

# Construction of Thioglycoside Bond via asymmetric organocatalyzed sulfa-Michael/Aldol reaction: Access to 4'-thionucleosides

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## Contents

1. General information .....	S2
2. The preparation of starting materials.....	S3
3. General procedure for the reaction .....	S4
4. Scale-up synthesis and transformation of products .....	S5
5. X-ray data of <b>3x</b> .....	S6
6. Characterization of compounds.....	S7
7. Copies of <sup>1</sup> H, <sup>13</sup> C NMR and <sup>19</sup> F NMR spectra .....	S51
8. Reference.....	S116

## 1. General information

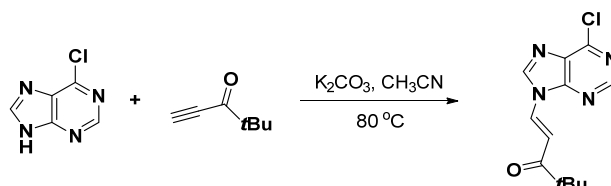
<sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on Bruker Avance III HD 600 or Avance 400 MHz spectrometer. Chemical shifts are recorded in ppm relative to tetramethylsilane with the solvent resonance as the internal standard. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet), coupling constants (J) are in Hertz (Hz), and integration. Enantiomer excesses were determined by chiral HPLC analysis on Chiralcel IA/AS-H/ID/OD-H/IE/IG in comparison with the authentic racemates. Chiral HPLC analysis was recorded on Thermo Scientific Dionex Ultimate 3000 and Agilent Technologies 1260 Infinity. Optical rotations were recorded on Autopol Automatic Polarimeter, and were reported as follows:  $[\alpha]_D^{25}$  (c: g/100 mL, in CH<sub>2</sub>Cl<sub>2</sub>). High resolution mass spectra (HRMS) was recorded on an ABI/Sciex QStar Mass Spectrometer (ESI). Single crystal X-ray crystallography data were obtained on Supernova Atlas S2 CCD detector. Melting point (m.p.) data were obtained on X-5 micro melting point apparatus. For column chromatography, silica gel (200-300 mesh) was used as the stationary phase. Unless stated otherwise, all the solvent and reagents were purchased from commercial suppliers and used without further purification.

## 2. The preparation of starting materials

### Synthesis of Variously (*E*)- $\beta$ -heteroaryl Propenyl Ketone (**1a-1aa**)<sup>1</sup>:

#### Method A:

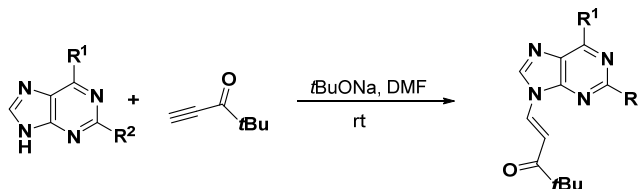
General Procedure for the Synthesis of **1a-1d**, **1j-1ad**:



Purine, benzimidazole, imidazoles, (2.0 mmol),  $K_2CO_3$  (1.0 mmol, 138 mg) and  $CH_3CN$  (8.0 mL) were mixed in a 15 mL flask. The mixture was stirred for 10 min at  $80\text{ }^\circ\text{C}$ , afterwards the acetylenic ketone (2.2 mmol) was added. After the reaction was completed, which was determined by TLC, the resulting mixture was filtered, and evaporated under reduced pressure. The mixture was directly purified by flash chromatography on silica gel (Pet/EtOAc = 7:1 - 3:1) to afford the products (*E*)- $\beta$ -heteroaryl acrylates.

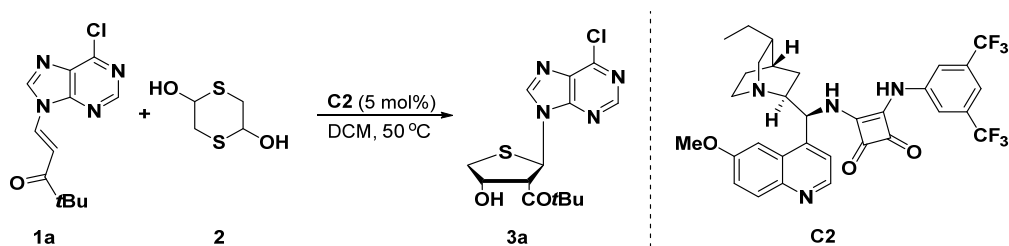
#### Method B:

General Procedure for the Synthesis of **1e-1i**:



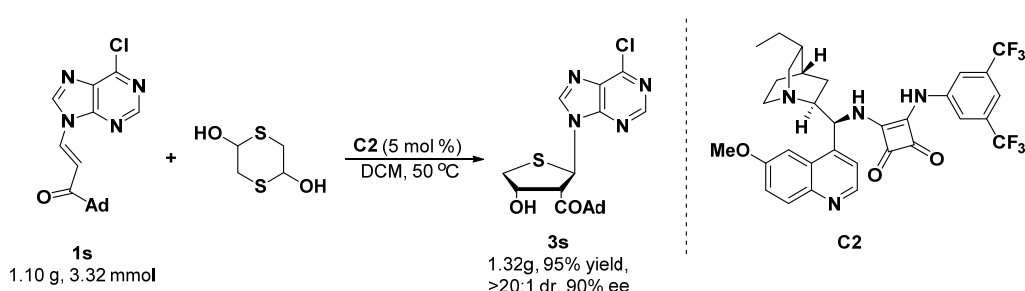
Purine, (2.0 mmol), sodium *tert*-butoxide (1.0 mmol) and  $DMF$  (5 mL) were mixed in a 15 mL flask. The mixture was stirred for 30 min at ambient temperature and then acetylenic ketone (2.2 mmol) was added. The reaction was complete after 6-12 h, as monitored by TLC, and the resulting mixture was partitioned between water and ethyl acetate, and the separated aqueous layer extracted with ethyl acetate (10 mL $\times$ 3). The combined organic layers were washed with brine (100 mL $\times$ 3), dried over anhydrous  $MgSO_4$ , filtered, and evaporated under reduced pressure. The mixture was directly purified by flash chromatography on silica gel (Pet/EtOAc = 7:1 - 1:1) to afford the products (*E*)- $\beta$ -heteroaryl acrylates.

### 3. General procedure for the reaction

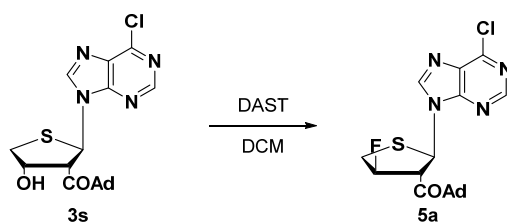


The synthetic procedure of **3a**: (*E*)-1-(6-chloro-9*H*-purin-9-yl)-4,4-dimethylpent-1-en-3-one **1a** (13.2 mg, 0.05 mmol), **2** (4.8 mg, 0.03 mmol), **C2** (1.58 mg, 5 mol %) in a reaction vessel. DCM (3.0 mL) was then added and the reaction mixture was stirred in oil bath at 50 °C for 48 h. Then the resulting mixture was cooled down to room temperature. The solvent was removed under reduced pressure. The residue was purified by column chromatography on a silica gel (eluent: Pet/EtOAc = 2:1-1:1) to give the pure product **3a**.

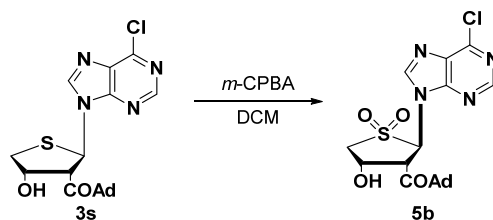
## 4. Scale-up synthesis and transformation of products



**Scale-up Synthesis:** To a round-bottom flask equipped with a stir bar was charged with (*E*)-1-(6-chloro-9*H*-purin-9-yl)-4,4-dimethylpent-1-en-3-one **1s** (1.10 g, 3.32 mmol), **2** (0.30 g, 1.99 mmol), **C2** (105 mg, 5 mol%) in a reaction vessel. DCM (100 mL) was then added and the reaction mixture was stirred in oil bath at 50 °C for 48 h. Then the resulting mixture was cooled down to room temperature. The solvent was removed under reduced pressure. The residue was purified by column chromatography on a silica gel (eluent: Pet/EtOAc = 2:1 - 1:1) to give the pure product **3s**.

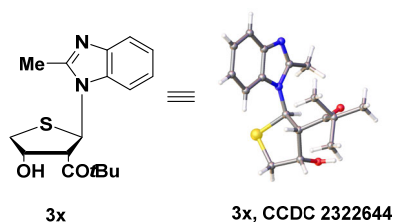


According to the literature,<sup>2</sup> In a test tube, **3s** (0.05 mmol, 20.9 mg, 90% ee) was dissolved in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL), DAST (2.3 equiv., 0.13 mmol, 21.0 mg) was added under N<sub>2</sub> atmosphere. The resulting solution was stirred at room temperature for 1.5 h. After the reaction was completed, which was determined by TLC, the mixture was directly purified by flash chromatography on silica gel was purified by silica gel flash chromatography (Pet/EtOAc = 1:2) to yield the product **5a** as a colorless oil (75% yield, 15.8 mg, 90% ee).



According to the literature,<sup>3</sup> In a test tube, **3s** (0.05 mmol, 20.9 mg, 90% ee) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL) and the reaction mixture was stirred at the room temperature. Then, *m*-CPBA (2.0 equiv, 0.1 mmol, 17.2 mg) was added. The reaction mixture was stirred overnight, After the reaction was completed, which was determined by TLC, the mixture was directly purified by flash chromatography on silica gel (Pet/EtOAc = 1:2) to afford product **5b** as a white solid (85% yield, 19.2 mg, 90% ee).

## 5. X-ray data of 3x

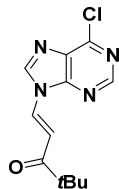


**Table S1 Crystal data and structure refinement for 3x.**

Identification code	<b>3x</b>
Empirical formula	C <sub>17</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub> S
Formula weight	318.42
Temperature/K	293(2)
Crystal system	monoclinic
Space group	P2 <sub>1</sub>
a/Å	10.90480(10)
b/Å	14.2184(2)
c/Å	11.99560(10)
α/°	90
β/°	110.3770(10)
γ/°	90
Volume/Å <sup>3</sup>	1743.51(3)
Z	4
ρ <sub>calc</sub> /cm <sup>3</sup>	1.213
μ/mm <sup>-1</sup>	1.713
F(000)	680.0
Crystal size/mm <sup>3</sup>	0.14 × 0.12 × 0.09
Radiation	Cu Kα (λ = 1.54184)
2θ range for data collection/°	7.862 to 142.782
Index ranges	-13 ≤ h ≤ 13, -16 ≤ k ≤ 17, -14 ≤ l ≤ 14
Reflections collected	44786
Independent reflections	6391 [R <sub>int</sub> = 0.0746, R <sub>sigma</sub> = 0.0345]
Data/restraints/parameters	6391/1/407
Goodness-of-fit on F <sup>2</sup>	1.137
Final R indexes [I ≥ 2σ(I)]	R <sub>1</sub> = 0.0732, wR <sub>2</sub> = 0.2000
Final R indexes [all data]	R <sub>1</sub> = 0.0768, wR <sub>2</sub> = 0.2085
Largest diff. peak/hole / e Å <sup>-3</sup>	0.26/-0.55
Flack/Hoof parameter	0.01(3)/0.01(6)

## 6. Characterization of compounds

### (*E*)-1-(6-chloro-9*H*-purin-9-yl)-4,4-dimethylpent-1-en-3-one (1a)



Pale-yellow solid, m.p. = 233.2-236.6 °C, 56% yield.

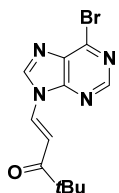
$R_f$  = 0.13 (Pet/EtOAc, 5/1, v/v).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.89 (s, 1H), 8.32 (s, 1H), 8.09 (d,  $J$  = 14.0 Hz, 1H), 7.92 (d,  $J$  = 14.0 Hz, 1H), 1.27 (s, 9H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  203.7, 153.3, 152.2, 151.6, 144.6, 133.1, 132.1, 114.1, 43.8, 26.2.

**HRMS** (ESI-TOF)  $m/z$ :  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{12}\text{H}_{14}\text{ClN}_4\text{O}$   $m/z$  265.0851, found 265.0845.

### (*E*)-1-(6-bromo-9*H*-purin-9-yl)-4,4-dimethylpent-1-en-3-one (1b)



Pale-yellow solid, m.p. 238.1-241.3 °C, 62% yield.

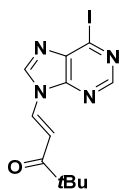
$R_f$  = 0.14 (Pet/EtOAc, 5/1, v/v).

$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.85 (s, 1H), 8.32 (s, 1H), 8.07 (d,  $J$  = 13.8 Hz, 1H), 7.92 (d,  $J$  = 13.8 Hz, 1H), 1.27 (s, 9H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  203.8, 153.2, 150.3, 144.5, 144.2, 135.7, 132.2, 114.1, 43.8, 26.2.

**HRMS** (ESI-TOF)  $m/z$ :  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{12}\text{H}_{14}\text{BrN}_4\text{O}$  309.0346, found 309.0342.

### (*E*)-1-(6-iodo-9*H*-purin-9-yl)-4,4-dimethylpent-1-en-3-one (1c)



Pale-yellow solid, m.p. 247.5-250.9 °C, 57% yield.

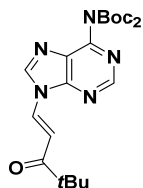
$R_f$  = 0.13 (Pet/EtOAc, 5/1, v/v).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.77 (s, 1H), 8.33 (s, 1H), 8.06 (d, *J* = 14.0 Hz, 1H), 7.92 (d, *J* = 14.0 Hz, 1H), 1.27 (s, 9H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 203.8, 153.2, 147.9, 144.0, 144.6, 132.3, 123.0, 114.1, 43.8, 26.2.

**HRMS** (ESI-TOF) *m/z*: [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O 357.0207, found 357.0200.

***tert*-butyl(*E*)-(tert-butoxycarbonyl)(9-(4,4-dimethyl-3-oxopent-1-en-1-yl)-9*H*-purin-6-yl)carbamate (1d)**



white solid, m.p. 37.6-46.4 °C, 39% yield.

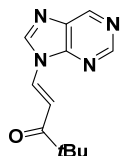
*R<sub>f</sub>* = 0.11 (Pet/EtOAc, 8/1, v/v).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.98 (s, 1H), 8.23 (s, 1H), 8.08 (d, *J* = 14.0 Hz, 1H), 7.93 (d, *J* = 14.0 Hz, 1H), 1.46 (s, 18H), 1.27 (s, 9H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 204.0, 153.4, 150.4, 144.0, 132.4, 113.4, 84.2, 43.8, 27.9, 26.3.

**HRMS** (ESI-TOF) *m/z*: [M+H]<sup>+</sup> calcd for C<sub>22</sub>H<sub>32</sub>N<sub>5</sub>O<sub>5</sub> 468.2217, found 468.2209.

**(*E*)-1-(6-methoxy-9*H*-purin-9-yl)-4,4-dimethylpent-1-en-3-one (1e)**



Pale-yellow solid, m.p. 178.5-182.8 °C, 49% yield.

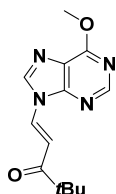
*R<sub>f</sub>* = 0.10 (Pet/EtOAc, 3/1, v/v).

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 9.22 (s, 1H), 9.13 (s, 1H), 8.27 (s, 1H), 8.10 (d, *J* = 13.8 Hz, 1H), 7.97 (d, *J* = 14.4 Hz, 1H), 1.28 (s, 9H).

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>) δ 204.1, 153.9, 151.3, 149.5, 144.8, 135.4, 132.4, 113.4, 43.8, 29.8, 26.3.

**HRMS** (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>15</sub>N<sub>4</sub>O 231.1240, found 231.1239.

**(*E*)-1-(6-methoxy-9*H*-purin-9-yl)-4,4-dimethylpent-1-en-3-one (1f)**





white solid, m.p. 196.7-201.2 °C, 65% yield.

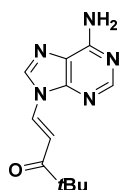
R<sub>f</sub> = 0.11 (Pet/EtOAc, 5/1, v/v).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.66 (s, 1H), 8.11 (s, 1H), 8.08 (d, *J* = 14.0 Hz, 1H), 7.88 (d, *J* = 14.0 Hz, 1H), 4.22 (s, 3H) 1.27 (s, 9H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 204.1, 161.5, 153.5, 151.9, 141.7, 132.8, 113.0, 54.6, 43.8, 26.3.

HRMS (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>17</sub>N<sub>4</sub>O<sub>2</sub> 261.1346, found 261.1340.

**(*E*)-1-(6-amino-9*H*-purin-9-yl)-4,4-dimethylpent-1-en-3-one (1g)**



Pale-yellow solid, m.p. 227.7-230.0 °C, 42% yield.

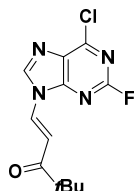
R<sub>f</sub> = 0.15 (EtOAc).

<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.72 (s, 1H), 8.28 (s, 1H), 8.11 (d, *J* = 14.0 Hz, 1H), 7.79 (d, *J* = 14.0 Hz, 1H), 7.51 (br, 1H), 1.18 (s, 9H).

<sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 203.3, 156.2, 153.8, 149.3, 140.0, 132.9, 119.3, 110.5, 43.0, 25.8.

HRMS (ESI-TOF): [M+Na]<sup>+</sup> calcd for C<sub>12</sub>H<sub>15</sub>N<sub>5</sub>NaO 268.1169 found 268.1168.

**(*E*)-1-(6-chloro-2-fluoro-9*H*-purin-9-yl)-4,4-dimethylpent-1-en-3-one (1h)**



Pale-yellow solid, m.p. 196.7-201.2 °C, 52% yield.

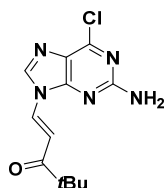
R<sub>f</sub> = 0.11 (Pet/EtOAc, 5/1, v/v).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.29 (s, 1H), 8.01 (d, *J* = 14.0 Hz, 1H), 7.76 (d, *J* = 14.0 Hz, 1H), 1.27 (s, 9H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 203.5, 159.0, 156.8, 154.1, 145.1 (d, *J*<sub>C-F</sub> = 4.0 Hz, 1H), 131.7, 125.8, 114.5, 113.8, 43.9, 26.4, 26.1.

HRMS (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>13</sub>ClFN<sub>4</sub>O 283.0756, found 283.0751.

**(E)-1-(2-amino-6-chloro-9H-purin-9-yl)-4,4-dimethylpent-1-en-3-one (1i)**



Pale-yellow solid, m.p. 234.1-237.0 °C, 52% yield.

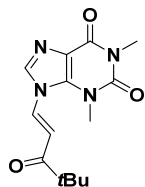
$R_f = 0.15$  (EtOAc).

$^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ )  $\delta$  8.70 (s, 1H), 7.99 (d,  $J = 14.0$  Hz, 1H), 7.69 (d,  $J = 14.4$  Hz, 1H), 7.27 (br, 1H), 1.18 (s, 9H).

$^{13}\text{C NMR}$  (100 MHz, DMSO- $d_6$ )  $\delta$  203.3, 160.4, 153.5, 150.0, 141.2, 132.1, 123.8, 110.7, 39.9, 25.7.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{12}\text{H}_{14}\text{ClN}_5\text{NaOS}$  302.0779 found 302.0775.

**(E)-9-(4,4-dimethyl-3-oxopent-1-en-1-yl)-1,3-dimethyl-3,9-dihydro-1H-purine-2,6-dione (1j)**



Pale-yellow solid, m.p. 216.1-219.0 °C, 53% yield.

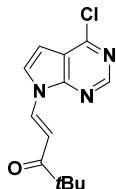
$R_f = 0.13$  (Pet/EtOAc, 2/1, v/v).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09 (d,  $J = 13.6$  Hz, 1H), 7.96 (s, 1H), 7.79 (d,  $J = 14.0$  Hz, 1H), 3.62 (s, 3H), 3.44 (s, 3H), 1.23 (s, 9H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  203.7, 154.7, 151.4, 150.8, 141.9, 133.8, 114.4, 43.8, 30.3, 28.8, 26.2.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{14}\text{H}_{18}\text{N}_4\text{NaO}_3$  313.1271 found 313.1269.

**(E)-1-(4-chloro-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-4,4-dimethylpent-1-en-3-one (1k)**



White solid, m.p. 162.8-166.3 °C, 70% yield.

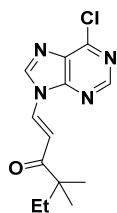
$R_f = 0.14$  (Pet/EtOAc, 6/1, v/v).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.73 (s, 1H), 8.32 (d,  $J = 14.0$  Hz, 1H), 7.51 (d,  $J = 4.0$  Hz, 1H), 7.31 (d,  $J = 14.0$  Hz, 1H), 6.75 (d,  $J = 4.0$  Hz, 1H), 1.23 (s, 9H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  203.8, 152.9, 152.3, 152.0, 134.6, 126.9, 119.5, 109.6, 103.7, 43.5, 26.4.

**HRMS** (ESI-TOF):  $[M+H]^+$  calcd for  $C_{13}H_{15}ClN_3O$  264.0898, found 264.0893.

**(E)-1-(6-chloro-9H-purin-9-yl)-4,4-dimethylhex-1-en-3-one (1l)**



white solid, m.p. 155.3-157.0 °C, 68% yield.

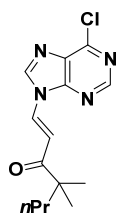
$R_f$  = 0.14 (Pet/EtOAc, 5/1, v/v).

**$^1H$  NMR** (600 MHz,  $CDCl_3$ )  $\delta$  8.90 (s, 1H), 8.33 (s, 1H), 8.09 (d,  $J$  = 13.8 Hz, 1H), 7.91 (d,  $J$  = 13.8 Hz, 1H), 1.70 (q,  $J$  = 7.8 Hz, 2H), 1.22 (s, 6H), 0.85 (t,  $J$  = 7.8 Hz, 3H).

**$^{13}C$  NMR** (150 MHz,  $CDCl_3$ )  $\delta$  203.7, 153.3, 152.1, 151.5, 144.7, 133.1, 132.1, 114.2, 47.6, 32.4, 23.6, 9.2.

**HRMS** (ESI-TOF):  $[M+H]^+$  calcd for  $C_{13}H_{16}ClN_4O$  279.1007, found 279.0999.

**(E)-1-(6-chloro-9H-purin-9-yl)-4,4-dimethylhept-1-en-3-one (1m)**



white solid; m.p. 130.3-135.5 °C; 69% yield.

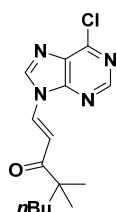
$R_f$  = 0.12 (Pet/EtOAc, 5/1, v/v).

**$^1H$  NMR** (600 MHz,  $CDCl_3$ )  $\delta$  8.90 (s, 1H), 8.32 (s, 1H), 8.08 (d,  $J$  = 13.8 Hz, 1H), 7.91 (d,  $J$  = 13.8 Hz, 1H), 1.60-1.63 (m, 2H), 1.24-1.26 (m, 2H), 1.23 (s, 6H), 0.91 (t,  $J$  = 7.2 Hz, 3H).

**$^{13}C$  NMR** (150 MHz,  $CDCl_3$ )  $\delta$  203.7, 153.3, 152.1, 151.5, 144.6, 133.1, 132.0, 114.2, 47.4, 42.2, 24.1, 18.2, 14.8.

**HRMS** (ESI-TOF):  $[M+H]^+$  calcd for  $C_{14}H_{18}ClN_4O$  293.1164, found 293.1159.

**(E)-1-(6-chloro-9H-purin-9-yl)-4,4-dimethyloct-1-en-3-one (1n)**



white solid, m.p. 130.3-135.5 °C, 75% yield.

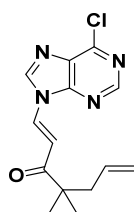
$R_f = 0.12$  (Pet/EtOAc, 5/1, v/v).

$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.89 (s, 1H), 8.35 (s, 1H), 8.10 (d,  $J = 13.8$  Hz, 1H), 7.92 (d,  $J = 13.8$  Hz, 1H), 1.62-1.65 (m, 2H), 1.26-1.31 (m, 2H), 1.22 (s, 6H), 1.16-1.20 (m, 2H), 0.86 (t,  $J = 7.2$  Hz, 3H).

$^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  203.8, 153.3, 152.1, 151.5, 144.7, 133.1, 132.1, 114.2, 47.3, 39.6, 27.1, 24.1, 23.4, 14.1.

**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{15}\text{H}_{20}\text{ClN}_4\text{O}$  307.1320, found 307.1320.

**(E)-1-(6-chloro-9H-purin-9-yl)-4,4-dimethylhepta-1,6-dien-3-one (1o)**



White solid, m.p. 110.9-114.5 °C, 71% yield.

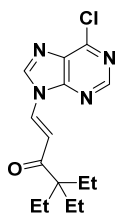
$R_f = 0.12$  (Pet/EtOAc, 5/1, v/v).

$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.89 (s, 1H), 8.35 (s, 1H), 8.09 (d,  $J = 13.8$  Hz, 1H), 7.94 (d,  $J = 13.8$  Hz, 1H), 5.67-5.74 (m, 1H), 5.05-5.09 (m, 2H), 2.39 (d,  $J = 7.2$  Hz, 2H), 1.24 (s, 6H).

$^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  203.0, 153.3, 152.2, 151.6, 144.7, 133.7, 133.1, 132.2, 118.6, 114.3, 47.2, 43.8, 23.9.

**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{14}\text{H}_{16}\text{ClN}_4\text{O}$  291.1007, found 291.1003.

**(E)-1-(6-chloro-9H-purin-9-yl)-4,4-diethylhex-1-en-3-one (1p)**



White solid, m.p. 185.5-188.1 °C, 62% yield.

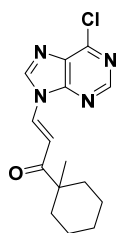
$R_f = 0.18$  (Pet/EtOAc, 5/1, v/v).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.90 (s, 1H), 8.33 (s, 1H), 8.10 (d,  $J = 13.6$  Hz, 1H), 7.94 (d,  $J = 14.0$  Hz, 1H), 1.70 (q,  $J = 7.6$  Hz, 6H), 0.78 (t,  $J = 7.6$  Hz, 9H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  203.9, 153.3, 152.1, 151.6, 144.7, 133.1, 131.9, 114.5, 54.5, 25.1, 8.3.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{15}\text{H}_{19}\text{ClN}_4\text{Na O}$  329.1140, found 329.1139.

**(E)-3-(6-chloro-9H-purin-9-yl)-1-(1-methylcyclohexyl)prop-2-en-1-one (1q)**



White solid, m.p. 172.2-176.7 °C, 86% yield.

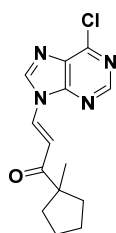
R<sub>f</sub> = 0.14 (Pet/EtOAc, 5/1, v/v).

<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 8.90 (s, 1H), 8.32 (s, 1H), 8.09 (d, *J* = 13.8 Hz, 1H), 7.92 (d, *J* = 13.8 Hz, 1H), 2.04-2.07 (m, 2H), 1.58-1.62 (m, 2H), 1.48-1.51 (m, 1H), 1.36-1.44 (m, 5H), 1.20 (s, 3H).

<sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 203.8, 153.3, 152.1, 151.5, 144.6, 133.1, 132.1, 114.3, 47.8, 34.6, 26.0, 23.0.

HRMS (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>15</sub>H<sub>18</sub>ClN<sub>4</sub>O 305.1164, found 305.1157.

**(E)-3-(6-chloro-9H-purin-9-yl)-1-(1-methylcyclopentyl)prop-2-en-1-one (1r)**



white solid, m.p. 182.1-182.9 °C, 81% yield.

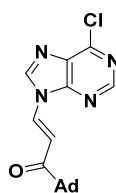
R<sub>f</sub> = 0.13 (Pet/EtOAc, 5/1, v/v).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.89 (s, 1H), 8.31 (s, 1H), 8.10 (d, *J* = 14.0 Hz, 1H), 7.82 (d, *J* = 14.0 Hz, 1H), 2.13-2.19 (m, 2H), 1.69-1.79 (m, 4H), 1.52-1.55 (m, 2H), 1.32 (s, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 202.9, 153.3, 152.2, 144.5, 133.1, 131.9, 115.2, 55.2, 36.5, 25.6, 24.5.

HRMS (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>16</sub>ClN<sub>4</sub>O 291.1007, found 291.0998.

**(E)-1-((3r,5r,7r)-adamantan-1-yl)-3-(6-chloro-9H-purin-9-yl)prop-2-en-1-one (1s)**



white solid, m.p. 280.8-283.0 °C, 75% yield.

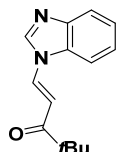
R<sub>f</sub> = 0.12 (Pet/EtOAc, 5/1, v/v).

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 8.92 (s, 1H), 8.31 (s, 1H), 8.07 (d, *J* = 13.8 Hz, 1H), 7.91 (d, *J* = 14.4 Hz, 1H), 2.11-2.15 (m, 3H), 1.87-1.95 (m, 6H), 1.73-1.83 (m, 6H).

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>) δ 203.3, 153.4, 144.6, 133.1, 132.1, 113.7, 46.1, 38.0, 36.6, 29.9, 29.9, 28.0.

**HRMS** (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>20</sub>ClN<sub>4</sub>O 343.1320, found 343.1313.

**(*E*)-1-(1*H*-benzo[d]imidazol-1-yl)-4,4-dimethylpent-1-en-3-one (1t)**



White solid, m.p. 151.9-155.6 °C, 76% yield.

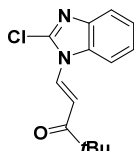
R<sub>f</sub> = 0.10 (Pet/EtOAc, 4/1, v/v).

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 8.24 (s, 1H), 8.15 (d, *J* = 13.8 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.38-7.45 (m, 2H), 6.97 (d, *J* = 13.8 Hz, 1H), 1.27 (s, 9H).

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>) δ 203.6, 144.7, 141.7, 134.6, 132.5, 125.1, 124.5, 121.4, 111.2, 108.2, 43.6, 26.5.

**HRMS** (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>17</sub>N<sub>2</sub>O 229.1335, found 229.3025.

**(*E*)-1-(2-chloro-1*H*-benzo[d]imidazol-1-yl)-4,4-dimethylpent-1-en-3-one (1u)**



White solid, m.p. 151.9-155.6 °C, 68% yield.

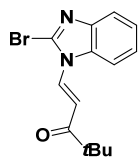
R<sub>f</sub> = 0.10 (Pet/EtOAc, 4/1, v/v).

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 8.17 (d, *J* = 14.4 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.34-7.42 (m, 2H), 7.09 (d, *J* = 13.8 Hz, 1H), 1.26 (s, 9H).

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>) δ 203.4, 142.4, 141.4, 134.1, 133.3, 125.0, 124.8, 120.5, 111.8, 111.0, 43.6, 26.4.

**HRMS** (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>16</sub>ClN<sub>2</sub>O 263.0946, found 263.0947.

**(E)-1-(2-bromo-1H-benzo[d]imidazol-1-yl)-4,4-dimethylpent-1-en-3-one (1v)**



White solid, m.p. 113.6-117.1 °C, 52% yield.

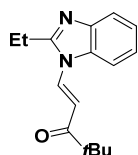
$R_f$  = 0.10 (Pet/EtOAc, 4/1, v/v).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19 (d,  $J$  = 14.0 Hz, 1H), 7.71-7.77 (m, 1H), 7.59-7.64 (m, 1H), 7.33-7.43 (m, 2H), 7.11 (d,  $J$  = 14.0 Hz, 1H), 1.27 (s, 9H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  203.4, 144.1, 135.5, 133.7, 131.1, 125.0, 124.7, 120.5, 111.8, 111.2, 43.6, 26.4.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{14}\text{H}_{16}\text{BrN}_2\text{NaO}$  329.0260 found 329.0252.

**(E)-1-(2-ethyl-1H-benzo[d]imidazol-1-yl)-4,4-dimethylpent-1-en-3-one (1w)**



White solid, m.p. 99.8-102.5 °C, 76% yield.

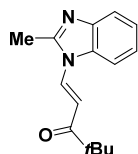
$R_f$  = 0.12 (Pet/EtOAc, 4/1, v/v).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.11 (d,  $J$  = 14.0 Hz, 1H), 7.72-7.78 (m, 1H), 7.56-7.63 (m, 1H), 7.29-7.38 (m, 2H), 7.00 (d,  $J$  = 14.0 Hz, 1H), 3.02 (q,  $J$  = 7.6 Hz, 2H), 1.48 (t,  $J$  = 7.6 Hz, 3H), 1.26 (s, 9H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  204.0, 157.3, 143.7, 135.0, 133.3, 124.1, 124.1, 120.3, 112.1, 109.2, 43.5, 26.5, 21.8, 11.6.

**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}$  243.1492 found 243.1484.

**(E)-4,4-dimethyl-1-(2-methyl-1H-benzo[d]imidazol-1-yl) pent-1-en-3-one (1x)**



White solid, m.p. 73.3-76.9 °C, 58% yield.

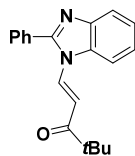
$R_f$  = 0.12 (Pet/EtOAc, 4/1, v/v).

$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24 (d,  $J$  = 13.8 Hz, 1H), 7.65-7.69 (m, 1H), 7.53-7.58 (m, 1H), 7.27-7.33 (m, 2H), 6.96 (d,  $J$  = 13.8 Hz, 1H), 2.68 (s, 3H), 1.24 (s, 9H).

$^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  203.8, 152.8, 143.6, 135.1, 133.1, 124.1, 124.0, 120.1, 111.9, 109.0, 43.4, 26.4, 14.9.

HRMS (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}$  257.1648 found 257.1650.

**(E)-4,4-dimethyl-1-(2-phenyl-1H-benzo[d]imidazol-1-yl)pent-1-en-3-one (1y)**



White solid, m.p. 157.8-161.8 °C, 66% yield.

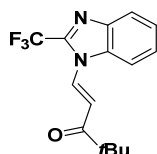
$R_f$  = 0.20 (Pet/EtOAc, 5/1, v/v).

$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (d,  $J$  = 13.8 Hz, 1H), 7.53-7.60 (m, 2H), 7.45-7.50 (m, 3H), 7.40 (s, 1H), 7.22 (s, 1H), 6.67 (d,  $J$  = 13.8 Hz, 1H), 1.19 (s, 9H).

$^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  203.5, 150.1, 136.4, 130.9, 129.9, 129.7, 129.2, 129.0, 116.6, 109.9, 43.5, 26.3.

HRMS (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}$  305.1648 found 305.1645.

**(E)-4,4-dimethyl-1-(2-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)pent-1-en-3-one (1z)**



White solid, m.p. 76.9-80.9 °C, 63% yield.

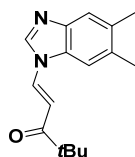
$R_f$  = 0.40 (Pet/EtOAc, 5/1, v/v).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15 (dq,  $J$  = 1.2, 14.0 Hz, 1H), 7.94 (d,  $J$  = 8.0 Hz, 1H), 7.69 (d,  $J$  = 8.4 Hz, 1H), 7.53-7.58 (m, 1H), 7.46-7.51 (m, 1H), 7.14 (d,  $J$  = 13.6 Hz, 1H), 1.27 (s, 9H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  202.9, 141.8, 133.8 (q,  $J_{\text{C-F}}$  = 12.0 Hz, 1H), 133.5 (q,  $J_{\text{C-F}}$  = 8.0 Hz, 1H), 127.2, 125.4, 122.7, 114.5, 112.7, 43.7, 27.1, 26.2.

HRMS (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{15}\text{H}_{16}\text{F}_3\text{N}_2\text{O}$  297.1209 found 297.1206.

**(E)-1-(5,6-dimethyl-1H-benzo[d]imidazol-1-yl)-4,4-dimethylpent-1-en-3-one (1aa)**



white solid, m.p. 174.2-177.9 °C, 54% yield.

$R_f$  = 0.10 (Pet/EtOAc, 3/1, v/v).

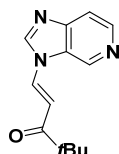


**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 8.12 (s, 1H), 8.10 (d, *J* = 14.4 Hz, 1H), 7.57 (s, 1H), 7.36 (s, 1H), 6.90 (d, *J* = 13.8 Hz, 1H), 2.42 (s, 3H), 2.37 (s, 3H), 1.26 (s, 9H).

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>) δ 203.7, 143.2, 141.0, 134.8, 134.3, 133.4, 130.9, 121.3, 111.5, 107.5, 43.5, 26.5, 20.9, 20.4.

**HRMS** (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>16</sub>H<sub>21</sub>N<sub>2</sub>O 257.1648 found 257.1652.

**(*E*)-1-(3*H*-imidazo[4,5-*c*]pyridin-3-yl)-4,4-dimethylpent-1-en-3-one (1ab)**



White solid, m.p. 203.0-207.1 °C, 62% yield.

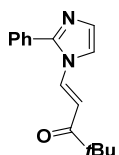
R<sub>f</sub> = 0.10 (Pet/EtOAc, 2/1, v/v).

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 9.18 (s, 1H), 8.61 (d, *J* = 5.4 Hz, 1H), 8.29 (s, 1H), 8.11 (d, *J* = 13.8 Hz, 1H), 7.57 (d, *J* = 5.4 Hz, 1H), 7.00 (d, *J* = 14.4 Hz, 1H), 1.27 (s, 9H).

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>) δ 203.1, 144.6, 144.2, 142.5, 141.4, 137.5, 133.6, 110.2, 106.5, 43.7, 26.4.

**HRMS** (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>16</sub>N<sub>3</sub>O 230.1288 found 230.1283.

**(*E*)-4,4-dimethyl-1-(2-phenyl-1*H*-imidazol-1-yl)pent-1-en-3-one (1ac)**



White solid, m.p. 85.1-88.3 °C, 71% yield.

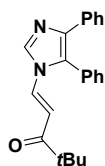
R<sub>f</sub> = 0.10 (Pet/EtOAc, 5/1, v/v).

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 7.97 (d, *J* = 13.8 Hz, 1H), 7.54-7.58 (m, 2H), 7.46-7.52 (m, 3H), 7.40 (s, 1H), 7.22 (s, 1H), 6.67 (d, *J* = 13.8 Hz, 1H), 1.19 (s, 9H).

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>) δ 203.5, 150.1, 136.4, 130.9, 129.9, 129.7, 129.2, 129.0, 116.6, 109.9, 43.5, 26.3.

**HRMS** (ESI-TOF): [M+H]<sup>+</sup> calcd for C<sub>16</sub>H<sub>19</sub>N<sub>2</sub>O 255.1492 found 255.1484.

**(*E*)-1-(4,5-diphenyl-1*H*-imidazol-1-yl)-4,4-dimethylpent-1-en-3-one (1ad)**



White solid, m.p. 222.6-225.4 °C, 65% yield.

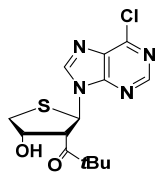
$R_f = 0.10$  (Pet/EtOAc, 5/1, v/v).

**$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (s, 1H), 7.62 (d,  $J = 14.4$  Hz, 1H), 7.46-7.52 (m, 5H), 7.32-7.39 (m, 2H), 7.16-7.25 (m, 3H), 6.54 (d,  $J = 14.0$  Hz, 1H), 1.12 (s, 9H).

**$^{13}\text{C NMR}$**  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  203.4, 135.4, 134.8, 131.2, 129.6, 129.6, 129.3, 128.4, 127.3, 127.1, 110.0, 43.4, 26.2.

**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}$  331.1805 found 331.1799.

**1-((2*R*, 3*S*, 4*S*)-2-(6-chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2, 2-dimethylpropan-1-one (3a)**



Pale yellow gum, 15.8 mg, 93% yield.

$R_f = 0.10$  (Pet/EtOAc, 2/1, v/v).

$[\alpha]_D^{22} = -85.1$  ( $c = 0.53$ ,  $\text{CH}_2\text{Cl}_2$ ).

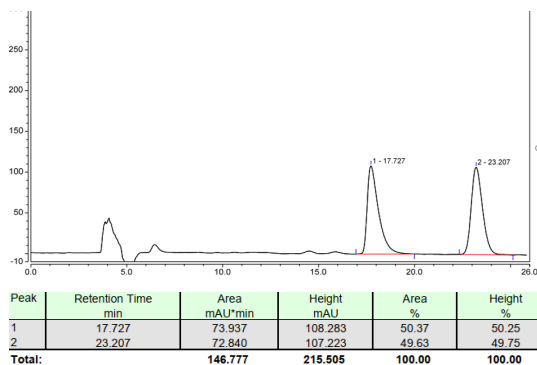
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 18.332 min (major), 25.393 min (minor), 91% ee, >20:1 dr.

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.77 (s, 1H), 8.23 (s, 1H), 6.66 (d,  $J = 8.4$  Hz, 1H), 4.94-4.98 (m, 1H), 4.64 (dd,  $J = 3.6, 8.0$  Hz, 1H), 3.98 (dd,  $J = 3.2, 11.6$  Hz, 1H), 3.27 (dd,  $J = 1.6, 11.6$  Hz, 1H), 0.93 (s, 9H).

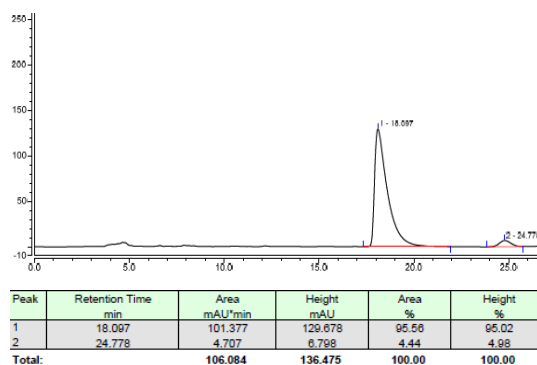
**$^{13}\text{C}$  NMR** (150 MHz,  $\text{CDCl}_3$ )  $\delta$  212.5, 152.1, 151.8, 151.2, 145.0, 132.9, 77.0, 64.8, 59.2, 45.1, 43.5, 25.6.

**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{14}\text{H}_{18}\text{ClN}_4\text{O}_2\text{S}$  341.0834 found 341.0833.

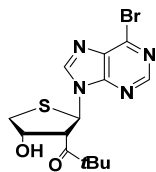
Racemic sample of **3a**



**3a**



**1-((2*R*, 3*S*, 4*S*)-2-(6-bromo-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (3b)**



Pale yellow solid, m.p. 129.2-134.6 °C, 18.5 mg, 96% yield.

$R_f = 0.12$  (Pet/EtOAc, 2/1, v/v).

$[\alpha]_D^{22} = -79.1$  ( $c = 0.92$ ,  $\text{CH}_2\text{Cl}_2$ ).

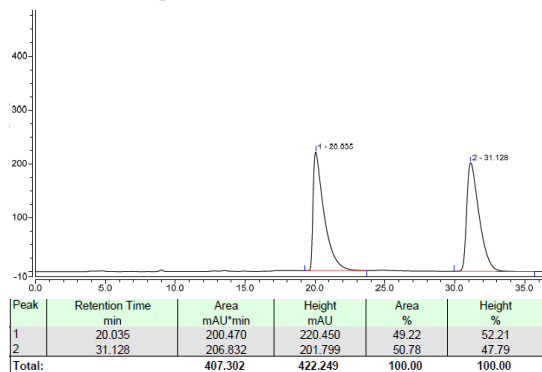
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 18.578 min (major), 31.713 min (minor), 90% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.73 (s, 1H), 8.23 (s, 1H), 6.64 (d,  $J = 8.4$  Hz, 1H), 4.96 (s, 1H), 4.63 (dd,  $J = 3.6, 8.4$  Hz, 1H), 3.98 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.27 (dd,  $J = 1.8, 12.0$  Hz, 1H), 3.01 (s, 1H), 0.94 (s, 9H).

