

## Supporting Information

### **Synthesis and Activation of Bench-Stable 3a-Fluoropyrroloindolines as Latent Electrophiles for the Synthesis of C-2-Thiol-substituted Tryptophans and C-3a-substituted Pyrroloindolines**

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## Materials and Methods

**General Information.** Reactions were performed in flame-dried borosilicate round-bottom flasks fitted with a rubber septum under a positive pressure of Ar, unless otherwise noted. Air/moisture sensitive liquids and solutions were transferred via syringe under positive Ar pressure. Controlled temperature reactions were performed using a mineral oil bath and a temperature controlled hot plate (Corning, PC 420D). Analytical thin layer chromatography (TLC) was performed using pre-coated Merck aluminum backed silica gel plates (Silica gel 60 F254). Visualization was achieved using ultraviolet light (254 nm) and chemical staining with silica gel impregnated with iodine, *p*-anisaldehyde, potassium permanganate, bromocresol green, and ninhydrin as appropriate. Flash column chromatography purification was performed using silica gel 60 (230-400 mesh, Silicycle, Quebec, Canada and 230-400 mesh, high purity 9385, Sigma Aldrich, Germany). Prior to use, silica gel was washed with four volumes of ammonium hydroxide/dichloromethane/ethanol (0.5:4:4.5) solution, filtered, and baked to neutralize small amounts of acid on silica gel. Solvents were dried according to standard methods.<sup>1</sup> Reagents and solvents were purchased from Sigma-Aldrich, Novabiochem, Alfa Aesar, Acros Organics, AK Scientific Inc., Oakwood Chemical, TCI America and used without further purification unless noted otherwise. Dipeptide substrates for fluorocyclization were synthesized following reported procedures: N-Tr-Trp-Gly-OMe,<sup>2</sup> N-Fmoc-Trp-Gly-OMe,<sup>3</sup> N-Boc-Trp-Gly-OMe.<sup>4</sup>

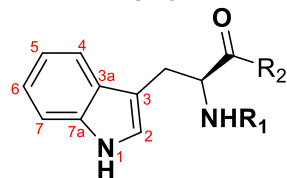
**Instrumentation.** <sup>1</sup>H, <sup>19</sup>F, <sup>13</sup>C, and 2D NMR spectra were recorded on Bruker Avance 300 (300 MHz), Bruker Avance 400dir (400 MHz), Bruker Avance 400inv (400 MHz), and Bruker Avance 600-CRP (600 MHz) spectrometers. Chemical shifts ( $\delta$ ) are reported in ppm and referenced to the appropriate residual solvent peaks (acetone-D<sub>6</sub>, CD<sub>3</sub>CN, CD<sub>2</sub>Cl<sub>2</sub>, or CDCl<sub>3</sub>). Low-resolution mass spectrometry (LRMS) in Electrospray Ionization (ESI) mode was obtained using Waters ZQ mass spectrometer equipped with ESCI ion source and Waters 2695 HPLC. High-resolution mass spectrometry (HRMS) in ESI mode was obtained using Water/Micromass LCT-TOF mass spectrometer equipped with ESI ion source. The X-Ray crystallographic measurements were performed on a Bruker APEX DUO diffractometer with a TRIUMPH curved-crystal monochromator with Mo-K $\alpha$  radiation. Infrared (IR) spectra (cm<sup>-1</sup>) was recorded neat using PerkinElmer FT-IR Frontier Spectrometer.

## General Fluorocyclization Procedure for Compounds 3-8a,b

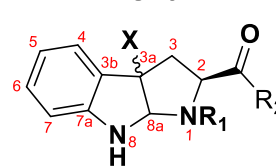
A flame-dried round bottom flask under positive Ar atmosphere was charged with the corresponding tryptophan analog dissolved in anhydrous dichloromethane (DCM) to reach a final concentration of 0.05-0.1 M with respect to the corresponding tryptophan analog. To this solution, added 1-fluoro-2,4,6-trimethylpyridinium triflate (1.8 equiv). The reaction contents were stirred for 3 h at 21 °C and the reaction progress was followed by TLC. Upon completion the crude was concentrated under reduced pressure and immediately purified using silica gel flash column chromatography. <sup>19</sup>F-NMR spectroscopy on the crude reaction was used to determine the diastereomeric ratios (*syn-cis*:*anti-cis*).

## Numbering Systems and Remarks on Characterization of Fluoropyrroloindoline Compounds

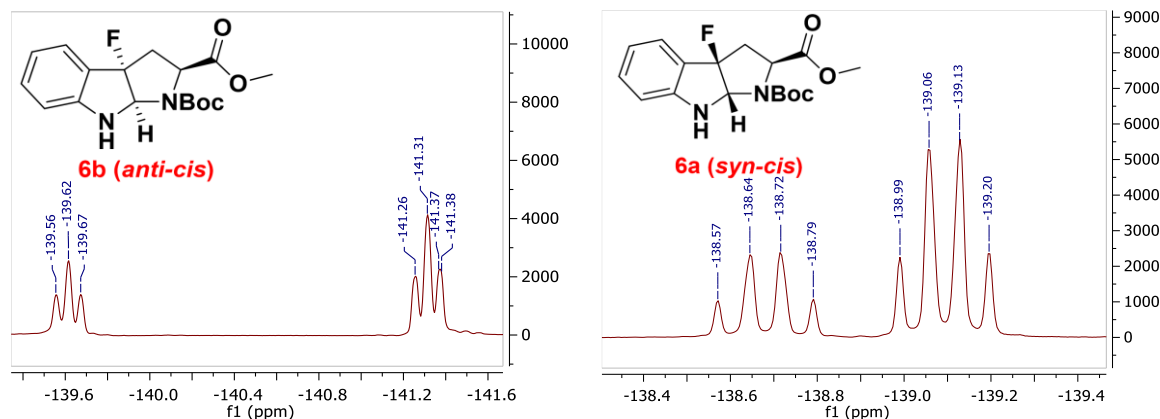
a) indole core numbering system



b) pyrroloindoline core numbering system



Diastereomeric assignments for compounds **5a,b** and **6a,b** were done based on the characteristic  $^1\text{H}$ -NMR proton chemical shift of -OMe ester group. Due to the geometry of the *anti-cis* diastereomer -OMe group is shielded by the aromatic ring resulting in an upfield shift ( $\sim 3$  ppm), whereas *syn-cis* does not experience the shielding effect of the aromatic ring and proton chemical shift of the -OMe appears in a characteristic range for esters ( $\sim 3.5$ - $3.7$  ppm).<sup>5-7</sup> During the course of this study it was also discovered that Fmoc- and Boc-protected fluoropyrroloindolines exhibit characteristic  $^{19}\text{F}$ -signal shapes. Upon inspection, it was determined that multiplet  $^{19}\text{F}$ -signal of the *syn-cis* diastereomer resembles a quartet and the multiplet  $^{19}\text{F}$ -signal of the *anti-cis* resembles a triplet (see below an example from N-Boc-fluoropyrroloindoline-OMe **6a** and **6b**). Diastereomeric assignment of **4a,b**, **7-8a,b** were determined based on the characteristic splitting pattern in  $^{19}\text{F}$ -NMR (**Figure S1**). Due to the presence of two rotamers, both diastereomers of compounds **3-8ab** exhibited an additional set of signals in  $^1\text{H}$ ,  $^{19}\text{F}$ ,  $^{13}\text{C}$ -NMR; this phenomenon has been previously documented for 3a-fluoropyrroloindolines.<sup>5, 8</sup> The ratio of rotamers was found to change depending on the NMR solvent used; in the case of compound **4a**, in  $\text{CD}_2\text{Cl}_2$  two rotamers appeared in a ratio of  $\sim 1.4:1$ , whereas in acetone- $\text{D}_6$  the ratio was 2.3:1 (determined by  $^{19}\text{F}$ -NMR). This observation also confirms that the observed signals are due to rotamer as opposed to epimers. To analyze  $^1\text{H}$ -spectra, -OMe of fluoropyrroloindoline compounds **3-6ab** were integrated to a cumulative value of 3H and the rest of the peaks were integrated with respect to this value. For compounds **7,8ab**, the  $^1\text{H}$ -spectra calibration was done using the upfield multiplet corresponding to  $\text{H}_2$ -3 (2H), which is well separated from other peaks, the rest of the peaks were integrated with respect to this multiplet. Note the characteristic 5-6 ppm range for H-8a in  $^1\text{H}$ -NMR; this signal was observed as a doublet with  $^3J_{\text{H-F}} \sim 20$  Hz for compounds **2b**, **3-8ab**. In  $^{13}\text{C}$ -NMR spectrum of **2-8a,b**,  $^1J_{\text{C-F}}$ ,  $^2J_{\text{C-F}}$ ,  $^3J_{\text{C-F}}$ ,  $^4J_{\text{C-F}}$  couplings were observed between F-atom and C3a, C8a, C3, C3b, C2, C4, C7a, C5, and C7. Variable temperature experiments were run for one of the fluoropyrroloindoline compounds (**4a,b**) in an attempt to observe a coalescence of both spectra due to the presence of rotamers; at two different temperatures, 45 and 72  $^\circ\text{C}$ , merging of rotamers was not observed.



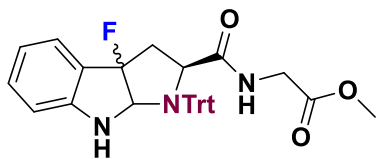
**Figure S1.** Characteristic Multiplicity of  $^{19}\text{F}$ -NMR Signals of *anti-cis* and *syn-cis* Diastereomers (compounds **6b** and **6a**, respectively)



**Table S1.** Description of Diastereomeric **2-8a,b** in Crude, Isolated, and Characterized Forms

Compd	Diastereomeric ratio based on <sup>19</sup> F-NMR spectrum acquired on crude reaction ( <i>syn-cis:anti-cis</i> )	Diastereomeric ratio of isolate used for yield determination ( <i>syn-cis:anti-cis</i> )	Full NMR Characterization performed on ( <i>syn-cis:anti-cis</i> )
<b>2a,b</b>	1:10	<i>anti-cis</i>	<i>anti-cis</i> (major, <b>2b</b> )
<b>3a,b</b>	1.2:1	1:1	<i>syn-cis</i> (major, <b>3a</b> ) 1:1 (mixture)
<b>4a,b</b>	1.2:1	1.4:1	<i>syn-cis</i> (major, <b>4a</b> ) 1.4:1 (mixture)
<b>5a,b</b>	1.2:1	1.2:1	1.2:1
<b>6a,b</b>	1.1:1	1.2:1	<i>syn-cis</i> (major, <b>6a</b> ) <i>anti-cis</i> (minor, <b>6b</b> )
<b>7a,b</b>	1.2:1	1.2:1	1.2:1 (mixture)
<b>8a,b</b>	1.1:1	1.4:1	1.4:1 (mixture)

## Synthesis and characterization of compound **2a,b**



**2a,b** (1:10)<sup>b</sup> 47 %

**Chemical Formula:** C<sub>33</sub>H<sub>30</sub>FN<sub>3</sub>O<sub>3</sub>

**Exact Mass:** 535.23

**Molecular Weight:** 535.62

**Methyl ((2S)-3a-fluoro-1-trityl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carbonyl)glycinate, N-Trt-FPI-Gly-OMe (**2a,b**).** A flame-dried round bottom flask under positive Ar atmosphere was charged with 1-fluoro-2,4,6-trimethylpyridinium triflate (2.15 eq., 144.3 mg, 0.499 mmol) in dichloromethane (DCM) (6.18 mL) and pH 6, 0.5 M citrate buffer (3.1 mL), followed by N-Trt-Trp-Gly-OMe (1 eq., 120 mg, 0.232 mmol). The reaction contents were stirred at 21 °C for 1.5 h and then another portion of 1-fluoro-2,4,6-trimethylpyridinium triflate (2.15 eq., 144 mg, 0.50 mmol) was added and the reaction was stirred for 18.5 h at 21 °C. The DCM layer (light orange and clear) was separated and concentrated under reduced pressure. The crude residue was immediately purified using silica gel (NH<sub>4</sub>OH treated and baked to neutralize small amounts of acid on silica gel, see general procedures) flash column chromatography (isocratic elution at 0.4/15/84.5 triethylamine/hexane/ethyl acetate) to afford pure *anti-cis* N-Trt-FPI-Gly-OMe **2a,b** (57 mg, 0.10 mmol, 47% yield) as a crystalline white solid. The product was crystallized out of hexane/ethyl acetate (3/1) as clear needle-like crystals. <sup>19</sup>F-NMR spectroscopy on the crude reaction mixture was used to determine the diastereomeric ratio of 10:1 (*anti-cis*:*syn-cis*), major diastereomer **2b** was isolated and characterized.

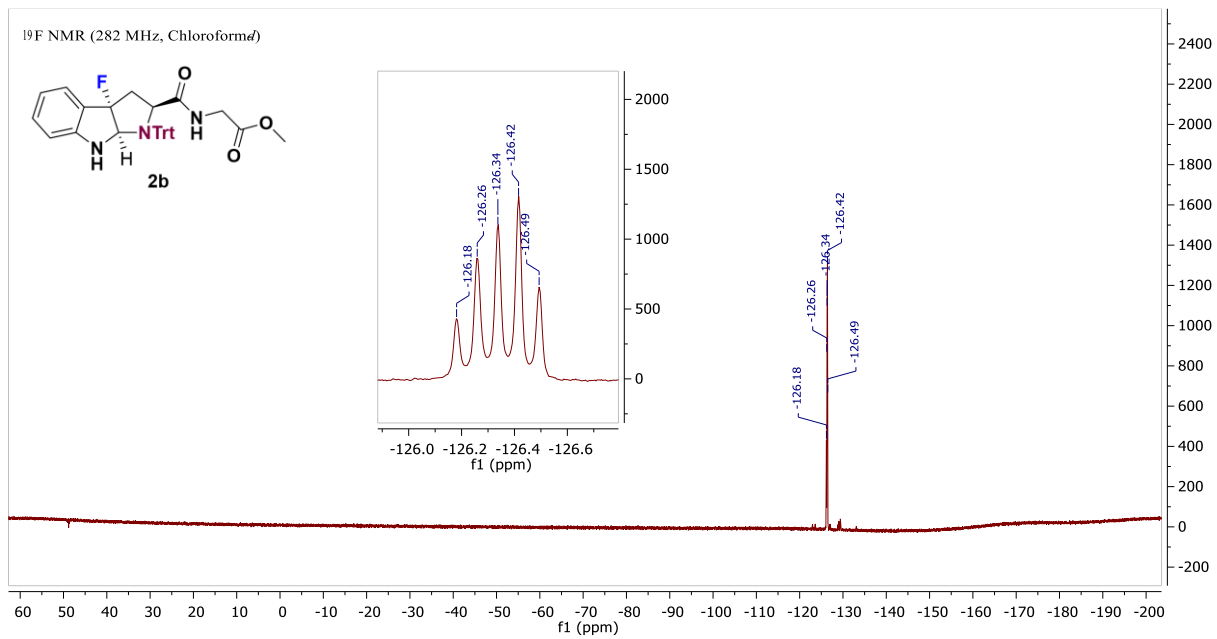
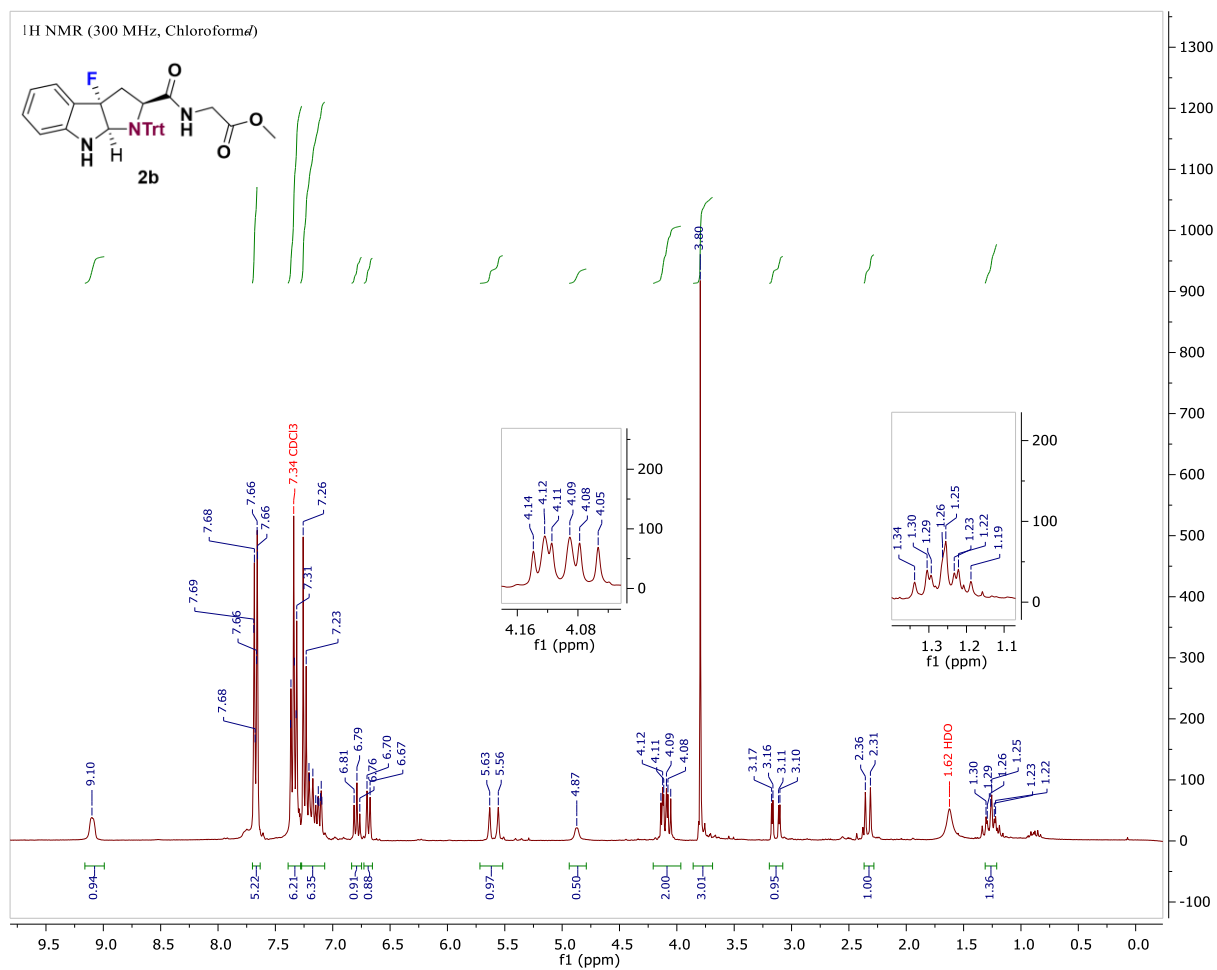
**<sup>1</sup>H NMR** (300 MHz, Chloroform-*d*) major diastereomer, *anti-cis* δ (ppm) 9.10 (s, 1H), 7.70 – 7.63 (m, 5H), 7.39 – 7.27 (m, 6H), 7.28 – 7.07 (m, 6H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.59 (d, *J* = 22.5 Hz, 1H), 4.87 (s, 1H), 4.21 – 3.97 (m, 2H), 3.80 (s, 3H), 3.14 (dd, *J* = 18.3, 3.5 Hz, 1H), 2.33 (d, *J* = 13.3 Hz, 1H), 1.26 (td, *J* = 11.2, 10.1, 3.4 Hz, 1H).

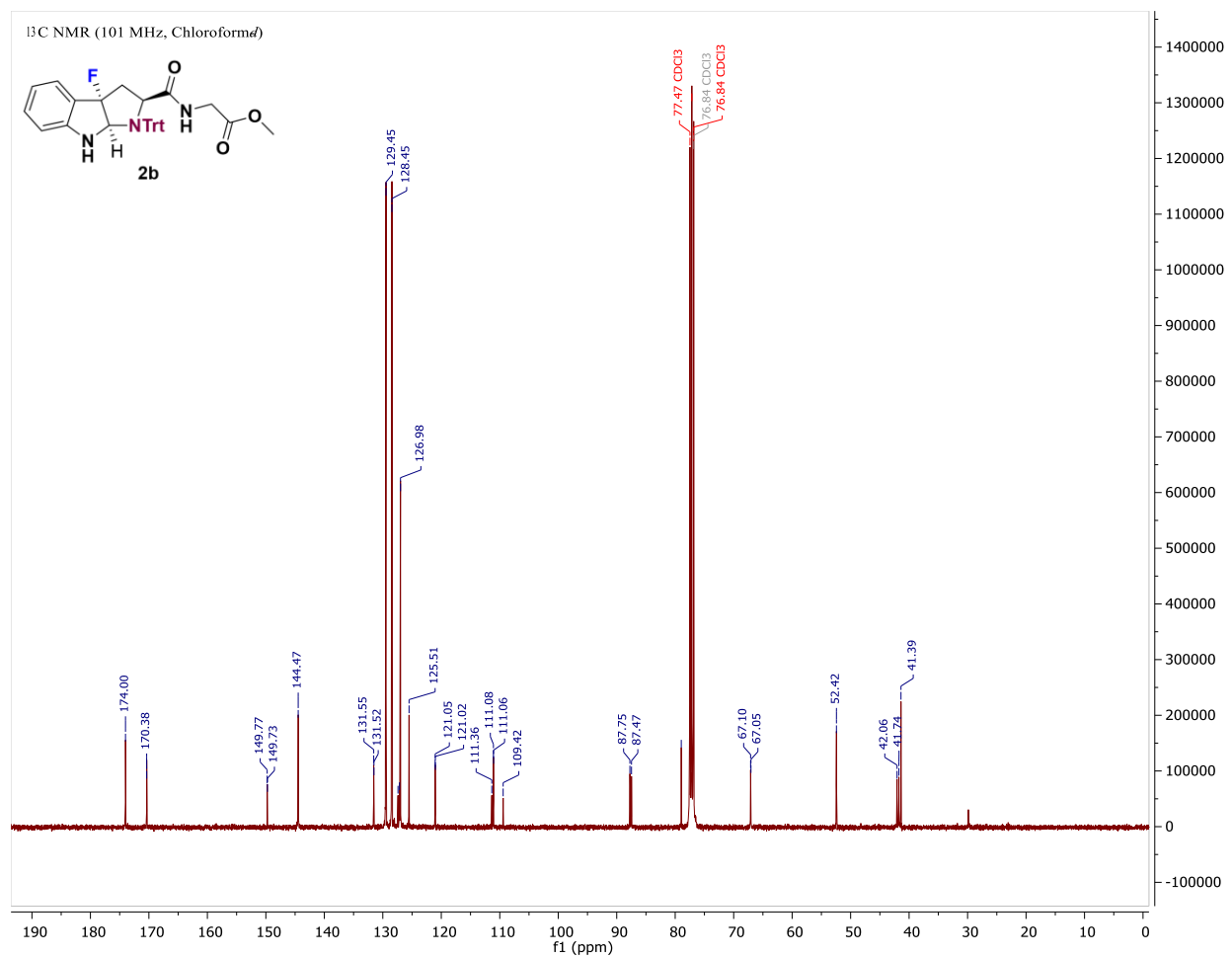
**<sup>19</sup>F NMR** (282 MHz, Chloroform-*d*, ref. CFC<sub>3</sub> = 0 ppm) major diastereomer, *anti-cis* δ (ppm) -126.34 (dt, *J* = 44.0, 22.0 Hz).

**<sup>13</sup>C NMR** (101 MHz, Chloroform-*d*) major diastereomer, *anti-cis* δ (ppm) 41.39, 41.90 (d, *J* = 32.3 Hz), 52.42, 67.07 (d, *J* = 5.9 Hz), 78.96, 87.61 (d, *J* = 27.7 Hz), 110.39 (d, *J* = 195.5 Hz), 111.07 (d, *J* = 2.3 Hz), 121.03 (d, *J* = 3.1 Hz), 125.51, 126.98, 127.28 (d, *J* = 25.2 Hz), 128.44, 129.45, 131.54 (d, *J* = 3.6 Hz), 144.47, 149.75 (d, *J* = 4.4 Hz), 170.38, 174.00.

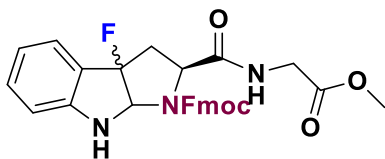
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> found 558.2171; calc. 558.2169 for C<sub>33</sub>H<sub>30</sub>FN<sub>3</sub>O<sub>3</sub>Na.

**TLC** (hexane:ethyl acetate 6:4 v/v): R<sub>f</sub> = 0.6 (UV, I<sub>2</sub>, p-anisaldehyde).





## Synthesis and characterization of compound **3a,b**



**3a,b** (1.2:1)<sup>c</sup> 76 %

**Chemical Formula:** C<sub>29</sub>H<sub>26</sub>FN<sub>3</sub>O<sub>5</sub>

**Exact Mass:** 515.19

**Molecular Weight:** 515.54

**(9H-fluoren-9-yl)methyl (2S)-3a-fluoro-2-((2-methoxy-2-oxoethyl)carbamoyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate, N-Fmoc-FPI-Gly-OMe (**3a,b**).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-Trp-Gly-OMe (1.0 equiv, 250 mg, 0.50 mmol) dissolved in 10.0 mL of anhydrous DCM. To this solution, added 1-fluoro-2,4,6-trimethylpyridinium triflate (1.8 equiv, 261 mg, 0.90 mmol). The reaction contents were stirred for 3 h at 21 °C and the reaction progress was monitored by TLC. Upon completion, the crude (light yellow, clear) was concentrated under reduced pressure and immediately purified using silica gel flash column chromatography (gradient elution, 2:3 to 4:1 diethyl ether/petroleum ether) to obtain 197 mg (0.382 mmol) of **3a,b** as a white solid in 76 % isolated yield. <sup>19</sup>F-NMR spectroscopy on the crude reaction was used to determine the diastereomeric ratio (*syn-cis:anti-cis*) of 1.2:1. Stability note: stable for >8 weeks at room temperature and > 3 months at -20 °C. Major diastereomer was isolated for NMR analysis following two additional silica gel re-purifications with a slow gradient of diethyl ether/petroleum ether.

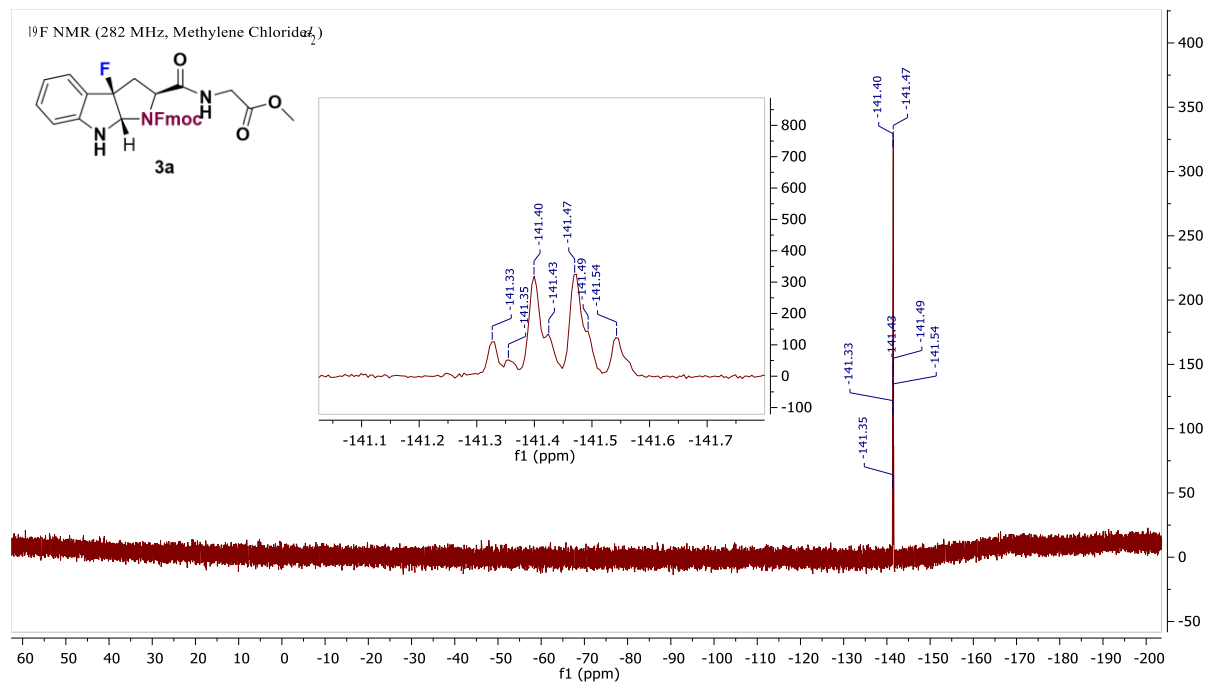
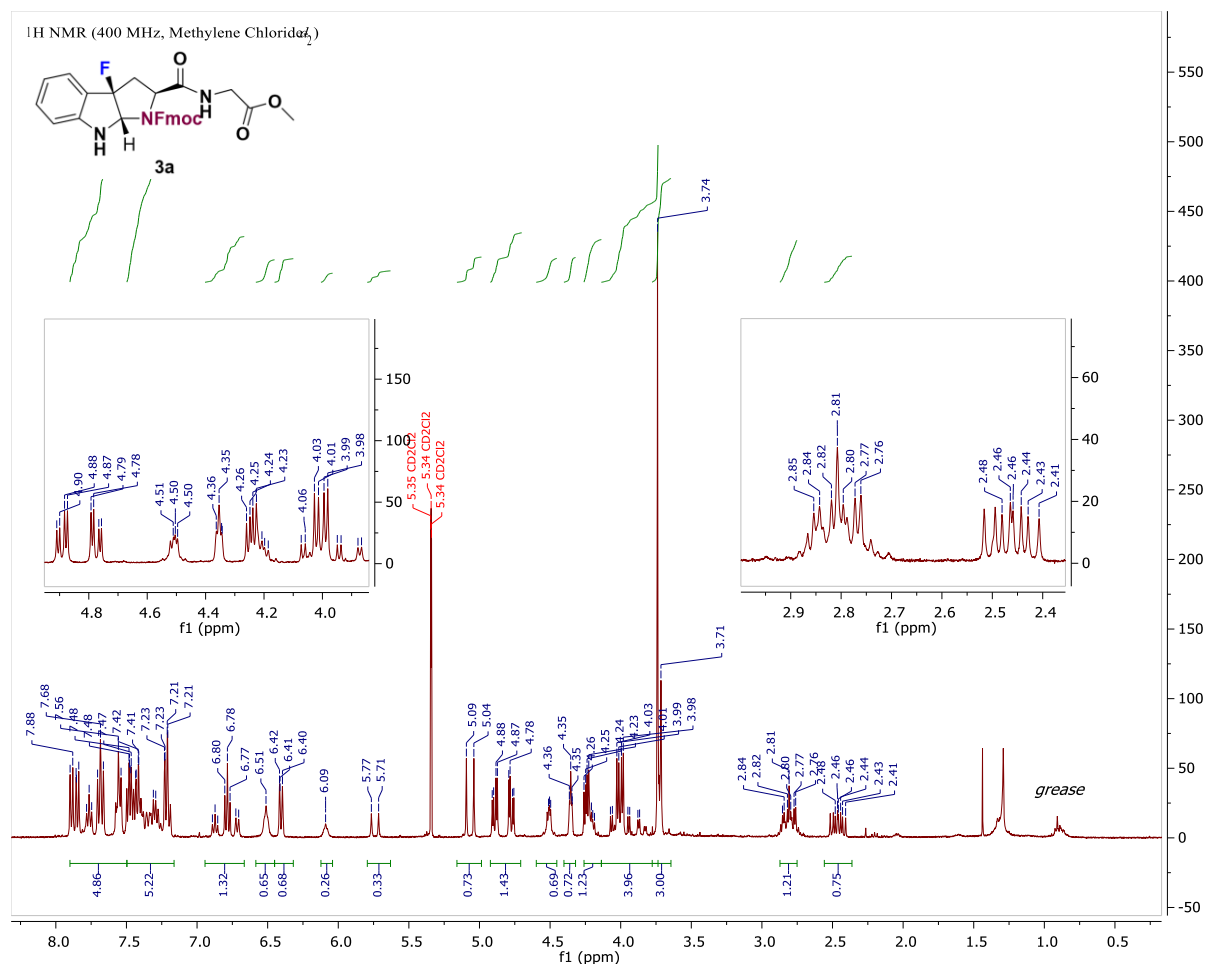
**<sup>1</sup>H NMR** (400 MHz, Methylene Chloride-*d*<sub>2</sub>) major diastereomer and rotamers, *syn-cis* δ (ppm) 7.90 – 7.50 (m, 5H), 7.50 – 7.16 (m, 5H), 6.94 – 6.67 (m, 1H), 6.51 (s, 1H), 6.45 – 6.32 (m, 1H), 5.07 (d, *J* = 21.2 Hz, 1H), 4.83 (ddd, *J* = 46.6, 10.7, 3.8 Hz, 1H), 4.60 – 4.45 (m, 1H), 4.40 – 4.32 (m, 1H), 4.26 – 4.14 (m, 1H), 4.14 – 3.74 (m, 4H), 3.7, 3.74 (s, 3H), 2.81 (ddd, *J* = 18.6, 14.0, 4.6 Hz, 1H), 2.56 – 2.36 (m, 1H).

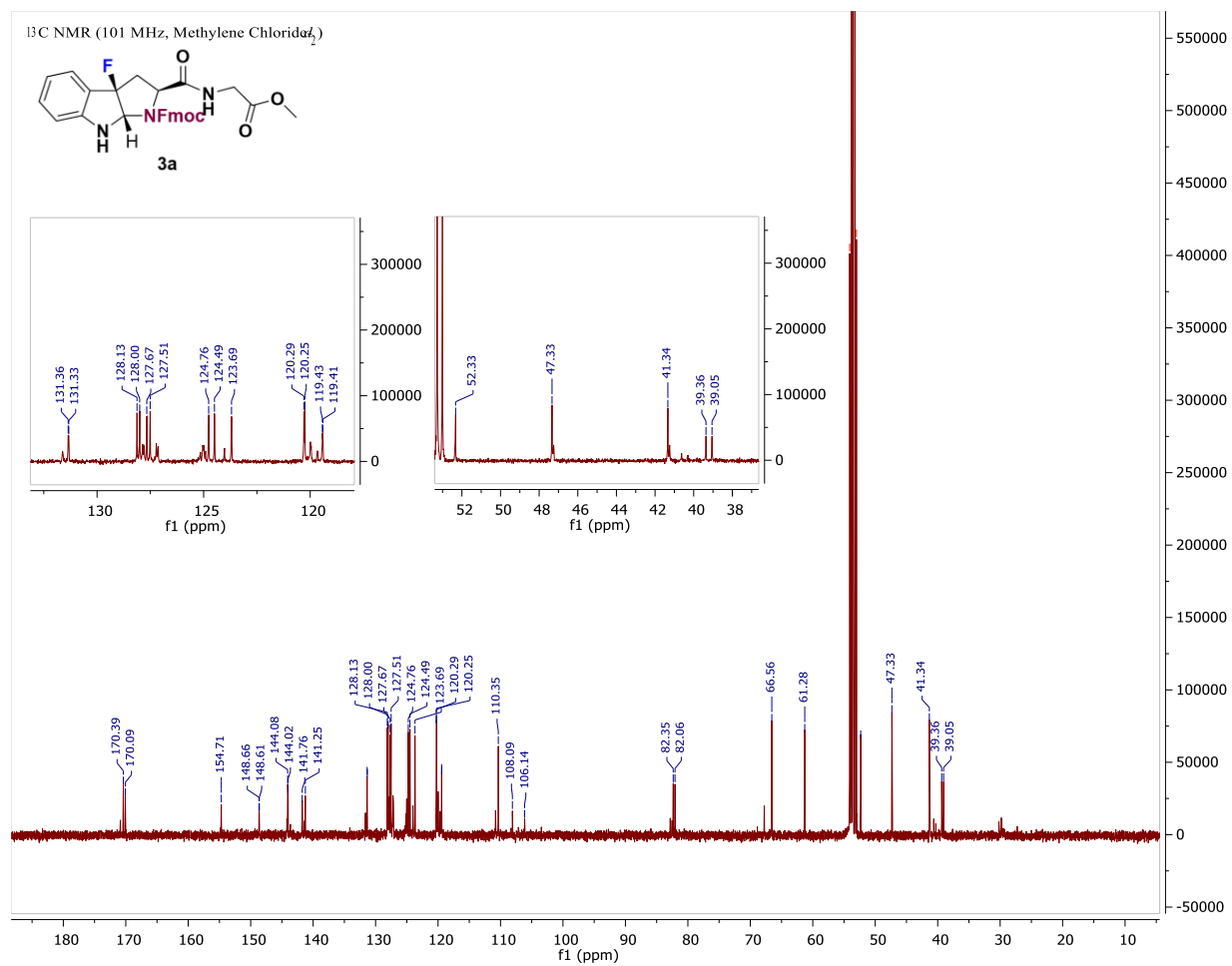
**<sup>19</sup>F NMR** (282 MHz, Methylene Chloride-*d*<sub>2</sub>, ref. CFCl<sub>3</sub> = 0 ppm) major diastereomer and rotamers, *syn-cis* δ (ppm) -134.77 – -149.07 (m).

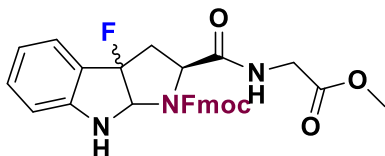
**<sup>13</sup>C NMR** (101 MHz, Methylene Chloride-*d*<sub>2</sub>) major diastereomer and major rotamer, *syn-cis* δ (ppm) 39.21 (d, *J* = 31.5 Hz), 41.34, 47.33, 52.33, 61.28, 66.56, 82.20 (d, *J* = 29.0 Hz), 107.12 (d, *J* = 196.8 Hz), 110.35, 119.42 (d, *J* = 1.9 Hz), 120.27 (d, *J* = 4.4 Hz), 123.69, 124.49, 124.76, 127.51, 127.67, 128.00, 128.13, 131.34 (d, *J* = 2.9 Hz), 141.25, 141.76, 144.05 (d, *J* = 6.2 Hz), 148.64 (d, *J* = 4.8 Hz), 154.71, 170.09, 170.39.

**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 538.1754; found 538.1746 M+Na for C<sub>29</sub>H<sub>26</sub>FN<sub>3</sub>O<sub>5</sub>Na.

**TLC** (diethyl ether:petroleum ether, 1:1 v/v): R<sub>f</sub> = 0.5 (UV, I<sub>2</sub>, p-anisaldehyde).







**3a,b** (1.2:1)<sup>c</sup> **76 %**  
**Chemical Formula:** C<sub>29</sub>H<sub>26</sub>FN<sub>3</sub>O<sub>5</sub>  
**Exact Mass:** 515.19  
**Molecular Weight:** 515.54

**<sup>1</sup>H NMR** (300 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1:1), δ (ppm) 7.94 – 7.64 (m, 4H), 7.60 – 7.04 (m, 7H), 6.85 – 6.22 (m, 2H), 5.58 (ddd, *J* = 117.9, 21.0, 2.5 Hz, 1H), 4.91 – 3.65 (m, 6H), 3.61, 3.64 (two s, 1.5H), 3.55, 3.50 (two s, 1.5H), 3.42 – 2.63 (m, 3H).

**<sup>19</sup>F NMR** (282 MHz, Acetone-*d*<sub>6</sub>, ref. CFC<sub>l</sub><sub>3</sub> = 0 ppm) two diastereomers and rotamers, *syn-cis:anti-cis* (1:1), δ (ppm) -134.46 - -134.79 (d, *J* = 19.6 Hz), -135.10 (t, *J* = 19.2 Hz), -136.68 (q, *J* = 18.6 Hz), -138.02 (q, *J* = 18.5 Hz).

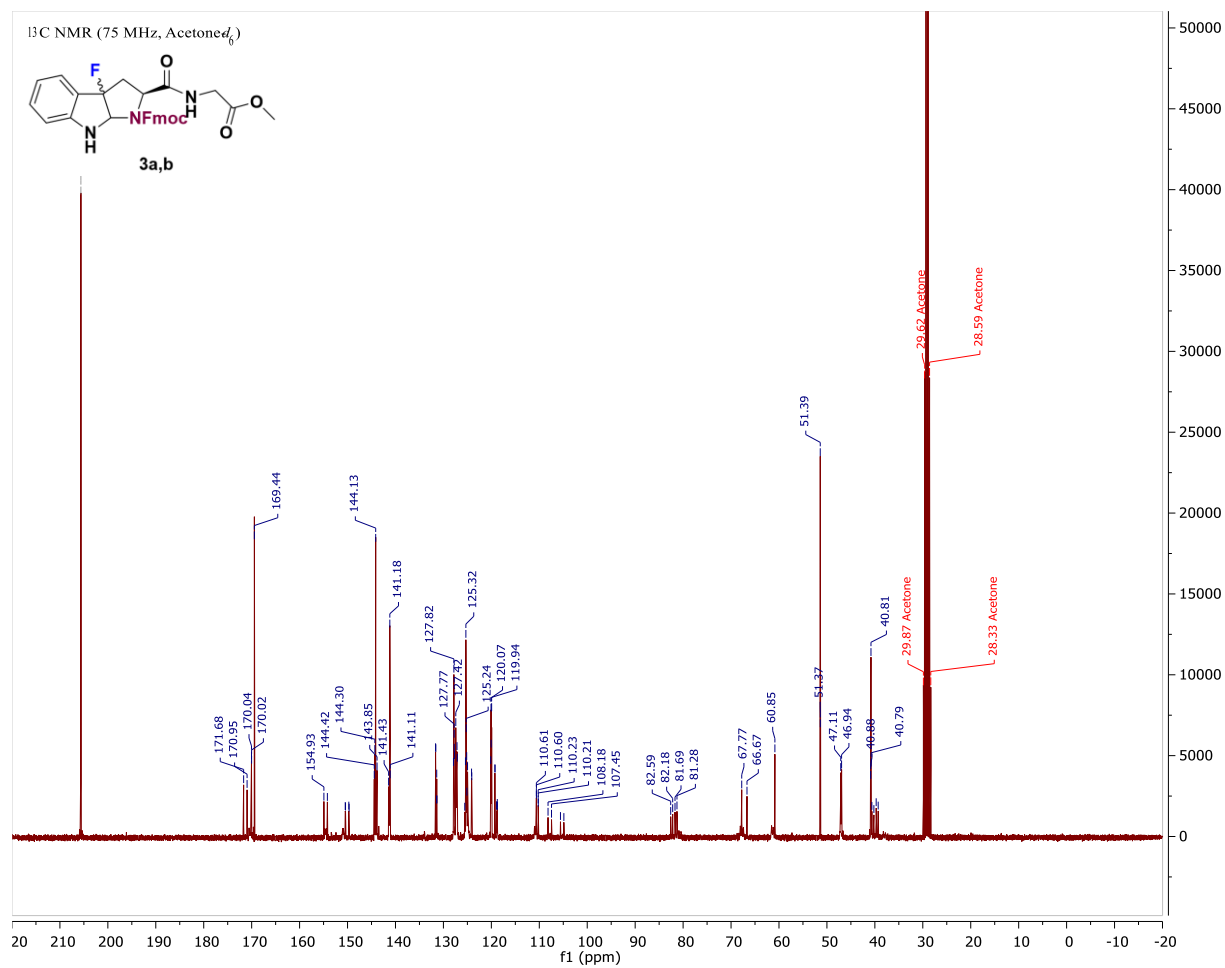
**<sup>13</sup>C NMR** (75 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1:1), δ (ppm) 39.31, 39.72, 40.20, 40.63, 40.79, 40.81, 40.88, 46.94, 47.11, 51.37, 51.39, 60.85, 66.67, 67.77, 81.28, 81.69, 82.18, 82.59, 104.87, 105.58, 107.45, 108.18, 110.21, 110.23, 110.60, 110.61, 118.73, 118.76, 118.88, 118.91, 119.23, 119.26, 119.94, 120.04, 120.07, 120.13, 124.09, 124.13, 124.97, 125.10, 125.14, 125.24, 125.32, 125.40, 125.55, 127.11, 127.17, 127.42, 127.68, 127.74, 127.77, 127.82, 127.90, 131.36, 131.40, 131.43, 131.59, 131.64, 141.11, 141.18, 141.43, 143.85, 144.13, 144.30, 144.42, 149.67, 149.73, 150.42, 150.48, 154.20, 154.93, 169.44, 170.02, 170.04, 170.95, 171.68.

**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 538.1754; found 538.1743 M+Na for C<sub>29</sub>H<sub>26</sub>FN<sub>3</sub>O<sub>5</sub>Na.

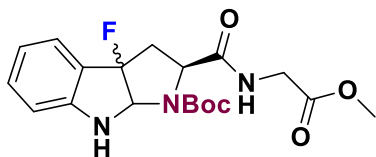
**TLC** (diethyl ether:petroleum ether, 1:1 v/v): R<sub>f</sub> = 0.5 (UV, I<sub>2</sub>, p-anisaldehyde).







## Synthesis and characterization of compound **4a,b**



**4a,b** (1.2:1)<sup>c</sup> **68 %**

**Chemical Formula:** C<sub>19</sub>H<sub>24</sub>FN<sub>3</sub>O<sub>5</sub>

**Exact Mass:** 393.17

**Molecular Weight:** 393.42

**Tert-butyl (2S)-3a-fluoro-2-((2-methoxy-2-oxoethyl)carbamoyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate, N-Boc-FPI-Gly-OMe (**4a,b**).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-Trp-Gly-OMe (1.0 equiv, 200 mg, 0.533 mmol) dissolved in 8.5 mL of anhydrous DCM. To this solution, added 1-fluoro-2,4,6-trimethylpyridinium triflate (1.8 equiv, 0.278 mg, 0.959 mmol) in 2.7 mL of anhydrous DCM. The reaction contents were stirred for 3 h at 21 °C and the reaction progress was monitored by TLC. Upon completion, the crude (light yellow, clear) was concentrated under reduced pressure and immediately purified using silica gel flash column chromatography (isocratic elution, 1:1:8 acetone:ethyl acetate:hexane to obtain 143 mg (0.362 mmol) of **4a,b** as a beige solid in 68 % isolated yield. <sup>19</sup>F-NMR spectroscopy on the crude reaction was used to determine the diastereomeric ratio (*syn-cis:anti-cis*) of 1.2:1. Stability note: stable > 1 year at room temperature. Major diastereomer was isolated for NMR analysis following two additional silica gel re-purifications with a slow gradient of diethyl ether/ethyl acetate/petroleum ether.

