

## Supporting Information

### **Isothiourea-Catalyzed Enantioselective Synthesis of Tetrahydro- $\alpha$ -carbolinones \*\***

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## Supporting Information

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## 1 General Information

Reactions involving moisture sensitive reagents were carried out in flame-dried glassware under an argon or nitrogen atmosphere using standard vacuum line techniques and using anhydrous solvents. Anhydrous solvents (THF, CH<sub>2</sub>Cl<sub>2</sub> and toluene) were obtained from an anhydrous solvent system (purified using an alumina column, Mbraun SPS-800). All other reactions were performed in standard glassware with no precautions to exclude air or moisture. Solvents and commercial reagents were used as supplied without further purification unless otherwise stated.

Room temperature (r.t.) refers to 20-25 °C. Temperatures of 0 °C and -78 °C were obtained using ice/water and CO<sub>2</sub>(s)/acetone baths, respectively. Temperatures of -40 °C for overnight reactions were obtained using an immersion cooler (HAAKE EK 90). Reflux conditions were obtained using a DrySyn, oil bath or sand bath equipped with a contact thermometer.

'*In vacuo*' refers to the use of either a Büchi Rotavapor R-200 with a Büchi V-491 heating bath and Büchi V-800 vacuum controller, a Büchi Rotavapor R-210 with a Büchi V-491 heating bath and Büchi V-850 vacuum controller, a Heidolph Laborota 4001 with vacuum controller, an IKA RV10 rotary evaporator with a IKA HB10 heating bath and ILMVAC vacuum controller, or an IKA RV10 rotary evaporator with a IKA HB10 heating bath and Vacuubrand CVC3000 vacuum controller. Rotary evaporator condensers are fitted to Julabo FL601 Recirculating Coolers filled with ethylene glycol and set to -5 °C.

Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 F<sub>254</sub> silica). TLC visualisation was carried out with ultraviolet light (254 nm), followed by staining with a 1% aqueous KMnO<sub>4</sub> solution. Manual column chromatography was performed in glass columns fitted with porosity 3 sintered discs over Kieselgel 60 silica using the solvent system stated. Automated chromatography was performed on a Biotage Isolera Four running Biotage OS578 with a UV/Vis detector using the method stated and cartridges filled with Kieselgel 60 silica.

Melting points were recorded on an Electrothermal 9100 melting point apparatus and are uncorrected.

Optical rotations were measured on a PerkinElmer Precisly/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell at 20 °C.

HPLC analyses were obtained using either a Shimadzu HPLC consisting of a DGU-20A5 degassing unit, LC-20AT liquid chromatography pump, SIL-20AHT autosampler, CMB-20A communications bus module, SPD-M20A diode array detector and a CTO-20A column oven; or a Shimadzu HPLC consisting of a DGU-20A5R degassing unit, LC-20AD liquid chromatography pump, SIL-20AHT autosampler, SPD-20A UV/Vis detector and a CTO-20A column oven. Separation was achieved using DAICEL CHIRALCEL OD-H and OJ-H columns or DAICEL CHIRALPAK AD-H, AS-H, IA, IB, IC and ID columns. All HPLC traces of enantiomerically-enriched compounds were compared with authentic racemic spectra.

<sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker Avance 300 (<sup>1</sup>H 300 MHz), Bruker Avance II 400 (<sup>1</sup>H 400 MHz; <sup>13</sup>C 101 MHz; <sup>19</sup>F 376 MHz) or a Bruker Avance II 500 (<sup>1</sup>H 500 MHz; <sup>13</sup>C 126 MHz) spectrometer at ambient temperature in the deuterated solvent stated. All chemical shifts are quoted in parts per million (ppm) and referenced to the residual solvent peak. All coupling constants, J, are quoted in Hz. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), sept (septet), dd (doublet of doublets), dt (doublet of triplets), dq (doublet of quartets), td

(triplet of doublets), tt (triplet of triplets), ddd (doublet of doublet of doublets), ddt (doublet of doublet of triplets) dddd (doublet of doublet of doublet of doublets), dddt (doublet of doublet of doublet of triplets), and m (multiplet). The abbreviation Ar is used to denote aromatic, Ph to denote phenyl, Bn to denote benzyl, br to denote broad and app to denote apparent.

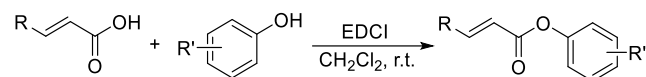
Infrared spectra were recorded on a Shimadzu IRAffinity-1 Fourier transform IR spectrophotometer fitted with a Specac Quest ATR accessory (diamond puck). Spectra were recorded of either thin films or solids, with characteristic absorption wave numbers (max) reported in  $\text{cm}^{-1}$ .

Mass spectrometry ( $m/z$ ) data were acquired by electrospray ionization (ESI), electron impact (EI), atmospheric pressure chemical ionization (APCI) or nanospray ionization (NSI) either at the University of St Andrews or the EPSRC National Mass Spectrometry Facility, Swansea.

## 2 General Procedures

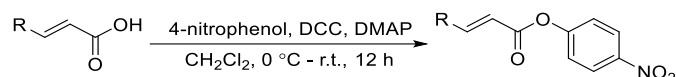
### General Procedure 1: Synthesis of $\alpha,\beta$ -unsaturated aryl esters

#### Method A<sup>1</sup>:



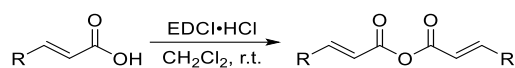
To a solution of  $\alpha,\beta$ -unsaturated acid (1.0 equiv.) and EDCI (1.2 equiv.) in anhydrous dichloromethane (0.67 M) was added phenol (1.1 equiv.) at room temperature. The resulting solution was stirred at r.t. for 2 h till the total consumption of starting material. The solvent was removed *in vacuo*, and the residue was purified by flash silica column chromatography using a mixture of petroleum ether and ethyl acetate as eluent.

#### Method B<sup>2</sup>:



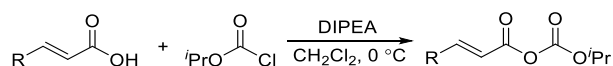
The appropriate alcohol (1.02 equiv.) was added dropwise to a solution of the appropriate carboxylic acid (1 equiv.), DCC (1.1 equiv.) and DMAP (0.2 equiv.) in  $\text{CH}_2\text{Cl}_2$  (1 M) at 0 °C. The reaction mixture was allowed to stir for 12 h at room temperature. The crude mixture was filtered to remove the by-product dicyclohexylurea and concentrated *in vacuo*. The residue was purified by flash silica column chromatography using a mixture of petroleum ether and ethyl acetate as eluent.

### General Procedure 2<sup>3</sup>: Synthesis of $\alpha,\beta$ -unsaturated homoanhydrides



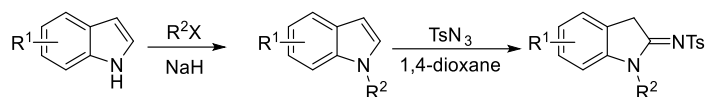
To a solution of carboxylic acid (1.4 equiv.) in  $\text{CH}_2\text{Cl}_2$  (0.8 M) was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide · HCl (EDCI · HCl) (1.0 equiv.) and the solution stirred for 1-2 h at room temperature. The solution was diluted with  $\text{CH}_2\text{Cl}_2$  (50 mL) and then washed sequentially with water (2×50 mL) and saturated aqueous  $\text{NaHCO}_3$  solution (50 mL). The organic layer was dried over anhydrous  $\text{MgSO}_4$ , filtered, and concentrated *in vacuo* to afford the homoanhydride.

### General Procedure 3<sup>4</sup>: Synthesis of $\alpha,\beta$ -unsaturated carbonic anhydrides



To a stirred solution of an  $\alpha,\beta$ -unsaturated carboxylic acid (1.0 equiv.) in  $\text{CH}_2\text{Cl}_2$  (0.72 M) was slowly added *i*-Pr<sub>2</sub>EtN (1.5 equiv.) and isopropyl chloroformate (1.1 equiv.) at 0 °C, and the mixture was stirred at 0 °C for 30 min.  $\text{H}_2\text{O}$  was added to the solution, and the mixture was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo*. Purification by flash silica gel column chromatography using a mixture of petroleum ether and ethyl acetate as an eluent gave the corresponding carbonic anhydride.

### General Procedure 4: Synthesis of indolin-2-imines

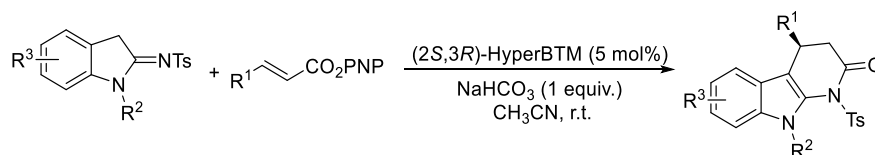


Following a reported procedure<sup>5</sup>, the indole derivative (1.0 equiv.) was dissolved in dry DMF and at 0 °C NaH (1.6 equiv., 60% dispersion in mineral oil) was added portion wise. The ice bath was removed and the reaction mixture was stirred at ambient temperature. After 30 minutes methyl iodide (1.2 equiv.) was added at 0 °C, afterwards the reaction mixture was allowed to warm to room temperature and stirred overnight. H<sub>2</sub>O was carefully added and the aqueous phase was extracted using CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were washed with H<sub>2</sub>O and NaCl aq. (sat.). Then the combined organic layers were dried using Na<sub>2</sub>SO<sub>4</sub> and after filtration the solvent was removed *in vacuo*. In case the *N*-methyl indole was insufficient pure, further purification was achieved by flash column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate.

NaH (1.08 equiv.) was added portion wise at 0 °C to a solution of indole (1.0 equiv.) in DMF. The ice bath was removed and the mixture was stirred for 30 minutes. Benzyl bromide (1.05 equiv.) was added dropwise at 0 °C and the reaction mixture was stirred overnight at room temperature. Addition of H<sub>2</sub>O was followed by extraction using EtOAc for three times. The combined organic layers were washed with NaCl aq. (sat.) and dried over MgSO<sub>4</sub>. All volatiles were removed *in vacuo* and after flash column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate.

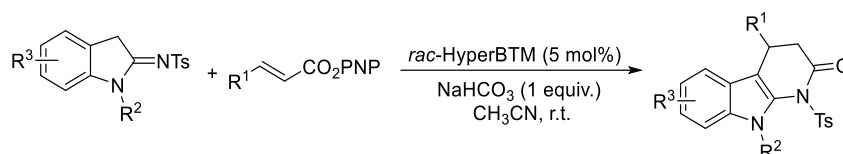
Following a reported procedure<sup>6</sup>, an oven-dried round-bottomed flask was charged with indole (1.0 equiv.) and *p*-toluenesulfonyl azide (1.4 equiv.) in dry 1,4-dioxane under nitrogen atmosphere. The mixture was stirred at 75-80 °C for 18-24 h and cooled. Addition of ethanol resulted in indolin-2-imines to precipitate from the solution.

**General Procedure 5:** *Asymmetric [3+3] cyclization of indolin-2-imines with  $\alpha,\beta$ -unsaturated aryl esters*



Indolin-2-imines (0.24 mmol),  $\alpha,\beta$ -unsaturated aryl esters (0.2 mmol) and (2*S*,3*R*)-HyperBTM (5 mol%) in CH<sub>3</sub>CN were allowed to stir for 24-72 h at room temperature. Then, the mixture was concentrated *in vacuo*, and the residue purified by flash column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluent.

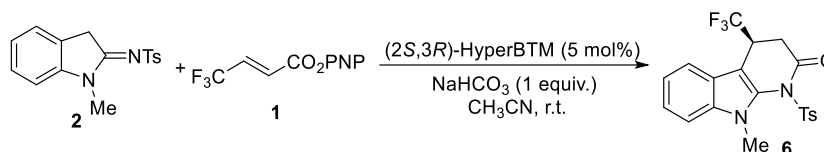
**General Procedure 6:** *Unasymmetric [3+3] cyclization of indolin-2-imines with  $\alpha,\beta$ -unsaturated aryl esters*



Indolin-2-imines (0.12 mmol),  $\alpha,\beta$ -unsaturated aryl esters (0.1 mmol) and *rac*-HyperBTM (5 mol%) in 1 mL CH<sub>3</sub>CN were allowed to stir for 24-72 h at room temperature. Then, the mixture was concentrated

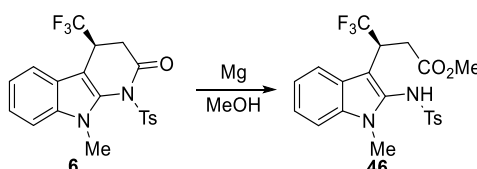
*in vacuo*, and the residue purified by flash column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluent.

**General Procedure 7:** Grams-scale preparation of **6**



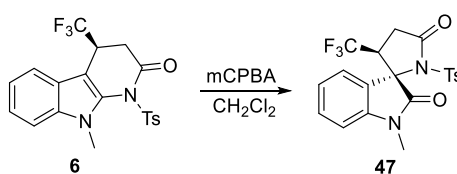
4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (1.08 g, 3.6 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (0.78 g, 3.0 mmol) and (2*S*,3*R*)-HyperBTM (46.3 mg, 0.15 mmol) in 30 mL CH<sub>3</sub>CN were allowed to stir for 72 h at room temperature. Then, the mixture was concentrated *in vacuo*, and the residue purified by flash column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product (1.10 g, 87% yield).

**General Procedure 8<sup>7</sup>:** Hydrolysis of tetrahydro- $\alpha$ -carbolinone **6**



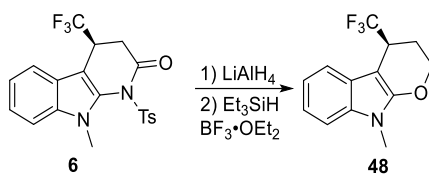
To a dry Schlenk tube equipped with a magnetic stir bar, was added **6** (84.5 mg, 0.2 mmol) and Mg-powder (28.8 mg, 6 equiv). The tube was sealed with a septum, evacuated and refilled with nitrogen for 3 times. Then, absolute MeOH (4 mL) was added and the reaction was sonicated at room temperature over night. The reaction mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub>, vacuum filtration through celite and the filtrate was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluent.

**General Procedure 9:** Synthesis of spiro compound **47**



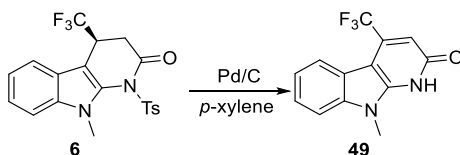
To a dry round-bottomed flask equipped with a magnetic stir bar, was added **6** (84.5 mg, 0.2 mmol) and 2 mL CH<sub>2</sub>Cl<sub>2</sub>, then *m*CPBA (50.3 mg, 0.204 mmol, 70%) was added at 0 °C. The mixture was stirred at 0 °C over night. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluent.

**General Procedure 10<sup>8</sup>:** Reduction of tetrahydro- $\alpha$ -carbolinone **6**



To a dry Schlenk tube equipped with a magnetic stir bar, was added **6** (84.5 mg, 0.2 mmol) and Mg-powder (28.8 mg, 6 equiv.). The tube was sealed with a septum, evacuated and refilled with nitrogen for 3 times. Then, absolute MeOH (2 mL) was added and the reaction was sonicated at room temperature until no more starting material remained monitored by TLC (around 5 h). The reaction mixture was diluted with DCM, vacuum filtration through celite and the filtrate was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluent.

**General Procedure 11<sup>7</sup>: Synthesis of carboline **49****

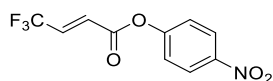


To a solution of **6** (84.5 mg, 0.2 mmol) in *p*-xylene (4 mL) was added 46 mg Pd/C (two times by each 23.0 mg, interval 12h), the reaction mixture was stirred at 145 °C under reflux for 24h. After cooling to r.t., then the reaction mixture was diluted with 20 mL MeOH, vacuum filtration through celite and the filtrate was removed under reduced pressure and the residue was purified by chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluent.

### 3 Preparation of Starting Materials

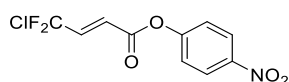
#### 3.1 Data for $\alpha,\beta$ -unsaturated aryl esters

##### 4-Nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (**1**)



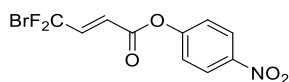
Following General Procedure **1** (Method **A**), the title compound was afforded from (*E*)-4,4,4-trifluorobut-2-enoic acid and 4-nitrophenol as a white solid; mp 93-95 °C;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 6.72–6.77 (1H, m,  $\text{F}_3\text{CCH}=\text{CH}$ ), 7.00–7.09 (1H, m,  $\text{F}_3\text{CCH}=\text{CH}$ ), 7.37–7.40 (2H, m,  $\text{ArC}(2,6)\text{H}$ ), 8.31–8.35 (2H, m,  $\text{ArC}(3,5)\text{H}$ ). Data in agreement with the literature.<sup>1</sup>

##### 4-Nitrophenyl (*E*)-4-chloro-4,4-difluorobut-2-enoate (**7**)



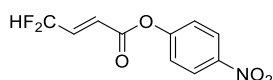
Following General Procedure **1** (Method **A**), the title compound was afforded from (*E*)-4-chloro-4,4-difluorobut-2-enoic acid and 4-nitrophenol as a white solid; mp 99-100 °C;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 6.63 (1H, dt,  $J$  15.6, 1.8,  $\text{F}_2\text{ClCCH}=\text{CH}$ ), 7.18 (1H, dt,  $J$  15.6, 9.0,  $\text{F}_2\text{ClCCH}=\text{CH}$ ), 7.37–7.41 (2H, m,  $\text{ArC}(2,6)\text{H}$ ), 8.32–8.36 (2H, m,  $\text{ArC}(3,5)\text{H}$ ). Data in agreement with the literature.<sup>9</sup>

##### 4-Nitrophenyl (*E*)-4-bromo-4,4-difluorobut-2-enoate (**8**)



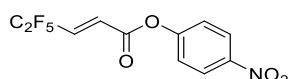
Following General Procedure **1** (Method **A**), the title compound was afforded from (*E*)-4-bromo-4,4-difluorobut-2-enoic acid and 4-nitrophenol as a white solid; mp 79-80 °C;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 6.54 (1H, dt,  $J$  15.6, 1.7,  $\text{F}_2\text{BrCCH}=\text{CH}$ ), 7.24 (1H, dt,  $J$  15.6, 9.9,  $\text{F}_2\text{BrCCH}=\text{CH}$ ), 7.37–7.41 (2H, m,  $\text{ArC}(2,6)\text{H}$ ), 8.31–8.35 (2H, m,  $\text{ArC}(3,5)\text{H}$ ). Data in agreement with the literature.<sup>9</sup>

##### 4-Nitrophenyl (*E*)-4,4-difluorobut-2-enoate (**9**)



Following General Procedure **1** (Method **A**), the title compound was afforded from (*E*)-4,4-difluorobut-2-enoic acid and 4-nitrophenol as a white solid; mp 74-76 °C;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 6.22–6.50 (1H, m,  $\text{CF}_2\text{H}$ ), 6.52–6.57 (1H, m,  $\text{F}_2\text{HCCH}=\text{CH}$ ), 7.03–7.14 (1H, m,  $\text{F}_2\text{HCCH}=\text{CH}$ ), 7.36–7.40 (2H, m,  $\text{ArC}(2,6)\text{H}$ ), 8.31–8.35 (2H, m,  $\text{ArC}(3,5)\text{H}$ ). Data in agreement with the literature.<sup>9</sup>

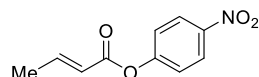
##### 4-Nitrophenyl (*E*)-4,4,5,5-pentafluoropent-2-enoate (**10**)



Following General Procedure **1** (Method **A**), the title compound was afforded from (*E*)-4,4,5,5,5-pentafluoropent-2-enoic acid and 4-nitrophenol as a white solid; mp 37-38 °C;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 6.80 (1H, dt,  $J$  15.8, 2.1,  $\text{F}_3\text{CF}_2\text{CCH}=\text{CH}$ ), 7.02–7.12 (1H, m,  $\text{F}_3\text{CF}_2\text{CCH}=\text{CH}$ ), 7.38–7.42 (2H, m,  $\text{ArC}(2,6)\text{H}$ ), 8.32–8.36 (2H, m,  $\text{ArC}(3,5)\text{H}$ );  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{F}}$ : -117.4 (m,  $\text{CF}_2$ ), -84.4 (m,  $\text{CF}_3$ );  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 108.2–120.2 (m,  $J$  236.7,  $\text{CF}_2\text{CF}_3$ ), 122.2 ( $2\times\text{ArCH}$ ),

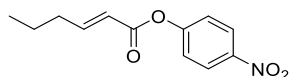
125.4 (2×ArCH), 129.5 (t, *J* 8.3, F<sub>3</sub>CF<sub>2</sub>CCH=CH), 133.3 (t, *J* 24.2, F<sub>3</sub>CF<sub>2</sub>CCH=CH), 145.8 (ArC), 154.5 (ArC), 161.1 (CO<sub>2</sub>Ar). Attempted mass spectrometry analysis did not give a satisfactory mass ion or recognized fragmentation; however **10** was readily transformed to compound **21** that was fully characterized.

#### 4-Nitrophenyl (*E*)-but-2-enoate (**11**)



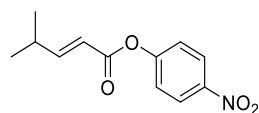
Following General Procedure **1** (Method **B**), the title compound was afforded from (*E*)-but-2-enoic acid and 4-nitrophenol as a white solid; mp 59-61 °C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ<sub>H</sub>: 2.01 (3H, dd, *J* 6.9, 1.7, CH<sub>3</sub>), 6.03–6.08 (1H, m, CH=CH–CO<sub>2</sub>PNP), 7.21–7.28 (1H, m, CH=CHCO<sub>2</sub>PNP), 7.29–7.31 (2H, m, CH–Ar<sub>PNP</sub>), 8.26–8.29 (2H, m, CH–Ar<sub>PNP</sub>). Data in agreement with the literature.<sup>2</sup>

#### 4-Nitrophenyl (*E*)-hex-2-enoate (**12**)



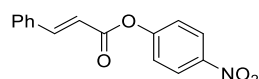
Following General Procedure **1** (Method **B**), the title compound was afforded from (*E*)-hex-2-enoic acid and 4-nitrophenol as a white solid; mp 95-96 °C; v<sub>max</sub> (film), 1520 (N–O), 1738 (C=O); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub>: 1.01 (3H, t, *J* 7.4, CH<sub>3</sub>), 1.58 (2H, h, *J* 7.4, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.32 (2H, qd, *J* 7.2, 1.6, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 6.05 (1H, dt, *J* 15.6, 1.6, <sup>n</sup>PrCH=CH), 7.26 (1H, dt, *J* 15.6, 7.0, <sup>n</sup>PrCH=CH), 7.32–7.35 (2H, m, ArC(2,6)*H*), 8.27–8.31 (2H, m, ArC(3,5)*H*); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub>: 13.7 (CH<sub>3</sub>), 21.2 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 34.5 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 119.8 (<sup>n</sup>PrCH=CH), 122.5 (2×ArCH), 125.2 (2×ArCH), 145.2 (ArC), 153.5 (<sup>n</sup>PrCH=CH), 155.7 (ArC), 163.9 (C=O); HRMS (ESI<sup>+</sup>) C<sub>12</sub>H<sub>13</sub>NNaO<sub>4</sub> [M+Na]<sup>+</sup> found 258.0736, requires 258.0737 (–0.31 ppm).

#### 4-Nitrophenyl (*E*)-4-methylpent-2-enoate (**13**)



Following General Procedure **1** (Method **B**), the title compound was afforded from (*E*)-4-methylpent-2-enoic acid and 4-nitrophenol as a white solid; mp 96-97 °C; v<sub>max</sub> (film), 1520 (N–O), 1738 (C=O); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub>: 1.16 (6H, d, *J* 6.8, (CH<sub>3</sub>)<sub>2</sub>CH), 2.55–2.64 (1H, m, (CH<sub>3</sub>)<sub>2</sub>CH), 6.00 (1H, dd, *J* 1.5, 15.7, <sup>i</sup>PrCH=CH), 7.24 (1H, dd, *J* 6.6, 15.7, <sup>i</sup>PrCH=CH), 7.21–7.36 (2H, m, ArC(2,6)*H*), 8.28–8.32 (2H, m, ArC(3,5)*H*); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub>: 21.1 ((CH<sub>3</sub>)<sub>2</sub>CH), 31.4 ((CH<sub>3</sub>)<sub>2</sub>CH), 117.2 (<sup>i</sup>PrCH=CH), 122.5 (2×ArCH), 125.2 (2×ArCH), 145.2 (ArC), 155.7 (<sup>i</sup>PrCH=CH), 159.6 (ArC), 164.3 (C=O); HRMS (ESI<sup>+</sup>) C<sub>12</sub>H<sub>13</sub>NNaO<sub>4</sub> [M+Na]<sup>+</sup> found 258.0733, requires 258.0737 (–1.47 ppm).

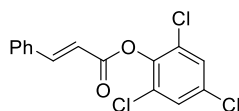
#### 4-Nitrophenyl cinnamate (**14**)



Following General Procedure **1** (Method **A**), the title compound was afforded from cinnamic acid and 4-nitrophenol as a white solid; mp 143-145 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub>: 6.63 (1H, d, *J* 16.0, CH=CH–CO<sub>2</sub>PNP), 7.37–7.39 (2H, m, CH–Ar<sub>PNP</sub>), 7.44–7.47 (3H, m, CH–Ph), 7.60–7.62 (2H, m, CHPh),

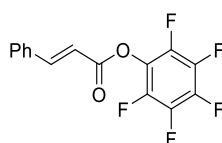
7.92 (1H, d, *J* 16.0, CH=CH-CO<sub>2</sub>PNP), 8.30–8.32 (2H, m, CH-Ar<sub>PNP</sub>). Data in agreement with the literature.<sup>10</sup>

### 2,4,6-Trichlorophenyl cinnamate (S1)



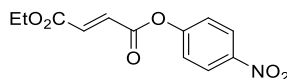
Following General Procedure **1** (Method **A**), the title compound was afforded from cinnamic acid and 2,4,6-trichlorophenol as a white solid; mp 74–76 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub>: 6.72 (1H, d, *J* 16.0, PhCH=CH), 7.43 (2H, s, ArC(3,5)H), 7.46–7.49 (3H, m, PhCH), 7.63–7.66 (2H, m, PhCH), 7.99 (1H, d, *J* 16.0, PhCH=CH). Data in agreement with the literature.<sup>11</sup>

### Perfluorophenyl cinnamate (S2)



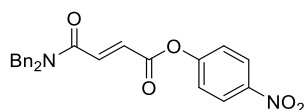
Following General Procedure **1** (Method **A**), the title compound was afforded from cinnamic acid and 2,3,4,5,6-pentafluorophenol as a white solid; mp 87–88 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub>: 6.64 (1H, d, *J* 16.0, PhCH=CH), 7.44 (1H, t, *J* 5.7, CH-Ar), 7.46 (2H, s, CH-Ar), 7.60 (2H, d, *J* 5.7, CH-Ar), 7.95 (1H, d, *J* 16.0, PhCH=CH). Data in agreement with the literature.<sup>12</sup>

### Ethyl (4-nitrophenyl) fumarate (15)



Following General Procedure **1** (Method **B**), the title compound was afforded from (*E*)-4-ethoxy-4-oxobut-2-enoic acid and 4-nitrophenol as a white solid; mp 67–68 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub>: 1.36 (3H, t, *J* 7.1, CH<sub>2</sub>CH<sub>3</sub>), 4.32 (2H, q, *J* 7.1, CH<sub>2</sub>CH<sub>3</sub>), 7.04 (1H, d, *J* 15.8, CH=CHCO<sub>2</sub>Ar), 7.09 (1H, d, *J* 15.8, CH=CHCO<sub>2</sub>Ar), 7.31–7.43 (2H, m, CH-Ar), 8.10–8.13 (2H, m, CH-Ar). Data in agreement with the literature.<sup>2</sup>

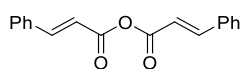
### 4-Nitrophenyl (*E*)-4-(dibenzylamino)-4-oxobut-2-enoate (16)



Following General Procedure **1** (Method **B**), the title compound was afforded from (*E*)-4-(dibenzylamino)-4-oxobut-2-enoic acid and 4-nitrophenol as a white solid; mp 62–64 °C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ<sub>H</sub>: 4.58 (2H, s, CH<sub>2</sub>Ph), 4.69 (2H, s, CH<sub>2</sub>Ph), 7.14 (1H, d, *J* 15.3, CH=CH-CO<sub>2</sub>PNP), 7.16–7.19 (2H, m, CH<sub>2</sub>Bn), 7.26–7.27 (2H, m, CH<sub>2</sub>Bn), 7.31–7.33 (2H, m, CH-Ar<sub>PNP</sub>), 7.34–7.40 (6H, m, CH-Ar), 7.64 (1H, d, *J* 15.3, CH=CH-CO<sub>2</sub>PNP), 8.28–8.29 (2H, m, CH-Ar<sub>PNP</sub>). Data in agreement with the literature.<sup>2</sup>

## 3.2 Data for homo anhydride

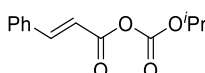
### Cinnamic anhydride (S4)



Following General Procedure 2, the title compound was afforded from cinnamic acid as a white solid;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 6.54 (2H, d,  $J$  16.0,  $\text{PhCH}=\text{CH}$ ), 7.40–7.47 (6H, m,  $\text{CH-Ph}$ ), 7.54–7.63 (4H, m,  $\text{CH-Ph}$ ), 7.86 (2H, d,  $J$  16.0,  $\text{PhCH}=\text{CH}$ ). Data in agreement with the literature.<sup>3</sup>

### 3.3 Data for carbonic anhydride

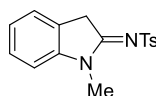
#### (*E*)-cinnamic (isopropyl carbonic) anhydride (17)



Following General Procedure 3, the title compound was afforded from cinnamic acid as a colourless oil;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 1.39 (6H, d,  $J$  6.0 Hz,  $\text{CH}(\text{CH}_3)_2$ ), 5.05 (1H, p,  $J$  6.0,  $\text{CH}(\text{CH}_3)_2$ ), 6.42 (1H, d,  $J$  16.0 Hz,  $\text{CH}$ ), 7.42 (2H, m,  $\text{CH-Ph}$ ), 7.55 (2H, m,  $\text{CH-Ph}$ ), 7.82 (1H, d,  $J$  16.0 Hz,  $\text{CH}$ ). Data in agreement with the literature.<sup>4</sup>

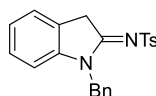
### 3.4 Data for indolin-2-imines

#### (*Z*)-4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (2)



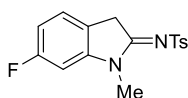
Following General Procedure 4, the title compound was afforded as a brown solid; mp 143–145 °C;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 2.44 (3H, s,  $\text{C}_6\text{H}_4\text{CH}_3$ ), 3.38 (3H, s,  $\text{N-CH}_3$ ), 4.24 (2H, s,  $\text{CH}_2$ ), 6.96–6.98 (1H, m,  $\text{CH-Ar}$ ), 7.14–7.16 (1H, m,  $\text{CH-Ar}$ ), 7.32–7.33 (4H, m,  $\text{CH-Ar}$ ), 7.90–7.92 (2H, m,  $\text{CH-Ar}$ ). Data in agreement with the literature.<sup>13</sup>

#### (*Z*)-*N*-(1-benzylindolin-2-ylidene)-4-methylbenzenesulfonamide (28)



Following General Procedure 4, the title compound was afforded as a brown solid; mp 119–121 °C;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 1.62 (2H, s,  $\text{CH}_2\text{Ph}$ ), 2.38 (3H, s,  $\text{CH}_3$ ), 5.26 (2H, s,  $\text{CH}_2\text{-C}=\text{N}$ ), 6.35 (1H, s,  $\text{CH}$ ), 7.00–7.07 (4H, m,  $\text{CH-Ar}$ ), 7.13–7.17 (3H, m,  $\text{CH-Ar}$ ), 7.23–7.25 (2H, m,  $\text{CH-Ar}$ ), 7.29–7.32 (2H, m,  $\text{CH-Ar}$ ), 7.63–7.64 (2H, m,  $\text{CH-Ar}$ ). Data in agreement with the literature.<sup>14</sup>

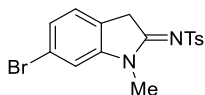
#### (*Z*)-*N*-(6-fluoro-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (29)



Following General Procedure 4, the title compound was afforded as a yellow solid; mp 164–165 °C;  $\nu_{\text{max}}$  (film), 1558 ( $\text{C}=\text{N}$ );  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ :  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 2.44 (3H, s,  $\text{C}_6\text{H}_4\text{CH}_3$ ), 3.34 (3H, s,  $\text{N-CH}_3$ ), 4.21 (2H, s,  $\text{CH}_2$ ), 6.68–6.71 (1H, m,  $\text{CH-Ar}$ ), 6.80–6.84 (1H, m,  $\text{CH-Ar}$ )

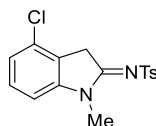
Ar), 7.25–7.33 (3H, m, *CH*-Ar), 7.89–7.91 (2H, m, *CH*-Ar);  $^{19}\text{F}\{^1\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{F}}$ : –112.4–112.3 (m, F);  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 21.6 ( $\text{C}_6\text{H}_4\text{CH}_3$ ), 28.7 (N- $\text{CH}_3$ ), 35.6 ( $\text{CH}_2$ ), 98.0 (d, *J* 27.9, ArCH), 109.9 (d, *J* 22.6, ArCH), 121.5 (ArC), 125.3 (d, *J* 9.7, ArC), 126.7 (2 $\times$ ArCH), 129.4 (2 $\times$  ArCH), 139.2 (ArC), 143.0 (ArC), 145.4 (d, *J* 11.5, ArC), 163.0 (d, *J* 245.4, ArC), 170.4 (C=N); HRMS (ESI $^+$ )  $\text{C}_{16}\text{H}_{15}\text{FN}_2\text{NaO}_2\text{S}$  [ $\text{M}+\text{Na}$ ] $^+$  found 341.0729, requires 341.0730 (–0.43 ppm).

**(Z)-N-(6-bromo-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (30)**



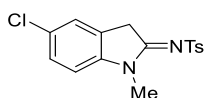
Following General Procedure 4, the title compound was afforded as a orange solid; mp 187-188 °C;  $\nu_{\text{max}}$  (film), 1558 (C=N);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 2.44 (3H, s,  $\text{C}_6\text{H}_4\text{CH}_3$ ), 3.34 (3H, s, N- $\text{CH}_3$ ), 4.21 (2H, s,  $\text{CH}_2$ ), 7.10 (1H, d, *J* 1.5 Hz, *CH*-Ar), 7.20 (1H, d, *J* 7.9 Hz, *CH*-Ar), 7.27 (1H, dd, *J* 7.9, 1.6 Hz, *CH*-Ar), 7.31–7.33 (2H, m, *CH*-Ar), 7.88–7.91 (2H, m, *CH*-Ar). Data in agreement with the literature.<sup>7</sup>

**(Z)-N-(4-chloro-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (31)**



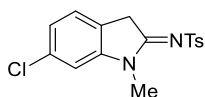
Following General Procedure 4, the title compound was afforded as a yellow solid; mp 186-187 °C;  $\nu_{\text{max}}$  (film), 1557 (C=N);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 2.44 (3H, s,  $\text{C}_6\text{H}_4\text{CH}_3$ ), 3.36 (3H, s, N- $\text{CH}_3$ ), 4.27 (2H, s,  $\text{CH}_2$ ), 6.86 (1H, d, *J* 7.8 Hz, *CH*-Ar), 7.11 (1H, d, *J* 7.8 Hz, *CH*-Ar), 7.27–7.34 (3H, m, *CH*-Ar), 7.92 (2H, d, *J* 8.3 Hz, *CH*-Ar). Data in agreement with the literature.<sup>4</sup>

**(Z)-N-(5-chloro-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (32)**



Following General Procedure 4, the title compound was afforded as a yellow solid; mp 193-194 °C;  $\nu_{\text{max}}$  (film), 1558 (C=N);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ :  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 2.44 (3H, s,  $\text{C}_6\text{H}_4\text{CH}_3$ ), 3.35 (3H, s, N- $\text{CH}_3$ ), 4.25 (2H, s,  $\text{CH}_2$ ), 6.88 (1H, d, *J* 8.4 Hz, *CH*-Ar), 7.30–7.33 (4H, m, *CH*-Ar), 7.89–7.91 (2H, m, *CH*-Ar);  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 21.6 ( $\text{C}_6\text{H}_4\text{CH}_3$ ), 28.7 (N- $\text{CH}_3$ ), 36.1 ( $\text{CH}_2$ ), 110.0 (ArCH), 124.9 (ArCH), 126.7 (2 $\times$ ArCH), 127.9 (ArC), 128.1 (ArCH), 129.2 (ArC), 129.4 (2 $\times$ ArCH), 139.2 (ArC), 142.6 (ArC), 143.0 (ArC), 169.2 (C=N); HRMS (ESI $^+$ )  $\text{C}_{16}\text{H}_{16}\text{ClN}_2\text{O}_2\text{S}$  [ $\text{M}+\text{H}$ ] $^+$  found 335.0615, requires 335.0616 (–0.16 ppm).

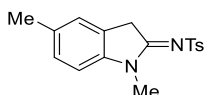
**(Z)-N-(6-chloro-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (33)**



Following General Procedure 4, the title compound was afforded as a yellow solid; mp 160-161 °C;  $\nu_{\text{max}}$

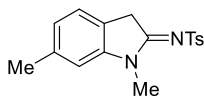
(film), 1562 (C=N);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 2.44 (3H, s,  $\text{C}_6\text{H}_4\text{CH}_3$ ), 3.35 (3H, s, N- $\text{CH}_3$ ), 4.24 (2H, s,  $\text{CH}_2$ ), 6.96 (1H, d,  $J$  1.7 Hz,  $\text{CH-Ar}$ ), 7.12 (1H, dd,  $J$  7.9, 1.7 Hz,  $\text{CH-Ar}$ ), 7.26 (1H, d,  $J$  7.9 Hz,  $\text{CH-Ar}$ ), 7.31–7.34 (2H, m,  $\text{CH-Ar}$ ), 7.90 (2H, d,  $J$  8.3 Hz,  $\text{CH-Ar}$ );  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 21.6 ( $\text{C}_6\text{H}_4\text{CH}_3$ ), 28.7 (N- $\text{CH}_3$ ), 35.8 ( $\text{CH}_2$ ), 109.9 (ArCH), 123.6 (ArCH), 124.6 (ArC), 125.2 (ArCH), 126.8 ( $2\times\text{ArCH}$ ), 129.4 ( $2\times\text{ArCH}$ ), 134.1 (ArC), 139.1 (ArC), 143.0 (ArC), 145.2 (ArC), 169.8 (C=N); **HRMS (ESI $^+$ )**  $\text{C}_{16}\text{H}_{16}\text{ClN}_2\text{O}_2\text{S}$  [ $\text{M}+\text{H}$ ] $^+$  found 335.0615, requires 335.0616 (–0.16 ppm).

**(Z)-N-(1,5-dimethylindolin-2-ylidene)-4-methylbenzenesulfonamide (34)**



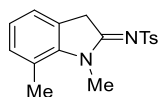
Following General Procedure 4, the title compound was afforded as a yellow solid; mp 177–179 °C;  $\nu_{\text{max}}$  (film), 1557 (C=N);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 2.37 (3H, s, Ar $\text{CH}_3$ ), 2.43 (3H, s, Ar $\text{CH}_3$ ), 3.36 (3H, s, N- $\text{CH}_3$ ), 4.19 (2H, s,  $\text{CH}_2$ ), 6.85 (1H, d,  $J$  8.0 Hz,  $\text{CH-Ar}$ ), 7.12–7.16 (2H, m,  $\text{CH-Ar}$ ), 7.31 (2H, d,  $J$  8.0 Hz,  $\text{CH-Ar}$ ), 7.91 (2H, d,  $J$  8.3 Hz,  $\text{CH-Ar}$ );  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 21.1 (Ar $\text{CH}_3$ ), 21.5 (Ar $\text{CH}_3$ ), 28.6 (N- $\text{CH}_3$ ), 36.2 ( $\text{CH}_2$ ), 108.9 (ArCH), 125.2 (ArCH), 126.4 (ArC), 126.7 ( $2\times\text{ArCH}$ ), 128.4 (ArCH), 129.3 ( $2\times\text{ArCH}$ ), 133.5 (ArC), 139.5 (ArC), 141.6 (ArC), 142.7 (ArC), 169.6 (C=N); **HRMS (ESI $^+$ )**  $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_2\text{S}$  [ $\text{M}+\text{H}$ ] $^+$  found 315.1161, requires 315.1162 (–0.24 ppm).

**(Z)-N-(1,6-dimethylindolin-2-ylidene)-4-methylbenzenesulfonamide (35)**



Following General Procedure 4, the title compound was afforded as a yellow solid; mp 163–165 °C;  $\nu_{\text{max}}$  (film), 1557 (C=N);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 2.41 (3H, s, Ar $\text{CH}_3$ ), 2.43 (3H, s, Ar $\text{CH}_3$ ), 3.36 (3H, s, N- $\text{CH}_3$ ), 4.18 (2H, s,  $\text{CH}_2$ ), 6.78 (1H, s,  $\text{CH-Ar}$ ), 6.95 (1H, d,  $J$  7.5 Hz,  $\text{CH-Ar}$ ), 7.21 (1H, d,  $J$  7.5 Hz,  $\text{CH-Ar}$ ), 7.30–7.32 (2H, m,  $\text{CH-Ar}$ ), 7.90–7.92 (2H, m,  $\text{CH-Ar}$ );  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 21.5 (Ar $\text{CH}_3$ ), 21.7 (Ar $\text{CH}_3$ ), 28.5 (N- $\text{CH}_3$ ), 35.9 ( $\text{CH}_2$ ), 110.1 (ArCH), 123.3 (ArC), 124.1 (ArCH), 124.3 (ArCH), 126.7 ( $2\times\text{ArCH}$ ), 129.4 ( $2\times\text{ArCH}$ ), 138.3 (ArC), 139.5 (ArC), 142.7 (ArC), 144.1 (ArC), 170.1 (C=N); **HRMS (ESI $^+$ )**  $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_2\text{S}$  [ $\text{M}+\text{H}$ ] $^+$  found 315.1158, requires 315.1162 (–1.19 ppm).

**(Z)-N-(1,7-dimethylindolin-2-ylidene)-4-methylbenzenesulfonamide (36)**



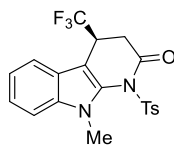
Following General Procedure 4, the title compound was afforded as a yellow solid; mp 151–152 °C;  $\nu_{\text{max}}$  (film), 1549 (C=N);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 2.43 (3H, s, Ar $\text{CH}_3$ ), 2.60 (3H, s, Ar $\text{CH}_3$ ), 3.66 (3H, s, N- $\text{CH}_3$ ), 4.18 (2H, s,  $\text{CH}_2$ ), 6.99–7.06 (2H, m,  $\text{CH-Ar}$ ), 7.16 (1H, d,  $J$  6.9 Hz,  $\text{CH-Ar}$ ), 7.30 (2H, d,  $J$  8.1 Hz,  $\text{CH-Ar}$ ), 7.89–7.91 (2H, m,  $\text{CH-Ar}$ );  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 19.3 (Ar $\text{CH}_3$ ), 21.5 (Ar $\text{CH}_3$ ), 32.1 (N- $\text{CH}_3$ ), 36.0 ( $\text{CH}_2$ ), 120.9 (ArC), 122.3 (ArCH), 123.7 (ArCH), 126.7 ( $2\times\text{ArCH}$ ), 126.9 (ArC), 129.4 ( $2\times\text{ArCH}$ ), 131.9 (ArCH), 139.5 (ArC), 141.8 (ArC), 142.7 (ArC), 170.5 (C=N); **HRMS (ESI $^+$ )**  $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_2\text{S}$  [ $\text{M}+\text{H}$ ] $^+$  found 315.1158, requires 315.1162 (–1.19 ppm).