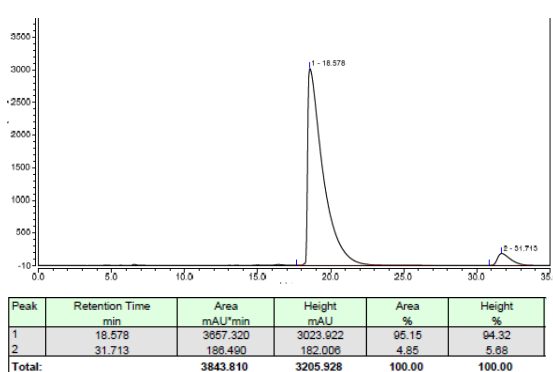
**$^{13}\text{C NMR}$**  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  212.6, 152.0, 149.9, 144.8, 144.0, 135.5, 77.0, 64.9, 59.2, 45.2, 43.6, 25.6.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{14}\text{H}_{17}\text{BrN}_4\text{NaO}_2\text{S}$  407.0148 found 407.0150.

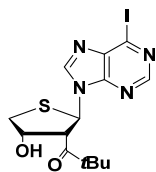
Racemic sample of **3b**



**3b**



**1-((2*R*, 3*S*, 4*S*)-4-hydroxy-2-(6-iodo-9*H*-purin-9-yl)tetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (3c)**



Colorless oil, 21 mg, 96% yield.

$R_f = 0.12$  (Pet/EtOAc, 2/1, v/v).

$[\alpha]_D^{22} = -67.8$  ( $c = 0.70$ ,  $\text{CH}_2\text{Cl}_2$ ).

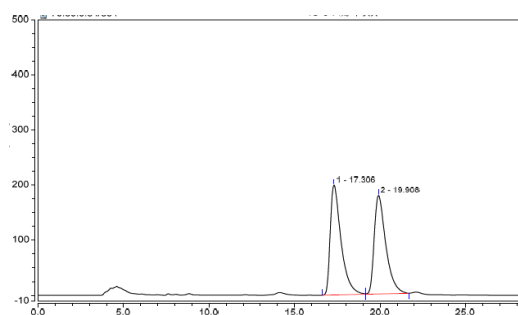
**HPLC** CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 17.593 min (minor), 19.765 min (major), 88% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.65 (s, 1H), 8.21 (s, 1H), 6.61 (d,  $J = 7.8$  Hz, 1H), 4.95 (s, 1H), 4.64 (dd,  $J = 4.2, 8.1$  Hz, 1H), 3.98 (dd,  $J = 3.0, 12.0$  Hz, 1H), 3.27 (dd,  $J = 1.8, 11.4$  Hz, 1H), 2.97 (d,  $J = 6.0$  Hz, 1H), 0.94 (s, 9H).

**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  212.7, 152.0, 147.4, 144.2, 139.8, 123.0, 77.1, 59.2, 45.2, 43.6, 25.6.

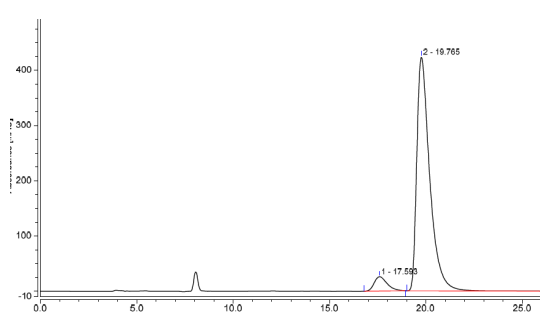
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{14}\text{H}_{17}\text{IN}_4\text{NaO}_2\text{S}$  455.0009 found 455.0006.

Racemic sample of **3c**



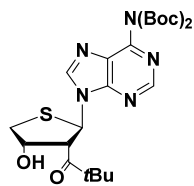
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	17.306	146.127	199.474	51.08	52.75
2	19.908	139.974	178.678	48.92	47.25
Total:		286.100	378.151	100.00	100.00

**3c**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	17.593	20.198	25.969	5.79	5.78
2	19.765	328.670	423.310	94.21	94.22
Total:		348.869	449.279	100.00	100.00

***tert*-butyl (*tert*-butoxycarbonyl)(9-((2*R*, 3*S*, 4*S*)-4-hydroxy-3-pivaloyltetrahydrothiophen-2-yl)-9*H*-purin-6-yl)carbamate (**3d**)**



White solid, m.p. 52.5-55.4 °C, 21.1 mg, 81% yield.

$R_f = 0.14$  (Pet/EtOAc, 2/1, v/v).

$[\alpha]_D^{22} = -68.2$  ( $c = 0.22$ ,  $\text{CH}_2\text{Cl}_2$ ).

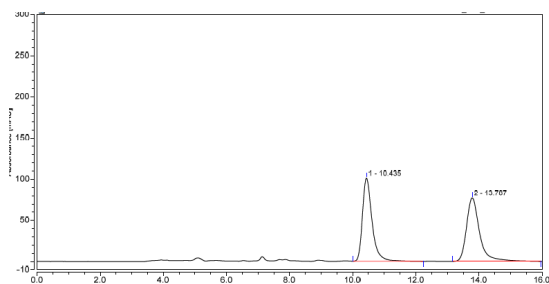
**HPLC** CHIRALCEL IF, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 10.440 min (major), 13.827 min (minor), 91% ee, >20:1 dr.

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.87 (s, 1H), 8.13 (s, 1H), 6.62 (d,  $J = 8.4$  Hz, 1H), 4.89-4.97 (m, 1H), 4.69 (dd,  $J = 3.6, 8.0$  Hz, 1H), 3.97 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.27 (dd,  $J = 1.6, 11.6$  Hz, 1H), 2.99 (d,  $J = 6.0$  Hz, 1H), 1.42 (s, 18H), 0.91 (s, 9H).

**$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  213.1, 152.7, 152.2, 151.0, 150.3, 144.3, 130.1, 84.0, 77.0, 64.7, 58.9, 45.2, 43.5, 27.9, 25.5.

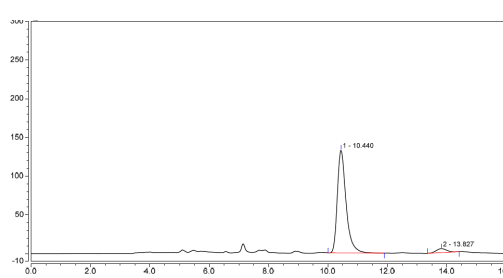
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{24}\text{H}_{35}\text{N}_5\text{NaO}_6\text{S}$  544.2200 found 544.2200.

**Racemic sample of **3d****



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.435	35.670	101.193	49.07	56.70
2	13.787	37.021	77.268	50.93	43.30
Total:		72.690	178.461	100.00	100.00

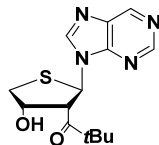
****3d****



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.440	45.407	132.856	95.70	96.29
2	13.827	2.042	5.117	4.30	3.71
Total:		47.448	137.974	100.00	100.00

1-((2*R*, 3*S*, 4*S*)-4-Hydroxy-2-(9*H*-purin-9-yl)tetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one

(3e)



Colorless oil, 21.1 mg, 84% yield.

$R_f = 0.10$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -54.0$  ( $c = 0.67$ ,  $\text{CH}_2\text{Cl}_2$ ).

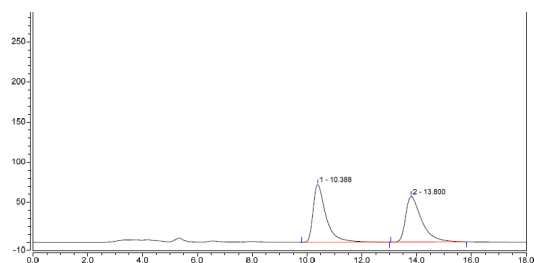
**HPLC** CHIRALCEL IA, n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min,  $\lambda = 256$  nm, retention time: 10.348 min (major), 14.007 min (minor), 87% ee, >20:1 dr.

**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  9.15 (s, 1H), 9.01 (s, 1H), 8.16 (s, 1H), 6.65 (d,  $J = 7.8$  Hz, 1H), 4.92-4.96 (m, 1H), 4.71 (dd,  $J = 3.6, 7.8$  Hz, 1H), 4.00 (dd,  $J = 3.0, 12.0$  Hz, 1H), 3.28 (dd,  $J = 1.2, 11.4$  Hz, 1H), 2.97 (br, 1H), 0.91 (s, 9H).

**$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  213.0, 152.7, 150.9, 149.4, 145.0, 135.3, 77.0, 64.5, 58.9, 45.2, 43.5, 25.6.

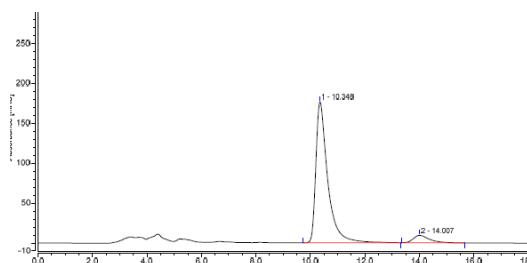
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{14}\text{H}_{18}\text{N}_4\text{NaO}_2\text{S}$  329.1043 found 329.1037.

Racemic sample of 3e



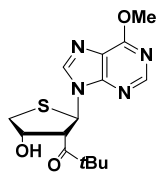
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.388	39.251	72.001	50.65	55.97
2	13.800	38.247	56.647	49.35	44.03
Total:		77.498	128.648	100.00	100.00

3e



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.348	98.949	177.212	93.39	95.05
2	14.007	6.207	2.228	6.61	4.95
Total:		95.246	186.440	100.00	100.00

**1-((2*R*, 3*S*, 4*S*)-4-Hydroxy-2-(6-methoxy-9*H*-purin-9-yl)tetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (3f)**



Colorless oil, 15.3 mg, 91% yield.

$R_f = 0.12$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -51.2$  ( $c = 1.43$ ,  $\text{CH}_2\text{Cl}_2$ ).

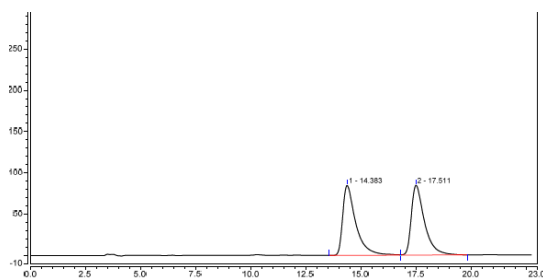
**HPLC** CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 13.910 min (major), 17.356 min (minor), 80% ee, >20:1 dr.

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.56 (s, 1H), 7.97 (s, 1H), 6.57 (d,  $J = 8.0$  Hz, 1H), 4.86-4.93 (m, 1H), 4.70 (dd,  $J = 3.6, 8.4$  Hz, 1H), 4.18 (s, 3H), 3.98 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.26 (dd,  $J = 1.2, 11.4$  Hz, 1H), 3.07 (br, 1H), 0.91 (s, 9H).

**$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  213.5, 161.4, 152.4, 151.4, 141.9, 122.9, 77.1, 64.7, 58.7, 54.4, 45.2, 43.5, 25.4.

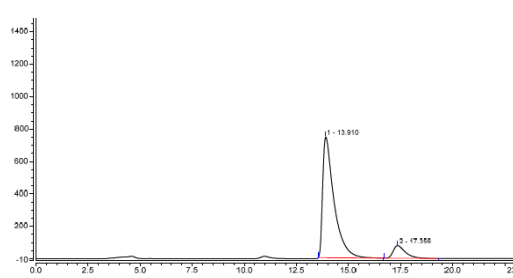
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{15}\text{H}_{20}\text{N}_4\text{NaO}_3\text{S}$  359.1148 found 359.1150.

Racemic sample of **3f**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.383	58.531	84.640	50.04	50.04
2	17.511	58.443	84.494	49.96	49.96
Total:		116.974	169.134	100.00	100.00

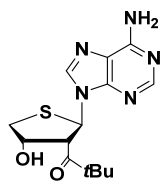
**3f**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.910	470.838	745.544	89.95	90.56
2	17.356	52.570	77.746	10.05	9.44
Total:		523.208	823.289	100.00	100.00



**1-((2*R*,3*S*,4*S*)-2-(6-Amino-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (3g)**



Light yellow oil, 15.1 mg, 94% yield.

$R_f = 0.10$  (EtOAc).

$[\alpha]_D^{24} = -27.6$  ( $c = 0.32$ ,  $\text{CH}_2\text{Cl}_2$ ).

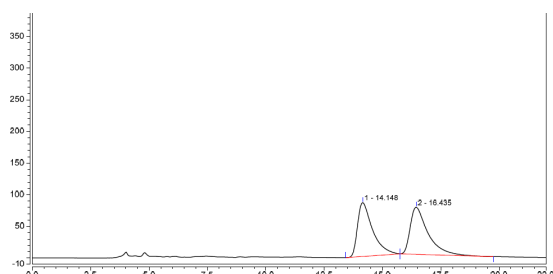
**HPLC** CHIRALCEL IA, n-hexane/2-propanol = 60/40, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 14.127 min (minor), 16.215 min (major), 68% ee, >20:1 dr.

**$^1\text{H NMR}$**  (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  8.28 (s, 1H), 8.21 (s, 1H), 6.75 (d,  $J = 9.2$  Hz, 1H), 4.98-5.03 (m, 1H), 4.70 (dd,  $J = 3.6, 8.8$  Hz, 1H), 3.93 (dd,  $J = 3.6, 11.2$  Hz, 1H), 3.09 (dd,  $J = 1.6, 11.2$  Hz, 1H), 0.97 (s, 9H).

**$^{13}\text{C NMR}$**  (100 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  211.6, 157.4, 153.7, 150.4, 142.3, 76.8, 64.2, 61.0, 45.7, 43.1, 26.0.

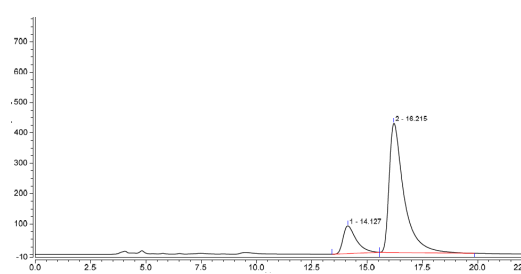
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{14}\text{H}_{19}\text{N}_5\text{NaO}_2\text{S}$  344.1152 found 344.1150.

Racemic sample of **3g**



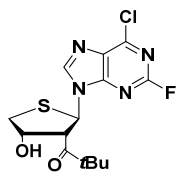
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.148	63.479	85.058	49.18	53.36
2	16.435	85.601	74.352	50.82	46.64
<b>Total:</b>		<b>129.080</b>	<b>159.410</b>	<b>100.00</b>	<b>100.00</b>

**3g**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.127	63.054	91.327	15.99	17.66
2	16.215	331.168	425.668	84.01	82.34
<b>Total:</b>		<b>394.222</b>	<b>516.996</b>	<b>100.00</b>	<b>100.00</b>

**1-((2*R*, 3*S*, 4*S*)-2-(6-Chloro-2-fluoro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3h**)**



Light yellow oil, 16.1 mg, 90% yield.

$R_f = 0.13$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -70.6$  ( $c = 0.74$ ,  $\text{CH}_2\text{Cl}_2$ ).

**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 11.898 min (major), 14.018 min (minor), 87% ee, >20:1 dr.

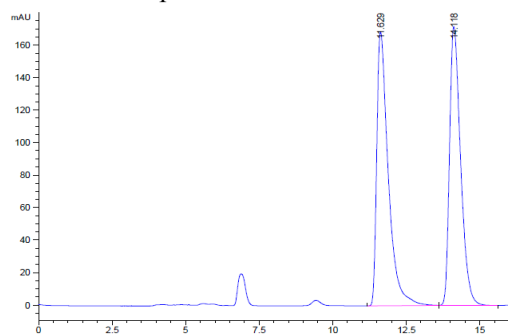
**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15 (s, 1H), 6.58 (d,  $J = 7.8$  Hz, 1H), 4.97 (s, 1H), 4.53 (dd,  $J = 3.6, 7.8$  Hz, 1H), 4.18 (s, 3H), 3.97 (dd,  $J = 3.0, 12.0$  Hz, 1H), 3.26 (dd,  $J = 1.8, 12.0$  Hz, 1H), 2.85 (br, 1H), 0.99 (s, 9H).

**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  212.2, 157.8, 156.3, 153.7 (d,  $J_{\text{C-F}} = 16.5$  Hz), 152.9 (d,  $J_{\text{C-F}} = 16.5$  Hz), 145.5 (d,  $J_{\text{C-F}} = 3.0$  Hz), 131.6 (d,  $J_{\text{C-F}} = 6.0$  Hz), 77.0, 64.9, 59.2, 45.1, 43.7, 25.7.

**$^{19}\text{F NMR}$**  (565 MHz,  $\text{CDCl}_3$ )  $\delta$  -47.9.

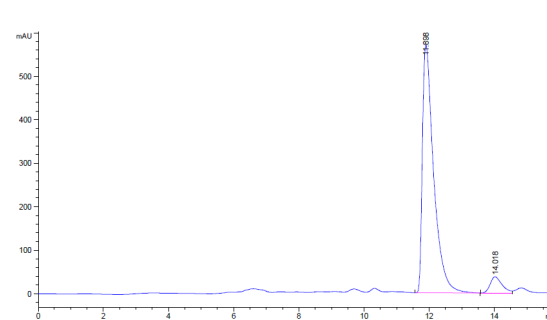
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{14}\text{H}_{16}\text{ClFN}_4\text{NaO}_2\text{S}$  381.0564 found 381.0563.

Racemic sample of **3h**



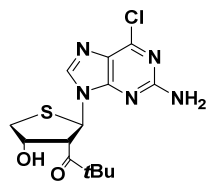
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.629	BB	0.4060	4580.69238	168.55084	50.6386
2	14.118	BB	0.3985	4465.16699	171.47868	49.3614

**3h**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.898	BB	0.3564	1.36609e4	570.90649	93.5984
2	14.018	EV	0.3738	934.32642	37.30988	6.4016

**1-((2*R*,3*S*,4*S*)-2-(2-Amino-6-chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3i**)**



Light yellow oil, 16.2 mg, 91% yield.

$R_f = 0.10$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{24} = -35.0$  ( $c = 0.44$ ,  $\text{CH}_2\text{Cl}_2$ ).

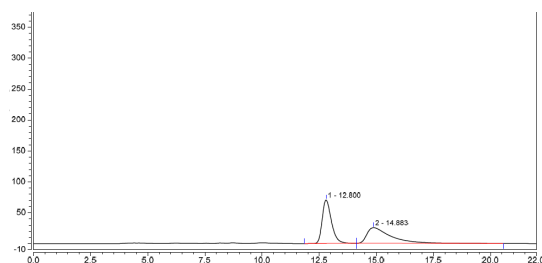
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 60/40, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 12.930 min (minor), 14.753 min (major), 95% ee, >20:1 dr.

**$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.91 (s, 1H), 6.48 (d,  $J = 8.0$  Hz, 1H), 5.34 (s, 2H), 4.88 (s, 1H), 4.40 (dd,  $J = 3.6, 8.4$  Hz, 1H), 3.84 (dd,  $J = 3.2, 11.6$  Hz, 1H), 3.27 (s, 1H), 3.24 (dd,  $J = 1.6, 11.6$  Hz, 1H), 0.96 (s, 9H).

**$^{13}\text{C NMR}$**  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  213.1, 159.1, 153.3, 151.9, 141.6, 126.0, 76.8, 63.9, 59.0, 45.2, 43.3, 25.5.

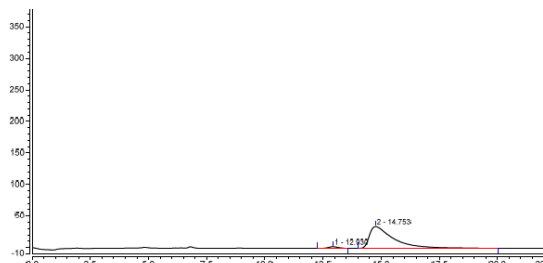
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{14}\text{H}_{18}\text{ClN}_5\text{NaO}_2\text{S}$  378.0762 found 378.0759.

Racemic sample of **3i**



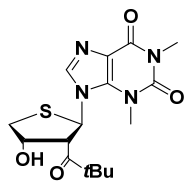
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	12.800	32.826	70.403	51.27	73.52
2	14.883	31.196	25.359	48.73	26.48
<b>Total:</b>		<b>64.022</b>	<b>95.761</b>	<b>100.00</b>	<b>100.00</b>

**3i**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	12.930	1.149	2.523	2.71	6.81
2	14.753	41.292	34.518	97.29	93.19
<b>Total:</b>		<b>42.441</b>	<b>37.041</b>	<b>100.00</b>	<b>100.00</b>

**9-((2*R*,3*S*,4*S*)-4-Hydroxy-3-pivaloyltetrahydrothiophen-2-yl)-1,3-dimethyl-3,9-dihydro-1*H*-purine-2,6-dione (**3j**)**



Colorless oil, 15.4 mg, 84% yield.

$R_f = 0.20$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{24} = -21.5$  ( $c = 0.38$ ,  $\text{CH}_2\text{Cl}_2$ ).

**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 31.978 min (major), 46.225 min (minor), 71% ee, >20:1 dr.

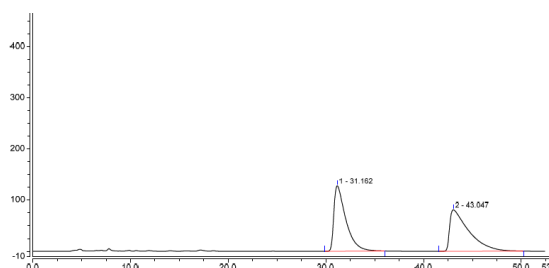
**$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.62 (s, 1H), 6.46 (d,  $J = 9.2$  Hz, 1H), 4.90 (dd,  $J = 3.2, 8.8$  Hz, 1H), 4.83-4.88 (m, 1H), 4.08-4.14 (m, 1H), 3.84 (dd,  $J = 3.2, 11.6$  Hz, 1H), 3.57 (s, 3H), 3.45 (s, 3H), 3.14 (dd,  $J = 1.6, 11.2$  Hz, 1H), 2.90 (d,  $J = 4.8$  Hz, 1H), 0.99 (s, 9H).

**$^{13}\text{C NMR}$**  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  213.9, 155.0, 151.5, 151.1, 142.4, 106.4, 77.1, 67.1, 59.2, 45.2, 43.1, 30.1, 28.7, 25.5.

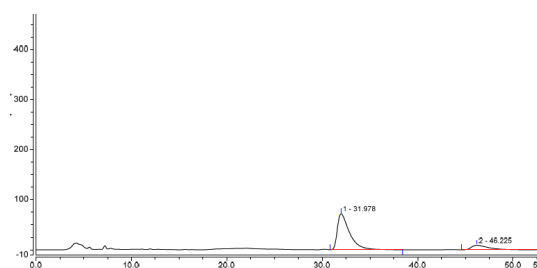
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{16}\text{H}_{22}\text{N}_4\text{NaO}_4\text{S}$  389.1254 found 389.1250.

Racemic sample of **3j**

**3j**

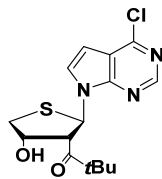


Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	31.162	181.507	127.851	49.78	61.27
2	43.047	183.112	80.817	50.22	38.73
Total:		364.620	208.668	100.00	100.00



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	31.978	105.737	71.842	85.39	88.99
2	46.225	18.089	8.886	14.61	11.01
Total:		123.826	80.728	100.00	100.00

**1-((2*R*, 3*S*, 4*S*)-2-(4-Chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (3k)**



Colorless oil, 17.9 mg, 90% yield.

$R_f = 0.12$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -48.6$  ( $c = 0.76$ ,  $\text{CH}_2\text{Cl}_2$ ).

**HPLC** CHIRALCEL IF, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 14.480 min (major), 16.372 min (minor), 88% ee, >20:1 dr.

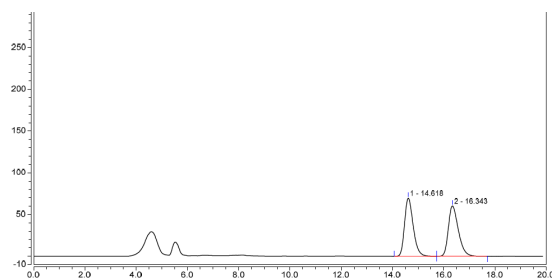
**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.65 (s, 1H), 7.44 (d,  $J = 3.6$  Hz, 1H), 6.75 (d,  $J = 8.4$  Hz, 1H), 6.62 (d,  $J = 3.6$  Hz, 1H), 4.79-4.84 (m, 1H), 4.42 (dd,  $J = 3.6, 8.4$  Hz, 1H), 3.85 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.26 (dd,  $J = 1.2, 11.7$  Hz, 1H), 3.23 (br, 1H), 0.84 (s, 9H).

**$^{13}\text{C}$  NMR** (150 MHz,  $\text{CDCl}_3$ )  $\delta$  214.2, 152.7, 151.1, 150.9, 128.2, 118.7, 100.9, 65.6, 59.0, 45.3, 43.0, 25.2.

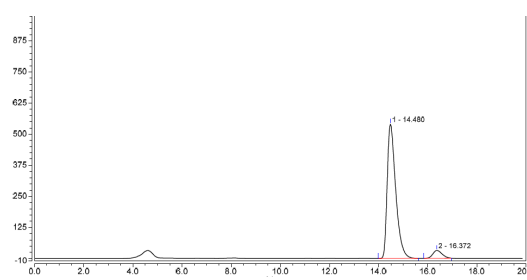
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{15}\text{H}_{18}\text{ClN}_3\text{NaO}_2\text{S}$  362.0700 found 362.0692.

Racemic sample of **3k**

**3k**

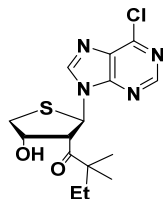


Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.618	27.327	69.847	49.95	53.60
2	16.343	27.377	60.454	50.05	46.40
<b>Total:</b>		<b>54.704</b>	<b>130.300</b>	<b>100.00</b>	<b>100.00</b>



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.480	215.805	540.016	94.03	94.48
2	16.372	13.702	31.575	5.97	5.52
<b>Total:</b>		<b>229.507</b>	<b>571.591</b>	<b>100.00</b>	<b>100.00</b>

**1-((2*R*, 3*S*, 4*S*)-2-(6-Chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylbutan-1-one (31)**



Colorless oil, 16.9 mg, 95% yield.

$R_f = 0.12$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -58.4$  ( $c = 0.90$ ,  $\text{CH}_2\text{Cl}_2$ ).

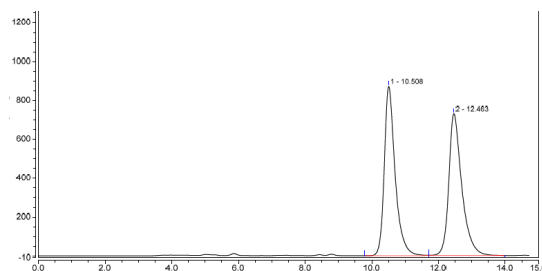
**HPLC** CHIRALCEL IA, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 10.493 min (major), 12.543 min (minor), 88% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.78 (s, 1H), 8.20 (s, 1H), 6.68 (d,  $J = 7.8$  Hz, 1H), 4.95 (s, 1H), 4.69 (dd,  $J = 3.0, 7.8$  Hz, 1H), 3.99 (dd,  $J = 3.0, 11.6$  Hz, 1H), 3.26 (dd,  $J = 1.2, 11.4$  Hz, 1H), 3.10 (br, 1H), 1.24-1.38 (m, 2H), 0.94 (s, 3H), 0.85 (s, 1H), 0.47 (q,  $J = 7.2$  Hz, 1H).

**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  212.8, 152.1, 151.8, 151.2, 145.0, 132.9, 64.9, 59.0, 48.9, 43.6, 31.6, 23.2, 22.6, 8.6.

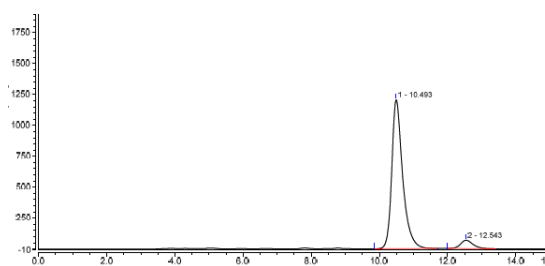
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{15}\text{H}_{19}\text{ClN}_4\text{NaO}_2\text{S}$  377.0809 found 377.0809.

Racemic sample of **31**



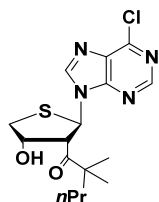
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.508	328.796	872.436	49.83	54.41
2	12.463	331.041	731.128	50.17	45.59
Total:		659.836	1603.564	100.00	100.00

**31**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.493	446.521	1205.413	94.02	94.71
2	12.543	28.412	87.303	5.98	5.29
Total:		474.933	1272.716	100.00	100.00

**1-((2*R*, 3*S*, 4*S*)-2-(6-Chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpentan-1-one (3m)**



Colorless oil, 15.9 mg, 86% yield.

$R_f = 0.13$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -85.3$  ( $c = 0.63$ ,  $\text{CH}_2\text{Cl}_2$ ).

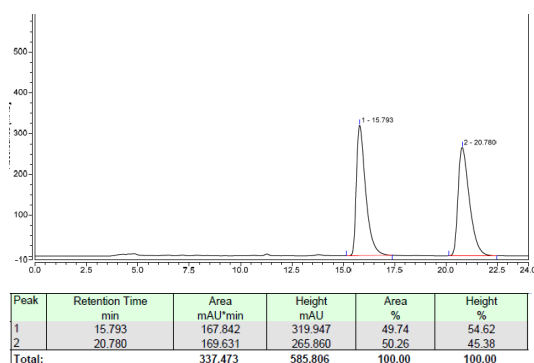
**HPLC** CHIRALCEL IF, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 15.738 min (major), 21.033 min (minor), 88% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.79 (s, 1H), 8.17 (s, 1H), 6.62 (d,  $J = 8.4$  Hz, 1H), 4.90-4.94 (m, 1H), 4.70 (dd,  $J = 3.6, 8.4$  Hz, 1H), 4.00 (dd,  $J = 3.0, 12.0$  Hz, 1H), 3.27 (dd,  $J = 1.2, 11.4$  Hz, 1H), 2.95 (d,  $J = 6.0$  Hz, 1H), 1.21-1.27 (m, 1H), 1.13-1.19 (m, 1H), 0.98 (s, 3H), 0.93-0.96 (m, 1H), 0.87 (s, 3H), 0.57-0.64 (m, 1H), 0.53 (t,  $J = 7.2$  Hz, 3H).

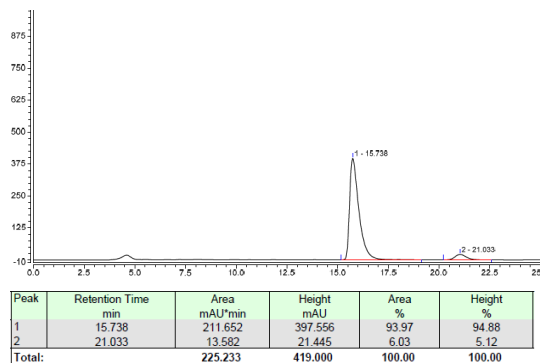
**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  212.8, 152.1, 151.9, 151.2, 145.0, 133.0, 77.0, 64.9, 58.8, 48.8, 43.6, 41.4, 23.8, 23.1, 17.8, 14.3.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{16}\text{H}_{21}\text{ClN}_4\text{NaO}_2\text{S}$  391.0966 found 391.0964.

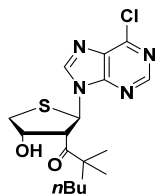
Racemic sample of **3m**



**3m**



**1-((2*R*, 3*S*, 4*S*)-2-(6-Chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylhexan-1-one (3n)**



Colorless oil, 17.6 mg, 92% yield.

$R_f = 0.18$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -35.8$  ( $c = 0.54$ ,  $\text{CH}_2\text{Cl}_2$ )

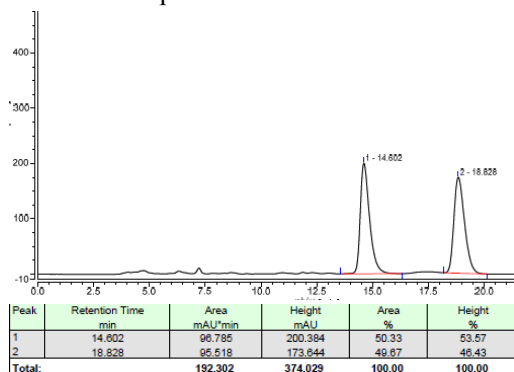
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 14.435 min (major), 18.947 min (minor), 88% ee, >20:1 dr.

**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.79 (s, 1H), 8.17 (s, 1H), 6.67 (d,  $J = 8.4$ , 1H), 4.94 (s, 1H), 4.72 (dd,  $J = 3.6, 8.4$  Hz, 1H), 4.00 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.26 (dd,  $J = 1.2, 11.4$  Hz, 1H), 2.95 (d,  $J = 4.8$  Hz, 1H), 1.22-1.28 (m, 2H), 1.14-1.20 (m, 1H), 1.00 (s, 3H), 0.90-0.97 (m, 1H), 0.88 (s, 3H), 0.71-0.80 (m, 1H), 0.63 (t,  $J = 7.2$  Hz, 1H), 0.45-0.53 (m, 1H).

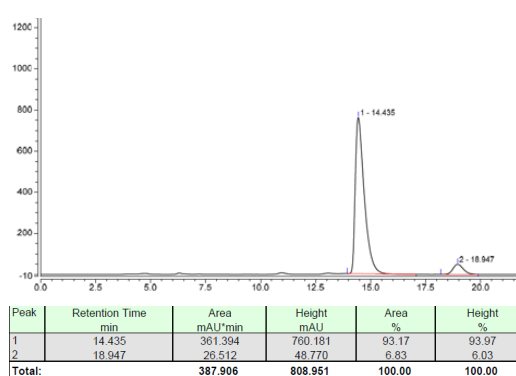
**$^{13}\text{C}$  NMR** (150 MHz,  $\text{CDCl}_3$ )  $\delta$  212.8, 152.1, 151.9, 151.2, 145.0, 133.0, 77.0, 64.9, 58.9, 48.6, 43.6, 39.1, 29.8, 26.6, 24.0, 23.1, 23.1, 13.8.

**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{24}\text{ClN}_4\text{O}_2\text{S}$  383.1303 found 383.1304.

Racemic sample of **3n**

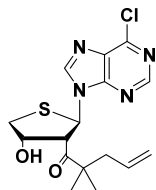


**3n**





**1-((2*R*, 3*S*, 4*S*)-2-(6-Chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpent-4-en-1-one (3o)**



Colorless oil, 17.8 mg, 97% yield.

$R_f = 0.3$  (Pet/EtOAc, 5/1, v/v).

$[\alpha]_D^{22} = -73.8$  ( $c = 0.69$ ,  $\text{CH}_2\text{Cl}_2$ ).

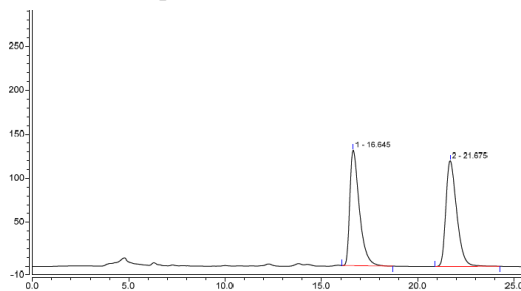
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 16.237 min (major), 21.788 min (minor), 90% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.78 (s, 1H), 8.17 (s, 1H), 6.68 (d,  $J = 7.8$  Hz, 1H), 5.31-5.40 (m, 1H), 5.00 (s, 1H), 4.68-4.78 (m, 2H), 4.65 (dd,  $J = 3.6, 7.8$  Hz, 1H), 4.02 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.25 (dd,  $J = 1.2, 11.4$  Hz, 1H), 2.90 (d,  $J = 6.6$  Hz, 1H), 2.03-2.14 (m, 2H), 0.97 (s, 3H), 0.95 (s, 3H).

**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  211.9, 152.1, 151.9, 151.2, 145.0, 133.0, 132.8, 118.6, 76.9, 64.6, 59.8, 48.3, 43.7, 43.5, 23.6, 23.5.

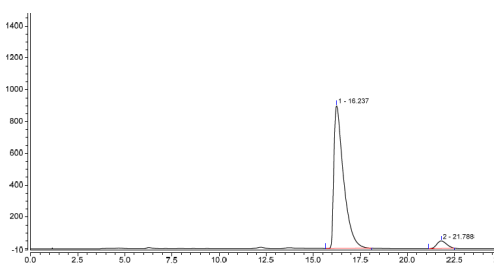
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{16}\text{H}_{19}\text{ClN}_4\text{NaO}_2\text{S}$  389.0809 found 389.0804.

**Racemic sample of 3o**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	16.645	75.522	131.605	49.05	52.23
2	21.675	78.434	120.365	50.95	47.77
Total:		153.957	251.970	100.00	100.00

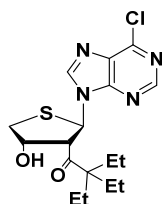
**3o**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	16.237	536.217	897.847	95.03	95.01
2	21.788	28.065	47.131	4.97	4.99
Total:		564.282	944.978	100.00	100.00

# 1-((2*R*, 3*S*, 4*S*)-2-(6-Chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-diethylbutan-

## 1-one (3p)



White solid, m.p. 125.1-128.6 °C, 16.3 mg, 85% yield.

$R_f = 0.32$  (Pet/EtOAc, 10/1, v/v).

$[\alpha]_D^{22} = -42.6$  ( $c = 0.52$ ,  $\text{CH}_2\text{Cl}_2$ ).

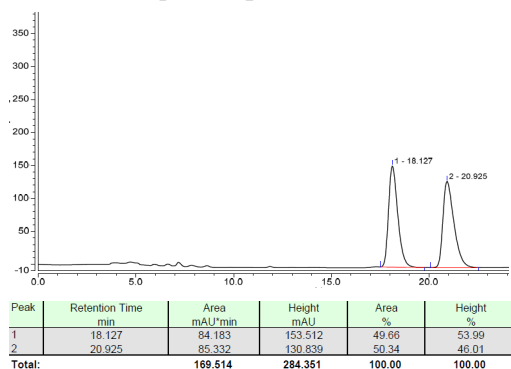
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 18.068 min (major), 21.178 min (minor), 88% ee, >20:1 dr.

**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.80 (s, 1H), 8.12 (s, 1H), 6.65 (d,  $J = 7.8$  Hz, 1H), 4.88-4.92 (m, 2H), 4.02 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.25 (dd,  $J = 1.2, 11.4$  Hz, 1H), 2.93 (br, 1), 1.42-1.50 (m, 3H), 1.30-1.37 (m, 3H), 0.43 (t,  $J = 7.8$  Hz, 9H).

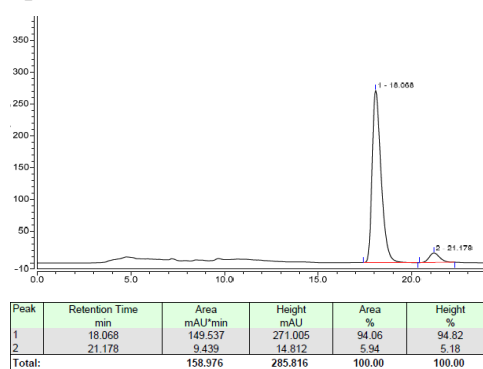
**$^{13}\text{C}$  NMR** (150 MHz,  $\text{CDCl}_3$ )  $\delta$  213.5, 152.1, 151.9, 151.2, 145.1, 133.0, 77.1, 65.3, 58.1, 56.2, 43.8, 24.7, 7.8.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{17}\text{H}_{23}\text{ClN}_4\text{NaO}_2\text{S}$  405.1122 found 405.1120.

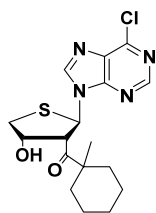
### Racemic sample of 3p



### 3p



**((2*R*, 3*S*, 4*S*)-2-(6-Chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)(1-methylcyclohexyl) methanone (3q)**



Colorless oil, 16.6 mg, 87% yield.

$R_f = 0.18$  (Pet/EtOAc, 2/1, v/v).

$[\alpha]_D^{22} = -82.7$  ( $c = 0.57$ ,  $\text{CH}_2\text{Cl}_2$ ).

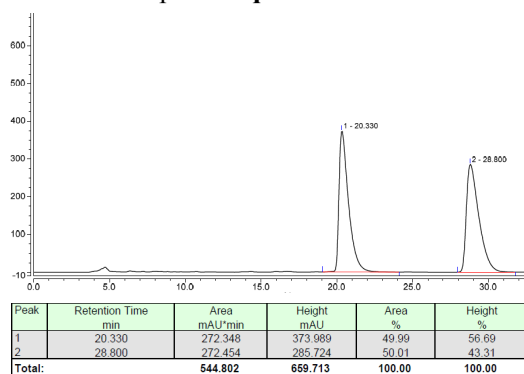
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 20.653 min (major), 29.555 min (minor), 91% ee, >20:1 dr.

**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.78 (s, 1H), 8.18 (s, 1H), 6.65 (d,  $J = 8.4$  Hz, 1H), 4.90-4.94 (m, 1H), 4.68 (dd,  $J = 3.6, 8.4$  Hz, 1H), 3.99 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.27 (dd,  $J = 1.2, 11.4$  Hz, 1H), 3.01 (d,  $J = 6.0$  Hz, 1H), 1.72-1.79 (m, 1H), 1.52-1.58 (m, 1H), 1.42-1.50 (m, 1H), 1.23-1.29 (m, 5H), 1.10-1.15 (m, 1H), 0.91-1.01 (m, 1H), 0.74 (s, 3H).

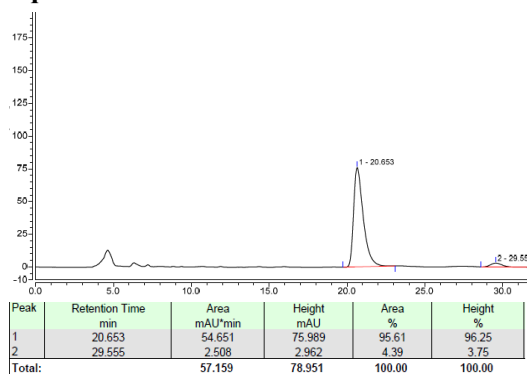
**$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  213.1, 152.1, 151.9, 151.2, 144.9, 132.9, 77.1, 65.1, 58.7, 49.0, 43.7, 34.0, 33.7, 25.6, 22.6, 22.3.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{17}\text{H}_{21}\text{ClN}_4\text{NaO}_2\text{S}$  403.0966 found 403.0959.

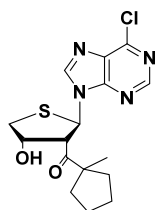
Racemic sample of **3q**



**3q**



**((2*R*, 3*S*, 4*S*)-2-(6-Chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)(1-methylcyclopentyl)methanone (**3r**)**



Colorless oil, 15.6 mg, 85% yield.