**<sup>1</sup>H NMR** (300 MHz, Acetone-*d*<sub>6</sub>) major diastereomer and rotamers, *syn-cis* δ (ppm) 7.74-7.61 (m, 4.2 Hz, 1H), 7.36 (t, *J* = 6.0 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.93 – 6.59 (m, 2H), 6.06 (d, *J* = 35.1 Hz, 1H), 5.61 (dd, *J* = 20.4, 9.2 Hz, 1H), 4.38 – 4.24 (m, 1H), 4.18 – 3.88 (m, 2H), 3.69 (s, 3H), 2.91 – 2.62 (m, 2H), 1.39, 1.51 (s, 9H).

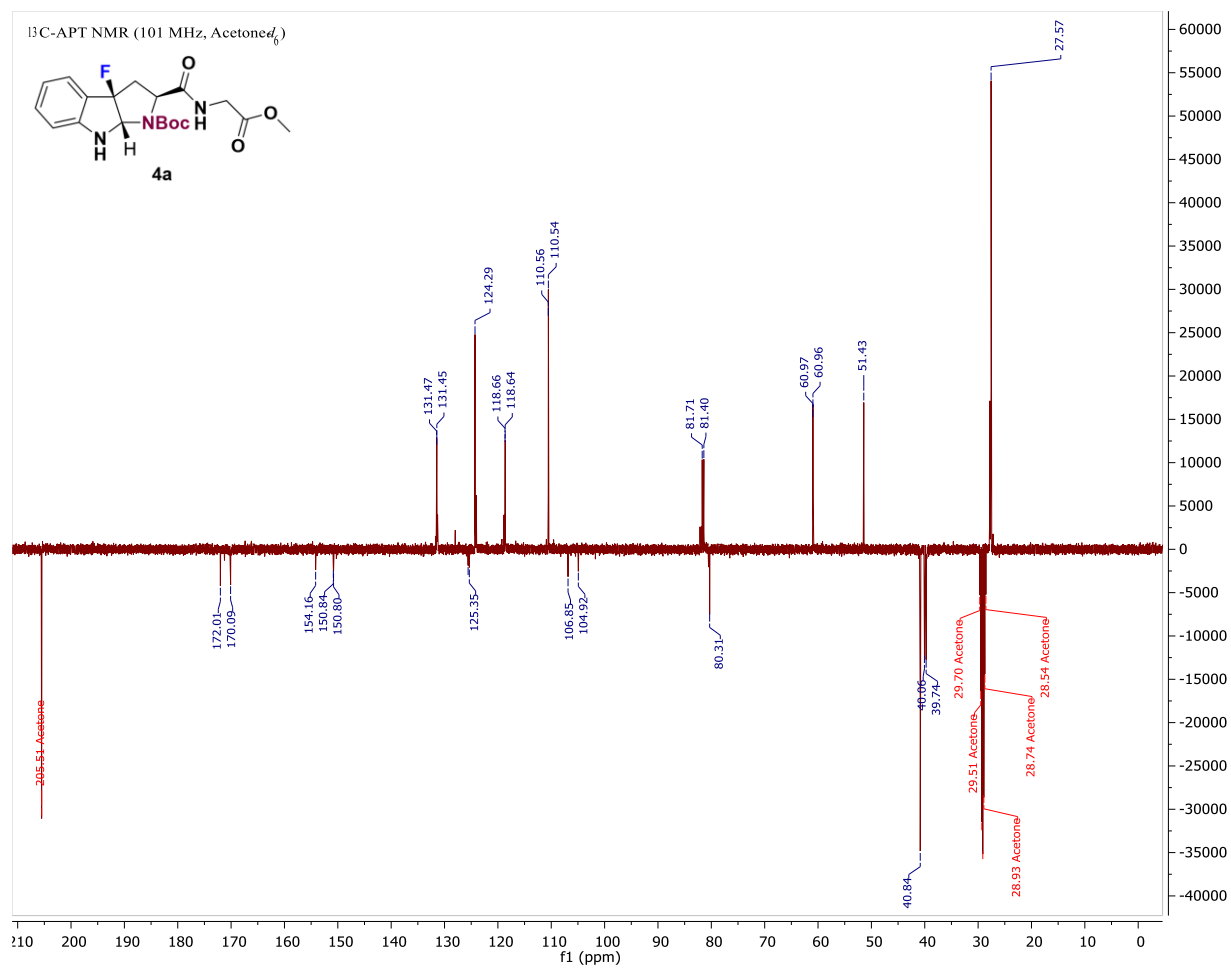
**<sup>19</sup>F NMR** (282 MHz, Acetone-*d*<sub>6</sub>, ref. CFC<sub>l</sub><sub>3</sub> = 0 ppm) major diastereomer and rotamers, *syn-cis* δ (ppm) -136.90 (q, *J* = 19.3, 18.7 Hz), -138.08 – -138.52 (m).

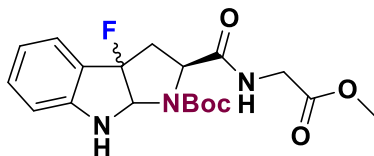
**<sup>13</sup>C NMR** (101 MHz, Acetone-*d*<sub>6</sub>) major diastereomer, major rotamer, *syn-cis* δ (ppm) 27.57, 39.90 (d, *J* = 31.5 Hz), 40.84, 51.43, 60.96, 60.97, 80.31, 81.55 (d, *J* = 31.3 Hz), 105.89 (d, *J* = 194.3 Hz), 110.55 (d, *J* = 1.5 Hz), 118.65 (d, *J* = 2.7 Hz), 124.29, 125.47 (d, *J* = 23.1 Hz), 131.46 (d, *J* = 2.9 Hz), 150.82 (d, *J* = 4.3 Hz), 154.16, 170.09, 172.01.

**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 416.1598; found 416.1594 for C<sub>19</sub>H<sub>24</sub>FN<sub>3</sub>O<sub>5</sub>Na.

**TLC** (acetone:ethyl acetate:hexane 1:1:8 v/v/v): R<sub>f</sub> = 0.5 (UV, I<sub>2</sub>, p-anisaldehyde).







**4a,b** (1.2:1)<sup>c</sup> **68 %**

**Chemical Formula:** C<sub>19</sub>H<sub>24</sub>FN<sub>3</sub>O<sub>5</sub>

**Exact Mass:** 393.17

**Molecular Weight:** 393.42

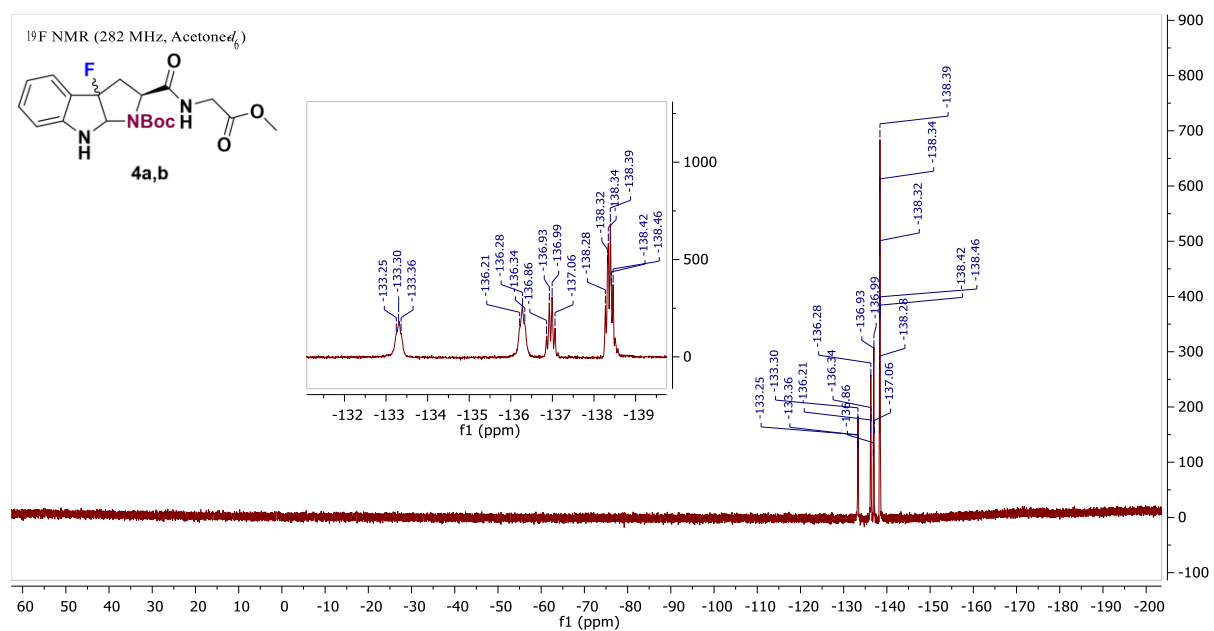
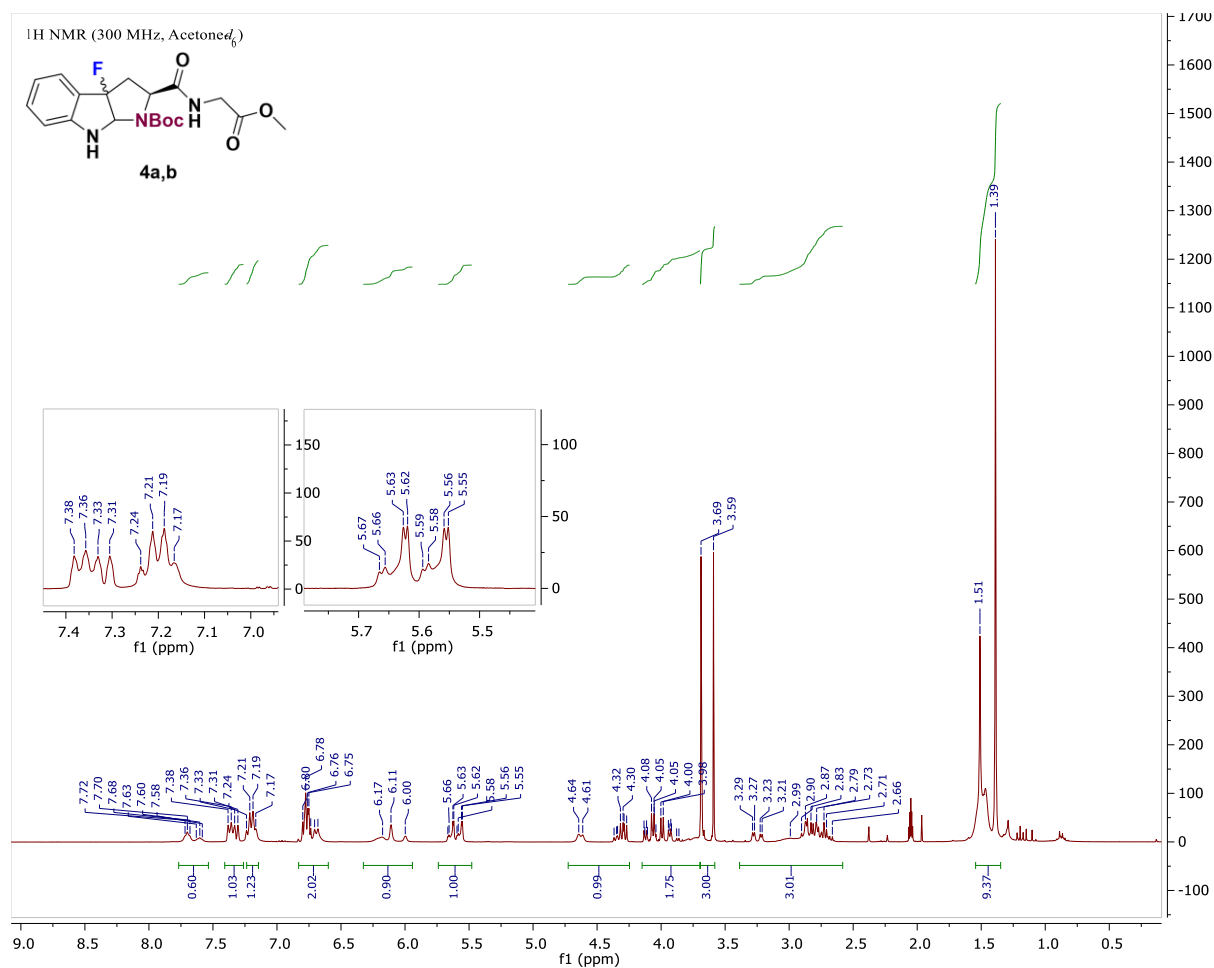
**<sup>1</sup>H NMR** (300 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1.4:1), δ (ppm) δ 7.77 – 7.54 (m, 1H), 7.34 (dd, *J* = 15.5, 7.6 Hz, 1H), 7.24 – 7.14 (m, 1H), 6.83 – 6.60 (m, 2H), 6.33 – 5.94 (m, 1H), 5.74 – 5.48 (m, 1H), 4.73 – 4.25 (m, 1H), 4.15 – 3.70 (m, 2H), 3.69, 3.59 (two s, 3H), 3.39 – 2.58 (m, 3H), 1.51, 1.39 (two s, 9H).

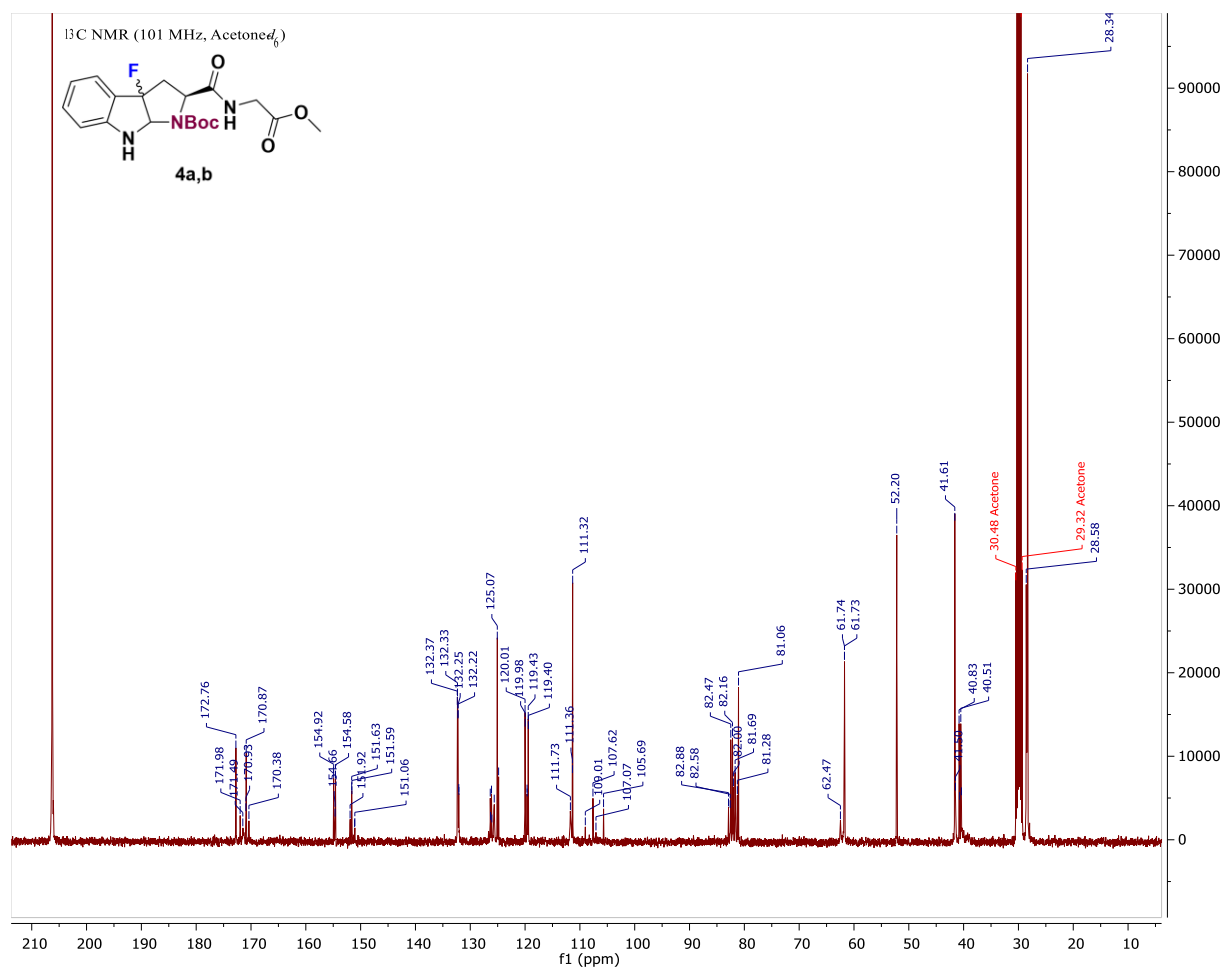
**<sup>19</sup>F NMR** (282 MHz, Acetone-*d*<sub>6</sub>, ref. CFC<sub>l</sub><sub>3</sub> = 0 ppm) two diastereomers and rotamers, *syn-cis:anti-cis* (1.4:1), δ (ppm) -132.95 – -133.78 (m), -132.21 – -133.64 (m), -136.96 (q, *J* = 19.3 Hz), -138.37 (td, *J* = 19.2, 13.0 Hz).

**<sup>13</sup>C NMR** (75 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1.4:1), due to the complexity of the spectrum, C-F couplings were could not be determined, δ (ppm) 28.34, 28.58, 40.40, 40.51, 40.72, 40.83, 41.50, 41.61, 52.20, 61.73, 61.74, 62.47, 81.06, 81.28, 81.69, 82.00, 82.16, 82.47, 82.58, 82.88, 105.69, 107.07, 107.62, 109.01, 111.32, 111.36, 111.73, 119.40, 119.43, 119.62, 119.64, 119.98, 120.01, 124.83, 125.07, 125.63, 126.06, 126.12, 126.30, 126.35, 132.08, 132.10, 132.22, 132.25, 132.33, 132.37, 151.06, 151.10, 151.59, 151.63, 151.92, 154.58, 154.66, 154.92, 170.38, 170.87, 170.93, 171.49, 171.98, 172.76.

**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 416.1598; found 416.1588 for C<sub>19</sub>H<sub>24</sub>FN<sub>3</sub>O<sub>5</sub>Na.

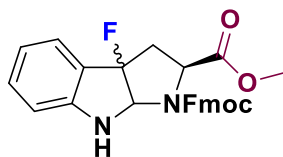
**TLC** (acetone:ethyl acetate:hexane 1:1:8 v/v/v): R<sub>f</sub> = 0.5 (UV, I<sub>2</sub>, p-anisaldehyde).







## Synthesis and characterization of compound **5a,b**



**5a,b** (1.2:1)<sup>c</sup> **85 %**  
**[ 2.0 g, 4.4 mmol ]**  
**Chemical Formula:** C<sub>27</sub>H<sub>23</sub>FN<sub>2</sub>O<sub>4</sub>  
**Exact Mass:** 458.16  
**Molecular Weight:** 458.49



**1-((9H-fluoren-9-yl)methyl) 2-methyl (2S)-3a-fluoro-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate, N-Fmoc-FPI-OMe (**5a,b**).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-Trp-OMe (1.0 equiv, 2.00 g, 4.54 mmol) dissolved in 70 mL of anhydrous DCM. To this solution, added 1-fluoro-2,4,6-trimethylpyridinium triflate (1.8 equiv, 2.36 g, 8.17 mmol) in 5.7 mL of anhydrous DCM. The reaction contents were stirred for 3 h at 21 °C and the reaction progress was monitored by TLC. Upon completion, the crude (light orange, clear) was concentrated under reduced pressure and immediately purified using silica gel flash column chromatography (gradient elution, 1:9 to 1:1 diethyl ether/petroleum ether) to obtain 1.77 g (3.86 mmol) of **5a,b** as a white solid in 85 % isolated yield. Crude <sup>19</sup>F-NMR was used to determine the diastereomeric ratio (*syn-cis*:*anti-cis*) of 1.2:1. The *syn-cis* diastereomer eluted from the column first (less polar). In <sup>19</sup>F-NMR (without <sup>1</sup>H-decoupling), *syn-cis* diastereomer was observed as a multiplet in a shape resembling a quartet, while *anti-cis* diastereomer was observed as a multiplet in a shape resembling a triplet. Stability note: solid material stable for > 9 months at -20 °C.

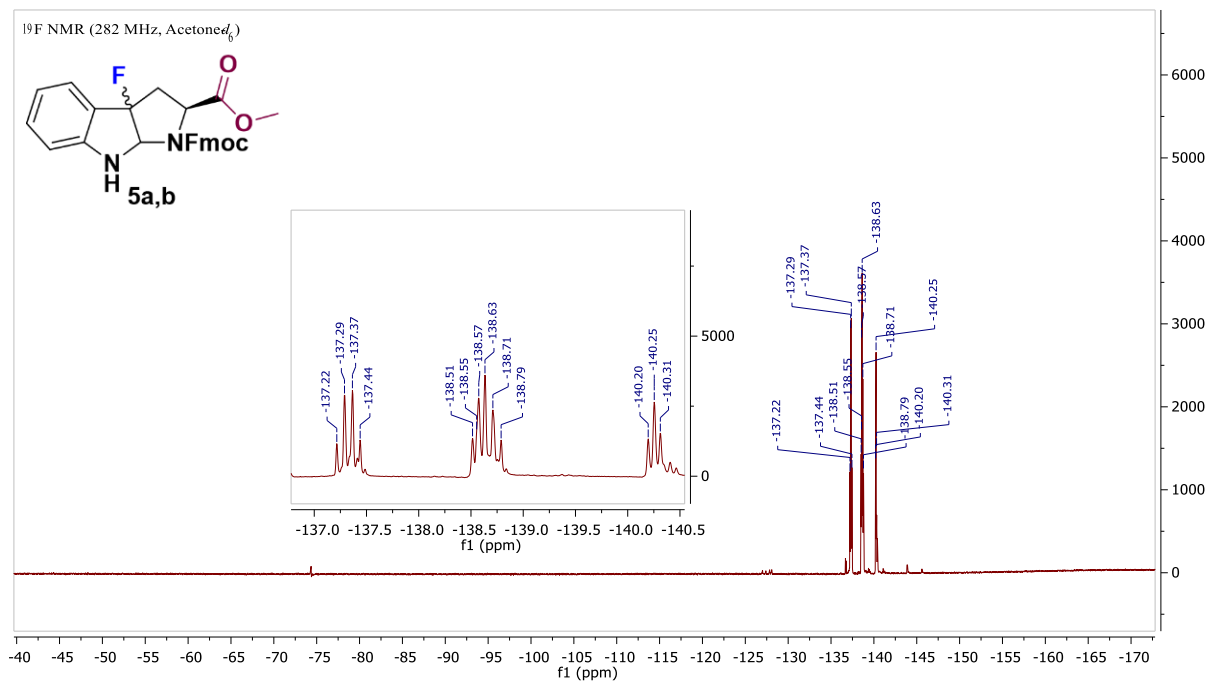
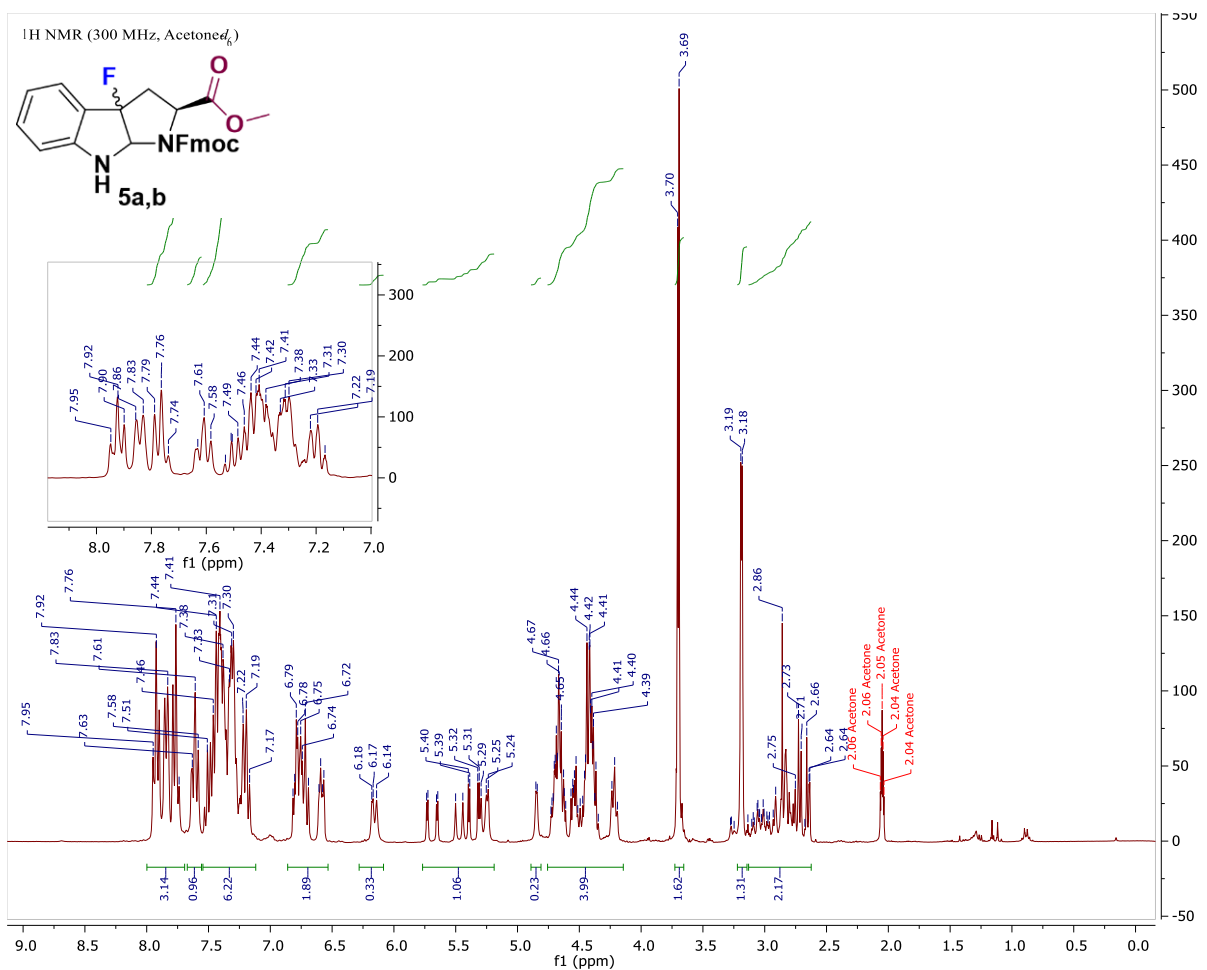
**<sup>1</sup>H NMR** (300 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis*:*anti-cis* (1.2:1), δ (ppm) 8.00 – 7.69 (m, 3H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.55 – 7.12 (m, 6H), 6.86 – 6.53 (m, 2H), 6.34 – 6.05 (m, 1/2H), 5.77 – 5.19 (m, 1H), 4.85 (d, *J* = 3.3 Hz, 1/2H), 4.76 – 4.14 (m, 4H), 3.70, 3.69 (s, 1.7H), 3.19, 3.19 (s, 1.3H), 3.13 – 2.62 (m, 2H).

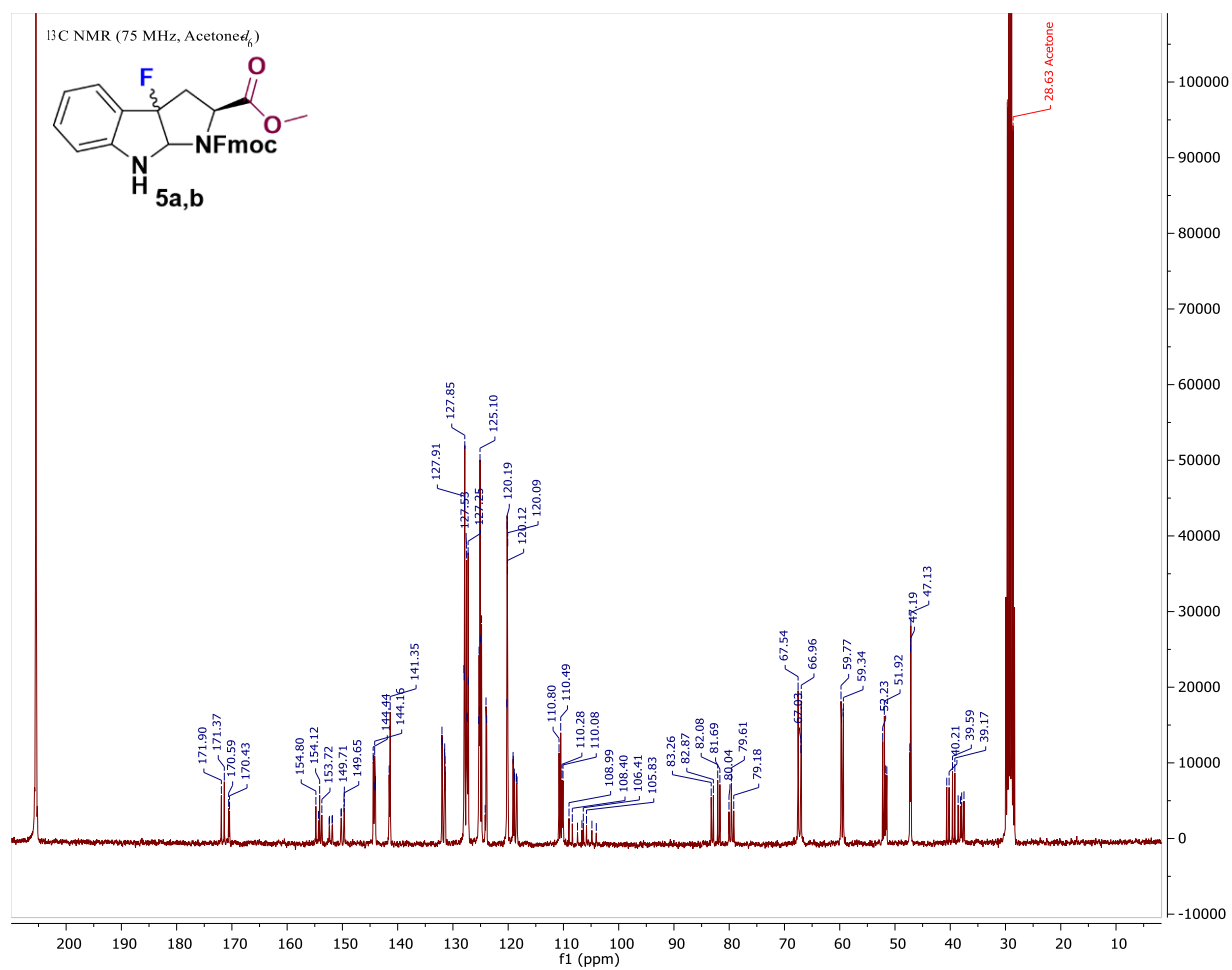
**<sup>19</sup>F NMR** (282 MHz, Acetone-*d*<sub>6</sub>, ref. CFCl<sub>3</sub> = 0 ppm) two diastereomers and rotamers, *syn-cis*:*anti-cis* (1.2:1), δ (ppm) -137.33 (q, *J* = 20.8 Hz), -138.23 – -139.02 (m), -140.33 (dt, *J* = 43.1, 16.6 Hz).

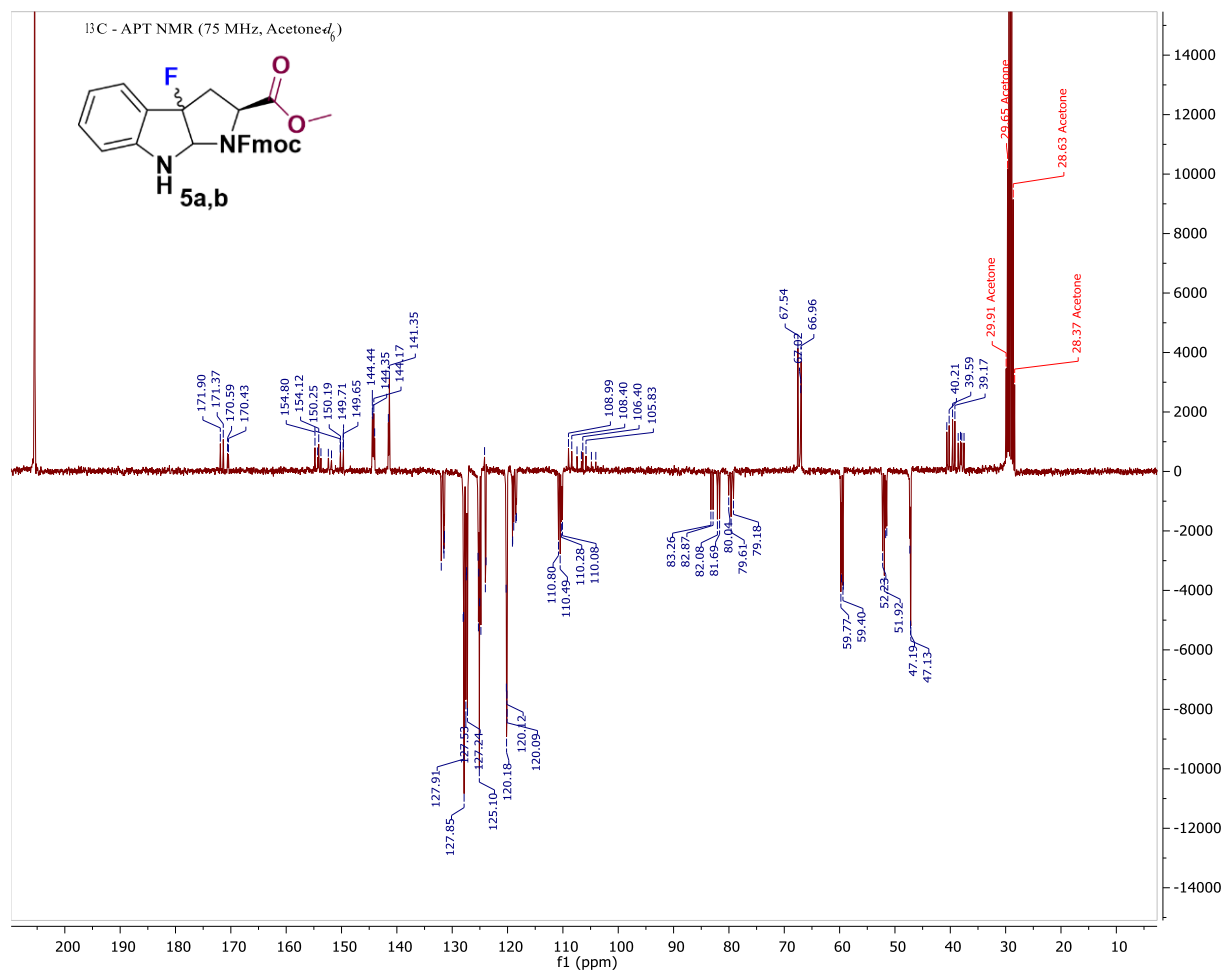
**<sup>13</sup>C NMR** (75 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis*:*anti-cis* (1.2:1), due to the complexity of the spectrum, C-F couplings were could not be determined), δ (ppm) 37.52, 37.93, 38.15, 38.57, 39.17, 39.59, 40.21, 40.63, 47.13, 47.19, 47.31, 51.47, 51.68, 51.92, 52.23, 59.34, 59.40, 59.66, 59.77, 66.96, 67.03, 67.54, 79.18, 79.61, 80.04, 81.69, 82.08, 82.87, 83.26, 104.05, 104.85, 105.83, 106.41, 106.65, 107.45, 108.40, 108.99, 110.08, 110.28, 110.49, 110.80, 118.40, 118.50, 118.53, 118.86, 118.89, 119.08, 119.11, 120.09, 120.12, 120.19, 120.25, 123.90, 124.01, 124.16, 124.82, 125.04, 125.10, 125.21, 125.26, 125.34, 127.20, 127.25, 127.40, 127.45, 127.53, 127.85, 127.91, 127.95, 128.02, 131.40, 131.43, 131.49, 131.52, 131.94, 131.98, 141.35, 141.54, 144.01, 144.10, 144.16, 144.24, 144.35, 144.44, 149.65, 149.71, 150.19, 150.25, 151.82, 151.86, 152.35, 152.40, 153.72, 154.12, 154.32, 154.80, 170.43, 170.59, 171.37, 171.90.

**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 481.1540; found 481.1544 for C<sub>27</sub>H<sub>23</sub>FN<sub>2</sub>O<sub>4</sub>Na.

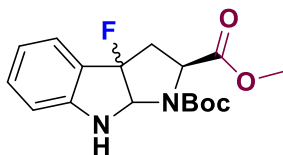
**TLC** (diethyl ether:petroleum ether, 6:4 v/v): R<sub>f</sub> = 0.7 (UV, I<sub>2</sub>, p-anisaldehyde).







## Synthesis and characterization of compound **6a,b**



**6a,b** (1.1:1)<sup>c</sup> 81 %

**Chemical Formula:** C<sub>17</sub>H<sub>21</sub>FN<sub>2</sub>O<sub>4</sub>

**Exact Mass:** 336.15

**Molecular Weight:** 336.36

**1-(Tert-butyl) 2-methyl (2S)-3a-fluoro-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate, N-Boc-FPI-OMe (**6a,b**).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-Trp-OMe (1.0 equiv, 200 mg, 0.63 mmol) dissolved in 10.0 mL of anhydrous DCM. To this solution, added 1-fluoro-2,4,6-trimethylpyridinium triflate (1.8 equiv, 327 mg, 1.13 mmol) in 2.6 mL of anhydrous DCM. The reaction contents were stirred for 3 h at 21 °C and the reaction progress was monitored by TLC. Upon completion, the crude (orange, clear) was concentrated under reduced pressure and immediately purified using silica gel flash column chromatography (gradient elution, 1:3 to 2:1 ethyl acetate/petroleum ether) to obtain 171 mg (0.51 mmol) of **6a,b** as a beige solid in 81 % isolated yield. <sup>19</sup>F-NMR spectroscopy on the crude reaction was used to determine the diastereomeric ratio (*syn-cis*:*anti-cis*) of 1.1:1. In the <sup>19</sup>F-NMR spectrum (obtained without 1H-decoupling), the *syn-cis* diastereomer was observed as a multiplet in a shape resembling a quartet, while the splitting for the *anti-cis* diastereomer was observed as a multiplet in a shape resembling a triplet. Both diastereomers were partially separated for NMR analysis following two additional silica gel re-purifications with a slow gradient elution of diethyl ether/petroleum ether.

**<sup>1</sup>H NMR** (300 MHz, Chloroform-*d*) major diastereomer and rotamers, *syn-cis* δ (ppm) 7.44 – 7.19 (m, 2H), 6.88 (td, *J* = 7.5, 4.4 Hz, 1H), 6.72 (dd, *J* = 8.1, 1.9 Hz, 1H), 5.72 (ddd, *J* = 23.2, 12.8, 1.9 Hz, 1H), 5.29, 4.82 (brs, 1H), 4.45 (ddd, *J* = 30.7, 8.3, 5.0 Hz, 1H), 3.82 (s, 3H), 2.90 – 2.59 (m, 2H), 1.59, 1.47 (s, 9H)

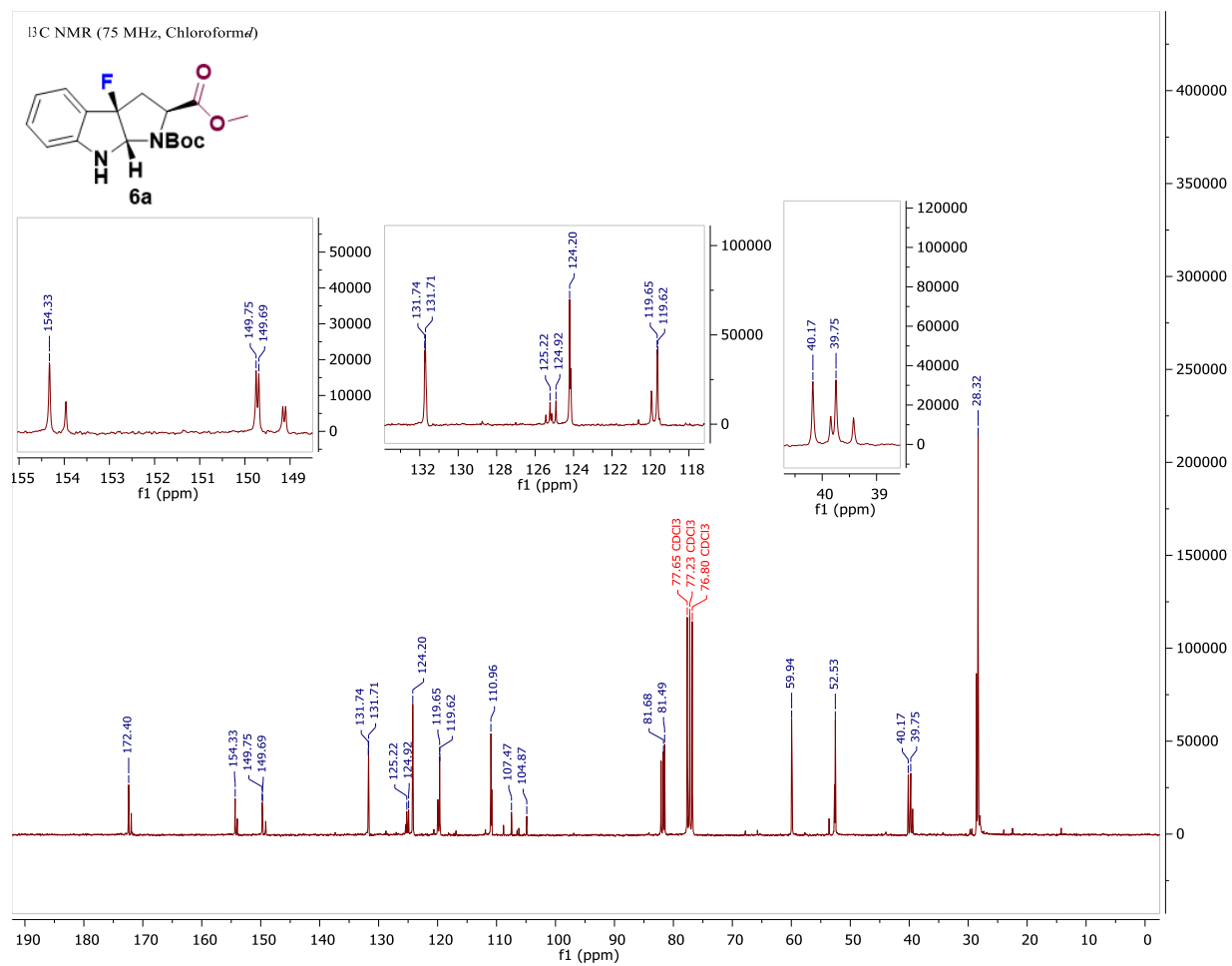
**<sup>19</sup>F NMR** (282 MHz, Chloroform-*d*, ref. CFCl<sub>3</sub> = 0 ppm) major diastereomer and rotamers, *syn-cis* δ (ppm) -138.68 (q, *J* = 21.0 Hz), -139.09 (q, *J* = 19.0 Hz).

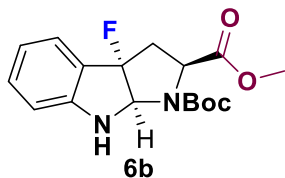
**<sup>13</sup>C NMR** (75 MHz, Chloroform-*d*) major diastereomer and major rotamer, *syn-cis* δ (ppm) 28.32, 39.96 (d, *J* = 32.1 Hz), 52.53, 59.94, 81.58 (d, *J* = 14.5 Hz), 106.17 (d, *J* = 195.9 Hz), 110.96, 119.64 (d, *J* = 2.4 Hz), 124.20, 125.07 (d, *J* = 23.3 Hz), 131.72 (d, *J* = 2.9 Hz), 149.72 (d, *J* = 4.6 Hz), 154.33, 172.40.

**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 359.1383; found 359.1376 for C<sub>17</sub>H<sub>21</sub>FN<sub>2</sub>O<sub>4</sub>Na.

**TLC** (ethyl acetate:hexane 6:4 v/v): R<sub>f</sub> = 0.75 (UV, I<sub>2</sub>, p-anisaldehyde).







**$^1\text{H}$  NMR** (300 MHz, Chloroform-*d*) minor diastereomer and rotamers, *anti-cis*  $\delta$  (ppm) 7.35 – 7.17 (m, 2H), 6.78 (ddt,  $J$  = 21.6, 15.4, 7.6 Hz, 2H), 5.58 - 5.46(m, 1H), 4.69 (ddd,  $J$  = 42.6, 9.0, 2.4 Hz, 1H), 3.32 (s, 3H), 3.12 – 2.72 (m, 2H), 1.59, 1.46 (s, 9H).