## 4 Products

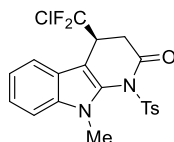
### 4.1 Data for tetrahydro-2*H*-pyrido[2,3-*b*]indol-2-ones

#### (*S*)-9-Methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2*H*-pyrido[2,3-*b*]indol-2-one (6)



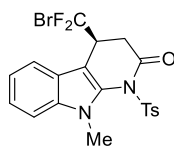
Following General Procedure 5, (*Z*)-4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (52.2 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.44) afforded the desired compound (83.6 mg, 99%) as white solid. mp: 133-134 °C;  $[\alpha]_D^{20} = +124.0$  (*c* 1.0, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (major): 17.0 min, *t<sub>R</sub>* (minor): 34.4 min, 97:3 er; *v<sub>max</sub>* (film), 1724 (C=O); **<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)** δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.89–2.91 (2H, m, CH<sub>2</sub>), 3.69–3.73 (1H, m, CHCF<sub>3</sub>), 3.96 (3H, d, *J* 1.5 Hz, N-CH<sub>3</sub>), 7.26–7.30 (1H, m, CH-Ar), 7.34–7.38 (3H, m, CH-Ar), 7.45–7.47 (1H, m, CH-Ar), 7.57 (1H, d, *J* 7.8 Hz, CH-Ar), 7.93 (2H, d, *J* 8.3 Hz, CH-Ar); **<sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz)** δ<sub>F</sub>: -71.6 (s, CF<sub>3</sub>); **<sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz)** δ<sub>C</sub>: 21.9 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 33.9 (N-CH<sub>3</sub>), 34.8 (q, <sup>2</sup>*J*<sub>C-F</sub> 31.4 Hz, CHCF<sub>3</sub>), 35.7 (CH<sub>2</sub>), 94.4 (ArC), 110.5 (ArCH), 118.1 (ArCH), 121.3 (ArCH), 122.8 (ArCH), 125.3 (q, <sup>1</sup>*J*<sub>C-F</sub> 280.0 Hz, CF<sub>3</sub>), 124.6 (ArC), 129.1 (2×ArCH), 130.8 (2×ArCH), 133.6 (ArC), 135.3 (ArC), 136.7 (ArC), 146.3 (ArC), 169.4 (C=O); **HRMS (ESI<sup>+</sup>)** C<sub>20</sub>H<sub>17</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 445.0797, requires 445.0804 (-1.62 ppm).

#### (*S*)-4-(Chlorodifluoromethyl)-9-methyl-1-tosyl-1,3,4,9-tetrahydro-2*H*-pyrido[2,3-*b*]indol-2-one (18)



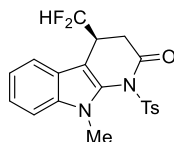
Following General Procedure 5, (*Z*)-4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4-chloro-4,4-difluorobut-2-enoate (55.5 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.46) afforded the desired compound (81.5 mg, 93%) as yellow solid. mp: 153-154 °C;  $[\alpha]_D^{20} = -147.6$  (*c* 1.1, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (major): 17.4 min, *t<sub>R</sub>* (minor): 41.0 min, 97:3 er; *v<sub>max</sub>* (film), 1722 (C=O); **<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)** δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.91 (1H, dd, *J* 17.1, 7.5 Hz, CH<sub>2</sub>), 3.00 (1H, dd, *J* 17.1, 1.6 Hz, CH<sub>2</sub>), 3.80–3.89 (1H, m, CHCF<sub>2</sub>Br), 3.96 (3H, s, N-CH<sub>3</sub>), 7.26–7.30 (1H, m, CH-Ar), 7.34–7.38 (3H, m, CH-Ar), 7.44–7.46 (1H, m, CH-Ar), 7.61–7.63 (1H, m, CH-Ar), 7.94–7.96 (2H, m, CH-Ar); **<sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz)** δ<sub>F</sub>: -58.6 (d, *J* 161.9, CF<sub>2</sub>Cl), -57.4 (d, *J* 161.9, CF<sub>2</sub>Cl); **<sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz)** δ<sub>C</sub>: 21.9 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 34.0 (N-CH<sub>3</sub>), 36.5 (CH<sub>2</sub>), 41.8 (t, <sup>2</sup>*J*<sub>C-F</sub> 26.7 Hz, CHCF<sub>2</sub>Cl), 95.5 (ArC), 110.5 (ArCH), 118.5 (ArCH), 121.3 (ArCH), 122.8 (ArCH), 124.8 (ArC), 128.8 (t, <sup>1</sup>*J*<sub>C-F</sub> 296.9 Hz, CF<sub>2</sub>Cl), 129.0 (2×ArCH), 131.0 (2×ArCH), 133.6 (ArC), 135.5 (ArC), 136.8 (ArC), 146.3 (ArC), 169.4 (C=O); **HRMS (ESI<sup>+</sup>)** C<sub>20</sub>H<sub>17</sub>ClF<sub>2</sub>N<sub>2</sub>O<sub>3</sub>S [M+H]<sup>+</sup> found 439.0680, requires 439.0689 (-2.10 ppm).

**(S)-4-(Bromodifluoromethyl)-9-methyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (19)**



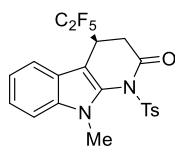
Following General Procedure 5, (Z)-4-methyl-N-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (E)-4-bromo-4,4-difluorobut-2-enoate (64.4 mg, 0.2 mmol), (2S,3R)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (91.8 mg, 95%) as yellow solid. mp: 144–146 °C; [α]<sub>D</sub><sup>20</sup> = –96.2 (c 0.6, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 18.8 min, t<sub>R</sub> (minor): 46.0 min, 94:6 er; v<sub>max</sub> (film), 1720 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.87 (1H, dd, J 17.1, 7.6 Hz, CH<sub>2</sub>), 3.02 (1H, dd, J 17.1, 1.1 Hz, CH<sub>2</sub>), 3.81–3.94 (1H, m, CHCF<sub>2</sub>Br), 3.95 (3H, s, N-CH<sub>3</sub>), 7.26–7.30 (1H, m, CH-Ar), 7.34–7.38 (3H, m, CH-Ar), 7.44–7.45 (1H, m, CH-Ar), 7.65–7.67 (1H, m, CH-Ar), 7.93–7.95 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: –52.4 (d, J 159.8, CF<sub>2</sub>Br), –51.1 (d, J 159.8, CF<sub>2</sub>Br); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.9 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 34.0 (N-CH<sub>3</sub>), 36.8 (CH<sub>2</sub>), 44.0 (t, <sup>2</sup>J<sub>C-F</sub> 24.1 Hz, CHCF<sub>2</sub>Br), 96.0 (ArC), 110.5 (ArCH), 118.7 (ArCH), 121.3 (ArCH), 122.4 (t, <sup>1</sup>J<sub>C-F</sub> 310.1 Hz, CF<sub>2</sub>Br), 122.8 (ArCH), 124.7 (ArC), 129.1 (2×ArCH), 130.9 (2×ArCH), 133.6 (ArC), 135.6 (ArC), 136.8 (ArC), 146.3 (ArC), 169.4 (C=O); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>17</sub>BrF<sub>2</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 504.9999, requires 505.0004 (–0.90 ppm).

**(S)-4-(Difluoromethyl)-9-methyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (20)**



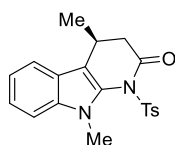
Following General Procedure 5, (Z)-4-methyl-N-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (E)-4,4-difluorobut-2-enoate (48.6 mg, 0.2 mmol), (2S,3R)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 72 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (53.4 mg, 66%) as yellow oil. [α]<sub>D</sub><sup>20</sup> = –32.1 (c 0.1, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 17.4 min, t<sub>R</sub> (minor): 41.0 min, 97:3 er; v<sub>max</sub> (film), 1732 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.81 (2H, d, J 4.9 Hz, CH<sub>2</sub>), 3.40–3.50 (1H, m, CHCF<sub>2</sub>H), 3.94 (3H, d, J 1.5 Hz, N-CH<sub>3</sub>), 5.55 (1H, t, J 56.0 Hz, CF<sub>2</sub>H), 7.23–7.27 (1H, m, CH-Ar), 7.32–7.37 (3H, m, CH-Ar), 7.43–7.45 (1H, m, CH-Ar), 7.55–7.57 (1H, m, CH-Ar), 7.90–7.92 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: –121.48–118.77 (m, CF<sub>2</sub>H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.8 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 33.5 (N-CH<sub>3</sub>), 34.7 (q, <sup>2</sup>J<sub>C-F</sub> 23.4 Hz, CHCF<sub>2</sub>H), 35.8 (CH<sub>2</sub>), 110.4 (ArCH), 115.5 (t, <sup>1</sup>J<sub>C-F</sub> 245.9 Hz, CF<sub>2</sub>H), 118.2 (ArCH), 121.1 (ArCH), 124.4 (ArC), 122.7 (ArCH), 124.7 (ArC), 129.2 (2×ArCH), 130.4 (2×ArCH), 133.9 (ArC), 134.8 (ArC), 136.7 (ArC), 146.2 (ArC), 169.4 (C=O); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>18</sub>F<sub>2</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 427.0893, requires 427.0898 (–1.27 ppm).

**(S)-9-Methyl-4-(perfluoroethyl)-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (21)**



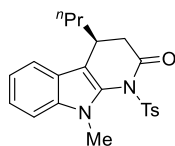
Following General Procedure 5, (*Z*)-4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,5,5,5-pentafluoropent-2-enoate (62.2 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.46) afforded the desired compound (91.6 mg, 97%) as yellow solid. mp: 148-150 °C;  $[\alpha]_D^{20} = -108.4$  (*c* 1.1, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL·min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (major): 12.3 min, *t<sub>R</sub>* (minor): 41.0 min, >99:1 er; *v<sub>max</sub>* (film), 1730 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.88 (1H, dd, *J* 16.9, 7.2 Hz, CH<sub>2</sub>), 2.97 (1H, dd, *J* 16.9, 1.5 Hz, CH<sub>2</sub>), 3.71–3.81 (1H, m, CHCF<sub>2</sub>CF<sub>3</sub>), 3.95 (3H, s, N-CH<sub>3</sub>), 7.25–7.29 (1H, m, CH-Ar), 7.34–7.38 (3H, m, CH-Ar), 7.44–7.46 (1H, m, CH-Ar), 7.50–7.52 (1H, m, CH-Ar), 7.93–7.95 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -122.0–-116.9 (m, CF<sub>2</sub>CF<sub>3</sub>), -82.3 (br, CF<sub>2</sub>CF<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.8 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 32.6 (t, <sup>2</sup>*J*<sub>C-F</sub> 23.8 Hz, CHCF<sub>2</sub>CF<sub>3</sub>), 33.9 (N-CH<sub>3</sub>), 35.6 (CH<sub>2</sub>), 94.5 (ArC), 110.5 (ArCH), 110.8–120.8 (m, C<sub>2</sub>F<sub>5</sub>), 118.1 (ArCH), 121.3 (ArCH), 122.8 (ArCH), 124.5 (ArC), 129.0 (2×ArCH), 130.9 (2×ArCH), 133.4 (ArC), 135.5 (ArC), 136.7 (ArC), 146.3 (ArC), 169.5 (C=O); HRMS (ESI<sup>+</sup>) C<sub>21</sub>H<sub>17</sub>F<sub>5</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 495.0763, requires 495.0772 (-1.87 ppm).

**(S)-4,9-Dimethyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (22)**



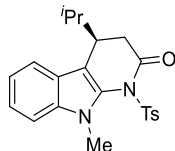
Following General Procedure 5, (*Z*)-4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (*E*)-but-2-enoate (41.4 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 72 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.46) afforded the desired compound (43.5 mg, 59%) as orange solid. mp: 124-125 °C;  $[\alpha]_D^{20} = +5.1$  (*c* 1.0, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak ID (90:10 hexane : IPA, flow rate 1.00 mL·min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (minor): 26.1 min, *t<sub>R</sub>* (major): 30.7 min, 1:99 er; *v<sub>max</sub>* (film), 1726 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 1.22 (3H, br, CHCH<sub>3</sub>), 2.39–2.45 (1H, m, CH<sub>2</sub>), 2.47 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.59–2.63 (1H, m, CH<sub>2</sub>), 3.69–3.73 (1H, m, CHCH<sub>3</sub>), 3.90 (3H, s, N-CH<sub>3</sub>), 7.17–7.21 (1H, m, CH-Ar), 7.30–7.35 (3H, m, CH-Ar), 7.41–7.43 (1H, m, CH-Ar), 7.63–7.64 (1H, m, CH-Ar), 7.88–7.90 (2H, m, CH-Ar); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.8 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>+CHCH<sub>3</sub>), 25.8 (CHCH<sub>3</sub>), 32.8 (N-CH<sub>3</sub>), 45.0 (CH<sub>2</sub>), 107.5 (ArC), 110.2 (ArCH), 118.9 (ArCH), 120.2 (ArCH), 122.0 (ArCH), 123.6 (ArC), 129.4 (2×ArCH), 129.8 (2×ArCH), 132.9 (ArC), 135.0 (ArC), 136.4 (ArC), 145.8 (ArC), 173.8 (C=O); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>20</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 391.1087, requires 391.1079 (-2.01 ppm).

**(S)-9-Methyl-4-propyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (23)**



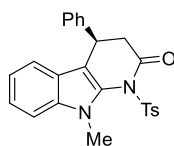
Following General Procedure 5, (*Z*)-4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (*E*)-but-2-enoate (41.4 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 72 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.46) afforded the desired compound (30.1 mg, 38%) as yellow solid. mp: 167-168 °C; [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -136.0 (*c* 0.7, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (major): 11.1 min, *t<sub>R</sub>* (minor): 18.7 min, 93:7 er; *v*<sub>max</sub> (film), 1719 (C=O); **<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)**  $\delta$ <sub>H</sub>: 0.81 (3H, t, *J* 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 0.91–1.15 (2H, m, CH<sub>3</sub>CH<sub>2</sub>), 1.29–1.42 (2H, m, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.47 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.47–2.52 (1H, m, CH<sub>2</sub>), 2.66–2.72 (1H, m, CH<sub>2</sub>), 2.97–3.02 (1H, m, CH<sup>*H*</sup>Pr), 3.91 (3H, s, N-CH<sub>3</sub>), 7.18–7.22 (1H, m, CH-Ar), 7.29–7.35 (3H, m, CH-Ar), 7.41–7.43 (1H, m, CH-Ar), 7.52–7.54 (1H, m, CH-Ar), 7.88–7.90 (2H, m, CH-Ar); **<sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz)**  $\delta$ <sub>C</sub>: 13.8 (CH<sub>3</sub>CH<sub>2</sub>), 21.1 (CH<sub>3</sub>CH<sub>2</sub>), 21.8 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 30.3 (CH<sup>*H*</sup>Pr), 33.0 (N-CH<sub>3</sub>), 37.7 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 42.9 (CH<sub>2</sub>CH), 106.9 (ArC), 110.2 (ArCH), 120.3 (ArCH), 122.1 (ArCH), 124.7 (ArC), 129.3 (2×ArCH), 130.2 (2×ArCH), 132.8 (ArC), 134.2 (ArC), 136.5 (ArC), 145.8 (ArC), 173.8 (C=O); **HRMS (ESI<sup>+</sup>)** C<sub>22</sub>H<sub>25</sub>N<sub>2</sub>O<sub>3</sub>S [M+H]<sup>+</sup> found 397.1576, requires 397.1580 (-1.11 ppm).

**(R)-4-Isopropyl-9-methyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (24)**



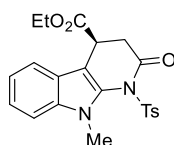
Following General Procedure 5, (*Z*)-4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4-methylpent-2-enoate (41.4 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 72 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.46) afforded the desired compound (30.0 mg, 38%) as yellow oil. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -148.8 (*c* 0.9, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (major): 9.3 min, *t<sub>R</sub>* (minor): 23.6 min, 96:4 er; *v*<sub>max</sub> (film), 1728 (C=O); **<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)**  $\delta$ <sub>H</sub>: 0.76–0.78 (3H, m, (CH<sub>3</sub>)<sub>2</sub>CH), 0.90–0.92 (3H, m, (CH<sub>3</sub>)<sub>2</sub>CH), 1.16–1.29 (1H, m, (CH<sub>3</sub>)<sub>2</sub>CH), 2.48 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.58–2.63 (2H, m, CH<sub>2</sub>), 2.70–2.73 (1H, m, CH<sup>*H*</sup>Pr), 3.90 (3H, s, N-CH<sub>3</sub>), 7.18–7.22 (1H, m, CH-Ar), 7.31–7.35 (3H, m, CH-Ar), 7.40–7.42 (1H, m, CH-Ar), 7.50–7.52 (1H, m, CH-Ar), 7.87–7.89 (2H, m, CH-Ar); **<sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz)**  $\delta$ <sub>C</sub>: 20.4 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 21.7 ((CH<sub>3</sub>)<sub>2</sub>CH), 21.9 ((CH<sub>3</sub>)<sub>2</sub>CH), 32.8 (CH<sup>*H*</sup>Pr), 33.0 (N-CH<sub>3</sub>), 37.9 ((CH<sub>3</sub>)<sub>2</sub>CH), 40.7 (CH<sub>2</sub>), 107.3 (ArC), 110.1 (ArCH), 118.7 (ArCH), 120.3 (ArCH), 122.1 (ArCH), 125.1 (ArC), 129.0 (2×ArCH), 130.1 (2×ArCH), 132.7 (ArC), 134.1 (ArC), 136.5 (ArC), 145.8 (ArC), 173.7 (C=O); **HRMS (ESI<sup>+</sup>)** C<sub>22</sub>H<sub>24</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 419.1395, requires 419.1400 (-1.16 ppm).

**(R)-9-Methyl-4-phenyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (25)**



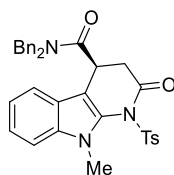
Following General Procedure 5, (*Z*)-4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl cinnamate (53.9 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 72 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.46) afforded the desired compound (34.4 mg, 40%) as yellow solid. mp: 152-153 °C;  $[\alpha]_D^{20} = +4.3$  (*c* 0.7, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (major): 19.2 min, *t<sub>R</sub>* (minor): 45.0 min, 88:12 er; *v<sub>max</sub>* (film), 1740 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.40 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.88–2.91 (1H, m, CH<sub>2</sub>), 3.14–3.18 (1H, m, CH<sub>2</sub>), 3.95 (3H, s, N-CH<sub>3</sub>), 4.30 (1H, br, CH), 7.02–7.06 (2H, m, CH-Ar), 7.15–7.16 (3H, m, CH-Ar), 7.20–7.33 (5H, m, CH-Ar), 7.44–7.46 (1H, m, CH-Ar), 7.54–7.56 (2H, m, CH-Ar); HRMS (ESI<sup>+</sup>) C<sub>25</sub>H<sub>22</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 453.1241, requires 453.1243 (–0.52 ppm). Data in agreement with the literature.<sup>7</sup>

**(S)-Ethyl 9-methyl-2-oxo-1-tosyl-2,3,4,9-tetrahydro-1H-pyrido[2,3-b]indole-4-carboxylate (26)**



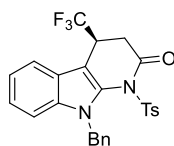
Following General Procedure 5, (*Z*)-4-methyl-*N*-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), ethyl (4-nitrophenyl) fumarate (53.0 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 72 h. The reaction mixture was concentrated and the crude residue was purified by column chromatograph mp: 162-164 °C; *y* (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.46) afforded the desired compound (50.3 mg, 59%) as yellow solid.  $[\alpha]_D^{20} = -95.7$  (*c* 0.1, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (major): 18.9 min, *t<sub>R</sub>* (minor): 53.2 min, 98:2 er; *v<sub>max</sub>* (film), 1732 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 1.22 (3H, t, *J* 7.1 Hz, CH<sub>3</sub>CH<sub>2</sub>), 2.48 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.70 (1H, dd, *J* 16.2, 6.3 Hz, CH<sub>2</sub>), 2.97 (1H, dd, *J* 16.2, 3.3 Hz, CH<sub>2</sub>), 3.91–2.93 (1H, m, CHCO<sub>2</sub>Et), 3.92 (3H, s, N-CH<sub>3</sub>), 4.05–4.09 (2H, m, CH<sub>3</sub>CH<sub>2</sub>), 7.22–7.26 (1H, m, CH-Ar), 7.31–7.35 (3H, m, CH-Ar), 7.41–7.43 (1H, m, CH-Ar), 7.58–7.60 (1H, m, CH-Ar), 7.86–7.88 (2H, m, CH-Ar); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 14.1 (CH<sub>3</sub>CH<sub>2</sub>), 21.9 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 33.2 (N-CH<sub>3</sub>), 35.2 (CH), 38.6 (CH<sub>2</sub>CH), 61.3 (CH<sub>3</sub>CH<sub>2</sub>), 107.5 (ArC), 110.3 (ArCH), 118.4 (ArCH), 119.2 (ArC), 120.8 (ArCH), 122.4 (ArCH), 129.2 (2×ArCH), 130.2 (2×ArCH), 132.5 (ArC), 134.4 (ArC), 136.5 (ArC), 145.7 (ArC), 166.5 (C=OOEt), 171.3 (C=O); HRMS (ESI<sup>+</sup>) C<sub>22</sub>H<sub>22</sub>N<sub>2</sub>NaO<sub>5</sub>S [M+Na]<sup>+</sup> found 449.1141, requires 449.1142 (–0.14 ppm).

**(S)-N,N-dibenzyl-9-methyl-2-oxo-1-tosyl-2,3,4,9-tetrahydro-1H-pyrido[2,3-b]indole-4-carboxamide (27)**



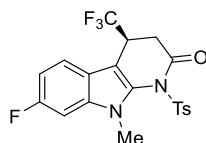
Following General Procedure 5, (Z)-4-methyl-N-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (E)-4-(dibenzylamino)-4-oxobut-2-enoate (83.3 mg, 0.2 mmol), (2S,3R)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 72 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (69.3 mg, 60%) as yellow solid. mp: 165–166 °C; [α]<sub>D</sub><sup>20</sup> = +175.0 (c 0.7, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralcel OD-H (85:15 hexane : IPA, flow rate 1.00 mL·min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 34.9 min, t<sub>R</sub> (minor): 56.0 min, 87:13 er; v<sub>max</sub> (film), 1761 (C=O), 1616 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.37 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.55 (1H, d, J 16.0 Hz, CH<sub>2</sub>CH), 3.02 (3H, s, N-CH<sub>3</sub>), 3.71 (1H, t, J 16.0 Hz, CH<sub>2</sub>CH), 4.15 (1H, d, J 16.0 Hz, CH<sub>2</sub>CH), 4.42 (1H, d, J 16.0 Hz, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 4.72 (2H, d, J 16.0 Hz, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 4.95 (1H, d, J 16.0 Hz, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 6.70–6.72 (2H, m, CH-Ar), 7.05–7.09 (3H, m, CH-Ar), 7.15–7.23 (4H, m, CH-Ar), 7.24–7.26 (2H, m, CH-Ar), 7.30–7.33 (2H, m, CH-Ar), 7.57–7.59 (2H, m, CH-Ar), 7.91–7.93 (1H, m, CH-Ar), 8.28–8.32 (2H, m, CH-Ar); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.7 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 28.8 (N-CH<sub>3</sub>), 36.5 (CH<sub>2</sub>CH), 37.1 (CH<sub>2</sub>CH), 49.0 (CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 49.8 (CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 109.7 (ArCH), 120.5 (ArCH), 122.6 (2×ArCH), 123.2 (ArCH), 124.5 (ArC), 125.2 (2×ArCH), 125.5 (ArCH), 127.1 (ArCH), 127.3 (ArCH), 127.4 (2×ArCH), 127.7 (2×ArCH), 128.5 (2×ArCH), 130.0 (2×ArCH), 135.2 (ArC), 136.2 (ArC), 136.4 (ArC), 136.7 (ArC), 144.7 (ArC), 145.2 (ArC), 155.7 (ArC), 170.4 (C=O), 172.5 (Bn<sub>2</sub>NC=O); HRMS (ESI<sup>+</sup>) C<sub>34</sub>H<sub>30</sub>N<sub>3</sub>O<sub>4</sub>S [M–H]<sup>-</sup> found 576.1964, requires 576.1963 (0.26 ppm).

**(S)-9-Benzyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (37)**



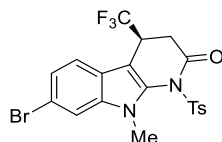
Following General Procedure 5, (Z)-4-methyl-N-(1-methylindolin-2-ylidene)benzenesulfonamide (72.1 mg, 0.24 mmol), 4-nitrophenyl (E)-4,4,4-trifluorobut-2-enoate (52.2 mg, 0.2 mmol), (2S,3R)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 72 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (31.9 mg, 32%) as yellow oil. Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL·min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 14.7 min, t<sub>R</sub> (minor): 27.2 min, 96:4 er; v<sub>max</sub> (film), 1732 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.48 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.82–2.93 (2H, m, CH<sub>2</sub>CH), 3.70–3.74 (1H, m, CHCF<sub>3</sub>), 5.67 (2H, q, J 16.8 Hz, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 7.06–7.08 (2H, m, CH-Ar), 7.22–7.30 (6H, m, CH-Ar), 7.32–7.34 (2H, m, CH-Ar), 7.55–7.57 (1H, m, CH-Ar), 7.9–7.92 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -71.4; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.8 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 34.9 (q, <sup>2</sup>J<sub>C-F</sub> 31.5 Hz, CHCF<sub>3</sub>), 35.8 (CH<sub>2</sub>CH), 50.2 (CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 112.1 (ArCH), 118.2 (ArCH), 121.5 (ArCH), 122.9 (ArCH), 125.2 (q, <sup>1</sup>J<sub>C-F</sub> 279.8 Hz, CF<sub>3</sub>), 126.8 (2×ArCH), 127.5 (ArCH), 128.6 (2×ArCH), 129.1 (2×ArCH), 130.8 (2×ArCH), 133.6 (ArC), 134.7 (ArC), 135.2 (ArC), 135.6 (ArC), 136.6 (ArC), 146.2 (ArC), 169.4 (C=O); HRMS (ESI<sup>+</sup>) C<sub>26</sub>H<sub>21</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 521.1109, requires 521.1117 (-1.57 ppm).

**(S)-7-Fluoro-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one**  
**(38)**



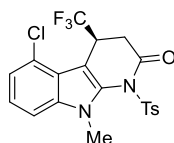
Following General Procedure **5**, (*Z*)-*N*-(6-fluoro-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (76.4 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (52.2 mg, 0.2 mmol), (2*S*,3*R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (66.9 mg, 76%) as orange solid. mp: 152-154 °C; [α]<sub>D</sub><sup>20</sup> = -161.6 (*c* 0.5, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 20.7 min, t<sub>R</sub> (minor): 43.6 min, 96:4 er; v<sub>max</sub> (film), 1728 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.89–2.91 (2H, m, CH<sub>2</sub>), 3.63–3.71 (1H, m, CHCF<sub>3</sub>), 3.91 (3H, s, N-CH<sub>3</sub>), 7.03 (1H, ddd, *J* 9.5, 8.8, 2.3 Hz, CH-Ar), 7.13 (1H, dd, *J* 9.5, 2.3 Hz, CH-Ar), 7.35 (2H, d, *J* 8.2 Hz, CH-Ar), 7.46 (1H, dd, *J* 8.8, 5.1 Hz, CH-Ar), 7.93 (2H, d, *J* 8.2 Hz, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -118.3 (Ar-F), -71.6 (CF<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.9 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 34.1 (N-CH<sub>3</sub>), 34.8 (q, <sup>2</sup>J<sub>C-F</sub> 31.5 Hz, CHCF<sub>3</sub>), 35.6 (CH<sub>2</sub>), 94.6 (ArC), 97.1 (d, <sup>2</sup>J<sub>C-F</sub> 26.7 Hz, ArCH), 110.1 (d, <sup>2</sup>J<sub>C-F</sub> 24.6 Hz, ArCH), 119.1 (d, <sup>3</sup>J<sub>C-F</sub> 10.0 Hz, ArCH), 121.0 (ArC), 125.2 (q, <sup>1</sup>J<sub>C-F</sub> 281.8 Hz, CF<sub>3</sub>), 129.1 (2×ArCH), 130.8 (2×ArCH), 133.5 (ArC), 135.5 (ArC), 136.8 (d, <sup>3</sup>J<sub>C-F</sub> 12.1 Hz, ArC), 146.3 (ArC), 160.1 (d, <sup>1</sup>J<sub>C-F</sub> 240.1 Hz, ArC), 169.2 (C=O); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>16</sub>F<sub>4</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 463.0705, requires 463.0710 (-1.07 ppm).

**(S)-7-Bromo-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one**  
**(39)**



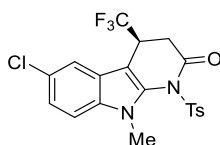
Following General Procedure **5**, (*Z*)-*N*-(6-bromo-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (76.4 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (91.0 mg, 0.2 mmol), (2*S*,3*R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (73.2 mg, 73%) as yellow solid. mp: 184-185 °C; [α]<sub>D</sub><sup>20</sup> = -117.5 (*c* 1.0, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 20.2 min, t<sub>R</sub> (minor): 31.4 min, 95:5 er; v<sub>max</sub> (film), 1732 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.85–2.95 (2H, m, CH<sub>2</sub>), 3.63–3.71 (1H, m, CHCF<sub>3</sub>), 3.92 (3H, s, N-CH<sub>3</sub>), 7.34–7.37 (3H, m, CH-Ar), 7.40–7.42 (1H, m, CH-Ar), 7.60–7.61 (1H, m, CH-Ar), 7.91–7.93 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -71.6; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.9 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 34.1 (N-CH<sub>3</sub>), 34.7 (q, <sup>2</sup>J<sub>C-F</sub> 31.5, CHCF<sub>3</sub>), 35.5 (CH<sub>2</sub>), 94.6 (ArC), 113.5 (ArCH), 116.2 (ArC), 119.4 (ArCH), 123.4 (ArC), 125.2 (q, <sup>1</sup>J<sub>C-F</sub> 280.8 Hz, CF<sub>3</sub>), 124.6 (ArCH), 129.1 (2×ArCH), 130.8 (2×ArCH), 133.5, (ArC), 135.7 (ArC), 137.4 (ArC), 146.4 (ArC), 169.1 (C=O); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>16</sub>BrF<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 522.9903, requires 522.9909 (-1.21 ppm).

**(S)-5-Chloro-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (40)**



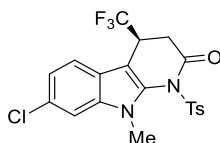
Following General Procedure **5**, (*Z*)-*N*-(4-chloro-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (76.4 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (80.4 mg, 0.2 mmol), (2*S*,3*R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (43.9 mg, 48%) as white solid. mp: 185-186 °C; [α]<sub>D</sub><sup>20</sup> = -38.3 (*c* 1.0, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 15.6 min, t<sub>R</sub> (minor): 39.8 min, 98:2 er; ν<sub>max</sub> (film), 1732 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.86–2.96 (2H, m, CH<sub>2</sub>), 3.95 (3H, s, N-CH<sub>3</sub>), 4.36–4.45 (1H, m, CHCF<sub>3</sub>), 7.20–7.26 (2H, m, CH-Ar), 7.33–7.36 (3H, m, CH-Ar), 7.94–7.97 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -70.5; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.9 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 34.3 (q, <sup>2</sup>J<sub>C-F</sub> 31.3 Hz, CHCF<sub>3</sub>), 34.4 (N-CH<sub>3</sub>), 36.1 (CH<sub>2</sub>), 109.2 (ArCH), 94.6 (ArC), 121.8 (ArC), 122.0 (ArCH), 123.1 (ArCH), 125.1 (q, <sup>1</sup>J<sub>C-F</sub> 281.8 Hz, CF<sub>3</sub>), 125.4 (ArC), 129.0 (2×ArCH), 131.2 (2×ArCH), 133.4 (ArC), 136.2 (ArC), 137.8 (ArC), 146.5 (ArC), 169.3 (C=O); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>16</sub>ClF<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 479.0408, requires 479.0414 (-1.35 ppm).

**(S)-6-Chloro-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (41)**



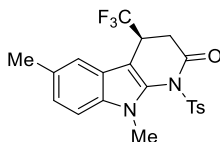
Following General Procedure **5**, (*Z*)-*N*-(5-chloro-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (76.4 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (80.4 mg, 0.2 mmol), (2*S*,3*R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (50.1 mg, 55%) as yellow solid. mp: 178-179 °C; [α]<sub>D</sub><sup>20</sup> = -180.0 (*c* 0.5, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 19.3 min, t<sub>R</sub> (minor): 43.5 min, 98:2 er; ν<sub>max</sub> (film), 1724 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.86–2.95 (2H, m, CH<sub>2</sub>), 3.60–3.70 (1H, m, CHCF<sub>3</sub>), 3.94 (3H, s, N-CH<sub>3</sub>), 7.28–7.30 (1H, m, CH-Ar), 7.34–7.37 (3H, m, CH-Ar), 7.51–7.52 (1H, m, CH-Ar), 7.91–7.93 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -71.7; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.9 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 34.2 (N-CH<sub>3</sub>), 34.7 (q, <sup>2</sup>J<sub>C-F</sub> 31.3 Hz, CHCF<sub>3</sub>), 35.5 (CH<sub>2</sub>), 111.6 (ArCH), 117.6 (ArCH), 123.1 (ArCH), 123.7 (ArC), 125.1 (q, <sup>1</sup>J<sub>C-F</sub> 284.8 Hz, CF<sub>3</sub>), 127.2 (ArC), 129.1 (2×ArCH), 130.9 (2×ArCH), 133.5 (ArC), 135.1 (ArC), 136.3 (ArC), 146.4 (ArC), 169.0 (C=O); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>16</sub>ClF<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 479.0412, requires 479.0414 (-0.51 ppm).

**(S)-7-Chloro-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-*b*]indol-2-one (42)**



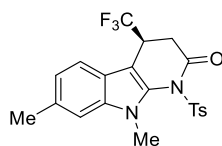
Following General Procedure **5**, (*Z*)-*N*-(6-chloro-1-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (76.4 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (80.4 mg, 0.2 mmol), (2*S*,3*R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (67.6 mg, 74%) as yellow solid. mp: 163-164 °C; [α]<sub>D</sub><sup>20</sup> = +147.2 (*c* 0.7, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 19.9 min, t<sub>R</sub> (minor): 33.8 min, 99:1 er; ν<sub>max</sub> (film), 1732 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.49 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 2.85–2.95 (2H, m, CH<sub>2</sub>), 3.62–3.72 (1H, m, CHCF<sub>3</sub>), 3.92 (3H, s, N-CH<sub>3</sub>), 7.21–7.24 (1H, m, CH-Ar), 7.34–7.36 (2H, m, CH-Ar), 7.44–7.46 (2H, m, CH-Ar), 7.91–7.93 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -71.6; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.9 (C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 34.1 (N-CH<sub>3</sub>), 34.7 (q, <sup>2</sup>J<sub>C-F</sub> 31.4 Hz, CHCF<sub>3</sub>), 35.5 (CH<sub>2</sub>), 94.6 (ArC), 110.5 (ArCH), 119.1 (ArCH), 122.0 (ArCH), 123.0 (ArC), 125.2 (q, <sup>1</sup>J<sub>C-F</sub> 281.8 Hz, CF<sub>3</sub>), 128.7 (ArC), 129.1 (2×ArCH), 130.8 (2×ArCH), 133.5 (ArC), 135.8 (ArC), 137.1 (ArC), 146.4 (ArC), 169.1 (C=O); HRMS (ESI<sup>+</sup>) C<sub>20</sub>H<sub>17</sub>ClF<sub>3</sub>N<sub>2</sub>O<sub>3</sub>S [M+H]<sup>+</sup> found 457.0584, requires 457.0595 (-2.41 ppm).

**(S)-6,9-Dimethyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-*b*]indol-2-one (43)**



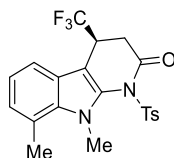
Following General Procedure **5**, (*Z*)-*N*-(1,5-dimethylindolin-2-ylidene)-4-methylbenzenesulfonamide (75.5 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (80.4 mg, 0.2 mmol), (2*S*,3*R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, R<sub>f</sub> 0.46) afforded the desired compound (32.3 mg, 37%) as yellow solid. mp: 169-170°C; [α]<sub>D</sub><sup>20</sup> = -46.6 (*c* 0.2, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 18.9 min, t<sub>R</sub> (minor): 30.7 min, 98:2 er; ν<sub>max</sub> (film), 1728 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.48 (3H, s, ArCH<sub>3</sub>), 2.50 (3H, s, ArCH<sub>3</sub>), 2.87–2.89 (2H, m, CH<sub>2</sub>), 3.62–3.72 (1H, m, CHCF<sub>3</sub>), 3.93 (3H, s, N-CH<sub>3</sub>), 7.16–7.18 (1H, m, CH-Ar), 7.32–7.35 (4H, m, CH-Ar), 7.91–7.93 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -71.7; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.5 (ArCH<sub>3</sub>), 21.8 (ArCH<sub>3</sub>), 33.9 (N-CH<sub>3</sub>), 34.4 (q, <sup>2</sup>J<sub>C-F</sub> 32.3 Hz, CHCF<sub>3</sub>), 35.7 (CH<sub>2</sub>), 110.2 (ArCH), 117.7 (ArCH), 119.5 (ArC), 124.3 (ArCH), 124.8 (ArC), 125.3 (q, <sup>1</sup>J<sub>C-F</sub> 280.8 Hz, CF<sub>3</sub>), 129.0 (2×ArCH), 130.8 (2×ArCH), 130.9 (ArC), 133.7 (ArC), 135.1 (ArC), 135.2 (ArC), 146.2 (ArC), 169.5 (C=O); HRMS (ESI<sup>+</sup>) C<sub>21</sub>H<sub>19</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 459.0954, requires 459.0961 (-1.46 ppm).

**(S)-7,9-Dimethyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (44)**



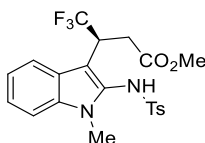
Following General Procedure 5, (*Z*)-*N*-(1,6-dimethylindolin-2-ylidene)-4-methylbenzenesulfonamide (75.5 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (80.4 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.46) afforded the desired compound (62.8 mg, 72%) as white solid. mp: 166-168 °C;  $[\alpha]_D^{20} = -172.4$  (*c* 0.9, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (major): 15.6 min, *t<sub>R</sub>* (minor): 26.1 min, 96:4 er; *v<sub>max</sub>* (film), 1722 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.48 (3H, s, ArCH<sub>3</sub>), 2.56 (3H, s, ArCH<sub>3</sub>), 2.84–2.93 (2H, m, CH<sub>2</sub>), 3.64–3.70 (1H, m, CHCF<sub>3</sub>), 3.92 (3H, s, N-CH<sub>3</sub>), 7.09–7.11 (1H, m, CH-Ar), 7.24 (1H, s, CH-Ar), 7.33–7.35 (2H, m, CH-Ar), 7.43–7.45 (1H, m, CH-Ar), 7.91–7.93 (2H, m, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -71.6; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 21.8 (ArCH<sub>3</sub>), 22.0 (ArCH<sub>3</sub>), 33.8 (N-CH<sub>3</sub>), 34.8 (q, <sup>2</sup>J<sub>C-F</sub> 31.4 Hz, CHCF<sub>3</sub>), 35.7 (CH<sub>2</sub>), 94.4 (ArC), 110.4 (ArCH), 117.8 (ArCH), 122.4 (ArC), 123.0 (ArCH), 125.3 (q, <sup>1</sup>J<sub>C-F</sub> 281.8 Hz, CF<sub>3</sub>), 129.1 (2×ArCH), 130.8 (2×ArCH), 132.9 (ArC), 133.7 (ArC), 134.7 (ArC), 137.1 (ArC), 146.2 (ArC), 169.5 (C=O); HRMS (ESI<sup>+</sup>) C<sub>21</sub>H<sub>20</sub>F<sub>3</sub>N<sub>2</sub>O<sub>3</sub>S [M+H]<sup>+</sup> found 437.1134, requires 437.1141 (-1.66 ppm).

**(S)-8,9-Dimethyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (45)**



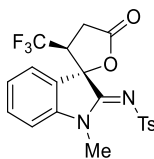
Following General Procedure 5, (*Z*)-*N*-(1,7-dimethylindolin-2-ylidene)-4-methylbenzenesulfonamide (75.5 mg, 0.24 mmol), 4-nitrophenyl (*E*)-4,4,4-trifluorobut-2-enoate (80.4 mg, 0.2 mmol), (*2S,3R*)-HyperBTM (3.2 mg, 0.01 mmol) in anhydrous CH<sub>3</sub>CN (2.0 mL) at room temperature for 48 h. The reaction mixture was concentrated and the crude residue was purified by column chromatography (80:20 Petrol : EtOAc, *R<sub>f</sub>* 0.46) afforded the desired compound (47.2 mg, 54%) as white solid. mp: 157-158 °C;  $[\alpha]_D^{20} = -272.7$  (*c* 1.2, CHCl<sub>3</sub>); Chiral HPLC analysis, Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) *t<sub>R</sub>* (major): 14.7 min, *t<sub>R</sub>* (minor): 17.4 min, 97:3 er; *v<sub>max</sub>* (film), 1728 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub>: 2.48 (3H, s, ArCH<sub>3</sub>), 2.83 (3H, s, ArCH<sub>3</sub>), 2.89–2.91 (2H, m, CH<sub>2</sub>), 3.64–3.73 (1H, m, CHCF<sub>3</sub>), 4.07 (3H, s, N-CH<sub>3</sub>), 7.07 (1H, d, *J* 7.2 Hz, CH-Ar), 7.15 (1H, t, *J* 7.5 Hz, CH-Ar), 7.34 (2H, d, *J* 8.2 Hz, CH-Ar), 7.38 (1H, d, *J* 7.8 Hz, CH-Ar), 7.92 (2H, d, *J* 8.3 Hz, CH-Ar); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ<sub>F</sub>: -71.6; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ<sub>C</sub>: 19.8 (ArCH<sub>3</sub>), 21.8 (ArCH<sub>3</sub>), 34.8 (q, <sup>2</sup>J<sub>C-F</sub> 31.3 Hz, CHCF<sub>3</sub>), 35.6 (CH<sub>2</sub>), 36.9 (N-CH<sub>3</sub>), 94.6 (ArC), 115.8 (ArCH), 121.6 (ArCH), 122.7 (ArC), 125.2 (q, <sup>1</sup>J<sub>C-F</sub> 280.8 Hz, CF<sub>3</sub>), 125.6 (ArCH), 128.7 (ArC), 129.0 (2×ArCH), 130.8 (2×ArCH), 133.5 (ArC), 136.4 (ArC), 136.5 (ArC), 146.2 (ArC), 169.5 (C=O); HRMS (ESI<sup>+</sup>) C<sub>21</sub>H<sub>19</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub>S [M+Na]<sup>+</sup> found 459.0954, requires 459.0961 (-1.46 ppm).