$R_f = 0.21$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -66.4$  ( $c = 0.59$ ,  $\text{CH}_2\text{Cl}_2$ ).

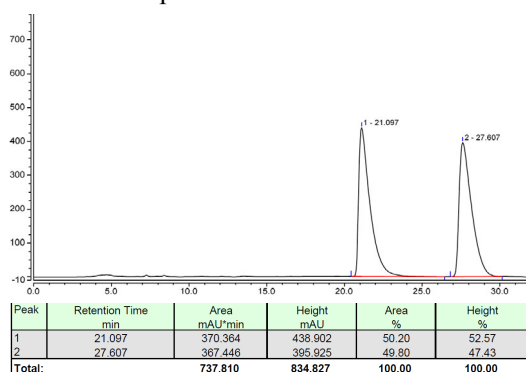
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 20.998 min (major), 28.325 min (minor), 87% ee, >20:1 dr.

**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.77 (s, 1H), 8.23 (s, 1H), 6.67 (d,  $J = 8.4$  Hz, 1H), 4.96 (s, 1H), 4.57 (dd,  $J = 3.6, 7.8$  Hz, 1H), 3.97 (dd,  $J = 3.0, 12.0$  Hz, 1H), 3.27 (dd,  $J = 1.8, 12.0$  Hz, 1H), 3.13 (br, 1H), 1.76-1.82 (m, 1H), 1.44-1.63 (m, 4H), 1.34-1.42 (m, 1H), 1.19-1.29 (m, 2H), 0.97 (s, 3H).

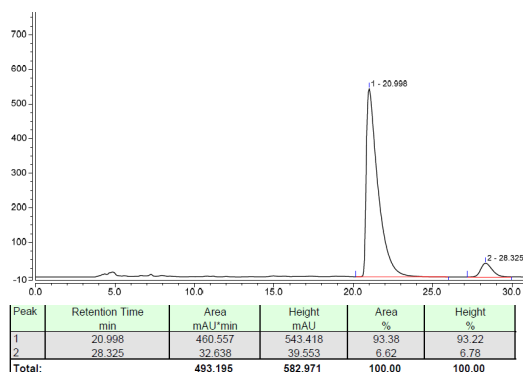
**$^{13}\text{C}$  NMR** (150 MHz,  $\text{CDCl}_3$ )  $\delta$  211.8, 152.1, 151.8, 151.2, 145.0, 132.9, 64.7, 60.0, 56.5, 43.5, 35.8, 35.7, 24.8, 24.6, 23.3.

**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{16}\text{H}_{20}\text{ClN}_4\text{O}_2\text{S}$  367.0990 found 367.0989.

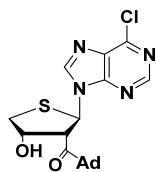
Racemic sample of **3r**



**3r**



**((3*S*, 5*S*, 7*S*)-Adamantan-1-yl)((2*R*,3*S*,4*S*)-2-(6-chloro-9*H*-purin-9-yl)-4-hydroxytetrahydrothiophen-3-yl)methanone (3s)**



Colorless oil, 19.1mg, 91% yield.

$R_f = 0.19$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -45.3$  ( $c = 1.1$ ,  $\text{CH}_2\text{Cl}_2$ ).

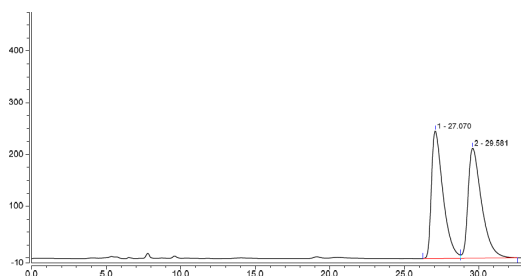
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 27.793 min (minor), 29.548 min (major), 92% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.78 (s, 1H), 8.23 (s, 1H), 6.68 (d,  $J = 8.4$  Hz, 1H), 4.92-4.97 (m, 1H), 4.62 (dd,  $J = 3.6, 7.8$  Hz, 1H), 3.98 (dd,  $J = 3.6, 12.0$  Hz, 1H), 3.26 (dd,  $J = 1.2, 11.4$  Hz, 1H), 3.03 (br, 1H), 1.88-1.95 (m, 3H), 1.60-1.70 (m, 3H), 1.46-1.57 (m, 9H), 1.19-1.29 (m, 2H), 0.97 (s, 3H).

**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  212.0, 152.1, 151.8, 151.2, 144.98, 144.96, 132.9, 76.9, 64.6, 58.7, 47.3, 43.6, 37.2, 36.2, 27.5.

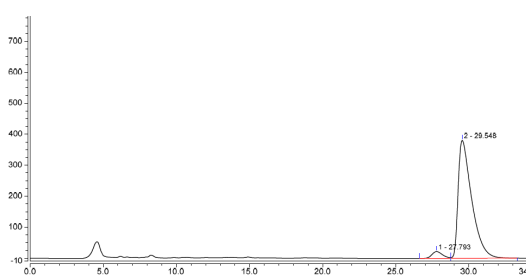
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{20}\text{H}_{24}\text{ClN}_4\text{NaO}_2\text{S}$  419.1303 found 419.1299.

Racemic sample of **3s**



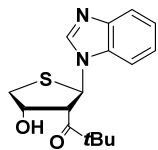
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	27.070	220.774	246.201	49.70	53.67
2	29.581	223.478	212.557	50.30	46.33
<b>Total:</b>		<b>444.253</b>	<b>458.758</b>	<b>100.00</b>	<b>100.00</b>

**3s**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	27.793	18.037	21.759	4.24	5.40
2	29.548	407.133	380.818	95.76	94.60
<b>Total:</b>		<b>425.171</b>	<b>402.577</b>	<b>100.00</b>	<b>100.00</b>

**1-((2*R*, 3*S*, 4*S*)-2-(1*H*-Benzo[d]imidazol-1-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3t**)**



White solid, m.p. 161.0-164.8 °C, 12.8 mg, 84% yield.

$R_f = 0.08$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -2.7$  ( $c = 0.78$ ,  $\text{CH}_2\text{Cl}_2$ ).

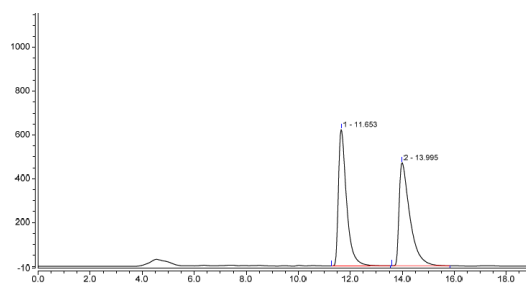
**HPLC** CHIRALCEL ID, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 13.078 min (major), 17.572 min (minor), 95% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.14 (s, 1H), 7.75-7.79 (m, 1H), 7.46-7.50 (m, 1H), 7.26-7.32 (m, 2H), 6.63 (d,  $J = 9.0$  Hz, 1H), 4.75-4.78 (m, 1H), 4.04 (dd,  $J = 3.0, 9.6$  Hz, 1H), 3.75 (dd,  $J = 3.0, 12.6$  Hz, 1H), 3.31 (dd,  $J = 1.8, 12.0$  Hz, 1H), 0.75 (s, 9H).

**$^{13}\text{C NMR}$**  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  214.7, 144.4, 142.1, 132.7, 123.6, 123.0, 121.0, 111.0, 76.2, 65.1, 59.8, 45.4, 42.2, 24.9.

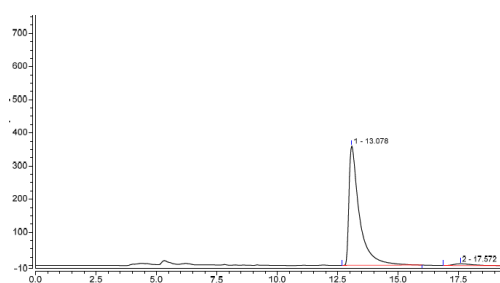
**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_2\text{S}$  305.1318 found 305.1318.

Racemic sample of **3t**



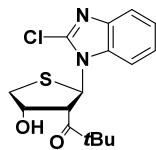
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.653	226.140	623.681	50.15	56.95
2	13.995	224.781	471.445	49.85	43.05
Total:		450.921	1095.126	100.00	100.00

**3t**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.078	180.669	360.388	97.32	98.56
2	17.572	4.973	5.262	2.68	1.44
Total:		185.643	365.650	100.00	100.00

**1-((2*R*, 3*S*, 4*S*)-2-(2-Chloro-1*H*-benzo[d]imidazol-1-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3u**)**



Colorless oil, 14.6 mg, 86% yield.

$R_f = 0.24$  (Pet/EtOAc, 2/1, v/v).

$[\alpha]_D^{22} = -22.8$  ( $c = 0.96$ ,  $\text{CH}_2\text{Cl}_2$ ).

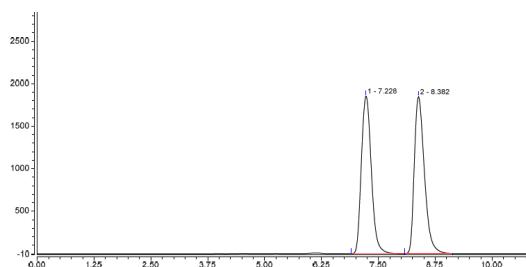
**HPLC** CHIRALCEL ID, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 7.493 min (major), 8.555 min (minor), 95% ee, >20:1 dr.

**$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.67-7.71 (m, 1H), 7.59-7.64 (m, 1H), 7.27-7.37 (m, 2H), 6.82 (d,  $J = 9.6$  Hz, 1H), 4.72-4.78 (m, 1H), 4.32 (dd,  $J = 3.2, 9.6$  Hz, 1H), 3.75 (dd,  $J = 3.2, 11.6$  Hz, 1H), 3.42 (br, 1H), 3.35 (dd,  $J = 1.2, 11.6$  Hz, 1H), 0.80 (s, 9H).

**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  214.6, 142.2, 140.2, 123.7, 123.5, 120.4, 111.2, 76.4, 65.1, 56.2, 45.5, 42.9, 24.9, 18.6.

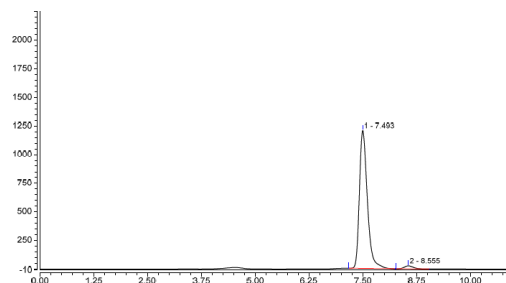
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{16}\text{H}_{19}\text{ClN}_2\text{NaO}_2\text{S}$  361.0748 found 361.0745.

Racemic sample of **3u**



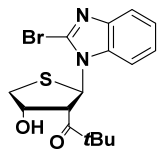
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.228	472.128	1855.654	50.01	50.11
2	8.382	471.962	1847.184	49.99	49.89
Total:		944.110	3702.838	100.00	100.00

**3u**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.493	256.928	1204.757	97.62	97.89
2	8.555	6.271	25.969	2.38	2.11
Total:		263.199	1230.725	100.00	100.00

**1-((2*R*, 3*S*, 4*S*)-2-(2-Bromo-1*H*-benzo[d]imidazol-1-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3v**)**



Colorless oil, 16.6 mg, 87% yield.

$R_f = 0.27$  (Pet/EtOAc, 2/1, v/v).

$[\alpha]_D^{22} = -24.2$  ( $c = 0.76$ ,  $\text{CH}_2\text{Cl}_2$ ).

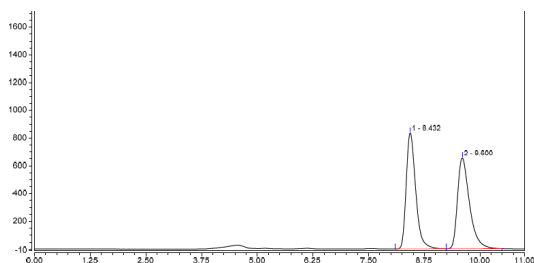
HPLC CHIRALCELID-H, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 8.417 min (major), 9.680 min (minor), 94% ee, >20:1 dr.

$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.71 (d,  $J = 7.2$  Hz, 1H), 7.65 (s, 1H), 7.27-7.35 (m, 2H), 7.26-7.32 (m, 2H), 6.83 (d,  $J = 9.6$  Hz, 1H), 4.76 (s, 1H), 4.34 (d,  $J = 7.2$  Hz, 1H), 3.75 (dd,  $J = 3.0, 12.0$  Hz, 1H), 3.50 (br, 1H), 3.36 (d,  $J = 12.0$  Hz, 1H), 0.78 (s, 9H).

$^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  214.6, 171.3, 143.9, 123.6, 123.4, 120.4, 111.2, 76.4, 66.3, 60.5, 56.0, 45.5, 42.9, 24.8, 21.2, 14.3.

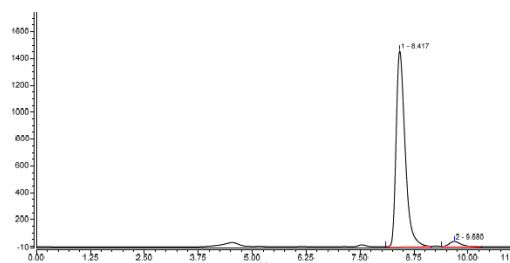
HRMS (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{16}\text{H}_{19}\text{BrN}_2\text{NaO}_2\text{S}$  405.0243 found 405.0245.

Racemic sample of **3v**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.432	206.212	838.179	50.19	56.09
2	9.600	204.662	656.254	49.81	43.91
Total:		410.874	1494.433	100.00	100.00

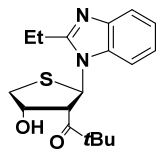
**3v**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.417	348.284	1461.247	96.98	97.52
2	9.680	10.642	37.231	3.04	2.48
Total:		360.226	1498.479	100.00	100.00



**1-((2*R*, 3*S*, 4*S*)-2-(2-Ethyl-1*H*-benzo[d]imidazol-1-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3w**)**



White solid, m.p. 201.9-205.2 °C, 11.8 mg, 71% yield.

$R_f = 0.12$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -55.7$  ( $c = 0.38$ ,  $\text{CH}_2\text{Cl}_2$ ).

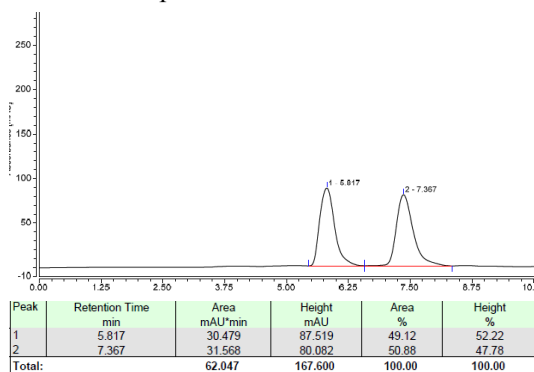
**HPLC** CHIRALCEL OD-H, n-hexane/2-propanol = 80/20, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 5.813 min (minor), 7.348 min (major), 94% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70-7.74 (m, 1H), 7.61-7.67 (m, 1H), 7.23-7.29 (m, 2H), 6.69 (d,  $J = 9.6$  Hz, 1H), 4.76 (s, 1H), 4.43 (dd,  $J = 3.0, 10.2$  Hz, 1H), 3.77 (dd,  $J = 3.0, 12.0$  Hz, 1H), 3.34 (d,  $J = 12.0$  Hz, 1H), 2.82-2.85 (m, 2H), 1.41 (t,  $J = 7.2$  Hz, 1H), 0.75 (s, 9H).

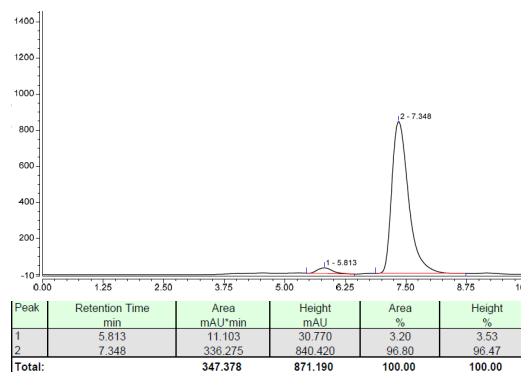
**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  215.5, 156.2, 143.5, 122.6, 122.5, 120.3, 111.5, 76.0, 64.3, 58.6, 56.2, 45.5, 42.5, 24.9, 20.9, 18.6, 12.0.

**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{25}\text{N}_2\text{O}_2\text{S}$  333.1631 found 333.1630.

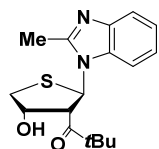
Racemic sample of **3w**



**3w**



**1-((2*R*, 3*S*, 4*S*)-4-Hydroxy-2-(2-methyl-1*H*-benzo[d]imidazol-1-yl)tetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3x**)**



White solid, m.p. 199.7-204.5 °C, 13.7 mg, 86% yield.

$R_f = 0.10$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -55.5$  ( $c = 0.61$ ,  $\text{CH}_2\text{Cl}_2$ ).

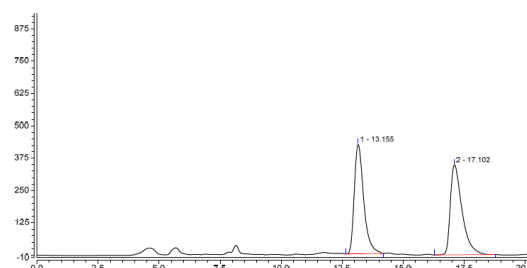
HPLC CHIRALCELID-H, n-hexane/2-propanol = 80/20, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 13.162 min (major), 17.343 min (minor), 94% ee, >20:1 dr.

$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.61-7.70 (m, 2H), 7.23-7.28 (m, 2H), 6.68 (d,  $J = 9.6$  Hz, 1H), 4.77 (s, 1H), 4.37 (dd,  $J = 3.0, 10.2$  Hz, 1H), 3.76 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.50 (br, 1H), 3.33 (d,  $J = 11.4$  Hz, 1H), 2.54 (s, 3H), 0.75 (s, 9H).

$^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  215.1, 151.7, 143.4, 132.8, 122.7, 122.5, 120.1, 111.5, 75.9, 64.6, 56.5, 45.5, 42.5, 24.9, 14.2.

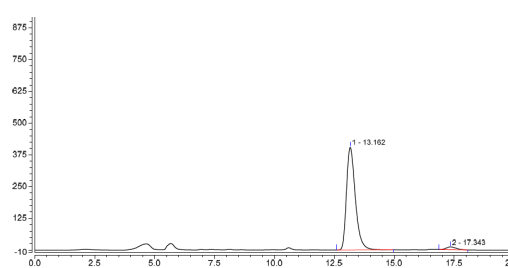
HRMS (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{17}\text{H}_{22}\text{N}_2\text{NaO}_2\text{S}$  341.1294 found 341.1290.

Racemic sample of **3x**



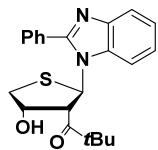
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.155	189.764	423.437	49.58	54.85
2	17.102	192.946	348.516	50.42	45.15
Total:		382.710	771.953	100.00	100.00

**3x**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.162	173.719	404.782	97.08	97.40
2	17.343	5.234	10.786	2.92	2.60
Total:		178.953	415.568	100.00	100.00

**1-((2*R*, 3*S*, 4*S*)-4-Hydroxy-2-(2-phenyl-1*H*-benzo[d]imidazol-1-yl)tetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3y**)**



White solid, m.p. 204.9-208.0 °C, 13.0 mg, 68% yield.

$R_f = 0.25$  (Pet/EtOAc, 2/1, v/v).

$[\alpha]_D^{22} = -48.3$  ( $c = 0.39$ ,  $\text{CH}_2\text{Cl}_2$ ).

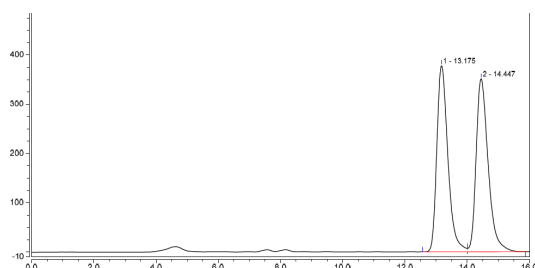
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 80/20, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 13.187 min (major), 14.562 min (minor), 89% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.77-7.86 (m, 2H), 7.57 (s, 5H), 7.32-7.38 (m, 2H), 6.72 (d,  $J = 9.6$  Hz, 1H), 4.63-4.68 (m, 1H), 4.46 (dd,  $J = 3.0, 9.6$  Hz, 1H), 3.74 (dd,  $J = 3.0, 12.0$  Hz, 1H), 3.30 (d,  $J = 12.0$  Hz, 1H), 3.23 (s, 1H), 0.68 (s, 9H).

**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  215.0, 154.3, 144.1, 133.1, 130.4, 129.5, 129.4, 129.1, 123.3, 123.2, 121.2, 112.3, 76.2, 66.0, 58.6, 55.3, 45.4, 42.4, 24.8, 18.6.

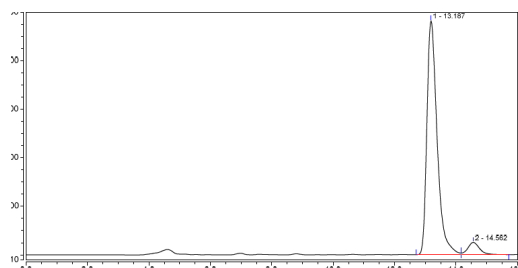
**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_2\text{S}$  381.1631 found 381.1628.

Racemic sample of **3y**



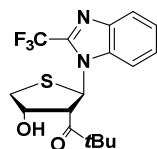
Peak	Retention Time min	Area mAU·min	Height mAU	Area %	Height %
1	13.175	155.840	378.281	49.76	51.84
2	14.447	157.364	351.460	50.24	48.16
<b>Total:</b>		<b>313.204</b>	<b>729.742</b>	<b>100.00</b>	<b>100.00</b>

**3y**



Peak	Retention Time min	Area mAU·min	Height mAU	Area %	Height %
1	13.187	185.547	481.713	94.34	95.04
2	14.562	11.137	25.164	5.66	4.96
<b>Total:</b>		<b>196.684</b>	<b>506.877</b>	<b>100.00</b>	<b>100.00</b>

**1-((2*R*, 3*S*, 4*S*)-4-Hydroxy-2-(2-(trifluoromethyl)-1*H*-benzo[d]imidazol-1-yl)tetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3z**)**



White solid, m.p. 169.9-173.8 °C, 17.9 mg, 96% yield.

$R_f = 0.30$  (Pet/EtOAc, 2/1, v/v).

$[\alpha]_D^{22} = -65.1$  ( $c = 0.61$ ,  $\text{CH}_2\text{Cl}_2$ ).

**HPLC** CHIRALCEL OD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min,  $\lambda = 256$  nm, retention time: 6.375 min (minor), 7.653 min (major), 93% ee, >20:1 dr.

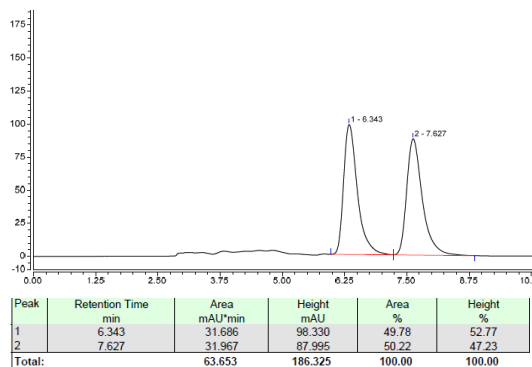
**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.91 (d,  $J = 8.4$  Hz, 1H), 7.76 (d,  $J = 8.4$  Hz, 1H), 7.50 (t,  $J = 7.8$  Hz, 1H), 7.43 (t,  $J = 7.2$  Hz, 1H), 6.72 (d,  $J = 9.0$  Hz, 1H), 4.77 (s, 1H), 4.44 (dd,  $J = 3.6, 9.6$  Hz, 1H), 3.77 (dd,  $J = 1.8, 12.0$  Hz, 1H), 3.70 (br, 1H), 3.40 (dd,  $J = 1.8, 12.0$  Hz, 1H), 0.74 (s, 9H).

**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  214.8, 142.0, 140.8 (d,  $J_{\text{C-F}} = 39.0$  Hz), 133.2, 125.8, 124.4, 122.9, 121.5, 119.7, 117.9, 112.9, 76.8, 65.8, 58.6, 55.4, 45.5, 42.8, 24.6, 18.6.

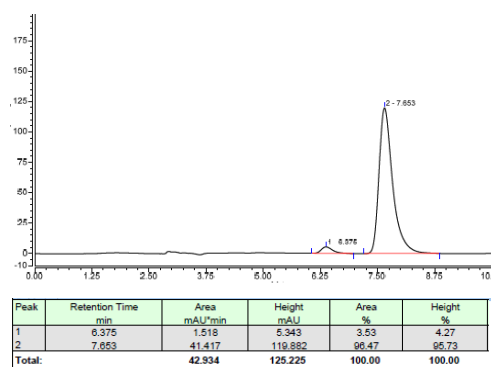
**$^{19}\text{F NMR}$**  (565 MHz,  $\text{CDCl}_3$ )  $\delta$  -60.8.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{17}\text{H}_{19}\text{F}_3\text{N}_2\text{NaO}_2\text{S}$  395.1012 found 395.1011.

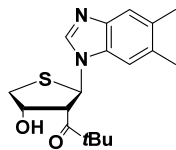
Racemic sample of **3z**



**3z**



**1-((2*R*, 3*S*, 4*S*)-2-(5,6-Dimethyl-1*H*-benzo[d]imidazol-1-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (3aa)**



White solid, m.p. 116.8-118.6 °C, 13.3 mg, 80% yield.

$R_f = 0.10$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -10.7$  ( $c = 0.93$ ,  $\text{CH}_2\text{Cl}_2$ ).

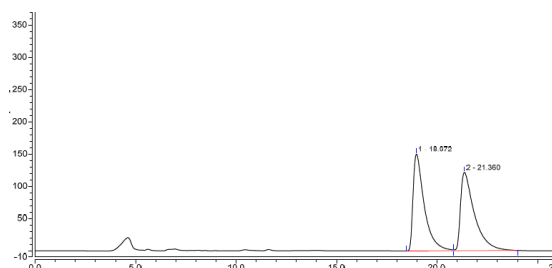
**HPLC** CHIRALCEL ID, n-hexane/2-propanol = 80/20, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 18.733 min (major), 21.970 min (minor), 98% ee, >20:1 dr.

**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (s, 1H), 7.51 (s, 1H), 7.22 (s, 1H), 6.56 (d,  $J = 9.6$  Hz, 1H), 4.75-4.78 (m, 1H), 4.03 (dd,  $J = 3.0, 9.6$  Hz, 1H), 3.73 (dd,  $J = 3.0, 12.0$  Hz, 1H), 3.30 (dd,  $J = 1.8, 12.0$  Hz, 1H), 2.39 (s, 3H), 2.35 (s, 3H), 0.78 (s, 9H).

**$^{13}\text{C}$  NMR** (150 MHz,  $\text{CDCl}_3$ )  $\delta$  214.9, 142.9, 141.3, 132.8, 132.0, 131.1, 120.9, 111.0, 76.3, 65.2, 59.6, 45.4, 42.2, 25.0, 20.9, 20.4.

**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{25}\text{N}_2\text{O}_2\text{S}$  333.1631 found 333.1627.

Racemic sample of **3aa**



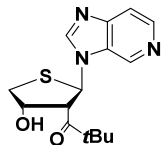
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	18.733	264.314	396.197	98.79	98.91
2	21.970	3.245	4.369	1.21	1.09
Total:		267.559	400.566	100.00	100.00

**3aa**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	18.733	264.314	396.197	98.79	98.91
2	21.970	3.245	4.369	1.21	1.09
Total:		267.559	400.566	100.00	100.00

**1-((2*R*, 3*S*, 4*S*)-4-Hydroxy-2-(3*H*-imidazo[4,5-*c*]pyridin-3-yl)tetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (3ab)**



Colorless oil, 13.0 mg, 85% yield.

$R_f = 0.10$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -4.44$  ( $c = 0.50$ ,  $\text{CH}_2\text{Cl}_2$ ).

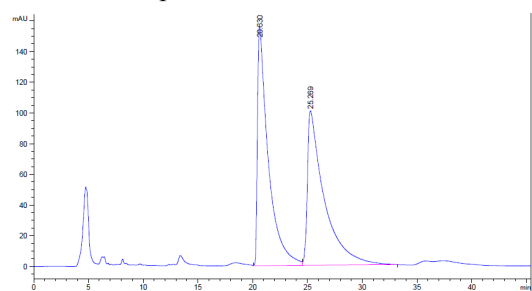
**HPLC** CHIRALCEL OD-H, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min,  $\lambda = 256$  nm, retention time: 20.916 min (major), 29.566 min (minor), 96% ee, >20:1 dr.

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.09 (s, 1H), 8.46 (d,  $J = 5.6$  Hz, 1H), 8.21 (s, 1H), 7.46 (d,  $J = 5.6$  Hz, 1H), 6.64 (d,  $J = 9.2$  Hz, 1H), 4.82 (br, 1H), 3.97 (dd,  $J = 2.8, 9.2$  Hz, 1H), 3.77 (dd,  $J = 3.2, 11.6$  Hz, 1H), 3.51 (br, 1H), 3.33 (dd,  $J = 1.2, 11.6$  Hz, 1H), 0.78 (s, 1H).

**$^{13}\text{C}$  NMR** (150 MHz,  $\text{CDCl}_3$ )  $\delta$  213.8, 144.0, 143.4, 142.7, 141.4, 137.7, 106.4, 76.1, 64.9, 60.4, 45.4, 42.3, 25.0, 18.6.

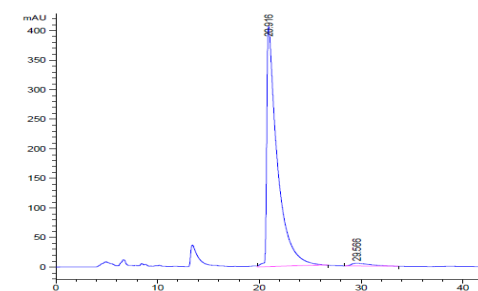
**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{15}\text{H}_{20}\text{N}_3\text{O}_2\text{S}$  306.1271 found 306.1269.

**Racemic sample of 3ab**



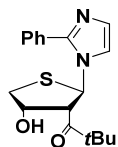
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.630	VV	0.9396	1.06752e4	155.74036	49.9754
2	25.269	VB	1.4030	1.06857e4	100.68083	50.0246

**3ab**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.916	MM	1.1906	2.90598e4	406.78839	97.9967
2	29.566	BB	1.4731	594.06274	4.73763	2.0033

**1-((2*R*, 3*S*, 4*S*)-4-Hydroxy-2-(2-phenyl-1*H*-imidazol-1-yl)tetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3ac**)**



White solid, m.p. 161.6-169.0 °C, 12.1 mg, 73% yield.

$R_f = 0.10$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -117.1$  ( $c = 1.02$ ,  $\text{CH}_2\text{Cl}_2$ ).

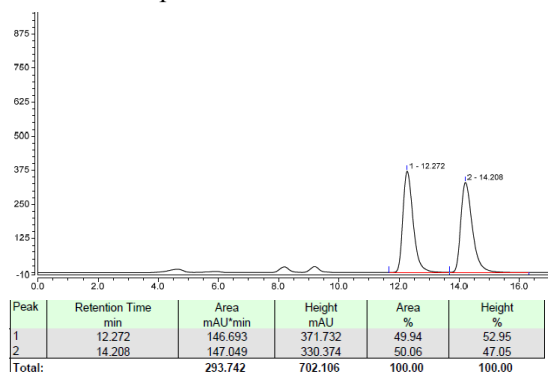
**HPLC** CHIRALCEL ID, n-hexane/2-propanol = 80/20, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 13.272 min (major), 15.257 min (minor), 99% ee, >20:1 dr.

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42-7.49 (m, 5H), 7.42 (d,  $J = 1.2$  Hz, 1H), 7.18 (s, 1H), 6.43 (d,  $J = 9.0$  Hz, 1H), 4.62-4.65 (m, 1H), 3.85 (dd,  $J = 3.0, 9.0$  Hz, 1H), 3.59 (dd,  $J = 3.6, 11.4$  Hz, 1H), 3.14 (dd,  $J = 1.8, 12.0$  Hz, 1H), 0.91 (s, 9H).

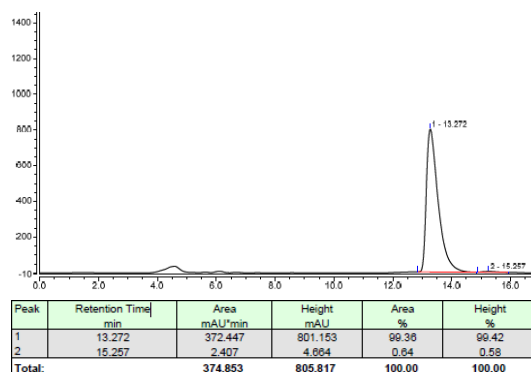
**$^{13}\text{C NMR}$**  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  214.0, 148.7, 130.1, 129.7, 129.4, 129.2, 128.9, 117.4, 76.1, 65.1, 60.9, 45.3, 41.9, 25.1.

**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{18}\text{H}_{22}\text{N}_2\text{NaO}_2\text{S}$  353.1294 found 353.1291.

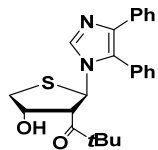
Racemic sample of **3ac**



**3ac**



**1-((2*R*, 3*S*, 4*S*)-2-(4,5-Diphenyl-1*H*-imidazol-1-yl)-4-hydroxytetrahydrothiophen-3-yl)-2,2-dimethylpropan-1-one (**3ad**)**



White solid, m.p. 156.5-161.3°C, 15.0 mg, 74% yield.

$R_f = 0.10$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = -88.2$  ( $c = 0.62$ ,  $\text{CH}_2\text{Cl}_2$ ).

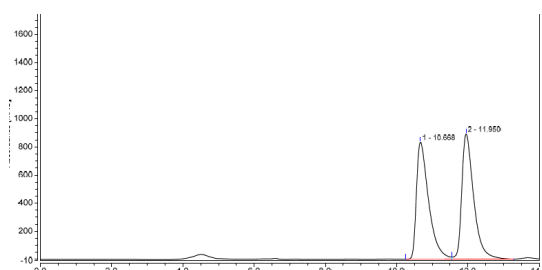
HPLC CHIRALCEL ID, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 10.873 min (major), 11.917 min (minor), 97% ee, >20:1 dr.

$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (s, 1H), 7.45-7.51 (m, 3H), 7.37-7.41 (m, 2H), 7.22-7.26 (m, 2H), 7.16-7.20 (m, 2H), 7.11-7.15 (m, 1H), 6.00 (d,  $J = 9.6$  Hz, 1H), 4.61-4.65 (m, 1H), 3.94 (dd,  $J = 3.6, 9.0$  Hz, 1H), 3.52 (dd,  $J = 3.0, 11.4$  Hz, 1H), 3.11 (dd,  $J = 1.8, 11.4$  Hz, 1H), 0.99 (s, 9H).

$^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  213.6, 138.4, 135.5, 134.1, 131.2, 129.4, 129.4, 129.3, 128.7, 128.3, 126.8, 126.8, 76.2, 63.3, 61.0, 45.3, 41.9, 25.2.

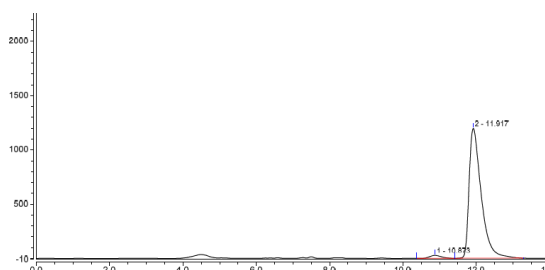
**HRMS** (ESI-TOF):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{24}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$  407.1788 found 407.1784.

Racemic sample of **3ad**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.668	329.926	832.885	48.93	48.32
2	11.950	344.287	890.947	51.07	51.68
Total:		674.213	1723.832	100.00	100.00

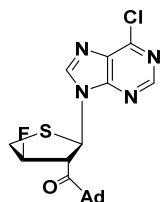
**3ad**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.873	9.777	26.511	2.09	2.17
2	11.917	457.618	1196.416	97.91	97.83
Total:		467.395	1222.927	100.00	100.00



**((3*R*,5*R*,7*R*)-Adamantan-1-yl)((2*R*,3*R*,4*R*)-2-(6-chloro-9*H*-purin-9-yl)-4-fluorotetrahydrothiophen-3-yl)methanone (5a)**



Colorless oil, 15.8 mg, 75% yield.

$R_f = 0.13$  (Pet/EtOAc, 4/1, v/v).

$[\alpha]_D^{22} = -1.8$  ( $c = 0.37$ ,  $\text{CH}_2\text{Cl}_2$ ).

HPLC CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 18.005 min (minor), 20.735 min (major), 90% ee, >20:1 dr.

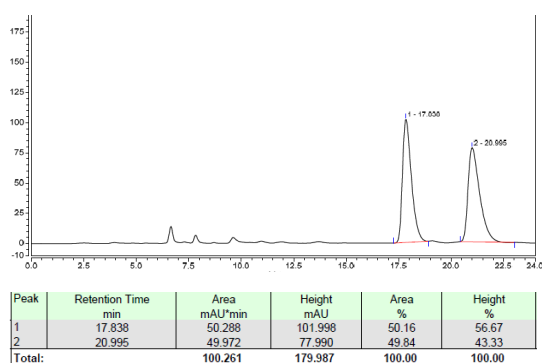
$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.76 (s, 1H), 8.51 (s, 1H), 6.29 (d,  $J = 3.0$  Hz, 1H), 5.31 (dq,  $J = 4.2, 50.4$  Hz, 1H), 4.33 (dt,  $J = 3.6, 17.4$  Hz, 1H), 3.67-3.75 (m, 1H), 3.51 (ddd,  $J = 4.2, 12.0, 28.2$  Hz, 1H), 2.00 (s, 3H), 1.64-1.75 (m, 9H), 1.58-1.63 (m, 3H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  210.4 (d,  $J = 7.0$  Hz, 1H), 152.25, 151.4 (d,  $J = 12.0$  Hz, 1H), 145.1 (d,  $J = 7.0$  Hz, 1H), 132.20, 96.7 (d,  $J = 187.0$  Hz), 62.0 (d,  $J = 3.0$  Hz), 60.1 (d,  $J = 20.0$  Hz), 47.76, 39.0 (d,  $J = 21.0$  Hz), 37.38, 36.22, 27.56.

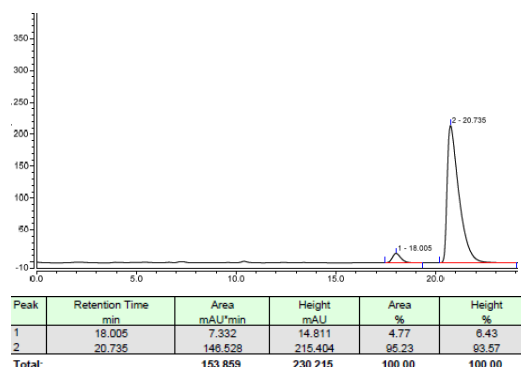
$^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -170.3.

HRMS (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{20}\text{H}_{22}\text{ClFN}_4\text{NaOS}$  443.1079 found 443.1073.

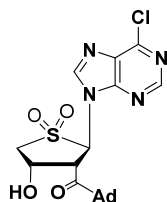
Racemic sample of **5a**



**5a**



**((3*S*,5*S*,7*S*)-Adamantan-1-yl)((2*R*,3*S*,4*S*)-2-(6-chloro-9*H*-purin-9-yl)-4-hydroxy-1,1-dioxidotetrahydrothiophen-3-yl)methanone (5b)**



Colorless oil, 19.2 mg, 85% yield.

$R_f = 0.10$  (Pet/EtOAc, 1/1, v/v).

$[\alpha]_D^{22} = 1.71$  ( $c = 0.35$ ,  $\text{CH}_2\text{Cl}_2$ ).

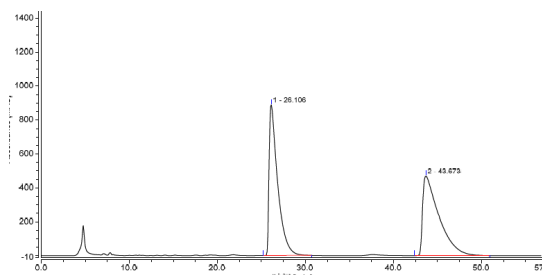
**HPLC** CHIRALCEL IE, n-hexane/2-propanol = 70/30, flow rate = 0.8 mL/min,  $\lambda = 256$  nm, retention time: 26.106 min (major), 43.673 min (minor), 90% ee, >20:1 dr.

**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.79 (s, 1H), 8.41 (s, 1H), 6.58 (d,  $J = 10.8$  Hz, 1H), 5.31 (dd,  $J = 4.2, 10.8$  Hz, 1H), 5.16 (s, 1H), 4.06-4.16 (m, 1H), 3.76-3.89 (m, 2H), 1.96 (s, 3H), 1.60-1.74 (m, 9H), 1.53-1.58 (m, 3H).

**$^{13}\text{C}$  NMR** (150 MHz,  $\text{CDCl}_3$ )  $\delta$  208.5, 152.5, 152.1, 151.9, 145.9, 132.1, 71.9, 65.9, 59.6, 51.0, 47.9, 37.5, 36.1, 27.5.

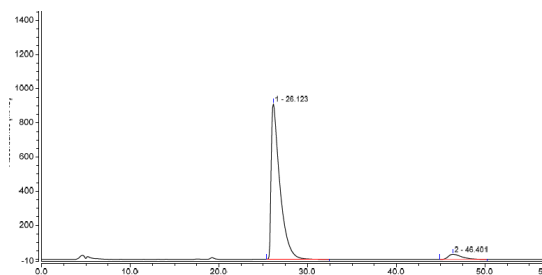
**HRMS** (ESI-TOF):  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{20}\text{H}_{23}\text{ClN}_4\text{NaO}_4\text{S}$  473.1021 found 473.1020.

