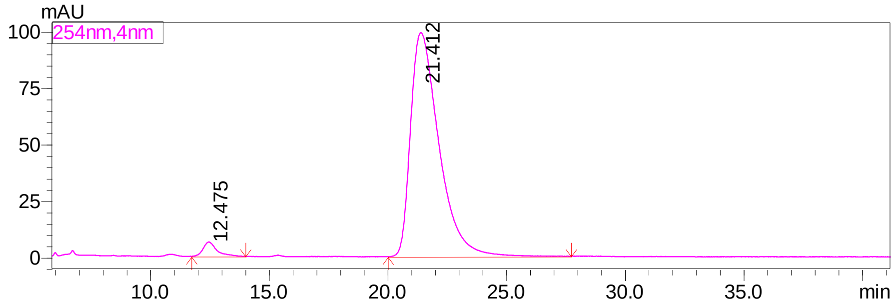
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{38}H_{35}F_2NNaO_3^+$ 614.2477, found 614.2478.

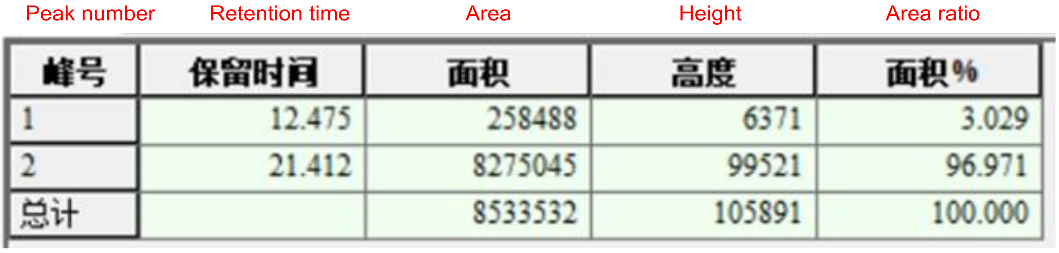
$[\alpha]^{25}_{D}$ = 43.2 °(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 97.0:3.0 (Chiralpak ID, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 21.412 min, $t_{minor}$ = 12.475 min.



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 12.723 | 1565214 | 43238 | 51.265 |
| 2 | 22.166 | 1487943 | 18150 | 48.735 |
| 总计 |  | 3053157 | 61388 | 100.000 |

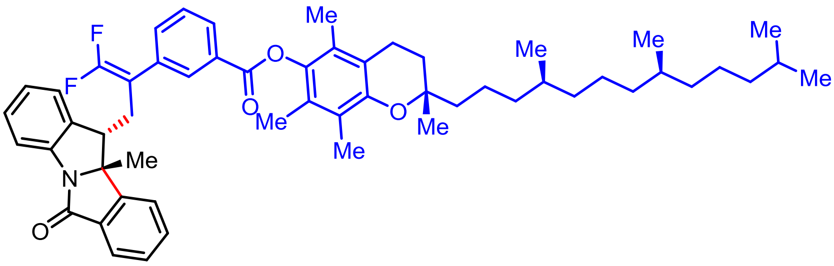
**Figure S81.** HPLC chromatography of the racemic product **43**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 12.475 | 258488 | 6371 | 3.029 |
| 2 | 21.412 | 8275045 | 99521 | 96.971 |
| 总计 |  | 8533532 | 105891 | 100.000 |

**Figure S82.** HPLC chromatography of chiral product **43**



**(*S*)-2,5,7,8-Tetramethyl-2-((4*S*,8*S*)-4,8,12-trimethyltridecyl)chroman-6-yl 3-(1,1-**

**difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzoate, 44**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **44** as colorless oil (107.8 mg, 0.128 mmol, 64% yield).

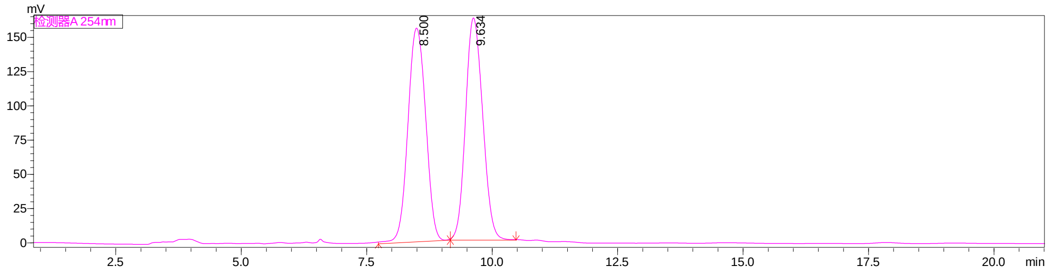
**$^1$H NMR (500 MHz, $CDCl_3$):** δ 8.21 (d, *J* = 7.0 Hz, 1H), 8.18 (s, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.58 – 7.53 (m, 4H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 3.11 (dd, *J* = 10.0, 4.0 Hz, 1H), 2.65 (t, *J* = 6.5 Hz, 2H), 2.35 – 2.29 (m, 1H), 2.16 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H), 1.88 – 1.78 (m, 2H), 1.75 – 1.70 (m, 1H), 1.61 – 1.58 (m, 1H), 1.53 – 1.50 (m, 4H), 1.44 – 1.38 (m, 3H), 1.29 – 1.24 (m, 11H), 1.16 – 1.06 (m, 6H), 0.89 – 0.85 (m, 14H) ppm.

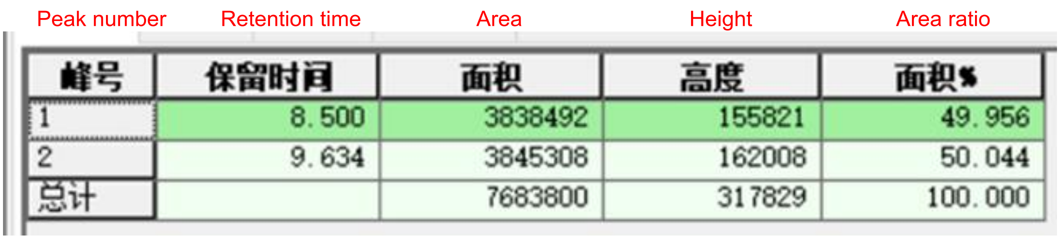
**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 167.3, 164.9, 154.4 (t, *J* = 292.4 Hz), 149.7, 147.6, 140.6, 138.3, 137.8, 133.8, 133.5, 133.1, 132.7, 130.4, 129.4, 129.2, 129.1, 128.9, 126.9, 125.8, 125.2, 124.5, 123.4, 123.0, 117.7, 117.5, 88.6 (dd, *J* = 21.9, 13.6 Hz), 75.3, 75.0, 47.4, 40.5, 39.8, 39.5, 37.6, 37.4, 32.92, 32.87, 32.81, 31.4, 31.3, 31.1, 28.1, 27.1, 24.9, 24.6, 24.3, 23.9, 22.9, 22.8, 21.2, 20.8, 19.9, 19.8, 13.3, 12.4, 12.0 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -86.7 (d, *J* = 33.4 Hz), -88.1 (d, *J* = 34.4 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{55}H_{67}F_2NNaO_4^+$ 866.4930, found 866.4928.

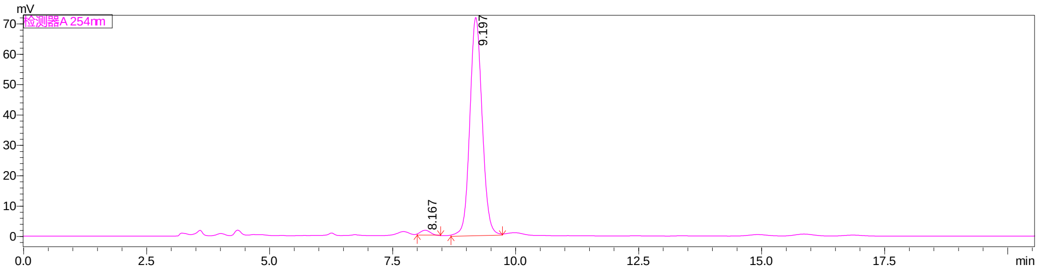
$[\alpha]^{25}_D$ = 10.4 °(c = 0.50 in $CHCl_3$). The enantiomeric excess was determined by HPLC: d.e. = 98.6:1.4 (Chiralpak ID, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm); $t_{major}$ = 9.197 min, $t_{minor}$ = 8.167 min.





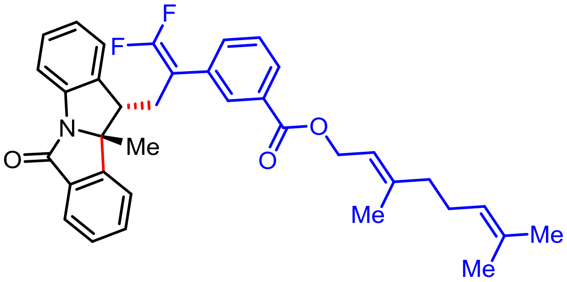
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 8.500 | 3838492 | 155821 | 49.956 |
| 2 | 9.634 | 3845308 | 162008 | 50.044 |
| 总计 |  | 7683800 | 317829 | 100.000 |

**Figure S83.** HPLC chromatography of the racemic product **44**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 8.167 | 17772 | 1490 | 1.406 |
| 2 | 9.197 | 1246012 | 71736 | 98.594 |
| 总计 |  | 1263784 | 73225 | 100.000 |

**Figure S84.** HPLC chromatography of chiral product **44**



**(*E*)-3,7-Dimethylocta-2,6-dien-1-yl 3-(1,1-difluoro-3-((10b*R*,11S)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzoate, 45**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7/1, v/v) afforded **45** as colorless oil (36.6 mg, 0.064 mmol, 32% yield).

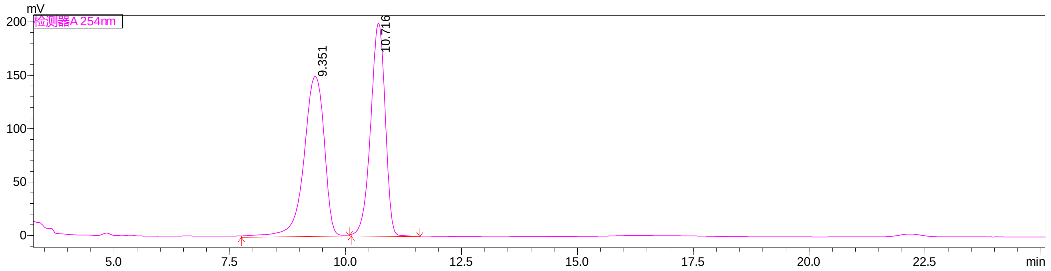
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 8.01 – 8.00 (m, 2H), 7.95 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.69 (td, *J* = 7.5, 1.0 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.51 – 7.47 (m, 2H), 7.36 (td, *J* = 8.0, 1.5 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 5.54 – 5.51 (m, 1H), 5.12 – 5.10 (m, 1H), 4.91 (d, *J* = 7.0 Hz, 2H), 3.06 (dd, *J* = 10.5, 4.5 Hz, 1H), 2.30 – 2.24 (m, 1H), 2.16 – 2.11 (m, 4H), 1.81 (s, 3H), 1.73 – 1.69 (m, 1H), 1.68 (s, 3H), 1.61 (s, 3H), 1.50 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.3, 166.4, 154.3 (t, *J* = 293.7 Hz), 147.7, 142.9, 138.3, 137.8, 137.8, 133.9, 133.2, 132.6, 132.5, 132.1, 131.3, 129.1, 129.0, 128.85, 128.78, 125.9, 125.2, 124.5, 123.8, 123.1, 118.3, 117.5, 88.6 (dd, *J* = 21.4, 13.6 Hz), 75.0, 62.3, 47.3, 39.7, 31.4, 27.1, 26.4, 25.8, 17.9, 16.8 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -87.1 (d, *J* = 33.9 Hz), -88.3 (d, *J* = 33.9 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{36}H_{35}F_2NNaO_3^+$ 590.2477, found 590.2477.

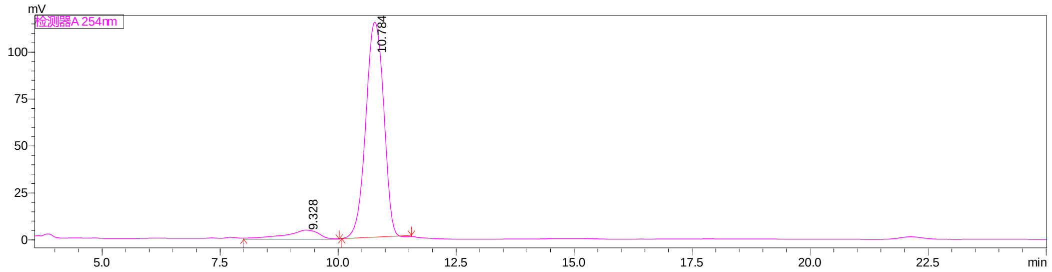
$[\alpha]^{25}_{D} = 76.0^{\circ}$ (c = 0.10 in $CHCl_3$). The enantiomeric excess was determined by HPLC: e.r. = 93.0:7.0 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); $t_{major}$ = 10.784 min, $t_{minor}$ = 9.328 min.



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 9. 351 | 4554475 | 149390 | 51. 242 |
| 2 | 10. 716 | 4333679 | 199335 | 48. 758 |
| 总计 | | 8888154 | 348725 | 100. 000 |

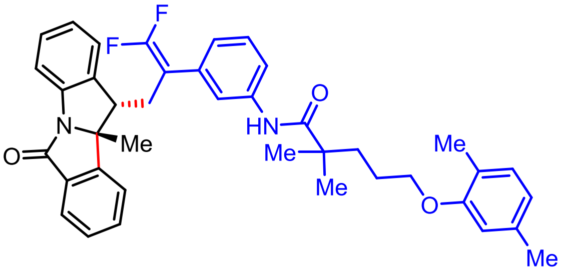
**Figure S85.** HPLC chromatography of the racemic product **45**



Peak number Retention time Area Height Area ratio

| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 9. 328 | 227698 | 4664 | 7. 050 |
| 2 | 10. 784 | 3002027 | 114216 | 92. 950 |
| 总计 | | 3229725 | 118880 | 100. 000 |

**Figure S86.** HPLC chromatography of chiral product **45**



***N*-(3-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-**

**isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl)-5-(2,5-dimethylphenoxy)-2,2-dimethylpentanamide, 46**

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1, v/v) afforded **46** as a white solid (64.7 mg, 0.102 mmol, 51% yield). **m.p.** 47.6 – 48.9 □.

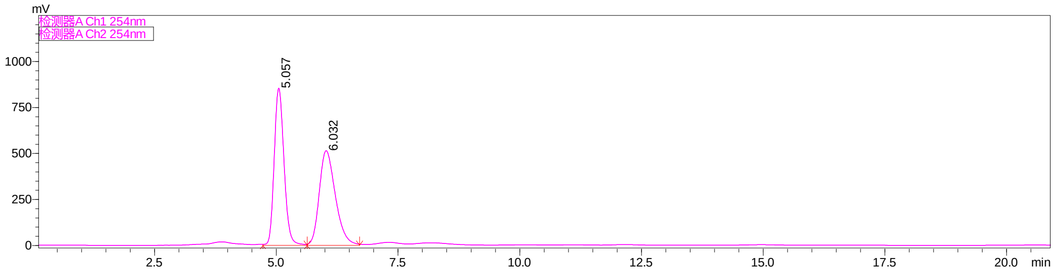
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.91 (d, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 1H), 7.67 – 7.64 (m, 2H), 7.54 – 7.49 (m, 3H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.08 – 7.04 (m, 2H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.65 (d, *J* = 7.5 Hz, 1H), 6.62 (s, 1H), 3.98 – 3.96 (m, 2H), 3.17 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.28 – 2.24 (m, 4H), 2.17 (s, 3H), 1.87 (s, 4H), 1.65 – 1.60 (m, 1H), 1.51 (s, 3H), 1.39 (s, 6H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 176.0, 167.5, 156.9, 154.2 (dd, *J* = 293.7, 289.7 Hz), 147.9, 138.61, 138.55, 137.8, 136.7, 133.7, 133.5 (t, *J* = 3.7 Hz), 132.6, 130.4, 129.4, 129.0, 128.6, 126.1, 125.0, 124.6, 123.9, 123.5, 123.4, 121.0, 119.9, 119.2, 117.3, 112.2, 88.8 (dd, *J* = 21.3, 13.2 Hz), 75.1, 68.0, 47.3, 43.0, 37.8, 31.4, 27.0, 25.8, 25.7, 25.3, 21.5, 16.0 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -87.5 (d, *J* = 35.3 Hz), -88.3 (d, *J* = 35.3 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: [M+H]$^+$ calcd for $C_{40}H_{41}F_2N_2O_3^+$ 635.3080, found 635.3080.

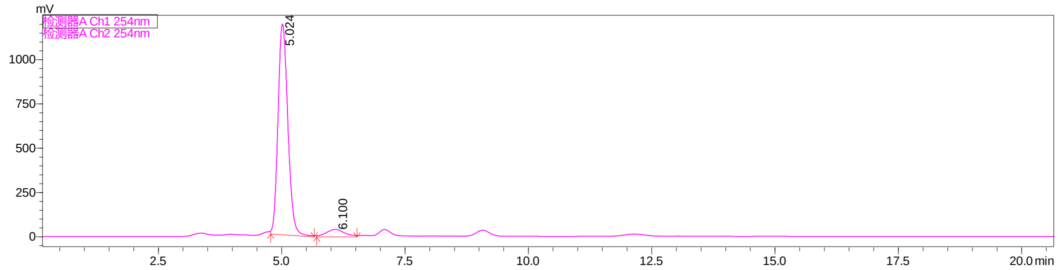
$[\alpha]^{25}_{D}$ = 27.2 ° (c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 94.2:5.8 (Chiralpak AD-H, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 5.024 min, $t_{minor}$ = 6.100 min.



Peak number Retention time Area Height Area ratio

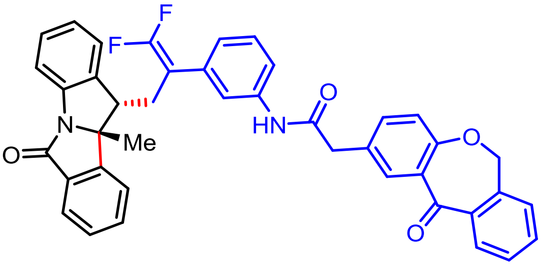
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 5.057 | 11858104 | 852304 | 50.272 |
| 2 | 6.032 | 11729874 | 512451 | 49.728 |
| 总计 |  | 23587978 | 1364755 | 100.000 |

**Figure S87.** HPLC chromatography of the racemic product **46**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 5.024 | 16425622 | 1188636 | 94.198 |
| 2 | 6.100 | 1011681 | 40317 | 5.802 |
| 总计 |  | 17437304 | 1228953 | 100.000 |

**Figure S88.** HPLC chromatography of chiral product **46**



### *N*-(3-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl)-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetamide, 47

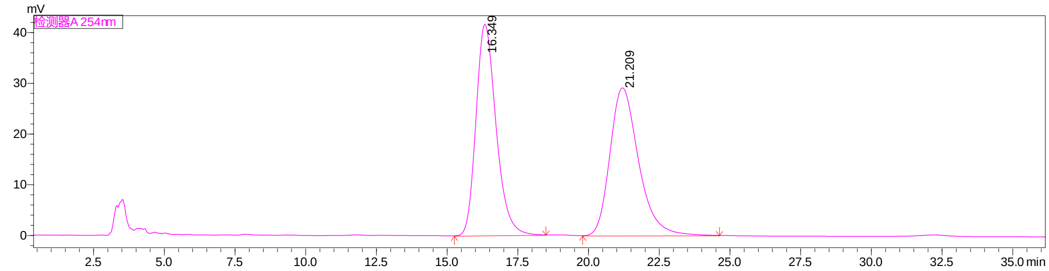
This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 2/1, v/v) afforded **47** as a white solid (58.3 mg, 0.089 mmol, 45% yield). **m.p.** 126.9 – 135.2 □.

**$^1$H NMR (500 MHz, CDCl$_3$):** δ 8.23 (d, *J* = 2.5 Hz, 1H), 7.97 (s, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 7.0 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 2H), 7.58 – 7.54 (m, 2H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.32 – 7.29 (m, 3H), 7.15 (d, *J* = 7.0 Hz, 1H), 7.08 (d, *J* = 8.5 Hz, 1H), 7.05 – 7.02 (m, 2H), 5.19 (s, 2H), 3.78 (s, 2H), 3.12 (dd, *J* = 10.5, 4.5 Hz, 1H), 2.23 – 2.18 (m, 1H), 1.64 – 1.59 (m, 1H), 1.48 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 191.1, 169.3, 167.6, 160.8, 154.1 (t, *J* = 290.8 Hz), 147.8, 140.4, 138.5, 137.7, 136.5, 135.6, 133.6, 133.4, 133.0, 132.7, 132.6, 129.5, 129.42, 129.38, 129.0, 128.6, 128.5, 128.0, 126.0, 125.4, 124.9, 124.6, 124.0, 123.4, 121.7, 119.5, 119.0, 117.3, 88.8 (dd, *J* = 21.3, 13.4 Hz), 75.2, 73.7, 47.2, 43.7, 31.3, 26.9 ppm.

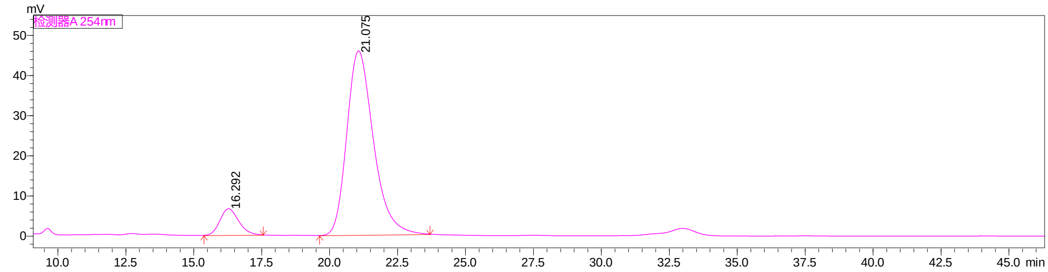
**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -87.7 (d, *J* = 35.3 Hz), -88.4 (d, *J* = 34.9 Hz) ppm.

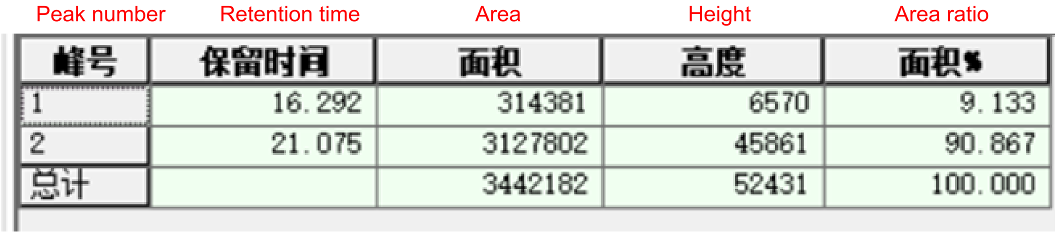
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{41}H_{30}F_2N_2NaO_4^+$ 675.2066, found 675.2064. $[\alpha]^{25}_{D}$ = 76.0˚(c = 0.25 in CHCl$_3$). The enantiomeric excess was determined by HPLC: e.r. = 90.9:9.1 (Chiralpak ID, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm); t$_{major}$ = 21.075 min, t$_{minor}$ = 16.292 min.



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 16.349 | 2057715 | 41632 | 50.110 |
| 2 | 21.209 | 2048707 | 29130 | 49.890 |
| 总计 | | 4106422 | 70762 | 100.000 |

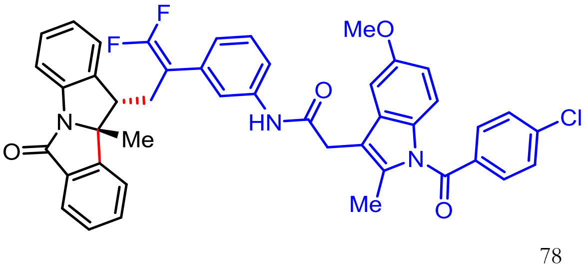
**Figure S89.** HPLC chromatography of the racemic product **47**





| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 16.292 | 314381 | 6570 | 9.133 |
| 2 | 21.075 | 3127802 | 45861 | 90.867 |
| 总计 | | 3442182 | 52431 | 100.000 |

**Figure S90.** HPLC chromatography of chiral product **47**



### 2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)-*N*-(3-(1,1-difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl)acetamide, 48

This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1 to 2/1, v/v) afforded **48** as a white solid (79.4 mg, 0.107 mmol, 53% yield). **m.p.** 53.1 – 55.2 □.

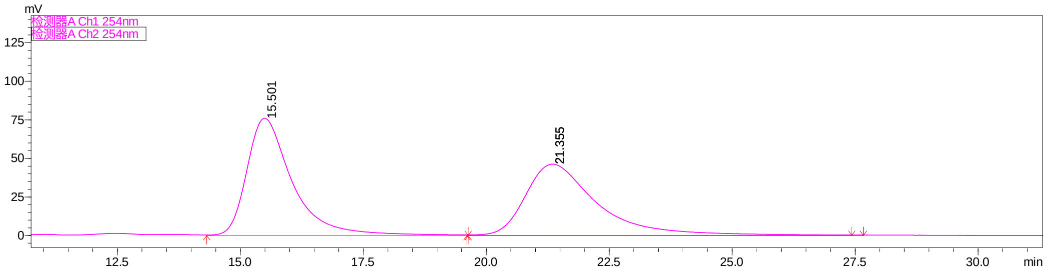
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.89 (d, *J* = 7.5 Hz, 1H), 7.71 (s, 1H), 7.68 – 7.64 (m, 4H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.49 – 7.47 (m, 3H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.5 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 3H), 6.92 (d, *J* = 9.0 Hz, 1H), 6.74 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.86 (s, 2H), 3.81 (s, 3H), 3.13 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.49 (s, 3H), 2.25 – 2.19 (m, 1H), 1.65 – 1.59 (m, 1H), 1.50 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 168.6, 168.5, 167.5, 156.4, 154.1 (dd, *J* = 293.3, 289.7 Hz), 147.8, 139.7, 138.5, 138.2, 137.7, 136.8, 133.7, 133.6, 133.5 (t, *J* = 4.2 Hz), 132.7, 131.3, 131.1, 130.4, 129.4, 129.3, 129.0, 128.6, 126.0, 125.0, 124.5, 124.2, 123.3, 119.7, 119.2, 117.3, 115.3, 112.5, 112.3, 101.2, 88.7 (dd, *J* = 21.3, 13.1 Hz), 75.1, 55.9, 47.2, 33.5, 31.3, 27.0, 13.6 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.35 (d, *J* = 36.3 Hz), -89.44 (dd, *J* = 36.3, 3.8 Hz) ppm.

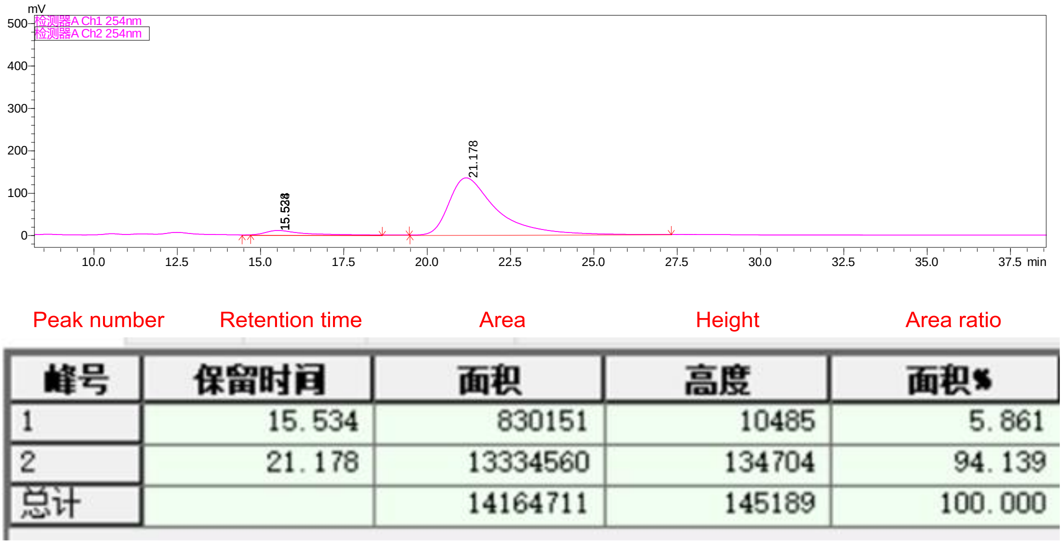
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{44}H_{34}ClF_2N_3NaO_4^+$ 764.2098, found 764.2098.

The enantiomeric excess was determined by HPLC: e.r. = 94.1:5.9 (Chiralpak AD-H, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, λ= 254 nm); t$_{major}$ = 21.178 min, t$_{minor}$ = 15.534 min. $[\alpha]^{25}_{D}$ = 27.2 ° (c = 0.50 in CHCl$_3$).



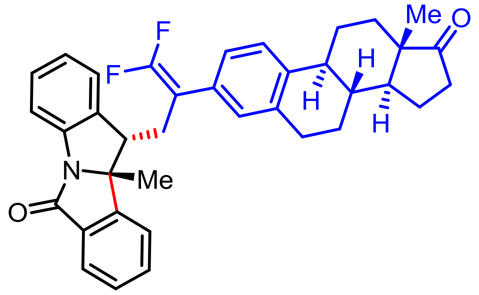
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 15.501 | 4826172 | 75731 | 51.228 |
| 2 | 21.355 | 4594818 | 45985 | 48.772 |
| 总计 |  | 9420989 | 121716 | 100.000 |

**Figure S91.** HPLC chromatography of the racemic product **48**



| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
|---|---|---|---|---|
| 1 | 15.534 | 830151 | 10485 | 5.861 |
| 2 | 21.178 | 13334560 | 134704 | 94.139 |
| 总计 |  | 14164711 | 145189 | 100.000 |

**Figure S92.** HPLC chromatography of chiral product **48**



**(10b*R*,11*S*)-11-(3,3-Difluoro-2-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 49**

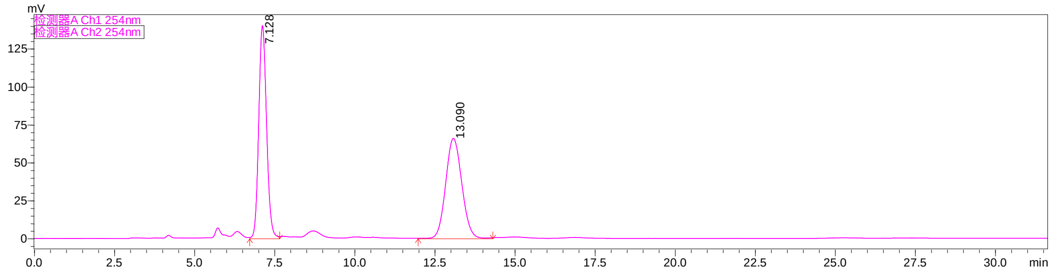
This compound was prepared according to the general procedure **3.2**. Purification by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 5/1 to 3/1, v/v) afforded **49** as a white solid (59.6 mg, 0.106 mmol, 53% yield). **m.p.** 137.1 – 139.9 □.

**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.68 (td, *J* = 7.0, 1.0 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.10 (td, *J* = 7.5, 1.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.93 (s, 1H), 3.11 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.95 – 2.93 (m, 1H), 2.55 – 2.53 (m, 1H), 2.46 – 2.43 (m, 1H), 2.33 (td, *J* = 11.0, 4.0 Hz, 1H), 2.23 – 2.06 (m, 4H), 2.01 – 1.98 (m, 1H), 1.70 – 1.52 (m, 8H), 1.51 (s, 3H), 0.93 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 220.9, 167.3, 154.1 (dd, *J* = 292.4, 289.7 Hz), 147.8, 139.3, 138.5, 137.8, 137.1, 133.9, 132.5, 130.3 (t, *J* = 3.2 Hz), 129.0, 128.8, 128.7, 126.1, 125.9, 125.3, 125.1, 124.4, 123.0, 117.4, 88.7 (dd, $J$ = 20.9, 14.1 Hz), 75.0, 50.6, 48.1, 47.4, 44.5, 38.1, 36.0, 31.7, 31.6, 29.6, 27.0, 26.5, 25.7, 21.7, 14.0 ppm.

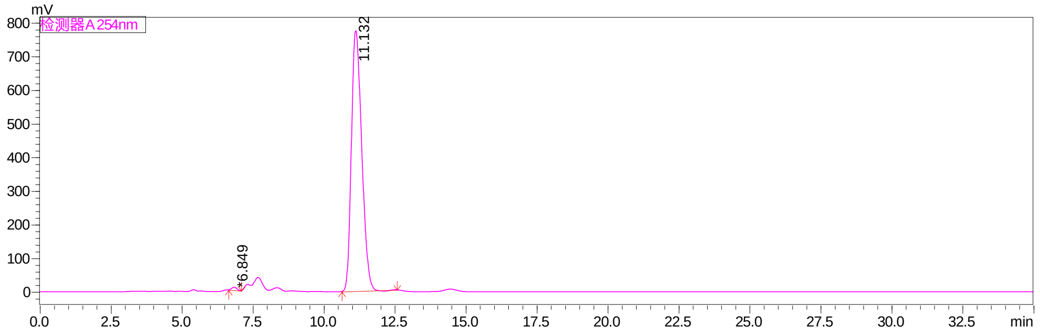
**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -88.8 (d, $J$ = 37.7 Hz), -89.8 (d, $J$ = 37.7 Hz) ppm.

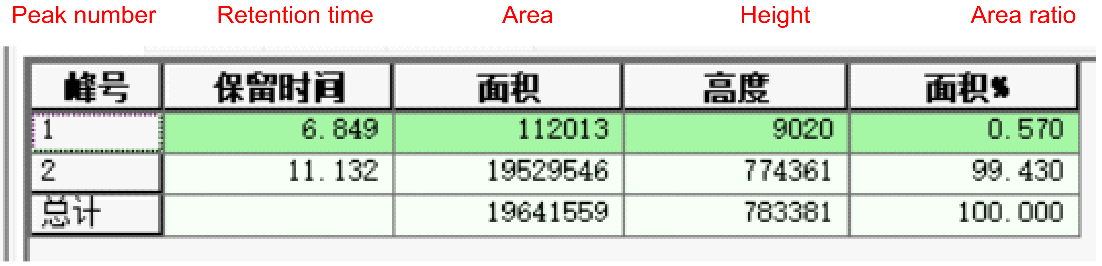
**HRMS (ESI$^+$):** *m/z*: [M+Na]$^+$ calcd for $C_{37}H_{35}F_2NNaO_2^+$ 586.2528, found 586.2528. $[\alpha]^{25}_{D}$ = 103.2°(c = 0.50 in CHCl$_3$). The enantiomeric excess was determined by HPLC: d.e. = 99.4:0.6 (Chiralpak AD-H, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 11.132 min, $t_{minor}$ = 6.849 min.



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 7.128 | 2392689 | 140266 | 50.906 |
| 2 | 13.090 | 2307485 | 65965 | 49.094 |
| 总计 | | 4700174 | 206231 | 100.000 |

**Figure S93.** HPLC chromatography of the racemic product **49**



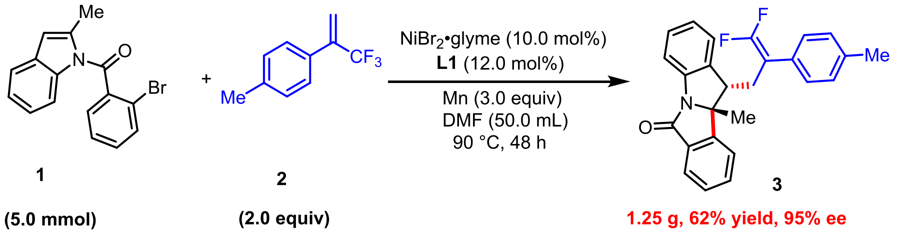


| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 6.849 | 112013 | 9020 | 0.570 |
| 2 | 11.132 | 19529546 | 774361 | 99.430 |
| 总计 | | 19641559 | 783381 | 100.000 |

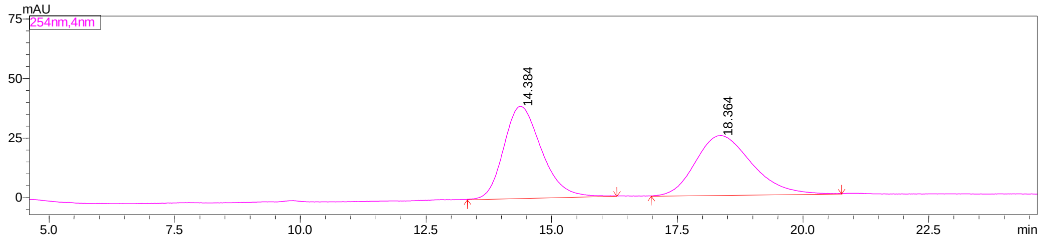
**Figure S94.** HPLC chromatography of chiral product **49**

# 5. Gram-Scale Synthesis and Further Derivatizations

## 5.1 Gram-Scale Synthesis of Product 3

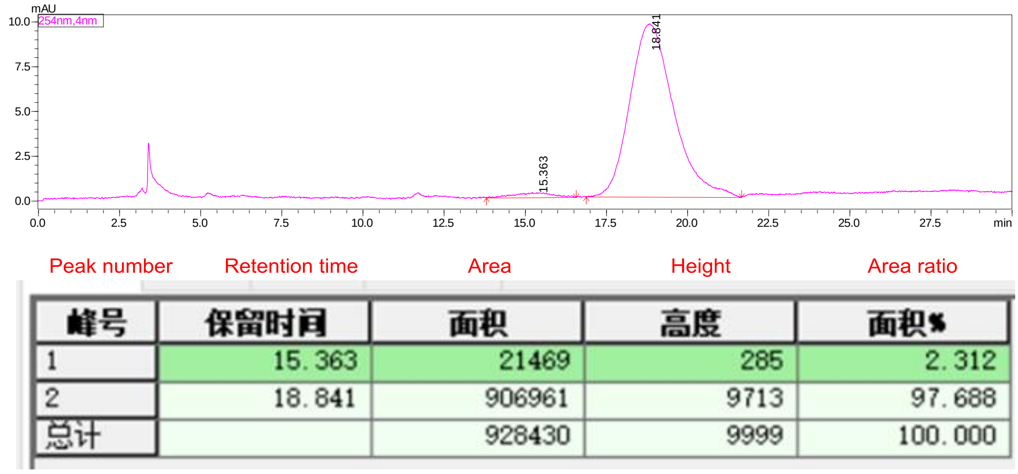


An oven-dried Schlenk tube (250 mL) was charged with NiBr$_2$•glyme (0.5 mmol, 154.3 mg, 10.0 mol%), **L1** (0.6 mmol, 198.8 mg, 12.0 mol%), Mn dust (15.0 mmol, 824.0 mg, 3.0 equiv.), **1** (5.0 mmol, 1.0 equiv, 1.57 g), **2** (10.0 mmol, 2.0 equiv, 1.86 g), and DMF (50.0 mL). The reaction mixture was allowed to stir under N$_2$ atmosphere at 90 °C (oil bath) for 48 h. After this time, the tube was cooled to room temperature then the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~50 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 10:1 to 7:1, v/v) to afford the desired product **3** as a yellow solid (1.25 g, 62%, 95% ee). The enantiomeric excess was determined by HPLC: e.r. = 97.7:2.3 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); t$_{\text{major}}$ = 18.841 min, t$_{\text{minor}}$ = 15.363 min.



| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 14.384 | 2013628 | 38769 | 50.903 |
| 2 | 18.364 | 1942172 | 25091 | 49.097 |
| 总计 | | 3955800 | 63859 | 100.000 |

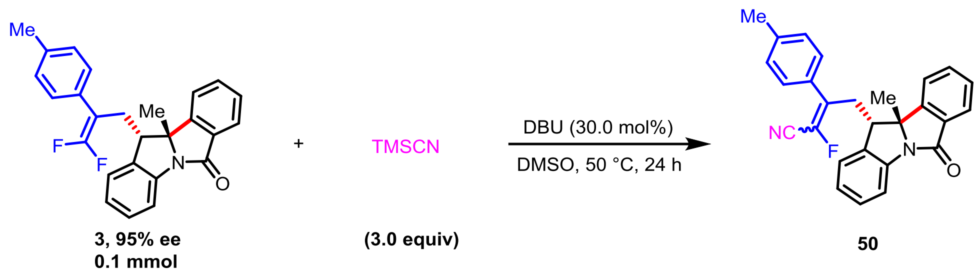
**Figure S95.** HPLC chromatography of the racemic product **3**



| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 15.363 | 21469 | 285 | 2.312 |
| 2 | 18.841 | 906961 | 9713 | 97.688 |
| 总计 |  | 928430 | 9999 | 100.000 |

**Figure S96.** HPLC chromatography of chiral product **3**

## 5.2 Further Transformations of 3$^{9-10}$



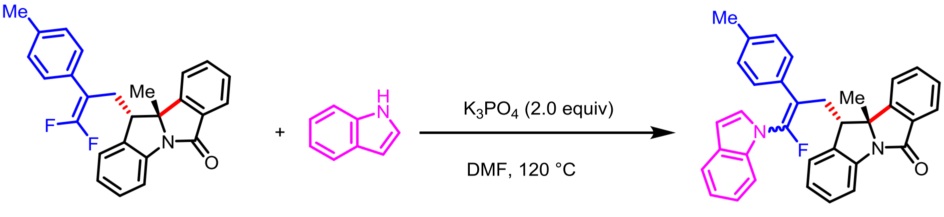
To a solution of **3** (0.1 mmol, 1.0 equiv, 40.1 mg) and trimethylsilyl cyanide (0.3 mmol, 3.0 equiv, 29.8 mg) in 2.0 mL anhydrous DMSO was added DBU (4.6 mg, 30.0 mol%). The mixture was stirred at 50 °C for 24 h. After completion of the reaction, the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~10 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. The crude product was purified by column chromatography on silica gel, eluting with petroleum ether/ethyl acetate = 10:1 (v/v) to afford the product **50** as colorless oil (31.0 mg, 0.076 mmol, 76% yield, E/Z = 1.1:1).

**$^{1}$H NMR (500 MHz, CDCl$_3$):** δ 7.95 (m, 1H), 7.76 – 7.67 (m, 2H), 7.60 – 7.53 (m, 1.5H), 7.48 (d, *J* = 8.0 Hz, 0.5H), 7.40 – 7.36 (m, 1H), 7.27 – 7.26 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.19 – 7.02 (m, 3H), 3.12 (dd, *J* = 10.5, 4.5 Hz, 1H), 2.53 (dt, *J* = 14.5, 4.5 Hz, 0.5H), 2.40 (d, *J* = 3.5 Hz, 3H), 2.36 (dt, *J* = 14.0, 4.5 Hz, 0.5H), 1.80 – 1.75 (m, 1H), 1.50 (d, *J* = 6.5 Hz, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.1, 166.8, 147.31, 147.26, 140.6, 140.5, 137.9, 137.8, 137.7, 137.0, 136.9, 136.8, 133.9, 133.8, 133.3 (d, *J* = 8.4 Hz), 132.75, 132.68, 131.1 (d, *J* = 6.9 Hz), 130.2, 129.9, 129.34, 129.31, 129.2, 129.1, 128.85, 128.83, 128.3 (d, *J* = 4.8 Hz), 128.0 (d, *J* = 2.6 Hz), 126.2, 125.6, 125.5, 125.3, 124.7, 124.4, 123.0, 117.7, 112.6 (d, $J$ = 47.4 Hz), 111.5 (d, $J$ = 47.6 Hz), 75.02, 74.96, 48.0 (d, $J$ = 2.5 Hz), 47.1 (d, $J$ = 2.3 Hz), 35.5, 34.5, 27.0, 26.8, 21.49, 21.45 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -121.8 (s), -125.0 (d, $J$ = 2.4 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{21}FN_2NaO^+$ 431.1530, found 431.1538.



**3, 95% ee**
**0.1 mmol**

**(2.0 equiv)**

**51**

An oven-dried Schlenk tube (20 mL) was charged with indole (0.2 mmol, 2.0 equiv, 23.4 mg), **3** (0.1 mmol, 1.0 equiv, 40.1 mg), $K_3PO_4$ (0.2 mmol, 2.0 equiv, 42.6 mg) and DMF (1.0 mL). Then the reaction was stirred at 120 ºC for 24 h. After completion of the reaction, the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~10 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 10:1, v/v) to afford **51** as a white solid (38.9 mg, 0.078 mmol, 78% yield, 94 % ee, E/Z = 6.5:1). **m.p.** 87.2 – 91.4 □.

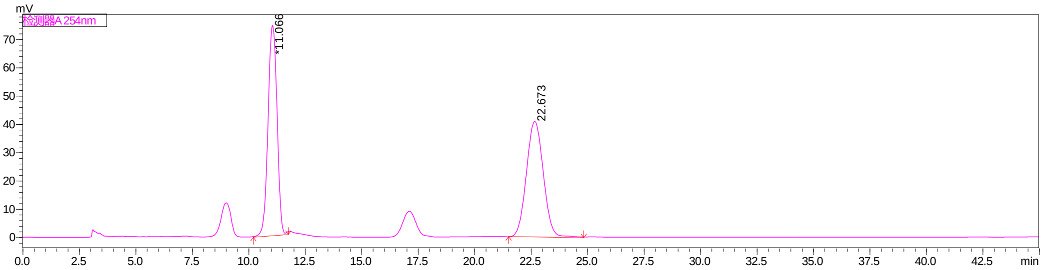
**$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.97 (d, $J$ = 7.5 Hz, 1H), 7.81 (d, $J$ = 7.5 Hz, 1H), 7.71 (t, $J$ = 7.5 Hz, 1H), 7.59 – 7.52 (m, 3H), 7.46 (t, $J$ = 7.5 Hz, 1H), 7.30 (d, $J$ = 7.0 Hz, 1H), 7.22 – 7.19 (m, 3H), 7.16 – 7.13 (m, 1H), 6.98 (d, $J$ = 7.5 Hz, 2H), 6.74 (d, $J$ = 8.0 Hz, 2H), 6.54 (d, $J$ = 3.5 Hz, 1H), 6.36 (d, $J$ = 3.5 Hz, 1H), 3.13 (dd, $J$ = 12.0, 4.0 Hz, 1H), 2.47 (dt, $J$ = 14.0, 4.0 Hz, 1H), 2.26 (s, 3H), 1.99 (t, $J$ = 12.5 Hz, 1H), 1.52 (s, 3H) ppm. $[\alpha]^{25}_{D}$ = 48.8° (c = 0.5 in $CHCl_3$).

**$^{13}$C NMR (126 MHz, $CDCl_3$):** 167.3, 148.1, 146.0 (d, $J$ = 266.2 Hz), 138.5, 138.0, 137.5, 135.9, 134.0, 132.6, 131.9 (d, $J$ = 3.2 Hz), 129.7, 129.0, 128.9, 128.7, 127.6, 127.5, 126.5, 125.3, 124.2, 123.1, 123.0, 121.4, 121.3, 121.0, 117.5, 110.5 (d, $J$ = 27.7 Hz), 105.1, 75.2, 47.3, 33.6, 27.0, 21.3.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** -87.7 (s, minor), -88.7 (s, major).

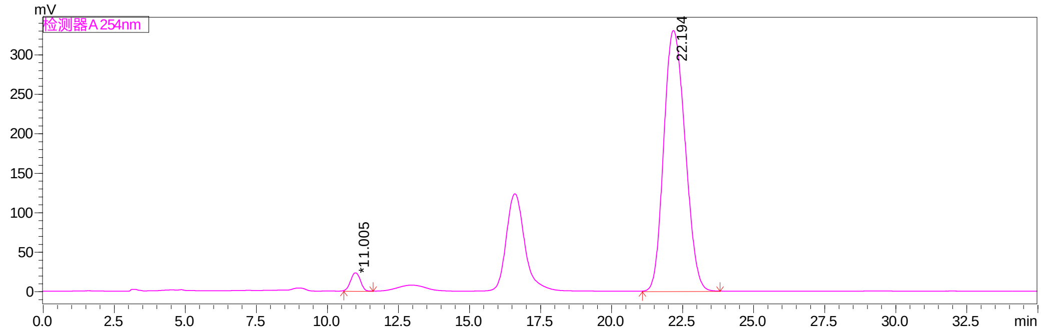
**HRMS (ESI$^+$):** *m/z*: $[M+Na]^+$ calcd for $C_{34}H_{27}FN_2NaO^+$ 521.2000, found 521.1994.

The enantiomeric excess was determined by HPLC: e.r. = 97.0:3.0 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 22.194 min, $t_{minor}$ = 11.005 min.



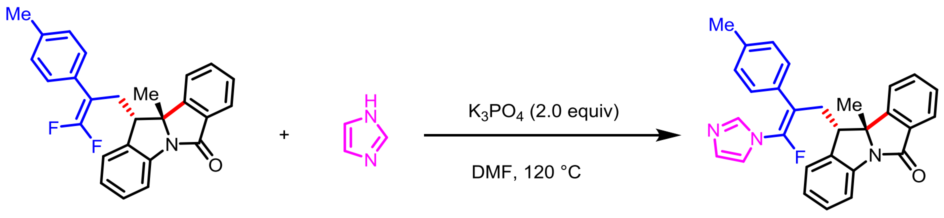
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 11.066 | 2054718 | 74257 | 49.412 |
| 2 | 22.673 | 2103611 | 40718 | 50.588 |
| 总计 | | 4158329 | 114975 | 100.000 |

**Figure S97.** HPLC chromatography of the racemic product **51**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 11.005 | 535821 | 22802 | 3.011 |
| 2 | 22.194 | 17259025 | 329936 | 96.989 |
| 总计 | | 17794846 | 352739 | 100.000 |

**Figure S98.** HPLC chromatography of chiral product **51**



**3, 95% ee**
**0.1 mmol**

**(2.0 equiv)**

**52**

An oven-dried Schlenk tube (20 mL) was charged with azole (0.2 mmol, 2.0 equiv, 20.2 mg), **3** (0.1 mmol, 1.0 equiv, 40.1 mg), $K_3PO_4$ (0.2 mmol, 2.0 equiv, 42.6 mg) and DMF (1.0 mL). Then the reaction was stirred at 120 °C for 24 h. After completion of the reaction, the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~10 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 3:1 to 2:1, v/v) to afford the product **52** as light yellow oil (32.8 mg, 0.073 mmol, 73% yield, 95 % ee). $[\alpha]^{25}_{D} = 60.8^{\circ}$ (c = 0.25 in $CHCl_3$).

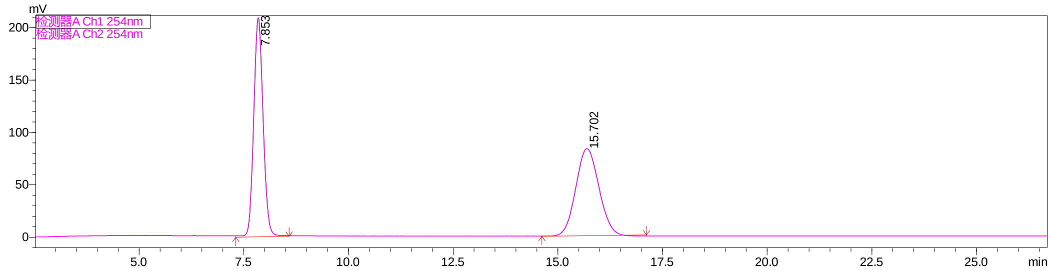
**$^1$H NMR (500 MHz, $CDCl_3$):** δ 7.96 (d, $J$ = 7.5 Hz, 1H), 7.77 (d, $J$ = 8.0 Hz, 1H), 7.69 (t, $J$ = 7.5 Hz, 1H), 7.58 (t, $J$ = 7.5 Hz, 1H), 7.50 (d, $J$ = 7.5 Hz, 1H), 7.40 (t, $J$ = 7.5 Hz, 1H), 7.23 (d, $J$ = 7.5 Hz, 1H), 7.16 – 7.10 (m, 4H), 6.96 (br, 1H), 6.83 (d, $J$ = 8.0 Hz, 2H), 6.72 (br, 1H), 3.12 (dd, $J$ = 10.5, 5.0 Hz, 1H), 2.37 – 2.33 (m, 4H), 1.97 – 1.92 (m, 1H), 1.51 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, $CDCl_3$):** δ 167.2, 147.7, 138.5, 138.3, 138.0, 134.0, 132.5, 130.21, 131.18, 130.1, 129.1, 128.9, 127.79, 127.76, 125.8, 125.2, 124.2, 123.1, 117.6, 110.6 (d, $J$ = 23.6 Hz), 75.1, 47.1, 34.2, 26.9, 21.3 ppm.

**$^{19}$F NMR (471 MHz, $CDCl_3$):** δ -91.5 (s) ppm.

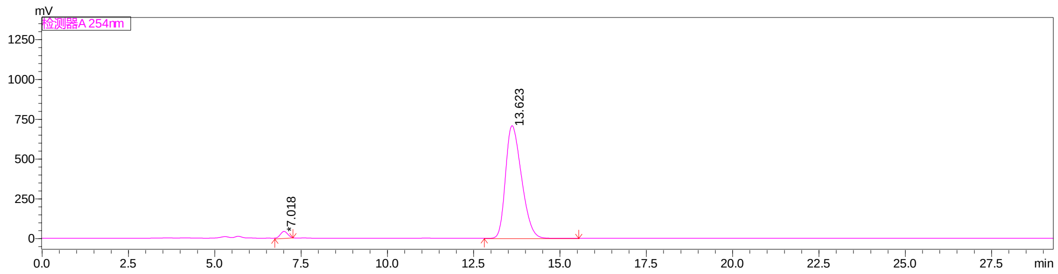
**HRMS (ESI$^+$):** *m/z*: $[M+H]^+$ calcd for $C_{29}H_{25}FN_3O^+$ 450.1976, found 450.1974.

The enantiomeric excess was determined by HPLC: e.r. = 97.3:2.7 (Chiralpak AD-H, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 13.623 min, $t_{minor}$ = 7.018 min.



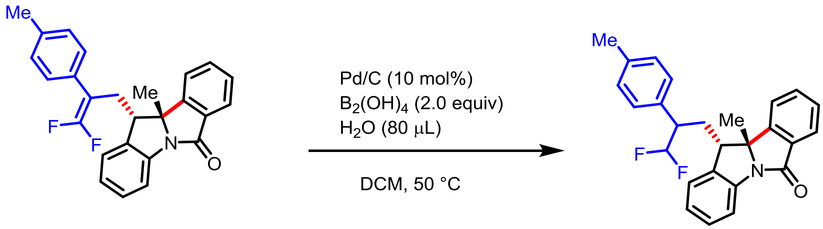
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 7.853 | 3254882 | 208662 | 51.108 |
| 2 | 15.702 | 3113727 | 82757 | 48.892 |
| 总计 |  | 6368608 | 291419 | 100.000 |

**Figure S99.** HPLC chromatography of the racemic product **52**



| Peak number<br>峰号 | Retention time<br>保留时间 | Area<br>面积 | Height<br>高度 | Area ratio<br>面积% |
|---|---|---|---|---|
| 1 | 7.018 | 622117 | 41891 | 2.678 |
| 2 | 13.623 | 22608816 | 706631 | 97.322 |
| 总计 |  | 23230933 | 748521 | 100.000 |

**Figure S100.** HPLC chromatography of chiral product **52**



**3, 95% ee**
**0.1 mmol**

**53**

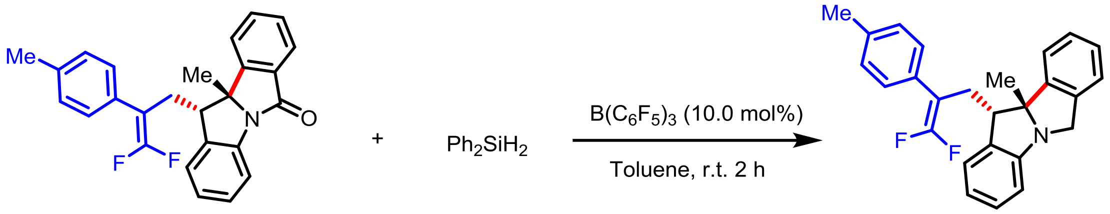
An oven-dried Schlenk tube (10 mL) was charged with tetrahydroxydiboron (0.2 mmol, 2.0 equiv, 17.9 mg), and Pd/C (0.01 mmol, 0.1 equiv, 10% wt, 10.2 mg). The tube was capped with a septum, degassed and backfilled with argon. The vial was charged with 2.0 mL of dichloromethane followed with *gem*-difluoroalkene **3** (0.12 mmol, 41.4 mg) and 80 µL of water. The mixture was heated at 50 ℃ for 36 h (monitored by TLC). The solution was then filtered through a celite plug and washed with DCM. The crude product was purified by column chromatography on silica gel, eluting with petroleum ether/ethyl acetate = 10:1 (v/v) to afford the product **53** as inseparable mixture of diastereoisomers (colorless oil, 27.8 mg, 0.069 mmol, 69%, dr = 1.3:1)

**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.94 (d, $J$ = 7.5 Hz, 1H), 7.89 (d, $J$ = 7.5 Hz, 1.3H), 7.75 – 7.66 (m, 5H), 7.58 – 7.51 (m, 4H), 7.48 (t, $J$ = 7.5 Hz, 1H), 7.39 – 7.33 (m, 2.4H), 7.29 – 7.28 (m, 3.5H), 7.20 – 7.19 (m, 3H), 7.13 (t, $J$ = 7.5 Hz, 2.5H), 7.07 (t, $J$ = 8.0 Hz, 2.7H), 6.90 (t, $J$ = 7.5 Hz, 2.7H), 5.80 – 5.33 (m, 1.5H), 3.28 – 3.25 (m, 1.3H), 3.07 – 2.98 (m, 2H), 2.90 (dd, $J$ = 12.5, 3.5 Hz, 1H), 2.41 (s, 3H), 2.28 (s, 3.8H), 1.75 – 1.67 (m, 3.9H), 1.53 (s, 4H), 1.43 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 167.2, 167.1, 147.9, 147.7, 139.6, 138.4, 138.0, 137.83, 137.78, 137.6, 134.0, 138.9, 132.7, 132.5, 132.0, 131.9, 130.0, 129.7, 129.2, 129.1, 128.8, 128.6, 128.4, 126.3, 126.2, 125.2, 125.1, 124.6, 124.3, 123.3, 122.9, 118.2, 117.9, 117.6, 75.52, 75.49, 47.7, 46.2, 33.4, 30.7, 27.2, 26.8, 21.3, 21.1 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** -114.8 (dd, *J* = 56.0, 13.2 Hz), -115.4 (dd, *J* = 56.5, 13.2 Hz), -120.7 (dd, *J* = 56.5, 15.1 Hz), -122.7 (dd, *J* = 57.0, 17.9 Hz), -123.2 (dd, *J* = 56.5, 17.4 Hz) ppm.

**HRMS (ESI$^+$):** *m/z*: $[M+H]^+$ calcd for $C_{26}H_{23}F_2NONa^+$ 426.1640, found 426.1635.



**3, 95% ee**
**0.2 mmol**

**(2.0 equiv)**

**54**

In the glove box, to a solution of **3** (0.2 mmol, 1.0 equiv, 80.3 mg), $B(C_6F_5)_3$ (0.02 mmol, 10.0 mol%, 10.2 mg) in toluene (1.0 mL) was added $Ph_2SiH_2$ (0.4 mmol, 2.0 equiv, 73.7 mg) and toluene (1.0 mL). Then the reaction was stirred at room temperature for 2 h. After completion of the reaction, the reaction mixture was concentrated under vacuum. The crude product was purified by column chromatography on silica gel, eluting with petroleum ether/ethyl acetate = 20:1 (v/v) to afford the product **54** (65.8 mg, 0.177 mmol, 85% yield, 94% ee). $[\alpha]^{25}_{D} = 36.0^{\circ}$ (c = 0.50 in CHCl$_3$).

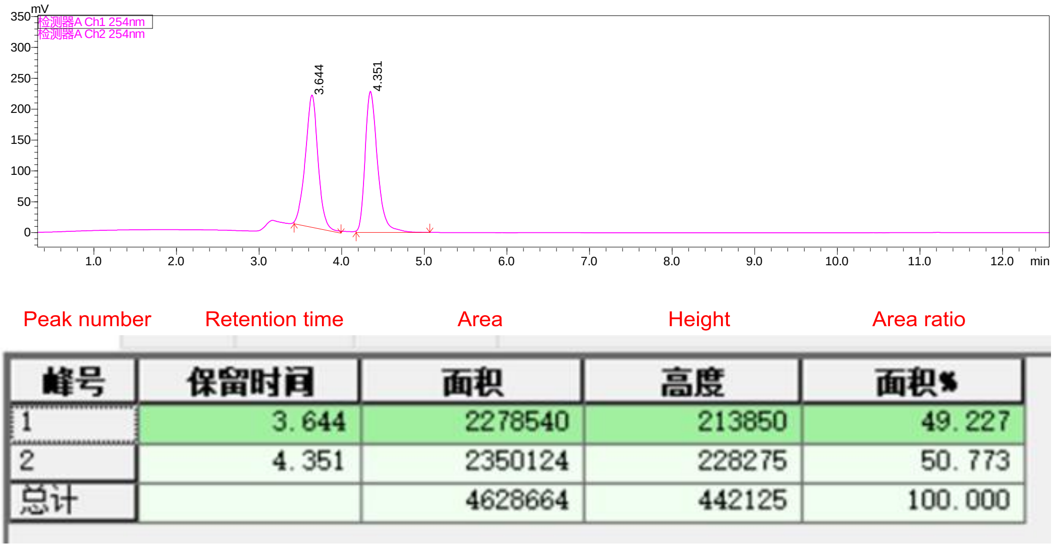
**$^1$H NMR (500 MHz, CDCl$_3$):** δ 7.33 – 7.26 (m, 5H), 7.24 – 7.22 (m, 3H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 6.86 – 6.82 (m, 2H), 4.78 (d, *J* = 14.0 Hz, 1H), 4.42 (d, *J* = 14.0 Hz, 1H), 2.97 (dd, *J* = 11.5, 4.5 Hz, 1H), 2.56 – 2.50 (m, 1H), 2.38 (s, 3H), 1.91 – 1.85 (m, 1H), 1.45 (s, 3H) ppm.

**$^{13}$C NMR (126 MHz, CDCl$_3$):** δ 153.8 (dd, *J* = 290.7, 287.8 Hz), 152.1, 143.1, 140.2, 137.4, 134.8, 130.1 (t, *J* = 3.5 Hz), 129.6, 128.3, 128.2 (t, *J* = 3.3 Hz), 127.8, 127.2, 125.0, 123.9, 123.1, 120.8, 113.6, 89.9 (dd, *J* = 21.0, 13.6 Hz), 80.0, 58.1, 49.2, 32.9, 30.0, 21.3 ppm.

**$^{19}$F NMR (471 MHz, CDCl$_3$):** δ -90.2 (d, *J* = 41.0 Hz), -90.7 (dd, *J* = 40.5, 4.7 Hz ) ppm.

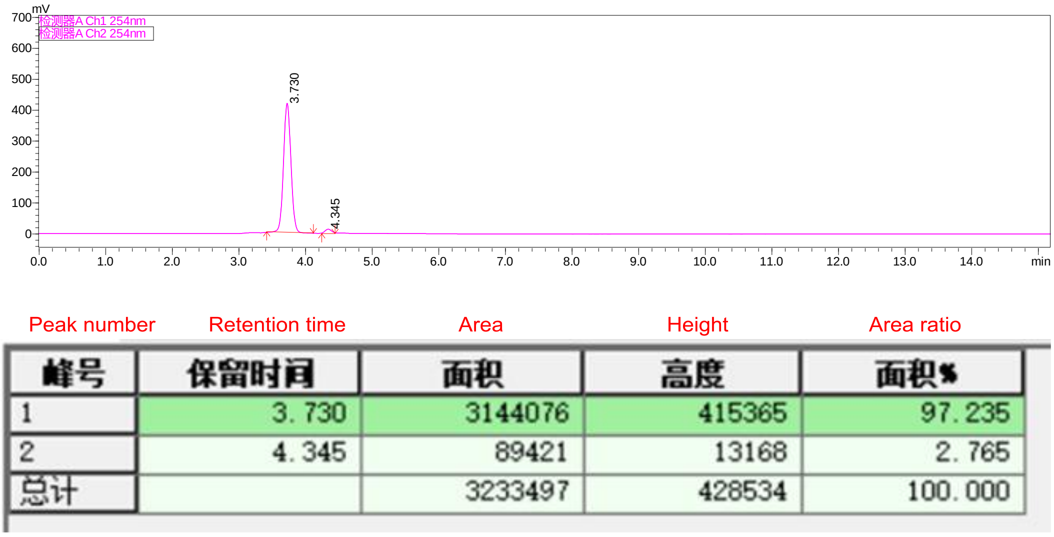
**HRMS (ESI$^+$):** *m/z*: $[M+H]^+$ calcd for $C_{26}H_{24}F_2N^+$ 388.1871, found 388.1891.

The enantiomeric excess was determined by HPLC: e.r. = 97.2:2.8 (Chiralpak AD-H, *i*-propanol/hexane = 1/99, flow rate 1.0 mL/min, λ= 254 nm); $t_{major}$ = 3.730 min, $t_{minor}$ = 4.345 min.



