

# Supporting Information

## Synthesis of Bisindoles Scaffolds by Palladium-Catalyzed Allylic Alkylation of *N*-aminoindole with *ortho*-Iodoaryl Allenes

Chenyue Ding<sup>a‡</sup>, Yuan Yin<sup>a‡</sup>, Enyu Hu<sup>a</sup>, Huiwen Dong<sup>a</sup>, Yanru He<sup>a</sup>, Shuaijie Wu<sup>a\*</sup>, Ying Han<sup>a\*</sup>,  
Lei Wang<sup>a\*</sup>

<sup>a</sup>*School of Chemistry and Materials, Yangzhou University, Yangzhou 225002, China*

<sup>‡</sup>*C. Ding and ‡ Y. Yin contributed to equally*

*Corresponding author: shuaijiewu\_chem@163.com, hanying@yzu.edu.cn, Lei.wang@yzu.edu.cn*

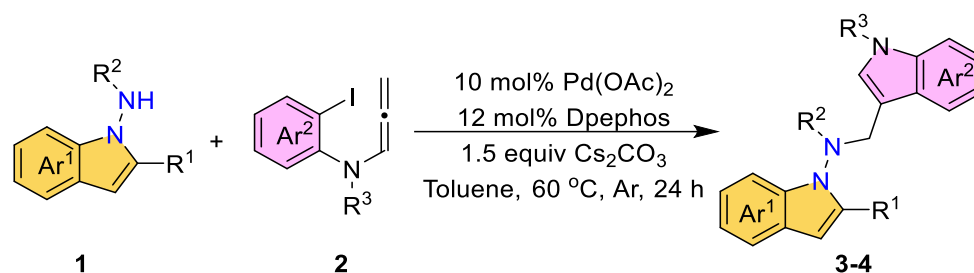
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## 1. General Information:

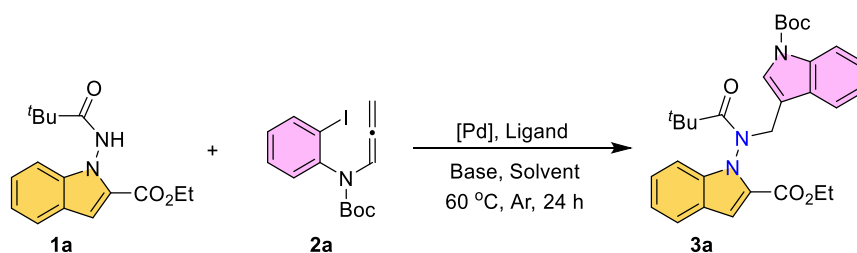
Unless otherwise noted, all reactions were carried out under the air atmosphere; materials obtained from commercial suppliers were used directly without further purification.  $^1\text{H}$  NMR spectra,  $^{13}\text{C}$  NMR spectra, and  $^{19}\text{F}$  NMR spectra were recorded on Agilent 400 or Bruker 400 MHz spectrometer in  $\text{CDCl}_3$ . NMR experiments are reported in  $\delta$  units, parts per million (ppm), and were referenced to  $\text{CDCl}_3$  ( $\delta$  7.26 or 77.0 ppm) as the internal standard. The data is being reported as (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet or unresolved, br = broad signal, coupling constant(s) in Hz, integration). All the solvents were used directly without further purification. Reactions were monitored by TLC. Flash column chromatography was performed on silica (particle size 300-400 mesh ASTM, purchased from Yantai, China) and eluted with petroleum ether/ethyl acetate. Copies of NMR were processed with MestReNova Software. Note,  $\text{Pd}(\text{OAc})_2$  was purchased from Bide Pharmatech Ltd. Dpephos and  $\text{Cs}_2\text{CO}_3$  were purchased from energy chemical. Toluene was purchased from Sinopharm Chemical Reagent Co., Ltd. All the *N*-aminoindole according to the literature,<sup>1-2</sup> and synthesis of *ortho*-iodoaryl allene according to the literature.<sup>3-5</sup>

## 2. General procedure:



A sealed tube (10 mL) equipped with a magnetic stir bar was charged with Pd(OAc)<sub>2</sub> (6.7 mg, 0.030 mmol, 0.10 equiv), Dpephos (19.4 mg, 0.036 mmol, 0.12 equiv), Cs<sub>2</sub>CO<sub>3</sub> (146.7 mg, 0.45 mmol, 1.5 equiv), *N*-aminoindole **1** (0.30 mmol, 1.0 equiv), *ortho*-iodoaryl allene **2** (0.36 mmol, 1.2 equiv) and 2.0 mL toluene were added sequentially. Degassed toluene and backfilled with argon for 3 times (3 × 1 min) at -78 °C. Under argon atmosphere, the reaction mixture was stirred at 60 °C for 24 h by use of module heating. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as eluent to give the desired products **3-4**.

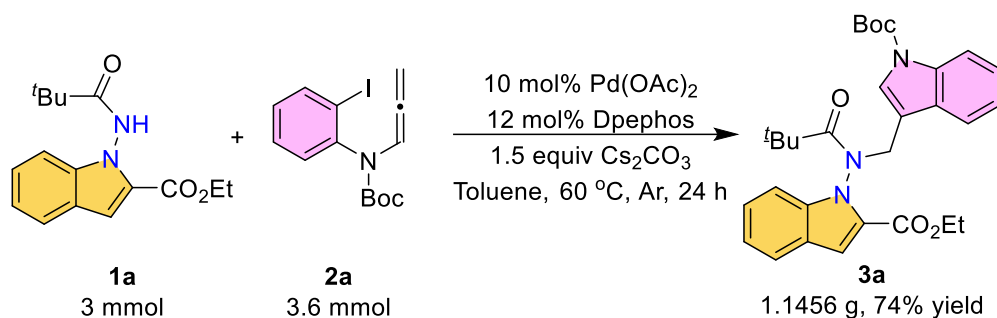
### 3. Table S1. Optimization of reaction conditions:



Entry	Ligand	Pd catalyst	Base	Solvent	Yield (%) <sup>b</sup>
1 <sup>c</sup>	Dpephos	Pd <sub>2</sub> (dba) <sub>3</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	84
2 <sup>c</sup>	PPh <sub>3</sub>	Pd <sub>2</sub> (dba) <sub>3</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	83
3 <sup>c</sup>	Xphos	Pd <sub>2</sub> (dba) <sub>3</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	trace
4 <sup>c</sup>	Dppf	Pd <sub>2</sub> (dba) <sub>3</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	34
5 <sup>c</sup>	--	Pd <sub>2</sub> (dba) <sub>3</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	0
6	Dpephos	Pd(OAc) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	92
7 <sup>c</sup>	Dpephos	PdCl <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	trace
8	Dpephos	Pd(acac) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	80
9	Dpephos	--	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	trace
10	Dpephos	Pd(OAc) <sub>2</sub>	CsOAc	Toluene	30
11	Dpephos	Pd(OAc) <sub>2</sub>	K <sub>2</sub> CO <sub>3</sub>	Toluene	53
12	Dpephos	Pd(OAc) <sub>2</sub>	NaO <sup>t</sup> Bu	Toluene	41
13	Dpephos	Pd(OAc) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub>	CH <sub>3</sub> CN	77
14	Dpephos	Pd(OAc) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub>	DCE	38
15	Dpephos	Pd(OAc) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub>	THF	90
16 <sup>d</sup>	Dpephos	Pd(OAc) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	21
17 <sup>e</sup>	Dpephos	Pd(OAc) <sub>2</sub>	Cs <sub>2</sub> CO <sub>3</sub>	Toluene	89

<sup>a</sup> Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), Pd catalyst (10 mol%), ligand (12 mol%), base (1.5 equiv), in the solvent (2.0 mL) at 60 °C under Ar for 24 h. <sup>b</sup> Isolated yield. <sup>c</sup> Pd catalyst (5 mol%) was used. <sup>d</sup> under air for 24 h. <sup>e</sup> **1a** (0.3 mmol), **2a** (0.36 mmol), Pd catalyst (10 mol%), ligand (12 mol%), Cs<sub>2</sub>CO<sub>3</sub> (1.5 equiv.), in the solvent (2.0 mL) at 60 °C under Ar for 24 h.

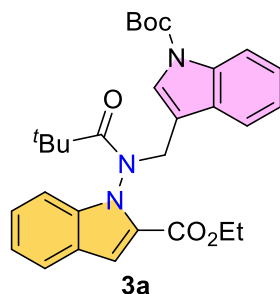
#### 4. Gram-scale synthesis of **3a**



An 100 mL Schlenk tube was charged with Pd(OAc)<sub>2</sub> (64.7 mg, 0.3 mmol, 0.1 equiv), Dpephos (193.9 mg, 0.36 mmol, 0.12 equiv), Cs<sub>2</sub>CO<sub>3</sub> (1.4662 g, 4.5 mmol, 1.5 equiv), **1a** (865.0 mg, 3 mmol, 1.0 equiv), **2a** (1.2859 g, 3.6 mmol, 1.2 equiv) and toluene (20 mL) were added sequentially. Degassed toluene and backfilled with argon for 3 times (3 × 1 min) at -78 °C. The reaction mixture was stirred at 80 °C for 24 h. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as eluent to give the desired product **3a** 1.1456 g in 74% yield.

## 5. Characterization data for the product

*tert*-butyl 3-((*N*-(2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (**3a**)

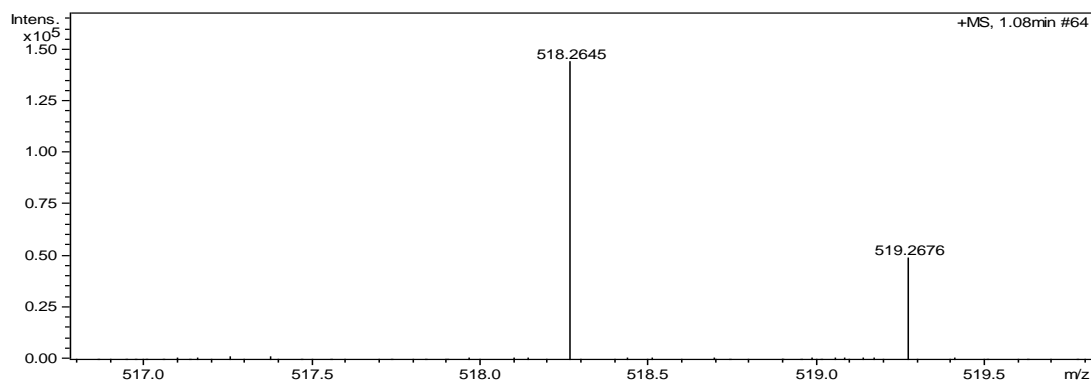


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **3a** (138.2 mg, 89% yield) as a white solid. Mp: 103-105 °C.

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  8.02 (d,  $J = 7.6$  Hz, 1H), 7.59 (d,  $J = 7.6$  Hz, 1H), 7.49 (d,  $J = 7.6$  Hz, 1H), 7.29-7.24 (m, 2H), 7.18 (t,  $J = 7.2$  Hz, 1H), 7.10-7.02 (m, 2H), 6.77 (d,  $J = 7.6$  Hz, 2H), 5.38 (d,  $J = 14.8$  Hz, 1H), 4.67 (d,  $J = 14.8$  Hz, 1H), 4.08 (q,  $J = 6.8$  Hz, 2H), 1.56 (s, 9H), 1.27 (t,  $J = 7.2$  Hz, 3H), 1.04 (s, 9H);

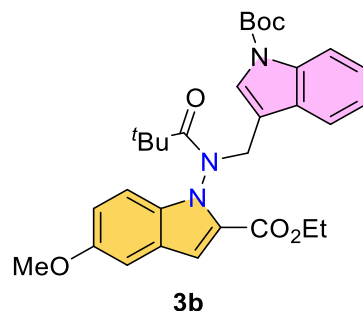
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  179.4, 160.1, 149.1, 139.3, 135.1, 129.8, 128.3, 126.7, 125.7, 124.4, 123.6, 122.6, 122.5, 121.9, 119.6, 114.8, 114.7, 111.4, 111.3, 83.4, 60.9, 44.8, 41.0, 28.7, 28.0, 14.1;

**HRMS** Calcd (ESI)  $m/z$  for  $\text{C}_{30}\text{H}_{36}\text{N}_3\text{O}_5$   $[\text{M} + \text{H}]^+$ : 518.2649, found: 518.2645;



*tert*-butyl

3-((N-(2-(ethoxycarbonyl)-5-methoxy-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (**3b**)

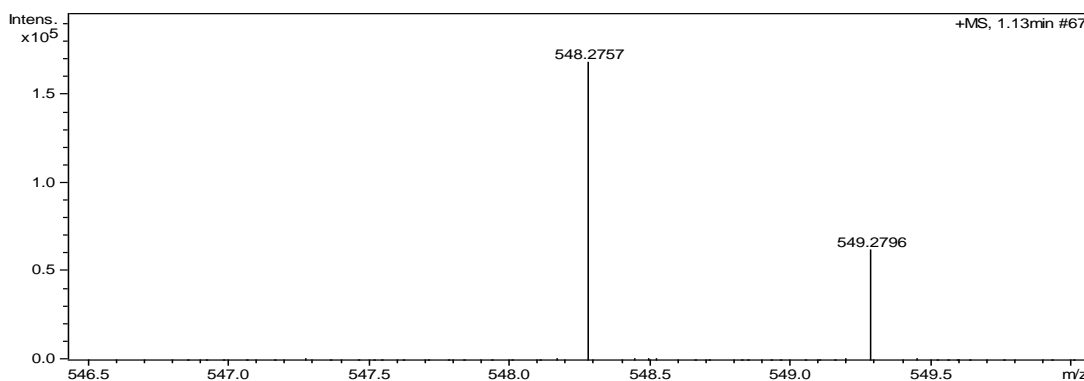


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:12) give the product **3b** (145.2 mg, 88% yield) as a white solid. Mp: 116-118 °C.

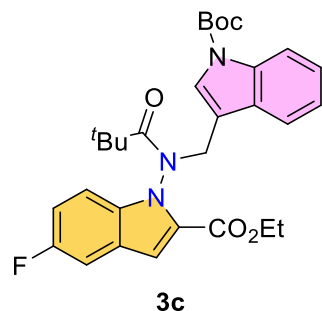
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 8.02 (d, *J* = 7.2 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.29-7.26 (m, 1H), 7.21-7.17 (m, 2H), 6.97 (d, *J* = 2.0 Hz, 1H), 6.80 (s, 1H), 6.70 (dd, *J*<sub>1</sub> = 9.2 Hz, *J*<sub>2</sub> = 2.4 Hz, 1H), 6.64 (d, *J* = 8.8 Hz, 1H), 5.40 (d, *J* = 14.8 Hz, 1H), 4.61 (d, *J* = 14.4 Hz, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 1.57 (s, 9H), 1.27 (t, *J* = 6.8 Hz, 3H), 1.04 (s, 9H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.4, 160.1, 155.3, 149.1, 135.1, 134.5, 129.8, 128.4, 126.7, 124.4, 124.0, 122.6, 119.5, 116.9, 114.8, 114.7, 112.2, 110.9, 102.5, 83.4, 60.8, 55.4, 44.8, 41.0, 28.6, 28.0, 14.1;

HRMS Calcd (ESI) *m/z* for C<sub>31</sub>H<sub>38</sub>N<sub>3</sub>O<sub>6</sub> [M + H]<sup>+</sup>: 548.2755, found: 548.2757;



***tert*-butyl 3-((N-(2-(ethoxycarbonyl)-5-fluoro-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (**3c**)**



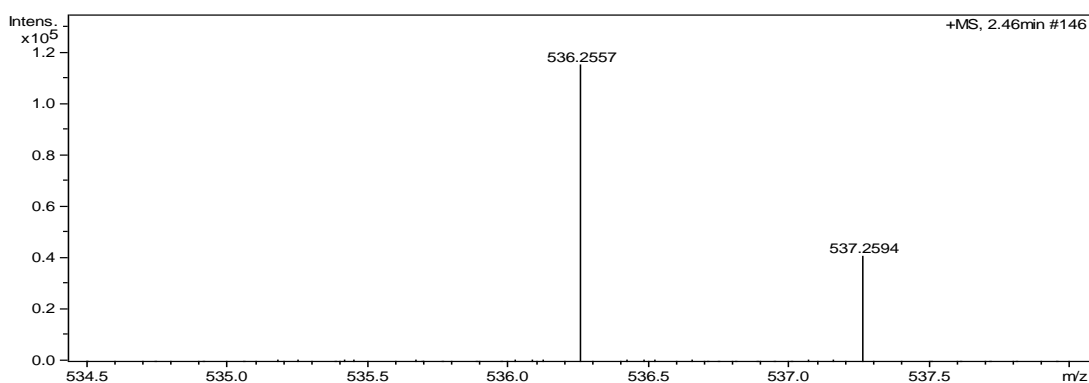
Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **3c** (127.7 mg, 79% yield) as a white solid. Mp: 116-118 °C.

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.30-7.17 (m, 4H), 6.78-6.73 (m, 2H), 6.63 (dd, *J*<sub>1</sub> = 9.2 Hz, *J*<sub>2</sub> = 4.4 Hz, 1H), 5.49 (d, *J* = 14.4 Hz, 1H), 4.56 (d, *J* = 14.4 Hz, 1H), 4.21-4.09 (m, 2H), 1.57 (s, 9H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.03 (s, 9H);

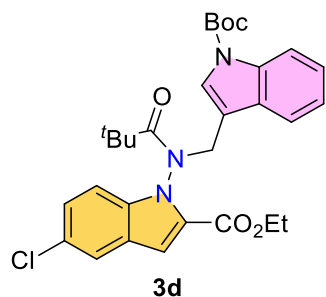
**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.3, 159.8, 158.5 (d, *J* = 237.5 Hz), 149.1, 135.9, 135.1, 129.7, 129.5, 126.7 (d, *J* = 4.0 Hz), 124.5, 123.6 (d, *J* = 10.4 Hz), 122.7, 119.4, 114.8 (2C), 114.5, 112.4, 111.0, 106.8 (d, *J* = 22.7 Hz), 83.5, 61.1, 44.8, 41.0, 28.6, 28.0, 14.1;

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -121.4;

**HRMS** Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>35</sub>FN<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 536.2555, found: 536.2557;



***tert*-butyl 3-((N-(5-chloro-2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (**3d**)**

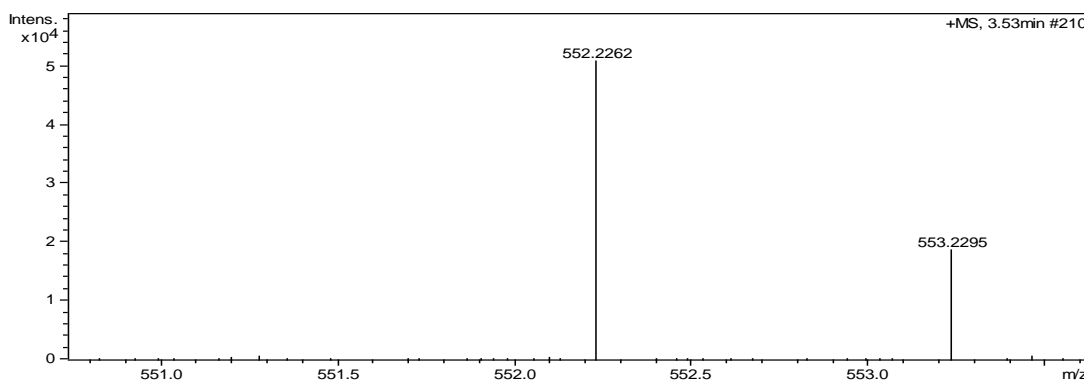


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **3d** (142.5 mg, 86% yield) as a white solid. Mp: 122-124 °C.

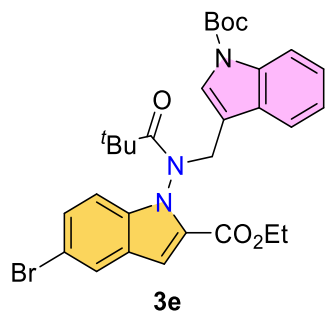
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 8.02 (d, *J* = 7.2 Hz, 1H), 7.55 (d, *J* = 1.6 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.22-7.18 (m, 2H), 6.94 (dd, *J*<sub>1</sub> = 8.8 Hz, *J*<sub>2</sub> = 1.6 Hz, 1H), 6.75 (s, 1H), 6.60 (d, *J* = 8.8 Hz, 1H), 5.50 (d, *J* = 14.8 Hz, 1H), 4.54 (d, *J* = 14.4 Hz, 1H), 4.20-4.08 (m, 2H), 1.57 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.01 (s, 9H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.2, 159.8, 149.1, 137.7, 135.1, 129.7, 129.2, 127.4, 126.7, 126.1, 124.5, 124.2, 122.7, 121.6, 119.4, 114.9, 114.5, 112.4, 110.6, 83.6, 61.2, 44.9, 41.0, 28.6, 28.0, 14.1;

HRMS Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>35</sub>ClN<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 552.2260, found: 552.2262;



***tert*-butyl 3-((N-(5-bromo-2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (**3e**)**

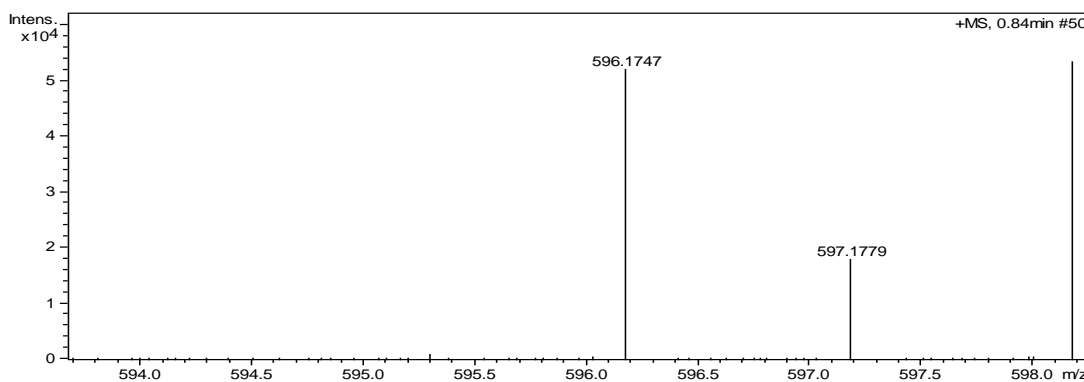


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **3e** (117.3 mg, 66% yield) as a white solid. Mp: 133-135 °C.

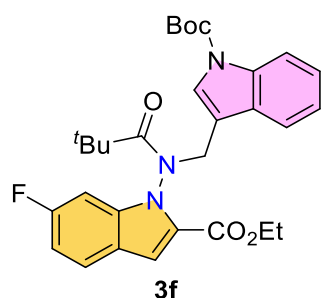
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 8.02 (d, *J* = 7.2 Hz, 1H), 7.72 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.31-7.26 (m, 1H), 7.23-7.18 (m, 2H), 7.07 (d, *J* = 8.8 Hz, 1H), 6.76 (s, 1H), 6.56 (d, *J* = 8.8 Hz, 1H), 5.50 (d, *J* = 14.4 Hz, 1H), 4.55 (d, *J* = 14.8 Hz, 1H), 4.19-4.09 (m, 2H), 1.58 (s, 9H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.01 (s, 9H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.3, 159.8, 149.1, 138.0, 135.1, 129.7, 129.1, 128.6, 126.7, 124.9, 124.8, 124.6, 122.8, 119.4, 114.9, 114.9, 114.5, 112.8, 110.4, 83.6, 61.2, 44.9, 41.0, 28.6, 28.0, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>35</sub>BrN<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 596.1755, found: 596.1747;



***tert*-butyl 3-((N-(2-(ethoxycarbonyl)-6-fluoro-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (3f)**



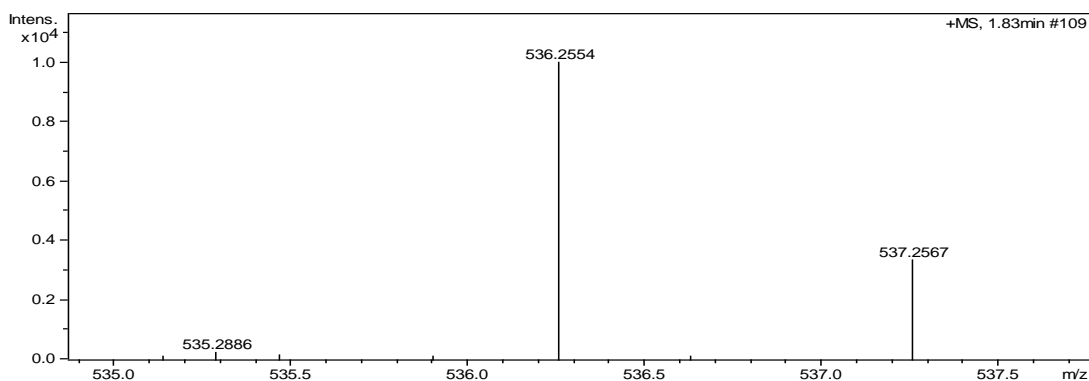
Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **3f** (127.1 mg, 79% yield) as a white solid. Mp: 104-106 °C.

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 8.01 (d, *J* = 7.6 Hz, 1H), 7.53-7.46 (m, 2H), 7.30-7.26 (m, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 6.86-6.81 (m, 2H), 6.40 (d, *J* = 9.2 Hz, 1H), 5.44 (d, *J* = 14.8 Hz, 1H), 4.60 (d, *J* = 14.8 Hz, 1H), 4.17-4.09 (m, 2H), 1.58 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.04 (s, 9H);

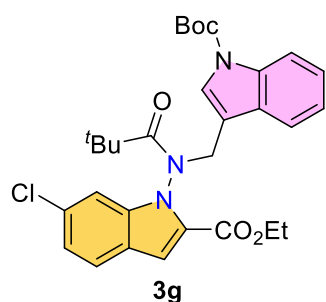
**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.4, 161.7 (d, *J* = 244.1 Hz), 159.9, 149.1, 139.9, 139.8, 135.0, 129.7, 126.6, 124.5, 123.9 (d, *J* = 10.2 Hz), 122.7, 119.9, 119.3, 114.9, 114.5, 111.5, 111.3, 97.7 (d, *J* = 27.4 Hz), 83.5, 61.0, 44.8, 41.0, 28.7, 28.0, 14.1;

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -113.6;

**HRMS** Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>35</sub>FN<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 536.2555, found: 536.2554;



***tert*-butyl 3-((N-(6-chloro-2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (**3g**)**

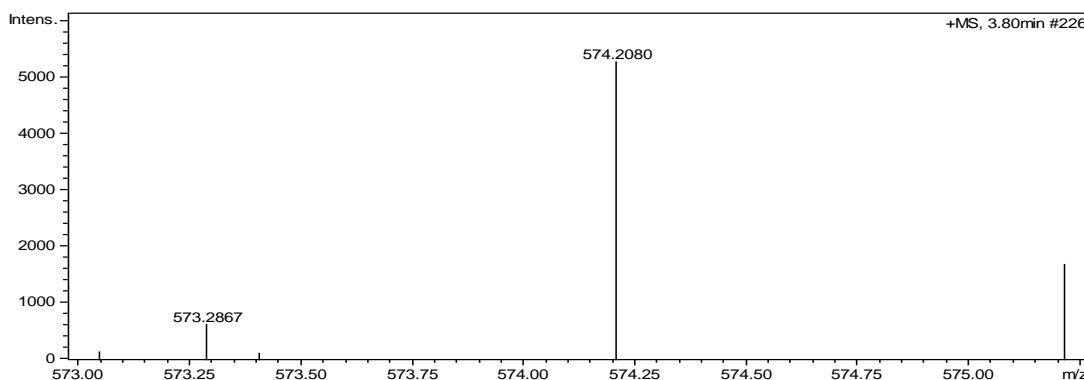


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **3g** (127.8 mg, 77% yield) as a white solid. Mp: 126-129 °C.