**Racemic sample of 5b**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	26.106	1004.380	887.911	50.04	65.42
2	43.673	1002.840	469.395	49.96	34.58
Total:		2007.220	1357.306	100.00	100.00

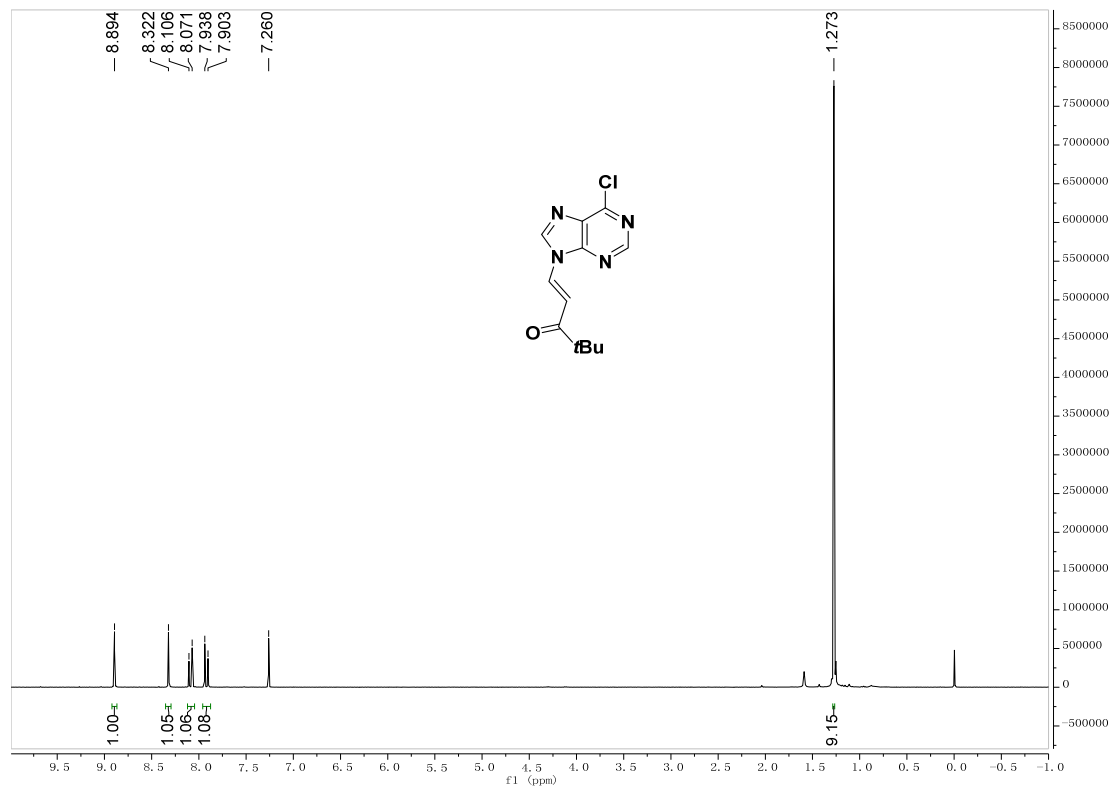
**5b**



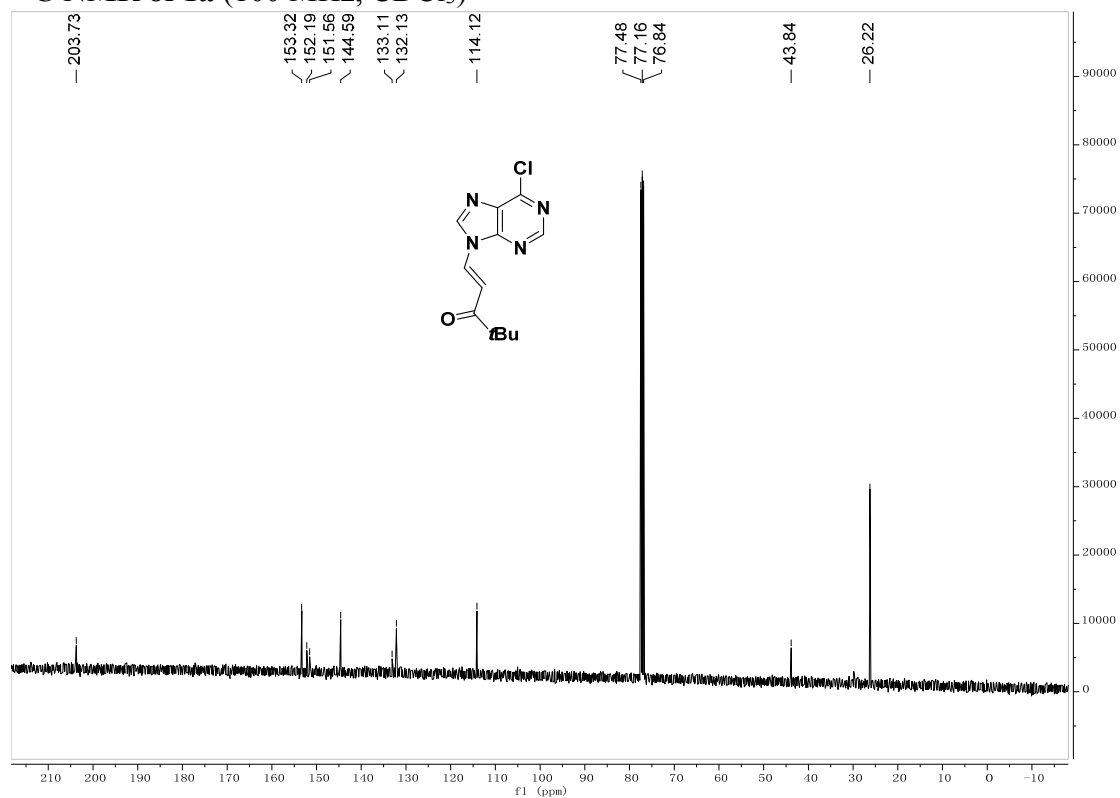
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	26.123	1034.850	909.736	95.14	96.80
2	46.401	52.853	30.079	4.86	3.20
Total:		1087.703	939.816	100.00	100.00

## 7. Copies of $^1\text{H}$ , $^{13}\text{C}$ NMR and $^{19}\text{F}$ NMR spectra

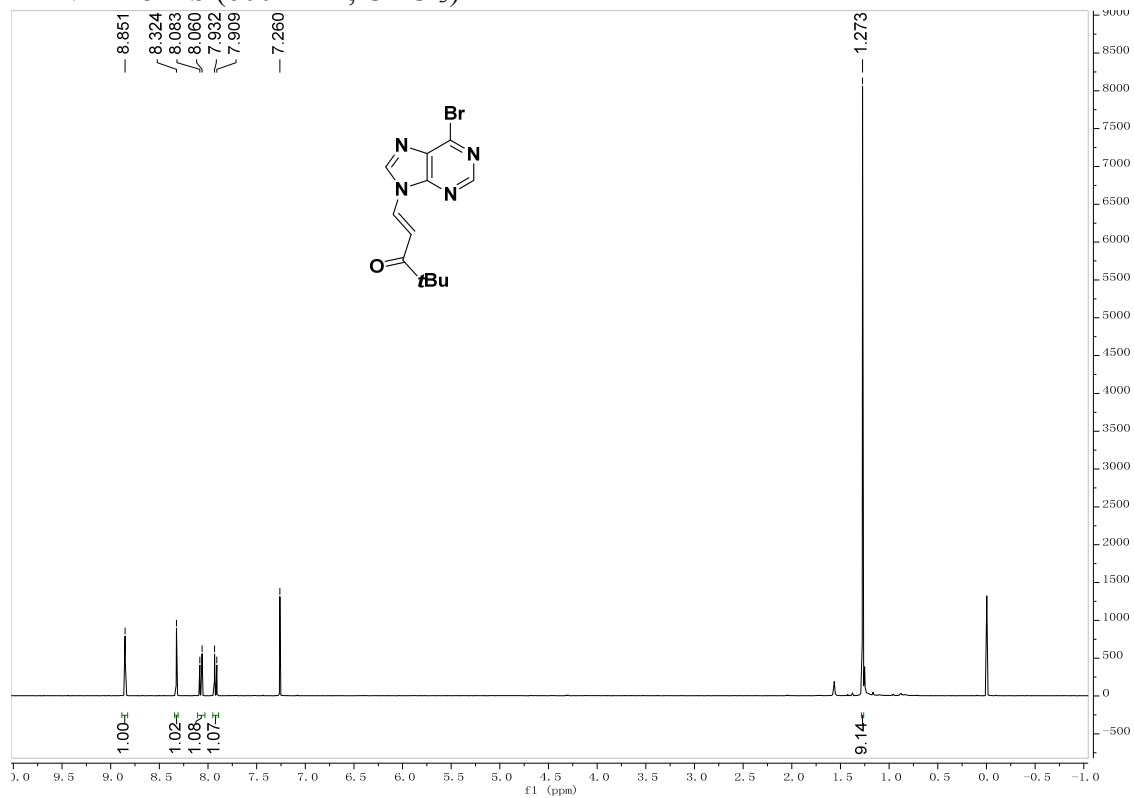
### $^1\text{H}$ NMR of **1a** (400 MHz, $\text{CDCl}_3$ )



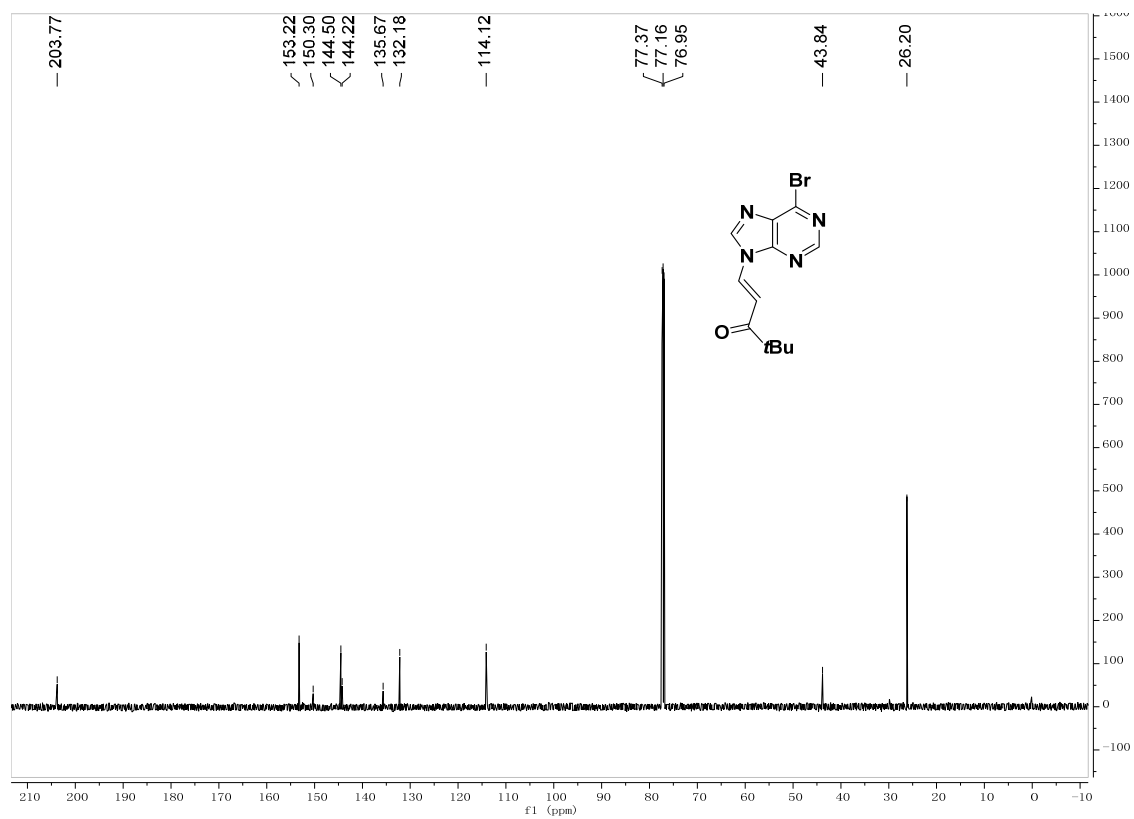
### $^{13}\text{C}$ NMR of **1a** (100 MHz, $\text{CDCl}_3$ )



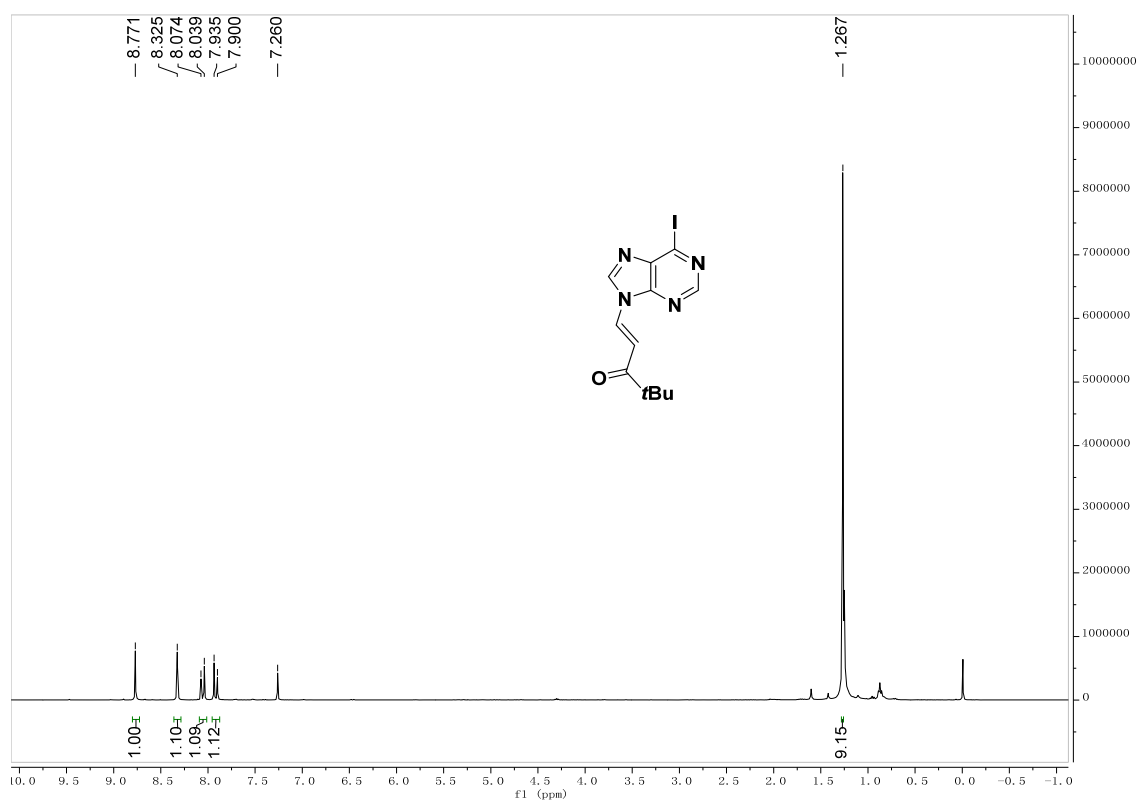
**<sup>1</sup>H NMR of 1b (600 MHz, CDCl<sub>3</sub>)**



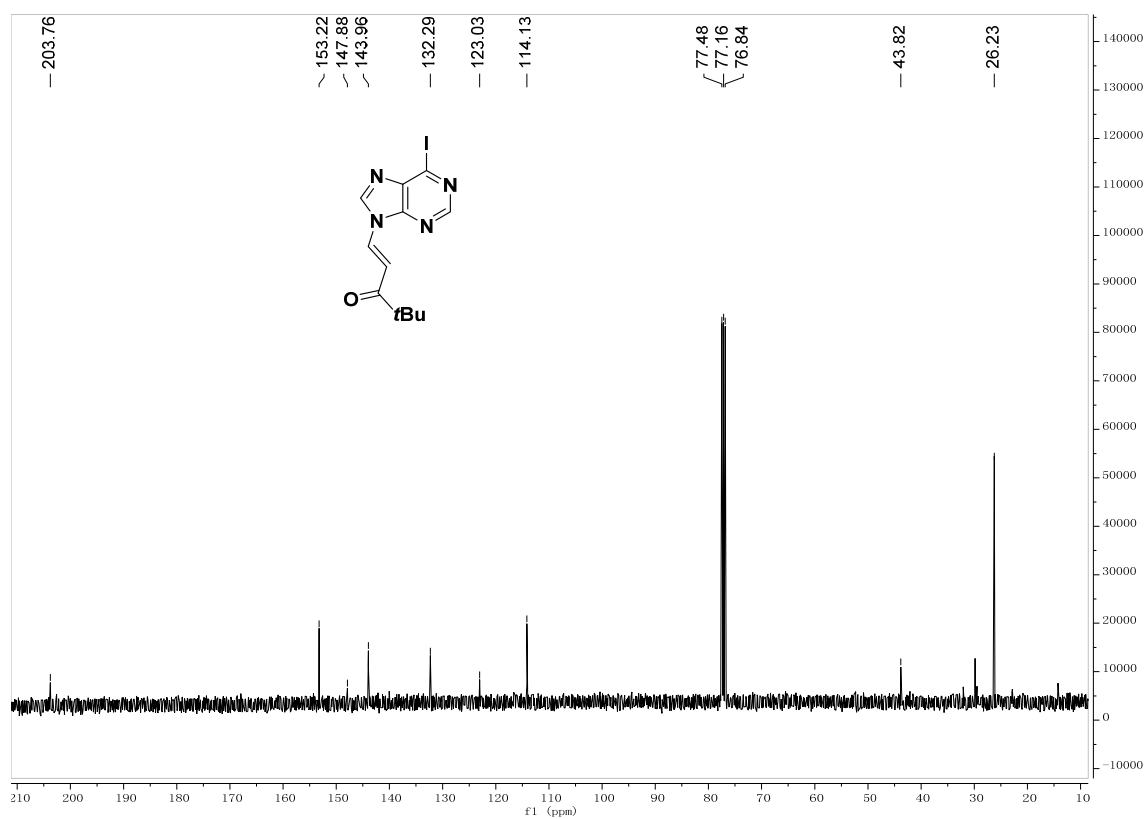
**<sup>13</sup>C NMR of 1b (150 MHz, CDCl<sub>3</sub>)**



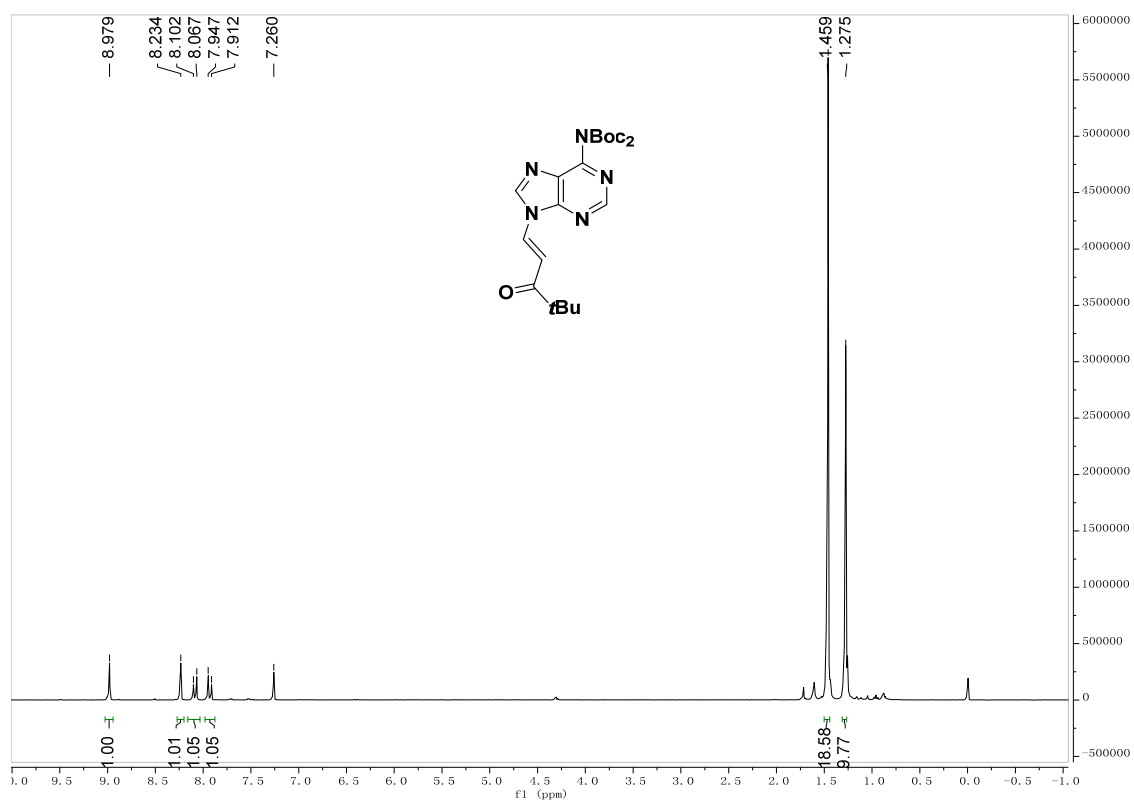
### <sup>1</sup>H NMR of 1c (400 MHz, CDCl<sub>3</sub>)



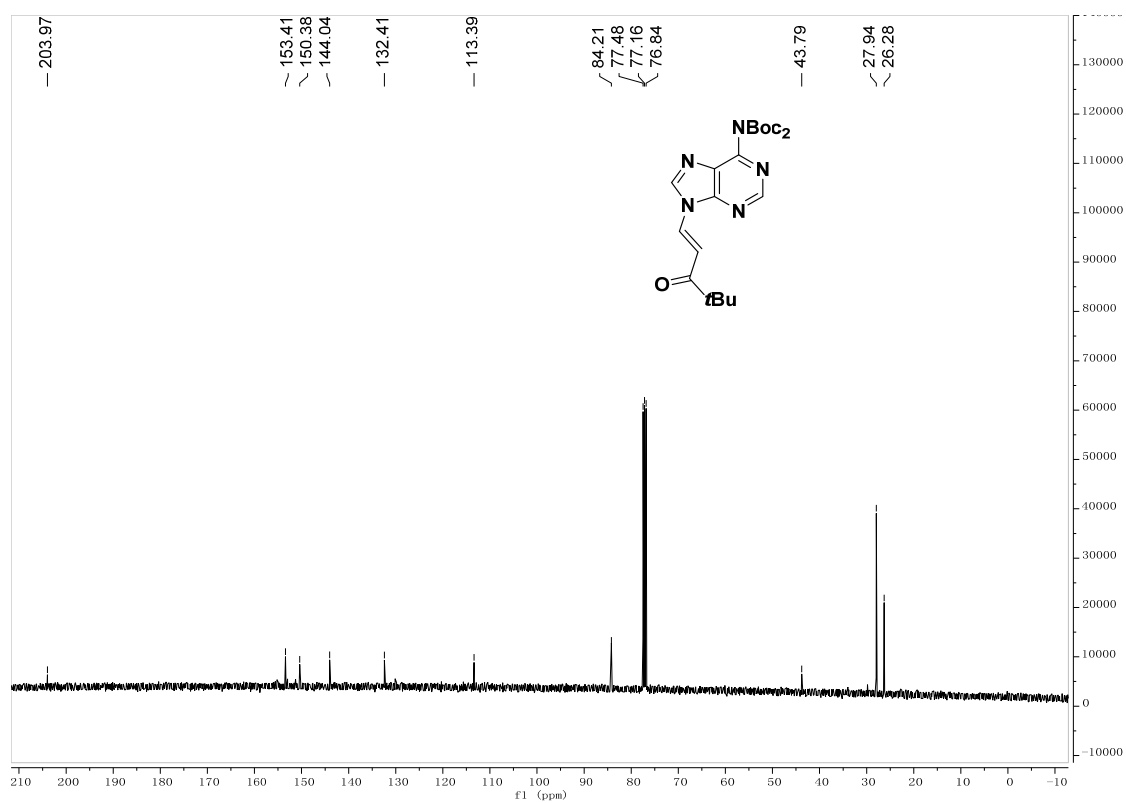
### <sup>13</sup>C NMR of 1c (100 MHz, CDCl<sub>3</sub>)



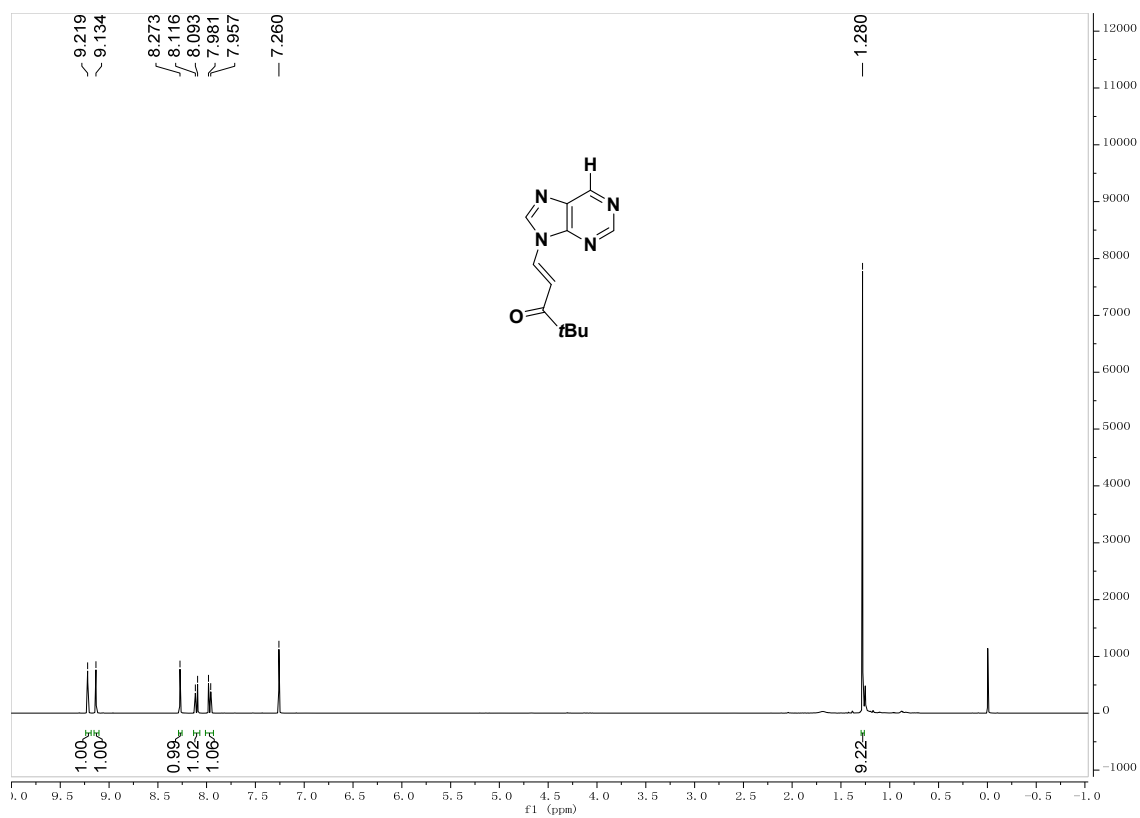
### <sup>1</sup>H NMR of 1d (400 MHz, CDCl<sub>3</sub>)



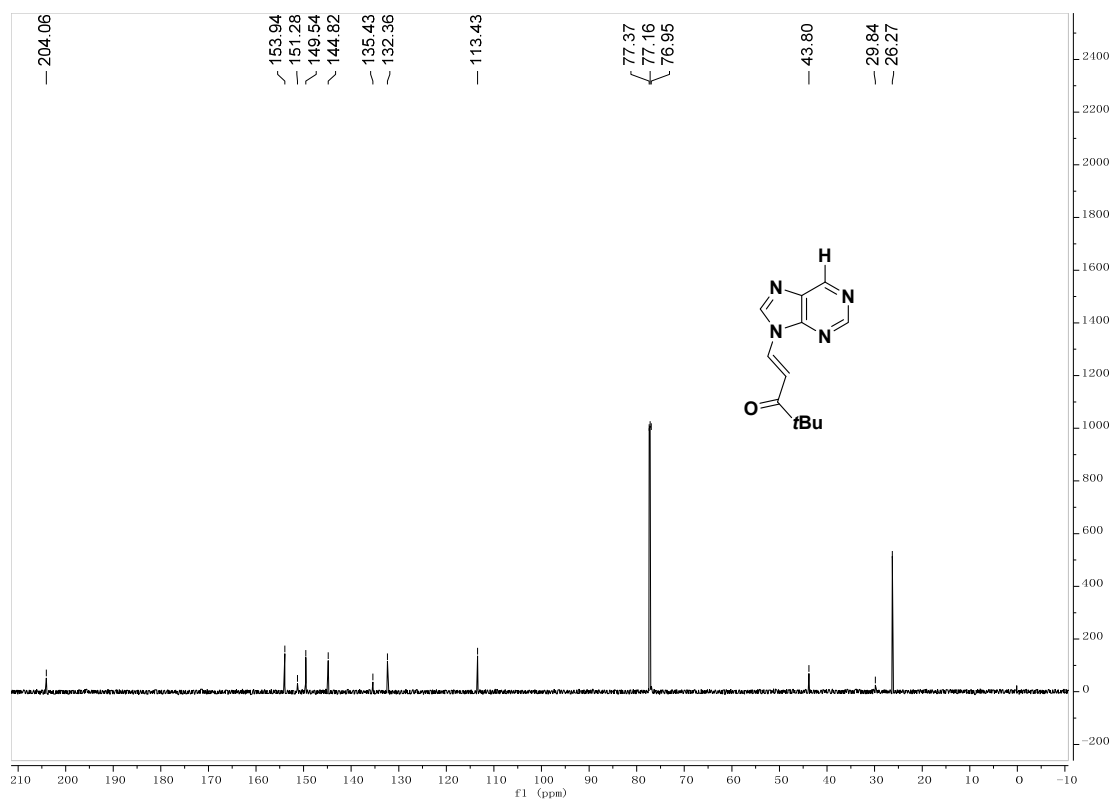
### <sup>13</sup>C NMR of 1d (100 MHz, CDCl<sub>3</sub>)



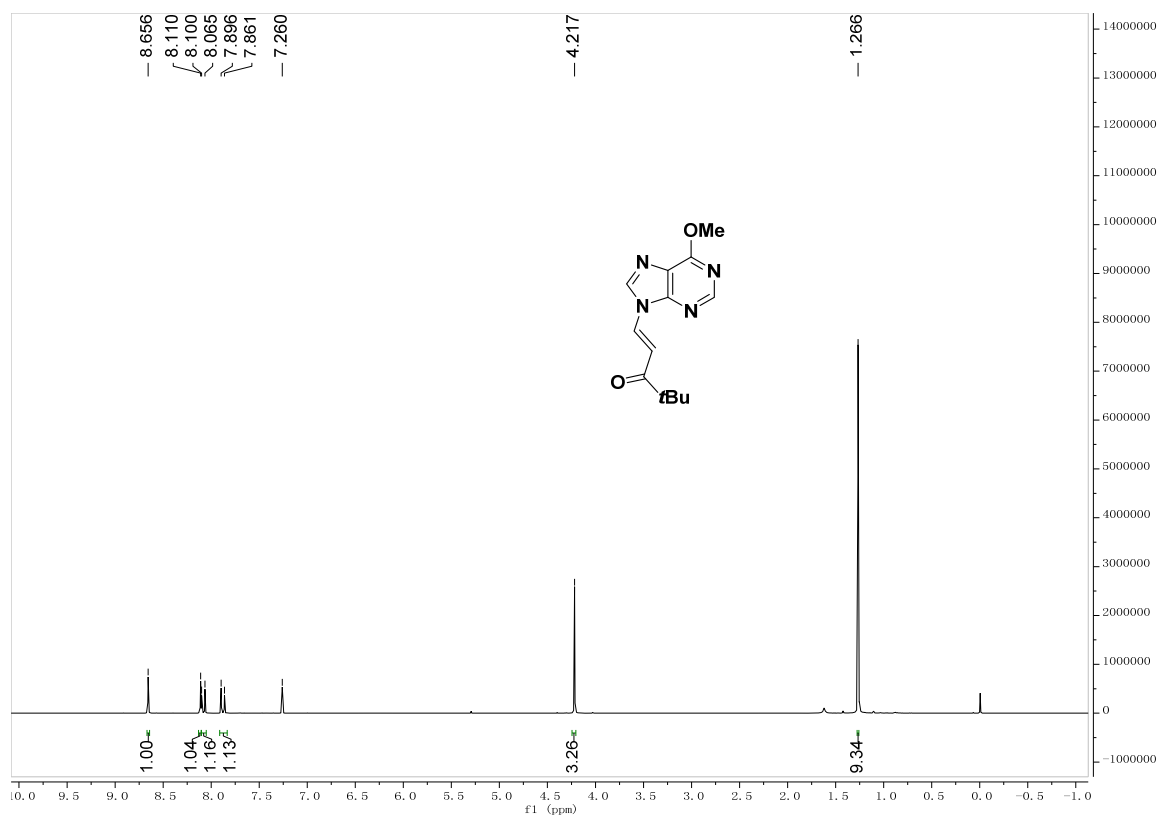
### <sup>1</sup>H NMR of 1e (600 MHz, CDCl<sub>3</sub>)



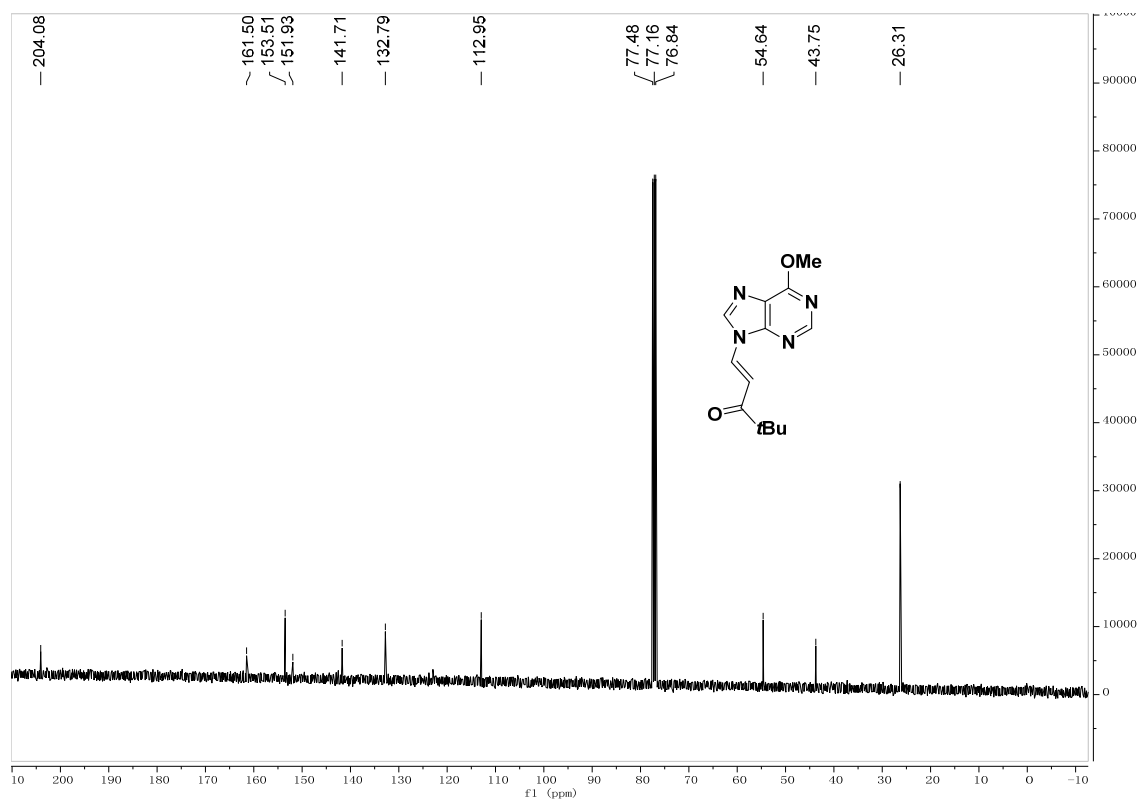
### <sup>13</sup>C NMR of 1e (150 MHz, CDCl<sub>3</sub>)



**<sup>1</sup>H NMR of 1f (400 MHz, CDCl<sub>3</sub>)**

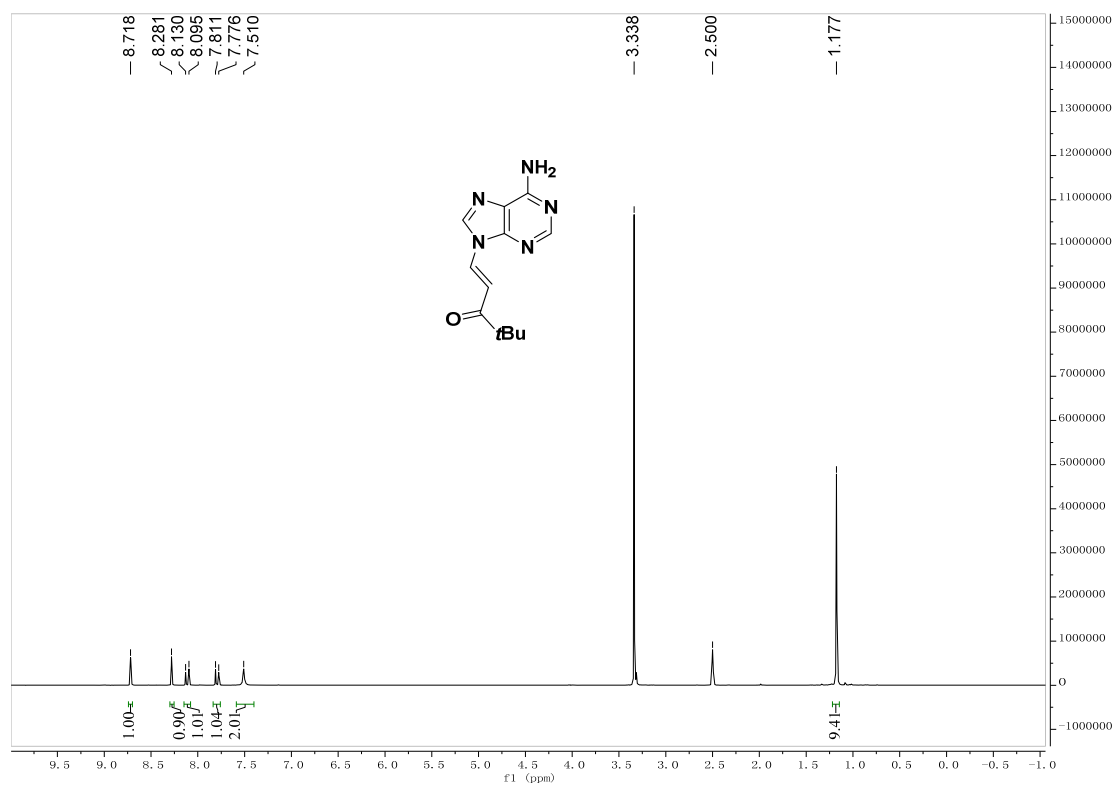


**<sup>13</sup>C NMR of 1f (100 MHz, CDCl<sub>3</sub>)**

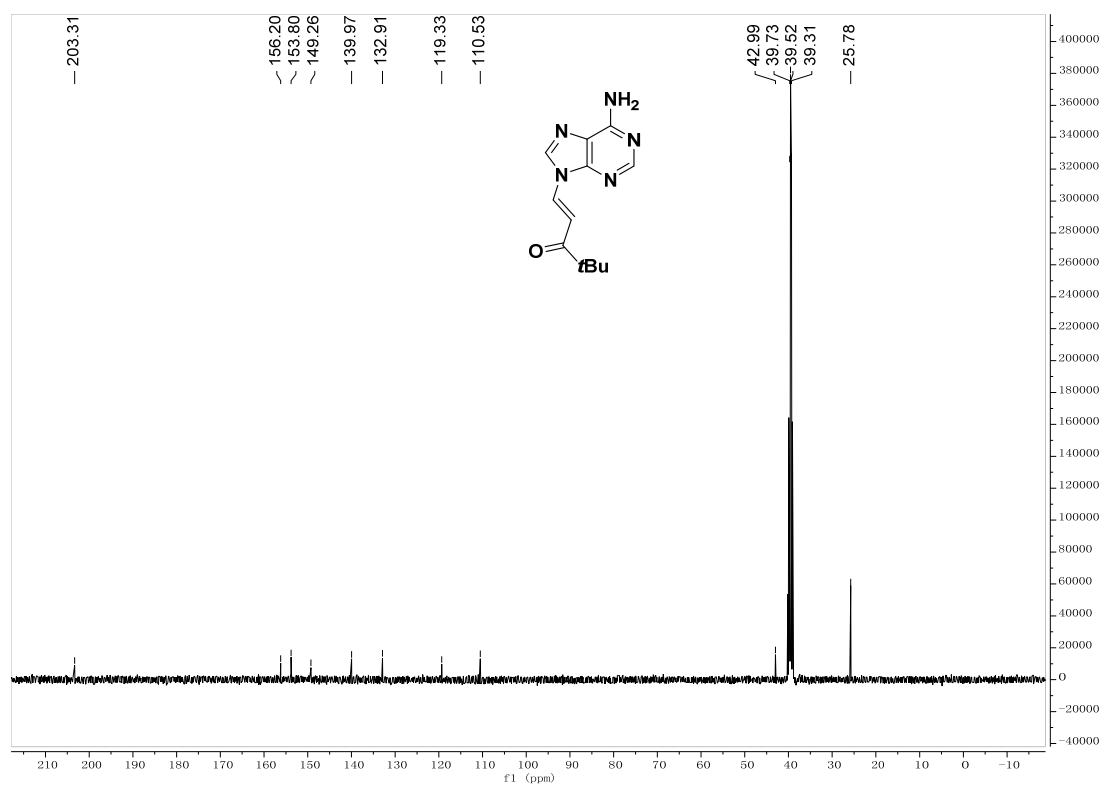




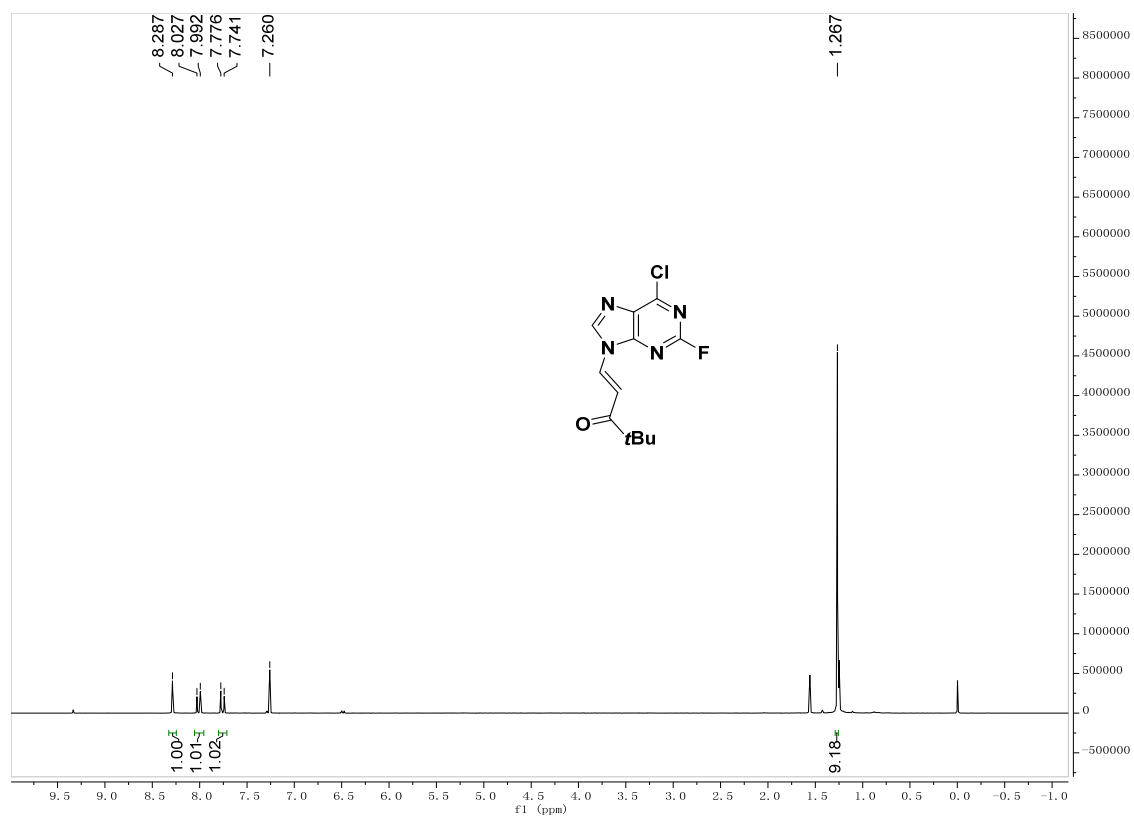
**<sup>1</sup>H NMR of 1g (400 MHz, DMSO-*d*<sub>6</sub>)**