**Methyl (S)-4,4,4-trifluoro-3-(1-methyl-2-((4-methylphenyl)sulfonamido)-1H-indol-3-yl)butanoate (46)**



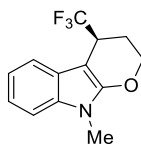
Following General Procedure **8**, the desired compound (90.0 mg, 99%) was achieved by column chromatography (80:20 Petrol : EtOAc,  $R_f$  0.22) afforded as white solid. mp: 88-89 °C;  $[\alpha]_D^{20} = +178.3$  ( $c$  1.1,  $\text{CHCl}_3$ ); Chiral HPLC analysis, HPLC Data for **mg**: Chiralpak AD-H (82:18 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C)  $t_R$  (major): 9.8 min,  $t_R$  (minor): 13.6 min, 97:3 er;  $v_{\max}$  (film), 1165 (C=O); **<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)**  $\delta_H$ : 2.44 (3H, s,  $\text{C}_6\text{H}_5\text{CH}_3$ ), 2.80–2.90 (2H, m,  $\text{CH}_2$ ), 3.29–3.42 (1H, m,  $\text{CHCF}_3$ ), 3.82 (3H, s,  $\text{CO}_2\text{CH}_3$ ), 3.82 (3H, s, N- $\text{CH}_3$ ), 7.13–7.17 (1H, m,  $\text{CH-Ar}$ ), 7.31–7.33 (3H, m,  $\text{CH-Ar}$ ), 7.37 (1H, d,  $J$  8.2 Hz,  $\text{CH-Ar}$ ), 7.60 (1H, d,  $J$  8.2 Hz,  $\text{CH-Ar}$ ), 7.77–7.79 (2H, m,  $\text{CH-Ar}$ ), 7.82 (1H, br, NH); **<sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz)**  $\delta_F$ : -66.6; **<sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz)**  $\delta_C$ : 21.6 ( $\text{C}_6\text{H}_4\text{CH}_3$ ), 30.3 ( $\text{CO}_2\text{CH}_3$ ), 33.6 ( $\text{CH}_2$ ), 37.3 (q,  $^2J_{\text{C-F}}$  30.3 Hz,  $\text{CHCF}_3$ ), 52.5 (N- $\text{CH}_3$ ), 102.6 (ArC), 110.2 (ArCH), 119.8 (ArCH), 120.4 (ArCH), 122.7 (ArCH), 123.9 (q,  $^1J_{\text{C-F}}$  192.9 Hz,  $\text{CF}_3$ ), 127.3 (2×ArCH), 130.0 (2×ArCH), 130.6 (ArC), 135.7 (ArC), 136.4 (ArC), 140.8 (ArC), 144.5 (ArC), 172.9 (C=O); **HRMS (ESI<sup>+</sup>)**  $\text{C}_{21}\text{H}_{21}\text{F}_3\text{N}_2\text{NaO}_4\text{S}$   $[\text{M}+\text{Na}]^+$  found 477.1060, requires 477.1066 (-1.33 ppm).

**4-Methyl-N-((2S,3S,Z)-1'-methyl-5-oxo-3-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-2'-ylidene)benzenesulfonamide (47)**



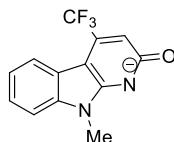
Following General Procedure **9**, the desired compound (28.1 mg, 32%) was achieved by column chromatography (80:20 Petrol : EtOAc,  $R_f$  0.14) afforded as white solid. mp: 137-138 °C;  $[\alpha]_D^{20} = -61.4$  ( $c$  0.1,  $\text{CHCl}_3$ ); Chiralpak AD-H (82:18 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C)  $t_R$  (major): 39.7 min,  $t_R$  (minor): 36.0 min, 97:3 er;  $v_{\max}$  (film), 1605 (C=O), 1636 (C=O); **<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)**  $\delta_H$ : 2.45 (3H, s,  $\text{C}_6\text{H}_4\text{CH}_3$ ), 2.76 (1H, dd,  $J$  17.0, 9.0 Hz,  $\text{CH}_2$ ), 3.18 (1H, dd,  $J$  17.0, 12.8 Hz,  $\text{CH}_2$ ), 3.53–3.64 (1H, m,  $\text{CHCF}_3$ ), 3.86 (3H, s, N- $\text{CH}_3$ ), 7.06 (1H, d,  $J$  8.0 Hz,  $\text{CH-Ar}$ ), 7.26–7.34 (3H, m,  $\text{CH-Ar}$ ), 7.41–7.43 (1H, m,  $\text{CH-Ar}$ ), 7.52–7.57 (1H, m,  $\text{CH-Ar}$ ), 7.84–7.86 (2H, m,  $\text{CH-Ar}$ ); **<sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz)**  $\delta_F$ : -65.8; **<sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz)**  $\delta_C$ : 21.6 ( $\text{C}_6\text{H}_5\text{CH}_3$ ), 23.8 (C), 28.6 ( $\text{CH}_2$ ), 32.3 (N- $\text{CH}_3$ ), 50.2 (q,  $^2J_{\text{C-F}}$  30.3 Hz,  $\text{CHCF}_3$ ), 85.1 (ArC), 110.6 (ArCH), 123.9 (ArCH), 125.1 (ArCH), 126.2 (2×ArCH), 126.7 (q,  $^1J_{\text{C-F}}$  292.9 Hz,  $\text{CF}_3$ ), 129.4 (2×ArCH), 132.4 (ArCH), 139.7 (ArC), 143.1 (ArC), 145.1 (ArC), 160.1 (C=N), 171.4 (C=O); **HRMS (ESI<sup>+</sup>)**  $\text{C}_{20}\text{H}_{17}\text{F}_3\text{N}_2\text{NaO}_4\text{S}$   $[\text{M}+\text{Na}]^+$  found 461.0746, requires 461.0753 (-1.59 ppm).

**(S)-9-Methyl-4-(trifluoromethyl)-2,3,4,9-tetrahydropyrano[2,3-b]indole (48)**



Following General Procedure **10**, the desired compound (34.7 mg, 68%) was achieved by column chromatography (80:20 Petrol : EtOAc,  $R_f$  0.69) afforded as colourless oil.  $[\alpha]_D^{20} = -14.0$  ( $c$  0.2,  $\text{CHCl}_3$ ); Chiral HPLC analysis, Chiralpak ID (99:1 hexane : IPA, flow rate  $1.00 \text{ mL}\cdot\text{min}^{-1}$ , 254 nm, 30 °C)  $t_R$  (major): 4.8 min,  $t_R$  (minor): 5.5 min, 97:3 er;  $v_{\text{max}}$  (film), 1117 (C–O–C);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta_{\text{H}}$ : 2.17–2.32 (2H, m,  $\text{CHCH}_2$ ), 3.59 (3H, s, N- $\text{CH}_3$ ), 3.61–3.69 (1H, m,  $\text{CHCF}_3$ ), 4.41–4.53 (2H, m,  $\text{OCH}_2$ ), 7.12–7.17 (2H, m,  $\text{CH-Ar}$ ), 7.19–7.22 (1H, m,  $\text{CH-Ar}$ ), 7.49–7.51 (1H, m,  $\text{CH-Ar}$ );  $^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta_{\text{F}}$ : -70.0;  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta_{\text{C}}$ : 22.6 ( $\text{CHCH}_2$ ), 27.4 ( $\text{CH}_3$ ), 34.0 (q,  $^2J_{\text{C-F}}$  29.3 Hz,  $\text{CHCF}_3$ ), 65.7 ( $\text{OCH}_2$ ), 108.2 (ArCH), 110.1 (ArC), 117.4 (ArCH), 119.7 (ArCH), 120.1 (ArCH), 126.0 (ArC), 127.5 (q,  $^1J_{\text{C-F}}$  282.8 Hz,  $\text{CF}_3$ ), 132.2 (ArC), 150.4 (ArC); **HRMS** (**ESI** $^+$ )  $\text{C}_{13}\text{H}_{13}\text{F}_3\text{NNaO}$   $[\text{M}+\text{H}]^+$  found 256.0939, requires 256.0944 (-1.87 ppm).

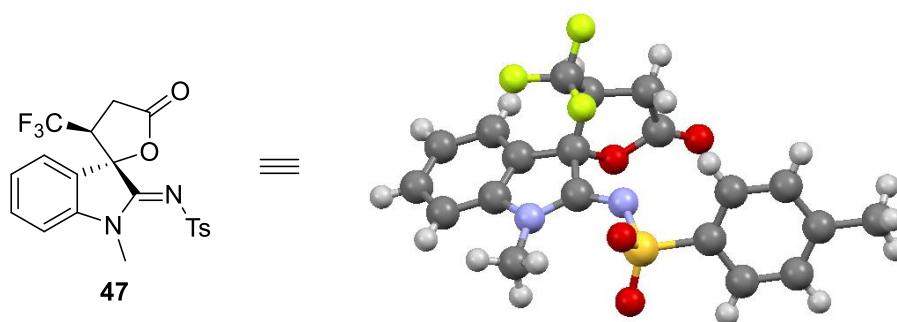
**9-Methyl-4-(trifluoromethyl)-1,9-dihydro-2H-pyrido[2,3-b]indol-2-one (49)**



Following General Procedure **10**, the desired compound (30.3 mg, 57%) was achieved by column chromatography (80:20 Petrol : EtOAc,  $R_f$  0.19) afforded as white solid. mp: 194–195 °C;  $v_{\text{max}}$  (film), 1656 (C=O);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta_{\text{H}}$ : 3.88 (3H, s, N- $\text{CH}_3$ ), 6.80 (1H, s,  $\text{CHC}=\text{O}$ ), 7.28–7.32 (1H, m,  $\text{CH-Ar}$ ), 7.48–7.52 (1H, m,  $\text{CH-Ar}$ ), 7.68 (1H, d,  $J$  8.0 Hz,  $\text{CH-Ar}$ ), 7.94 (1H, d,  $J$  8.0 Hz,  $\text{CH-Ar}$ );  $^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta_{\text{F}}$ : -63.6;  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta_{\text{C}}$ : 28.3 ( $\text{CH}_3$ ), 110.5 (ArCH), 118.1 (ArC), 121.1 (ArCH), 121.4 (ArCH), 123.7 (ArC), 123.9 (q,  $^1J_{\text{C-F}}$  274.7 Hz,  $\text{CCF}_3$ ), 125.6 (ArC), 126.1 (ArCH), 130.1 (ArCH), 132.5 (q,  $^2J_{\text{C-F}}$  34.3 Hz,  $\text{CCF}_3$ ), 139.6 (ArC), 163.0 (C=O). **HRMS** (**ESI** $^-$ )  $\text{C}_{13}\text{H}_8\text{F}_3\text{N}_2\text{O}$   $[\text{M}-\text{H}]^-$  found 265.0595, requires 265.0594 (+0.30 ppm).

## 5 Determination of Product Configuration

### 5.1 X-ray crystal structure of 47.



**Figure S1:** X-Ray crystal structures confirming the relative and absolute stereochemistry of **47**.

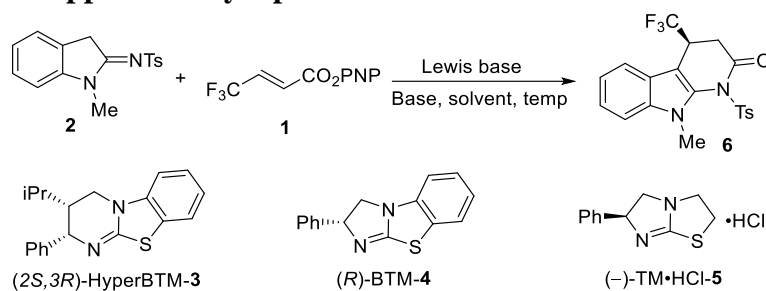
### 5.1 Crystal data of 47.

Crystal data for **47**: C<sub>21</sub>H<sub>19</sub>Cl<sub>2</sub>F<sub>3</sub>N<sub>2</sub>O<sub>4</sub>S, M = 493.52, colourless prism, orthorhombic space group *P* 2<sub>1</sub> 2<sub>1</sub> 2<sub>1</sub>; *a* = 8.5492(3) Å, *b* = 10.7773(4) Å, *c* = 24.8410(7) Å,  $\alpha = 90^\circ$ ,  $\beta = 90^\circ$ ,  $\gamma = 90^\circ$ , *V* = 2288.78 Å<sup>3</sup>, *Z* = 4, *Z'* = 0, *R* = 0.0695. Data were recorded at 173 K on Rigaku XtaLAB P100 diffractometer using multi-layer mirror monochromated Cu-K $\sigma$  radiation and the structures were solved by direct methods and refined using full-matrix least square analysis.

## 6 References

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## Appendix I : Supplementary Optimisation Studies



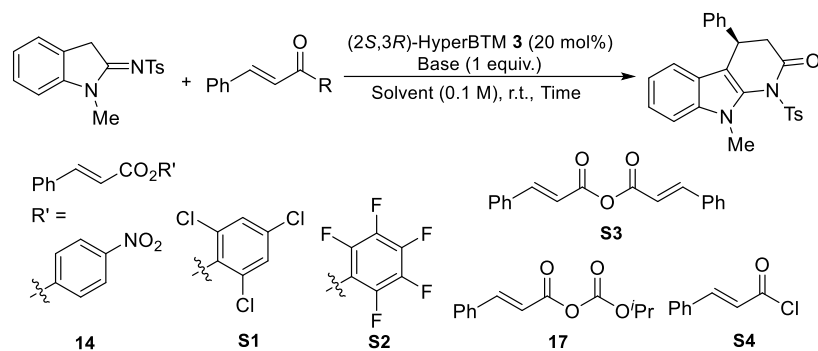
Entry	Cat. (x mol%)	2 : 1	Base	Solvent	Con. (M)	Temp (°C)	Time (h)	Yield (%) <sup>a</sup>	er <sup>b</sup>
1	5 (20 mol%)	1:1	DIPEA	THF	0.1	r.t.	2	6	85:15
2	4 (20 mol%)	1:1	DIPEA	THF	0.1	r.t.	2	37	98:2
3	3 (20 mol%)	1:1	DIPEA	THF	0.1	r.t.	2	53	98:2
4	3 (20 mol%)	1:1	Et <sub>3</sub> N	THF	0.1	r.t.	2	40	98:2
5	3 (20 mol%)	1:1	DBU	THF	0.1	r.t.	2	25	64:36
6	3 (20 mol%)	1:1	KOAc	THF	0.1	r.t.	24	45	84:16
7	3 (20 mol%)	1:1	K <sub>3</sub> PO <sub>4</sub>	THF	0.1	r.t.	2	50	66:34
8	3 (20 mol%)	1:1	K <sub>2</sub> CO <sub>3</sub>	THF	0.1	r.t.	24	12	60:40
9	3 (20 mol%)	1:1	Na <sub>2</sub> CO <sub>3</sub>	THF	0.1	r.t.	2	12	>99:1
10	3 (20 mol%)	1:1	NaHCO <sub>3</sub>	THF	0.1	r.t.	2	68	>99:1
11	3 (20 mol%)	1:1	NaHCO <sub>3</sub>	toluene	0.1	r.t.	72	81	98:2
12	3 (20 mol%)	1:1	NaHCO <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	0.1	r.t.	72	80	98:2
13	3 (20 mol%)	1:1	NaHCO <sub>3</sub>	CHCl <sub>3</sub>	0.1	r.t.	72	62	98:2
14	3 (20 mol%)	1:1	NaHCO <sub>3</sub>	Et <sub>2</sub> O	0.1	r.t.	72	84	99:1
15	3 (20 mol%)	1:1	NaHCO <sub>3</sub>	1,4-dioxane	0.1	r.t.	24	80	83:17
16	3 (20 mol%)	1:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	r.t.	5	91	97:3
17	3 (20 mol%)	1:1	NaHCO <sub>3</sub>	DMF	0.1	r.t.	5	43	84:16
18	3 (10 mol%)	1:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	r.t.	48	81	97:3
19	3 (5 mol%)	1:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	r.t.	48	83	96:4
20	3 (1 mol%)	1:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	r.t.	72	47	90:10
21	3 (5 mol%)	1:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.2	r.t.	48	72	96:4
22	3 (5 mol%)	1:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.05	r.t.	48	79	96:4
23	3 (5 mol%)	1.2:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	r.t.	48	99	97:3
24	3 (5 mol%)	1:1.2	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	r.t.	48	85	96:4
25	3 (5 mol%)	1.2:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	0	72	99	97:3
26	3 (5 mol%)	1.2:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	-10	72	76	97:3
27	3 (5 mol%)	1.2:1	-	CH <sub>3</sub> CN	0.1	r.t.	72	65	97:3
28 <sup>c</sup>	3 (5 mol%)	1.2:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	r.t.	72	68	97:3
29 <sup>d</sup>	3 (5 mol%)	1.2:1	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	0.1	r.t.	72	77	97:3

<sup>a</sup> Isolated yield given.

<sup>b</sup> Determined by HPLC analysis of purified products.

<sup>c</sup> 20% of NaHCO<sub>3</sub> used.

<sup>d</sup> 50% of NaHCO<sub>3</sub> used.



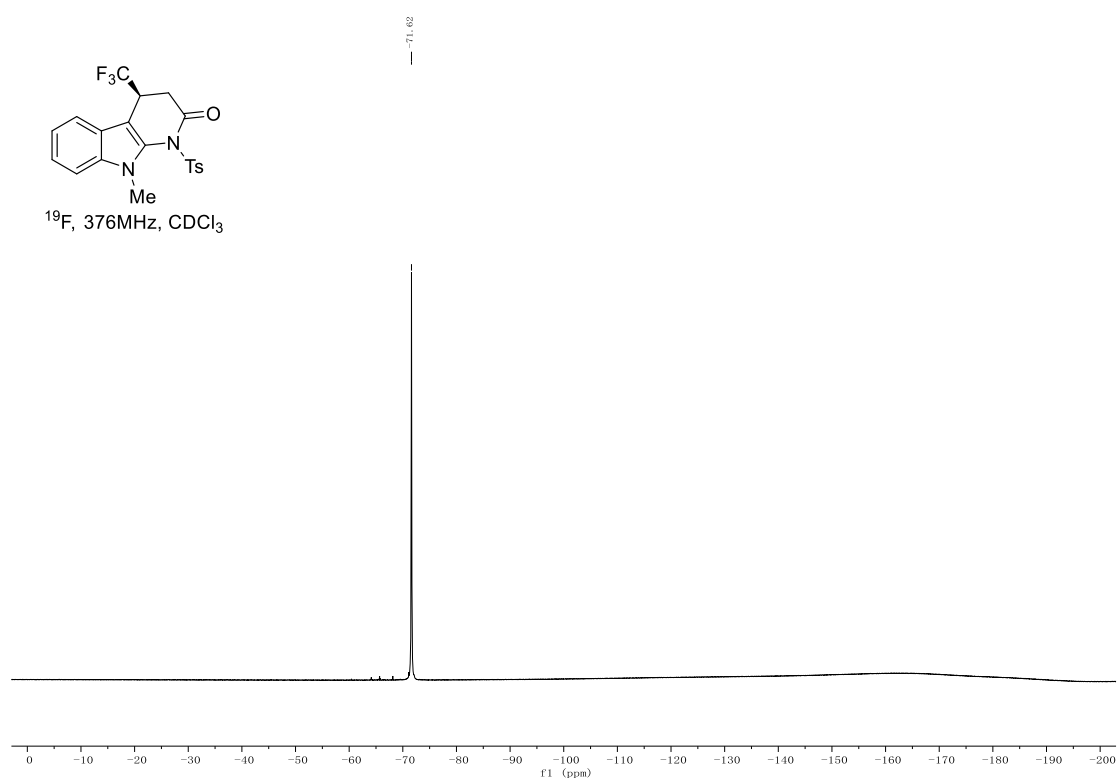
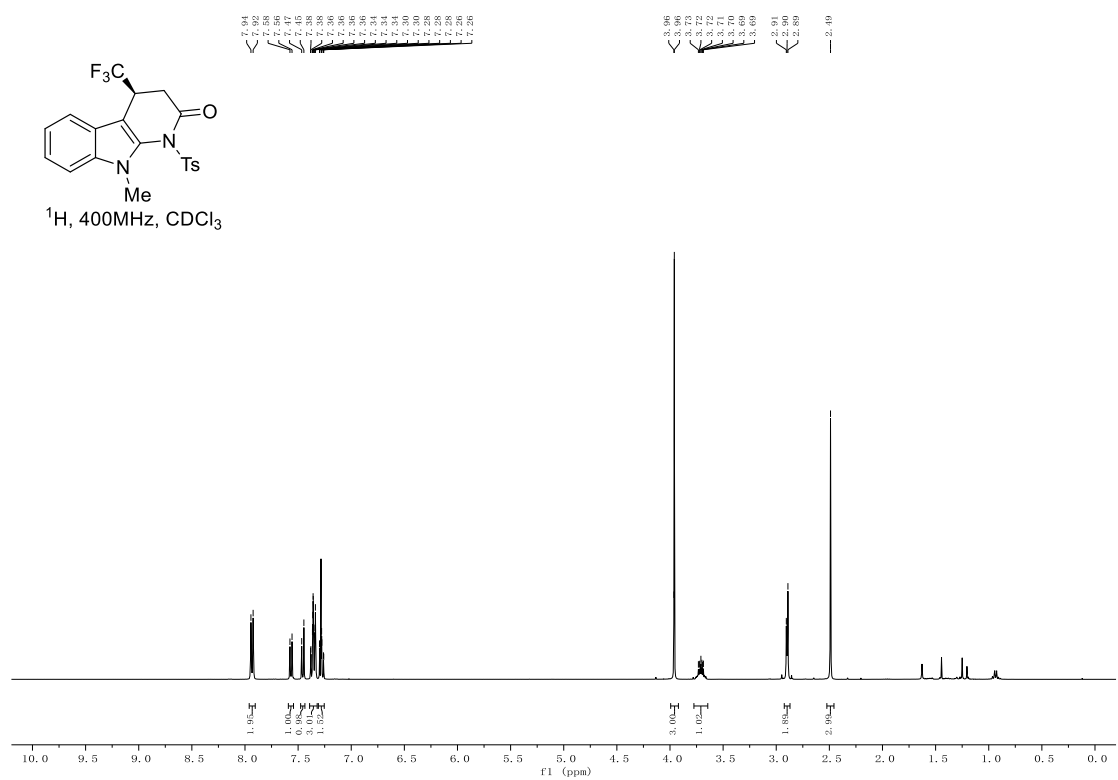
Entry	Substrate	Base	Solvent	Time (h)	Yield (%) <sup>a</sup>	er <sup>b</sup>
1	<b>14</b>	DIPEA	THF	72	24	87:13
2	<b>14</b>	NaHCO <sub>3</sub>	THF	48	43	77:23
3	<b>14</b>	Et <sub>3</sub> N	THF	72	37	80:20
4	<b>14</b>	NaHCO <sub>3</sub>	CH <sub>3</sub> CN	48	53	57:43
5	<b>14</b>	DIPEA	CH <sub>3</sub> CN	20	46	60:40
6	<b>14</b>	DIPEA	CH <sub>2</sub> Cl <sub>2</sub>	72	36	61:39
7	<b>14</b>	DIPEA	CHCl <sub>3</sub>	72	37	69:31
8	<b>14</b>	DIPEA	toluene	72	31	85:15
9	<b>S1</b>	DIPEA	THF	72	-	-
10	<b>S2</b>	DIPEA	THF	72	18	60:40
11	<b>S4</b>	DIPEA	THF	3	56	65:35
12	<b>17</b>	DIPEA	THF	72	40	89:11
13	<b>S6</b>	DIPEA	THF	72	NR	-

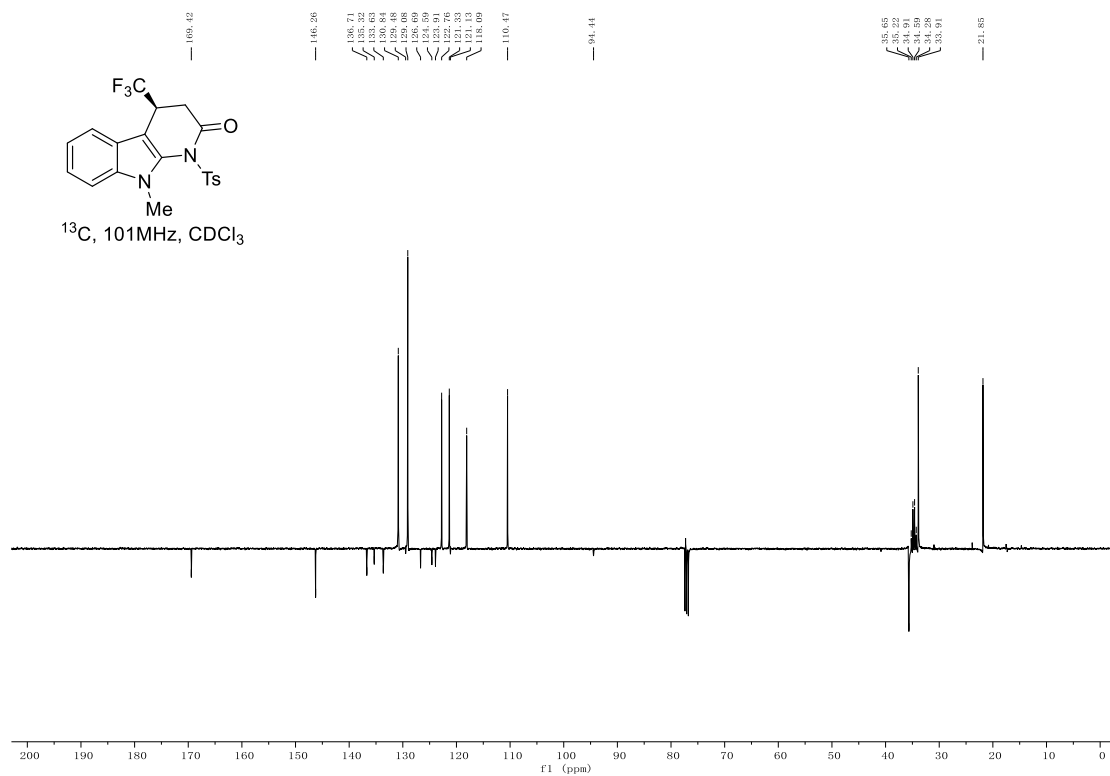
<sup>a</sup> Isolated yield given.

<sup>b</sup> Determined by HPLC analysis of purified products.

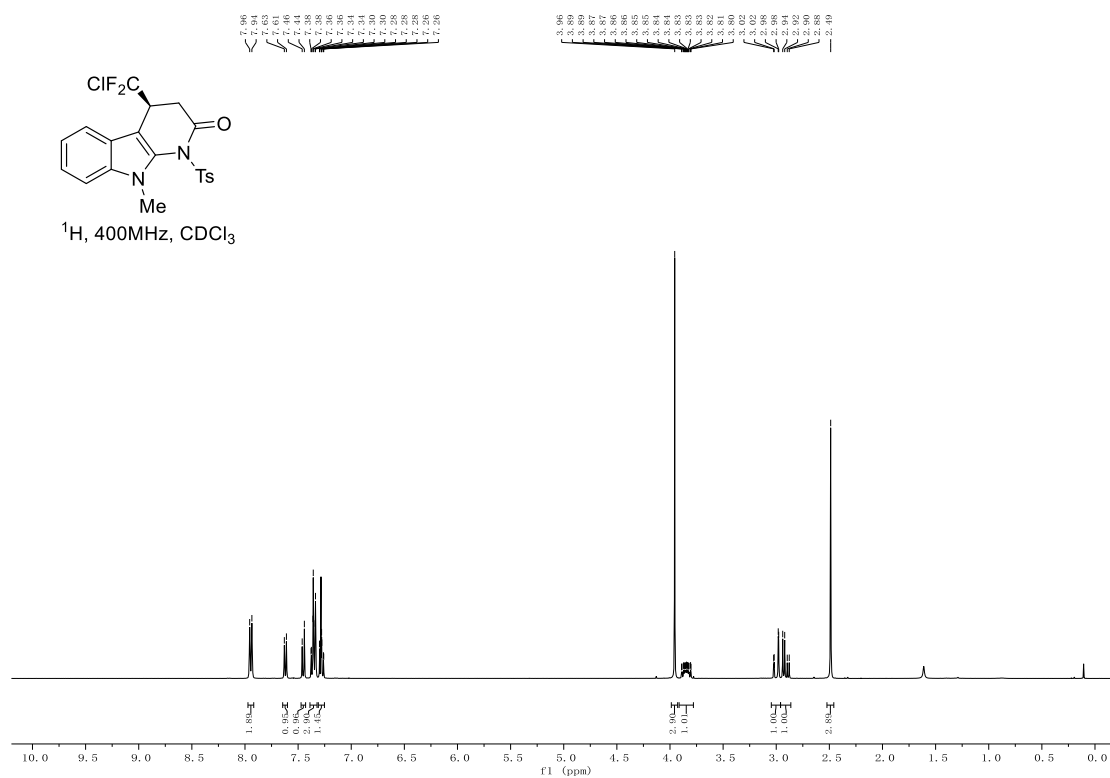
## Appendix II : NMR Spectra

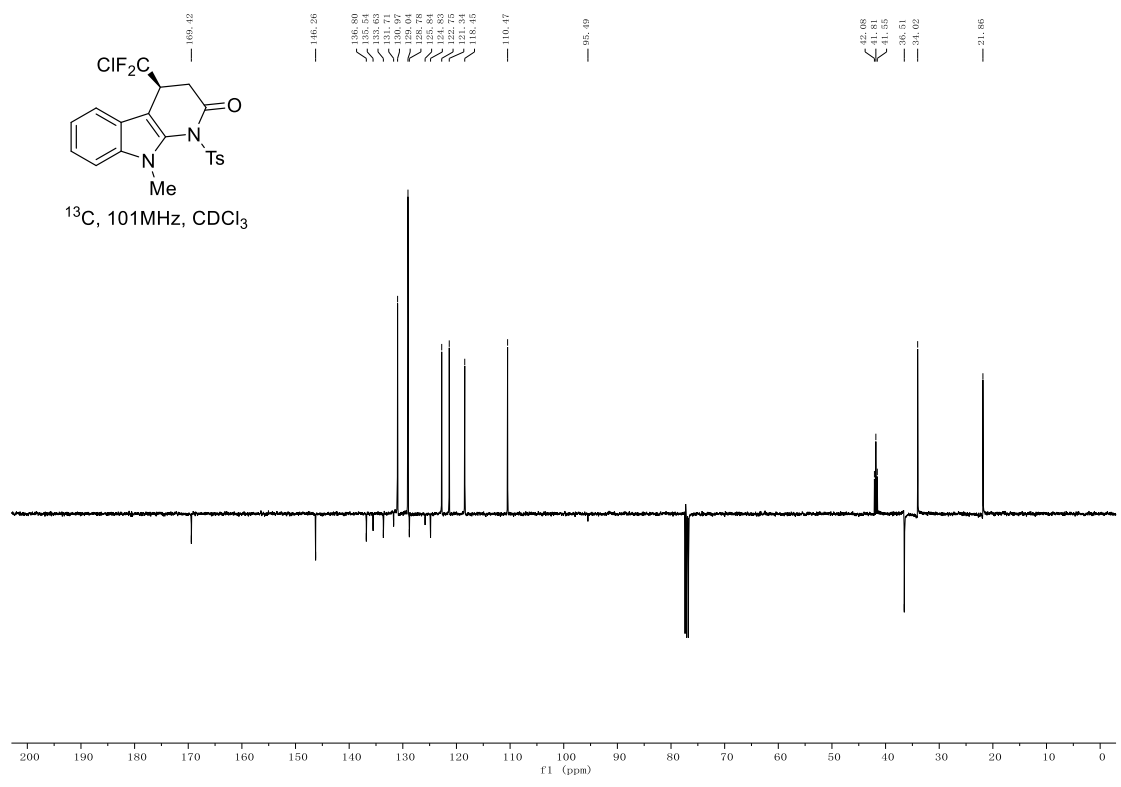
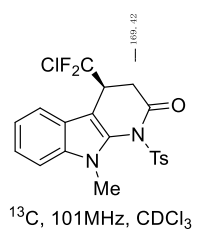
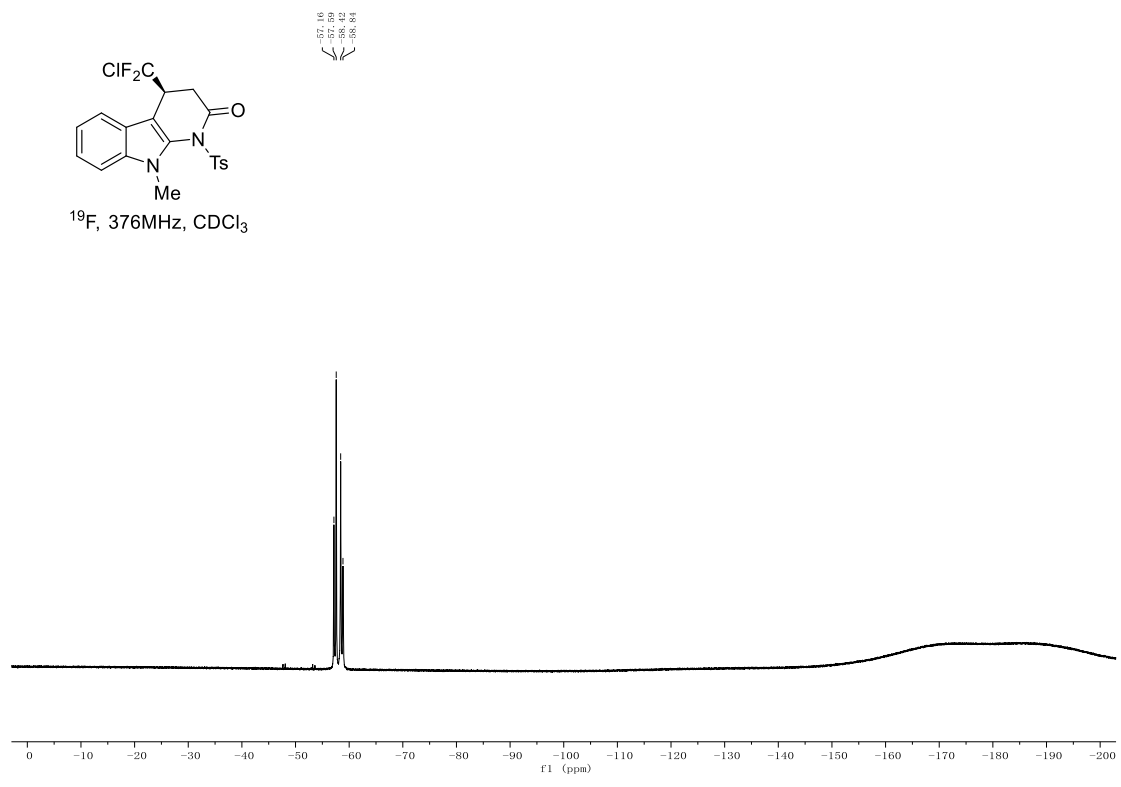
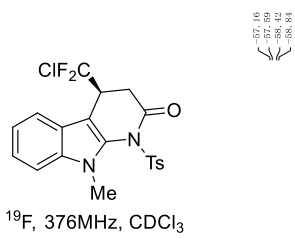
### (S)-9-Methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (6)



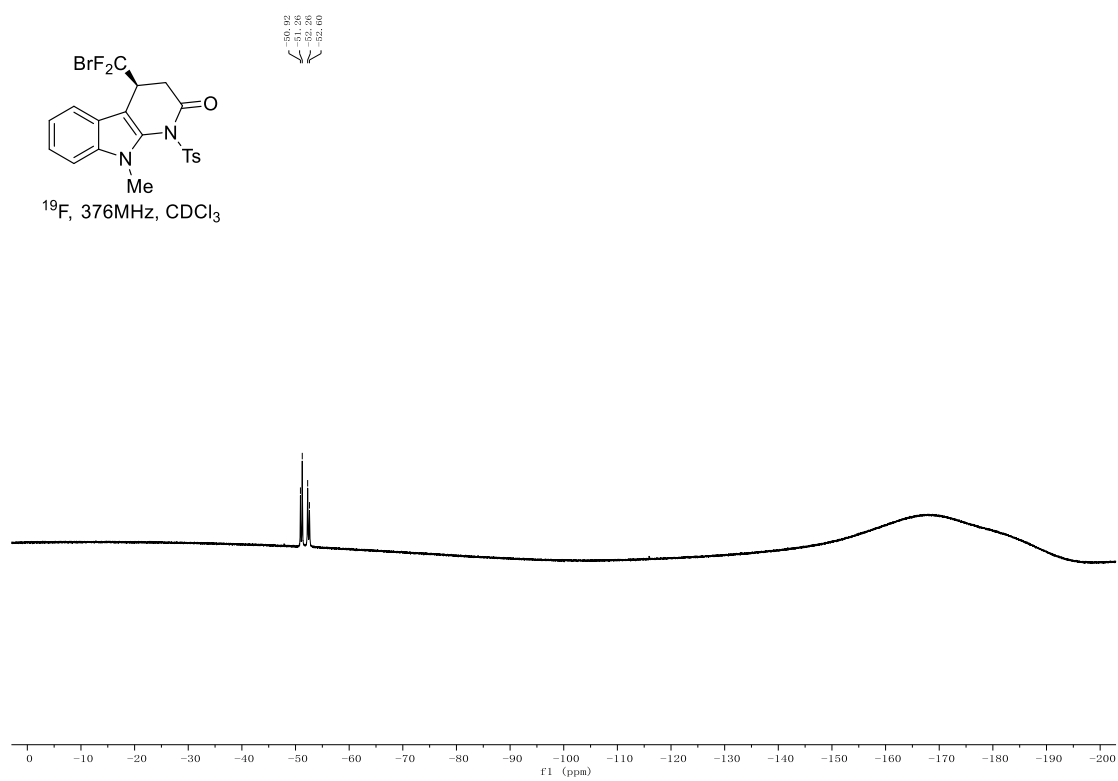
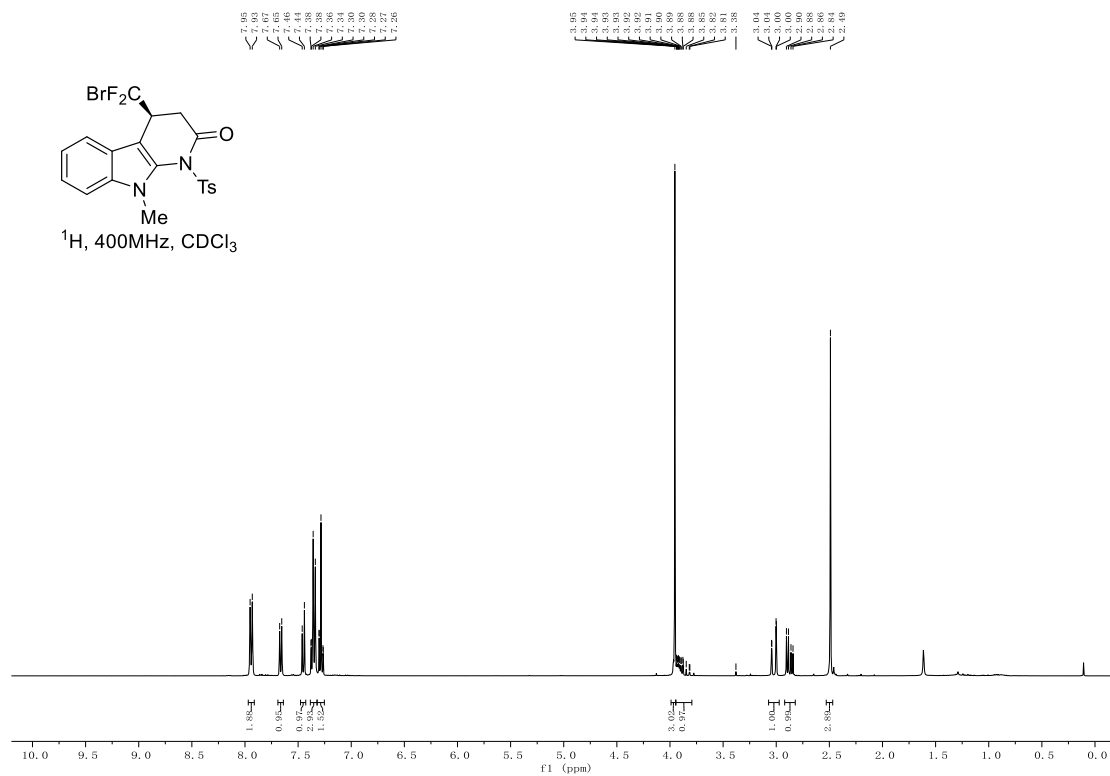


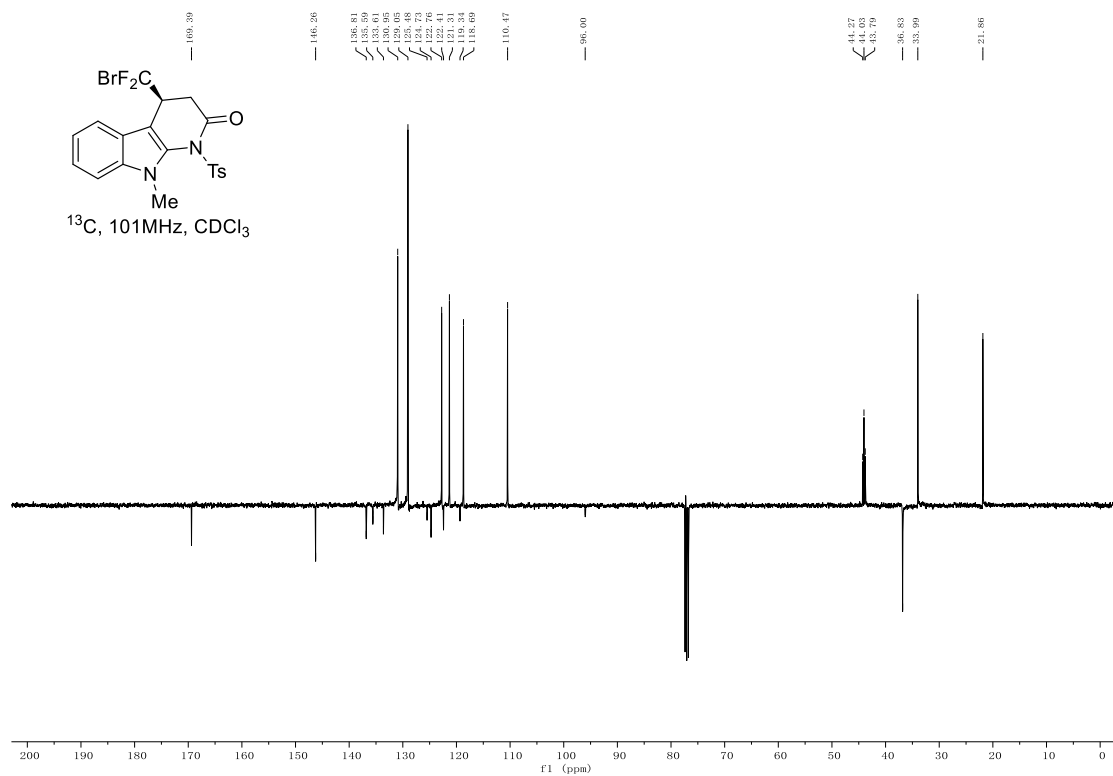
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**(18)**