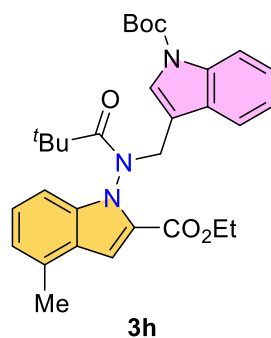
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 8.02 (d, *J* = 7.2 Hz, 1H), 7.50-7.46 (m, 2H), 7.30-7.27 (m, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.80 (s, 1H), 6.63 (s, 1H), 5.49 (d, *J* = 14.8 Hz, 1H), 4.55 (d, *J* = 14.0 Hz, 1H), 4.17-4.11 (m, 2H), 1.58 (s, 9H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.03 (s, 9H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.3, 159.9, 149.1, 139.7, 135.0, 132.0, 129.7, 128.9, 126.7, 124.6, 123.4, 122.8 (2C), 121.8, 119.3, 115.0, 114.5, 111.4, 111.2, 83.5, 61.1, 44.8, 41.0, 28.7, 28.0, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>34</sub>ClN<sub>3</sub>NaO<sub>5</sub> [M + Na]<sup>+</sup>: 574.2079, found: 574.2080;



**tert-butyl 3-((N-(2-(ethoxycarbonyl)-4-methyl-1H-indol-1-yl)pivalamido)methyl)-1H-indole-1-carboxylate (3h)**

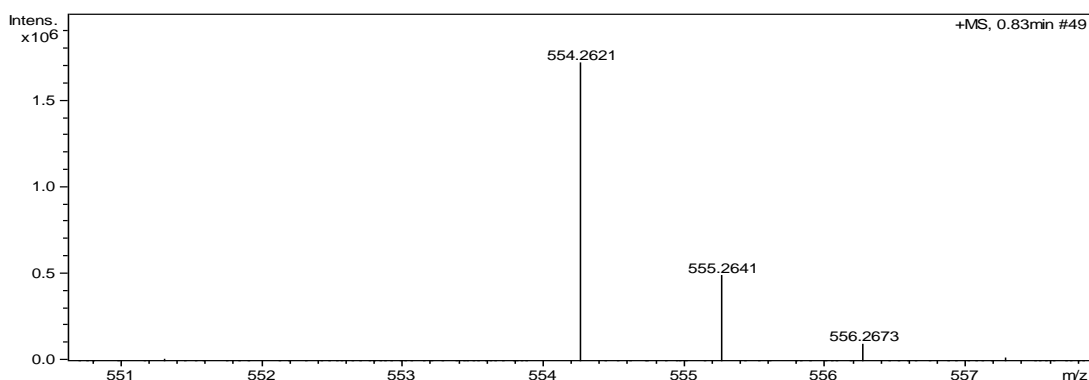


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **3h** (117.4 mg, 74% yield) as a white solid. Mp: 96-99 °C.

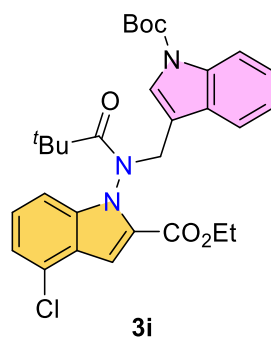
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 8.02 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.32 (s, 1H), 7.26 (t, *J* = 9.2 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 7.2 Hz, 1H), 6.77 (s, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 5.31 (d, *J* = 14.8 Hz, 1H), 4.71 (d, *J* = 14.4 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 2.53 (s, 3H), 1.56 (s, 9H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.03 (s, 9H);

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.4, 160.1, 149.2, 139.1, 135.1, 132.1, 129.8, 127.8, 126.7, 126.0, 124.3, 123.6, 122.6, 121.9, 119.6, 114.7 (2C), 109.9, 108.9, 83.3, 60.8, 44.7, 41.0, 28.7, 28.0, 18.1, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>31</sub>H<sub>37</sub>N<sub>3</sub>NaO<sub>5</sub> [M + Na]<sup>+</sup>: 554.2625, found: 554.2621;



***tert*-butyl 3-((N-(4-chloro-2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (**3i**)**

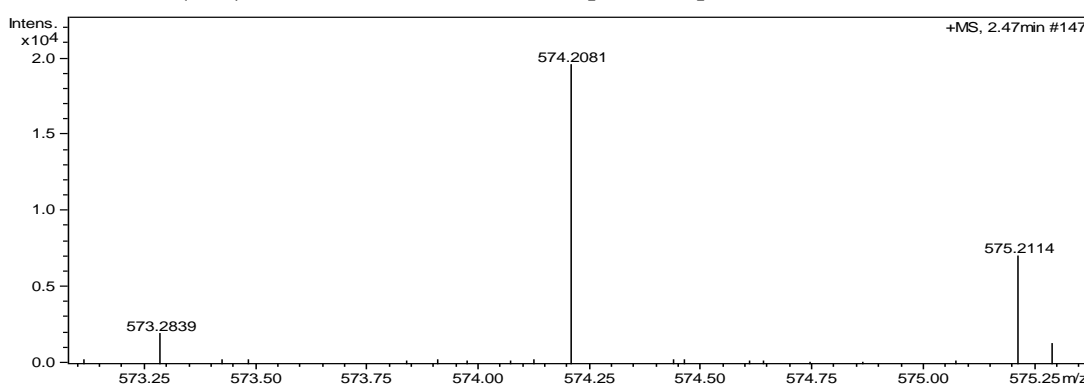


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **3i** (140.0 mg, 85% yield) as a white solid. Mp: 122-124 °C.

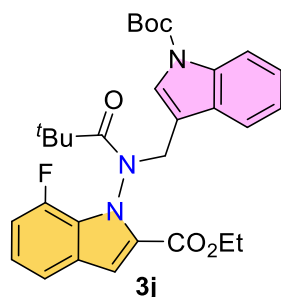
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 8.03 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.40 (s, 1H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 6.91 (t, *J* = 8.0 Hz, 1H), 6.70 (s, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 5.47 (d, *J* = 14.8 Hz, 1H), 4.60 (d, *J* = 14.4 Hz, 1H), 4.21-4.07 (m, 2H), 1.56 (s, 9H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.03 (s, 9H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.2, 159.8, 149.0, 140.0, 135.2, 129.7, 128.8, 127.7, 126.7, 126.1, 124.5, 122.7, 122.4, 121.5, 119.4, 114.8, 114.3, 109.9, 109.4, 83.5, 61.2, 44.8, 41.0, 28.6, 28.0, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>34</sub>ClN<sub>3</sub>NaO<sub>5</sub> [M + Na]<sup>+</sup>: 574.2079, found: 574.2081;



**tert-butyl 3-((N-(2-(ethoxycarbonyl)-7-fluoro-1H-indol-1-yl)pivalamido)methyl)-1H-indole-1-carboxylate (3j)**



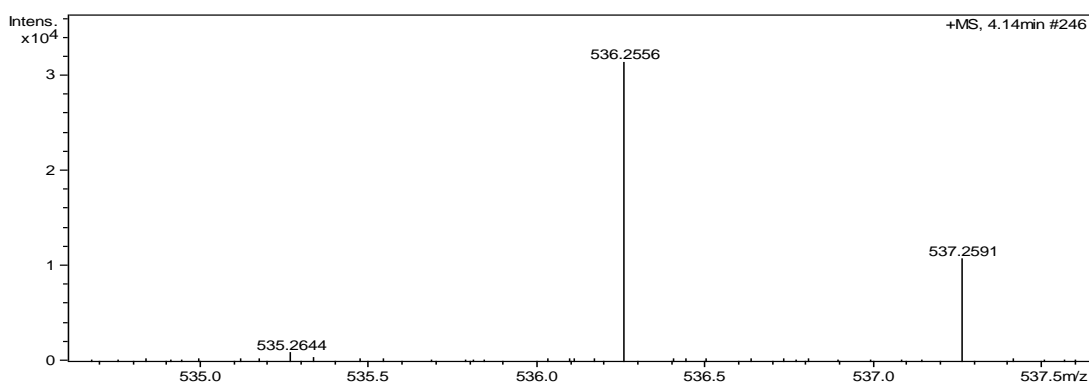
Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **3j** (105.4 mg, 66% yield) as a white solid, Mp: 86-88 °C.

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.36 (s, 1H), 7.29-7.26 (m, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 6.97-6.91 (m, 1H), 6.76-6.71 (m, 2H), 6.51 (d, *J* = 8.4 Hz, 1H), 5.43 (d, *J* = 14.4 Hz, 1H), 4.65 (d, *J* = 14.4 Hz, 1H), 4.18-4.05 (m, 2H), 1.57 (s, 9H), 1.29 (t, *J* = 6.8 Hz, 3H), 1.03 (s, 9H);

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.3, 159.7, 156.7 (d, *J* = 250.8 Hz), 149.1, 141.4 (d, *J* = 9.2 Hz), 135.1, 129.7, 128.5, 126.7, 126.4 (d, *J* = 7.8 Hz), 124.5, 122.7, 119.4, 114.8, 114.3, 113.3 (d, *J* = 23.2 Hz), 107.3, 107.0, 106.3 (d, *J* = 18.4 Hz), 83.5, 61.1, 44.7, 41.1, 28.6, 28.0, 14.1;

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -120.8;

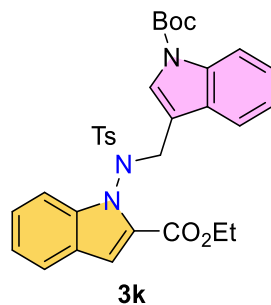
**HRMS** Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>35</sub>FN<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 536.2555, found: 536.2556;



*tert*-butyl

3-(((N-(2-(ethoxycarbonyl)-1*H*-indol-1-yl)-4-

methylphenyl)sulfonamido)methyl)-1*H*-indole-1-carboxylate (**3k**)

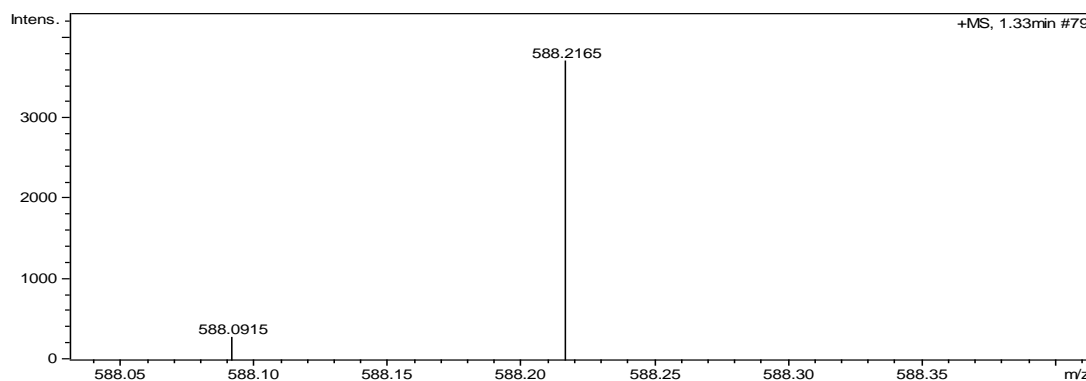


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:10) give the product **3k** (61.0 mg, 35% yield) as a white solid, Mp: 157-159 °C.

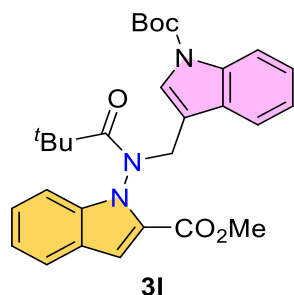
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 8.03 (d, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.24-7.21 (m, 4H), 7.14 (s, 1H), 6.98 (t, *J* = 7.2 Hz, 1H), 6.87 (t, *J* = 8.0 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 5.58 (d, *J* = 14.4 Hz, 1H), 5.19 (d, *J* = 14.4 Hz, 1H), 4.07-3.96 (m, 2H), 2.41 (s, 3H), 1.56 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 160.0, 149.3, 144.1, 140.6, 135.7, 129.6, 129.5, 128.2, 127.8, 126.6, 125.9, 124.6, 123.2, 122.8, 121.8, 121.7, 119.4, 115.1, 114.5, 112.6, 111.8, 83.7, 60.5, 46.6, 28.1, 21.5, 14.1;

HRMS Calcd (ESI) *m/z* for C<sub>32</sub>H<sub>34</sub>N<sub>3</sub>O<sub>6</sub>S [M + H]<sup>+</sup>: 588.2163, found: 588.2165;



**tert-butyl 3-((N-(2-(methoxycarbonyl)-1H-indol-1-yl)pivalamido)methyl)-1H-indole-1-carboxylate (31)**

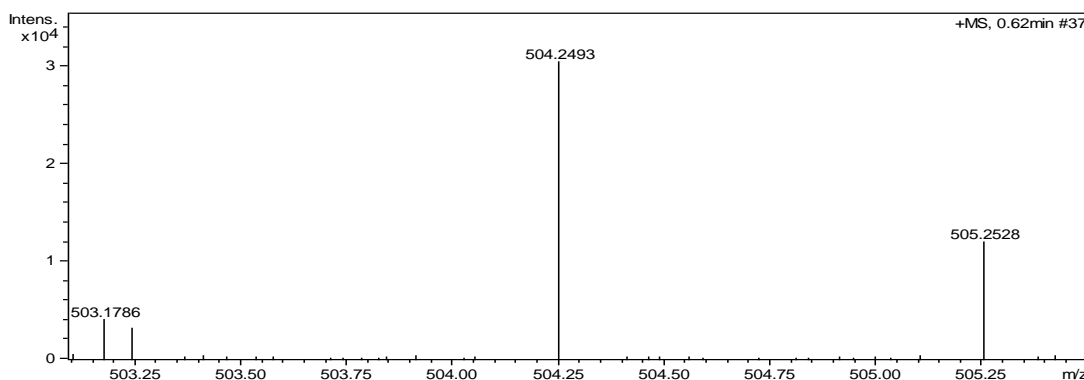


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **31** (122.0 mg, 81% yield) as a colorless oil.

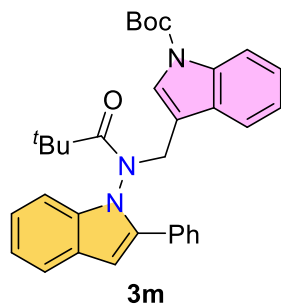
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 8.02 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 6.8 Hz, 1H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.29-7.25 (m, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.12-7.06 (m, 2H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.74 (s, 1H), 5.28 (d, *J* = 14.8 Hz, 1H), 4.76 (d, *J* = 14.4 Hz, 1H), 3.59 (s, 3H), 1.56 (s, 9H), 1.03 (s, 9H);

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.4, 160.4, 149.1, 139.2, 135.1, 129.8, 128.1, 126.8, 125.9, 124.4, 123.6, 122.6 (2C), 122.0, 119.6, 114.8, 114.6, 111.4, 111.2, 83.4, 51.6, 44.6, 41.0, 28.7, 28.0;

**HRMS** Calcd (ESI) *m/z* for C<sub>29</sub>H<sub>34</sub>N<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 504.2493, found: 504.2493;



***tert*-butyl 3-((N-(2-phenyl-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (3m)**

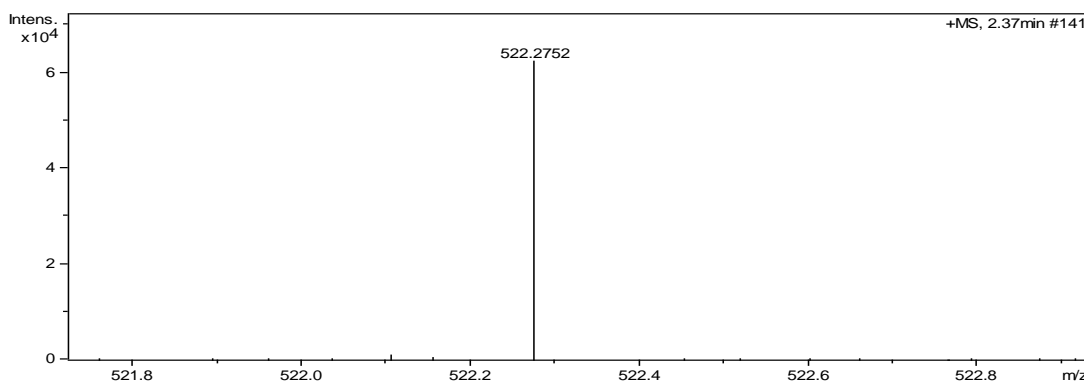


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:30) give the product **3m** (82.5 mg, 53% yield) as a white solid. Mp: 109-112 °C.

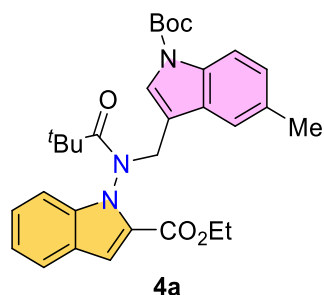
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.89 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.37-7.31 (m, 3H), 7.22-7.13 (m, 4H), 7.11-7.01 (m, 3H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.78 (s, 1H), 6.73 (s, 1H), 5.00 (q, *J* = 14.4 Hz, 2H), 1.59 (s, 9H), 1.11 (s, 9H);

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 149.1, 139.0, 135.0, 131.6, 130.5, 129.8, 128.2, 127.6, 126.8, 126.7, 125.7, 124.1, 122.7, 122.5, 121.3, 120.8, 119.3, 114.7, 114.2, 109.9, 101.9, 83.3, 44.5, 41.3, 28.8, 28.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>33</sub>H<sub>36</sub>N<sub>3</sub>O<sub>3</sub> [M + H]<sup>+</sup>: 522.2751, found: 522.2752;



***tert*-butyl 3-((*N*-(2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-5-methyl-1*H*-indole-1-carboxylate (**4a**)**

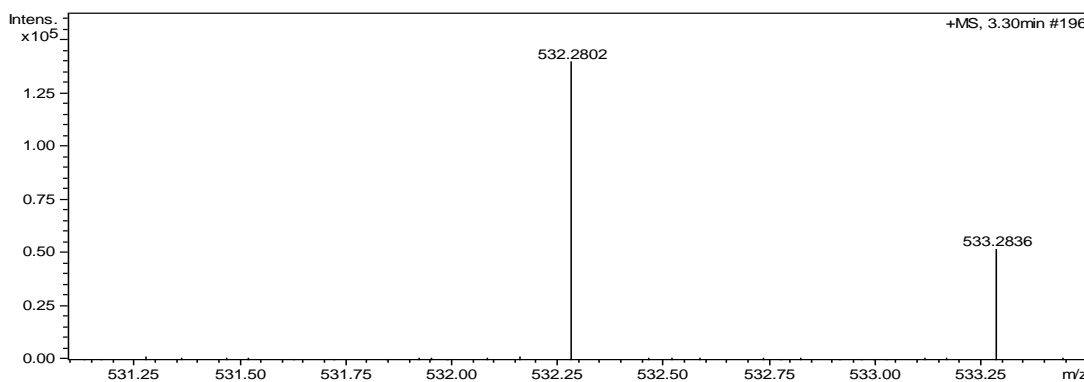


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **4a** (154.4 mg, 97% yield) as a white solid. Mp: 99-102 °C.

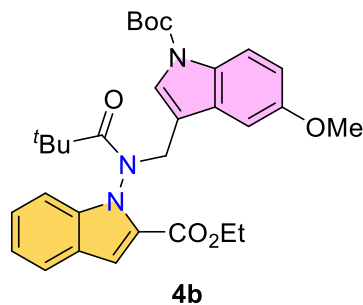
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.87 (d, *J* = 7.2 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.28 (s, 1H), 7.10-7.03 (m, 4H), 6.79-6.77 (m, 2H), 6.78 (d, *J* = 8.0 Hz, 2H), 5.37 (d, *J* = 14.8 Hz, 1H), 4.61 (d, *J* = 14.8 Hz, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 1.55 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.04 (s, 9H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.4, 160.2, 149.2, 139.4, 133.3, 132.0, 130.0, 128.3, 126.8, 125.7 (2C), 123.6, 122.4, 121.9, 119.2, 114.4, 114.3, 111.4 (2C), 83.2, 60.9, 44.8, 41.0, 28.7, 28.1, 21.3, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>31</sub>H<sub>38</sub>N<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 532.2806, found: 532.2802;



**tert-butyl 3-((N-(2-(ethoxycarbonyl)-1H-indol-1-yl)pivalamido)methyl)-5-methoxy-1H-indole-1-carboxylate (4b)**

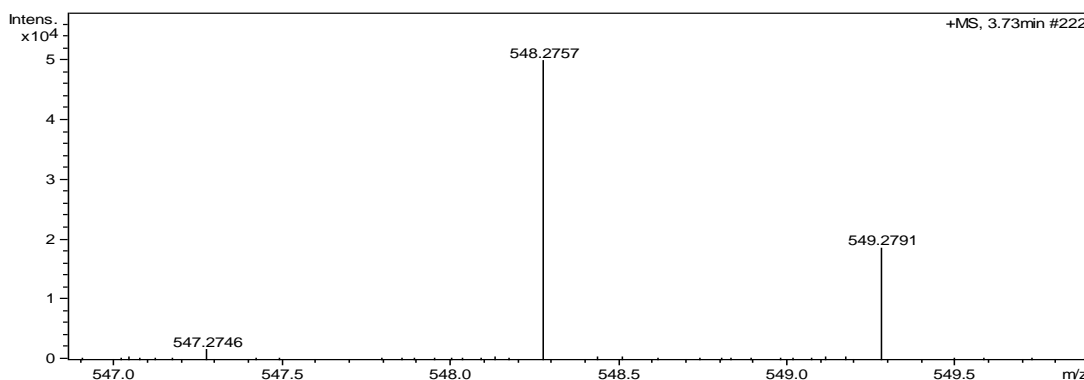


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:12) give the product **4b** (151.1 mg, 92% yield) as a white solid. Mp: 102-105 °C.

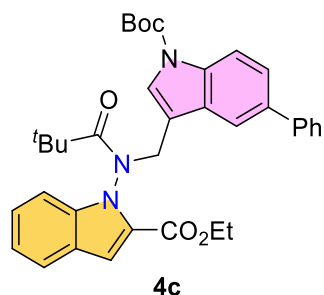
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.88 (d, *J* = 6.8 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.29 (s, 1H), 7.10-7.02 (m, 2H), 6.87-6.75 (m, 4H), 5.37 (d, *J* = 14.8 Hz, 1H), 4.60 (d, *J* = 14.8 Hz, 1H), 4.16-4.09 (m, 2H), 3.75 (s, 3H), 1.55 (s, 9H), 1.29 (t, *J* = 6.8 Hz, 3H), 1.03 (s, 9H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.4, 160.1, 155.8, 149.1, 139.3, 130.6, 129.8, 128.3, 127.2, 125.8, 123.6, 122.4, 121.9, 115.6, 114.7, 113.8, 111.4, 111.3, 101.3, 83.3, 60.9, 55.4, 45.0, 41.0, 28.7, 28.1, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>31</sub>H<sub>38</sub>N<sub>3</sub>O<sub>6</sub> [M + H]<sup>+</sup>: 548.2755, found: 548.2757;



***tert*-butyl 3-((N-(2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-5-phenyl-1*H*-indole-1-carboxylate (**4c**)**

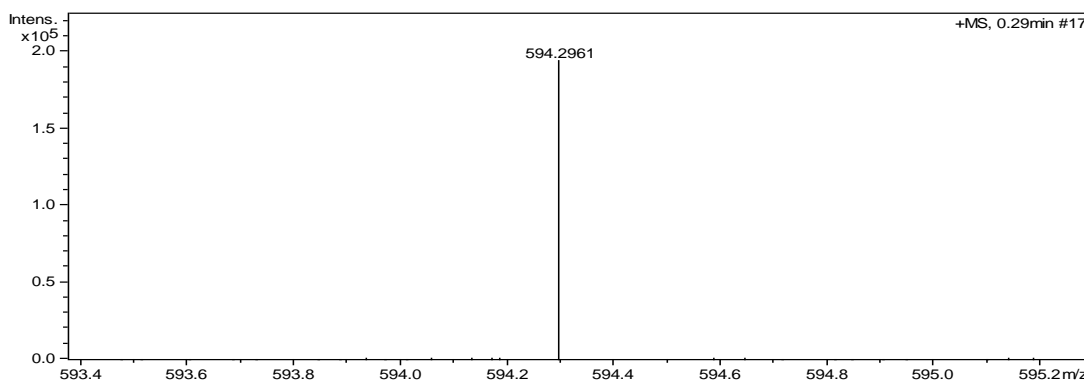


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **4c** (174.7 mg, 98% yield) as a white solid, Mp: 83-86 °C.