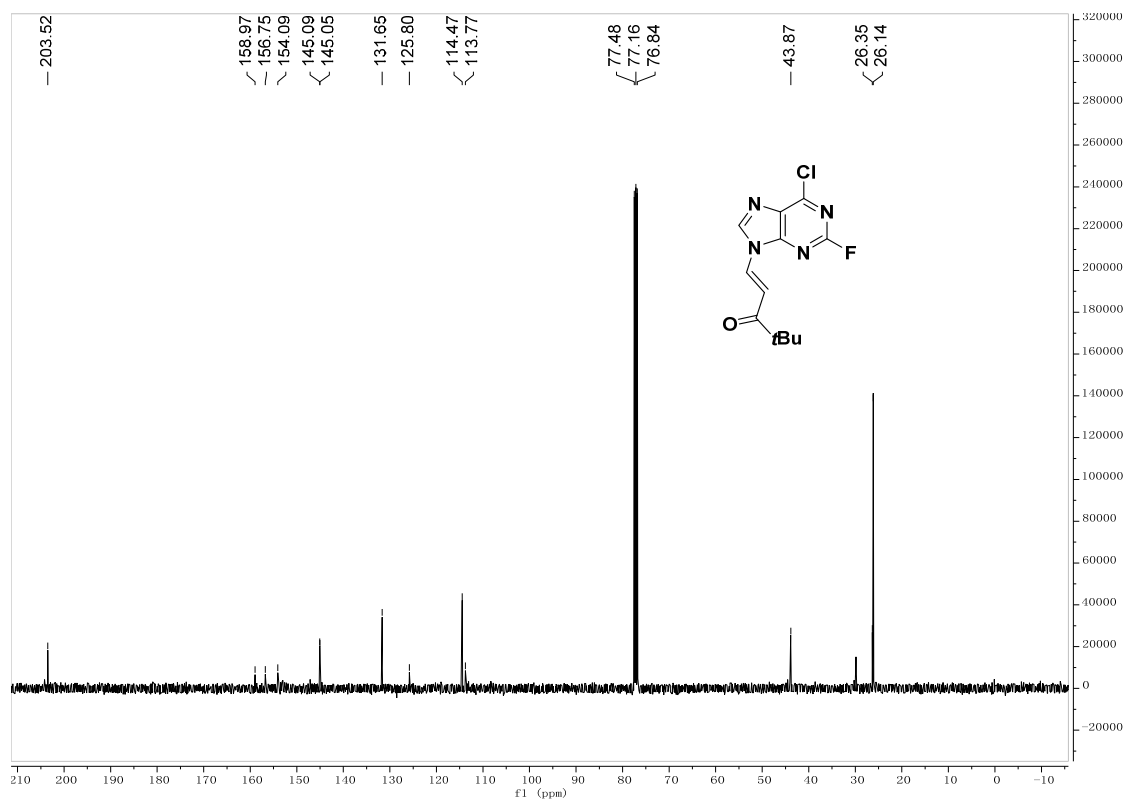
**<sup>13</sup>C NMR of 1g (100 MHz, DMSO-*d*<sub>6</sub>)**



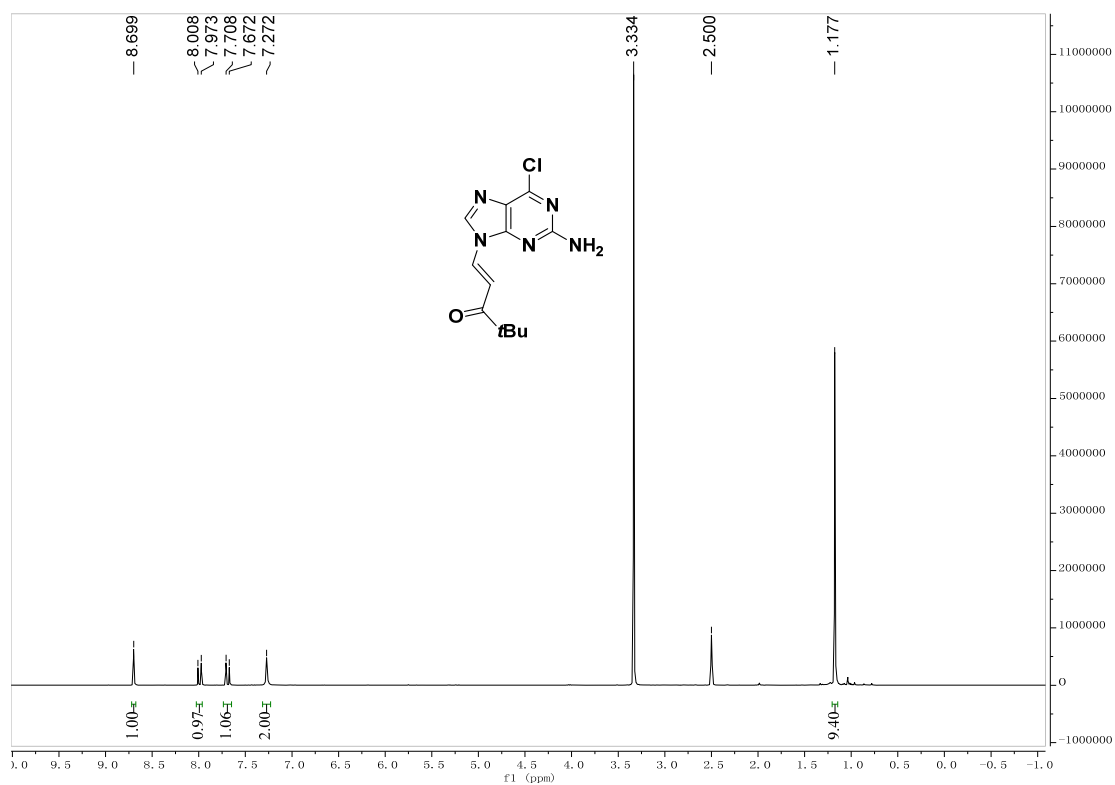
**<sup>1</sup>H NMR of 1h (400 MHz, CDCl<sub>3</sub>)**



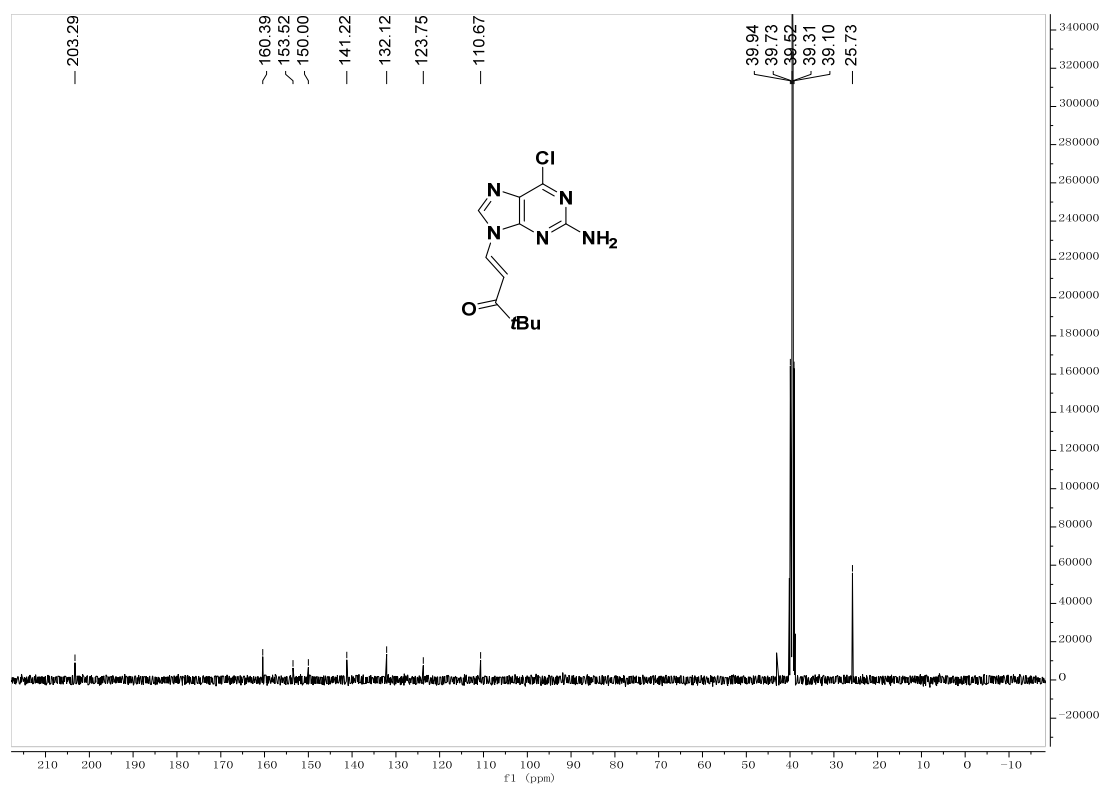
**<sup>13</sup>C NMR of 1h (100 MHz, CDCl<sub>3</sub>)**



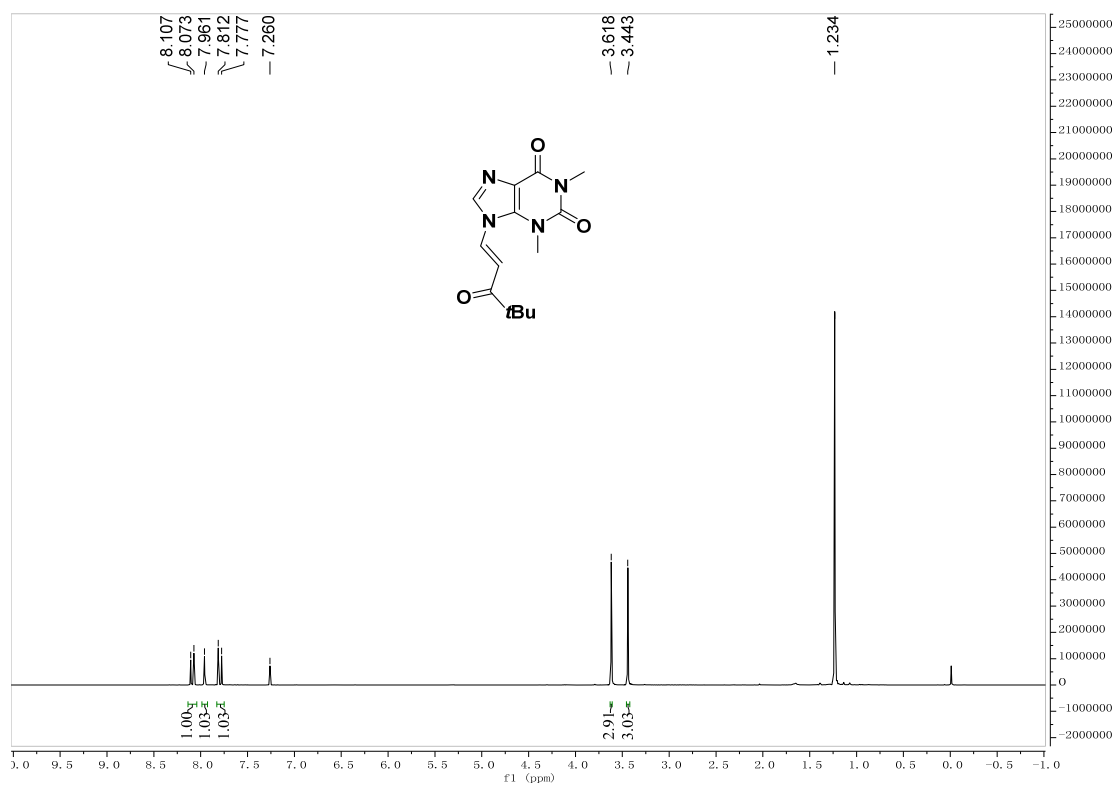
### <sup>1</sup>H NMR of 1i (400 MHz, DMSO-d<sub>6</sub>)



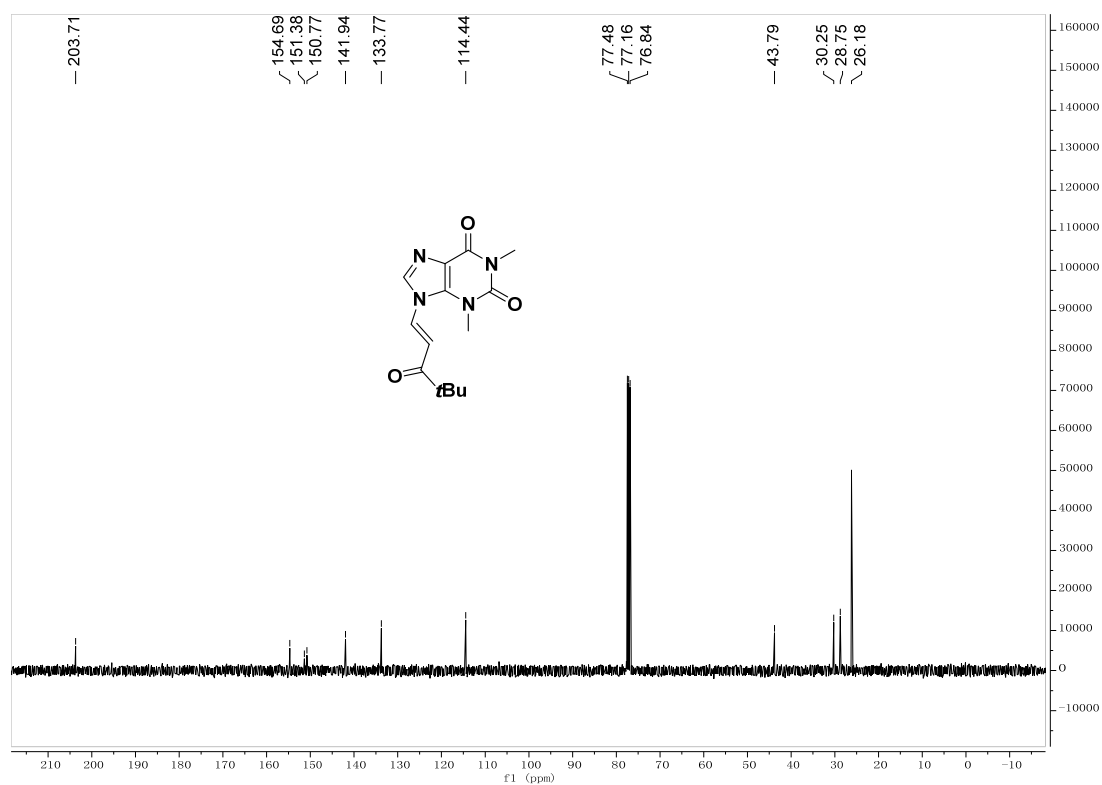
### <sup>13</sup>C NMR of 1i (100 MHz, DMSO-d<sub>6</sub>)



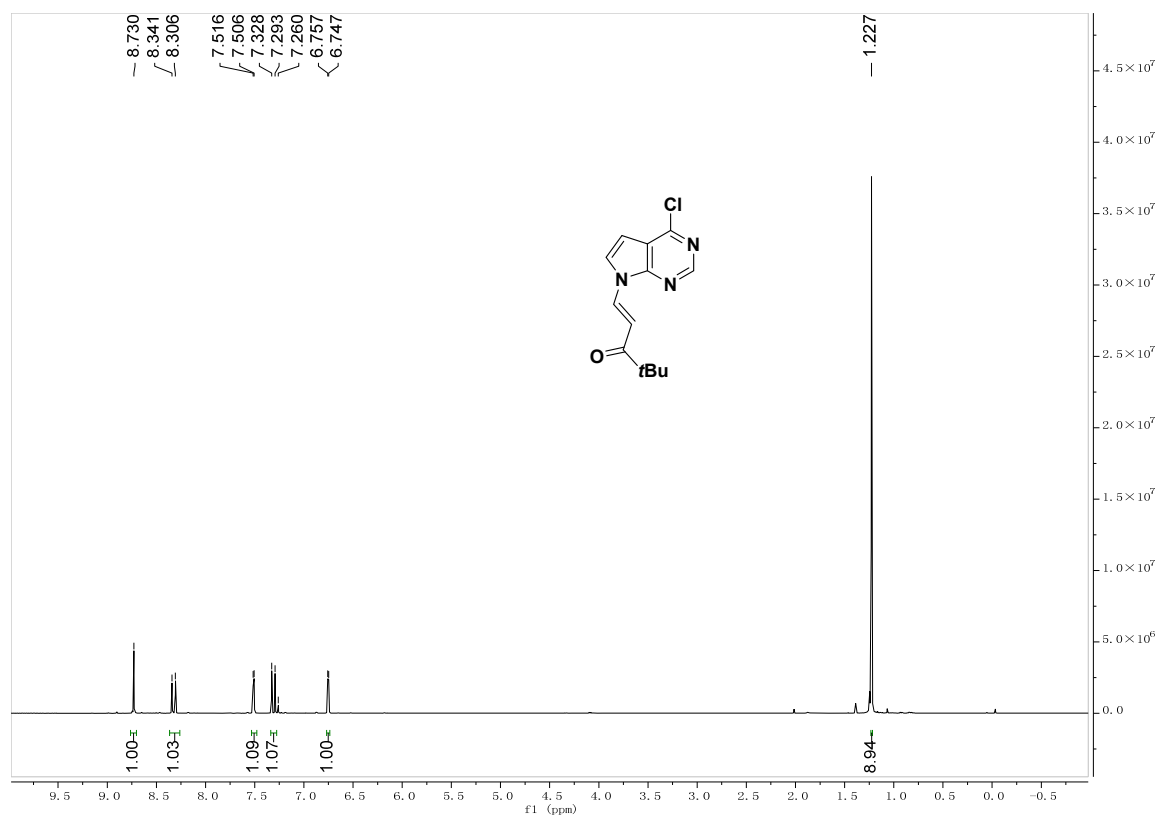
### <sup>1</sup>H NMR of 1j (400 MHz, CDCl<sub>3</sub>)



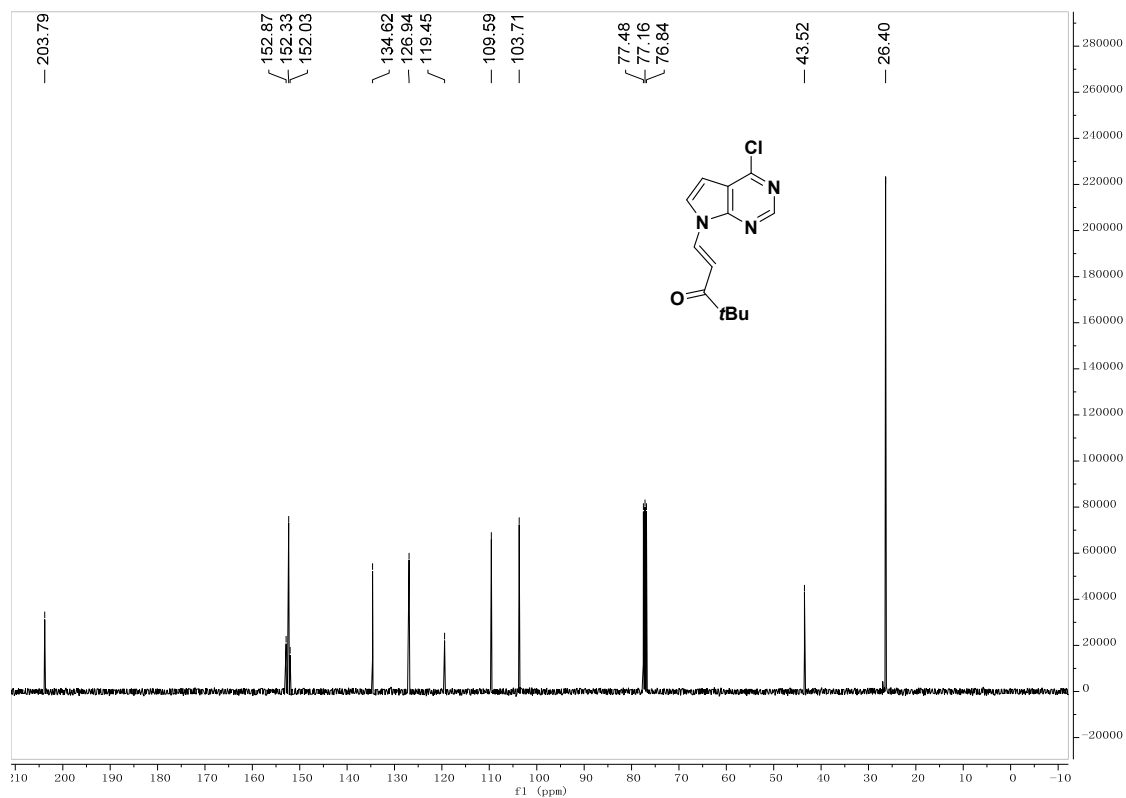
### <sup>13</sup>C NMR of 1j (100 MHz, CDCl<sub>3</sub>)



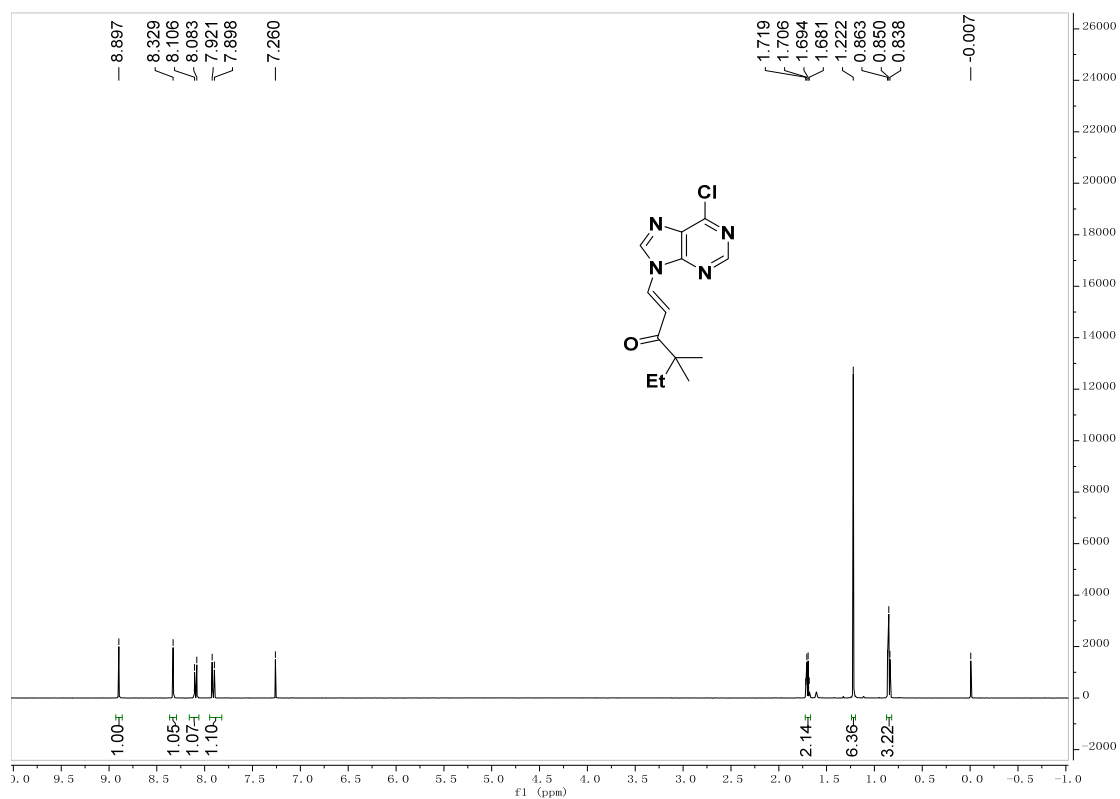
### <sup>1</sup>H NMR of 1k (400 MHz, CDCl<sub>3</sub>)



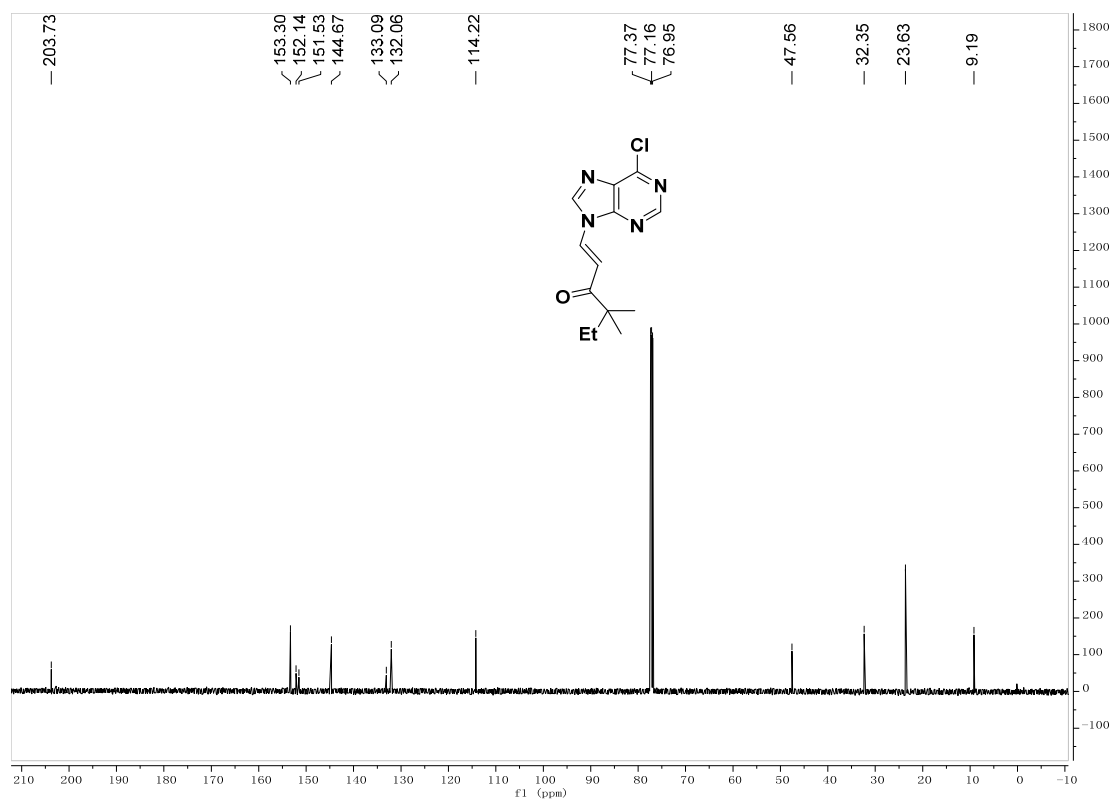
### <sup>13</sup>C NMR of 1k (100 MHz, CDCl<sub>3</sub>)



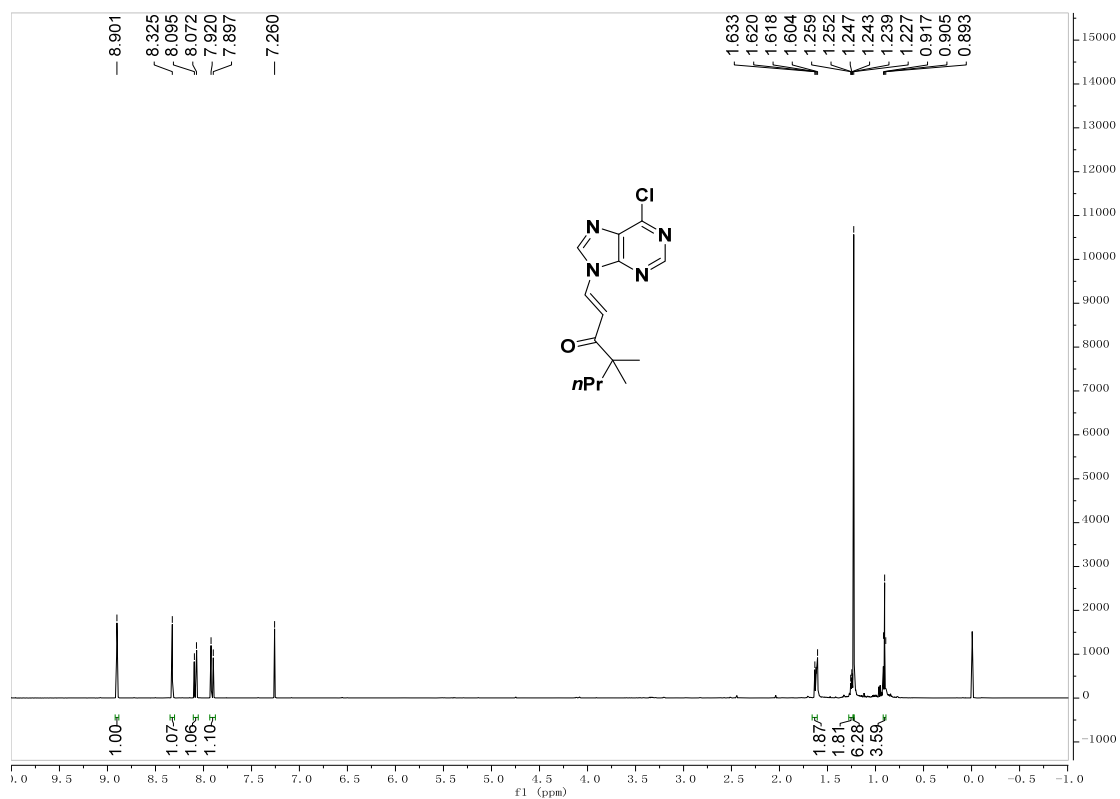
### <sup>1</sup>H NMR of 11 (600 MHz, CDCl<sub>3</sub>)



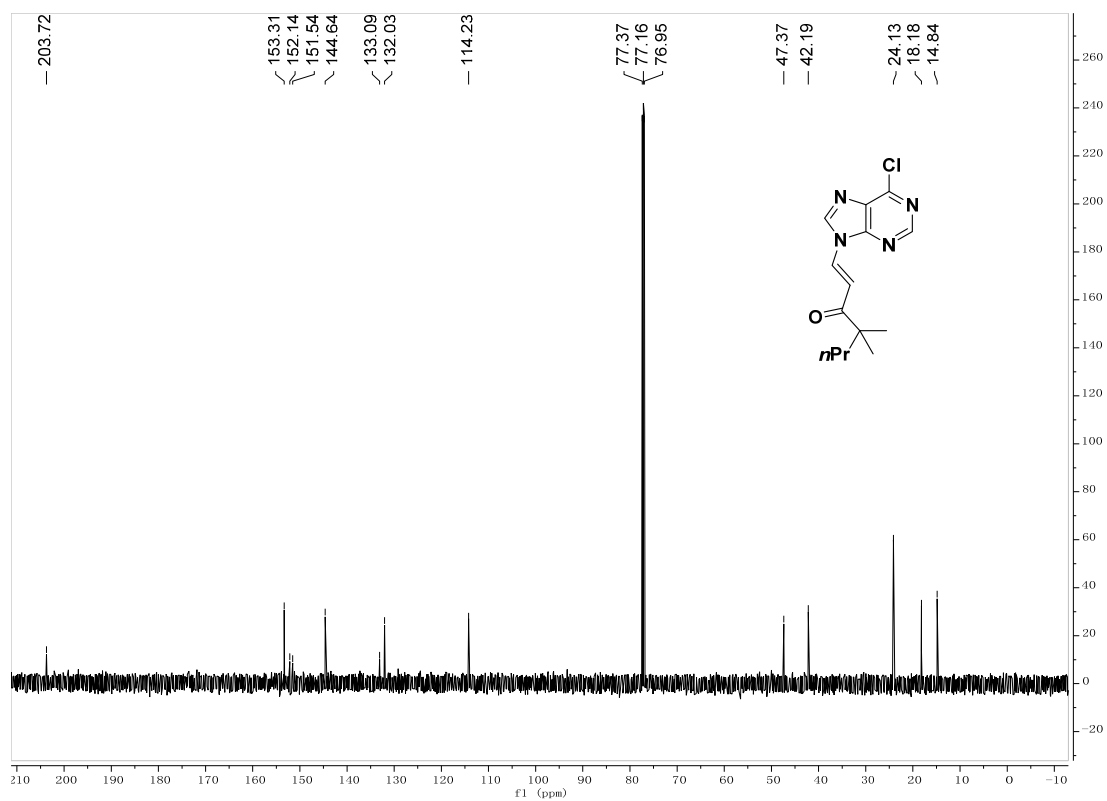
### <sup>13</sup>C NMR of 11 (150 MHz, CDCl<sub>3</sub>)



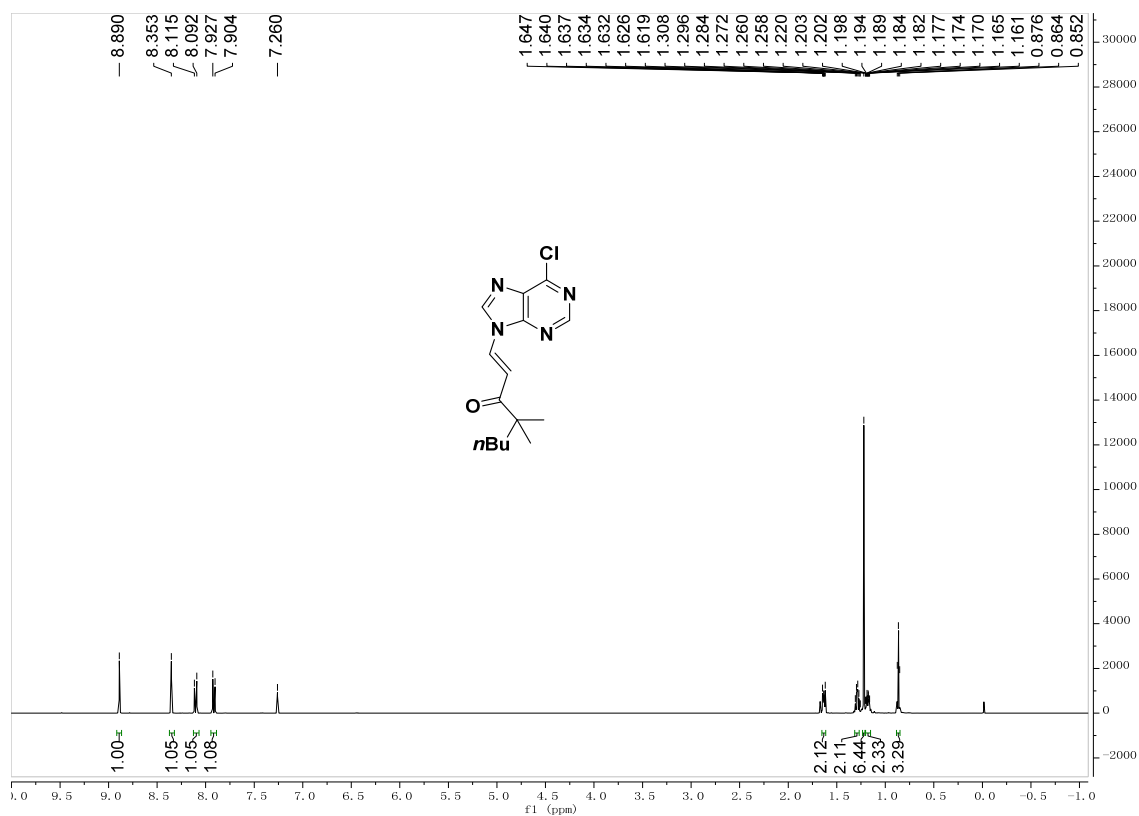
### <sup>1</sup>H NMR of 1m (600 MHz, CDCl<sub>3</sub>)



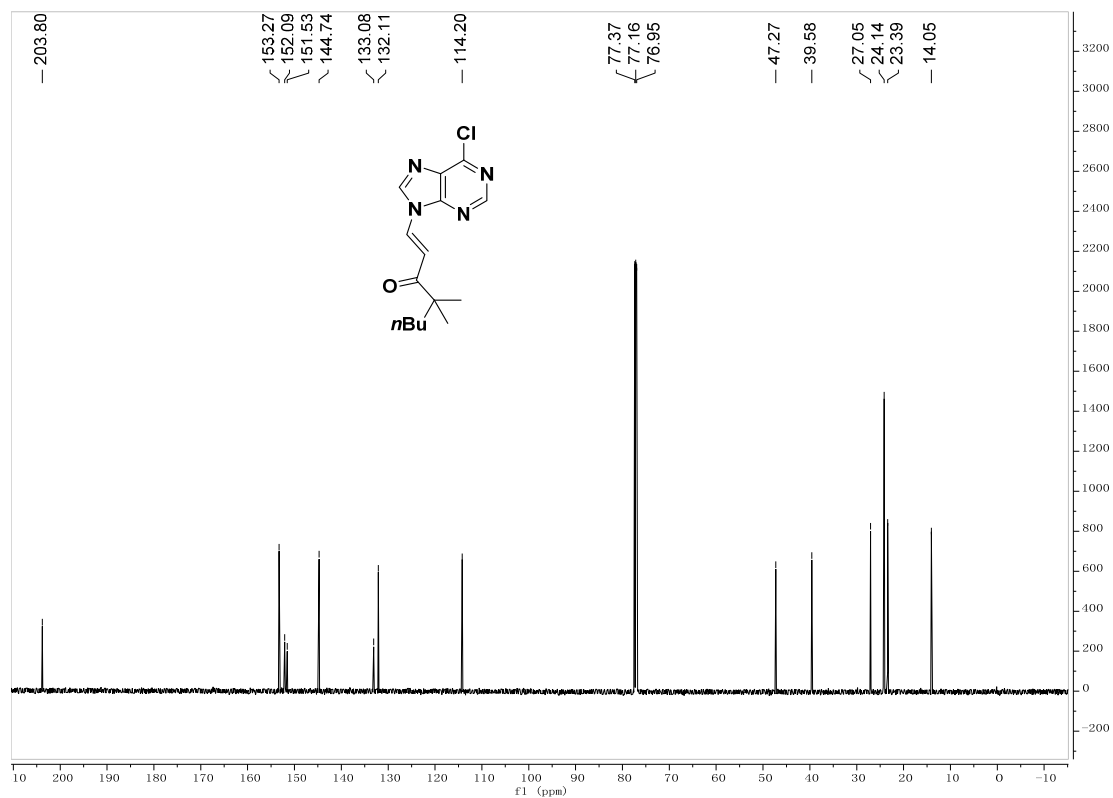
### <sup>13</sup>C NMR of 1m (150 MHz, CDCl<sub>3</sub>)



### <sup>1</sup>H NMR of 1n (600 MHz, CDCl<sub>3</sub>)

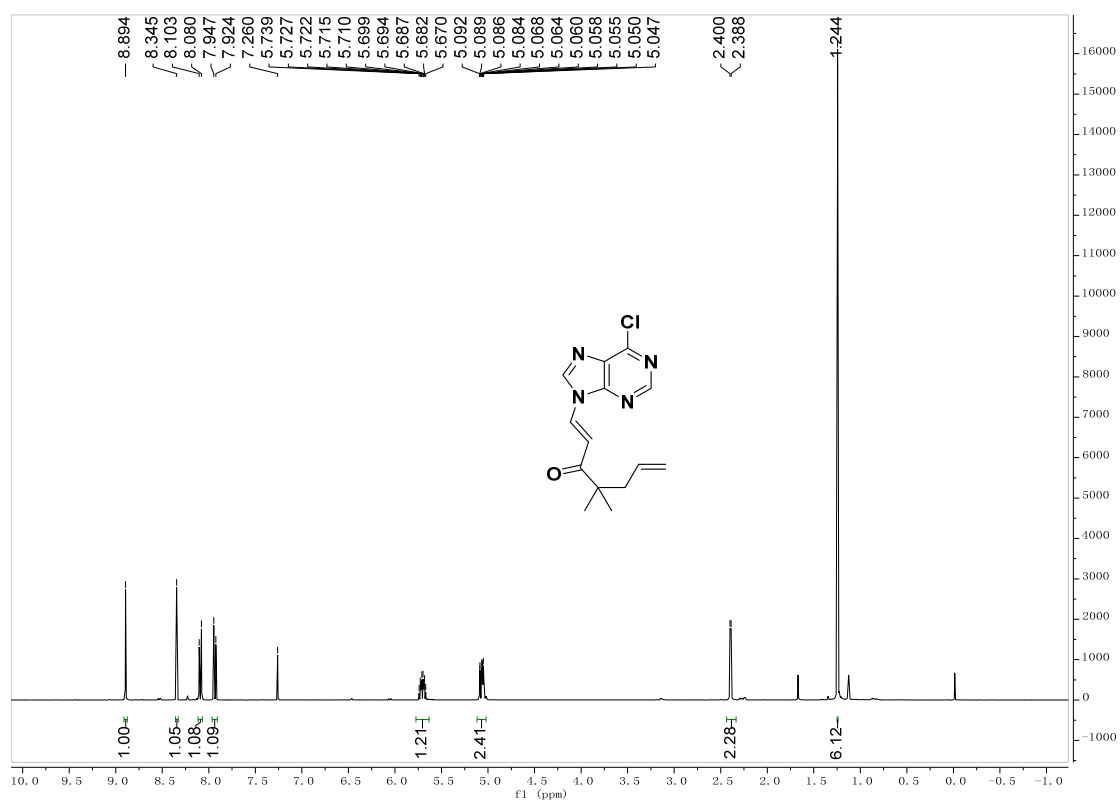


### <sup>13</sup>C NMR of 1n (150 MHz, CDCl<sub>3</sub>)

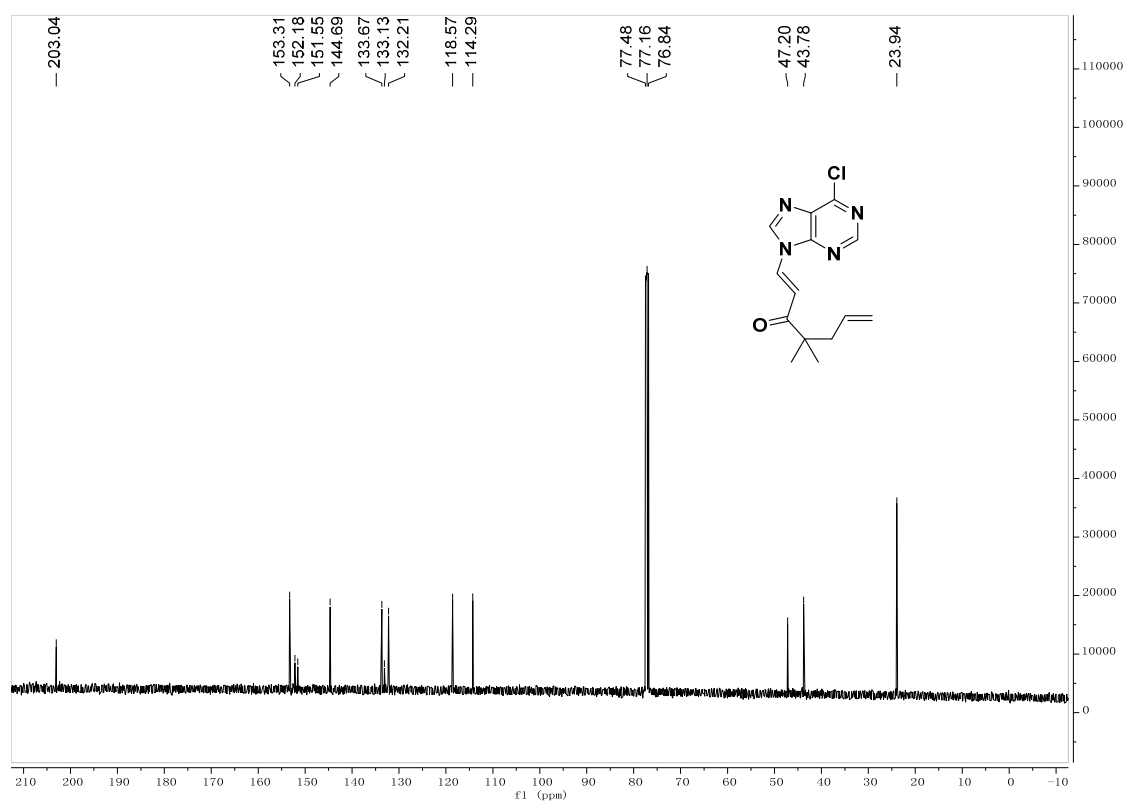




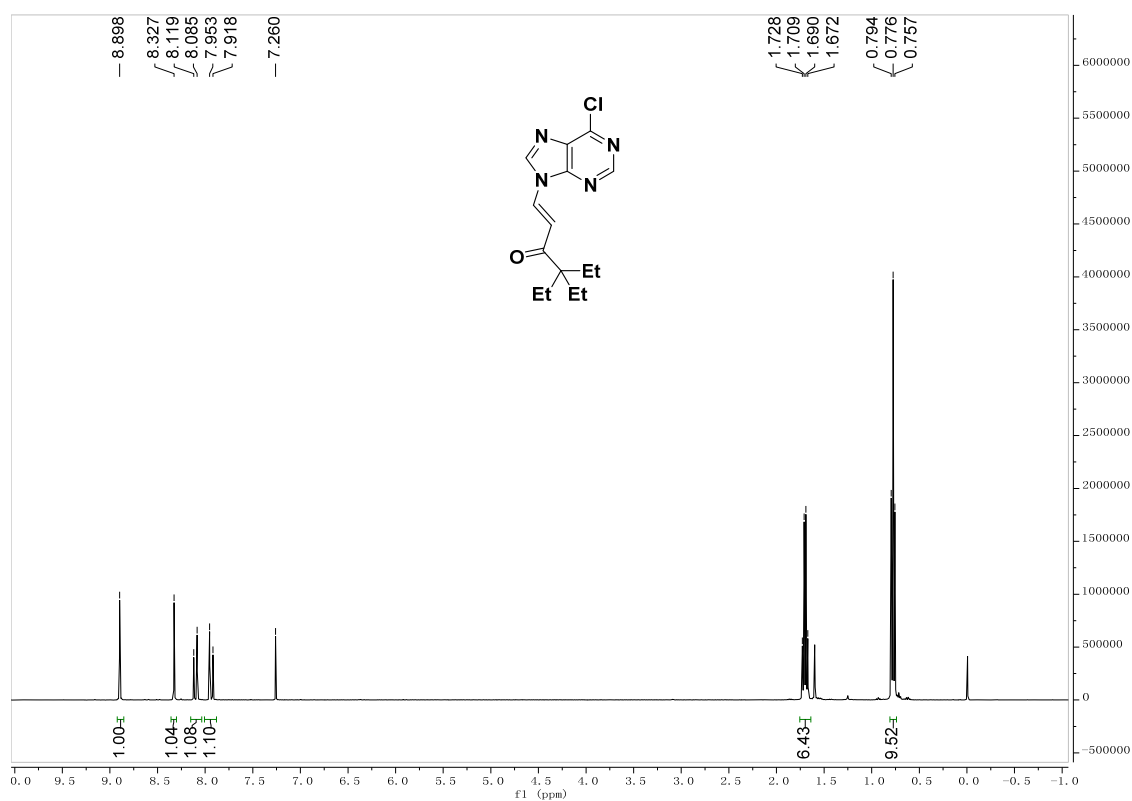
### <sup>1</sup>H NMR of **1o** (600 MHz, CDCl<sub>3</sub>)