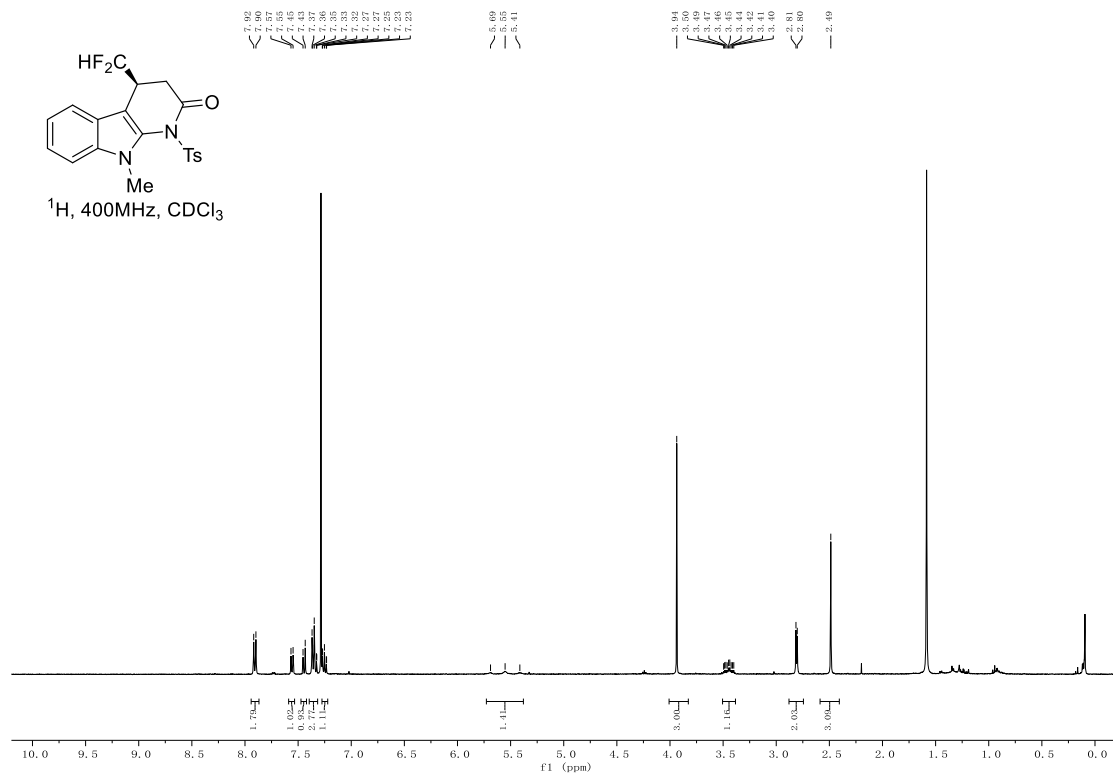


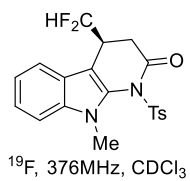
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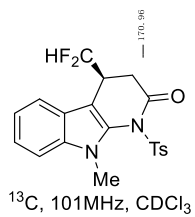
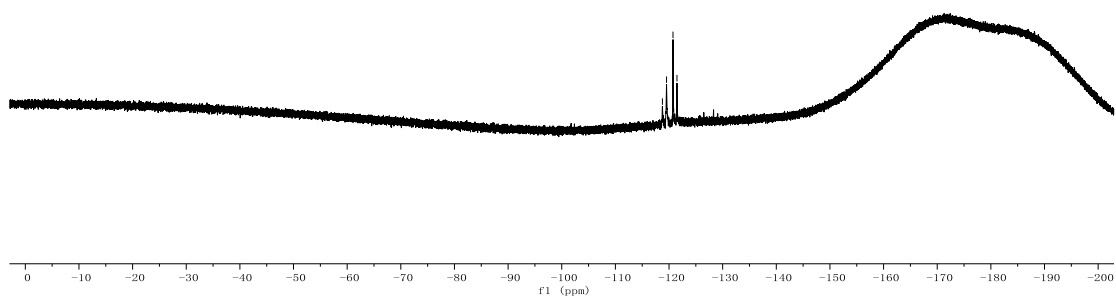


**(S)-4-(Difluoromethyl)-9-methyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (20)**



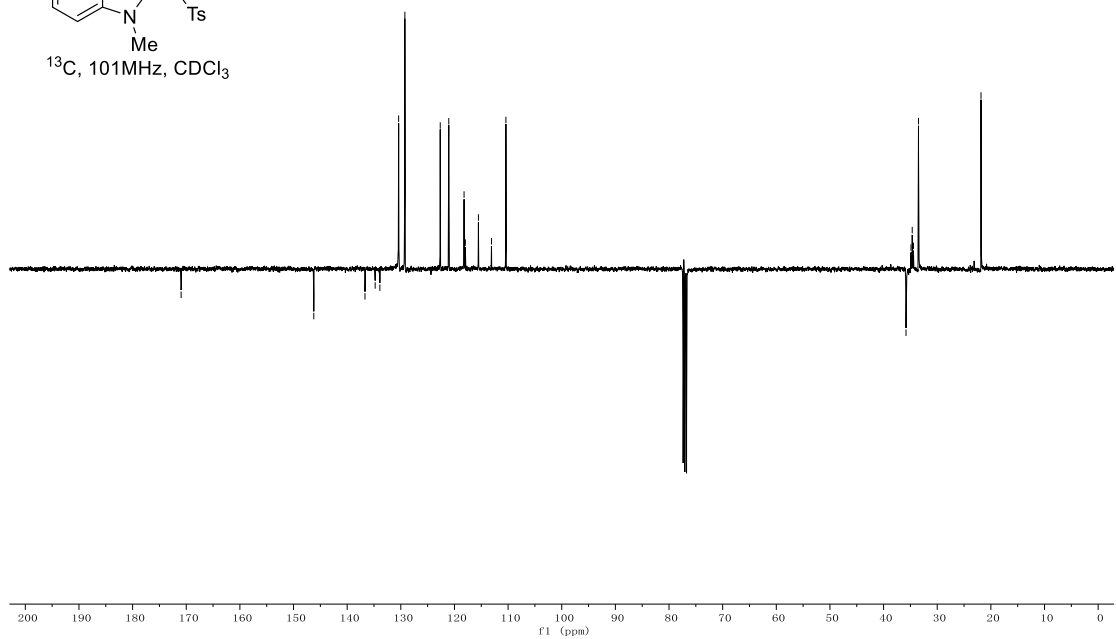


-118.77  
 -119.51  
 -121.48

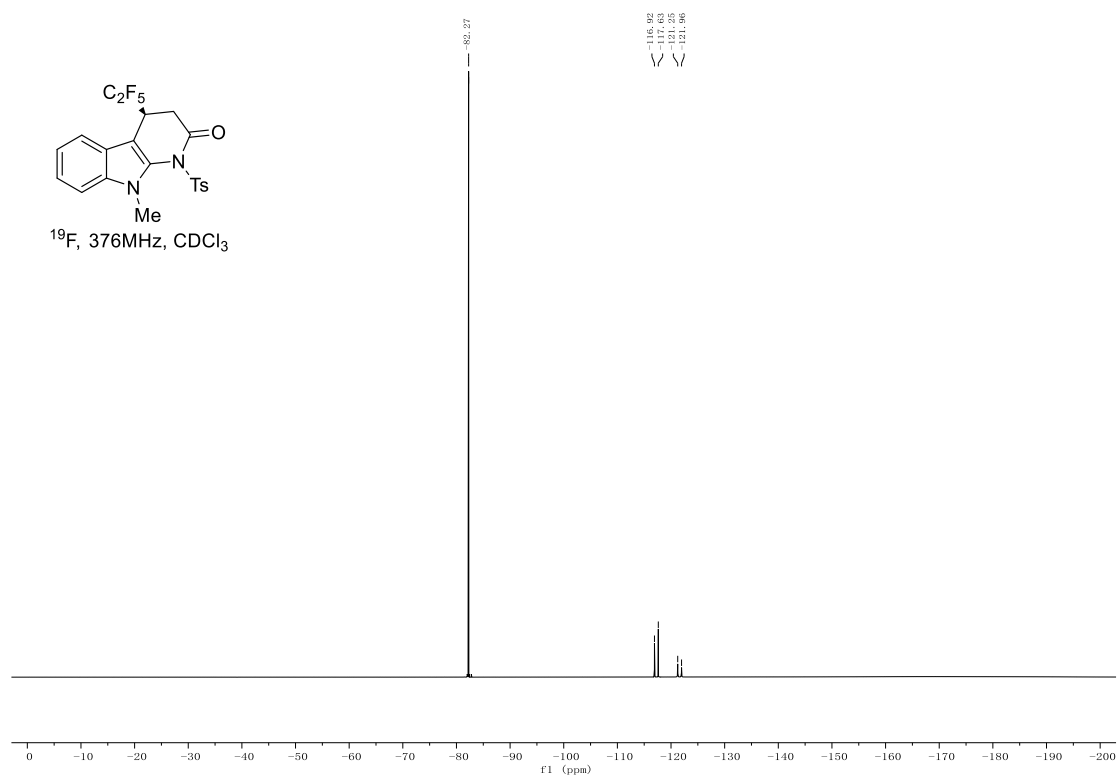
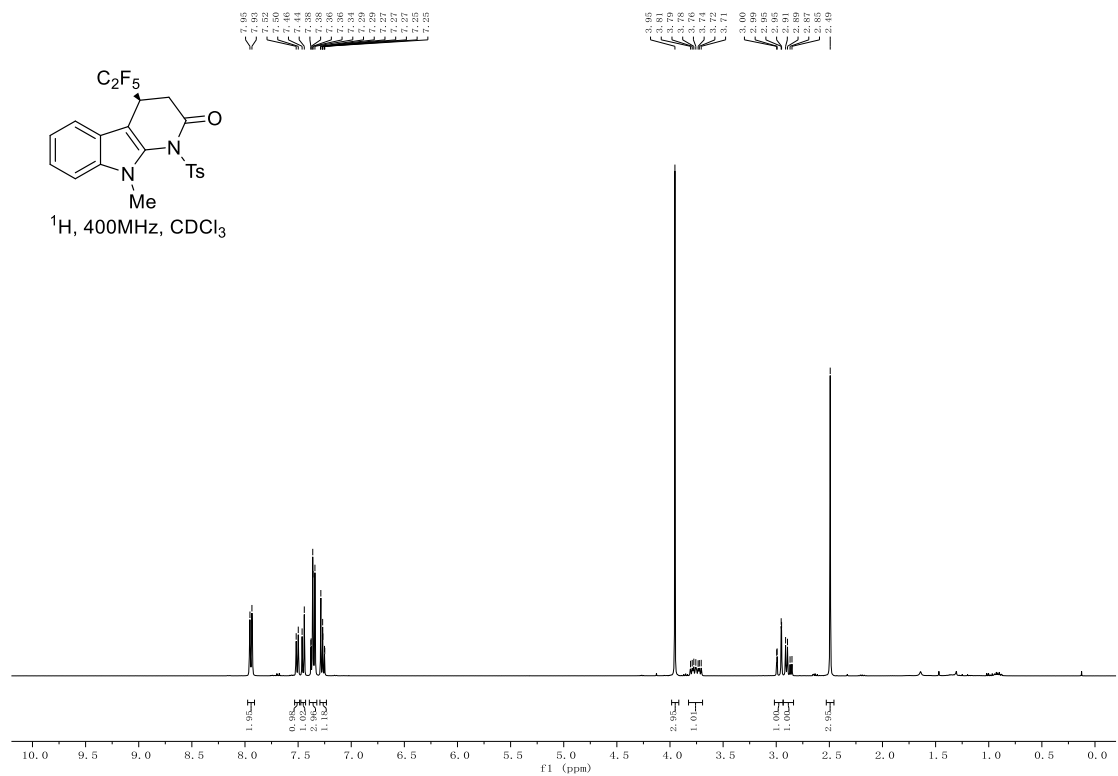


170.86  
 136.68  
 133.90  
 130.40  
 128.24  
 124.39  
 122.65  
 118.21  
 117.57  
 113.10  
 110.41

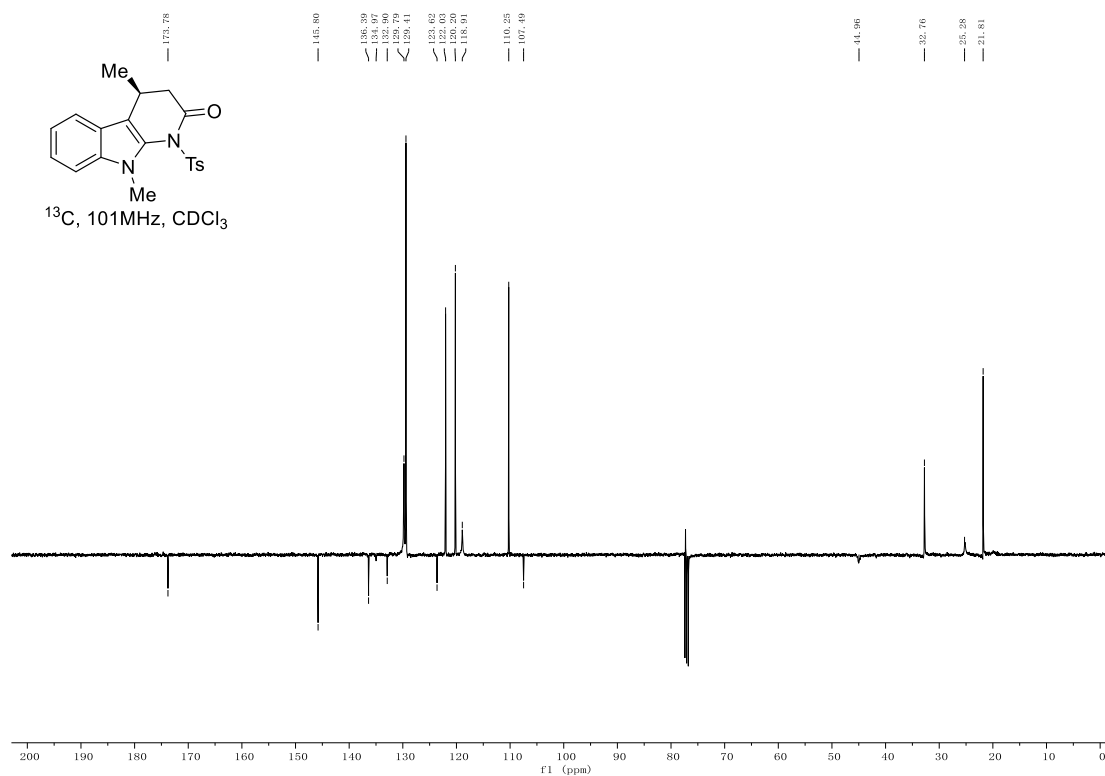
35.82  
 31.86  
 34.43  
 33.49  
 21.84



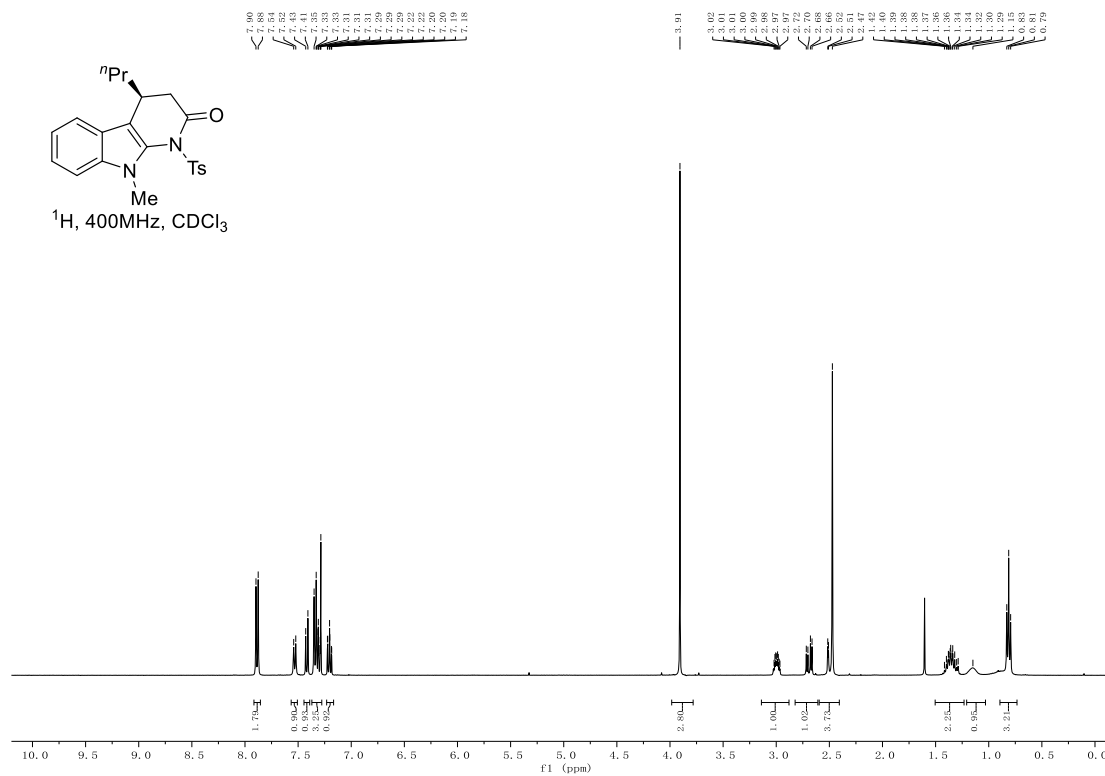
**(S)-9-Methyl-4-(perfluoroethyl)-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (21)**

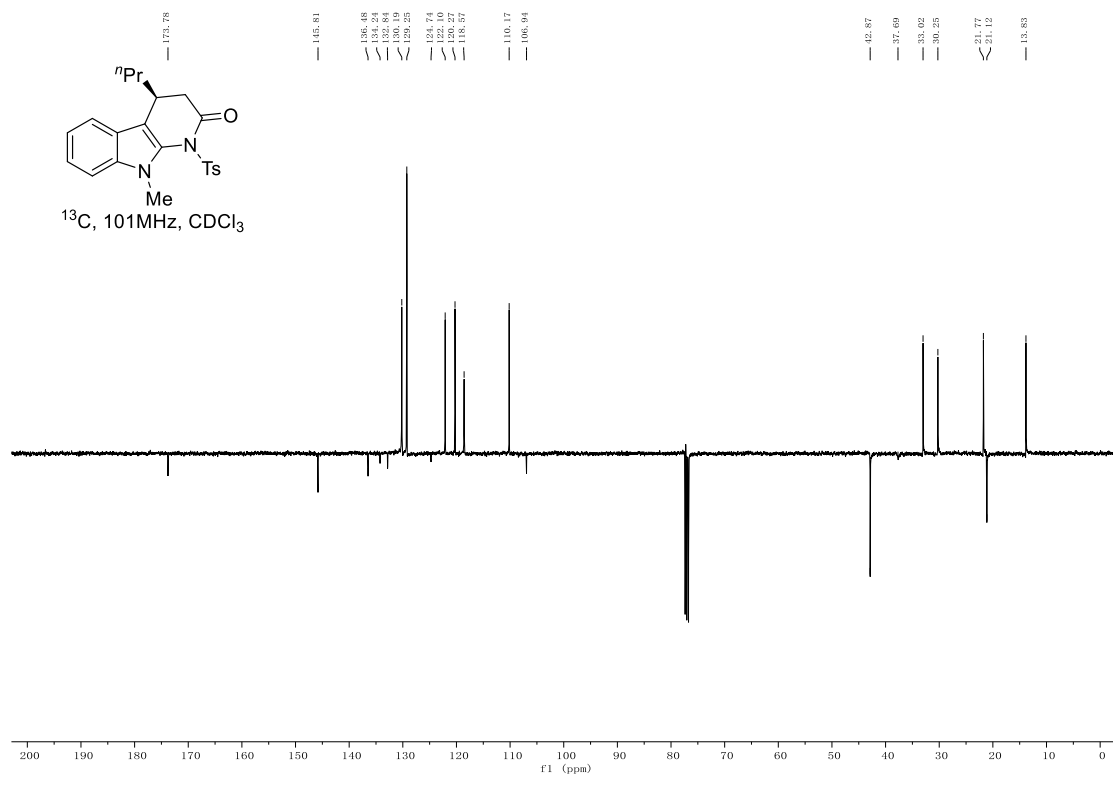




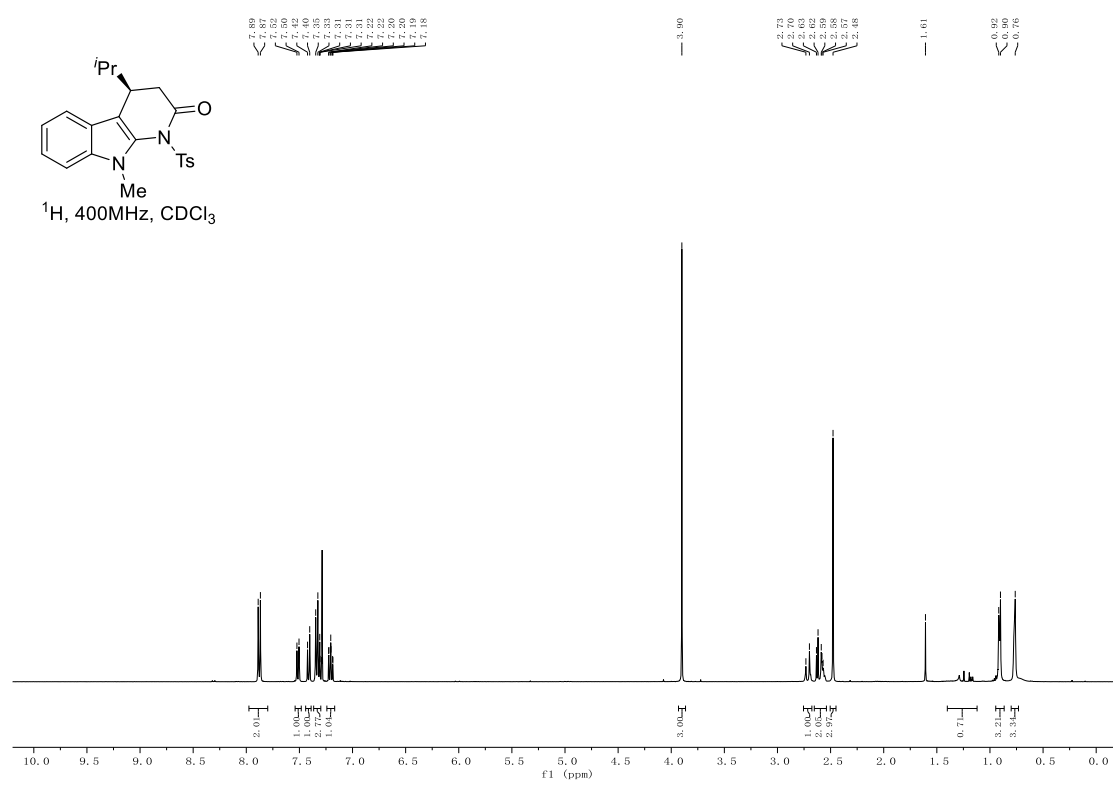


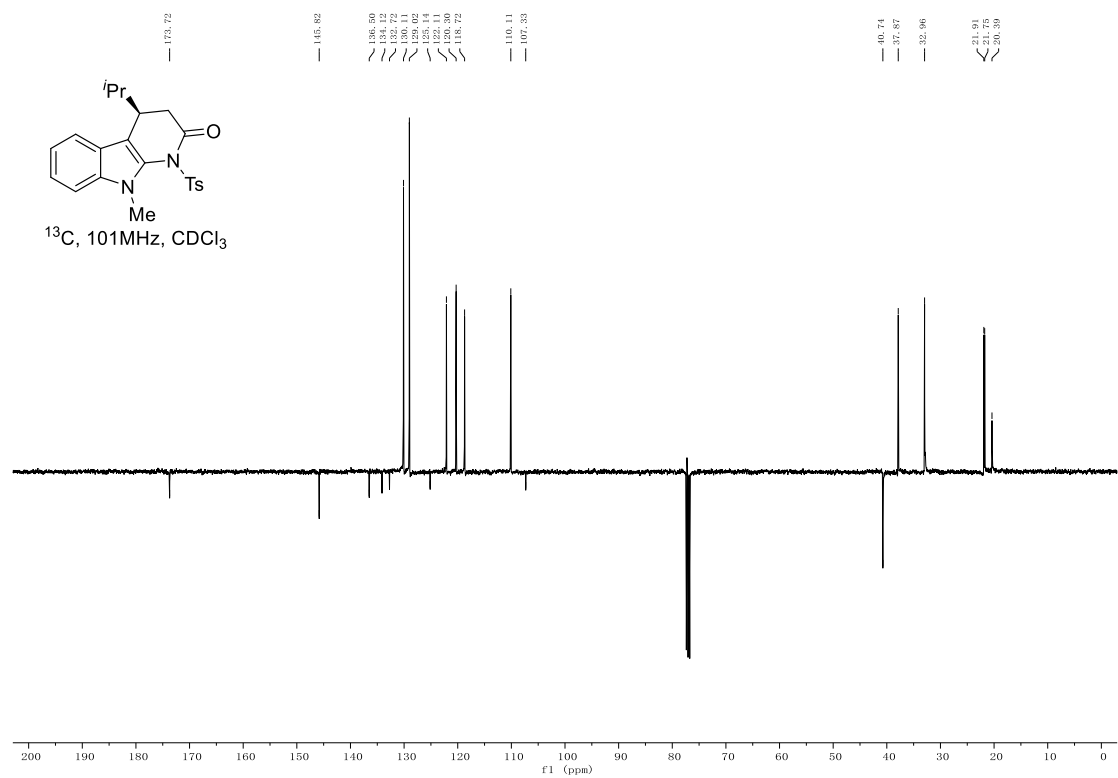
**(S)-9-Methyl-4-propyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (23)**



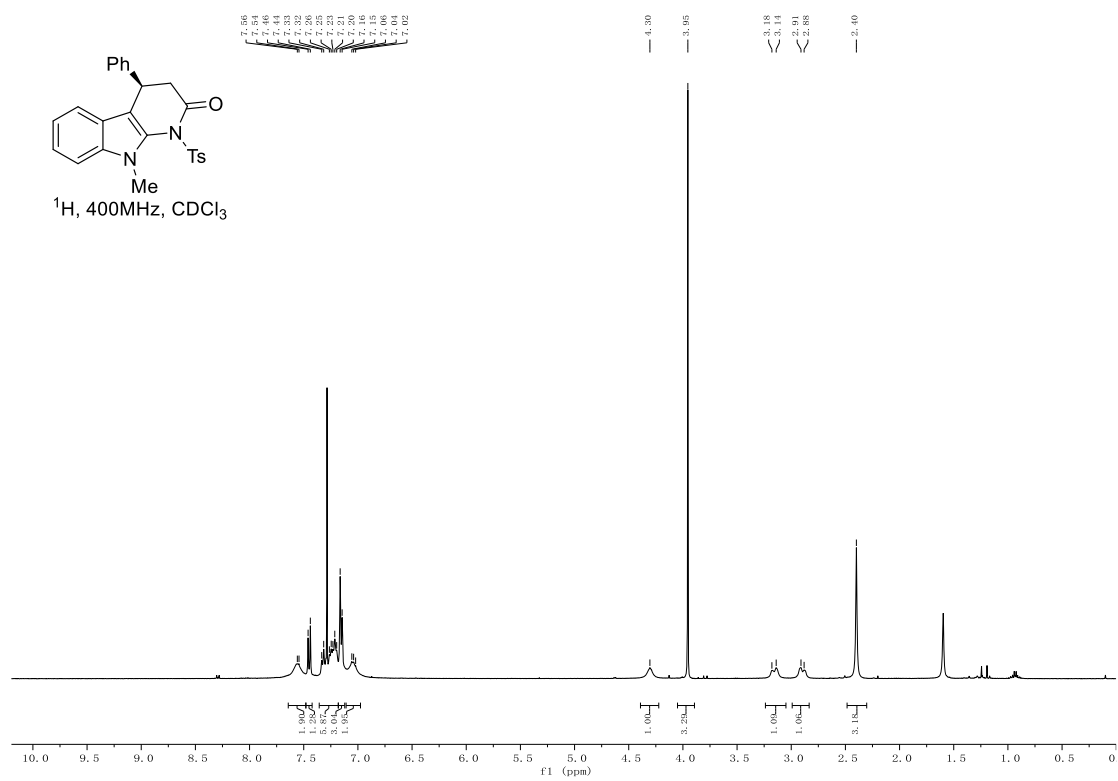


**(R)-4-Isopropyl-9-methyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (24)**

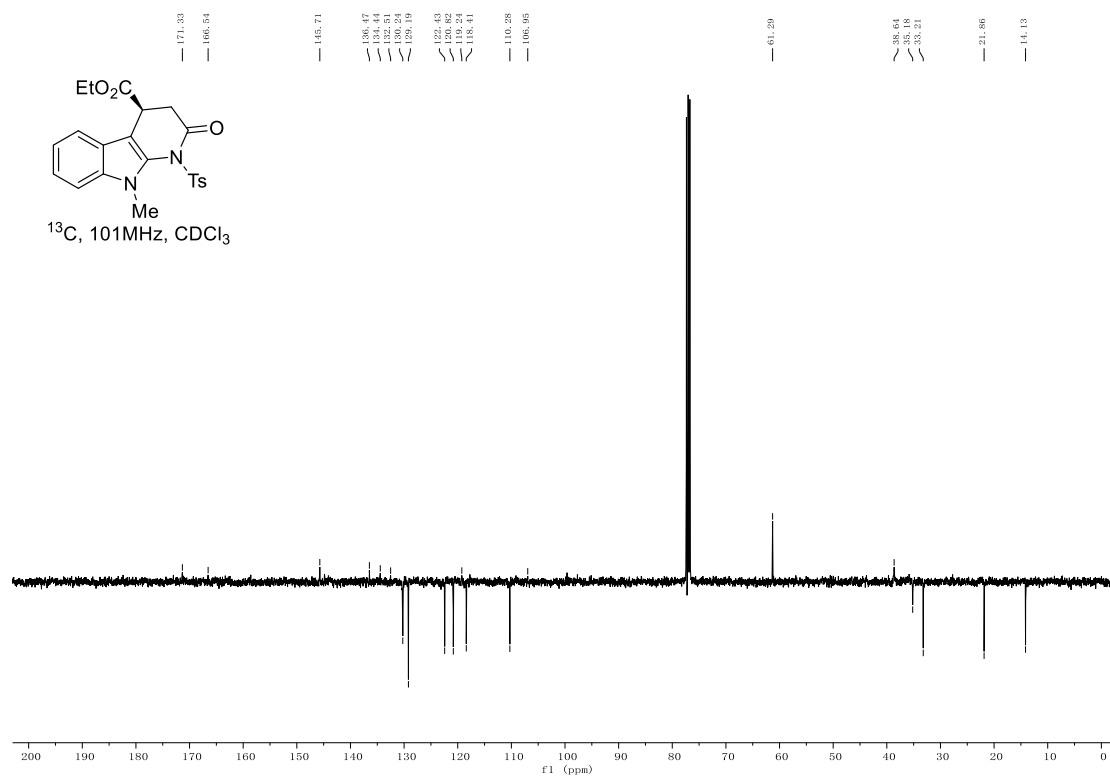
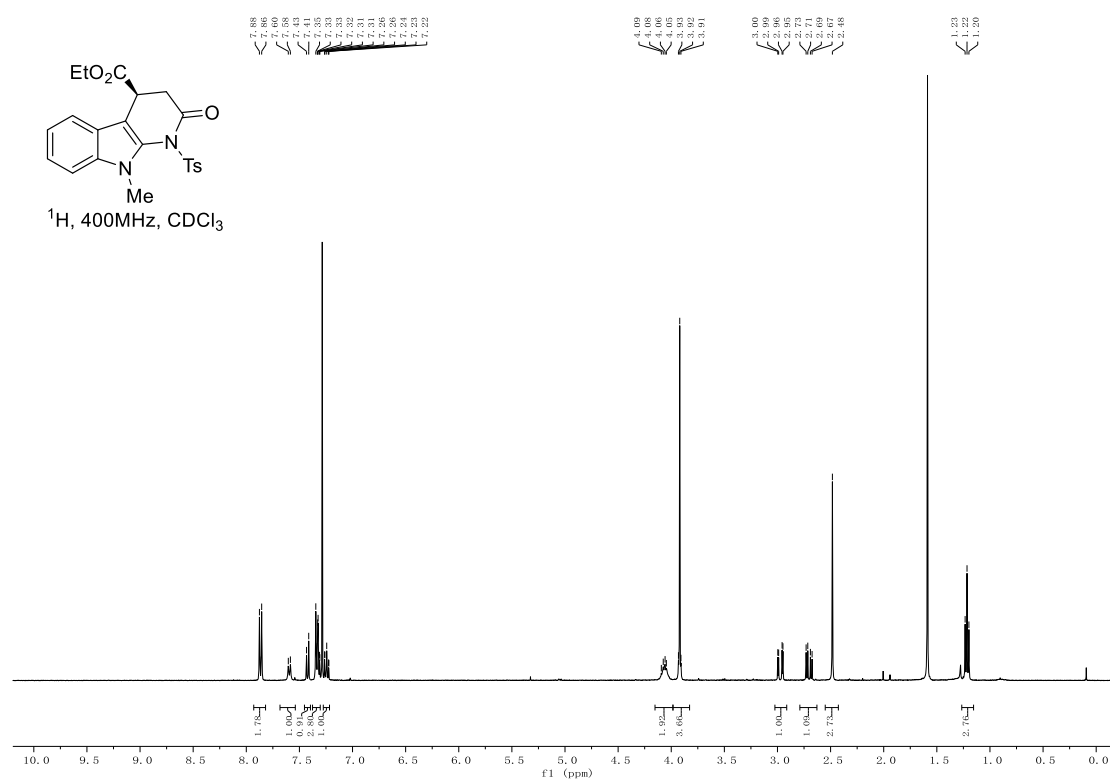




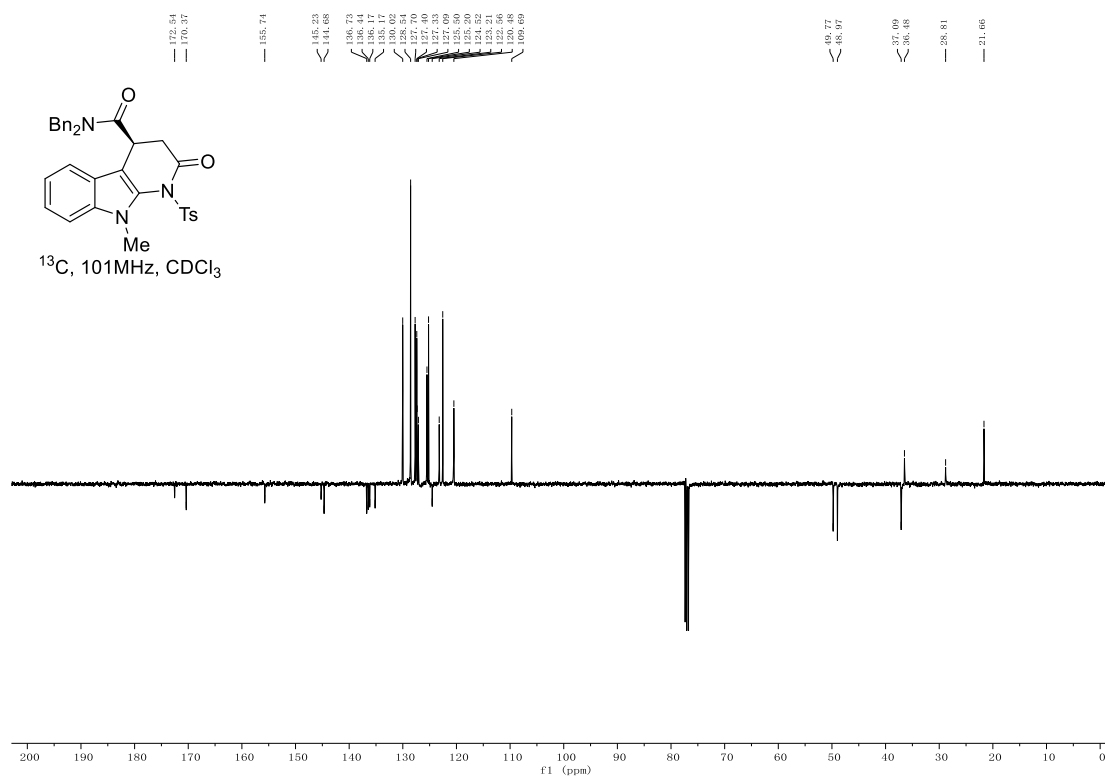
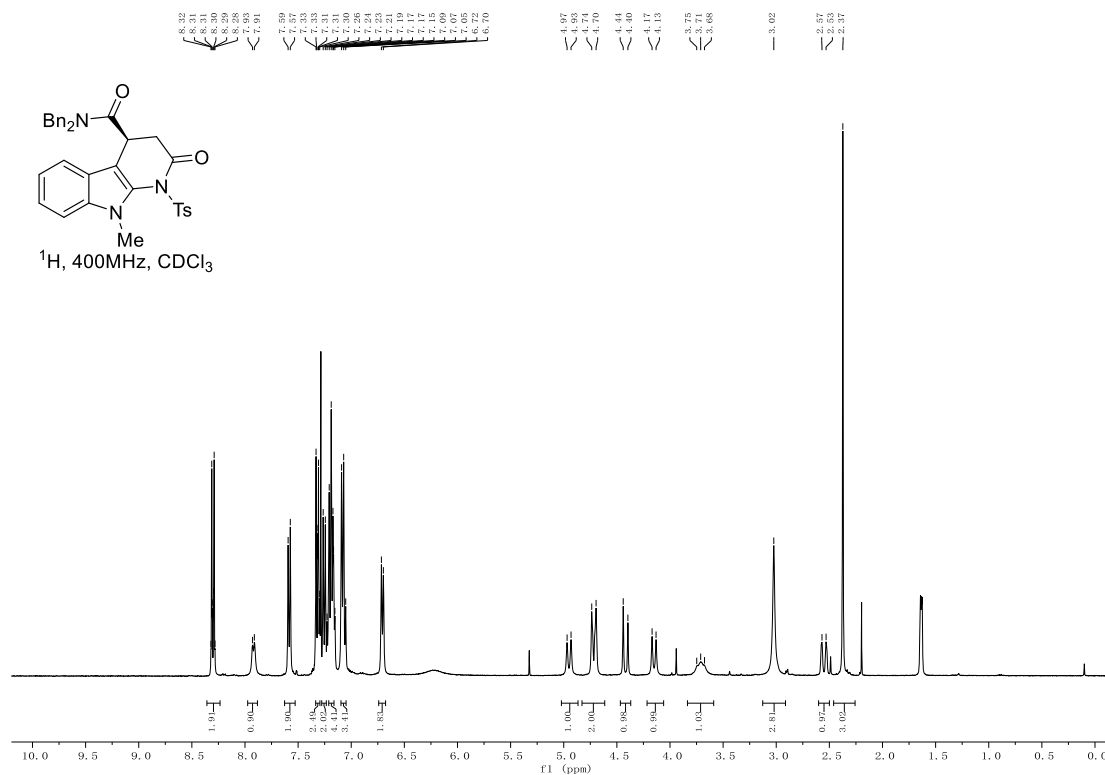
**(R)-9-Methyl-4-phenyl-1-tosyl-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (25)**



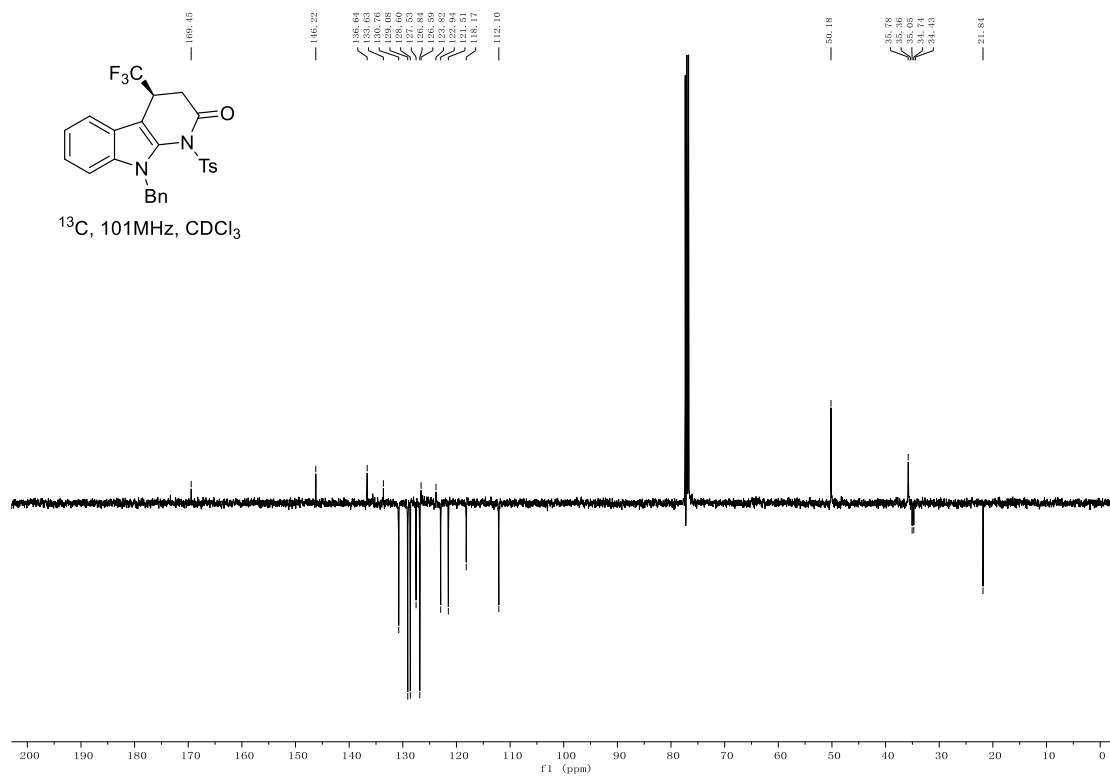
**(S)-Ethyl 9-methyl-2-oxo-1-tosyl-2,3,4,9-tetrahydro-1H-pyrido[2,3-b]indole-4-carboxylate (26)**



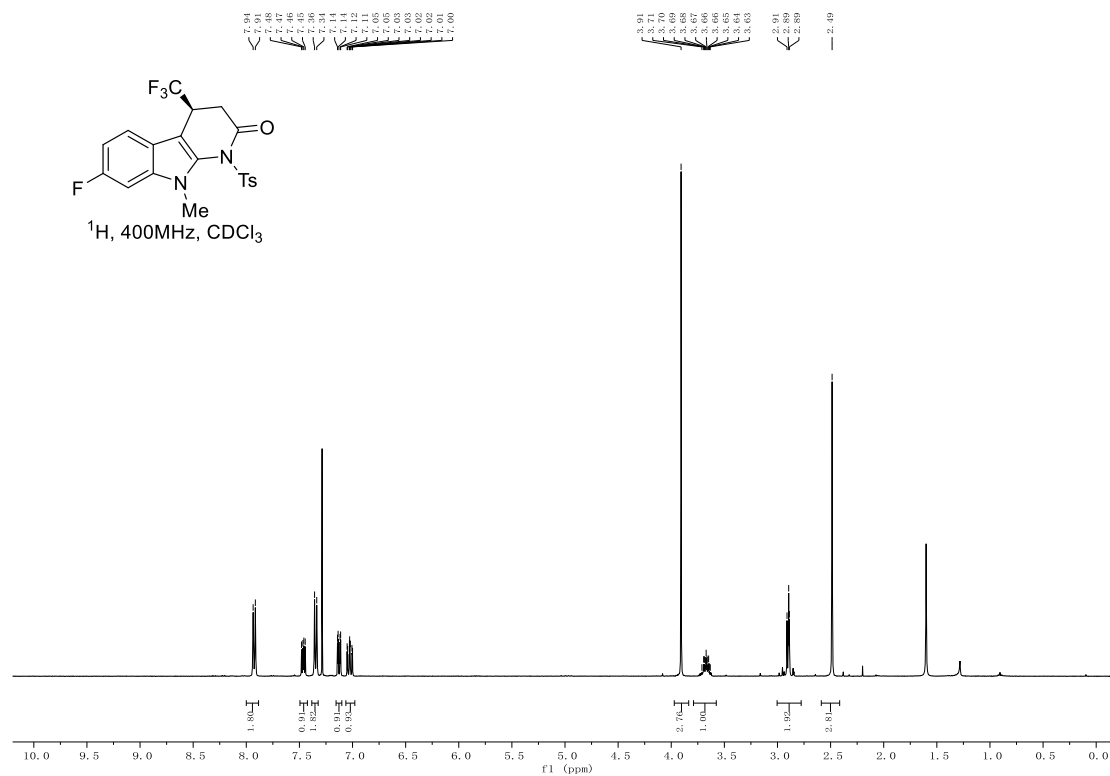
**(S)-N,N-dibenzyl-9-methyl-2-oxo-1-tosyl-2,3,4,9-tetrahydro-1H-pyrido[2,3-b]indole-4-carboxamide (27)**