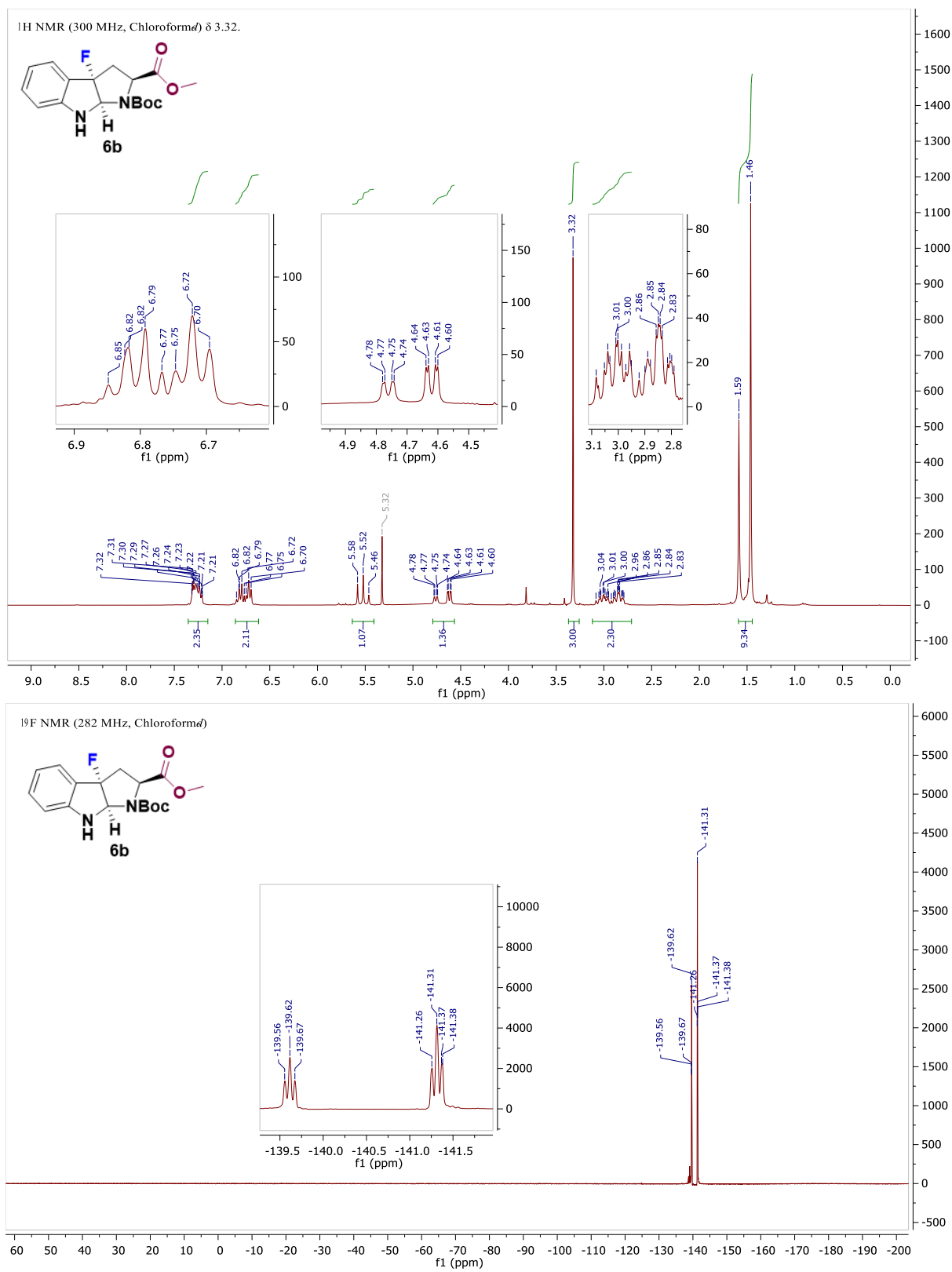
**$^{19}\text{F}$  NMR** (282 MHz, Chloroform-*d*, ref.  $\text{CFCl}_3$  = 0 ppm) minor diastereomer and rotamers, *anti-cis*  $\delta$  (ppm) -139.61 (t,  $J$  = 16.6 Hz), -141.11 – -141.87 (m).

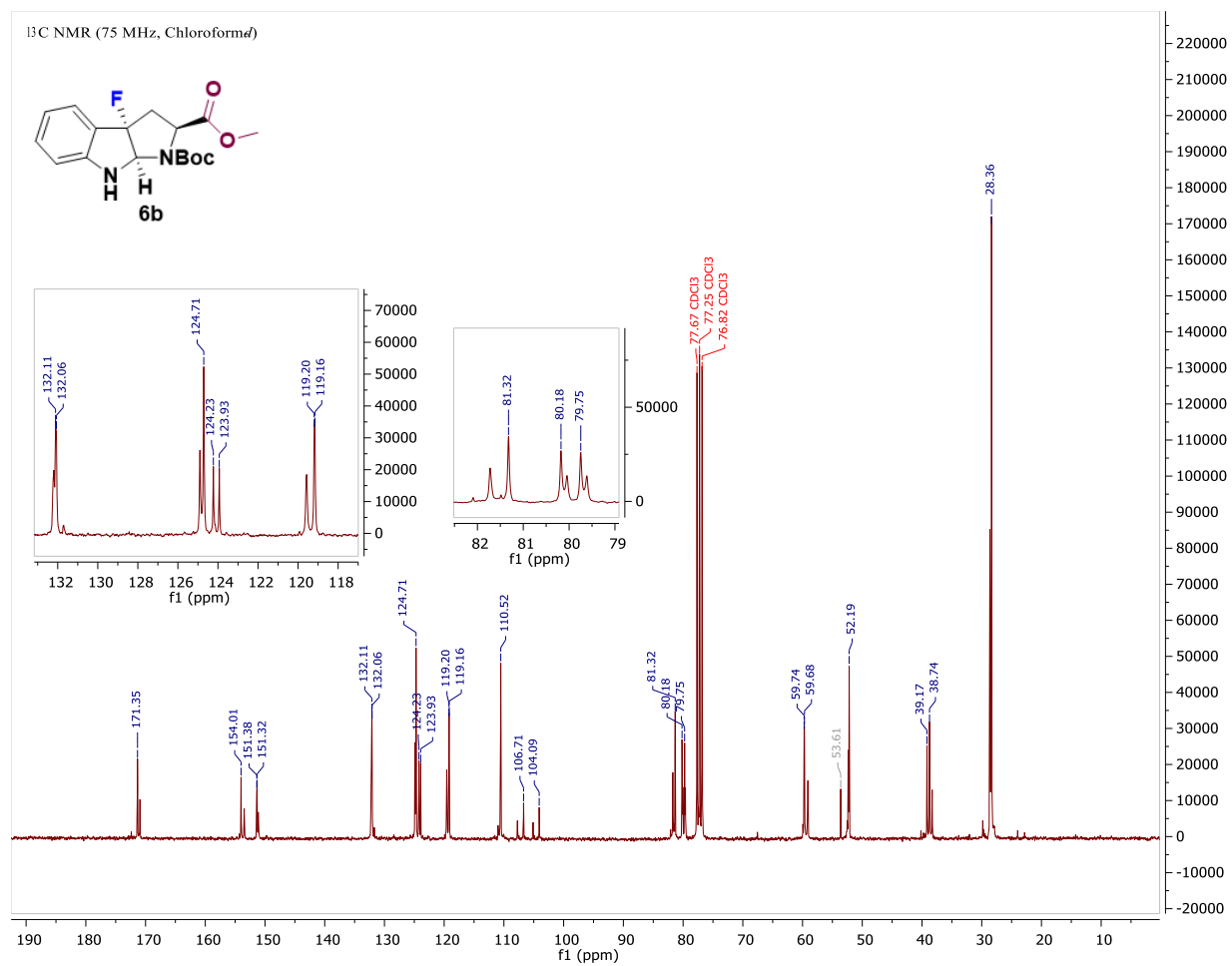
**$^{13}\text{C}$  NMR** (75 MHz, Chloroform-*d*) minor diastereomer and major rotamer, *anti-cis*  $\delta$  (ppm) 28.36, 38.95 (d,  $J$  = 32.2 Hz), 52.19, 59.71 (d,  $J$  = 4.5 Hz), 79.96 (d,  $J$  = 32.6 Hz), 81.32, 105.40 (d,  $J$  = 197.4 Hz), 110.52, 119.18 (d,  $J$  = 2.9 Hz), 123.93, 124.08 (d,  $J$  = 22.4 Hz), 132.09 (d,  $J$  = 3.3 Hz), 151.35 (d,  $J$  = 4.3 Hz), 154.01, 171.35.

**HRMS** (ESI-TOF,  $m/z$ ):  $[\text{M}+\text{Na}]^+$  calculated 359.1383; found 359.1386 for  $\text{C}_{17}\text{H}_{21}\text{FN}_2\text{O}_4\text{Na}$ .

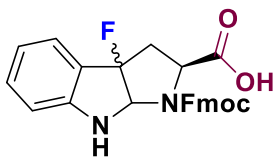
**TLC** (ethyl acetate:hexane 6:4 v/v):  $R_f$  = 0.7 (UV,  $\text{I}_2$ , p-anisaldehyde).







## Synthesis and characterization of compound **7a,b**



**7a,b** (1.2:1)<sup>c</sup> **85 %**

**Chemical Formula:** C<sub>26</sub>H<sub>21</sub>FN<sub>2</sub>O<sub>4</sub>

**Exact Mass:** 444.15

**Molecular Weight:** 444.46

**(2S)-1-(((9H-fluoren-9-yl)methoxy)carbonyl)-3a-fluoro-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylic acid, N-Fmoc-FPI-OH (**7a,b**).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-Trp-OH (1.0 equiv, 300 mg, 7.04 mmol) dissolved in 8.0 mL of anhydrous DCM. To this solution, added 1-fluoro-2,4,6-trimethylpyridinium triflate (1.8 equiv, 367 mg, 1.27 mmol) in 2.0 mL of anhydrous DCM. The reaction contents were stirred for 3 h at 21 °C and the reaction progress was monitored by TLC. Upon completion, the crude (light yellow/orange, clear) was concentrated under reduced pressure and immediately purified using silica gel flash column chromatography (gradient elution, 0.5:99.5 to 6:94 methanol/DCM) to obtain 266 mg (0.598 mmol) of **7a,b** as a light orange solid in 85 % isolated yield. <sup>19</sup>F-NMR spectroscopy on the crude reaction was used to determine the diastereomeric ratio (*syn-cis:anti-cis*) of 1.2:1.

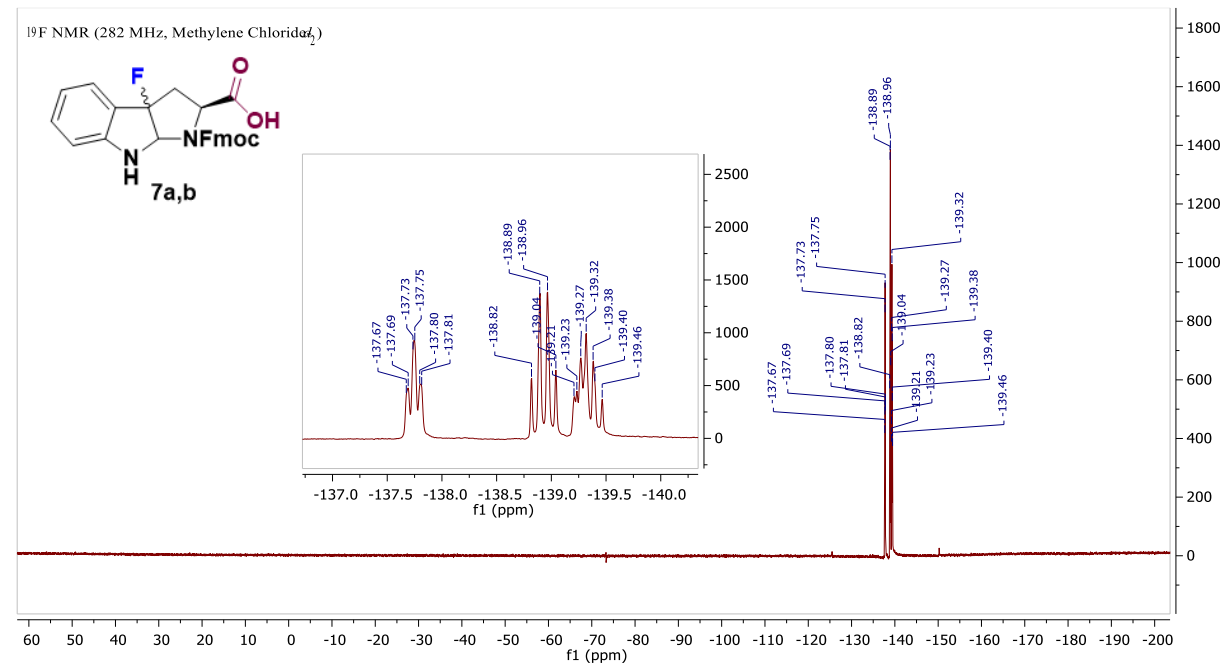
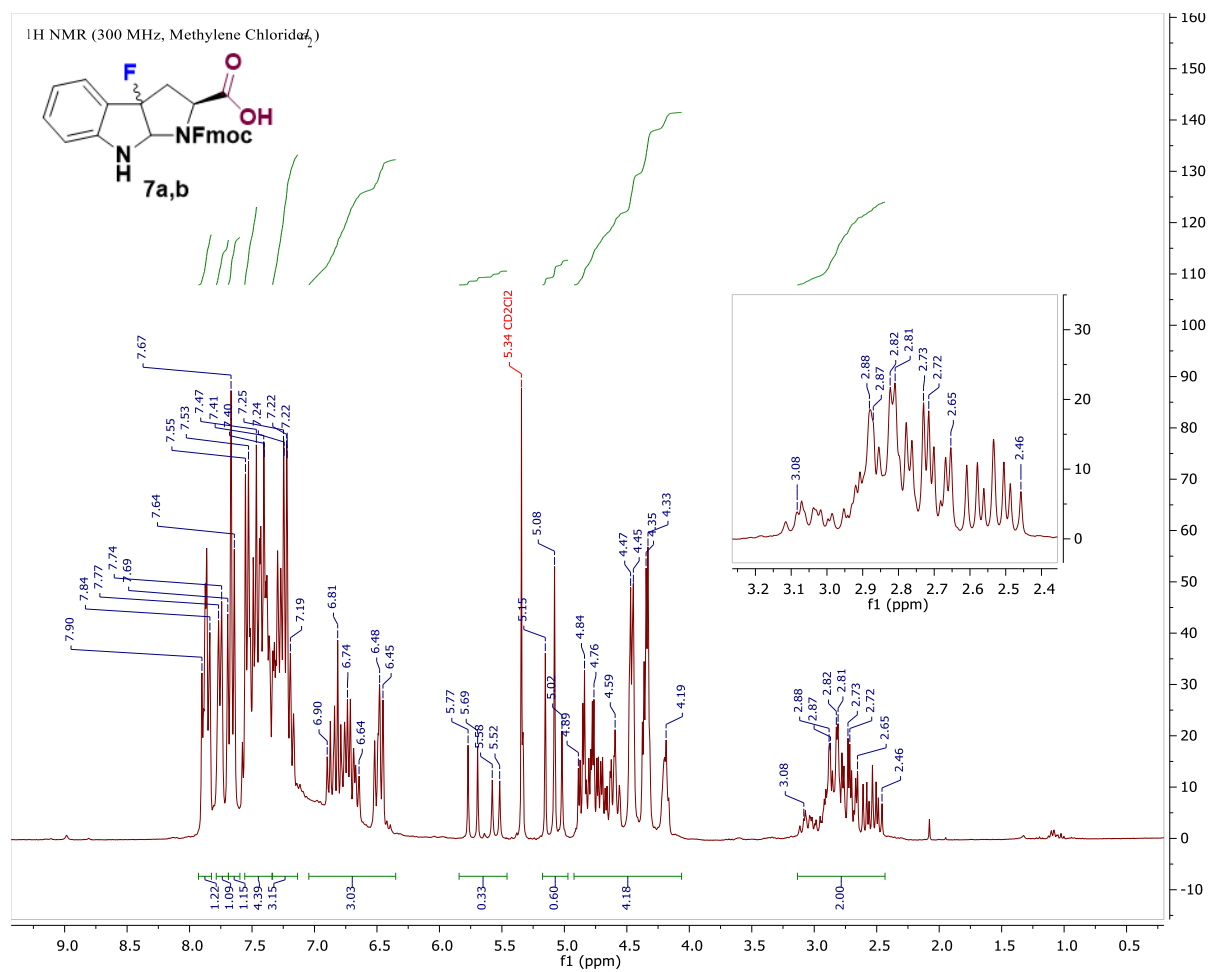
**<sup>1</sup>H NMR** (300 MHz, Methylene Chloride-*d*<sub>2</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1.2:1), δ (ppm) 7.87 (td, *J* = 7.9, 2.9 Hz, 1H), 7.79 – 7.69 (m, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.56 – 7.34 (m, 4H), 7.34 – 7.14 (m, 3H), 7.05 – 6.35 (m, 3H), 5.80 – 5.50 (m, 0H), 5.17 – 4.97 (m, 1H), 4.92 – 4.06 (m, 4H), 3.13 – 2.43 (m, 2H).

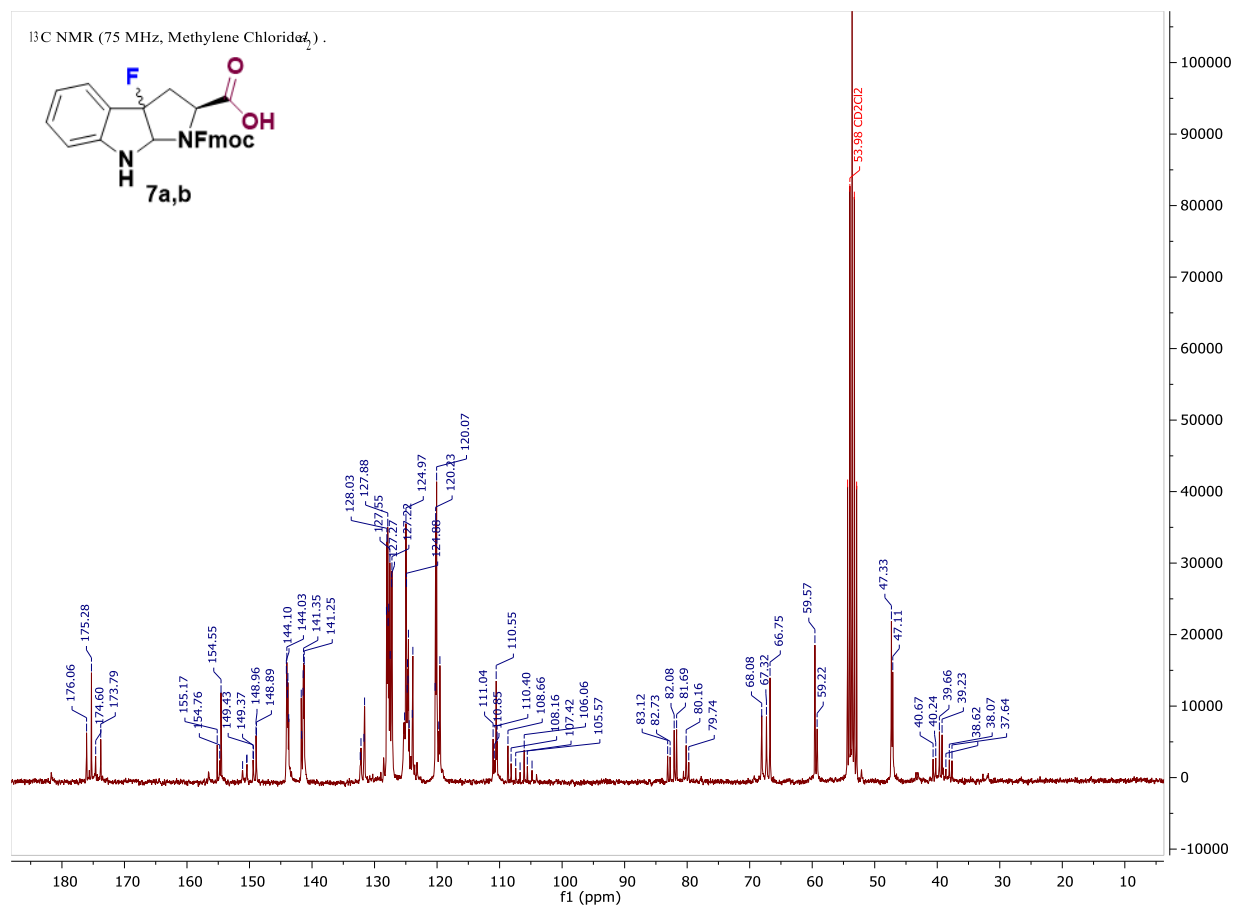
**<sup>19</sup>F NMR** (282 MHz, Methylene Chloride-*d*<sub>2</sub>, ref. CFCl<sub>3</sub> = 0 ppm) two diastereomers and rotamers, *syn-cis:anti-cis* (1.2:1), δ (ppm) -137.74 (td, *J* = 17.5, 5.0 Hz), -138.82, -138.88 – -139.13 (m), -139.32 (tt, *J* = 23.5, 13.1 Hz).

**<sup>13</sup>C NMR** (75 MHz, Methylene Chloride-*d*<sub>2</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1.2:1) due to the complexity of the spectrum, C-F couplings were could not be determined, δ (ppm) 37.64, 38.07, 38.62, 39.23, 39.66, 40.24, 40.67, 47.11, 47.33, 59.22, 59.57, 66.75, 67.32, 68.08, 79.74, 80.16, 81.69, 82.08, 82.73, 83.12, 104.81, 105.57, 106.06, 106.72, 107.42, 108.16, 108.66, 110.40, 110.55, 110.85, 111.04, 119.55, 119.73, 120.07, 120.23, 120.31, 123.87, 123.96, 124.46, 124.58, 124.66, 124.73, 124.78, 124.88, 124.97, 125.20, 127.22, 127.27, 127.50, 127.55, 127.73, 127.83, 127.88, 128.03, 128.10, 131.60, 131.70, 132.17, 132.29, 141.25, 141.35, 141.41, 141.44, 141.66, 141.73, 143.73, 143.86, 143.94, 143.98, 144.03, 144.10, 148.89, 148.96, 149.37, 149.43, 150.41, 150.45, 151.10, 154.55, 154.76, 155.17, 173.79, 174.60, 175.28, 176.06.

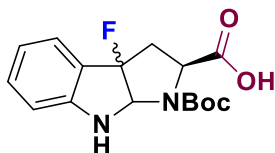
**HRMS** (ESI-TOF, *m/z*): [M+H]<sup>+</sup> calculated 445.1564; found 445.1549 for C<sub>26</sub>H<sub>22</sub>FN<sub>2</sub>O<sub>4</sub>.

**TLC** (acetic acid:methanol:DCM 0.1:5:95.9 v/v): R<sub>f</sub> = 0.7 (UV, I<sub>2</sub>, bromocresol green).





## Synthesis and characterization of compound **8a,b**



**8a,b** (1.1:1)<sup>c</sup> 74 %

**Chemical Formula:** C<sub>16</sub>H<sub>19</sub>FN<sub>2</sub>O<sub>4</sub>

**Exact Mass:** 322.13

**Molecular Weight:** 322.34

**(2S)-1-(tert-butoxycarbonyl)-3a-fluoro-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylic acid, N-Boc-FPI-OH (**8a,b**).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-Trp-OH (1.0 equiv, 150 mg, 0.493 mmol) dissolved in 6.0 mL of anhydrous DCM. To this solution, added 1-fluoro-2,4,6-trimethylpyridinium triflate (1.8 equiv, 257 mg, 0.89 mmol) in 1.0 mL of anhydrous DCM. The reaction contents were stirred for 3 h at 21 °C and the reaction progress was monitored by TLC. Upon completion, the crude (light orange-brown, clear) was concentrated under reduced pressure and immediately purified using silica gel flash column chromatography (gradient elution, 0.2:99.8 to 5:95 methanol:chloroform) to obtain 118 mg (0.365 mmol) of **8a,b** as a beige solid in 74 % isolated yield. <sup>19</sup>F-NMR spectroscopy on the crude reaction was used to determine the diastereomeric ratio (*syn-cis:anti-cis*) of 1.1:1.

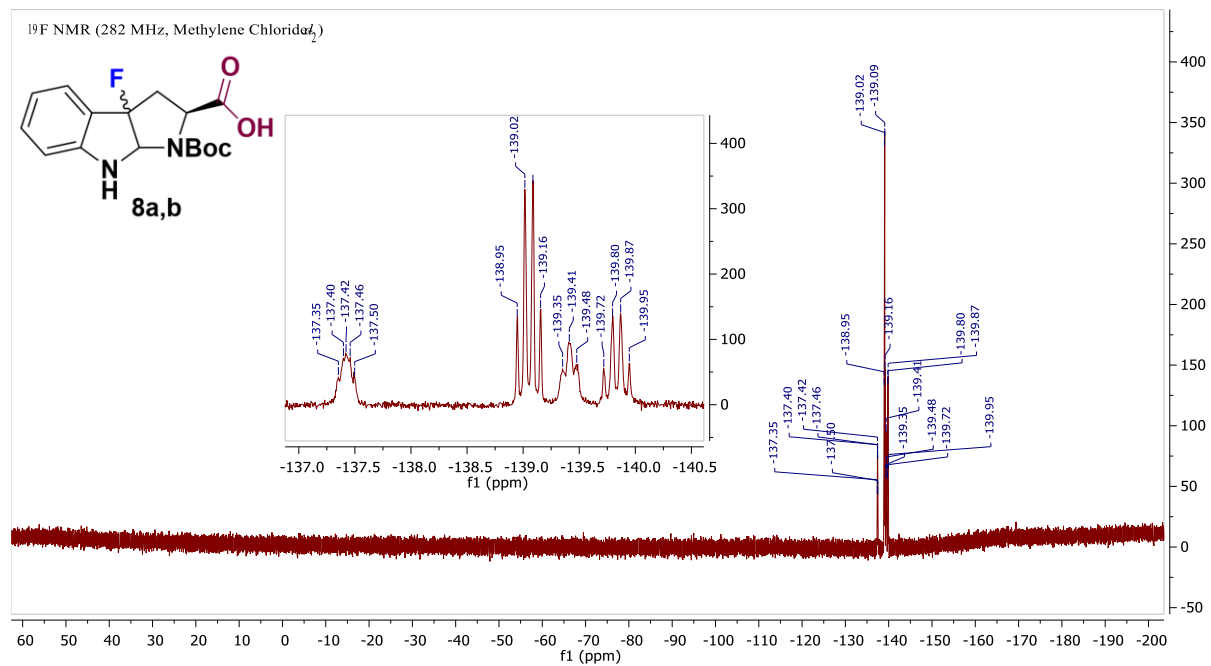
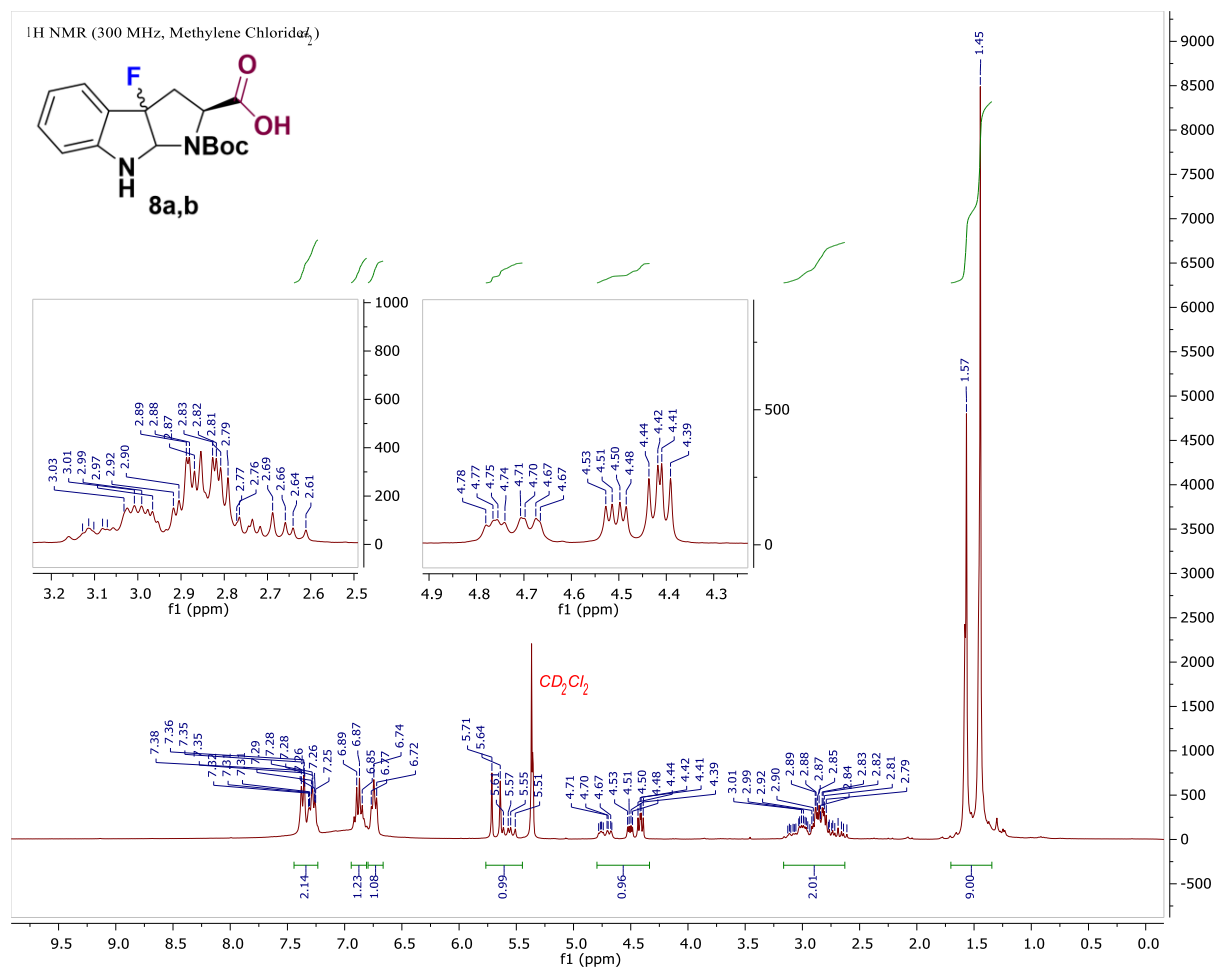
**<sup>1</sup>H NMR** (300 MHz, Methylene Chloride-*d*<sub>2</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1.4:1), δ (ppm) 7.44 – 7.23 (m, 2H), 6.87 (t, *J* = 7.2 Hz, 1H), 6.74 (t, *J* = 7.1 Hz, 1H), 5.77 – 5.45 (m, 1H), 4.80 – 4.34 (m, 1H), 3.16 – 2.63 (m, 2H), 1.51 (d, *J* = 36.4 Hz, 9H).

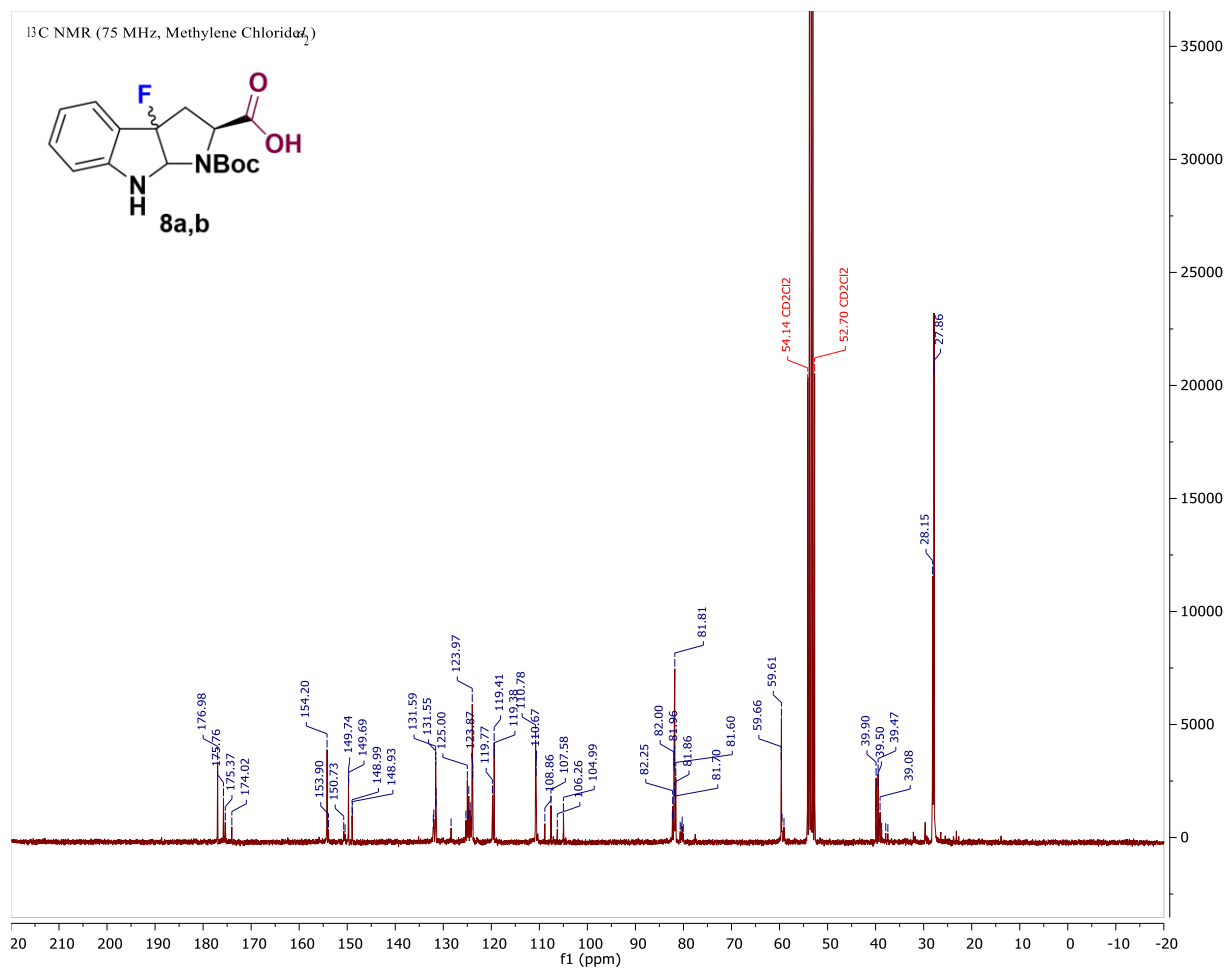
**<sup>19</sup>F NMR** (282 MHz, Methylene Chloride-*d*<sub>2</sub>, ref. CFCl<sub>3</sub> = 0 ppm) two diastereomers and rotamers, *syn-cis:anti-cis* (1.4:1), δ (ppm) -137.43 (dt, *J* = 21.6, 12.0 Hz), -139.05 (q, *J* = 19.3 Hz), -139.25 – -139.57 (m), -139.83 (q, *J* = 22.0 Hz).

**<sup>13</sup>C NMR** (75 MHz, Methylene Chloride-*d*<sub>2</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1.4:1), due to the complexity of the spectrum, C-F couplings could not be determined, δ (ppm) 27.86, 28.15, 37.45, 37.89, 38.75, 39.08, 39.17, 39.47, 39.50, 39.90, 59.08, 59.49, 59.61, 59.66, 80.04, 80.27, 80.47, 80.69, 81.60, 81.70, 81.81, 81.86, 81.96, 82.00, 82.25, 82.32, 104.99, 106.26, 107.58, 108.86, 110.67, 110.78, 119.38, 119.41, 119.74, 119.77, 123.87, 123.97, 124.15, 124.40, 124.69, 124.79, 125.00, 125.30, 128.38, 131.48, 131.51, 131.55, 131.59, 131.97, 132.08, 148.93, 148.99, 149.69, 149.74, 150.45, 150.73, 153.90, 154.20, 174.02, 175.37, 175.76, 176.98.

**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 345.1227; found 345.1233 for C<sub>16</sub>H<sub>19</sub>FN<sub>2</sub>O<sub>4</sub>Na.

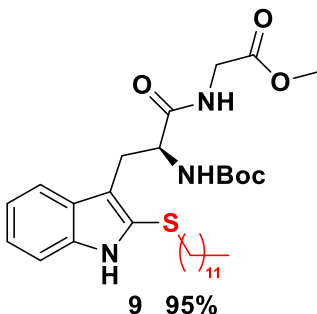
**TLC** (acetic acid:methanol:DCM, 0.1:6:93.9 v/v): R<sub>f</sub> = 0.65 (UV, I<sub>2</sub>, bromocresol green).







## Synthesis and characterization of compound **9**



Chemical Formula: C<sub>31</sub>H<sub>49</sub>N<sub>3</sub>O<sub>5</sub>S

Exact Mass: 575.34

Molecular Weight: 575.81

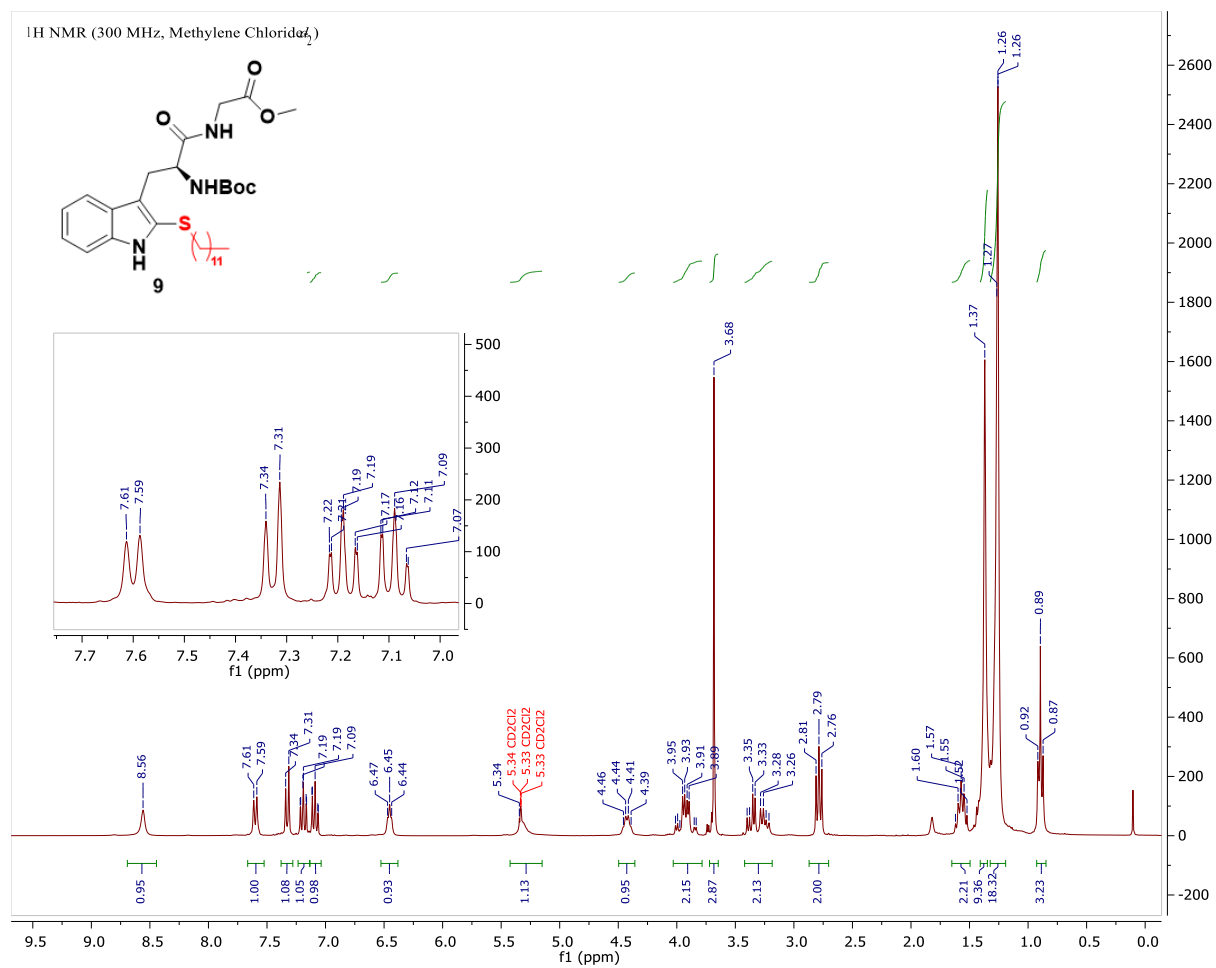
**Methyl (S)-2-(((tert-butoxycarbonyl)amino)-3-(2-(dodecylthio)-1H-indol-3-yl)propanoyl)glycinate (**9**).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-FPI-Gly-OMe (**4a,b**, 1 equiv, 35 mg, 0.089 mmol) in 1.42 mL of anhydrous DCM, followed by 1-dodecanethiol (2.5 equiv, 44.9 mg, 53.2  $\mu$ L, 0.222 mmol) and 0.36 mL of HFIP. The reaction contents were stirred for 30 min at 21°C. Upon completion, the crude (light yellow, clear) was concentrated under reduced pressure. The crude was purified by silica gel flash column chromatography (gradient elution, 9:1 to 8:2 petroleum ether/ethyl acetate) to obtain 49 mg (0.085 mmol) of **9** as a beige solid in 95 % yield.

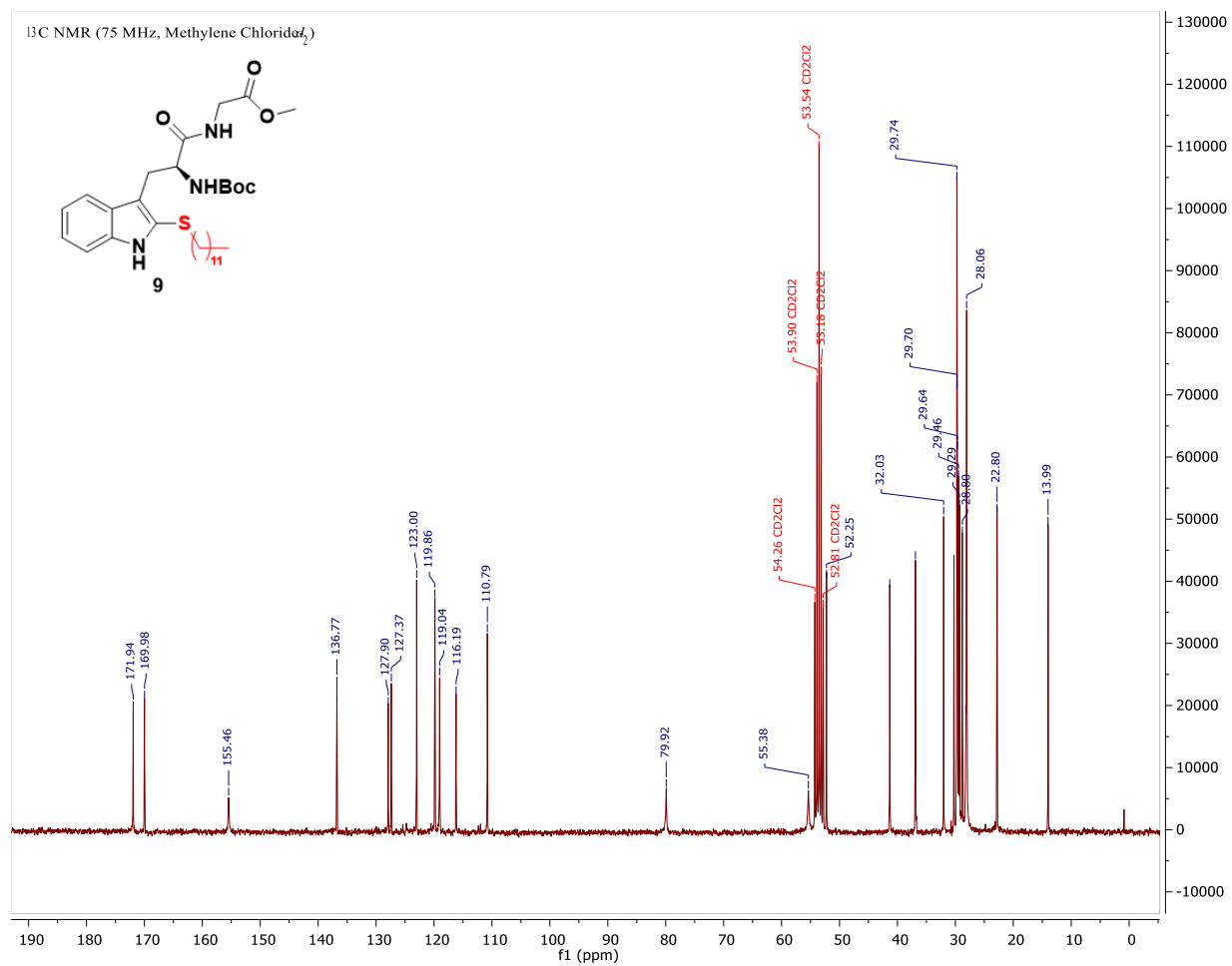
**<sup>1</sup>H NMR** (300 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  (ppm) 8.56 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.23 – 7.13 (m, 1H), 7.13 – 7.04 (m, 1H), 6.45 (t, *J* = 5.2 Hz, 1H), 5.34 (s, 1H), 4.42 (q, *J* = 7.0, 6.3 Hz, 1H), 4.03 – 3.78 (m, 2H), 3.68 (s, 3H), 3.42 – 3.19 (m, 2H), 2.87 – 2.70 (m, 2H), 1.57 (p, *J* = 7.5, 7.0 Hz, 2H), 1.37 (s, 9H), 1.32 – 1.19 (m, 18H), 0.93 – 0.85 (m, 3H).

**<sup>13</sup>C NMR** (75 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  (ppm) 13.99, 22.80, 28.06, 28.19, 28.80, 29.29, 29.46, 29.64, 29.70, 29.74, 30.25, 32.03, 36.90, 41.33, 52.25, 55.38, 79.92, 110.79, 116.19, 119.04, 119.86, 123.00, 127.37, 127.90, 136.77, 155.46, 169.98, 171.94.

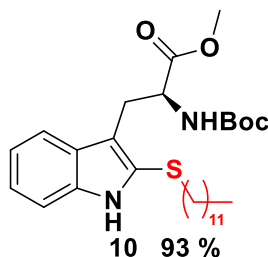
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 598.3291; found 598.3293 for C<sub>31</sub>H<sub>49</sub>N<sub>3</sub>O<sub>5</sub>SNa.