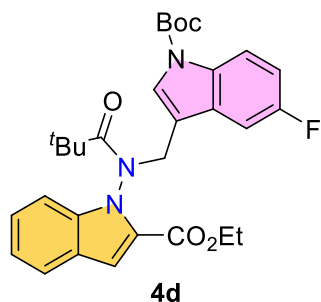
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 8.06 (d, *J* = 8.4 Hz, 1H), 7.59-7.57 (m, 1H), 7.54-7.50 (m, 3H), 7.47-7.41 (m, 3H), 7.34-7.29 (m, 2H), 7.11-7.05 (m, 2H), 6.99 (s, 1H), 6.89-6.86 (m, 1H), 5.40 (d, *J* = 14.8 Hz, 1H), 4.72 (d, *J* = 14.8 Hz, 1H), 4.18-4.06 (m, 2H), 1.60 (s, 9H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.05 (s, 9H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.5, 160.2, 149.1, 141.2, 139.3, 135.6, 134.5, 130.4, 128.6, 128.4, 127.4, 127.2, 126.7, 125.9, 123.7, 123.6, 122.5, 121.9, 117.6, 115.0, 114.8, 111.4, 111.3, 83.6, 60.9, 44.9, 41.0, 28.7, 28.1, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>36</sub>H<sub>40</sub>N<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 594.2962, found: 594.2961;



**tert-butyl 3-((N-(2-(ethoxycarbonyl)-1H-indol-1-yl)pivalamido)methyl)-5-fluoro-1H-indole-1-carboxylate (4d)**



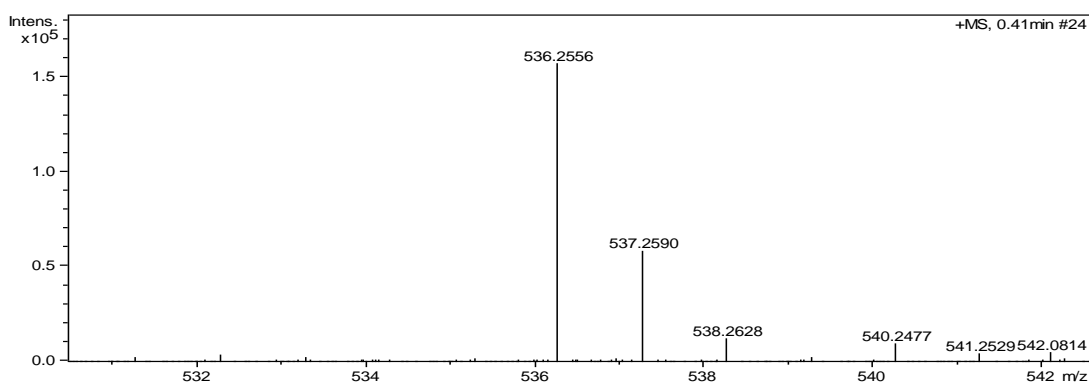
Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **4d** (149.9 mg, 93% yield) as a white solid, Mp: 79-83 °C.

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.96 (s, 1H), 7.59 (d, *J* = 6.8 Hz, 1H), 7.29 (s, 1H), 7.11-7.05 (m, 3H), 6.99-6.94 (m, 1H), 6.84 (s, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.30 (d, *J* = 14.8 Hz, 1H), 4.61 (d, *J* = 14.4 Hz, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 1.55 (s, 9H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.03 (s, 9H);

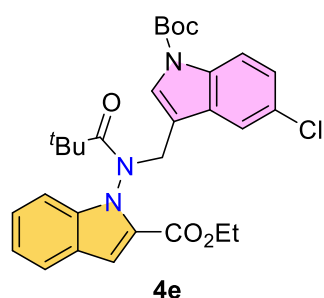
**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.5, 160.1, 159.2 (d, *J* = 238.2 Hz), 148.9, 139.3, 131.5, 130.9 (d, *J* = 10.0 Hz), 128.3, 128.2, 125.9, 123.6, 122.6, 122.0, 115.8 (d, *J* = 9.0 Hz), 114.5 (d, *J* = 4.2 Hz), 112.2 (d, *J* = 25.0 Hz), 111.5, 111.2, 105.2 (d, *J* = 23.2 Hz), 83.7, 60.9, 44.7, 41.0, 28.7, 28.0, 14.1;

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 282 MHz) δ -120.2;

**HRMS** Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>35</sub>FN<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 536.2555, found: 536.2556;



***tert*-butyl 5-chloro-3-((N-(2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (4e)**

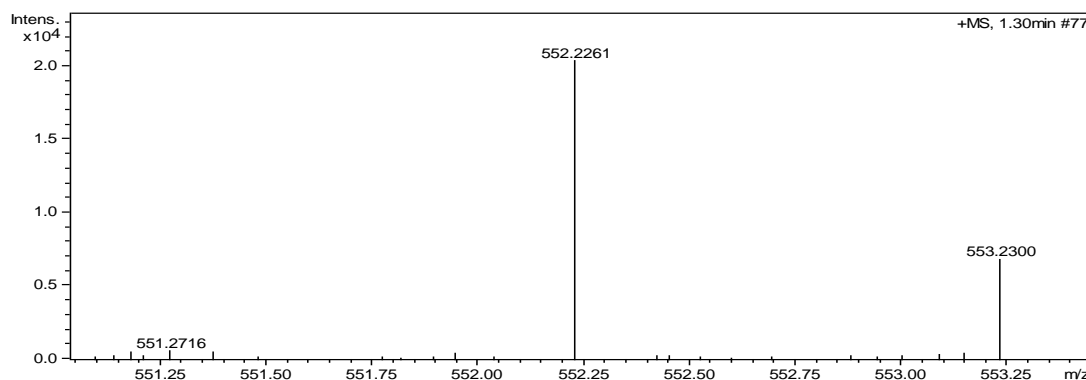


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **4e** (160.1 mg, 97% yield) as a white solid, Mp: 98-101 °C.

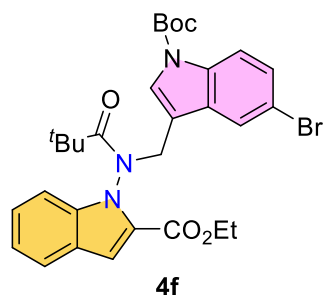
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.94 (d, *J* = 8.4 Hz, 1H), 7.63-7.59 (m, 1H), 7.29-7.27 (m, 2H), 7.19 (dd, *J*<sub>1</sub> = 8.8 Hz, *J*<sub>2</sub> = 2.0 Hz, 1H), 7.13-7.07 (m, 2H), 6.88 (s, 1H), 6.82-6.80 (m, 1H), 5.31 (d, *J* = 14.8 Hz, 1H), 4.62 (d, *J* = 14.8 Hz, 1H), 4.14 (q, *J* = 6.8 Hz, 2H), 1.56 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.04 (s, 9H);

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.5, 160.1, 148.8, 139.3, 133.4, 131.0, 128.4, 128.3, 128.0, 125.9, 124.5, 123.7, 122.6, 122.0, 119.1, 115.8, 114.0, 111.6, 111.2, 83.9, 60.9, 44.6, 41.0, 28.7, 28.0, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>35</sub>ClN<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 552.2260, found: 552.2261;



***tert*-butyl 5-bromo-3-((N-(2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-1*H*-indole-1-carboxylate (4f)**

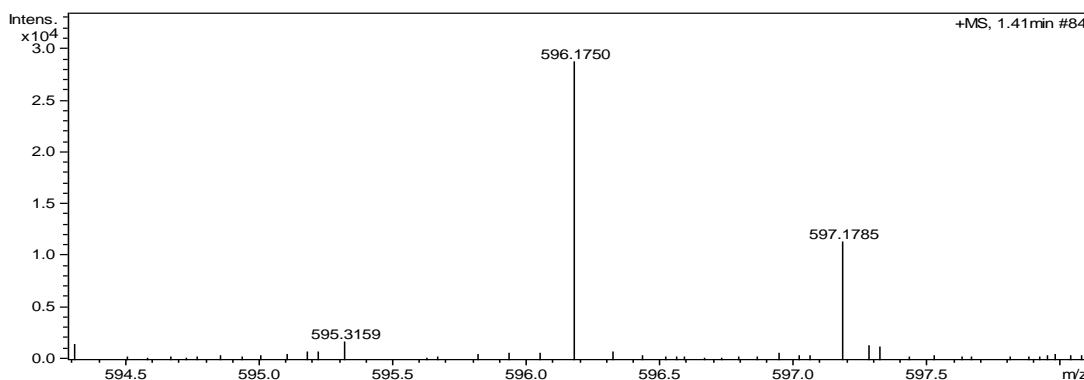


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **4f** (146.7 mg, 82% yield) as a white solid, Mp: 82-84 °C.

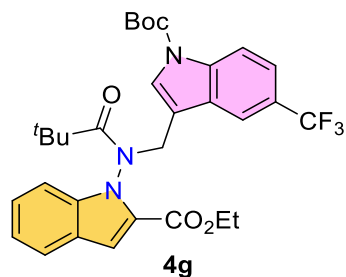
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.88 (d, *J* = 8.4 Hz, 1H), 7.62-7.58 (m, 1H), 7.37 (s, 1H), 7.32 (dd, *J*<sub>1</sub> = 8.8 Hz, *J*<sub>2</sub> = 1.6 Hz, 1H), 7.29 (s, 1H), 7.12-7.06 (m, 2H), 6.89 (s, 1H), 6.82-6.79 (m, 1H), 5.29 (d, *J* = 14.4 Hz, 1H), 4.61 (d, *J* = 14.8 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 1.56 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.04 (s, 9H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.5, 160.1, 148.8, 139.3, 133.4, 131.0, 128.4, 128.3, 128.0, 125.9, 124.5, 123.7, 122.6, 122.0, 119.11, 115.8, 114.0, 111.6, 111.2, 83.9, 60.9, 44.6, 41.0, 28.7, 28.0, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>30</sub>H<sub>35</sub>BrN<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 596.1755, found: 596.1750;



**tert-butyl 3-((N-(2-(ethoxycarbonyl)-1H-indol-1-yl)pivalamido)methyl)-5-(trifluoromethyl)-1H-indole-1-carboxylate (4g)**



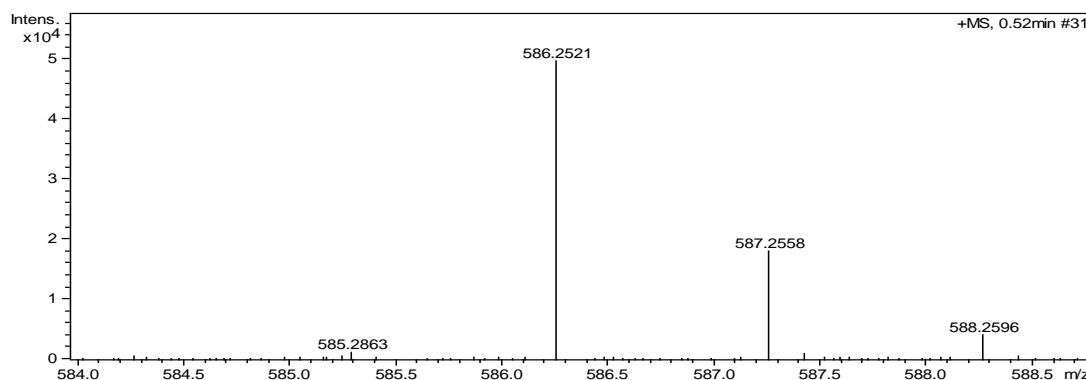
Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **4g** (171.1 mg, 97% yield) as a white solid, Mp: 86-88 °C.

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  8.11 (d,  $J = 8.4$  Hz, 1H), 7.58 (d,  $J = 7.2$  Hz, 1H), 7.47-7.43 (m, 2H), 7.28 (s, 1H), 7.12-7.04 (m, 3H), 6.80 (d,  $J = 7.2$  Hz, 1H), 5.35 (d,  $J = 14.8$  Hz, 1H), 4.67 (d,  $J = 14.8$  Hz, 1H), 4.12 (q,  $J = 6.8$  Hz, 2H), 1.59 (s, 9H), 1.27 (t,  $J = 7.2$  Hz, 3H), 1.03 (s, 9H);

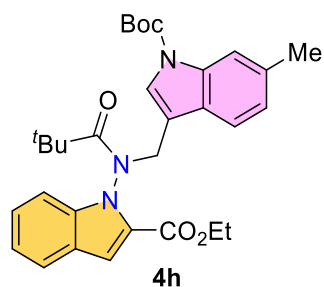
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  179.6, 160.2, 148.8, 139.2, 136.6, 129.5, 128.4, 128.2, 126.0, 124.6 (q,  $J = 270.5$  Hz), 124.8 (q,  $J = 31.9$  Hz), 123.7, 122.7, 122.1, 121.1 (q,  $J = 3.3$  Hz), 116.8 (q,  $J = 4.0$  Hz), 115.1, 115.0, 111.7, 111.1, 84.3, 60.9, 44.8, 41.0, 28.6, 28.0, 14.1;

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 282 MHz)  $\delta$  -61.0;

**HRMS** Calcd (ESI)  $m/z$  for  $\text{C}_{31}\text{H}_{35}\text{F}_3\text{N}_3\text{O}_5$   $[\text{M} + \text{H}]^+$ : 586.2523, found: 586.2521;



**tert-butyl 3-((N-(2-(ethoxycarbonyl)-1*H*-indol-1-yl)pivalamido)methyl)-6-methyl-1*H*-indole-1-carboxylate (4h)**

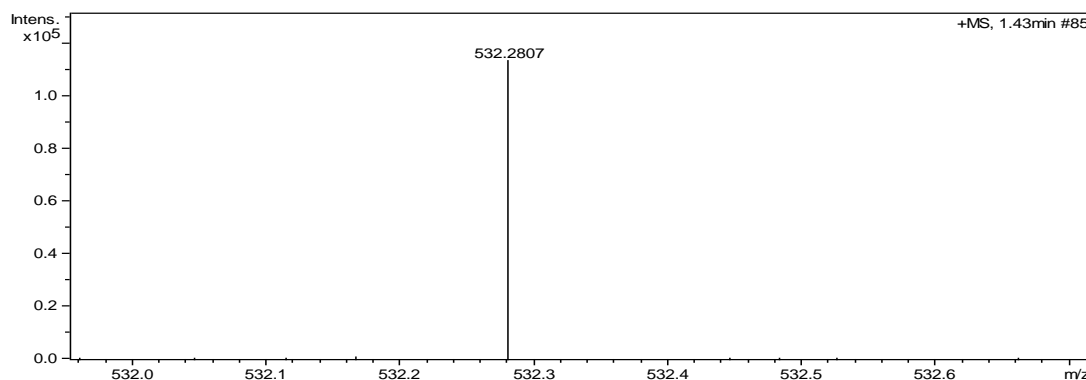


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) give the product **4h** (143.3 mg, 90% yield) as a white solid, Mp: 99-103 °C.

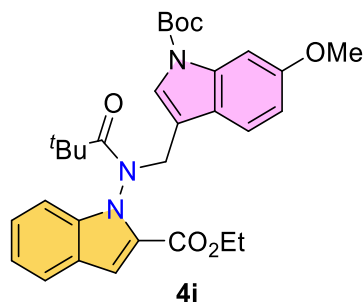
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.88 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.28 (s, 1H), 7.11-7.01 (m, 3H), 7.76 (d, *J* = 8.0 Hz, 1H), 6.64 (s, 1H), 5.37 (d, *J* = 14.4 Hz, 1H), 4.61 (d, *J* = 14.8 Hz, 1H), 4.14-4.06 (m, 2H), 2.45 (s, 3H), 1.54 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.03 (s, 9H);

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.4, 160.1, 149.2, 139.4, 135.6, 134.4, 128.3, 127.5, 126.1, 125.7, 124.1, 123.6, 122.4, 121.9, 119.2, 115.0, 114.6, 111.4, 111.3, 83.1, 60.9, 44.8, 41.0, 28.7, 28.0, 21.9, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>31</sub>H<sub>38</sub>N<sub>3</sub>O<sub>5</sub> [M + H]<sup>+</sup>: 532.2806, found: 532.2807;



**tert-butyl 3-((N-(2-(ethoxycarbonyl)-1H-indol-1-yl)pivalamido)methyl)-6-methoxy-1H-indole-1-carboxylate (4i)**

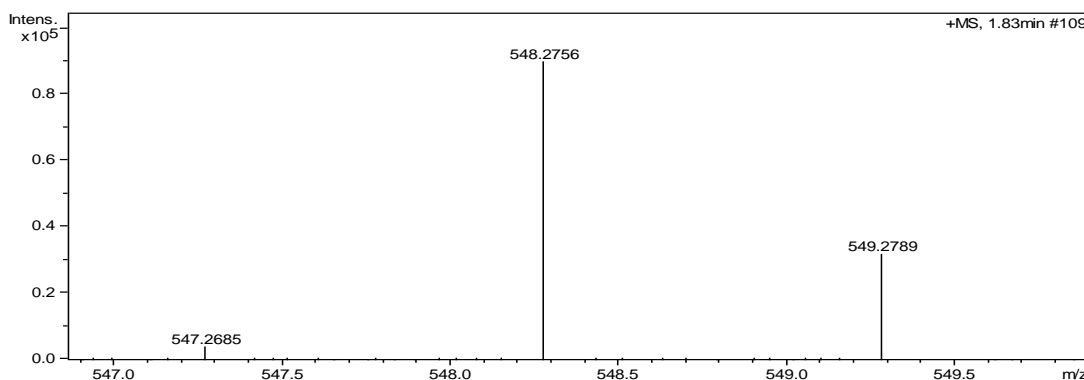


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:12) give the product **4i** (147.6 mg, 90% yield) as a white solid, Mp: 106-108 °C.

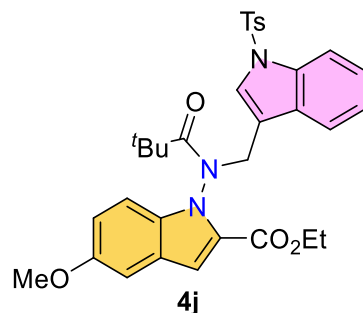
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.61-7.57 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.28 (s, 1H), 7.11-7.03 (m, 2H), 6.82 (dd, *J*<sub>1</sub> = 8.8 Hz, *J*<sub>2</sub> = 2.4 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.62 (s, 1H), 5.35 (d, *J* = 14.8 Hz, 1H), 4.59 (d, *J* = 14.8 Hz, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 1.54 (s, 9H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.02 (s, 9H);

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 179.4, 160.1, 157.8, 149.2, 139.3, 136.2, 128.3, 125.7, 125.4, 123.6 (2C), 122.4, 121.7, 120.2, 114.7, 112.0, 111.4, 111.3, 98.9, 83.2, 60.9, 55.5, 44.9, 41.0, 28.7, 28.0, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>31</sub>H<sub>38</sub>N<sub>3</sub>O<sub>6</sub> [M + H]<sup>+</sup>: 548.2755, found: 548.2756;



**ethyl 5-methoxy-1-(N-((1-tosyl-1*H*-indol-3-yl)methyl)pivalamido)-1*H*-indole-2-carboxylate (4j)**

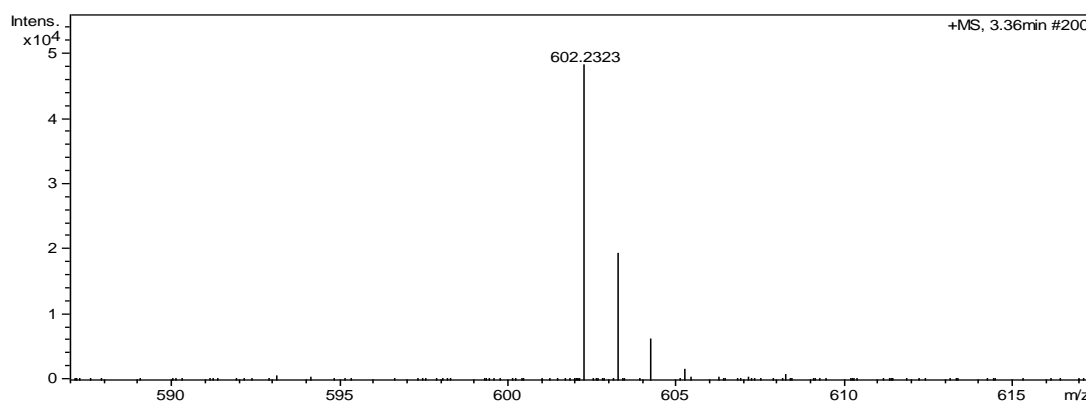


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:12) give the product **4j** (145.4 mg, 81% yield) as a white solid, Mp: 134-136 °C.

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.81 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.26-7.18 (m, 5H), 6.99 (d, *J* = 10.0 Hz, 2H), 6.56-6.49 (m, 2H), 5.42 (d, *J* = 14.8 Hz, 1H), 4.57 (d, *J* = 14.4 Hz, 1H), 4.13-4.04 (m, 2H), 3.81 (s, 3H), 2.34 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.01 (s, 9H);

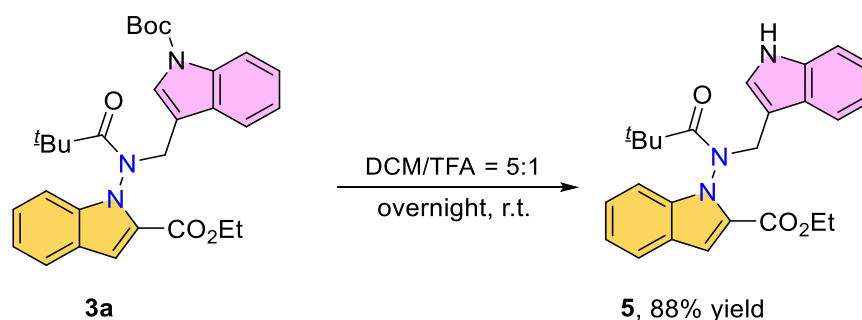
<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.4, 160.0, 155.3, 144.8, 135.1, 134.6, 134.2, 130.1, 129.8, 128.1, 126.7, 126.6, 124.7, 124.0, 123.2, 120.2, 117.2, 116.9, 113.1, 111.9, 111.0, 102.7, 60.8, 55.5, 45.0, 41.0, 28.6, 21.5, 14.1;

**HRMS** Calcd (ESI) *m/z* for C<sub>33</sub>H<sub>36</sub>N<sub>3</sub>O<sub>6</sub> [M + H]<sup>+</sup>: 602.2319, found: 602.2323;

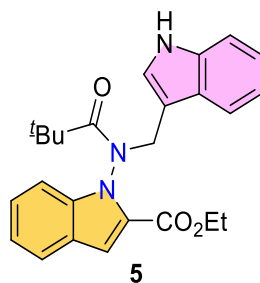


## 6. Synthetic transformations

### 6.1 Experimental procedure for synthesis of 5



A round-bottom flask (25 mL) equipped with a magnetic stir bar was charged with **3a** (103.5 mg, 0.2 mmol, 1.0 equiv) in DCM (5.0 mL). Subsequently, trifluoroacetic acid (1 mL) was slowly added. The resulting mixture was stirred at room temperature overnight. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as eluent to give the desired product **5**.  
**ethyl 1-(N-((1H-indol-3-yl)methyl)pivalamido)-1H-indole-2-carboxylate (5)**

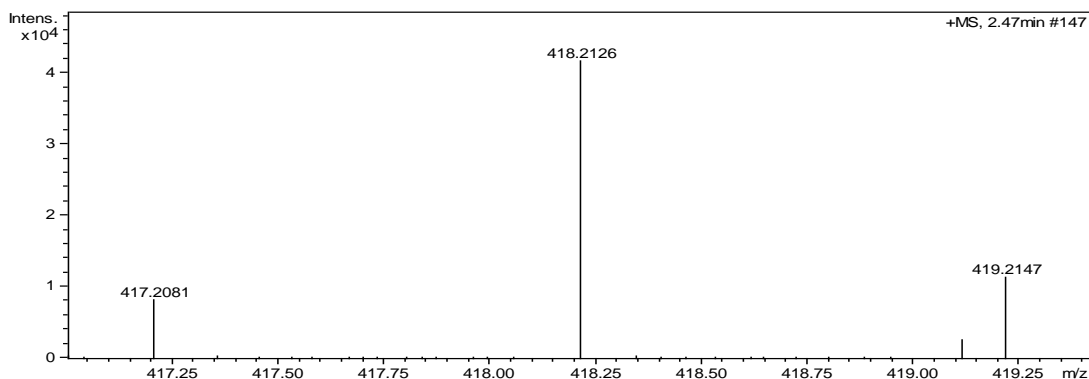


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:5) give the product **5** (73.5 mg, 88% yield) as a white solid, Mp: 179-181 °C.

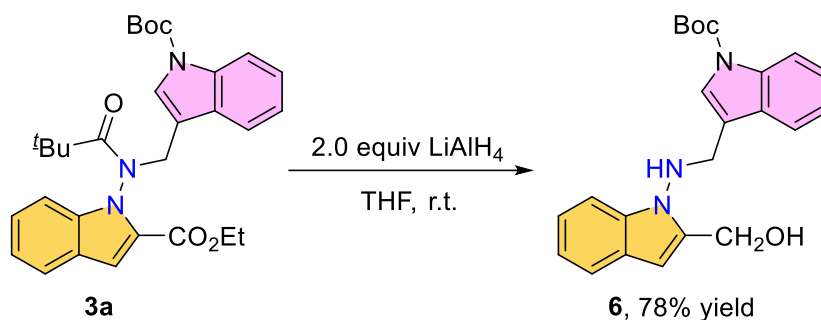
$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.98 (s, 1H), 7.50-7.44 (m, 2H), 7.18-7.16 (m, 2H), 7.08-7.96 (m, 4H), 6.77 (d,  $J = 7.6$  Hz, 1H), 6.41 (s, 1H), 5.21 (d,  $J = 14.8$  Hz, 1H), 4.82 (d,  $J = 14.8$  Hz, 1H), 3.95-3.78 (m, 2H), 1.13 (t,  $J = 7.2$  Hz, 3H), 0.95 (s, 9H);

$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  179.4, 160.2, 139.0, 135.7, 128.8, 127.2, 125.6, 125.5, 123.6, 122.3, 122.0, 121.7, 119.7, 119.4, 111.4, 110.9, 110.8, 110.1, 60.8, 45.1, 41.0, 28.7, 14.1;

**HRMS** Calcd (ESI)  $m/z$  for  $\text{C}_{25}\text{H}_{28}\text{N}_3\text{O}_3$   $[\text{M} + \text{H}]^+$ : 418.2125, found: 418.2126;

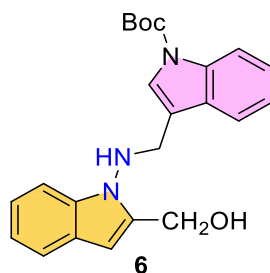


## 6.2 Experimental procedure for synthesis of **6**



A sealed tube (10 mL) equipped with a magnetic stir bar was charged with **3a** (103.5 mg, 0.2 mmol, 1.0 equiv) in THF (2.0 mL). Subsequently, lithium aluminum hydride (15.2 mg, 0.4 mmol, 2.0 equiv) was slowly added. The resulting mixture was stirred at room temperature overnight. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as eluent to give the desired product **6**.