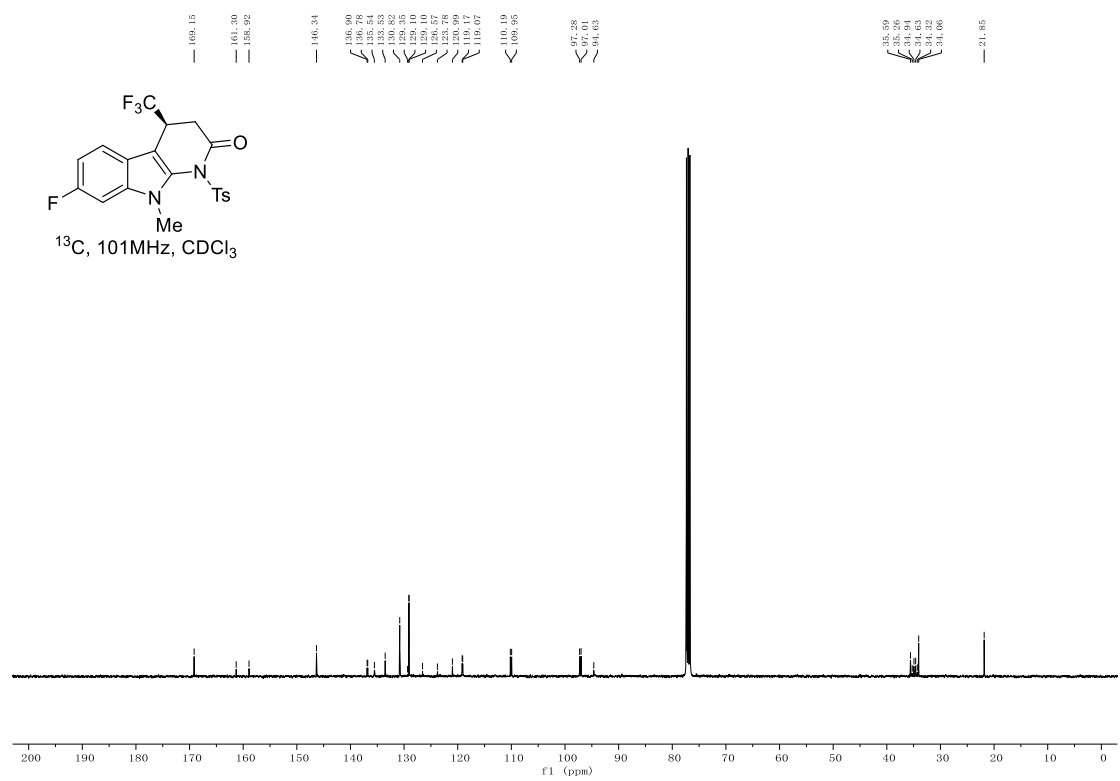
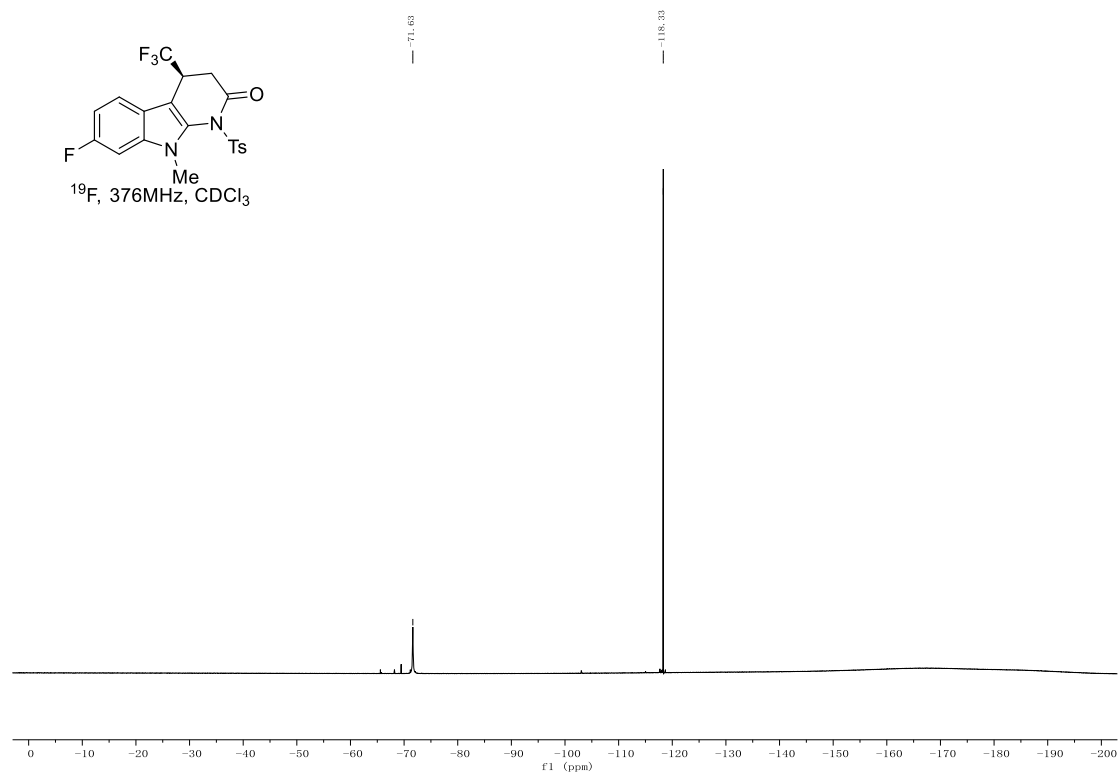




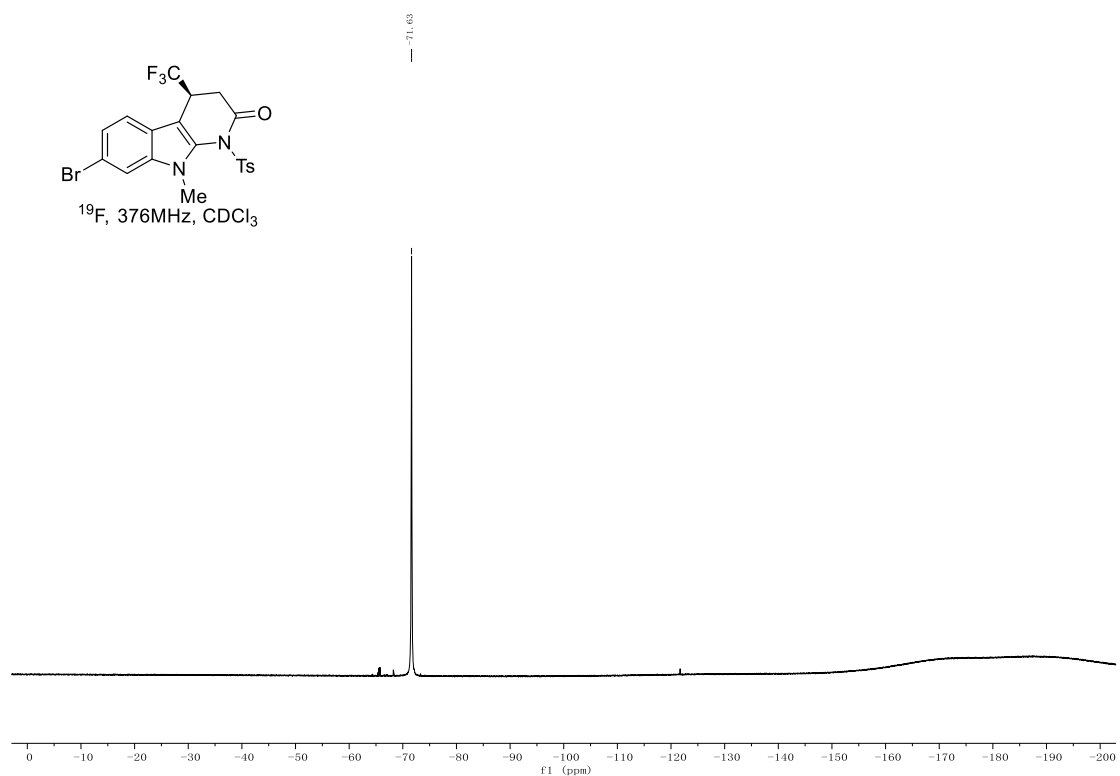
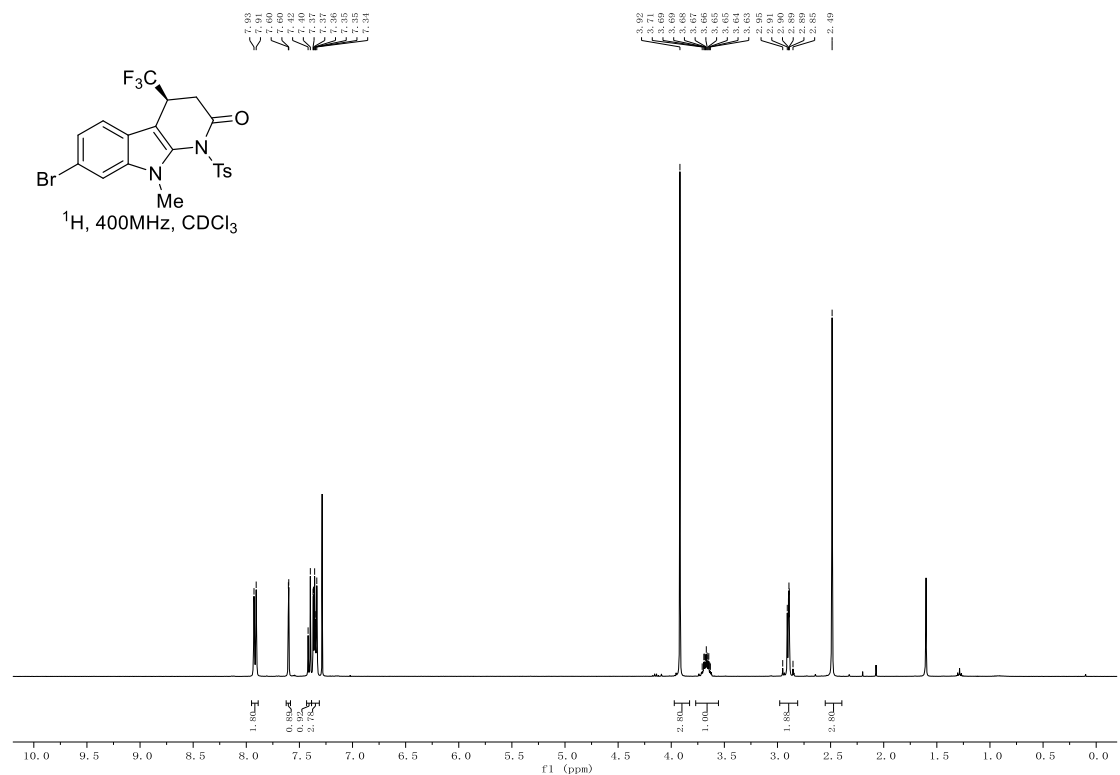


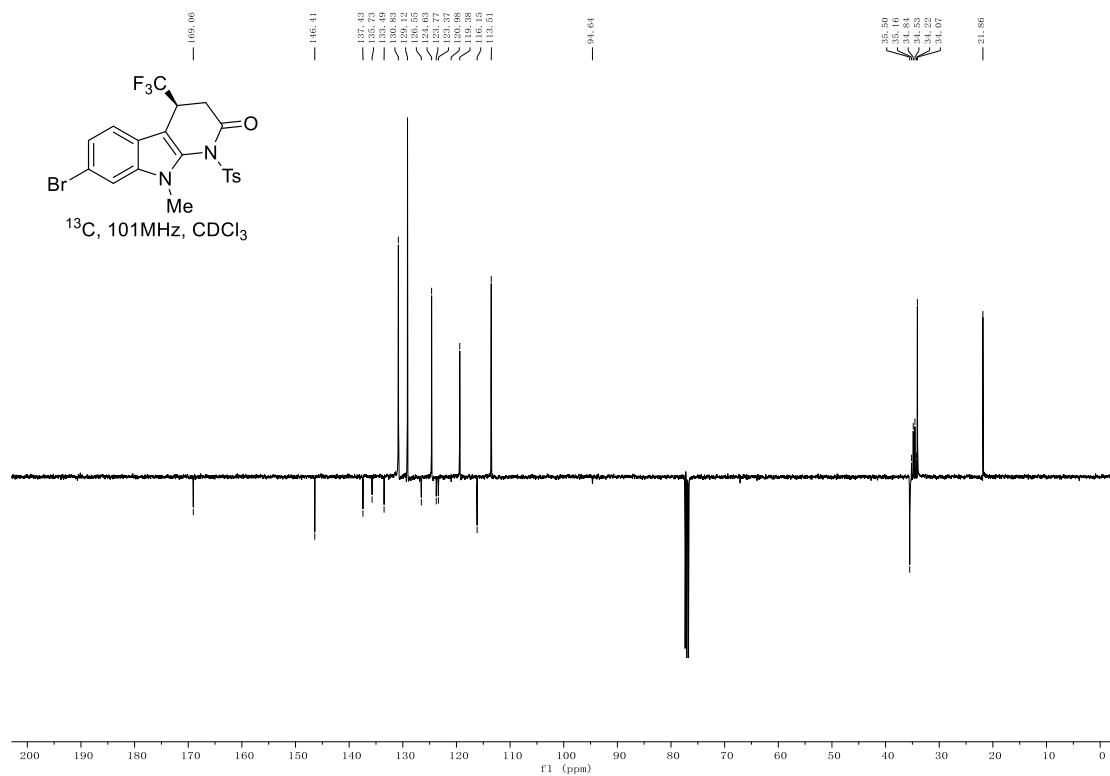
**(S)-7-Fluoro-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (38)**



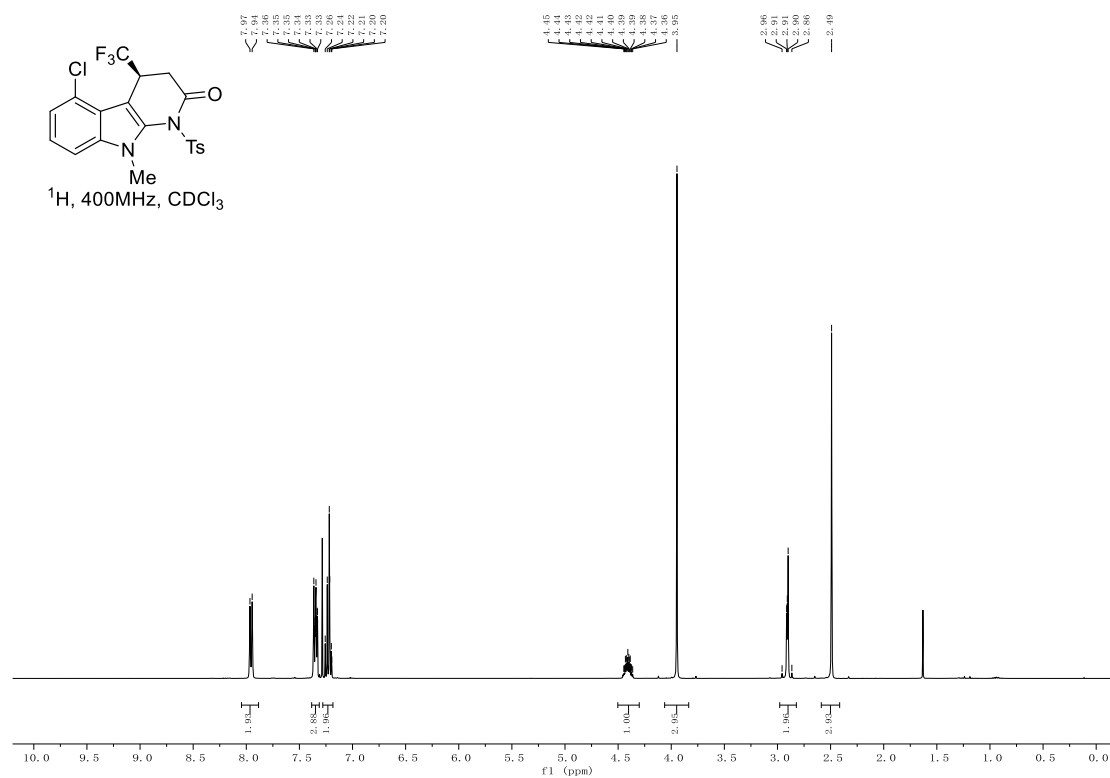


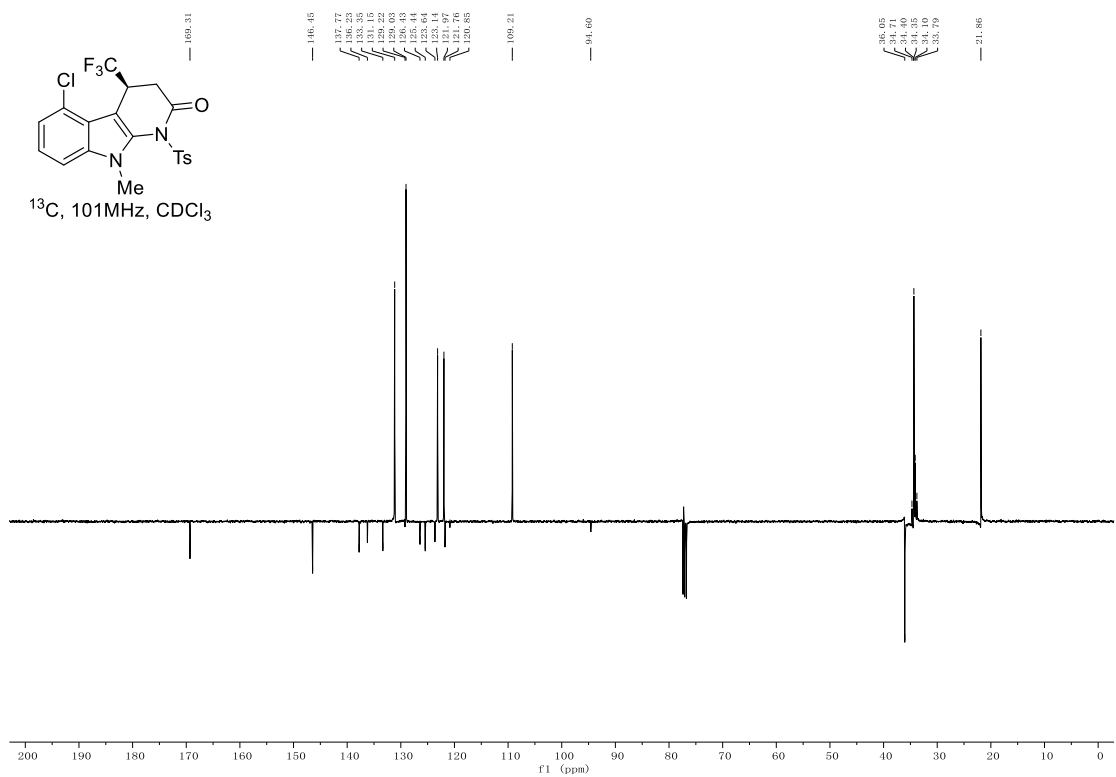
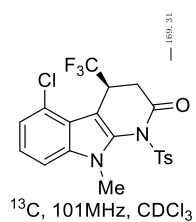
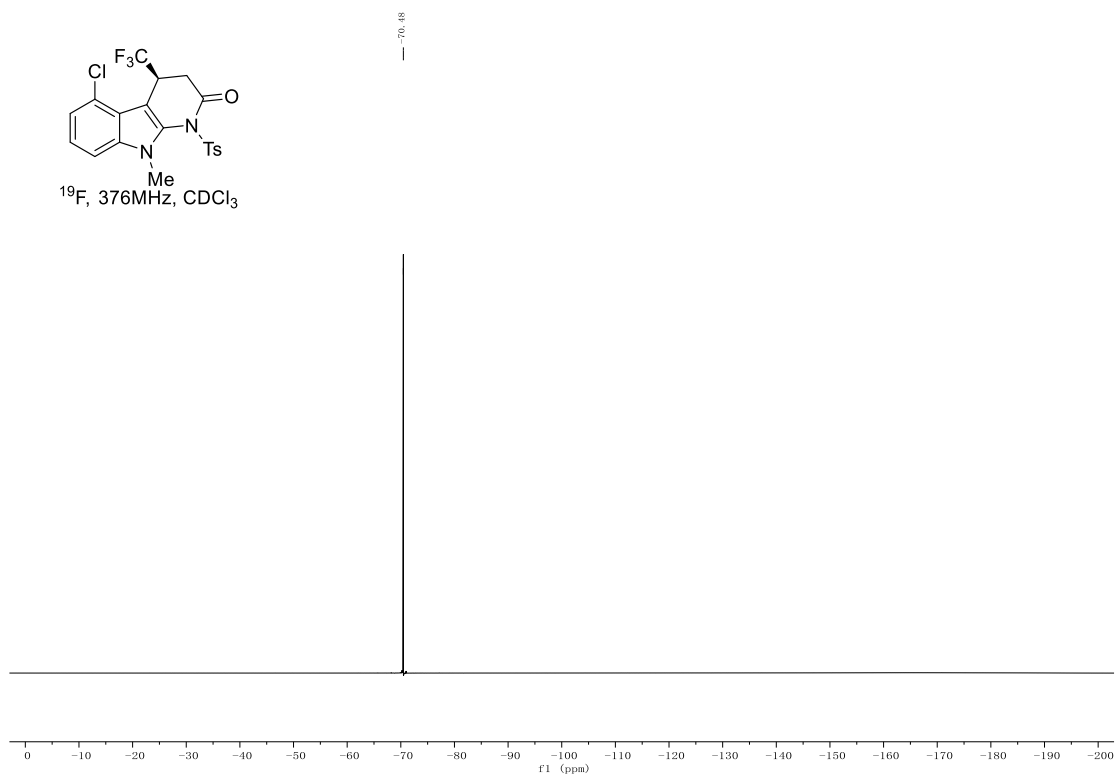
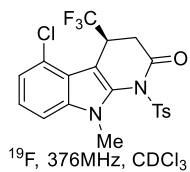
**(S)-7-Bromo-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one**  
**(39)**



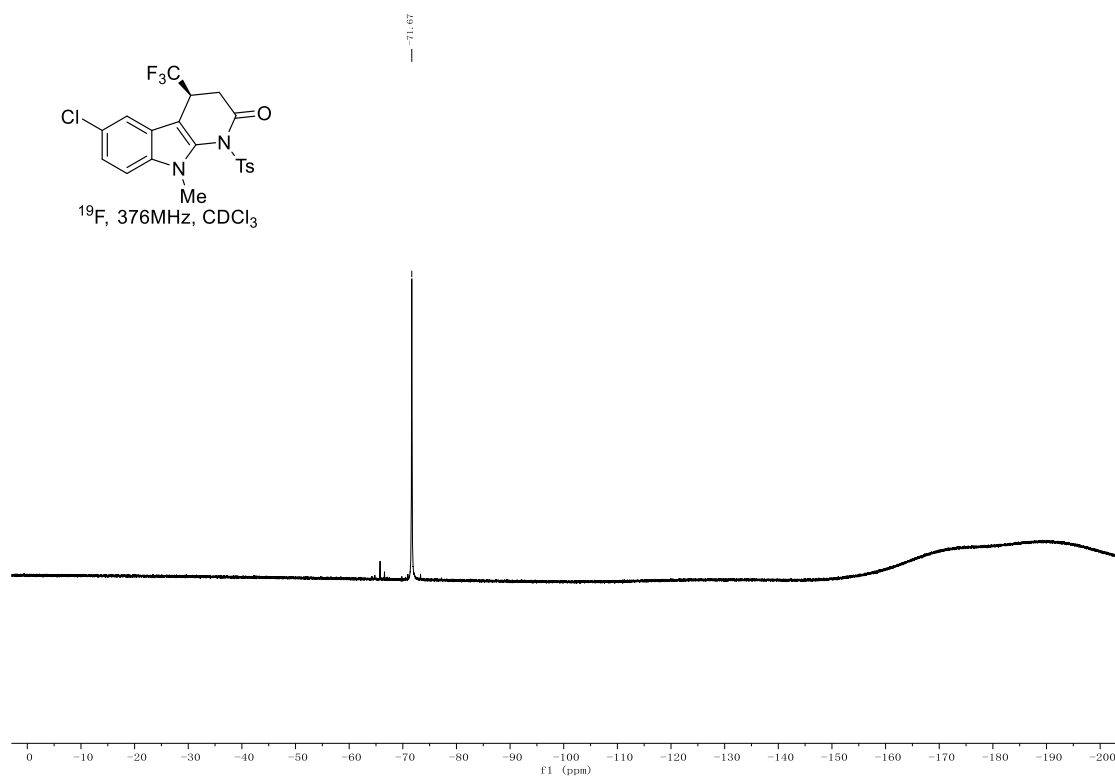
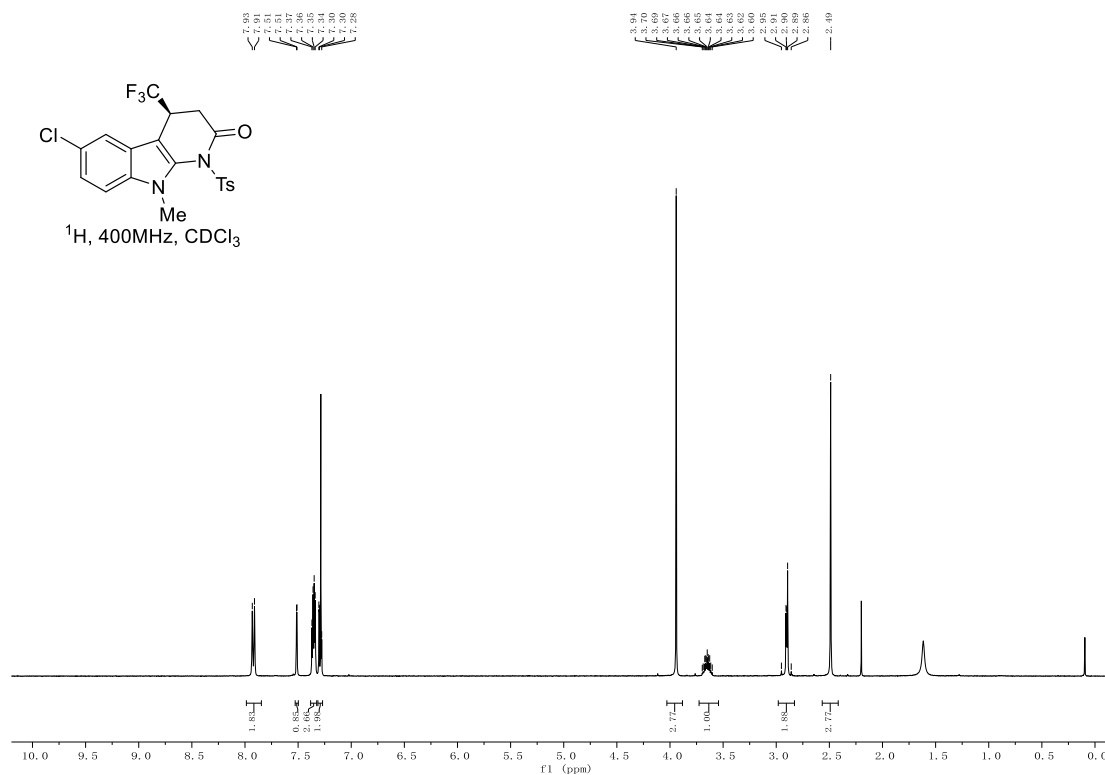


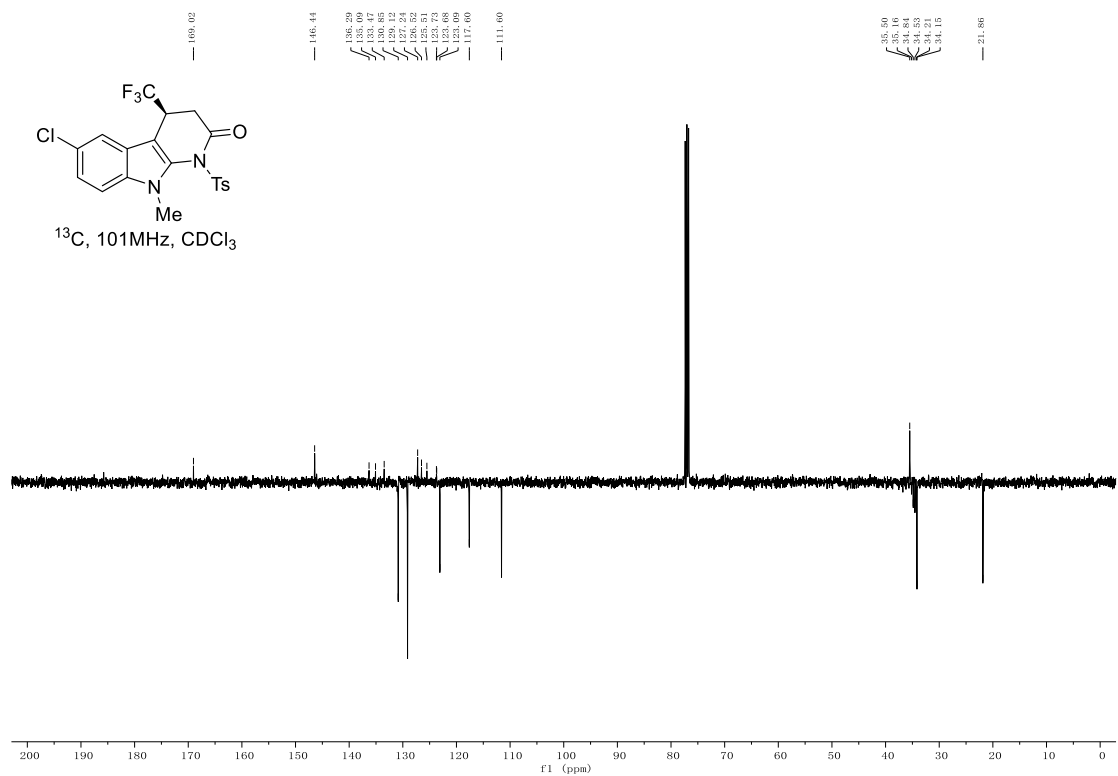
**(S)-4-Chloro-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (40)**



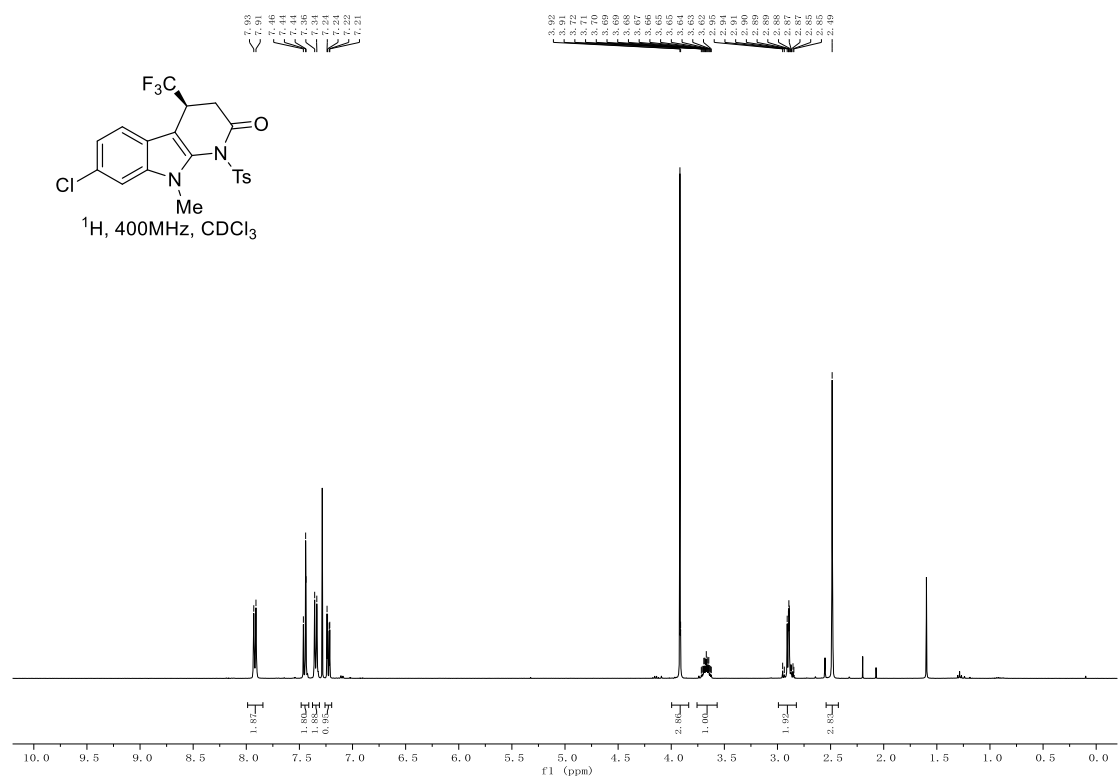


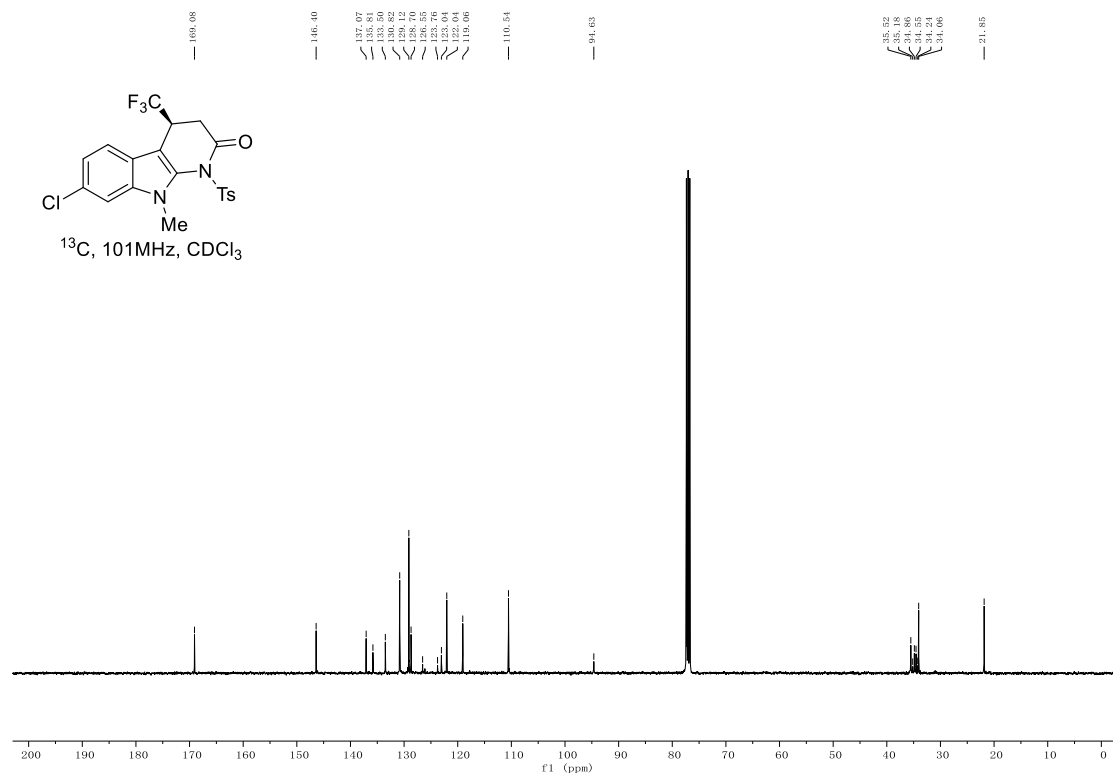
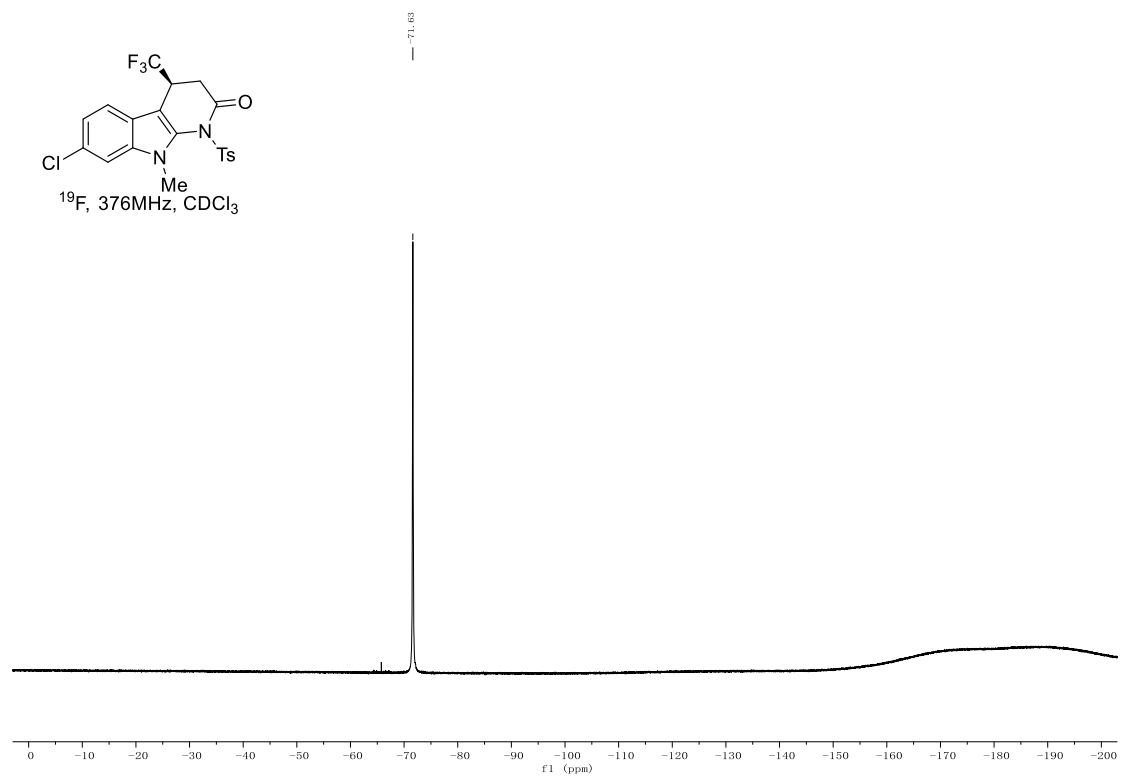
**(S)-6-Chloro-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one**  
**(41)**



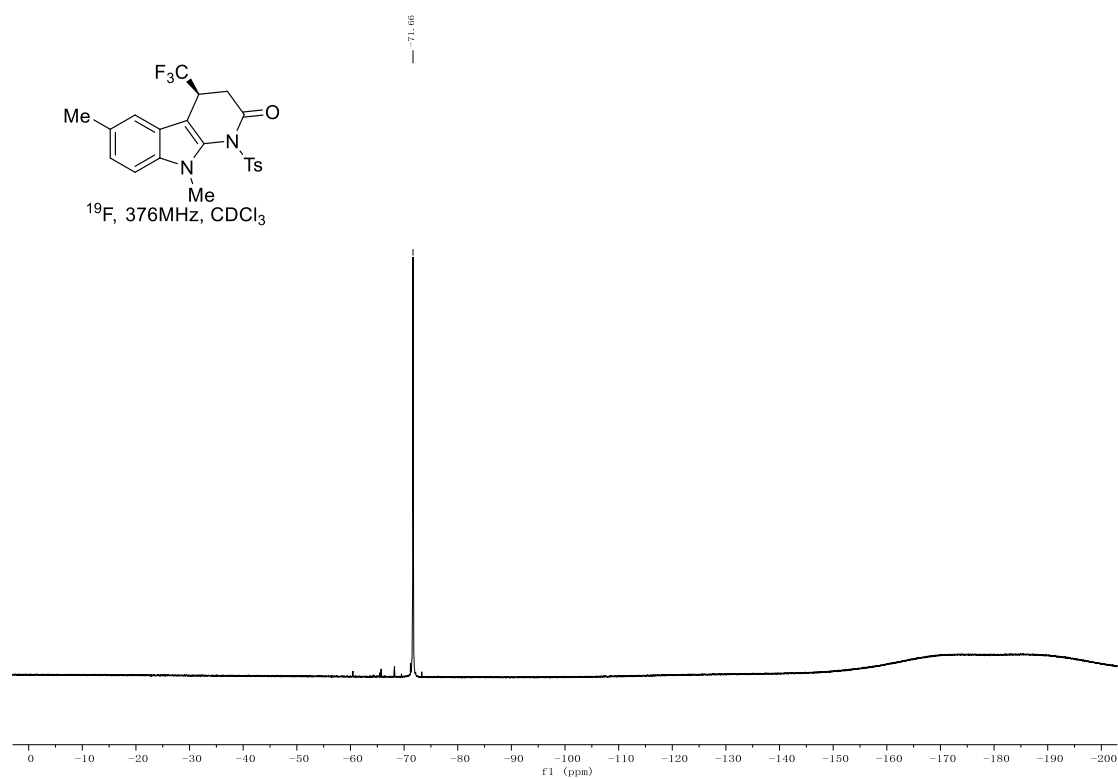
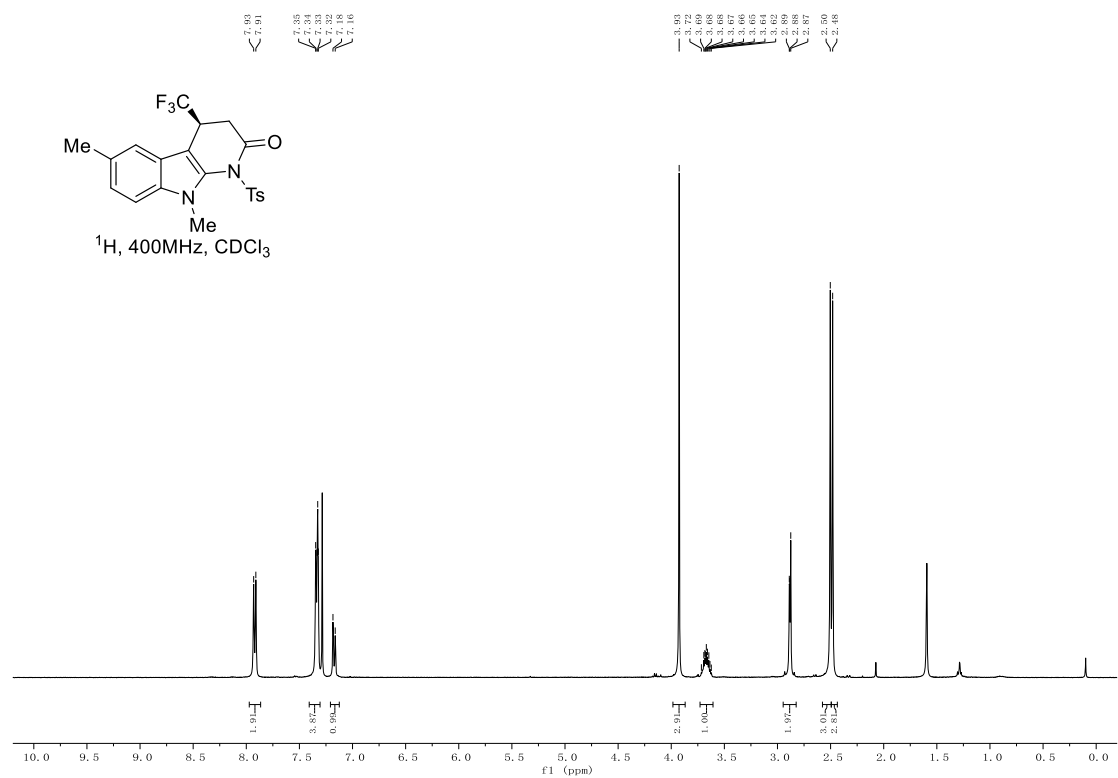