**TLC** (petroleum ether:ethyl acetate 8:2 v/v): R<sub>f</sub> = 0.5 (UV, I<sub>2</sub>, potassium permanganate).





## Synthesis and characterization of compound **10**



**Chemical Formula:** C<sub>29</sub>H<sub>46</sub>N<sub>2</sub>O<sub>4</sub>S

**Exact Mass:** 518.3178

**Molecular Weight:** 518.7570

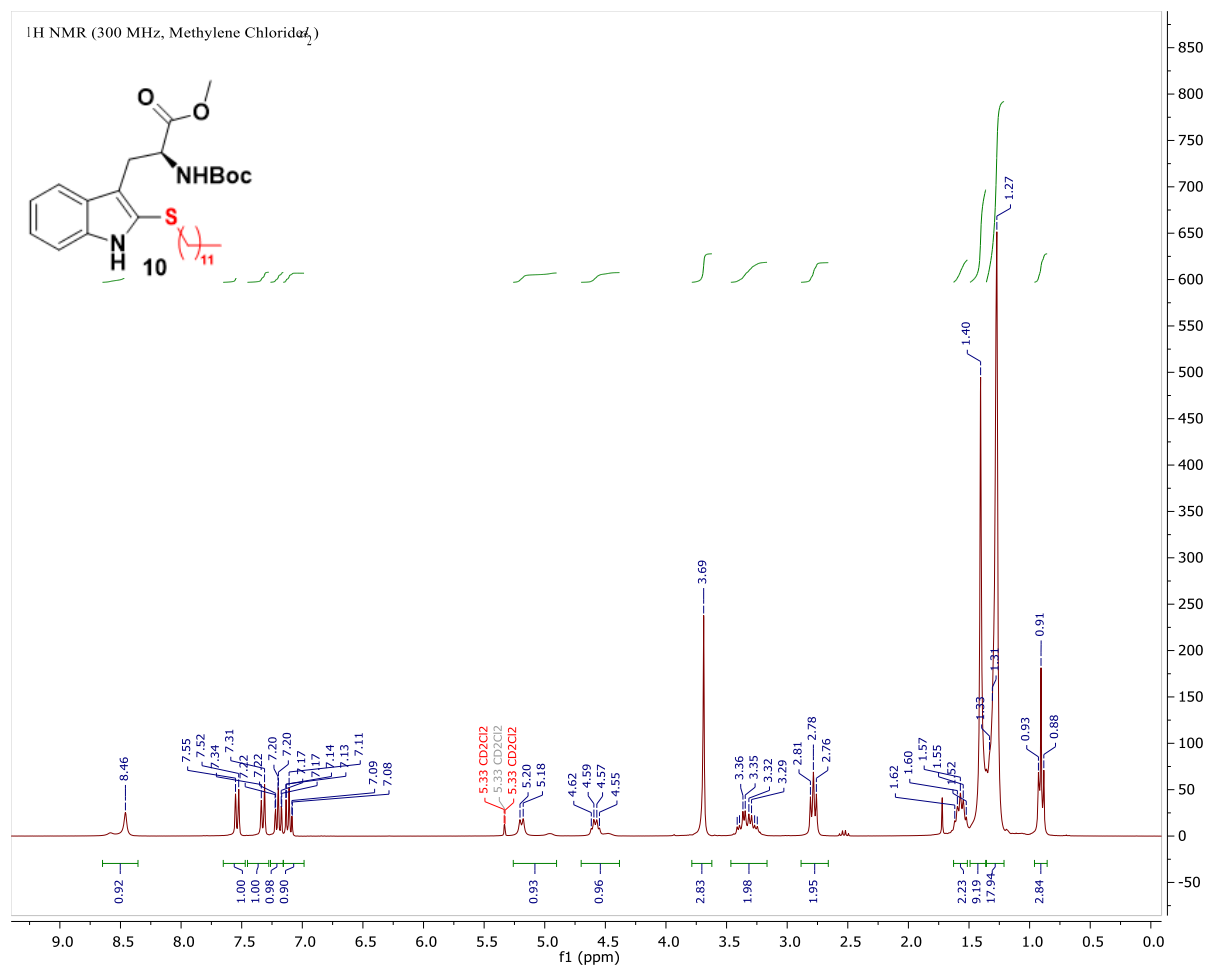
**Methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(2-(dodecylthio)-1H-indol-3-yl)propanoate (10).** A flame-dried round bottom flask was charged with N-Boc-FPI-OMe (**6a,b**, 1 equiv, 100 mg, 0.30 mmol) in 4.1 mL of anhydrous DCM, followed by 1-dodecanethiol (2.5 equiv, 150 mg, 178  $\mu$ L, 0.74 mmol) and 1.8 mL of HFIP. The reaction contents were stirred for 30 min at 21 °C. Upon completion, the crude reaction mixture (light yellow, clear) was concentrated under reduced pressure. The concentrate was purified by silica gel flash column chromatography (isocratic elution, 1:9 ethyl acetate/hexane) to obtain 143 mg (0.28 mmol) of **10** as a white solid in 93 % yield.

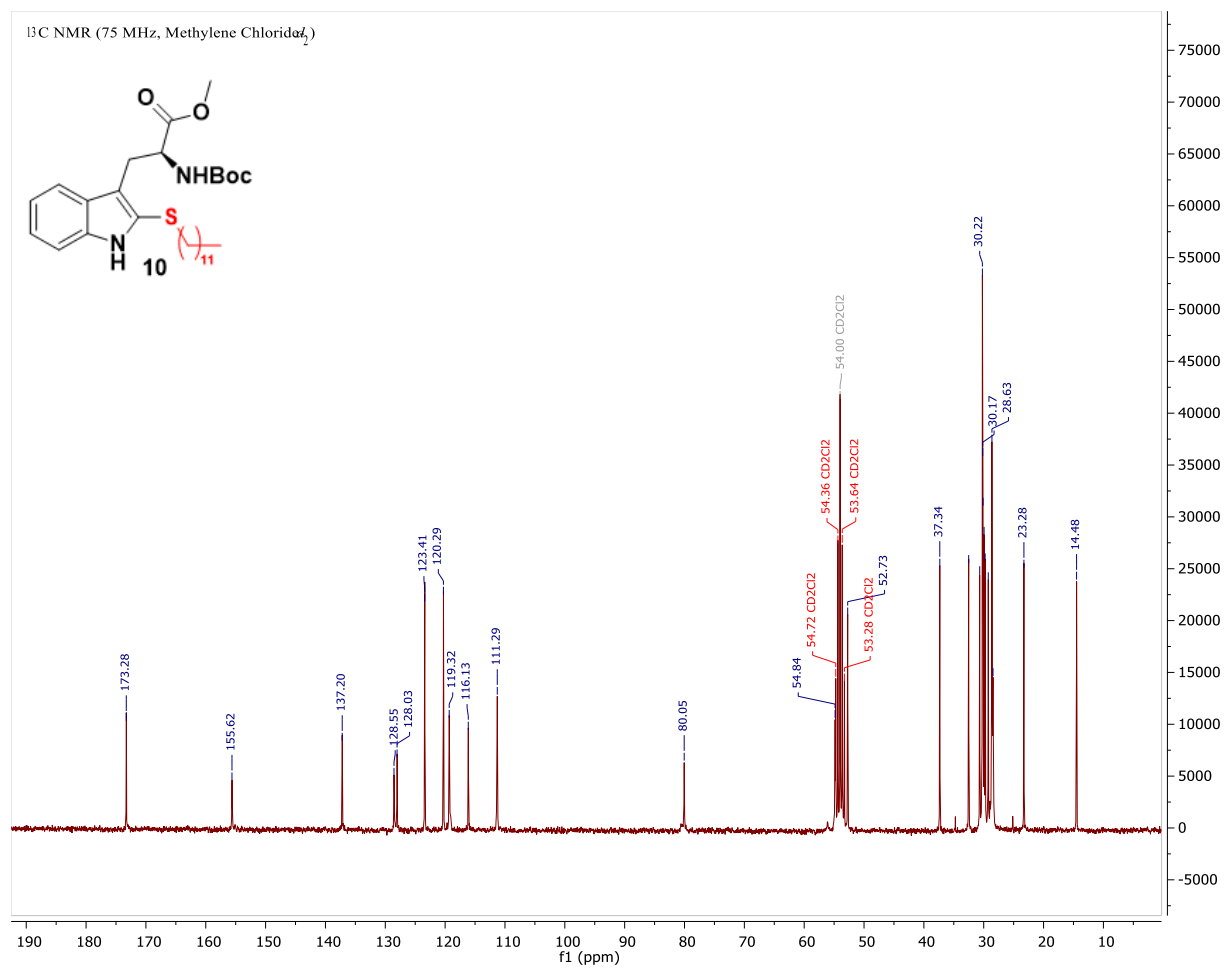
**<sup>1</sup>H NMR** (300 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  (ppm) 8.46 (br s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.26 – 7.16 (m, 1H), 7.16 – 6.99 (m, 1H), 5.19 (br d, *J* = 7.9 Hz, 1H), 4.58 (q, *J* = 6.4 Hz, 1H), 3.69 (s, 3H), 3.33 (tq, *J* = 14.2, 6.6, 6.2 Hz, 2H), 2.78 (t, *J* = 7.4 Hz, 2H), 1.62 – 1.52 (m, 2H), 1.40 (s, 9H), 1.33 – 1.27 (m, 18H), 0.91 (t, *J* = 6.7 Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  (ppm) 14.48, 23.28, 28.45, 28.63, 29.24, 29.76, 29.94, 30.11, 30.17, 30.22, 30.67, 32.51, 37.34, 52.73, 54.84, 80.05, 111.30, 116.13, 119.32, 120.29, 123.41, 128.03, 128.55, 137.20, 155.62, 173.28.

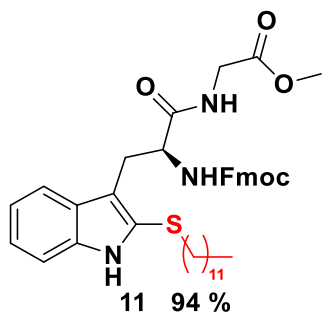
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 518.3178; found 518.3179 for C<sub>29</sub>H<sub>46</sub>N<sub>2</sub>O<sub>4</sub>SNa.

**TLC** (ethyl acetate:hexane 1:2 v/v): R<sub>f</sub> = 0.7 (UV, I<sub>2</sub>, potassium permanganate).





## Synthesis and characterization of compound **11**



**Chemical Formula:** C<sub>41</sub>H<sub>51</sub>N<sub>3</sub>O<sub>5</sub>S

**Exact Mass:** 697.3549

**Molecular Weight:** 697.9350

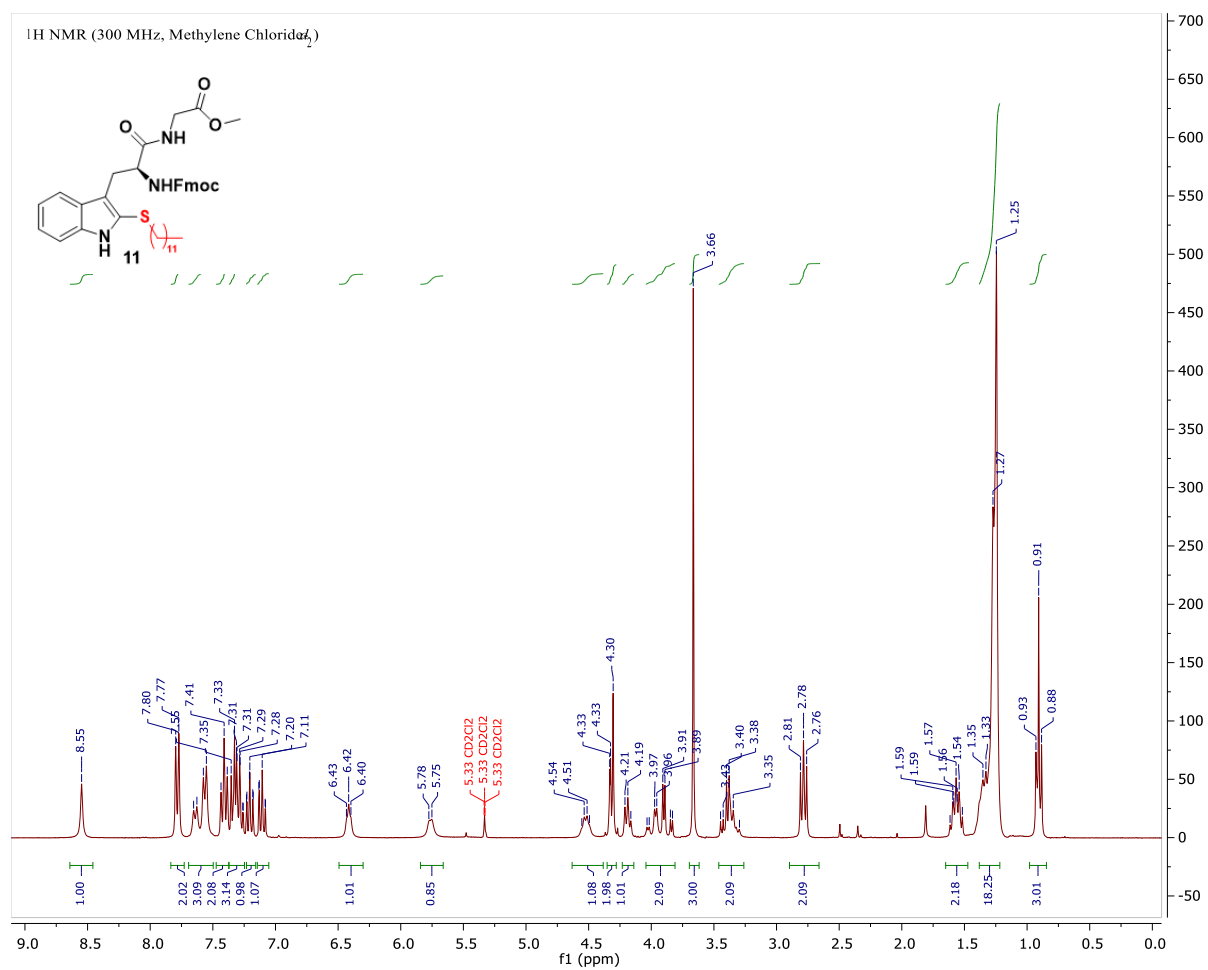
**Methyl (S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(2-(dodecylthio)-1H-indol-3-yl)propanoyl)glycinate (**11**).** A flame-dried round bottom flask was charged with N-Fmoc-FPI-Gly-OMe (**3a,b**, 1 equiv, 78 mg, 0.15 mmol) in 2.1 mL of anhydrous DCM, followed by 1-dodecanethiol (2.5 equiv, 76.6 mg, 90  $\mu$ L, 0.38 mmol) and 0.9 mL of HFIP. The reaction contents were stirred for 30 min at 21°C. Upon completion, the crude reaction mixture (light yellow, clear) was concentrated under reduced pressure. The concentrate was purified by silica gel flash column chromatography (gradient elution, 3:7 to 4.5:5.5 ethyl acetate/hexane) to obtain 98 mg (0.085 mmol) of **11** as a white solid in 94 % yield.

**<sup>1</sup>H NMR** (300 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  (ppm) 8.55 (br s, 1H), 7.78 (d, *J* = 7.5 Hz, 2H), 7.60 (dd, *J* = 23.0, 7.6 Hz, 3H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.37 – 7.25 (m, 3H), 7.23 – 7.16 (m, 1H), 7.15 – 7.05 (m, 1H), 6.42 (br t, *J* = 5.4 Hz, 1H), 5.76 (br d, *J* = 7.3 Hz, 1H), 4.52 (q, *J* = 5.7 Hz, 1H), 4.35 – 4.28 (m, 2H), 4.19 (t, *J* = 7.0 Hz, 1H), 3.93 (qd, *J* = 18.2, 5.1 Hz, 2H), 3.66 (s, 3H), 3.46 – 3.26 (m, 2H), 2.78 (t, *J* = 7.5 Hz, 2H), 1.65 – 1.47 (m, 2H), 1.37 – 1.25 (m, 18H), 0.98 – 0.85 (t, *J* = 6.5 Hz, 3H).

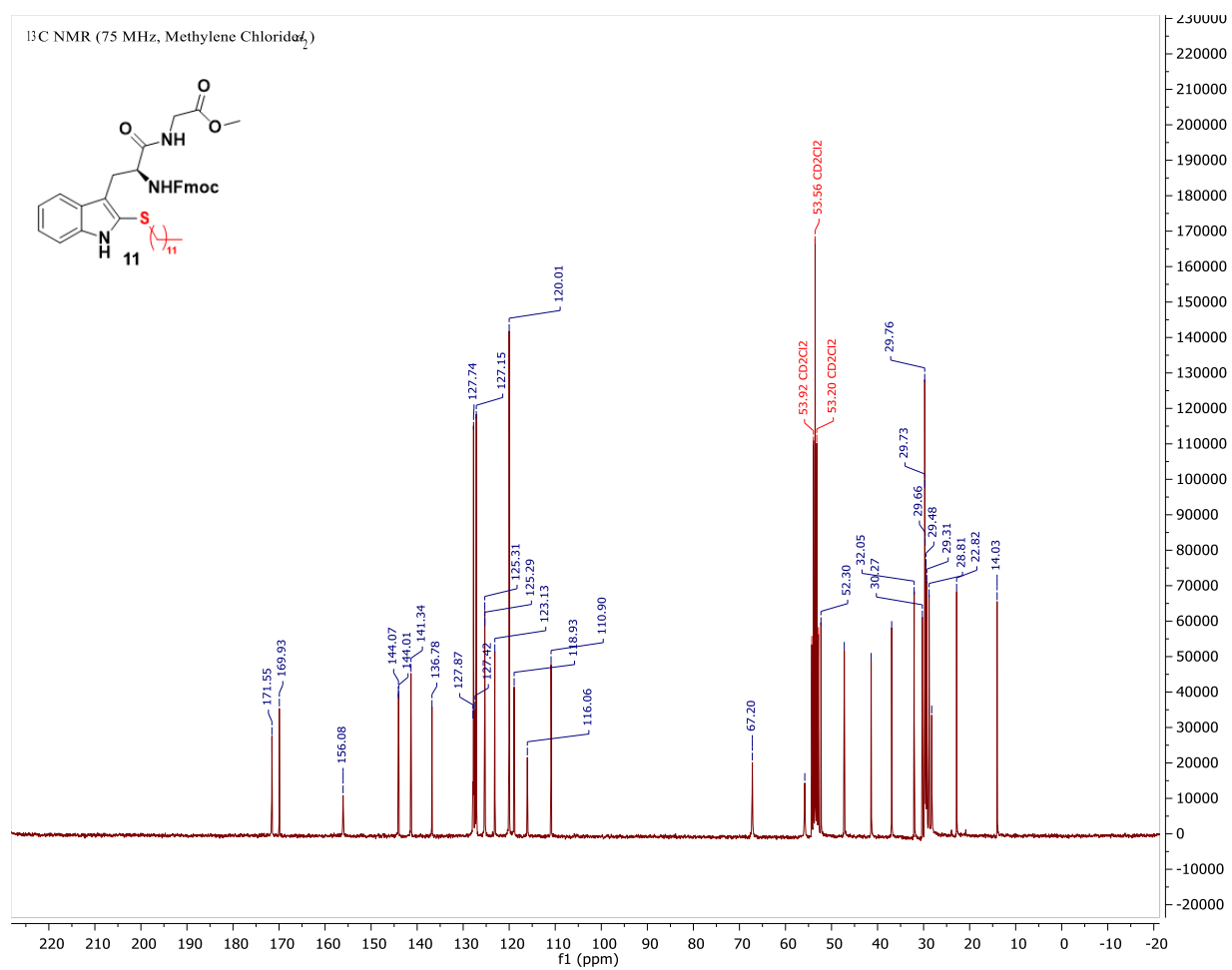
**<sup>13</sup>C NMR** (75 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  (ppm) 14.03, 22.82, 28.24, 28.81, 29.31, 29.48, 29.66, 29.73, 29.76, 30.27, 32.05, 36.93, 41.39, 47.23, 52.30, 55.81, 67.20, 110.90, 116.06, 118.93, 120.01, 123.13, 125.29, 125.31, 127.15, 127.42, 127.74, 127.87, 136.78, 141.34, 144.01, 144.07, 156.08, 169.93, 171.55.

**HRMS** (ESI-TOF, *m/z*): [M+H]<sup>+</sup> calculated 687.3549; found 697.3552 for C<sub>41</sub>H<sub>52</sub>N<sub>3</sub>O<sub>5</sub>S.

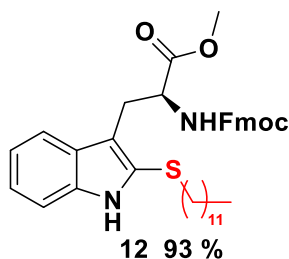
**TLC** (ethyl acetate:hexane 3:7 v/v): R<sub>f</sub> = 0.4 (UV, I<sub>2</sub>, potassium permanganate).







## Synthesis and characterization of compound **12**



**Chemical Formula:** C<sub>39</sub>H<sub>48</sub>N<sub>2</sub>O<sub>4</sub>S

**Exact Mass:** 640.33

**Molecular Weight:** 640.88

### **Methyl (S)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(2-(dodecylthio)-1H-indol-3-yl)propanoate (**12**).**

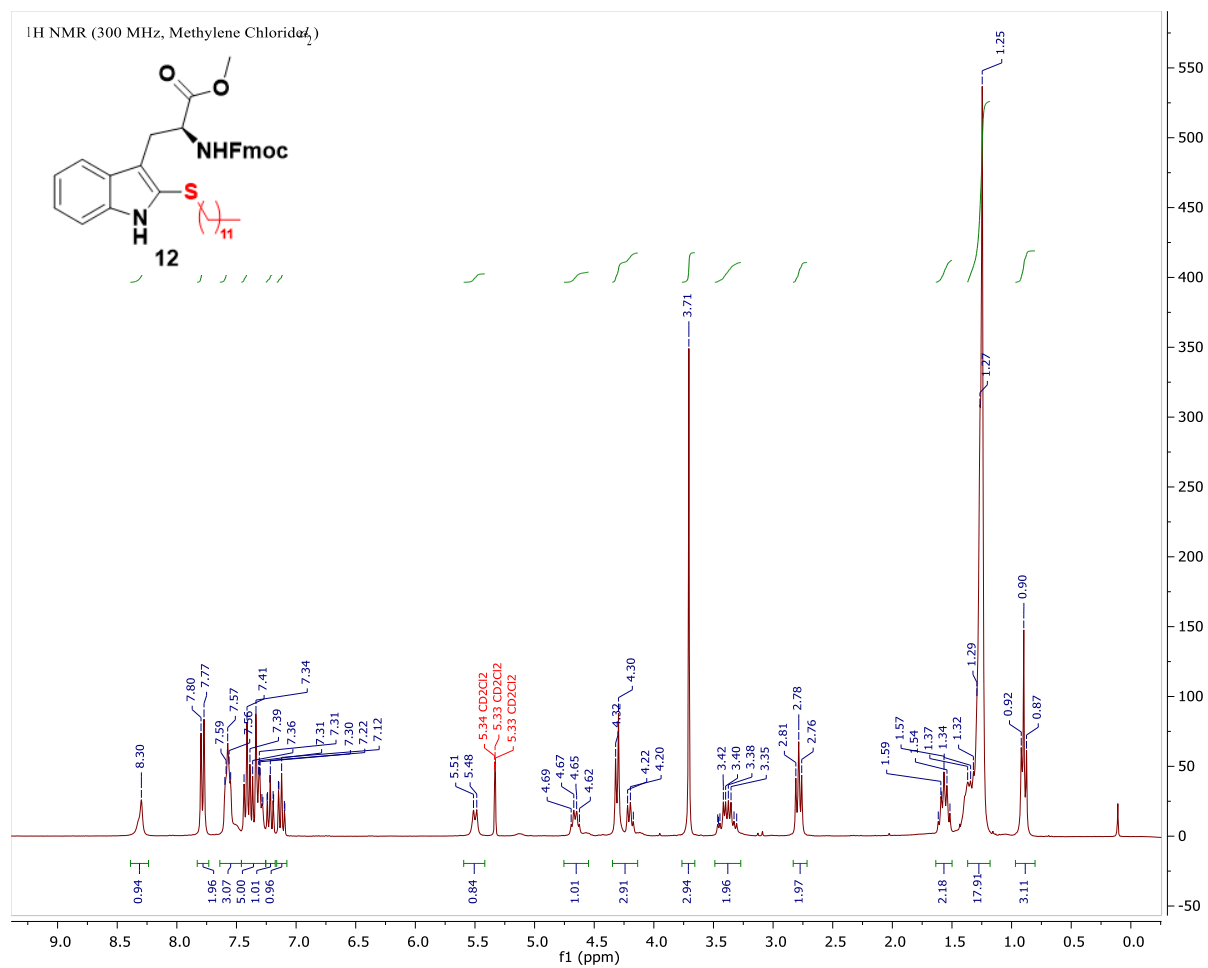
A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 100 mg, 0.22 mmol) in 2.5 mL of anhydrous DCM, followed by 1-dodecanethiol (2.5 equiv, 110 mg, 131  $\mu$ L, 0.55 mmol) and 0.62 mL of HFIP. The reaction contents were stirred for 30 min at 21 °C. Upon completion, the crude (yellow, clear) was concentrated under reduced pressure. The crude was purified by silica gel flash column chromatography (gradient elution, 9:1 to 8:2 petroleum ether/ethyl acetate) to obtain 130 mg (0.20 mmol) of **12** as a light yellow solid in 93 % yield.

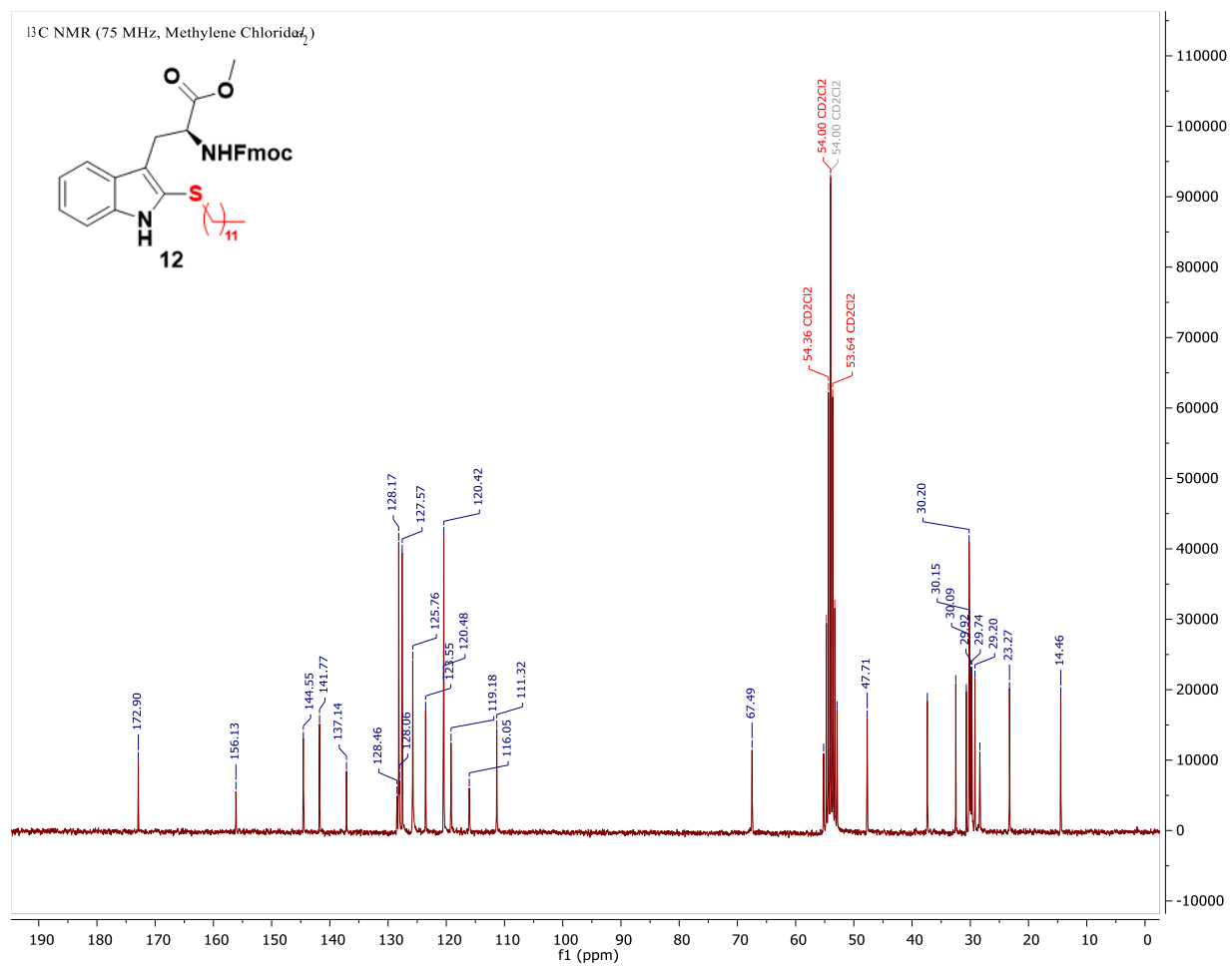
**<sup>1</sup>H NMR** (300 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  (ppm) 8.30 (s, 1H), 7.78 (d, *J* = 7.5 Hz, 2H), 7.64 – 7.46 (m, 3H), 7.46 – 7.26 (m, 5H), 7.25 – 7.18 (m, 1H), 7.16 – 7.08 (m, 1H), 5.50 (d, *J* = 8.3 Hz, 1H), 4.66 (q, *J* = 6.8 Hz, 1H), 4.35 – 4.14 (m, 3H), 3.71 (s, 3H), 3.39 (qd, *J* = 14.3, 6.2 Hz, 2H), 2.78 (t, *J* = 7.4 Hz, 2H), 1.64 – 1.50 (m, 2H), 1.26 (d, *J* = 5.7 Hz, 18H), 0.90 (t, *J* = 6.6 Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  (ppm) 14.46, 23.27, 28.36, 29.20, 29.74, 29.92, 30.09, 30.15, 30.20, 30.68, 32.49, 37.38, 47.71, 52.89, 55.19, 67.49, 111.32, 116.05, 119.18, 120.42, 120.48, 123.55, 125.76, 127.57, 128.06, 128.17, 128.46, 137.14, 141.77, 144.55, 156.13, 172.90.

**HRMS** (ESI-TOF, *m/z*): [M+H]<sup>+</sup> calculated 641.3413; found 641.3414 for C<sub>39</sub>H<sub>49</sub>N<sub>2</sub>O<sub>4</sub>S.

**TLC** (petroleum ether:ethyl acetate 8:2 v/v): R<sub>f</sub> = 0.6 (UV, I<sub>2</sub>, potassium permanganate).





## Procedures for Table 1, Entries 1 – 8

**Table 1, Entry 1.** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-FPI-Gly-OMe (**4a,b**, 1 equiv, 35 mg, 0.089 mmol) in 1.78 mL of anhydrous DCM, followed by 1-dodecanethiol (2.5 equiv, 44.9 mg, 53.2  $\mu$ L, 0.222 mmol) and B-chlorocatecholborane (1.2 equiv, 17 mg, 0.110 mmol). The reaction contents were stirred for 1 h at 21 °C. Upon completion, the crude (light brown, clear) was concentrated under reduced pressure. The crude was purified by silica gel flash column chromatography (gradient elution, 9:1 to 8:2 petroleum ether/ethyl acetate) to obtain 45 mg (0.079 mmol) of **9** as a beige solid in 89 % yield.

**Table 1, Entry 2.** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-FPI-Gly-OMe (**4a,b**, 1 equiv, 35 mg, 0.089 mmol) in 1.78 mL of anhydrous ACN, followed by 1-dodecanethiol (2.5 equiv, 44.9 mg, 53.2  $\mu$ L, 0.222 mmol) and anhydrous CeCl<sub>3</sub> (1.5 equiv, 33 mg, 0.134 mmol). The reaction contents were stirred for 3 h at 50 °C. Upon completion, the crude (yellow, clear) was filtered and concentrated under reduced pressure. The crude was purified by silica gel flash column chromatography (gradient elution, 9:1 to 8:2 petroleum ether/ethyl acetate) to obtain 46 mg (0.080 mmol) of **9** as a beige solid in 90 % yield.

**Table 1, Entry 3.** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-FPI-Gly-OMe (**4a,b**, 1 equiv, 35 mg, 0.089 mmol) in 1.78 mL of anhydrous DMF, followed by 1-dodecanethiol (2.5 equiv, 44.9 mg, 53.2  $\mu$ L, 0.222 mmol) and BaCl<sub>2</sub> (1.5 equiv, 28 mg, 0.134 mmol). The reaction contents were stirred for 3 h at 65 °C. Upon completion, the crude (yellow, clear) was filtered and concentrated under reduced pressure. The crude was purified by silica gel flash column chromatography (gradient elution, 9:1 to 8:2 petroleum ether/ethyl acetate) to obtain 44 mg (0.076 mmol) of **9** as a beige solid in 85 % yield.

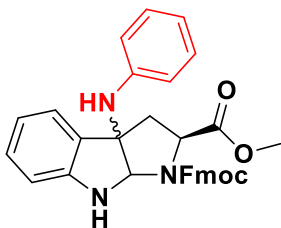
**Table 1, Entry 4.** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-FPI-Gly-OMe (**4a,b**, 1 equiv, 35 mg, 0.089 mmol) in 1.78 mL of anhydrous DCM, followed by 1-dodecanethiol (2.5 equiv, 44.9 mg, 53.2  $\mu$ L, 0.222 mmol) and BF<sub>3</sub>·O(Et)<sub>2</sub> (1.2 equiv, 15.6 mg, 13.8  $\mu$ L, 0.110 mmol). The reaction contents were stirred for 1 h at 21 °C. Upon completion, the crude (light brown, clear) was concentrated under reduced pressure. The crude was purified by silica gel flash column chromatography (gradient elution, 9:1 to 8:2 petroleum ether/ethyl acetate) to obtain 42 mg (0.072 mmol) of **9** as a beige solid in 81 % yield.

**Table 1, Entry 5.** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-FPI-Gly-OMe (**4a,b**, 1 equiv, 35 mg, 0.089 mmol) in 1.78 mL of anhydrous DCM, followed by 1-dodecanethiol (2.5 equiv, 44.9 mg, 53.2  $\mu$ L, 0.222 mmol) and trifluoroacetic acid (2 equiv, 20.3 mg, 13.6  $\mu$ L, 0.178 mmol). The reaction contents were stirred for 30 min at 21 °C. Upon completion, the crude (beige, clear) was concentrated under reduced pressure. The crude was purified by silica gel flash column chromatography (gradient elution, 9:1 to 8:2 petroleum ether/ethyl acetate) to obtain 49 mg (0.085 mmol) of **9** as a beige solid in 95 % yield.

**Table 1, Entry 6.** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-FPI-Gly-OMe (**4a,b**, 1 equiv, 35 mg, 0.089 mmol) in 1.78 mL of anhydrous ACN, followed by 1-dodecanethiol (2.5 equiv, 44.9 mg, 53.2  $\mu$ L, 0.222 mmol) and anhydrous CeCl<sub>3</sub> (0.2 equiv, 4.4 mg, 17.8  $\mu$ mol). The reaction contents were stirred for 5 h at 60 °C. Upon completion, the crude (yellow, clear) was filtered and concentrated under reduced pressure. The crude was purified by silica gel flash column chromatography (gradient elution, 9:1 to 8:2 petroleum ether/ethyl acetate) to obtain 48 mg (0.083 mmol) of **9** as a beige solid in 93 % yield.

**Table 1, Entry 8.** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-FPI-Gly-OMe (**4a,b**, 1 equiv, 35 mg, 0.089 mmol) in 1.42 mL of anhydrous DCM, followed by 1-dodecanethiol (2.5 equiv, 44.9 mg, 53.2  $\mu$ L, 0.222 mmol) and 0.36 mL of trifluoroethanol. The reaction contents were stirred for 2 h at 21 °C. Upon completion, the crude (light yellow, clear) was concentrated under reduced pressure. The was purified by silica gel flash column chromatography (gradient elution, 9:1 to 8:2 petroleum ether/ethyl acetate) obtain 46 mg (0.080 mmol) of **9** as a beige solid in 90 % yield.

## Synthesis and characterization of compound **13a,b**



**13a,b** 95%<sup>c,e,f</sup>

Chemical Formula: C<sub>33</sub>H<sub>29</sub>N<sub>3</sub>O<sub>4</sub>

Exact Mass: 531.22

Molecular Weight: 531.61

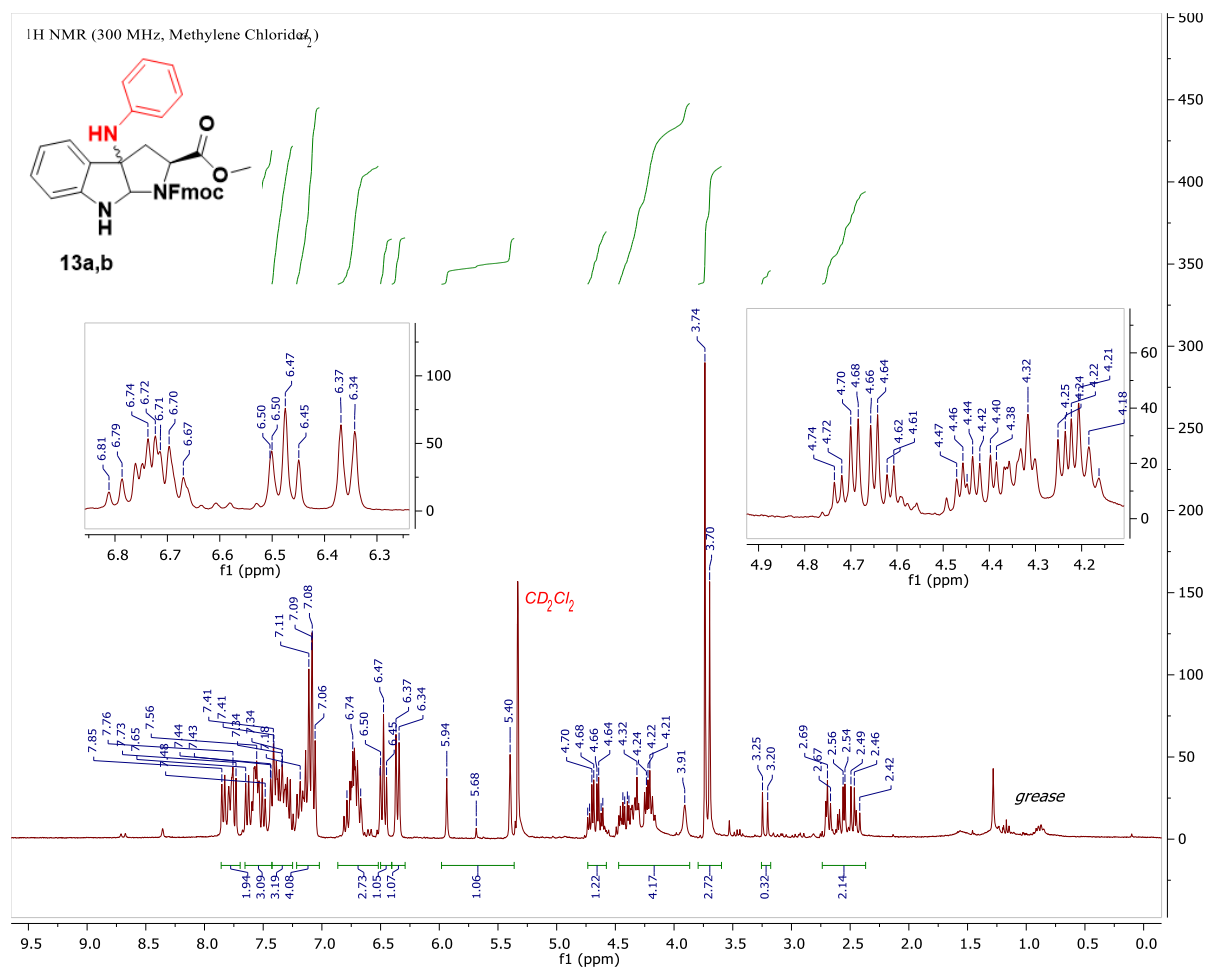
**1-((9H-fluoren-9-yl)methyl) 2-methyl (2S)-3a-(phenylamino)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (13a,b).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 0.070 mg, 0.153 mmol) in 2.4 mL of anhydrous dichloroethane (DCE) followed by aniline (5 equiv, 71 mg, 70  $\mu$ L, 0.764 mmol) and 0.6 mL of HFIP. The reaction contents were stirred at 50°C for 2 h. Upon completion, the solvent was evaporated under reduced pressure and the crude was purified by silica gel flash column chromatography (gradient elution, 100 % petroleum ether to 2:8 petroleum ether/diethyl ether) to afford 77 mg (0.145 mmol) of **13a,b** as a white solid in 95 % yield.

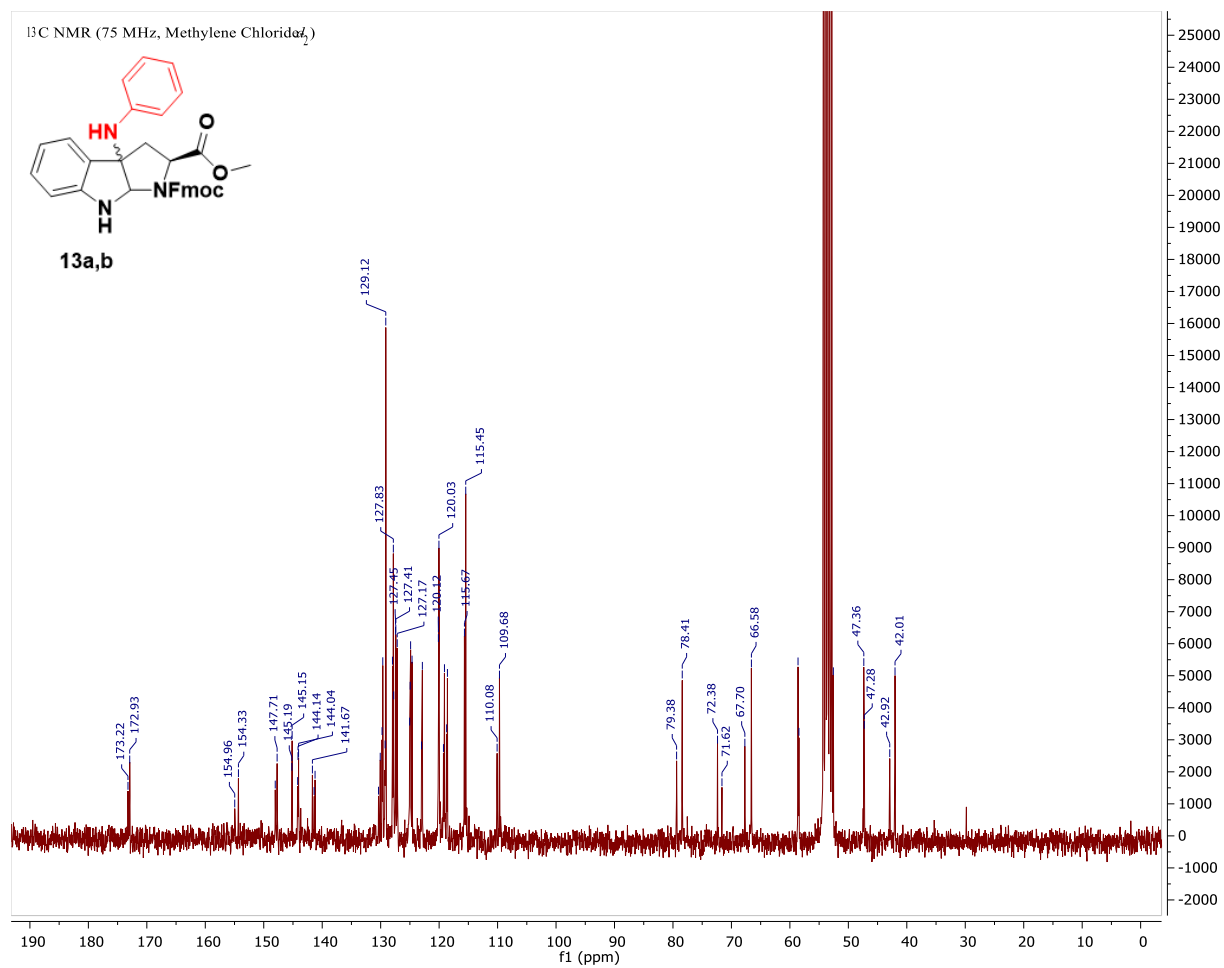
**<sup>1</sup>H NMR** (300 MHz, Methylene Chloride-*d*<sub>2</sub>) major diastereomer and rotamers, *syn-cis*,  $\delta$  (ppm) 7.86 – 7.70 (m, 2H), 7.66 – 7.43 (m, 3H), 7.43 – 7.25 (m, 3H), 7.22 – 7.02 (m, 4H), 6.86 – 6.52 (m, 3H), 6.46 (d, *J* = 7.7 Hz, 1H), 6.40 – 6.29 (m, 1H), 5.94, 5.68, 5.40 (two s, 1H), 4.74 – 4.58 (m, 1H), 4.47 – 3.87 (m, 4H), 3.70, 3.74, 3.25, 3.20 (four s, 3H), 2.74 – 2.37 (m, 2H).

**<sup>13</sup>C NMR** (75 MHz, Methylene Chloride-*d*<sub>2</sub>) major diastereomer and rotamers, *syn-cis*,  $\delta$  (ppm) 42.01, 42.92, 47.28, 47.36, 52.56, 58.45, 58.61, 66.58, 67.70, 71.62, 72.38, 78.41, 79.38, 109.68, 110.08, 115.45, 115.67, 118.58, 118.72, 119.09, 119.26, 120.03, 120.12, 122.87, 123.01, 124.63, 124.88, 124.95, 125.04, 127.17, 127.41, 127.45, 127.77, 127.83, 127.98, 129.12, 129.24, 129.64, 129.76, 130.07, 130.36, 141.22, 141.33, 141.39, 141.67, 144.04, 144.14, 144.20, 145.15, 145.19, 147.71, 148.03, 154.33, 154.96, 172.93, 173.22.