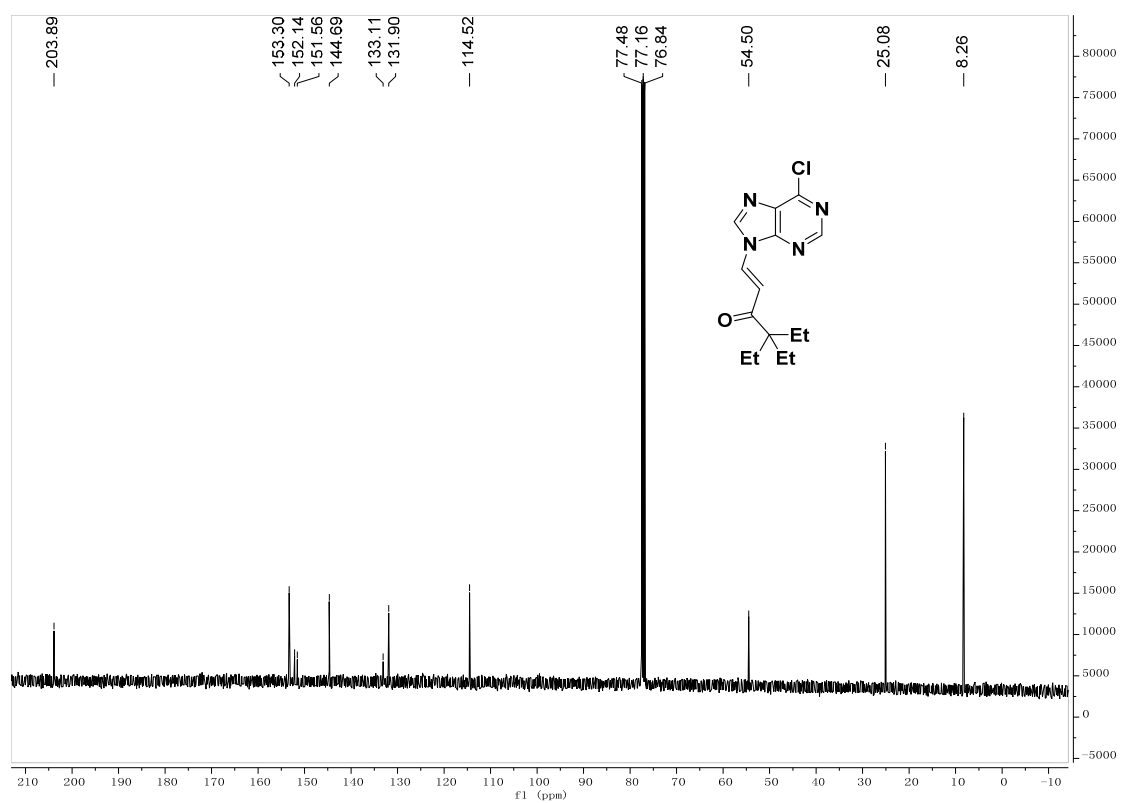
### <sup>13</sup>C NMR of **1o** (150 MHz, CDCl<sub>3</sub>)



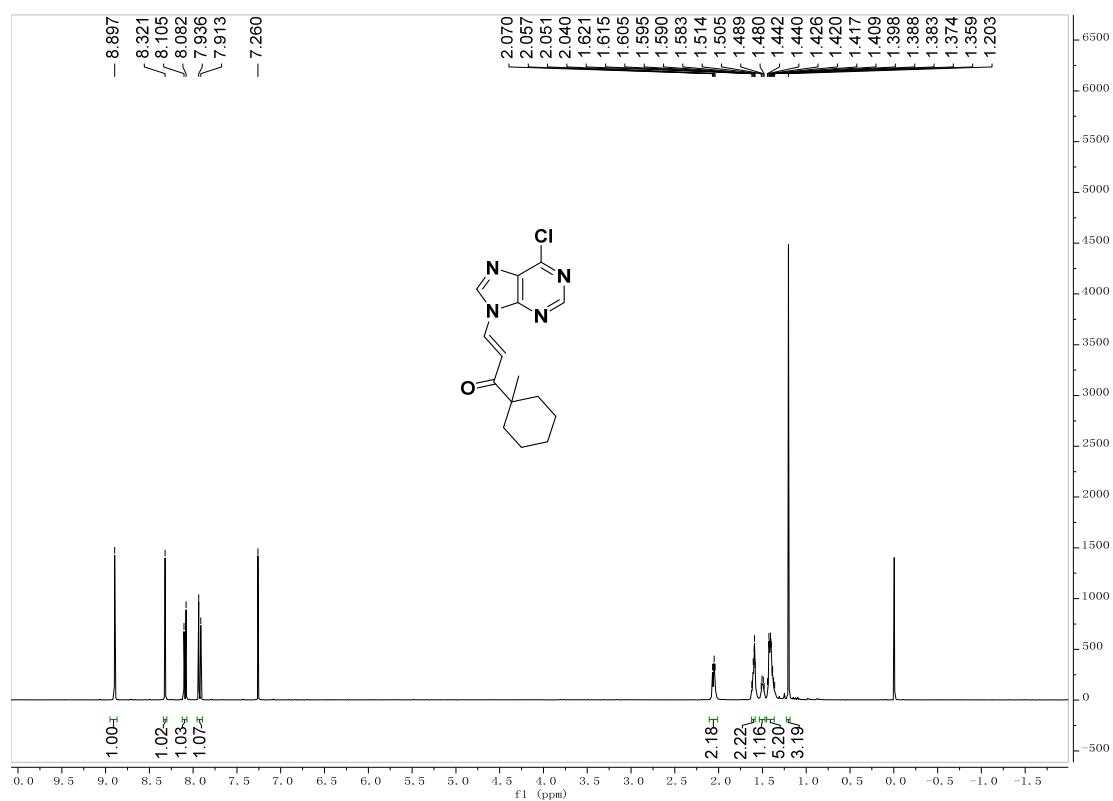
### <sup>1</sup>H NMR of 1p (400 MHz, CDCl<sub>3</sub>)



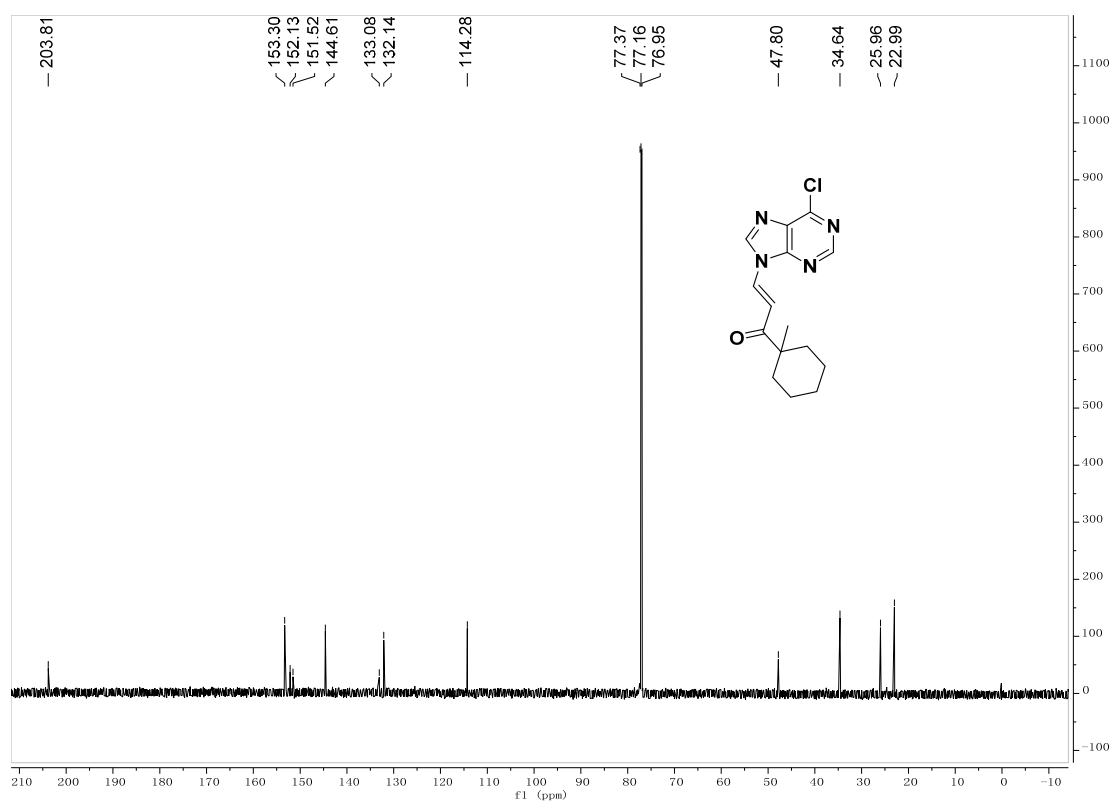
### <sup>13</sup>C NMR of 1p (100 MHz, CDCl<sub>3</sub>)



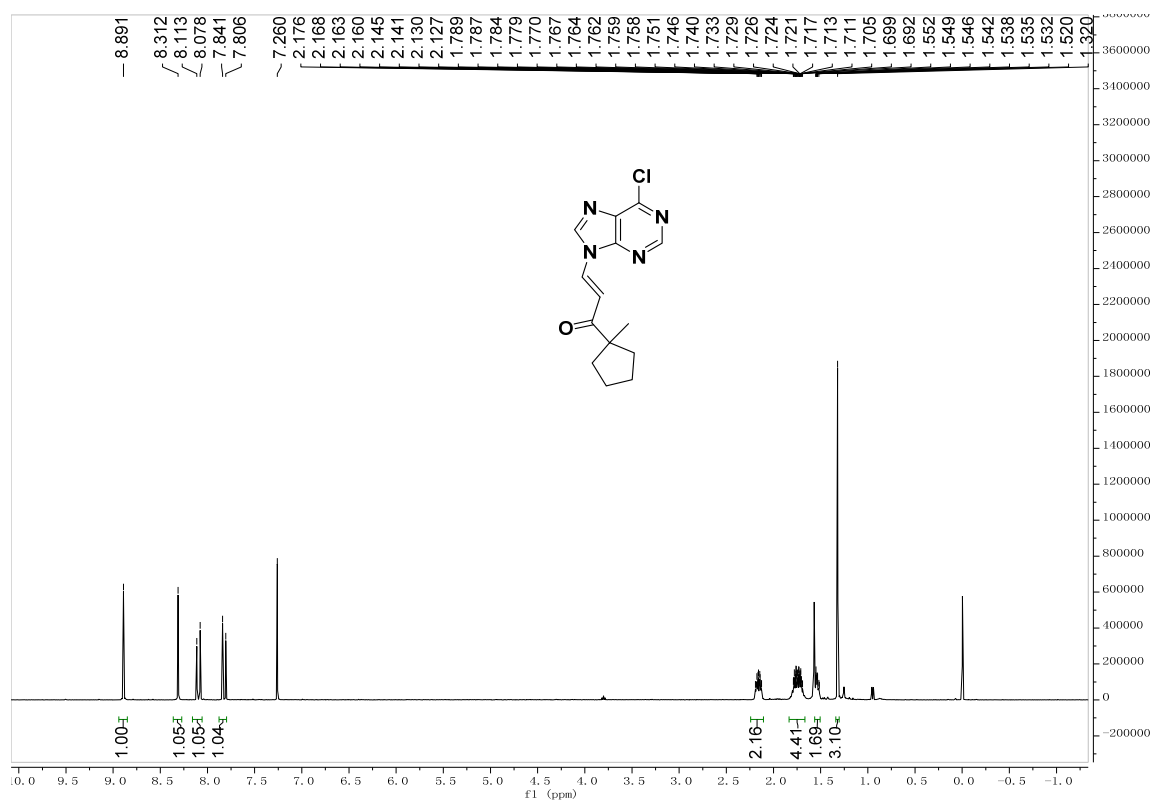
### <sup>1</sup>H NMR of 1q (600 MHz, CDCl<sub>3</sub>)



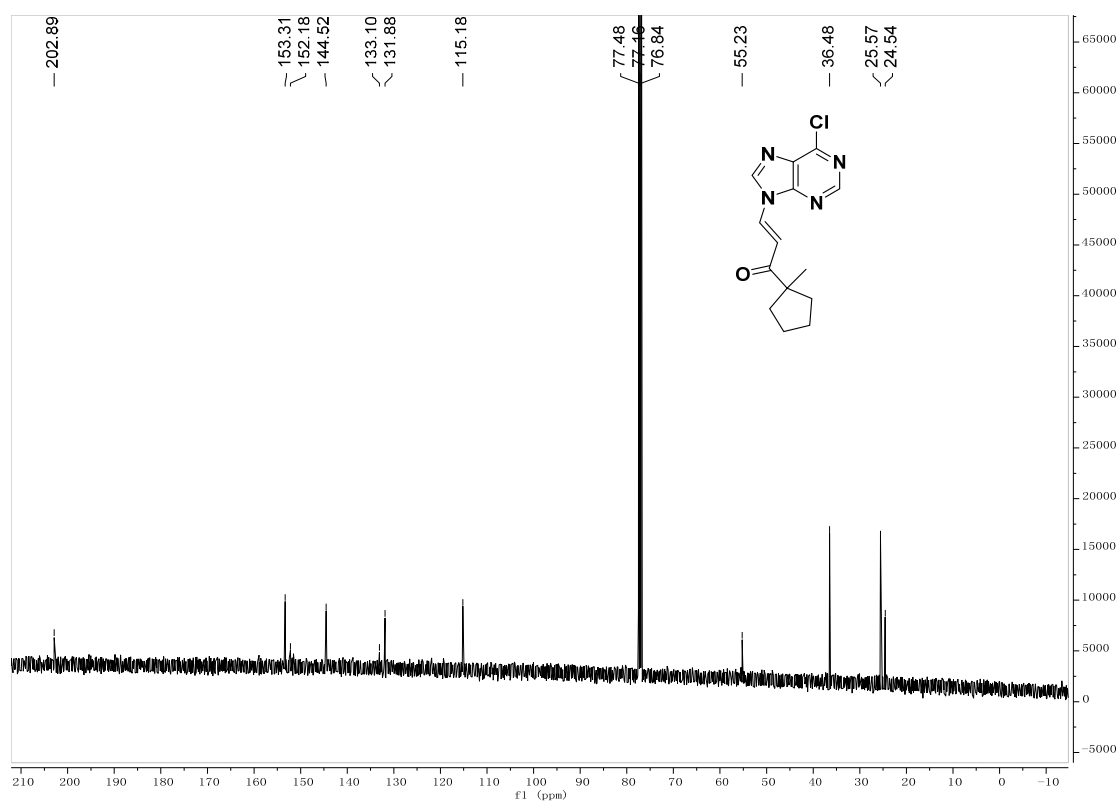
### <sup>13</sup>C NMR of 1q (150 MHz, CDCl<sub>3</sub>)



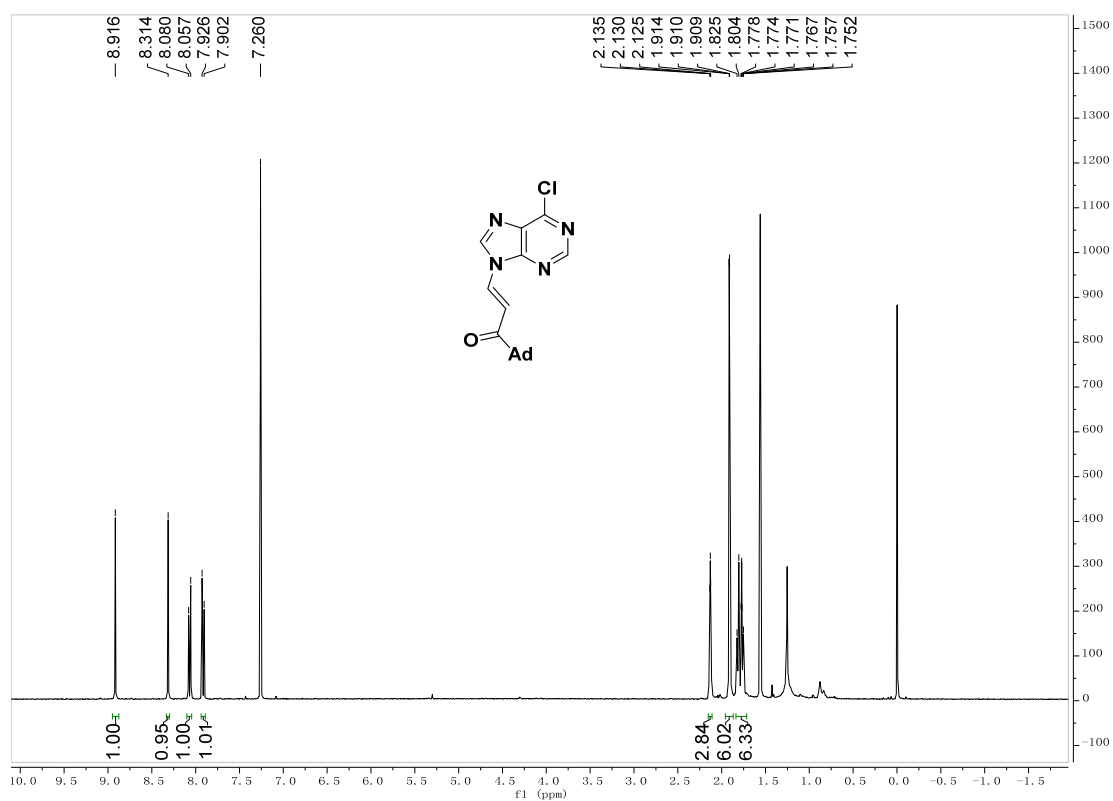
### <sup>1</sup>H NMR of 1r (400 MHz, CDCl<sub>3</sub>)



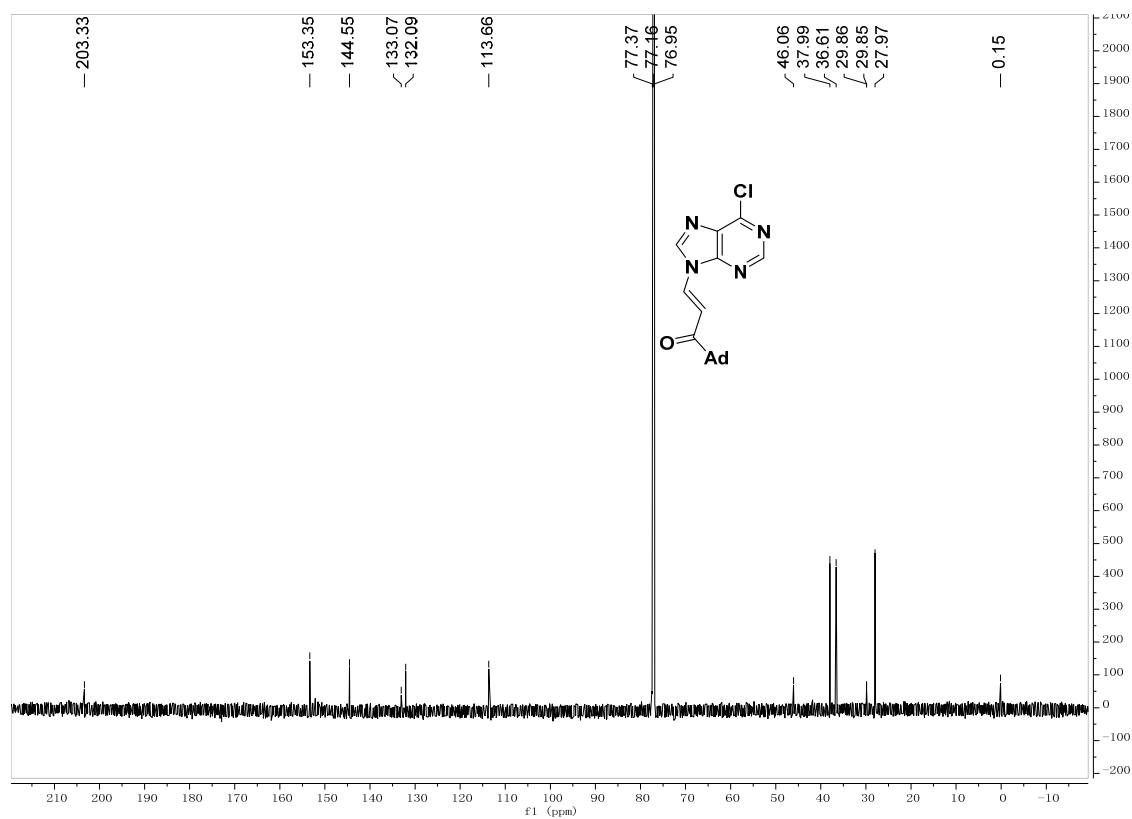
### <sup>13</sup>C NMR of 1r (100 MHz, CDCl<sub>3</sub>)



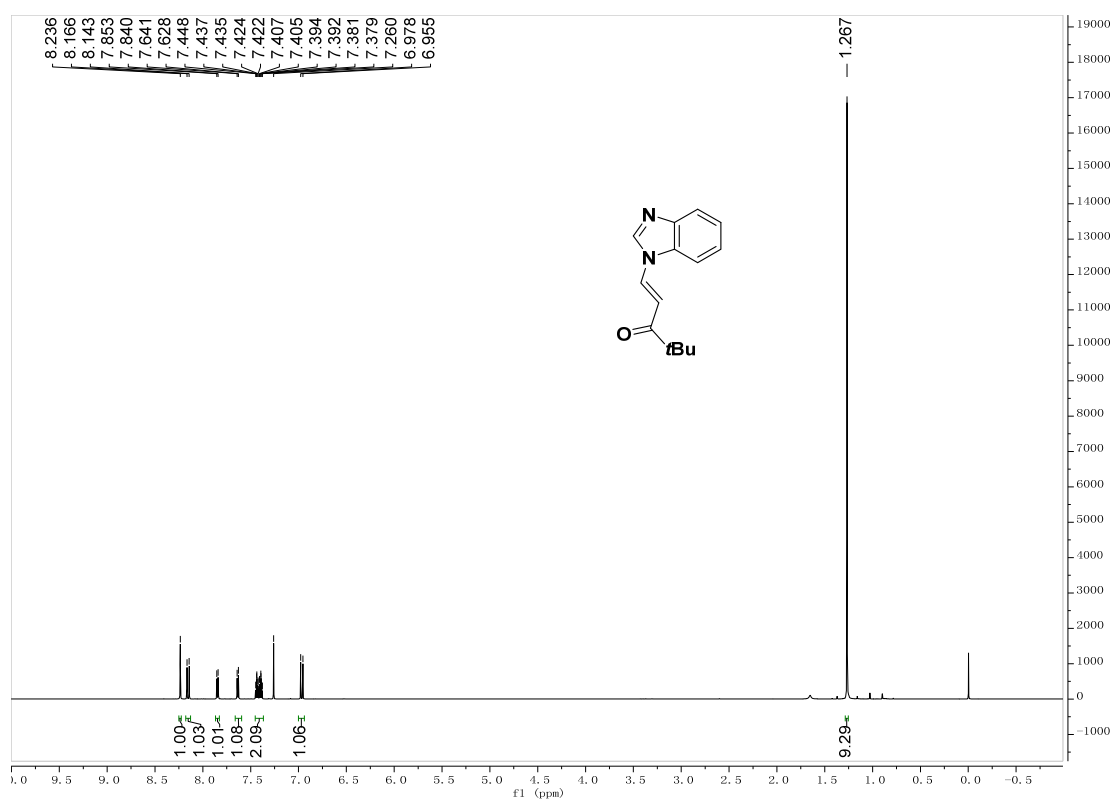
**<sup>1</sup>H NMR of 1s (600 MHz, CDCl<sub>3</sub>)**



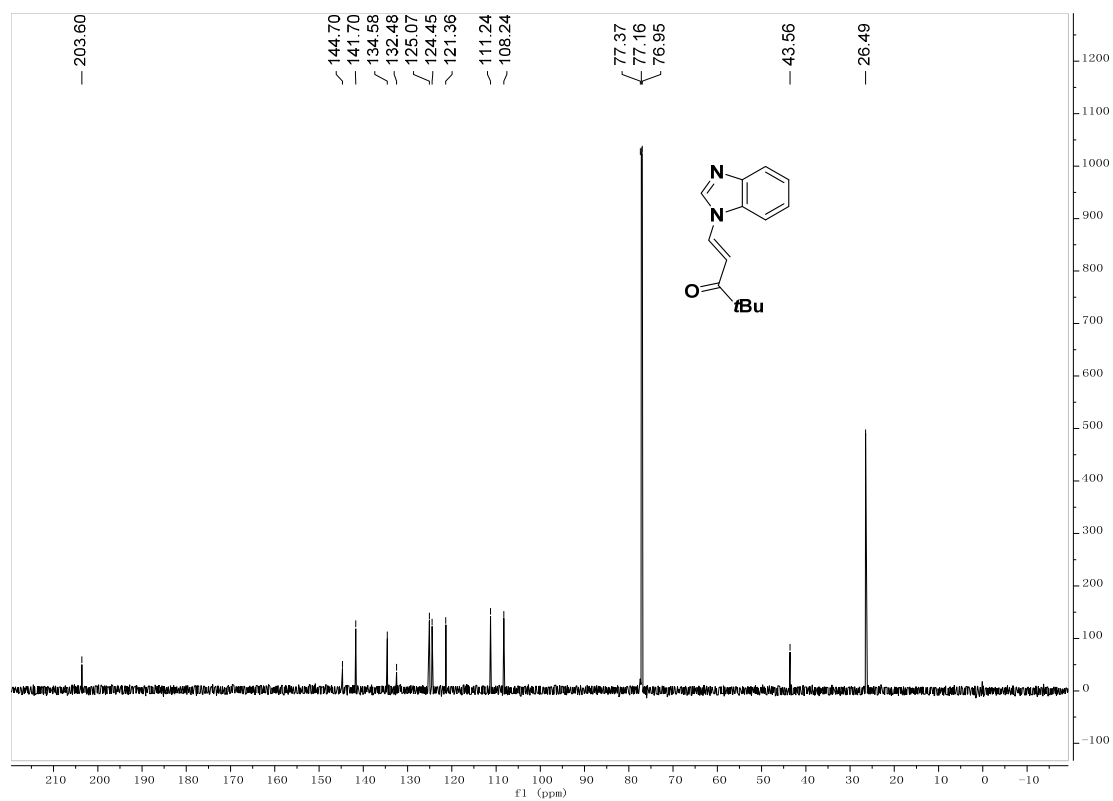
**<sup>13</sup>C NMR of 1s (150 MHz, CDCl<sub>3</sub>)**



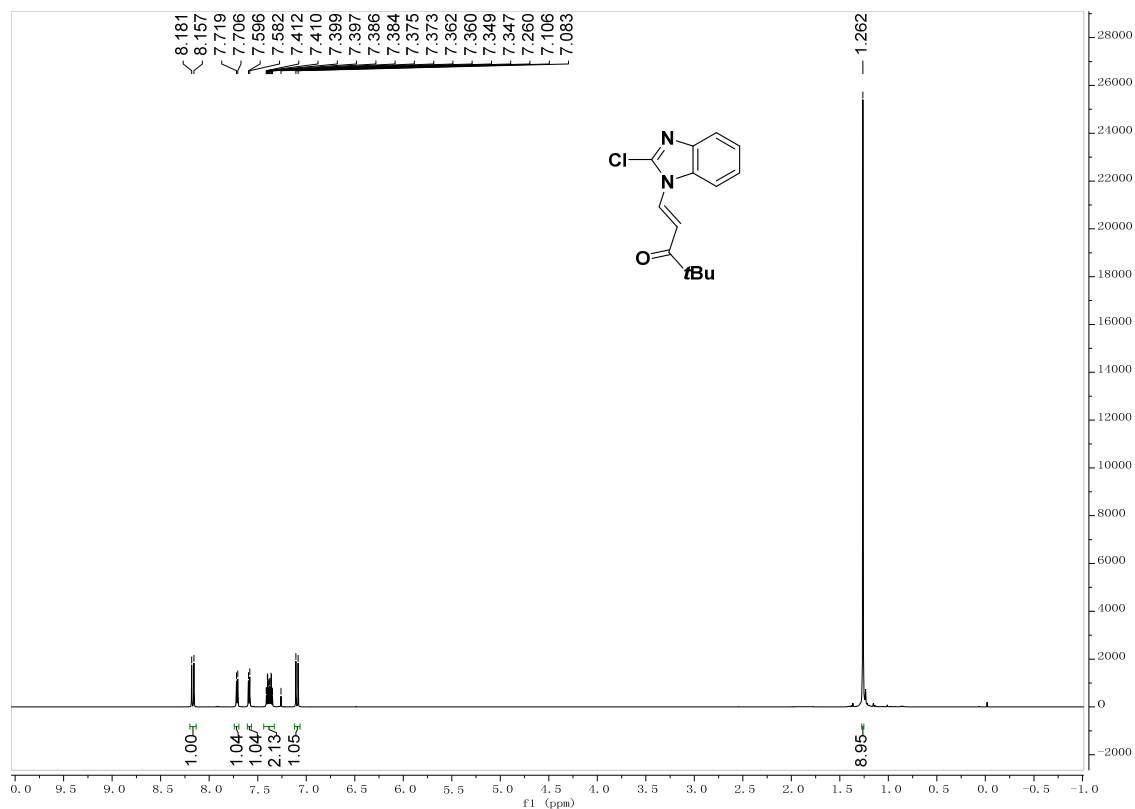
### <sup>1</sup>H NMR of 1t (600 MHz, CDCl<sub>3</sub>)



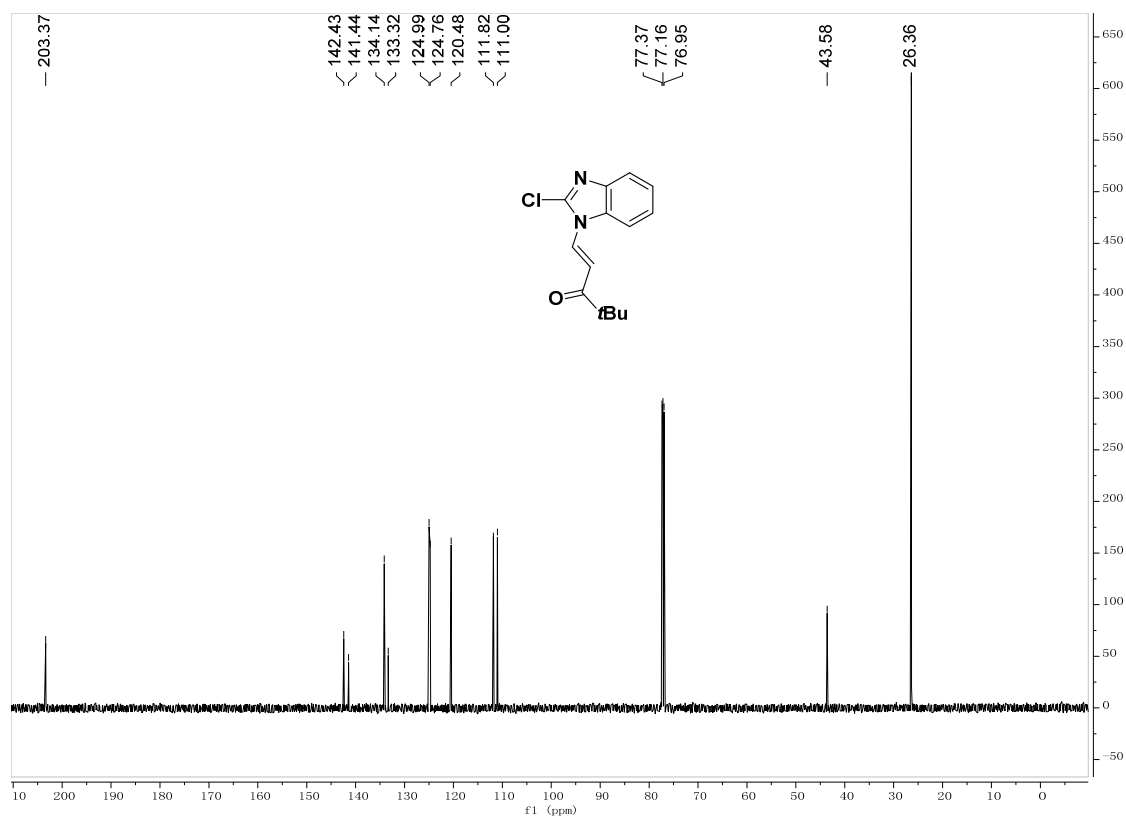
### <sup>13</sup>C NMR of 1t (150 MHz, CDCl<sub>3</sub>)



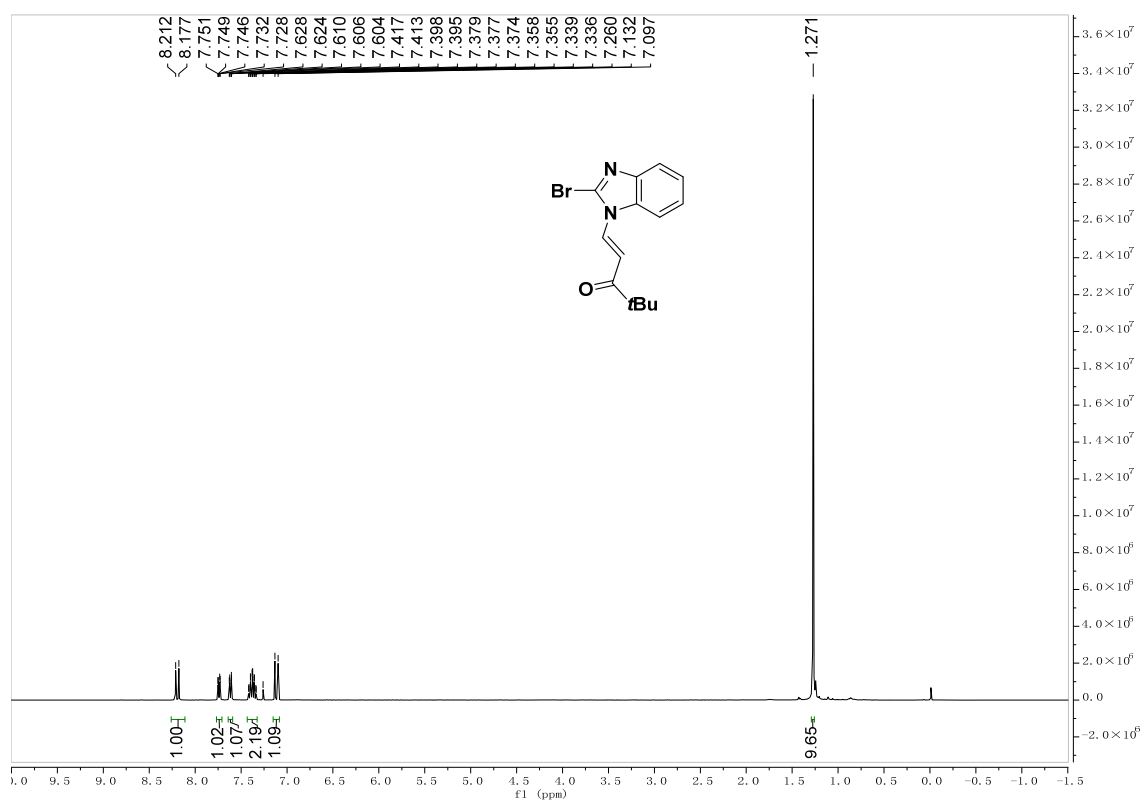
### <sup>1</sup>H NMR of **1u** (600 MHz, CDCl<sub>3</sub>)



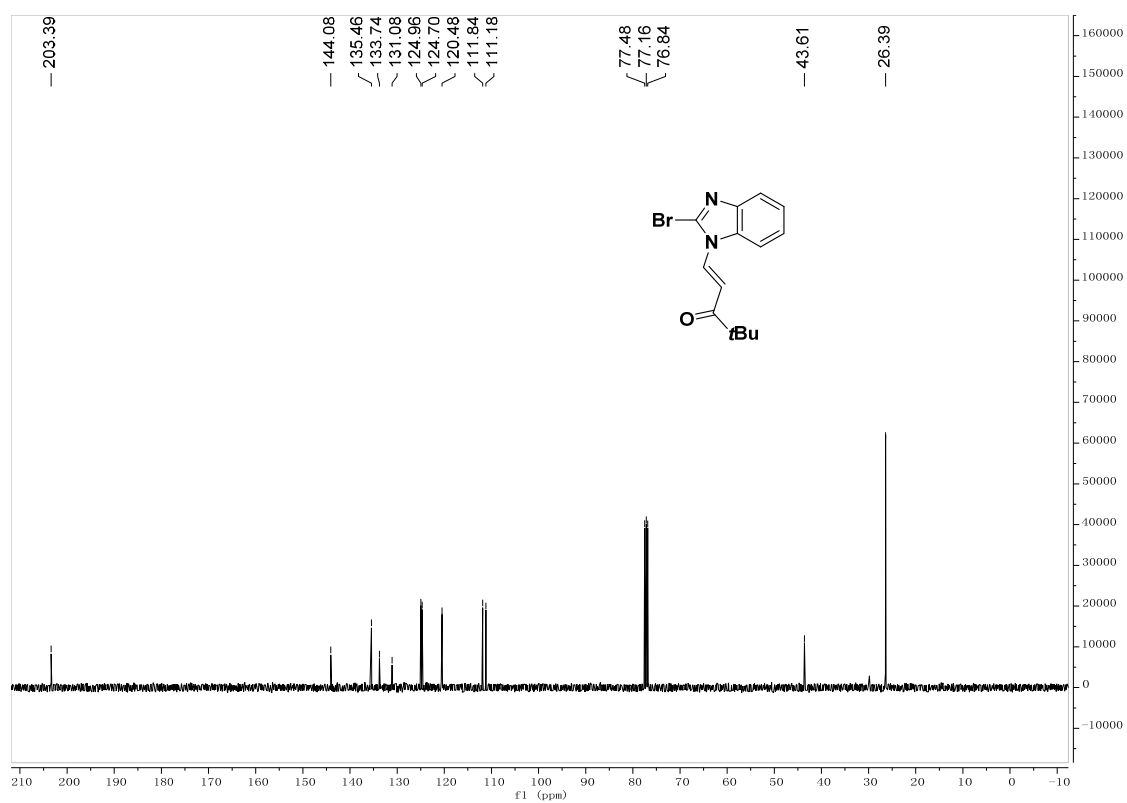
### <sup>13</sup>C NMR of **1u** (150 MHz, CDCl<sub>3</sub>)