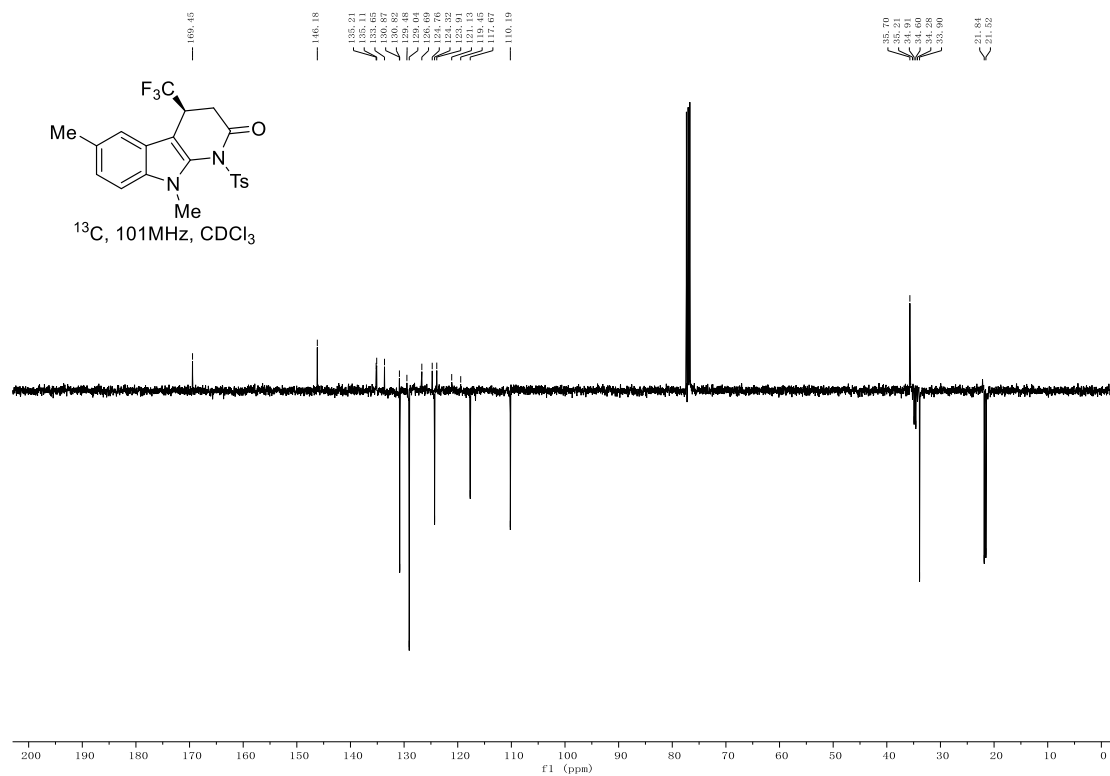
**(S)-7-Chloro-9-methyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (42)**



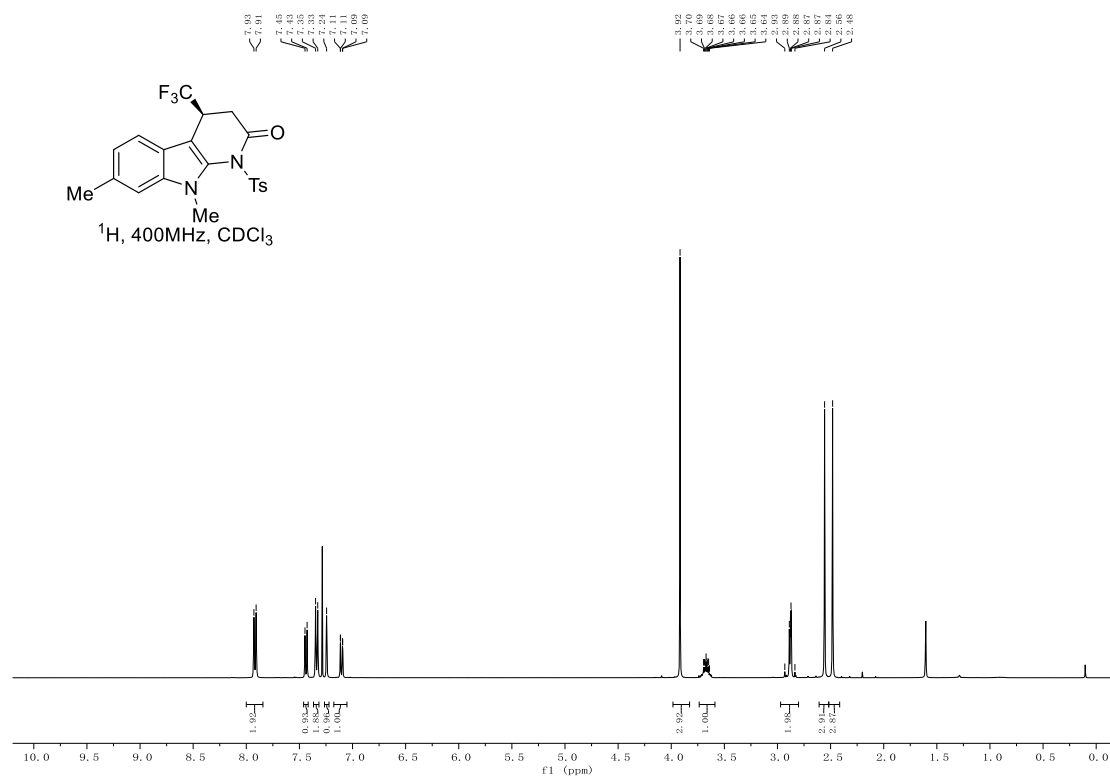


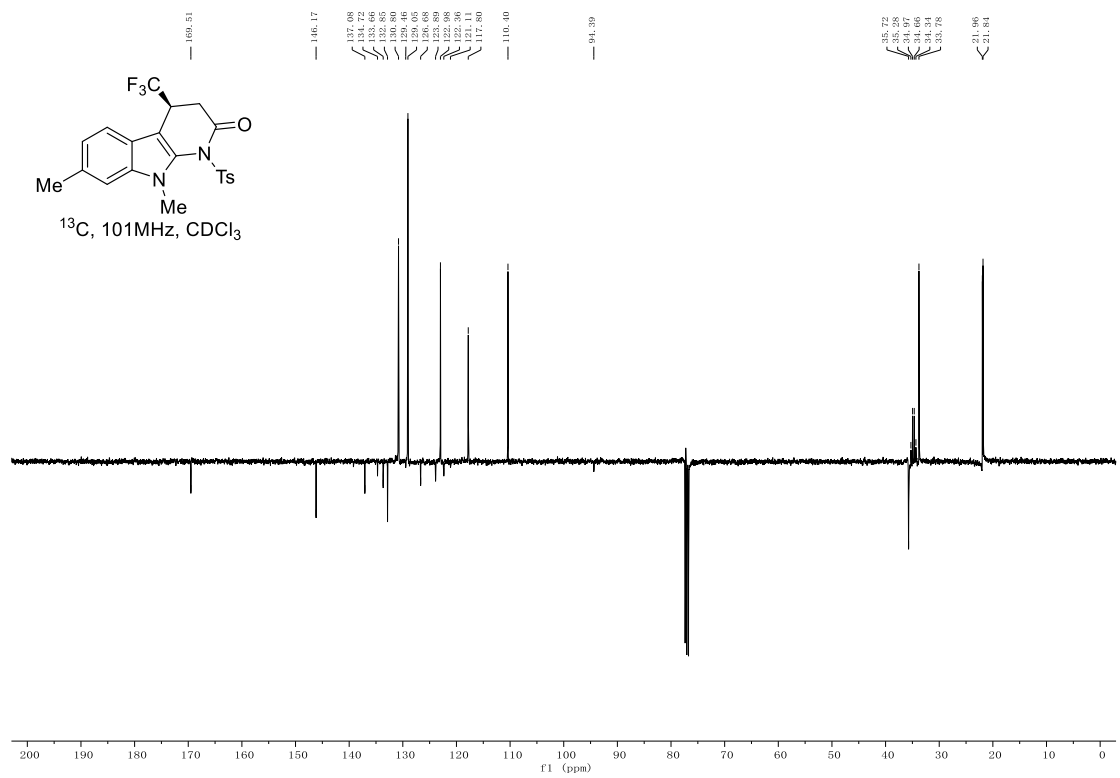
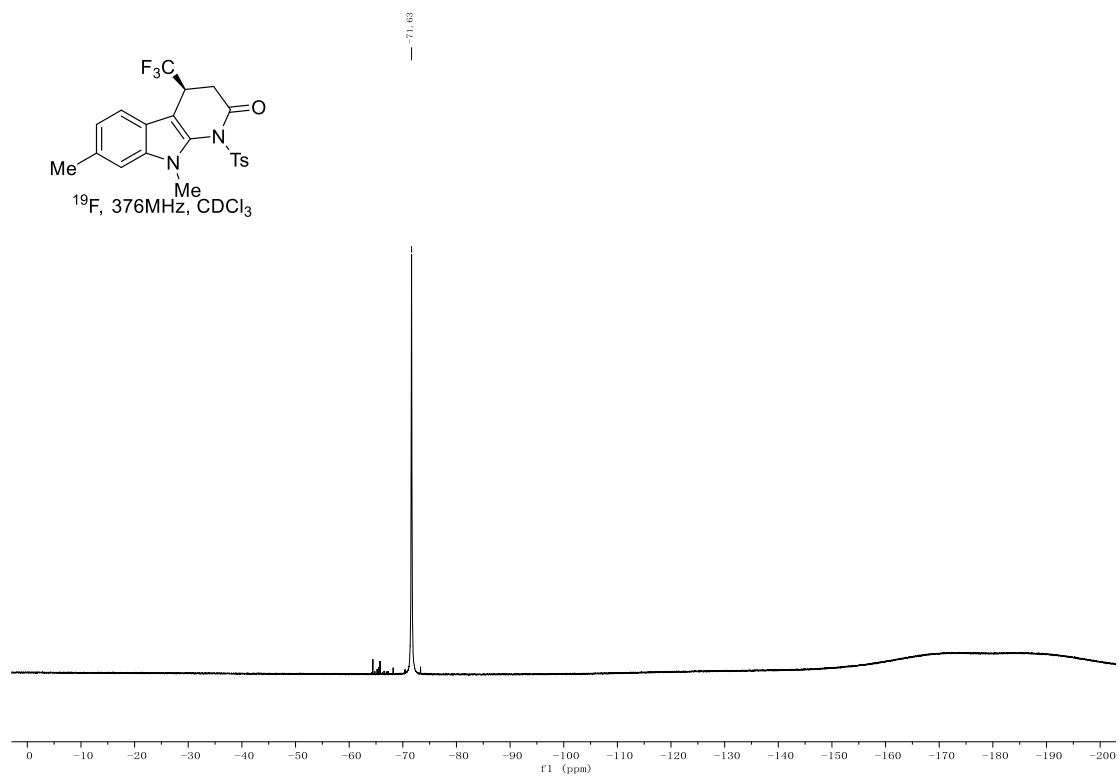
(S)-6,9-Dimethyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (43)



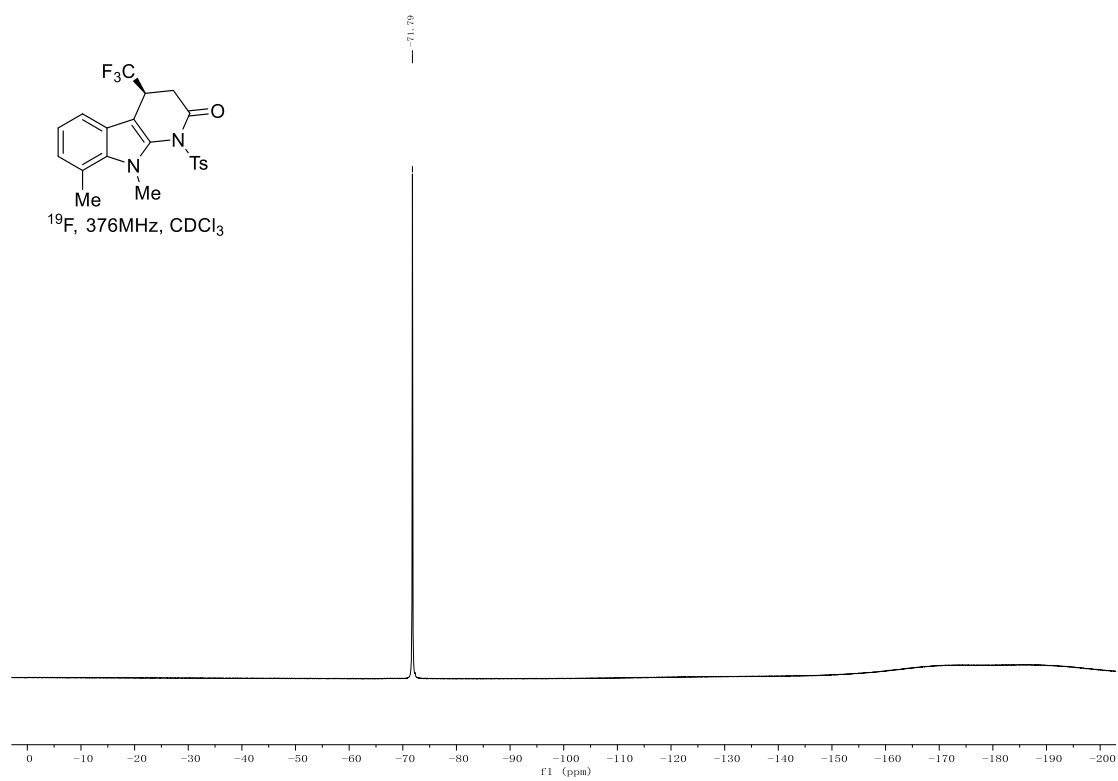
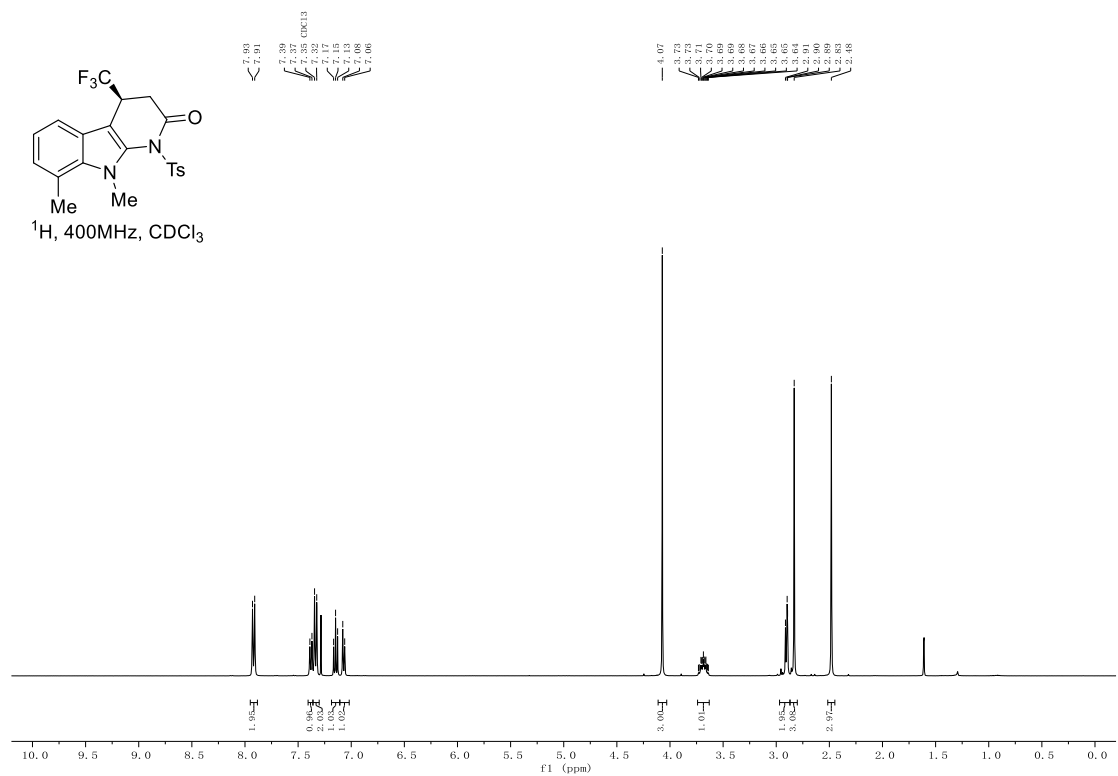


**(S)-7,9-Dimethyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (44)**

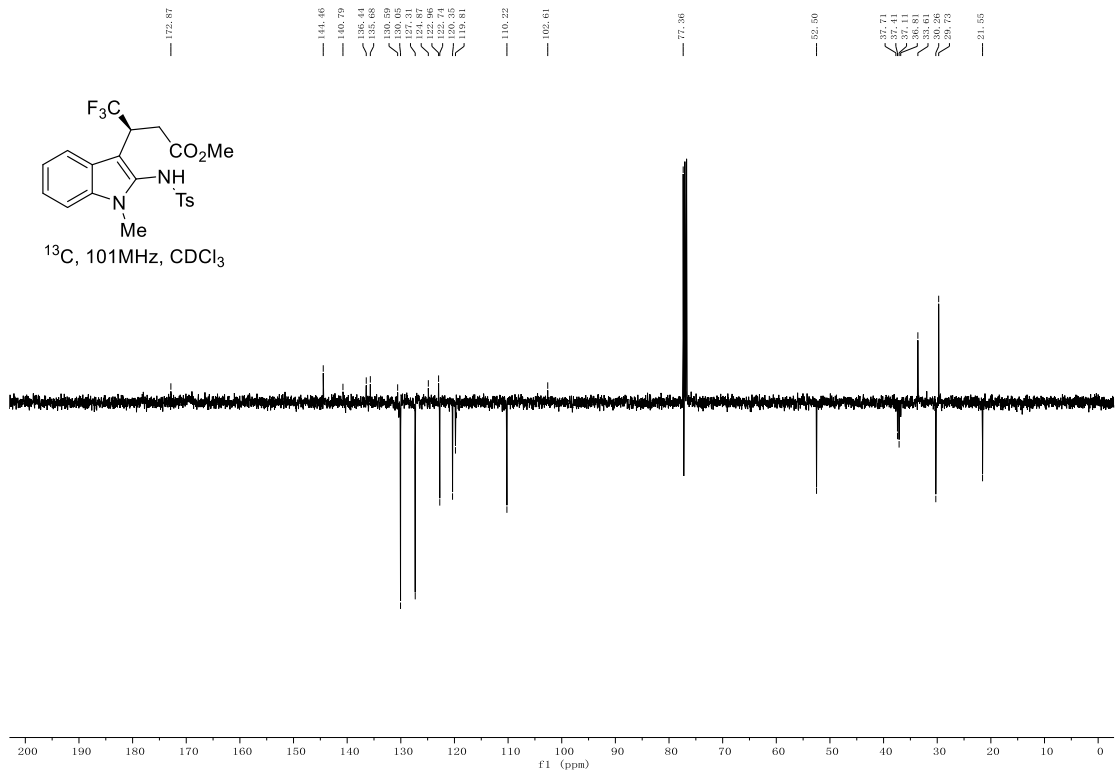
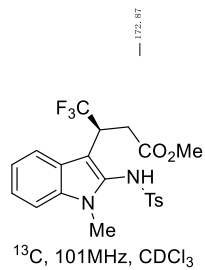
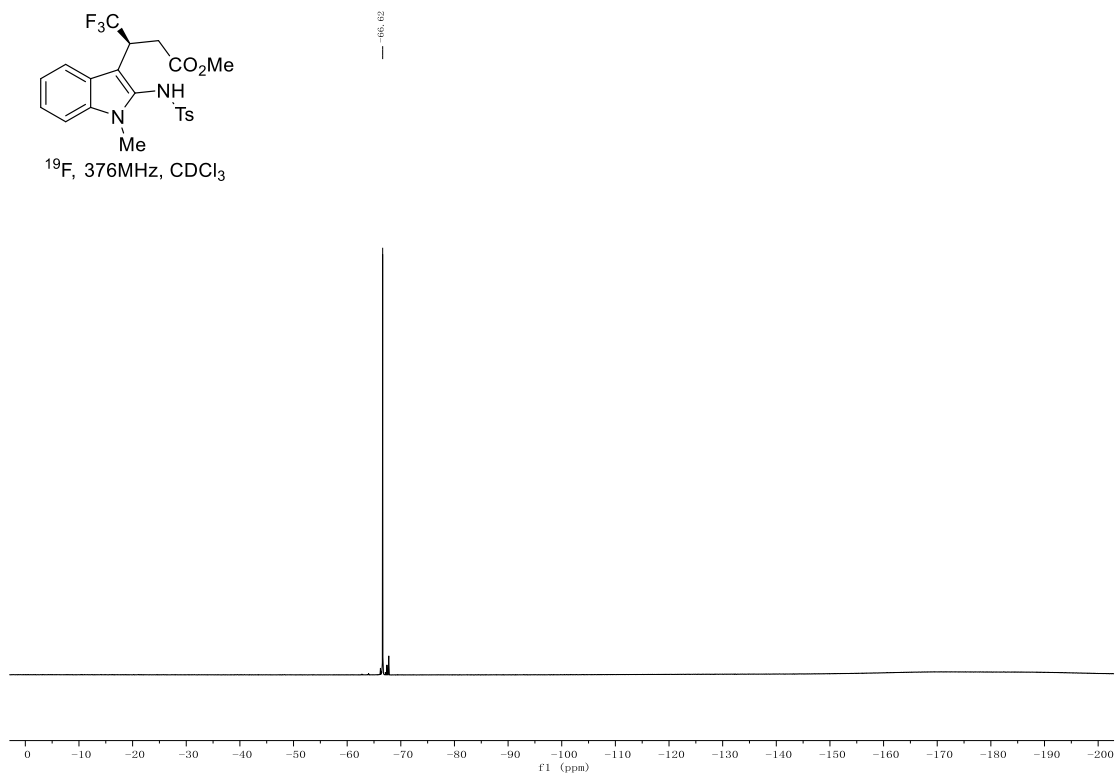
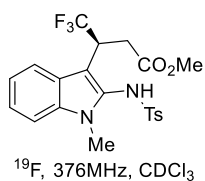




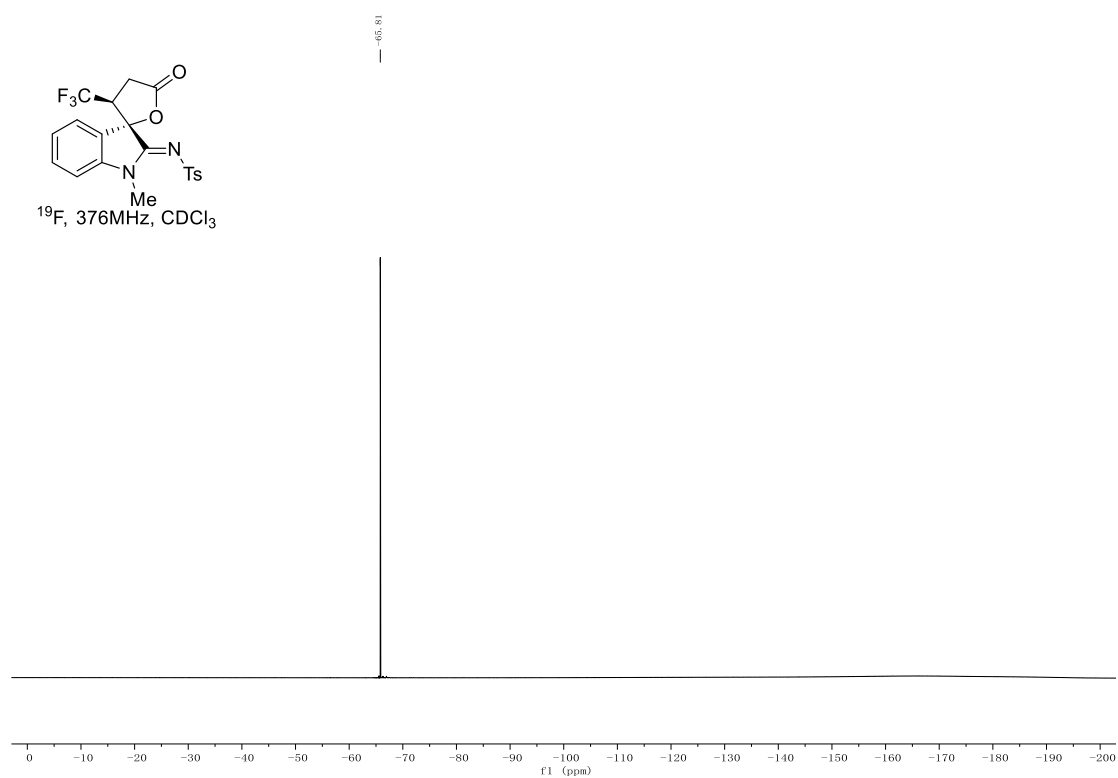
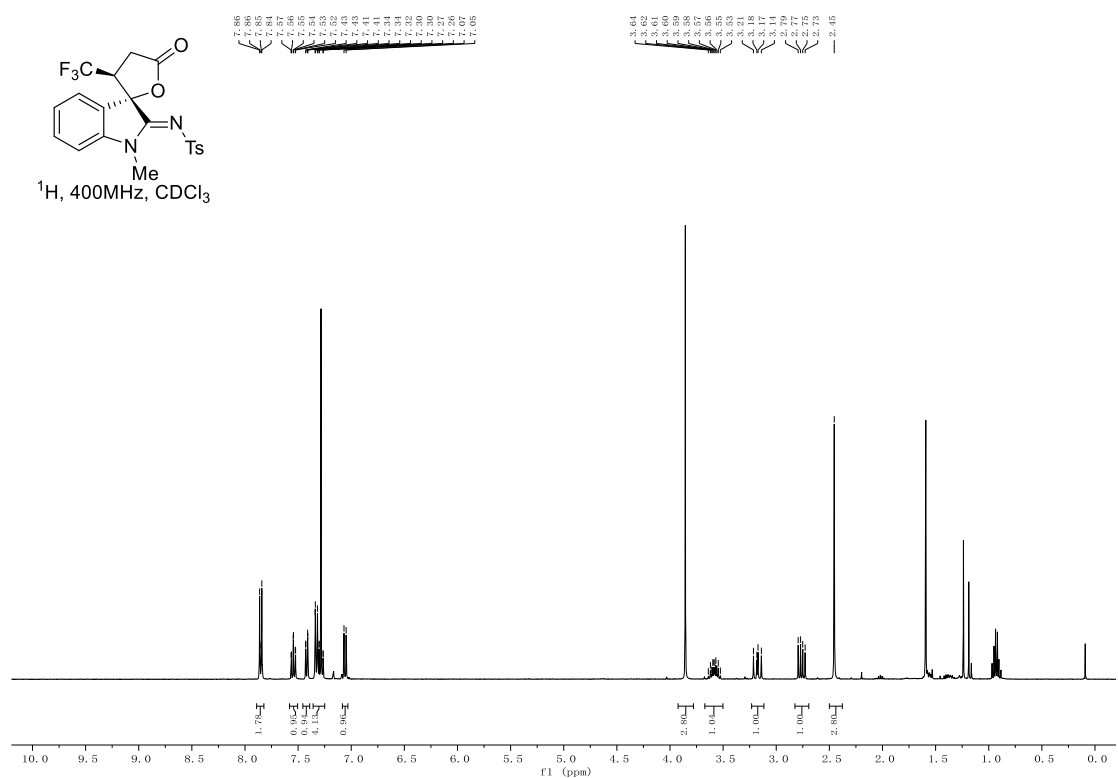
**(S)-8,9-Dimethyl-1-tosyl-4-(trifluoromethyl)-1,3,4,9-tetrahydro-2H-pyrido[2,3-b]indol-2-one (45)**



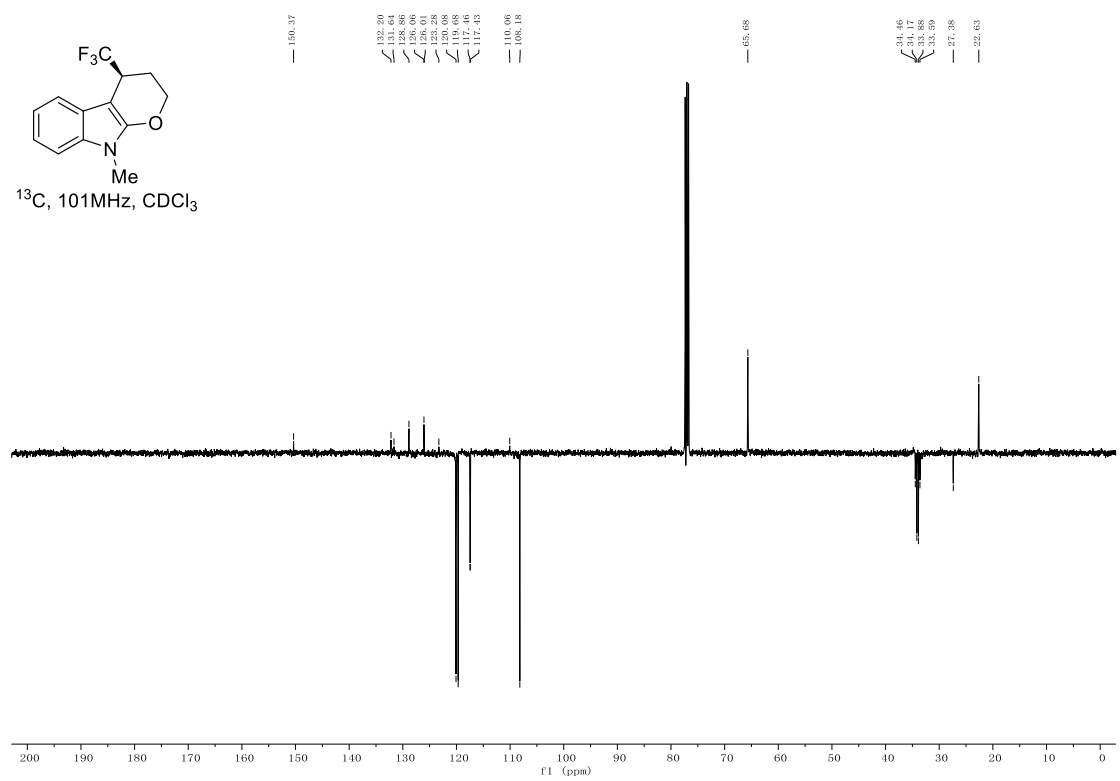
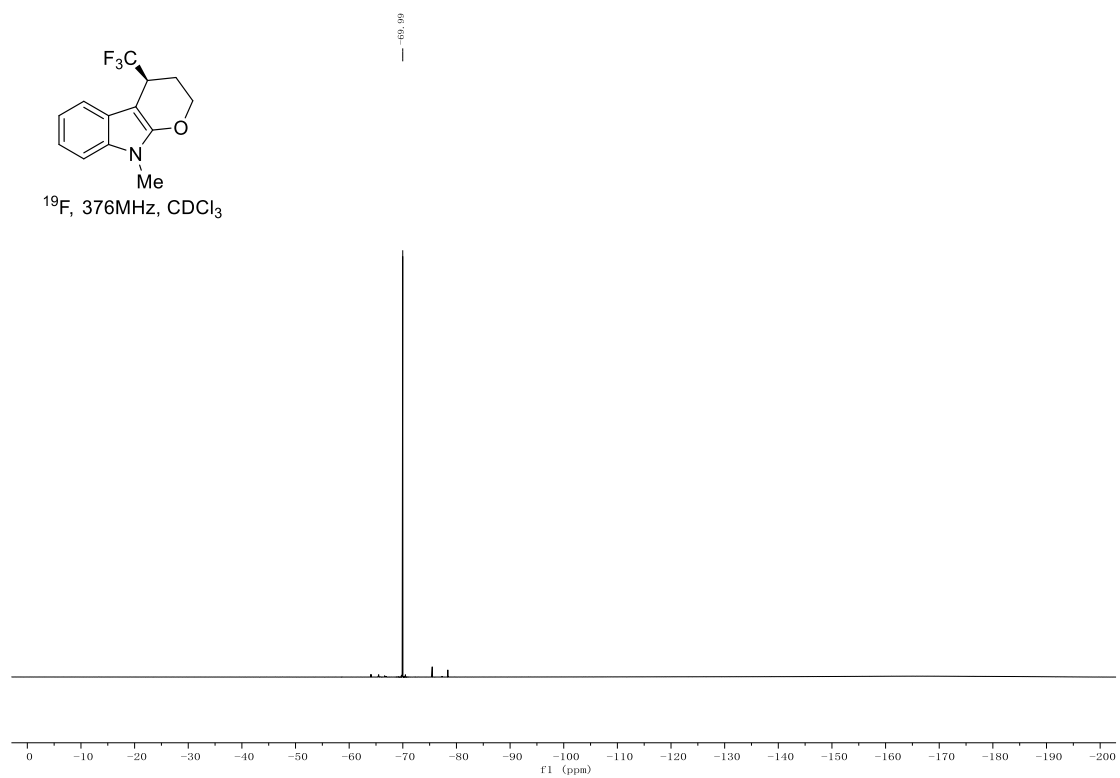




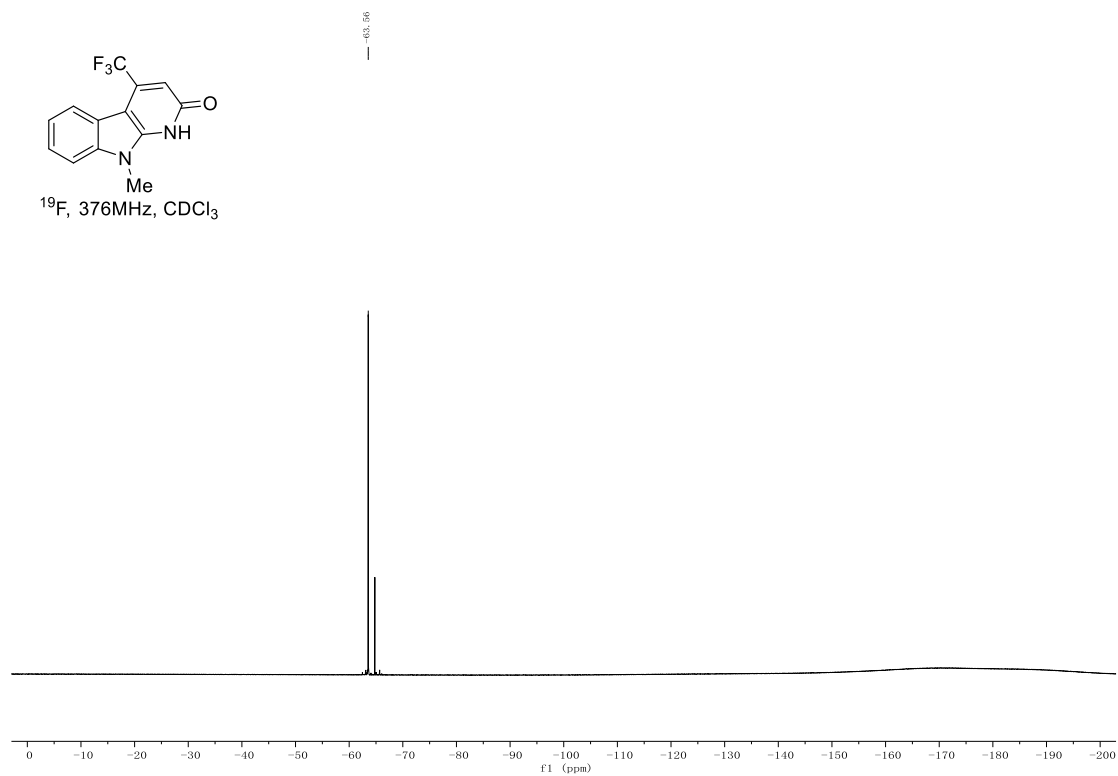
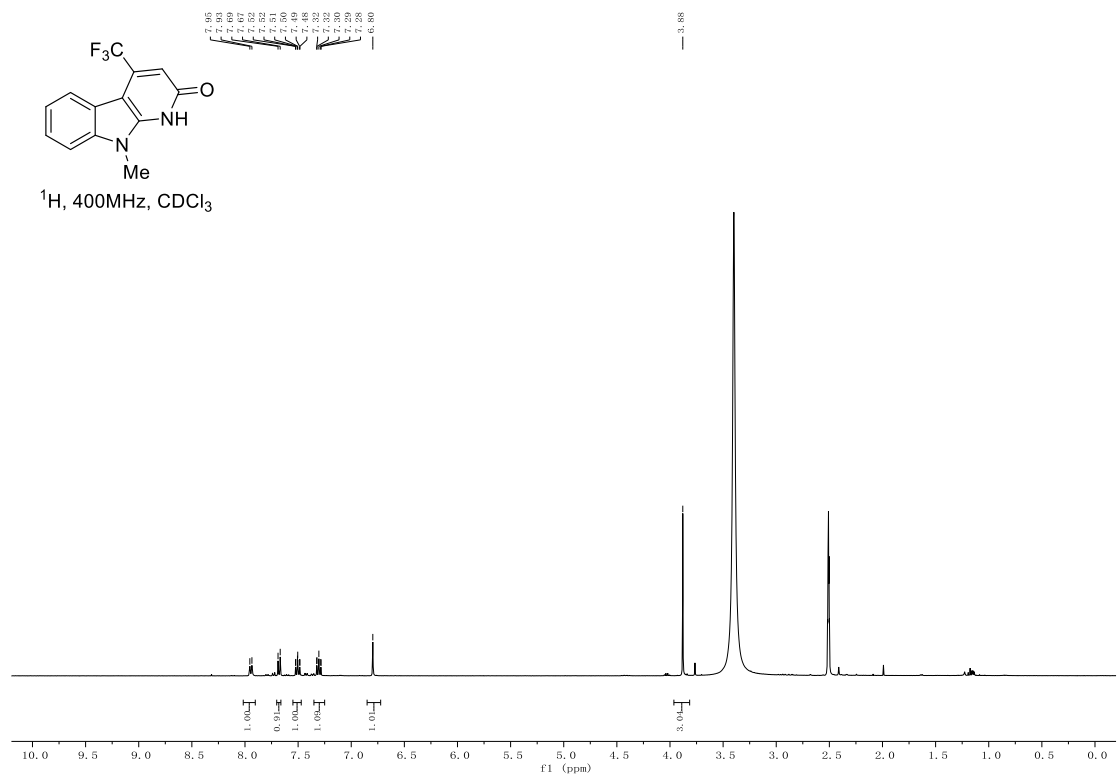
**4-Methyl-N-((2*S*,3*S*,*Z*)-1'-methyl-5-oxo-3-(trifluoromethyl)-4,5-dihydro-3*H*-spiro[furan-2,3'-indolin]-2'-ylidene)benzenesulfonamide (47)**

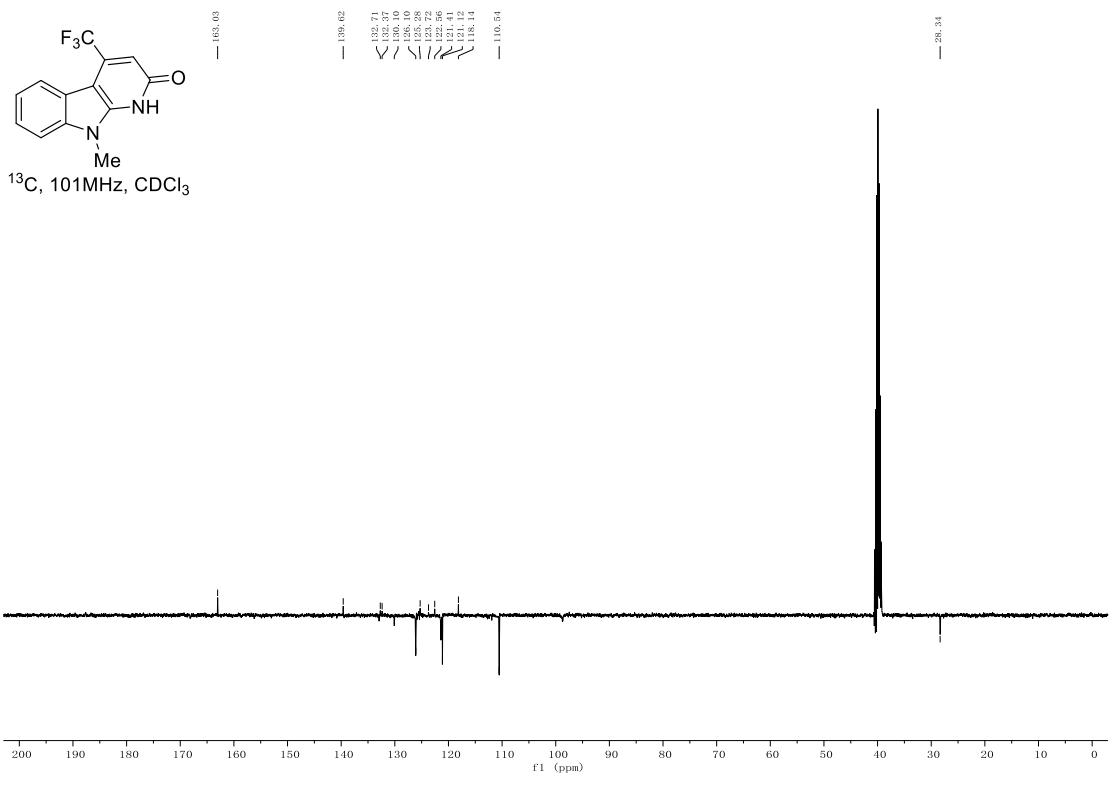






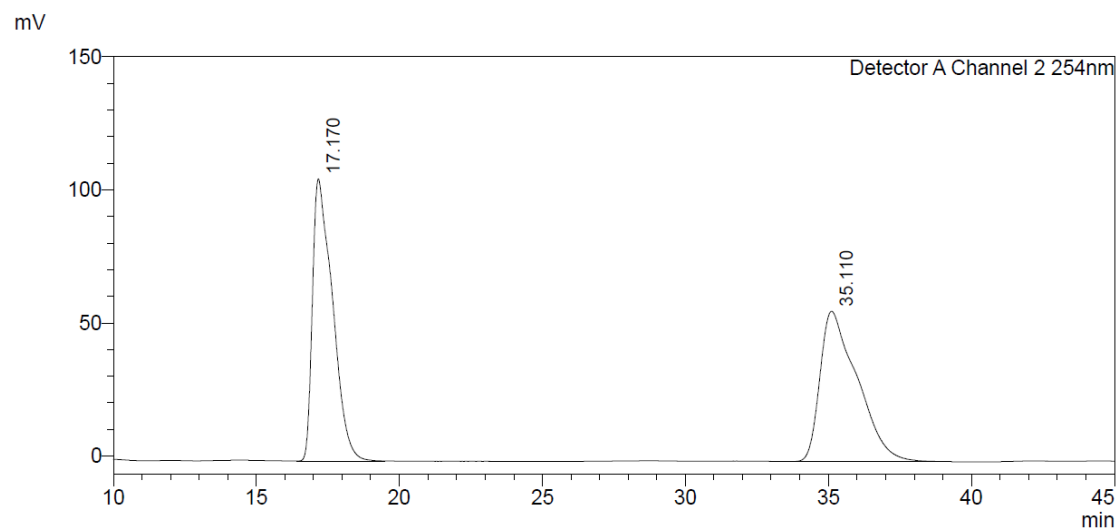
**9-Methyl-4-(trifluoromethyl)-1,9-dihydro-2H-pyrido[2,3-b]indol-2-one (49)**



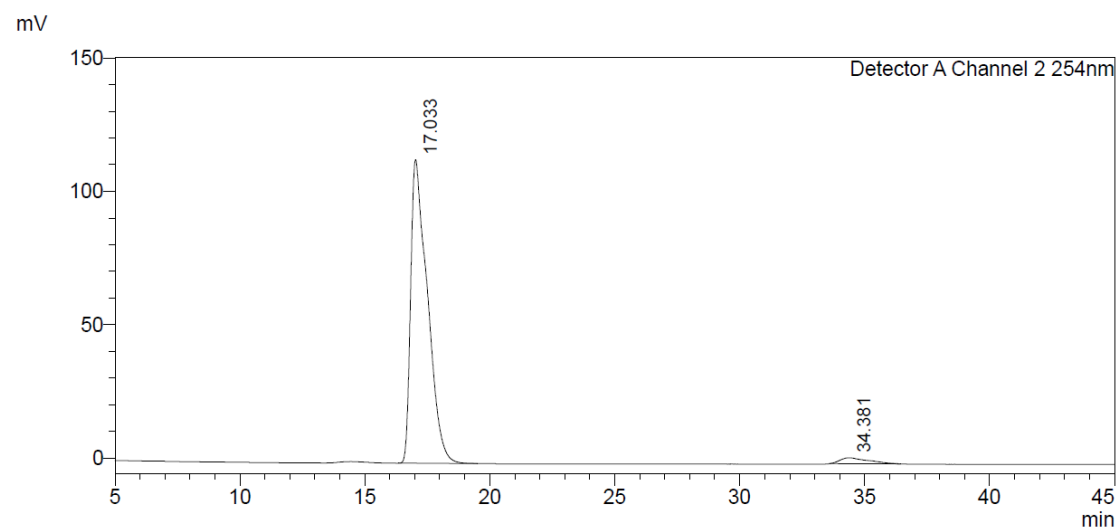


## Appendix IV: HPLC Spectra

HPLC Data for **6**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 17.0 min , t<sub>R</sub> (minor): 34.4 min, 97:3 er.