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 3.644 | 2278540 | 213850 | 49.227 |
| 2 | 4.351 | 2350124 | 228275 | 50.773 |
| 总计 | | 4628664 | 442125 | 100.000 |

**Figure S101.** HPLC chromatography of the racemic product **54**

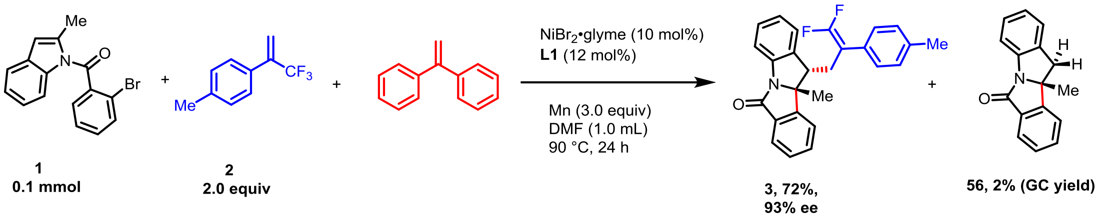


| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 3.730 | 3144076 | 415365 | 97.235 |
| 2 | 4.345 | 89421 | 13168 | 2.765 |
| 总计 | | 3233497 | 428534 | 100.000 |

**Figure S102.** HPLC chromatography of chiral product **54**

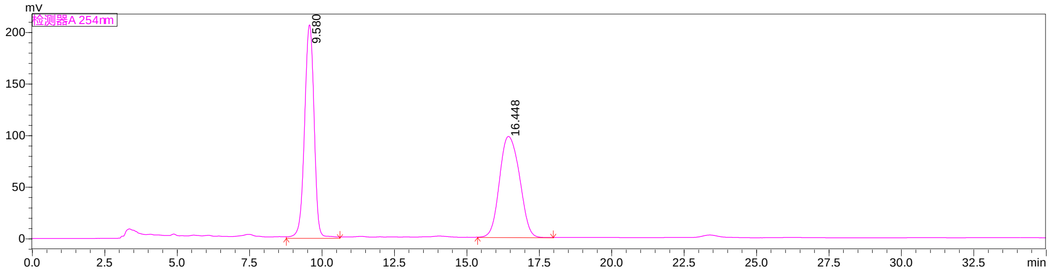
# 6. Mechanistic Studies

## 6.1 Radical Capture Experiments



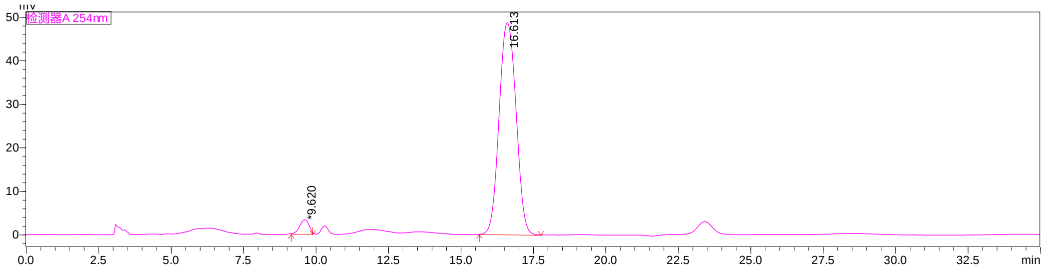
An oven-dried Schlenk tube (20 mL) was charged with $NiBr_2$•glyme (0.01 mmol, 3.1 mg, 10.0 mol%), **L1** (0.012 mmol, 4.0 mg, 12.0 mol%), Mn dust (0.3 mmol, 16.5 mg, 3.0 equiv), **1** (0.1 mmol, 1.0 equiv, 31.4 mg), **2** (0.2 mmol, 2.0 equiv, 37.2 mg), 1,1-diphenylethylene (0.1 mmol, 1.0 equiv, 18.1 mg) and DMF (1.0 mL). The reaction mixture was allowed to stir under $N_2$ atmosphere at 90 □ (oil bath) for 24 h. After this time, the tube was cooled to room temperature then the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~10 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7:1, v/v)) to afford the desired product **3** as a yellow solid (28.9 mg, 0.072 mmol, 72% yield, 93% ee). The yield of **56** was confirmed by GC using 1,3,5-trimethoxybenzene as an internal standard.

The enantiomeric excess was determined by HPLC: e.r. = 96.3:3.7 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); $t_{major}$ = 16.613 min, $t_{minor}$ = 9.620 min.



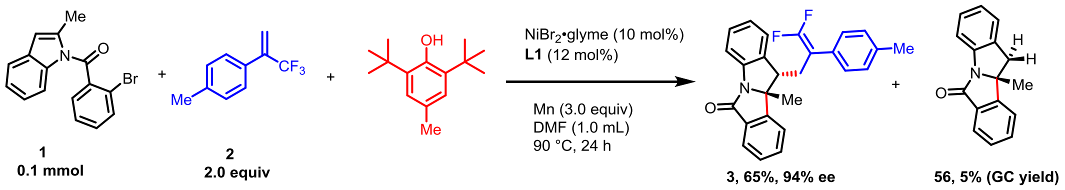
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.580 | 4746850 | 206548 | 50.243 |
| 2 | 16.448 | 4700853 | 97764 | 49.757 |
| 总计 | | 9447703 | 304312 | 100.000 |

**Figure S103.** HPLC chromatography of the racemic product **3**



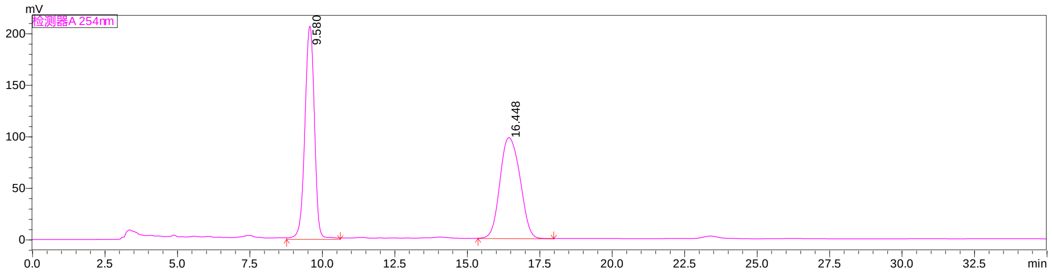
| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.620 | 75839 | 3341 | 3.695 |
| 2 | 16.613 | 1976646 | 48617 | 96.305 |
| 总计 |  | 2052486 | 51958 | 100.000 |

**Figure S104.** HPLC chromatography of chiral product **3**



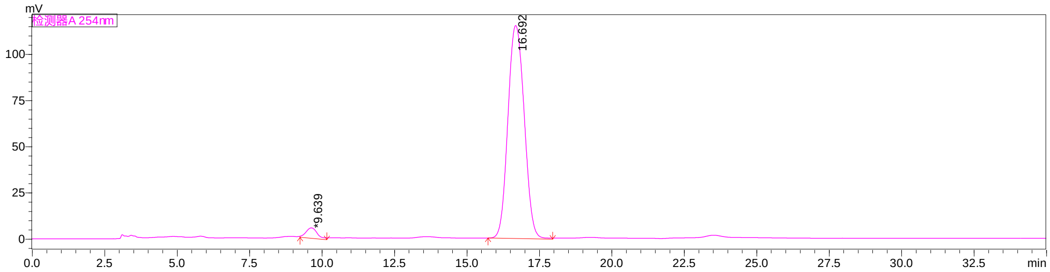
An oven-dried Schlenk tube (20 mL) was charged with $NiBr_2$•glyme (0.01 mmol, 3.1 mg, 10.0 mol%), **L1** (0.012 mmol, 4.0 mg, 12.0 mol%), Mn dust (0.3 mmol, 16.5 mg, 3.0 equiv), **1** (0.1 mmol, 1.0 equiv, 31.4 mg), **2** (0.2 mmol, 2.0 equiv, 37.2 mg), BHT (0.1 mmol, 1.0 equiv, 22.0 mg) and DMF (1.0 mL). The reaction mixture was allowed to stir under $N_2$ atmosphere at 90 □ (oil bath) for 24 h. After this time, the tube was cooled to room temperature then the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~10 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7:1, v/v)) to afford the desired product **3** as a yellow solid (26.1 mg, 0.065 mmol, 65% yield). The yield of **56** was confirmed by GC using 1,3,5-trimethoxybenzene as an internal standard.

The enantiomeric excess was determined by HPLC: e.r. = 96.8:3.2 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); $t_{major}$ = 16.692 min, $t_{minor}$ = 9.639 min.



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9. 580 | 4746850 | 206548 | 50. 243 |
| 2 | 16. 448 | 4700853 | 97764 | 49. 757 |
| 总计 | | 9447703 | 304312 | 100. 000 |

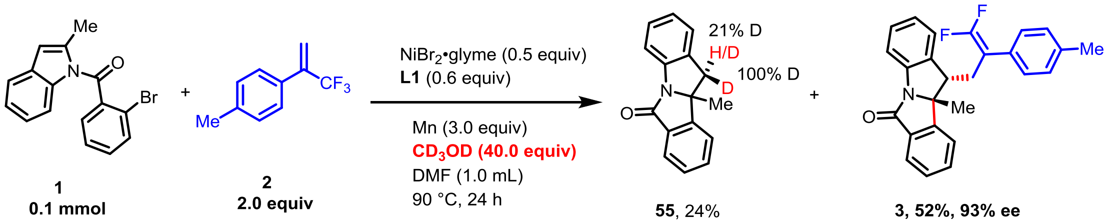
**Figure S105.** HPLC chromatography of the racemic product **3**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9. 639 | 146915 | 5476 | 3. 166 |
| 2 | 16. 692 | 4494195 | 115094 | 96. 834 |
| 总计 | | 4641110 | 120570 | 100. 000 |

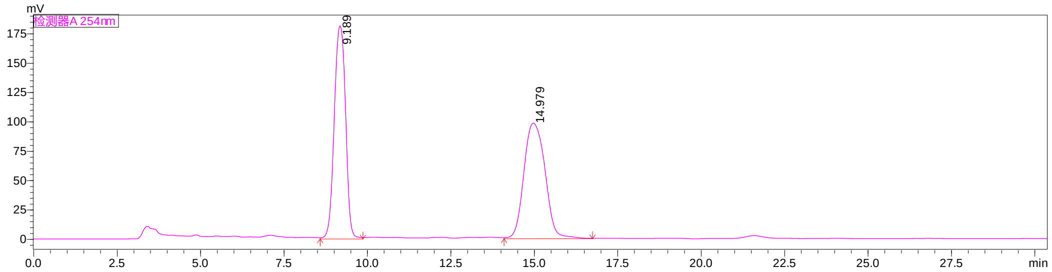
**Figure S106.** HPLC chromatography of chiral product **3**

## 6.2 Deuterium-Labelling Experiments



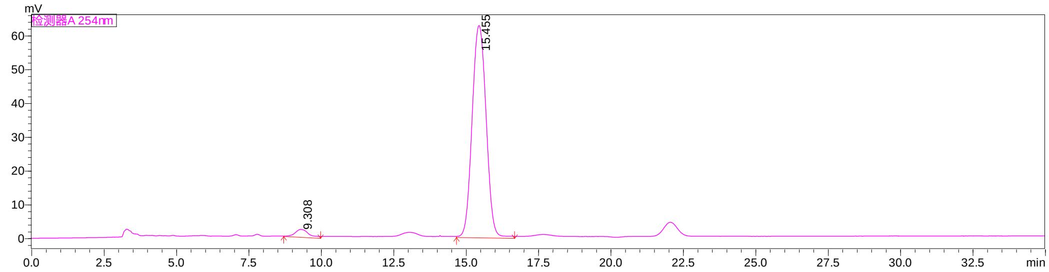
An oven-dried Schlenk tube (20.0 mL) was charged with NiBr$_2$•glyme (0.05 mmol, 15.4 mg, 50.0 mol%), **L1** (0.06 mmol, 19.9 mg, 60.0 mol%), Mn dust (0.3 mmol, 16.5 mg, 3.0 equiv), **1** (0.1 mmol, 1.0 equiv, 31.4 mg), **2** (0.2 mmol, 2.0 equiv, 37.2 mg), CD$_3$OD (4.0 mmol, 40.0 equiv, 144.3 mg) and DMF (1.0 mL). The reaction mixture was allowed to stir under N$_2$ atmosphere at 90 □ (oil bath) for 24 h. After this time, the tube was cooled to room temperature then the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~10 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7:1, v/v) to afford the desired product **3** as a white solid (20.9 mg, 0.052 mmol, 52% yield).

The enantiomeric excess was determined by HPLC: e.r. = 96.5:3.5 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, $\lambda$ = 254 nm); $t_{major}$ = 15.455 min, $t_{minor}$ = 9.308 min.



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.189 | 4274555 | 181173 | 49.752 |
| 2 | 14.979 | 4317177 | 98112 | 50.248 |
| 总计 | | 8591732 | 279285 | 100.000 |

**Figure S107.** HPLC chromatography of the racemic product **3**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.308 | 75571 | 2253 | 3.451 |
| 2 | 15.455 | 2114461 | 62746 | 96.549 |
| 总计 | | 2190032 | 64999 | 100.000 |

**Figure S108.** HPLC chromatography of chiral product **3**

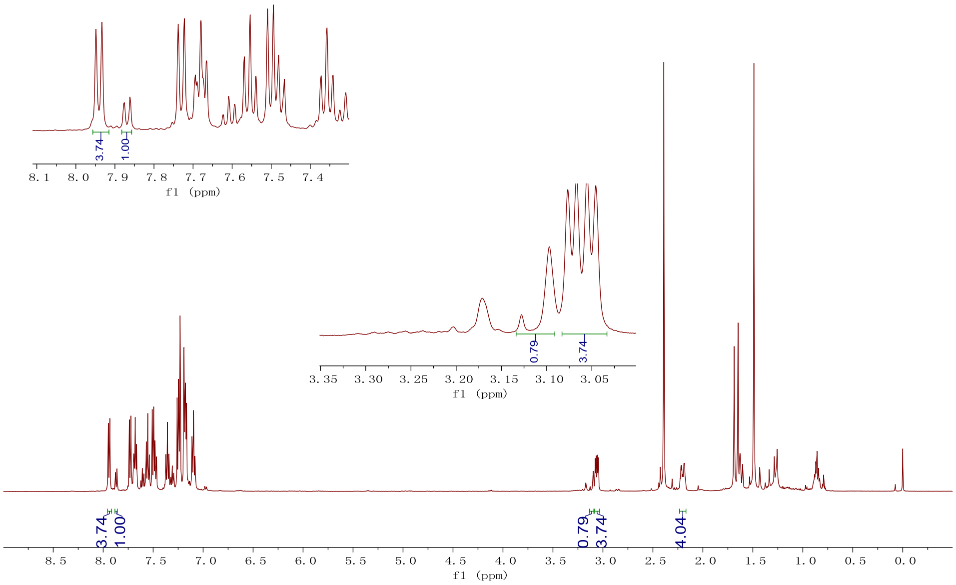
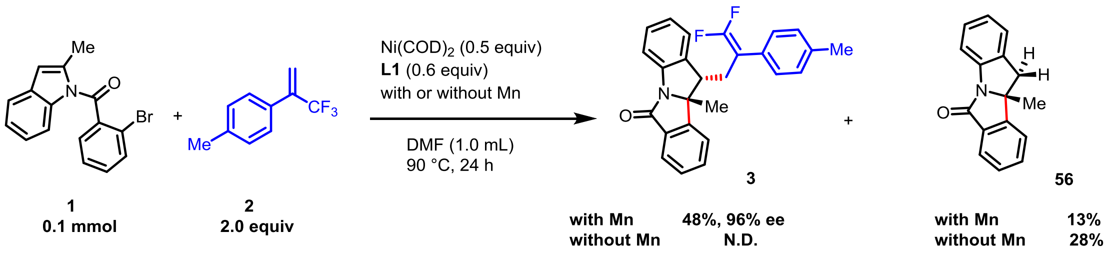


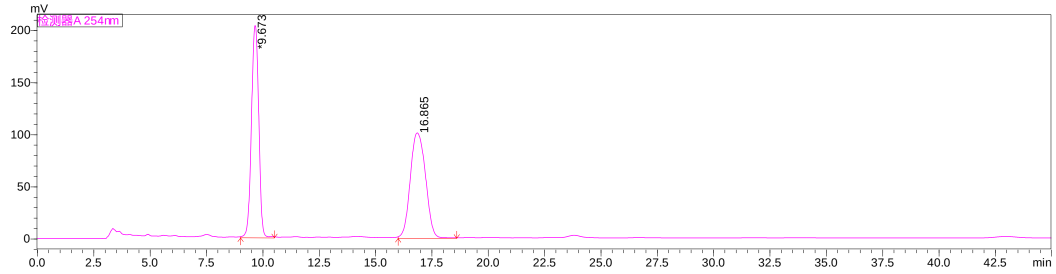
**Figure S109.** $^1$H NMR spectra (500 MHz, $CDCl_3$) of the mixture of products **3** and **55**

## 6.3 The Profile of Reductant in Nickel-Catalyzed Dearomative Reductive Coupling



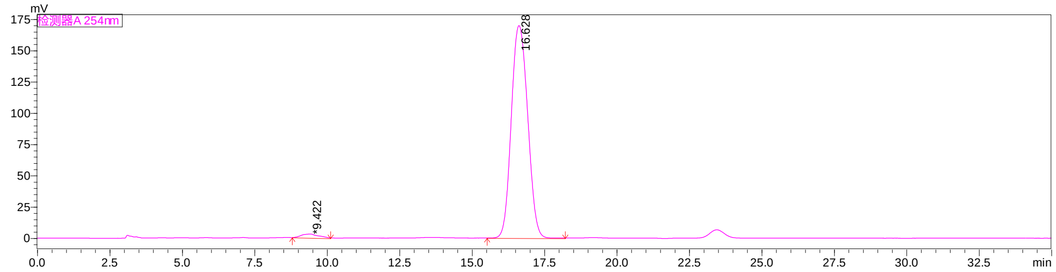
An oven-dried Schlenk tube (20.0 mL) was charged with $Ni(COD)_2$ (0.05 mmol, 13.8 mg, 0.5 equiv), **L1** (0.06 mmol, 20.0 mg, 0.3 equiv), Mn dust (0.3 mmol, 16.50mg, 3.0 equiv or without), **1** (0.1 mmol, 1.0 equiv, 31.4 mg), **2** (0.2 mmol, 2.0 equiv, 37.4 mg), and DMF (1.0 mL). The reaction mixture was allowed to stir under $N_2$ atmosphere at 90 □ (oil bath) for 24 h. After this time, the tube was cooled to room temperature then the reaction mixture was vacuumed to remove the volatiles. The residue was diluted with DCM (~10 mL) and filtered through a triangular suction filter funnel with a thin layer of celite, and the filtrate was concentrated under vacuum. The crude mixture was then purified by column chromatography on silica gel (Petroleum ether/Ethyl acetate = 7:1, v/v) to afford the desired product **3** as a yellow solid (19.3 mg, 0.048 mmol, 48% yield, 96% ee). The yield of **56** was confirmed by GC using 1,3,5-trimethoxybenzene as an internal standard.

The enantiomeric excess was determined by HPLC: e.r. = 98.2:1.8 (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm); $t_{major}$ = 16.628 min, $t_{minor}$ = 9.422 min.



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.673 | 4569983 | 203307 | 49.086 |
| 2 | 16.865 | 4740145 | 100877 | 50.914 |
| 总计 | | 9310128 | 304184 | 100.000 |

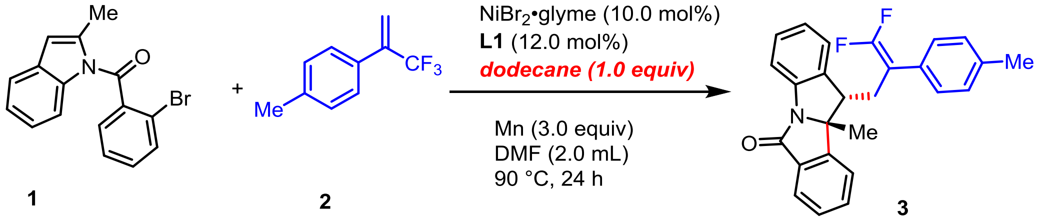
**Figure S110.** HPLC chromatography of the racemic product **3**



| Peak number | Retention time | Area | Height | Area ratio |
|---|---|---|---|---|
| 峰号 | 保留时间 | 面积 | 高度 | 面积% |
| 1 | 9.422 | 123197 | 3021 | 1.810 |
| 2 | 16.628 | 6683565 | 169910 | 98.190 |
| 总计 | | 6806762 | 172931 | 100.000 |

**Figure S111.** HPLC chromatography of chiral product **3**

## 6.4 Kinetic Studies



An oven-dried Schlenk tube (20.0 mL) was charged with $NiBr_2$•glyme (0.02 mmol, 6.2 mg, 10.0 mol%), **L1** (0.024 mmol, 8.0 mg, 12.0 mol%), Mn dust (0.6 mmol, 33.0 mg, 3.0 equiv), **1** (0.2 mmol, 1.0 equiv), **2** (0.4 mmol, 2.0 equiv), dodecane (0.2 mmol, 1.0 equiv, 34.1 mg) and DMF (2.0 mL). The reaction mixture was allowed to stir under $N_2$ atmosphere at 90 □ (oil bath). At 1, 2, 3, 4, 5, 7, 9, 11, 13, 16, 19, 22 and 24 h, a 25 $\mu$L aliquot of the reaction mixture was removed with microsampler under $N_2$ atmosphere and transferred into another vial. The measured mixture was diluted with ethyl acetate (2 mL) and filtered through a 0.22-μm filter membranes and the resulting filtrate was collected in a GC vial. The sample was analyzed by GC and the yields were determined based on the peak area of the analyte compared to dodecane as an internal standard. Enantiomeric excess was determined by HPLC analysis with a chiral column (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm).

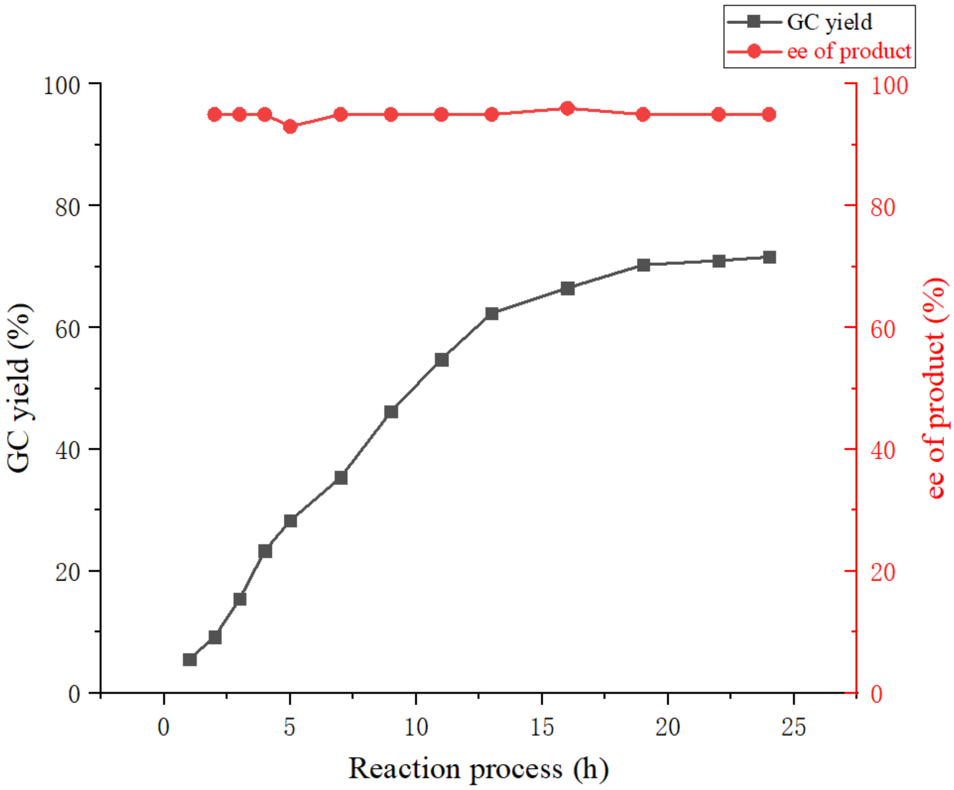
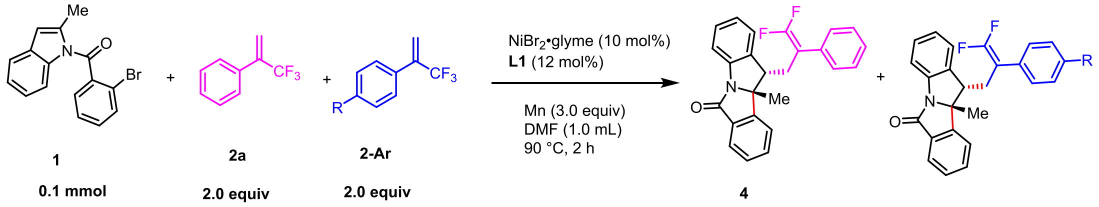


**Figure S112** Kinetic profiles of reactions with yield and ee values of product **3**

### 6.5 Hammett Plot of Different Substituents on Trifluoromehtyl Alkenes



An oven-dried Schlenk tube (20.0 mL) was charged with $NiBr_2$•glyme (0.01 mmol, 3.1 mg, 10.0 mol%), **L1** (0.012 mmol, 4.0 mg, 12.0 mol%), Mn dust (0.3 mmol, 16.5 mg, 3.0 equiv), **1** (0.1 mmol, 1.0 equiv), **2a** (0.2 mmol, 2.0 equiv), trifluoromethyl alkenes (0.2 mmol, 2.0 equiv) and DMF (1.0 mL). The reaction mixture was allowed to stir under $N_2$ atmosphere at 90 □ (oil bath) for 2 h. After this time, the tube was cooled to room temperature. The yields of products were confirmed by GC using dodecane as an internal standard.

**Table S1** Hammett plot varying the electronics on alkenes

| **R** | **Hammett $\sigma_p$** | **[2-Ar]/[4]** | **log(k/k$_0$)** |
|---|---|---|---|
| OMe | -0.27 | 0.5248 | -0.2800 |
| *t*Bu | -0.15 | 0.5631 | -0.2494 |
| H | 0 | 1 | 0 |
| CHO | 0.42 | 2.4434 | 0.3880 |
| Ac | 0.47 | 3.7905 | 0.5787 |
| CN | 0.70 | 3.8557 | 0.5861 |

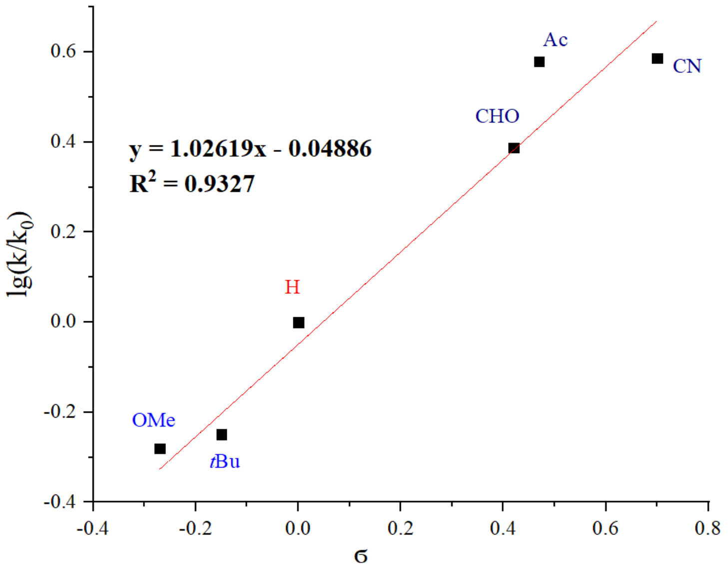


**Figure S113** Hammett plot varying the electronics on alkenes

# 7. X-ray Crystallographic Studies

### The Absolute Configuration Determination of Compounds 14 and 16 Produced by Asymmetric Dearomative Reductive Coupling

**Procedure for the sample preparation of 14**: In an oven-dried 10.0 mL vial, **14** (30 mg) was dissolved in ethyl acetate/hexane (10:1, v/v). After slow evaporation at room temperature, the crystal was afforded.

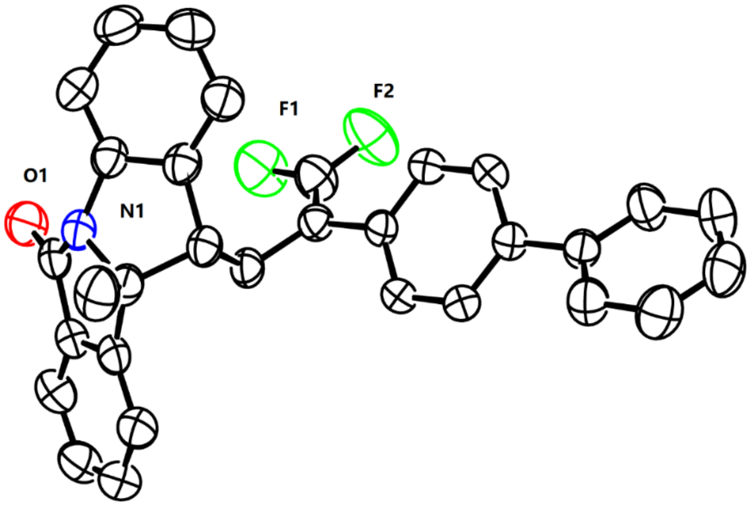


**Figure S114.** Crystal structure of compound **14** with 50% thermal ellipsoids (Solvent molecules, and carbon hydrogenatoms were omitted for clarity.) (CCDC 2268960)

**Crystal data and structure refinement for 14.**

| | |
|---|---|
| Identification code | exp_3118 |
| Empirical formula | $C_{31}H_{23}F_2NO$ |
| Formula weight | 463.50 |
| Temperature/K | 293 |
| Crystal system | tetragonal |
| Space group | $P4_32_12$ |
| a/Å | 11.38010(10) |
| b/Å | 11.38010(10) |
| c/Å | 37.2074(6) |
| α/° | 90 |
| β/° | 90 |
| γ/° | 90 |
| Volume/Å$^3$ | 4818.61(11) |
| Z | 8 |
| $\rho_{calc}$g/cm$^3$ | 1.278 |
| μ/mm$^{-1}$ | 0.710 |
| F(000) | 1936.0 |
| Crystal size/mm$^3$ | 0.3 × 0.3 × 0.3 |
| Radiation | CuKα (λ = 1.54184) |
| 2Θ range for data collection/° | 8.124 to 139.232 |
| Index ranges | $-13 \le h \le 13$, $-13 \le k \le 13$, $-45 \le l \le 42$ |
| Reflections collected | 55480 |
| Independent reflections | 4531 [$R_{int}$ = 0.0382, $R_{sigma}$ = 0.0156] |
| Data/restraints/parameters | 4531/0/317 |
| Goodness-of-fit on F$^2$ | 1.071 |

| | |
|---|---|
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0346, $wR_2$ = 0.0829 |
| Final R indexes [all data] | $R_1$ = 0.0366, $wR_2$ = 0.0847 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.09/-0.16 |
| Flack parameter | 0.05(4) |

**Procedure for the sample preparation of 16**: In an oven-dried 10.0 mL vial, **16** (60 mg) was dissolved in ethyl acetate/hexane (1:1, v/v). After slow evaporation in a refrigerator (−5 °C), the crystal was afforded.

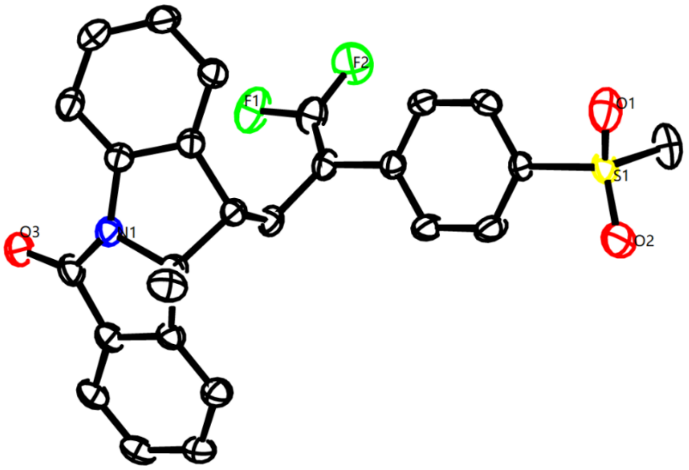


**Figure S115.** Crystal structure of compound **16** with 50% thermal ellipsoids (Solvent molecules, and carbon hydrogenatoms were omitted for clarity.) (CCDC 2256727)

**Crystal data and structure refinement for 16.**

| | |
|---|---|
| Identification code | exp_2833 |
| Empirical formula | $C_{26}H_{21}F_2NO_3S$ |
| Formula weight | 465.50 |
| Temperature/K | 293(10) |
| Crystal system | orthorhombic |
| Space group | $P2_12_12_1$ |
| a/Å | 8.3223(4) |
| b/Å | 14.4055(8) |
| c/Å | 18.9688(14) |
| α/° | 90 |
| β/° | 90 |
| γ/° | 90 |
| Volume/Å$^3$ | 2274.1(2) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.360 |
| μ/mm$^{-1}$ | 1.654 |
| F(000) | 968.0 |
| Crystal size/mm$^3$ | 0.2 × 0.1 × 0.05 |
| Radiation | CuKα (λ = 1.54184) |

| | |
|---|---|
| 2Θ range for data collection/° | 7.706 to 133.184 |
| Index ranges | $-9 \leq h \leq 9$, $-17 \leq k \leq 17$, $-22 \leq l \leq 22$ |
| Reflections collected | 29182 |
| Independent reflections | 4020 [$R_{int}$ = 0.0618, $R_{sigma}$ = 0.0405] |
| Data/restraints/parameters | 4020/0/300 |
| Goodness-of-fit on $F^2$ | 0.944 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0350, $wR_2$ = 0.0754 |
| Final R indexes [all data] | $R_1$ = 0.0449, $wR_2$ = 0.0786 |
| Largest diff. peak/hole / e $Å^{-3}$ | 0.11/-0.19 |
| Flack parameter | 0.008(12) |

# 8. References

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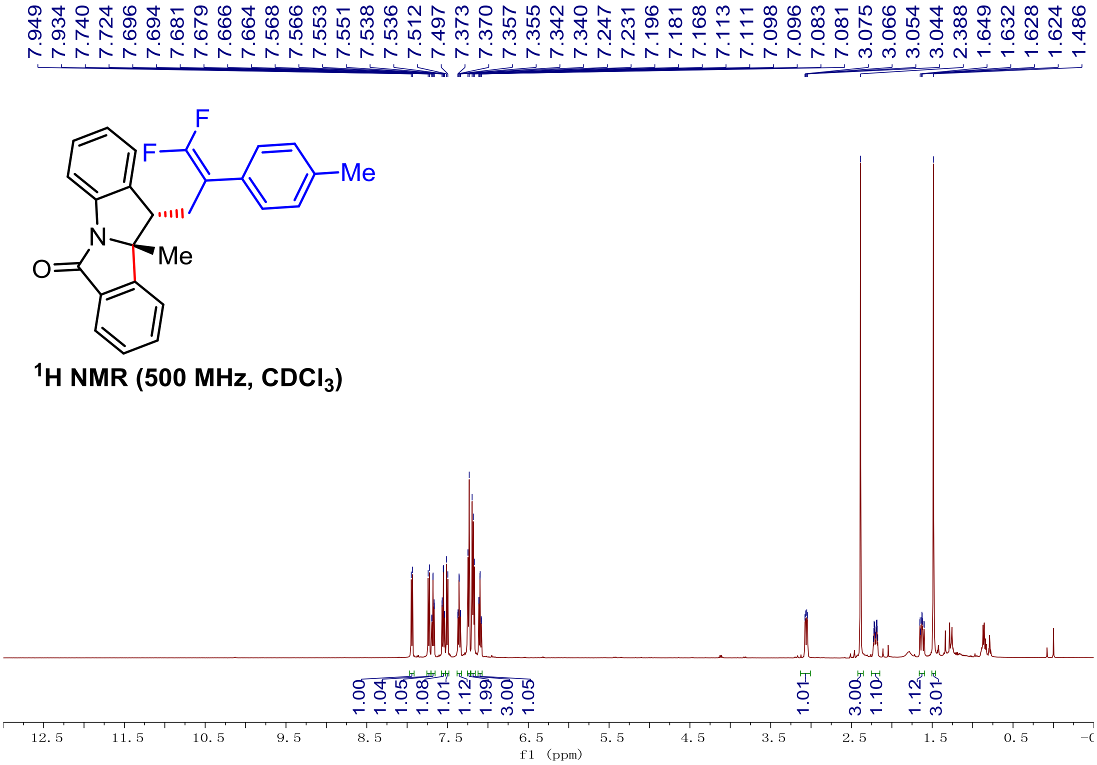
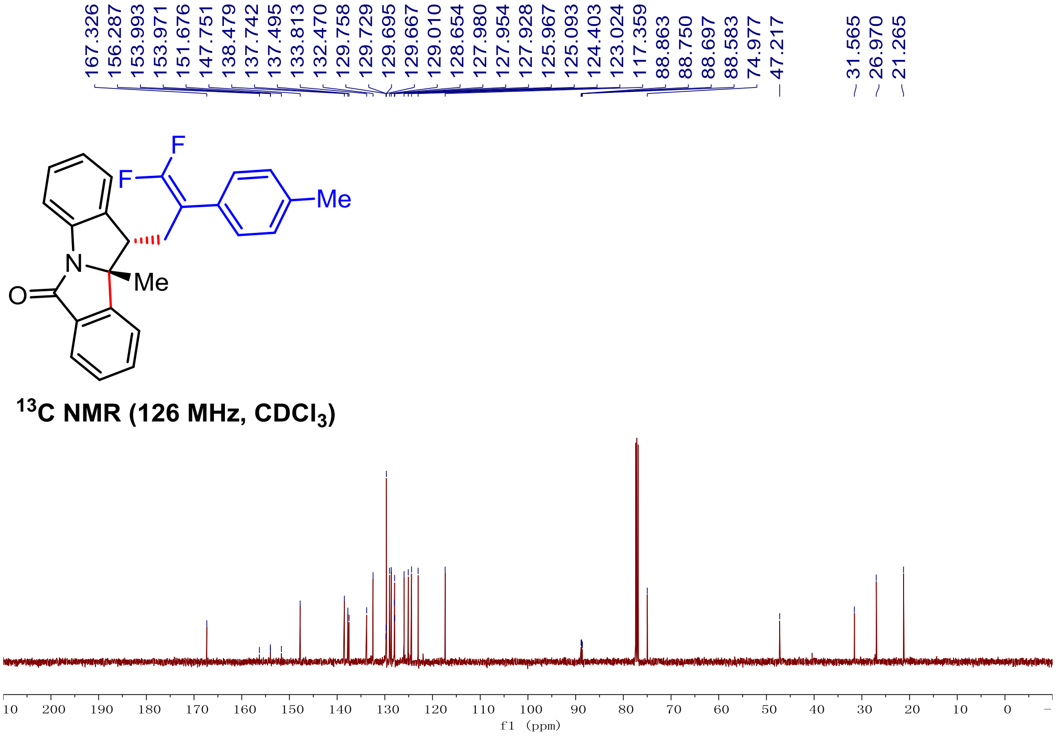
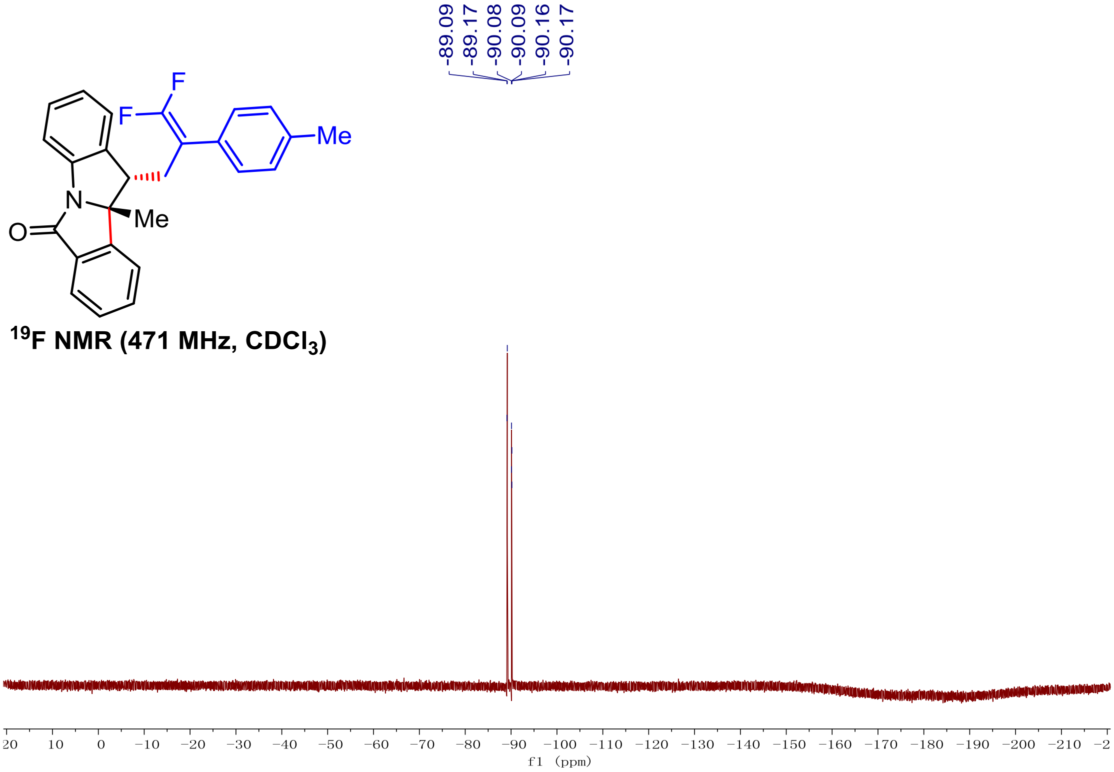
# 9. NMR Spectra

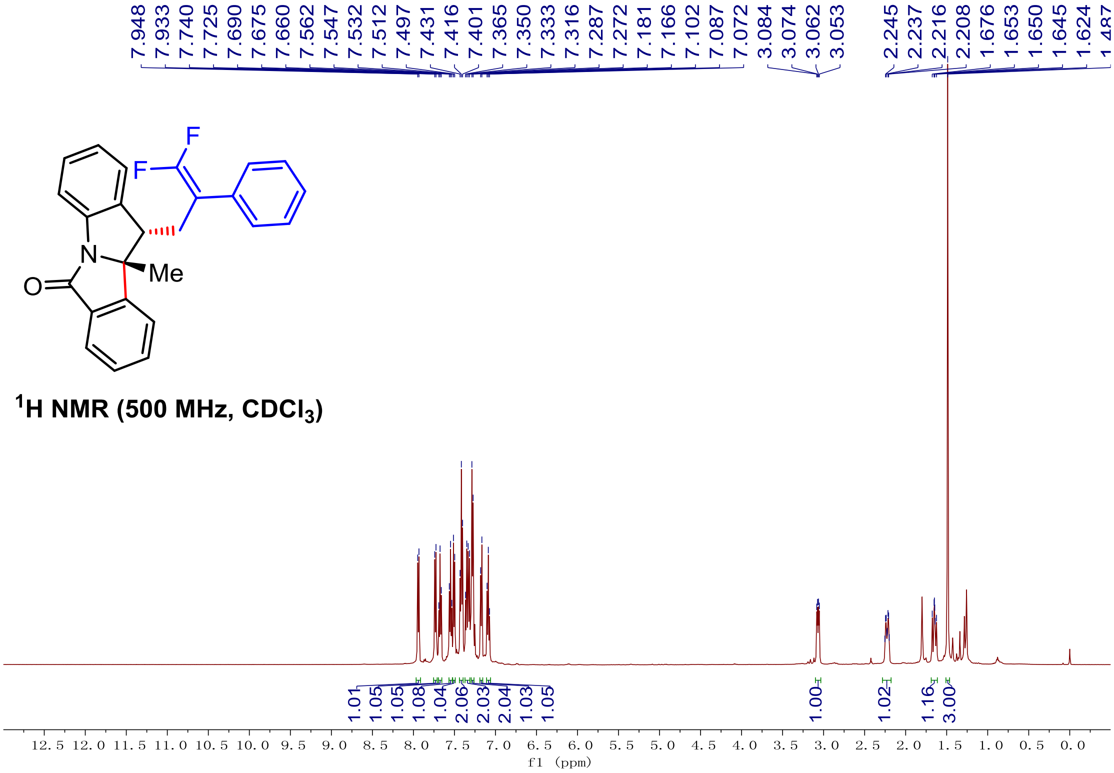
## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 3

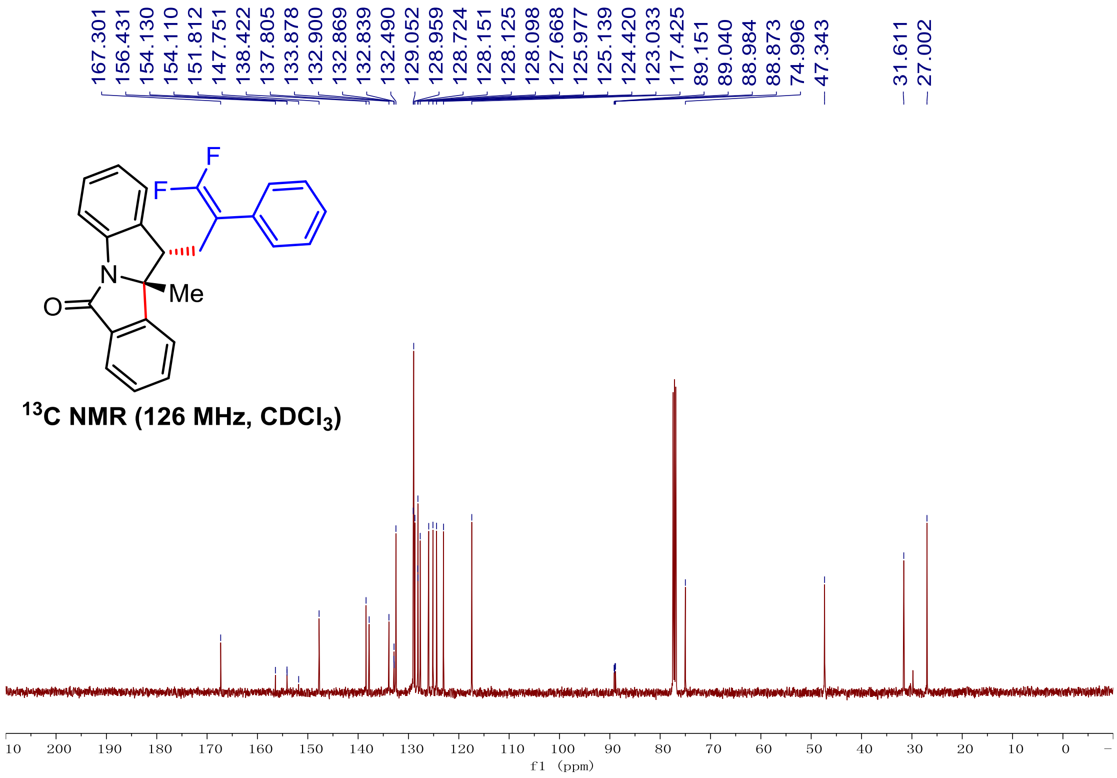




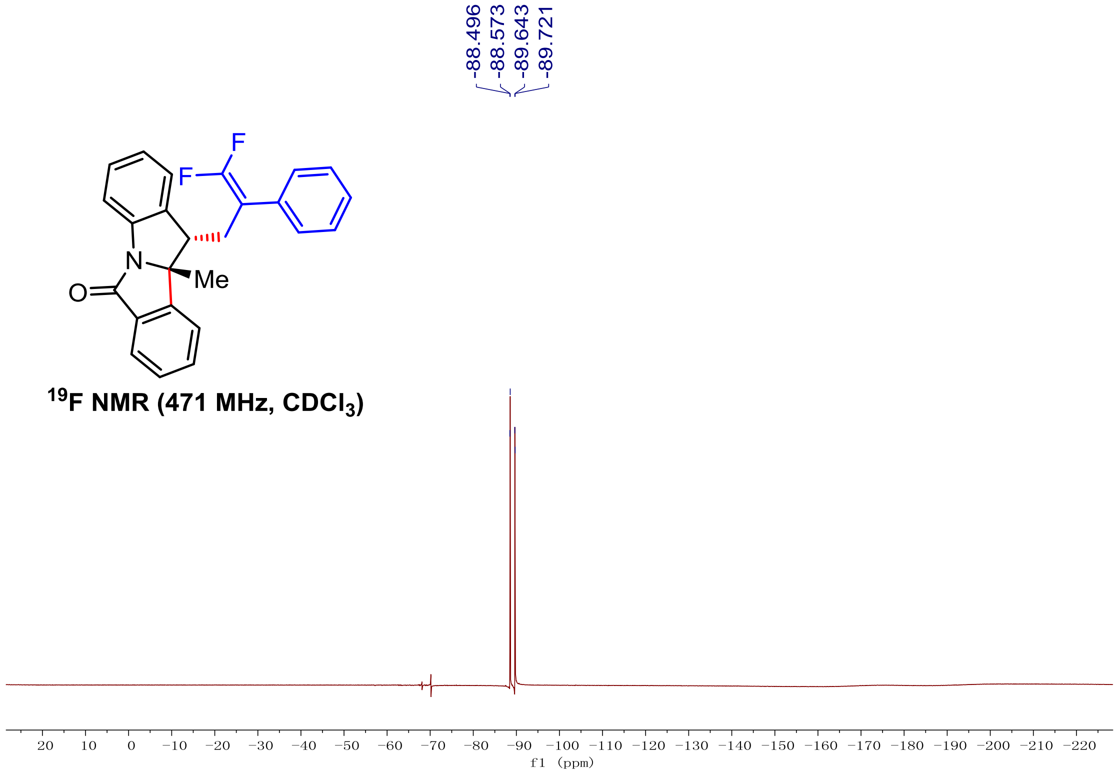


## (10b*R*,11*S*)-11-(3,3-Difluoro-2-phenylallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 4



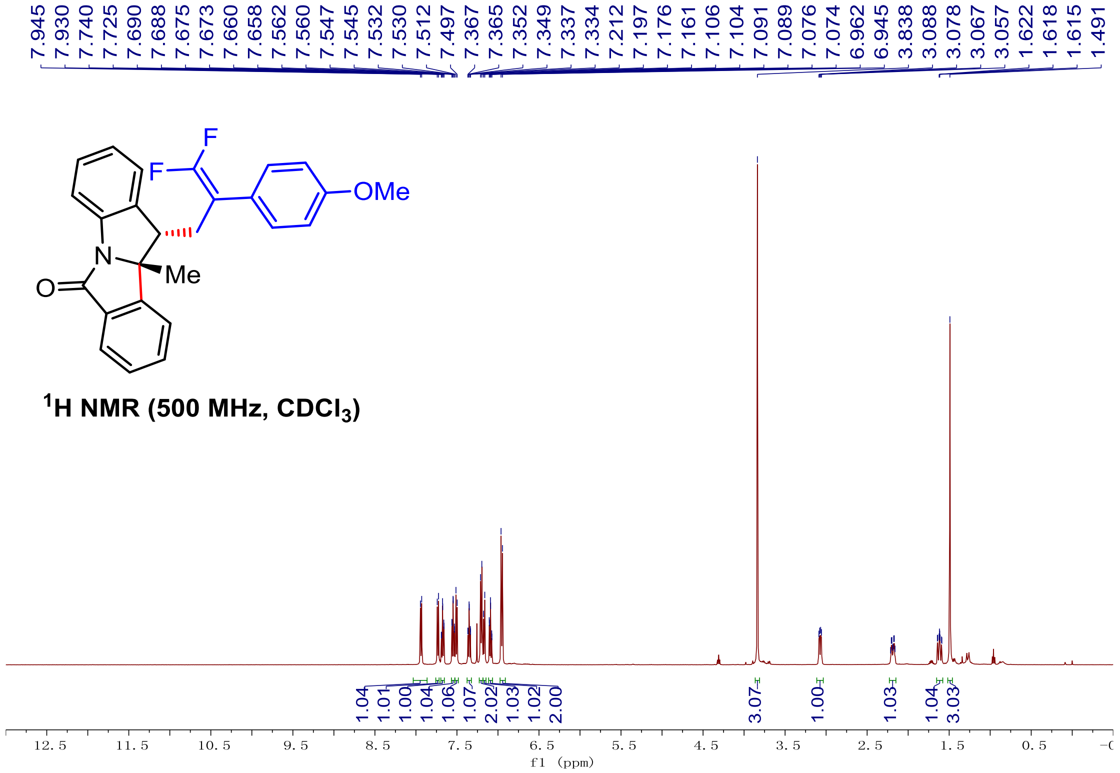


$^{13}$C NMR (126 MHz, CDCl$_3$)

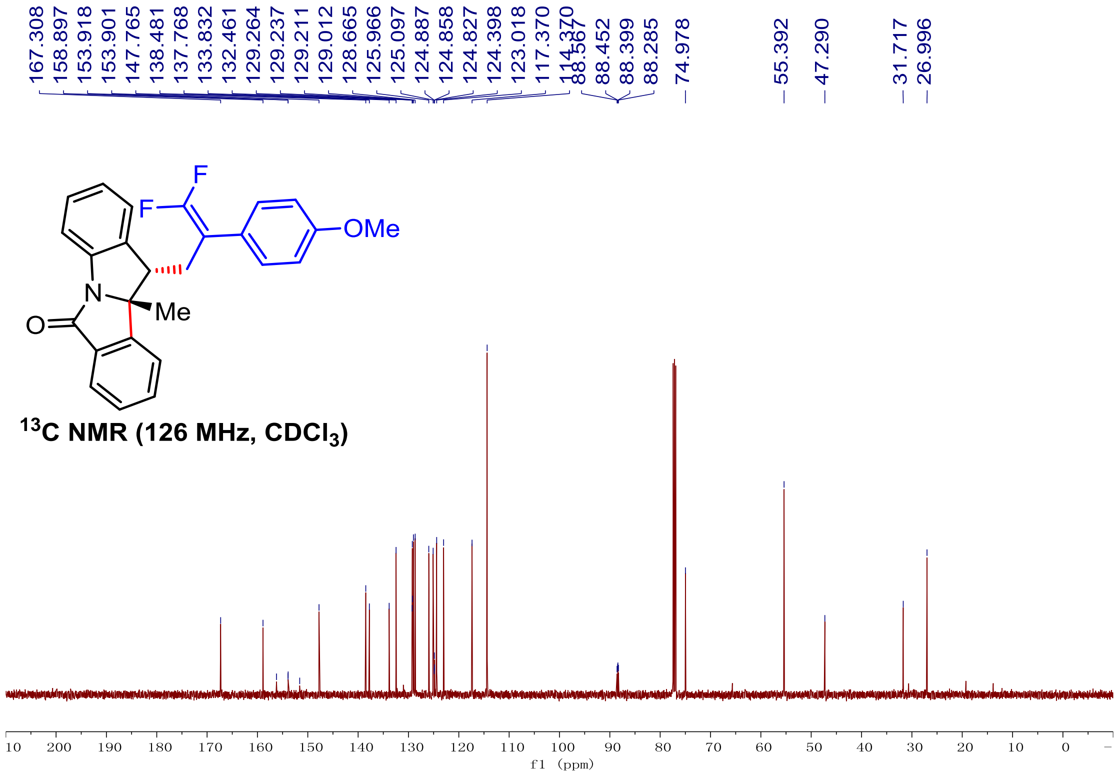


$^{19}$F NMR (471 MHz, CDCl$_3$)

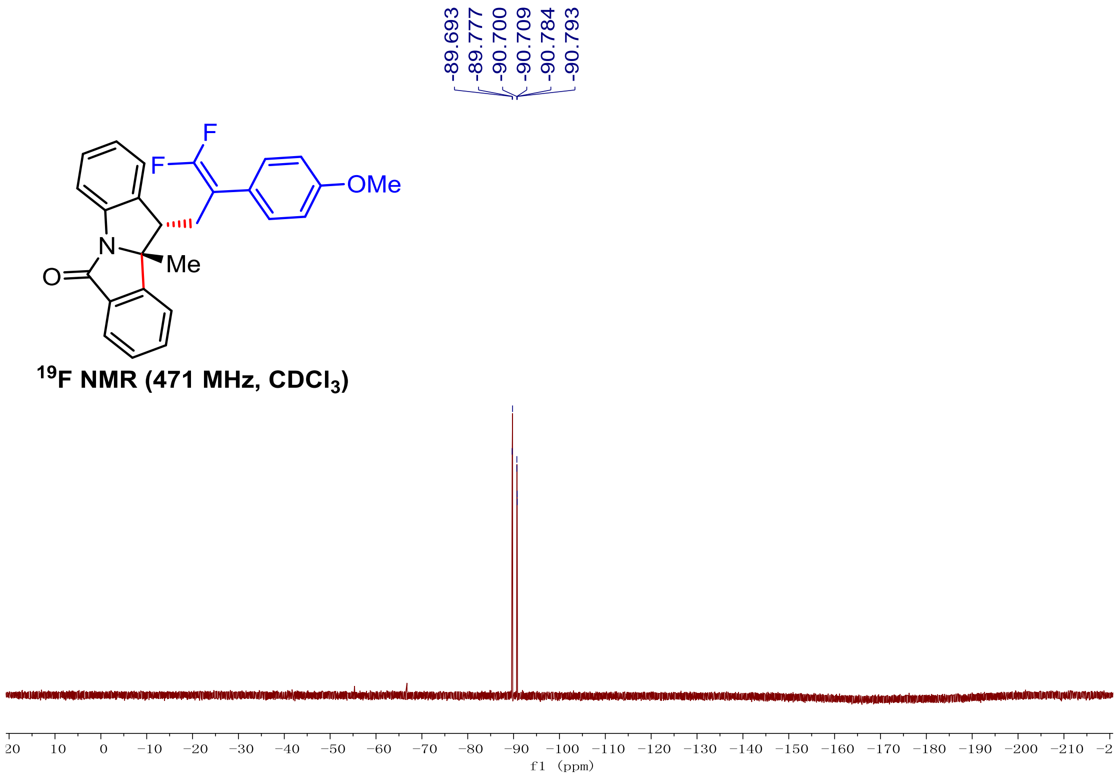
## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-methoxyphenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 5



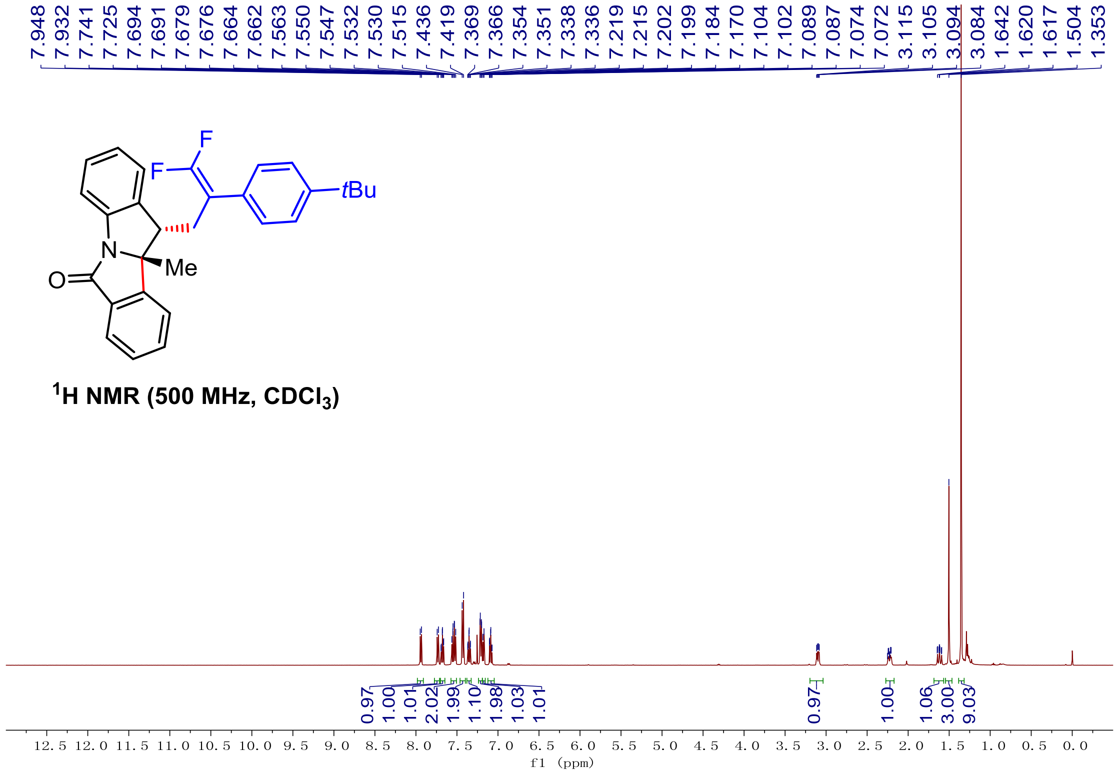
$^1$H NMR (500 MHz, CDCl$_3$)

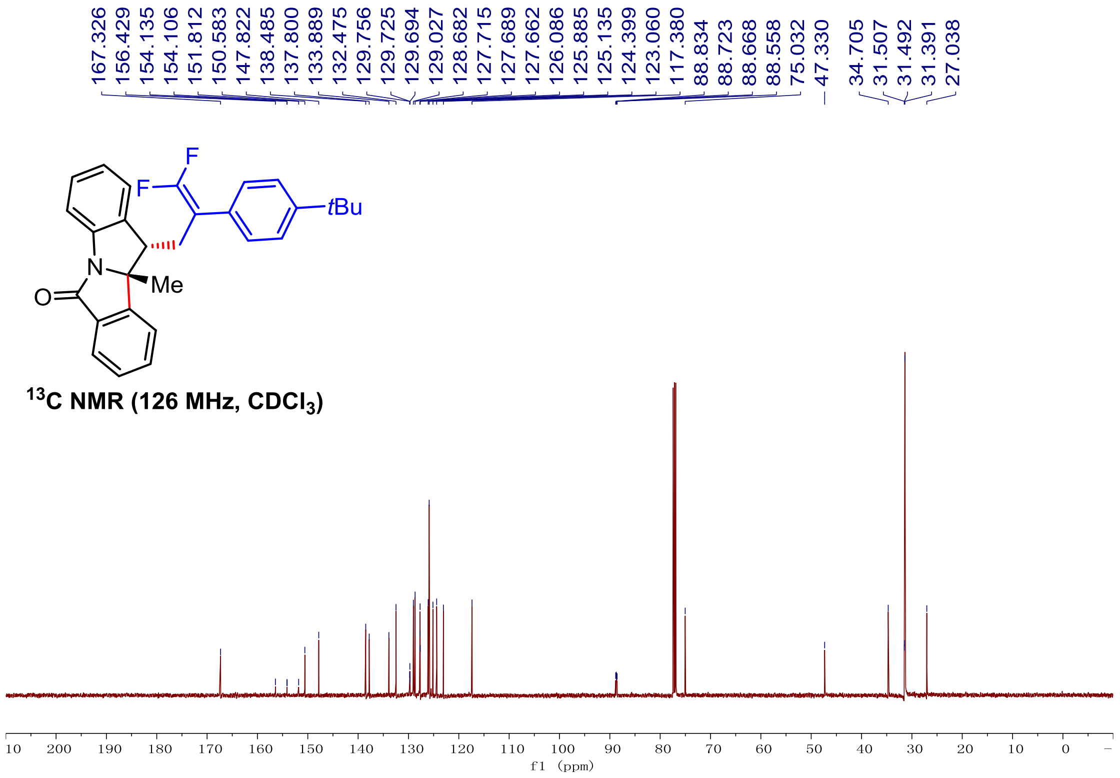


$^{13}$C NMR (126 MHz, CDCl$_3$)