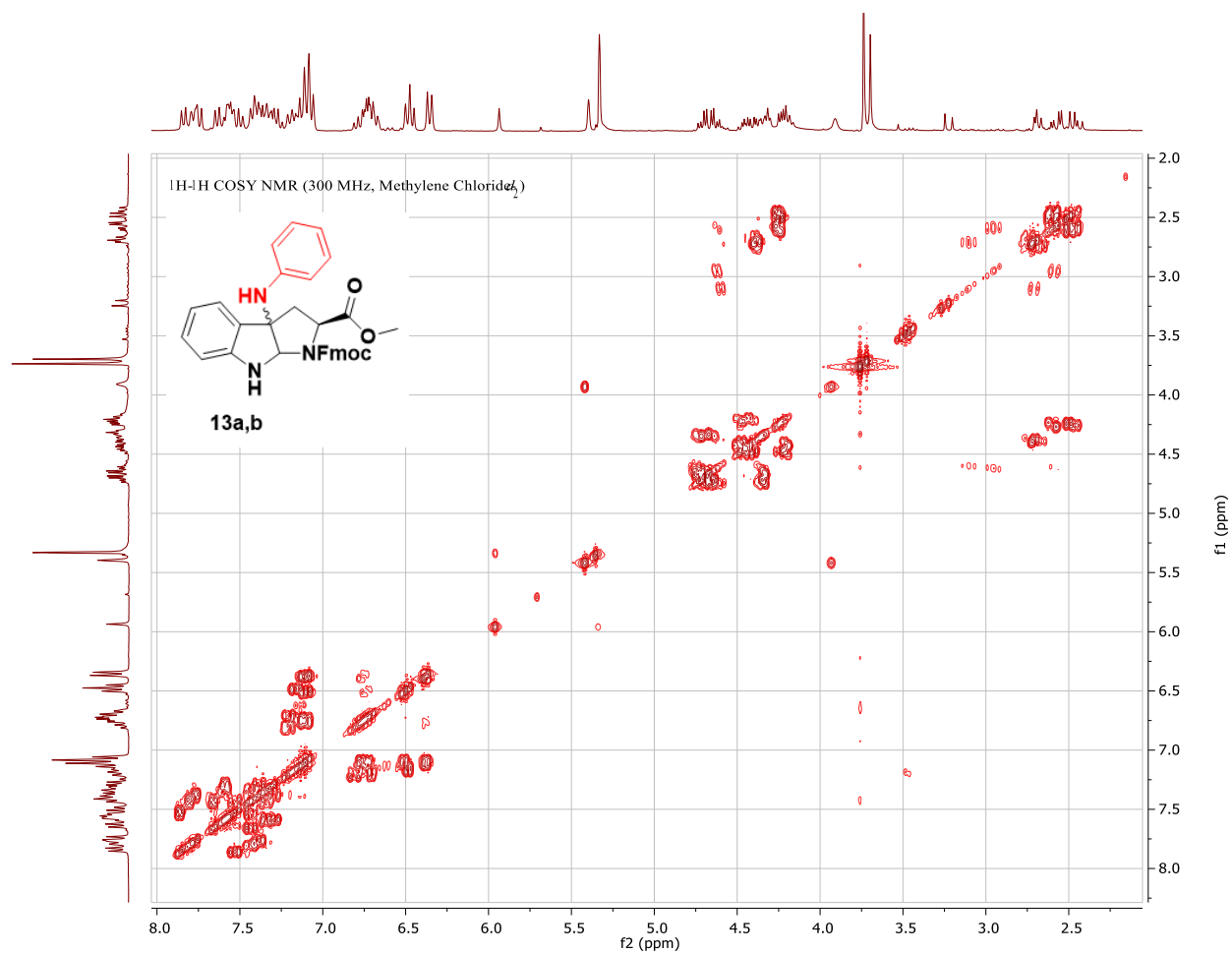
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 554.2056; found 554.2076 C<sub>33</sub>H<sub>29</sub>N<sub>3</sub>O<sub>4</sub>Na.

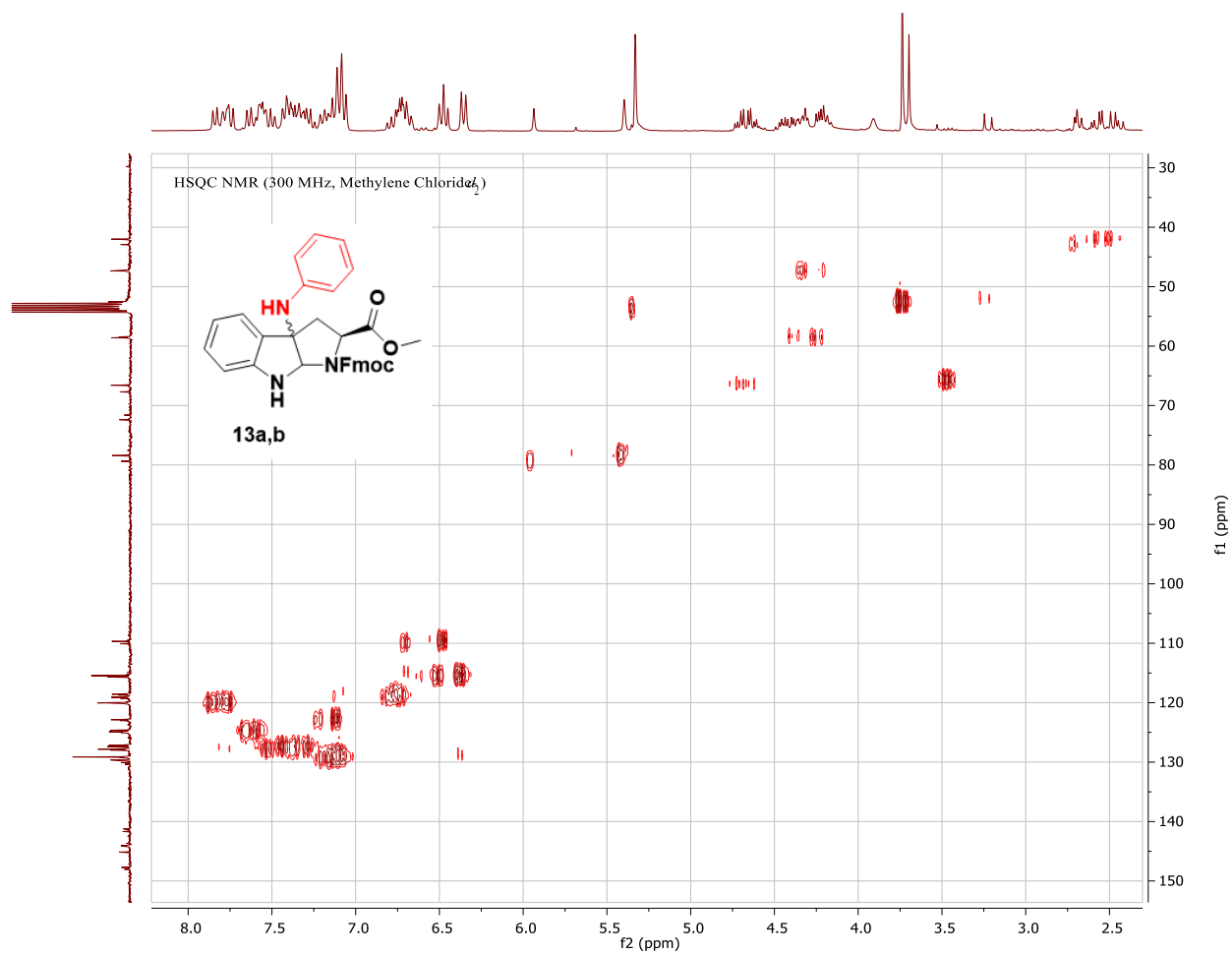
**TLC** (hexane:ethyl acetate, 1:1 v/v): R<sub>f</sub> = 0.65 (UV, I<sub>2</sub>, potassium permanganate).

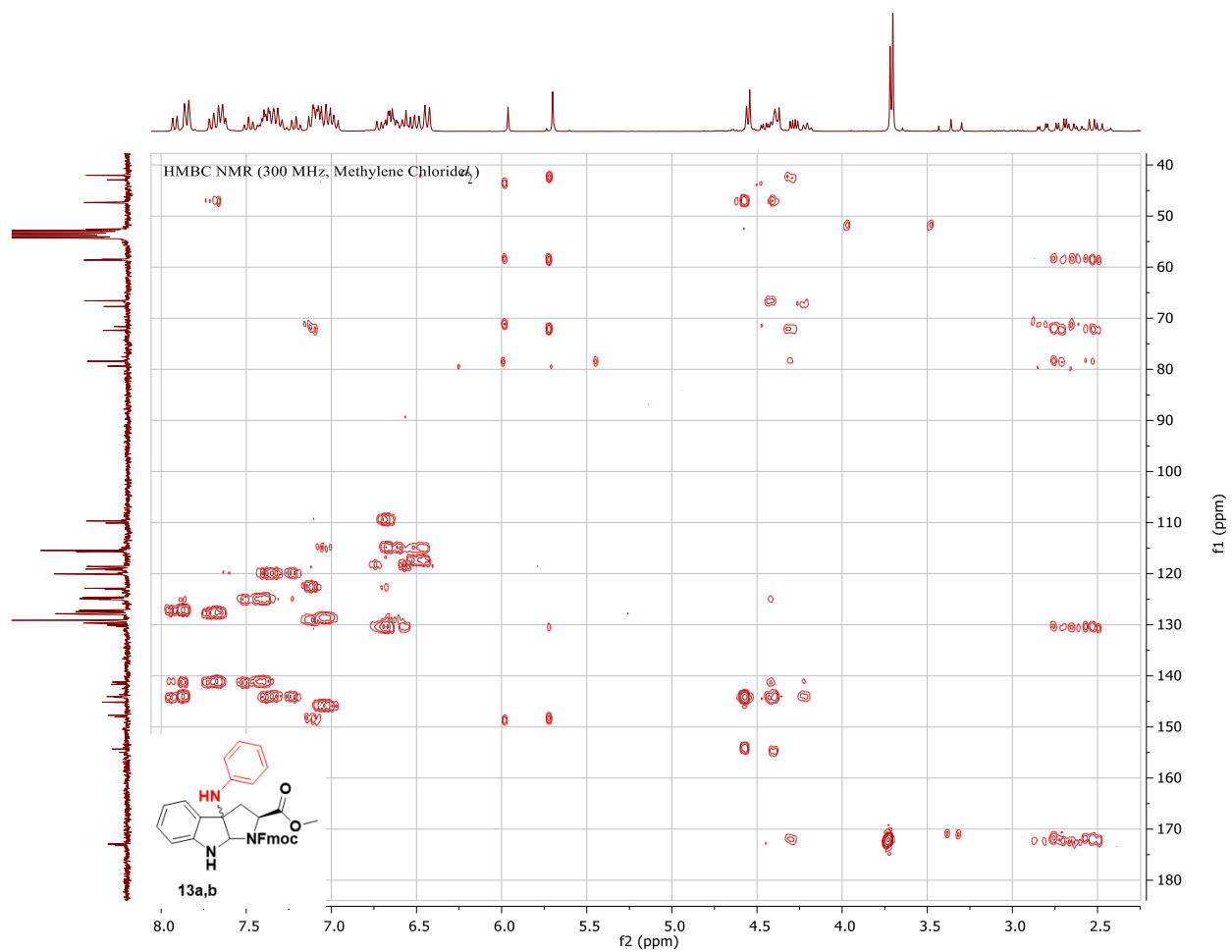




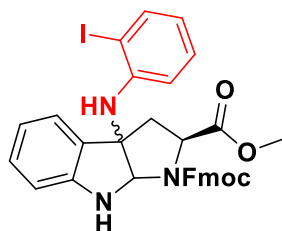








## Synthesis and characterization of compound **14a,b**



**14a,b** 63%<sup>c,e,f</sup>

Chemical Formula: C<sub>33</sub>H<sub>28</sub>IN<sub>3</sub>O<sub>4</sub>

Exact Mass: 657.11

Molecular Weight: 657.51

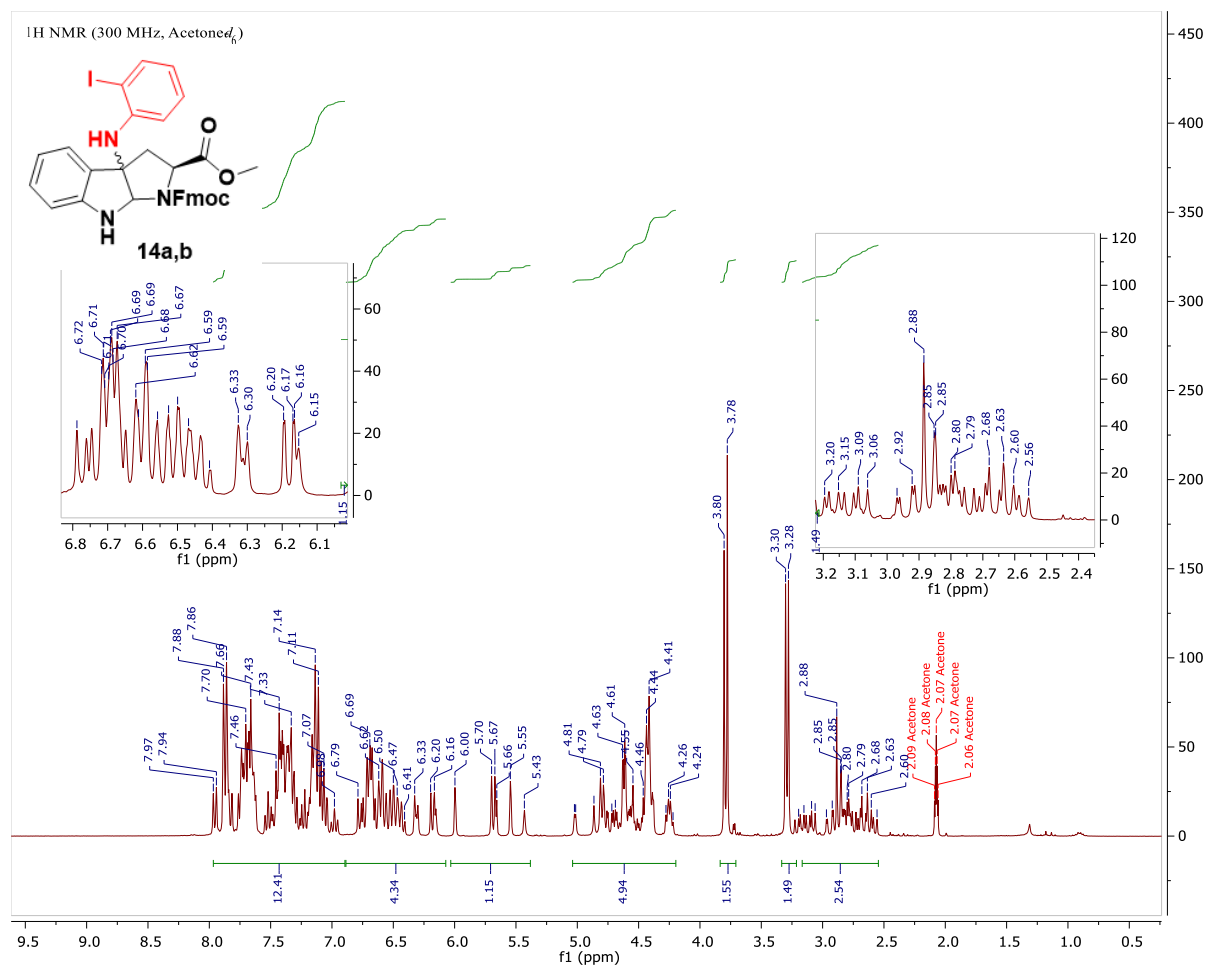
**1-((9H-fluoren-9-yl)methyl) 2-methyl (2S)-3a-((2-iodophenyl)amino)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (14a,b).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 0.120 mg, 0.26 mmol) in 3.36 mL of anhydrous DCE followed by 2-iodoaniline (1.5 equiv, 86 mg, 0.39 mmol) and 0.84 mL of HFIP. The reaction contents were stirred at 50°C for 45 min. Upon completion, the crude (yellow, clear) was concentrated under reduced pressure and purified by silica gel flash column chromatography (gradient elution, 100% petroleum ether to 3:7 petroleum ether/diethyl ether) to afford 109 mg (0.166 mmol) of **14a,b** as a white solid in 63 % yield.

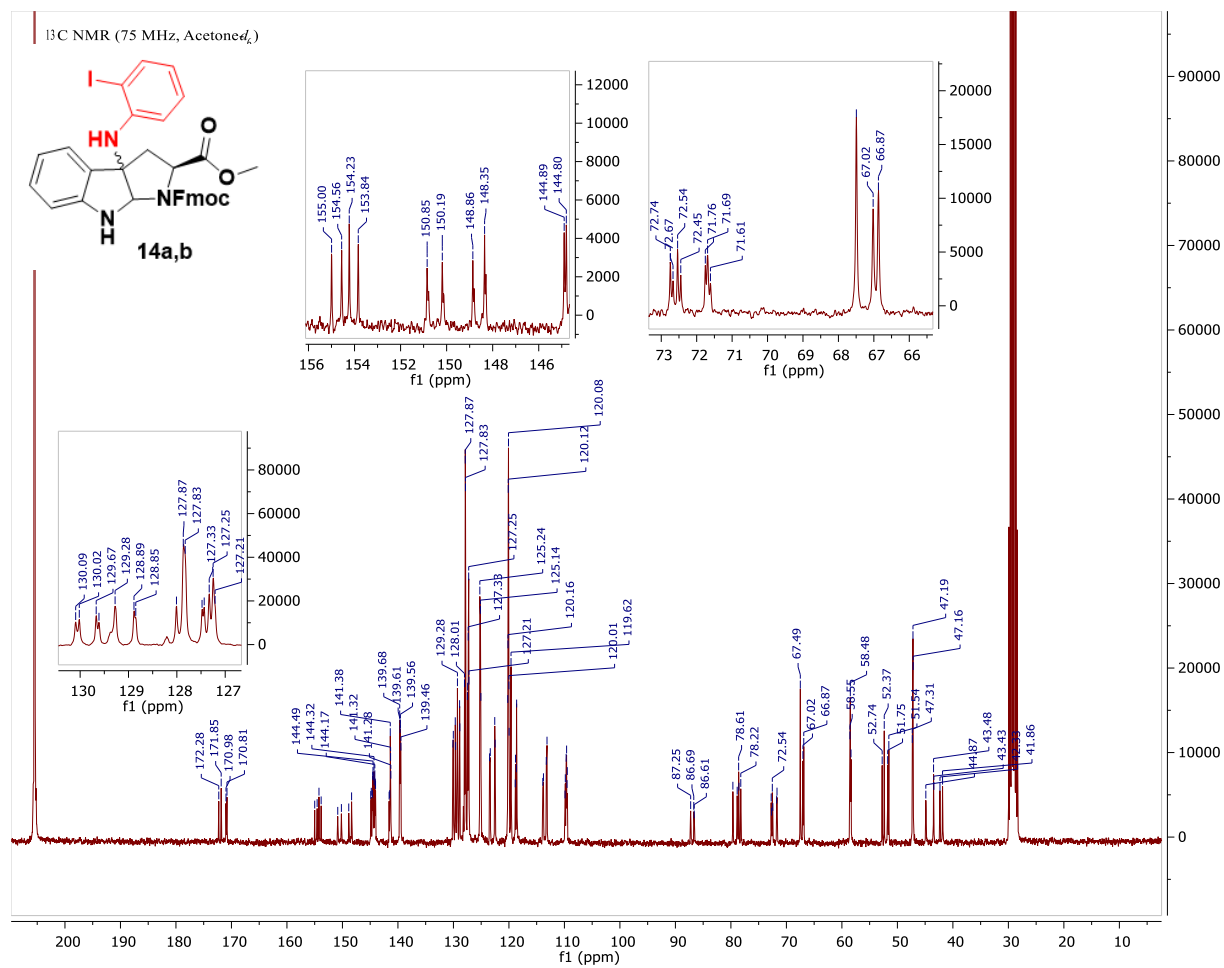
**<sup>1</sup>H NMR** (300 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1:1) δ (ppm) 7.97 – 6.89 (m, 12H), 6.89 – 6.07 (m, 4H), 6.03 – 5.38 (m, 1H), 5.04 – 4.20 (m, 5H), 3.80, 3.78 (two s, 1.5H), 3.20, 3.28 (two s, 1.5H), 3.18 – 2.48 (m, 2H).

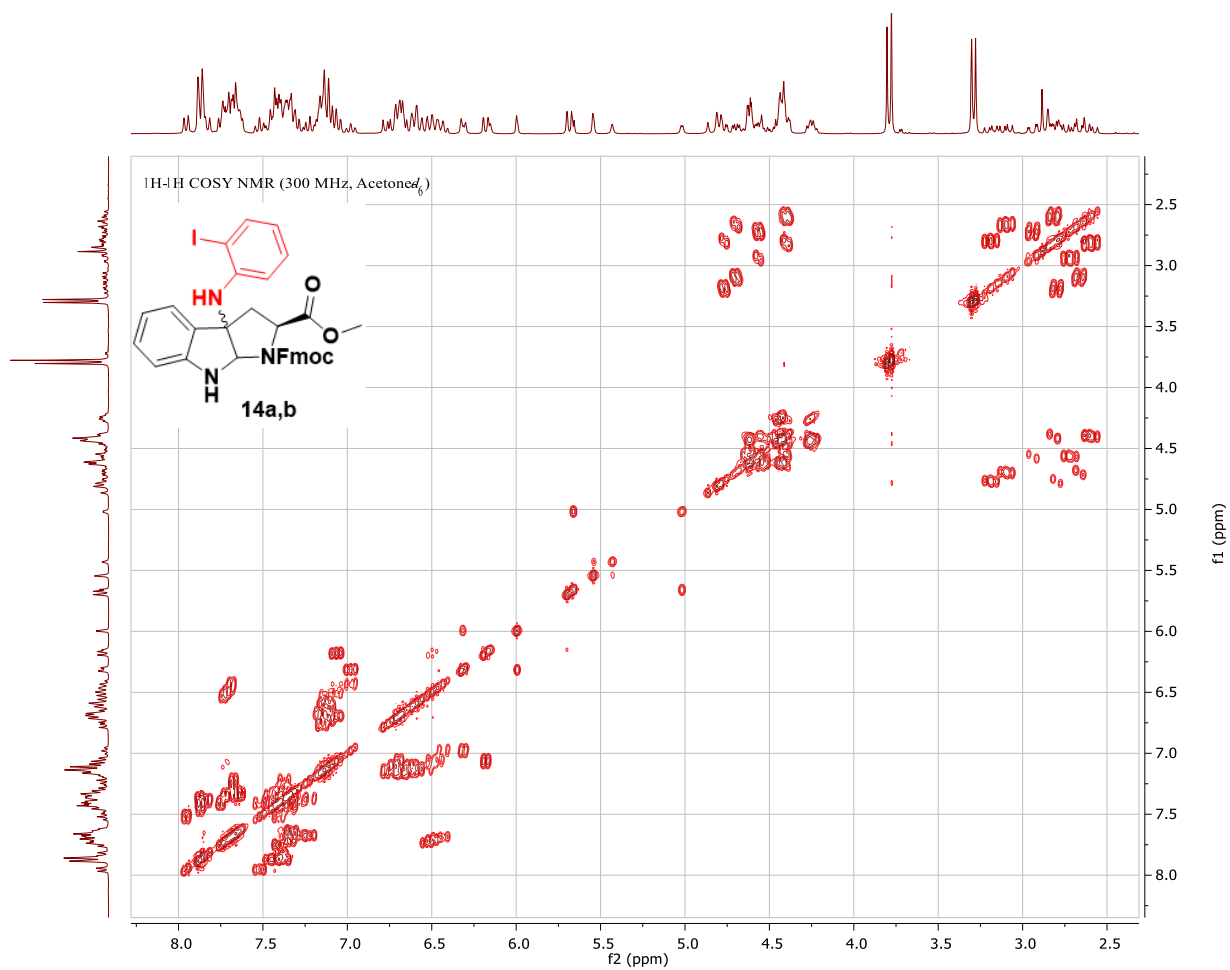
**<sup>13</sup>C NMR** (75 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1:1) δ (ppm) 41.86, 42.33, 43.43, 43.48, 44.87, 47.16, 47.19, 47.31, 51.54, 51.75, 52.37, 52.74, 58.36, 58.48, 58.55, 66.87, 67.02, 67.49, 71.69, 71.76, 72.45, 72.54, 72.67, 72.74, 78.22, 78.56, 78.61, 78.87, 79.64, 86.61, 86.69, 87.25, 109.49, 109.53, 109.61, 109.69, 109.84, 109.89, 113.14, 113.27, 113.78, 113.90, 118.61, 118.67, 118.81, 118.86, 119.62, 119.97, 120.01, 120.08, 120.12, 120.16, 120.21, 122.49, 122.55, 123.36, 123.49, 125.06, 125.14, 125.24, 127.21, 127.25, 127.33, 127.43, 127.48, 127.83, 127.87, 128.01, 128.85, 128.89, 129.28, 129.61, 129.67, 130.02, 130.09, 139.46, 139.56, 139.61, 139.68, 141.28, 141.32, 141.38, 141.48, 141.59, 144.03, 144.08, 144.17, 144.28, 144.32, 144.45, 144.49, 144.54, 144.61, 144.80, 144.89, 148.35, 148.86, 150.19, 150.85, 153.84, 154.23, 154.56, 155.00, 170.81, 170.98, 171.85, 172.28.

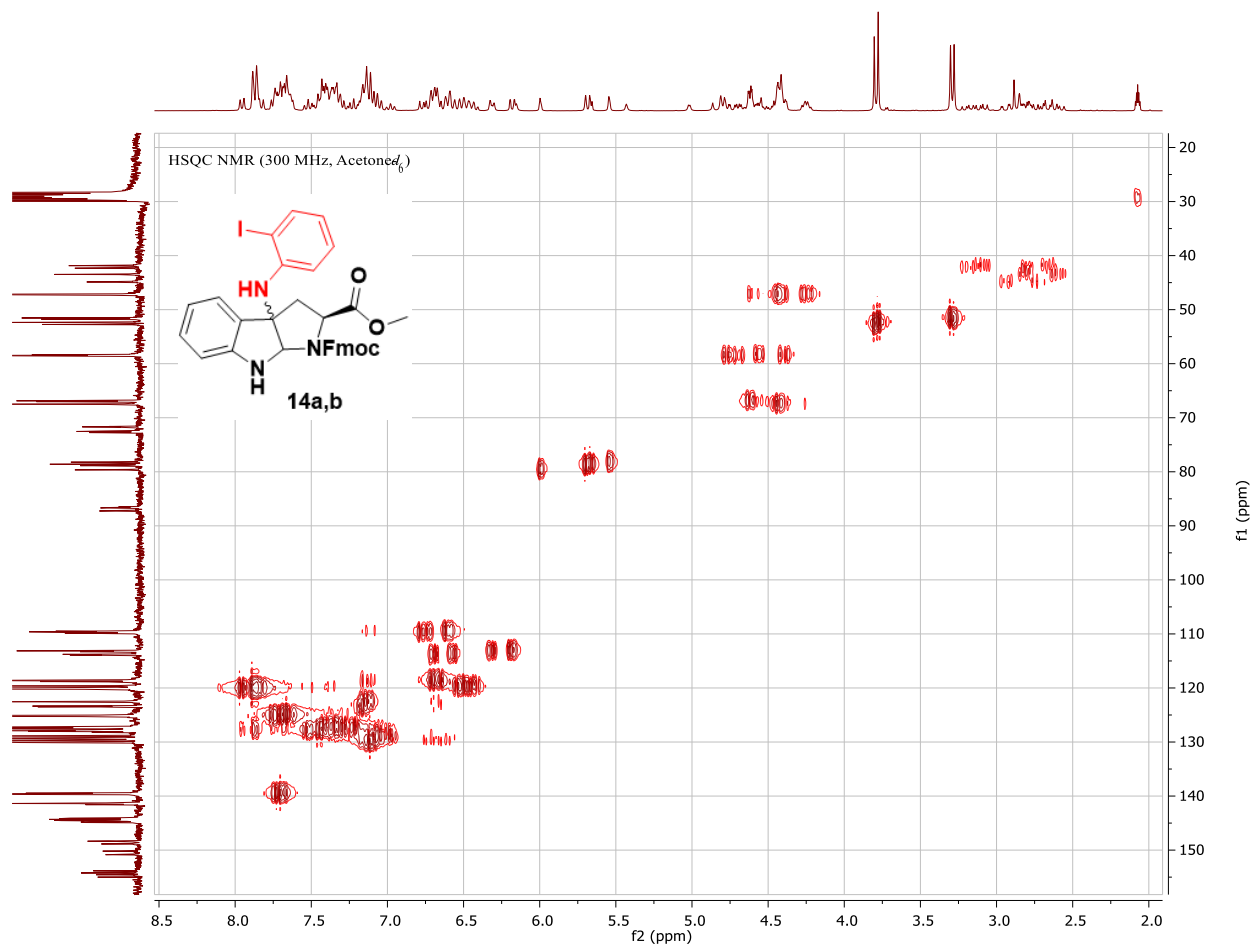
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 680.1022; found 680.0993 for C<sub>33</sub>H<sub>28</sub>IN<sub>3</sub>O<sub>4</sub>Na.

**TLC** (hexane:ethyl acetate, 1:1 v/v): R<sub>f</sub> = 0.6 (UV, I<sub>2</sub>, potassium permanganate).

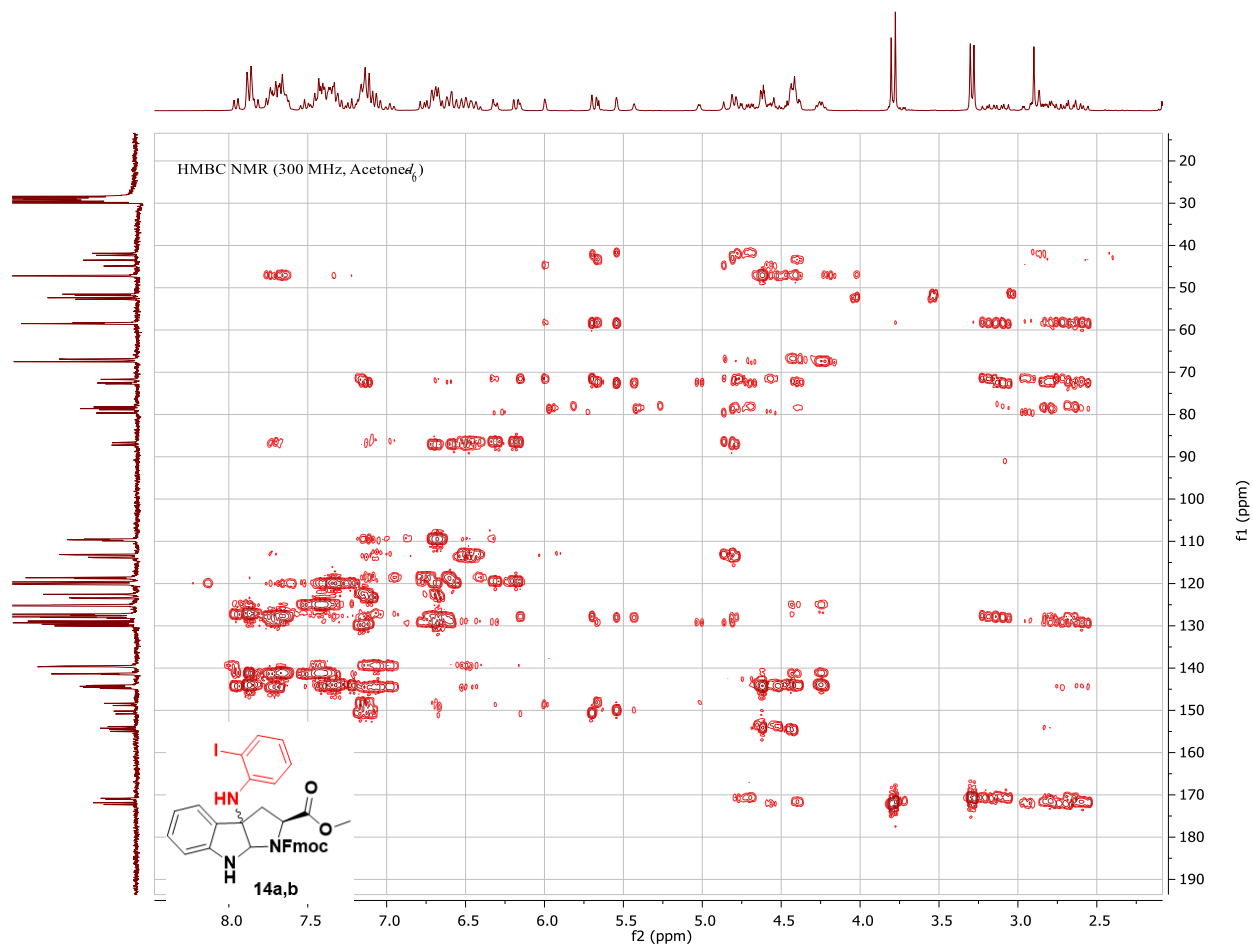




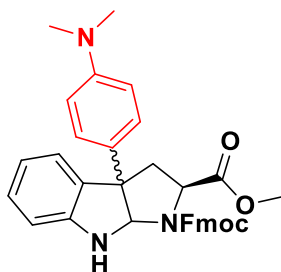








## Synthesis and characterization of compound **15a,b**



**15a,b** 79%<sup>c,e,f</sup>

Chemical Formula: C<sub>35</sub>H<sub>33</sub>N<sub>3</sub>O<sub>4</sub>

Exact Mass: 559.25

Molecular Weight: 559.67

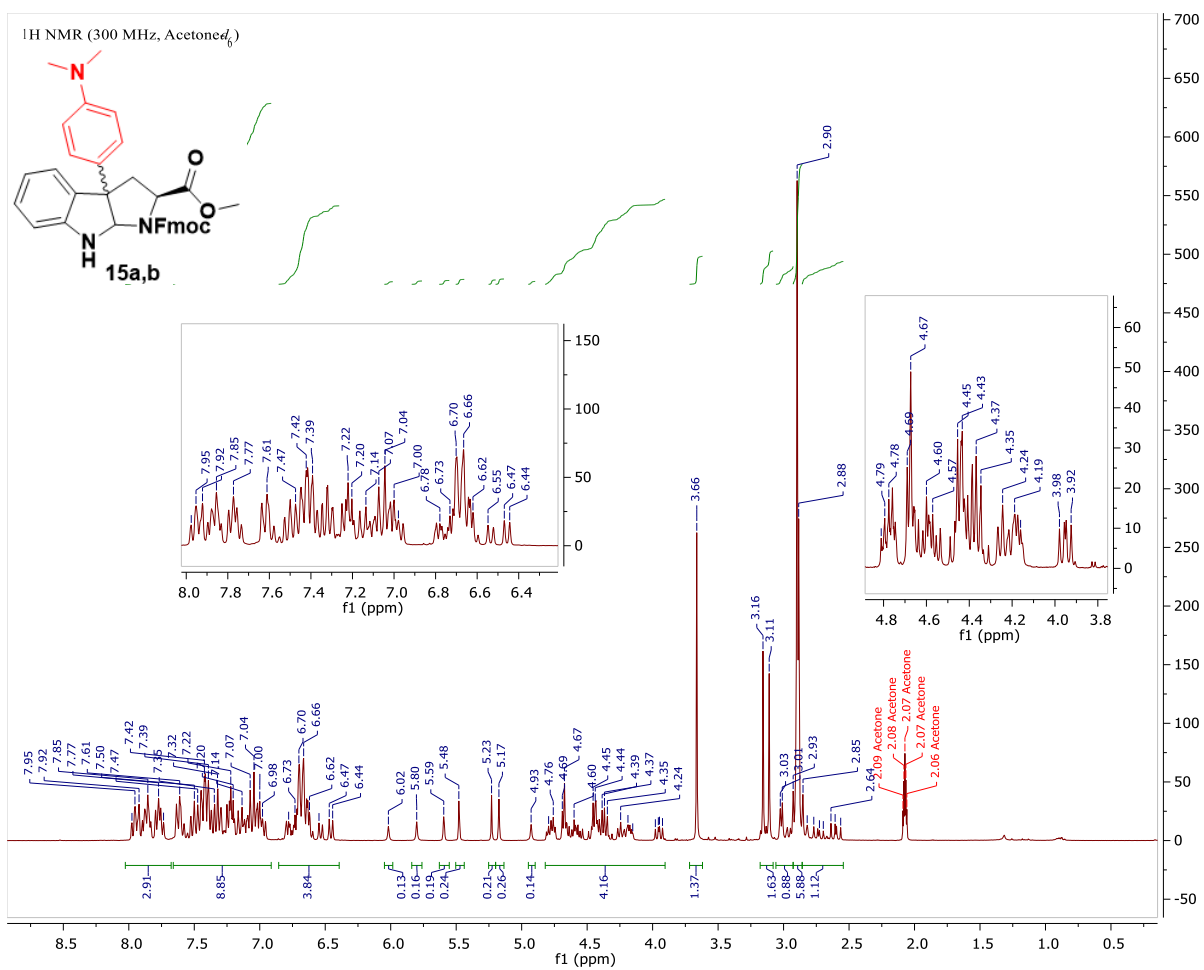
**1-((9H-fluoren-9-yl)methyl) 2-methyl (2S)-3a-(4-(dimethylamino)phenyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (15a,b)** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 0.100 mg, 0.22 mmol) in 3.5 mL of anhydrous DCE followed by *N,N*-dimethylaniline (5 equiv, 132 mg, 138  $\mu$ L, 1.09 mmol) and 0.87 mL of HFIP. The reaction contents were stirred at 50°C for 1 h. Upon completion, the solvent was evaporated under reduced pressure and the crude was purified by silica gel flash column chromatography (gradient elution, 100% petroleum ether to 2:8 petroleum ether/diethyl ether) to afford 96 mg (0.17 mmol) of **15a,b** as a white solid in 79 % yield.

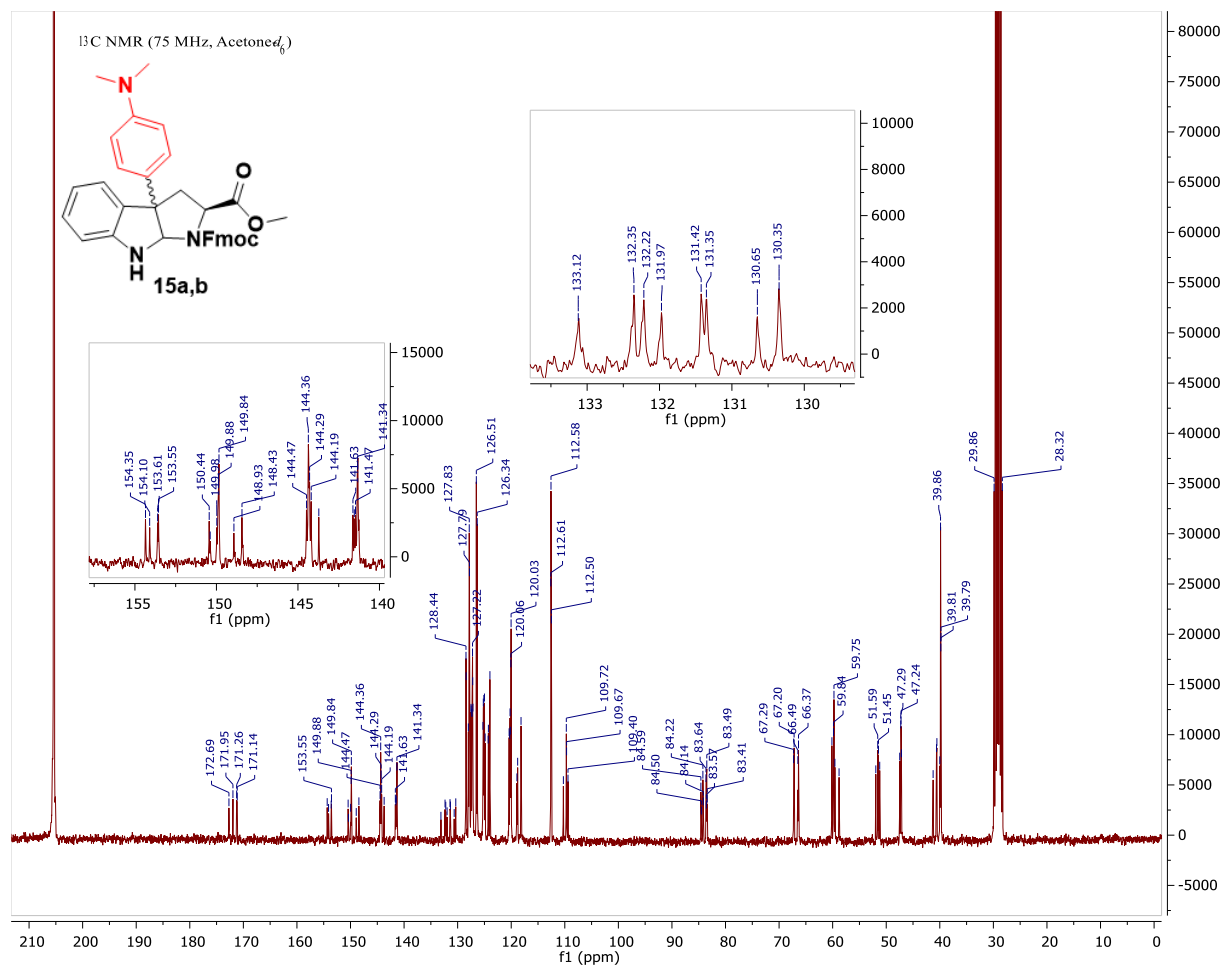
**<sup>1</sup>H NMR** (300 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1:1.1)  $\delta$  (ppm) 8.03 – 7.68 (m, 3H), 7.66 – 6.91 (m, 9H), 6.86 – 6.39 (m, 4H), 6.02, 5.8, 5.6, 5.48, 5.23, 5.17, 4.93 (s, 1H), 4.82 – 3.90 (m, 4H), 3.66 (s, 1.4H), 3.16, 3.11 (two s, 1.6H), 3.03-2.94 (m, 1H), 2.89 (s, 3H), 2.88 (s, 3H), 2.86 – 2.54 (m, 1H).

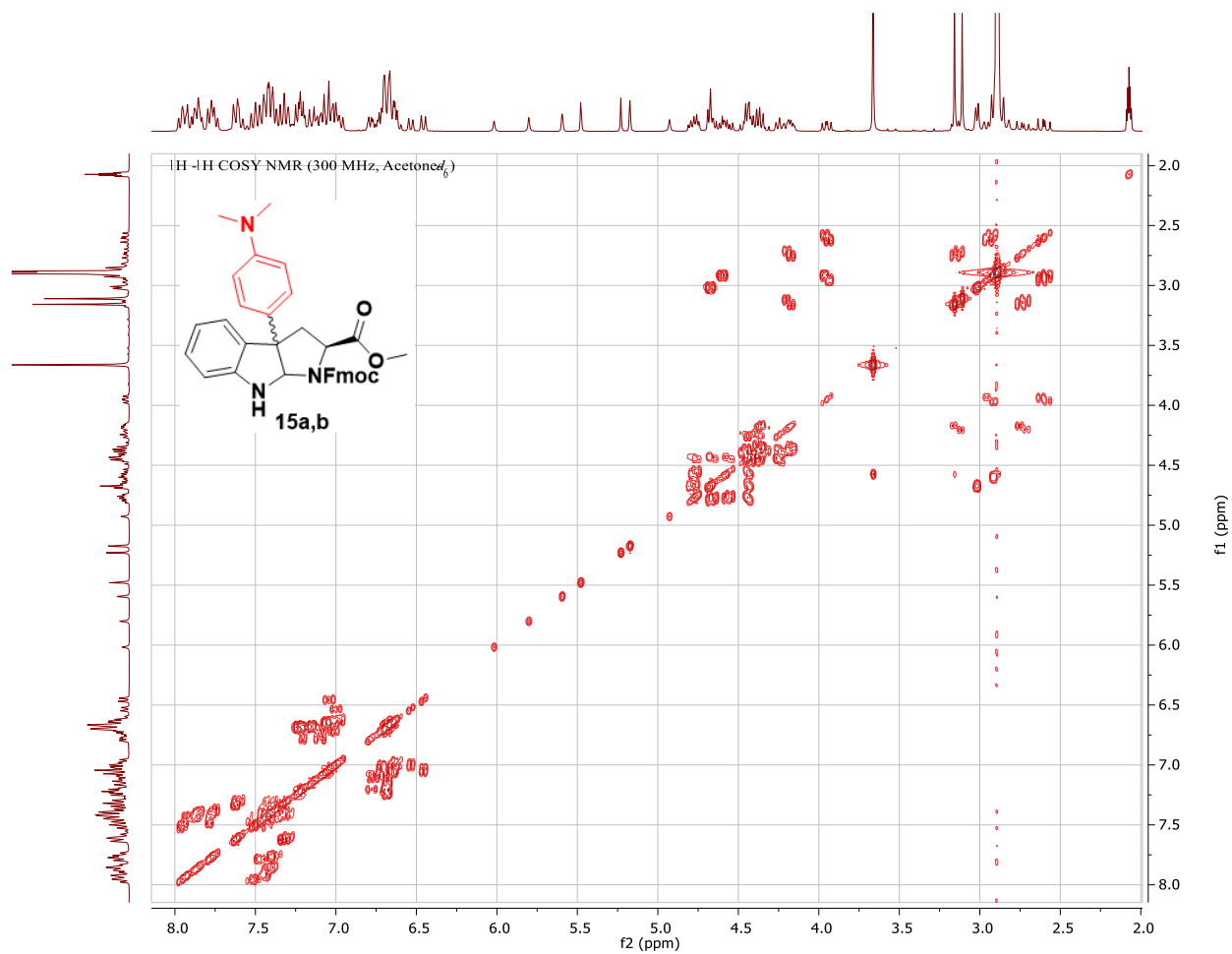
**<sup>13</sup>C NMR** (75 MHz, Acetone-*d*<sub>6</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1:1.1)  $\delta$  (ppm) 28.32, 28.58, 28.84, 29.09, 29.35, 29.61, 29.86, 39.79, 39.81, 39.86, 40.00, 40.54, 40.62, 41.25, 47.16, 47.24, 47.29, 47.48, 51.21, 51.45, 51.59, 51.94, 58.81, 59.58, 59.75, 59.84, 60.14, 66.37, 66.49, 67.20, 67.29, 83.41, 83.49, 83.57, 83.64, 84.14, 84.22, 84.50, 84.59, 109.40, 109.67, 109.72, 110.26, 112.50, 112.58, 112.61, 118.17, 118.80, 118.94, 120.03, 120.06, 120.17, 120.22, 120.27, 120.39, 123.97, 124.26, 124.30, 124.87, 124.99, 125.11, 125.21, 125.28, 126.34, 126.51, 127.15, 127.19, 127.22, 127.33, 127.34, 127.47, 127.50, 127.79, 127.83, 128.00, 128.41, 128.44, 130.35, 130.65, 131.35, 131.42, 131.97, 132.22, 132.35, 133.12, 141.34, 141.47, 141.54, 141.63, 143.72, 144.19, 144.29, 144.36, 144.47, 148.43, 148.93, 149.84, 149.88, 149.98, 150.38, 150.44, 153.55, 153.61, 154.10, 154.35, 171.14, 171.26, 171.95, 172.69, 205.37.