**tert-butyl 3-(((2-(hydroxymethyl)-1H-indol-1-yl)amino)methyl)-1H-indole-1-carboxylate (6)**

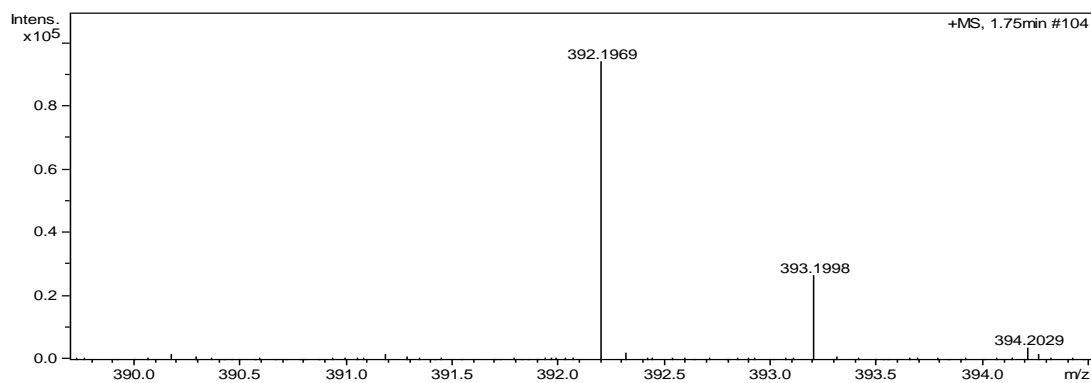


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:3) give the product **6** (61.3 mg, 78% yield) as a white solid, Mp: 179-181 °C.

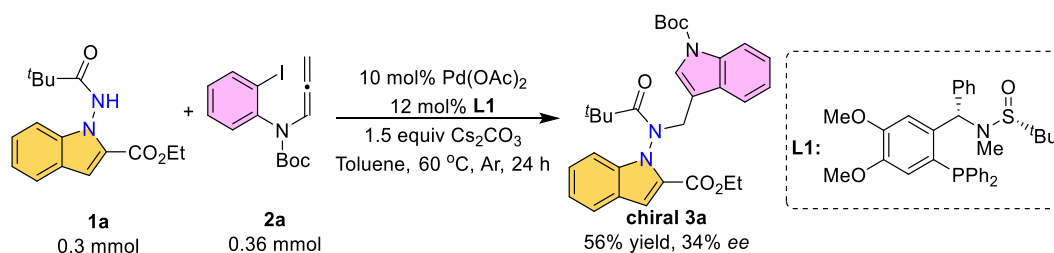
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.50 (s, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.31-7.24 (m, 2H), 7.14 (t, *J* = 7.2 Hz, 1H), 6.28 (s, 1H), 5.07 (t, *J* = 4.8 Hz, 1H), 4.66 (d, *J* = 3.2 Hz, 2H), 4.49 (d, *J* = 4.8 Hz, 2H), 2.64 (s, 1H), 1.67 (s, 9H);

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz) δ 138.9, 135.6, 129.6, 126.0, 125.1 (2C), 124.8, 123.0, 122.1, 121.3, 120.1, 119.0, 115.7, 115.4, 108.4, 98.4, 98.3, 84.0, 57.4, 46.5, 28.2;

**HRMS** Calcd (ESI) *m/z* for C<sub>23</sub>H<sub>26</sub>N<sub>3</sub>O<sub>3</sub> [M + H]<sup>+</sup>: 392.1969, found: 392.1969;



## 7. The attempt to achieve chirality in **3a**:



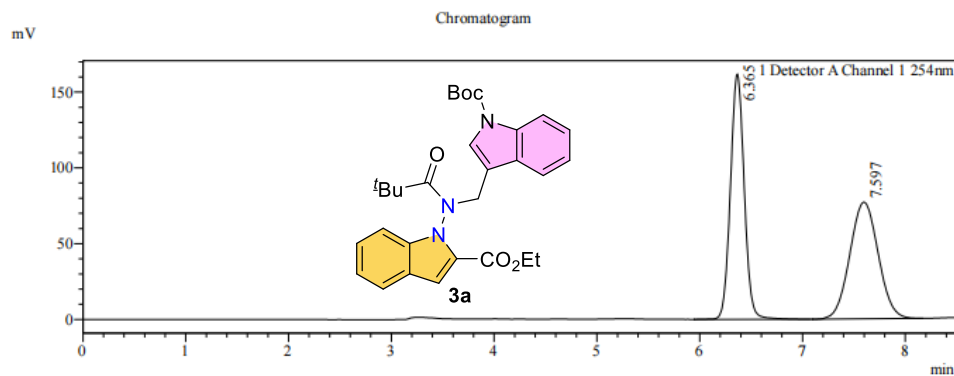
A sealed tube (10 mL) equipped with a magnetic stir bar was charged with Pd(OAc)<sub>2</sub> (6.7 mg, 0.030 mmol, 0.10 equiv), **L1** (19.6 mg, 0.036 mmol, 0.12 equiv) and 2.0 mL toluene. After the catalyst/ligand solution was stirred for 0.5 h at 25 °C. *N*-aminoindole **1a** (86.5 mg, 0.30 mmol, 1.0 equiv), *ortho*-iodoaryl allene **2a** (128.6 mg, 0.36 mmol, 1.2 equiv) and Cs<sub>2</sub>CO<sub>3</sub> (146.7 mg, 0.45 mmol, 1.5 equiv) were successively added. Degassed toluene and backfilled with argon for 3 times (3 × 1 min) at -78 °C. Under argon atmosphere, the reaction mixture was stirred at 60 °C for 24 h by use of module heating. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as eluent to give the desired product **chiral 3a** (86.9 mg, 56% yield).

**chiral 3a HPLC conditions:** Daicel Chiralpak IC column (1 mL/min, hexane/2-propanol = 85/15), 254 nm; tr (minor) = 6.30 min, tr (major) = 7.48 min, 34% *ee*.

### <Sample Information>

Sample Information  
Acquired by : System Administrator  
Sample Name : YY-2-37-WX  
Sample ID :  
Tray# : 1  
Vial# : 2  
Injection Volume : 20  
Data File : YY-2-37-WX-1-15-85-IC-254.lcd  
Method File : 15-85-1-30min-254.lcm  
Batch File : DFG.lcb  
Report Format File : DEFAULT.lsr  
Date Acquired : 06/22/2024 11:31:04  
Date Processed : 06/22/2024 17:10:32

### <Chromatogram>



### <Peak Table>

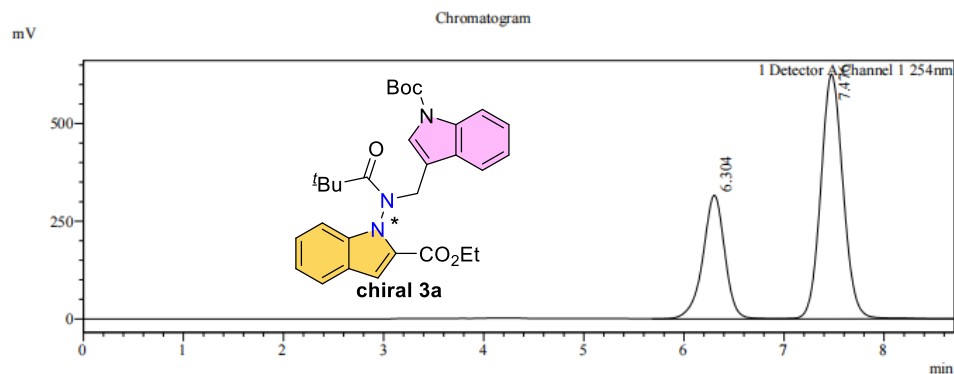
Peak Table

Peak#	Ret. Time	Area	Height	Area%
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2	7.597	1481335	76985	49.513
Total		2991789	238555	100.000

### <Sample Information>

Sample Information  
Acquired by : System Administrator  
Sample Name : WSJ-8-72-IC-85-15-1  
Sample ID :  
Tray# : 1  
Vial# : 1  
Injection Volume : 30  
Data File : WSJ-8-72-IC-85-15-1.lcd  
Method File : 15-85-1-10MIN.lcm  
Batch File : AFASF.lcb  
Report Format File : DEFAULT.lsr  
Date Acquired : 01/27/2026 11:42:09  
Date Processed : 01/27/2026 14:28:36

### <Chromatogram>



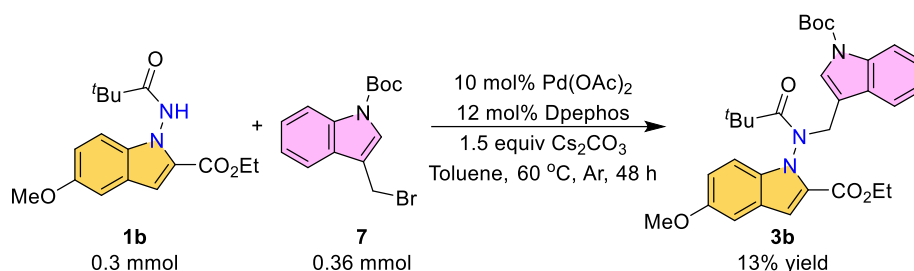
### <Peak Table>

Peak Table

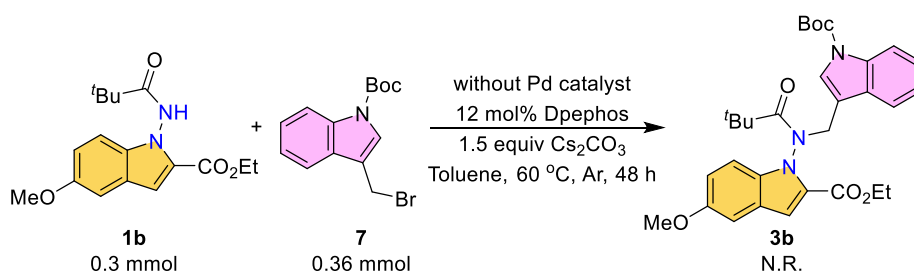
Peak#	Ret. Time	Area	Height	Area%
1	6.304	4839121	316141	33.194
2	7.476	9739044	626020	66.806
Total		14578165	942161	100.000

## 8. Mechanistic study

### 8.1 Control experiment of *tert*-butyl 3-(bromomethyl)-1*H*-indole-1-carboxylate



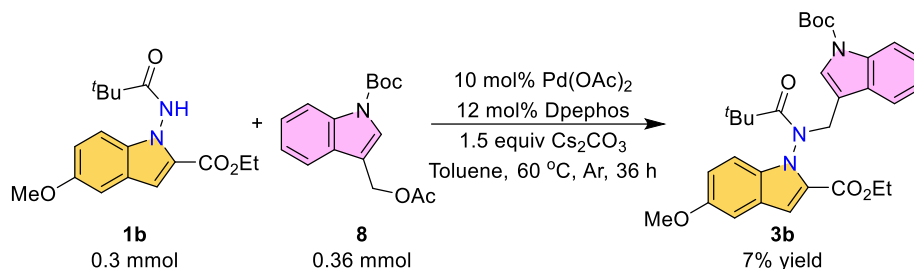
A sealed tube (10 mL) equipped with a magnetic stir bar was charged with Pd(OAc)<sub>2</sub> (6.7 mg, 0.030 mmol, 0.10 equiv), Dpephos (19.4 mg, 0.036 mmol, 0.12 equiv), Cs<sub>2</sub>CO<sub>3</sub> (146.7 mg, 0.45 mmol, 1.5 equiv), *N*-aminoindole **1b** (95.5 mg, 0.3 mmol, 1.0 equiv), *tert*-butyl 3-(bromomethyl)-1*H*-indole-1-carboxylate **7** (111.7 mg, 0.36 mmol, 1.2 equiv) and 2.0 mL toluene were added sequentially. Degassed toluene and backfilled with argon for 3 times (3 × 1 min) at -78 °C. Under argon atmosphere, the reaction mixture was stirred at 60 °C for 24 h by use of module heating. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as eluent to give the desired products **3b** 22.1 mg in 13% yield.



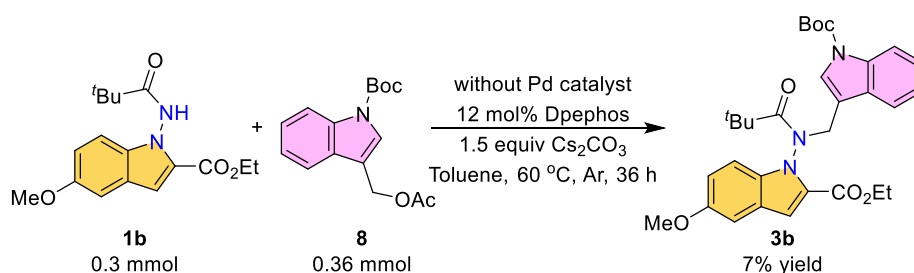
A sealed tube (10 mL) equipped with a magnetic stir bar was charged with Dpephos (19.4 mg, 0.036 mmol, 0.12 equiv), Cs<sub>2</sub>CO<sub>3</sub> (146.7 mg, 0.45 mmol, 1.5 equiv), *N*-aminoindole **1b** (95.5 mg, 0.3 mmol, 1.0 equiv), *tert*-butyl 3-(bromomethyl)-1*H*-indole-1-carboxylate **7** (111.7 mg, 0.36 mmol, 1.2 equiv) and 2.0 mL toluene were added sequentially. Degassed toluene and backfilled with argon for 3 times (3 × 1 min) at -78 °C. Under argon atmosphere, the reaction mixture was stirred at 60 °C for 24 h

by use of module heating. After completion of the reaction (monitored by TLC), no product of **3b** was detected.

## 8.2 Control experiment of *tert*-butyl 3-(acetoxymethyl)-1*H*-indole-1-carboxylate



A sealed tube (10 mL) equipped with a magnetic stir bar was charged with Pd(OAc)<sub>2</sub> (6.7 mg, 0.030 mmol, 0.10 equiv), Dpephos (19.4 mg, 0.036 mmol, 0.12 equiv), Cs<sub>2</sub>CO<sub>3</sub> (146.7 mg, 0.45 mmol, 1.5 equiv), *N*-aminoindole **1b** (95.5 mg, 0.3 mmol, 1.0 equiv), *tert*-butyl 3-(acetoxymethyl)-1*H*-indole-1-carboxylate **8** (104.2 mg, 0.36 mmol, 1.2 equiv) and 2.0 mL toluene were added sequentially. Degassed toluene and backfilled with argon for 3 times (3 × 1 min) at -78 °C. Under argon atmosphere, the reaction mixture was stirred at 60 °C for 24 h by use of module heating. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as eluent to give the desired products **3b** 10.9 mg in 7% yield.



A sealed tube (10 mL) equipped with a magnetic stir bar was charged with Dpephos (19.4 mg, 0.036 mmol, 0.12 equiv), Cs<sub>2</sub>CO<sub>3</sub> (146.7 mg, 0.45 mmol, 1.5 equiv), *N*-aminoindole **1b** (95.5 mg, 0.3 mmol, 1.0 equiv), *tert*-butyl 3-(acetoxymethyl)-1*H*-indole-1-carboxylate **8** (104.2 mg, 0.36 mmol, 1.2 equiv) and 2.0 mL toluene were added sequentially. Degassed toluene and backfilled with argon for 3 times (3 × 1 min) at -78 °C. Under argon atmosphere, the reaction mixture was stirred at 60 °C for 24 h

by use of module heating. After completion of the reaction (monitored by TLC), no product of **3b** was detected.

## 9. Single Crystal X-Ray Diffraction

Crystals of **3g**, **3m** were obtained by slow diffusion from a solution of the compounds in ethyl acetate, trichloromethane and petroleum ether at room temperature for several days (Figure S1-S2). Crystal data and details of the structure determination are presented in Table S2.

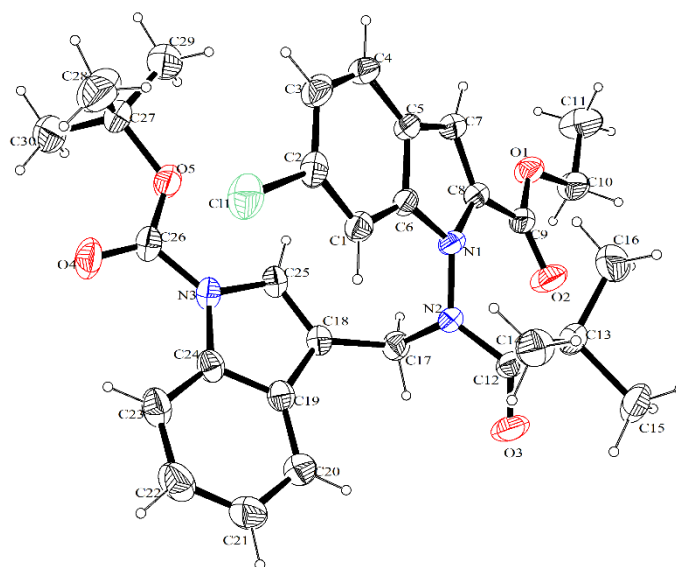


Figure S1. ORTEP drawing (30%) of the crystal structure of **3g**

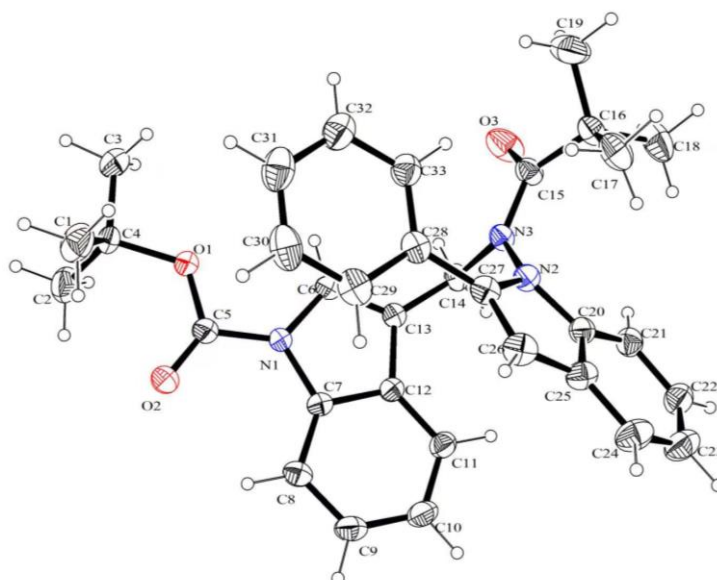


Figure S2. ORTEP drawing (25%) of the crystal structure of **3m**

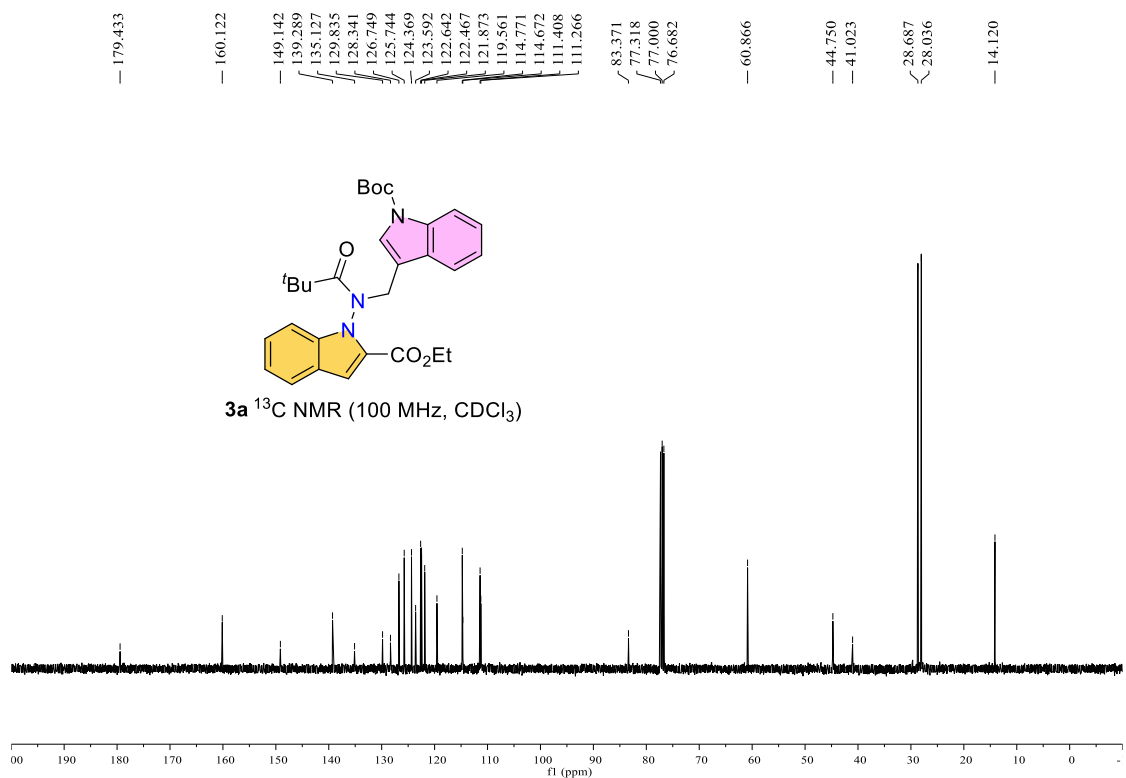
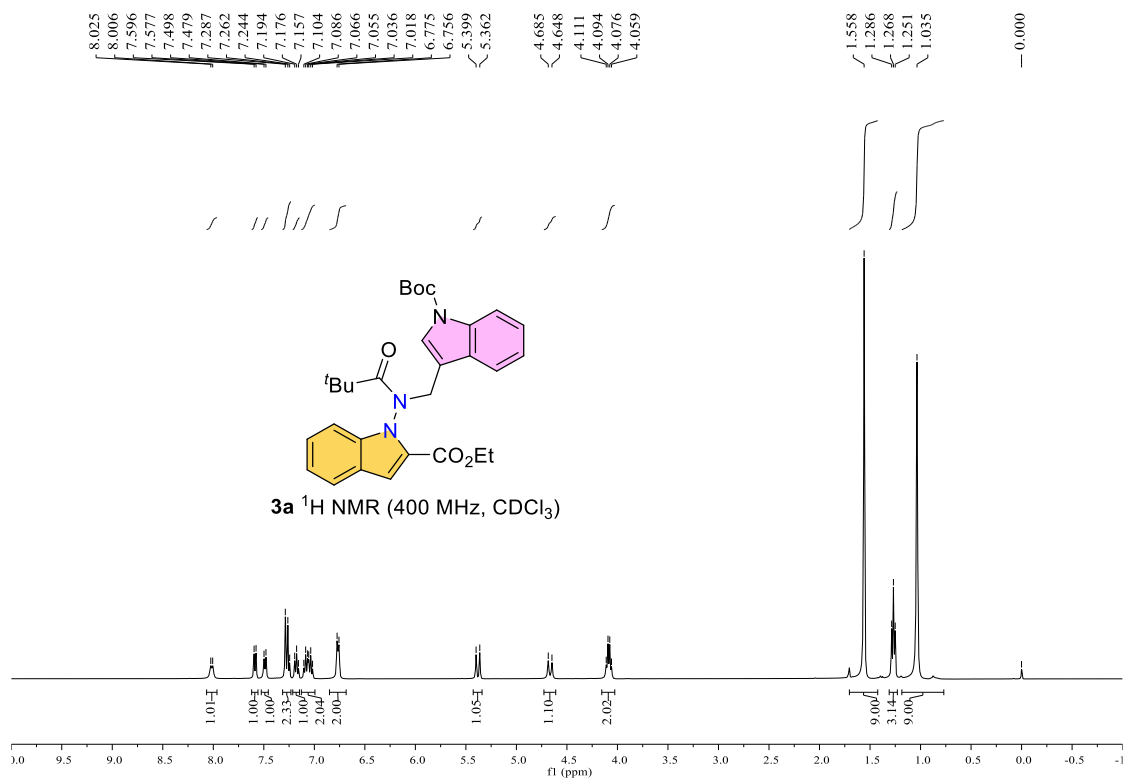
**Table S2** The single crystal data of compounds **3g**, **3m**