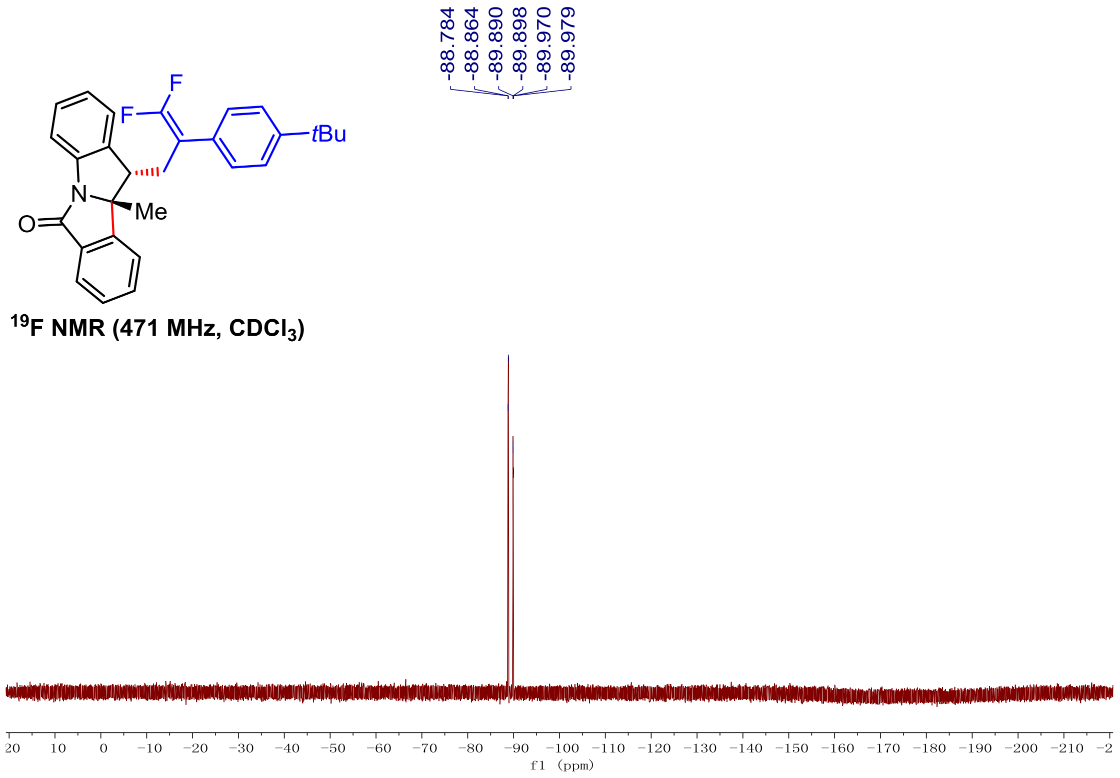


## (10b*R*,11*S*)-11-(2-(4-(*tert*-Butyl)phenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 6



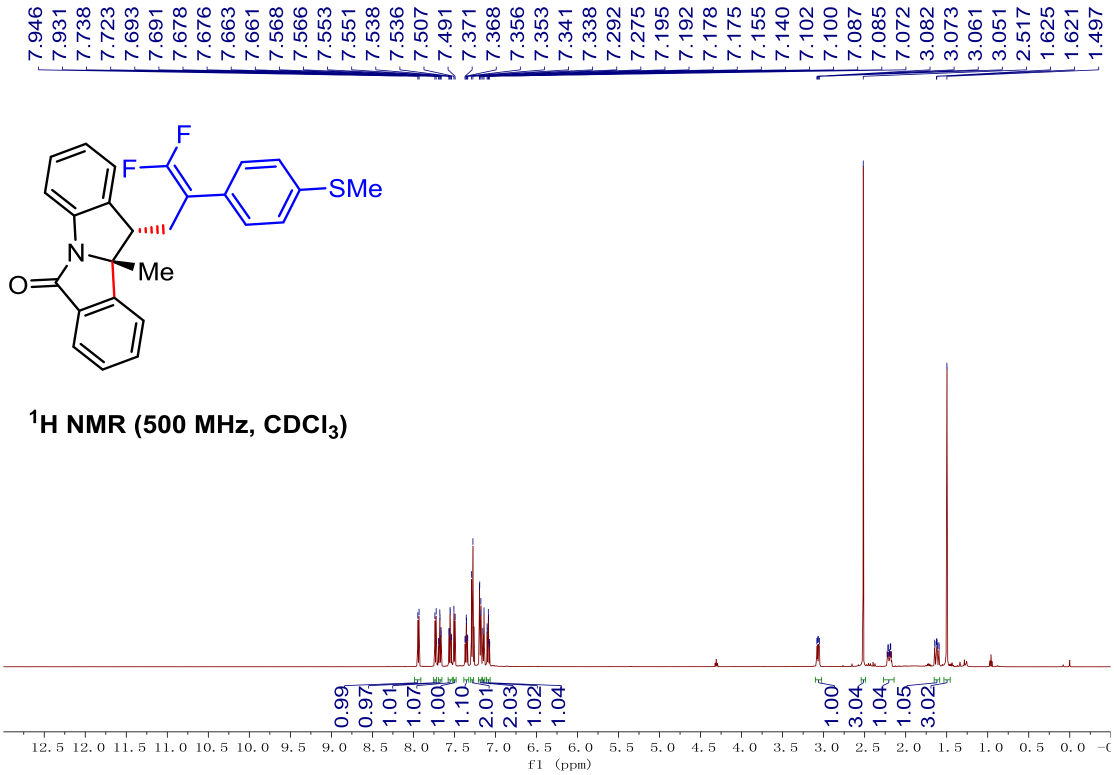


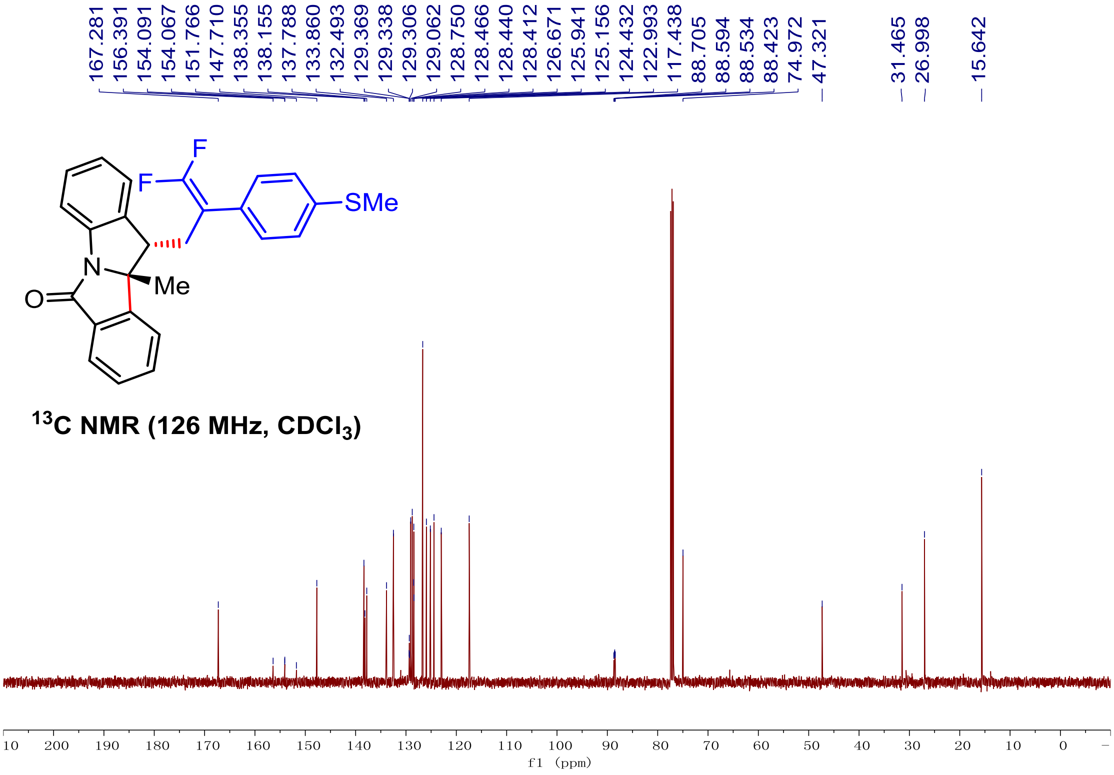
$^{13}$C NMR (126 MHz, CDCl$_3$)

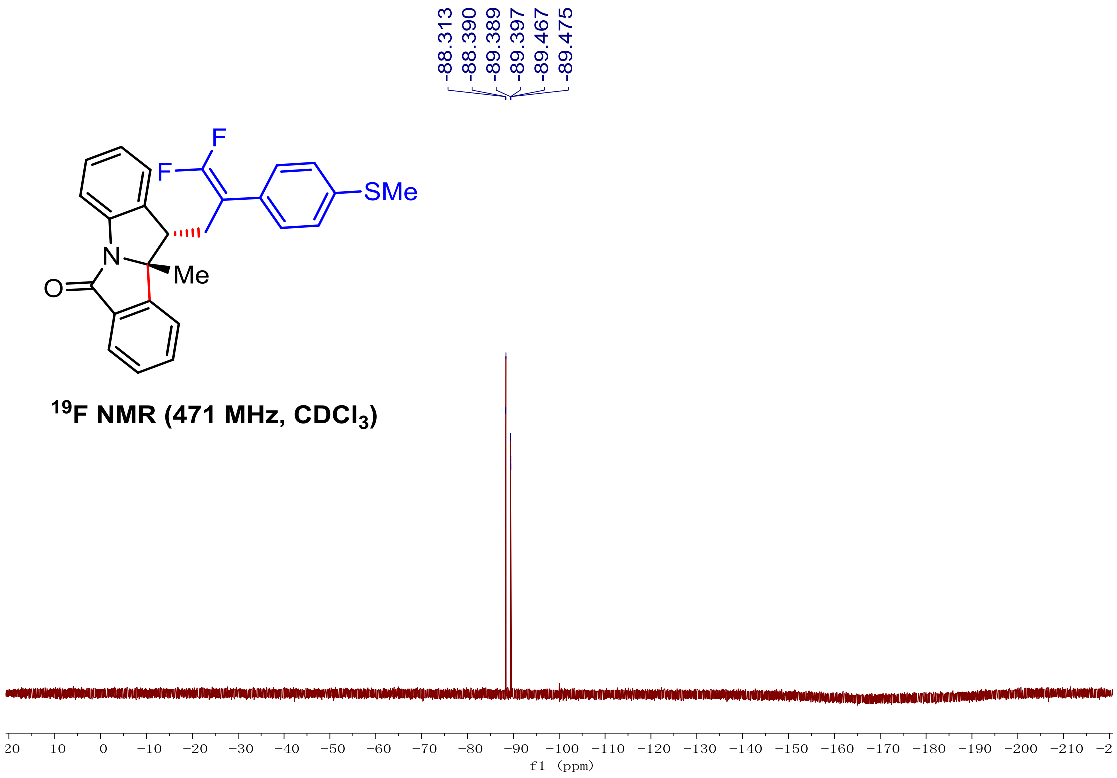


$^{19}$F NMR (471 MHz, CDCl$_3$)

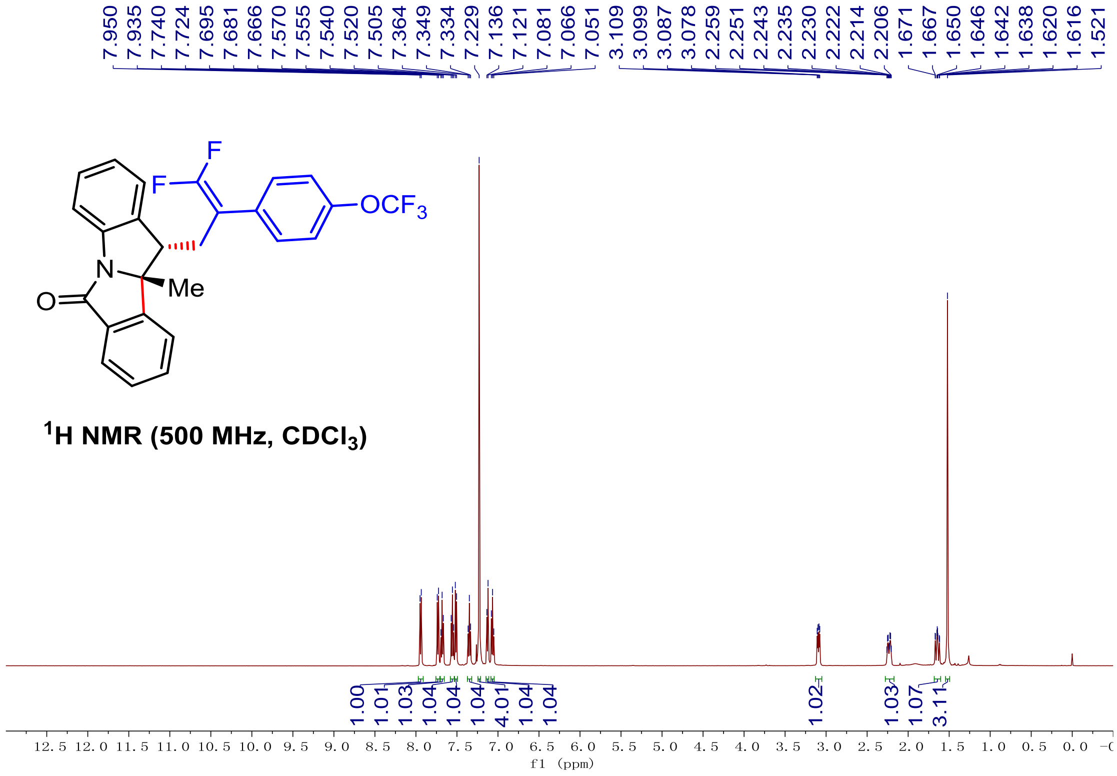
## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-(methylthio)phenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 7

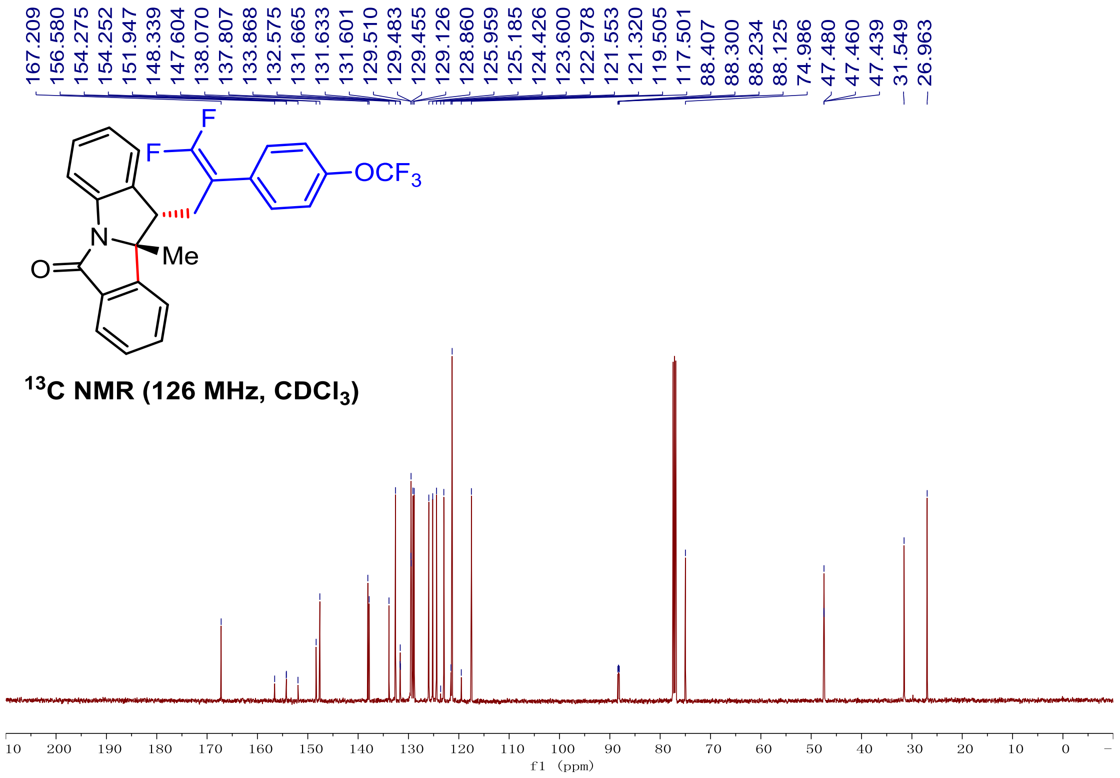




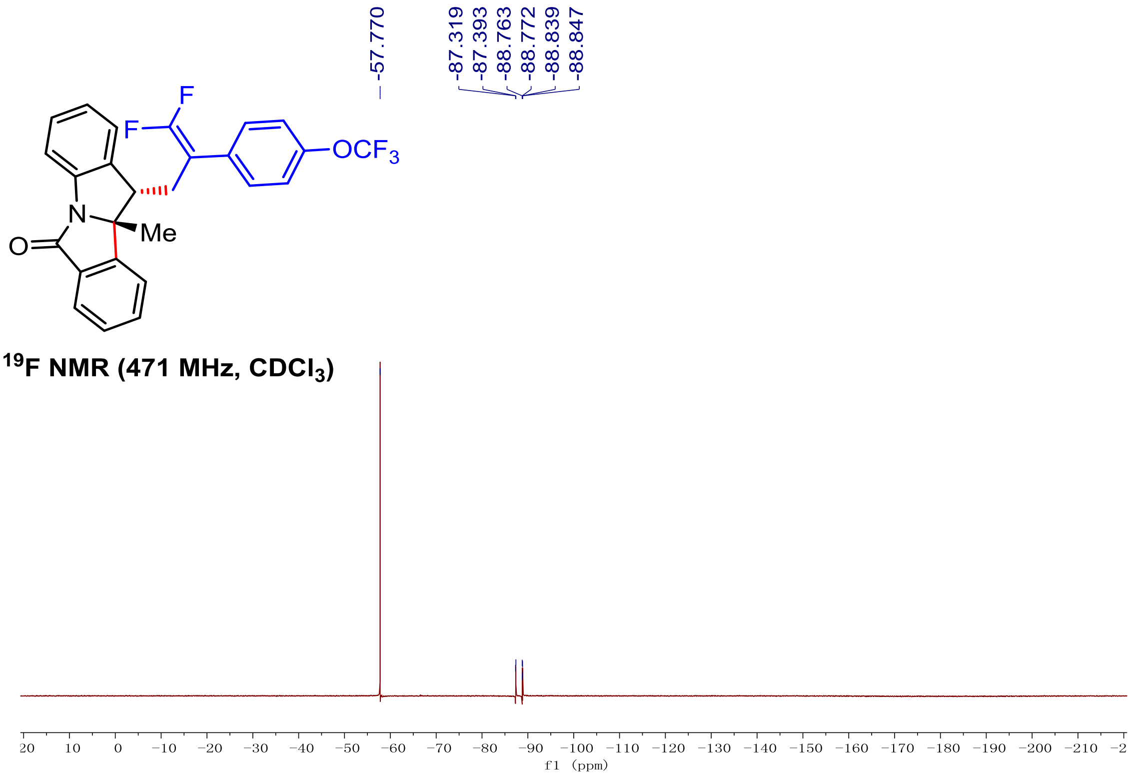


### (10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-(trifluoromethoxy)phenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 8



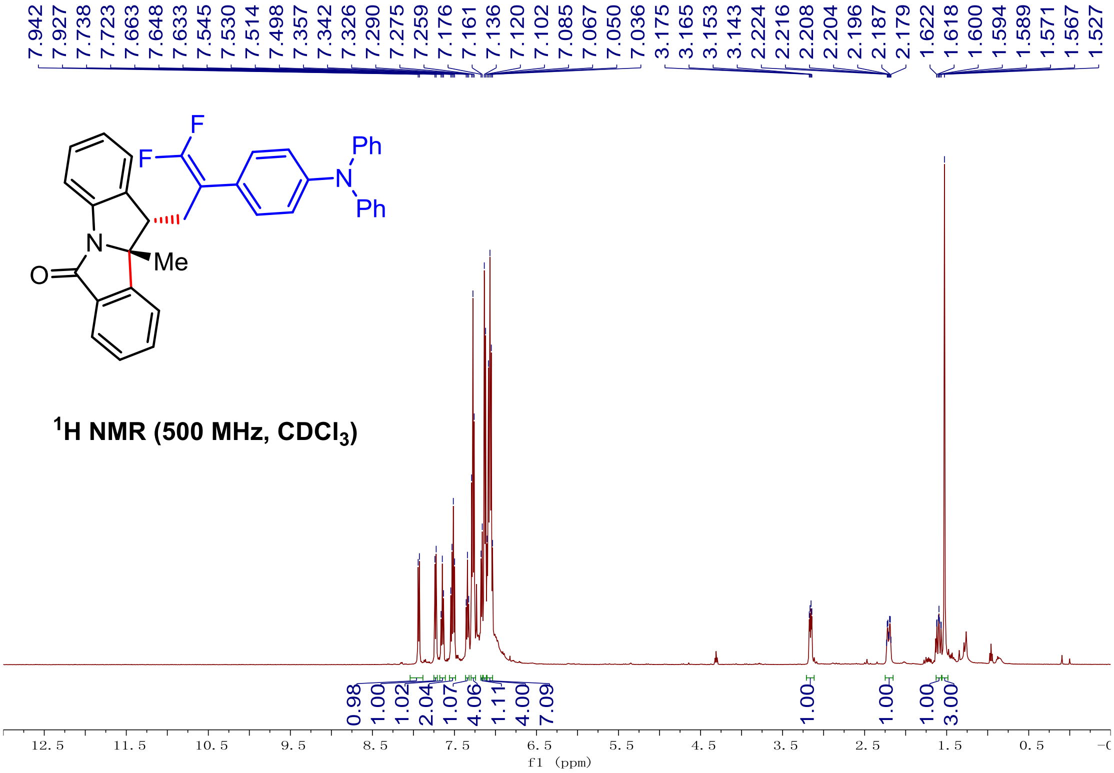


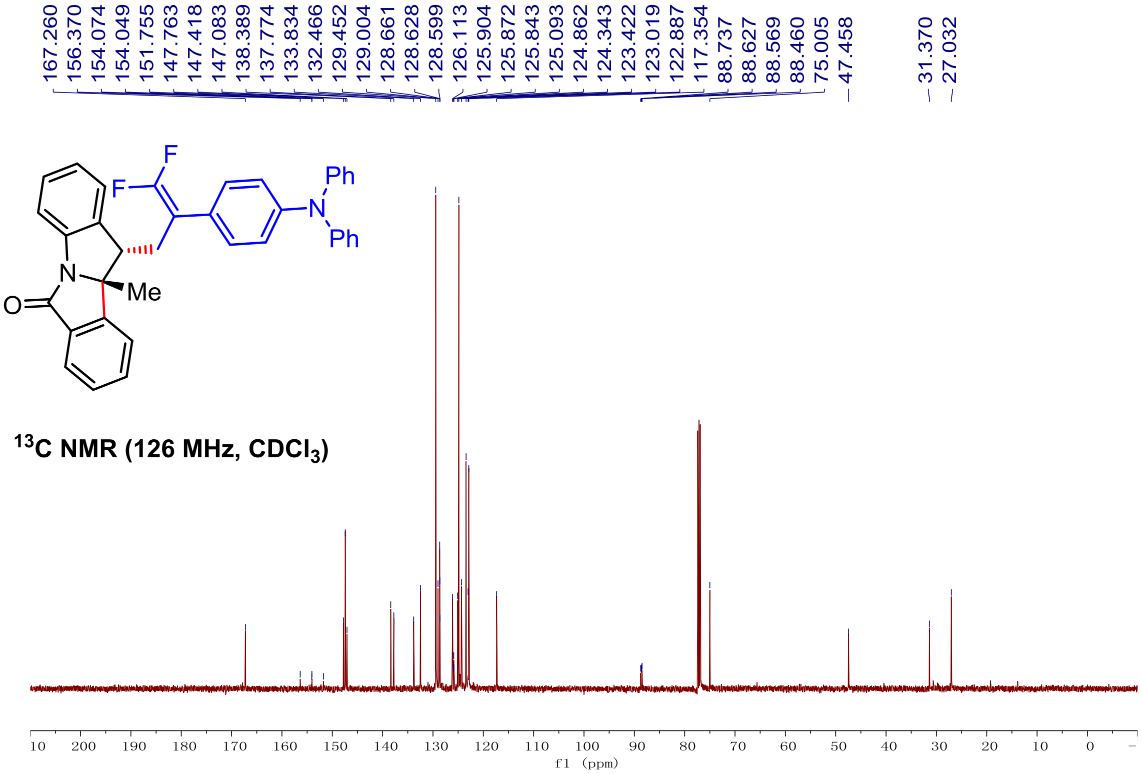
**$^{13}$C NMR (126 MHz, CDCl$_3$)**

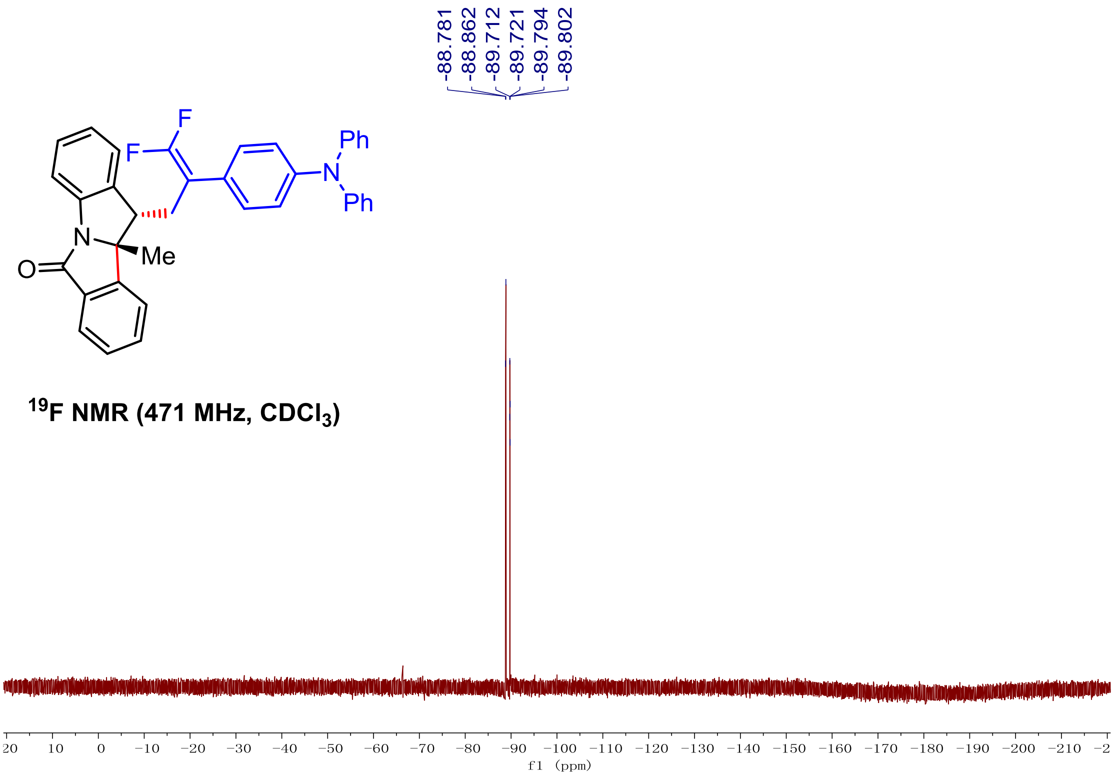


**$^{19}$F NMR (471 MHz, CDCl$_3$)**

## (10b*R*,11*R*)-11-(2-(4-(Diphenylamino)phenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 9

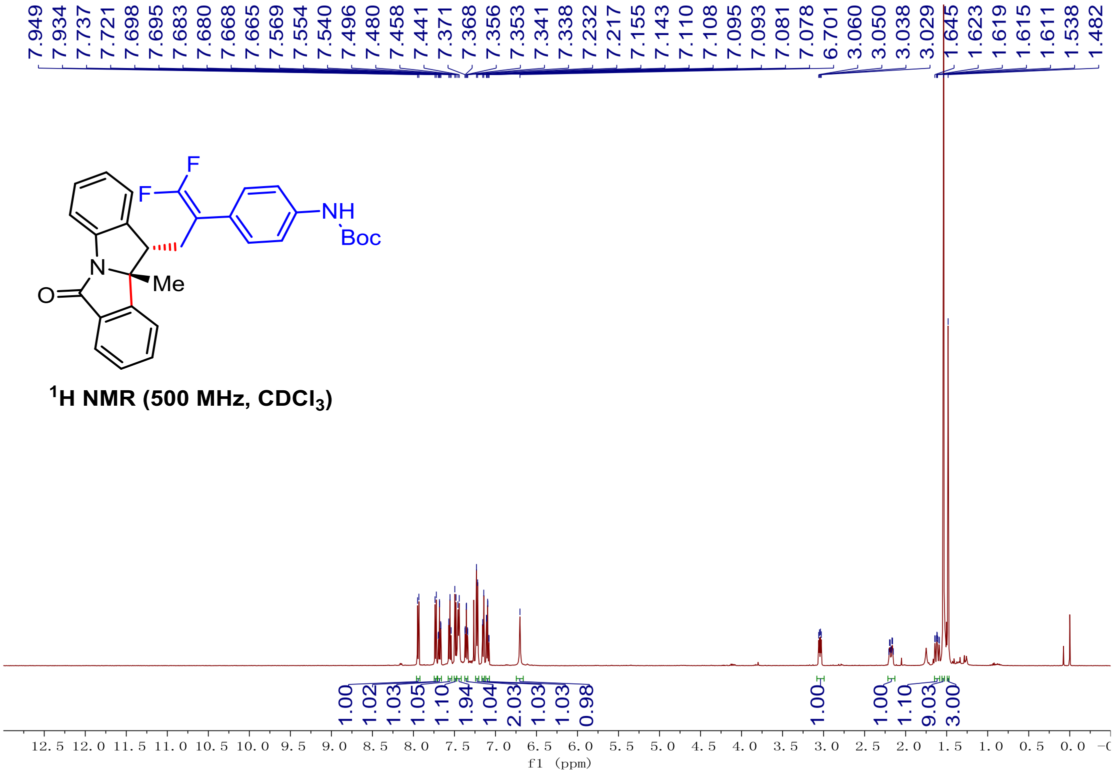




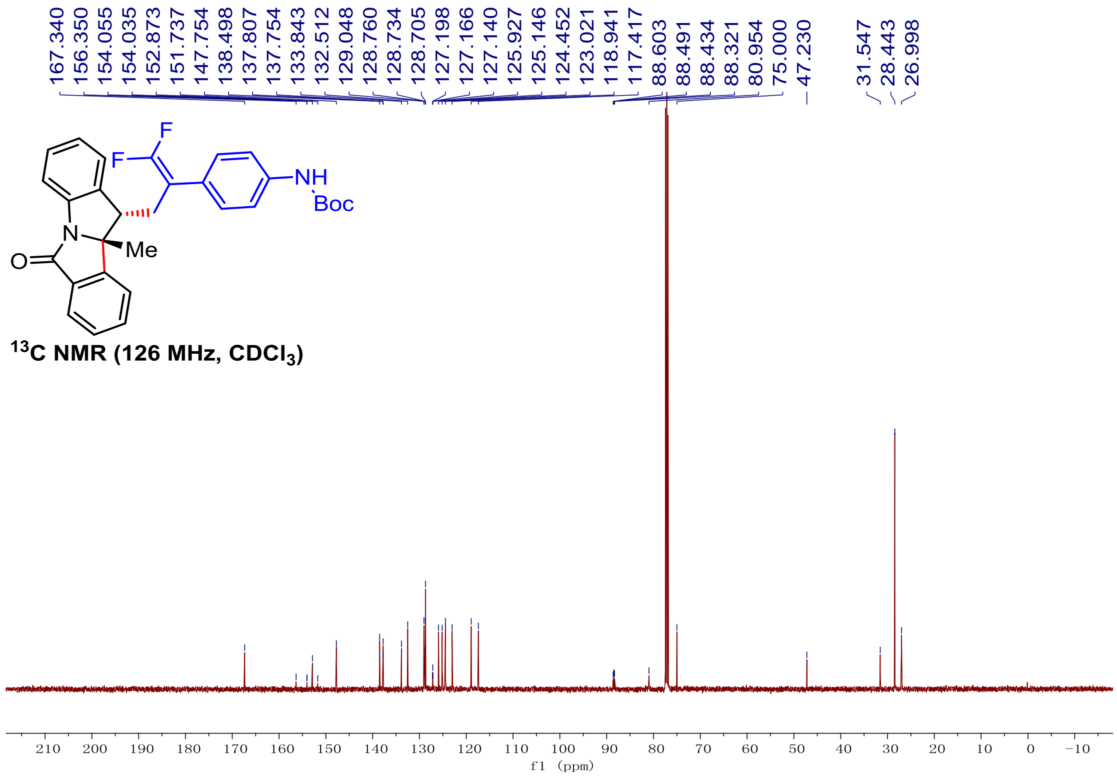


**$^{19}$F NMR (471 MHz, CDCl$_3$)**

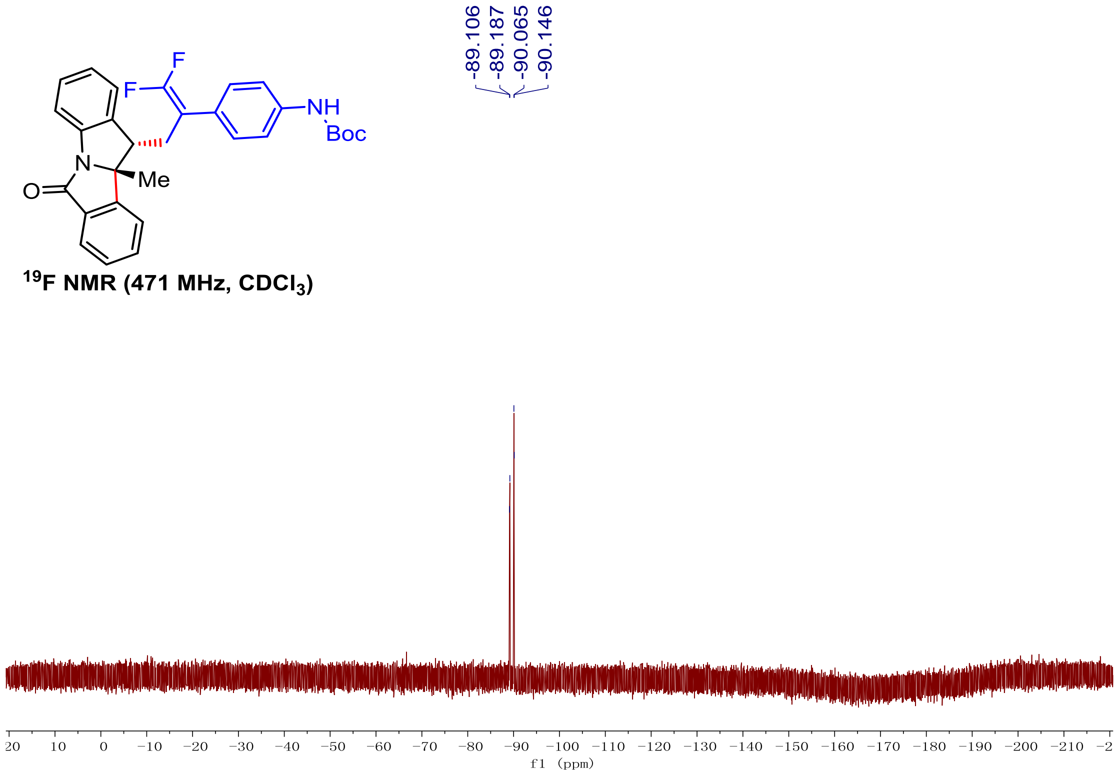
### ***tert*-Butyl (4-(1,1-difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl)carbamate, 10**



**$^1$H NMR (500 MHz, CDCl$_3$)**

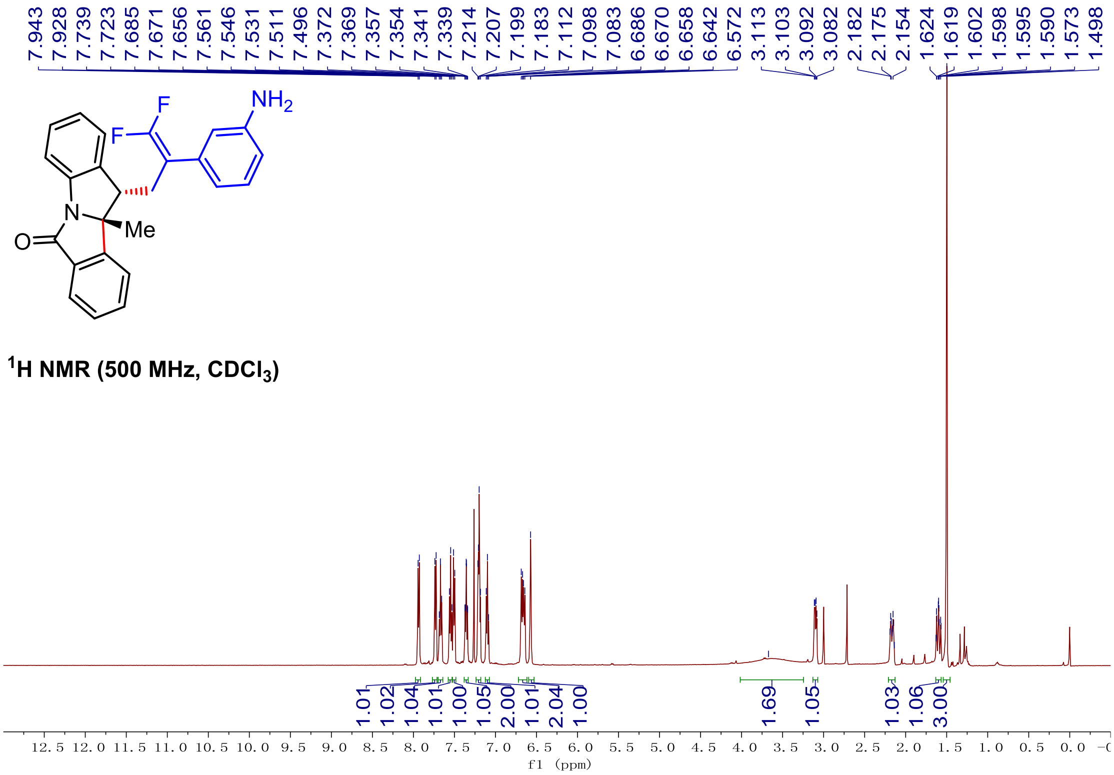


$^{13}$C NMR (126 MHz, CDCl$_3$)

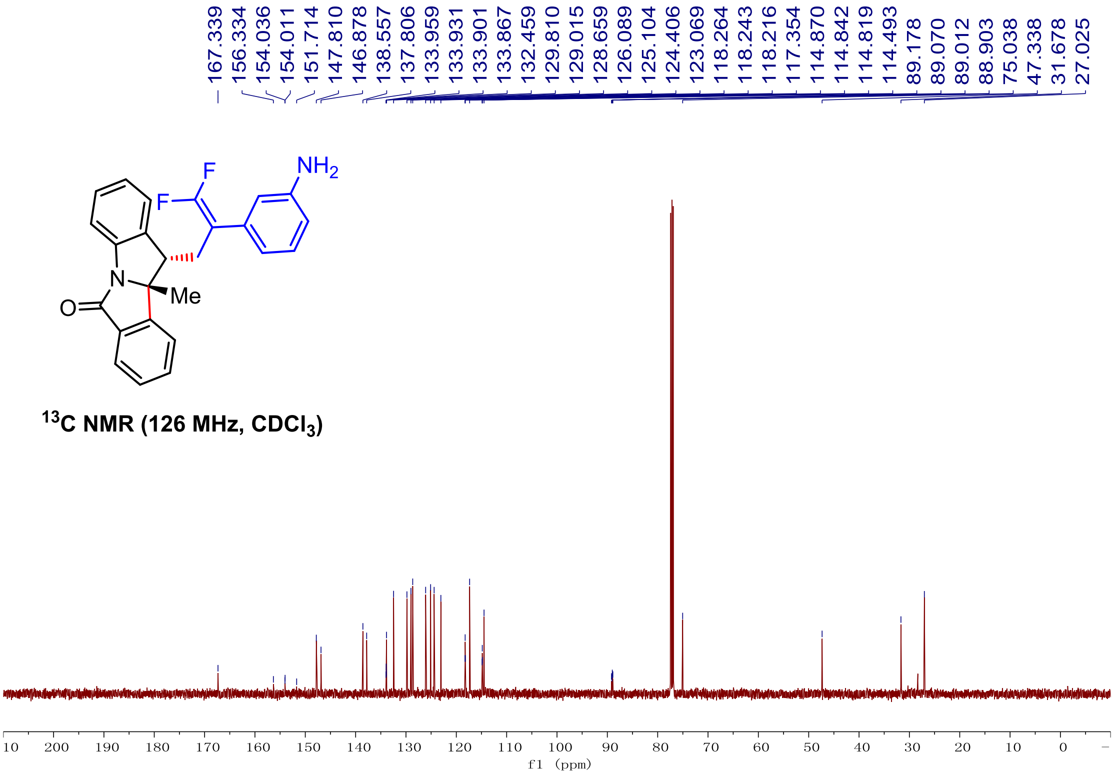


$^{19}$F NMR (471 MHz, CDCl$_3$)

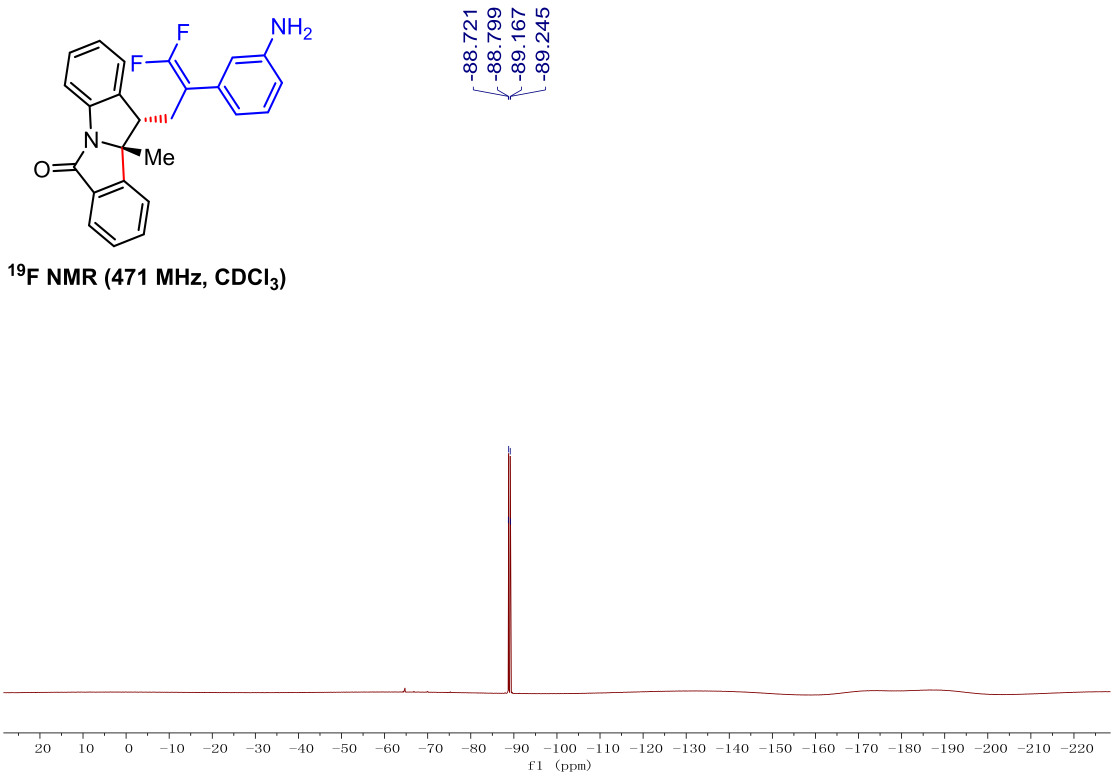
## (10b*R*,11*S*)-11-(2-(3-Aminophenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 11



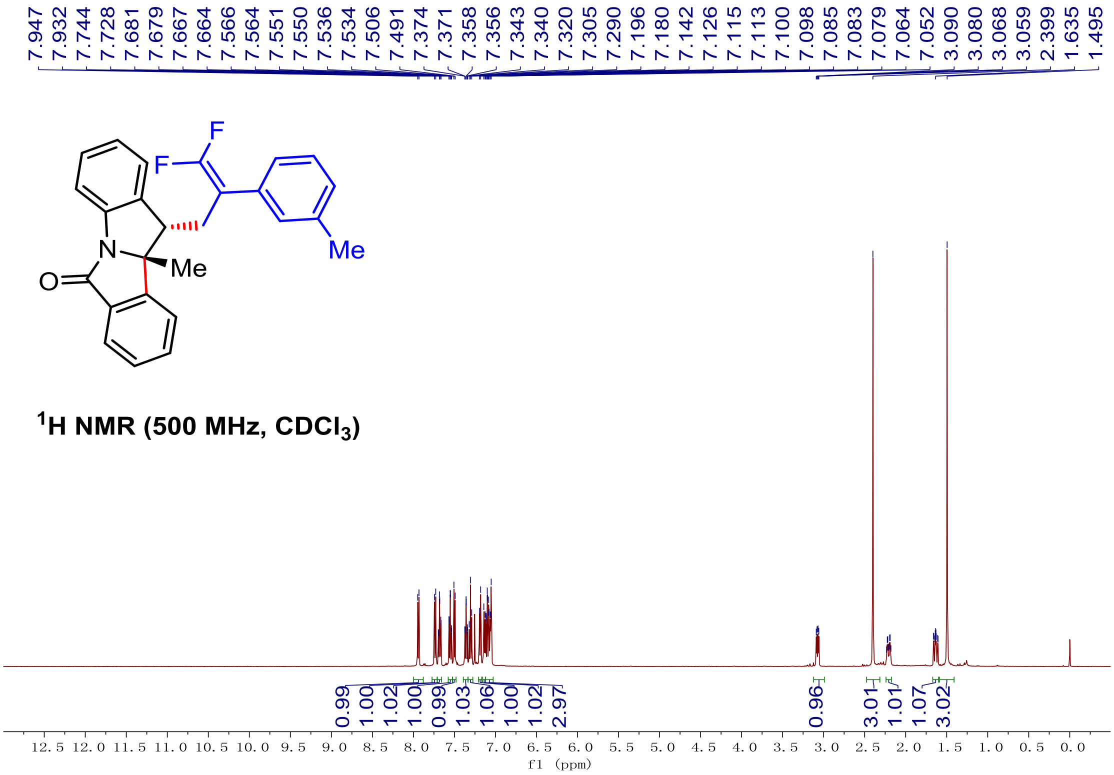
**$^1$H NMR (500 MHz, CDCl$_3$)**

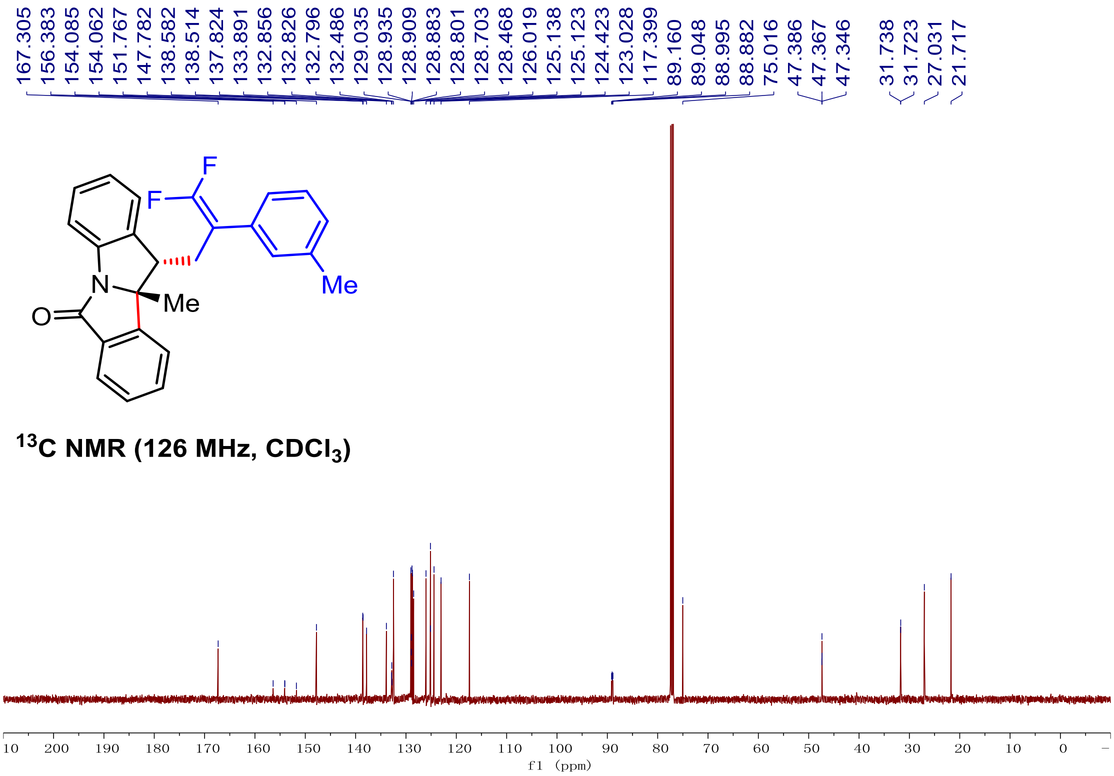


**$^{13}$C NMR (126 MHz, CDCl$_3$)**

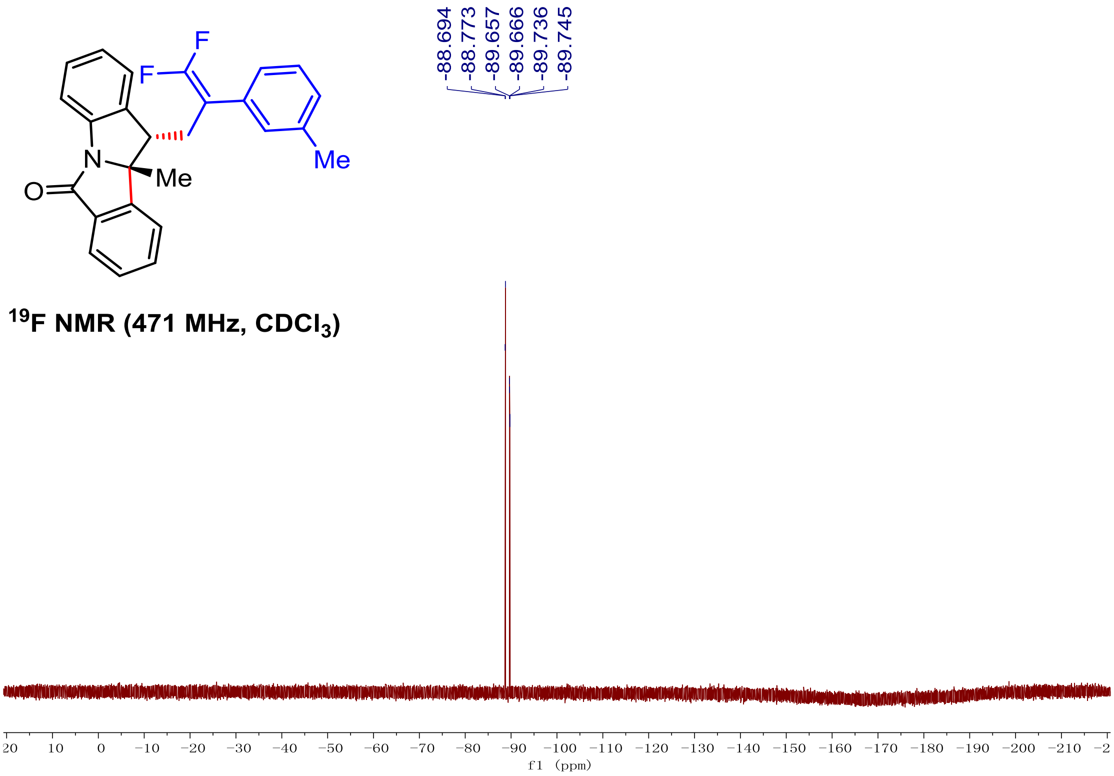


## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*m*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 12



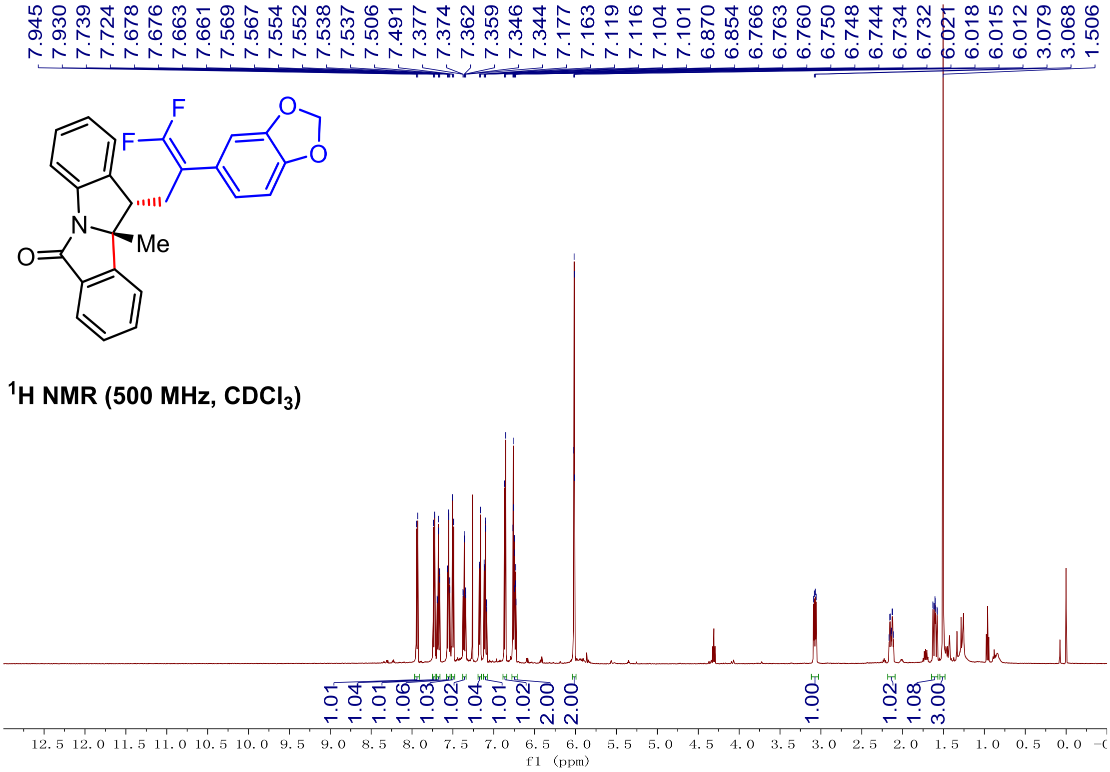


$^{13}C$ NMR (126 MHz, $CDCl_3$)

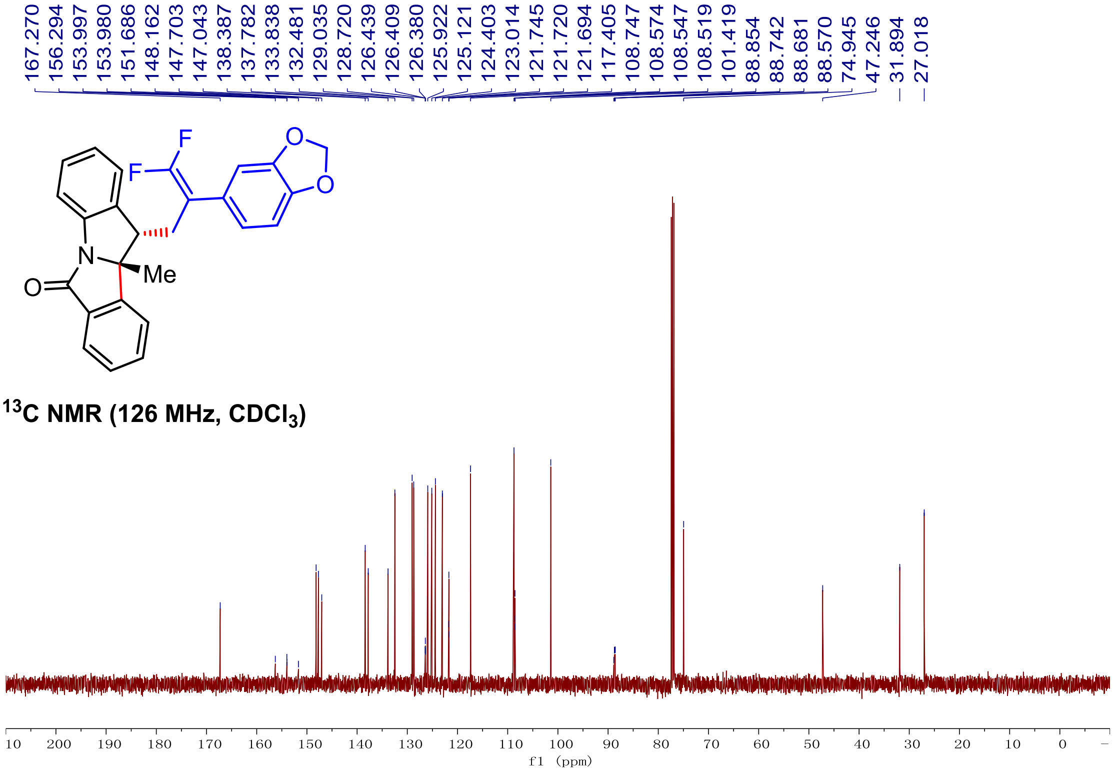


$^{19}F$ NMR (471 MHz, $CDCl_3$)

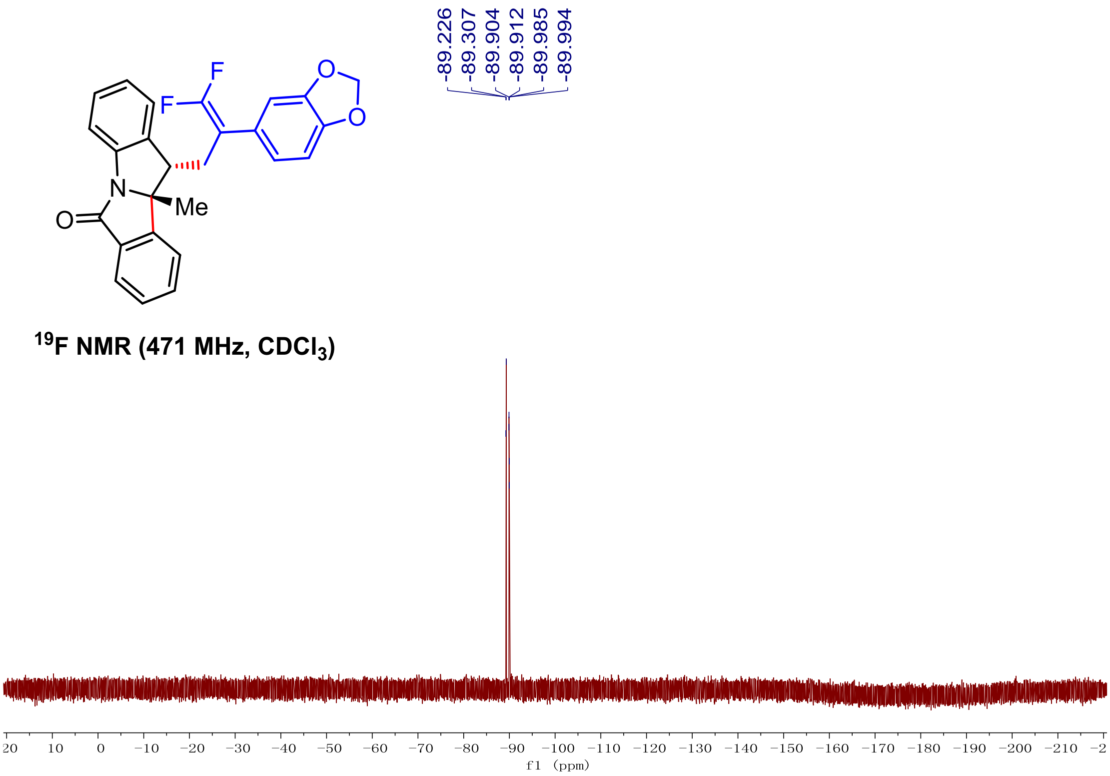
### (10b*R*,11*S*)-11-(2-(Benzo[*d*][1,3]dioxol-5-yl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 13



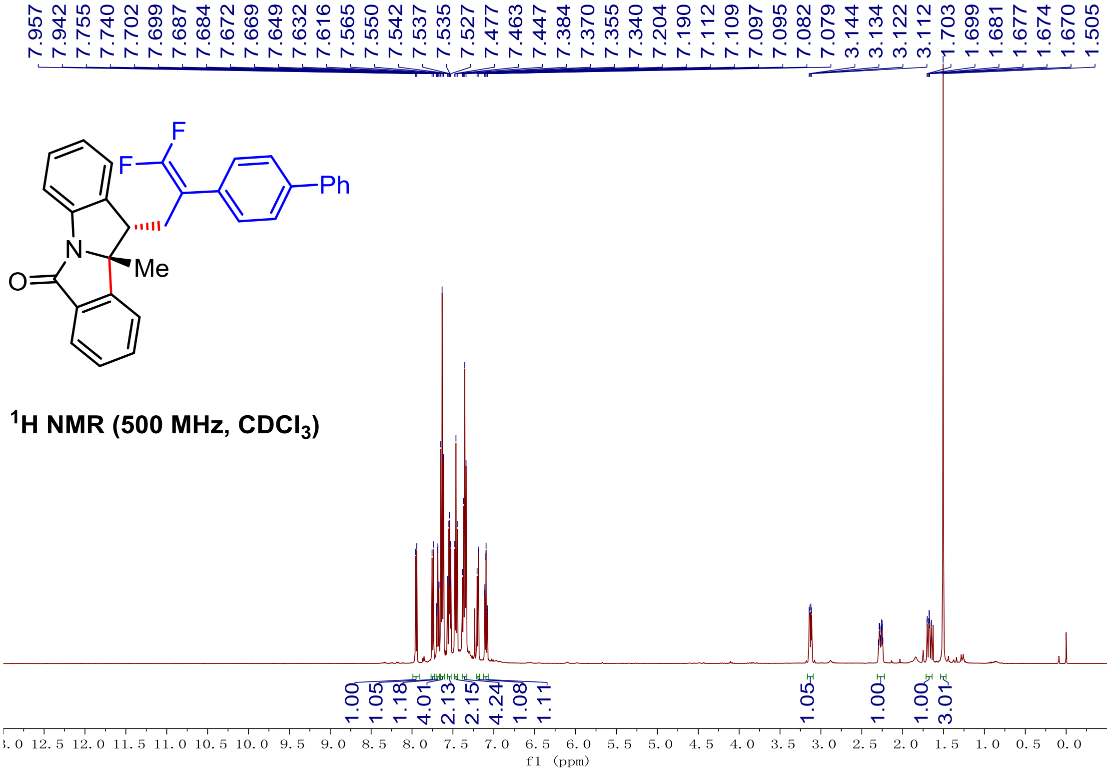
$^1$H NMR (500 MHz, CDCl$_3$)

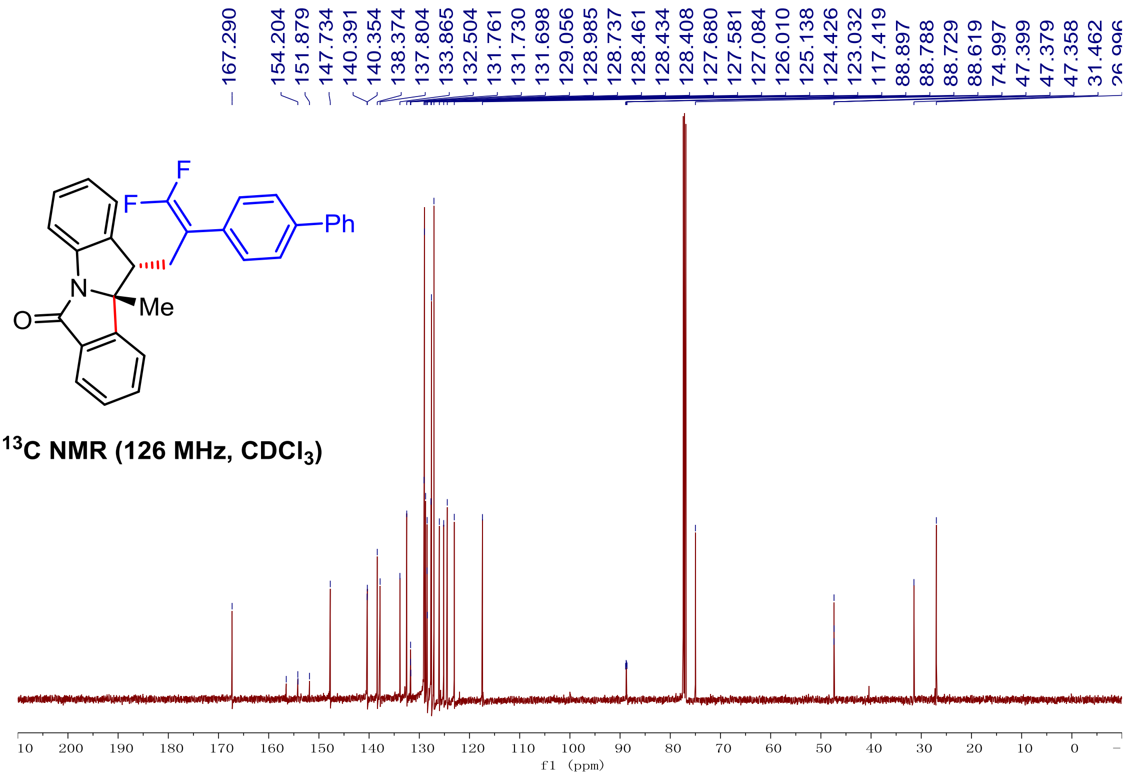


$^{13}$C NMR (126 MHz, CDCl$_3$)