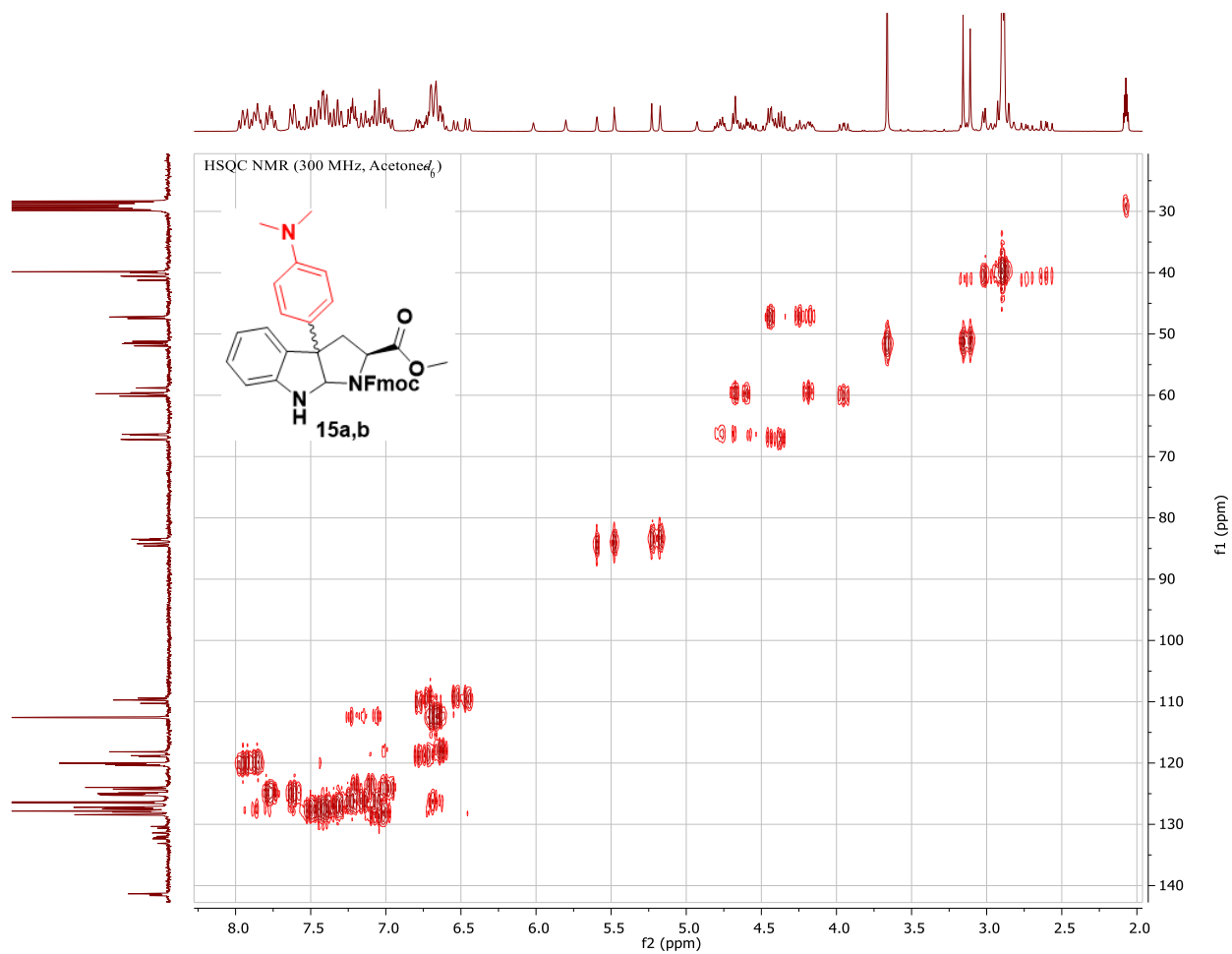
**HRMS** (ESI-TOF, *m/z*): [M+H]<sup>+</sup> calculated 560.2549; found 560.2553 for C<sub>35</sub>H<sub>35</sub>N<sub>3</sub>O<sub>4</sub>.

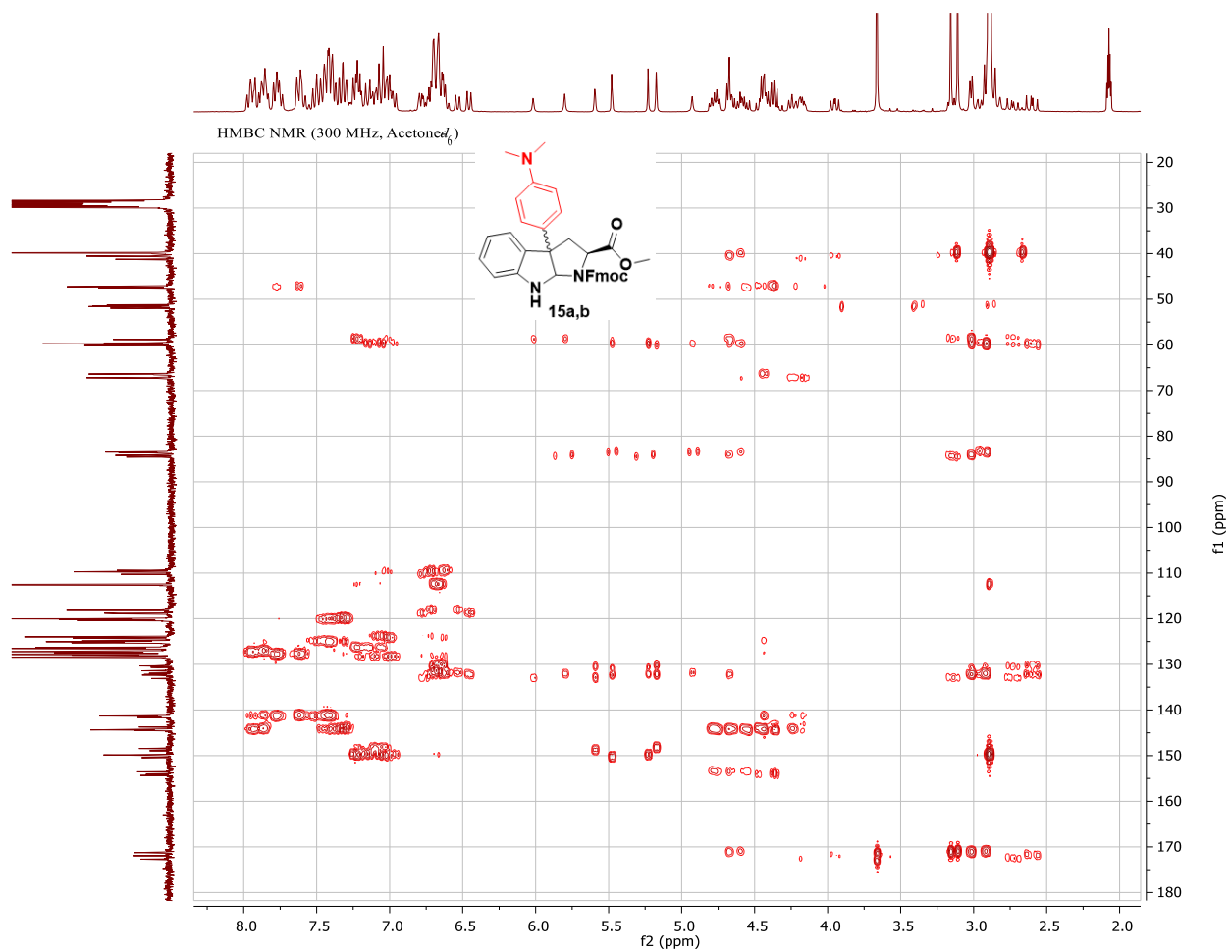
**TLC** (petroleum ether:diethyl ether, 1:1 v/v): R<sub>f</sub> = 0.3 (UV, I<sub>2</sub>, potassium permanganate).



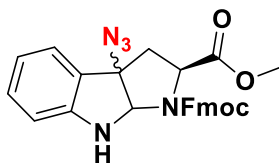








## Synthesis and characterization of compound **16a,b**



**16a,b** 84%<sup>b,f</sup>

Chemical Formula: C<sub>27</sub>H<sub>23</sub>N<sub>5</sub>O<sub>4</sub>

Exact Mass: 481.18

Molecular Weight: 481.51

**1-((9H-fluoren-9-yl)methyl) 2-methyl (2S)-3a-azido-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (16a,b)** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 43 mg, 94  $\mu$ mol) in 0.75 mL of anhydrous DCM followed by azidotrimethylsilane (3.3 equiv, 35.7 mg, 40.7  $\mu$ L, 0.031 mmol) and 0.19 mL of HFIP. The reaction contents were stirred at 21 °C for 2 h. Upon completion, the crude (beige and clear) was concentrated under reduced pressure and purified by silica gel flash column chromatography (isocratic elution, 2:3 petroleum ether/diethyl ether) to afford 38 mg (79  $\mu$ mol) of **16a,b** as a white solid in 84 % yield. Note: product has the same R<sub>f</sub> as the starting material (diethyl ether:petroleum ether, 6:4 v/v).

**<sup>1</sup>H NMR**(300 MHz, Methylene Chloride-*d*<sub>2</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1.5:1)  $\delta$  (ppm) 7.98 – 7.83 (m, 1H), 7.82 – 7.72 (m, 1H), 7.72 – 7.62 (m, 1H), 7.60 – 7.34 (m, 4H), 7.34 – 7.09 (m, 3H), 6.95 – 6.69 (m, 1H), 6.53 (d, *J* = 7.9 Hz, 0H), 6.41 (d, *J* = 7.9 Hz, 0H), 5.56 (s, 0H), 5.37 (s, 0H), 4.95 – 4.78 (m, 1H), 4.72 (dd, *J* = 10.7, 3.9 Hz, 0H), 4.63 (dd, *J* = 10.7, 4.8 Hz, 0H), 4.55 – 4.30 (m, 2H), 4.29 – 4.03 (m, 1H), 3.70, 3.67 (two s, 1.7H), 3.15, 3.14 (two s, 1.1H), 2.86 – 2.23 (m, 2H).

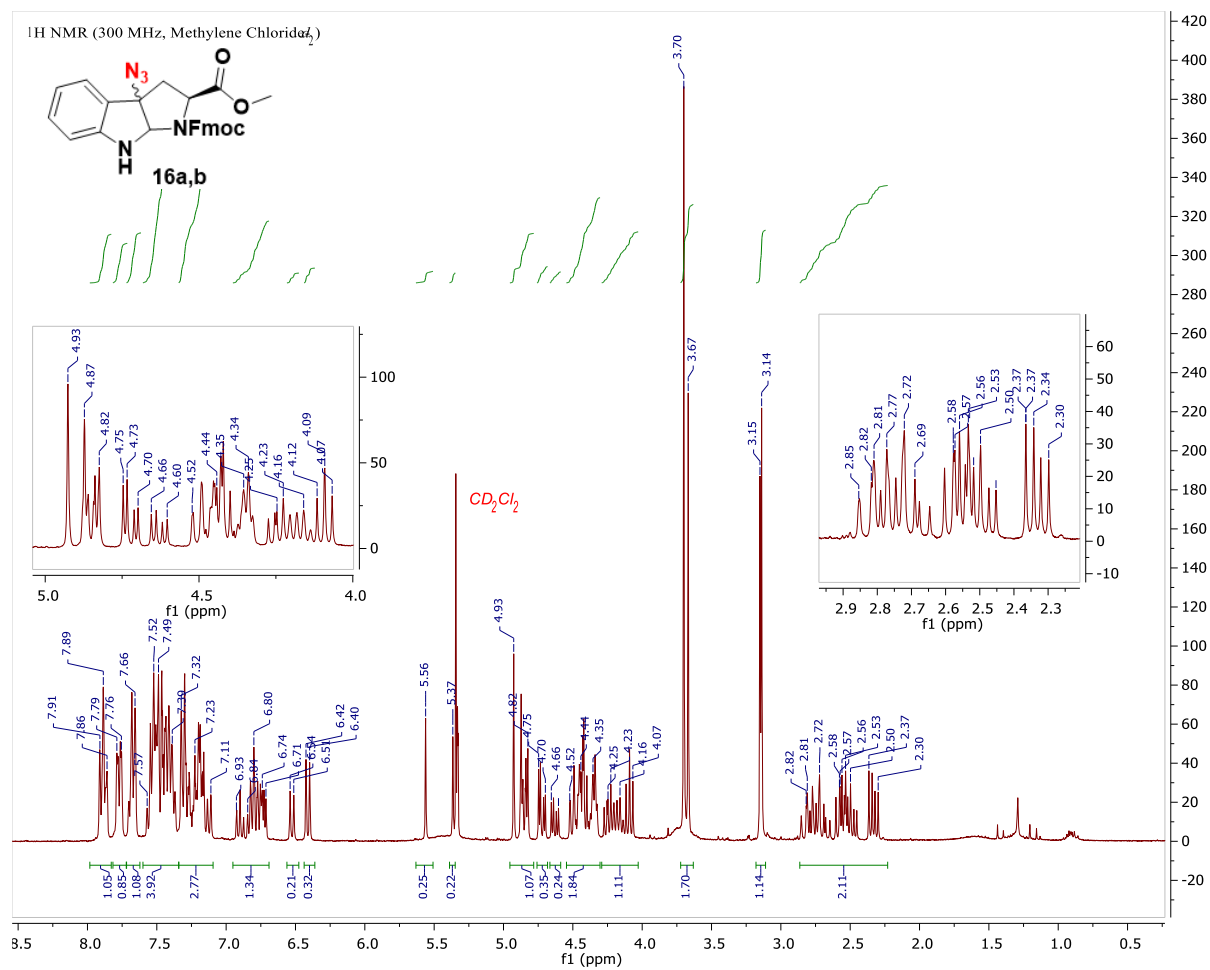
**<sup>13</sup>C NMR** (75 MHz, Methylene Chloride-*d*<sub>2</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1.5:1)  $\delta$  (ppm) 38.91, 39.65, 39.72, 40.51, 47.64, 47.67, 47.81, 47.98, 52.54, 52.67, 52.91, 53.09, 59.62, 59.85, 66.85, 67.11, 68.16, 75.46, 75.91, 76.20, 76.56, 81.15, 81.81, 81.86, 82.98, 110.45, 110.67, 110.84, 111.24, 119.51, 119.73, 120.10, 120.47, 120.68, 120.72, 120.81, 123.98, 124.17, 124.24, 124.66, 124.73, 124.95, 125.10, 125.17, 125.36, 125.43, 127.56, 127.62, 127.83, 127.94, 128.10, 128.25, 128.44, 128.54, 131.42, 131.56, 131.82, 131.94, 141.71, 141.78, 141.81, 142.18, 144.02, 144.39, 144.43, 144.51, 149.05, 149.56, 150.74, 151.28, 153.96, 154.12, 154.86, 154.96, 170.93, 171.06, 171.76, 172.21.

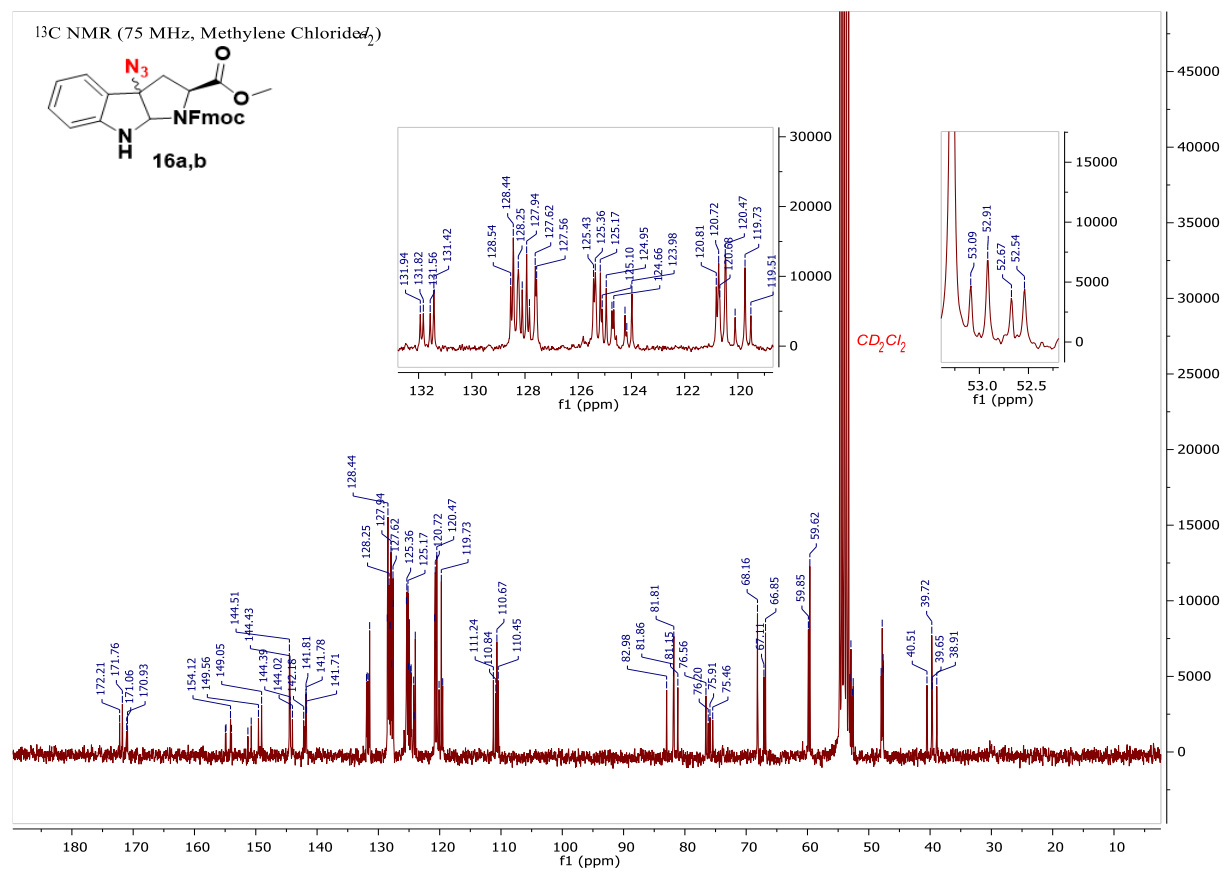
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 504.1648; found 504.1656 for C<sub>27</sub>H<sub>23</sub>N<sub>5</sub>O<sub>4</sub>Na

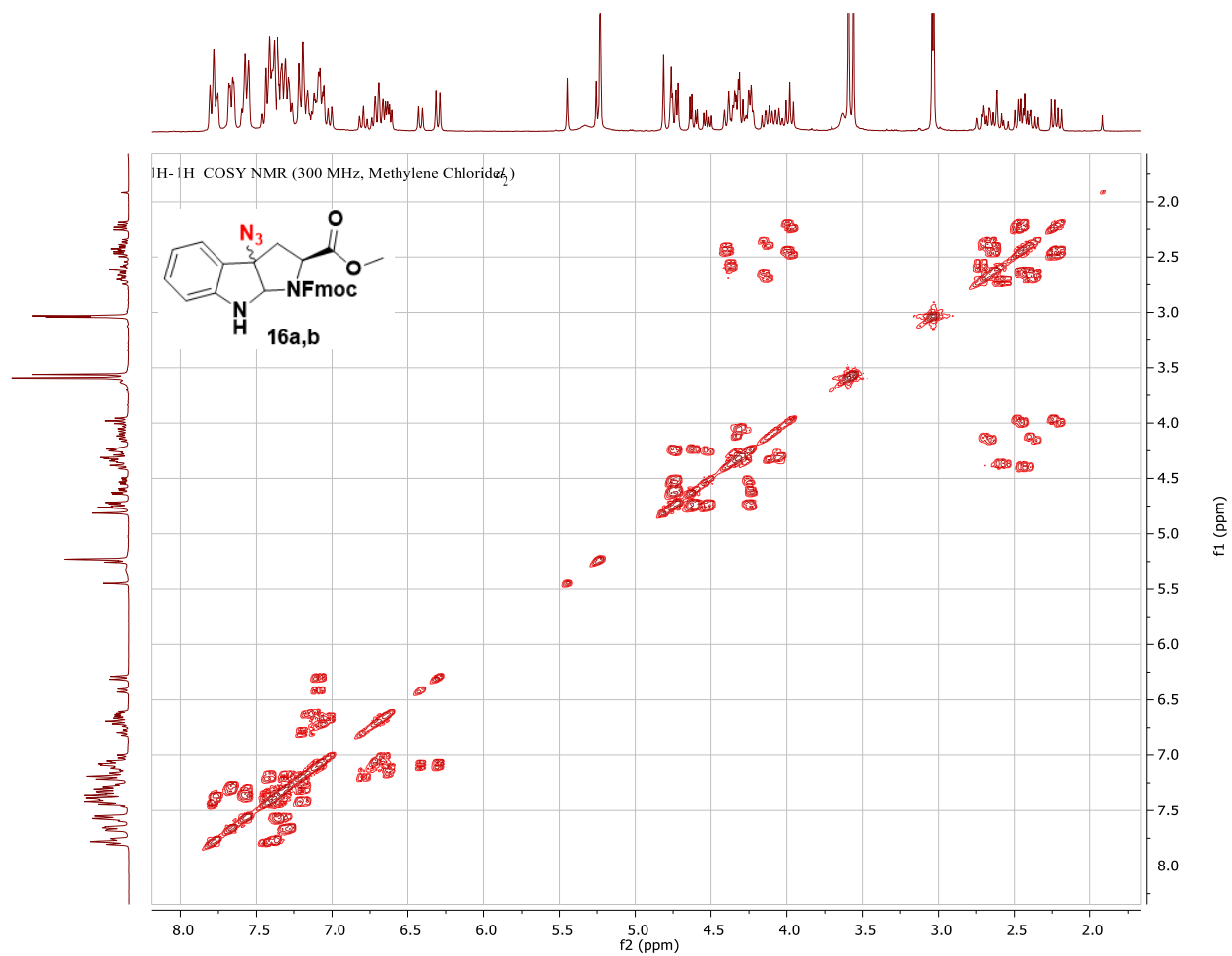
**TLC** (diethyl ether:petroleum ether, 6:4 v/v): R<sub>f</sub> = 0.7 (UV, I<sub>2</sub>, p-anisaldehyde).

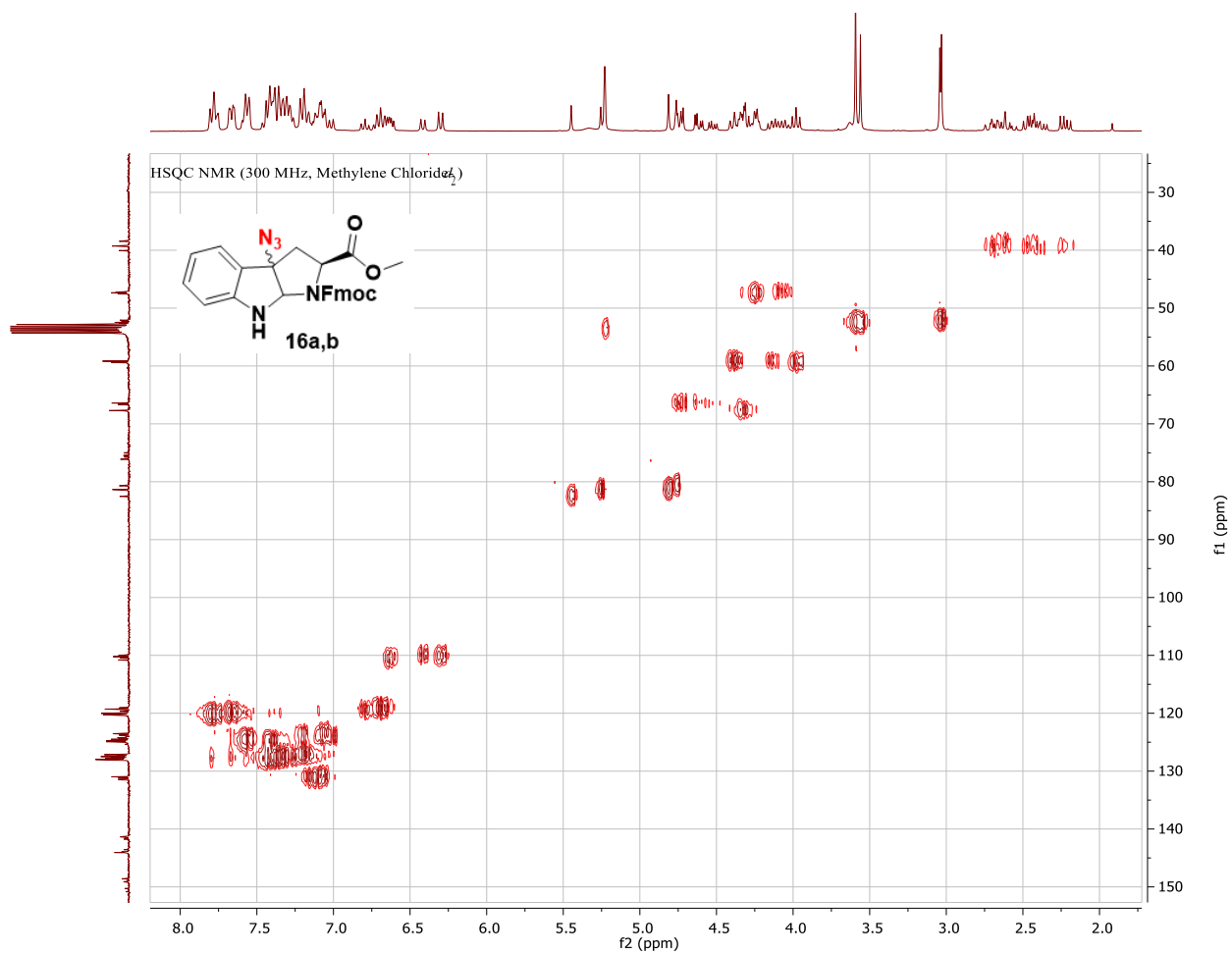
**FT-IR**  $\nu$  (cm<sup>-1</sup>): 2101 (strong, N=N=N).

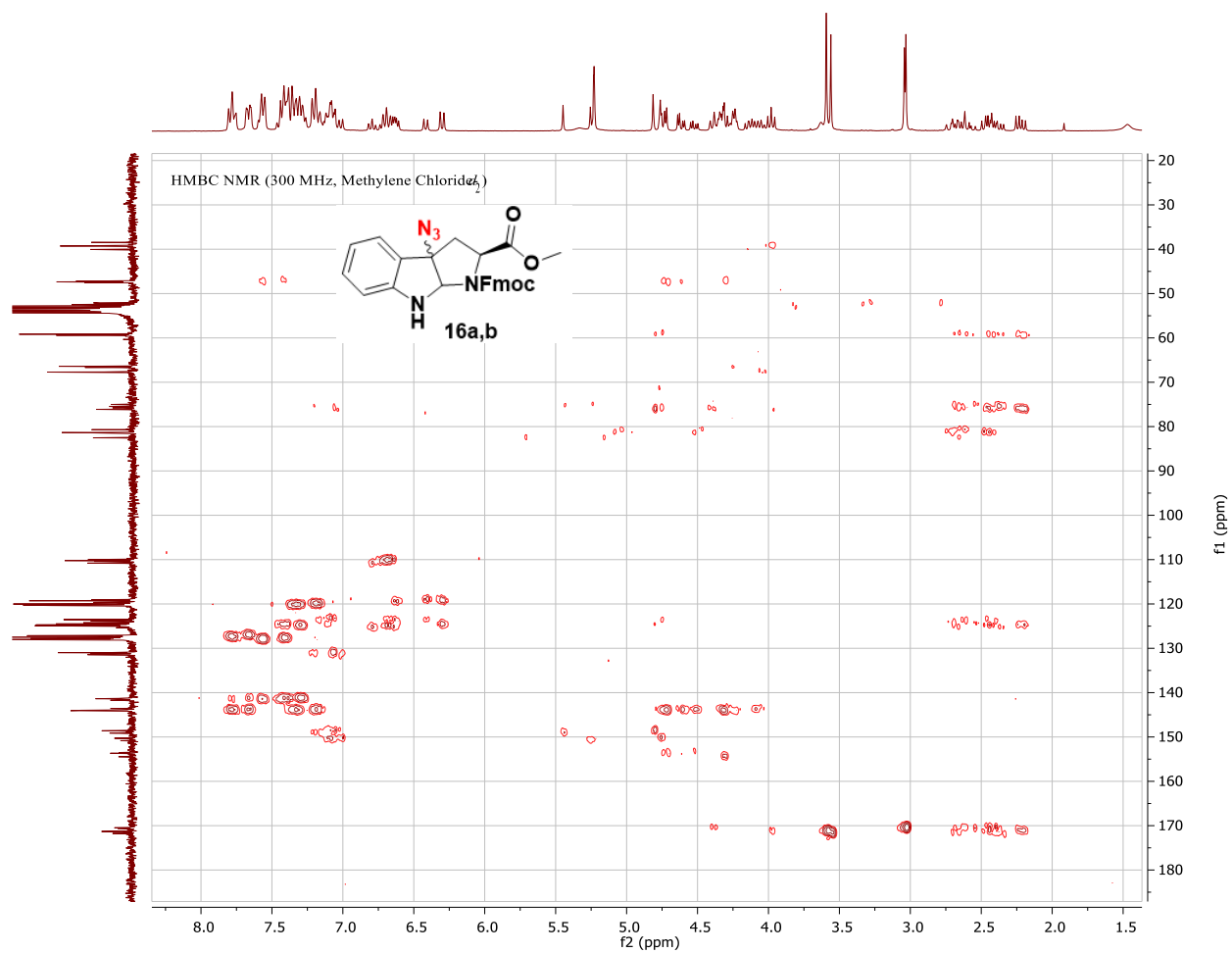




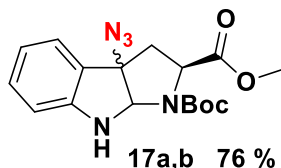








## Synthesis and characterization of compound **17a,b**



**Chemical Formula:** C<sub>17</sub>H<sub>21</sub>N<sub>5</sub>O<sub>4</sub>

**Exact Mass:** 359.1594

**Molecular Weight:** 359.3860

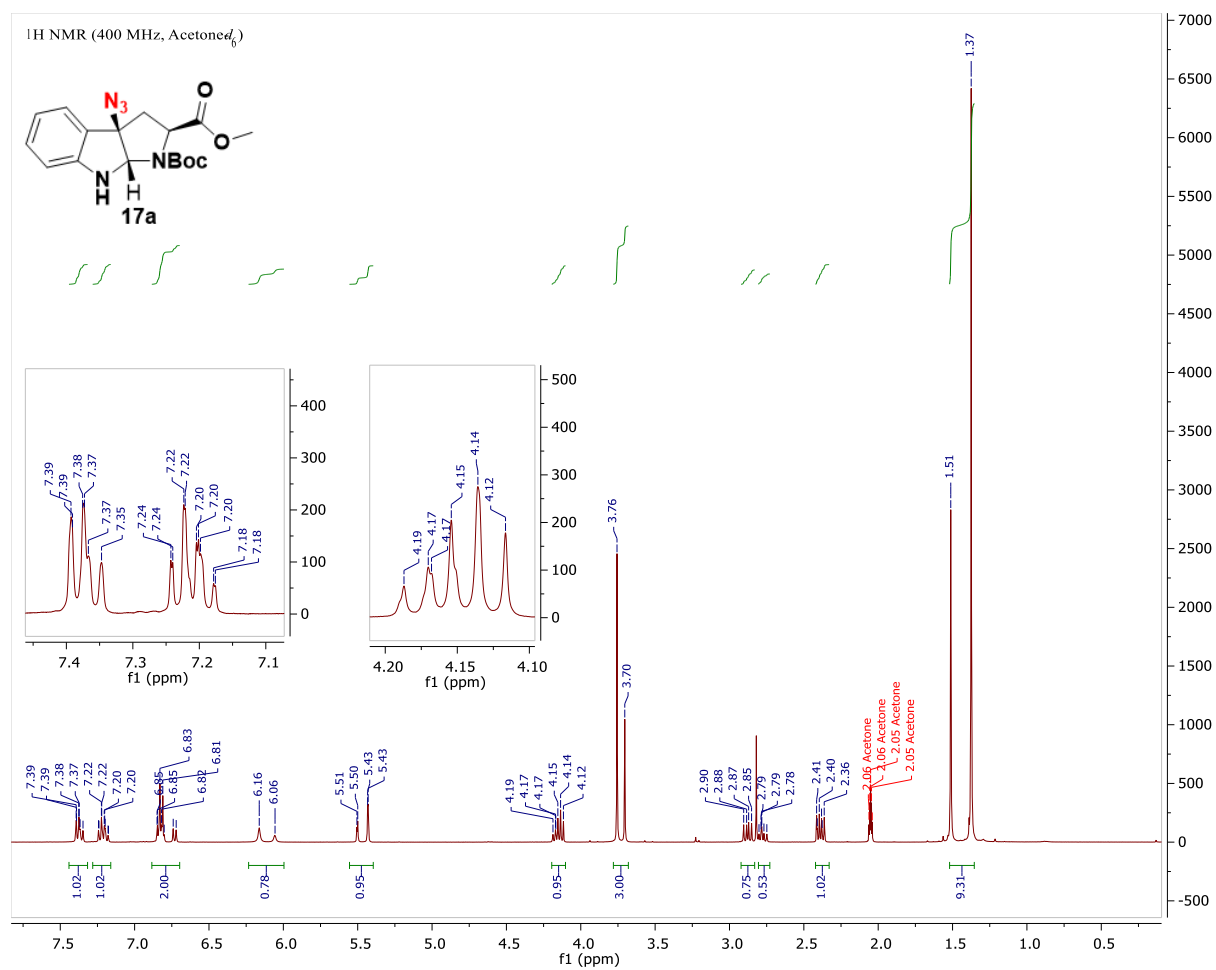
**1-((9H-fluoren-9-yl)methyl) 2-methyl (2S)-3a-azido-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (**17a,b**)** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Boc-FPI-OMe (**6a,b**, 1 equiv, 100 mg, 0.30 mmol) in 4.1 mL of anhydrous DCM followed by azidotrimethylsilane (3 equiv, 103 mg, 117  $\mu$ L, 0.89 mmol) and 1.8 mL of HFIP. The reaction contents were stirred at 21 °C for 2 h. Upon completion, the crude (beige and clear) was concentrated under reduced pressure and purified by silica gel flash column chromatography (isocratic elution, 9:1 hexane/ethyl acetate) to afford 82 mg (0.23 mmol) of **17a,b** as a beige solid in 76 % yield.

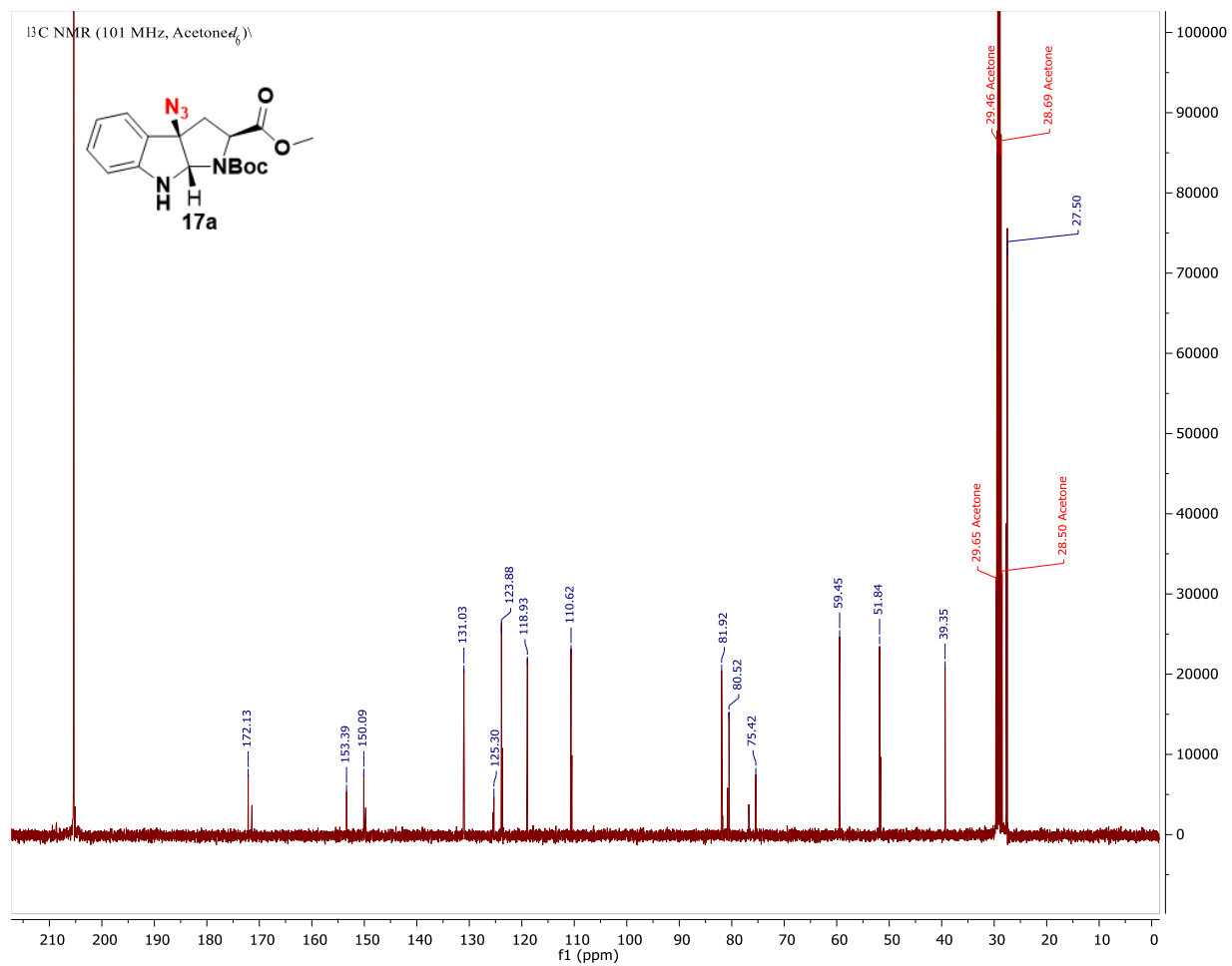
**<sup>1</sup>H NMR**(400 MHz, Acetone-*d*<sub>6</sub>) major diastereomer and rotamers, *syn-cis*  $\delta$  (ppm) 7.44 – 7.32 (m, 1H), 7.28 – 7.16 (m, 1H), 6.88 – 6.70 (m, 2H), 6.16 (br s, 1H), 5.51, 5.43 (two d, *J* = 1.7 Hz, 1H), 4.20 – 4.10 (m, 1H), 3.76, 3.70 (two s, 3H), 2.90 – 2.73 (m, 1H), 2.42 – 2.33 (m, 1H), 1.51, 1.37 (two s, 9H).

**<sup>13</sup>C NMR** (101 MHz, Acetone-*d*<sub>6</sub>) major diastereomer and major rotamer, *syn-cis*  $\delta$  (ppm) 27.50, 39.35, 51.84, 59.45, 75.42, 80.52, 81.92, 110.62, 118.93, 123.88, 125.30, 131.03, 150.09, 153.39, 172.13.

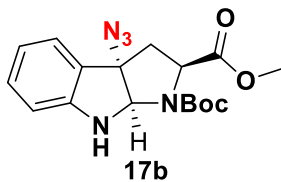
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 359.1594; found 359.1597 for C<sub>17</sub>H<sub>21</sub>N<sub>5</sub>O<sub>4</sub>Na

**TLC** (ethyl acetate:hexane, 1:4 v/v): R<sub>f</sub> = 0.7 (UV, I<sub>2</sub>, p-anisaldehyde).









**Chemical Formula:** C<sub>17</sub>H<sub>21</sub>N<sub>5</sub>O<sub>4</sub>

**Exact Mass:** 359.1594

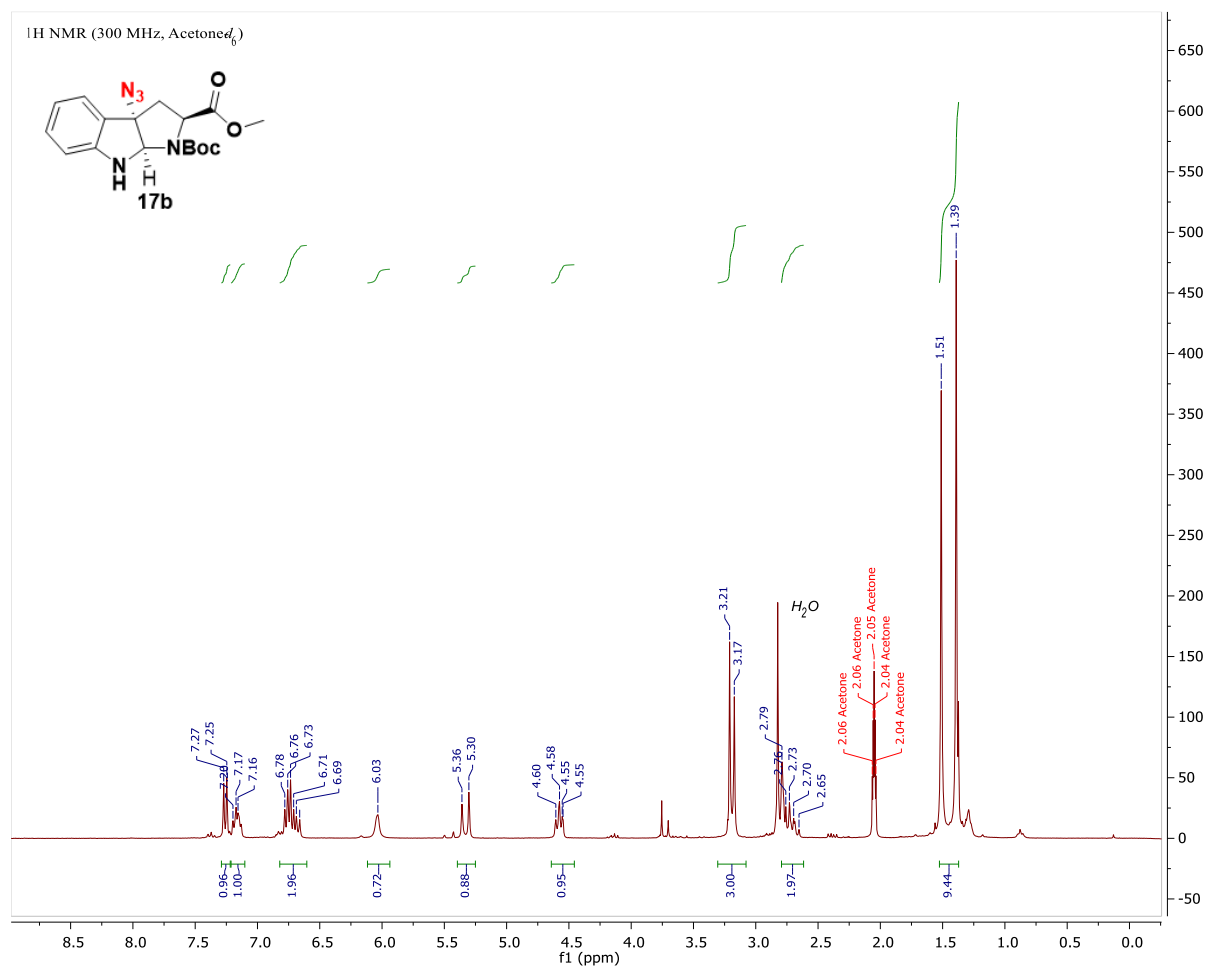
**Molecular Weight:** 359.3860

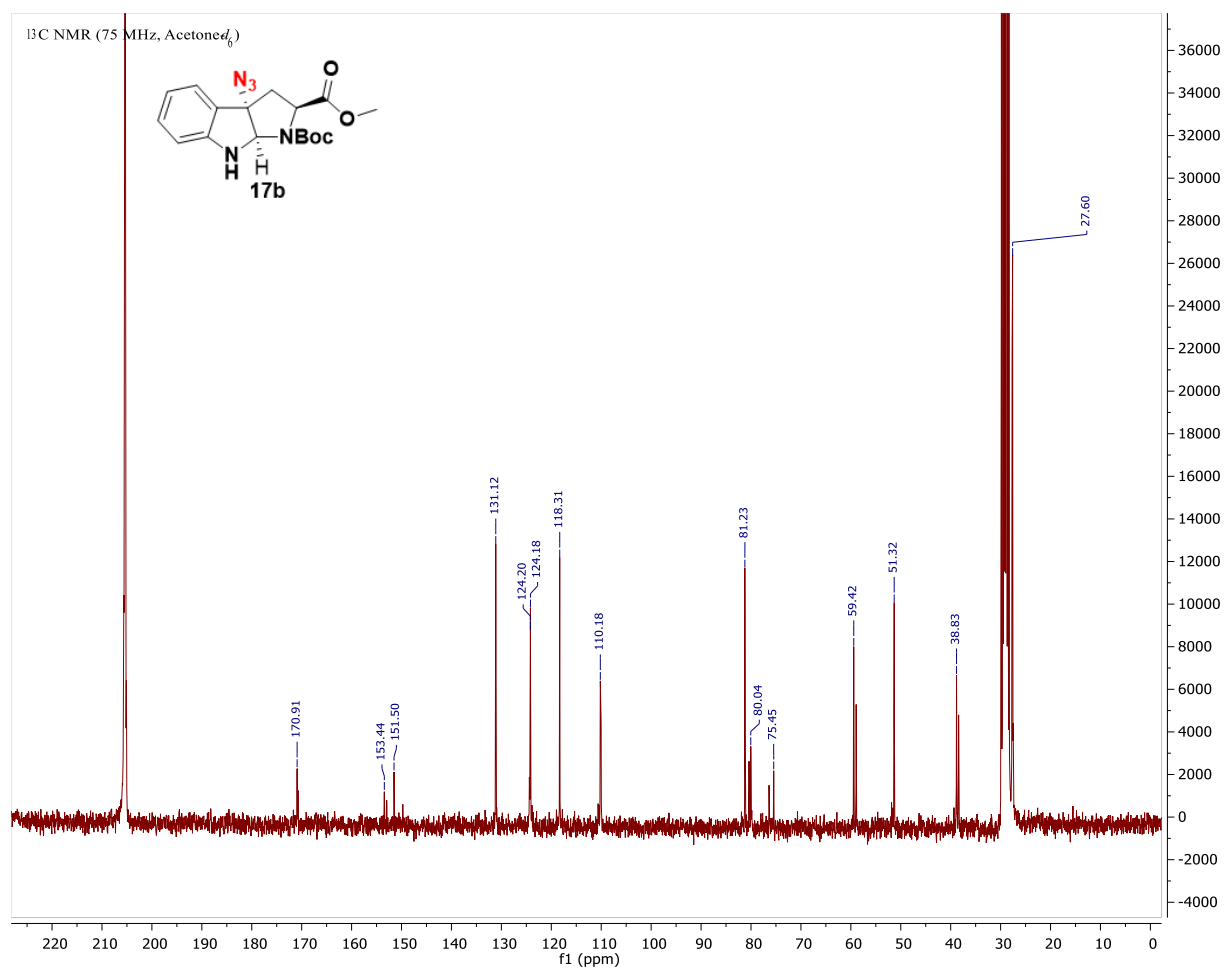
**<sup>1</sup>H NMR**(300 MHz, Acetone-*d*<sub>6</sub>) minor diastereomer and rotamers, *anti-cis* δ (ppm) 7.26 (d, *J* = 7.5 Hz, 1H), 7.21 – 7.10 (m, 1H), 6.79 – 6.67 (m, 2H), 6.03 (br s, 1H), 5.36, 5.30 (two s, 1H), 4.64 – 4.46 (m, 1H), 3.21, 3.17 (two s, 3H), 2.79 – 2.62 (m, 2H), 1.51, 1.39 (two s, 9H).