### <sup>1</sup>H NMR of 1v (400 MHz, CDCl<sub>3</sub>)

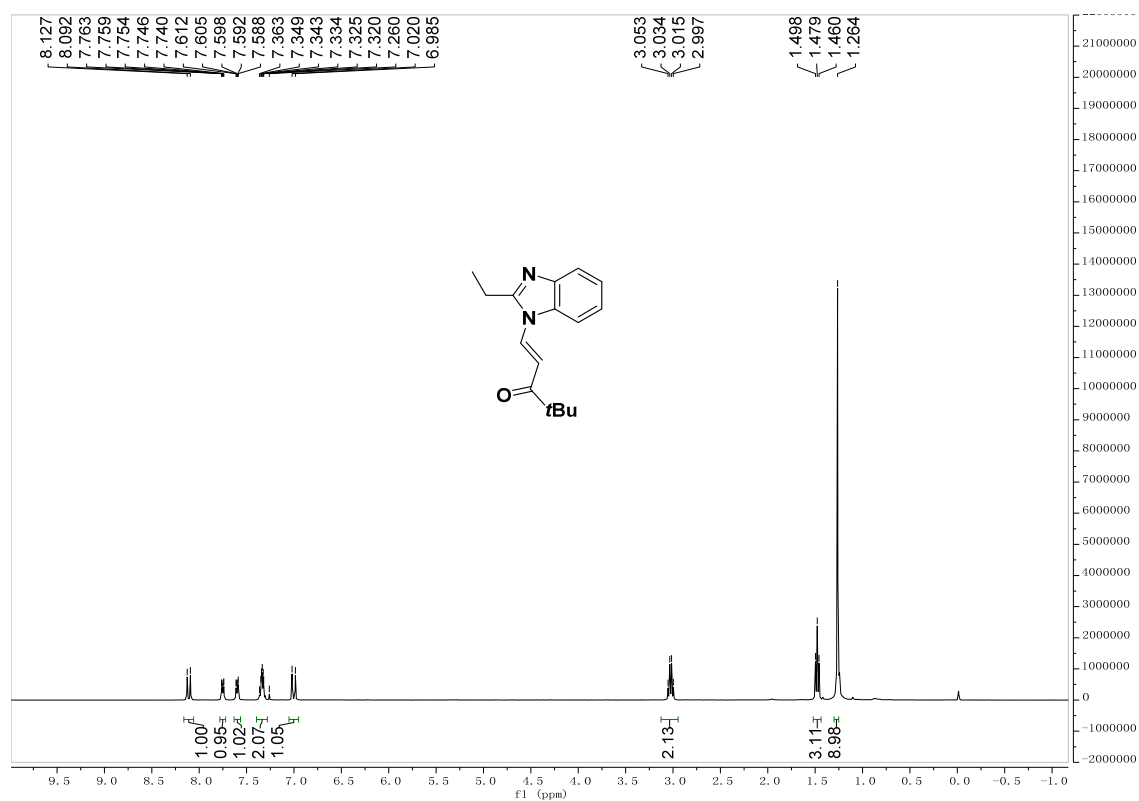


### <sup>13</sup>C NMR of 1v (100 MHz, CDCl<sub>3</sub>)

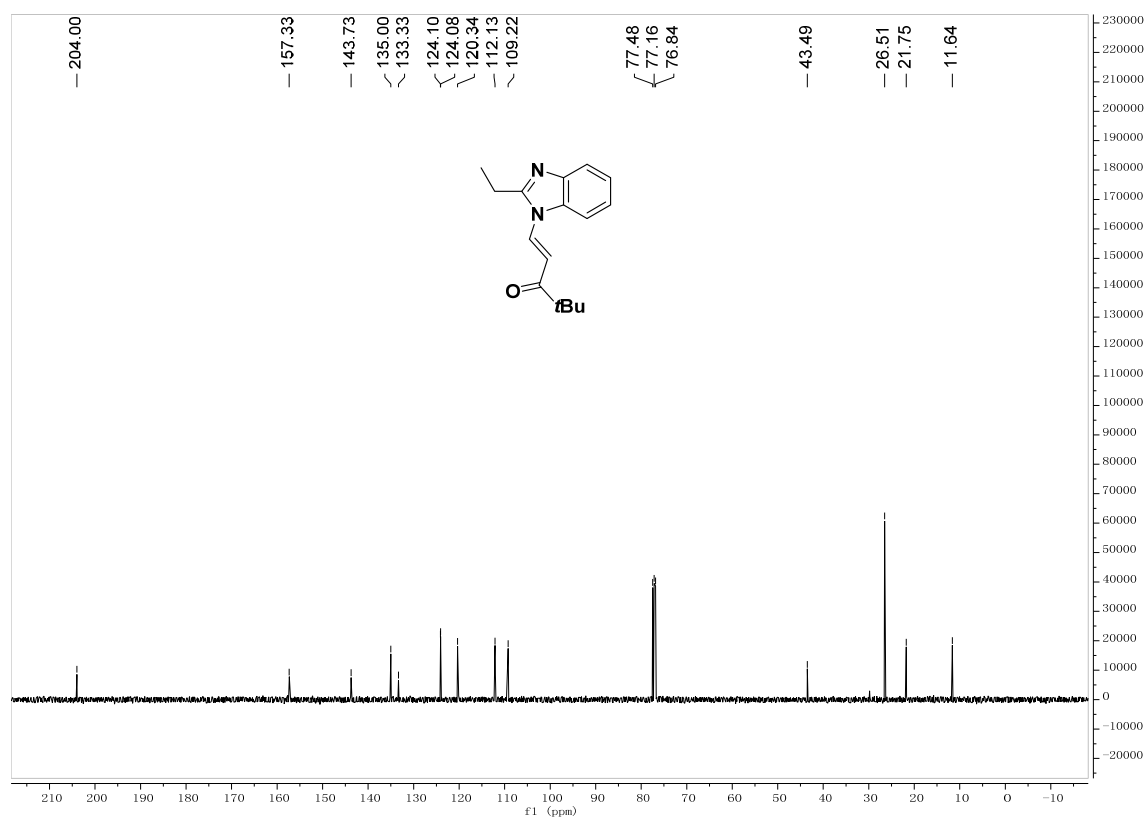




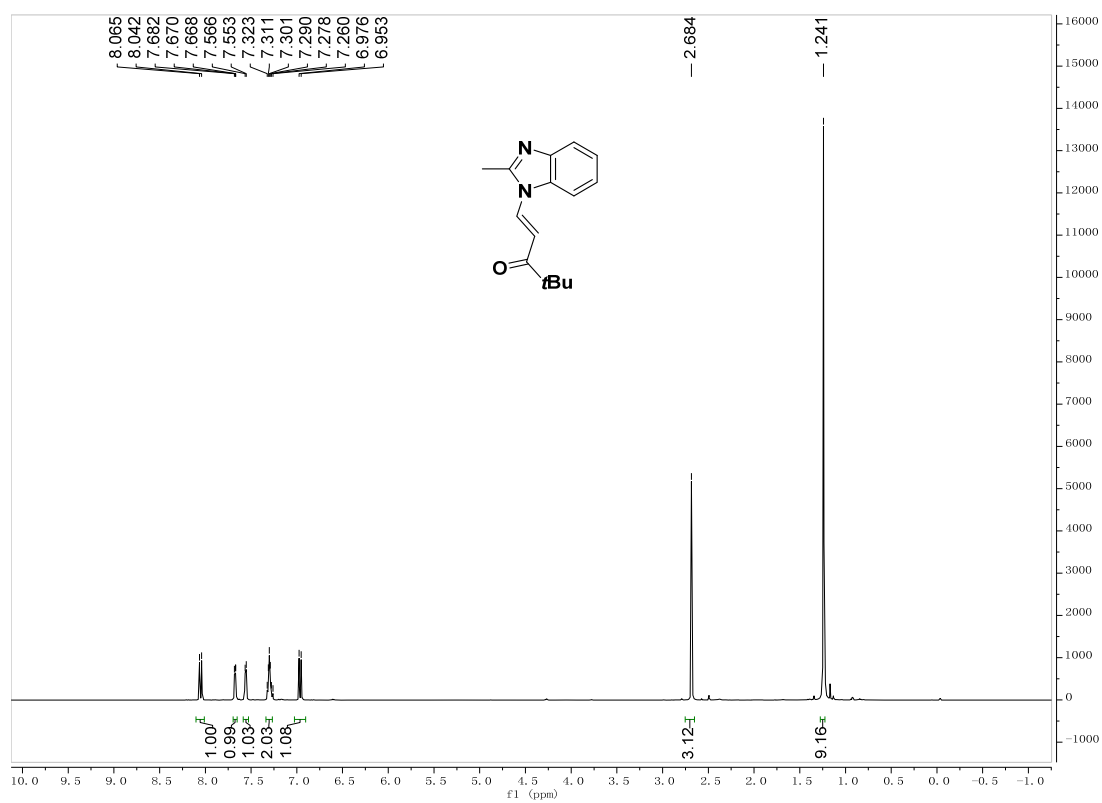
**<sup>1</sup>H NMR of 1w (400 MHz, CDCl<sub>3</sub>)**



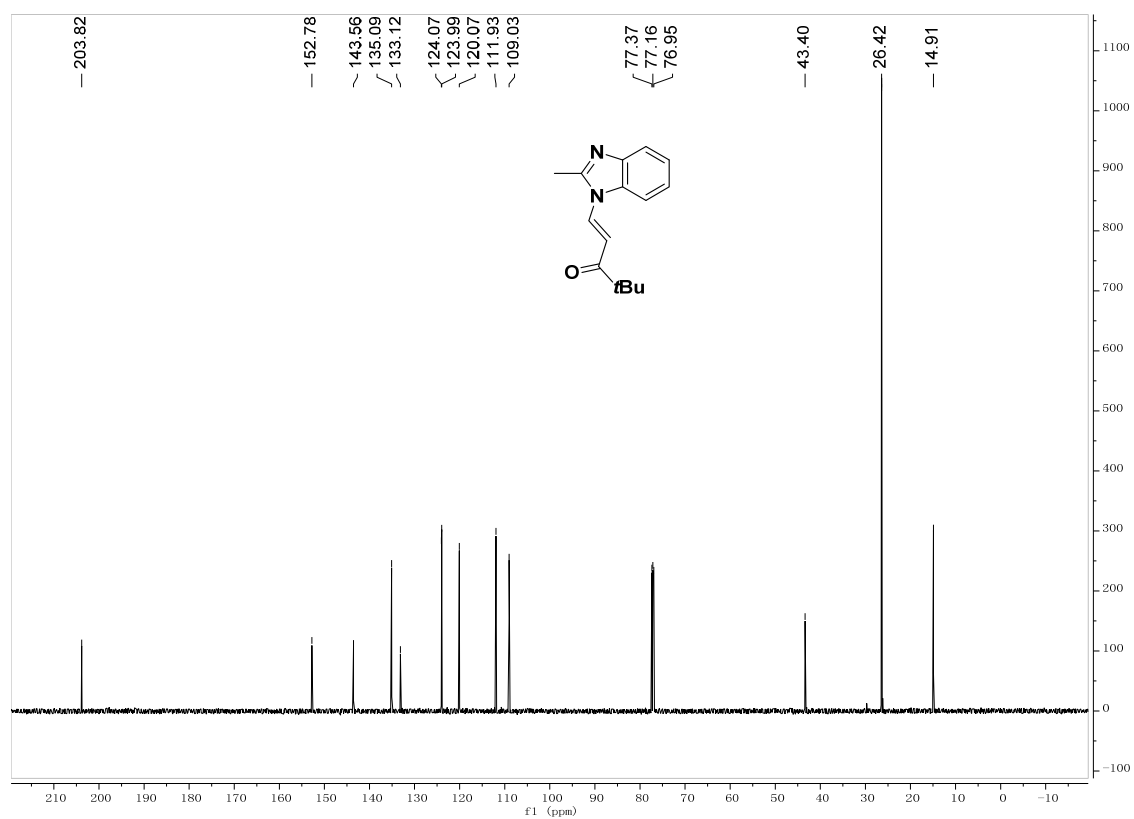
**<sup>13</sup>C NMR of 1w (100 MHz, CDCl<sub>3</sub>)**



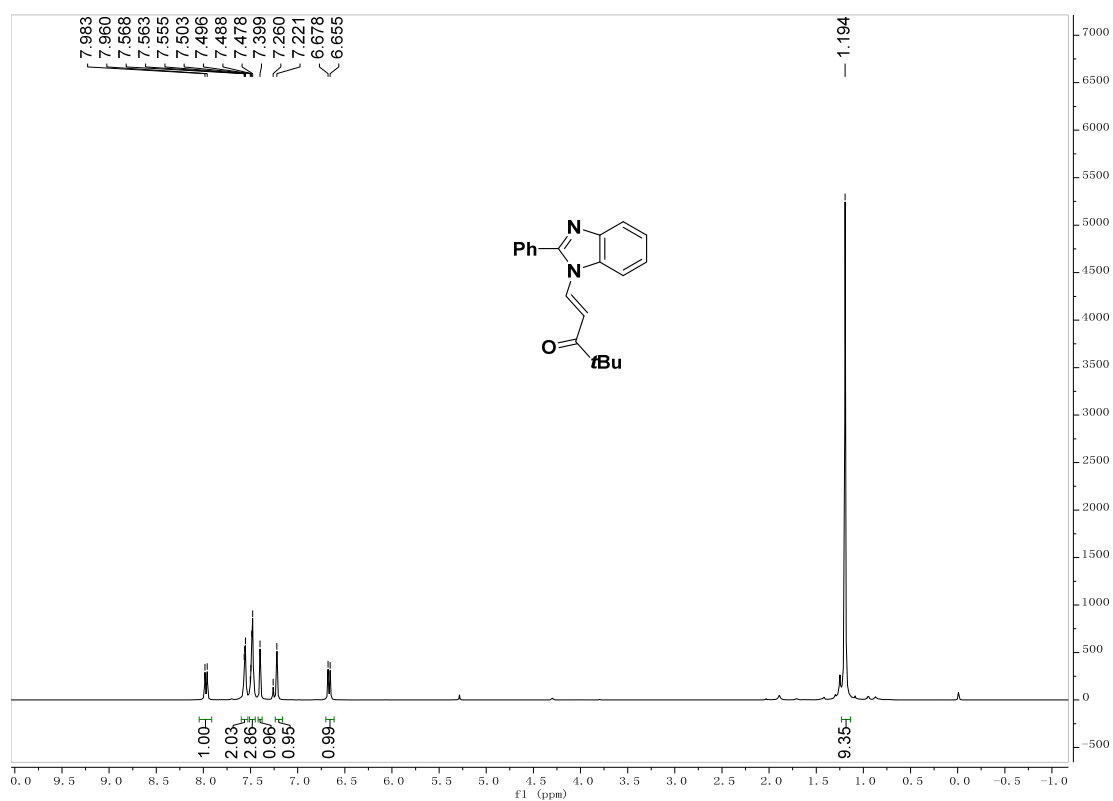
### <sup>1</sup>H NMR of 1x (600 MHz, CDCl<sub>3</sub>)



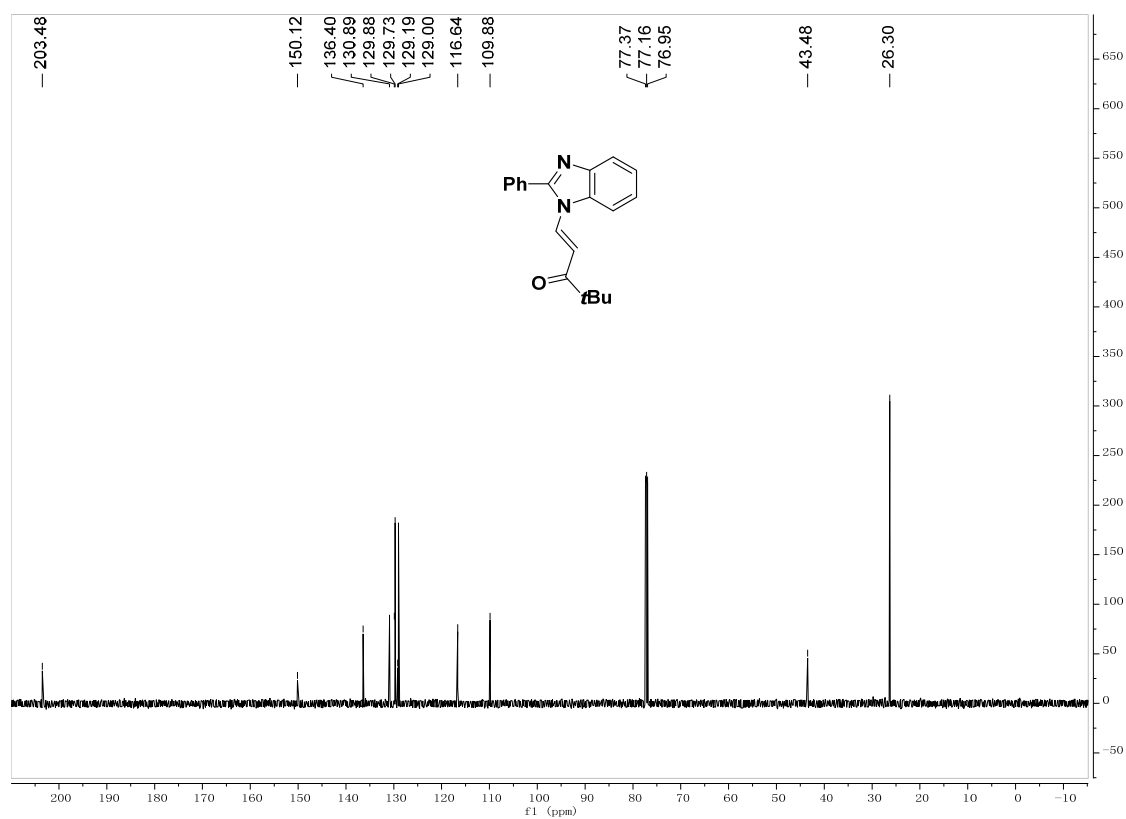
### <sup>13</sup>C NMR of 1x (150 MHz, CDCl<sub>3</sub>)



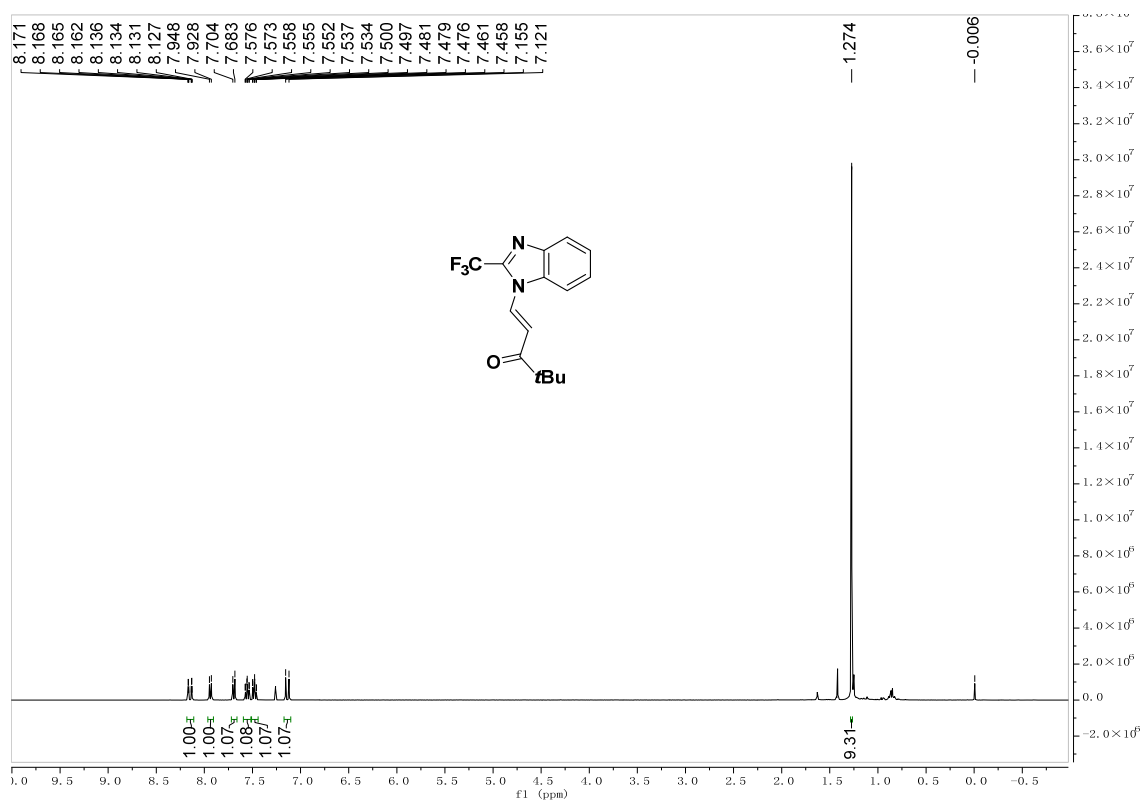
**<sup>1</sup>H NMR of 1y (600 MHz, CDCl<sub>3</sub>)**



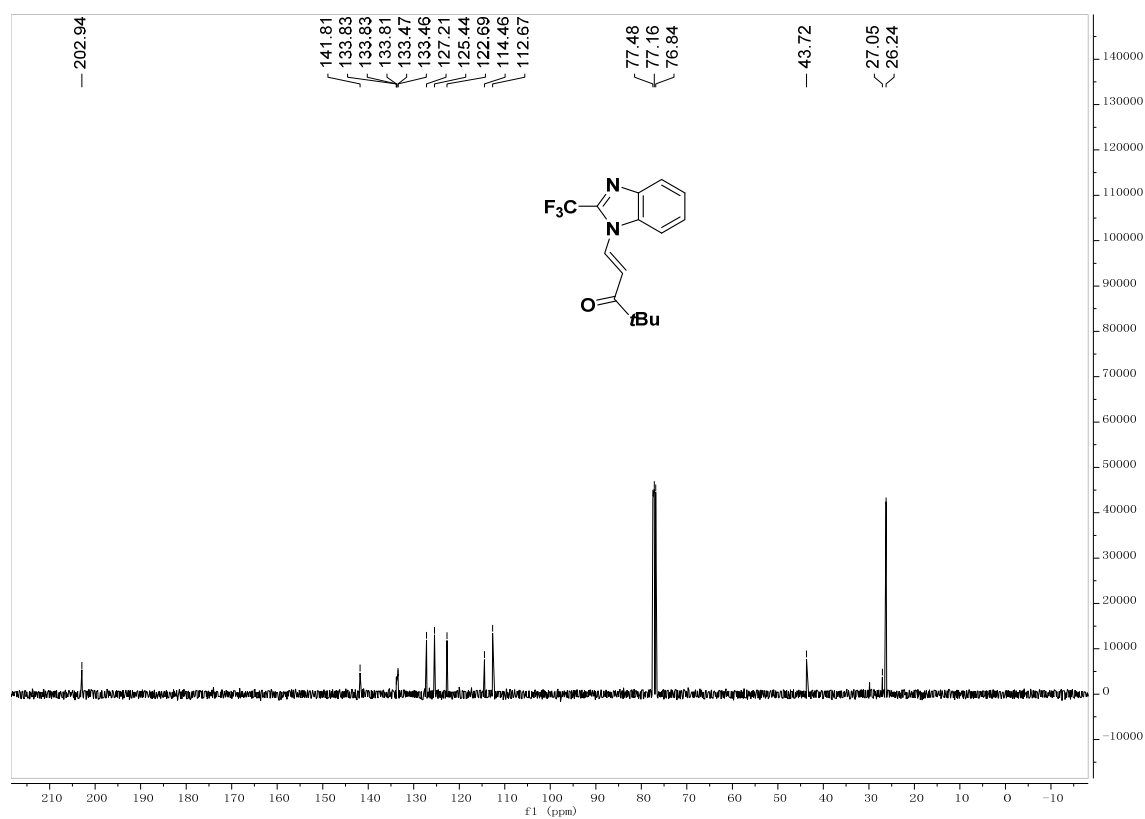
**<sup>13</sup>C NMR of 1y (150 MHz, CDCl<sub>3</sub>)**



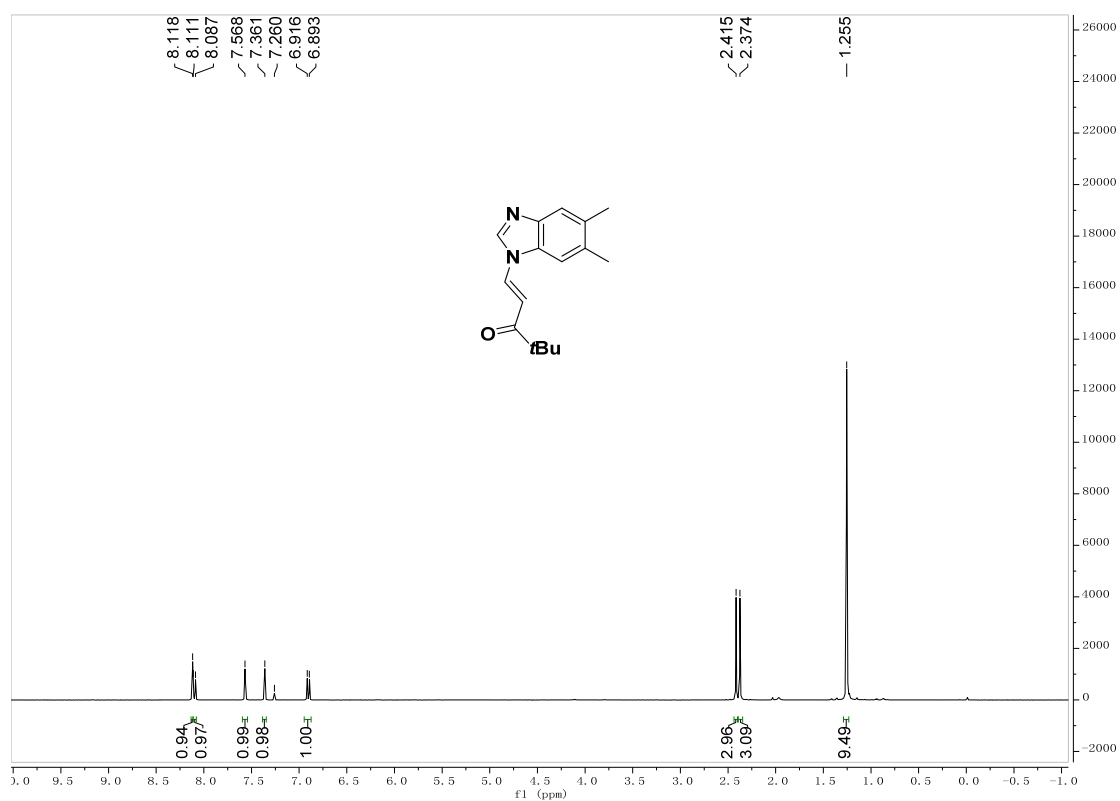
### <sup>1</sup>H NMR of 1z (400 MHz, CDCl<sub>3</sub>)



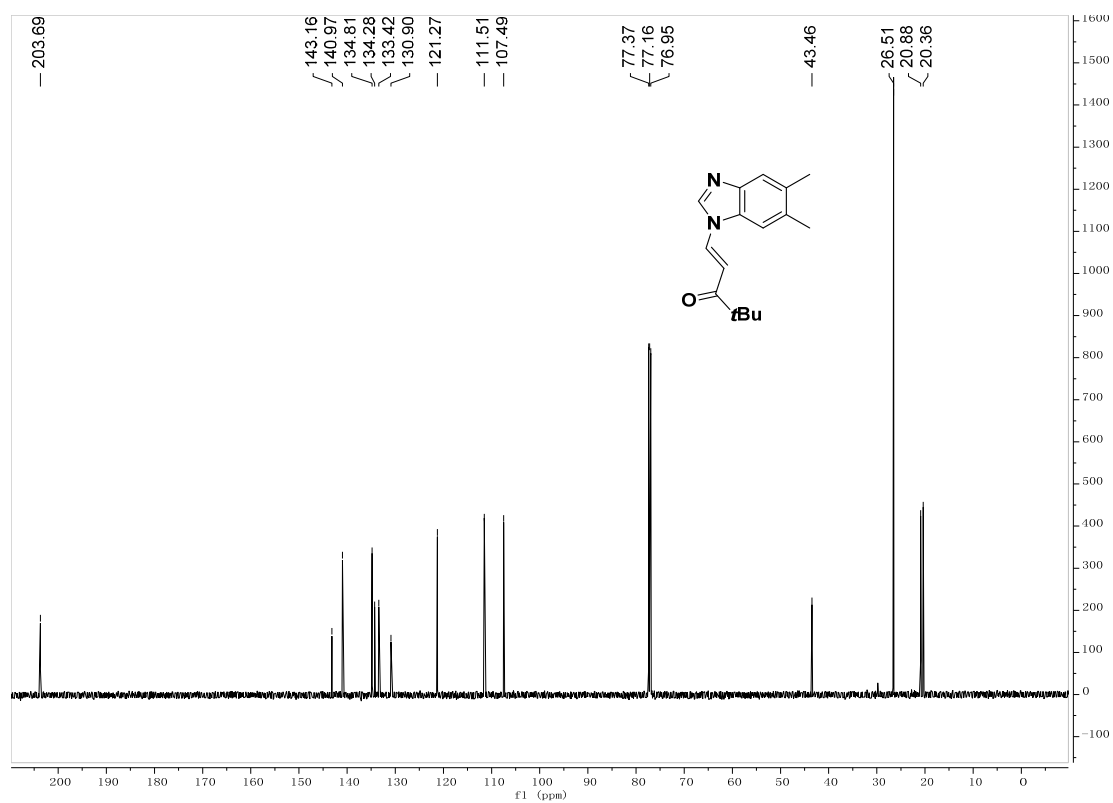
### <sup>13</sup>C NMR of 1z (100 MHz, CDCl<sub>3</sub>)



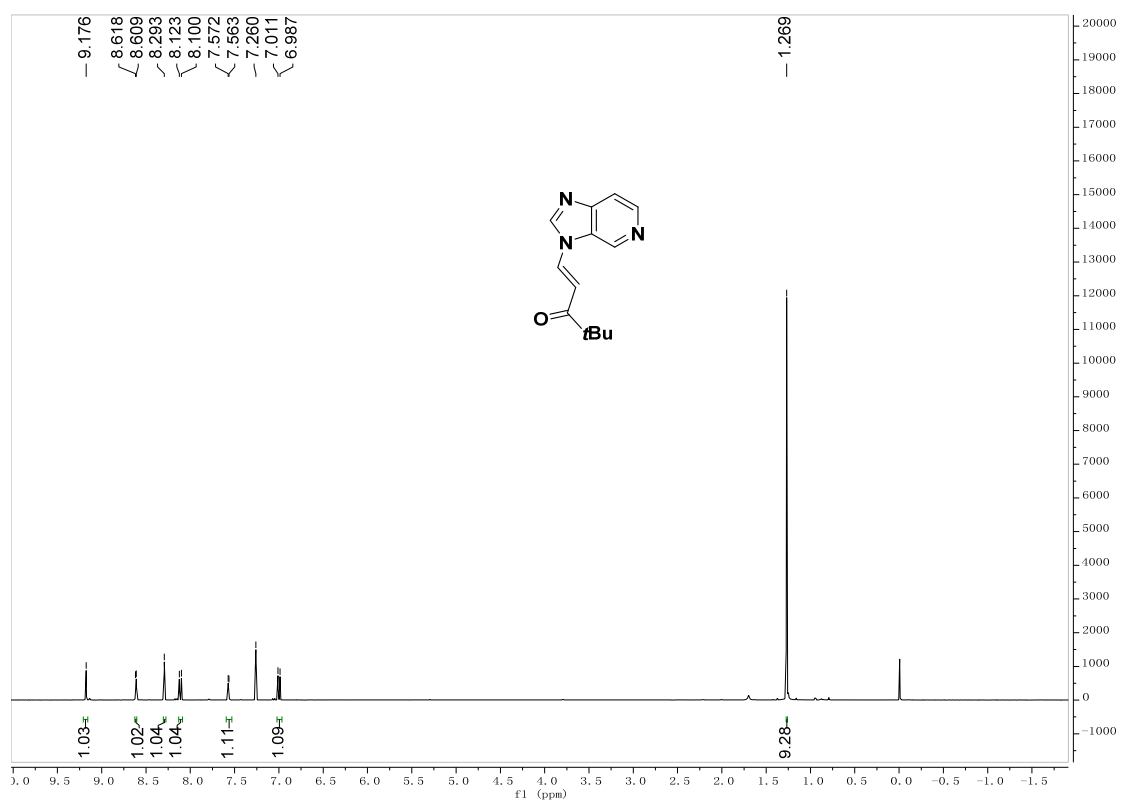
**<sup>1</sup>H NMR of 1aa (600 MHz, CDCl<sub>3</sub>)**



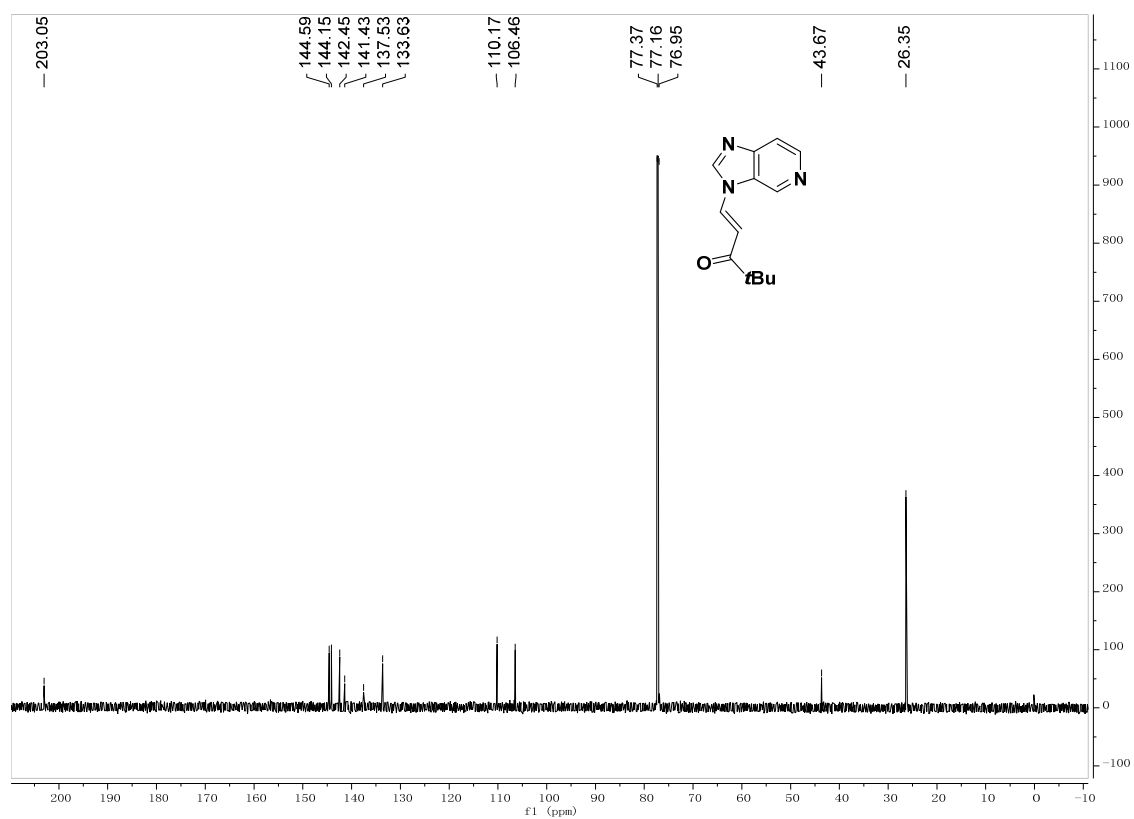
**<sup>13</sup>C NMR of 1aa (150 MHz, CDCl<sub>3</sub>)**



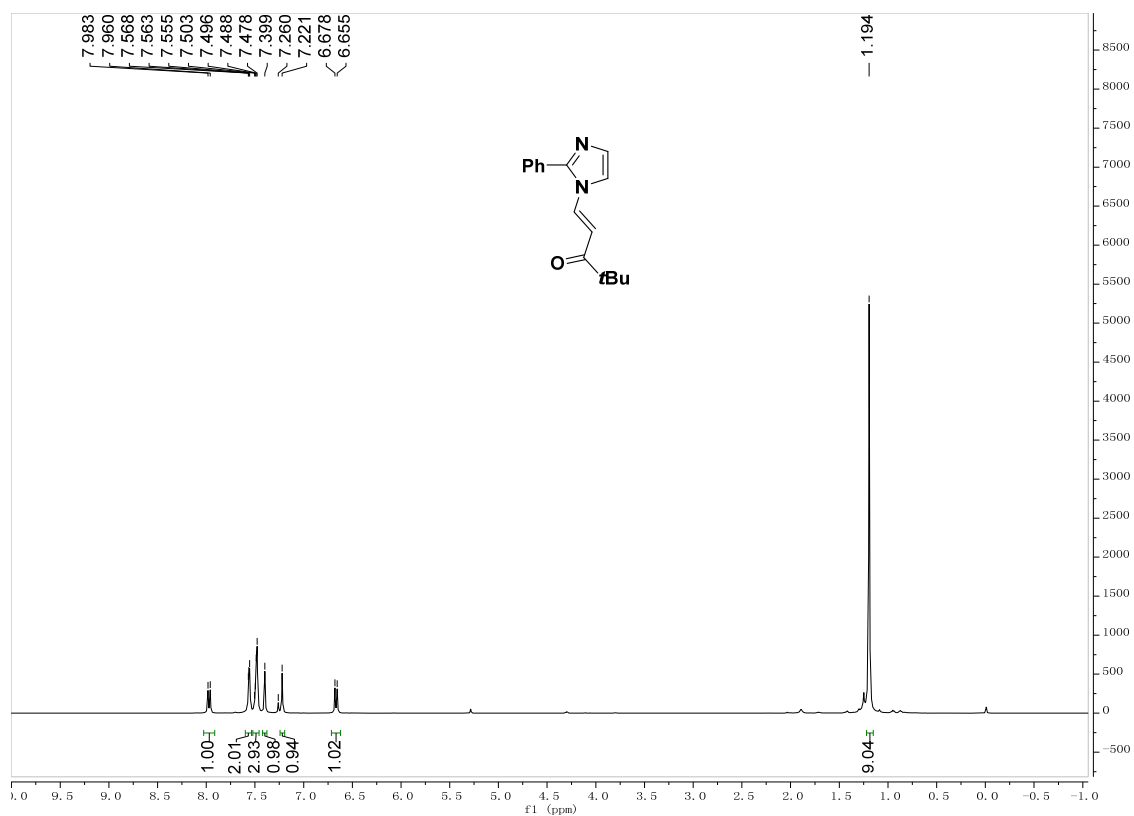
### <sup>1</sup>H NMR of 1ab (600 MHz, CDCl<sub>3</sub>)



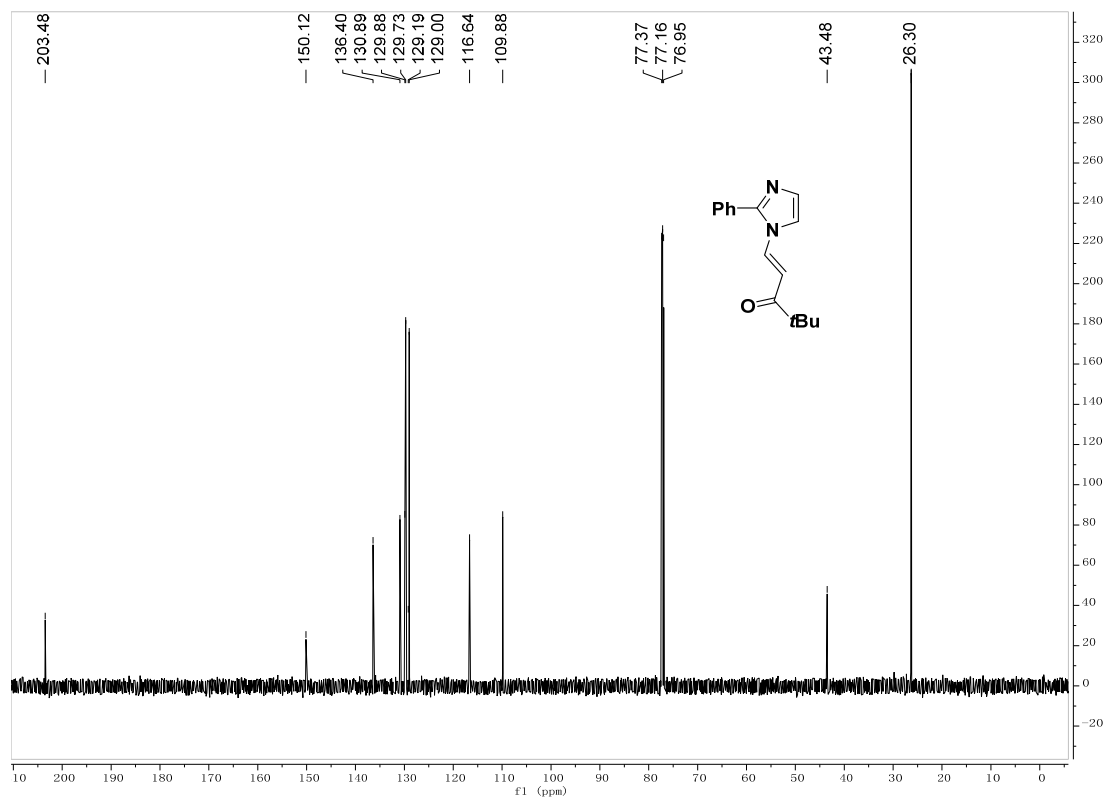
### <sup>13</sup>C NMR of 1ab (150 MHz, CDCl<sub>3</sub>)



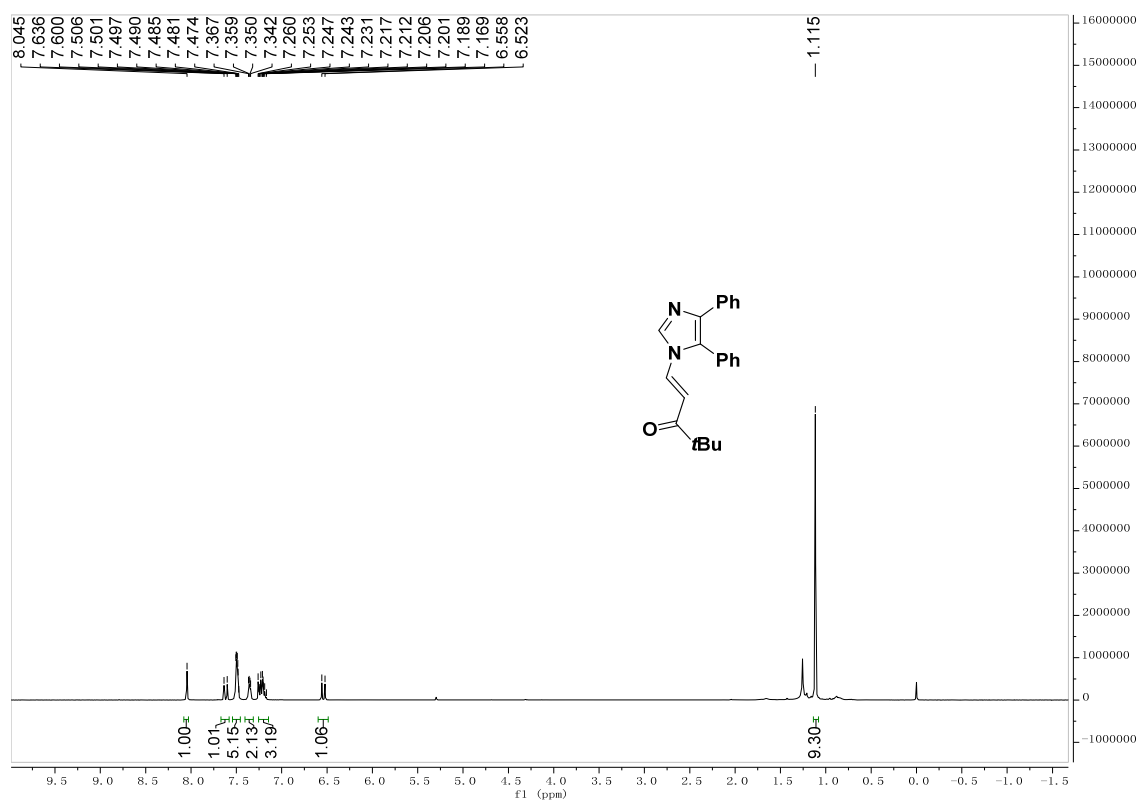
### <sup>1</sup>H NMR of 1ac (600 MHz, CDCl<sub>3</sub>)