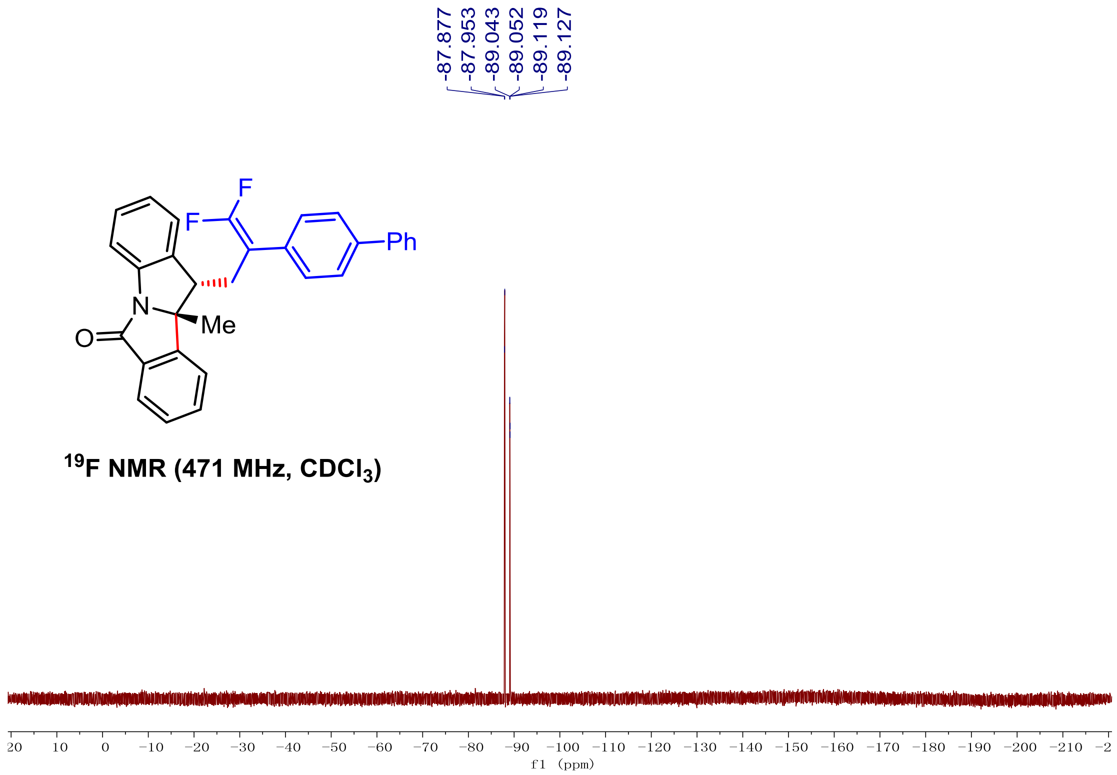


## (10b*R*,11*S*)-11-(2-([1,1'-Biphenyl]-4-yl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 14



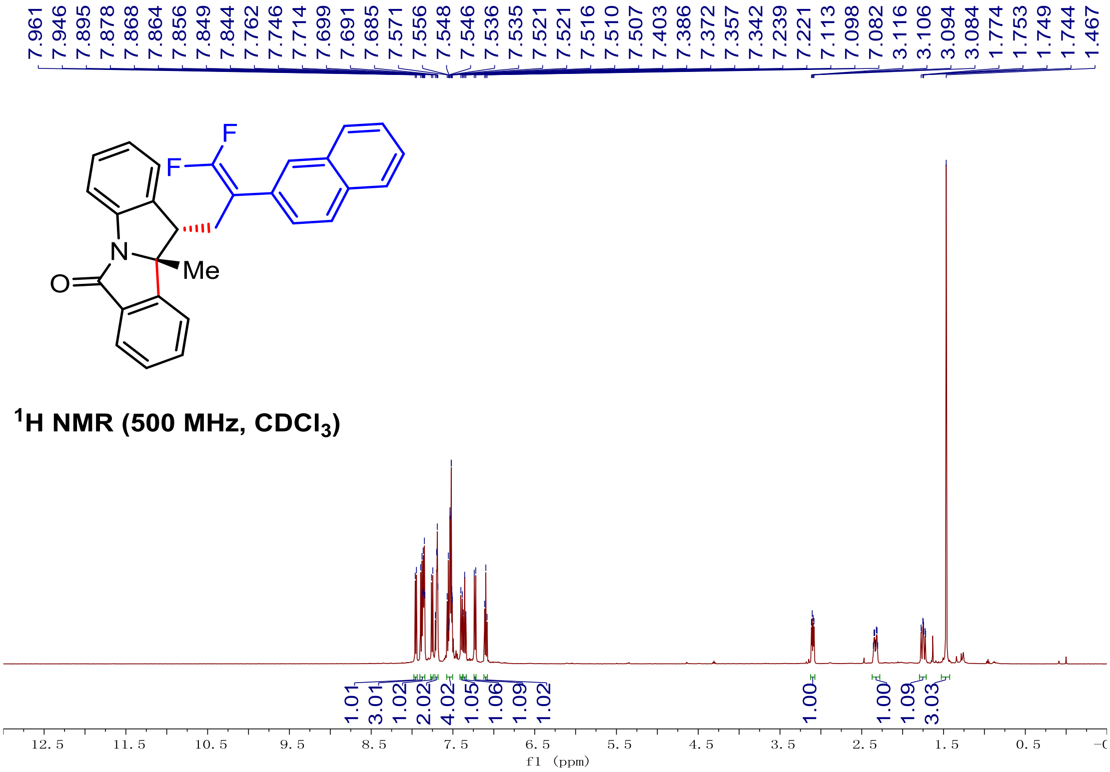


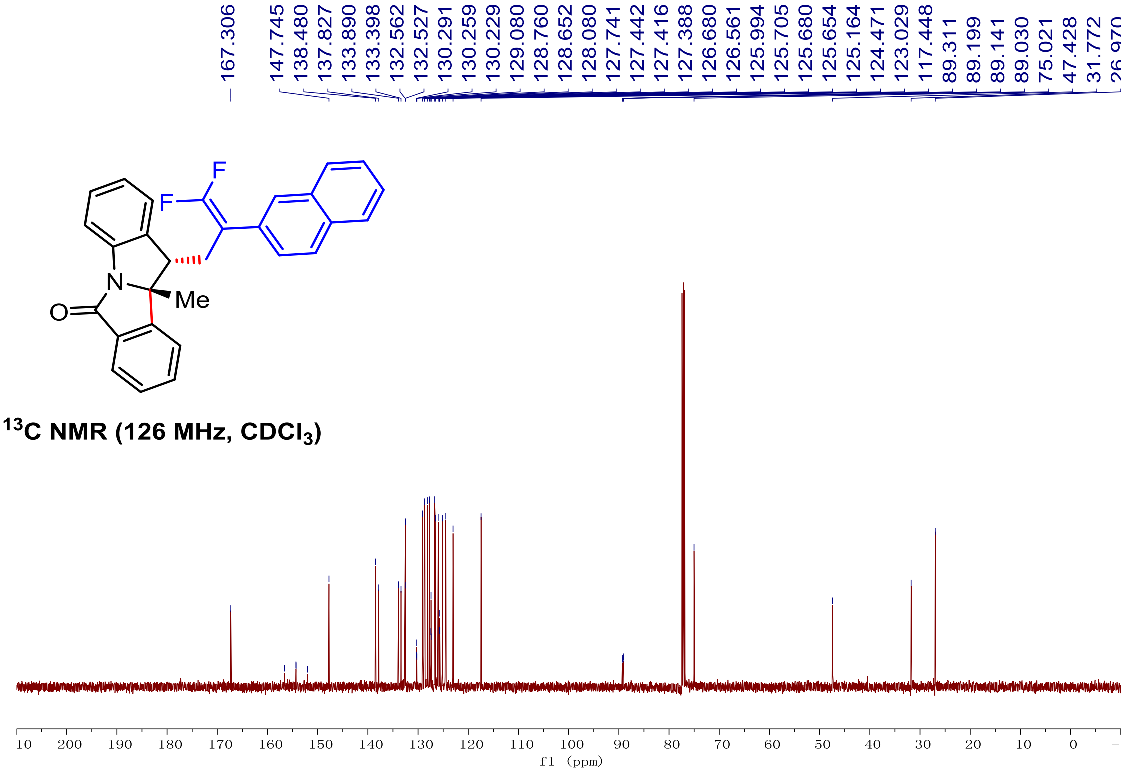
$^{13}$C NMR (126 MHz, CDCl$_3$)

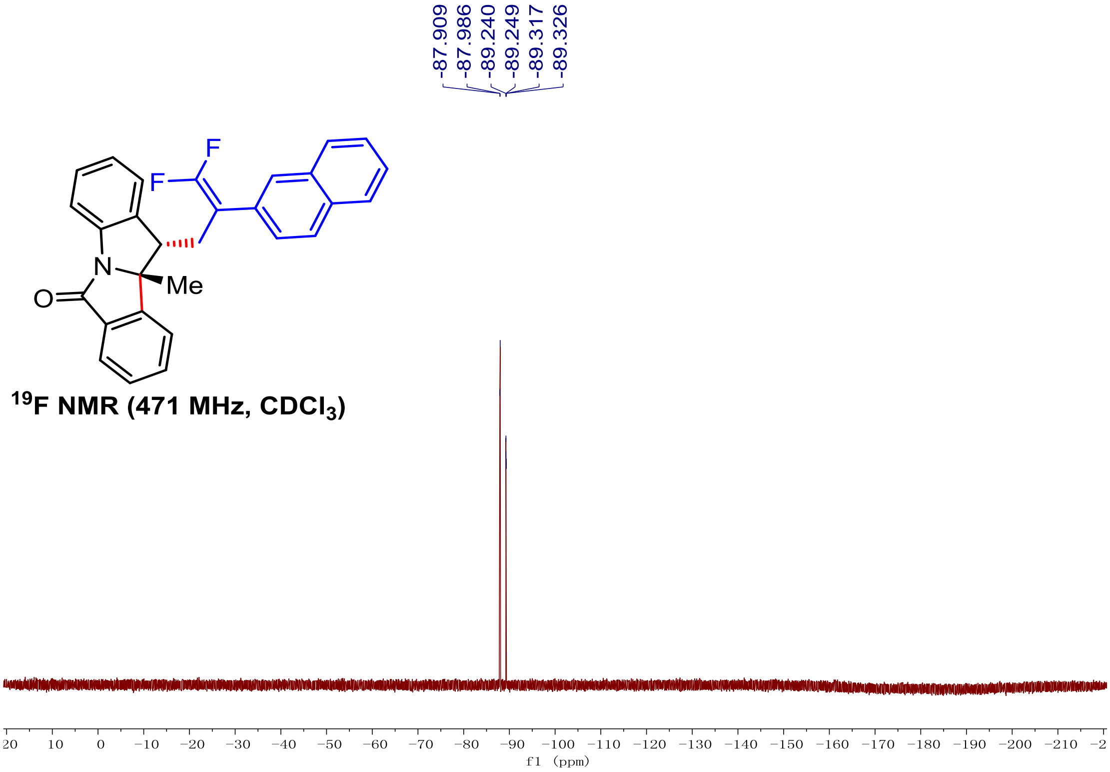


$^{19}$F NMR (471 MHz, CDCl$_3$)

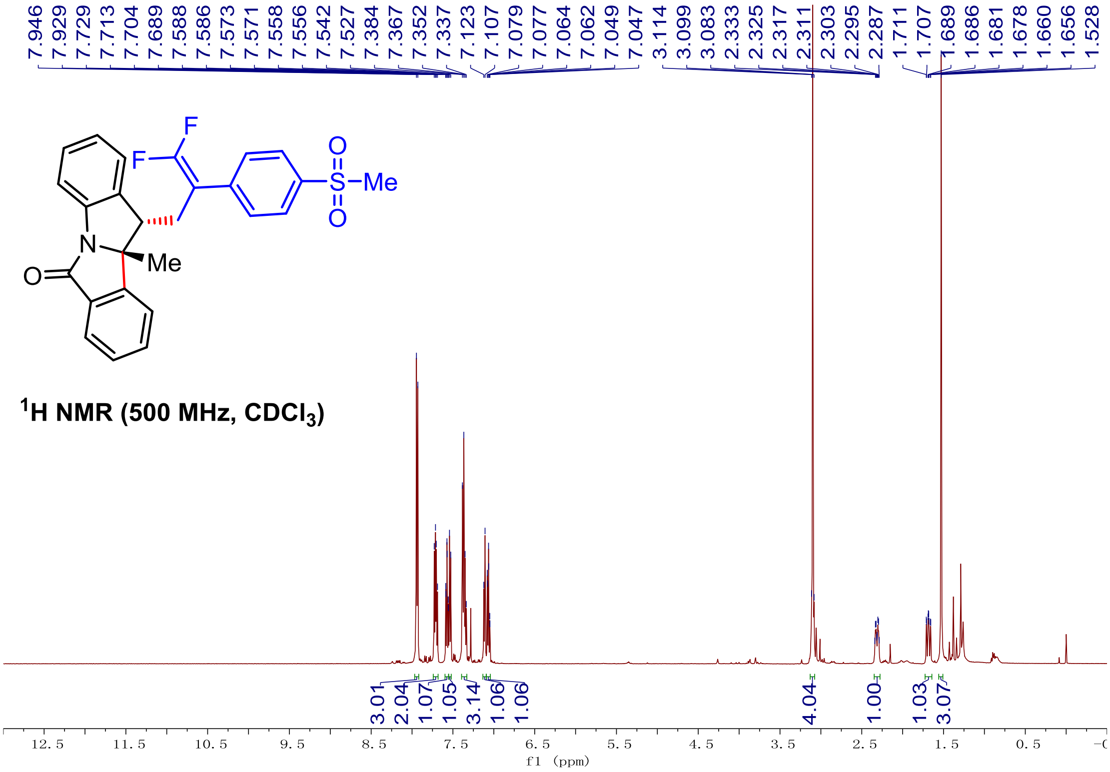
### (10b*R*,11*S*)-11-(3,3-Difluoro-2-(naphthalen-2-yl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 15

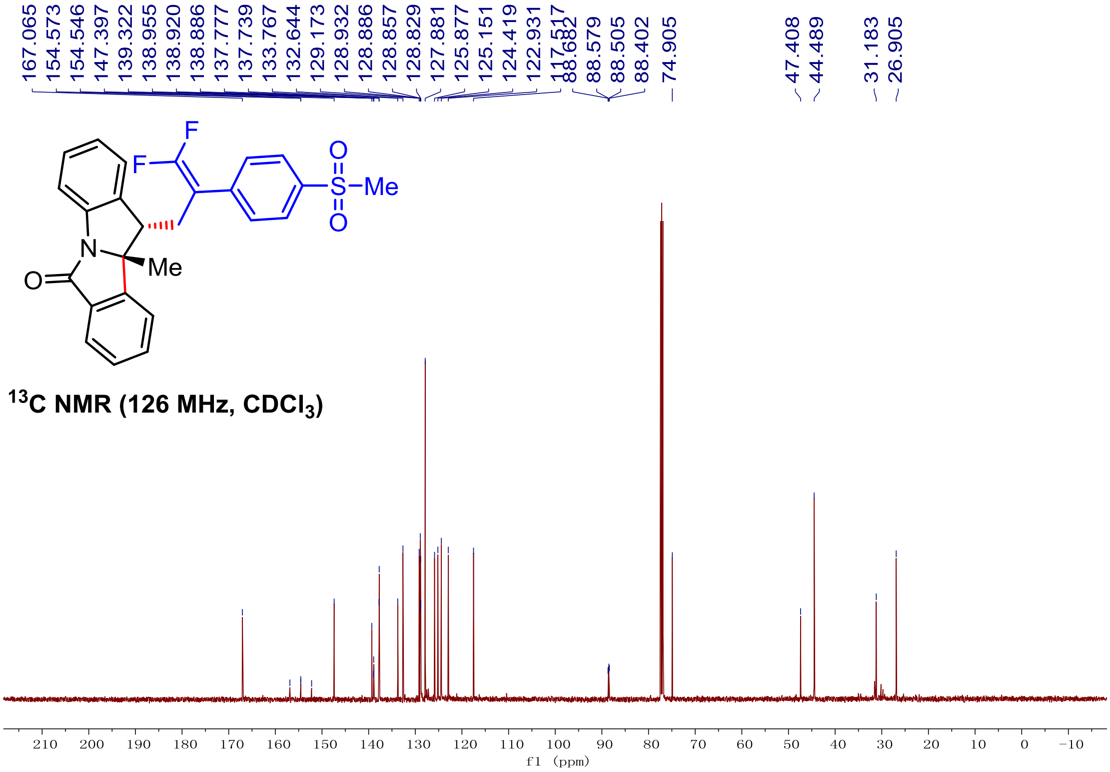




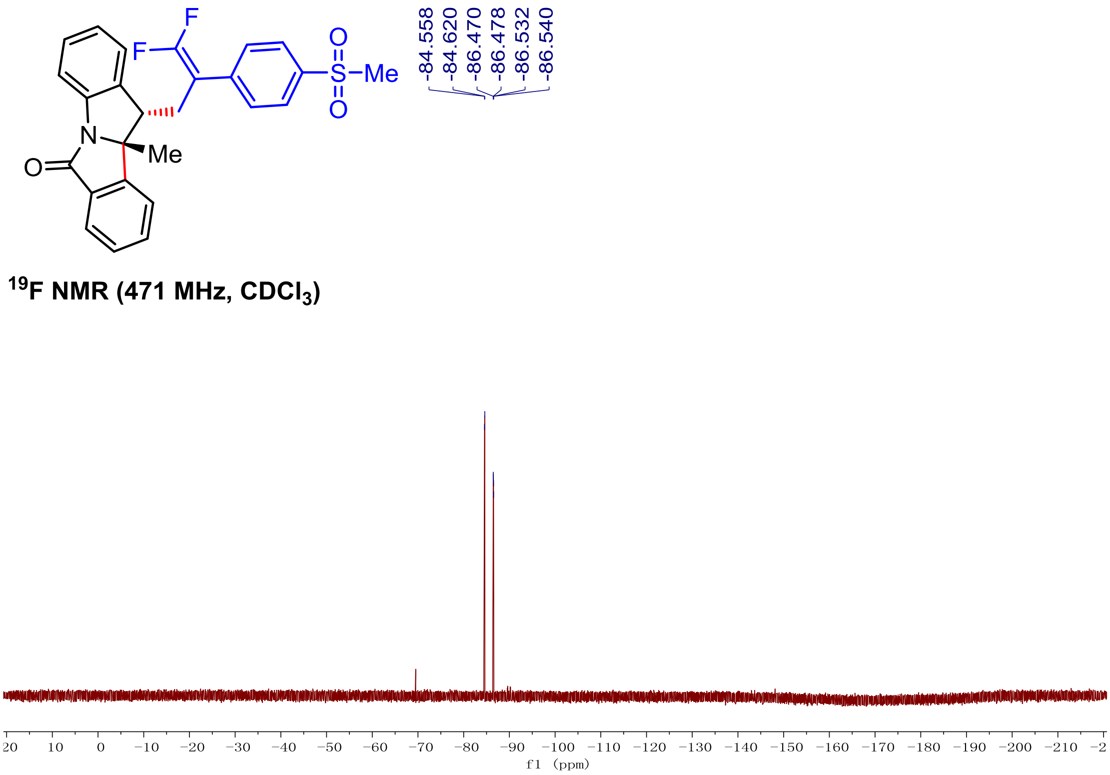


## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-(methylsulfonyl)phenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 16



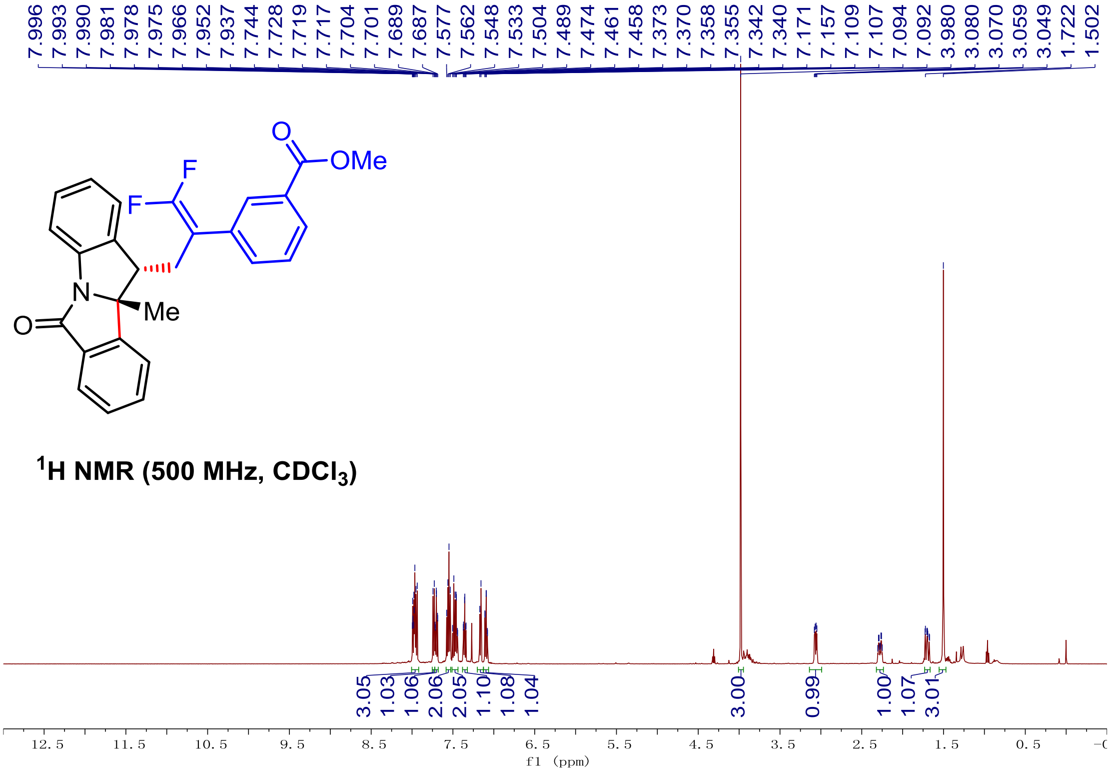


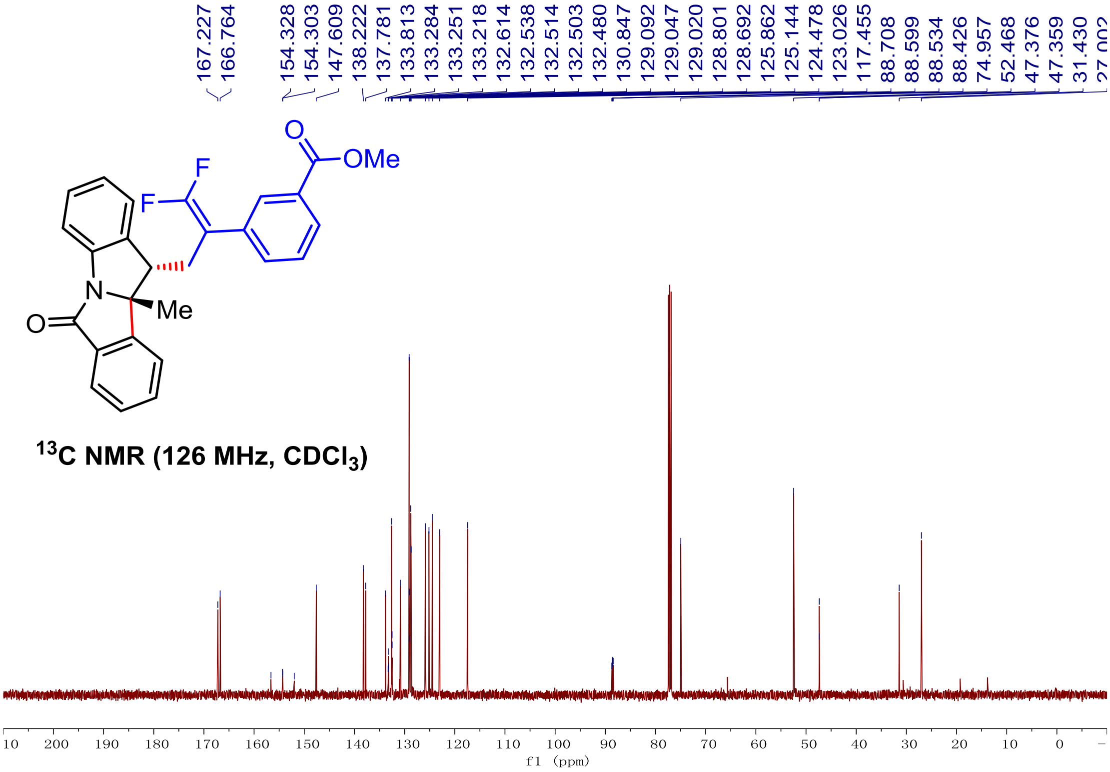
**$^{13}$C NMR (126 MHz, CDCl$_3$)**

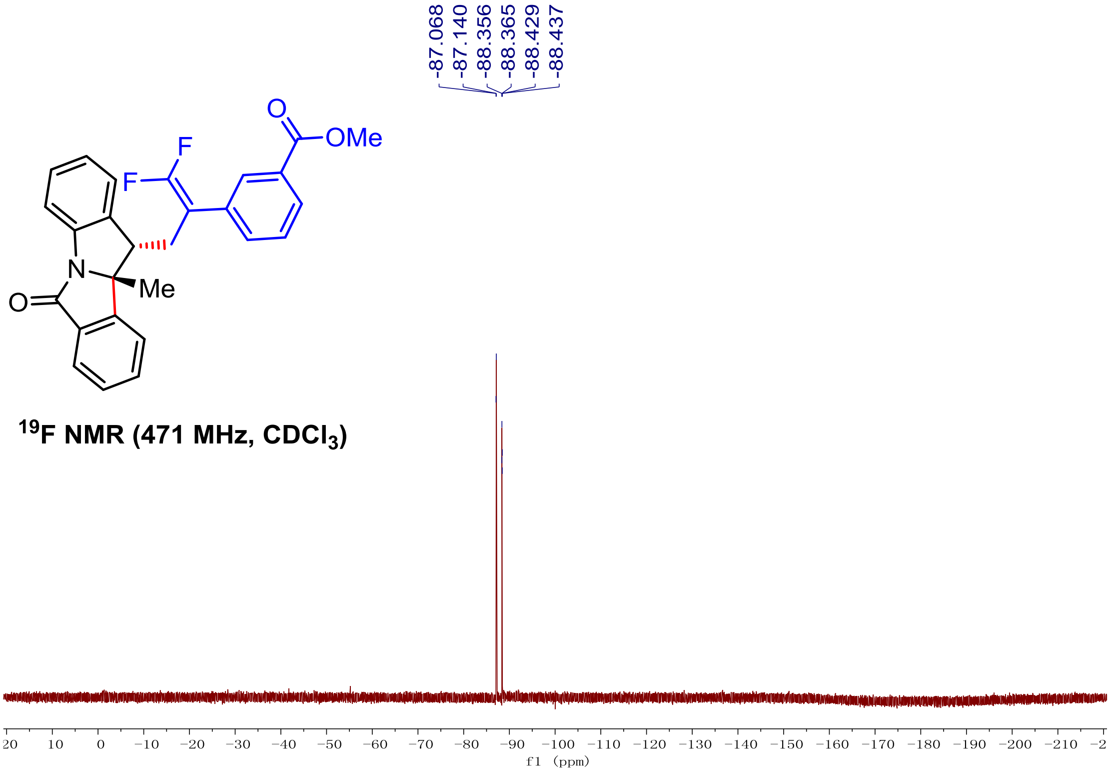


**$^{19}$F NMR (471 MHz, CDCl$_3$)**

## Methyl 3-(1,1-difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzoate, 17

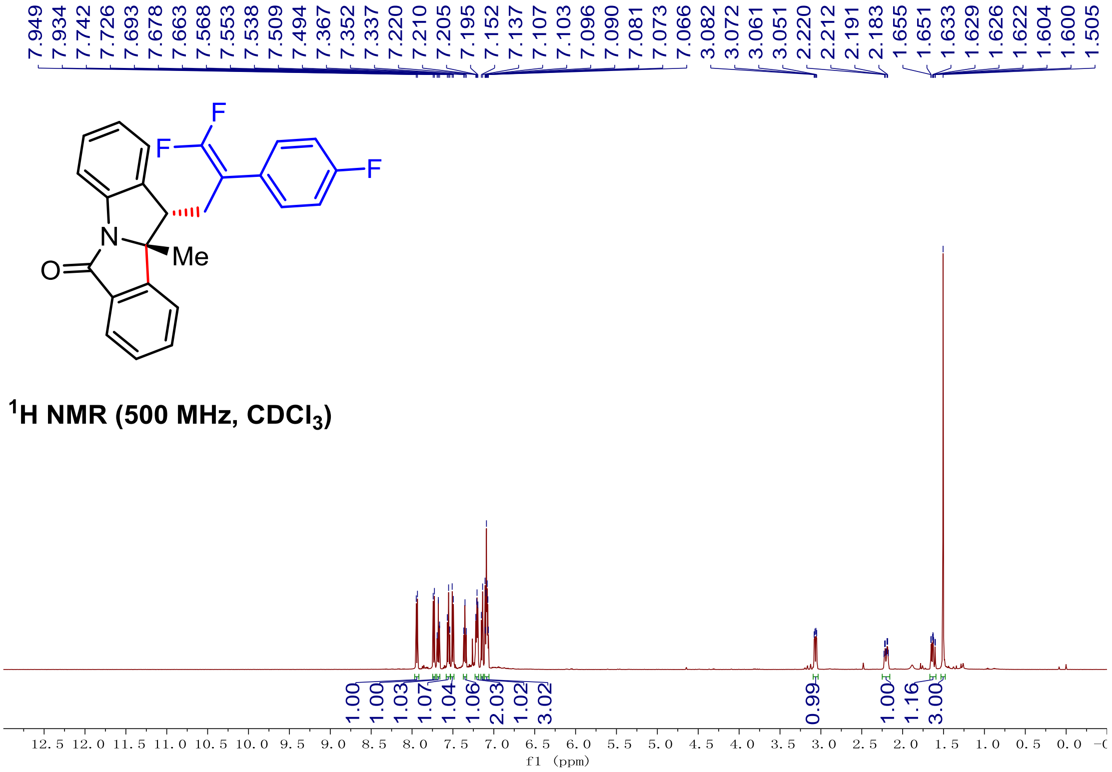




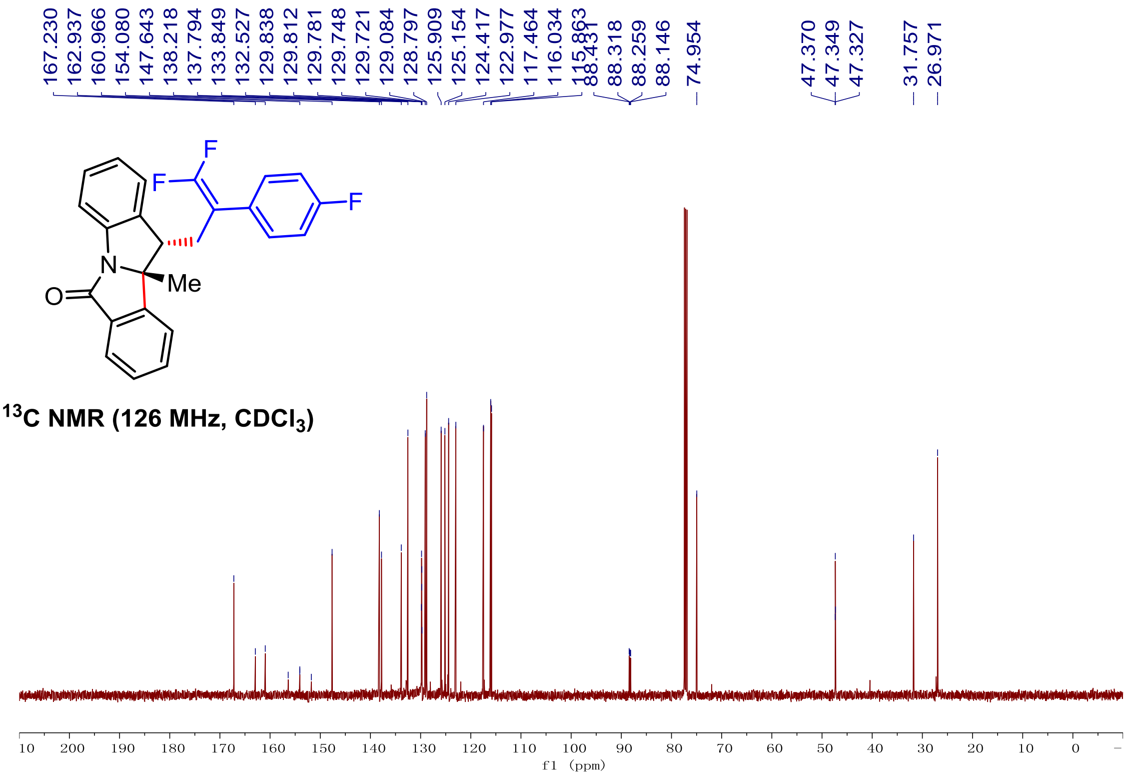


**$^{19}$F NMR (471 MHz, CDCl$_3$)**

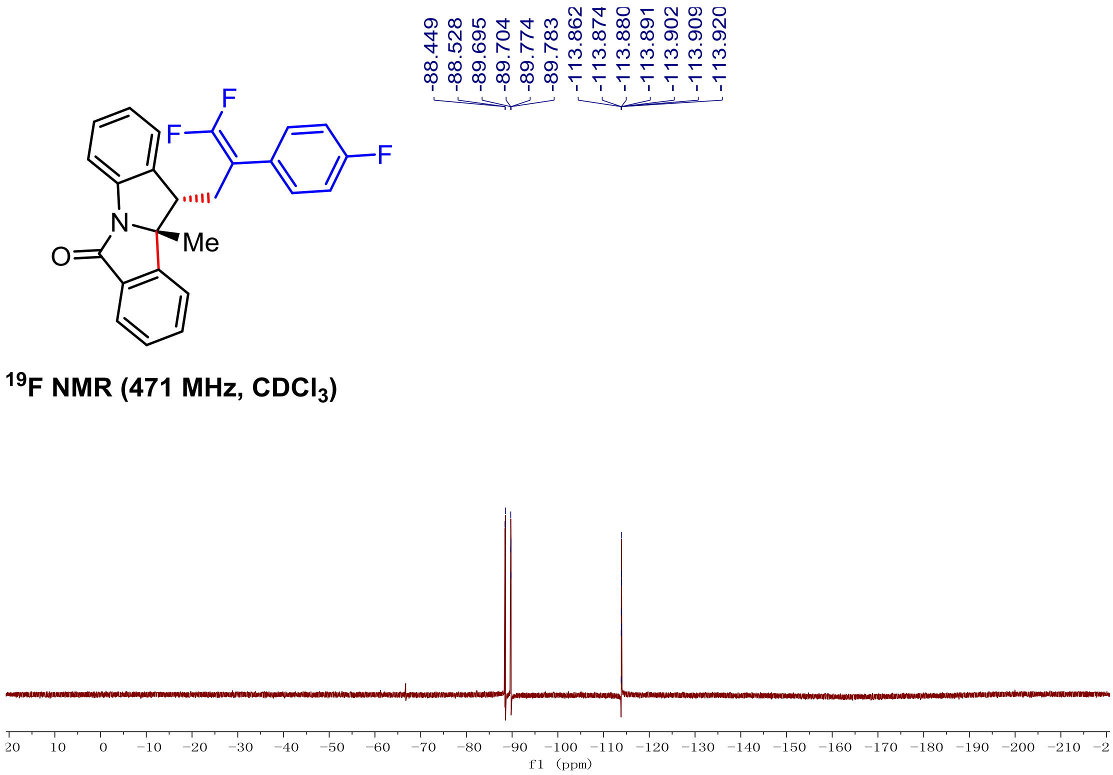
## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(4-fluorophenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 18



**$^{1}$H NMR (500 MHz, CDCl$_3$)**

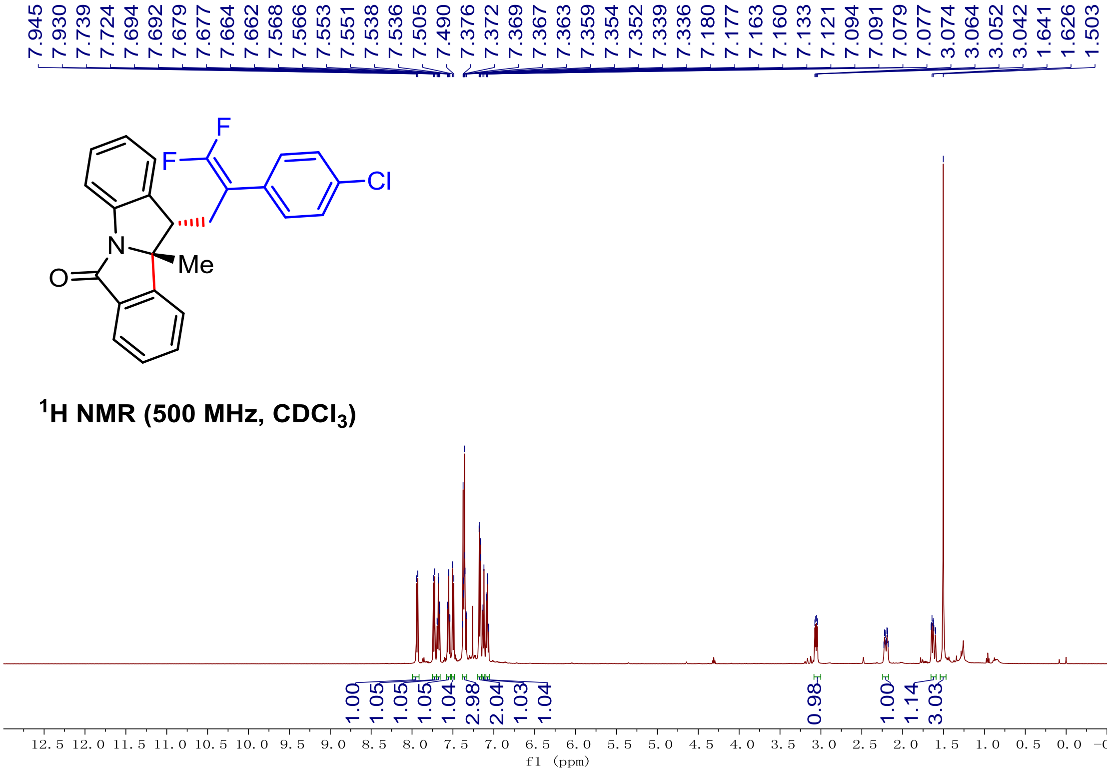


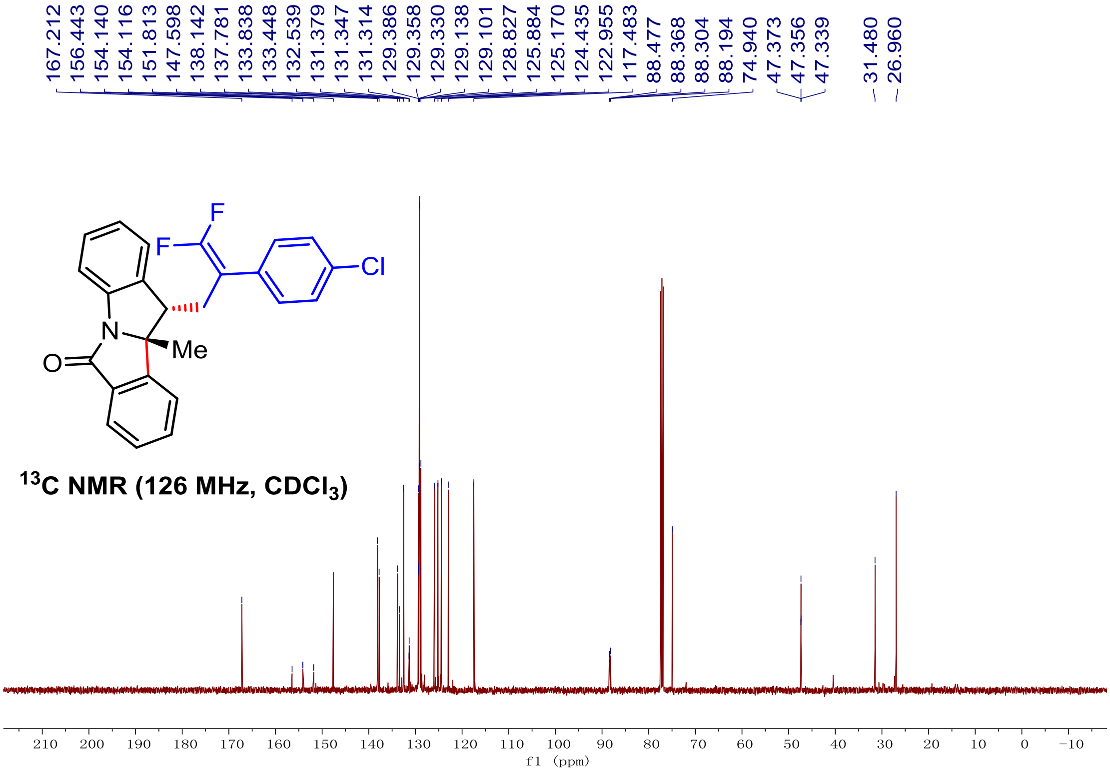
**$^{13}$C NMR (126 MHz, CDCl$_3$)**

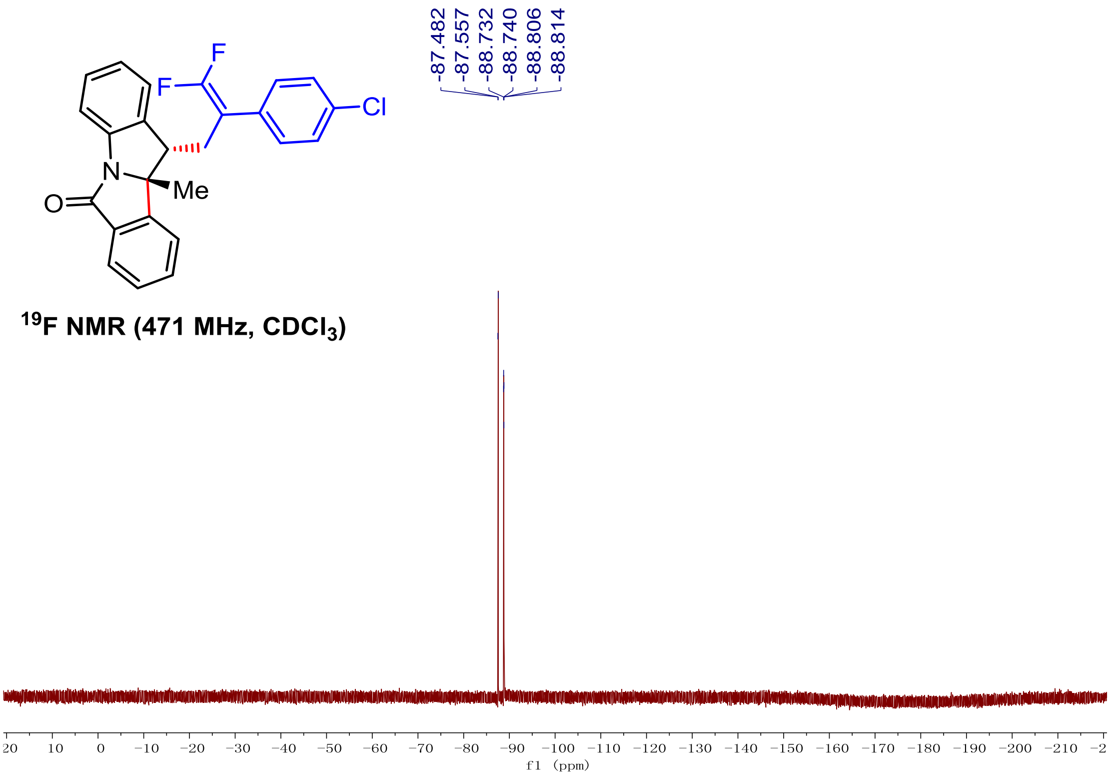


**$^{19}$F NMR (471 MHz, CDCl$_3$)**

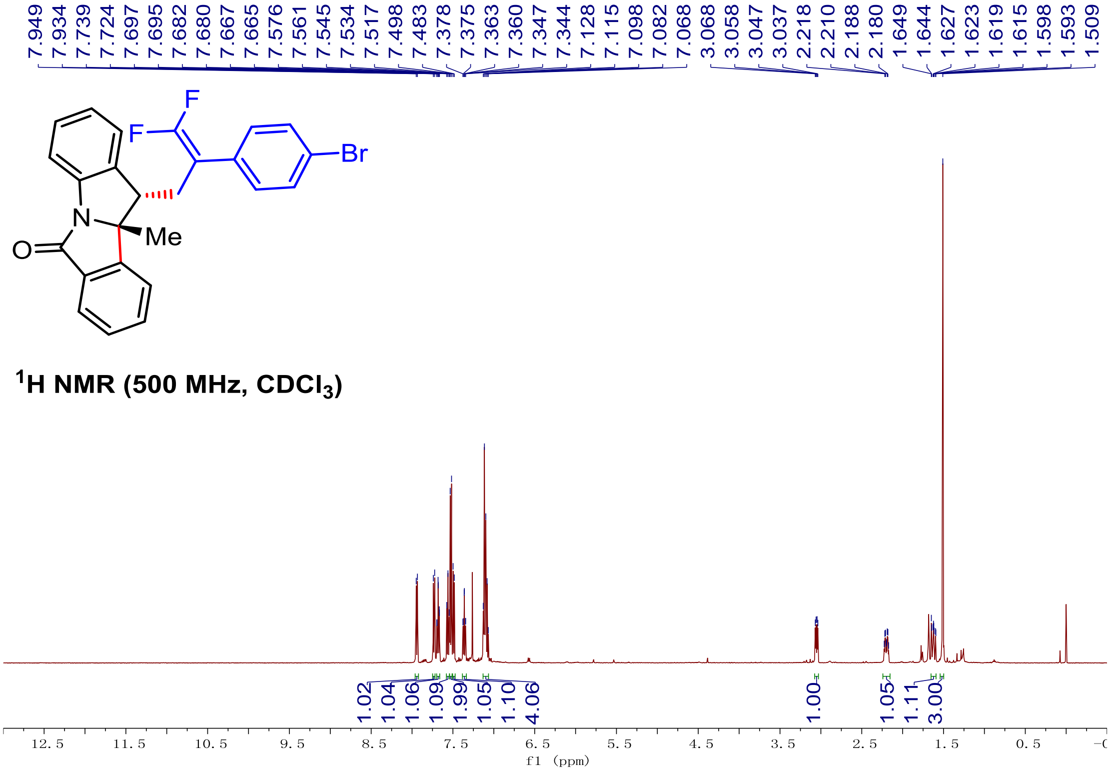
## (10b*R*,11*S*)-11-(2-(4-Chlorophenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 19

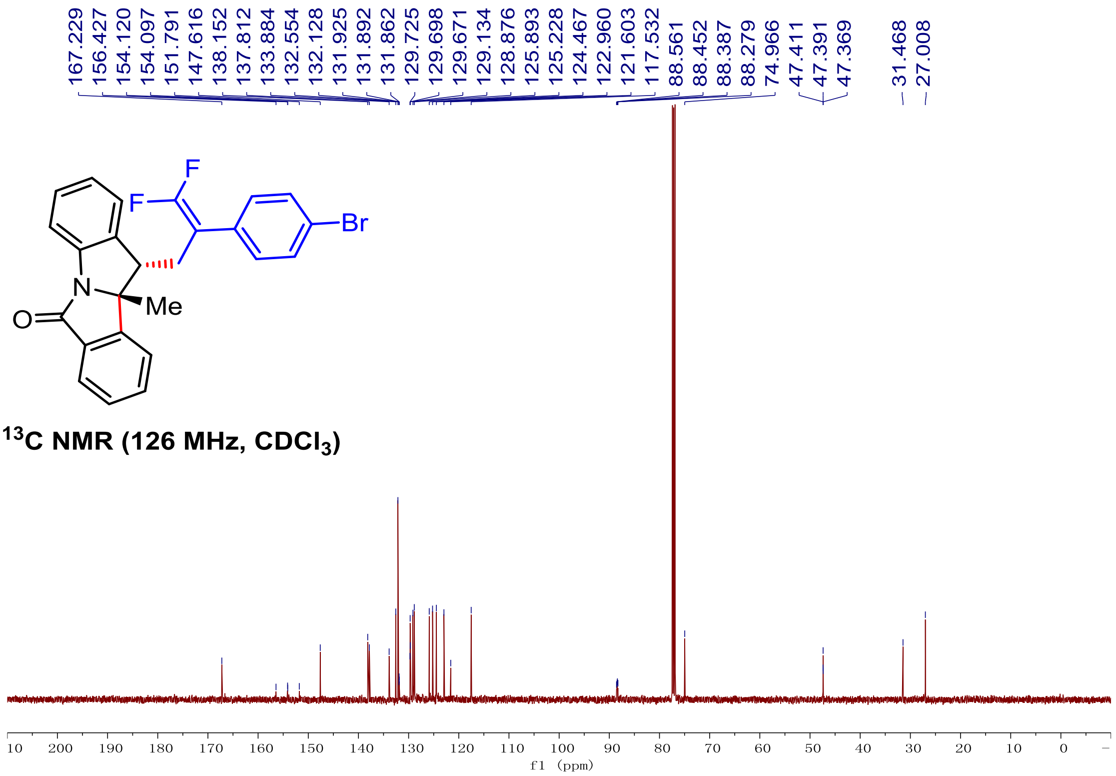




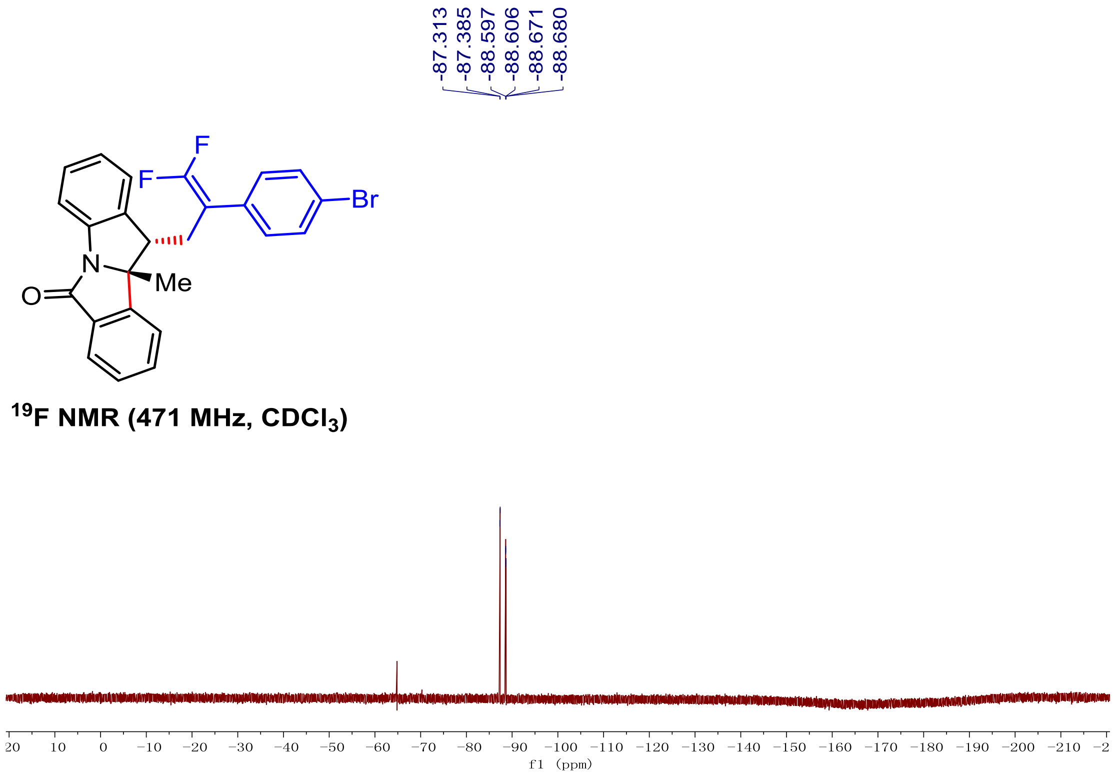


## (10b*R*,11*S*)-11-(2-(4-Bromophenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 20



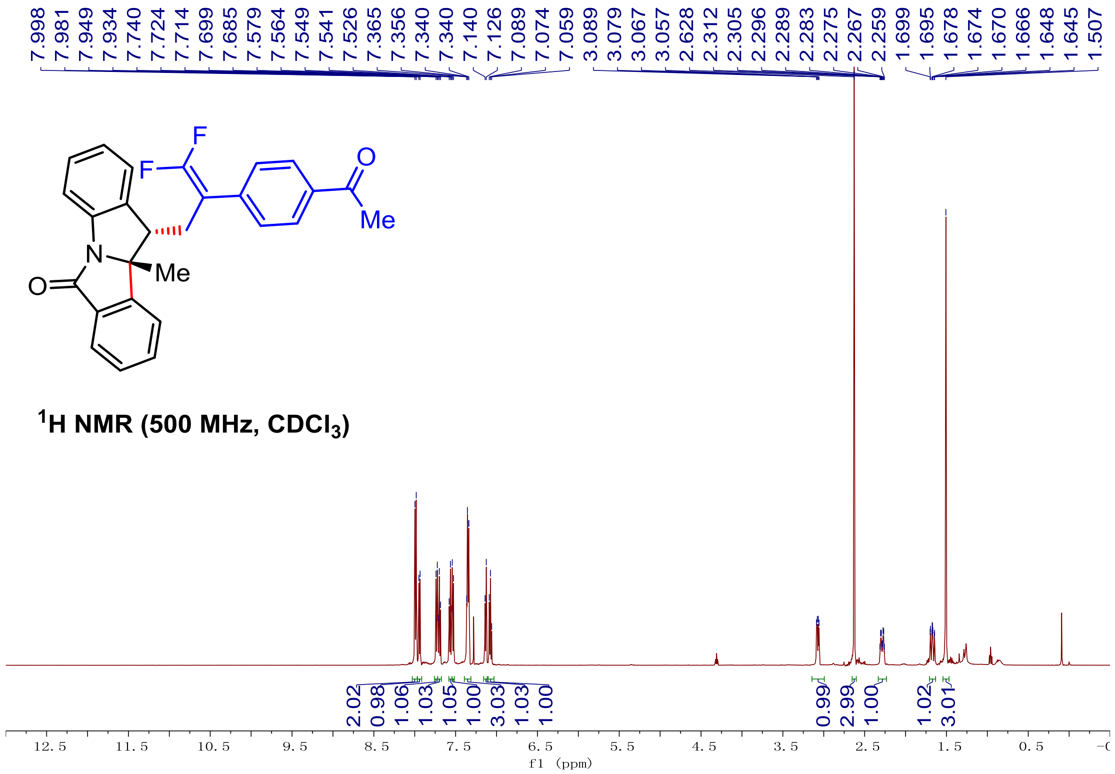


**$^{13}$C NMR (126 MHz, CDCl$_3$)**

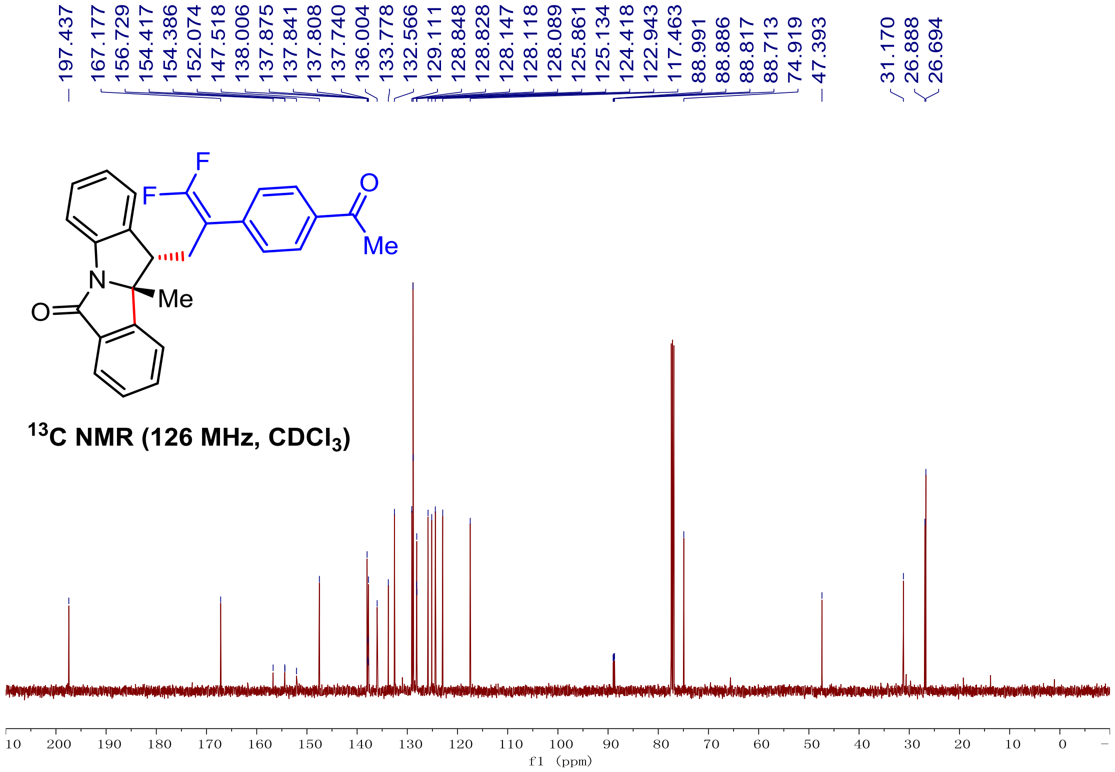


**$^{19}$F NMR (471 MHz, CDCl$_3$)**

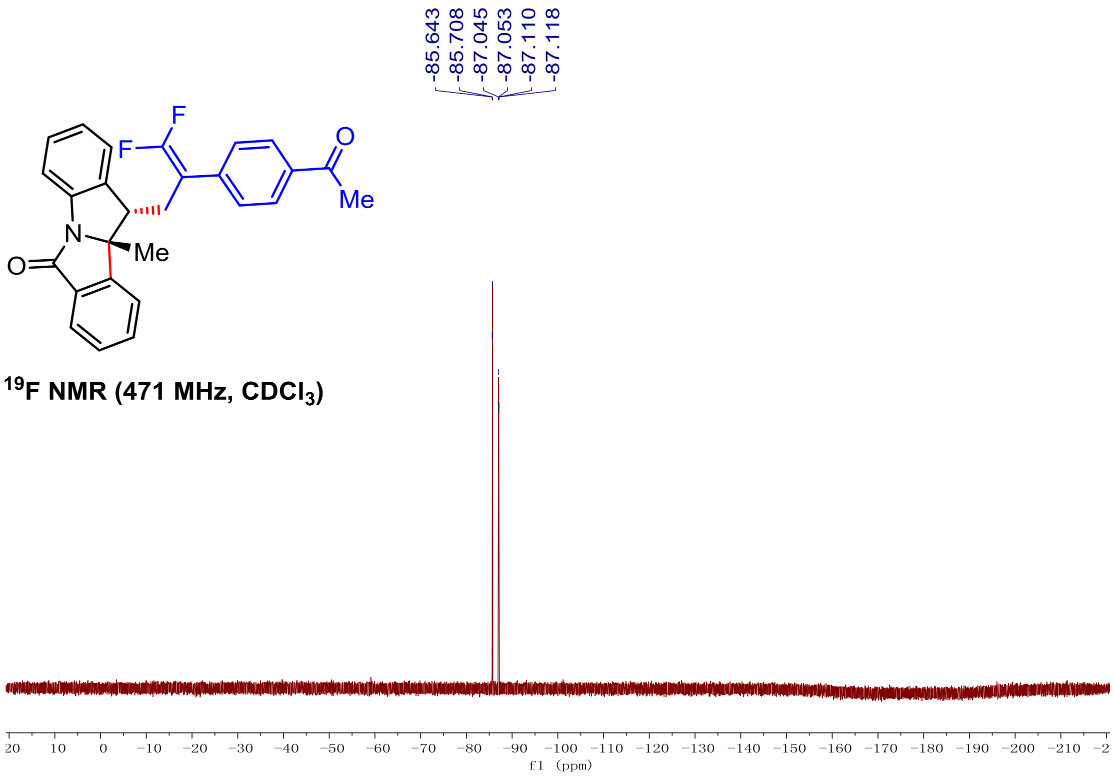
**(10b*R*,11*S*)-11-(2-(4-Acetylphenyl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 21**



$^1$H NMR (500 MHz, CDCl$_3$)

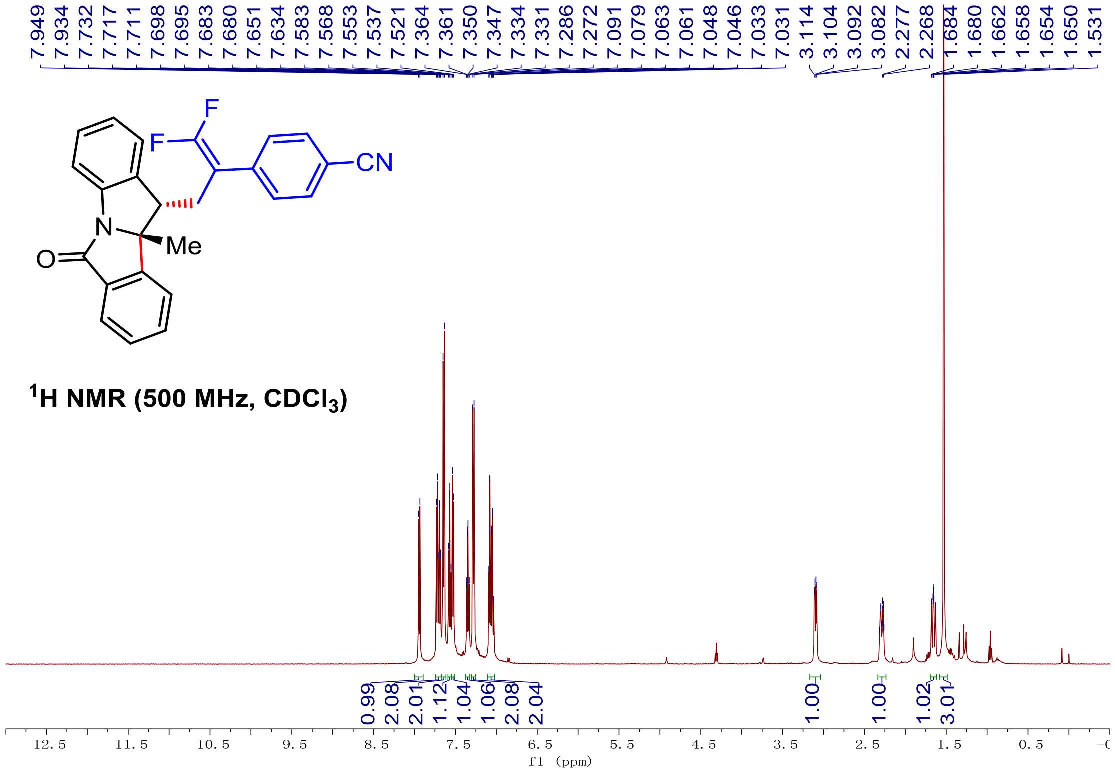


$^{13}$C NMR (126 MHz, CDCl$_3$)

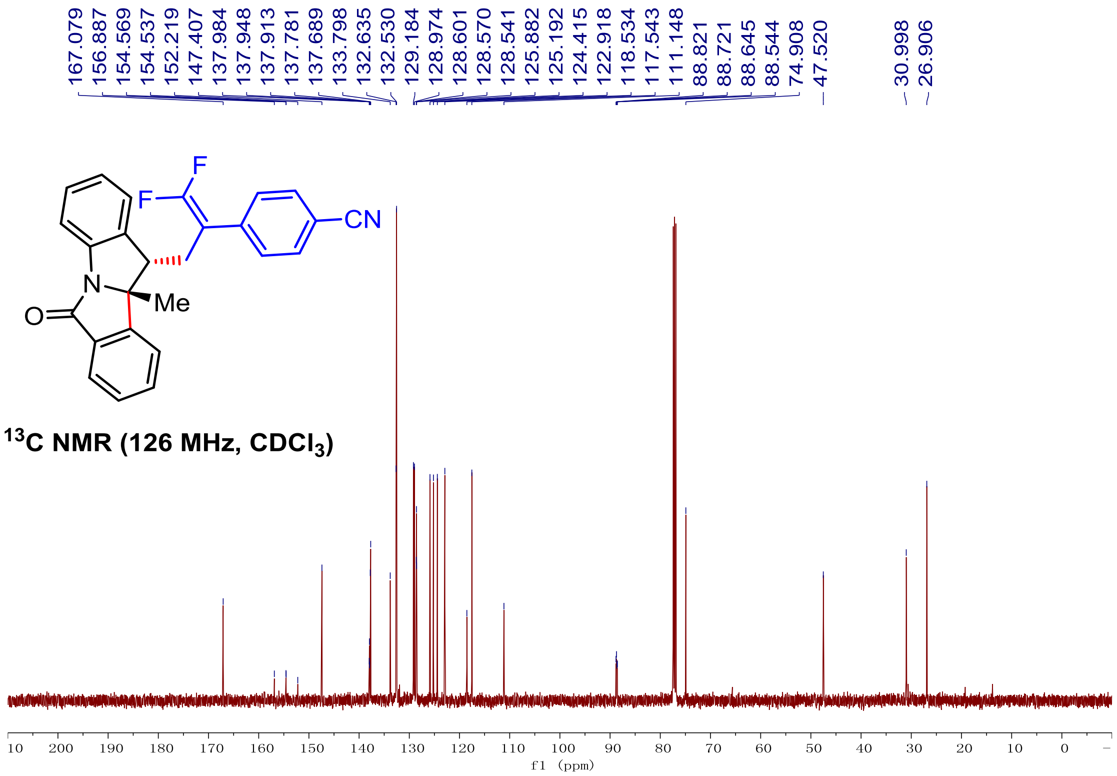


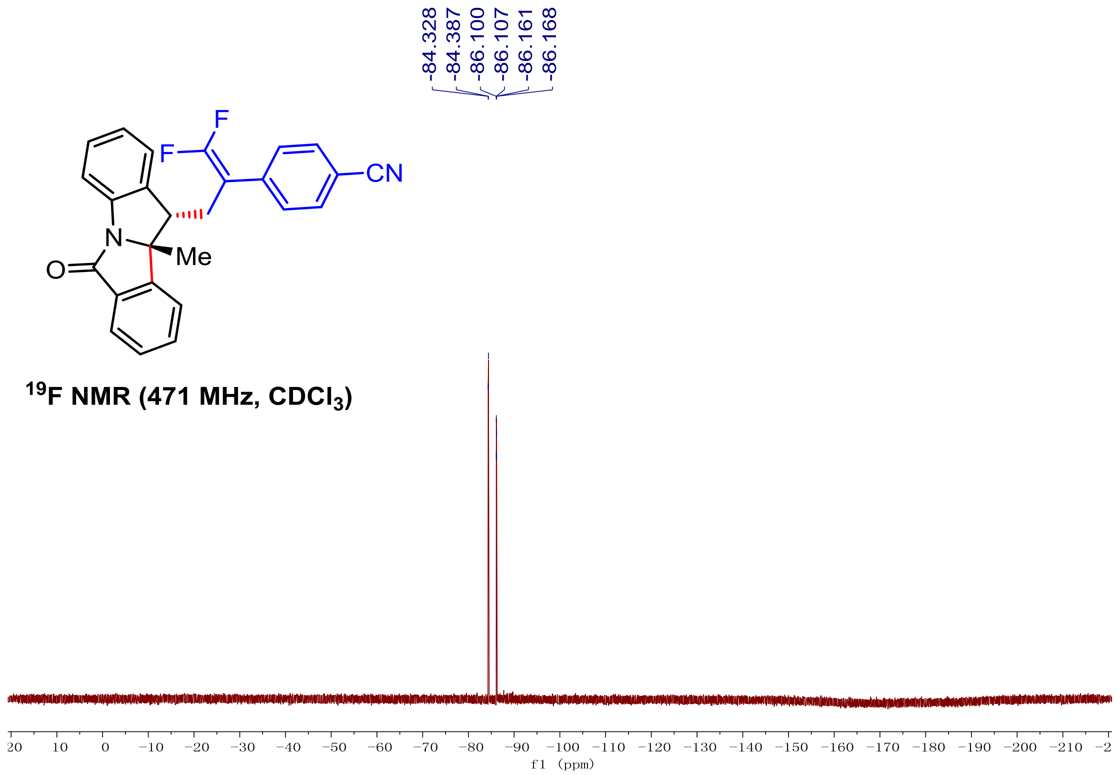
**$^{19}$F NMR (471 MHz, CDCl$_3$)**

## 4-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzonitrile, 22

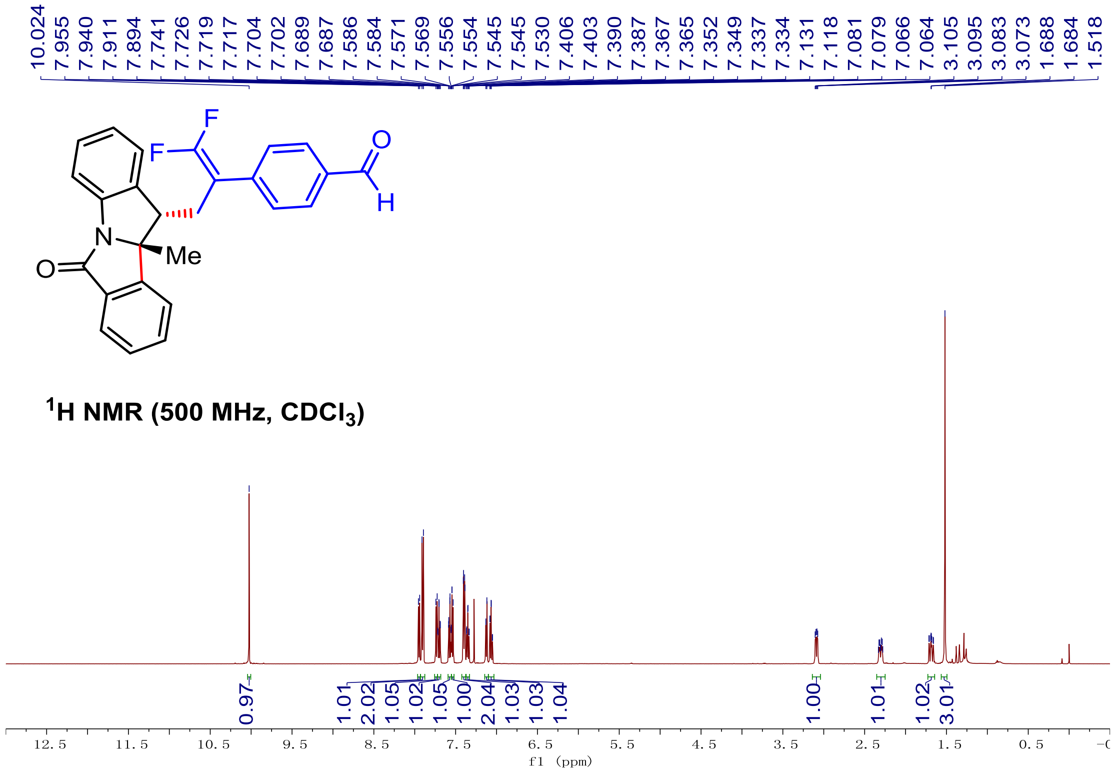


**$^{1}$H NMR (500 MHz, CDCl$_3$)**

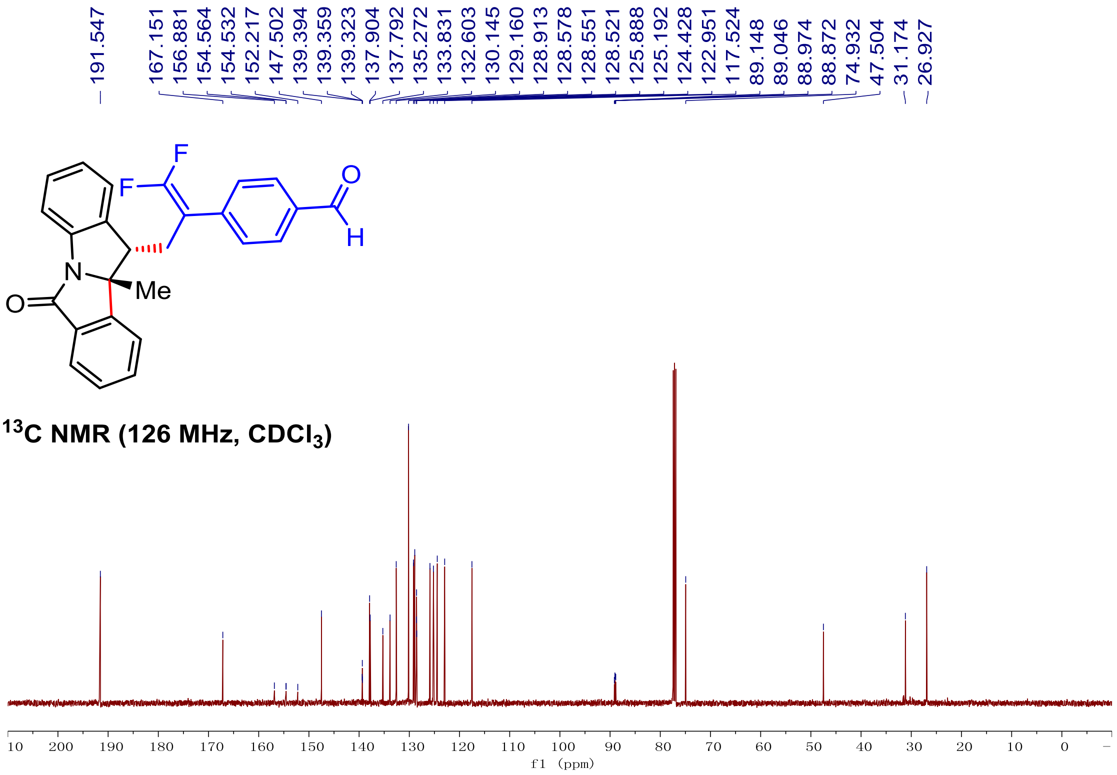

167.079
156.887
154.569
154.537
152.219
147.407
137.984
137.948
137.913
137.781
137.689
133.798
132.635
132.530
129.184
128.974
128.601
128.570
128.541
125.882
125.192
124.415
122.918
118.534
117.543
111.148
88.821
88.721
88.645
88.544
74.908
47.520
30.998
26.906
F
F
CN
N
Me
O
$^{13}$C NMR (126 MHz, CDCl$_3$)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-84.328
-84.387
-86.100
-86.107
-86.161
-86.168
F
F
CN
N
Me
O
$^{19}$F NMR (471 MHz, CDCl$_3$)
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −2
f1 (ppm)