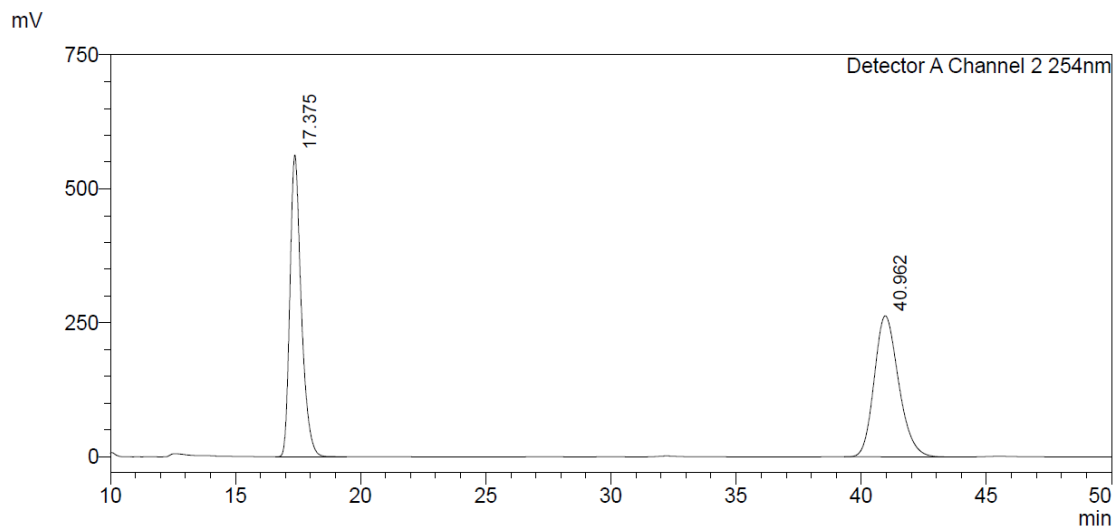


Peak#	Ret. Time	Area%
1	17.170	50.257
2	35.110	49.743
Total		100.000

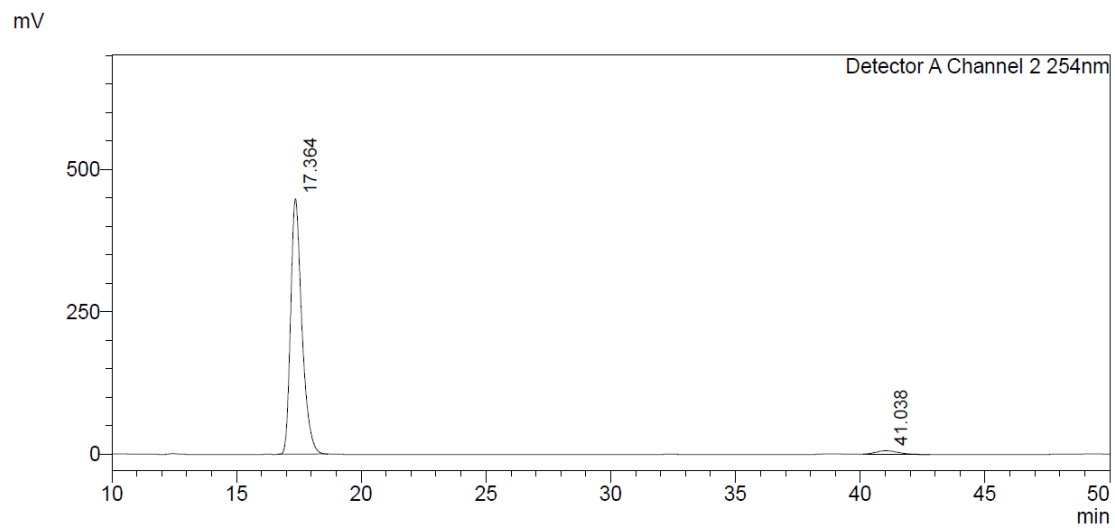


Peak#	Ret. Time	Area%
1	17.033	96.890
2	34.381	3.110
Total		100.000

HPLC Data for **18**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 17.4 min , t<sub>R</sub> (minor): 41.0 min, 97:3 er.

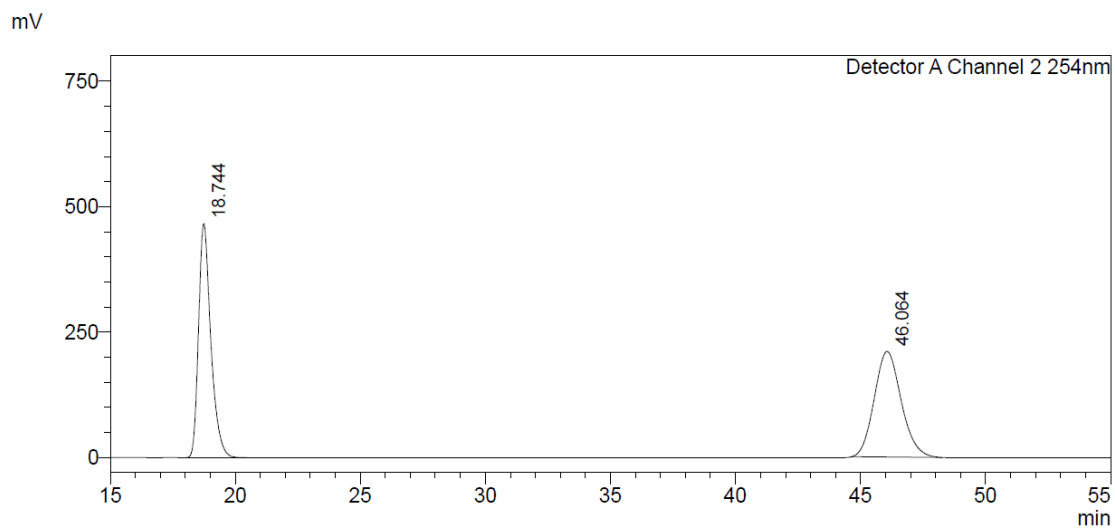


Peak#	Ret. Time	Area%
1	17.375	49.849
2	40.962	50.151
Total		100.000

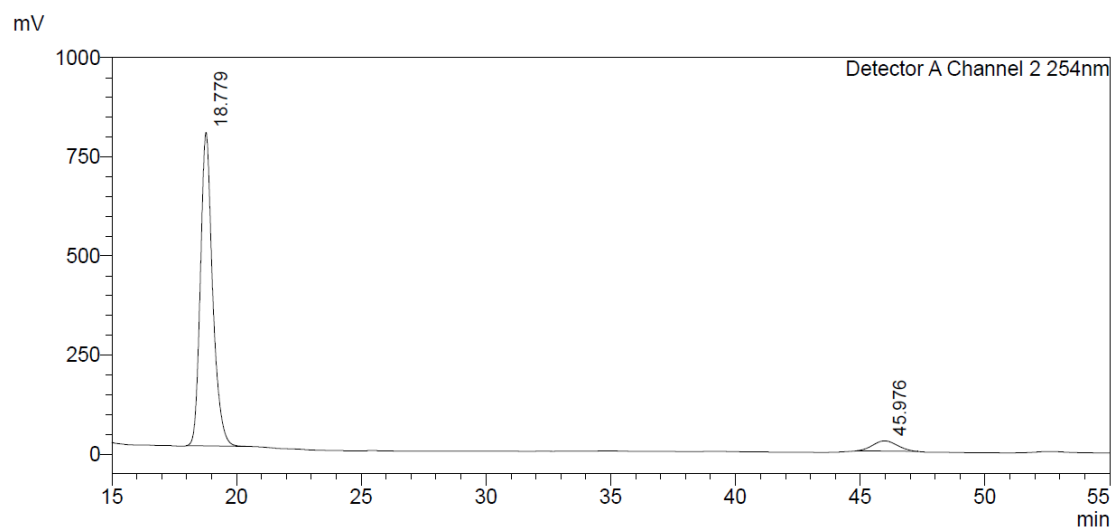


Peak#	Ret. Time	Area%
1	17.364	97.289
2	41.038	2.711
Total		100.000

HPLC Data for **19**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 18.8 min , t<sub>R</sub> (minor): 46.0 min, 94:6 er.

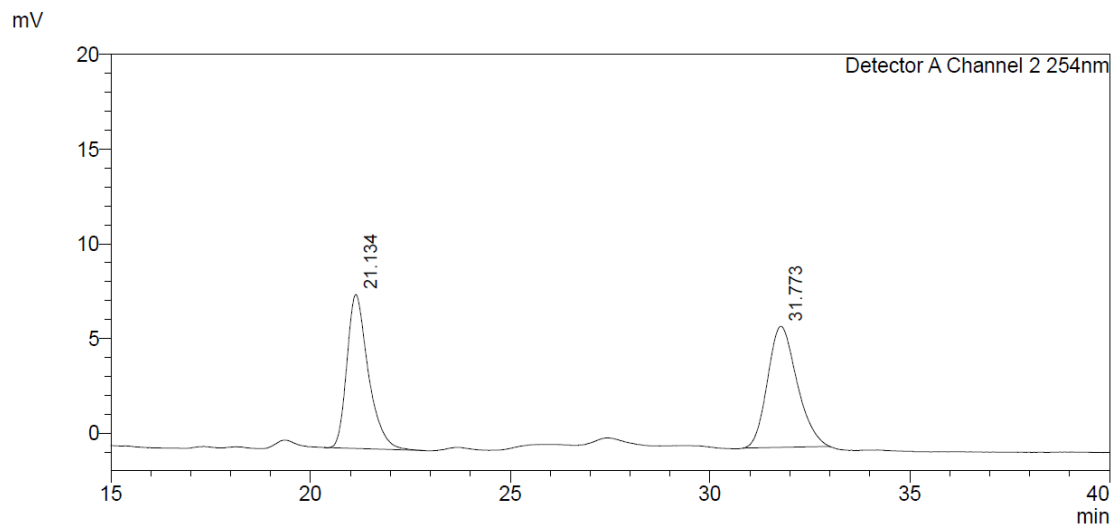


Peak#	Ret. Time	Area%
1	18.744	50.256
2	46.064	49.744
Total		100.000

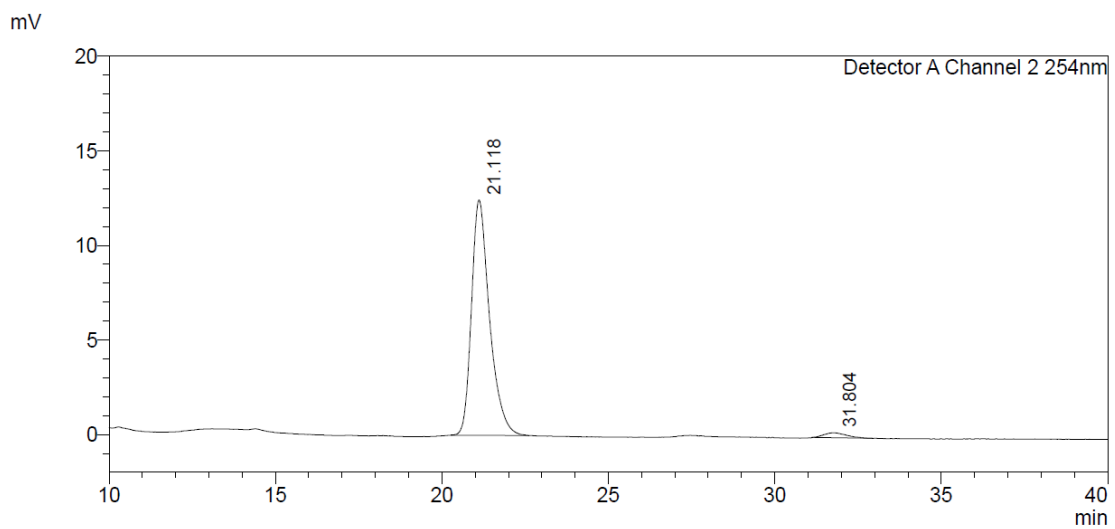


Peak#	Ret. Time	Area%
1	18.779	93.864
2	45.976	6.136
Total		100.000

HPLC Data for **20**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 21.1 min , t<sub>R</sub> (minor): 31.8 min, 97:3 er.

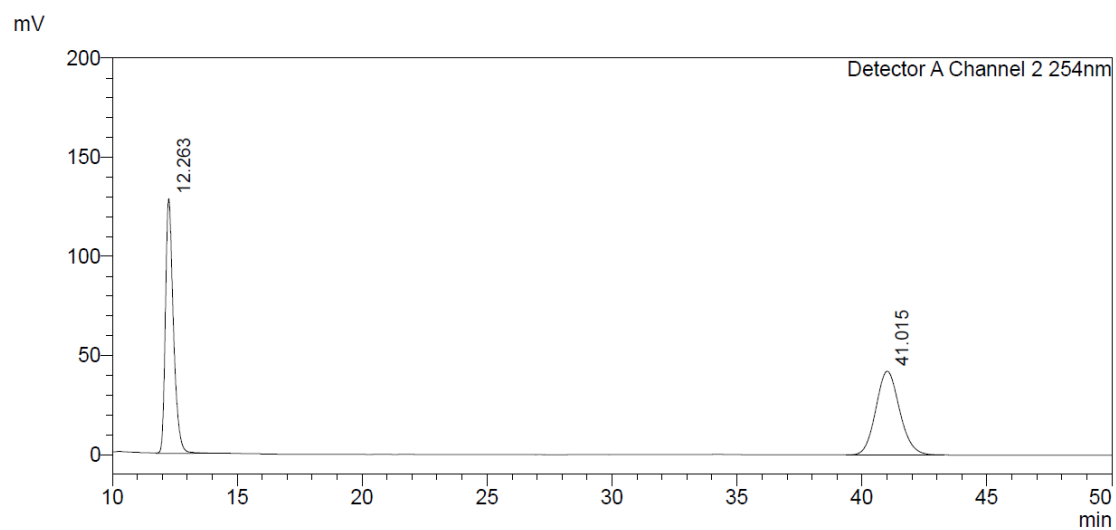


Peak#	Ret. Time	Area%
1	21.134	48.003
2	31.773	51.997
Total		100.000

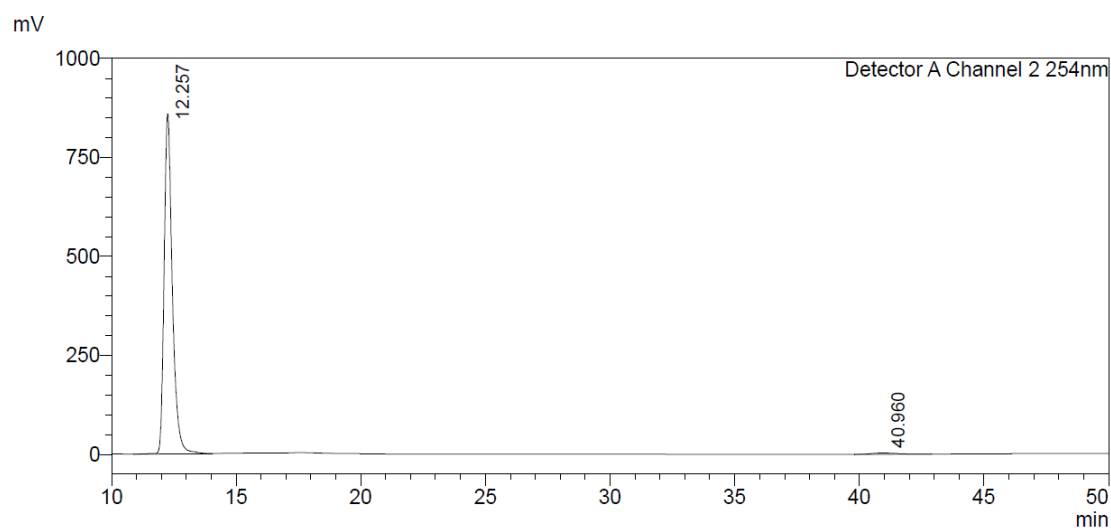


Peak#	Ret. Time	Area%
1	21.118	97.373
2	31.804	2.627
Total		100.000

HPLC Data for **21**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 12.3 min , t<sub>R</sub> (minor): 41.0 min, >99:1 er.



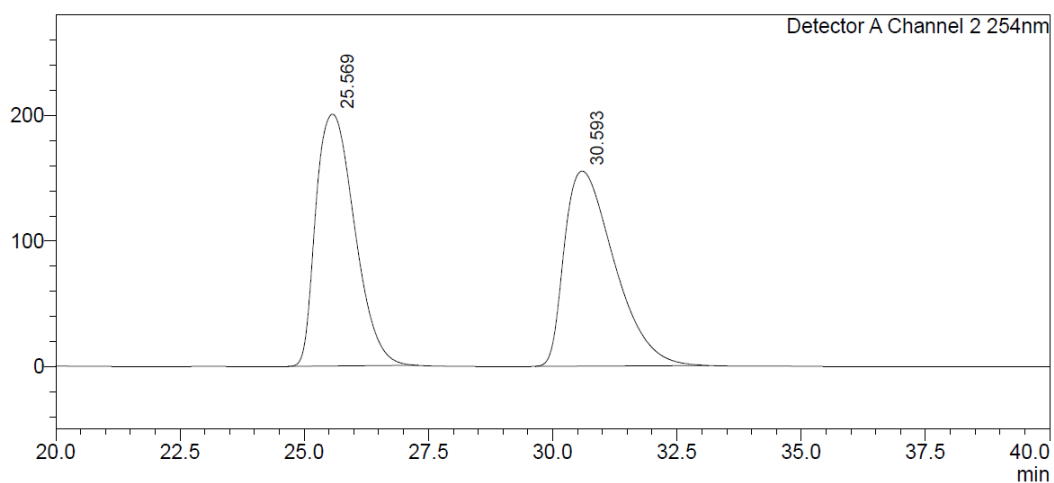
Peak#	Ret. Time	Area%
1	12.263	50.616
2	41.015	49.384
Total		100.000



Peak#	Ret. Time	Area%
1	12.257	99.042
2	40.960	0.958
Total		100.000

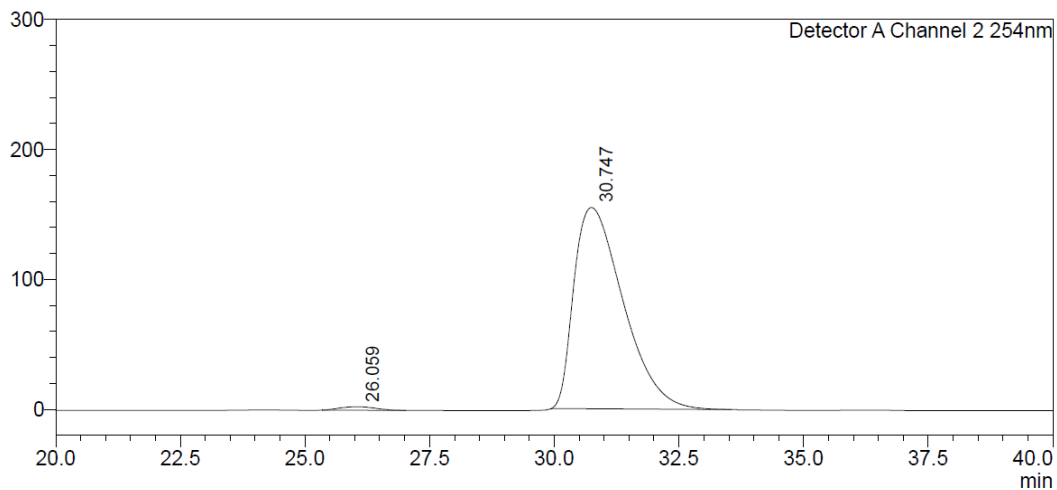
HPLC Data for **22**: Chiralpak ID (90:10 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (minor): 26.1 min , t<sub>R</sub> (major): 30.7 min, 1:99 er.

mV



Peak#	Ret. Time	Area%
1	25.569	50.103
2	30.593	49.897
Total		100.000

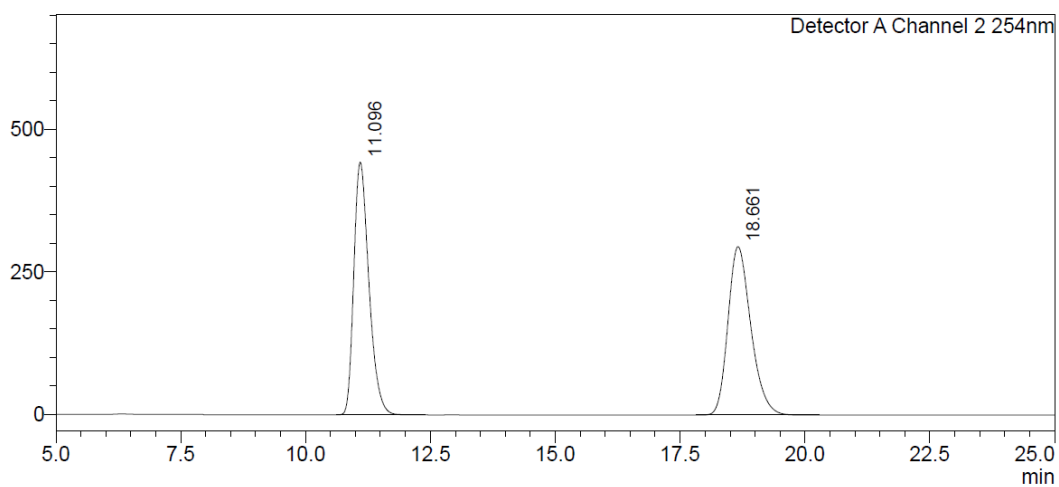
mV



Peak#	Ret. Time	Area%
1	26.059	1.224
2	30.747	98.776
Total		100.000

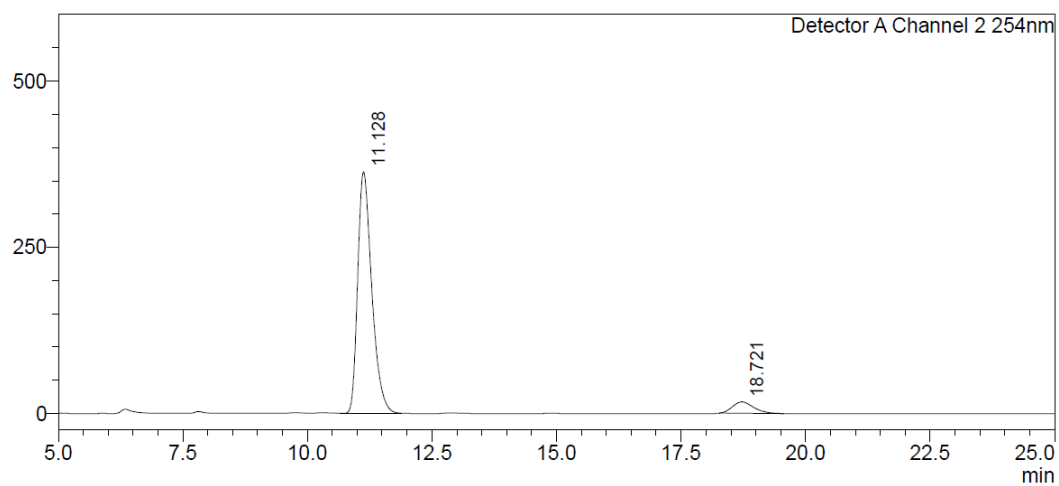
HPLC Data for **23**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 11.1 min , t<sub>R</sub> (minor): 18.7 min, 93:7 er.

mV



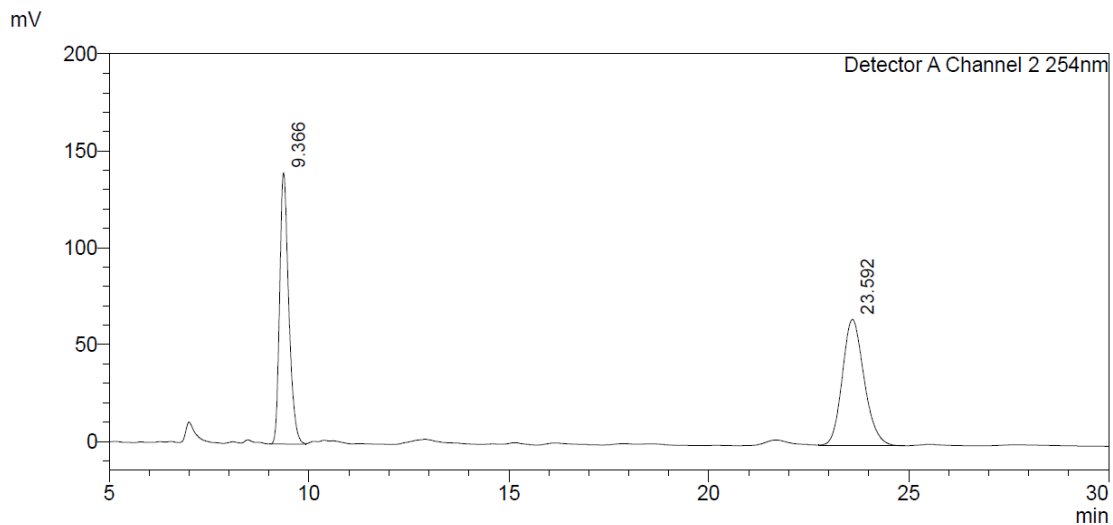
Peak#	Ret. Time	Area%
1	11.096	49.672
2	18.661	50.328
Total		100.000

mV

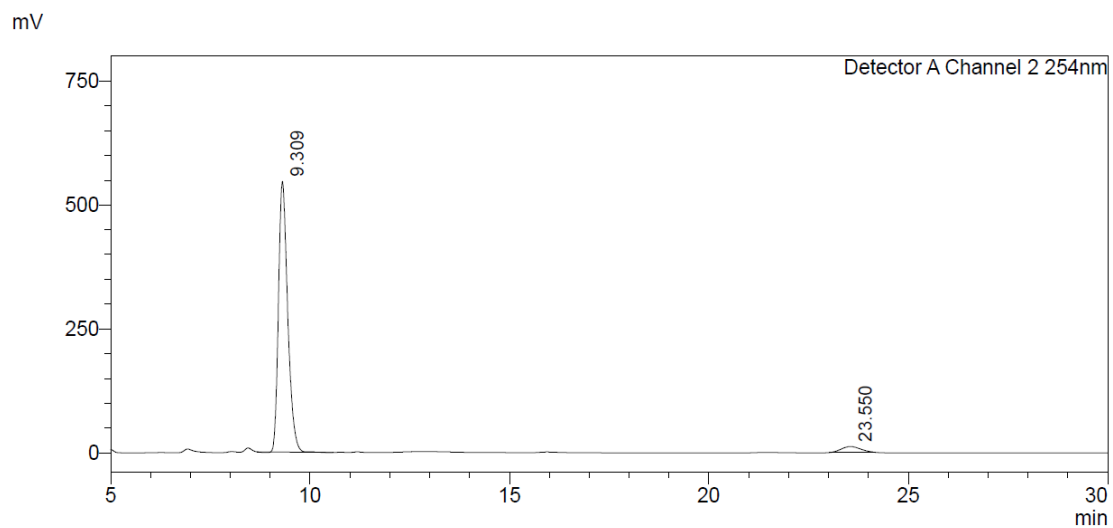


Peak#	Ret. Time	Area%
1	11.128	93.420
2	18.721	6.580
Total		100.000

HPLC Data for **24**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 9.3 min , t<sub>R</sub> (minor): 23.6 min, 96:4 er.

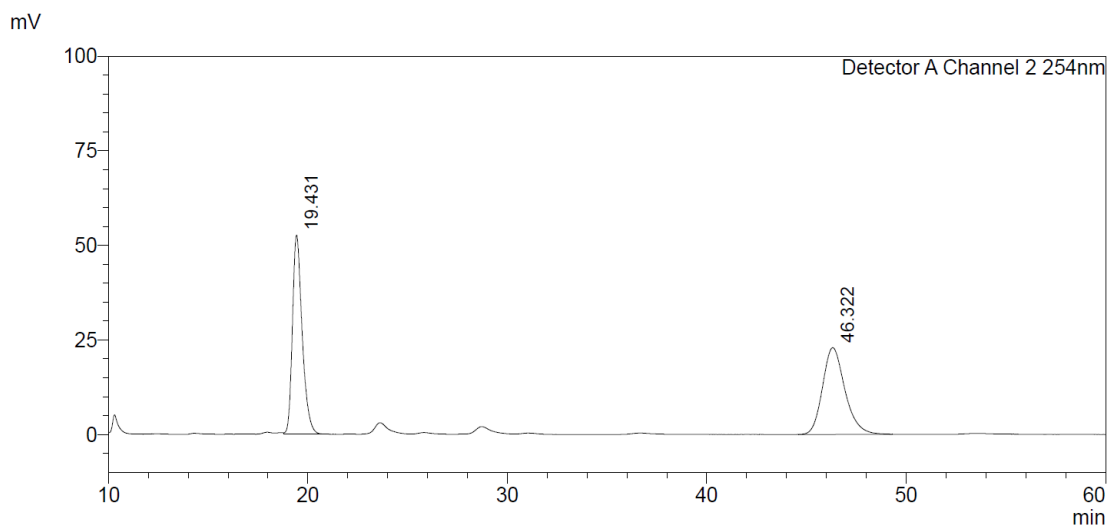


Peak#	Ret. Time	Area%
1	9.366	47.046
2	23.592	52.954
Total		100.000

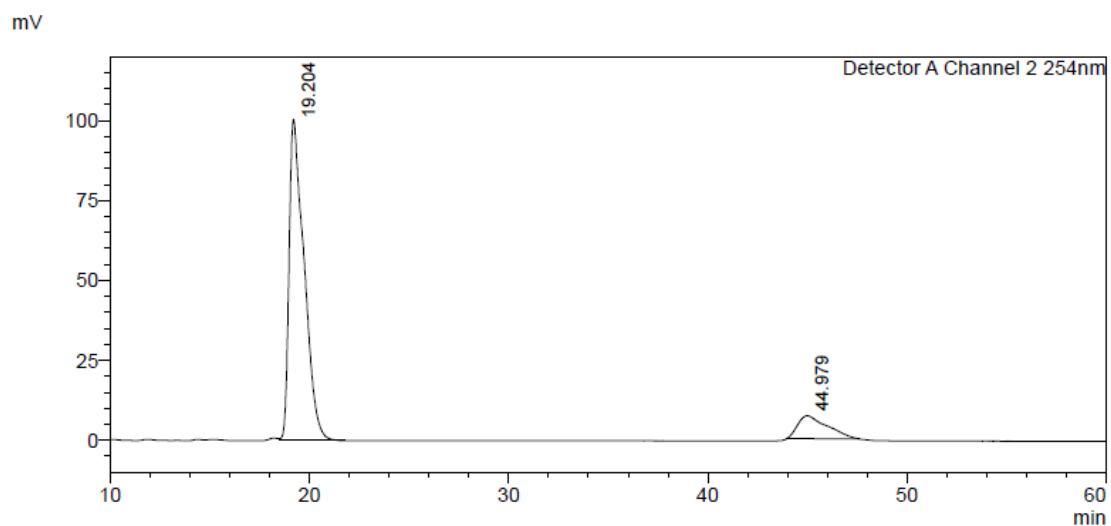


Peak#	Ret. Time	Area%
1	9.309	95.626
2	23.550	4.374
Total		100.000

HPLC Data for **25**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 19.2 min , t<sub>R</sub> (minor): 45.0 min, 88:12 er.



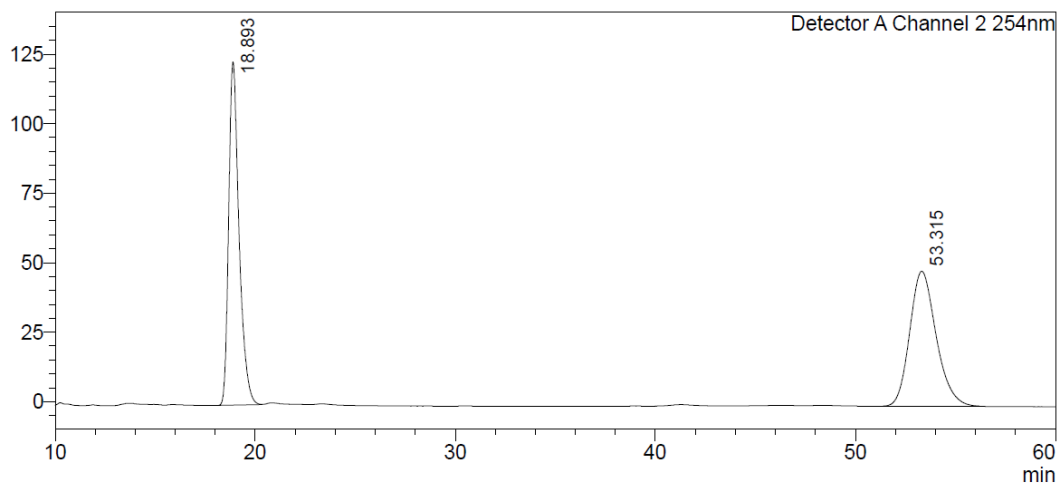
Detector A Channel 2 254nm		
Peak#	Ret. Time	Area%
1	19.431	49.945
2	46.322	50.055
Total		100.000



Detector A Channel 2 254nm		
Peak#	Ret. Time	Area%
1	19.204	87.633
2	44.979	12.367
Total		100.000

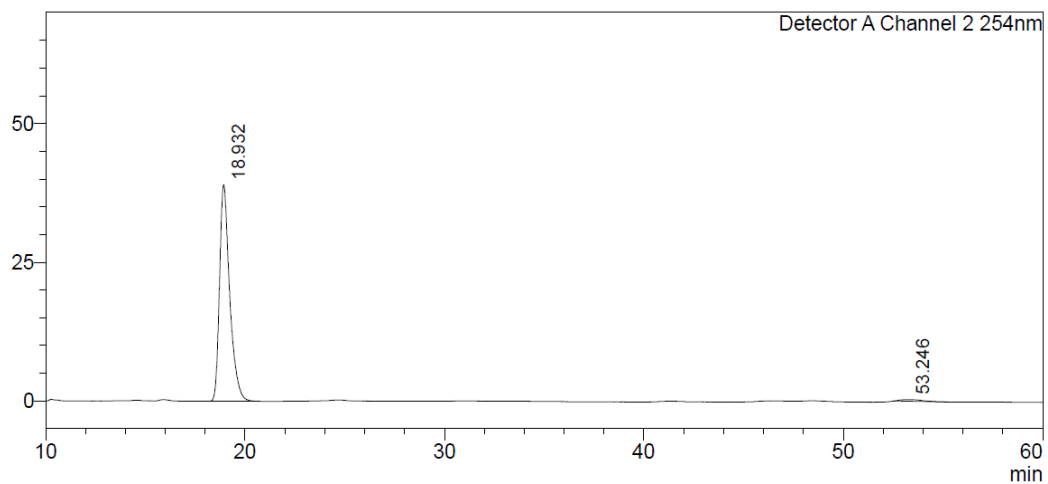
HPLC Data for **26**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 18.9 min , t<sub>R</sub> (minor): 53.2 min, 98:2 er.

mV



Peak#	Ret. Time	Area%
1	18.893	49.928
2	53.315	50.072
Total		100.000

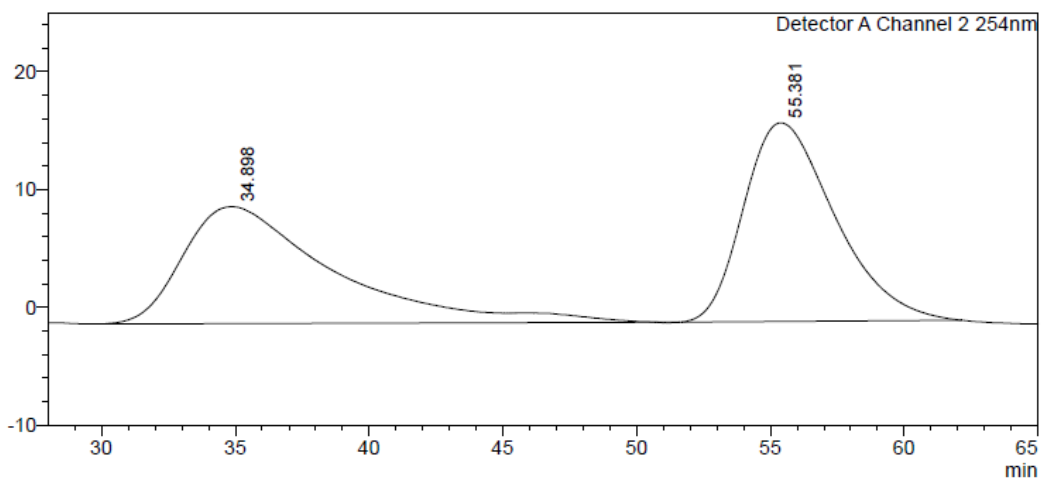
mV



Peak#	Ret. Time	Area%
1	18.932	98.410
2	53.246	1.590
Total		100.000

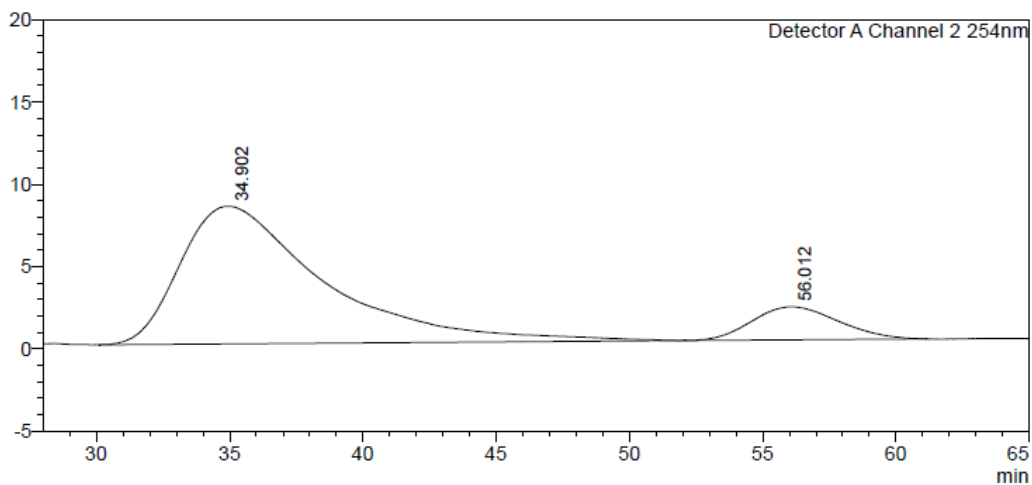
HPLC Data for **27**: Chiralcel OD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C)  $t_R$  (major): 34.9 min ,  $t_R$  (minor): 56.0 min, 87:13 er.

mV



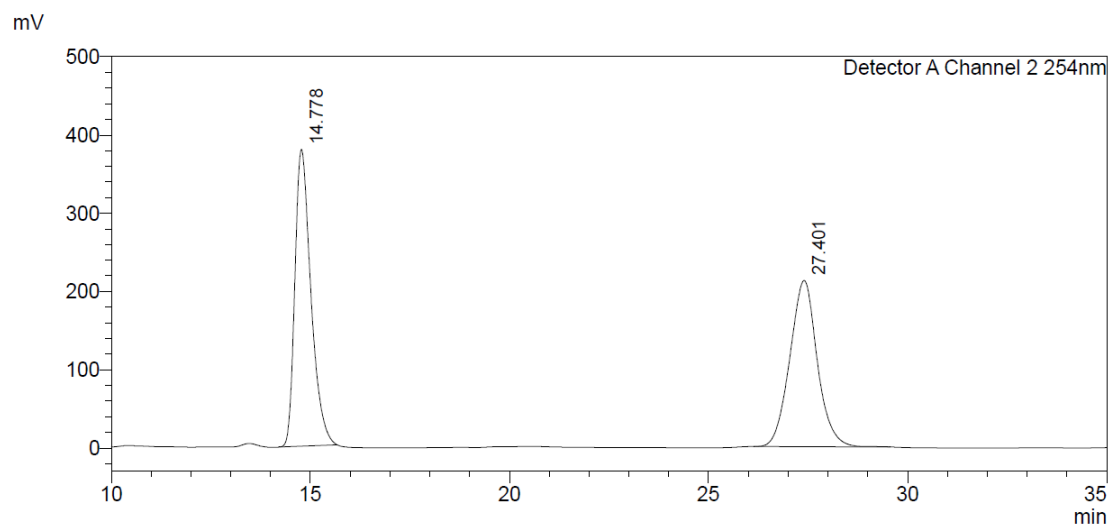
Peak#	Ret. Time	Area%
1	34.898	49.162
2	55.381	50.838
Total		100.000

mV

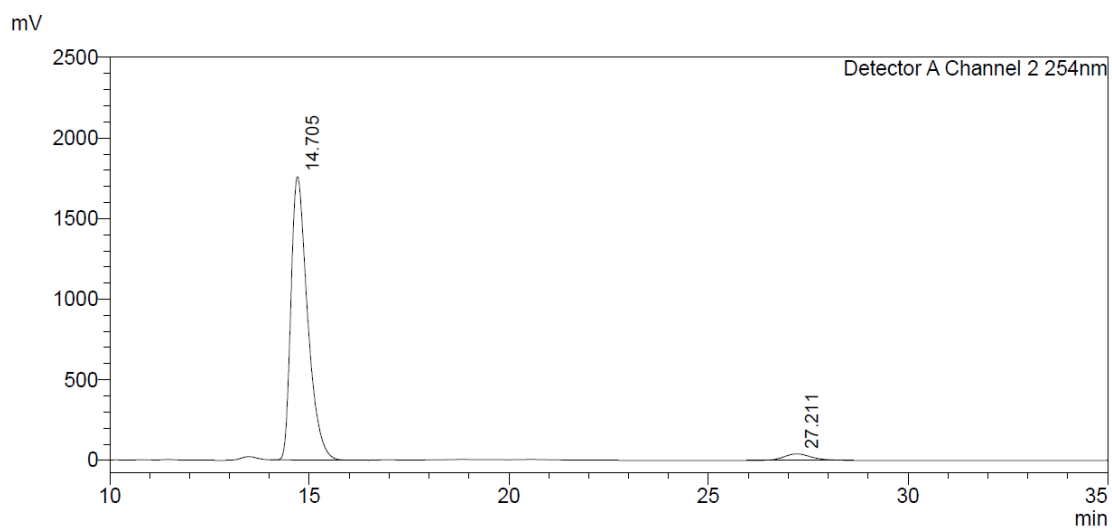


Peak#	Ret. Time	Area%
1	34.902	87.361
2	56.012	12.639
Total		100.000

HPLC Data for **37**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 14.7 min , t<sub>R</sub> (minor): 27.2 min, 96:4 er.