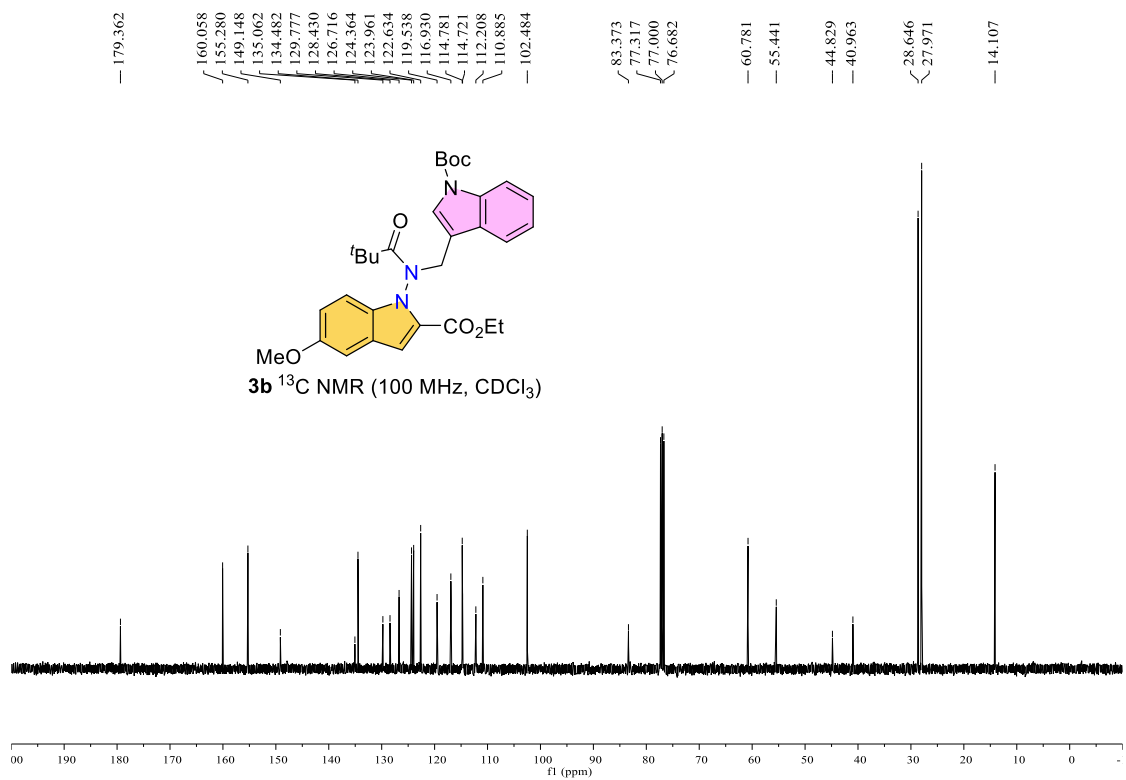
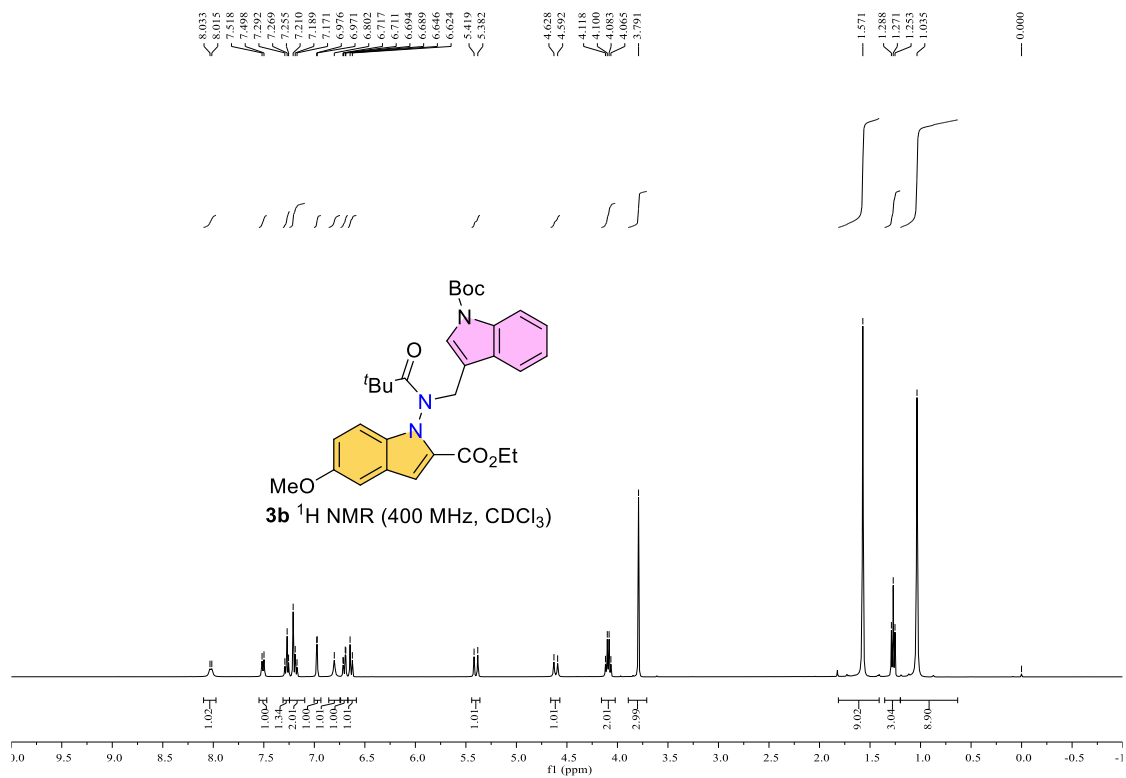
Phase	<b>3g</b>	<b>3m</b>
Identification code	123_a	20260310a_0m_pl
Empirical formula	C <sub>30</sub> H <sub>34</sub> ClN <sub>3</sub> O <sub>5</sub>	C <sub>33</sub> H <sub>35</sub> N <sub>3</sub> O <sub>3</sub>
Formula weight	552.05	521.64
Temperature/K	273.15	100
Crystal system	monoclinic	monoclinic
Space group	C2/c	P2 <sub>1</sub> /c
<i>a</i> / Å	20.503(2)	10.7544(8)
<i>b</i> / Å	16.785(2)	15.4745(11)
<i>c</i> / Å	17.144(2)	17.0735(14)
$\alpha$ (°)	90	90
$\beta$ (°)	94.575(5)	92.652(3)
$\gamma$ (°)	90	90
Volume (Å <sup>3</sup> )	5881.2(12)	2838.3(4)
Z	8	4
$\rho_{\text{calc}}/\text{cm}^3$	1.247	1.221
$\mu/\text{mm}^{-1}$	0.172	0.079
<i>F</i> (000)	2336.0	1112.0
Crystal size/mm <sup>3</sup>	0.13 × 0.11 × 0.1	0.11 × 0.1 × 0.08
Radiation	MoK $\alpha$ ( $\lambda$ = 0.71073)	MoK $\alpha$ ( $\lambda$ = 0.71073)
2 $\theta$ range for data collection/°	4.768 to 55.028	4.616 to 51.406
Index ranges	-26 ≤ <i>h</i> ≤ 26, -21 ≤ <i>k</i> ≤ 21, -22 ≤ <i>l</i> ≤ 22	-13 ≤ <i>h</i> ≤ 11, -18 ≤ <i>k</i> ≤ 18, -20 ≤ <i>l</i> ≤ 16
Reflections collected	45160	15091
Independent reflections	6758 [R <sub>int</sub> = 0.0510, R <sub>sigma</sub> = 0.0414]	5365 [R <sub>int</sub> = 0.0470, R <sub>sigma</sub> = 0.0676]
Data/restraints/parameters	6758/63/390	5365/0/358
Goodness-of-fit on F <sup>2</sup>	1.006	1.025
Final <i>R</i> indices[I ≥ 2 $\sigma$ (I)]	R <sub>1</sub> = 0.0531, wR <sub>2</sub> = 0.1061	R <sub>1</sub> = 0.0511, wR <sub>2</sub> = 0.1127
Final <i>R</i> indexes (all data)	R <sub>1</sub> = 0.0999, wR <sub>2</sub> = 0.1239	R <sub>1</sub> = 0.1153, wR <sub>2</sub> = 0.1339
Largest diff. peak and hole / (e Å <sup>-3</sup> )	0.14/-0.20	0.17/-0.18

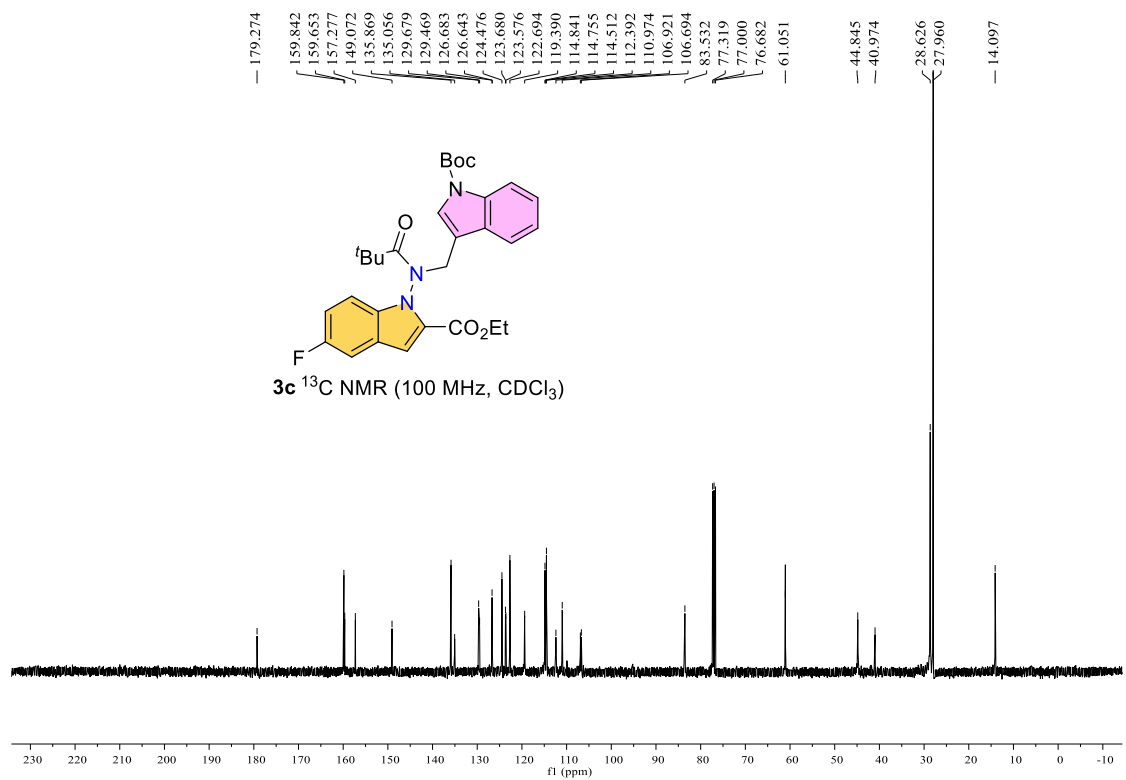
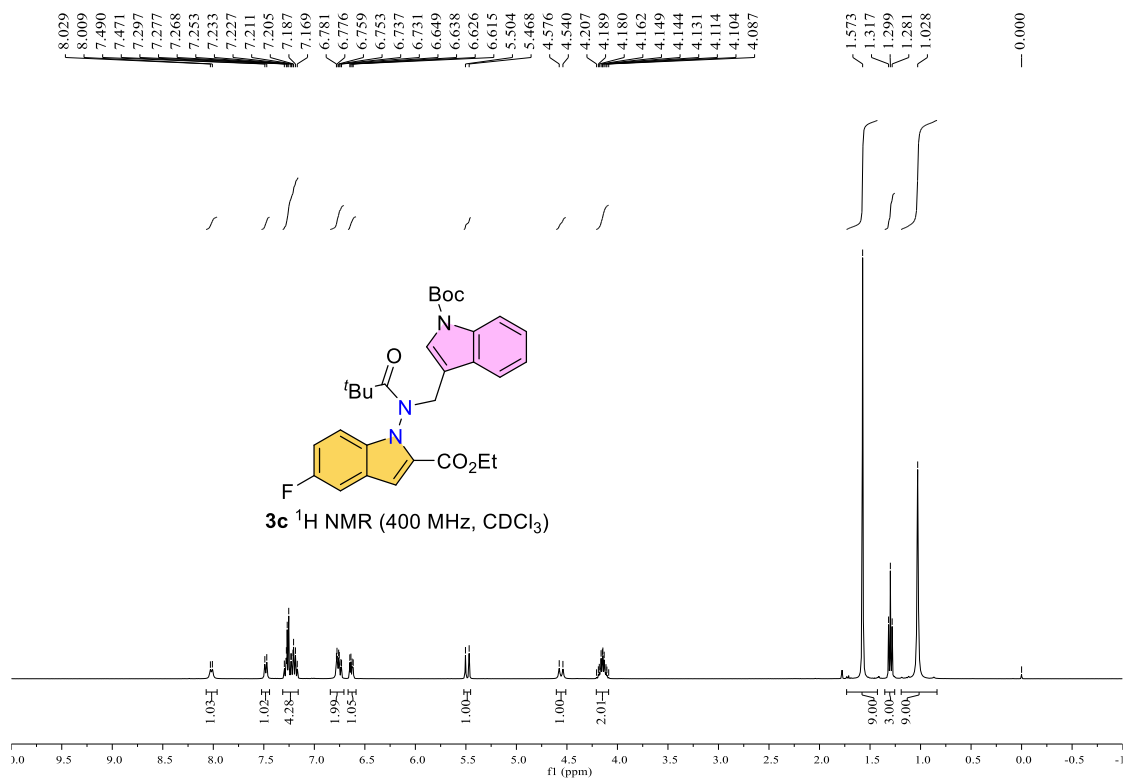
## 10. References:

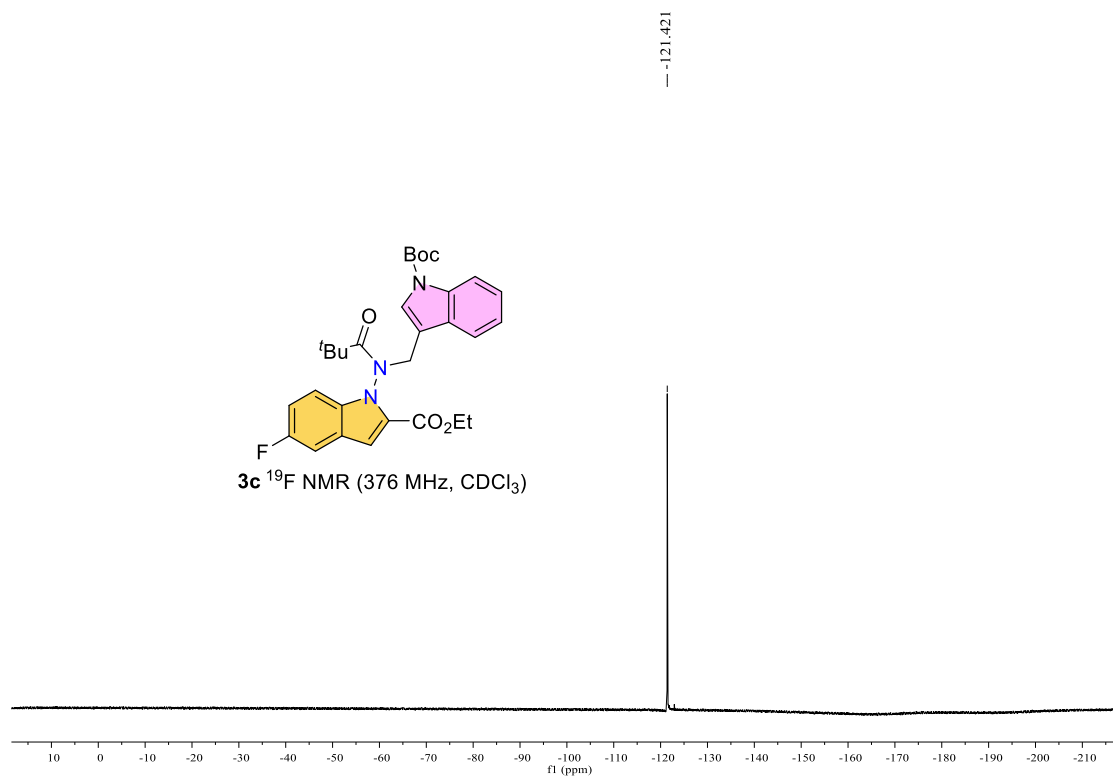
1. Z. Huang, Y. Xu, W. Lin, R. Qian, W. Zhang and X. Li, *Org. Chem. Front.* 2024, **11**, 5437–5442.
2. T.-Z. Li, S.-F. Wu, N.-Y. Wang, C.-S. Hong, Y.-C. Zhang and F. Shi, *J. Org. Chem.* 2024, **89**, 12559–12575.
3. X. Chen, G. Qiu, R. Liu, D. Chen and Z. Chen, *Org. Chem. Front.* 2020, **7**, 890–895.
4. J. Tang, L. Ren, J. Li, Y. Wang, D. Hu, X. Tong and C. Xia, *Org. Lett.* 2022, **24**, 3582–3587.
5. L. Wang, S. Wu, S. Zhang, Q. Hu, Q. Wang, J. Sun, Y. Han and C.-G. Yan. *J. Org. Chem.* 2022, **87**, 14646–14656.

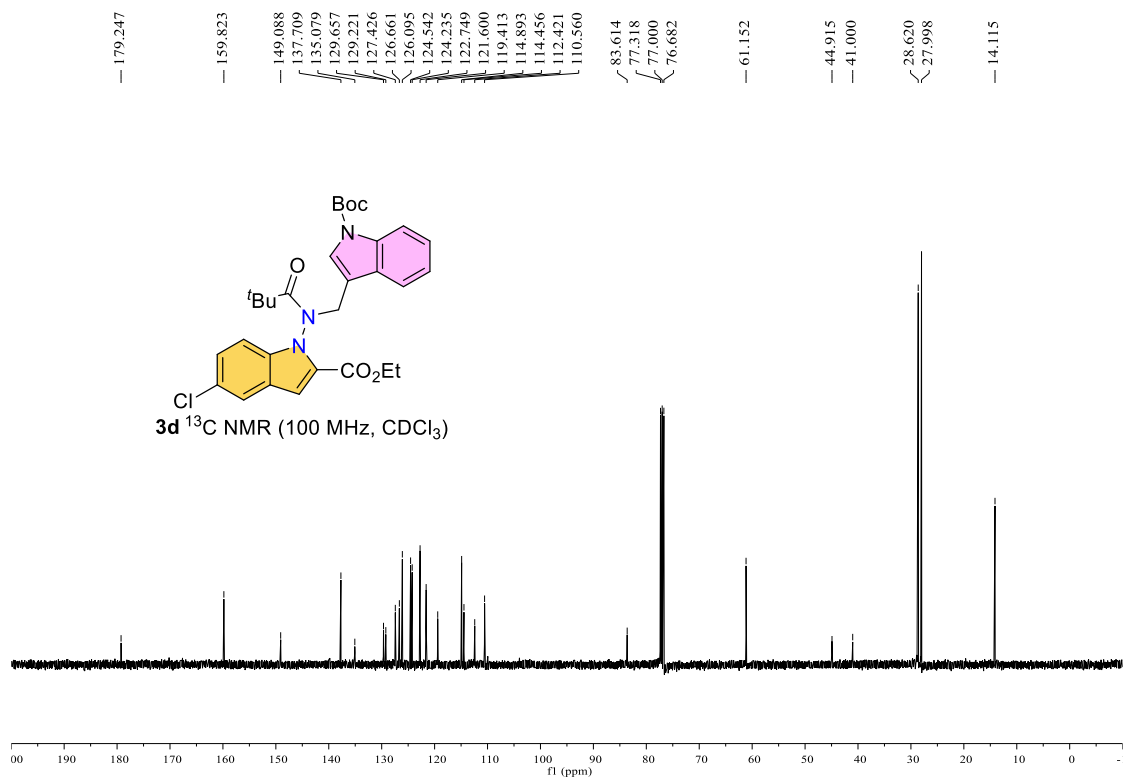
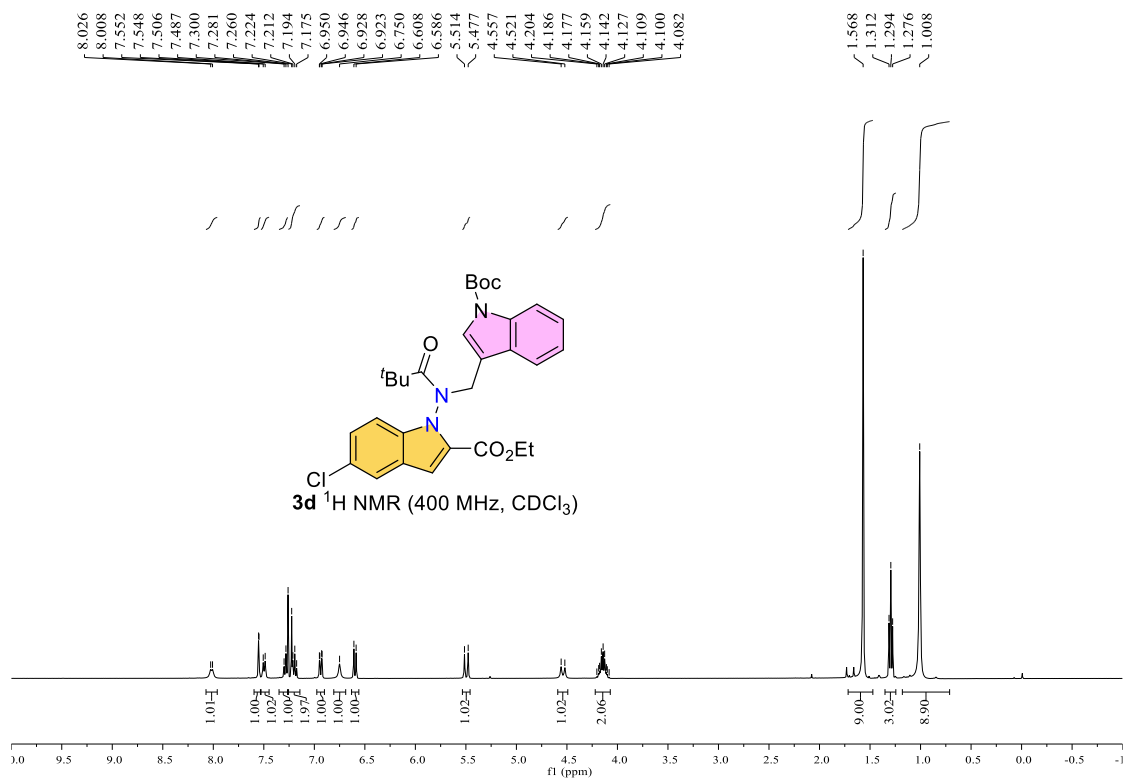
# 11. Copies of NMR spectra for new compounds

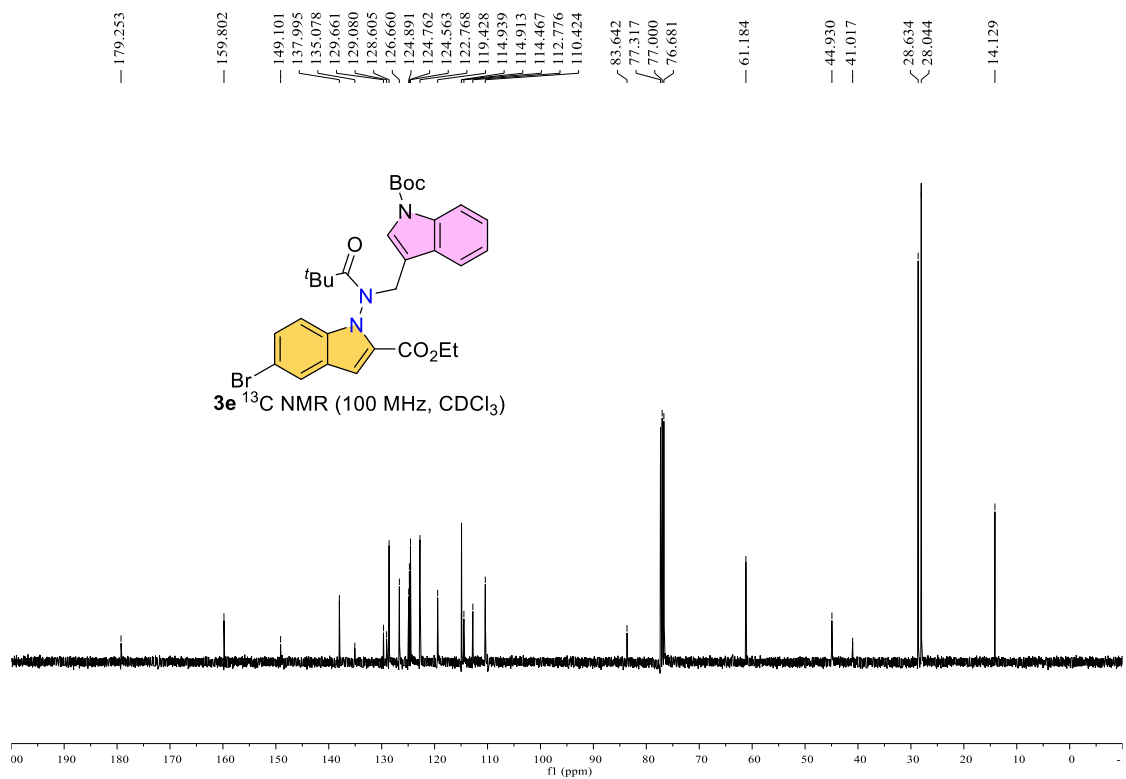
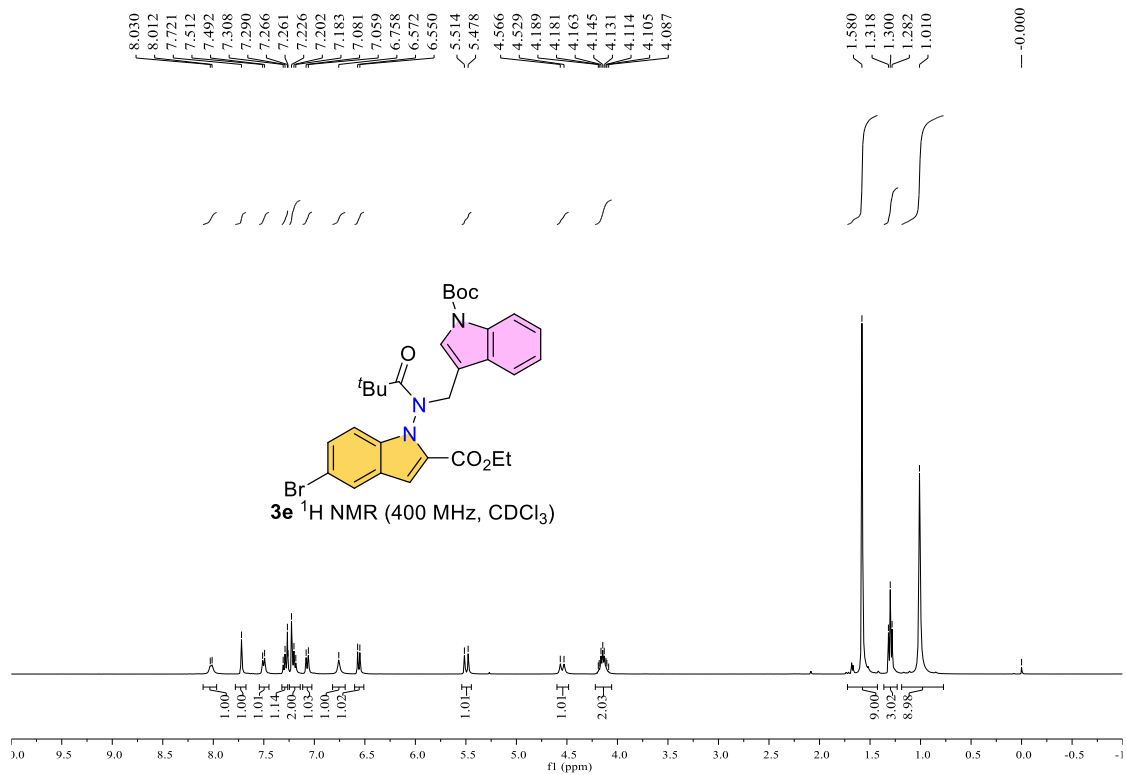