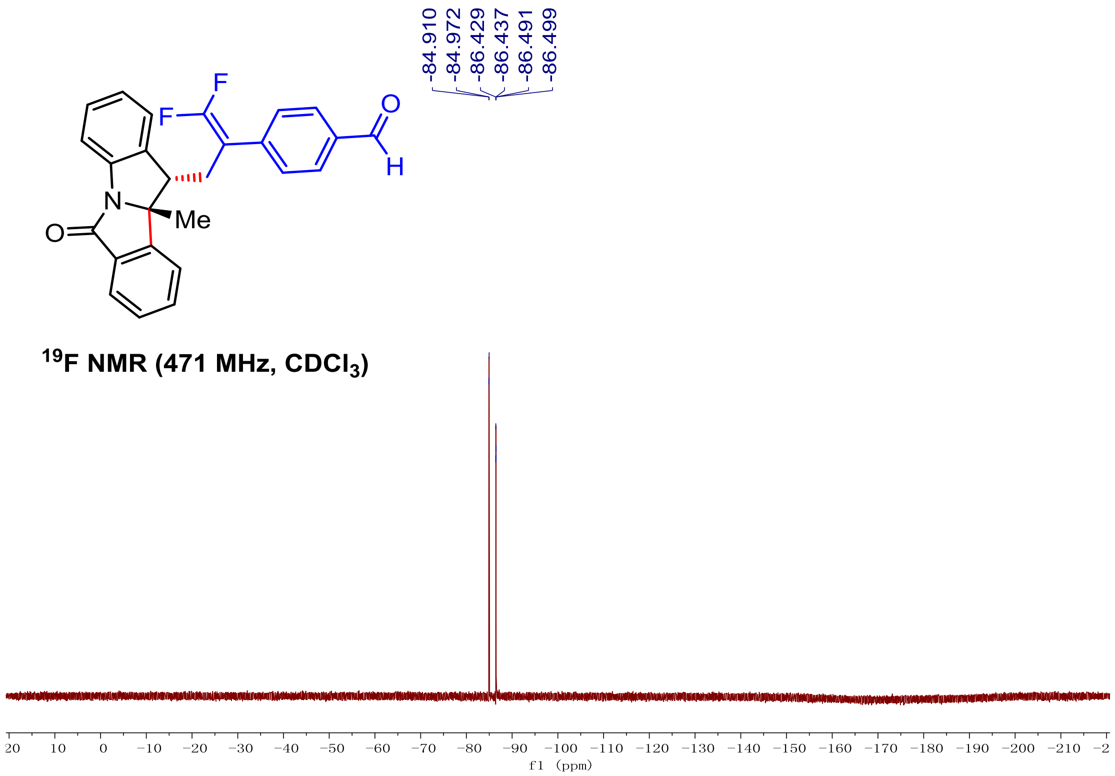
## 4-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzaldehyde, 23



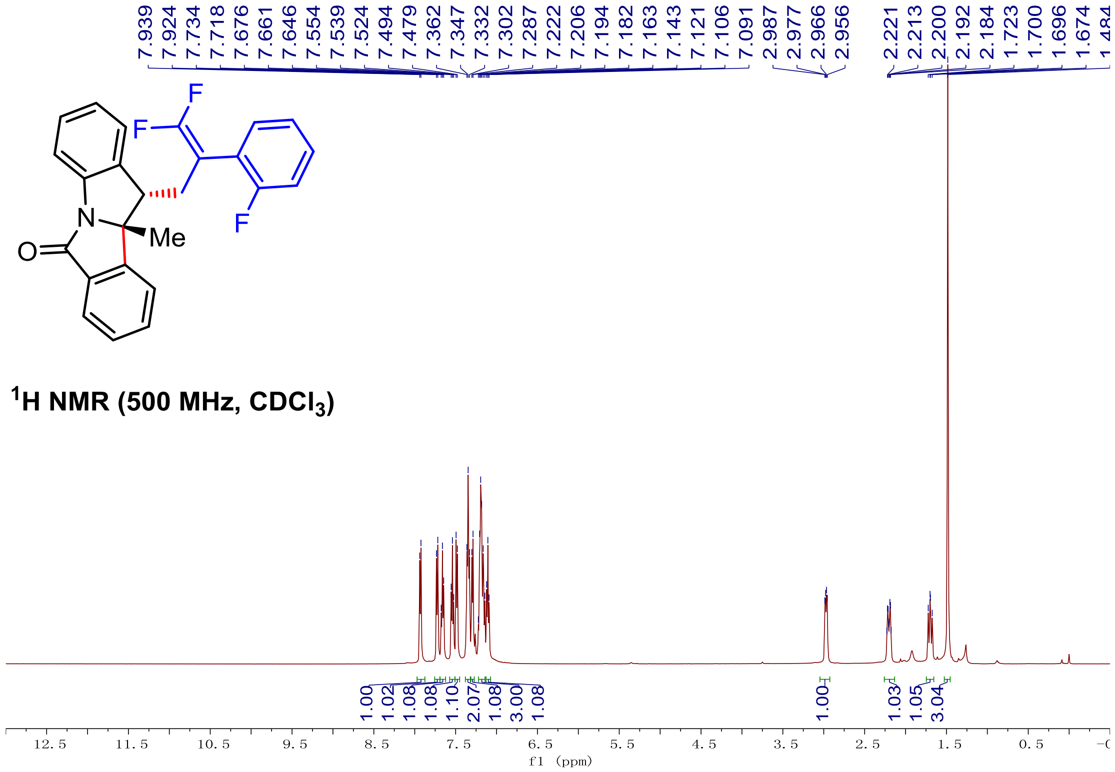
**$^1$H NMR (500 MHz, CDCl$_3$)**

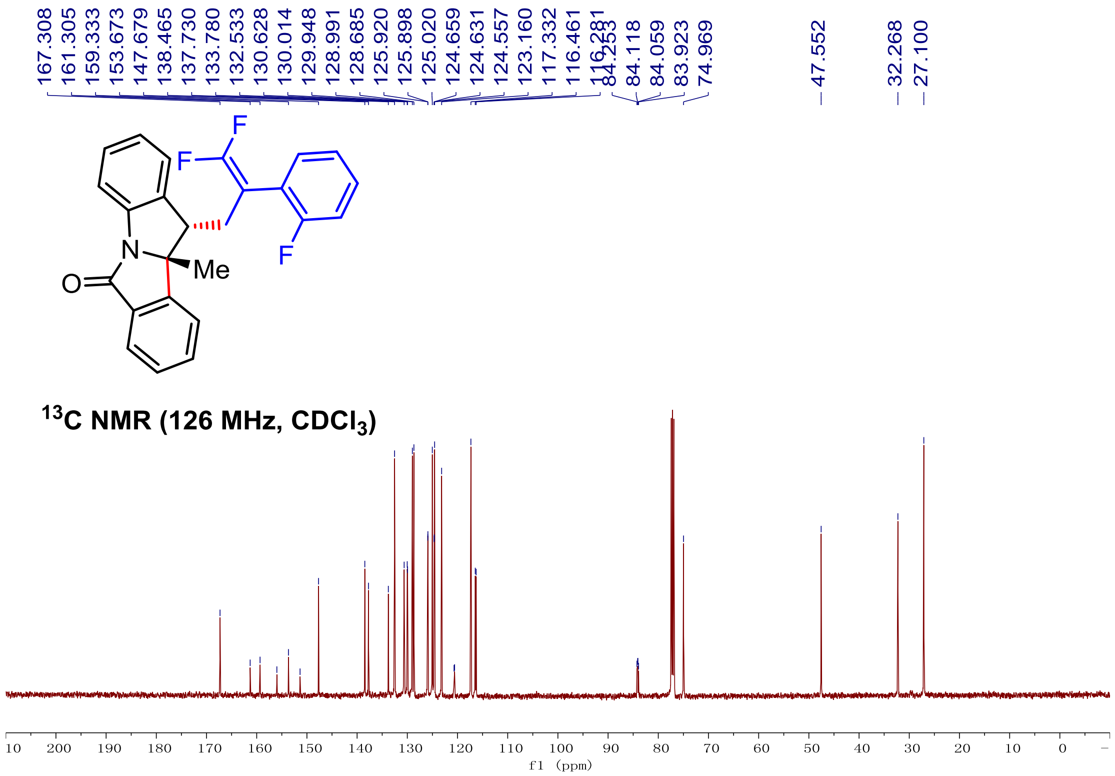


**$^{13}$C NMR (126 MHz, CDCl$_3$)**

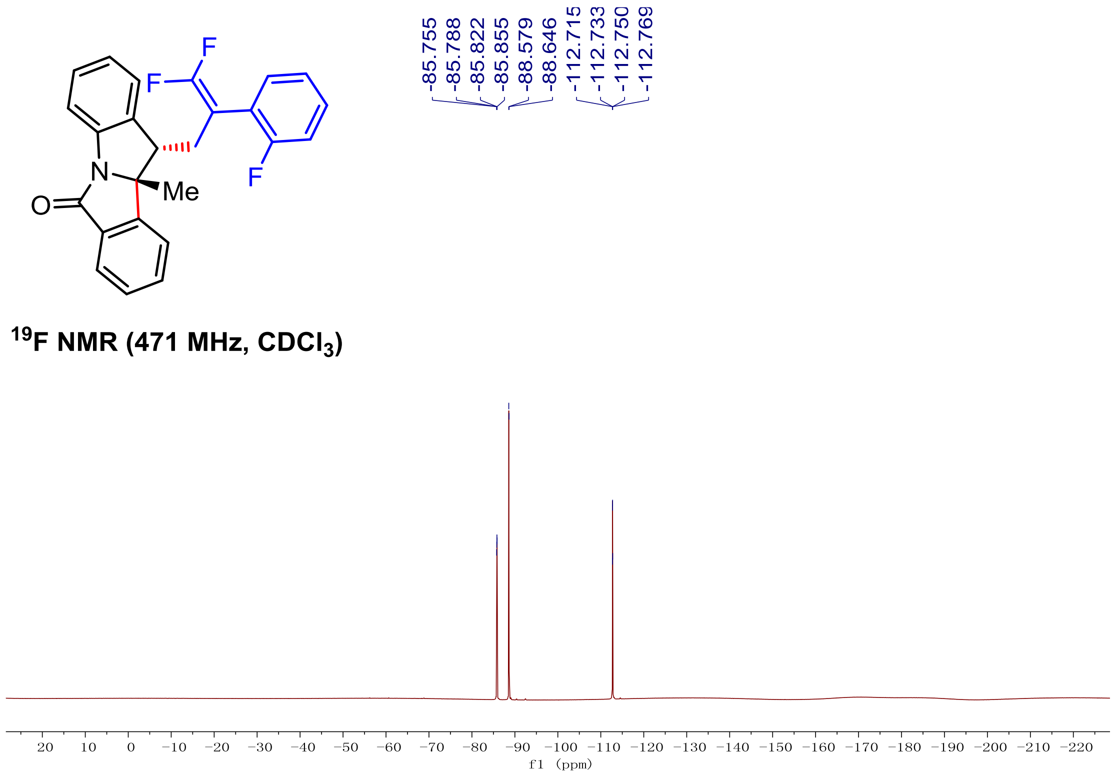


## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(2-fluorophenyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 24



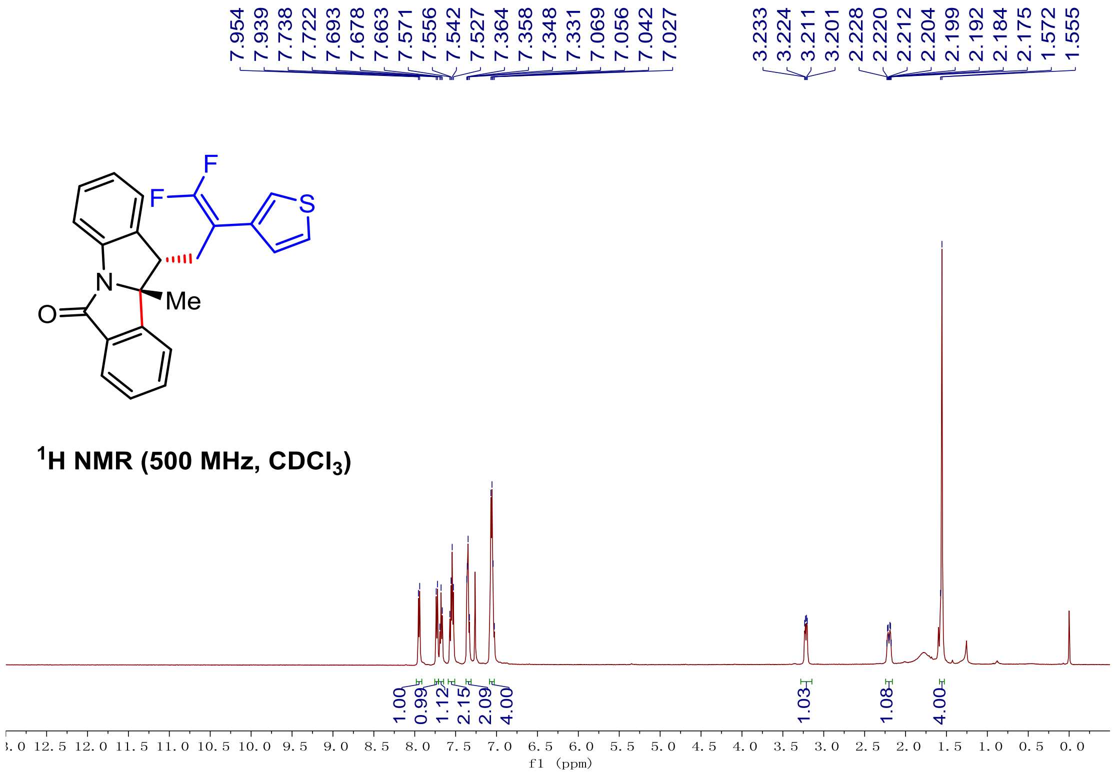


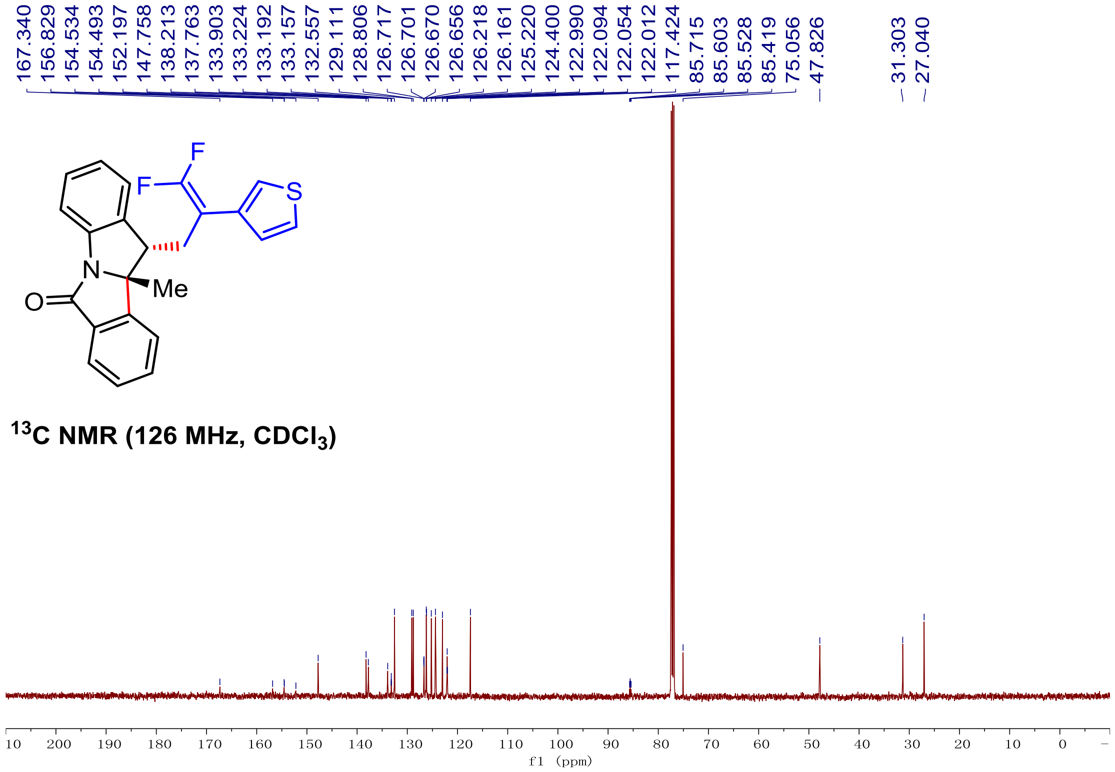
$^{13}$C NMR (126 MHz, CDCl$_3$)

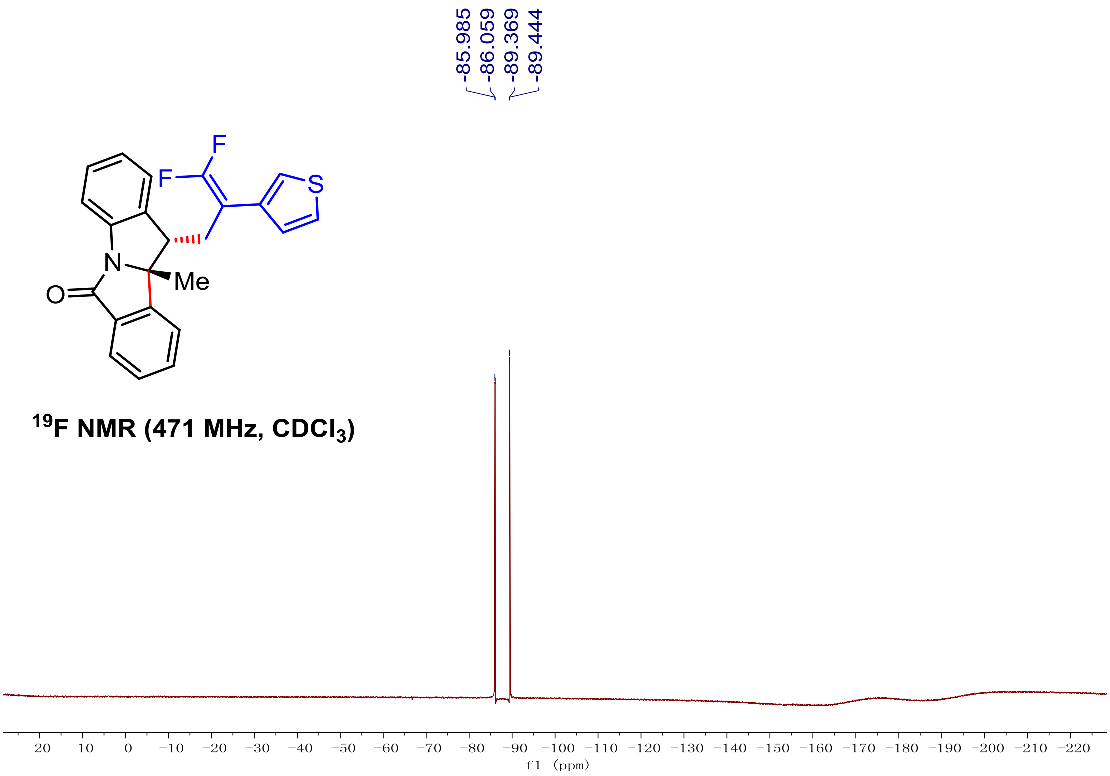


$^{19}$F NMR (471 MHz, CDCl$_3$)

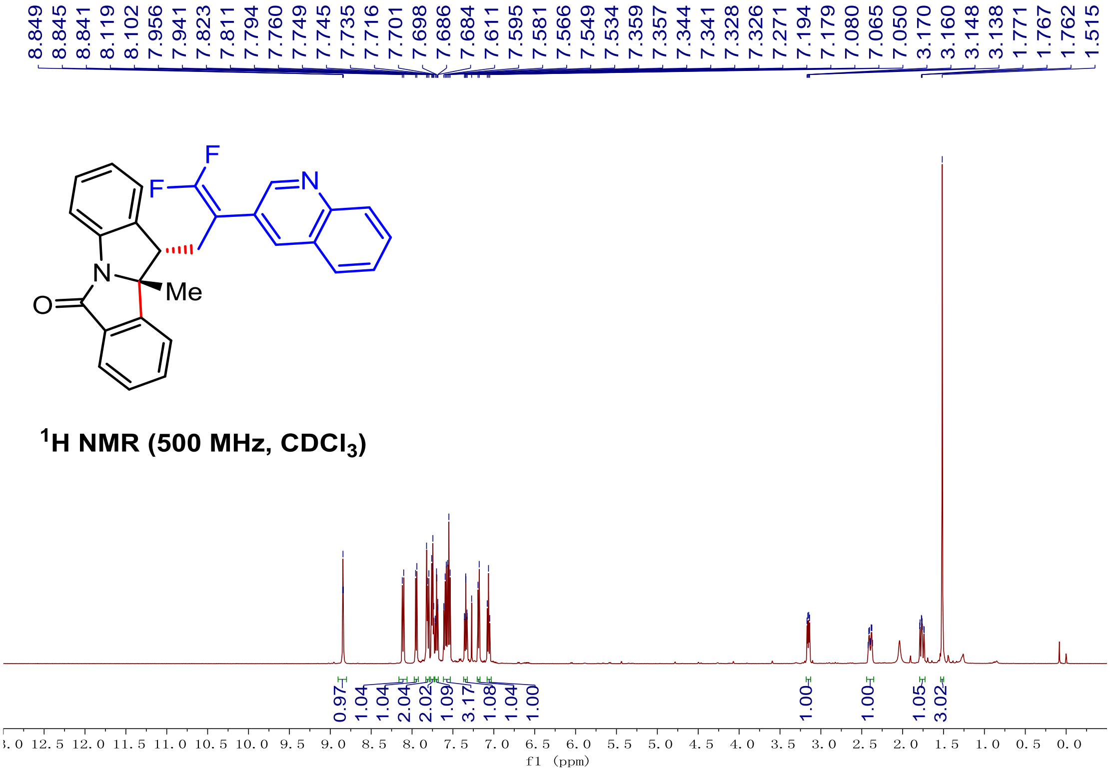
**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(thiophen-3-yl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 25**

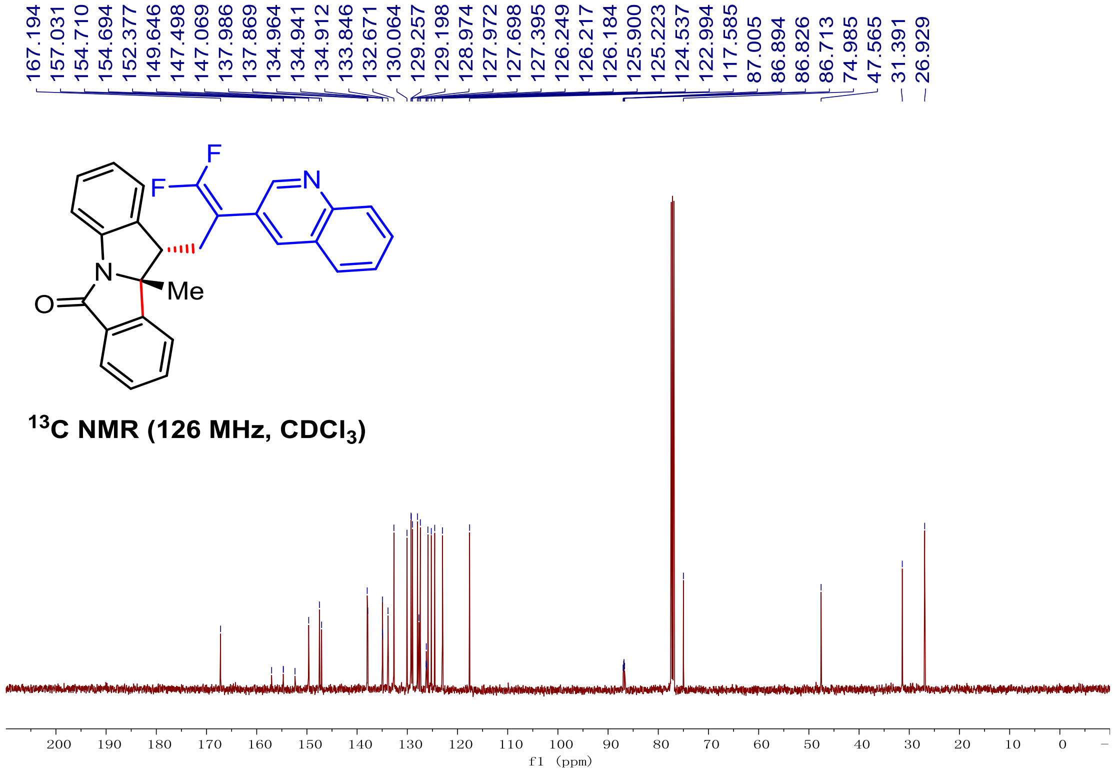




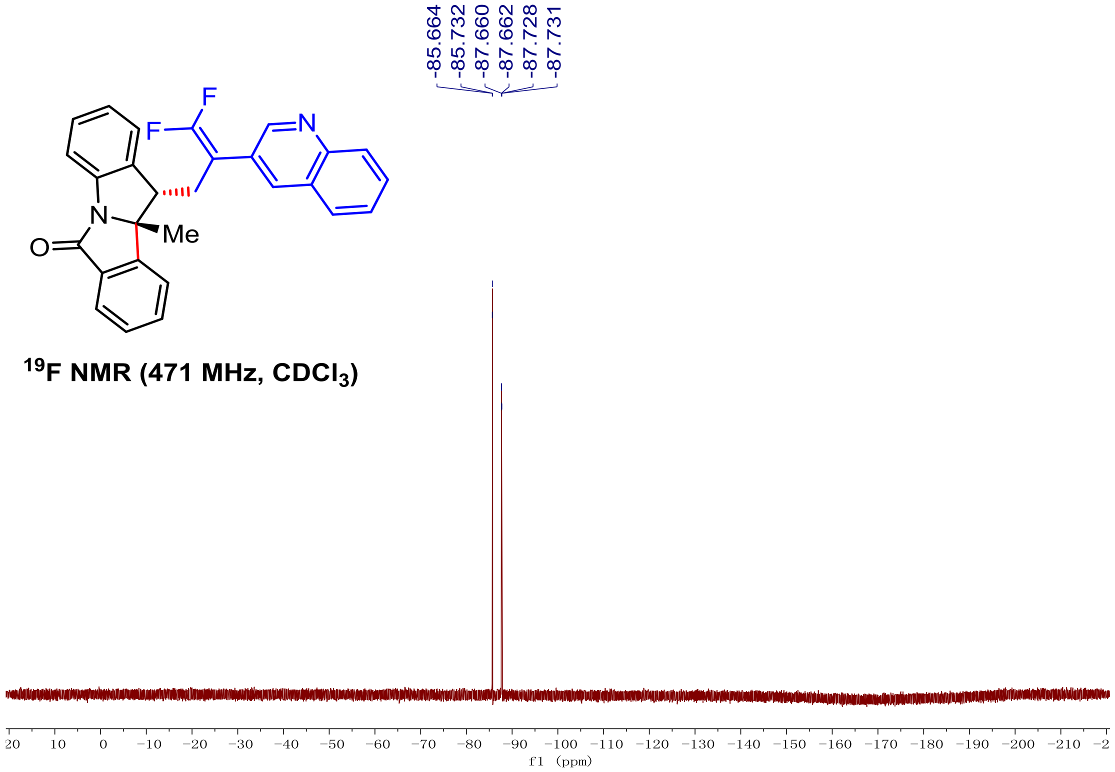


## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(quinolin-3-yl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 26



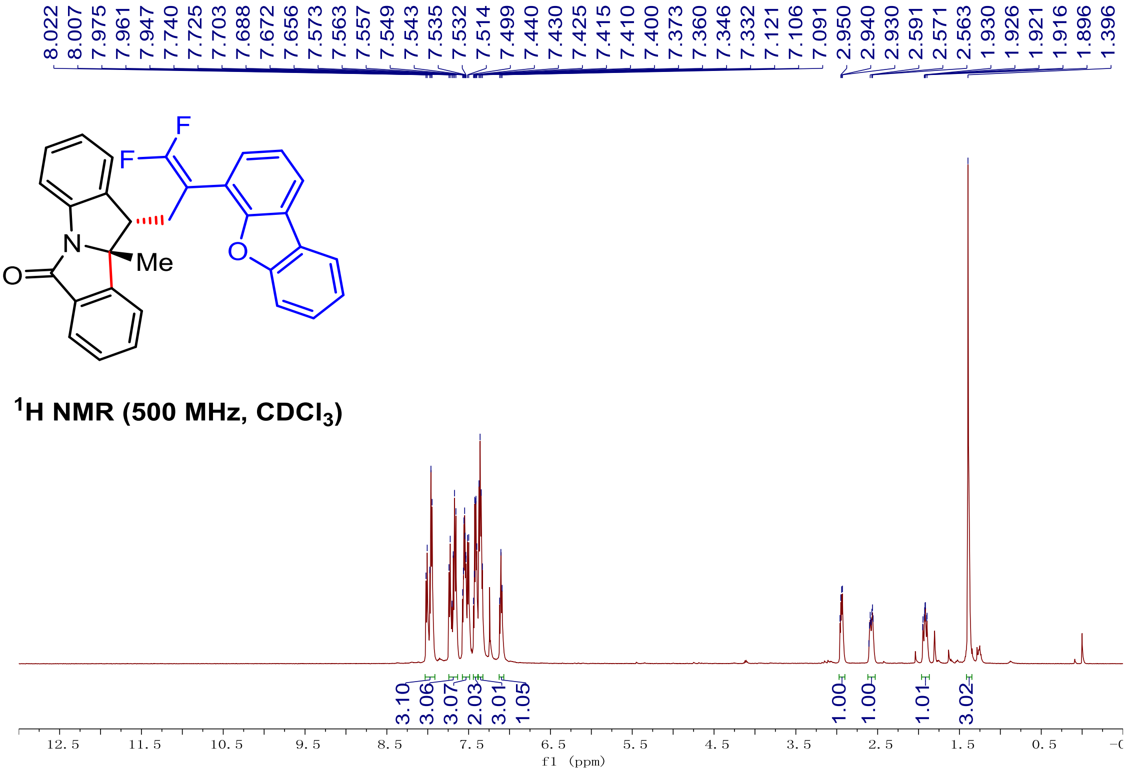


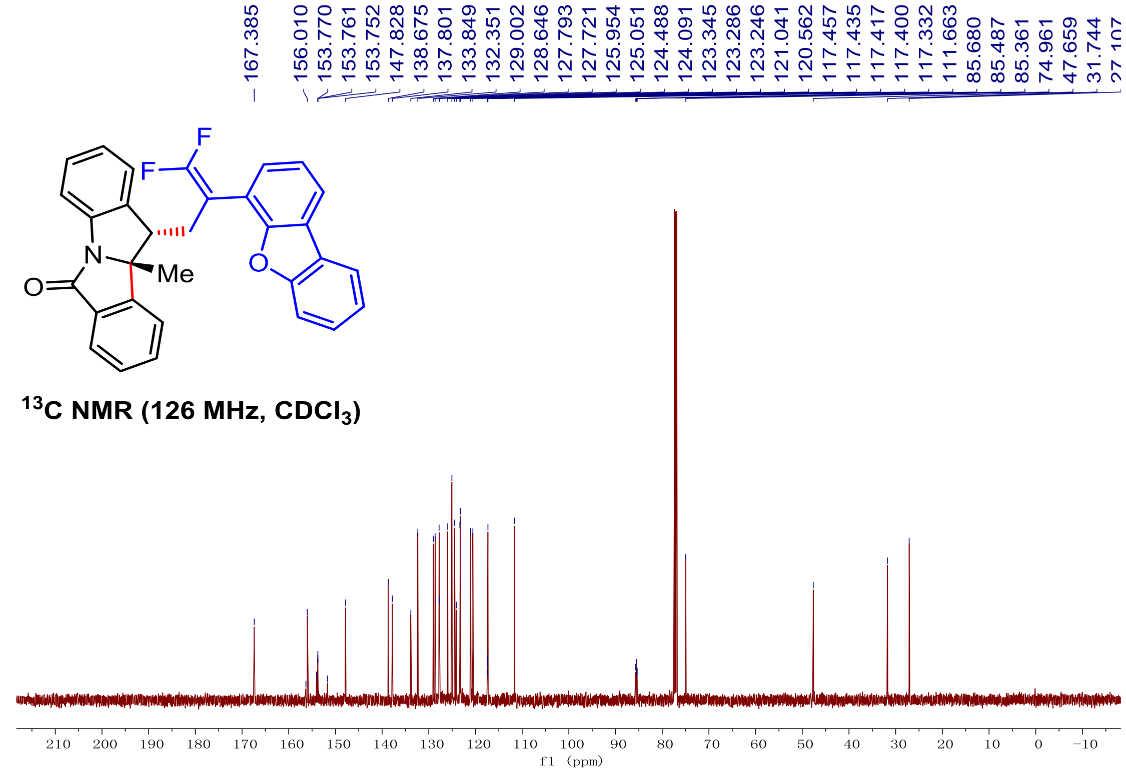
$^{13}$C NMR (126 MHz, CDCl$_3$)

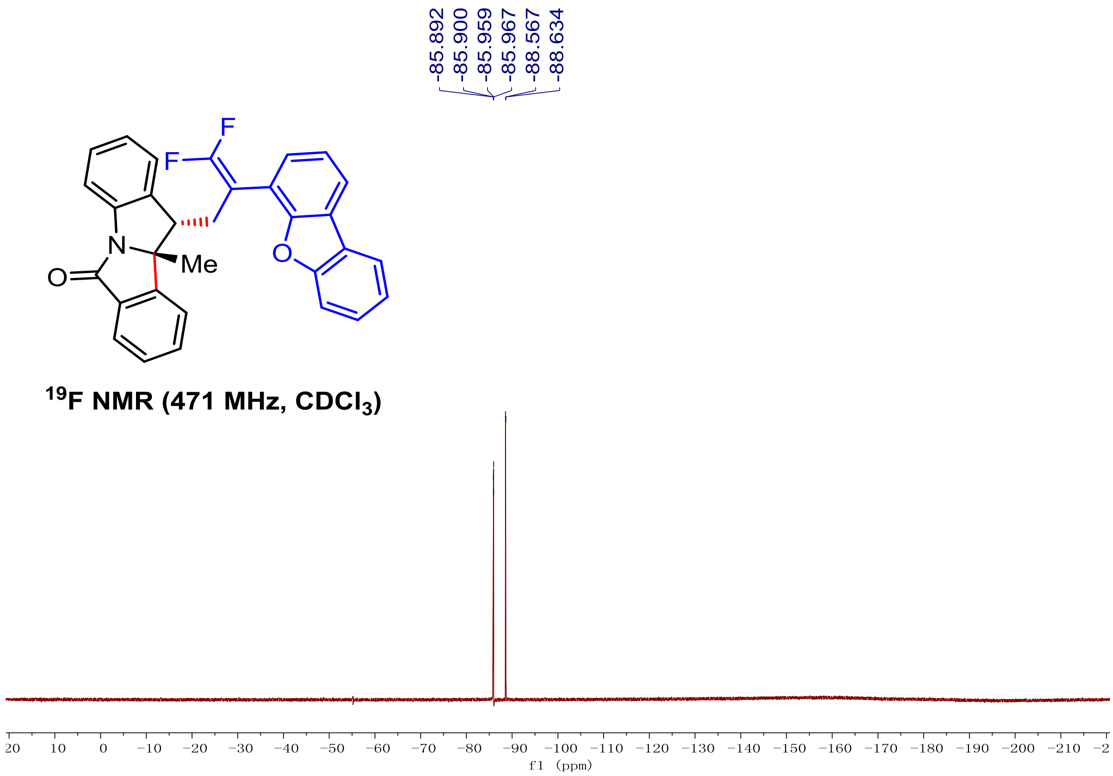


$^{19}$F NMR (471 MHz, CDCl$_3$)

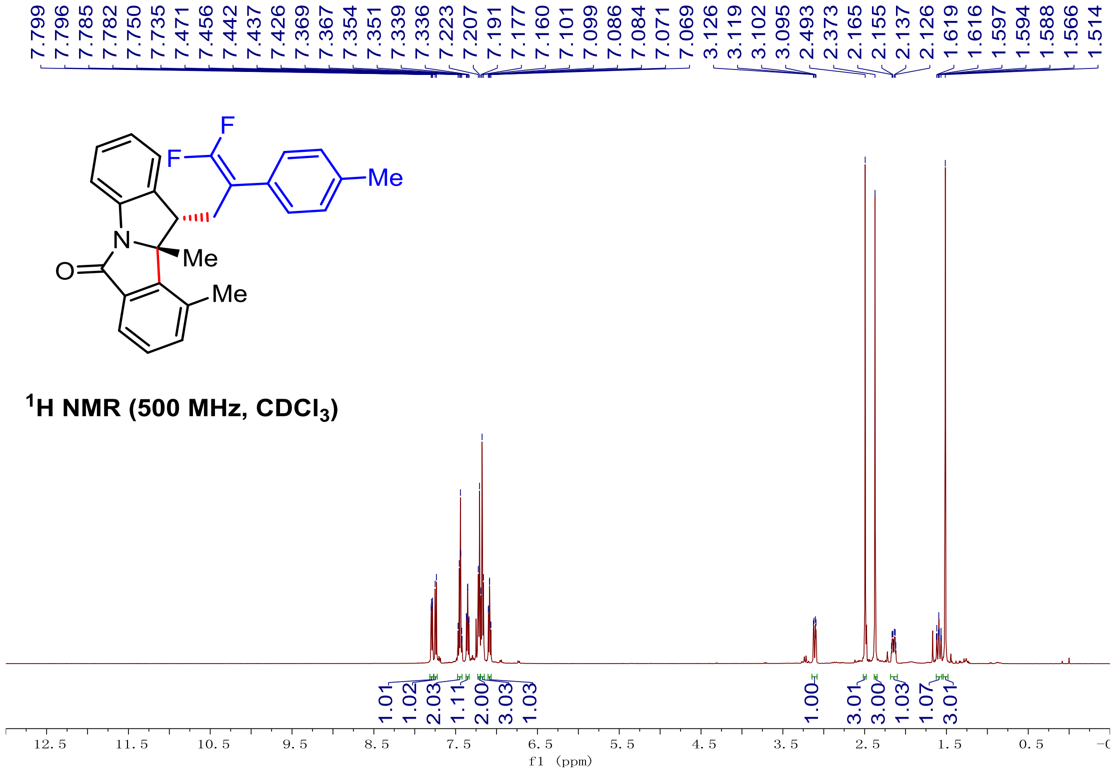
## (10b*R*,11*S*)-11-(2-(Dibenzo[*b*,*d*]furan-4-yl)-3,3-difluoroallyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 27

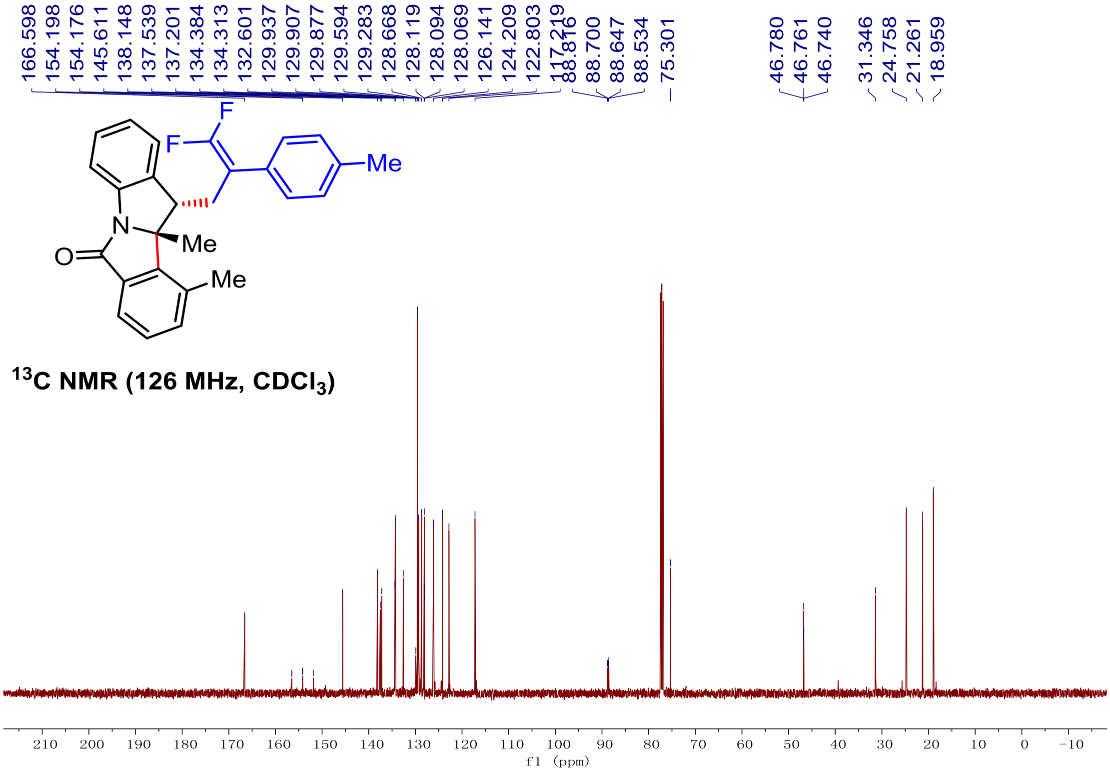




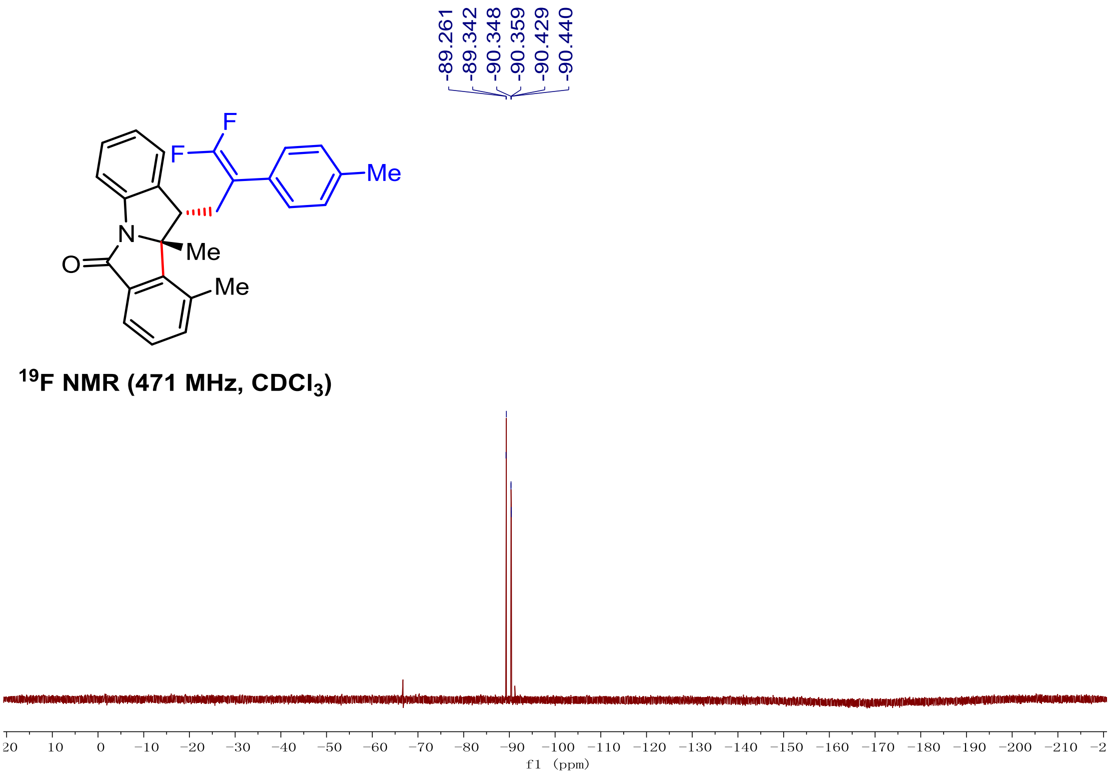


## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-10,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 28



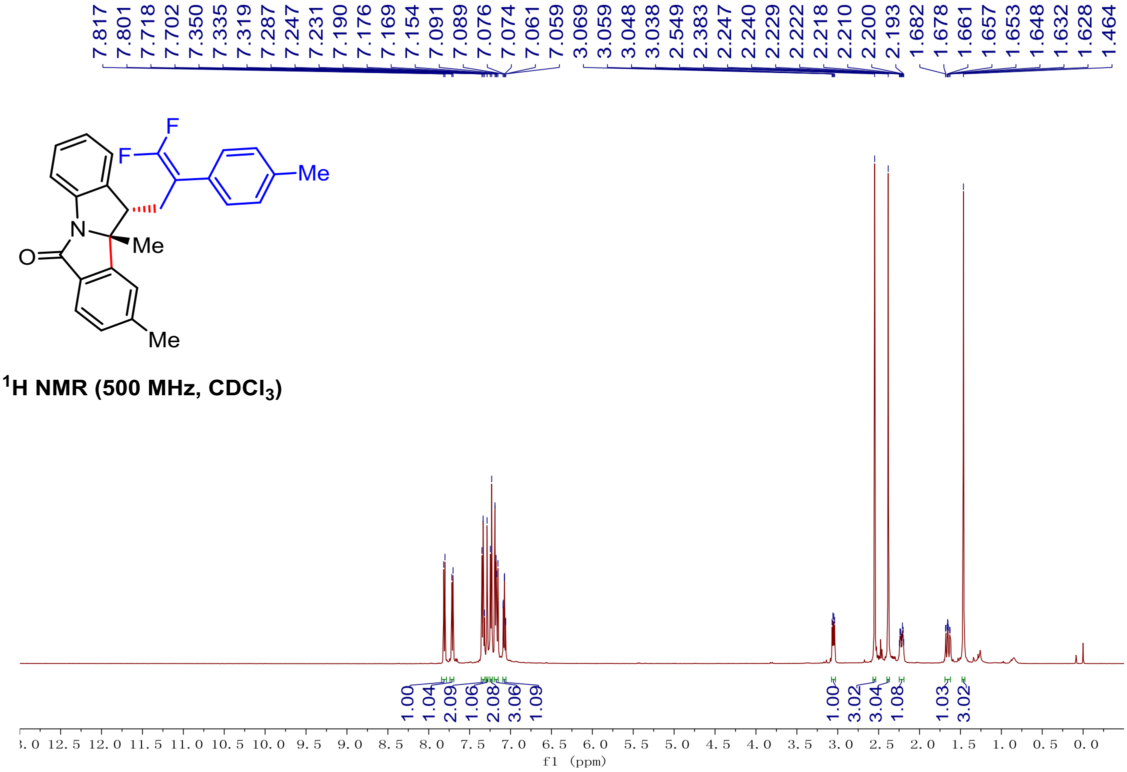


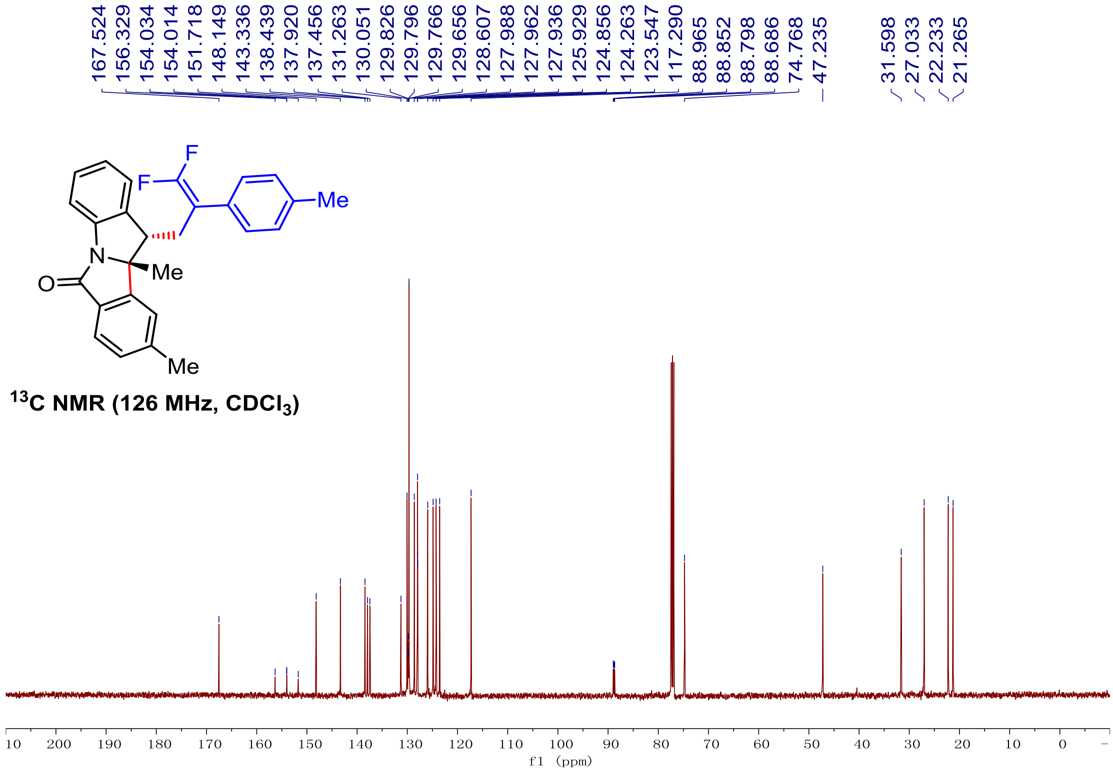
$^{13}$C NMR (126 MHz, CDCl$_3$)

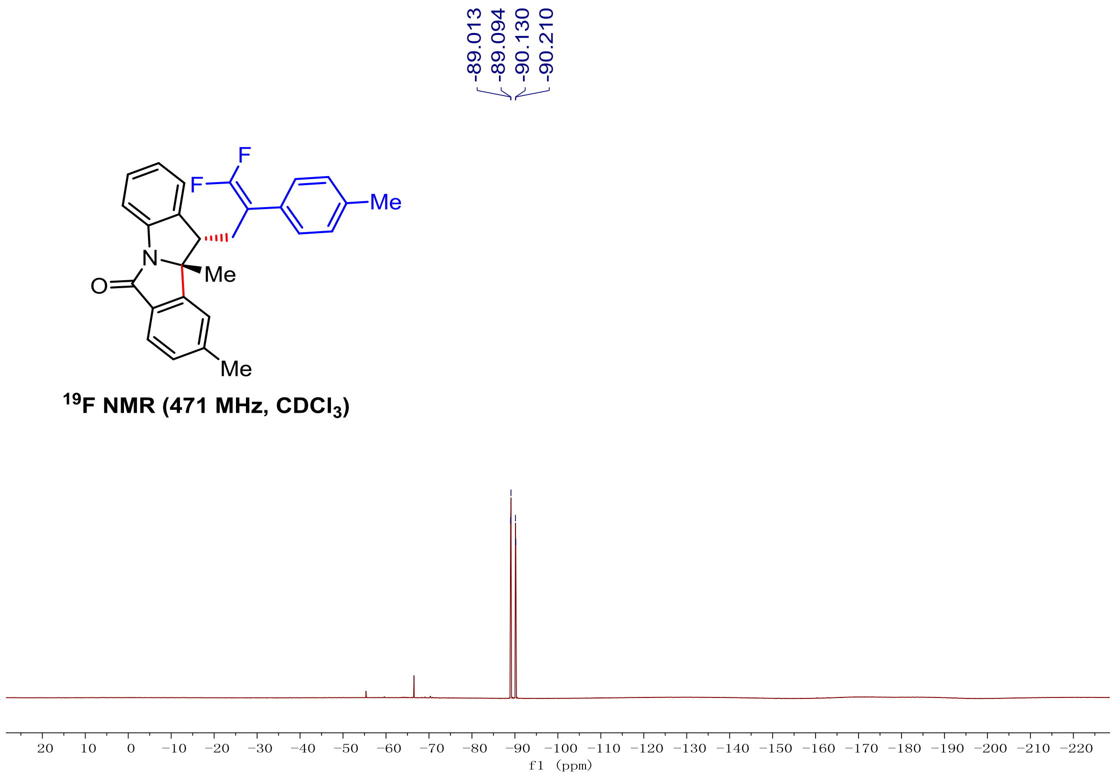


$^{19}$F NMR (471 MHz, CDCl$_3$)

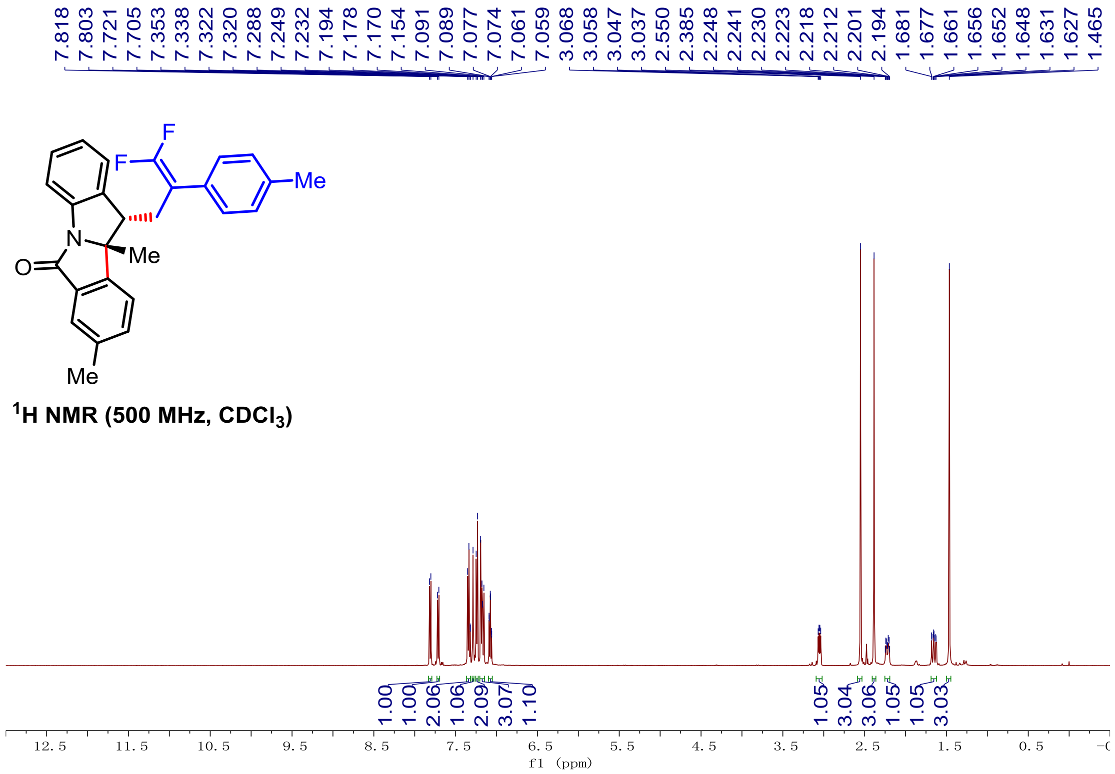
## (10b*R*,11*S)*-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-9,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 29

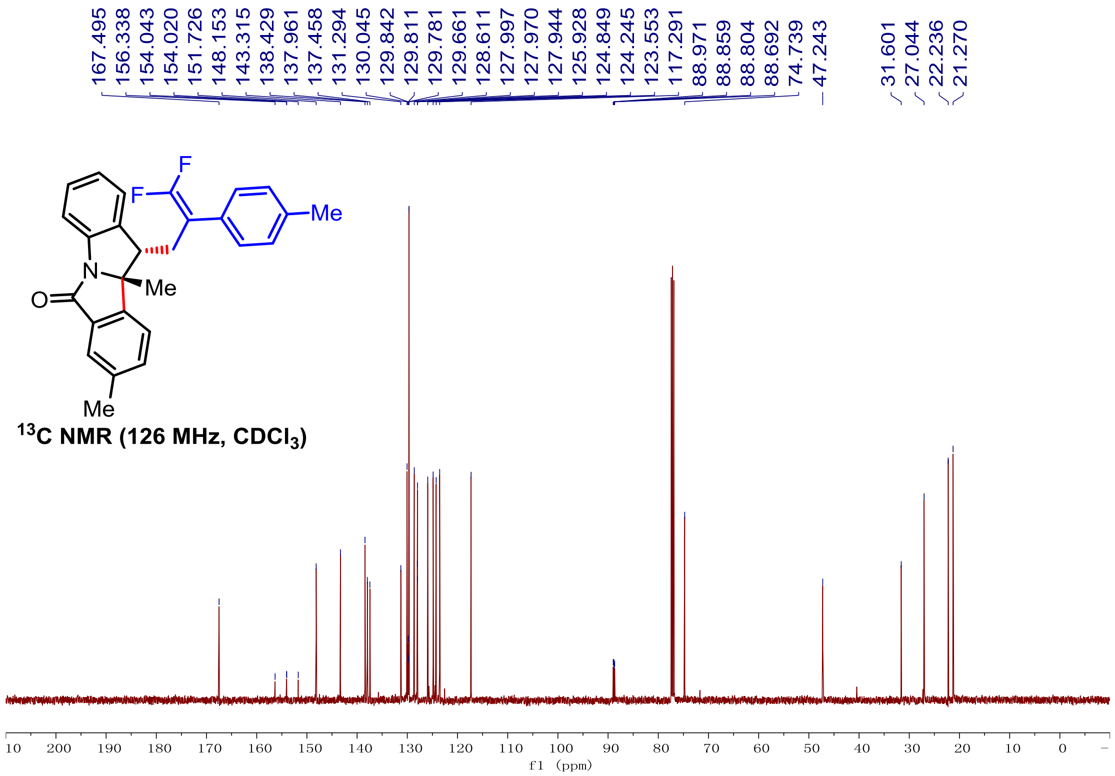


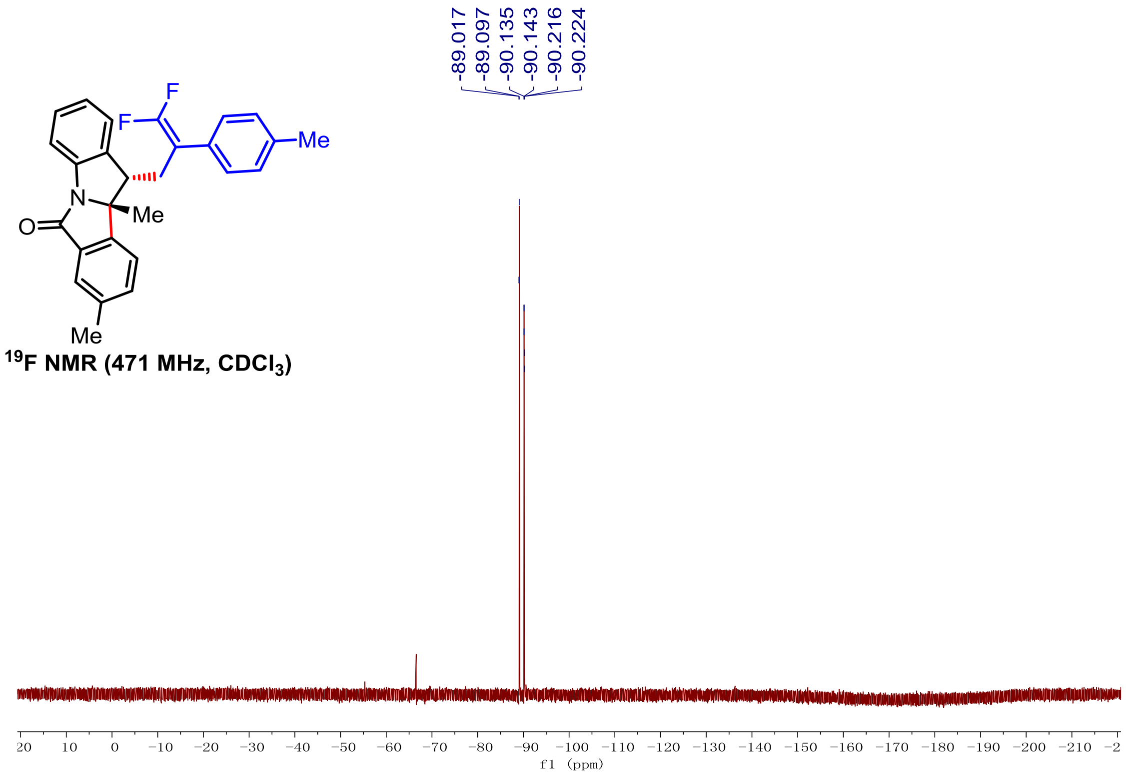




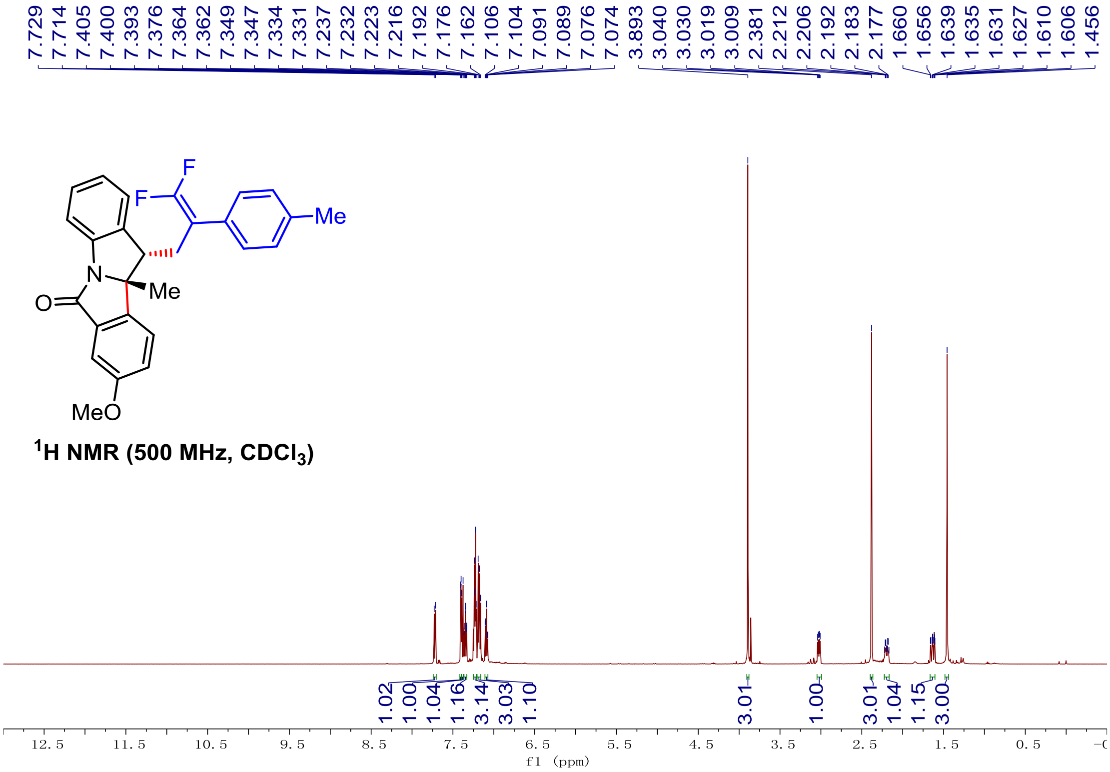
## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-8,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 30