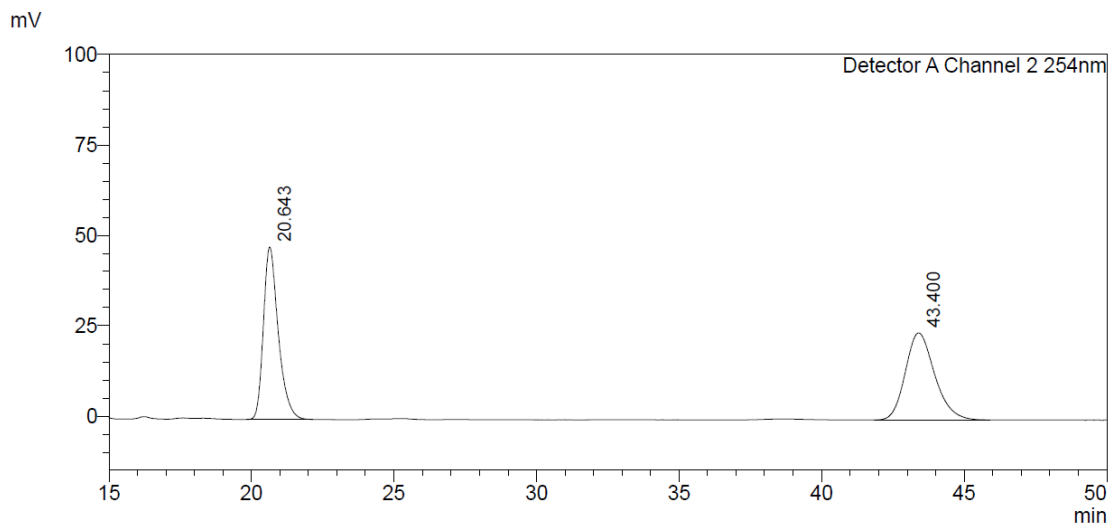


Peak#	Ret. Time	Area%
1	17.170	50.257
2	35.110	49.743
Total		100.000

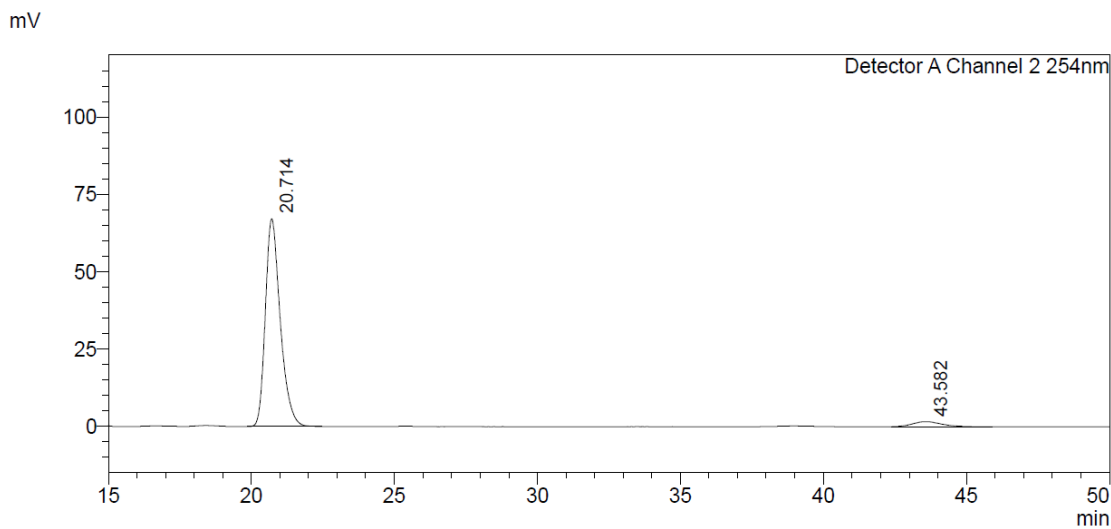


Peak#	Ret. Time	Area%
1	14.705	96.282
2	27.211	3.718
Total		100.000

HPLC Data for **38**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 20.7 min , t<sub>R</sub> (minor): 43.6 min, 96:4 er.

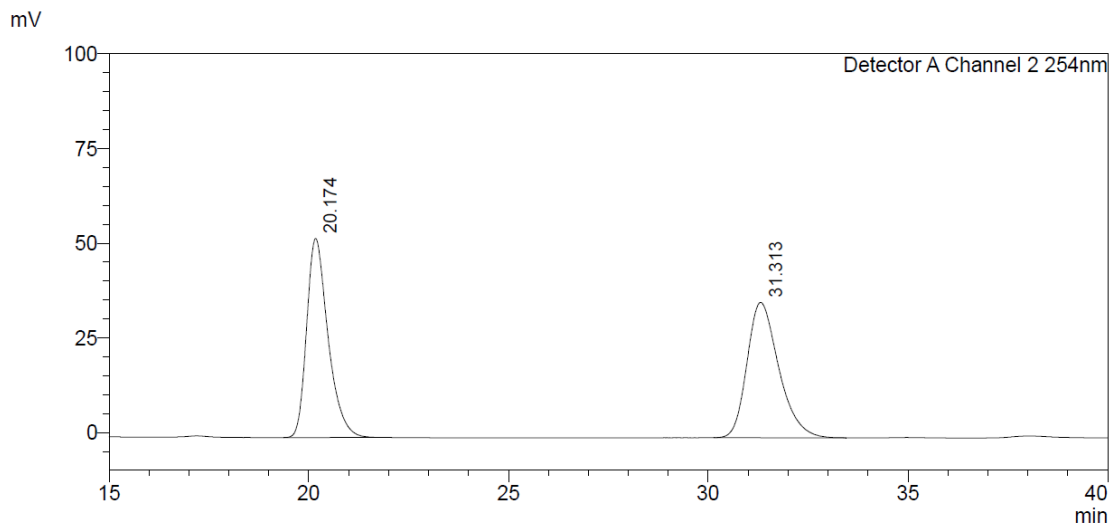


Peak#	Ret. Time	Area%
1	20.643	50.077
2	43.400	49.923
Total		100.000

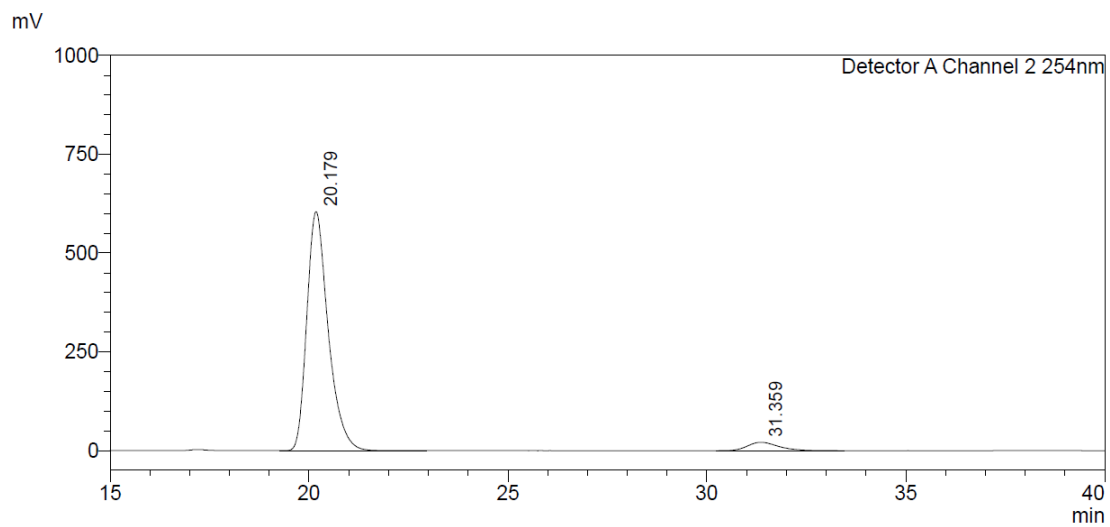


Peak#	Ret. Time	Area%
1	20.714	95.589
2	43.582	4.411
Total		100.000

HPLC Data for **39**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 20.2 min , t<sub>R</sub> (minor): 31.4 min, 95:5 er.

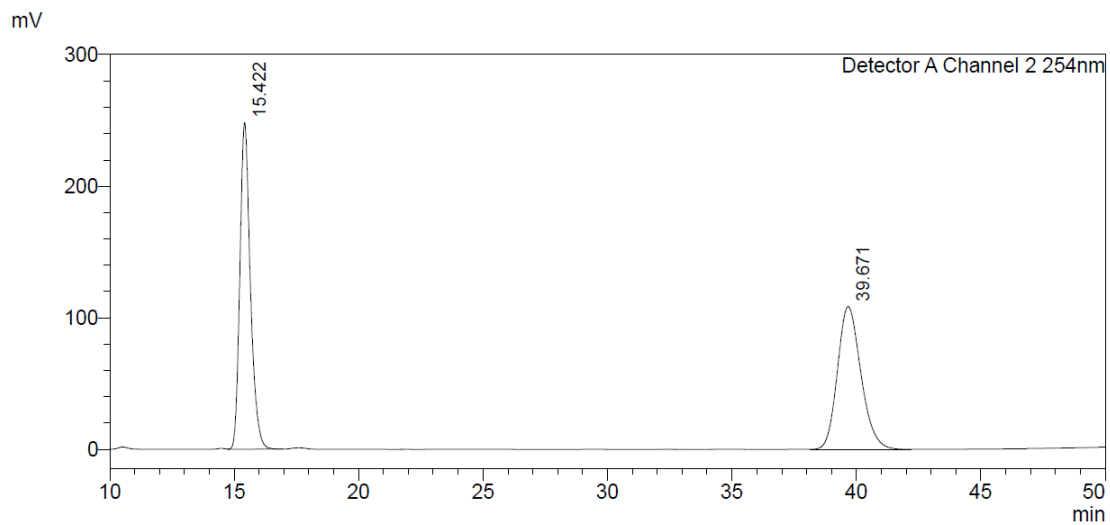


Peak#	Ret. Time	Area%
1	20.174	49.765
2	31.313	50.235
Total		100.000

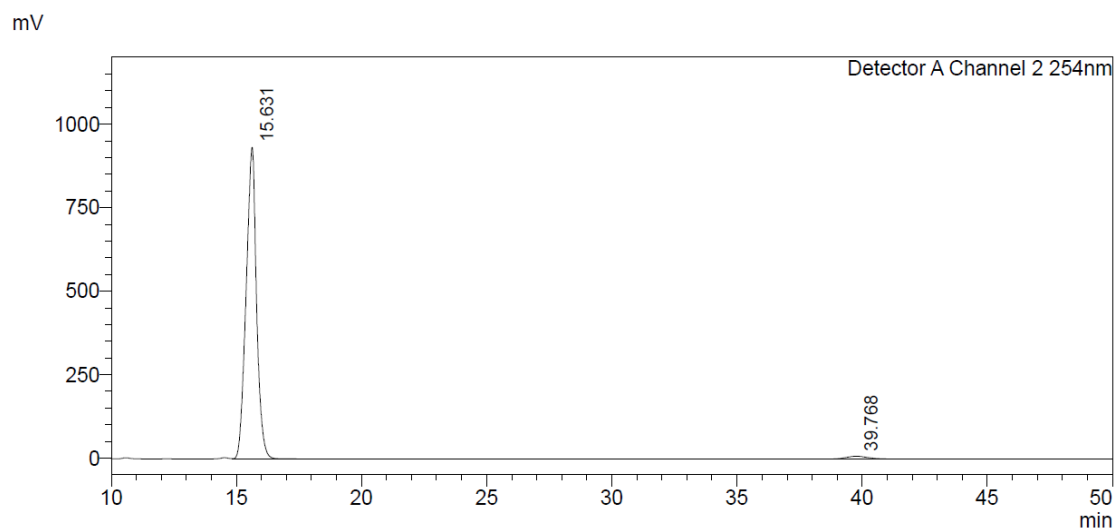


Peak#	Ret. Time	Area%
1	20.179	95.116
2	31.359	4.884
Total		100.000

HPLC Data for **40**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 15.6 min , t<sub>R</sub> (minor): 39.8 min, 98:2 er.

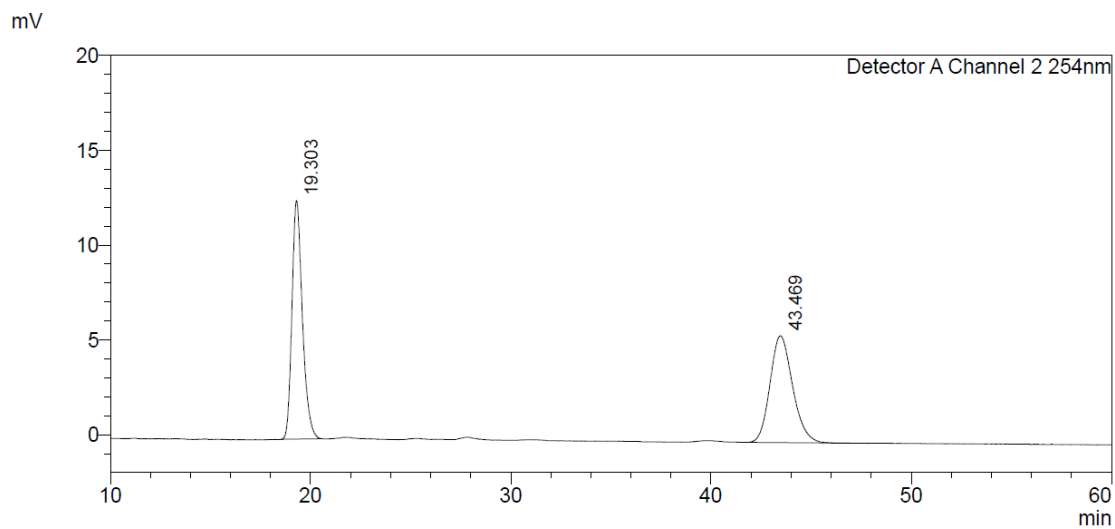


Peak#	Ret. Time	Area%
1	15.422	50.503
2	39.671	49.497
Total		100.000

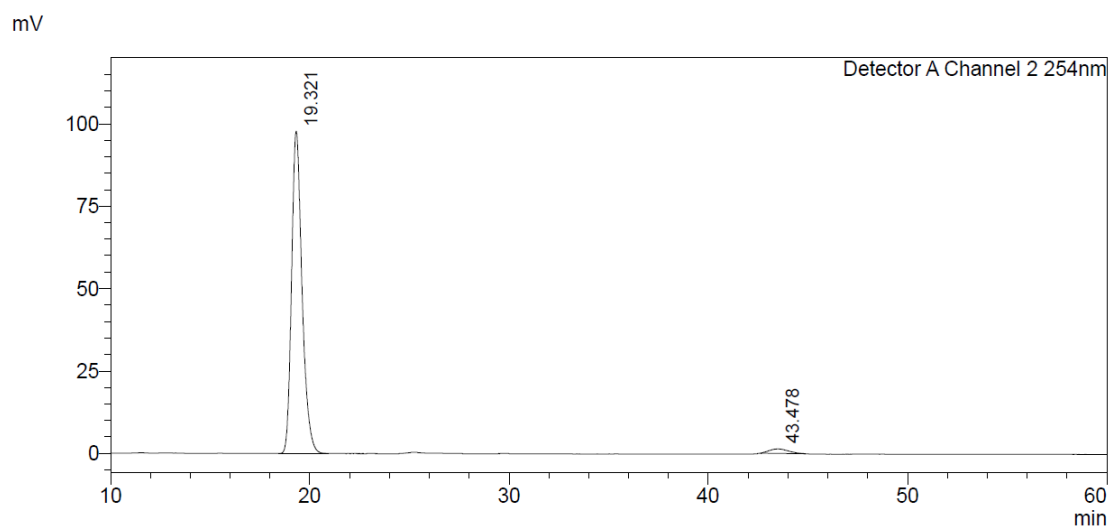


Peak#	Ret. Time	Area%
1	15.631	98.048
2	39.768	1.952
Total		100.000

HPLC Data for **41**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 19.3 min , t<sub>R</sub> (minor): 43.5 min, 98:2 er.

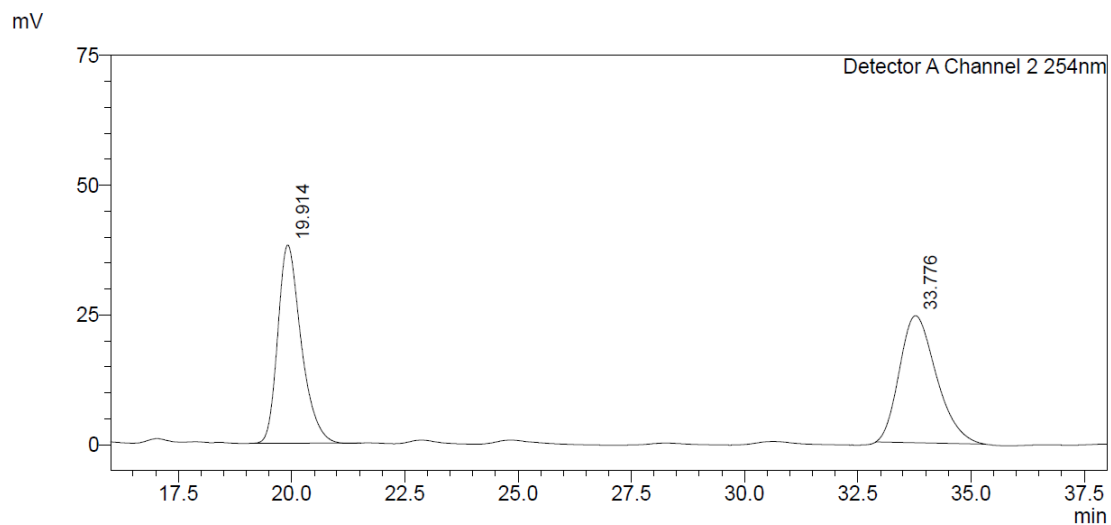


Peak#	Ret. Time	Area%
1	19.303	50.786
2	43.469	49.214
Total		100.000

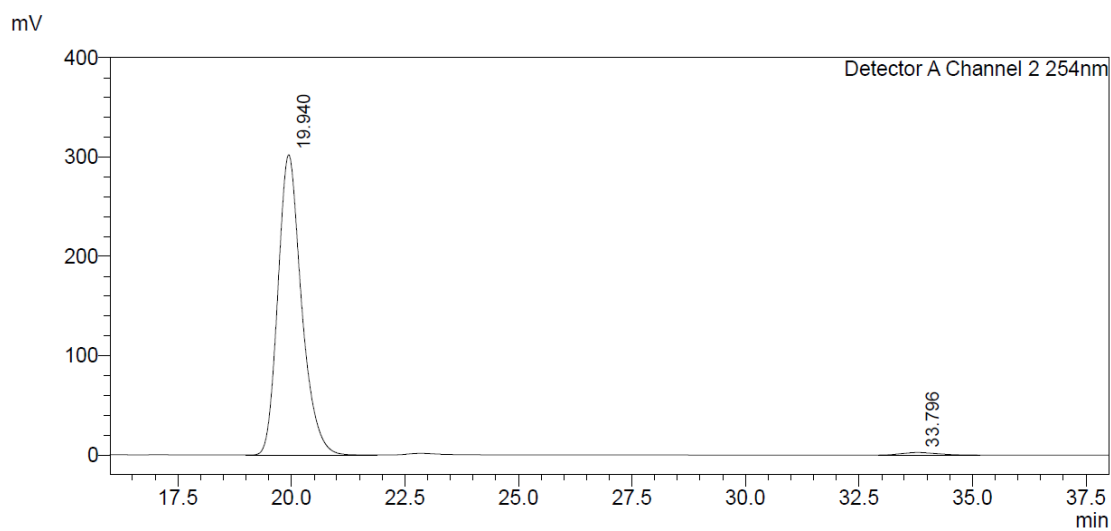


Peak#	Ret. Time	Area%
1	19.321	97.561
2	43.478	2.439
Total		100.000

HPLC Data for **42**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 19.9 min , t<sub>R</sub> (minor): 33.8 min, 99:1 er.

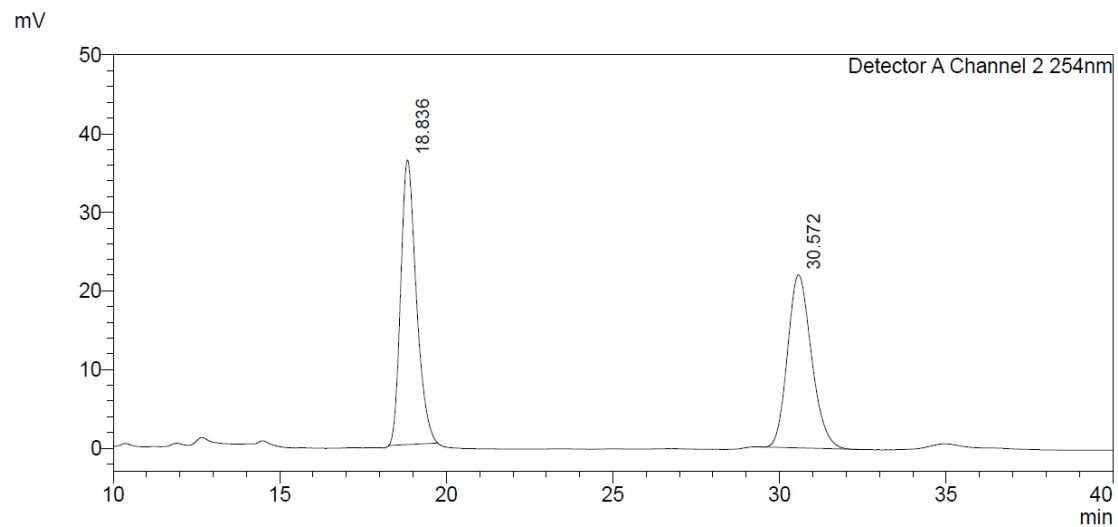


Peak#	Ret. Time	Area%
1	19.914	49.694
2	33.776	50.306
Total		100.000

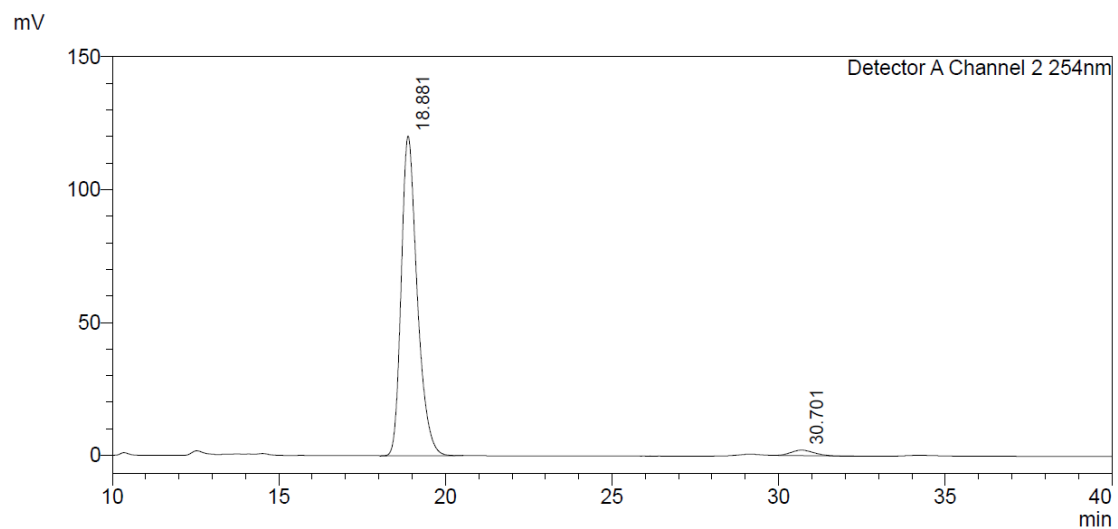


Peak#	Ret. Time	Area%
1	19.940	98.735
2	33.796	1.265
Total		100.000

HPLC Data for **43**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 18.9 min , t<sub>R</sub> (minor): 30.7 min, 98:2 er.

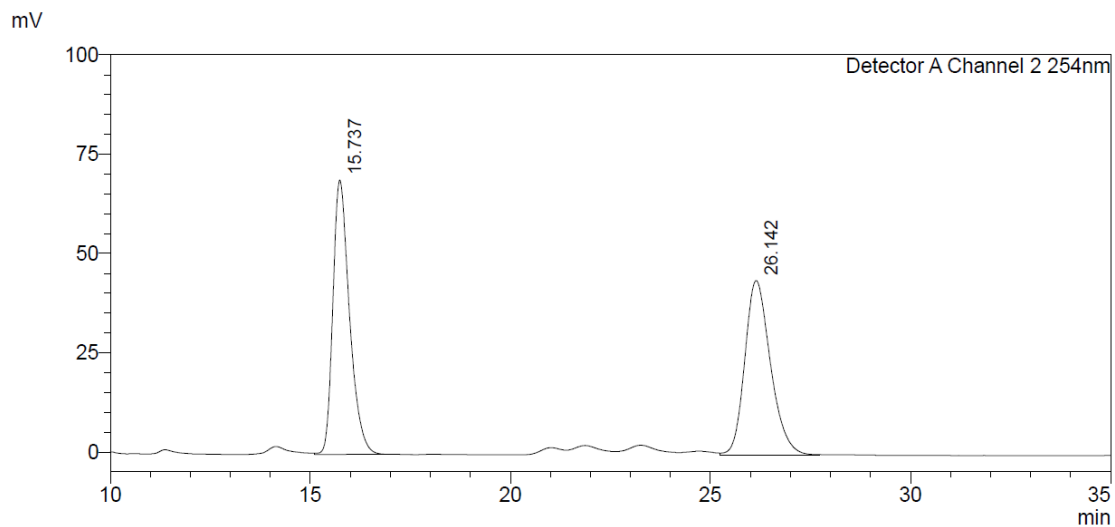


Peak#	Ret. Time	Area%
1	18.836	51.647
2	30.572	48.353
Total		100.000

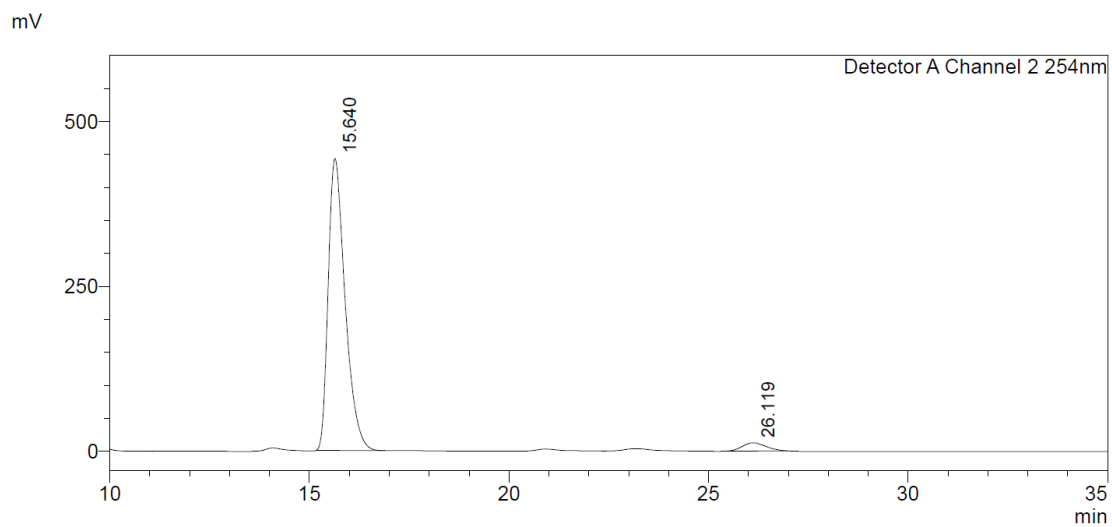


Peak#	Ret. Time	Area%
1	18.881	97.640
2	30.701	2.360
Total		100.000

HPLC Data for **44**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 15.6 min , t<sub>R</sub> (minor): 26.1 min, 96:4 er.

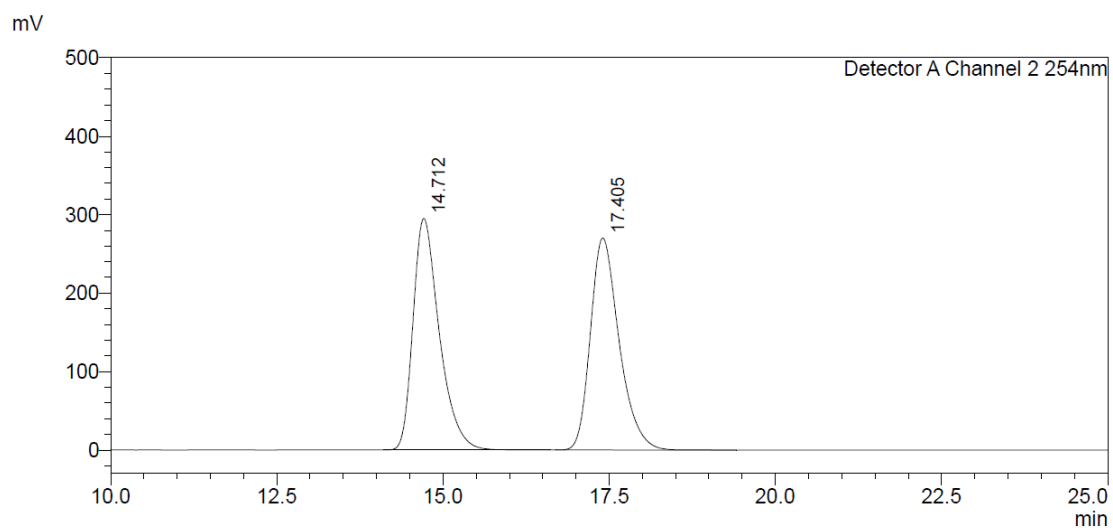


Peak#	Ret. Time	Area%
1	15.737	50.504
2	26.142	49.496
Total		100.000

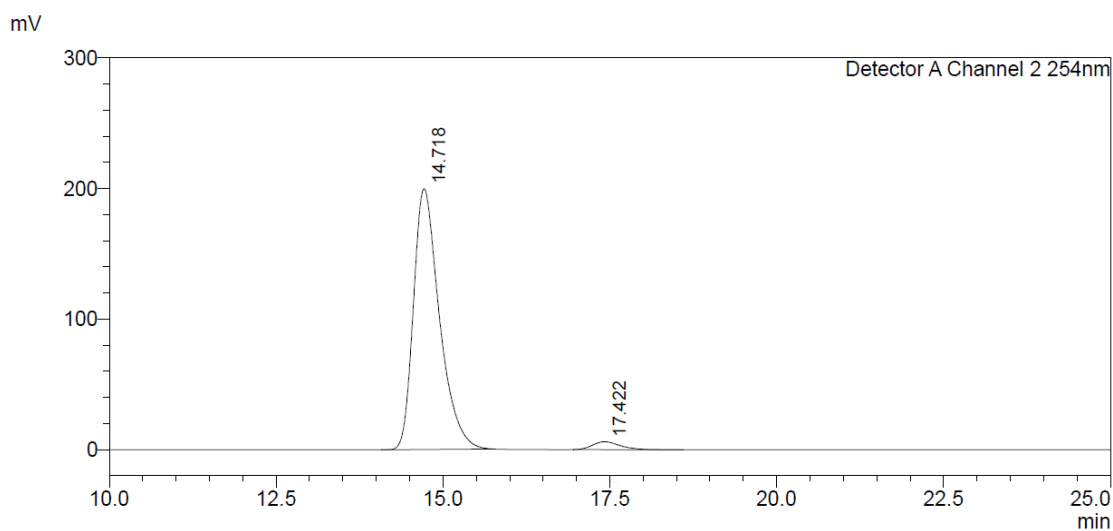


Peak#	Ret. Time	Area%
1	15.640	96.191
2	26.119	3.809
Total		100.000

HPLC Data for **45**: Chiralpak AD-H (85:15 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 14.7 min , t<sub>R</sub> (minor): 17.4 min, 97:3 er.

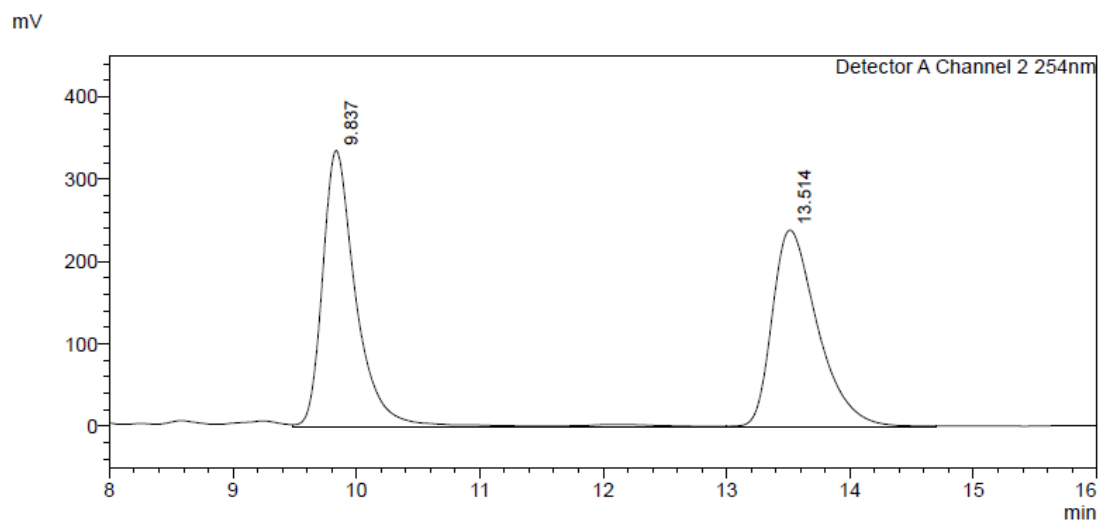


Peak#	Ret. Time	Area%
1	14.712	49.982
2	17.405	50.018
Total		100.000



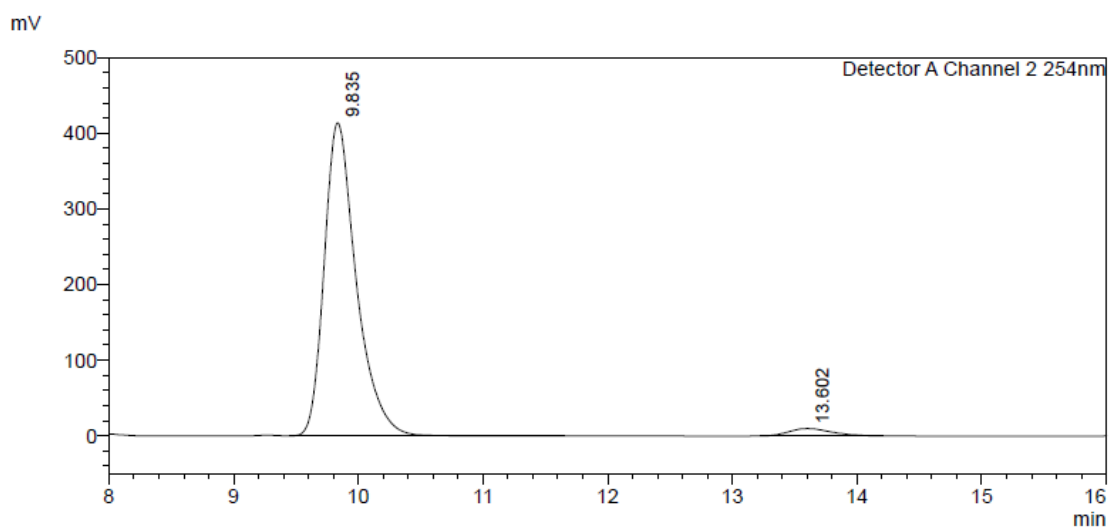
Peak#	Ret. Time	Area%
1	14.718	96.831
2	17.422	3.169
Total		100.000

HPLC Data for **46**: Chiralpak AD-H (82:18 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 9.8 min , t<sub>R</sub> (minor): 13.6 min, 97:3 er.



Detector A Channel 2 254nm

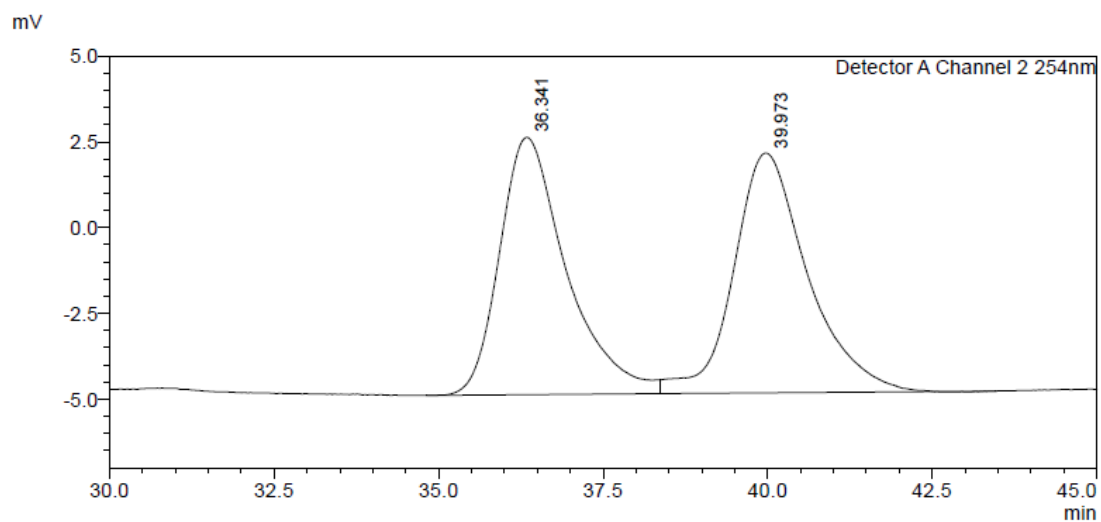
Peak#	Ret. Time	Area%
1	9.837	50.868
2	13.514	49.132
Total		100.000



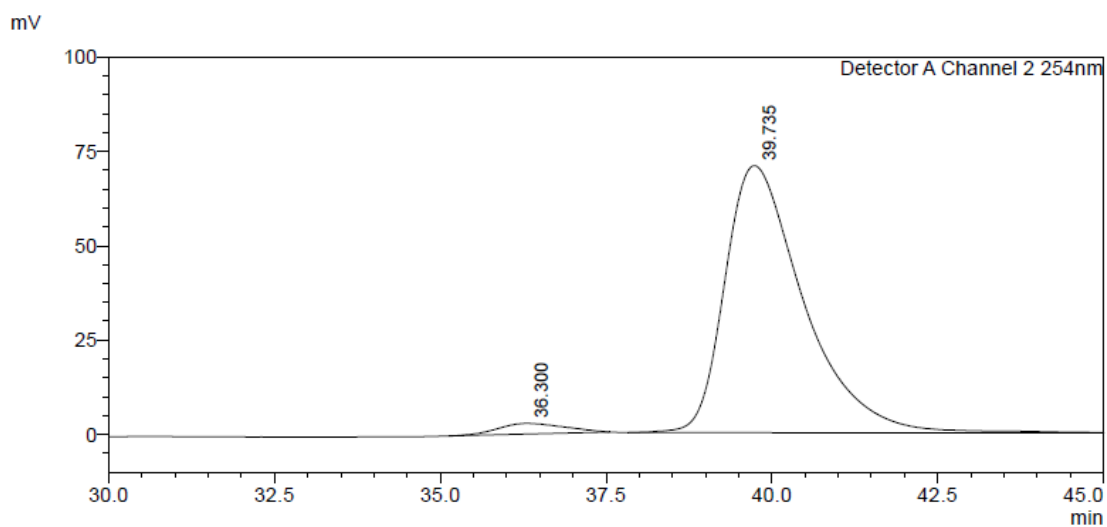
Detector A Channel 2 254nm

Peak#	Ret. Time	Area%
1	9.835	96.898
2	13.602	3.102
Total		100.000

HPLC Data for **47**: Chiralpak AD-H (82:18 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub> (major): 39.7 min , t<sub>R</sub> (minor): 36.0 min, 97:3 er.

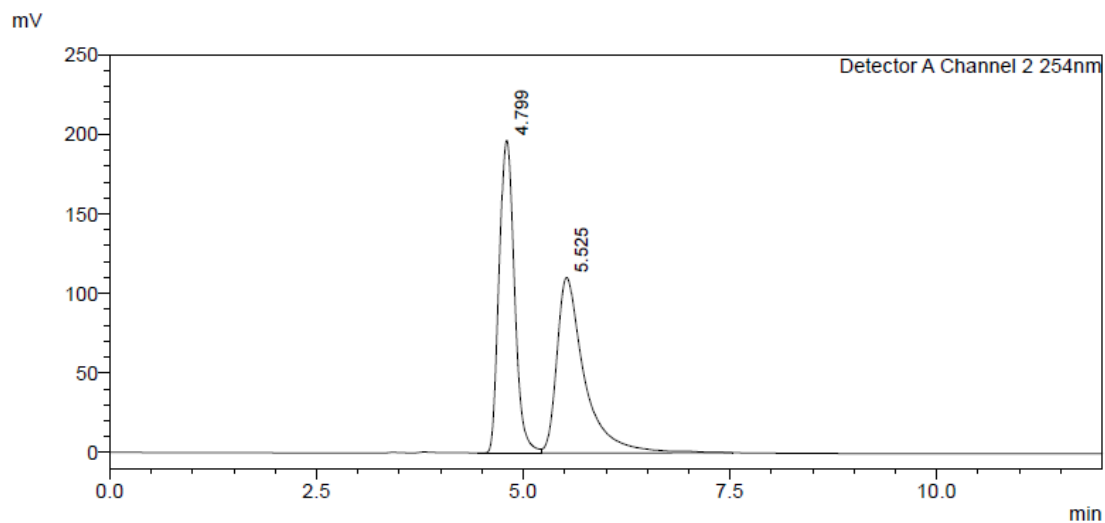


Detector A Channel 2 254nm		
Peak#	Ret. Time	Area%
1	36.341	49.244
2	39.973	50.756
Total		100.000

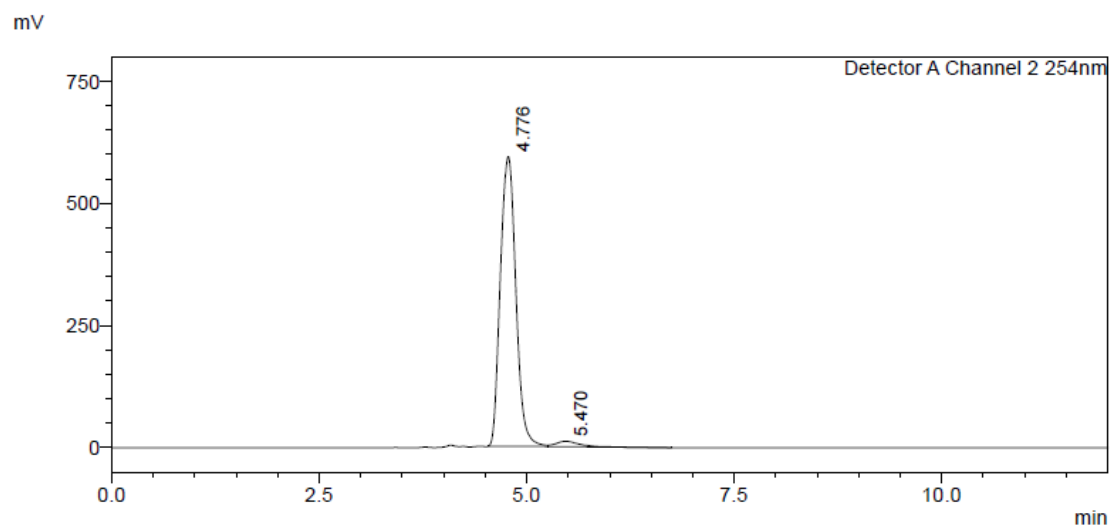


Detector A Channel 2 254nm		
Peak#	Ret. Time	Area%
1	36.300	3.215
2	39.735	96.785
Total		100.000

HPLC Data for **48**: Chiralpak ID (99:1 hexane : IPA, flow rate 1.00 mL.min<sup>-1</sup>, 254 nm, 30 °C) t<sub>R</sub>  
(major): 4.8 min, t<sub>R</sub> (minor): 5.5 min, 97:3 er.



Peak#	Ret. Time	Area%
1	4.799	49.774
2	5.525	50.226
Total		100.000



Peak#	Ret. Time	Area%
1	4.776	97.079
2	5.470	2.921
Total		100.000