**<sup>13</sup>C NMR** (75 MHz, Acetone-*d*<sub>6</sub>) minor diastereomer and major rotamer, *anti-cis* δ (ppm) 27.60, 38.83, 51.32, 59.42, 75.45, 80.04, 81.23, 110.18, 118.31, 124.18, 124.20, 131.12, 151.50, 153.44, 170.91.

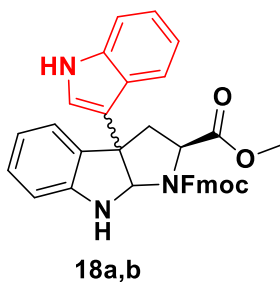
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 359.1594; found 359.1592 for C<sub>17</sub>H<sub>21</sub>N<sub>5</sub>O<sub>4</sub>Na

**TLC** (ethyl acetate:hexane, 1:4 v/v): R<sub>f</sub> = 0.65 (UV, I<sub>2</sub>, p-anisaldehyde).





## Synthesis and characterization of compound **18a,b**



Chemical Formula: C<sub>35</sub>H<sub>29</sub>N<sub>3</sub>O<sub>4</sub>

Exact Mass: 555.22

Molecular Weight: 555.63

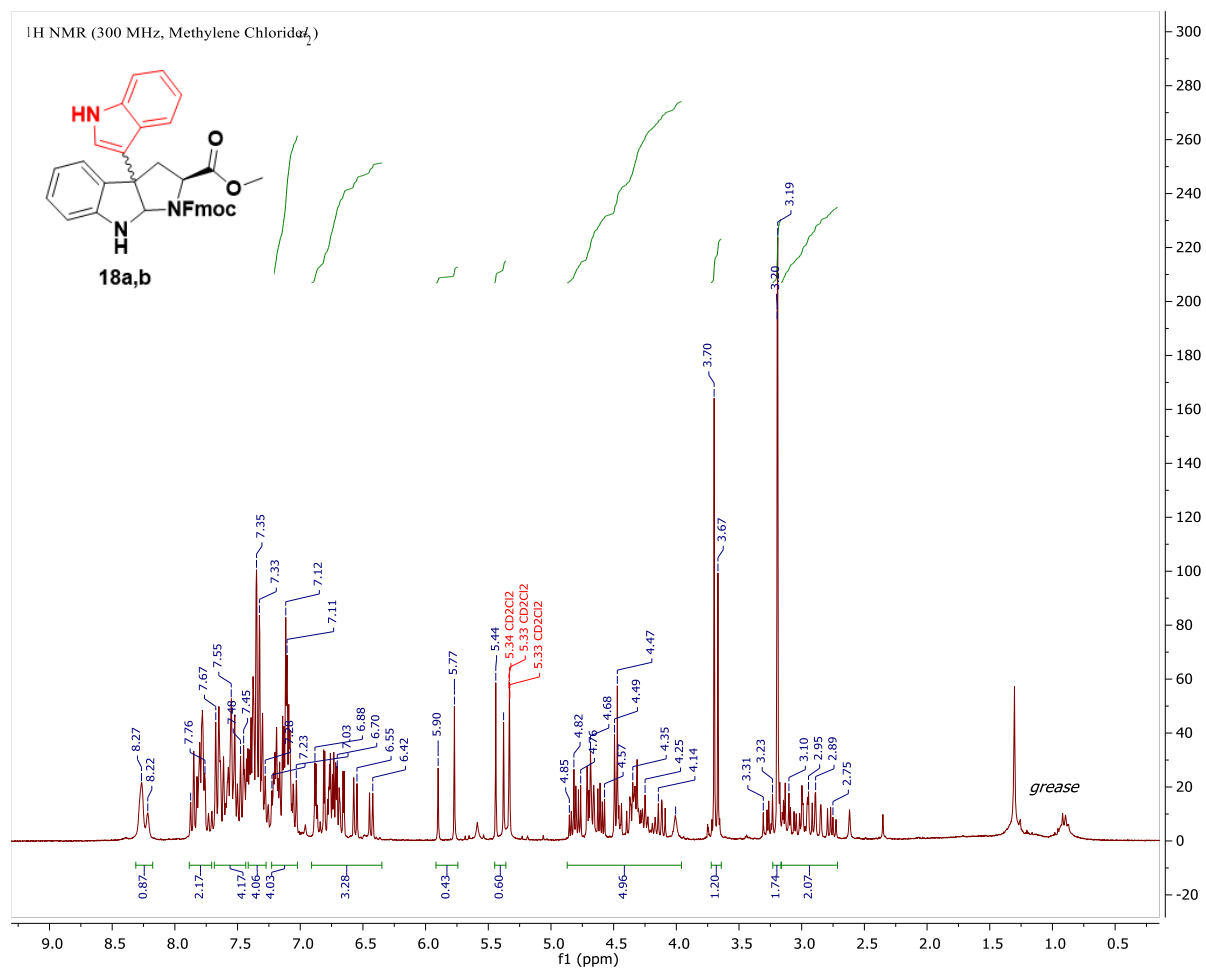
**1-((9H-fluoren-9-yl)methyl) 2-methyl (2S)-3a-(1H-indol-3-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (18a,b).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 150 mg, 0.33mmol) in 5.24 mL of anhydrous DCM followed by indole (recrystallized from hexanes prior to use, 1.15 equiv, 44 mg, 0.38 mmol) and 1.3 mL of HFIP. The reaction contents were stirred at 21 °C for 2 h. Upon completion, the crude (yellow and clear) was concentrated under reduced pressure and purified by silica gel flash column chromatography (gradient elution, 3:7 to 4.5:6.5 diethyl ether:petroleum ether) to afford 78.3 mg (0.141 mmol) of **18a,b** and 49 mg (0.088 mmol) of **19** as beige solids in 70 % overall yield.

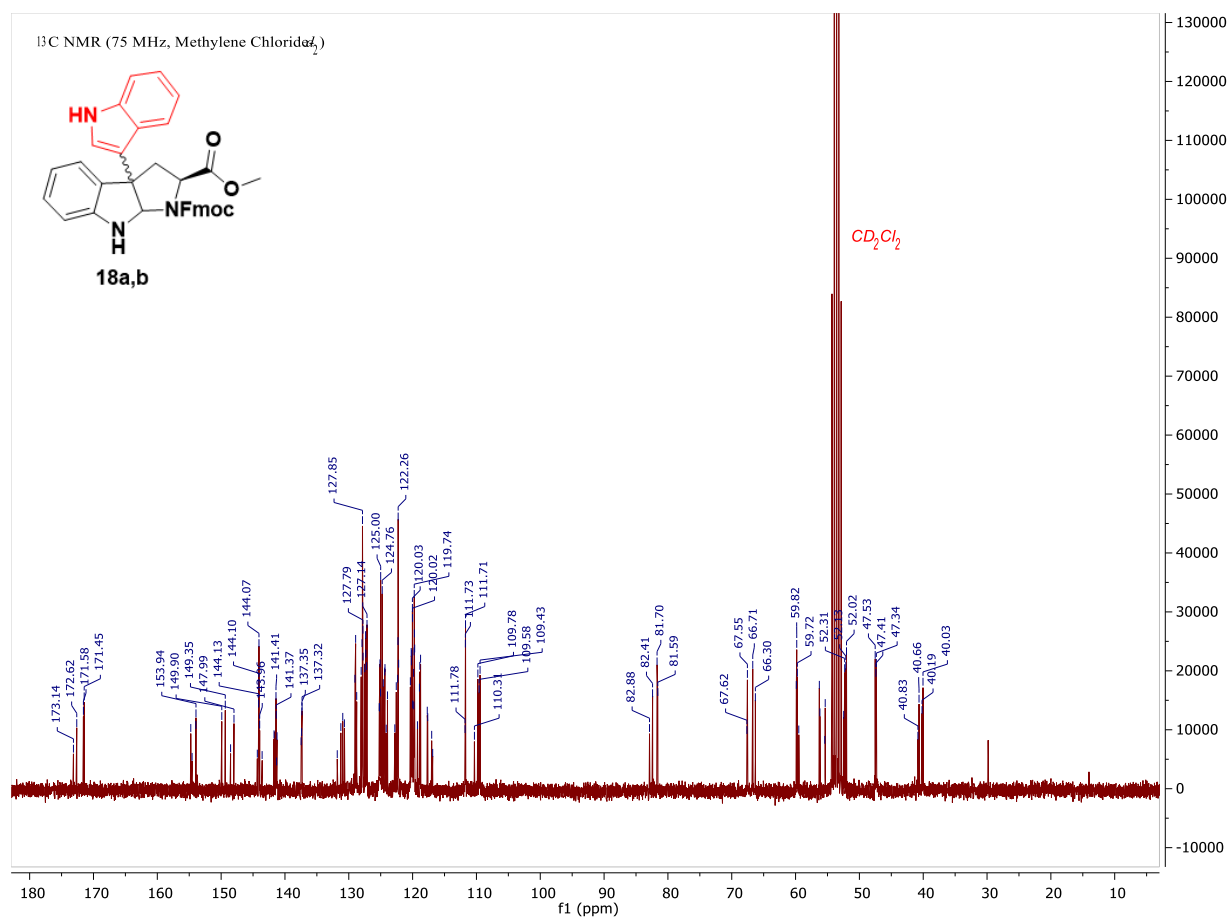
**<sup>1</sup>H NMR** (300 MHz, Methylene Chloride-*d*<sub>2</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1:1.4) δ (ppm) 8.24 (d, *J* = 15.1 Hz, 1H), 7.82 (d, *J* = 34.4 Hz, 2H), 7.69 – 7.43 (m, 4H), 7.42 – 7.27 (m, 4H), 7.23 – 7.02 (m, 4H), 6.91 – 6.35 (m, 3H), 5.90 (s, 0H), 5.77 (s, 0H), 5.44 (s, 0H), 5.38 (s, 0H), 4.87 – 3.96 (m, 5H), 3.70 (s, 1.2H), 3.19-3.20 (s, 0.8 H; s, 0.9 H), 3.16 – 2.71 (m, 2H).

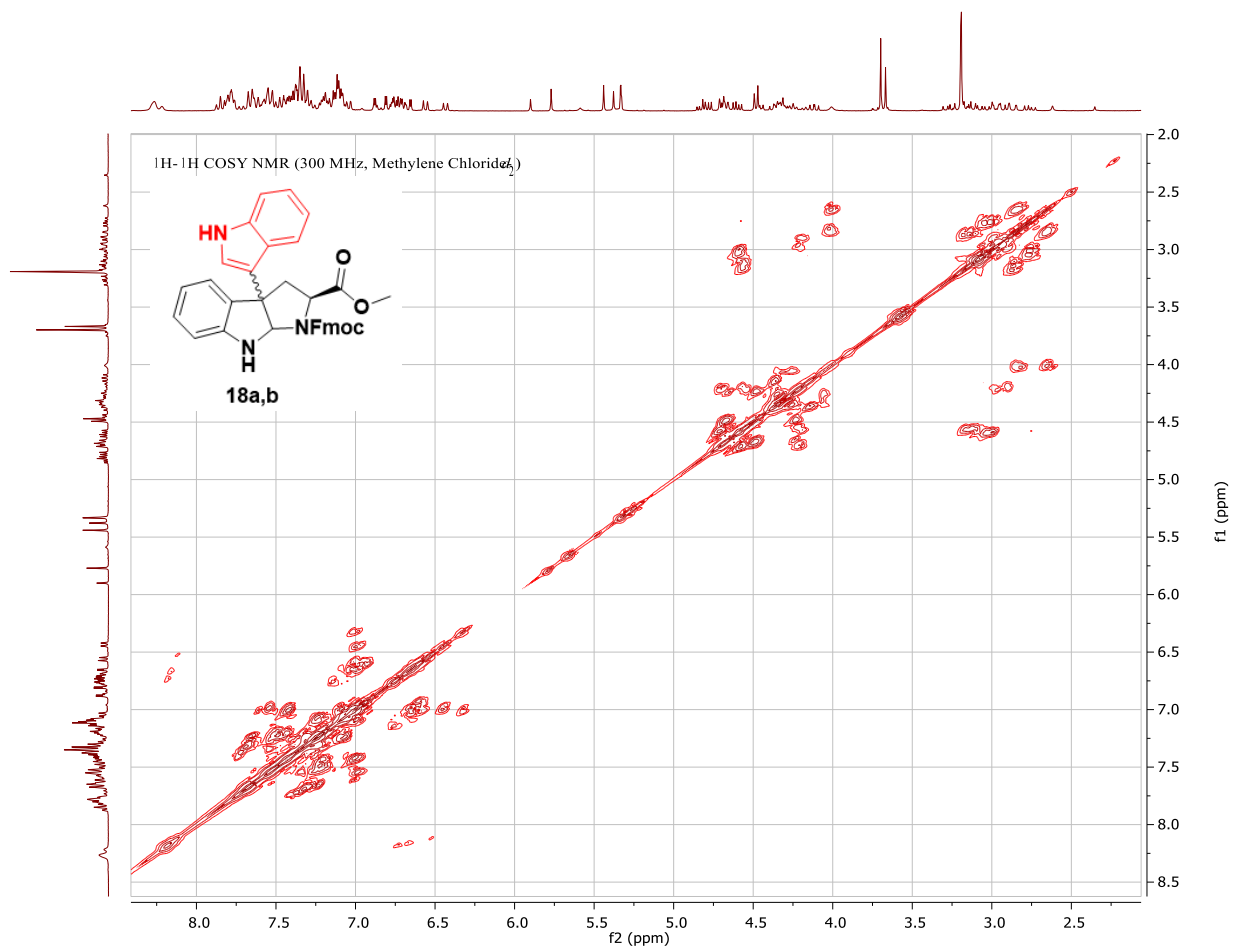
**<sup>13</sup>C NMR** (75 MHz, Methylene Chloride-*d*<sub>2</sub>) two diastereomers and rotamers, *syn-cis:anti-cis* (1:1.4) δ (ppm) 40.03, 40.19, 40.66, 40.83, 47.34, 47.41, 47.53, 52.02, 52.13, 52.31, 52.46, 55.35, 55.42, 56.18, 56.28, 59.49, 59.72, 59.82, 59.88, 66.30, 66.71, 67.55, 67.62, 81.59, 81.70, 82.41, 82.88, 109.43, 109.58, 109.78, 110.31, 111.71, 111.73, 111.78, 116.86, 117.01, 117.63, 117.70, 118.75, 118.87, 118.93, 119.24, 119.68, 119.71, 119.74, 119.77, 119.81, 119.84, 119.99, 120.02, 120.03, 120.13, 120.18, 120.22, 120.35, 122.19, 122.26, 122.29, 122.34, 122.56, 122.78, 123.94, 124.14, 124.33, 124.37, 124.60, 124.76, 125.00, 125.03, 125.11, 125.18, 125.23, 127.14, 127.21, 127.34, 127.37, 127.50, 127.77, 127.79, 127.85, 127.92, 128.06, 128.76, 128.93, 129.03, 130.69, 130.94, 131.24, 131.81, 137.32, 137.35, 137.39, 137.46, 141.25, 141.31, 141.37, 141.41, 141.71, 143.58, 143.96, 144.07, 144.10, 144.13, 144.33, 147.99, 148.52, 149.35, 149.90, 153.94, 153.96, 154.55, 154.76, 171.45, 171.58, 172.62, 173.14.

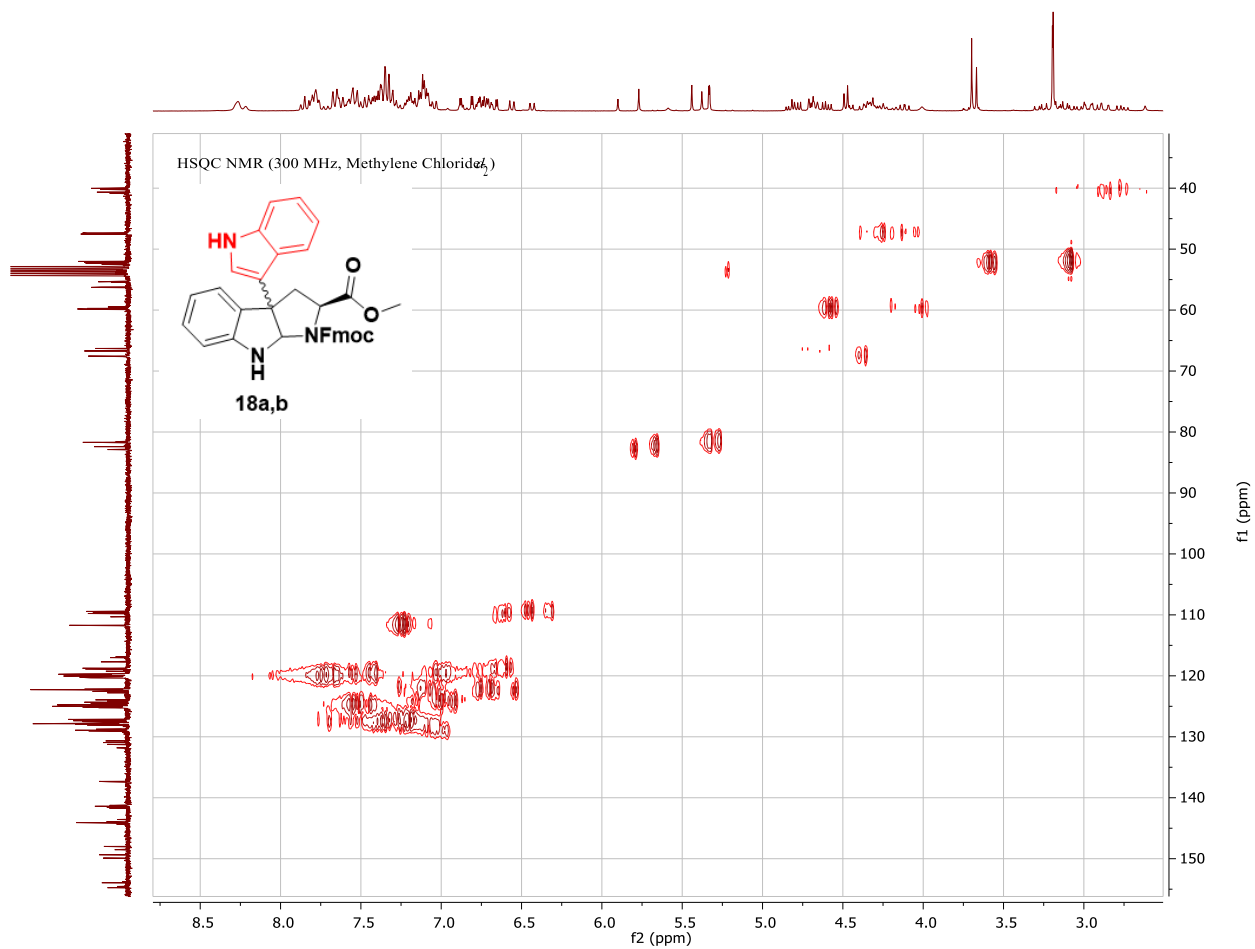
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 578.2056; found 578.2062.

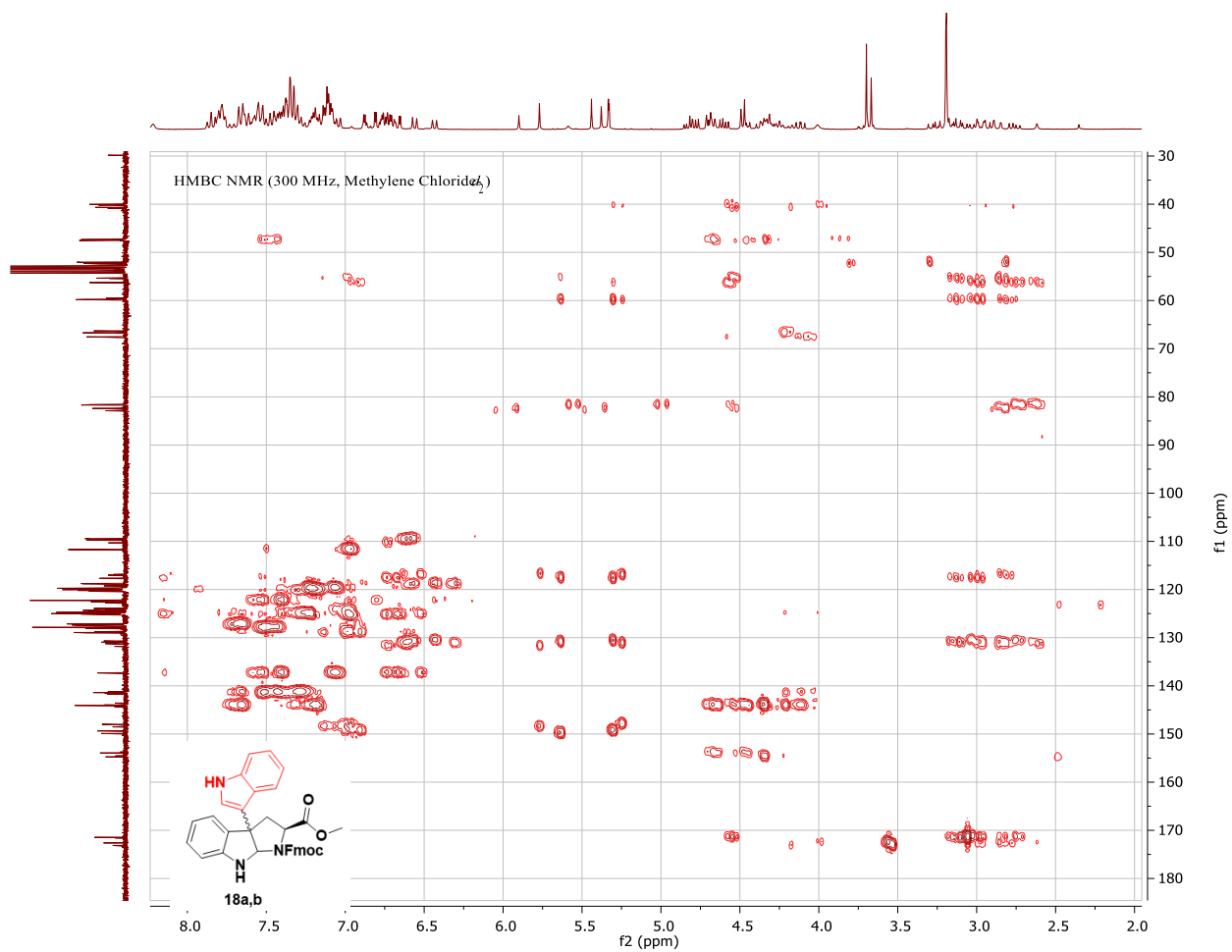
**TLC** (diethyl ether:petroleum ether, 6:4 v/v): R<sub>f</sub> = 0.45 (UV, I<sub>2</sub>, p-anisaldehyde).





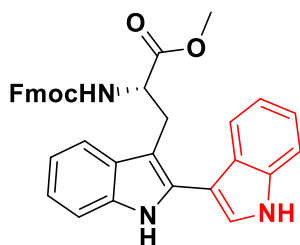








## Synthesis and characterization of compound **19**



**19** 27%<sup>b,e</sup>

**19** 63%<sup>d,e</sup>

Chemical Formula: C<sub>35</sub>H<sub>29</sub>N<sub>3</sub>O<sub>4</sub>

Exact Mass: 555.22

Molecular Weight: 555.63

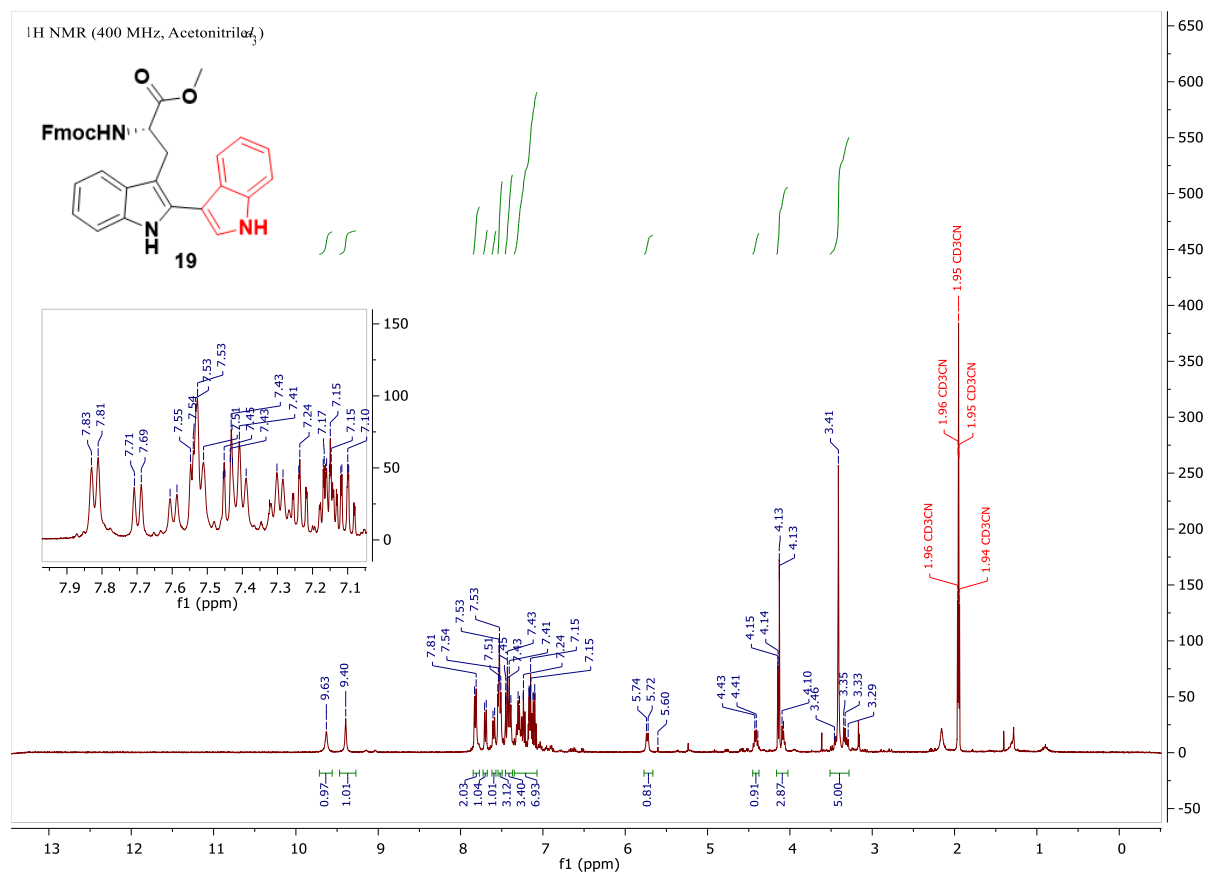
**Methyl (S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(1H,1'H-[2,3'-biindol]-3-yl)propanoate (19).** A flame-dried round bottom flask under positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 140.3 mg, 0.306 mmol) added indole (recrystallized from hexanes prior to use, 1.15 equiv, 41.2 mg, 0.35 mmol) dissolved in 5.7 mL of DCM, followed by HFIP (1.42 mL). The reaction contents were stirred at 41°C for 3 h. Upon completion, the crude (yellow and clear) was concentrated under reduced pressure and purified by silica gel flash column chromatography (gradient elution 3:7 4.5:6.5 to diethyl ether:petroleum) to afford 19.6 mg (0.035 mmol) of **18a,b** and 107 mg (0.19 mmol) of **19** as beige solids in 73 % overall yield.

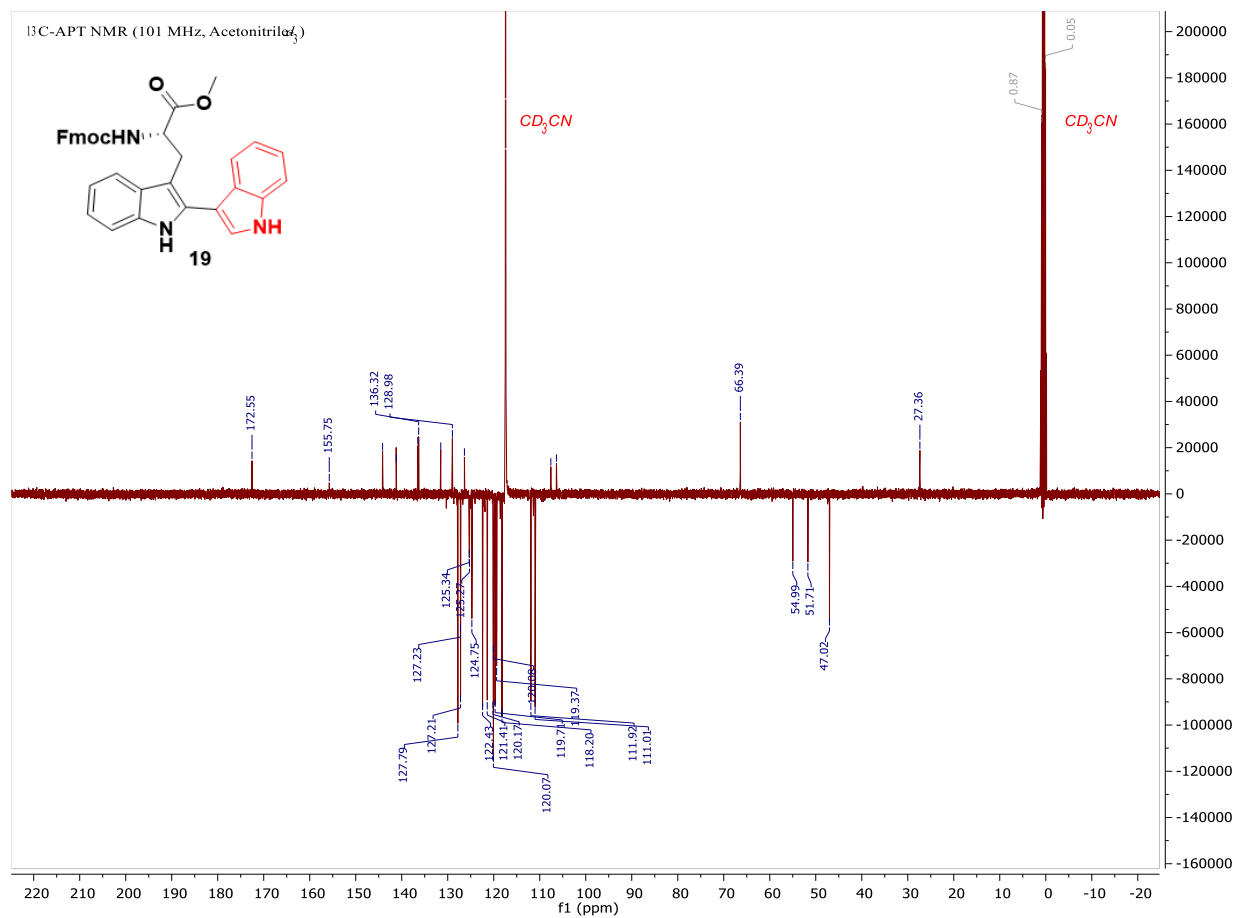
**<sup>1</sup>H NMR** (400 MHz, Acetonitrile-*d*<sub>3</sub>) δ (ppm) 9.63 (s, 1H), 9.40 (s, 1H), 7.82 (d, *J* = 7.7 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.50 (m, 3H), 7.46 – 7.37 (m, 3H), 7.35 – 7.07 (m, 7H), 5.73 (d, *J* = 8.1 Hz, 1H), 4.45 – 4.38 (m, 1H), 4.16 – 4.02 (m, 3H), 3.46–3.29 (m, 5H).

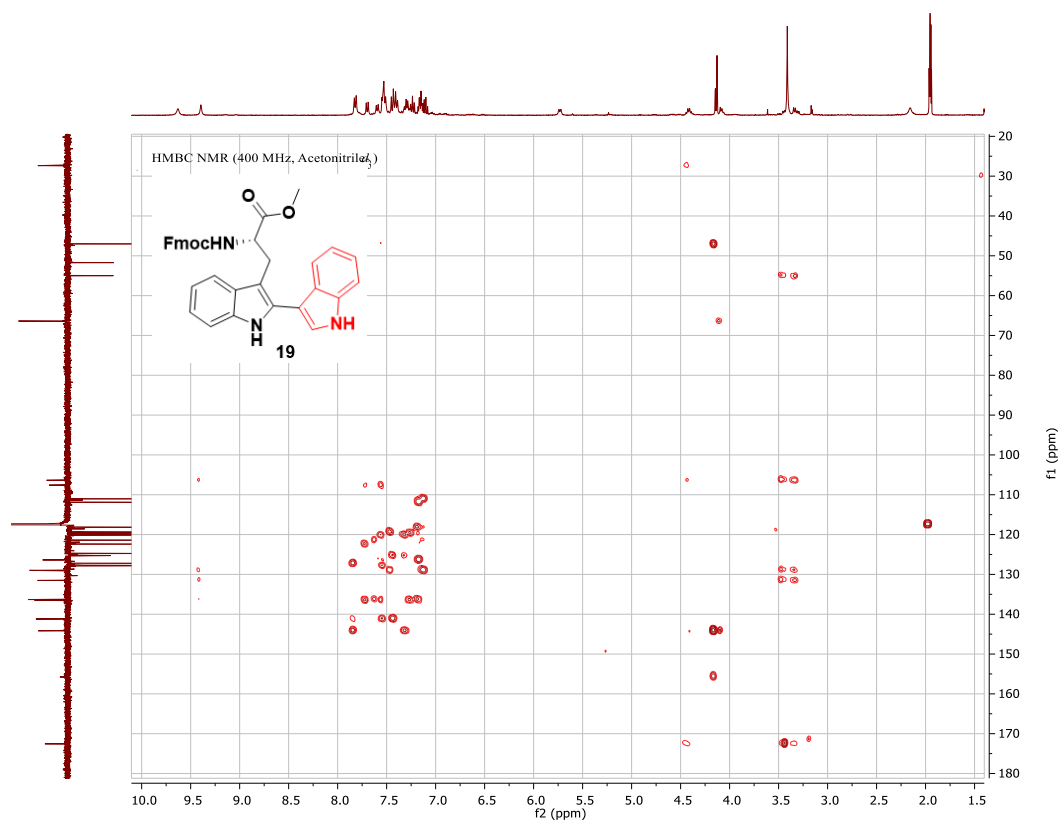
**<sup>13</sup>C NMR** (101 MHz, Acetonitrile-*d*<sub>3</sub>) δ (ppm) 27.36, 47.02, 51.71, 54.99, 66.39, 106.37, 107.59, 111.01, 111.92, 117.42, 118.20, 119.37, 119.71, 120.07, 120.08, 120.17, 121.41, 122.43, 124.75, 125.27, 125.34, 126.37, 127.21, 127.23, 127.79, 128.98, 131.52, 136.32, 136.51, 141.20, 144.16, 155.75, 172.55.

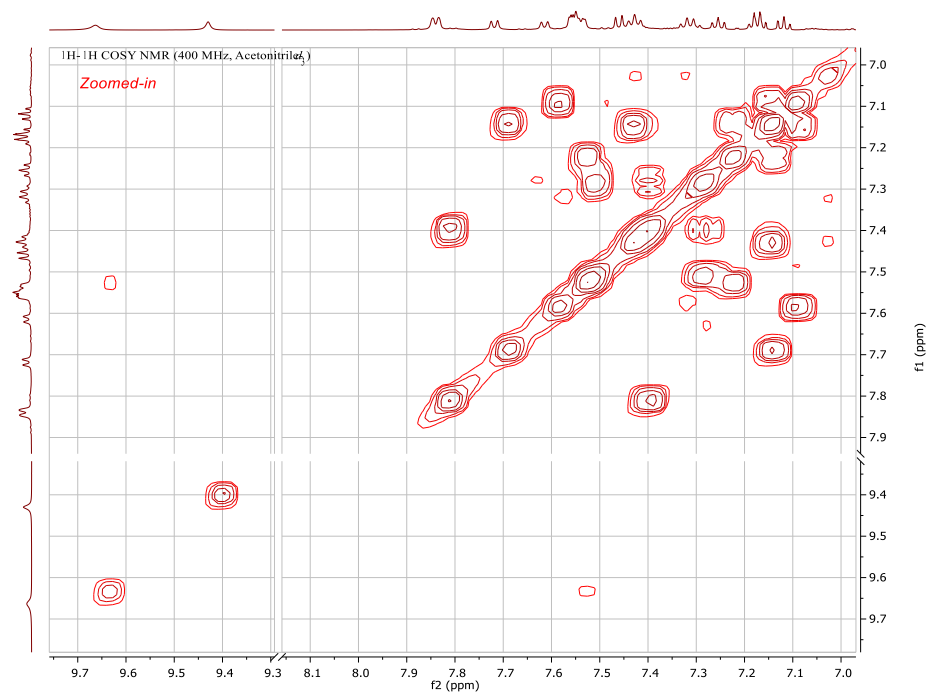
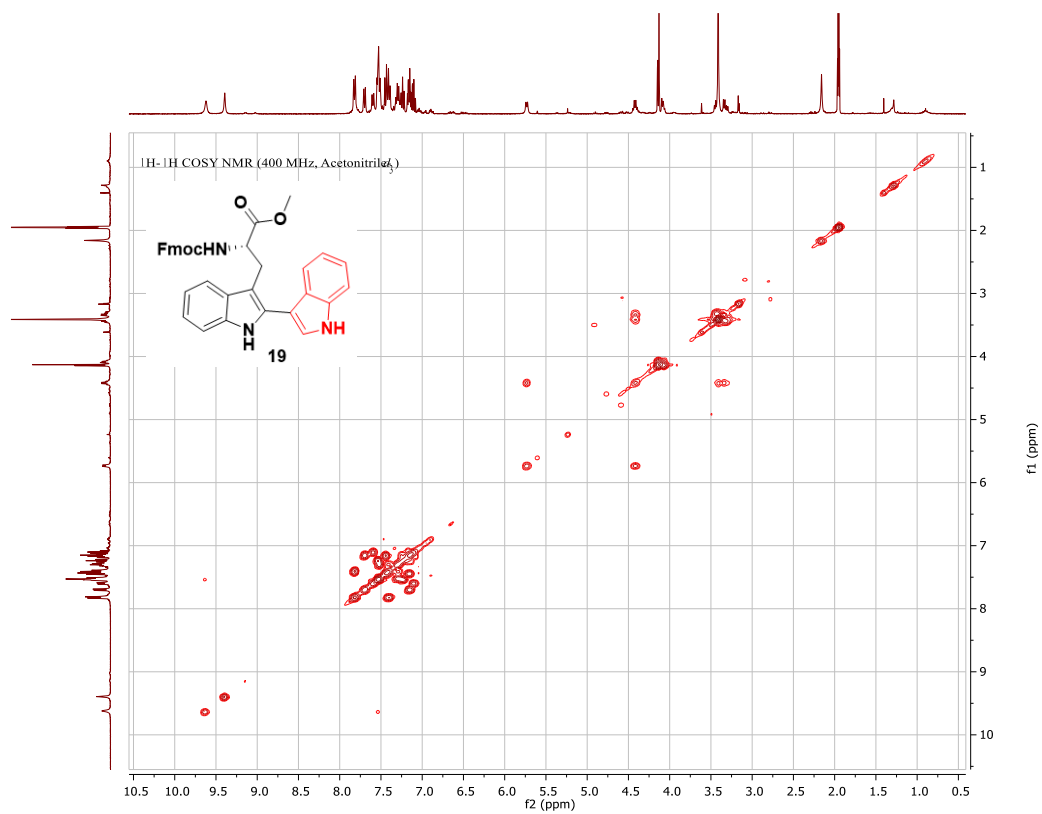
**HRMS** (ESI-TOF, *m/z*): [M+Na]<sup>+</sup> calculated 578.2056; found 578.2050.

**TLC** (diethyl ether:petroleum ether, 6:4 v/v): R<sub>f</sub> = 0.4 (UV, I<sub>2</sub>, p-anisaldehyde).



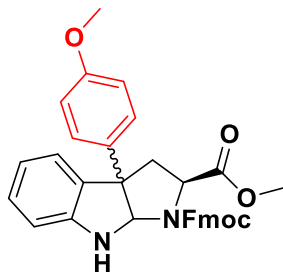






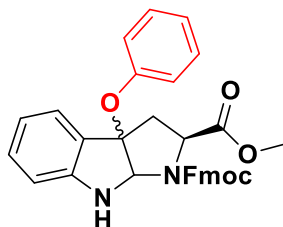


## Attempted synthesis of 20-22a,b



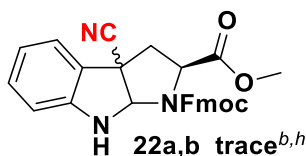
**20a,b** trace<sup>b,g</sup>

A small glass vial under a positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 5 mg, 11  $\mu\text{mol}$ ) in 176  $\mu\text{L}$  of anhydrous DCM, followed by anisole (2.5 equiv, 3.0 mg, 3.0  $\mu\text{L}$ , 27.5  $\mu\text{mol}$ ) and 44  $\mu\text{L}$  of HFIP. The reaction contents were stirred for 2 h at 21°C. TLC analysis (3:2 diethyl ether/pet ether) revealed numerous byproducts.



**21a,b** trace<sup>b,g</sup>

A small glass vial under a positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 5 mg, 11  $\mu\text{mol}$ ) in 176  $\mu\text{L}$  of anhydrous DCM, followed by phenol (2.5 equiv, 2.6 mg, 27.5  $\mu\text{mol}$ ) and 44  $\mu\text{L}$  of HFIP. The reaction contents were stirred for 2 h at 21°C. TLC analysis (3:2 diethyl ether/pet ether) revealed numerous byproducts.



**22a,b** trace<sup>b,h</sup>

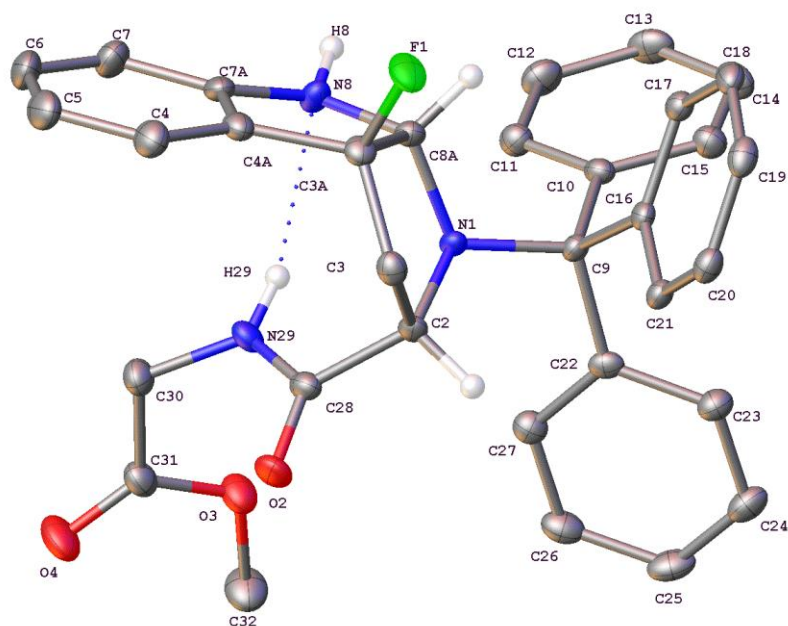
A small glass vial under a positive Ar atmosphere was charged with N-Fmoc-FPI-OMe (**5a,b**, 1 equiv, 10 mg, 22  $\mu\text{mol}$ ) in 352  $\mu\text{L}$  of anhydrous DCM, followed by TMSCN (2.5 equiv, 5.5 mg, 6.9  $\mu\text{L}$ , 55  $\mu\text{mol}$ ) and 88  $\mu\text{L}$  of HFIP. The reaction contents were stirred for 2 h at 21°C. TLC analysis (3:2 diethyl ether/pet ether), crude  $^1\text{H}$ - and  $^{19}\text{F}$ -NMR revealed no conversion, starting material was recovered. The reaction was also attempted with KCN as a cyanide source under same conditions as described for TMSCN, starting material was recovered.