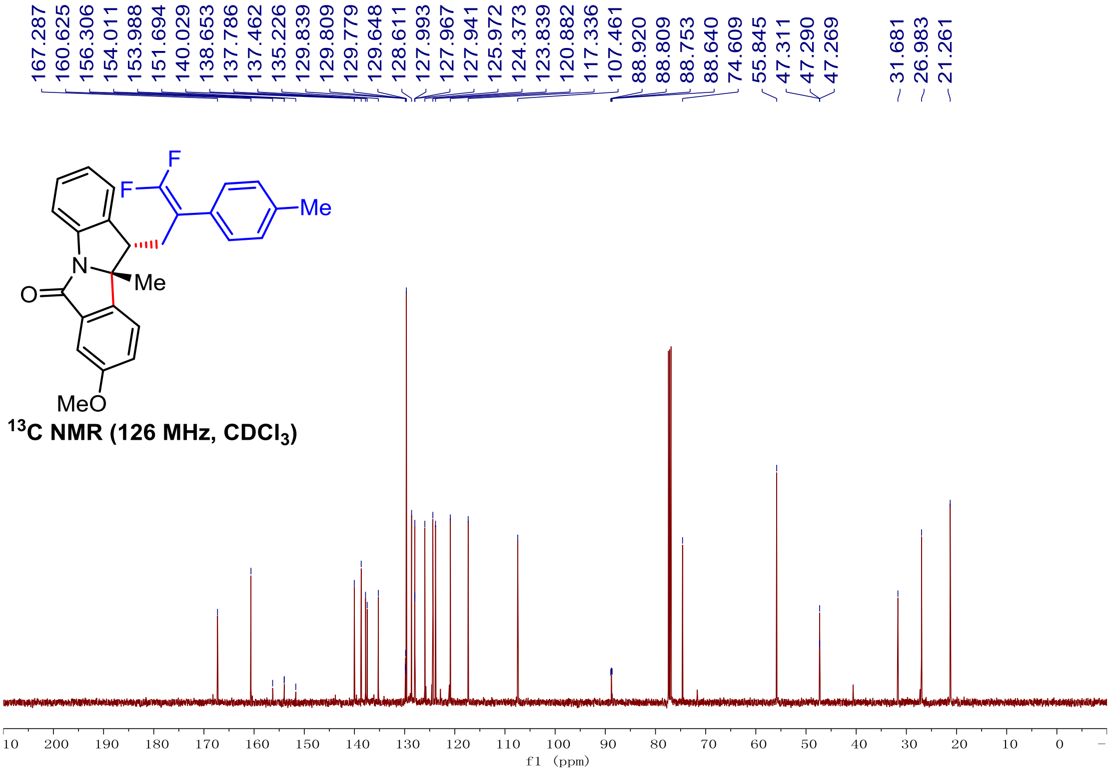

167.495
156.338
154.043
154.020
151.726
148.153
143.315
138.429
137.961
137.458
131.294
130.045
129.842
129.811
129.781
129.661
128.611
127.997
127.970
127.944
125.928
124.849
124.245
123.553
117.291
88.971
88.859
88.804
88.692
74.739
47.243
31.601
27.044
22.236
21.270
F
F
Me
N
Me
O
Me
$^{13}$C NMR (126 MHz, CDCl$_3$)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-89.017
-89.097
-90.135
-90.143
-90.216
-90.224
F
F
Me
N
Me
O
Me
$^{19}$F NMR (471 MHz, CDCl$_3$)
20
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
−2
f1 (ppm)

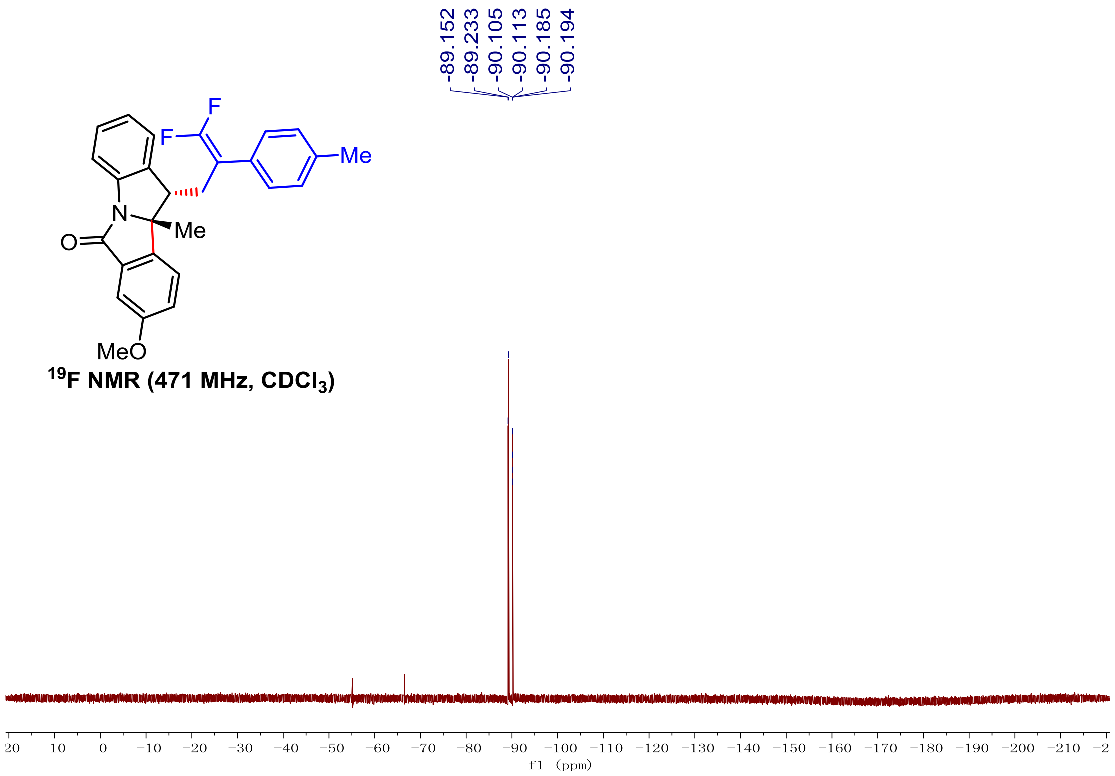
**(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-8-methoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 31**



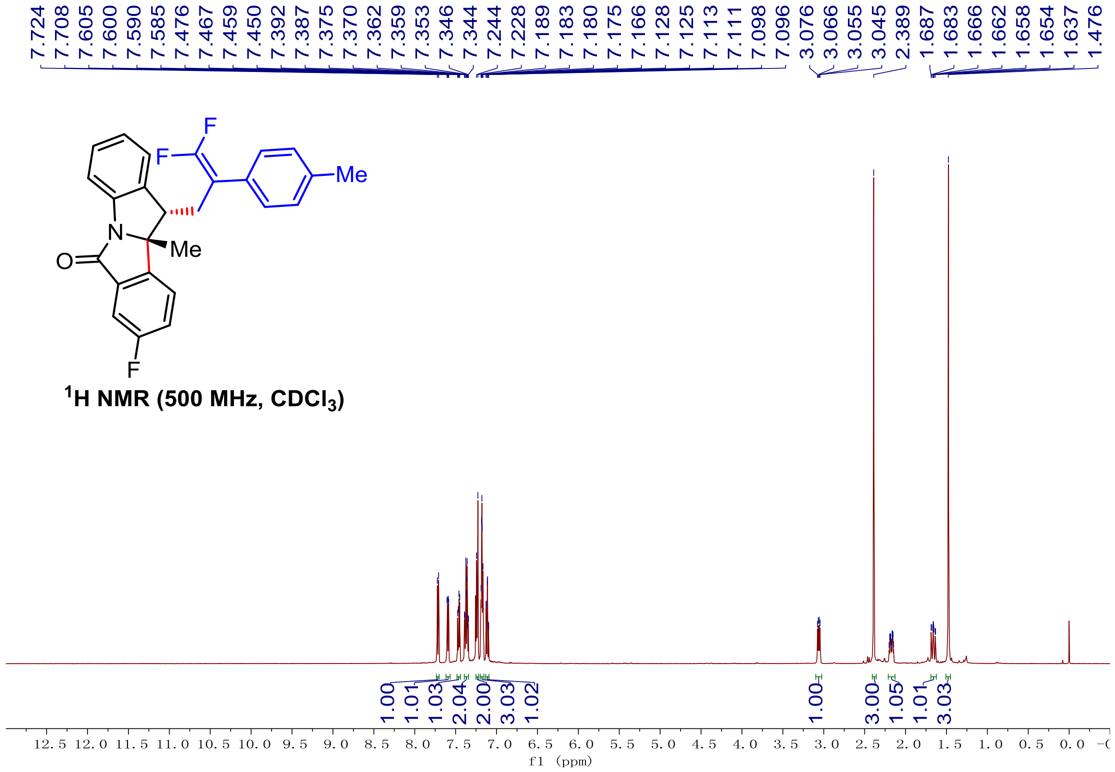
$^{1}$H NMR (500 MHz, CDCl$_3$)

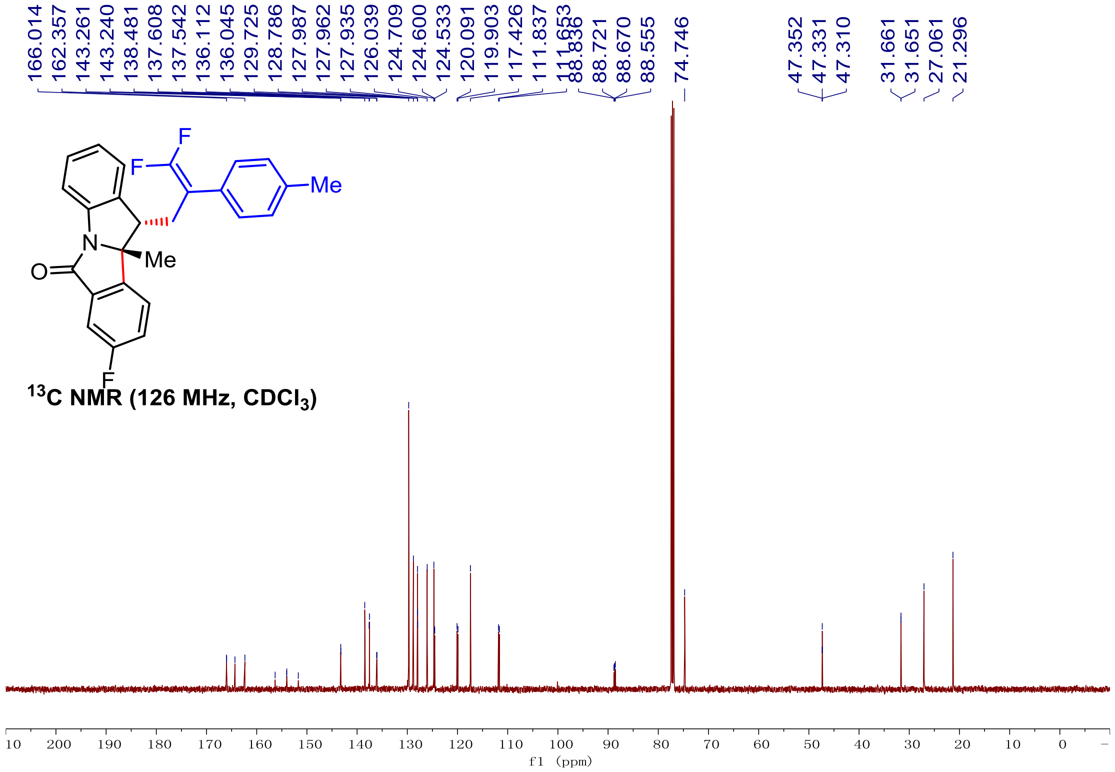


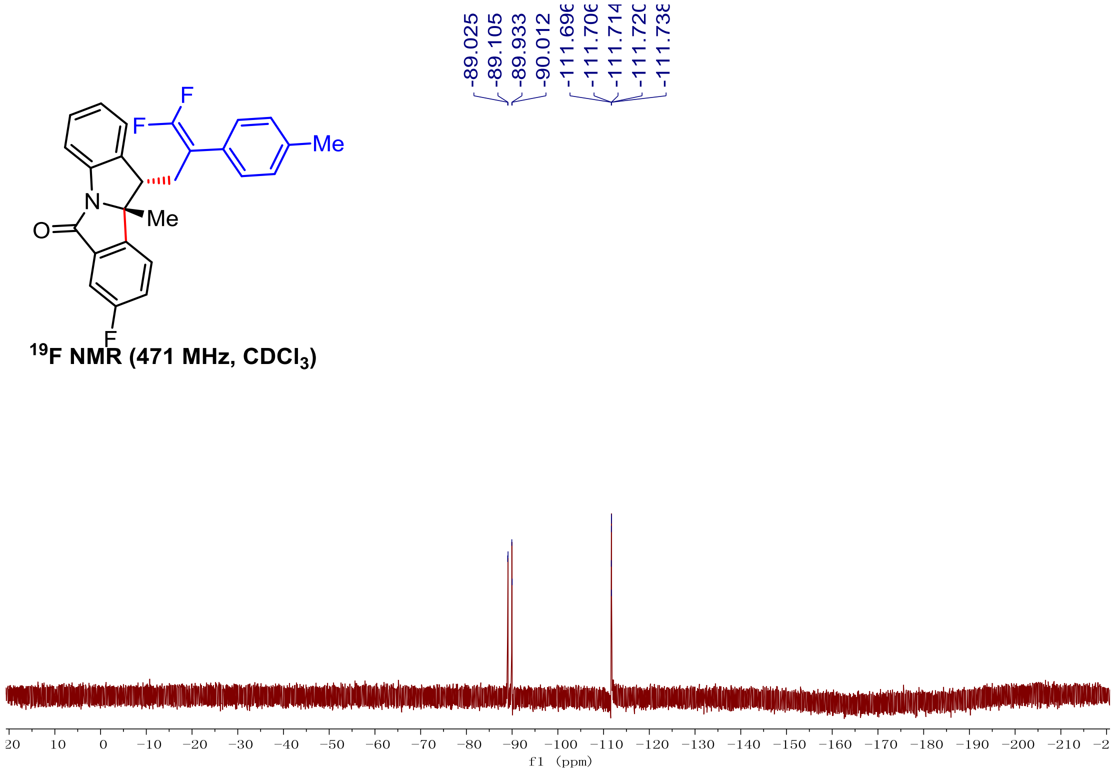
$^{13}$C NMR (126 MHz, CDCl$_3$)



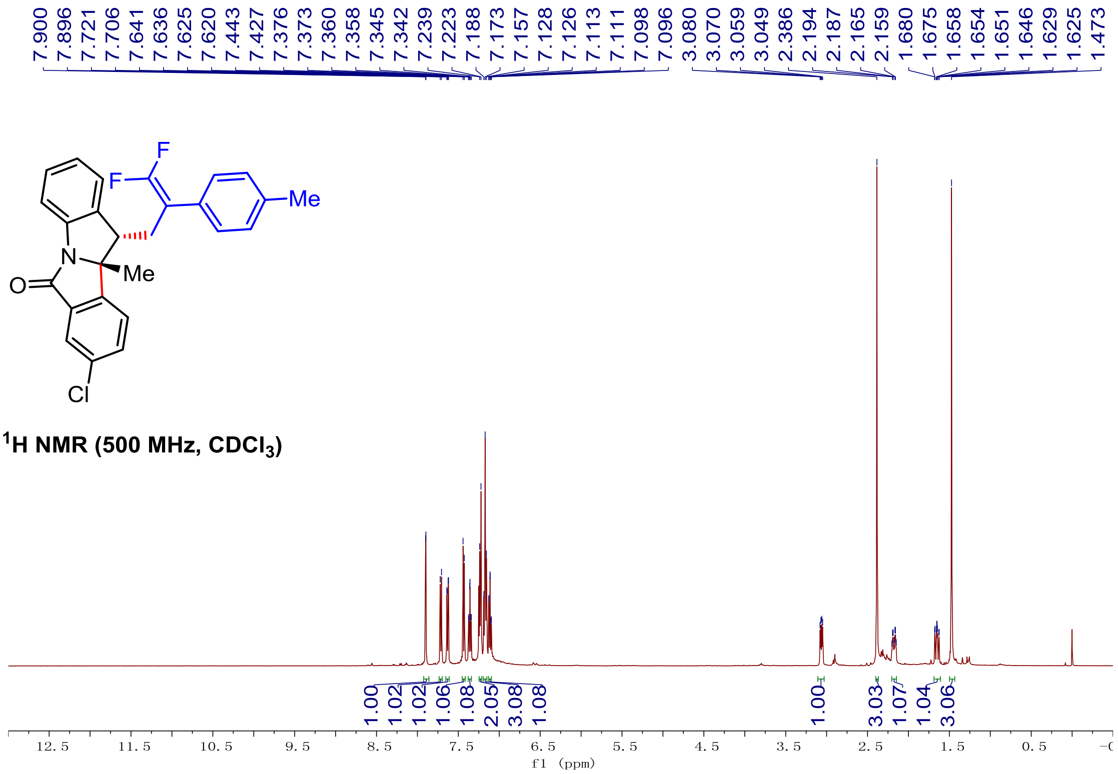
## **(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-8-fluoro-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 32**



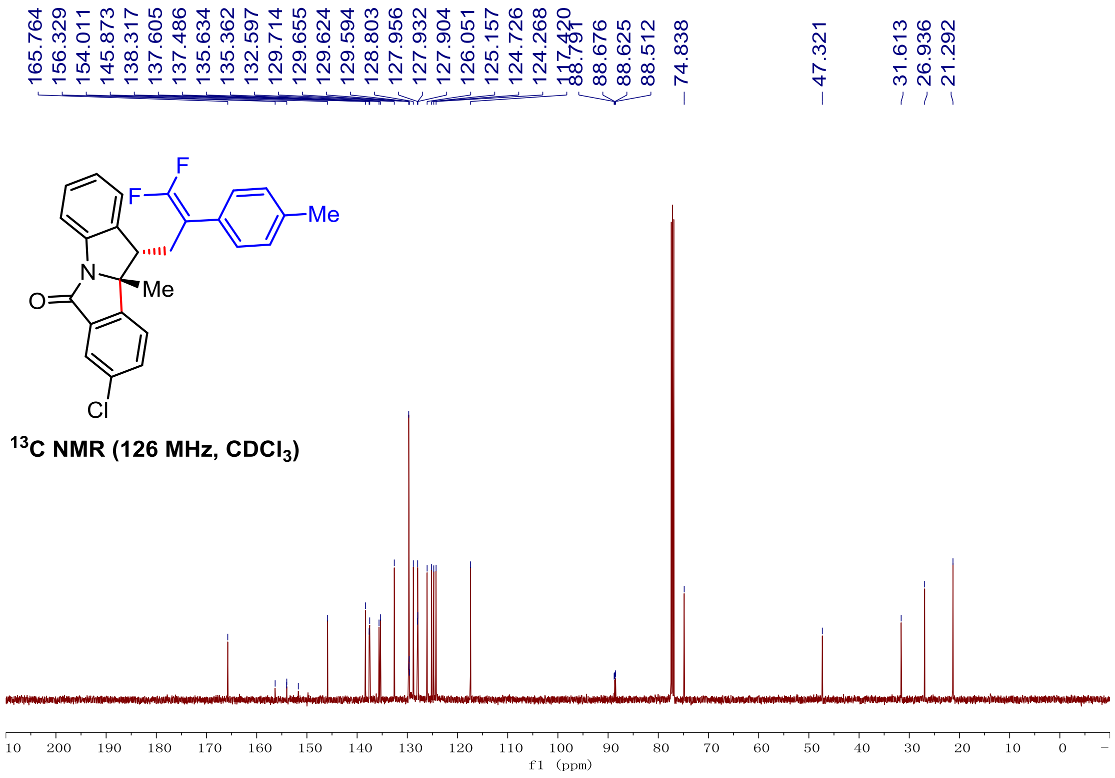

166.014
162.357
143.261
143.240
138.481
137.608
137.542
136.112
136.045
129.725
128.786
127.987
127.962
127.935
126.039
124.709
124.600
124.533
120.091
119.903
117.426
111.837
111.653
88.836
88.721
88.670
88.555
74.746
47.352
47.331
47.310
31.661
31.651
27.061
21.296
F
F
Me
N
Me
O
F
13C NMR (126 MHz, CDCl3)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-89.025
-89.105
-89.933
-90.012
-111.696
-111.706
-111.714
-111.720
-111.738
F
F
Me
N
Me
O
F
19F NMR (471 MHz, CDCl3)
20
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

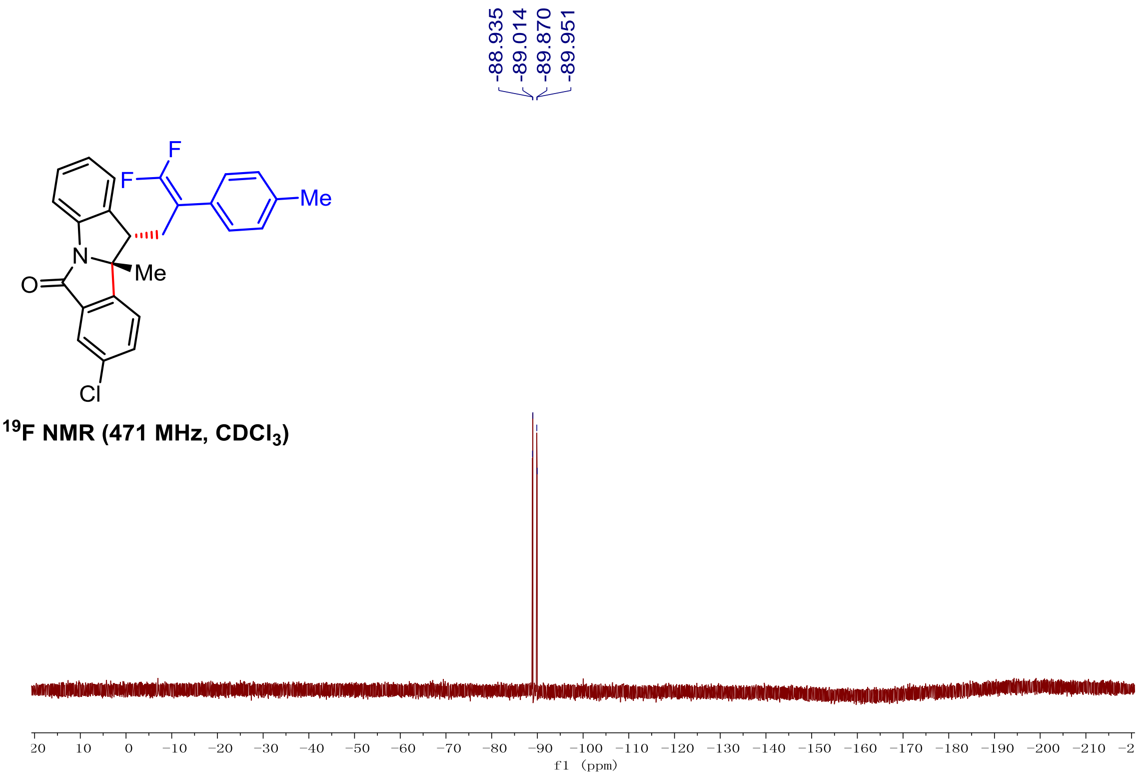
## (10b*R*,11*S*)-8-Chloro-11-(3,3-difluoro-2-(*p*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 33



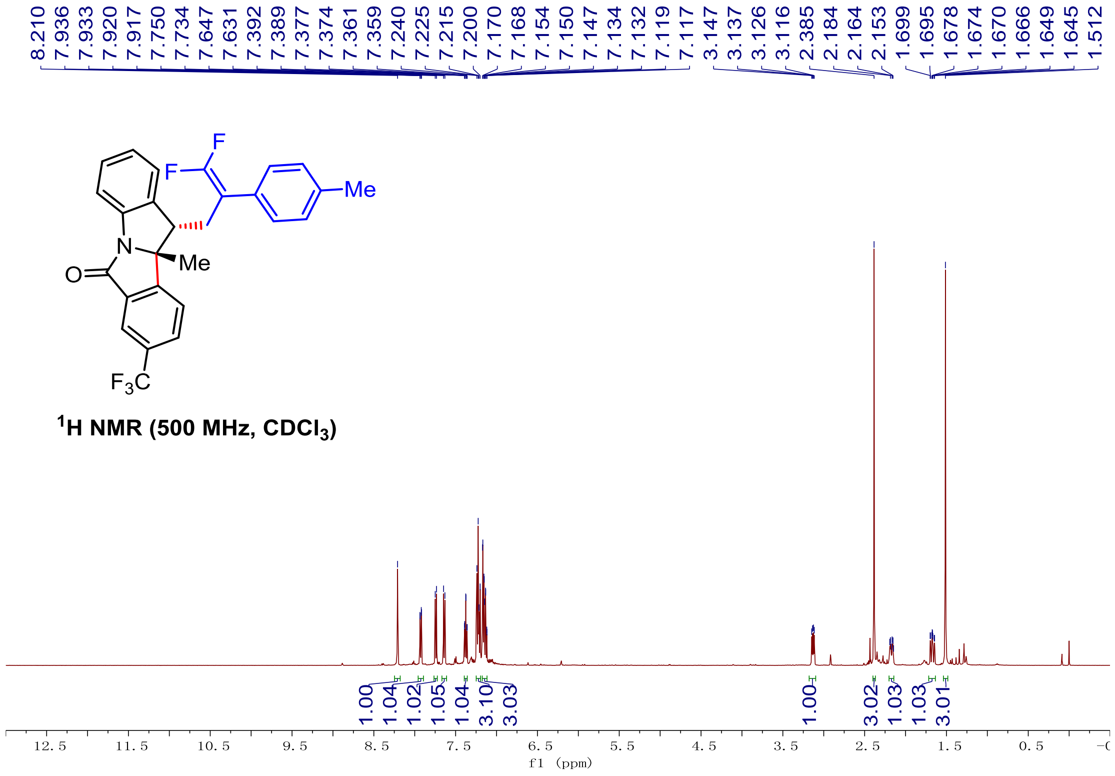
**$^1$H NMR (500 MHz, CDCl$_3$)**

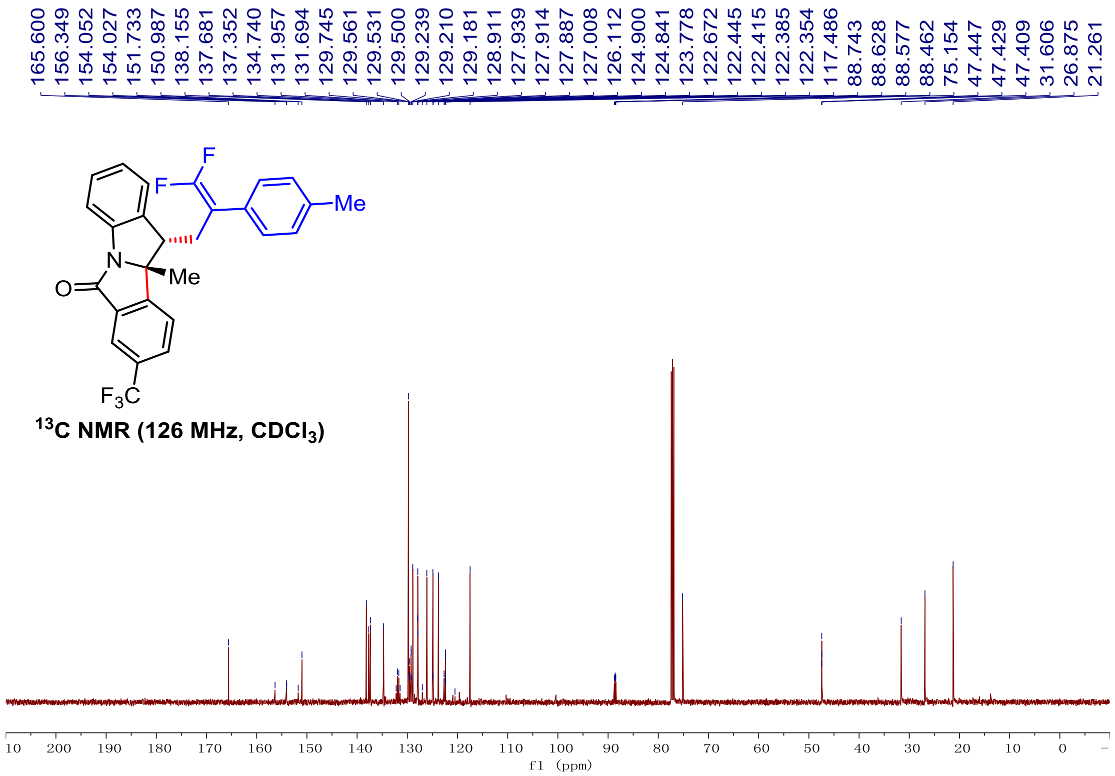


**$^{13}$C NMR (126 MHz, CDCl$_3$)**



## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-10b-methyl-8-(trifluoromethyl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 34

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156.349
154.052
154.027
151.733
150.987
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137.681
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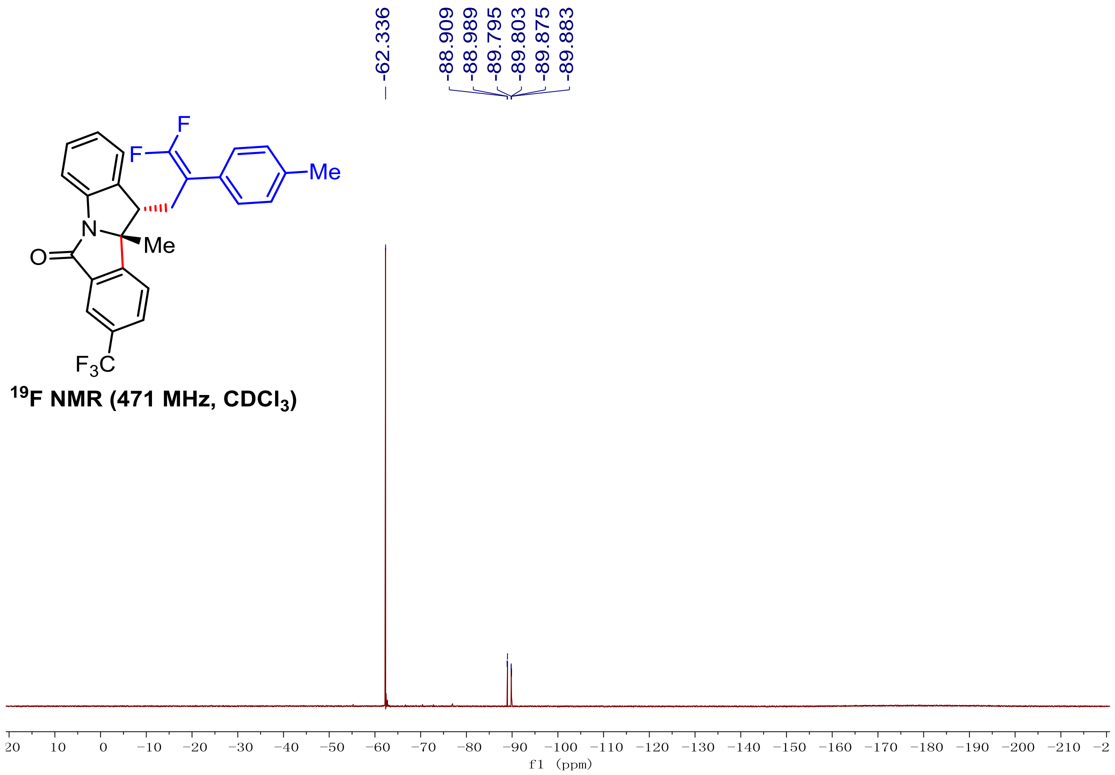
131.694
129.745
129.561
129.531
129.500
129.239
129.210
129.181
128.911
127.939
127.914
127.887
127.008
126.112
124.900
124.841
123.778
122.672
122.445
122.415
122.385
122.354
117.486
88.743
88.628
88.577
88.462
75.154
47.447
47.429
47.409
31.606
26.875
21.261
F
F
Me
N
Me
O
F3C
13C NMR (126 MHz, CDCl3)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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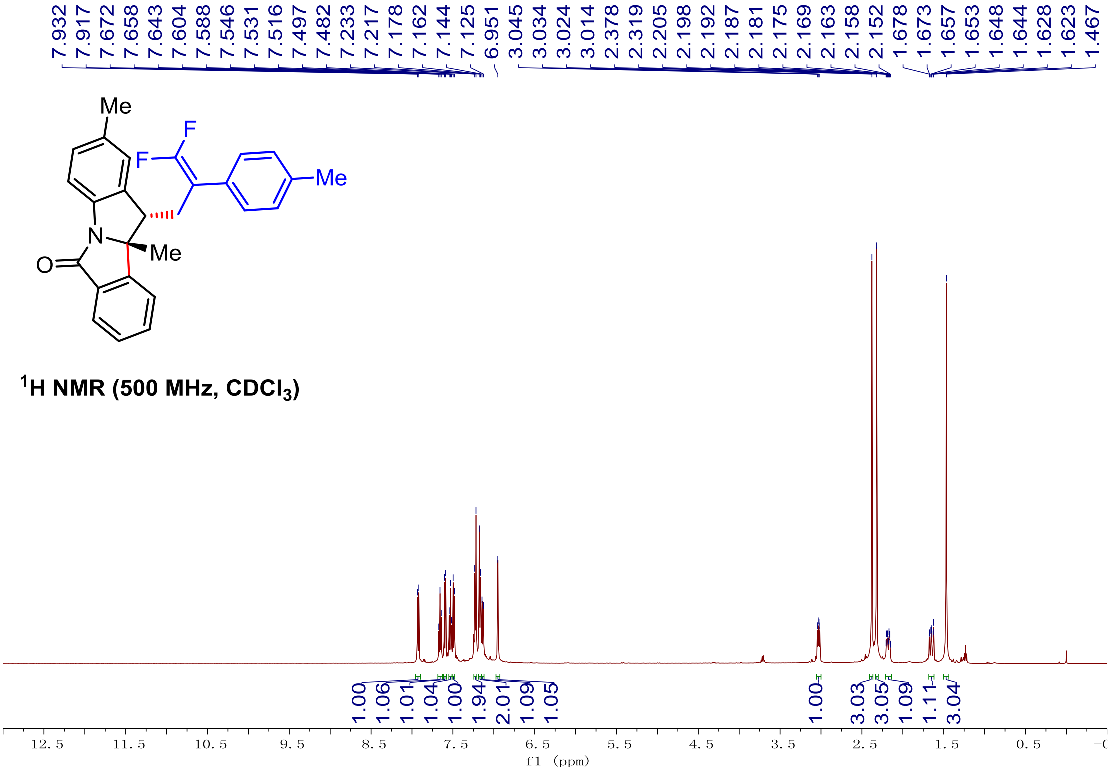
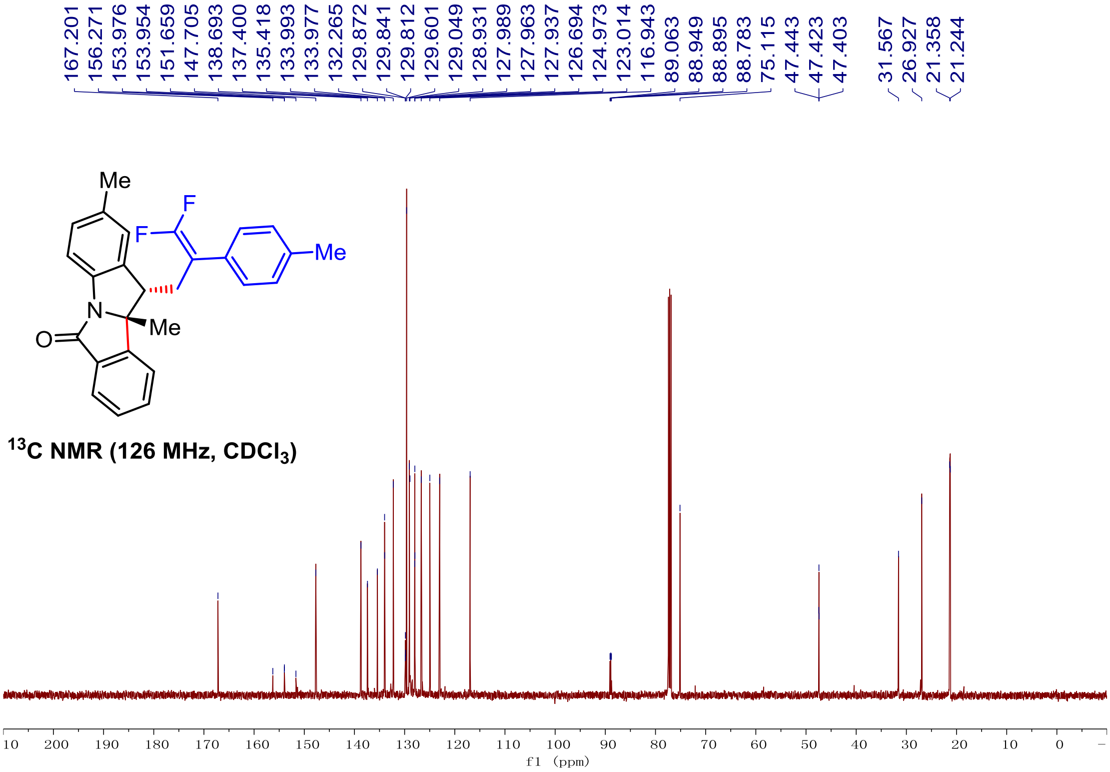
-88.909
-88.989
-89.795
-89.803
-89.875
-89.883
F
F
Me
N
Me
O
F3C
19F NMR (471 MHz, CDCl3)
20
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
−2
f1 (ppm)

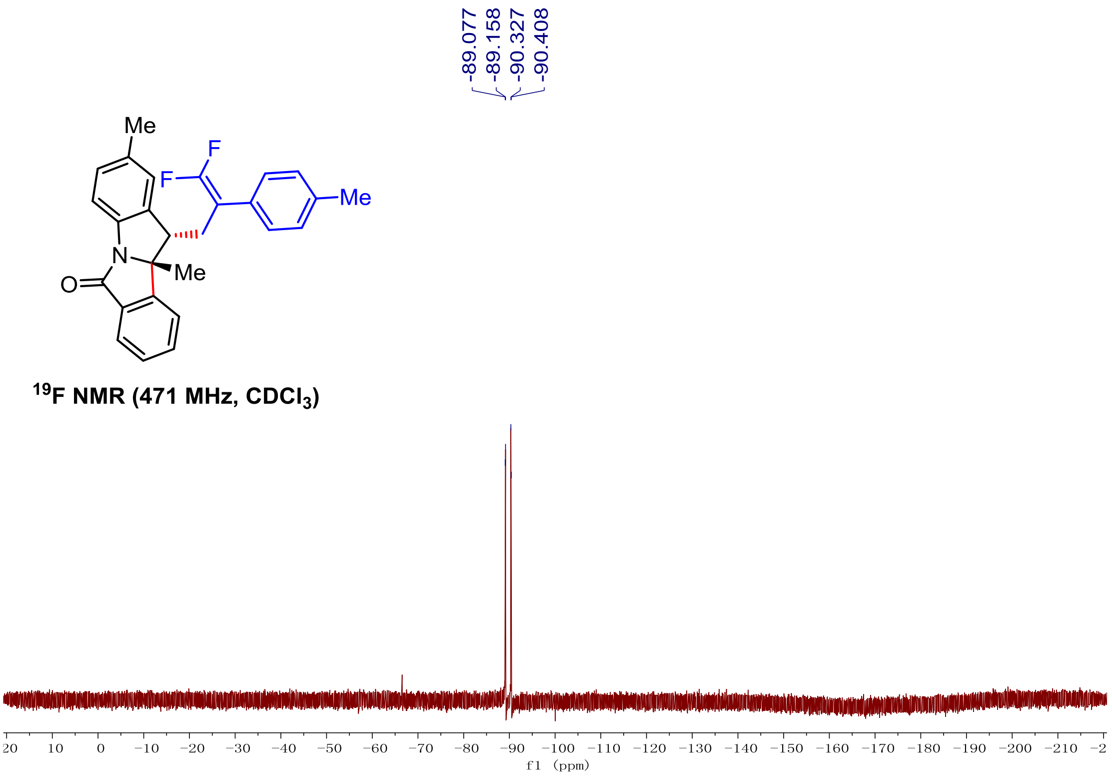
## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-2,10b-dimethyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 35



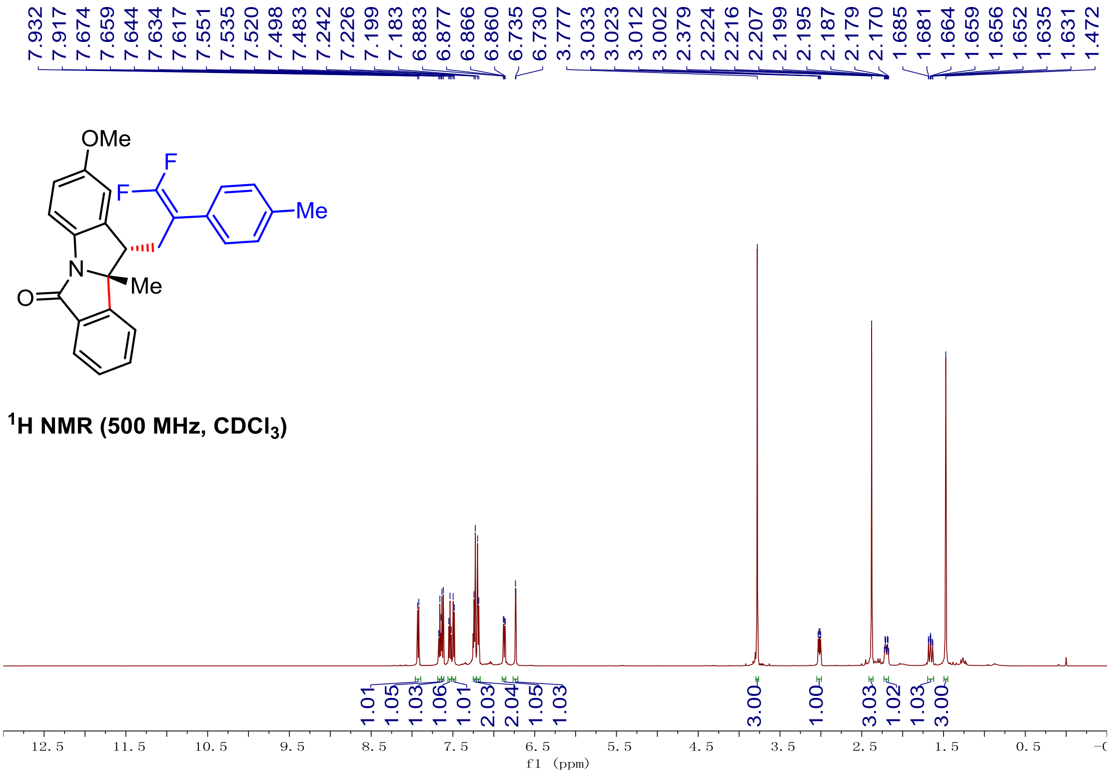
**$^{1}H$ NMR (500 MHz, $CDCl_3$)**

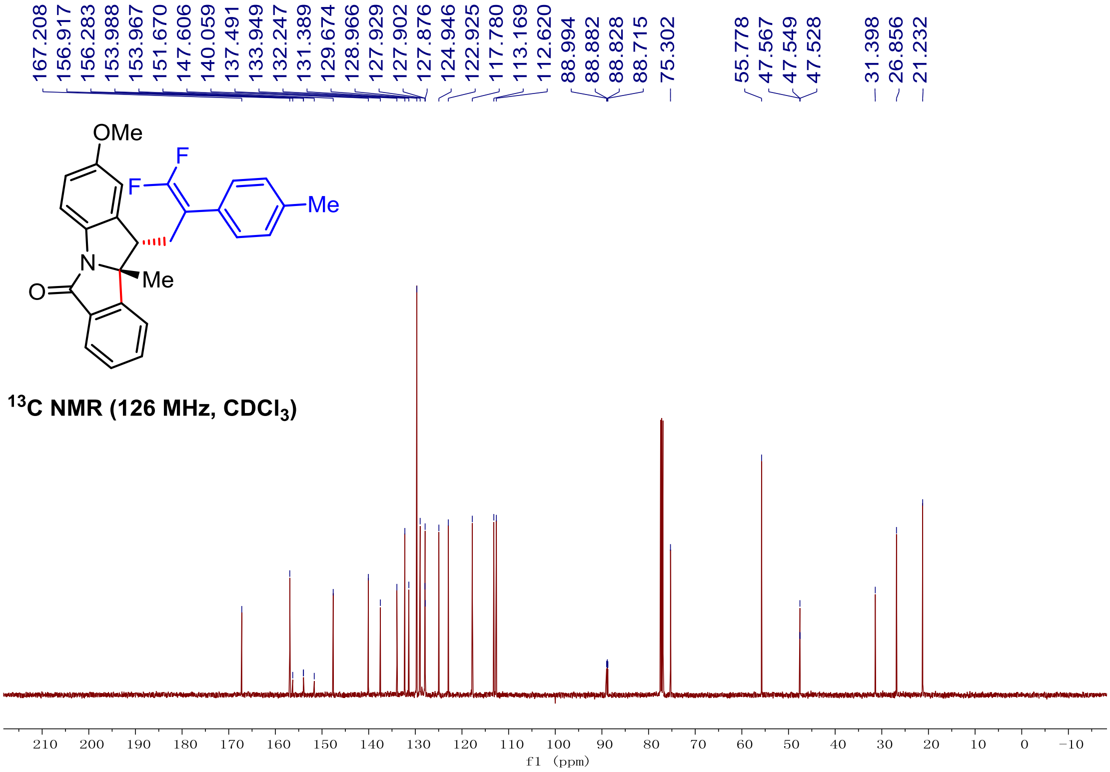


**$^{13}C$ NMR (126 MHz, $CDCl_3$)**

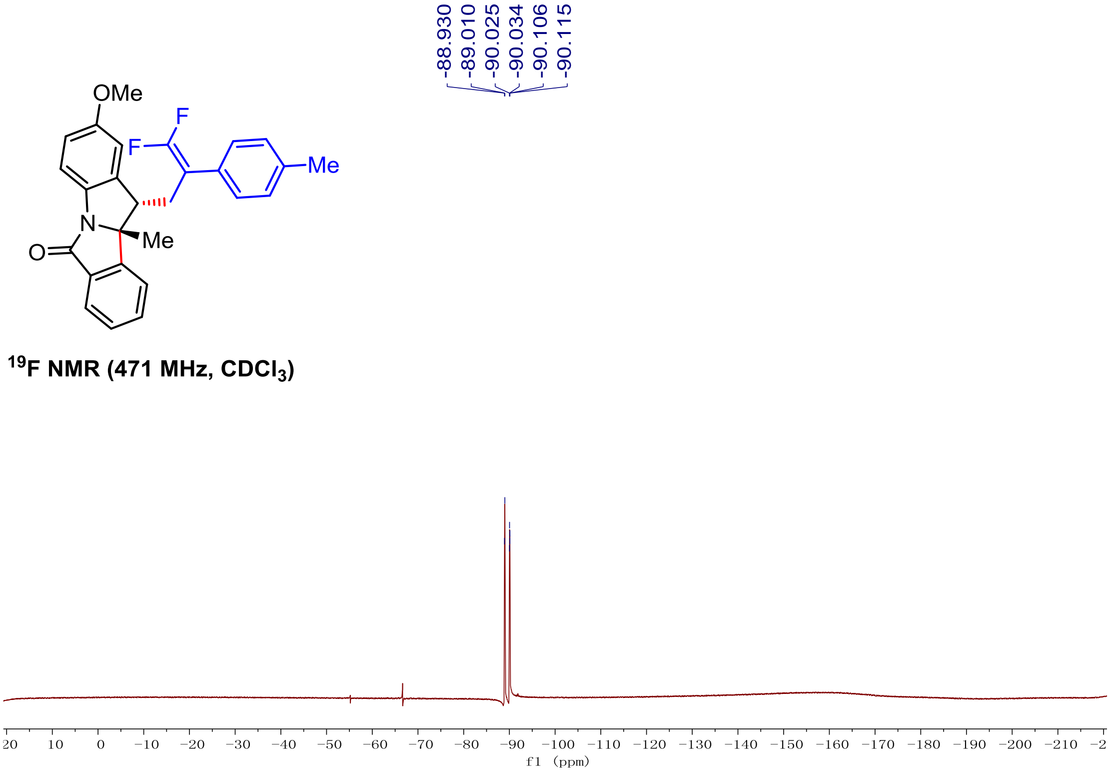


## **(10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-2-methoxy-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 36**



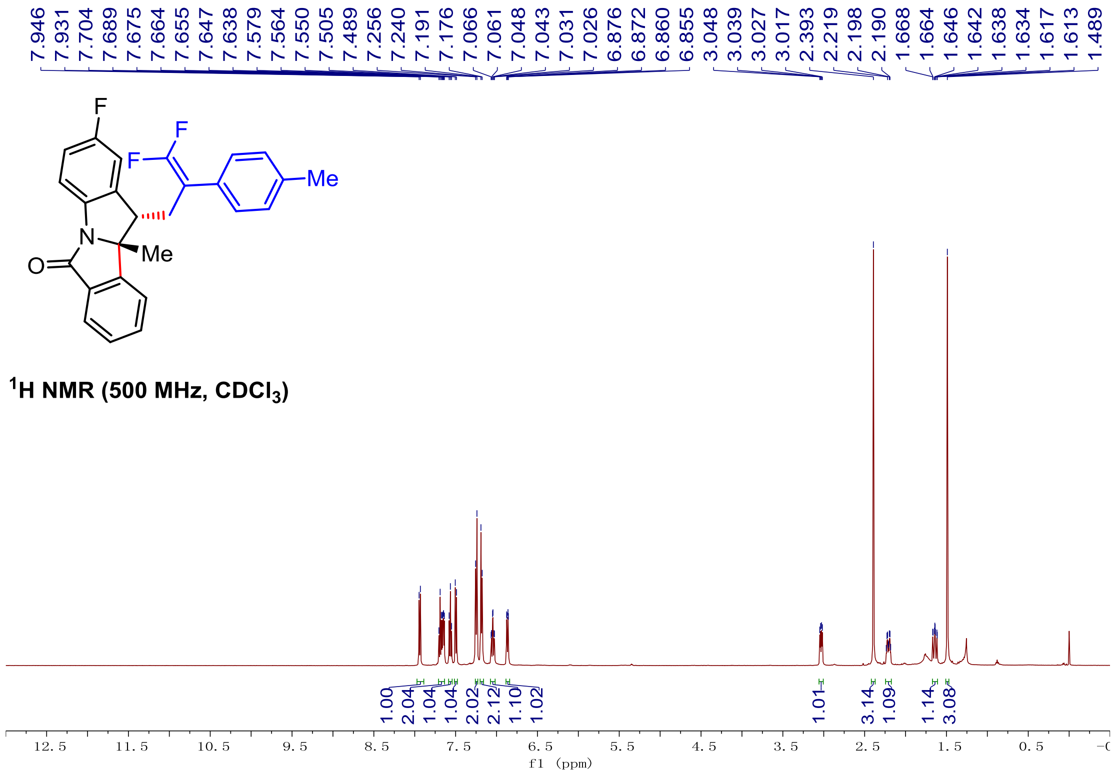


**$^{13}$C NMR (126 MHz, CDCl$_3$)**

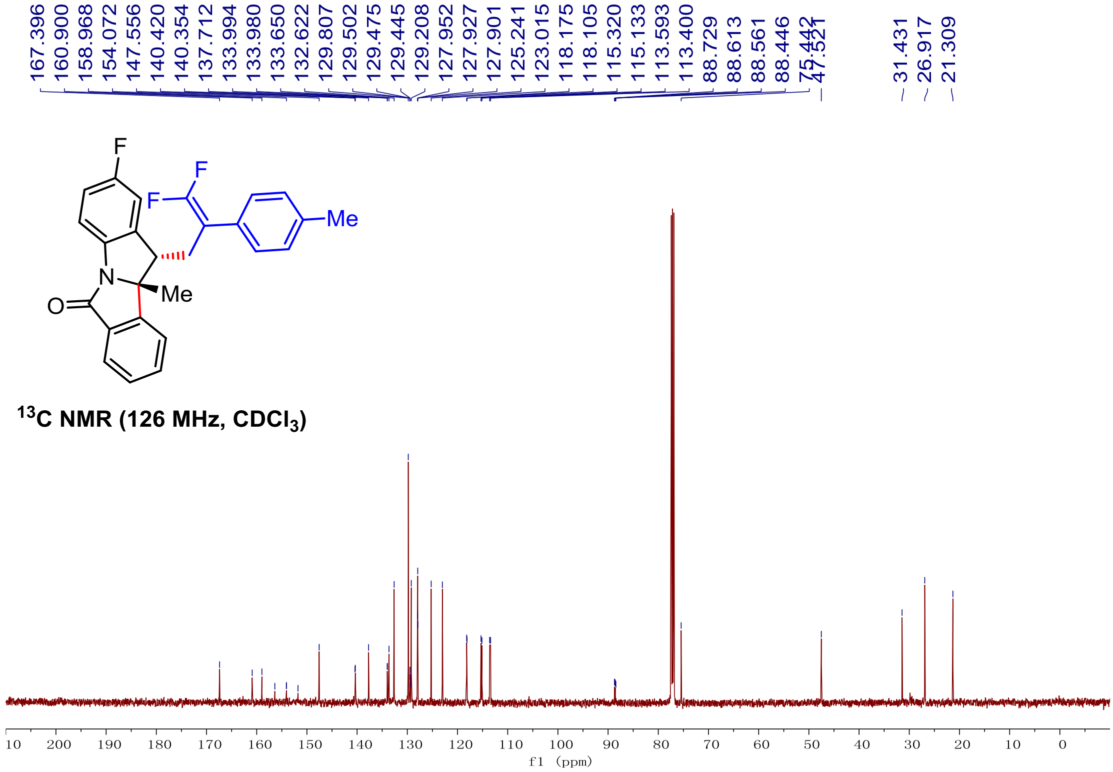


**$^{19}$F NMR (471 MHz, CDCl$_3$)**

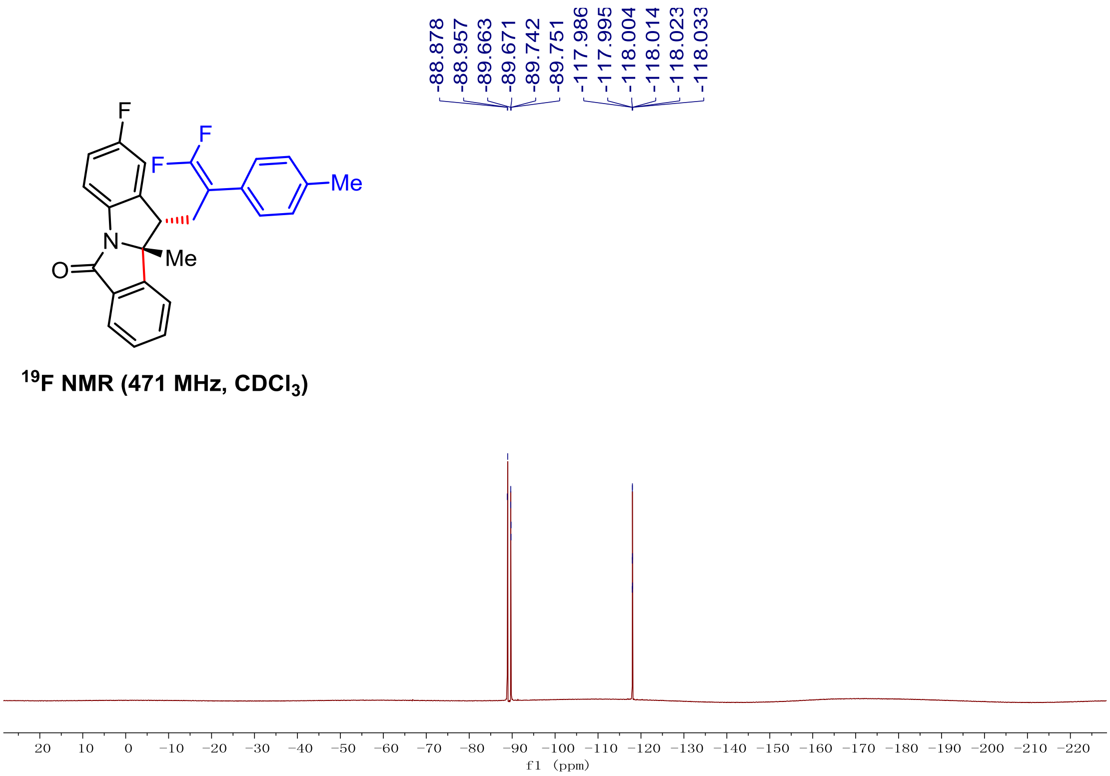
## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-2-fluoro-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 37



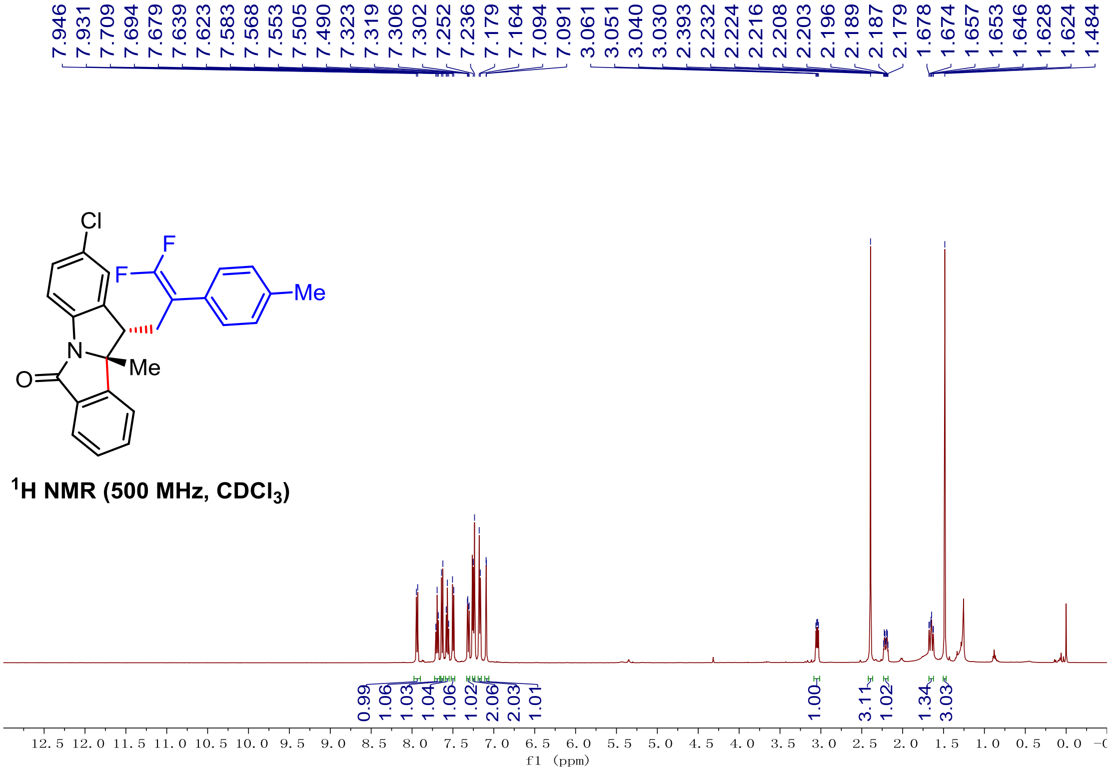
$^1$H NMR (500 MHz, CDCl$_3$)

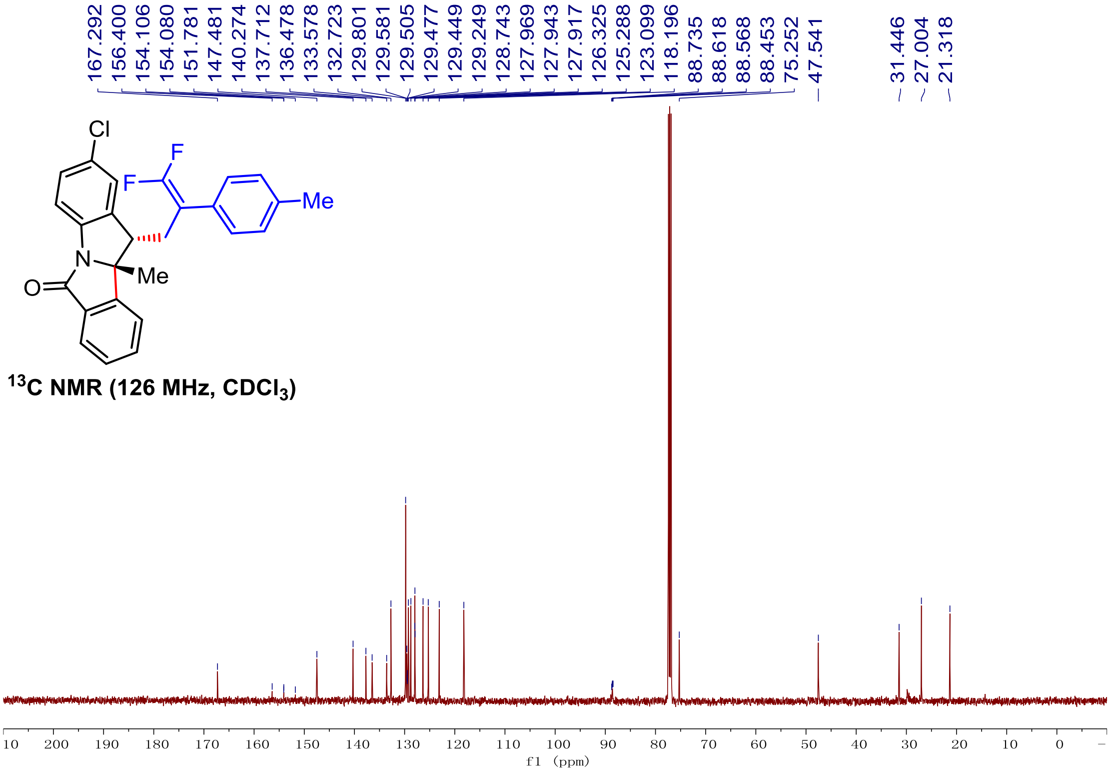


$^{13}$C NMR (126 MHz, CDCl$_3$)