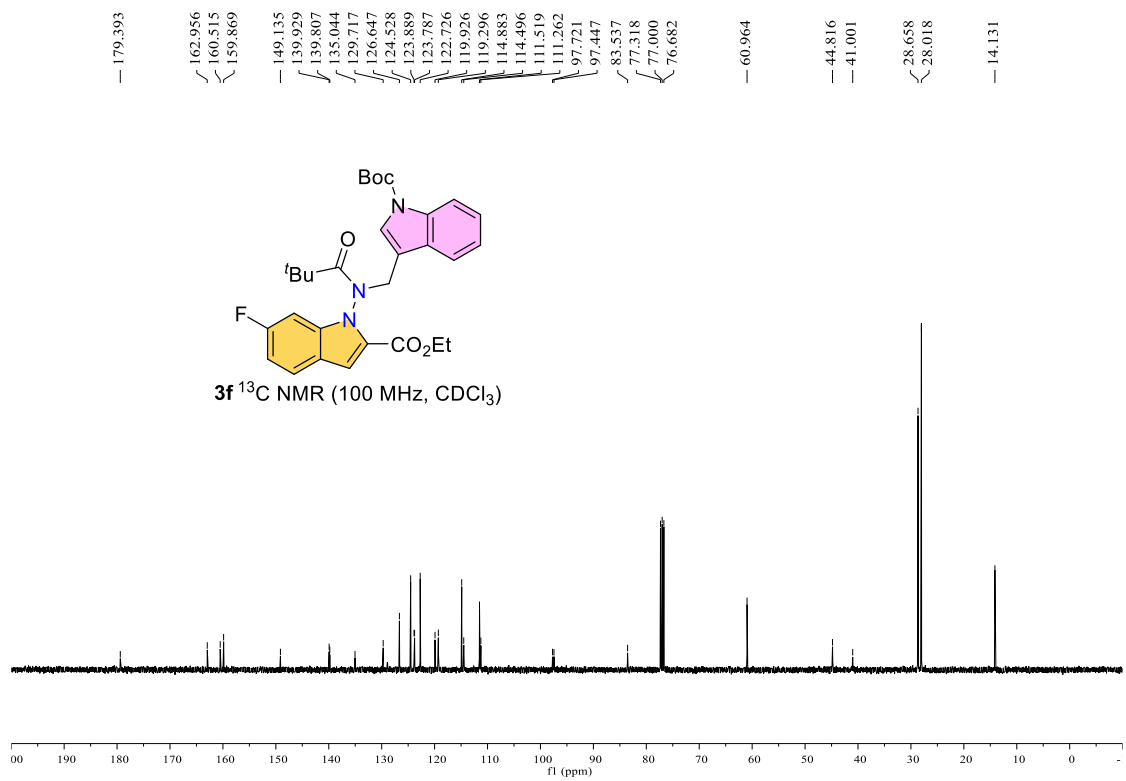
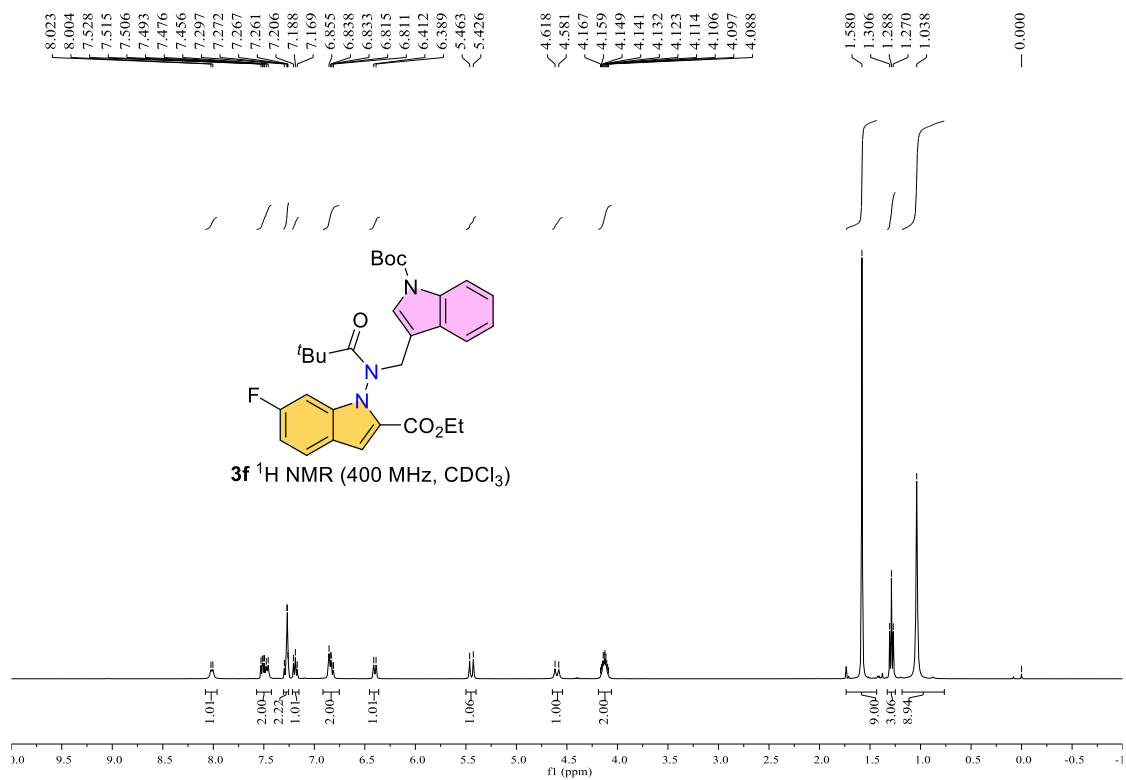


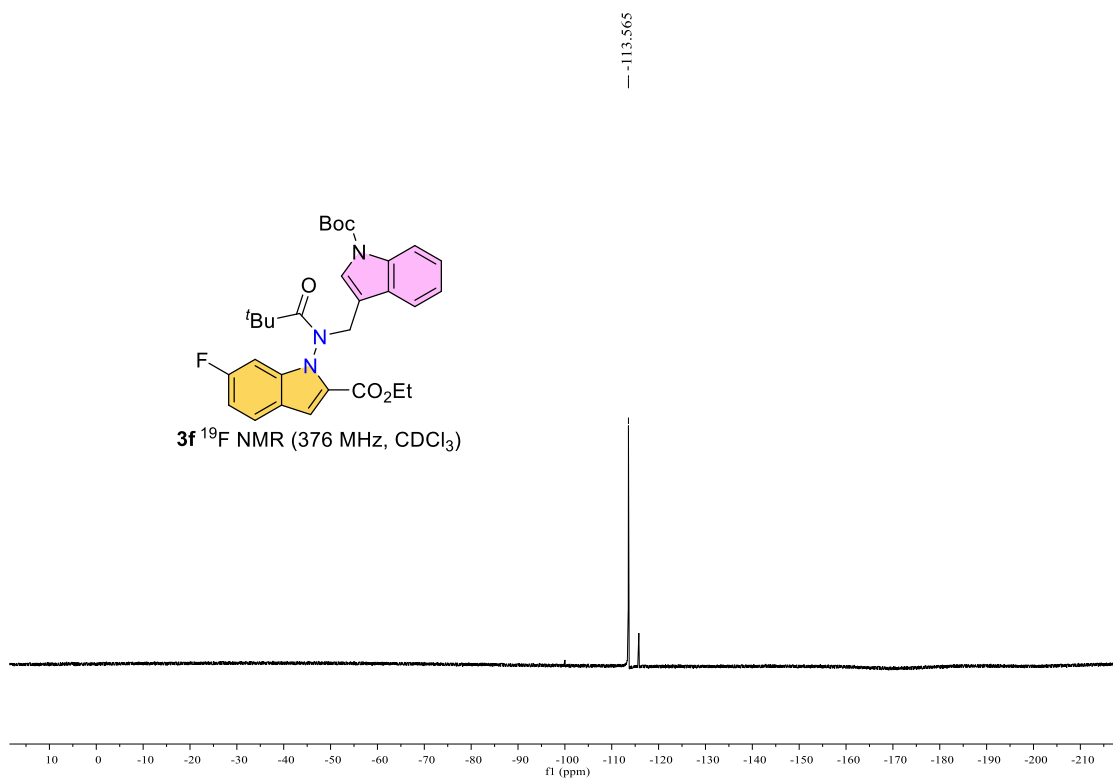
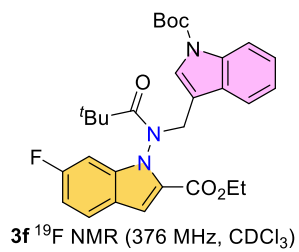


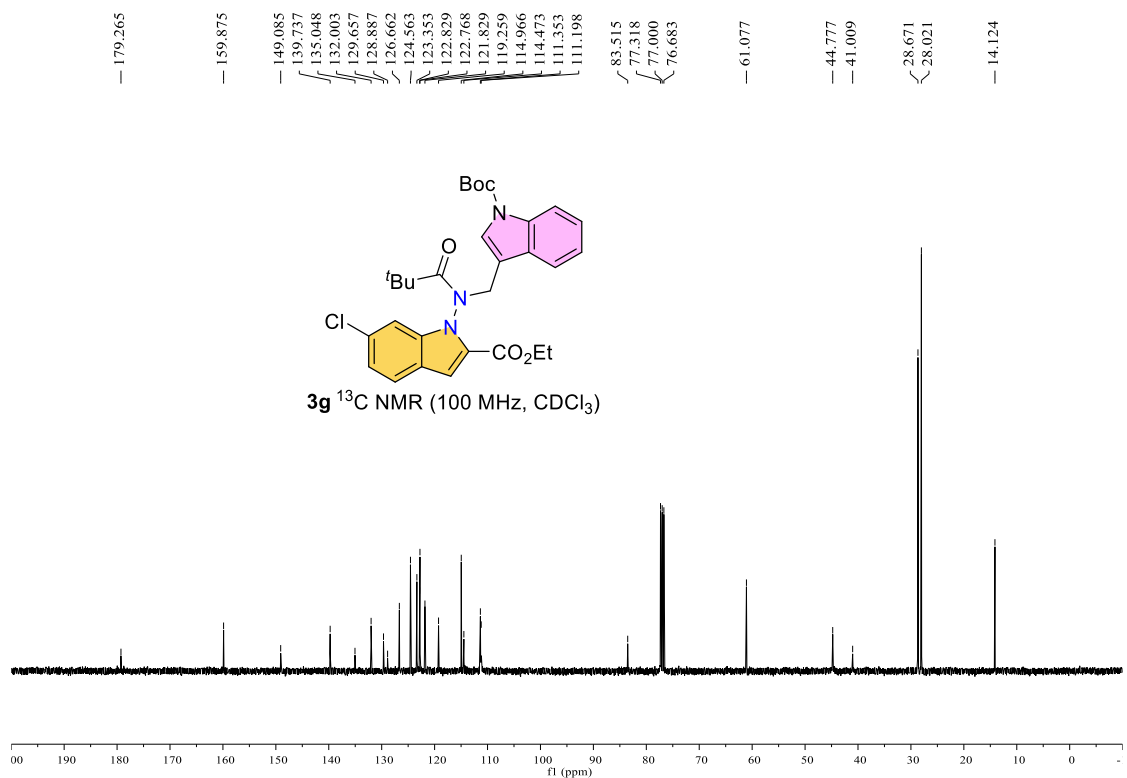
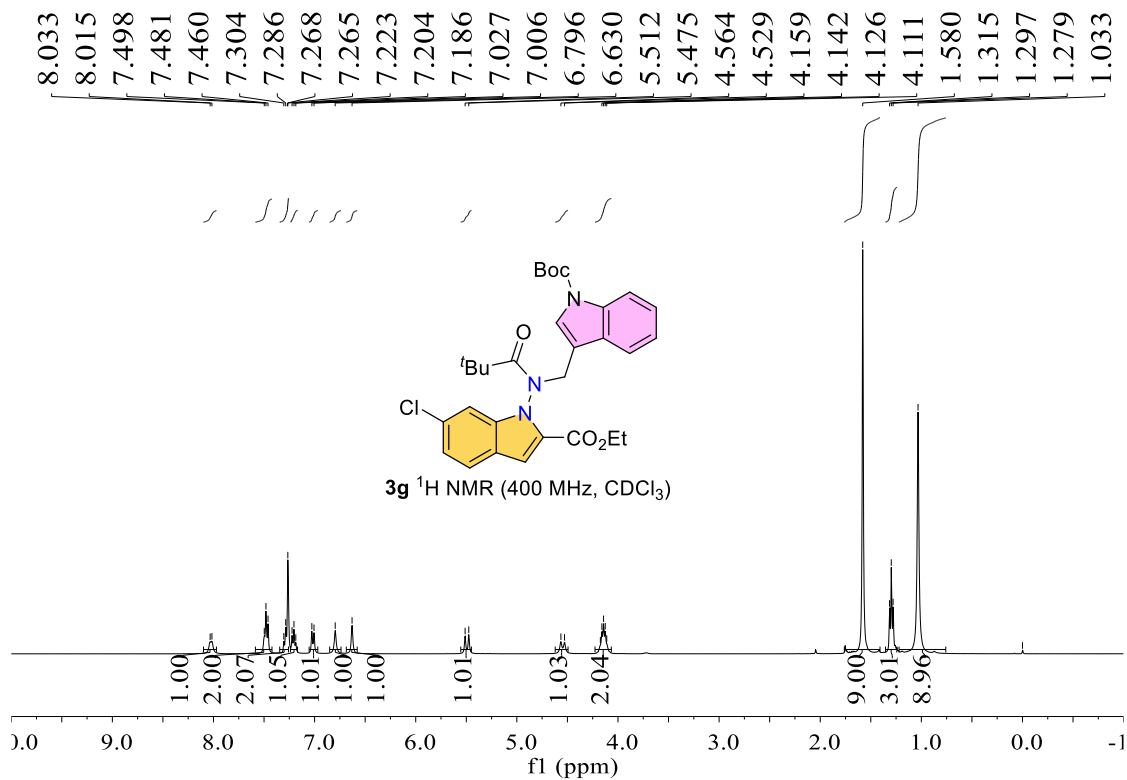


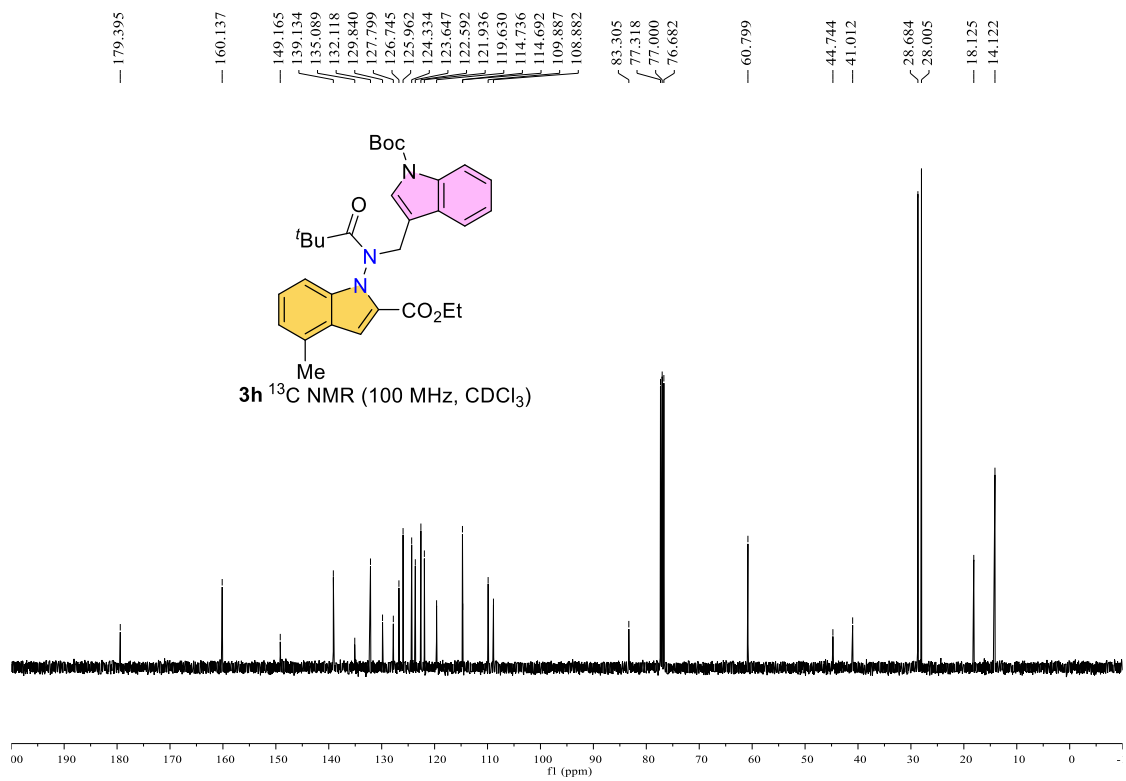
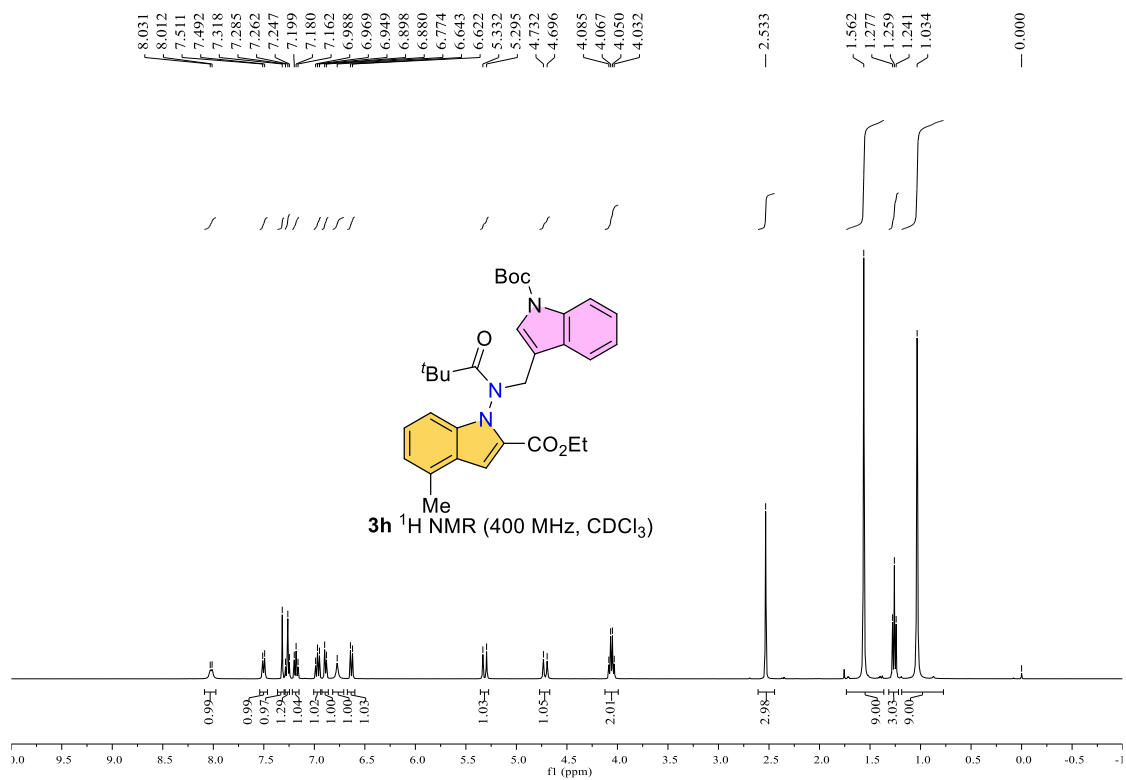




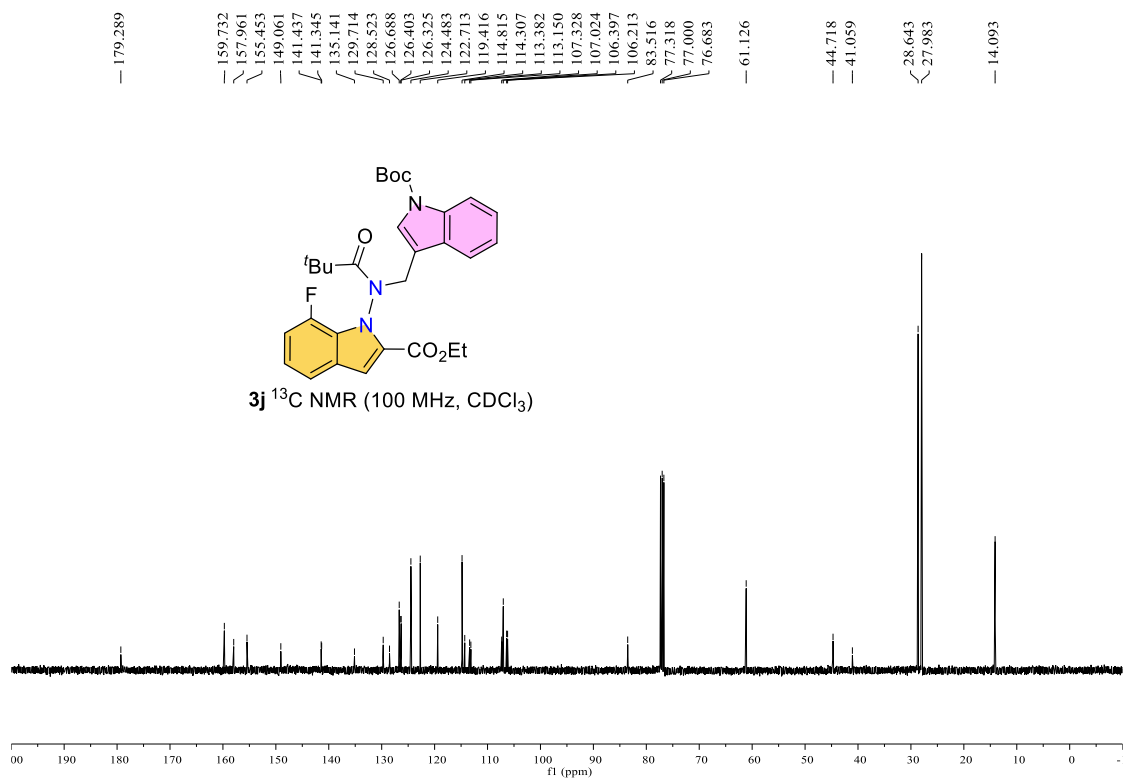
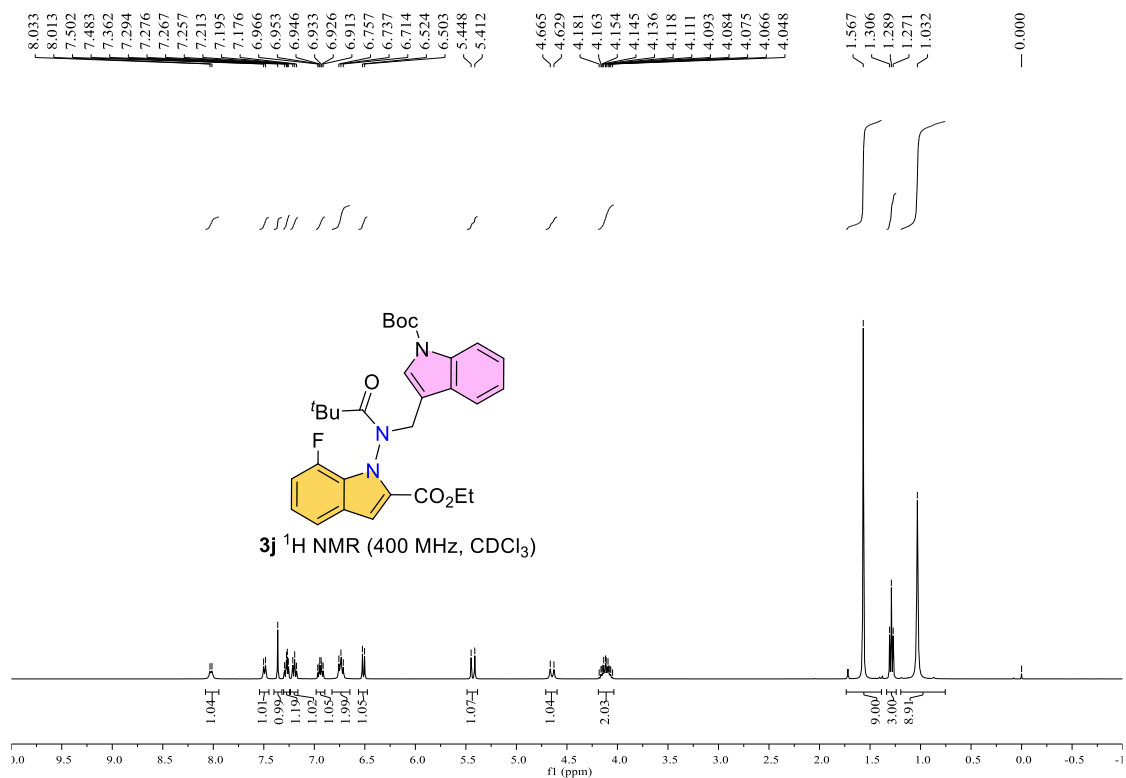