## References

1. Armarego, W. L. F.; Chai, C. L. L., Chapter 4 - Purification of Organic Chemicals. In *Purification of Laboratory Chemicals (Fifth Edition)*, Butterworth-Heinemann: Burlington, 2003; pp 80-388.
2. May, J. P.; Perrin, D. M., Intraannular Savige-Fontana reaction: One-step conversion of one class of monocyclic peptides into another class of bicyclic peptides. *Chem.-Eur. J.* **2008**, *14* (11), 3404-3409.
3. Cousins, B. G.; Das, A. K.; Sharma, R.; Li, Y. N.; McNamara, J. P.; Hillier, I. H.; Kinloch, I. A.; Ulijn, R. V., Enzyme-Activated Surfactants for Dispersion of Carbon Nanotubes. *Small* **2009**, *5* (5), 587-590.
4. Wu, W. B.; Li, Z.; Zhou, G. B.; Jiang, S., Total synthesis of argyrins A and E. *Tetrahedron Letters* **2011**, *52* (19), 2488-2491.
5. Fujiwara, T.; Yasuda, H.; Nishimura, Y.; Nambu, H.; Yakura, T., Synthesis of 10b-fluorinated analogues of protubonine A and its 11a-epimer via fluorocyclisation of tryptophan-containing dipeptides. *RSC Adv.* **2015**, *5* (7), 5464-5473.
6. Taniguchi, M.; Hino, T., CYCLIC TAUTOMERS OF TRYPTOPHANS AND TRYPTAMINES .4. SYNTHESIS OF CYCLIC TAUTOMERS OF TRYPTOPHANS AND TRYPTAMINES. *Tetrahedron* **1981**, *37* (8), 1487-1494.
7. Crich, D.; Banerjee, A., Chemistry of the hexahydropyrrolo 2,3-b indoles: Configuration, conformation, reactivity, and applications in synthesis. *Accounts of Chemical Research* **2007**, *40* (2), 151-161.
8. Fujiwara, T.; Seki, T.; Yakura, T.; Takeuchi, Y., Useful procedures for fluorocyclization of tryptamine and tryptophol derivatives to 3a-fluoropyrrolo 2,3-b indoles and 3a-fluorofuro 2,3-b indoles. *Journal of Fluorine Chemistry* **2014**, *165*, 7-13.



## Crystal Structure of compound **2b**: Data and Experimental



### Sample ID: dp062

**Experimental.** Single colourless rod-shaped crystals of **dp062** were recrystallised from a mixture of hexane and EtOAc by slow evaporation. A suitable crystal 0.40×0.11×0.10 mm<sup>3</sup> was selected and mounted on a mylar loop in oil on a Bruker APEX II area detector diffractometer. The crystal was kept at a steady  $T = 90(2)$  K during data collection. The structure was solved with the **XT** (Sheldrick, 2015) structure solution program using the Intrinsic Phasing solution method and by using **Olex2** (Dolomanov et al., 2009) as the graphical interface. The model was refined with version 2018/3 of **XL** (Sheldrick, 2015) using Least Squares minimisation.

**Crystal Data.** C<sub>37</sub>H<sub>38</sub>FN<sub>3</sub>O<sub>5</sub>,  $M_r = 623.70$ , monoclinic,  $P2_1$  (No. 4),  $a = 11.8601(2)$  Å,  $b = 14.1617(3)$  Å,  $c = 20.1222(4)$  Å,  $\beta = 105.4830(10)^\circ$ ,  $\alpha = \gamma = 90^\circ$ ,  $V = 3257.06(11)$  Å<sup>3</sup>,  $T = 90(2)$  K,  $Z = 4$ ,  $Z' = 2$ ,  $\mu(\text{CuK}\alpha) = 0.723$ , 84520 reflections measured, 11434 unique ( $R_{\text{int}} = 0.0406$ ) which were used in all calculations. The final  $wR_2$  was 0.0951 (all data) and  $R_1$  was 0.0353 ( $I > 2(I)$ ).

**Compound****AP-E512-F45-48**

Formula	C <sub>37</sub> H <sub>38</sub> FN <sub>3</sub> O <sub>5</sub>
$D_{calc.}/\text{g cm}^{-3}$	1.272
$\mu/\text{mm}^{-1}$	0.723
Formula Weight	623.70
Colour	colourless
Shape	rod
Size/mm <sup>3</sup>	0.40×0.11×0.10
$T/\text{K}$	90(2)
Crystal System	monoclinic
Flack Parameter	-0.05(5)
Hooft Parameter	-0.03(3)
Space Group	$P2_1$
$a/\text{\AA}$	11.8601(2)
$b/\text{\AA}$	14.1617(3)
$c/\text{\AA}$	20.1222(4)
$\alpha/^\circ$	90
$\beta/^\circ$	105.4830(10)
$\gamma/^\circ$	90
$V/\text{\AA}^3$	3257.06(11)
$Z$	4
$Z'$	2
Wavelength/ $\text{\AA}$	1.54178
Radiation type	CuK $_{\alpha}$
$\Theta_{min}/^\circ$	2.278
$\Theta_{max}/^\circ$	66.689
Measured Refl.	84520
Independent Refl.	11434
Reflections with $I > 2(I)$	11129
$R_{int}$	0.0406
Parameters	872
Restraints	1377
Largest Peak	0.572
Deepest Hole	-0.339
GooF	1.020
$wR_2$ (all data)	0.0951
$wR_2$	0.0940
$R_1$ (all data)	0.0364
$R_1$	0.0353

## Structure Quality Indicators

Reflections:	d min (Cu)	0.84	I/ $\sigma$	47.2	R <sub>int</sub>	4.06%
	complete	99%				
Refinement:	Shift	0.004	Max Peak	0.6	Min Peak	-0.3
	Flack	-0.05(5)			Goof	1.020

A colourless rod-shaped crystal with dimensions 0.40×0.11×0.10 mm<sup>3</sup> was mounted on a mylar loop in oil. Data were collected using a Bruker APEX II area detector diffractometer equipped with an Oxford Cryosystems low-temperature device operating at  $T = 90(2)$  K.

Data were measured using  $\phi$  and  $\omega$  scans of 1.0 ° per frame for between 2 and 10 s using CuK $\alpha$  radiation (microfocus sealed X-ray tube, 45 kV, 0.60 mA). The total number of runs and images was based on the strategy calculation from the program APEX3. The maximum resolution that was achieved was  $\theta = 66.689^\circ$  (0.84 Å).

The diffraction pattern was indexed and the unit cell was refined using **SAINT** (Bruker, V8.38A, after 2013) on 9951 reflections, 12% of the observed reflections. Data reduction, scaling and absorption corrections were performed using **SAINT** (Bruker, V8.38A, after 2013). The final completeness is 99.90 % out to 66.689° in  $\theta$ .

A numerical absorption correction was performed using **SADABS**-2016/2 (Bruker, 2016/2).  $wR_2(\text{int})$  was 0.0934 before and 0.0552 after correction. The ratio of minimum to maximum transmission is 0.8381. The  $\lambda/2$  correction factor is not present. The absorption coefficient  $\mu$  of this material is 0.723 mm<sup>-1</sup> at this wavelength ( $\lambda = 1.542\text{Å}$ ) and the minimum and maximum transmissions are 0.787 and 0.940.

The structure was solved and the space group  $P2_1$  (# 4) determined by the **XT** (Sheldrick, 2015) structure solution program using Intrinsic Phasing and refined by Least Squares using version 2018/3 of **XL** (Sheldrick, 2015). There are two chemically identical but crystallographically different molecules in the asymmetric unit. Additionally, the material crystallizes with two molecules of EtOAc in the asymmetric unit. One solvent molecule is disordered and was modeled in two orientations. Each molecule contains three chiral carbons, C2, C3A and C8A, whose absolute configurations were determined to be S, S and R, respectively. All non-hydrogen atoms were refined anisotropically. Most hydrogen atom positions were calculated geometrically and refined using the riding model, however all N—H hydrogen atoms were located in difference maps and refined freely.

The value of  $Z'$  is 2. This means that there are two independent molecules in the asymmetric unit.

The Flack parameter was refined to -0.05(5). Determination of absolute structure using Bayesian statistics on Bijvoet differences using the Olex2 results in -0.03(3). Note: The Flack parameter is used to determine chirality of the crystal studied, the value should be near 0, a value of 1 means that the stereochemistry is wrong and the model should be inverted. A value of 0.5 means that the crystal consists of a racemic mixture of the two enantiomers.

**Table 1:** Fractional Atomic Coordinates ( $\times 10^4$ ) and Equivalent Isotropic Displacement Parameters ( $\text{\AA}^2 \times 10^3$ ) for **dp062**.  $U_{eq}$  is defined as 1/3 of the trace of the orthogonalised  $U_{ij}$ .

Atom	x	y	z	$U_{eq}$
C35A	10143(13)	2200(20)	3407(15)	62(8)
C36A	9013(9)	2617(9)	3050(6)	52(4)
F1_1	9757.7(14)	3077.4(12)	7068.0(8)	24.1(4)
O2_1	10130.6(17)	5733.4(13)	5272.5(11)	24.5(4)
O3_1	9772.4(17)	4957.9(15)	3608.9(10)	24.7(4)
O4_1	11583.7(18)	5500.8(17)	3696.6(11)	32.7(5)
O5_1	12170(3)	1682(2)	3708(2)	83.1(12)
O6_1	11023(3)	2873(2)	3267.5(15)	53.5(7)
N1_1	8476.0(17)	3593.0(14)	5337.6(10)	12.8(4)
N8_1	10031.6(19)	2411.2(16)	5522.5(12)	18.5(5)
N29_1	10302.0(19)	4266.2(16)	4876.3(11)	17.3(4)
C2_1	8933(2)	4539.6(17)	5576.5(13)	14.1(5)
C3_1	9504(2)	4462.2(18)	6355.1(13)	16.3(5)
C3A_1	9931(2)	3447.5(18)	6447.9(13)	16.0(5)
C4_1	12200(2)	3657(2)	6824.7(14)	23.1(6)
C4A_1	11167(2)	3265.7(19)	6430.2(13)	17.9(5)
C5_1	13248(2)	3366(2)	6703.2(16)	27.3(6)
C6_1	13242(2)	2702(2)	6196.0(17)	29.0(7)
C7_1	12210(2)	2317(2)	5787.6(16)	25.6(6)
C7A_1	11163(2)	2616.5(18)	5909.4(14)	18.3(5)
C8A_1	9175(2)	2890.7(18)	5817.3(13)	15.0(5)
C9_1	7174(2)	3481.9(17)	5174.5(12)	13.2(5)
C10_1	6817(2)	2535.8(17)	4794.5(13)	14.5(5)
C11_1	7531(2)	2078.6(18)	4449.8(13)	17.5(5)
C12_1	7152(2)	1265(2)	4069.5(14)	22.5(6)
C13_1	6050(2)	898.6(19)	4021.4(14)	24.2(6)
C14_1	5317(2)	1370(2)	4345.1(14)	23.5(6)
C15_1	5696(2)	2177.3(18)	4728.3(13)	18.4(5)
C16_1	6789(2)	3555.5(18)	5845.6(12)	13.4(5)
C17_1	6647(2)	2763.7(18)	6231.6(13)	15.6(5)
C18_1	6418(2)	2862.8(19)	6869.9(13)	18.0(5)
C19_1	6359(2)	3752(2)	7145.9(13)	19.0(5)
C20_1	6491(2)	4542.4(19)	6773.7(13)	17.7(5)
C21_1	6693(2)	4444.0(18)	6128.5(13)	14.7(5)
C22_1	6571(2)	4222.1(17)	4635.2(12)	14.5(5)
C23_1	5432(2)	4517.4(19)	4593.8(13)	18.5(5)
C24_1	4824(2)	5098.8(19)	4060.9(14)	21.6(5)
C25_1	5351(3)	5393(2)	3558.2(14)	23.8(6)
C26_1	6481(3)	5111.5(19)	3595.1(14)	21.9(6)
C27_1	7088(2)	4524.4(18)	4124.6(13)	17.4(5)
C28_1	9833(2)	4900.1(18)	5217.5(13)	16.4(5)
C30_1	11262(2)	4522(2)	4595.9(14)	21.3(5)
C31_1	10904(2)	5052.6(19)	3920.1(14)	20.3(5)
C32_1	9373(3)	5442(3)	2954.6(15)	31.0(7)
C33_1	12032(4)	2447(3)	3419(2)	53.5(10)
C34_1	12940(4)	3018(4)	3189(3)	74.5(15)
C35_1	10005(9)	2406(13)	3425(7)	45(3)

Atom	x	y	z	$U_{eq}$
C36_1	9292(7)	1916(6)	2823(4)	58(2)
F1_2	4952.7(13)	5886.6(11)	1908.9(7)	20.4(3)
O2_2	4967.4(16)	9094.3(13)	569.9(10)	20.5(4)
O3_2	4706.1(18)	8423.3(16)	-1391.1(10)	29.9(5)
O4_2	6588.4(19)	8603.9(17)	-1396.3(11)	34.0(5)
O4A_2	5878(4)	6457(2)	-1059.9(15)	68.9(9)
O5A_2	6690(3)	5729(2)	-1795.9(14)	55.2(7)
N1_2	3544.6(18)	6794.6(14)	290.3(11)	12.5(4)
N8_2	5193.7(19)	5768.5(16)	292.2(12)	17.1(4)
N29_2	5242.3(19)	7846.1(16)	-78.7(11)	16.1(4)
C2_2	3916(2)	7688.6(16)	660.4(12)	13.4(5)
C3_2	4516(2)	7419.1(18)	1415.4(12)	15.1(5)
C3A_2	5054(2)	6463.3(18)	1353.6(12)	14.4(5)
C4_2	7301(2)	6788.5(19)	1746.0(14)	19.7(5)
C4A_2	6285(2)	6435.3(18)	1298.1(13)	15.4(5)
C5_2	8354(2)	6649.9(19)	1579.9(15)	22.8(6)
C6_2	8384(2)	6161(2)	989.3(15)	22.6(6)
C7_2	7373(2)	5808(2)	536.3(14)	20.8(5)
C7A_2	6310(2)	5965.4(17)	693.1(13)	16.2(5)
C8A_2	4327(2)	6037.5(17)	654.5(12)	13.7(5)
C9_2	2255(2)	6592.5(17)	133.8(13)	13.8(5)
C10_2	1985(2)	5683.8(18)	-295.6(13)	16.2(5)
C11_2	2593(2)	5485.8(19)	-783.7(14)	19.0(5)
C12_2	2287(3)	4710(2)	-1221.6(15)	26.8(6)
C13_2	1381(3)	4127(2)	-1180.1(17)	32.7(7)
C14_2	779(3)	4315(2)	-699.3(17)	35.0(7)
C15_2	1063(3)	5090(2)	-261.7(16)	26.6(6)
C16_2	1897(2)	6549.6(18)	817.4(13)	15.0(5)
C17_2	2059(2)	5727.3(19)	1219.3(14)	18.7(5)
C18_2	1887(2)	5732(2)	1876.4(14)	22.6(6)
C19_2	1534(2)	6547(2)	2143.5(14)	22.8(6)
C20_2	1358(2)	7366(2)	1748.5(14)	20.7(5)
C21_2	1542(2)	7362.4(19)	1095.4(13)	17.3(5)
C22_2	1577(2)	7364.9(18)	-355.2(12)	16.0(5)
C23_2	375(2)	7480(2)	-440.8(14)	22.7(6)
C24_2	-256(3)	8147(2)	-899.0(15)	28.7(7)
C25_2	297(3)	8703(2)	-1282.2(15)	30.4(7)
C26_2	1478(3)	8581(2)	-1215.4(15)	26.1(6)
C27_2	2110(2)	7915.7(19)	-758.8(13)	19.1(5)
C28_2	4757(2)	8272.7(17)	366.6(13)	14.6(5)
C30_2	6160(2)	8270.2(19)	-328.5(14)	19.5(5)
C31_2	5850(2)	8445.1(19)	-1095.9(14)	21.9(6)
C32_2	4375(3)	8582(3)	-2126.2(16)	41.3(8)
C33A_2	5802(4)	5953(3)	-1551.6(18)	45.6(9)
C34A_2	4683(4)	5587(3)	-1965(2)	57.0(11)
C35A_2	7821(4)	6056(5)	-1437(3)	80.5(17)
C36A_2	8675(4)	5818(4)	-1843(2)	59.2(11)

**Table 2:** Anisotropic Displacement Parameters ( $\times 10^4$ ) **dp062**. The anisotropic displacement factor exponent takes the form:  $-2\pi^2[h^2a^{*2} \times U_{11} + \dots + 2hka^* \times b^* \times U_{12}]$

Atom	$U_{11}$	$U_{22}$	$U_{33}$	$U_{23}$	$U_{13}$	$U_{12}$
C35A	52(8)	48(11)	86(15)	23(9)	20(8)	1(7)
C36A	45(6)	58(8)	52(6)	17(5)	15(5)	-3(5)
F1_1	23.0(8)	32.7(9)	17.3(7)	8.3(6)	6.6(6)	-3.0(7)
O2_1	23.5(9)	13.3(9)	37.4(11)	1.7(8)	9.6(9)	-5.5(8)
O3_1	21.6(9)	32.1(11)	20.8(10)	7.2(8)	6.3(8)	-3.2(8)
O4_1	27.2(10)	41.9(13)	31.2(11)	12.0(10)	11.6(9)	-7.6(10)
O5_1	86(2)	46.3(19)	122(3)	37(2)	36(2)	27.2(17)
O6_1	63.3(17)	45.2(15)	52.9(16)	11.4(13)	17.0(14)	5.9(13)
N1_1	11.4(9)	8.5(9)	17.6(10)	-0.3(8)	2.4(8)	-0.4(8)
N8_1	14.1(10)	12.5(11)	28.1(12)	-2.4(9)	4.1(9)	1.4(9)
N29_1	18.6(11)	15.8(11)	19.5(11)	1.8(8)	8.7(9)	-4.0(9)
C2_1	14.0(11)	8.9(11)	19.5(12)	-0.6(9)	4.5(10)	-0.8(9)
C3_1	15.1(12)	16.1(13)	17.7(12)	-3.1(10)	4.6(10)	-2.7(10)
C3A_1	16.7(12)	18.4(13)	13.0(11)	3.7(10)	4.1(9)	0.0(10)
C4_1	18.0(13)	25.1(14)	23.8(14)	3.3(11)	1.5(11)	0.0(11)
C4A_1	15.8(12)	17.3(12)	19.7(12)	6.2(10)	3.1(10)	-1.2(10)
C5_1	15.0(12)	28.3(15)	34.9(16)	5.7(13)	0.0(12)	-1.6(11)
C6_1	14.4(13)	26.6(16)	46.3(18)	6.6(13)	8.7(13)	4.0(11)
C7_1	18.7(13)	20.7(14)	37.9(16)	1.4(12)	8.3(12)	4.7(11)
C7A_1	15.0(12)	12.3(12)	26.8(13)	6.5(10)	4.4(10)	1.6(9)
C8A_1	15.1(12)	10.6(11)	19.2(12)	1.8(10)	4.4(10)	0.0(9)
C9_1	10.9(11)	11.6(12)	16.7(12)	0.5(9)	2.8(9)	1.3(9)
C10_1	14.3(11)	11.4(12)	16.5(12)	2.2(9)	2.0(9)	-1.0(9)
C11_1	16.4(12)	15.4(12)	19.7(12)	-1.3(10)	2.8(10)	-1.0(10)
C12_1	25.1(14)	18.1(13)	23.7(14)	-3.8(11)	5.3(11)	4.1(11)
C13_1	29.6(14)	14.0(13)	24.4(14)	-4.4(11)	-0.8(12)	-3.0(11)
C14_1	21.4(13)	19.7(13)	26.7(14)	-0.4(11)	1.7(11)	-8.2(11)
C15_1	18.6(12)	15.8(12)	20.7(12)	-0.6(10)	5.2(10)	-1.5(10)
C16_1	8.5(10)	15.0(12)	16.0(12)	1.5(9)	1.9(9)	0.7(9)
C17_1	12.1(11)	14.8(12)	18.7(12)	0.8(10)	2.2(10)	0.6(9)
C18_1	12.0(11)	22.0(13)	19.2(12)	6.0(10)	2.6(10)	1.4(10)
C19_1	13.7(12)	29.0(14)	13.7(12)	-0.3(10)	2.8(10)	2.0(10)
C20_1	13.2(11)	18.8(13)	20.3(13)	-2.4(10)	2.9(10)	2.2(10)
C21_1	11.2(11)	14.0(12)	18.4(12)	0.6(9)	3.1(9)	2.0(9)
C22_1	18.8(12)	9.8(11)	13.2(12)	-2.0(9)	1.4(10)	-0.7(9)
C23_1	18.9(12)	17.7(13)	18.1(12)	1.7(10)	3.3(10)	2.6(10)
C24_1	21.9(13)	19.8(13)	21.0(13)	-1.5(10)	2.0(11)	7.0(11)
C25_1	32.3(15)	19.1(13)	16.3(12)	2.8(10)	0.1(11)	5.8(11)
C26_1	30.2(15)	19.0(13)	16.9(13)	2.2(10)	7.0(11)	-2.3(11)
C27_1	19.2(12)	16.7(13)	16.3(12)	-1.3(10)	4.7(10)	-1.0(10)
C28_1	15.2(12)	14.0(12)	18.6(12)	2.7(10)	2.0(10)	-1.5(9)
C30_1	17.0(12)	25.1(14)	23.5(13)	4.0(11)	8.5(11)	0.2(11)
C31_1	20.6(13)	19.7(13)	23.1(13)	0.8(11)	10.3(11)	-2.0(11)
C32_1	28.1(15)	42.9(18)	20.7(14)	11.3(13)	4.7(12)	0.2(13)
C33_1	64(3)	47(2)	50(2)	1.6(19)	18(2)	9(2)
C34_1	62(3)	69(3)	83(3)	23(3)	3(3)	-7(2)
C35_1	50(5)	50(7)	38(5)	19(4)	18(4)	-2(4)
C36_1	62(5)	53(5)	62(5)	13(3)	19(4)	2(4)
F1_2	23.0(8)	21.0(8)	17.3(7)	7.2(6)	5.3(6)	-1.5(6)

Atom	$U_{11}$	$U_{22}$	$U_{33}$	$U_{23}$	$U_{13}$	$U_{12}$
O2_2	26.2(10)	12.0(9)	23.1(9)	0.4(7)	6.3(8)	-4.2(7)
O3_2	28.7(10)	36.4(12)	22.4(10)	7.7(9)	2.7(8)	-1.7(9)
O4_2	36.4(12)	42.8(13)	26.5(11)	3.2(10)	14.7(9)	-11.0(10)
O4A_2	124(3)	41.5(16)	45.4(16)	-9.8(13)	29.6(18)	4.1(18)
O5A_2	57.3(16)	71(2)	38.3(14)	-22.4(14)	13.9(13)	-2.0(15)
N1_2	12.0(10)	8.4(9)	16.5(10)	-0.7(8)	2.8(8)	-0.9(8)
N8_2	15.7(10)	14.1(11)	21.2(11)	-5.1(9)	4.3(9)	1.0(9)
N29_2	18.7(11)	11.0(10)	19.6(11)	1.5(9)	6.6(9)	-3.3(9)
C2_2	13.7(11)	9.9(11)	16.2(12)	-1.2(9)	3.6(10)	-0.5(9)
C3_2	15.0(12)	15.7(12)	14.7(12)	-2.1(9)	4.1(10)	-1.1(10)
C3A_2	16.1(12)	13.8(12)	12.4(11)	2.2(9)	2.2(9)	-1.5(9)
C4_2	18.8(13)	16.6(12)	20.8(13)	2.4(10)	0.4(11)	0.6(10)
C4A_2	14.9(12)	13.4(11)	16.9(12)	3.1(9)	2.7(10)	1.5(9)
C5_2	14.8(13)	20.4(14)	29.3(14)	7.5(11)	-0.7(11)	-0.2(10)
C6_2	14.5(12)	22.0(14)	32.0(15)	9.8(11)	7.3(11)	3.3(10)
C7_2	19.0(12)	21.1(13)	23.7(13)	3.1(11)	8.4(11)	6.7(10)
C7A_2	15.3(12)	10.7(11)	20.9(12)	3.2(10)	2.0(10)	1.5(9)
C8A_2	14.5(11)	9.0(11)	17.4(12)	0.1(9)	4.2(10)	0.9(9)
C9_2	11.4(11)	13.4(12)	17.0(12)	-0.8(9)	4.3(10)	-0.6(9)
C10_2	15.4(11)	13.2(12)	18.0(12)	1.0(10)	0.9(10)	0.2(10)
C11_2	18.5(12)	17.4(13)	19.9(12)	-4.3(10)	2.8(10)	0.1(10)
C12_2	27.5(14)	24.2(14)	26.0(14)	-9.6(11)	2.6(12)	3.6(12)
C13_2	40.4(17)	18.5(14)	31.9(16)	-9.5(12)	-3.2(14)	-5.6(13)
C14_2	37.2(17)	28.6(16)	36.4(17)	-6.7(13)	4.6(14)	-18.7(14)
C15_2	25.7(14)	26.2(15)	27.1(14)	-4.4(12)	5.7(12)	-12.4(12)
C16_2	9.9(11)	18.7(12)	16.3(12)	-1.3(10)	3.2(10)	-3.2(9)
C17_2	13.6(11)	18.9(13)	23.5(13)	0.2(10)	4.9(10)	-4.0(10)
C18_2	18.4(12)	26.0(14)	22.7(13)	6.5(11)	4.3(11)	-5.8(11)
C19_2	15.3(12)	35.3(16)	17.8(13)	-2.1(11)	4.7(10)	-7.7(11)
C20_2	14.4(12)	26.5(14)	21.7(13)	-4.6(11)	6.0(10)	-2.1(10)
C21_2	10.8(11)	20.9(13)	19.1(12)	-1.4(10)	2.3(10)	-1.0(10)
C22_2	18.6(12)	13.8(12)	13.9(11)	-3.7(9)	1.3(10)	1.9(10)
C23_2	18.2(13)	29.0(15)	19.5(13)	-2.6(11)	2.5(11)	2.6(11)
C24_2	20.6(13)	36.0(17)	25.0(14)	-2.9(12)	-1.7(12)	13.7(12)
C25_2	36.3(16)	26.4(15)	23.5(15)	3.2(12)	-0.7(13)	12.0(13)
C26_2	33.7(15)	20.2(14)	21.9(14)	3.4(11)	3.3(12)	2.4(12)
C27_2	19.6(13)	15.9(12)	19.9(13)	-0.1(10)	2.0(10)	0.1(10)
C28_2	15.9(11)	10.9(11)	14.7(11)	2.6(9)	0.3(9)	0.9(9)
C30_2	18.0(12)	18.7(13)	23.2(13)	2.0(10)	8.0(11)	-2.6(10)
C31_2	25.2(13)	17.6(13)	23.7(14)	1.2(11)	8.0(11)	-4.4(11)
C32_2	48(2)	47(2)	22.7(15)	7.9(14)	-1.1(14)	-8.1(17)
C33A_2	78(3)	35.0(19)	29.0(17)	-7.7(14)	23.9(18)	0.5(18)
C34A_2	66(3)	66(3)	49(2)	-4(2)	32(2)	12(2)
C35A_2	64(3)	123(5)	49(3)	-27(3)	6(2)	-22(3)
C36A_2	43(2)	82(3)	43(2)	-12(2)	-3.5(17)	-5(2)

**Table 3:** Bond Lengths in Å for **dp062**.

Atom	Atom	Length/Å
C35A	C36A	1.464(17)
C35A	O6_1	1.492(11)
F1_1	C3A_1	1.418(3)
O2_1	C28_1	1.228(3)
O3_1	C31_1	1.327(3)
O3_1	C32_1	1.447(3)
O4_1	C31_1	1.204(3)
O5_1	C33_1	1.219(5)
O6_1	C33_1	1.301(5)
O6_1	C35_1	1.484(8)
N1_1	C2_1	1.477(3)
N1_1	C8A_1	1.477(3)
N1_1	C9_1	1.499(3)
N8_1	C7A_1	1.391(3)
N8_1	C8A_1	1.472(3)
N29_1	C28_1	1.338(4)
N29_1	C30_1	1.446(3)
C2_1	C3_1	1.536(3)
C2_1	C28_1	1.527(3)
C3_1	C3A_1	1.518(4)
C3A_1	C4A_1	1.498(4)
C3A_1	C8A_1	1.558(3)
C4_1	C4A_1	1.386(4)
C4_1	C5_1	1.391(4)
C4A_1	C7A_1	1.393(4)
C5_1	C6_1	1.387(5)
C6_1	C7_1	1.390(4)
C7_1	C7A_1	1.395(4)
C9_1	C10_1	1.545(3)
C9_1	C16_1	1.540(3)
C9_1	C22_1	1.540(3)
C10_1	C11_1	1.390(4)
C10_1	C15_1	1.395(4)
C11_1	C12_1	1.390(4)
C12_1	C13_1	1.385(4)
C13_1	C14_1	1.389(4)
C14_1	C15_1	1.385(4)
C16_1	C17_1	1.400(4)
C16_1	C21_1	1.398(4)
C17_1	C18_1	1.389(4)
C18_1	C19_1	1.386(4)
C19_1	C20_1	1.379(4)
C20_1	C21_1	1.389(4)
C22_1	C23_1	1.396(4)
C22_1	C27_1	1.397(4)
C23_1	C24_1	1.391(4)
C24_1	C25_1	1.387(4)
C25_1	C26_1	1.381(4)
C26_1	C27_1	1.391(4)
C30_1	C31_1	1.512(4)



Atom	Atom	Length/Å
C33_1	C34_1	1.515(7)
C35_1	C36_1	1.456(15)
F1_2	C3A_2	1.415(3)
O2_2	C28_2	1.237(3)
O3_2	C31_2	1.329(4)
O3_2	C32_2	1.443(4)
O4_2	C31_2	1.210(3)
O4A_2	C33A_2	1.204(4)
O5A_2	C33A_2	1.315(5)
O5A_2	C35A_2	1.420(6)
N1_2	C2_2	1.475(3)
N1_2	C8A_2	1.478(3)
N1_2	C9_2	1.504(3)
N8_2	C7A_2	1.383(3)
N8_2	C8A_2	1.460(3)
N29_2	C28_2	1.332(3)
N29_2	C30_2	1.445(3)
C2_2	C3_2	1.544(3)
C2_2	C28_2	1.530(3)
C3_2	C3A_2	1.515(4)
C3A_2	C4A_2	1.495(3)
C3A_2	C8A_2	1.561(3)
C4_2	C4A_2	1.390(4)
C4_2	C5_2	1.391(4)
C4A_2	C7A_2	1.395(4)
C5_2	C6_2	1.384(4)
C6_2	C7_2	1.391(4)
C7_2	C7A_2	1.397(4)
C9_2	C10_2	1.535(3)
C9_2	C16_2	1.545(3)
C9_2	C22_2	1.545(3)
C10_2	C11_2	1.393(4)
C10_2	C15_2	1.395(4)
C11_2	C12_2	1.395(4)
C12_2	C13_2	1.376(5)
C13_2	C14_2	1.373(5)
C14_2	C15_2	1.392(4)
C16_2	C17_2	1.402(4)
C16_2	C21_2	1.393(4)
C17_2	C18_2	1.391(4)
C18_2	C19_2	1.384(4)
C19_2	C20_2	1.390(4)
C20_2	C21_2	1.388(4)
C22_2	C23_2	1.399(4)
C22_2	C27_2	1.393(4)
C23_2	C24_2	1.391(4)
C24_2	C25_2	1.383(5)
C25_2	C26_2	1.382(4)
C26_2	C27_2	1.388(4)
C30_2	C31_2	1.509(4)
C33A_2	C34A_2	1.461(6)

Atom	Atom	Length/Å
C35A_2	C36A_2	1.500(7)

**Table 4:** Bond Angles in ° for **dp062**.

Atom	Atom	Atom	Angle/°
C36A	C35A	O6_1	104.2(12)
C31_1	O3_1	C32_1	115.2(2)
C33_1	O6_1	C35A	107.8(10)
C33_1	O6_1	C35_1	119.6(7)
C2_1	N1_1	C9_1	115.69(18)
C8A_1	N1_1	C2_1	107.78(18)
C8A_1	N1_1	C9_1	115.99(19)
C7A_1	N8_1	C8A_1	110.2(2)
C28_1	N29_1	C30_1	120.7(2)
N1_1	C2_1	C3_1	106.89(19)
N1_1	C2_1	C28_1	113.0(2)
C28_1	C2_1	C3_1	109.4(2)
C3A_1	C3_1	C2_1	103.6(2)
F1_1	C3A_1	C3_1	109.6(2)
F1_1	C3A_1	C4A_1	109.3(2)
F1_1	C3A_1	C8A_1	110.0(2)
C3_1	C3A_1	C8A_1	106.1(2)
C4A_1	C3A_1	C3_1	117.1(2)
C4A_1	C3A_1	C8A_1	104.3(2)
C4A_1	C4_1	C5_1	118.4(3)
C4_1	C4A_1	C3A_1	129.7(3)
C4_1	C4A_1	C7A_1	121.3(2)
C7A_1	C4A_1	C3A_1	108.9(2)
C6_1	C5_1	C4_1	120.1(3)
C5_1	C6_1	C7_1	122.1(3)
C6_1	C7_1	C7A_1	117.5(3)
N8_1	C7A_1	C4A_1	111.6(2)
N8_1	C7A_1	C7_1	127.6(3)
C4A_1	C7A_1	C7_1	120.6(3)
N1_1	C8A_1	C3A_1	107.0(2)
N8_1	C8A_1	N1_1	112.0(2)
N8_1	C8A_1	C3A_1	104.63(19)
N1_1	C9_1	C10_1	109.27(19)
N1_1	C9_1	C16_1	109.26(19)
N1_1	C9_1	C22_1	109.88(19)
C16_1	C9_1	C10_1	112.7(2)
C16_1	C9_1	C22_1	112.41(19)
C22_1	C9_1	C10_1	103.13(18)
C11_1	C10_1	C9_1	121.8(2)
C11_1	C10_1	C15_1	118.4(2)
C15_1	C10_1	C9_1	119.4(2)
C12_1	C11_1	C10_1	120.6(2)
C13_1	C12_1	C11_1	120.7(3)
C12_1	C13_1	C14_1	119.0(2)
C15_1	C14_1	C13_1	120.4(3)

Atom	Atom	Atom	Angle/°
C14_1	C15_1	C10_1	120.9(2)
C17_1	C16_1	C9_1	122.7(2)
C21_1	C16_1	C9_1	119.6(2)
C21_1	C16_1	C17_1	117.4(2)
C18_1	C17_1	C16_1	121.0(2)
C19_1	C18_1	C17_1	120.4(2)
C20_1	C19_1	C18_1	119.7(2)
C19_1	C20_1	C21_1	120.0(2)
C20_1	C21_1	C16_1	121.6(2)
C23_1	C22_1	C9_1	120.4(2)
C23_1	C22_1	C27_1	118.2(2)
C27_1	C22_1	C9_1	121.0(2)
C24_1	C23_1	C22_1	121.2(2)
C25_1	C24_1	C23_1	119.9(3)
C26_1	C25_1	C24_1	119.6(2)
C25_1	C26_1	C27_1	120.7(2)
C26_1	C27_1	C22_1	120.5(2)
O2_1	C28_1	N29_1	122.8(2)
O2_1	C28_1	C2_1	119.9(2)
N29_1	C28_1	C2_1	117.2(2)
N29_1	C30_1	C31_1	114.4(2)
O3_1	C31_1	C30_1	112.4(2)
O4_1	C31_1	O3_1	124.8(3)
O4_1	C31_1	C30_1	122.8(3)
O5_1	C33_1	O6_1	121.4(4)
O5_1	C33_1	C34_1	127.2(5)
O6_1	C33_1	C34_1	111.4(4)
C36_1	C35_1	O6_1	111.0(10)
C31_2	O3_2	C32_2	114.9(2)
C33A_2	O5A_2	C35A_2	118.2(3)
C2_2	N1_2	C8A_2	107.97(18)
C2_2	N1_2	C9_2	114.78(19)
C8A_2	N1_2	C9_2	115.76(18)
C7A_2	N8_2	C8A_2	110.4(2)
C28_2	N29_2	C30_2	123.1(2)
N1_2	C2_2	C3_2	106.37(19)
N1_2	C2_2	C28_2	114.00(19)
C28_2	C2_2	C3_2	109.7(2)
C3A_2	C3_2	C2_2	103.50(19)
F1_2	C3A_2	C3_2	108.95(19)
F1_2	C3A_2	C4A_2	109.52(19)
F1_2	C3A_2	C8A_2	110.25(19)
C3_2	C3A_2	C8A_2	106.01(19)
C4A_2	C3A_2	C3_2	118.1(2)
C4A_2	C3A_2	C8A_2	103.7(2)
C5_2	C4_2	C4A_2	118.1(3)
C4_2	C4A_2	C3A_2	129.5(2)
C4_2	C4A_2	C7A_2	121.4(2)
C7A_2	C4A_2	C3A_2	109.1(2)
C6_2	C5_2	C4_2	120.5(3)
C5_2	C6_2	C7_2	121.9(2)

Atom	Atom	Atom	Angle/°
C6_2	C7_2	C7A_2	117.8(3)
N8_2	C7A_2	C4A_2	111.4(2)
N8_2	C7A_2	C7_2	128.1(2)
C4A_2	C7A_2	C7_2	120.3(2)
N1_2	C8A_2	C3A_2	106.80(19)
N8_2	C8A_2	N1_2	112.0(2)
N8_2	C8A_2	C3A_2	104.96(19)
N1_2	C9_2	C10_2	108.98(19)
N1_2	C9_2	C16_2	109.08(19)
N1_2	C9_2	C22_2	108.99(19)
C10_2	C9_2	C16_2	113.7(2)
C10_2	C9_2	C22_2	103.88(19)
C22_2	C9_2	C16_2	112.0(2)
C11_2	C10_2	C9_2	119.7(2)
C11_2	C10_2	C15_2	118.2(2)
C15_2	C10_2	C9_2	121.7(2)
C10_2	C11_2	C12_2	120.5(3)
C13_2	C12_2	C11_2	120.6(3)
C14_2	C13_2	C12_2	119.2(3)
C13_2	C14_2	C15_2	121.0(3)
C14_2	C15_2	C10_2	120.3(3)
C17_2	C16_2	C9_2	121.2(2)
C21_2	C16_2	C9_2	120.6(2)
C21_2	C16_2	C17_2	117.7(2)
C18_2	C17_2	C16_2	120.8(3)
C19_2	C18_2	C17_2	120.6(3)
C18_2	C19_2	C20_2	119.2(2)
C21_2	C20_2	C19_2	120.0(3)
C20_2	C21_2	C16_2	121.6(3)
C23_2	C22_2	C9_2	120.0(2)
C27_2	C22_2	C9_2	121.9(2)
C27_2	C22_2	C23_2	117.9(2)
C24_2	C23_2	C22_2	120.7(3)
C25_2	C24_2	C23_2	120.3(3)
C26_2	C25_2	C24_2	119.6(3)
C25_2	C26_2	C27_2	120.2(3)
C26_2	C27_2	C22_2	121.2(3)
O2_2	C28_2	N29_2	124.3(2)
O2_2	C28_2	C2_2	118.4(2)
N29_2	C28_2	C2_2	117.2(2)
N29_2	C30_2	C31_2	115.1(2)
O3_2	C31_2	C30_2	113.2(2)
O4_2	C31_2	O3_2	124.7(3)
O4_2	C31_2	C30_2	122.1(3)
O4A_2	C33A_2	O5A_2	124.0(4)
O4A_2	C33A_2	C34A_2	122.5(4)
O5A_2	C33A_2	C34A_2	113.4(3)
O5A_2	C35A_2	C36A_2	109.5(4)

**Table 5:** Hydrogen Fractional Atomic Coordinates ( $\times 10^4$ ) and Equivalent Isotropic Displacement Parameters ( $\text{\AA}^2 \times 10^3$ ) for **dp062**.  $U_{eq}$  is defined as 1/3 of the trace of the orthogonalised  $U_{ij}$ .

Atom	x	y	z	$U_{eq}$
H35A	10233.26	1566.05	3221.47	74
H35B	10223.57	2148.44	3907.84	74
H36A	8943.43	2643.74	2553.48	77
H36B	8960.54	3256.42	3224.38	77
H36C	8380.29	2227.98	3131.64	77
H2_1	8266.36	4995.91	5494.75	17
H3A_1	10163.52	4910.62	6503.18	20
H3B_1	8927.81	4587.74	6621.18	20
H4_1	12193.92	4112.83	7169.93	28
H5_1	13967.78	3622.72	6967.97	33
H6_1	13966.76	2503.15	6125.32	35
H7_1	12218.31	1866.94	5438.74	31
H8A_1	8657.8	2423.16	5964.87	18
H11_1	8286.65	2324.57	4474.5	21
H12_1	7652.81	957.13	3840.25	27
H13_1	5799.93	333.59	3770.97	29
H14_1	4549.52	1137.57	4303.32	28
H15_1	5187.14	2490.86	4949.12	22
H17_1	6708.02	2149.52	6054.57	19
H18_1	6300.42	2317.82	7118.54	22
H19_1	6227.6	3816.73	7589.28	23
H20_1	6444.12	5153.88	6958.56	21
H21_1	6766.57	4993.81	5872.93	18
H23_1	5065.04	4317.78	4935.68	22
H24_1	4049.55	5293.97	4041.15	26
H25_1	4936.88	5785.56	3190.99	29
H26_1	6846.77	5321	3255.33	26
H27_1	7860.32	4327.66	4138.87	21
H30A_1	11678.49	3938.99	4527.18	26
H30B_1	11820.11	4916.32	4937.88	26
H32A_1	9829.75	5228.22	2642.93	46
H32B_1	9473.9	6124.09	3027.54	46
H32C_1	8543.33	5300.44	2750.36	46
H34A_1	13018.98	3640.72	3409.13	112
H34B_1	12693.72	3094.16	2686.82	112
H34C_1	13693.42	2689.07	3322.43	112
H35A_1	10284.85	1947.96	3805.6	53
H35B_1	9522.38	2885.3	3579.74	53
H36A_1	9058.23	2359.79	2436.49	88
H36B_1	8591.93	1659.06	2928.05	88
H36C_1	9745.25	1399.33	2697.27	88
H29_1	10030(30)	3700(30)	4864(17)	23(8)
H8_1	9810(30)	1840(30)	5325(19)	33(9)
H2_2	3207.17	8077.07	648.18	16
H3A_2	5124.44	7885.78	1632.54	18
H3B_2	3938.71	7375.86	1690.09	18
H4_2	7275.71	7115.44	2154.04	24
H5_2	9058.55	6892.43	1874.14	27

Atom	x	y	z	<i>U</i> <sub>eq</sub>
H6_2	9114.85	6064.76	890.4	27
H7_2	7405.16	5470.9	133.55	25
H8A_2	3867.36	5476.43	732.95	16
H11_2	3219.96	5882.68	-818.57	23
H12_2	2710.03	4582.06	-1551.63	32
H13_2	1173.11	3600.84	-1480.78	39
H14_2	159.21	3909.37	-664.83	42
H15_2	627.33	5216.17	61.84	32
H17_2	2288.59	5159.56	1040.63	22
H18_2	2012.46	5170.71	2144.57	27
H19_2	1413.44	6546.67	2591.69	27
H20_2	1112.46	7928.8	1925.55	25
H21_2	1423.07	7927.8	831.76	21
H23_2	-14.33	7098.03	-183.1	27
H24_2	-1070.31	8221.38	-949.09	34
H25_2	-132.88	9165.24	-1589.36	36
H26_2	1859.34	8954.03	-1482.92	31
H27_2	2919.54	7834.34	-720.66	23
H30A_2	6855.26	7854.35	-202.77	23
H30B_2	6379.69	8879.82	-88.05	23
H32A_2	4678.52	8068.39	-2355.51	62
H32B_2	4700.87	9184.27	-2227.12	62
H32C_2	3519.8	8600.88	-2295.17	62
H34A_2	4669.83	5602.31	-2454.44	86
H34B_2	4045.66	5977.65	-1891.56	86
H34C_2	4583.82	4934.85	-1828.08	86
H35A_2	8067.64	5754.59	-977.26	97
H35B_2	7801.39	6747.77	-1371.48	97
H36A_2	8441	6134.5	-2292.29	89
H36B_2	8683.46	5133.2	-1912.16	89
H36C_2	9458.32	6030.69	-1590.68	89
H8_2	5060(30)	5340(30)	60(20)	33(10)
H29_2	5050(30)	7300(30)	-183(16)	15(7)

**Table 6:** Hydrogen Bond information for **dp062**.

D	H	A	d(D-H)/Å	d(H-A)/Å	d(D-A)/Å	D-H-A/deg
N29_1	H29_1	N8_1	0.87(4)	2.25(4)	2.986(3)	143(3)
N8_1	H8_1	O2_1 <sup>1</sup>	0.91(4)	1.99(4)	2.842(3)	156(3)
N8_2	H8_2	O2_2 <sup>2</sup>	0.75(4)	2.18(4)	2.914(3)	169(4)
N29_2	H29_2	N8_2	0.82(4)	2.36(3)	3.040(3)	141(3)

<sup>1</sup>2-x,-1+y,1-z; <sup>2</sup>1-x,-1/2+y,-z

**Table 7:** Atomic Occupancies for all atoms that are not fully occupied in **dp062**.

<b>Atom</b>	<b>Occupancy</b>
C35A	0.395(13)
H35A	0.395(13)
H35B	0.395(13)
C36A	0.395(13)
H36A	0.395(13)
H36B	0.395(13)
H36C	0.395(13)
C35_1	0.605(13)
H35A_1	0.605(13)
H35B_1	0.605(13)
C36_1	0.605(13)
H36A_1	0.605(13)
H36B_1	0.605(13)
H36C_1	0.605(13)

## References

- O.V. Dolomanov and L.J. Bourhis and R.J. Gildea and J.A.K. Howard and H. Puschmann, Olex2: A complete structure solution, refinement and analysis program, *J. Appl. Cryst.*, (2009), **42**, 339-341.
- Parsons, S., Flack, H.D., and Wagner, T., *Acta Cryst.*, (2013), **B69** 249-259
- Sheldrick, G.M., XT, *Acta Cryst.*, (2015), **A71**, 3-8.
- Sheldrick, G.M., XL, *Acta Cryst.*, (2015), **C71**, 3-8.
- Software for the Integration of CCD Detector System Bruker Analytical X-ray Systems, Bruker Axs, Madison, WI (after 2013).