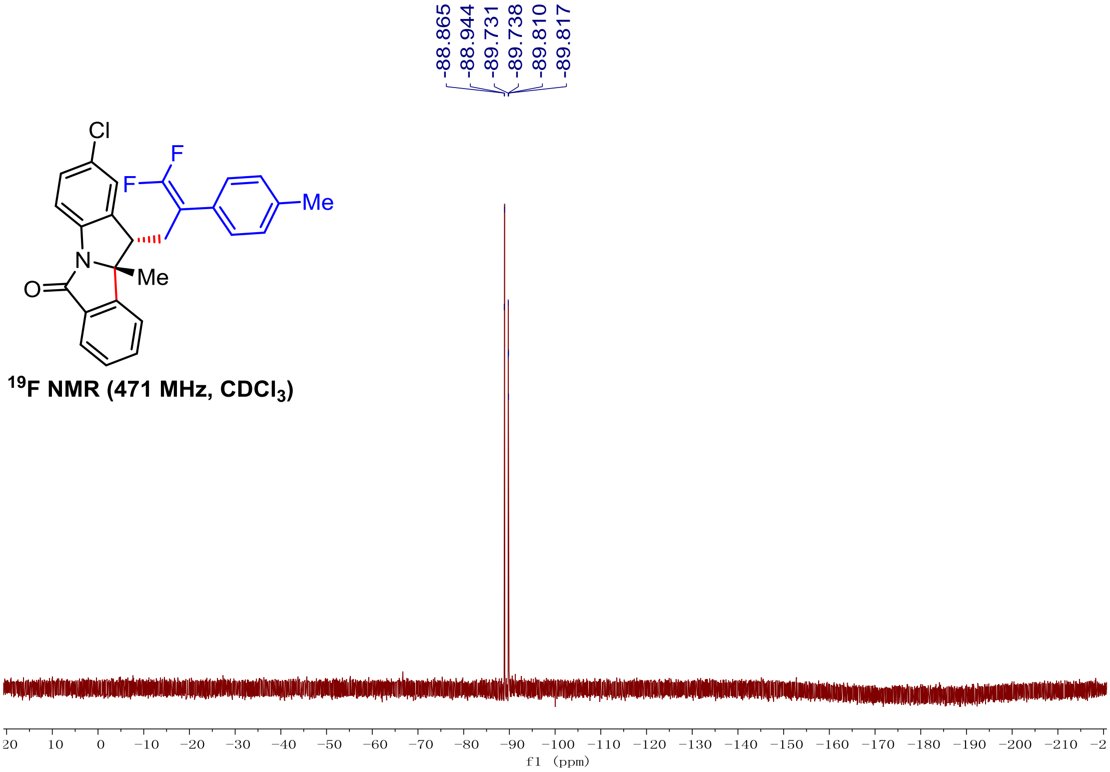


## (10b*R*,11*S*)-2-Chloro-11-(3,3-difluoro-2-(*p*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 38



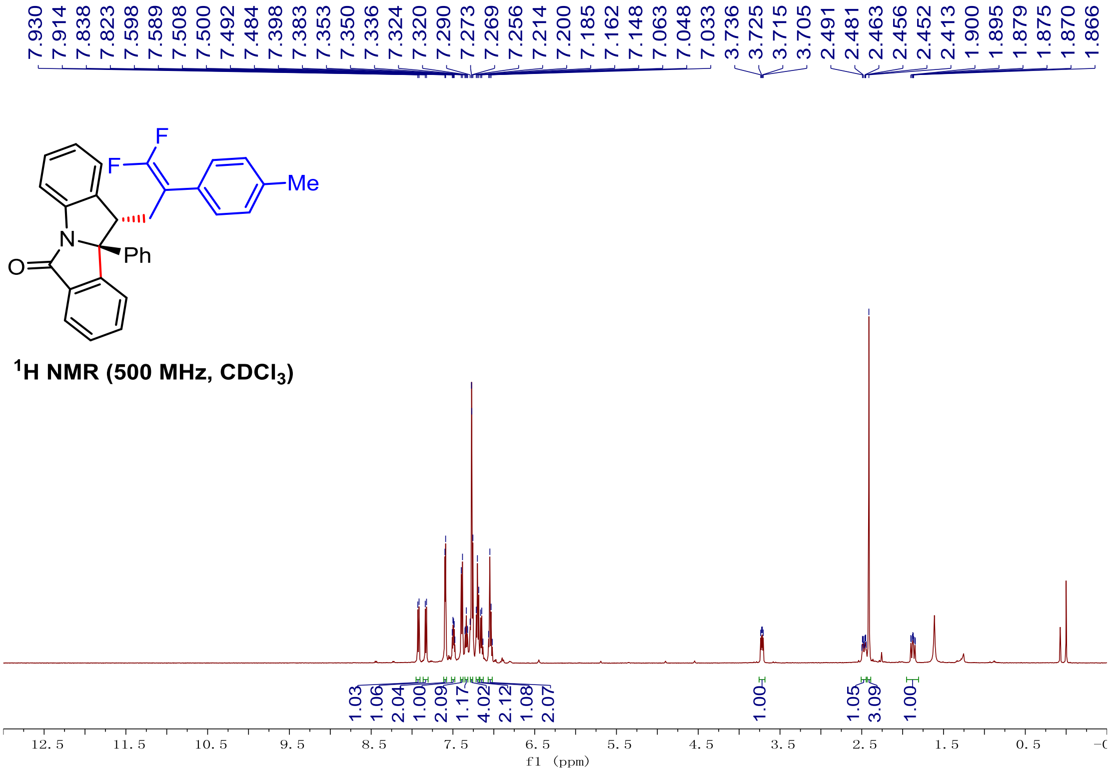


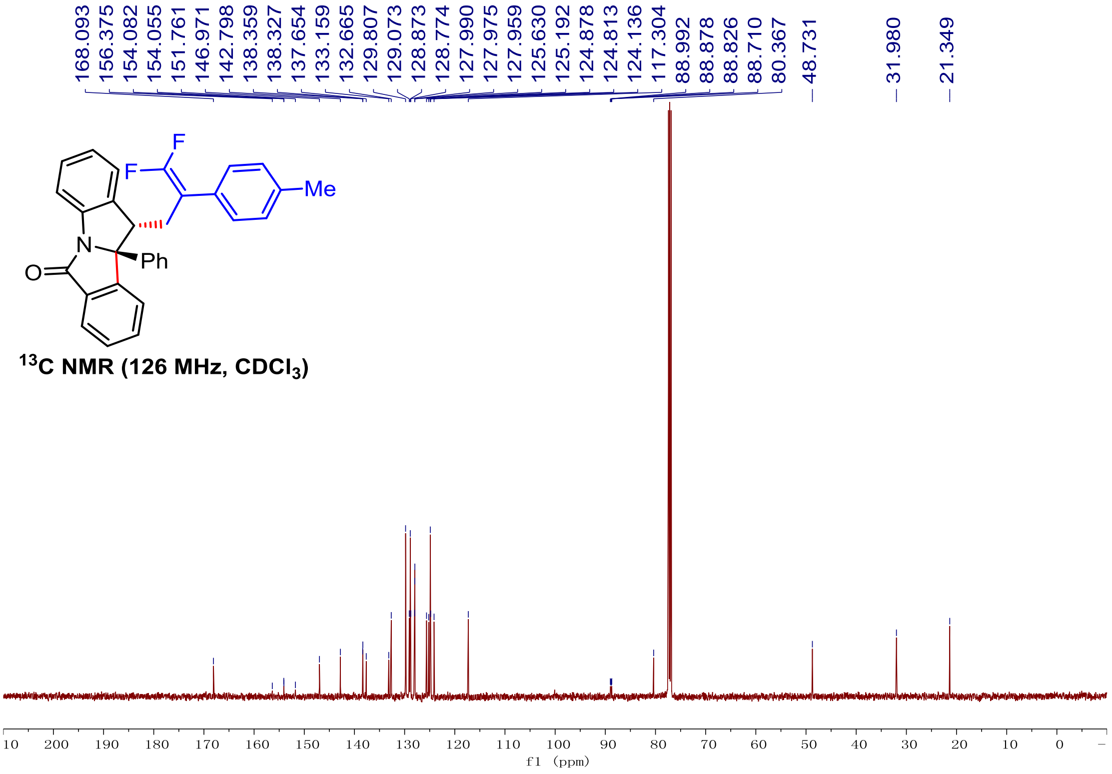
$^{13}$C NMR (126 MHz, CDCl$_3$)

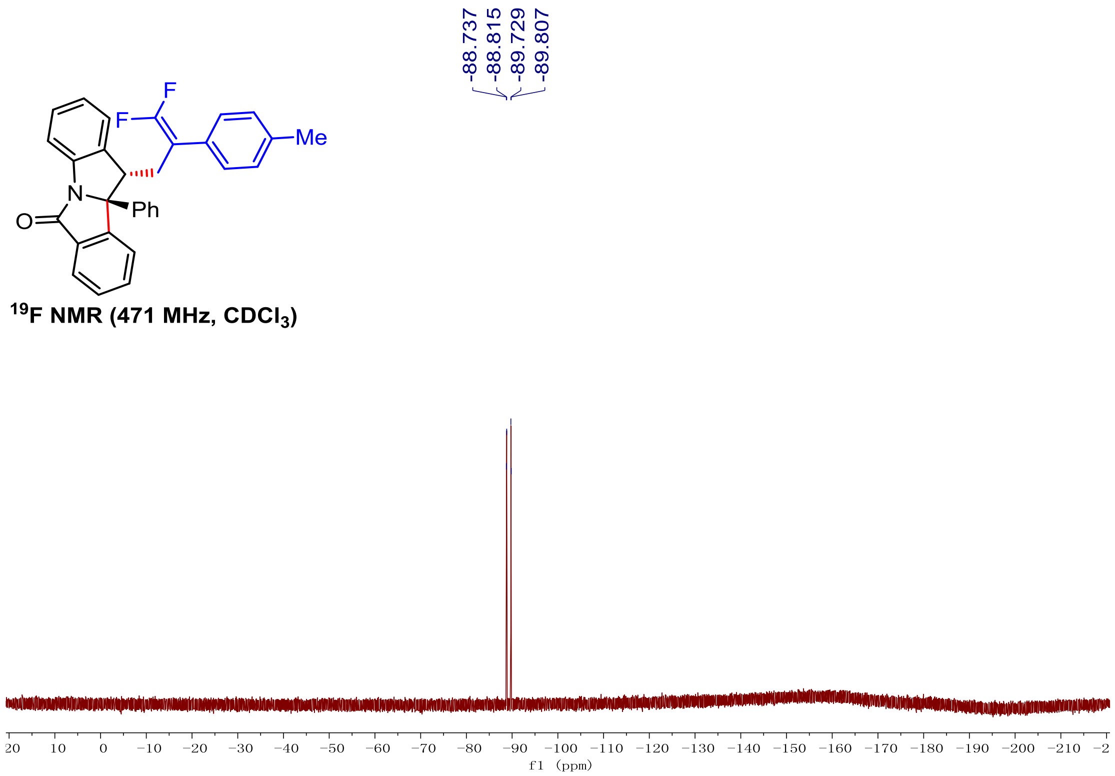


$^{19}$F NMR (471 MHz, CDCl$_3$)

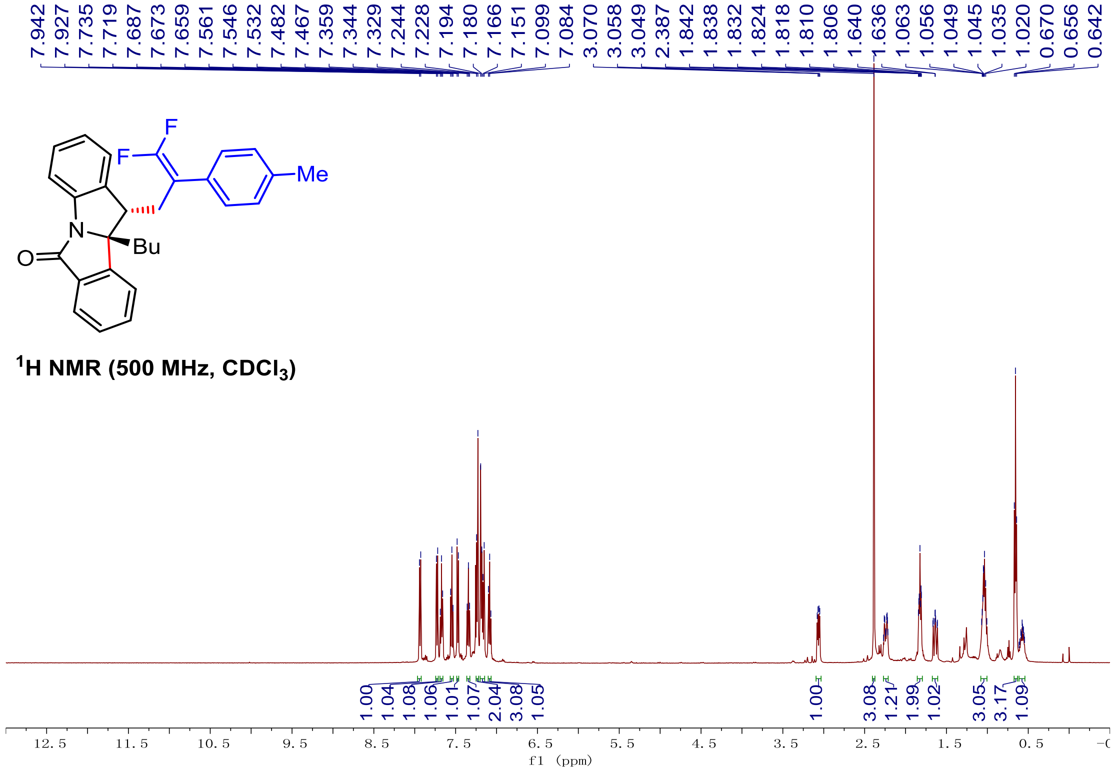
## (10b*S*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-10b-phenyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 39

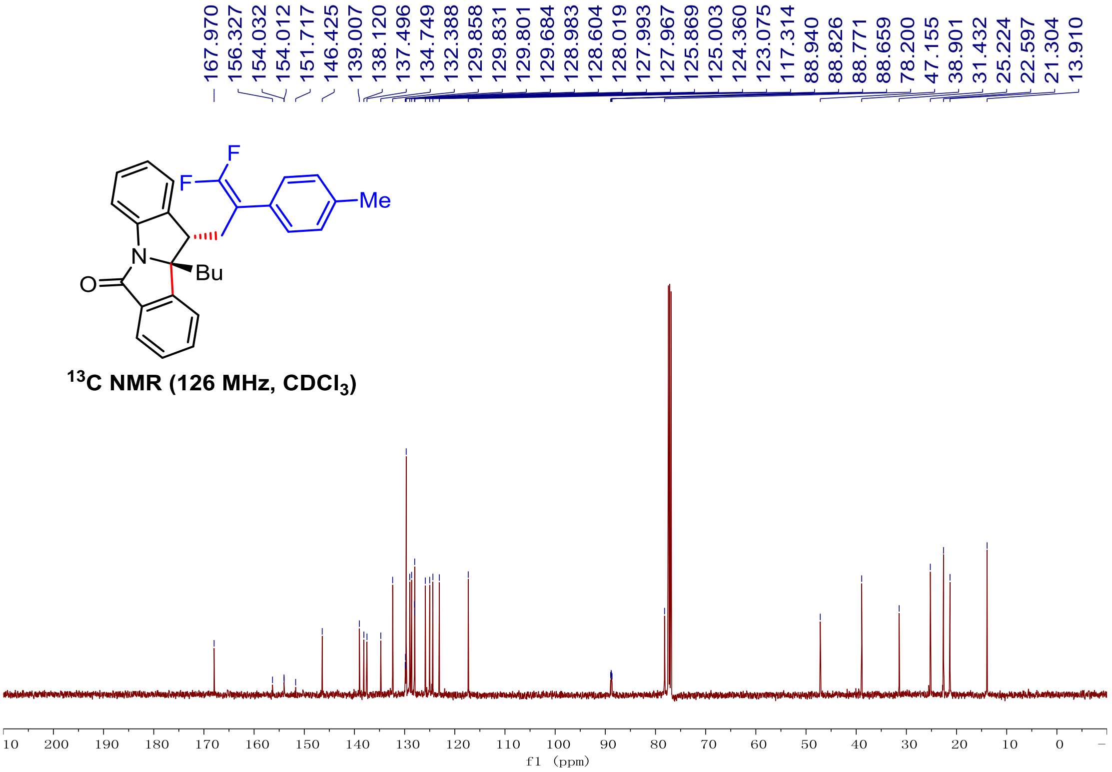


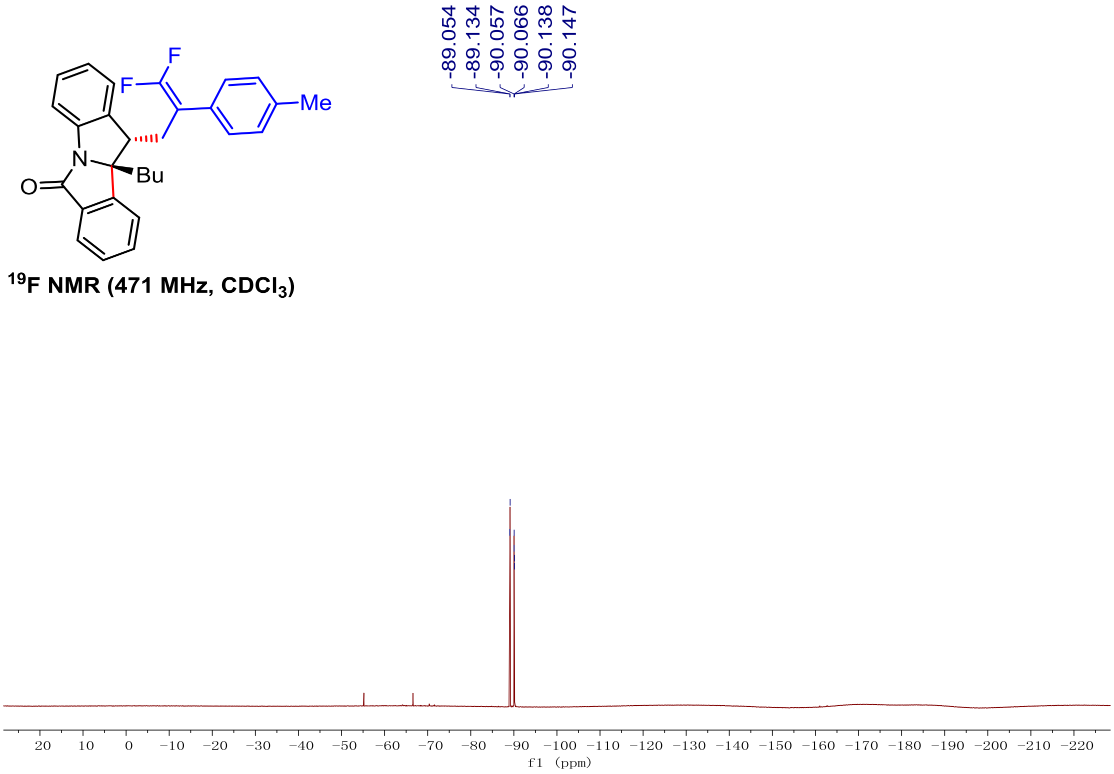




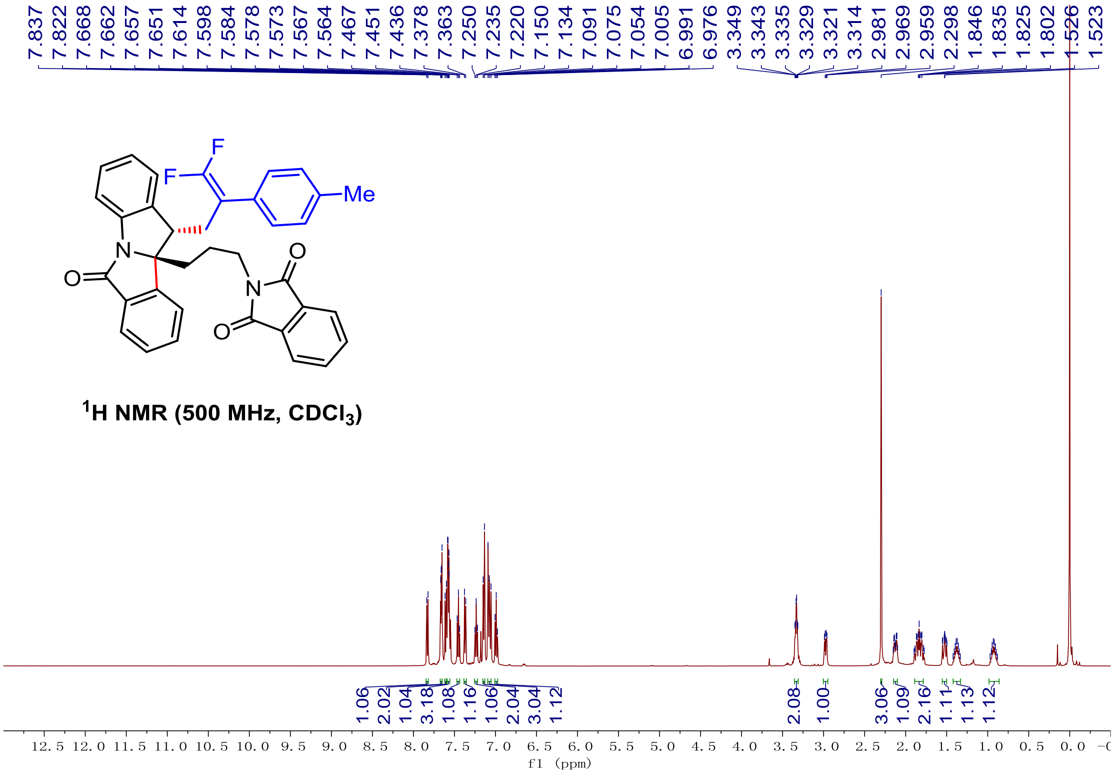
## (10b*R*,11*S*)-10b-Butyl-11-(3,3-difluoro-2-(*p*-tolyl)allyl)-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 40

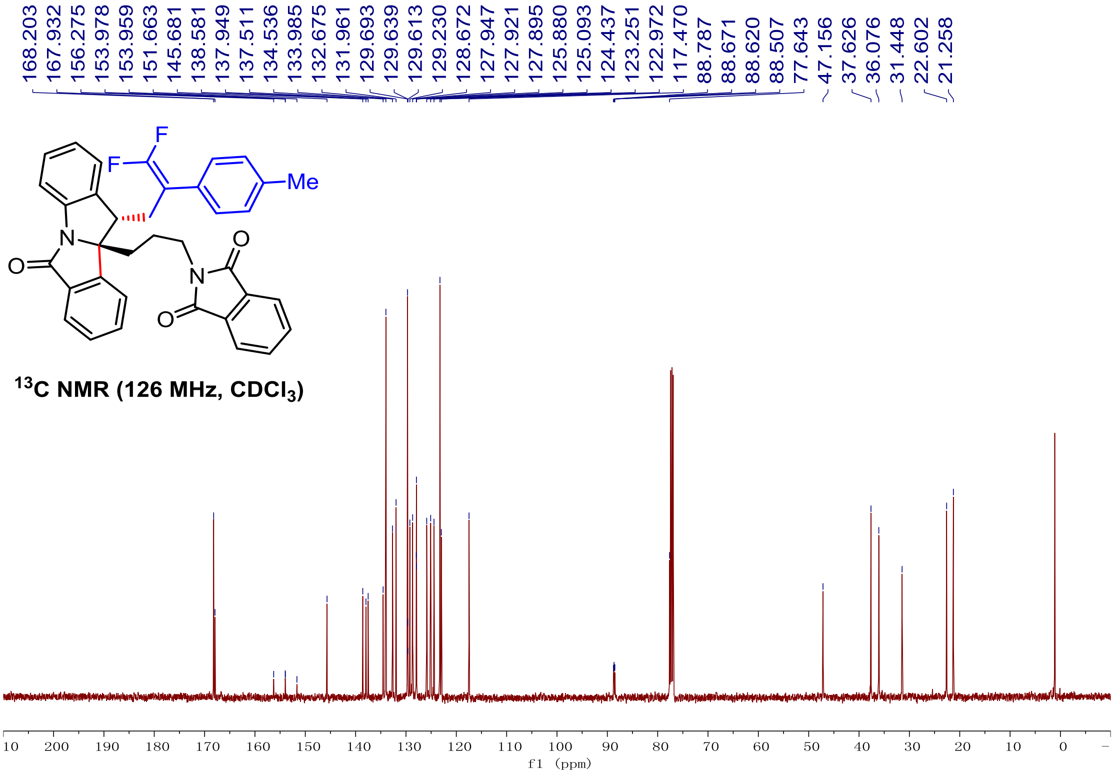


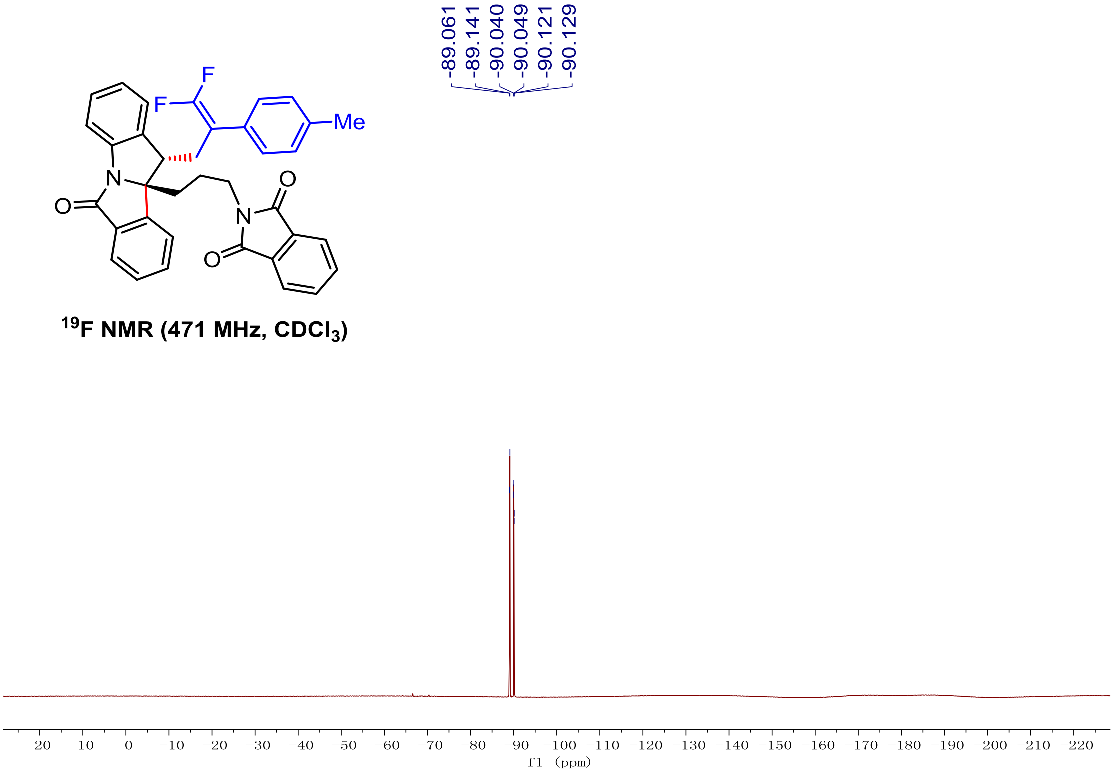

$^{13}$C NMR (126 MHz, CDCl$_3$)


$^{19}$F NMR (471 MHz, CDCl$_3$)

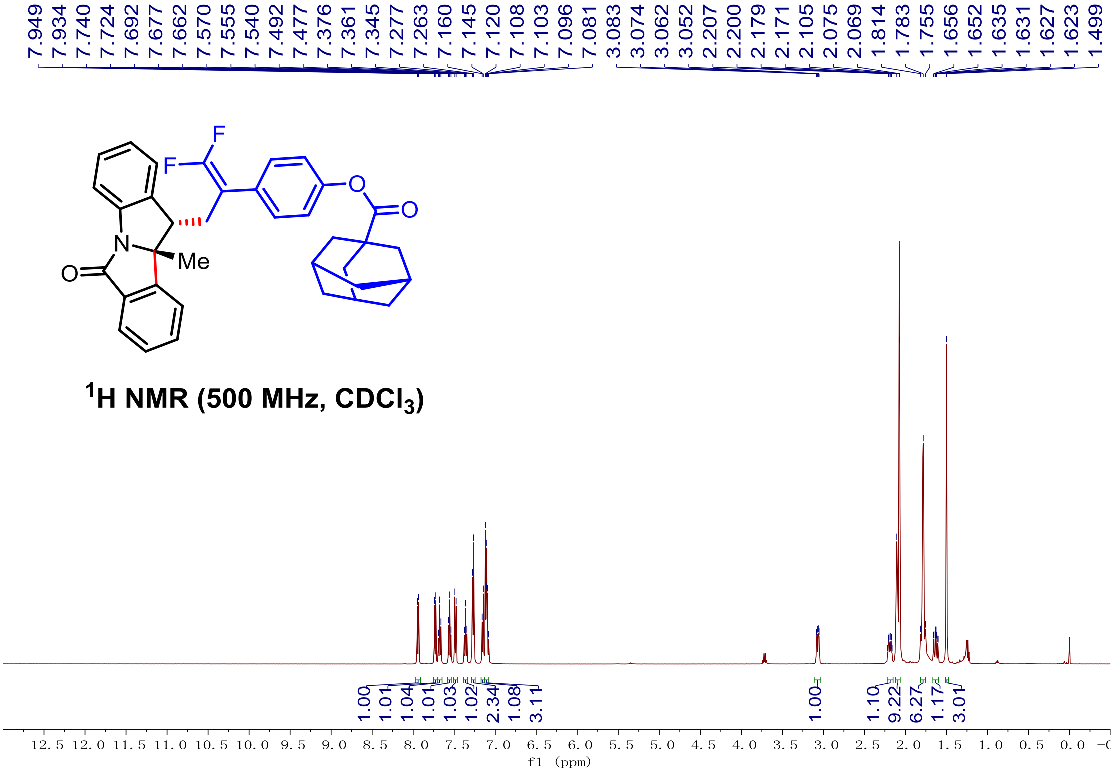
## 2-(3-((10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-6-oxo-6*H*-isoindolo[2,1-*a*]indol-10b(11H)-yl)propyl)isoindoline-1,3-dione, 41

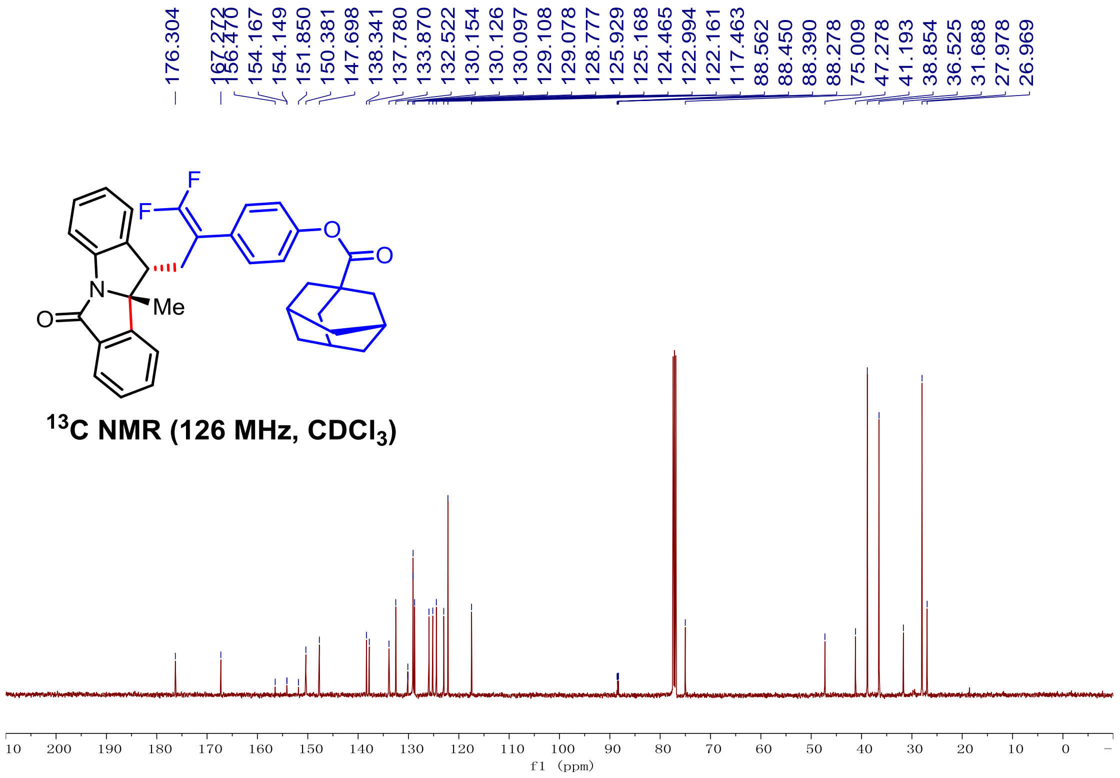




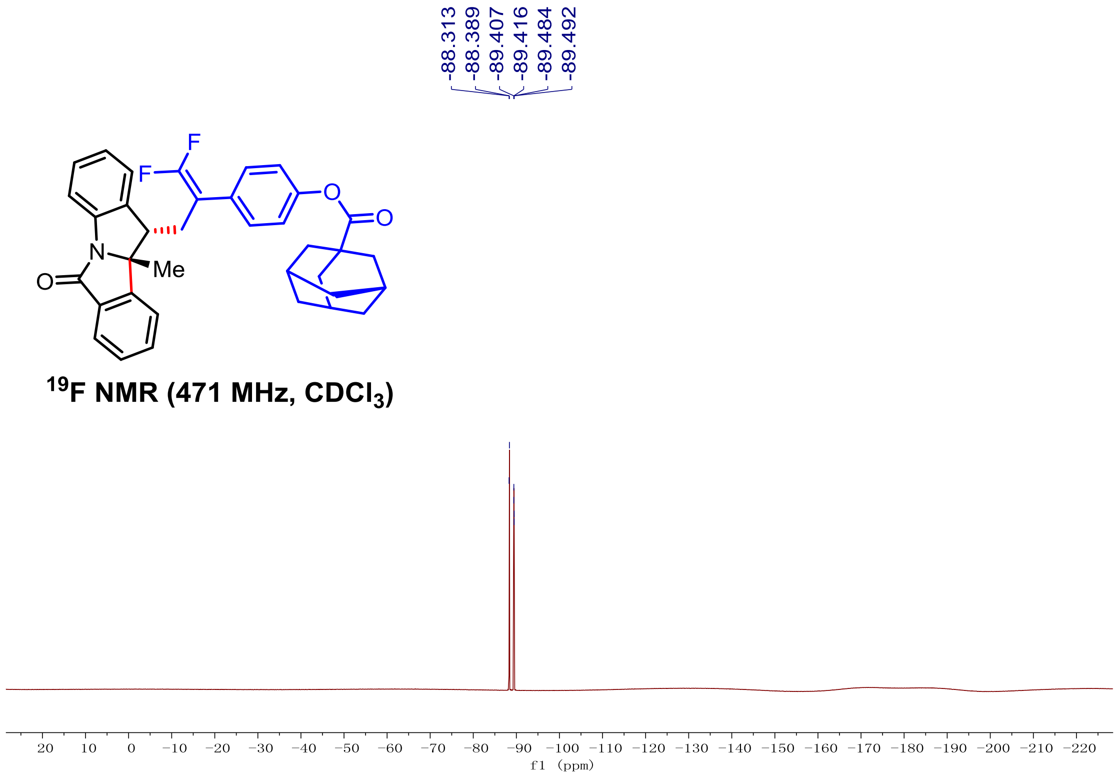


## 4-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl adamantane-1-carboxylate, 42



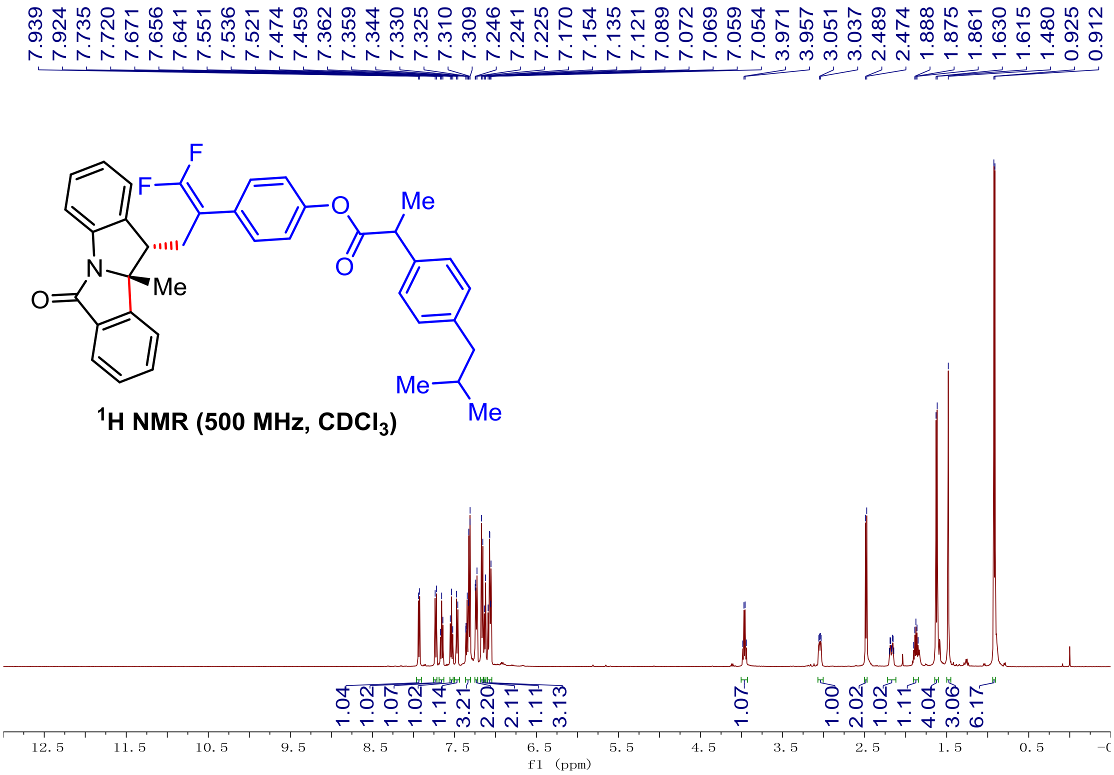


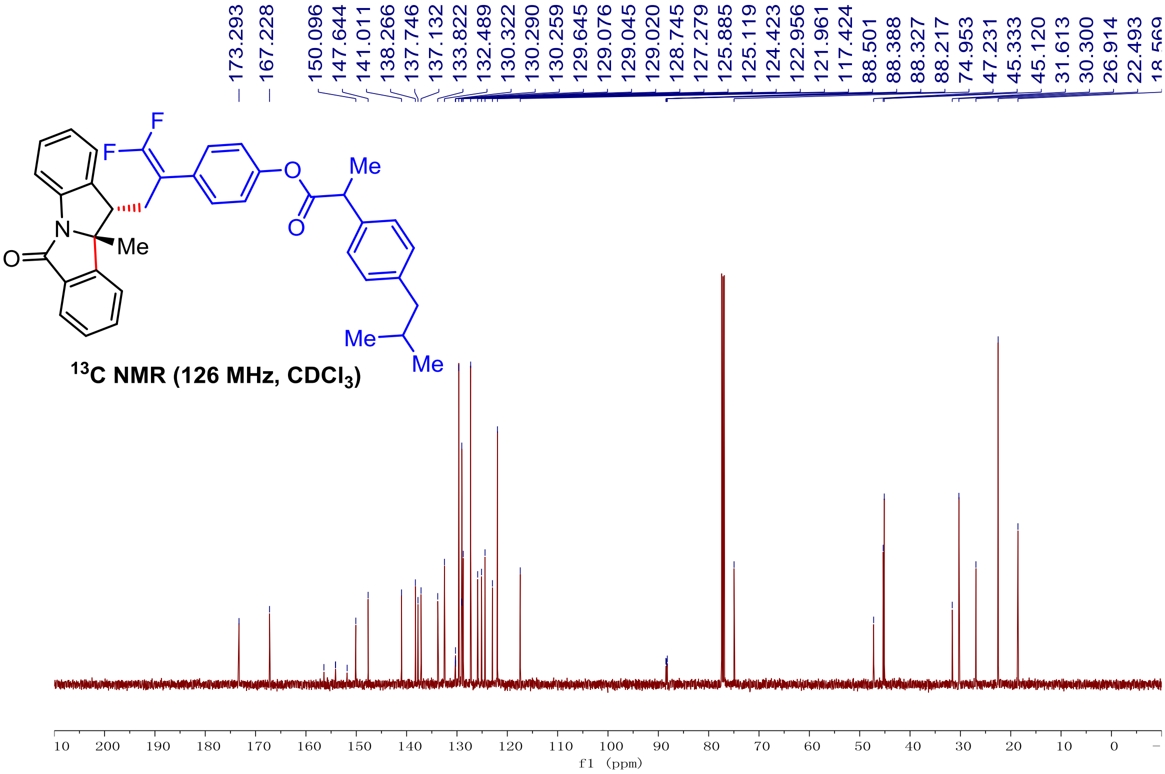
**$^{13}$C NMR (126 MHz, CDCl$_3$)**

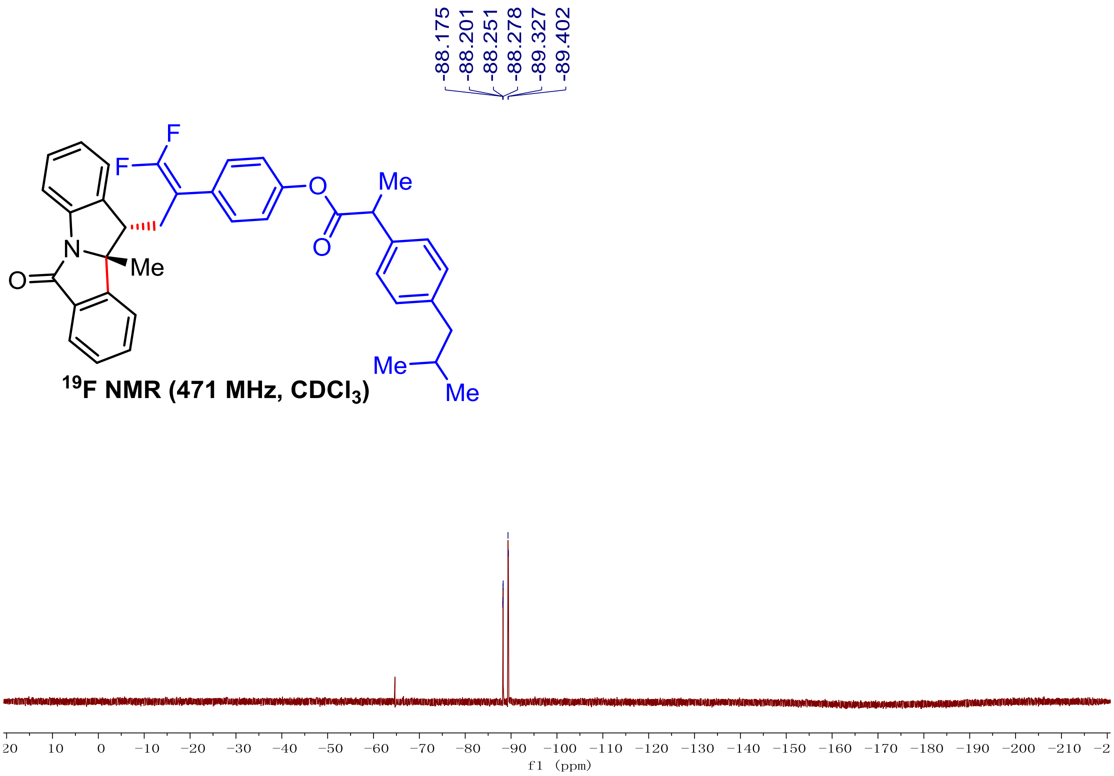


**$^{19}$F NMR (471 MHz, CDCl$_3$)**

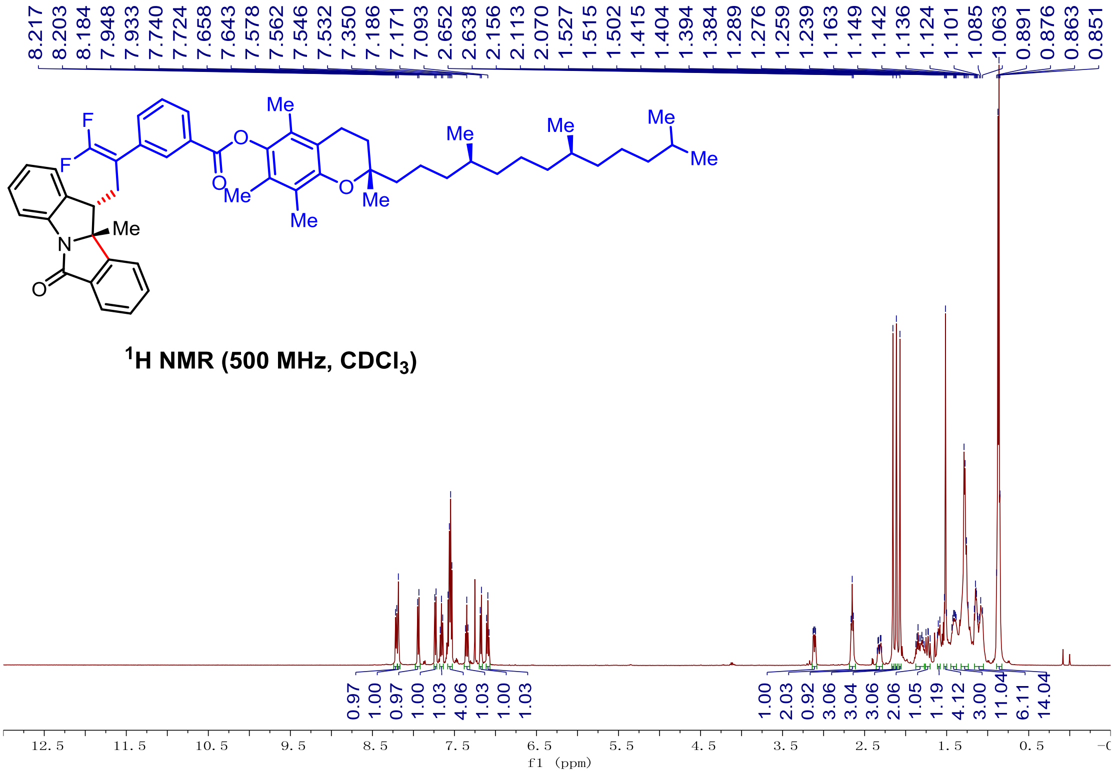
## 4-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl 2-(4-isobutylphenyl)propanoate, 43

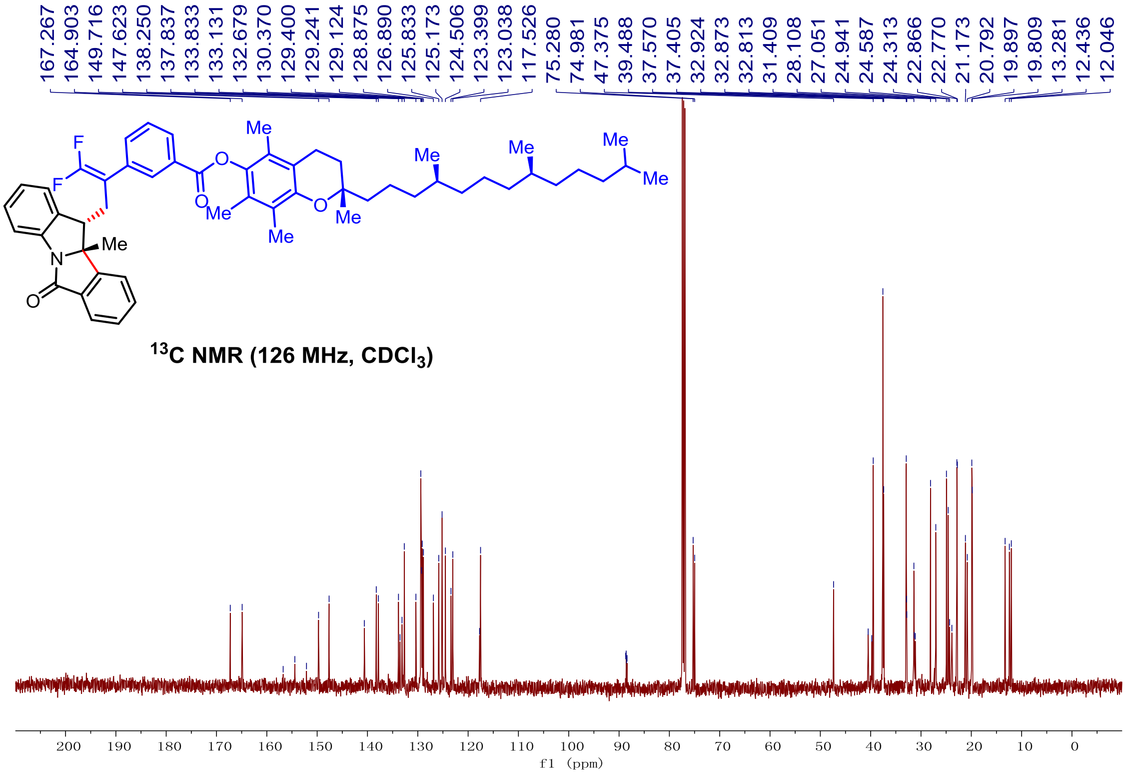




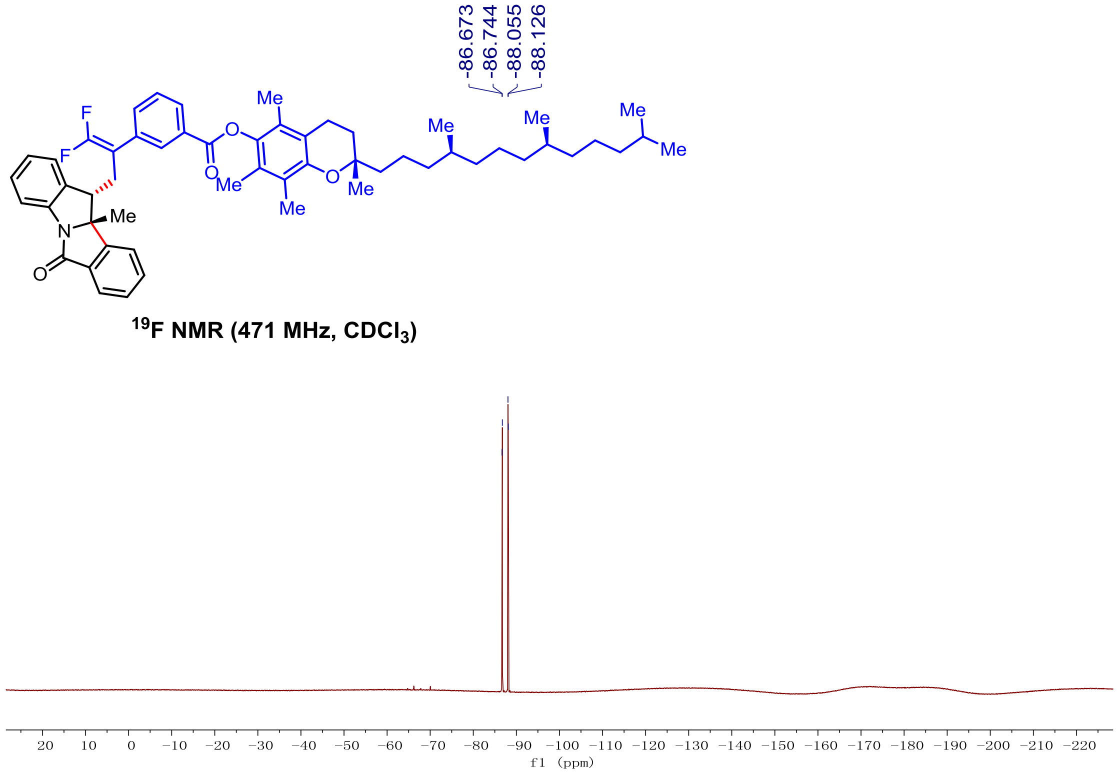


### (*S*)-2,5,7,8-Tetramethyl-2-((4*S*,8*S*)-4,8,12-trimethyltridecyl)chroman-6-yl 3-(1,1-difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzoate, 44



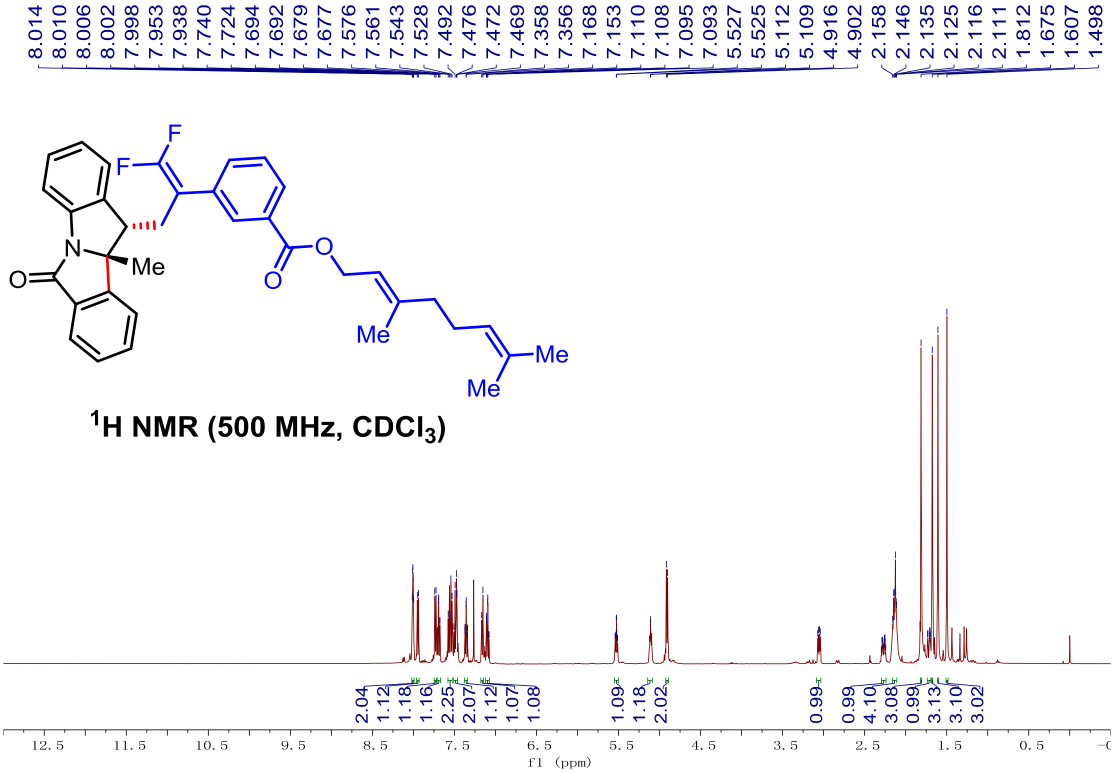


$^{13}$C NMR (126 MHz, CDCl$_3$)

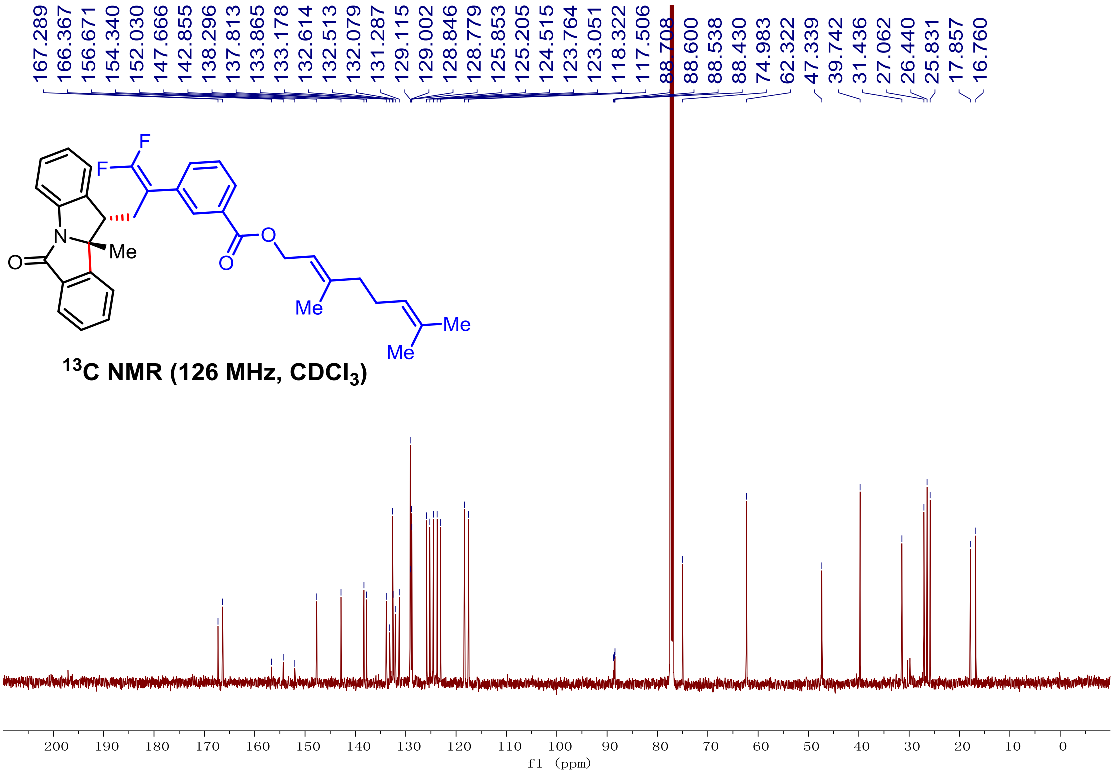


$^{19}$F NMR (471 MHz, CDCl$_3$)

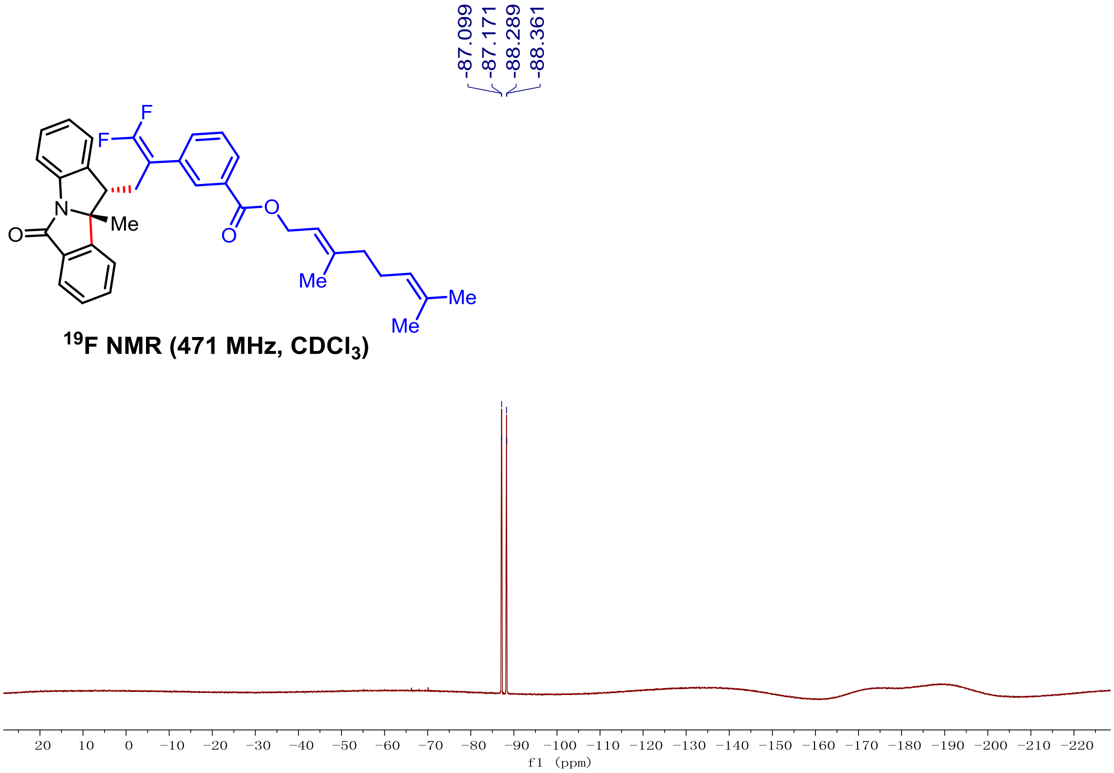
**(*E*)-3,7-Dimethylocta-2,6-dien-1-yl 3-(1,1-difluoro-3-((10b*R*,11S)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)benzoate, 45**



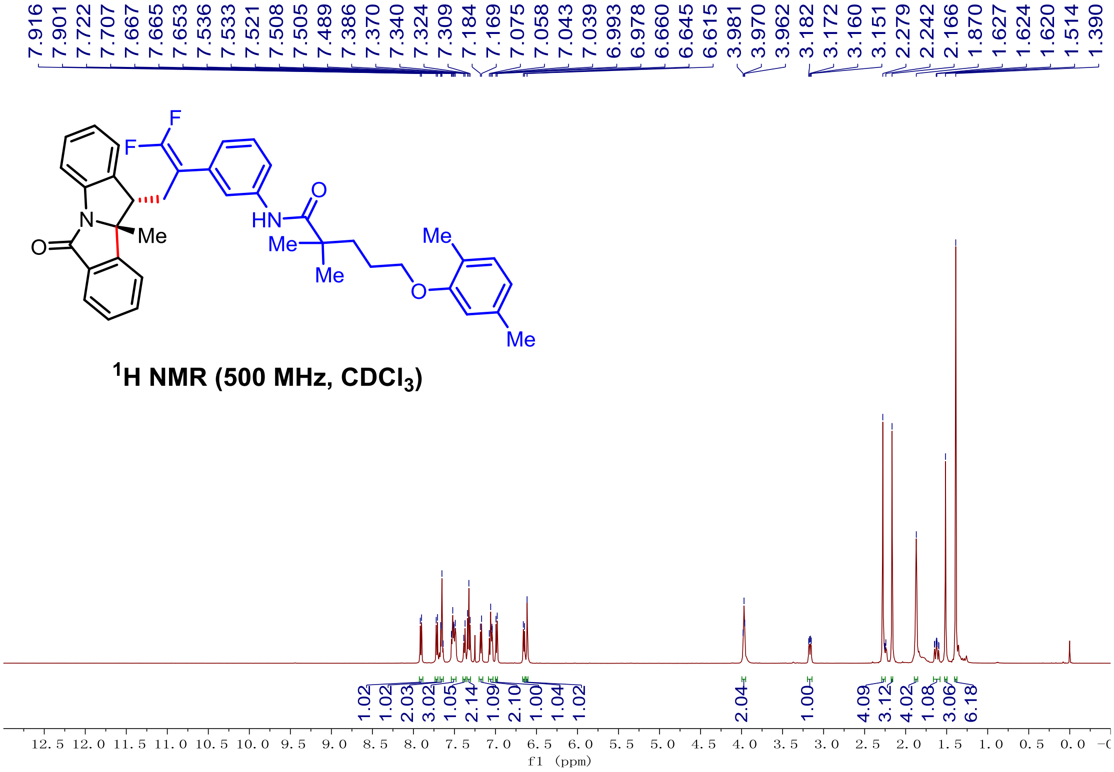
$^{1}$H NMR (500 MHz, CDCl$_3$)

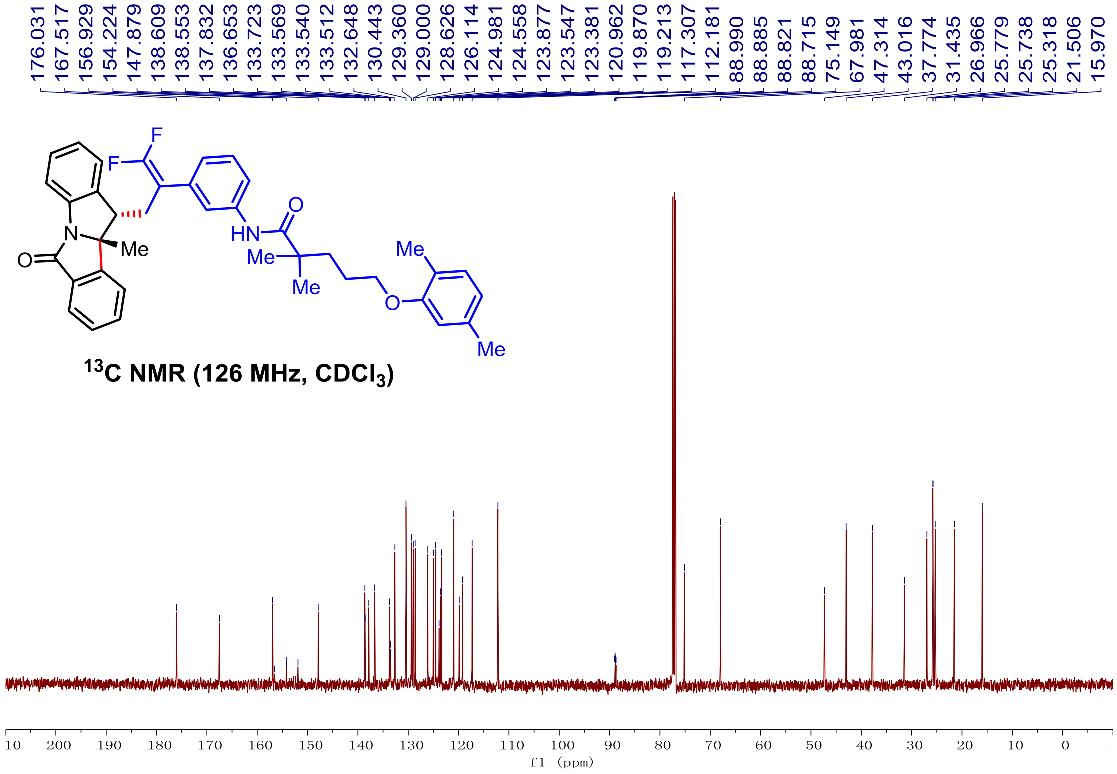


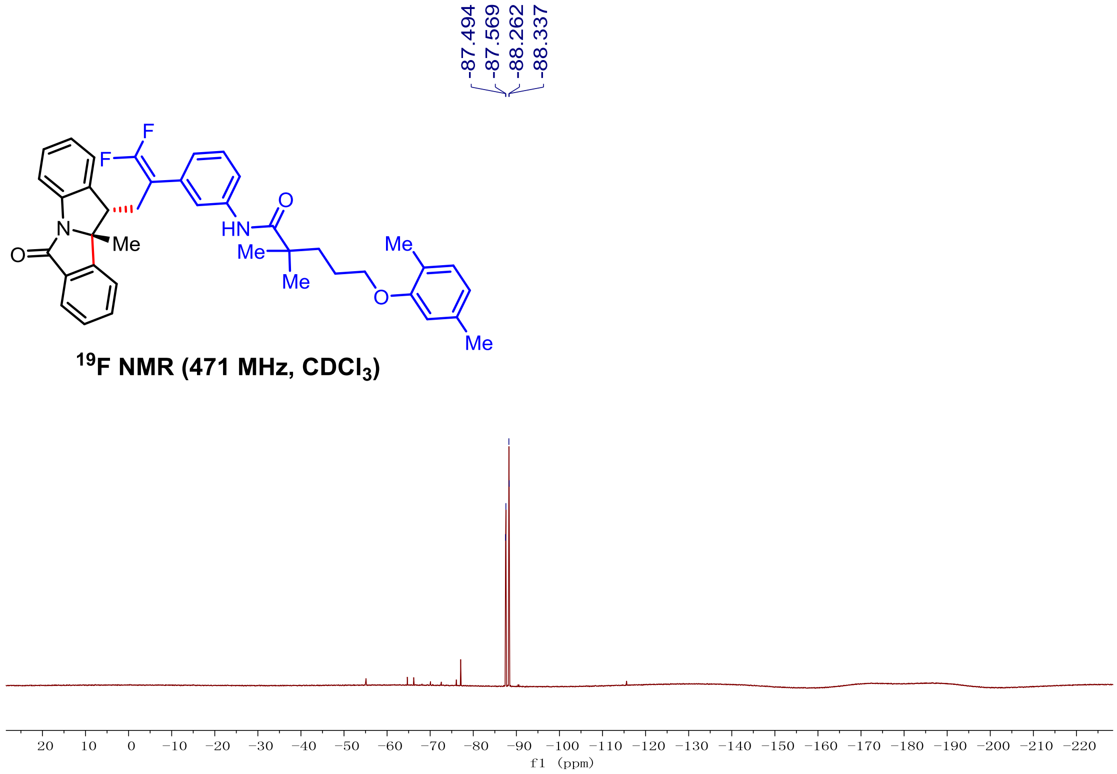
$^{13}$C NMR (126 MHz, CDCl$_3$)