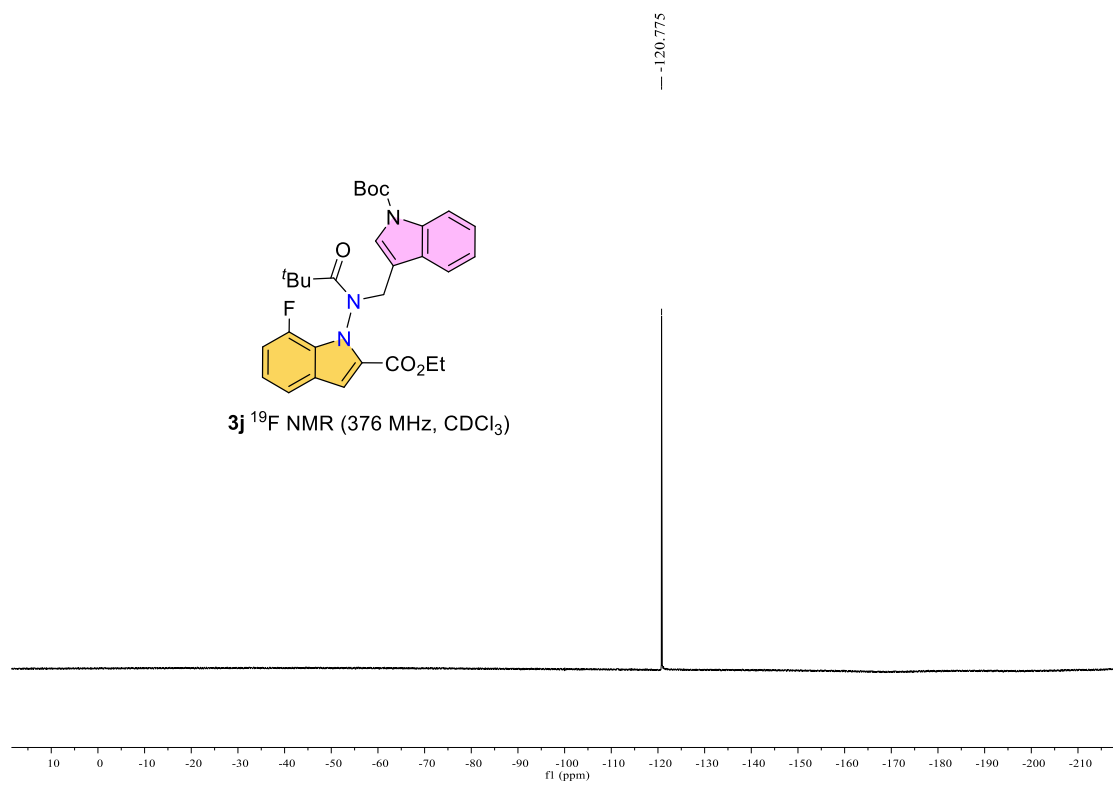


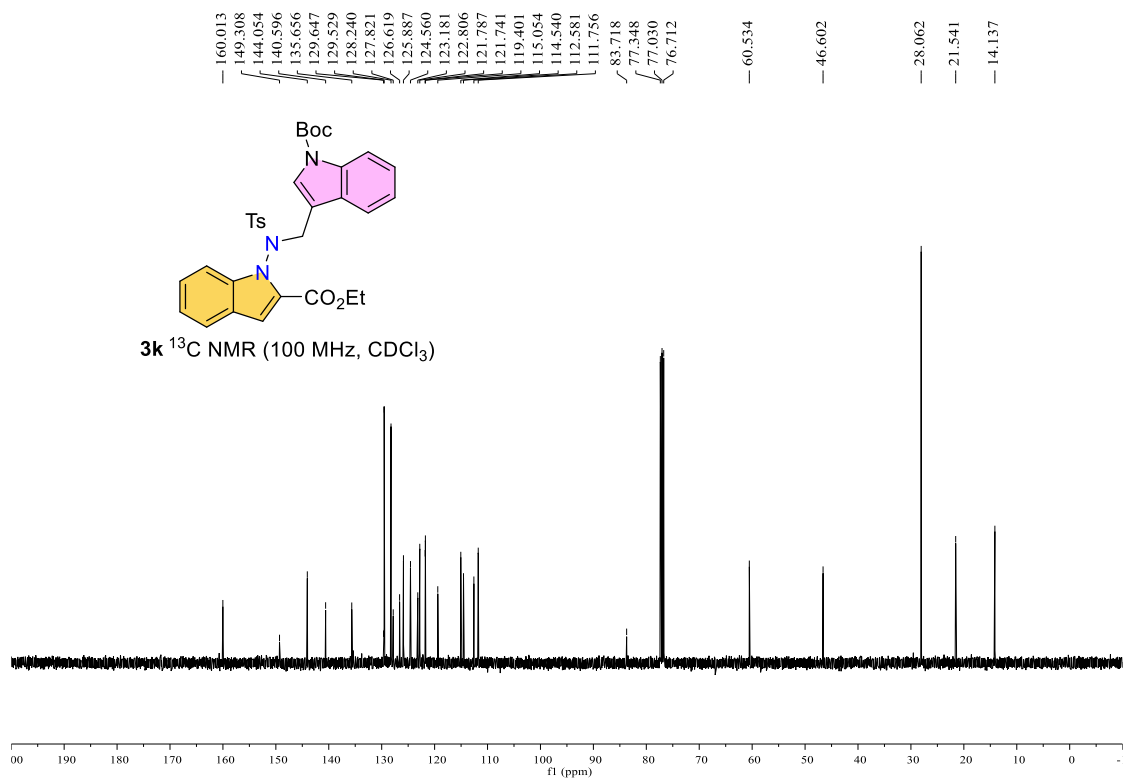
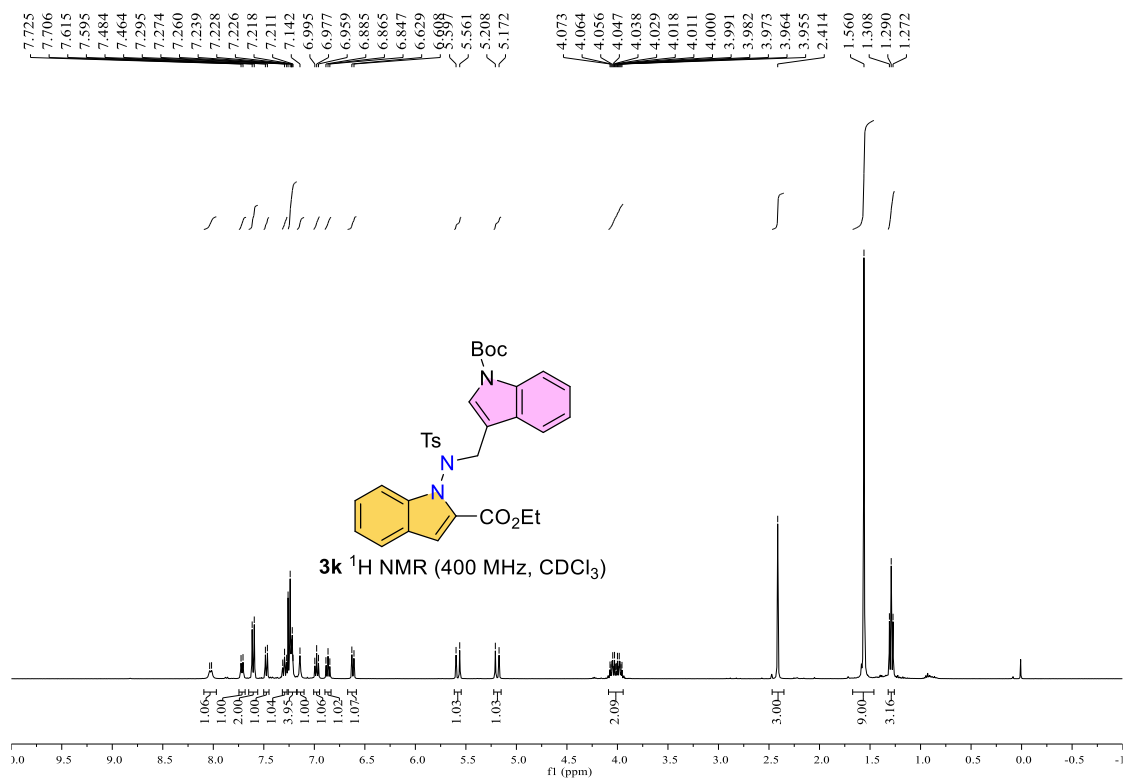


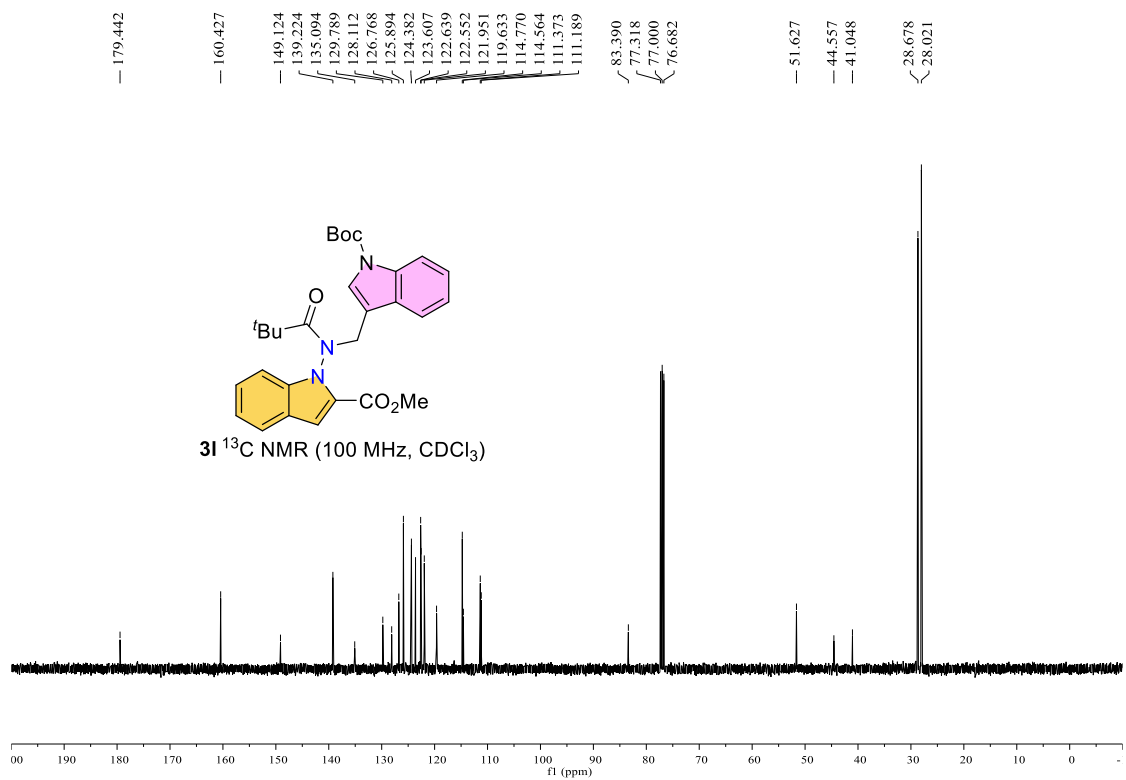
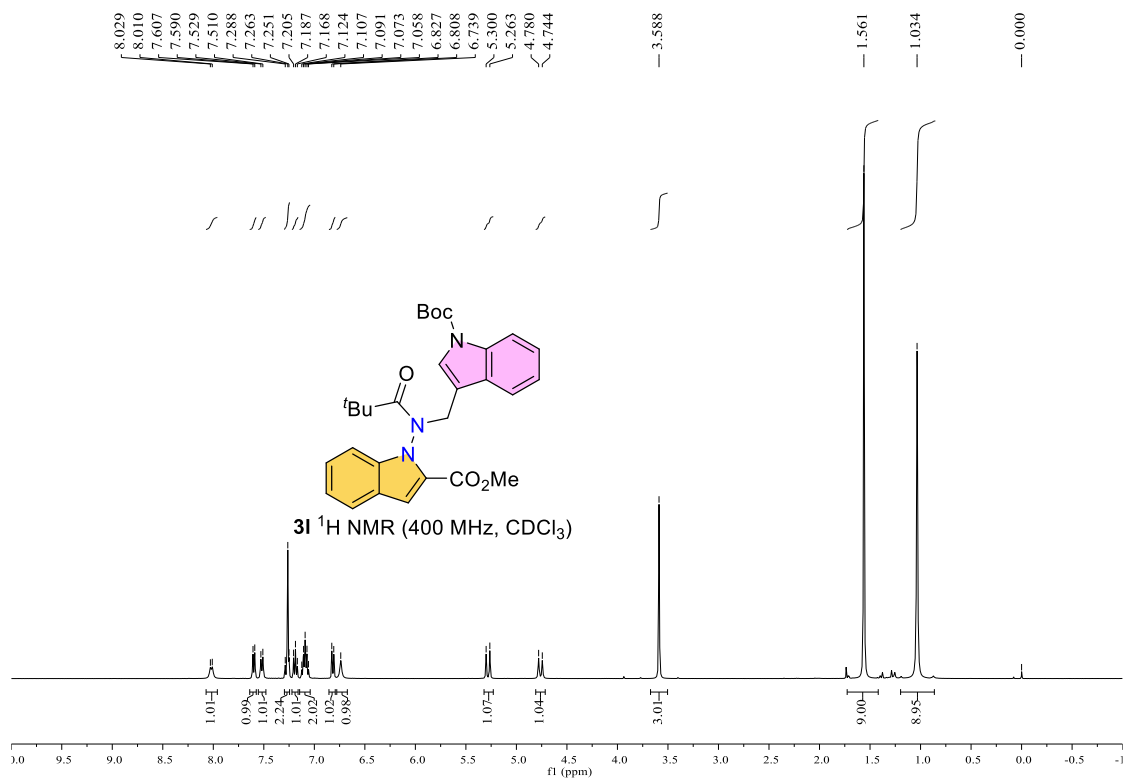


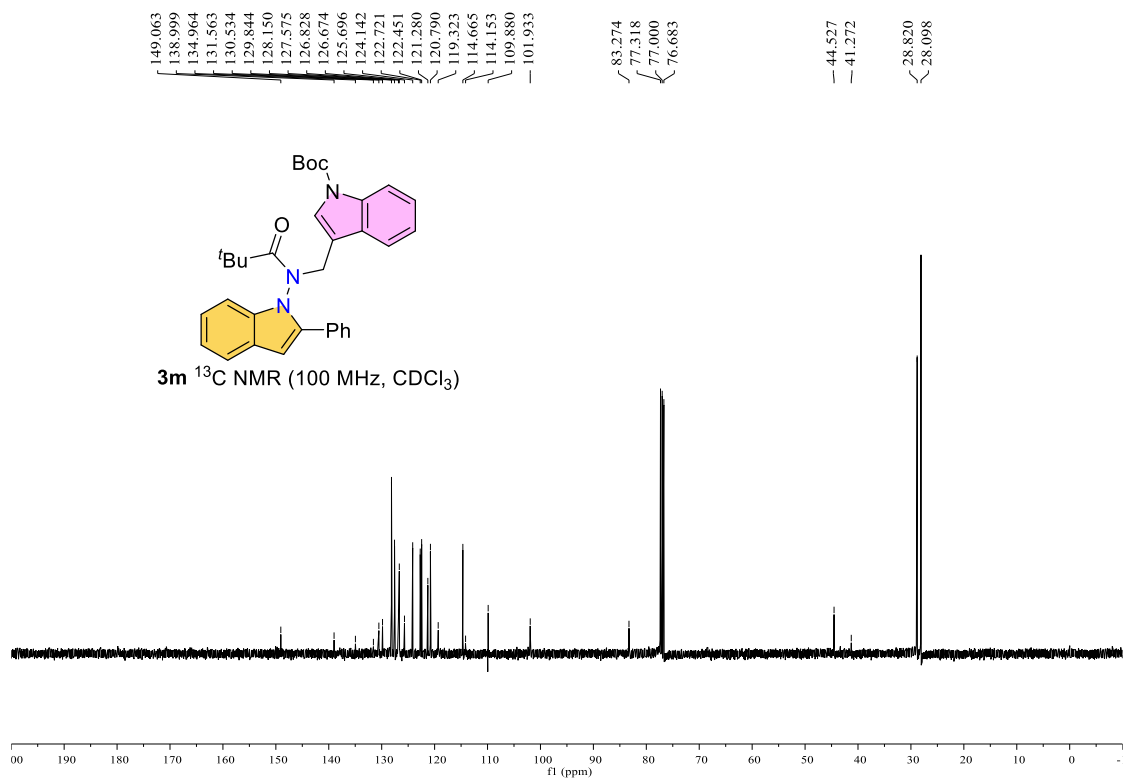
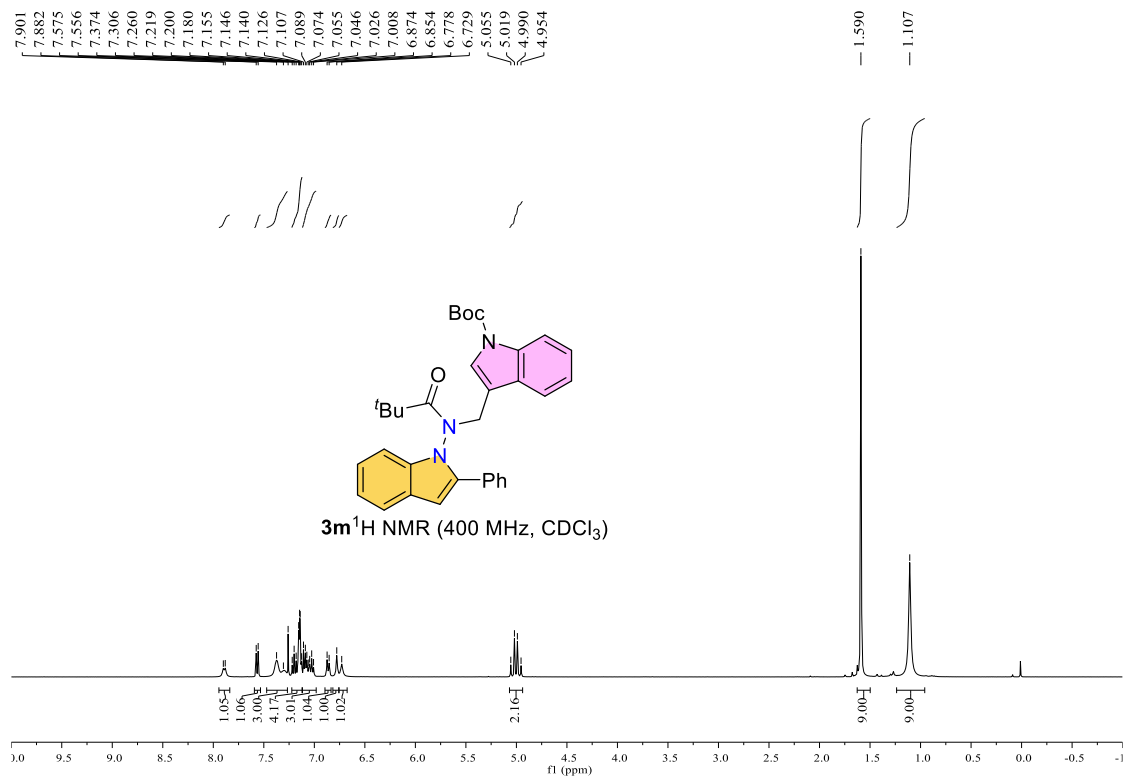


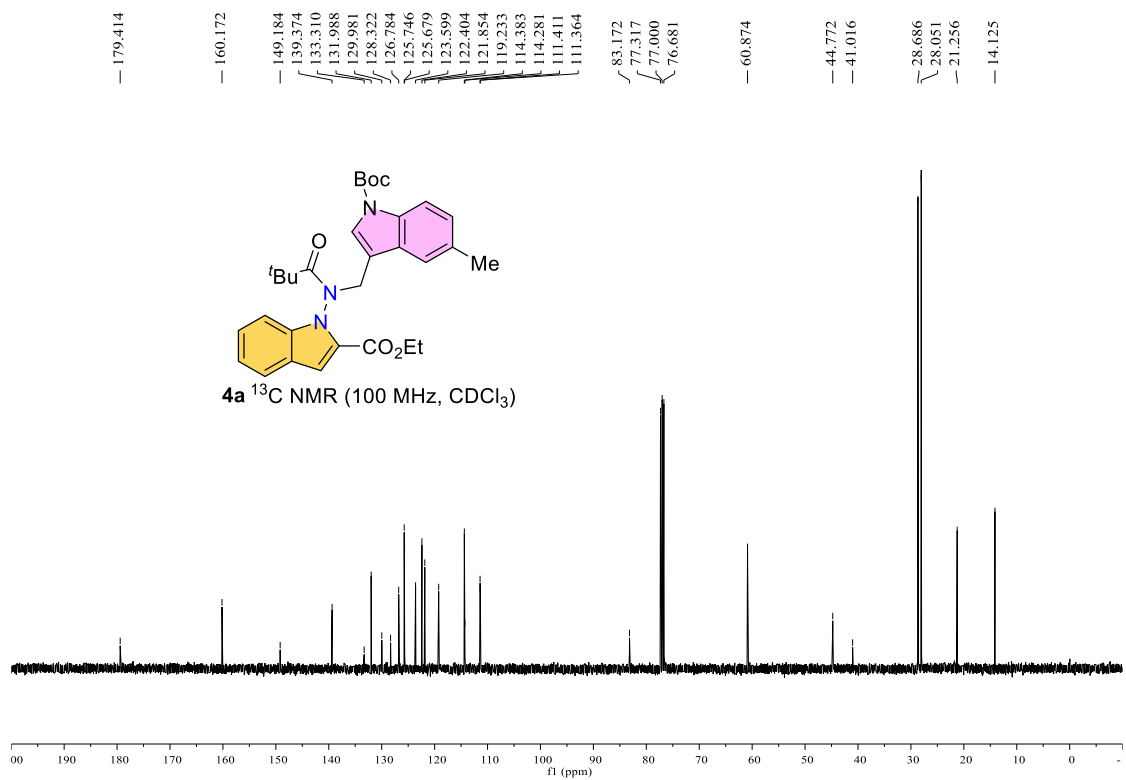
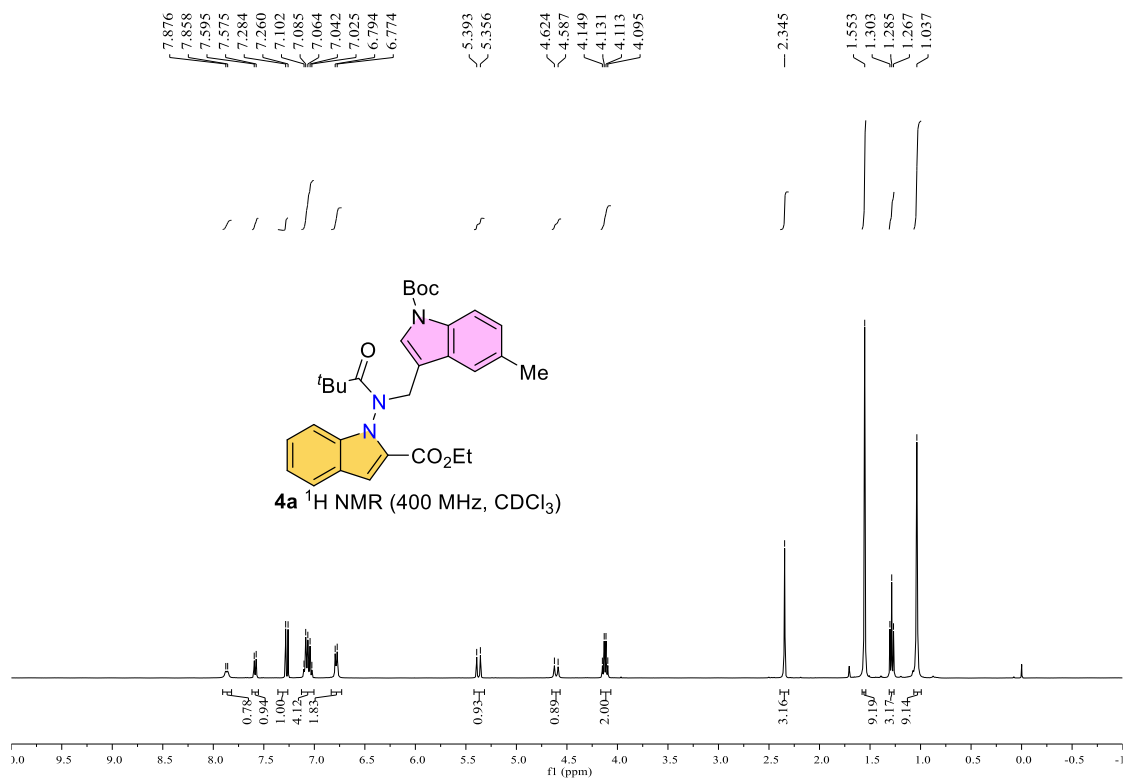


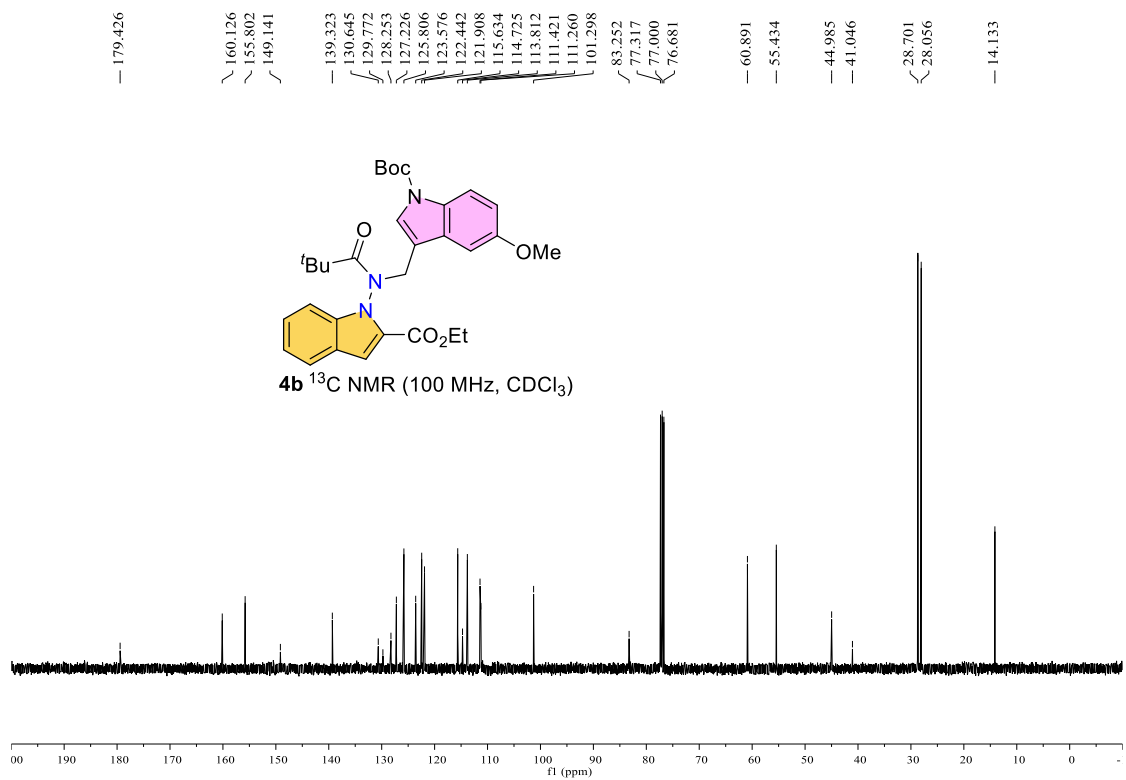
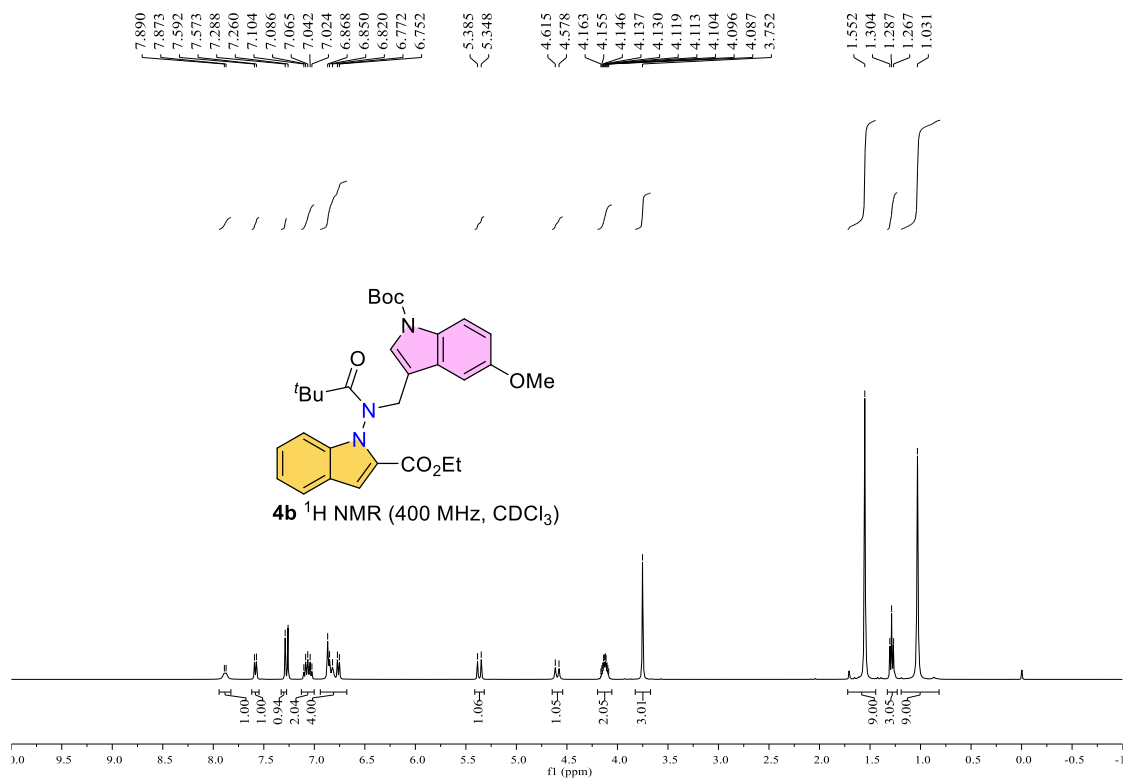