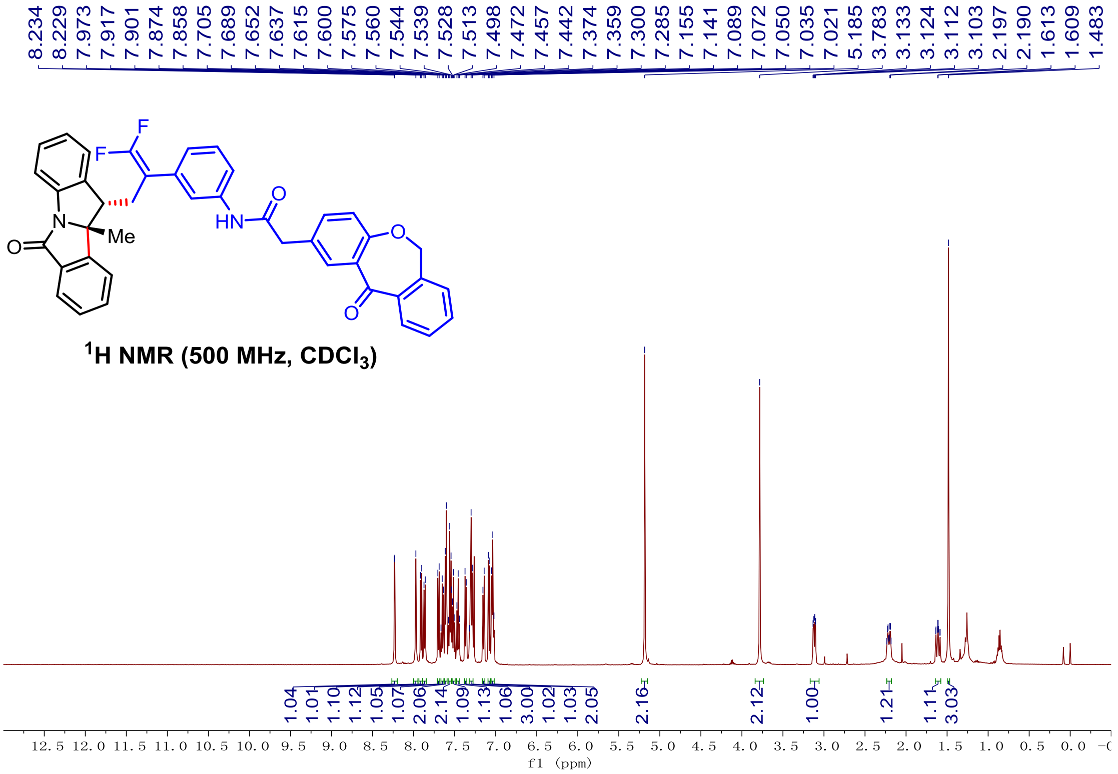
## *N*-(3-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl)-5-(2,5-dimethylphenoxy)-2,2-dimethylpentanamide, 46



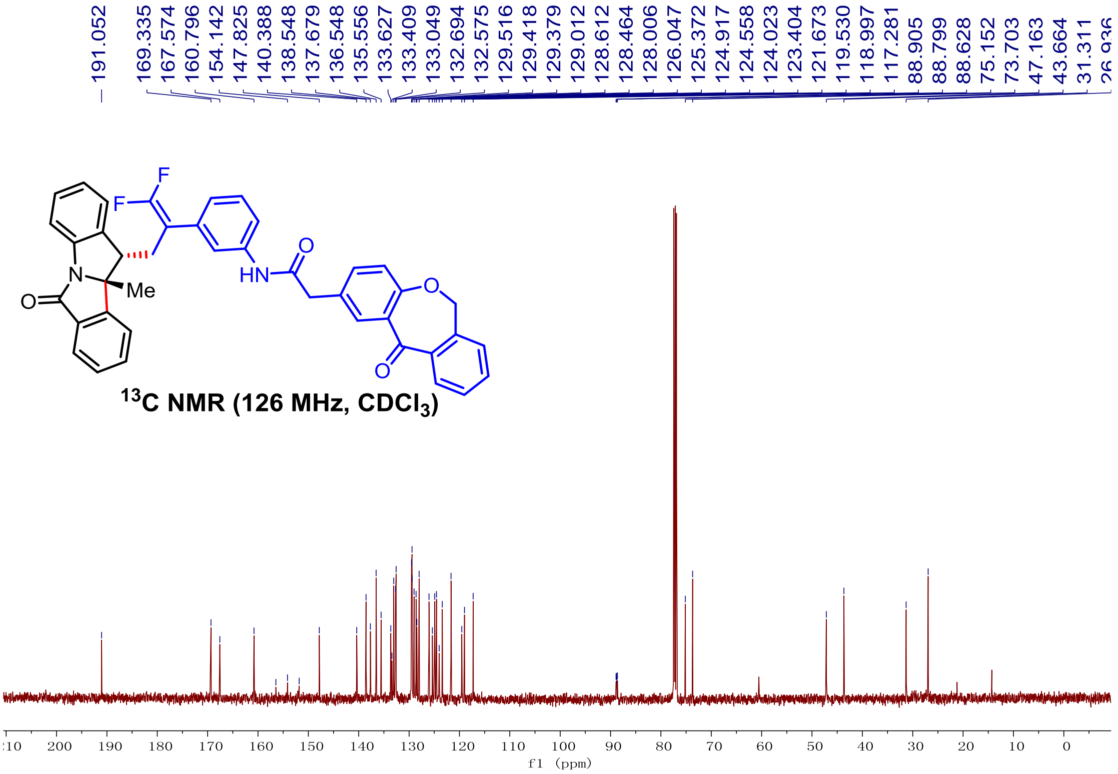

176.031
167.517
156.929
154.224
147.879
138.609
138.553
137.832
136.653
133.723
133.569
133.540
133.512
132.648
130.443
129.360
129.000
128.626
126.114
124.981
124.558
123.877
123.547
123.381
120.962
119.870
119.213
117.307
112.181
88.990
88.885
88.821
88.715
75.149
67.981
47.314
43.016
37.774
31.435
26.966
25.779
25.738
25.318
21.506
15.970
F
F
N
O
Me
HN
O
Me
Me
O
Me
Me
$^{13}$C NMR (126 MHz, CDCl$_3$)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-87.494
-87.569
-88.262
-88.337
F
F
N
O
Me
HN
O
Me
Me
O
Me
Me
$^{19}$F NMR (471 MHz, CDCl$_3$)
20
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
−220
f1 (ppm)

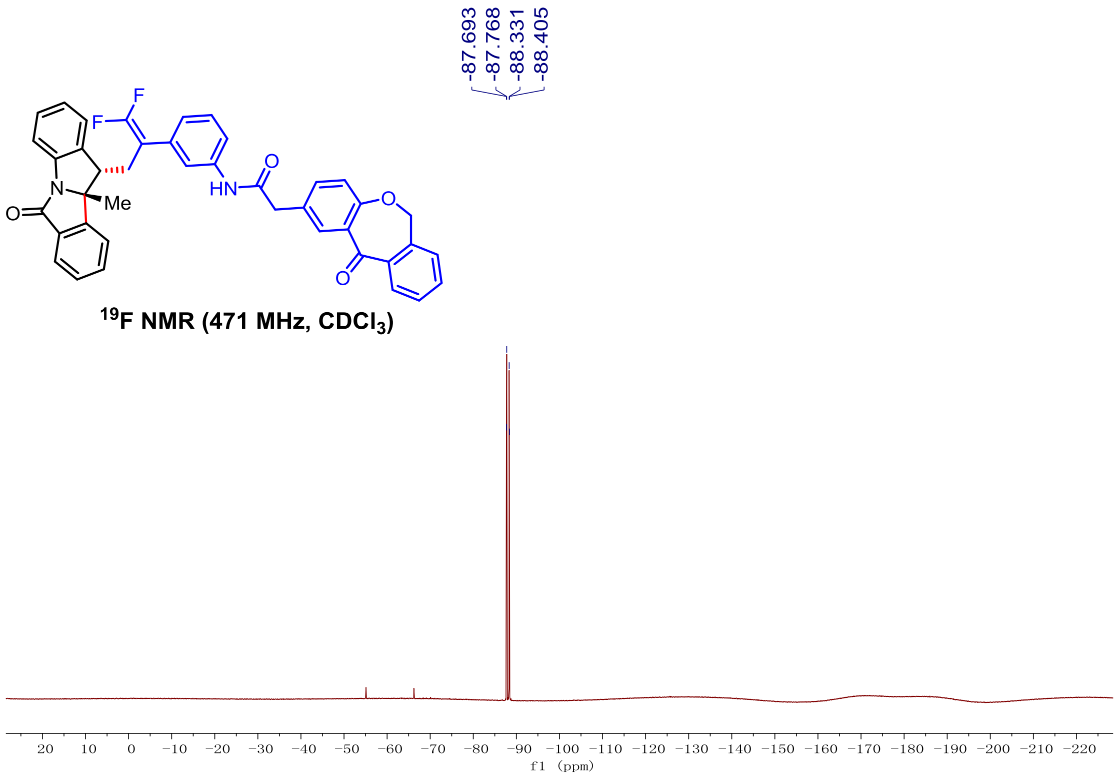
### *N*-(3-(1,1-Difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl)-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetamide, 47



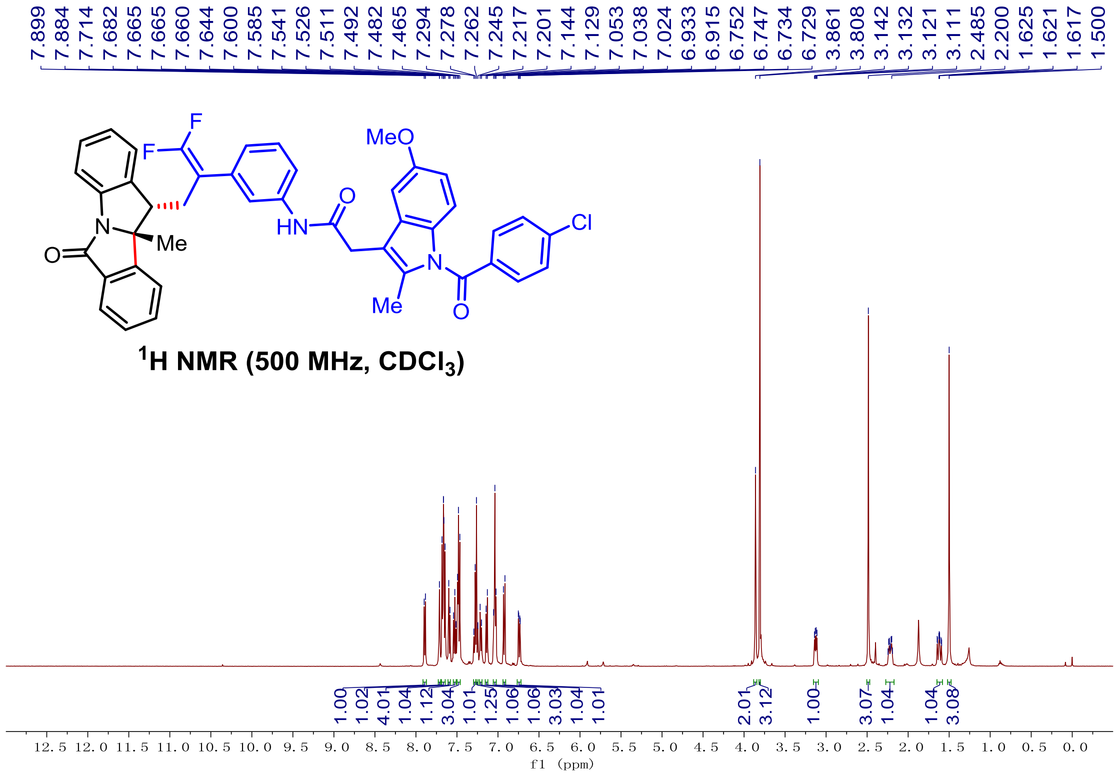
$^1$H NMR (500 MHz, CDCl$_3$)

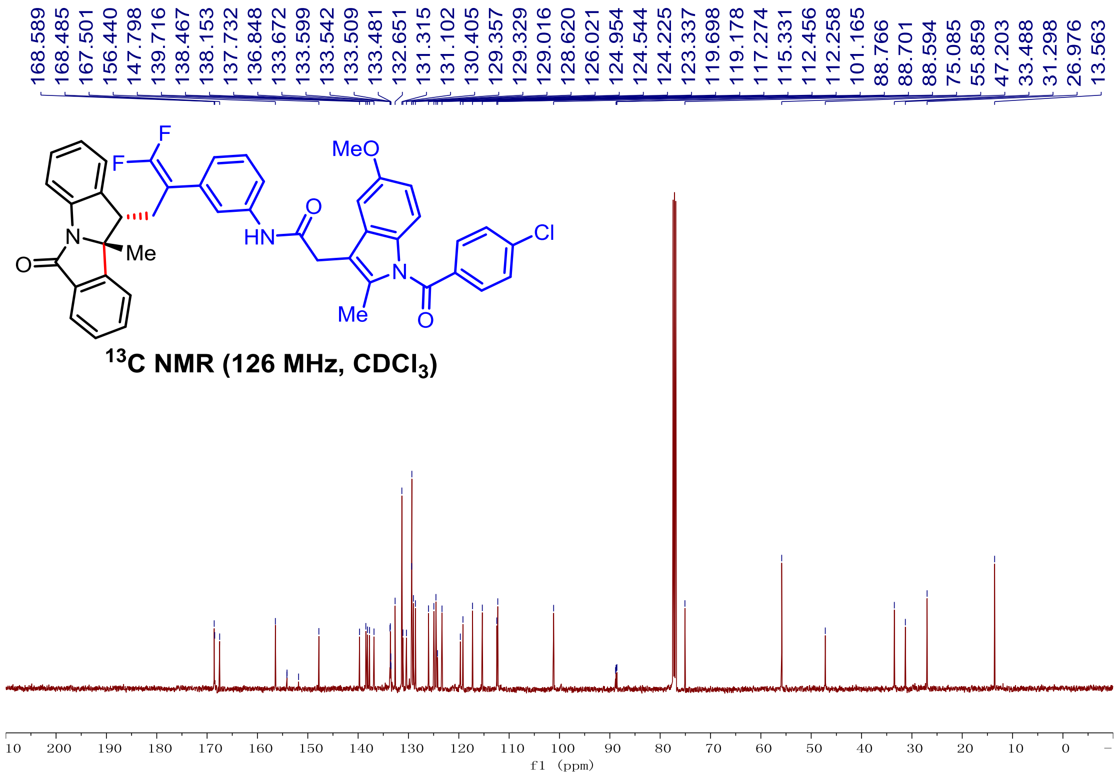


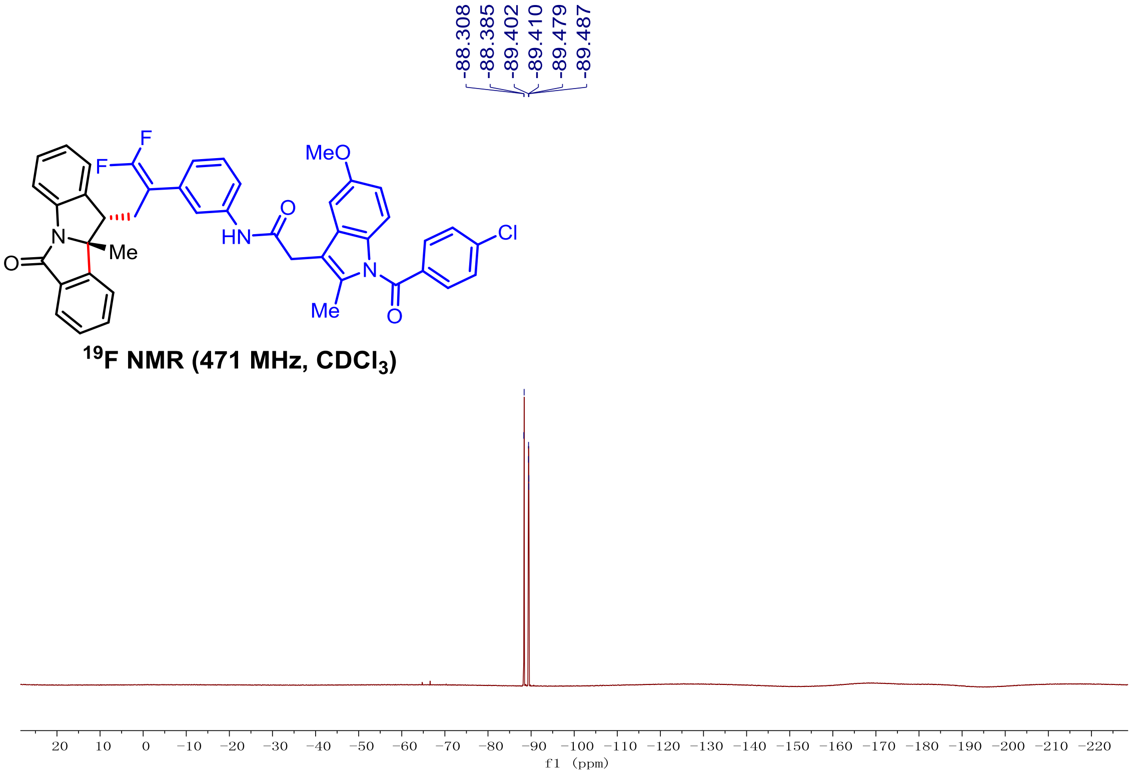
$^{13}$C NMR (126 MHz, CDCl$_3$)



## 2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)-*N*-(3-(1,1-difluoro-3-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)prop-1-en-2-yl)phenyl)acetamide, 48

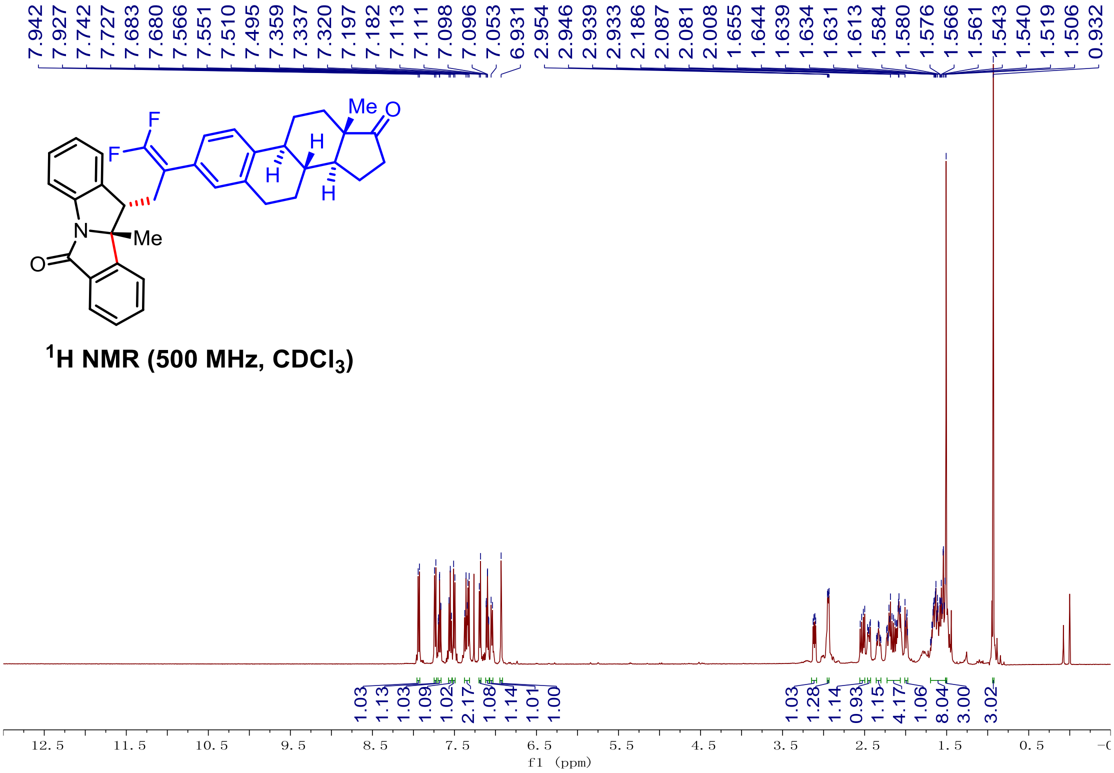


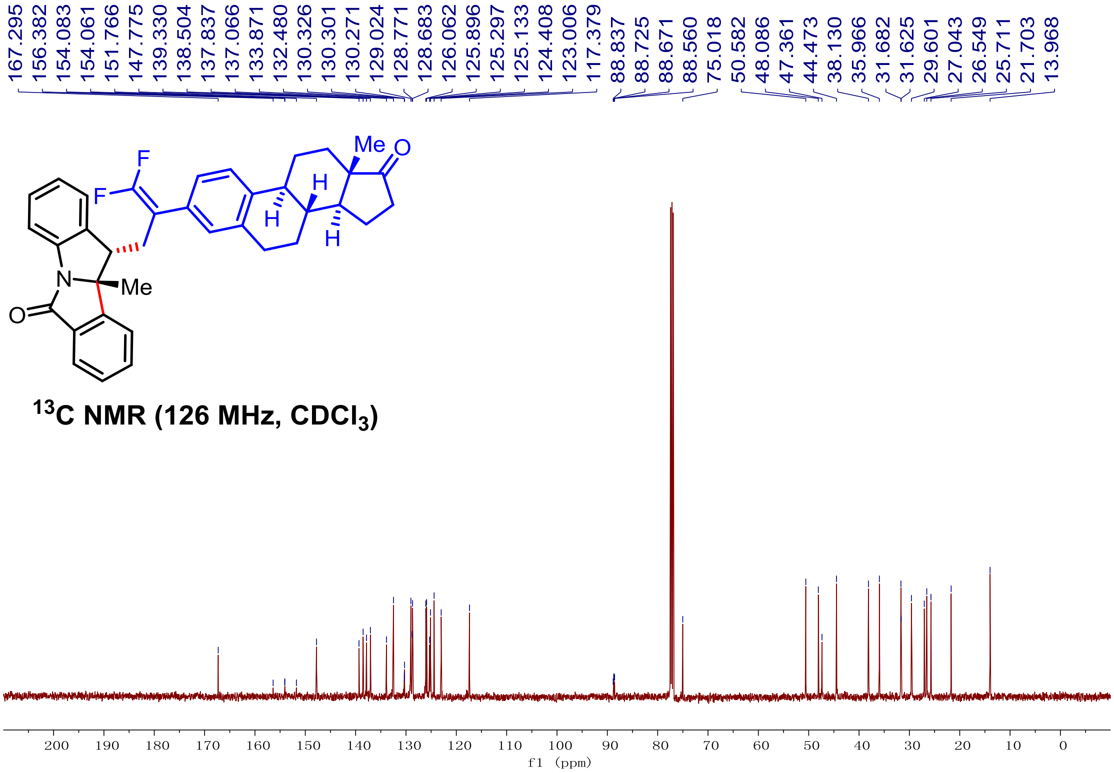


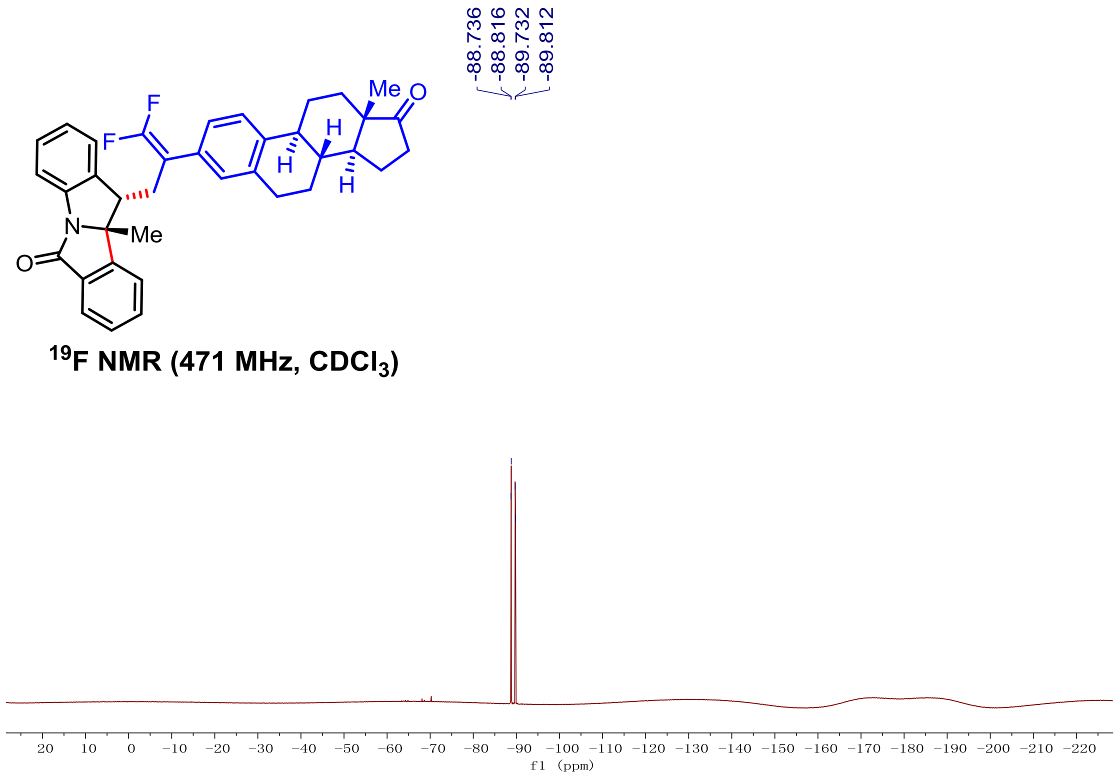


**(10b*R*,11*S*)-11-(3,3-Difluoro-2-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-**

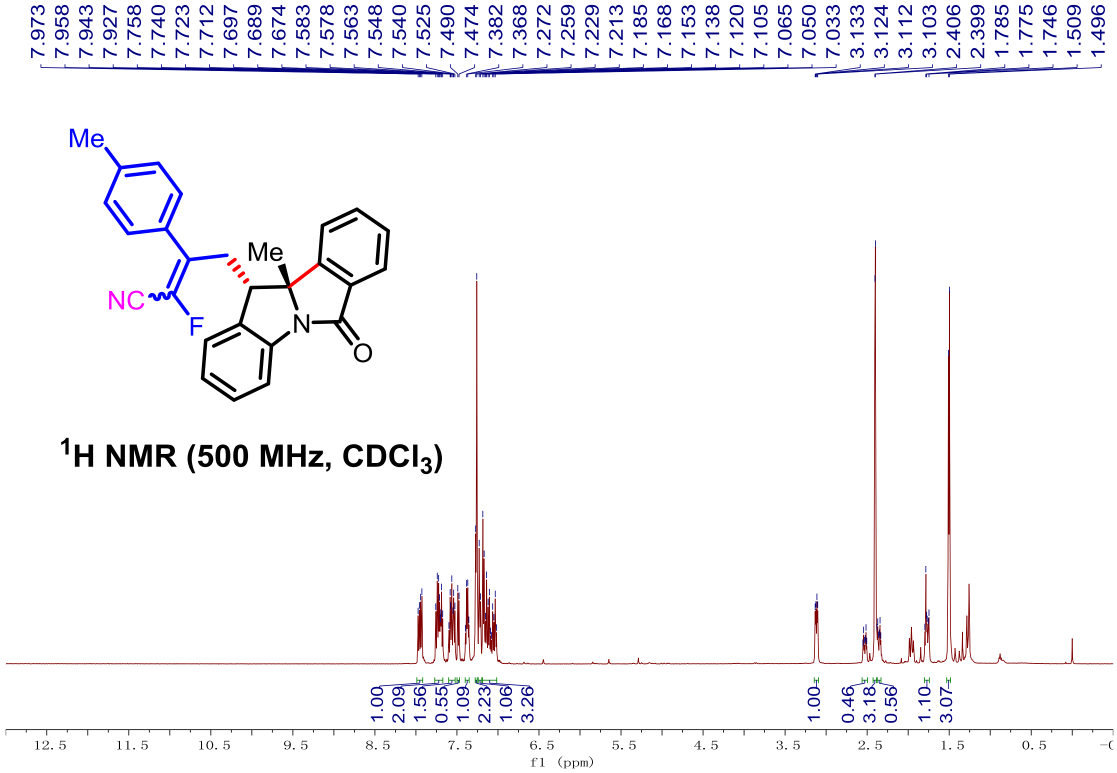
## 7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 49

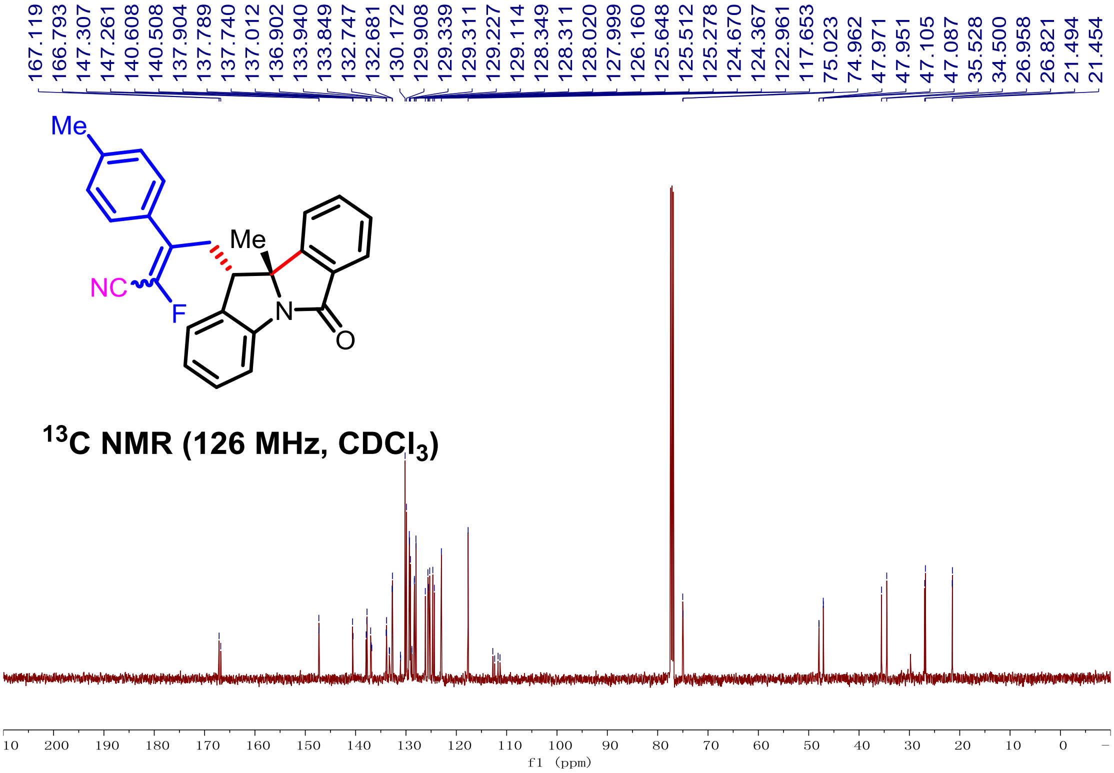




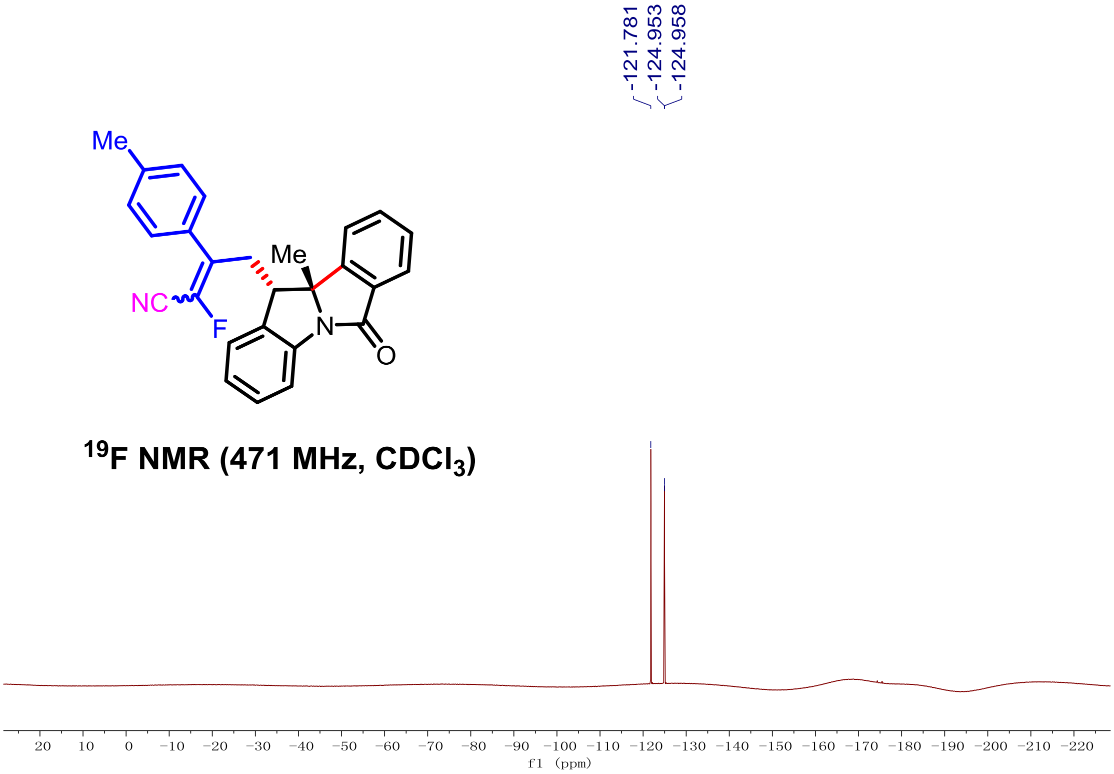


## 2-Fluoro-4-((10b*R*,11*S*)-10b-methyl-6-oxo-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-11-yl)-3-(*p*-tolyl)but-2-enenitrile, 50



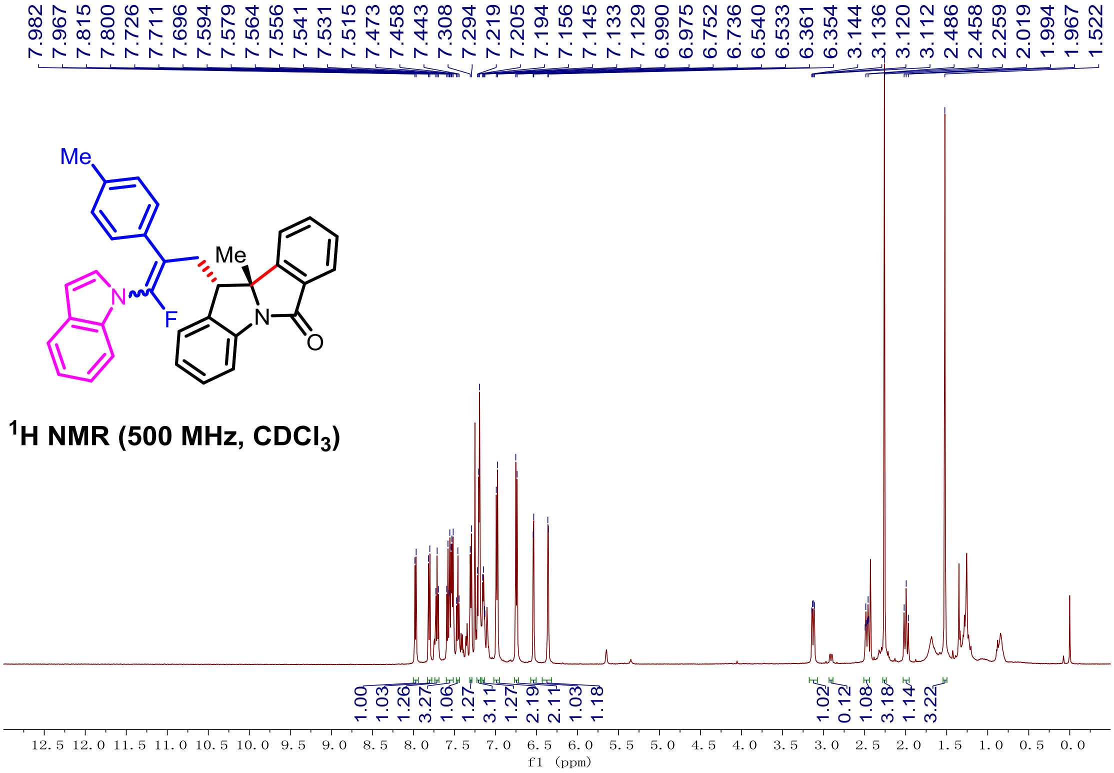


$^{13}C$ NMR (126 MHz, $CDCl_3$)

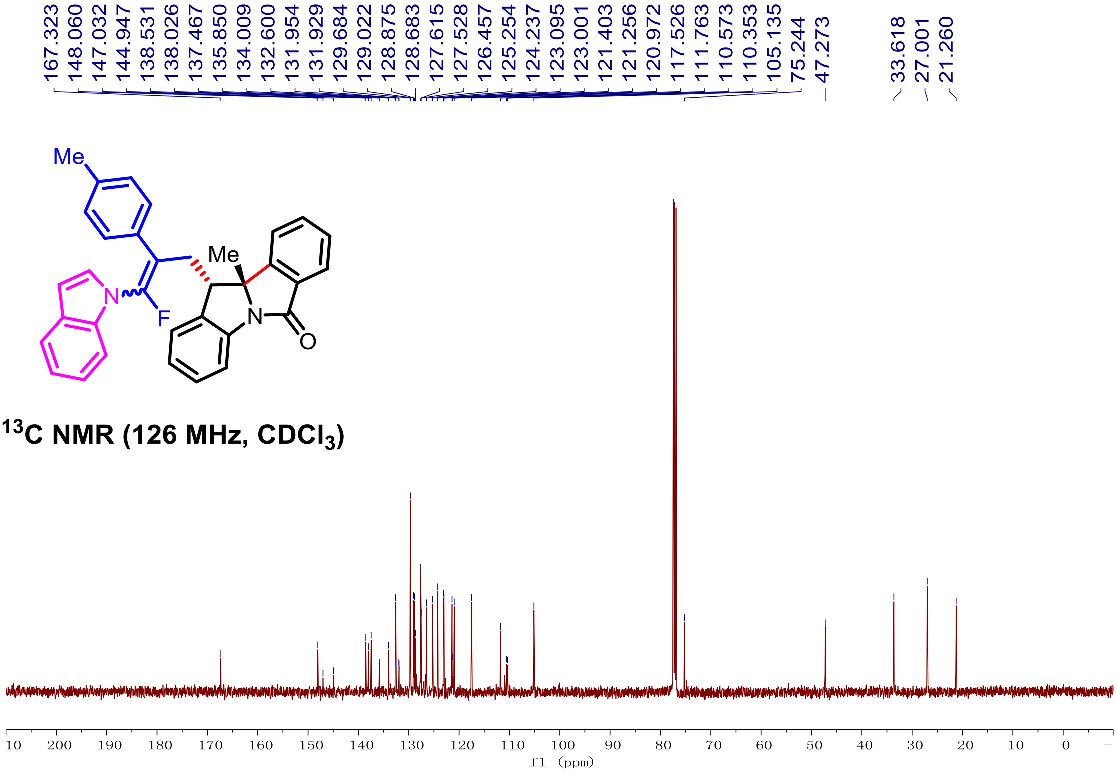


$^{19}F$ NMR (471 MHz, $CDCl_3$)

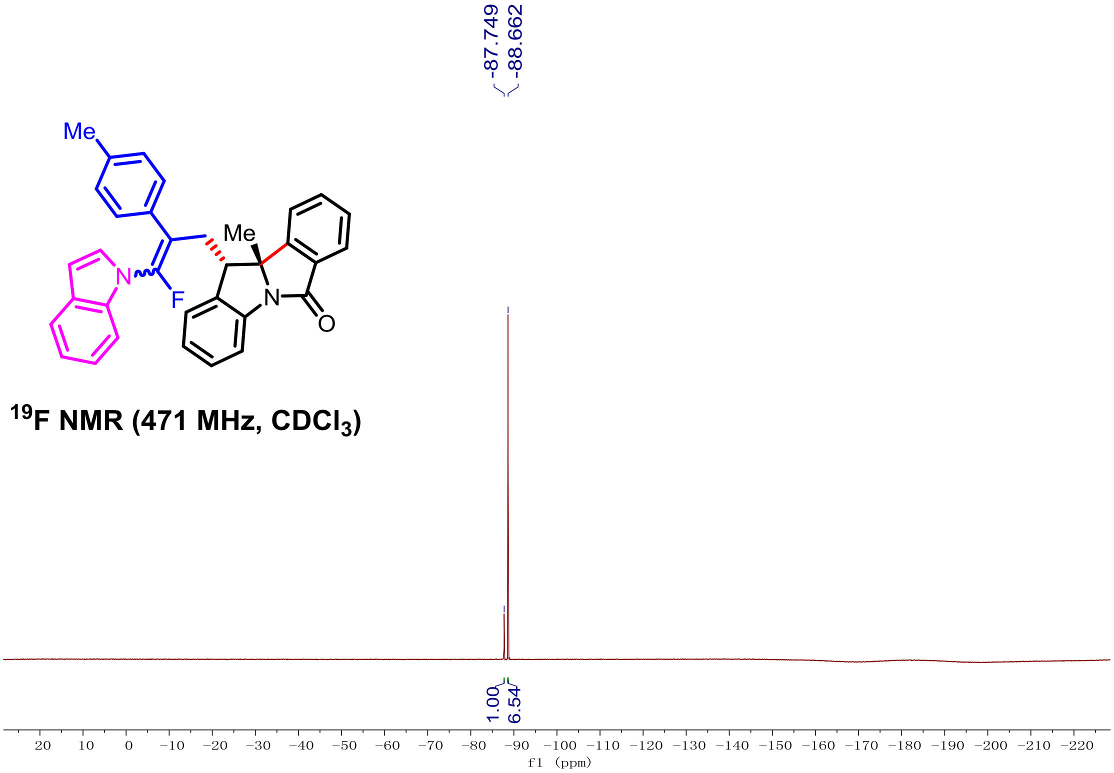
## (10b*R*,11*S*)-11-(3-Fluoro-3-(1*H*-indol-1-yl)-2-(*p*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 51



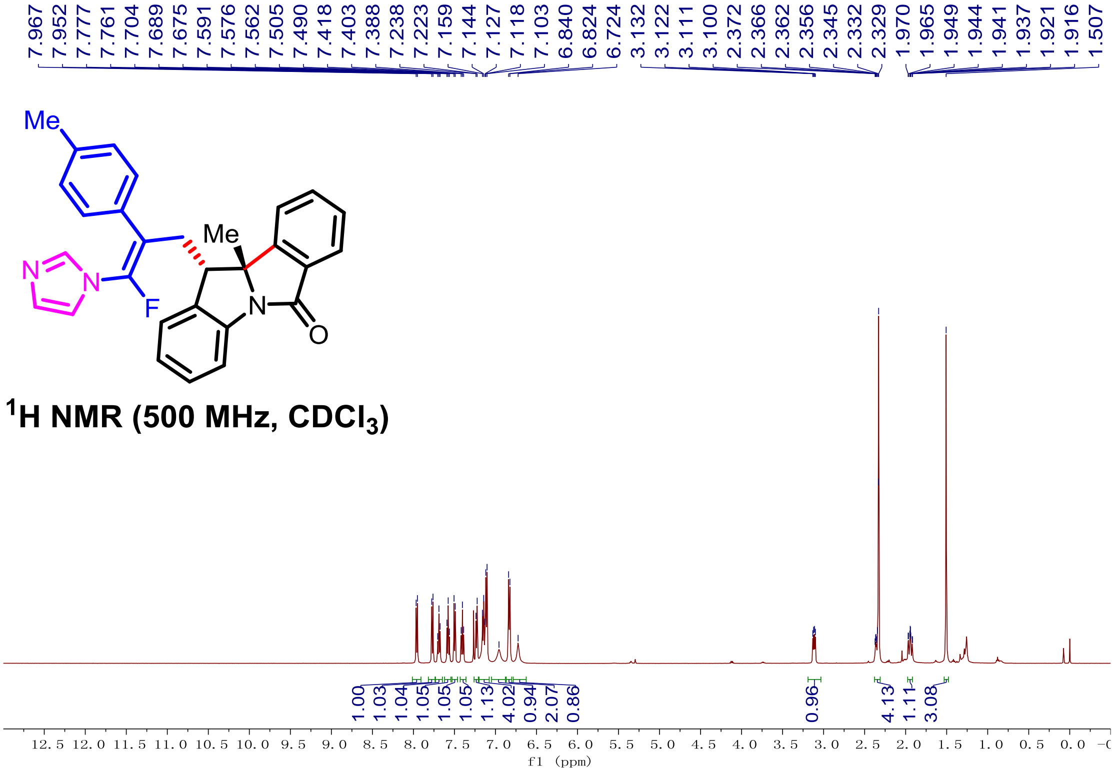
**$^1$H NMR (500 MHz, CDCl$_3$)**

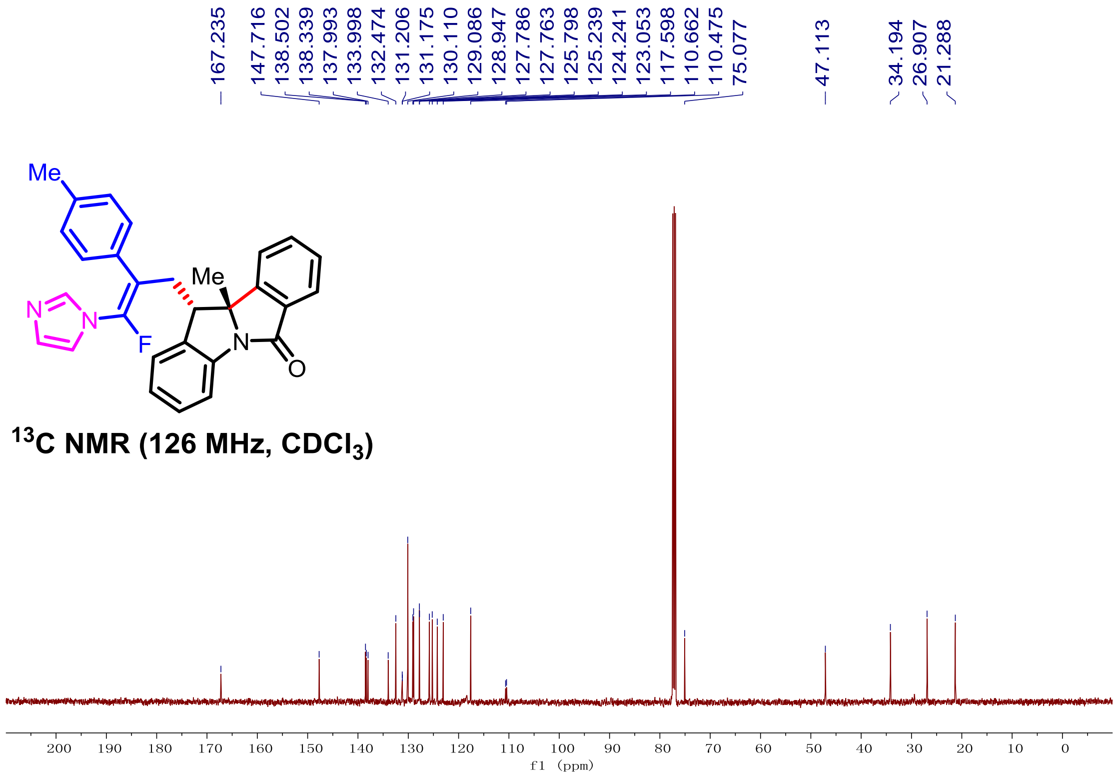


**$^{13}$C NMR (126 MHz, CDCl$_3$)**

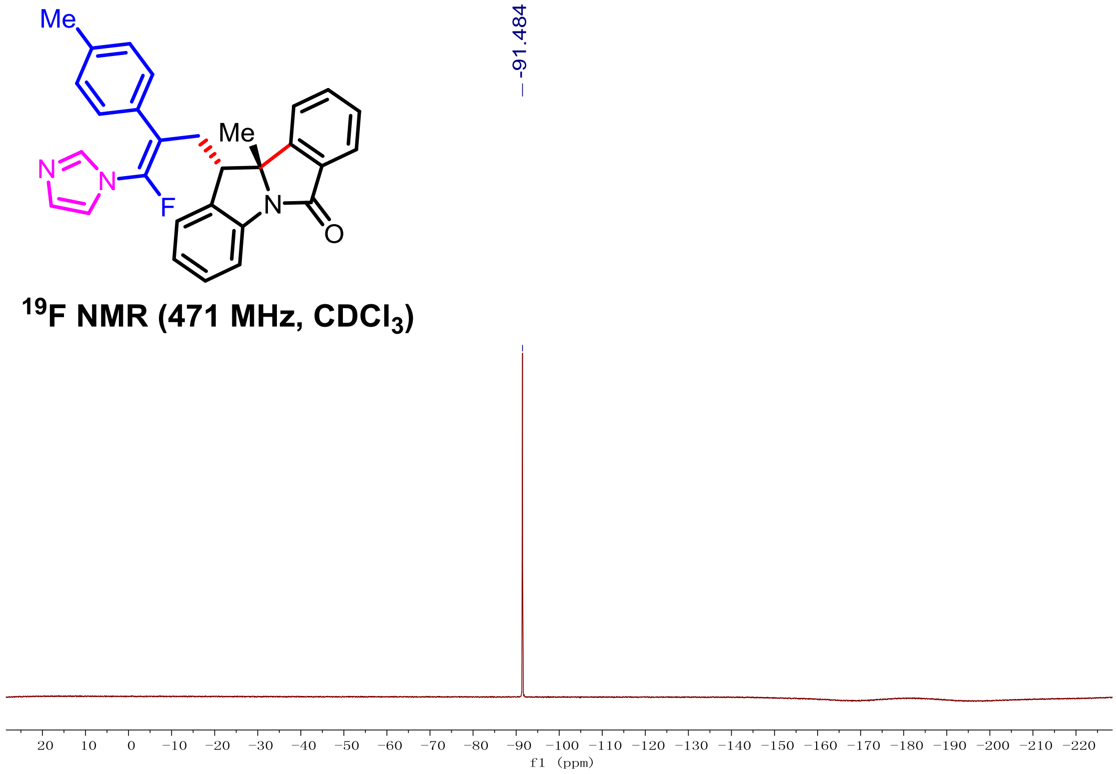


## (10b*R*,11*S*)-11-((*E*)-3-Fluoro-3-(1*H*-imidazol-1-yl)-2-(*p*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 52



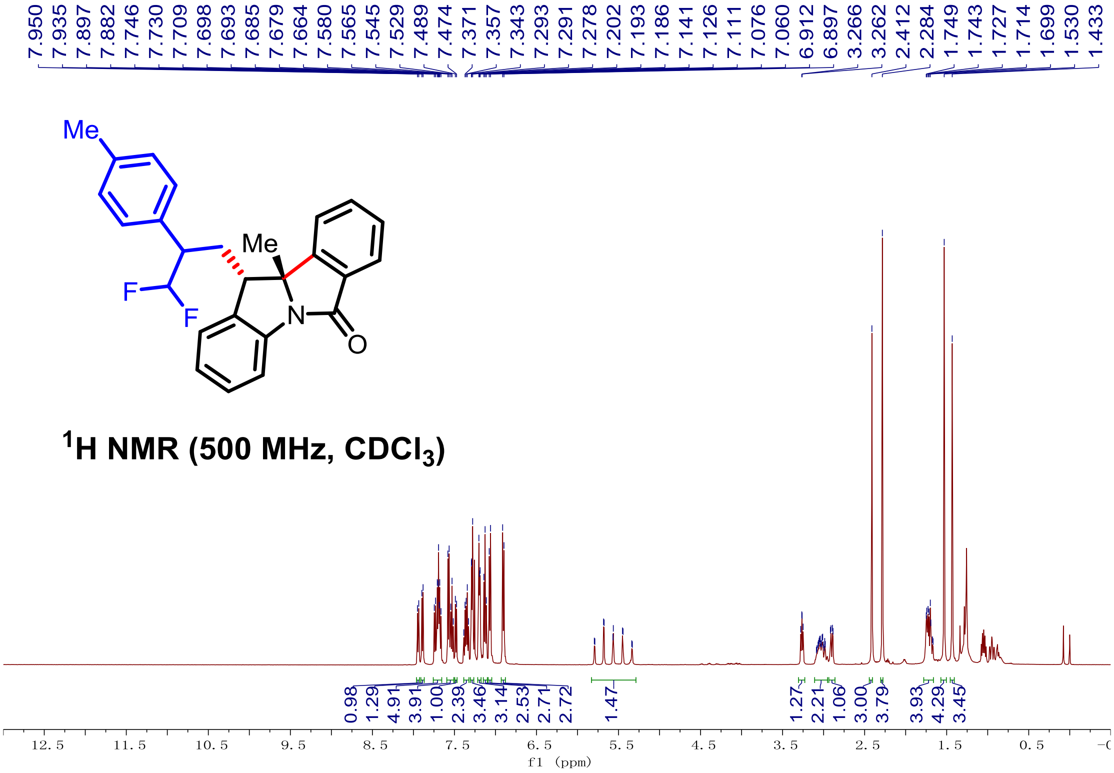


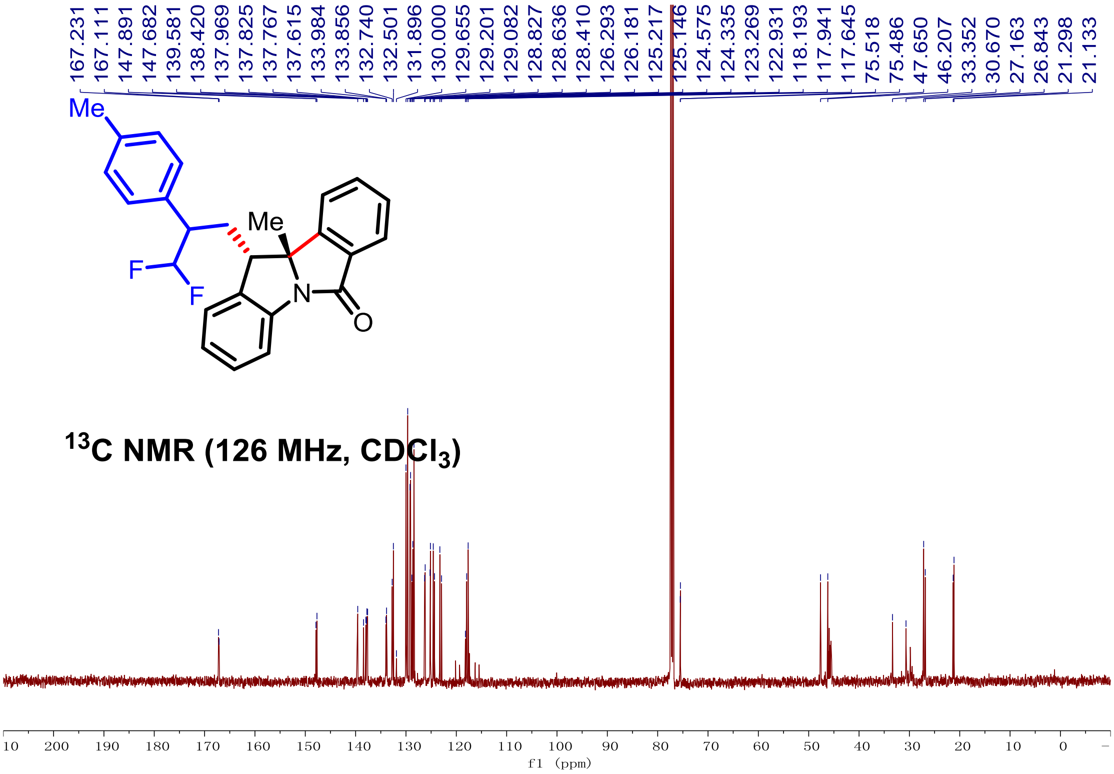
$^{13}$C NMR (126 MHz, $CDCl_3$)

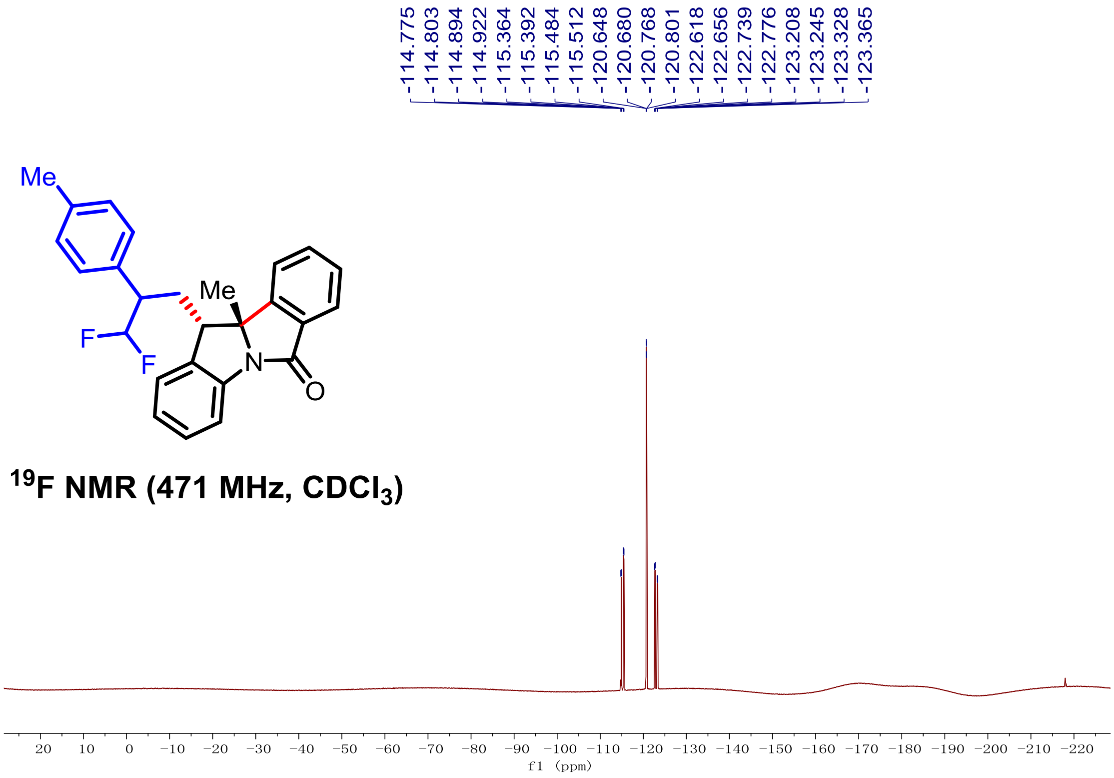


$^{19}$F NMR (471 MHz, $CDCl_3$)

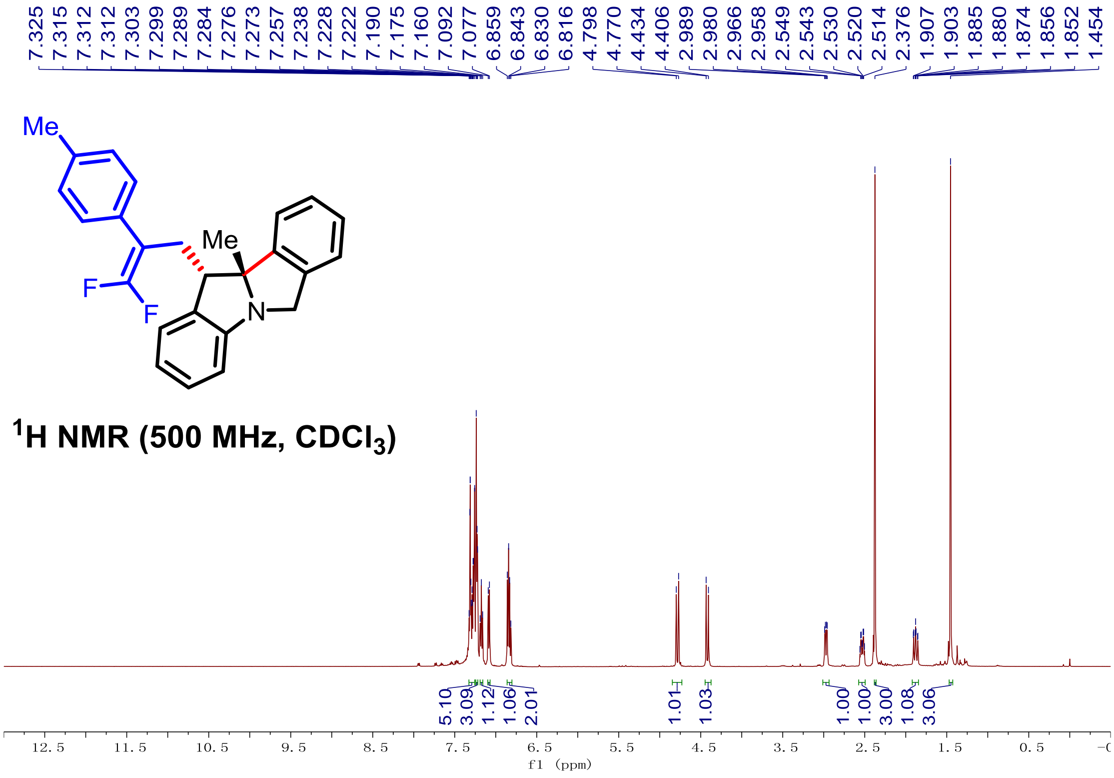
## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)propyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indol-6-one, 53

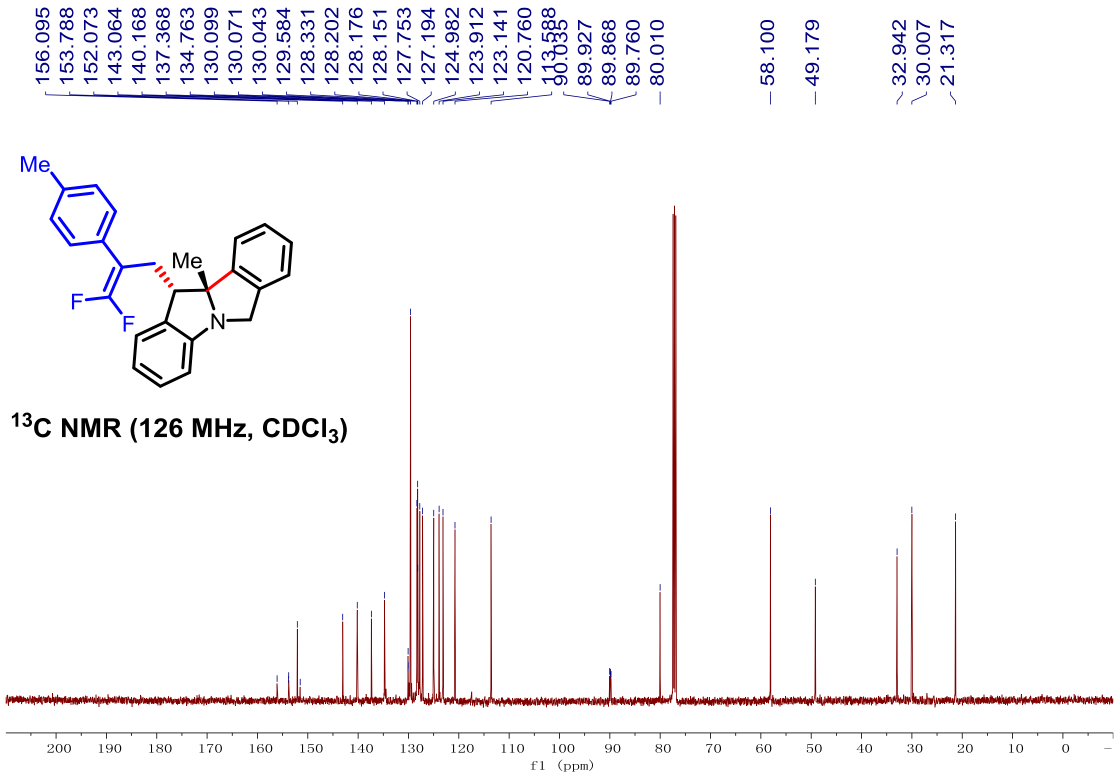




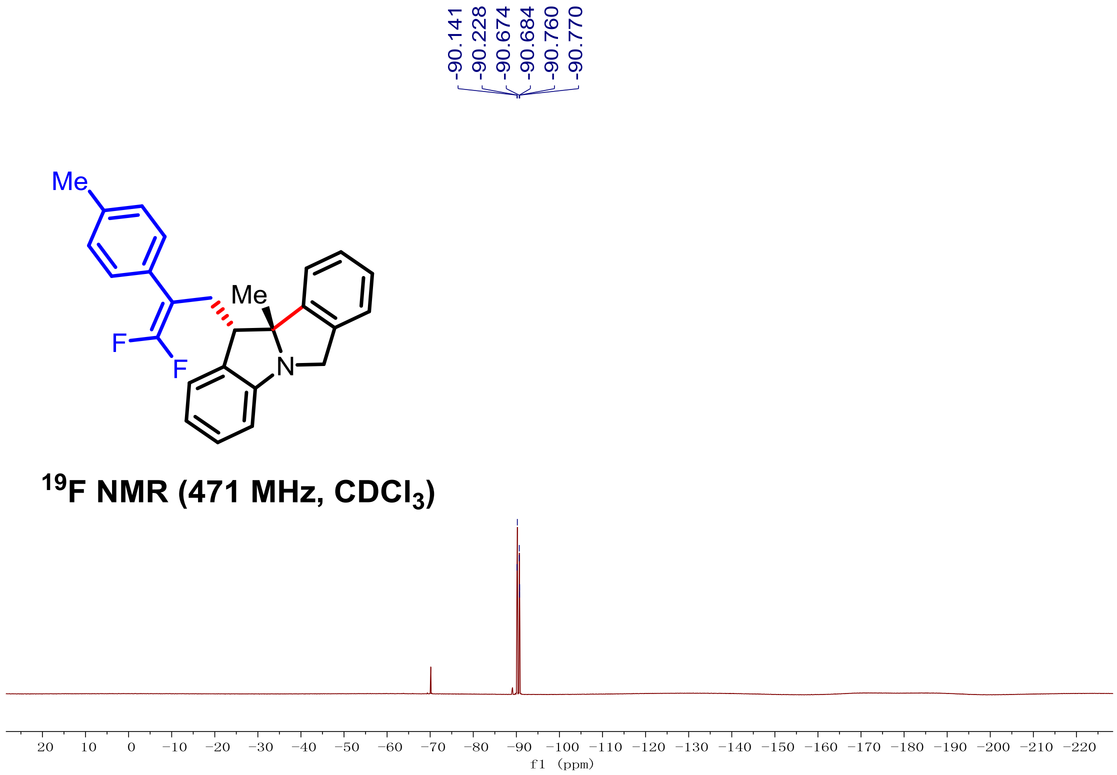


## (10b*R*,11*S*)-11-(3,3-Difluoro-2-(*p*-tolyl)allyl)-10b-methyl-10b,11-dihydro-6*H*-isoindolo[2,1-*a*]indole, 54





$^{13}$C NMR (126 MHz, CDCl$_3$)



$^{19}$F NMR (471 MHz, CDCl$_3$)