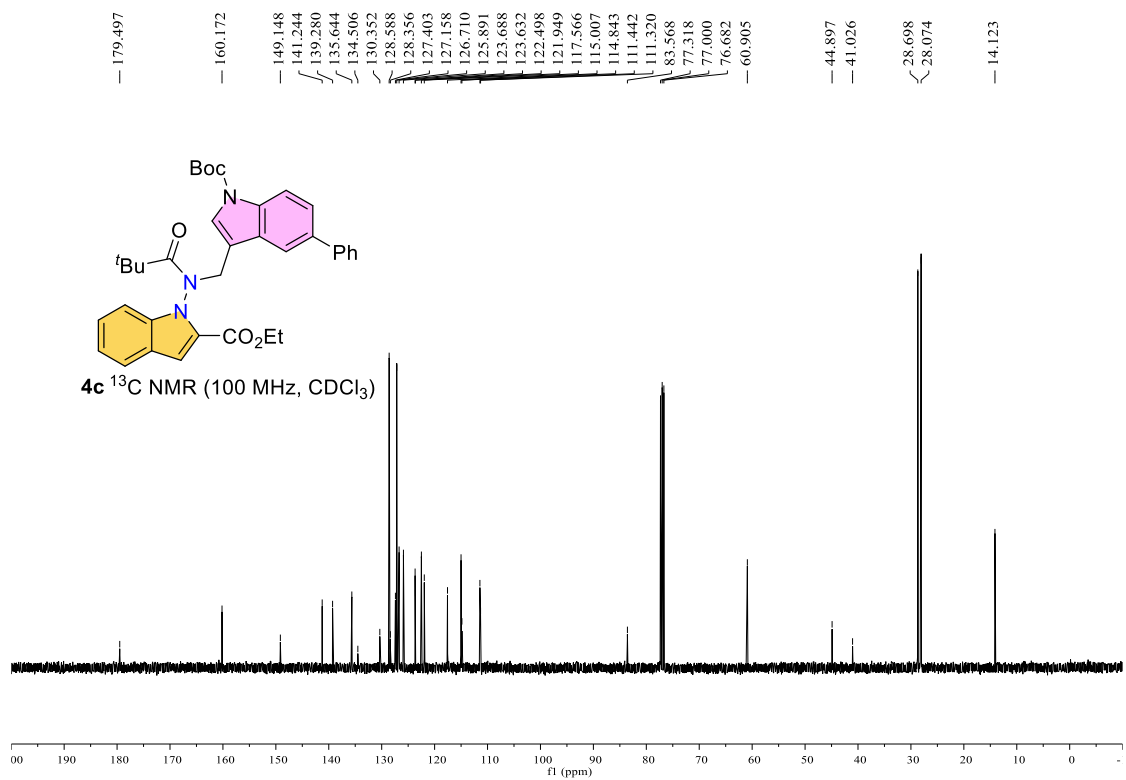
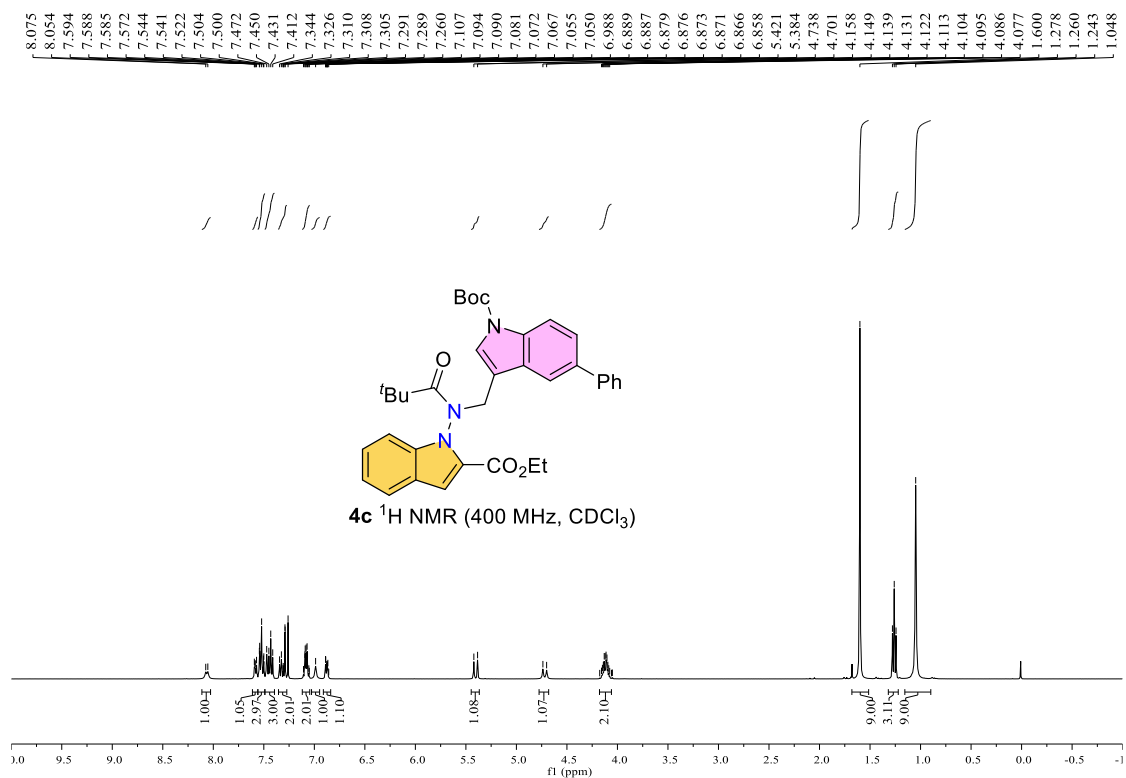


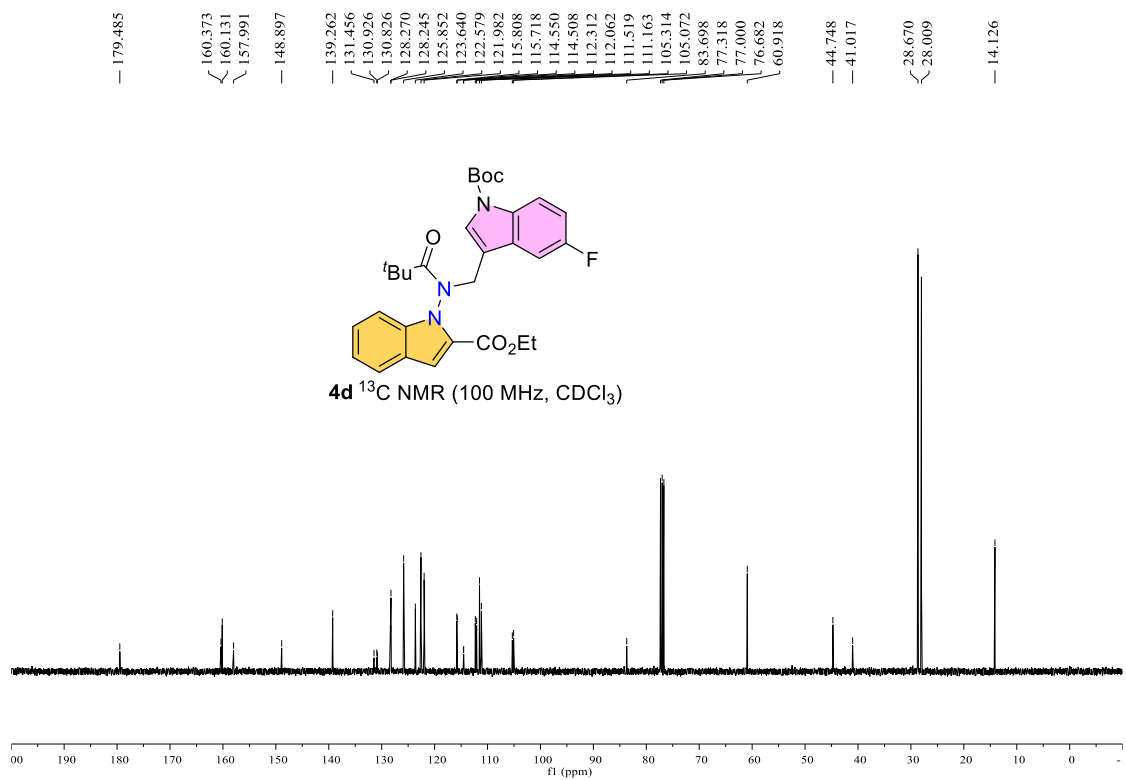
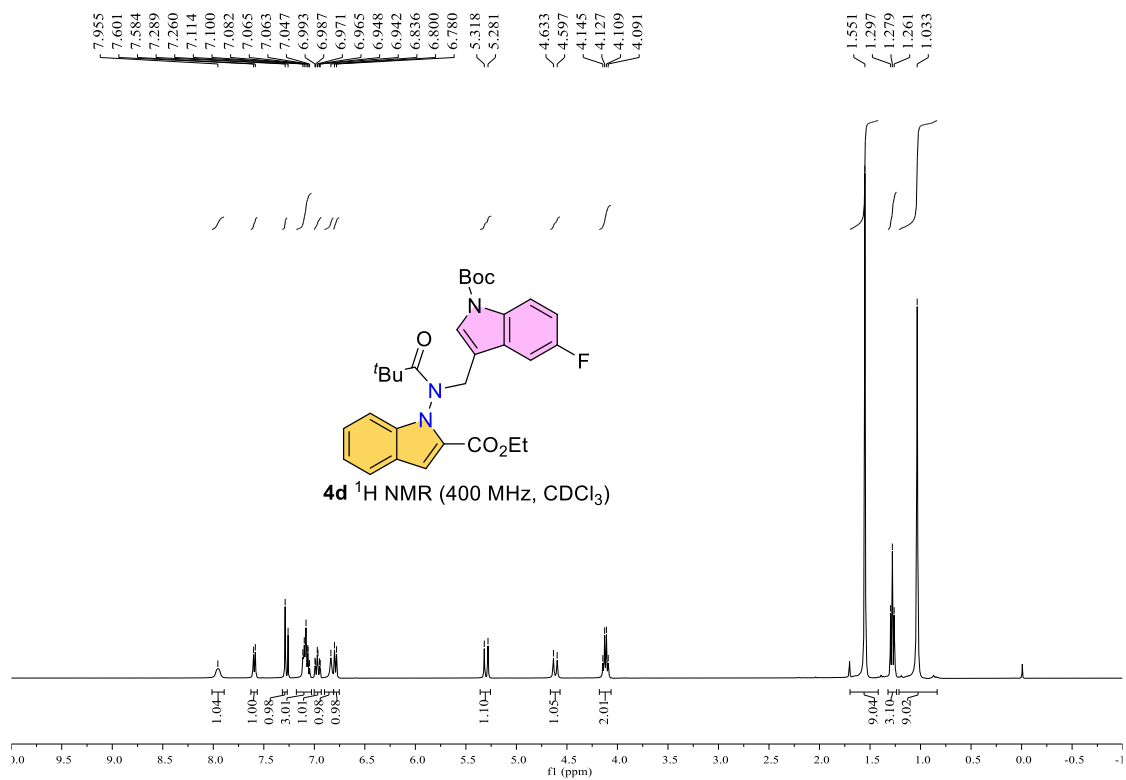


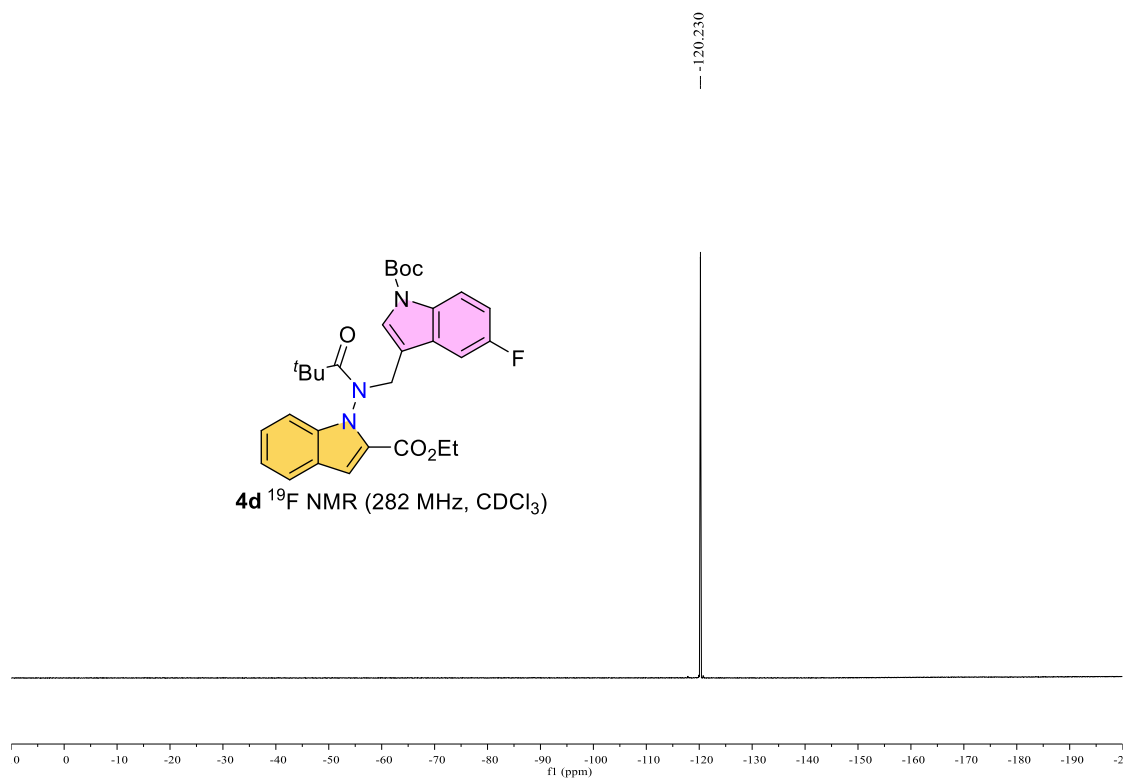


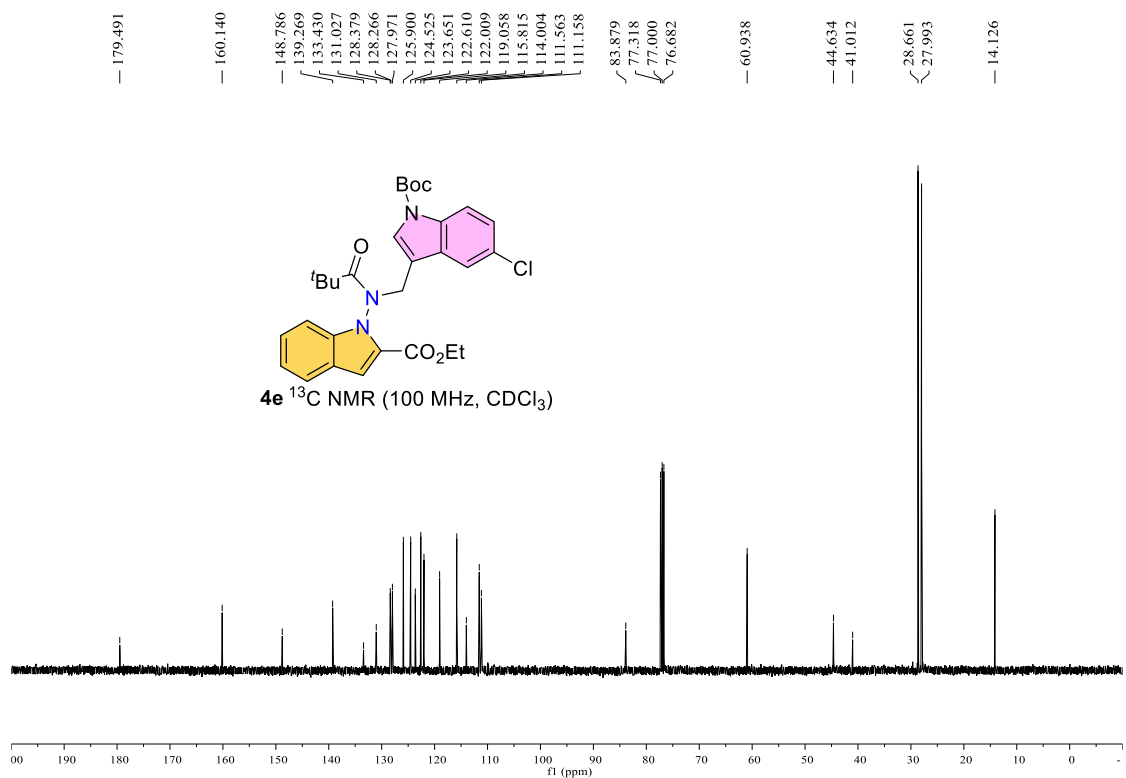
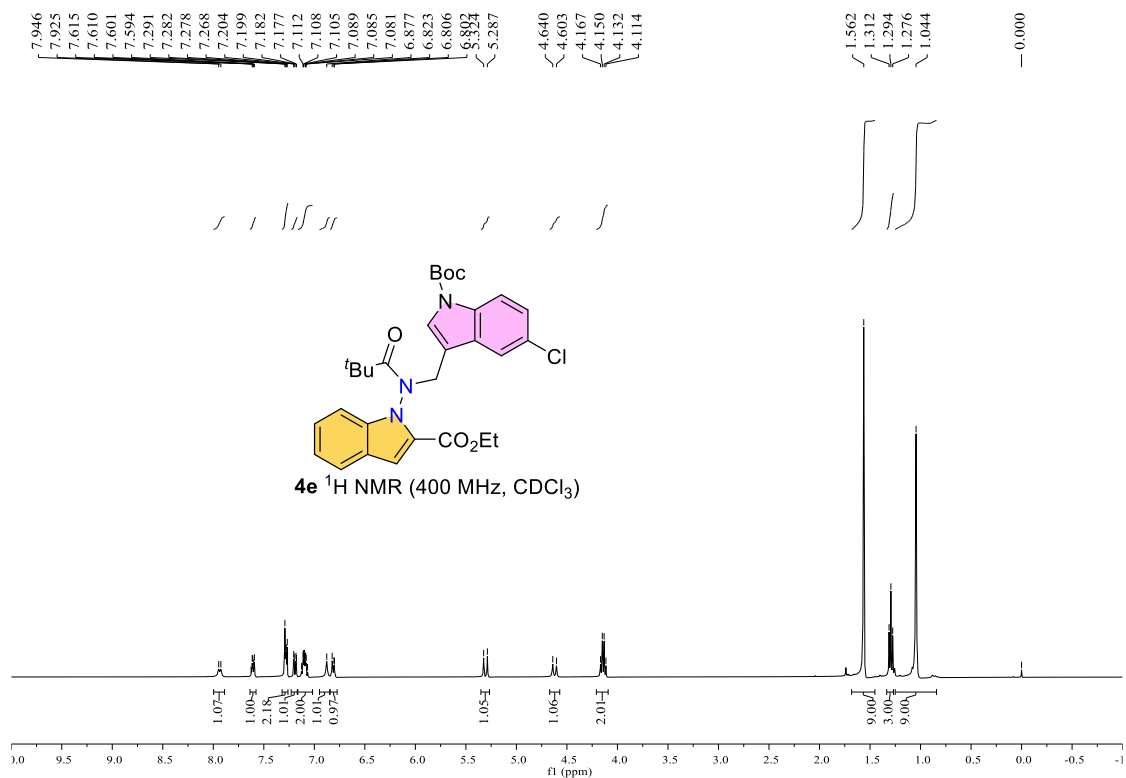




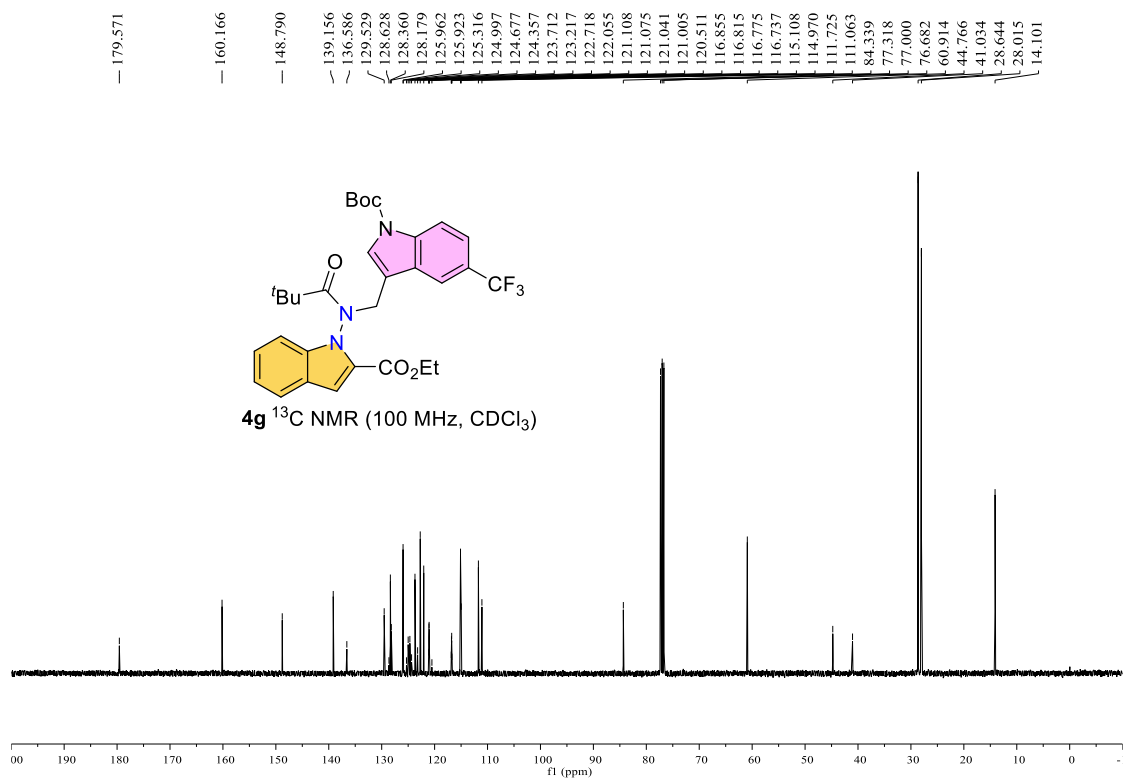
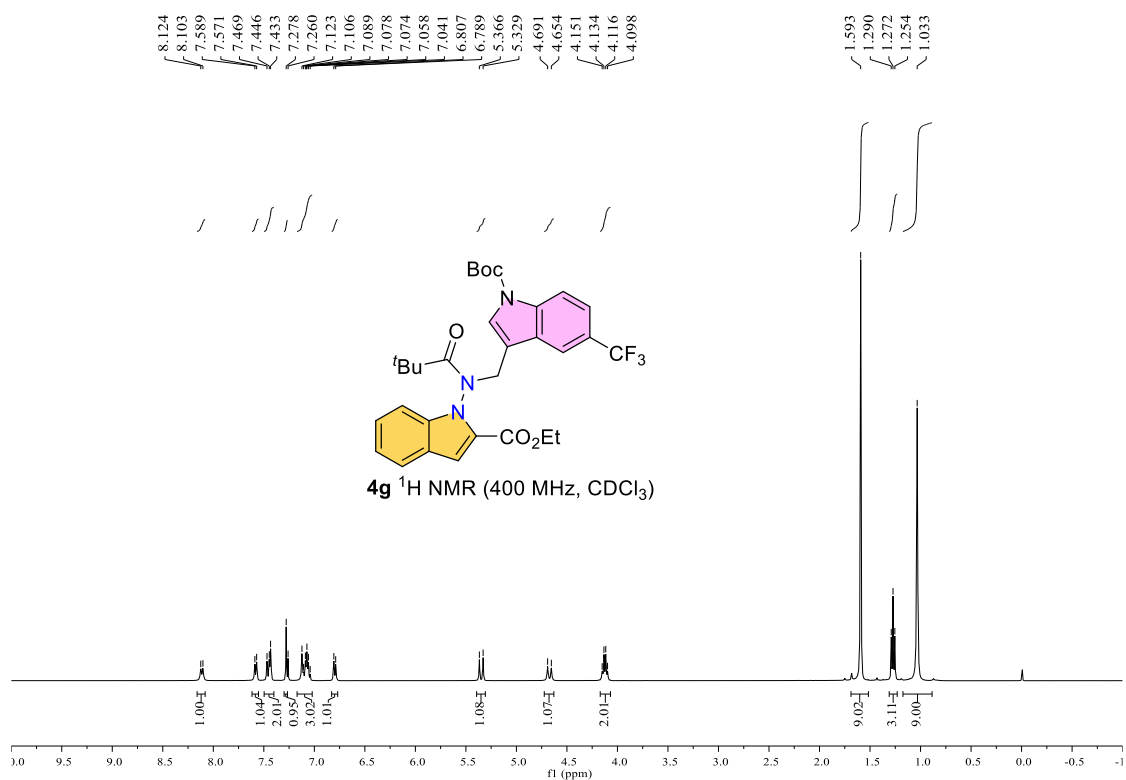




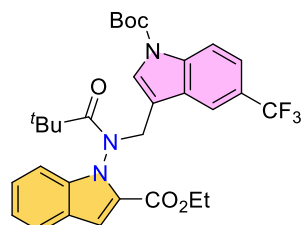








-61.046



**4g** <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>)