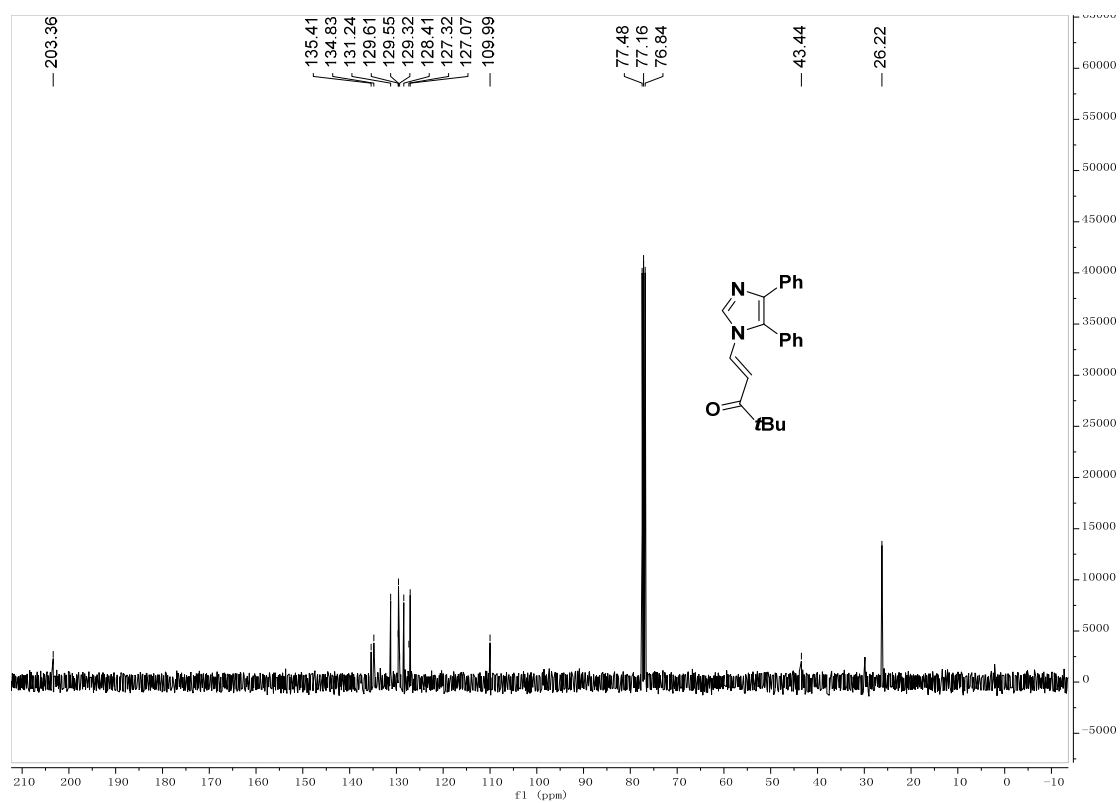
### <sup>13</sup>C NMR of 1ac (150 MHz, CDCl<sub>3</sub>)



### <sup>1</sup>H NMR of 1ad (400 MHz, CDCl<sub>3</sub>)

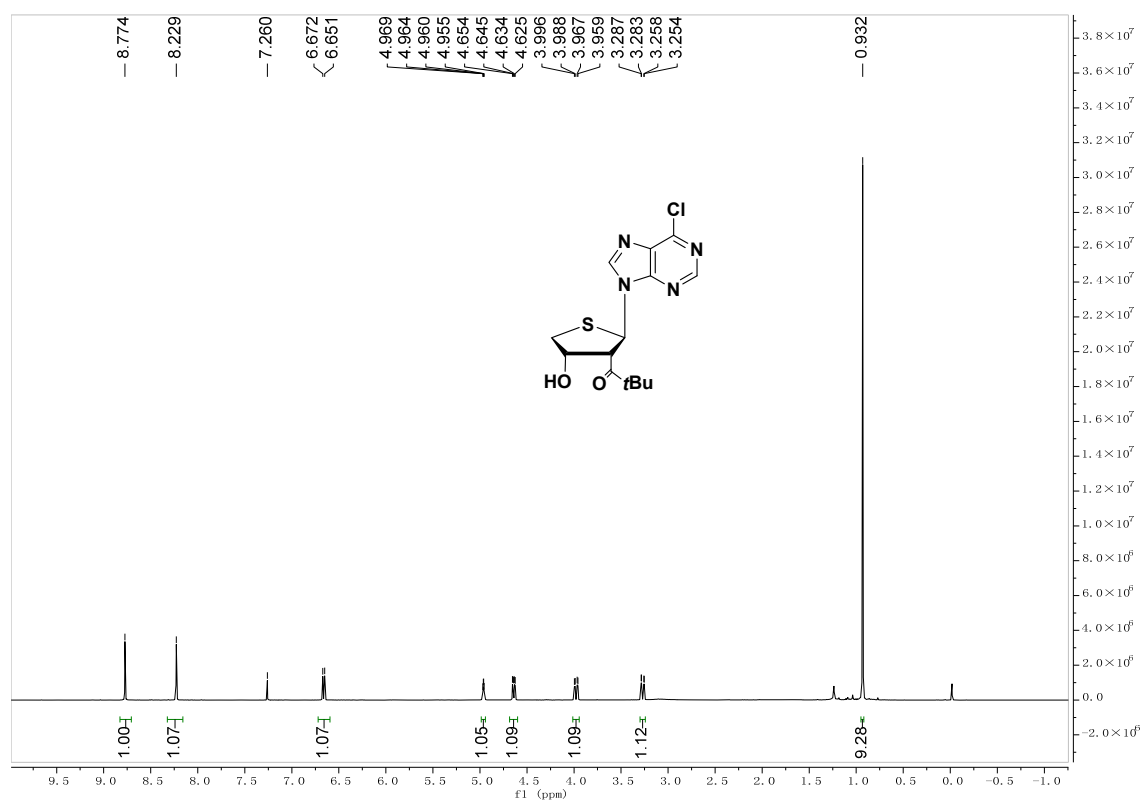


### <sup>13</sup>C NMR of 1ad (100 MHz, CDCl<sub>3</sub>)

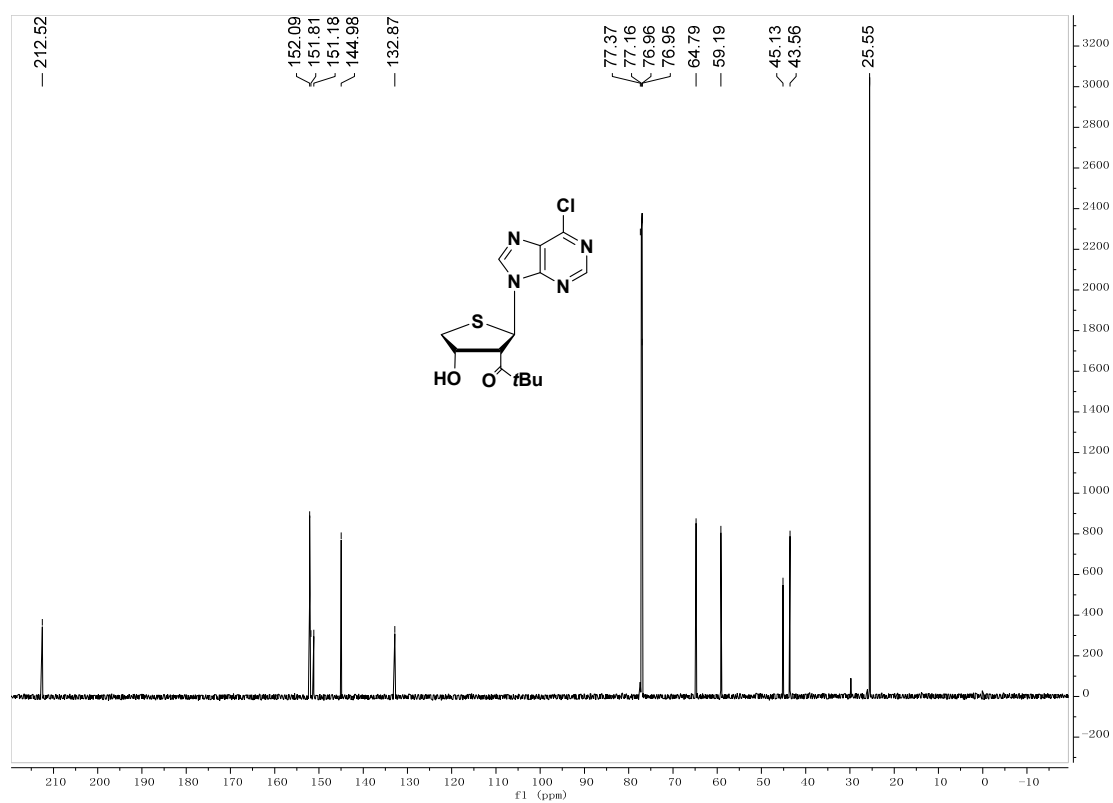




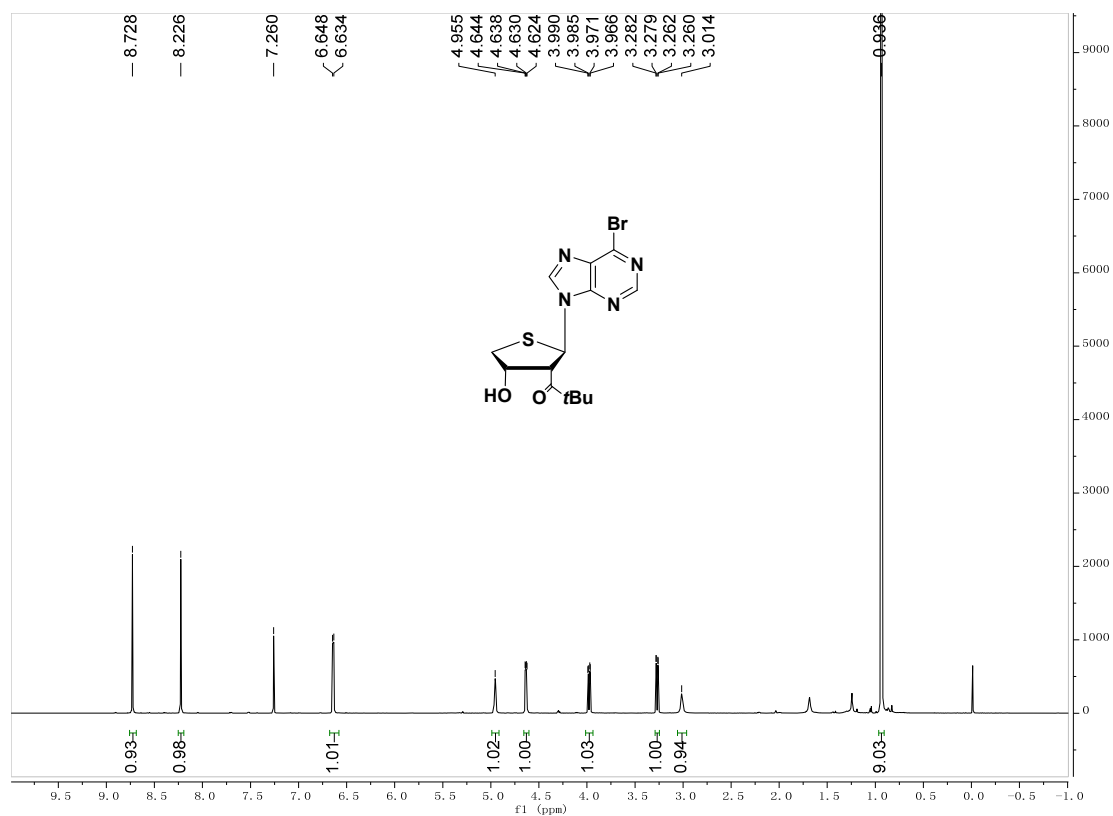
### <sup>1</sup>H NMR of 3a (400 MHz, CDCl<sub>3</sub>)



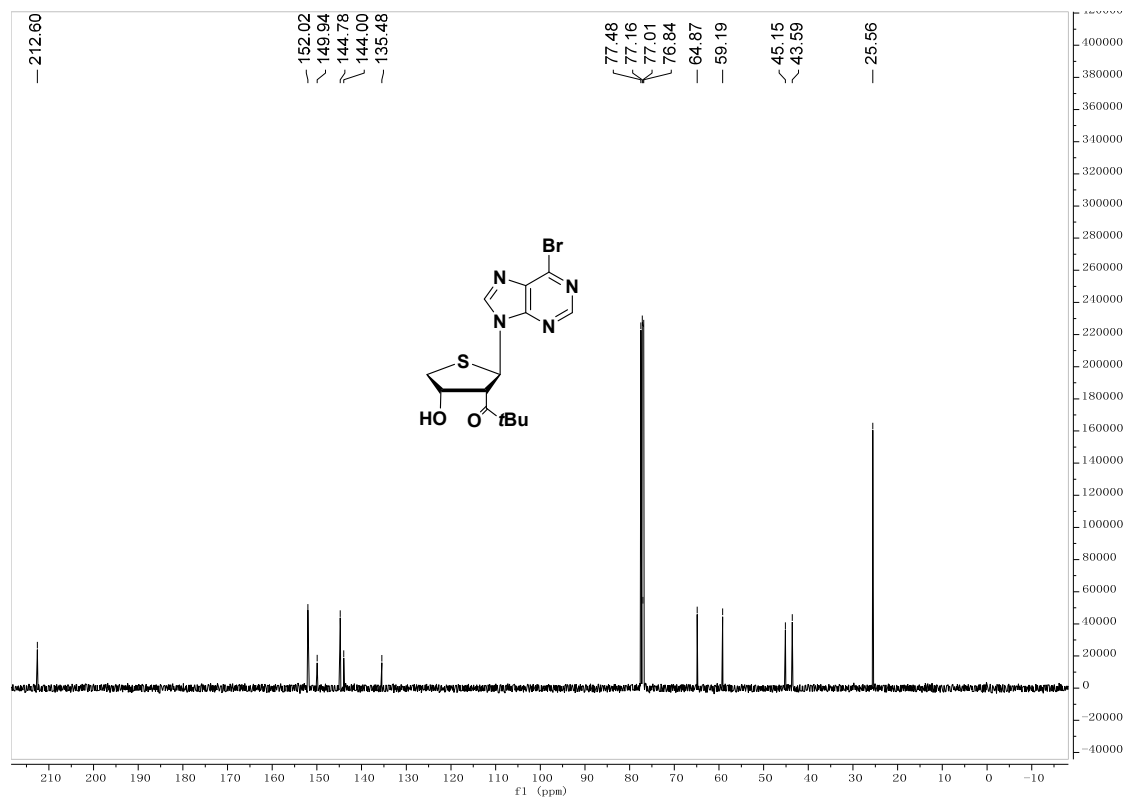
### <sup>13</sup>C NMR of 3a (150 MHz, CDCl<sub>3</sub>)



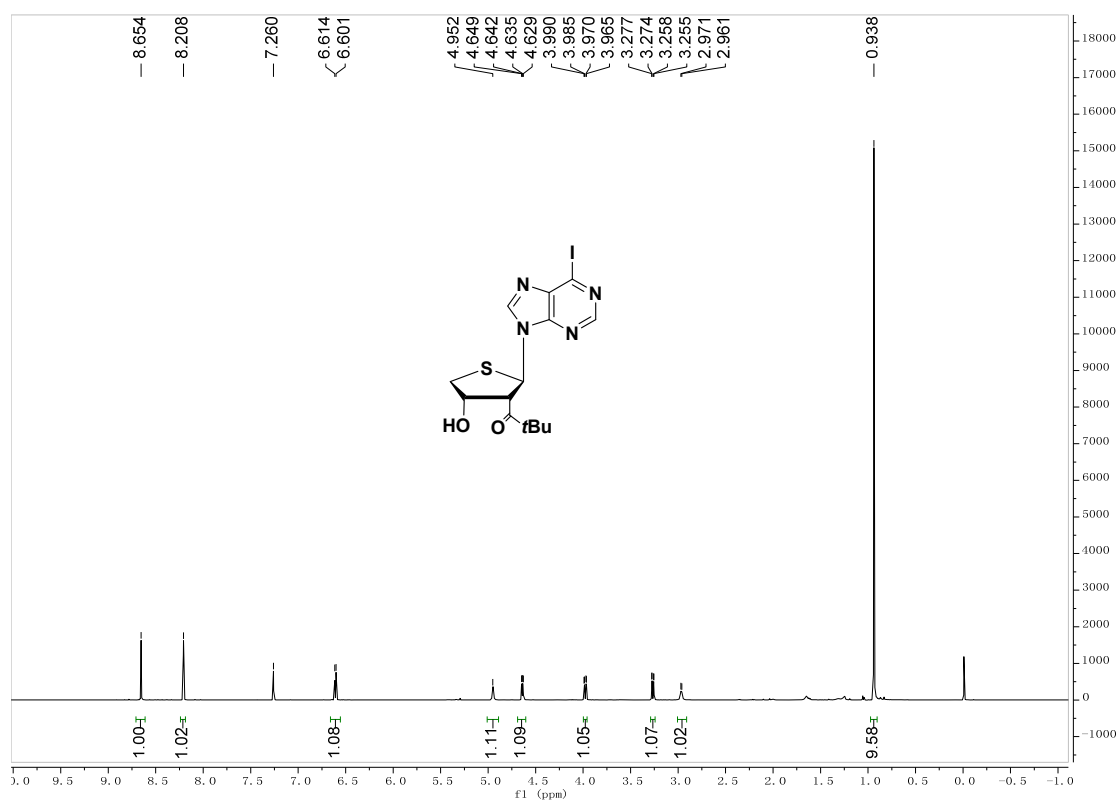
### $^1\text{H}$ NMR of **3b** (400 MHz, $\text{CDCl}_3$ )



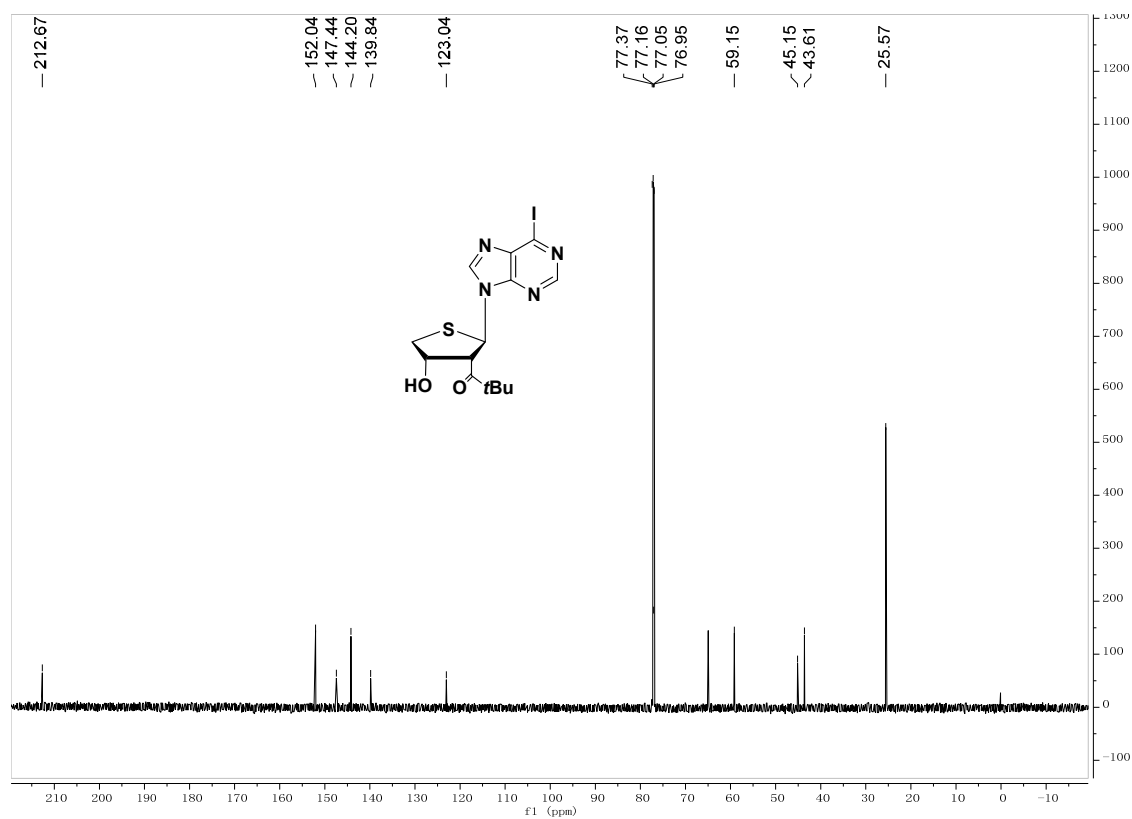
### $^{13}\text{C}$ NMR of **3b** (100 MHz, $\text{CDCl}_3$ )



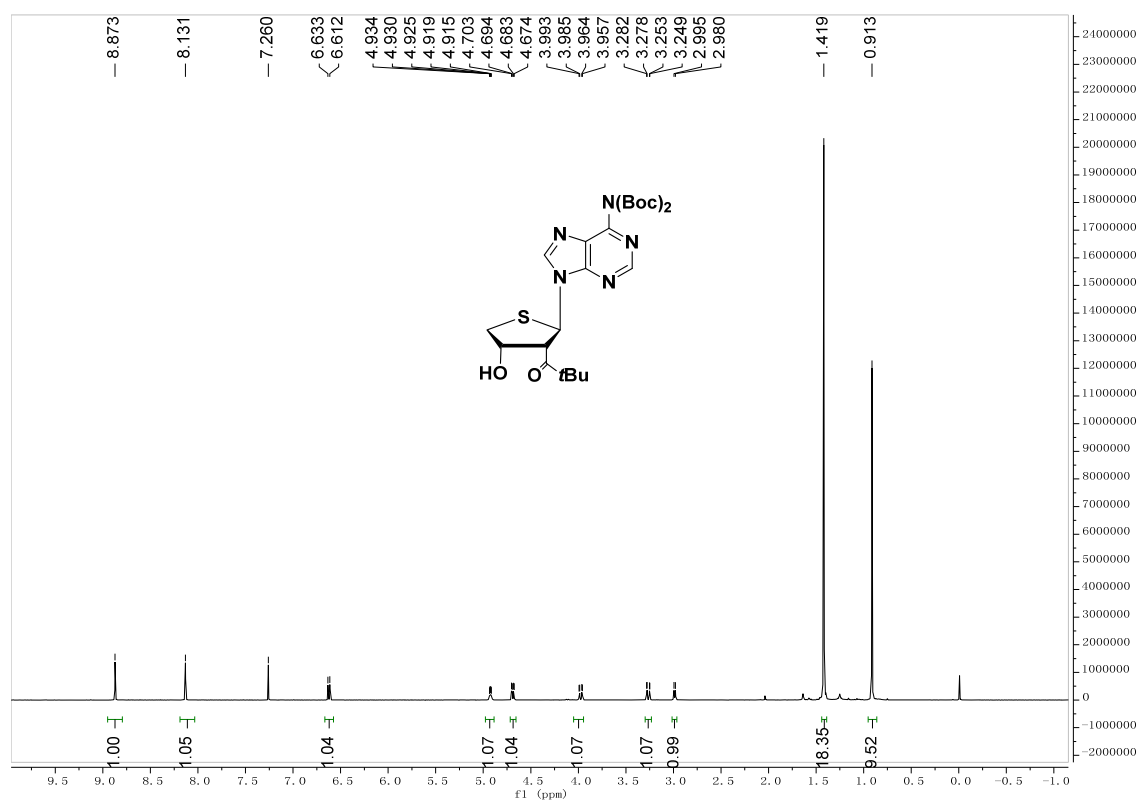
### $^1\text{H}$ NMR of **3c** (600 MHz, $\text{CDCl}_3$ )



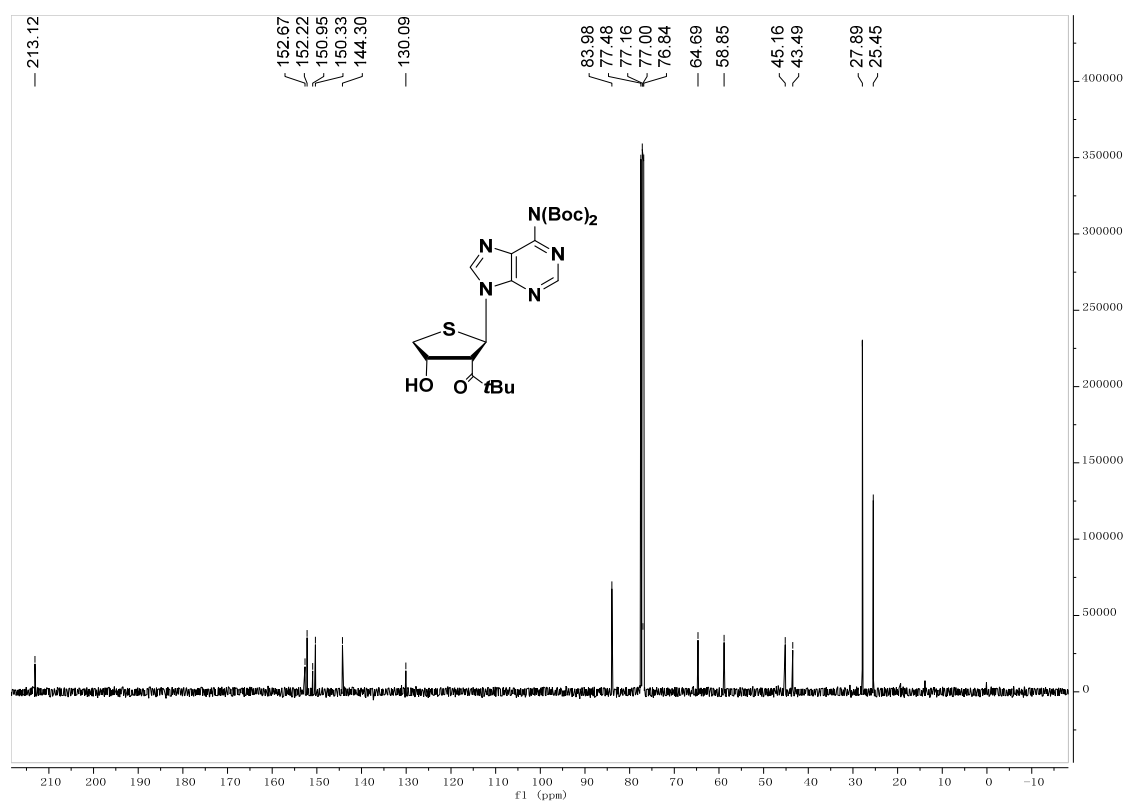
### $^{13}\text{C}$ NMR of **3c** (150 MHz, $\text{CDCl}_3$ )



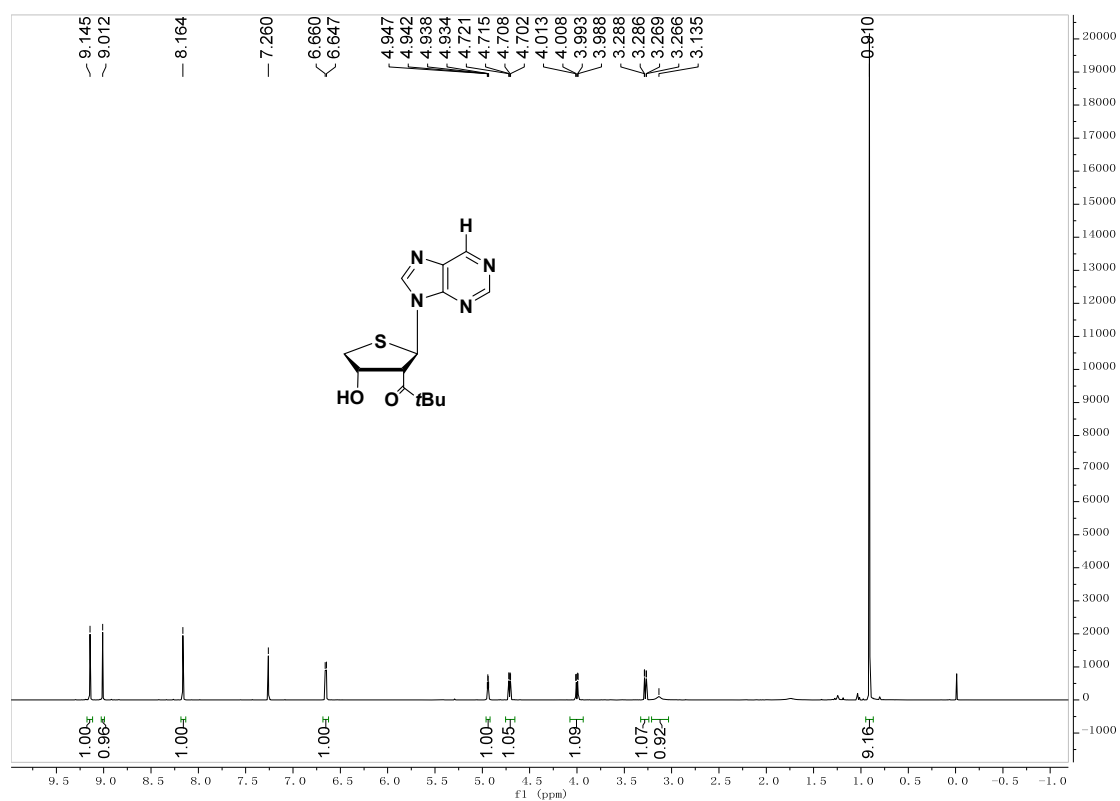
### <sup>1</sup>H NMR of 3d (400 MHz, CDCl<sub>3</sub>)



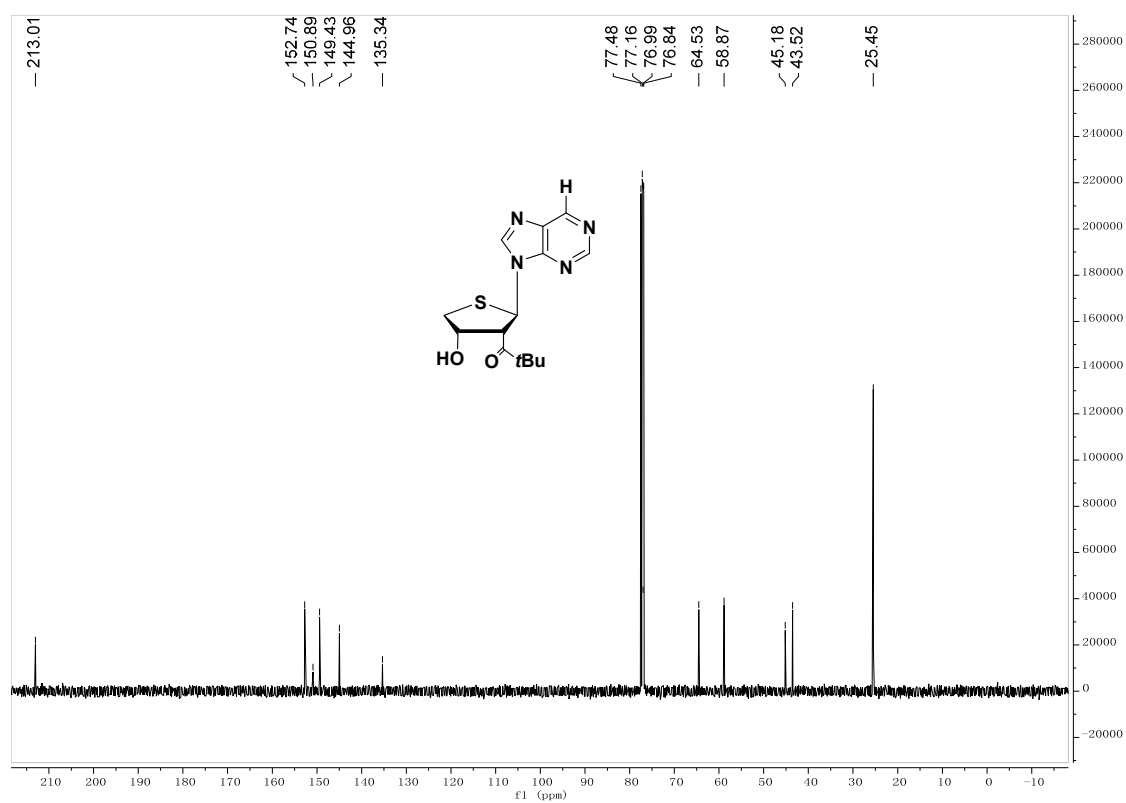
### <sup>13</sup>C NMR of 3d (100 MHz, CDCl<sub>3</sub>)



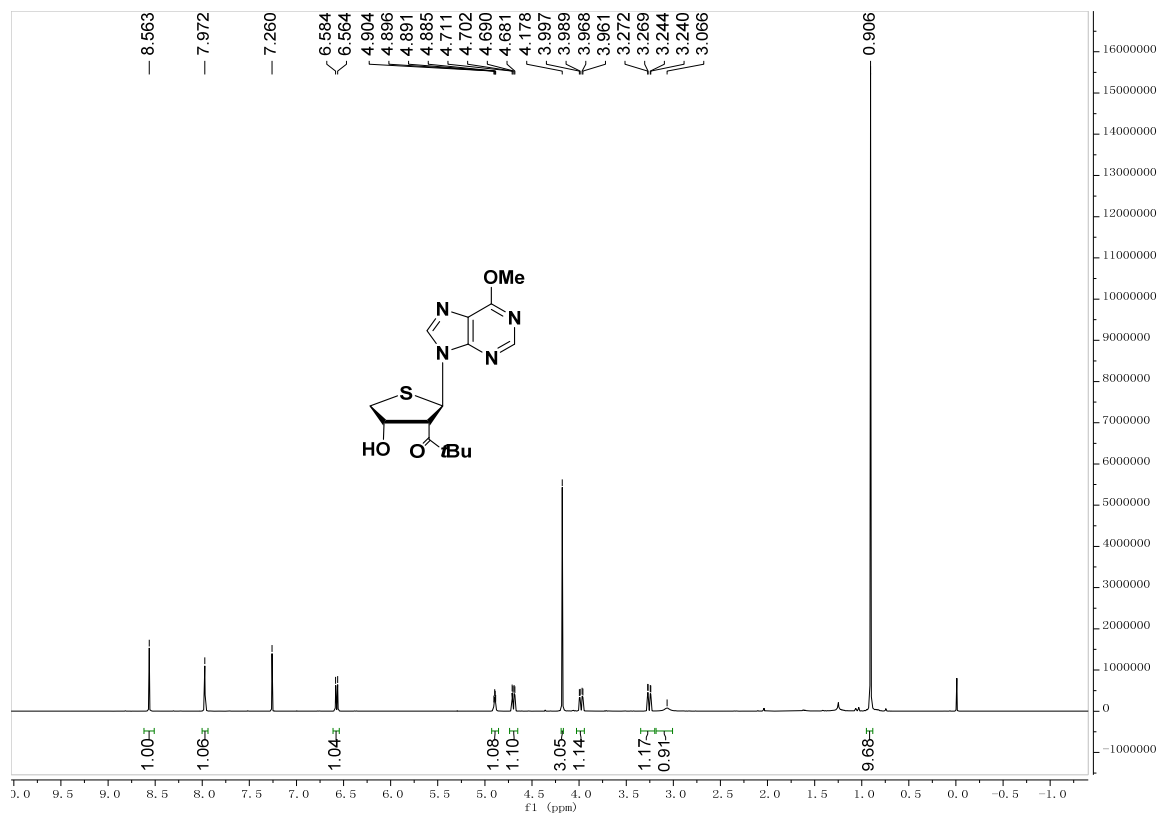
### $^1\text{H}$ NMR of **3e** (600 MHz, $\text{CDCl}_3$ )



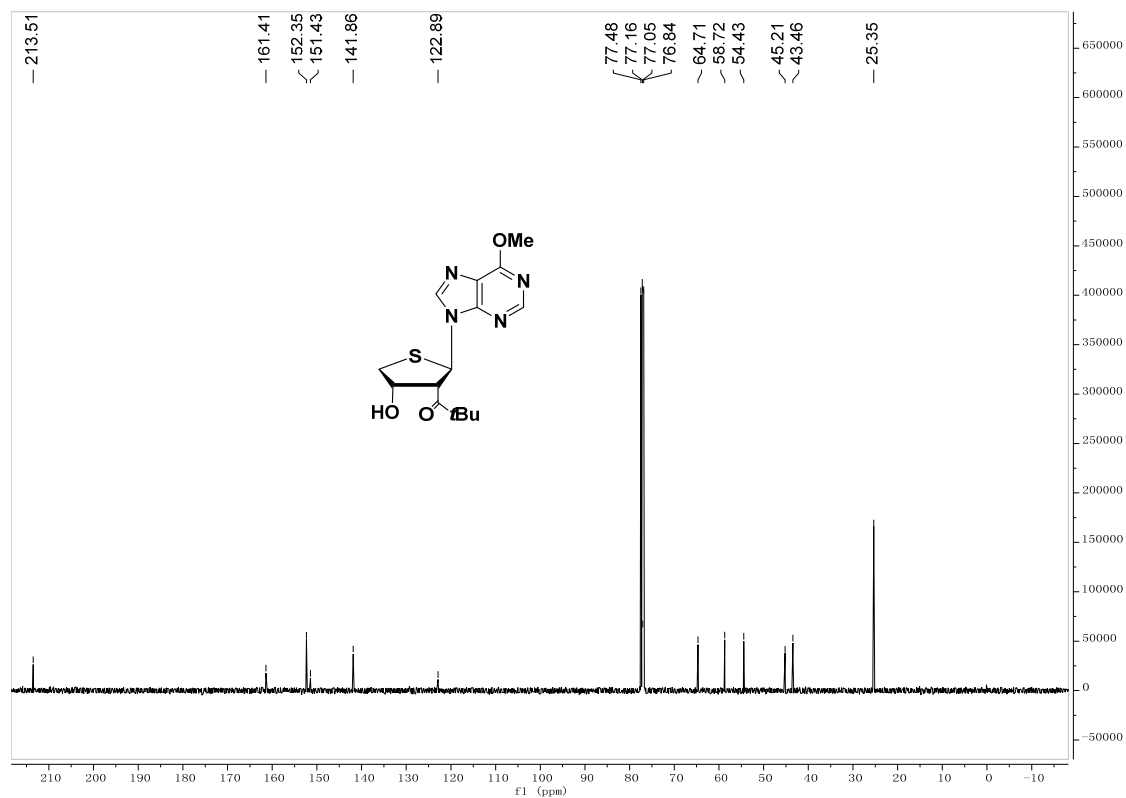
### $^{13}\text{C}$ NMR of **3e** (100 MHz, $\text{CDCl}_3$ )



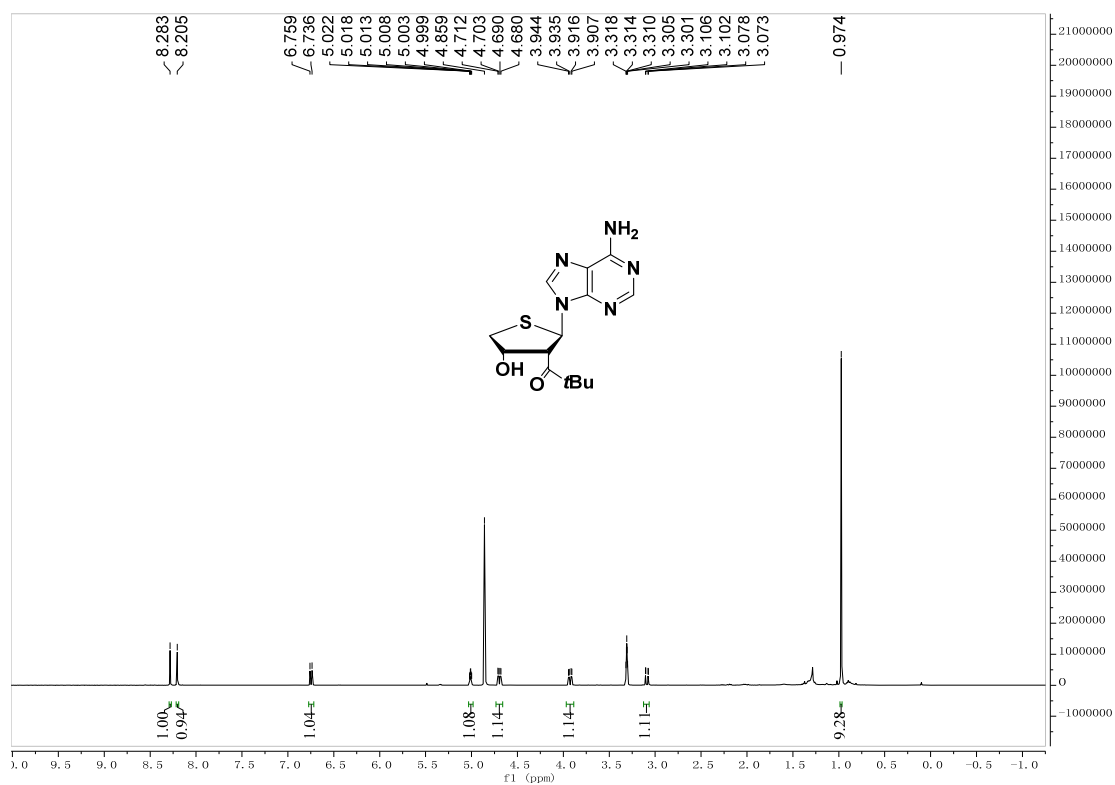
### $^1\text{H}$ NMR of 3f (400 MHz, $\text{CDCl}_3$ )



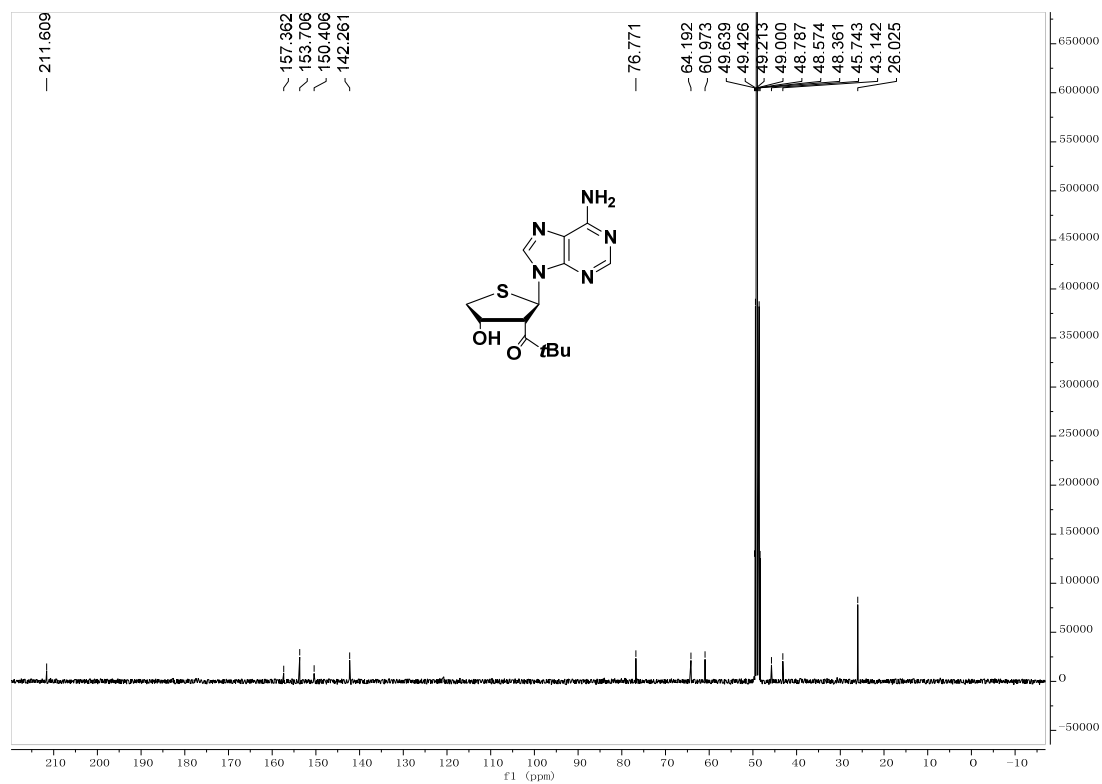
### $^{13}\text{C}$ NMR of 3f (100 MHz, $\text{CDCl}_3$ )



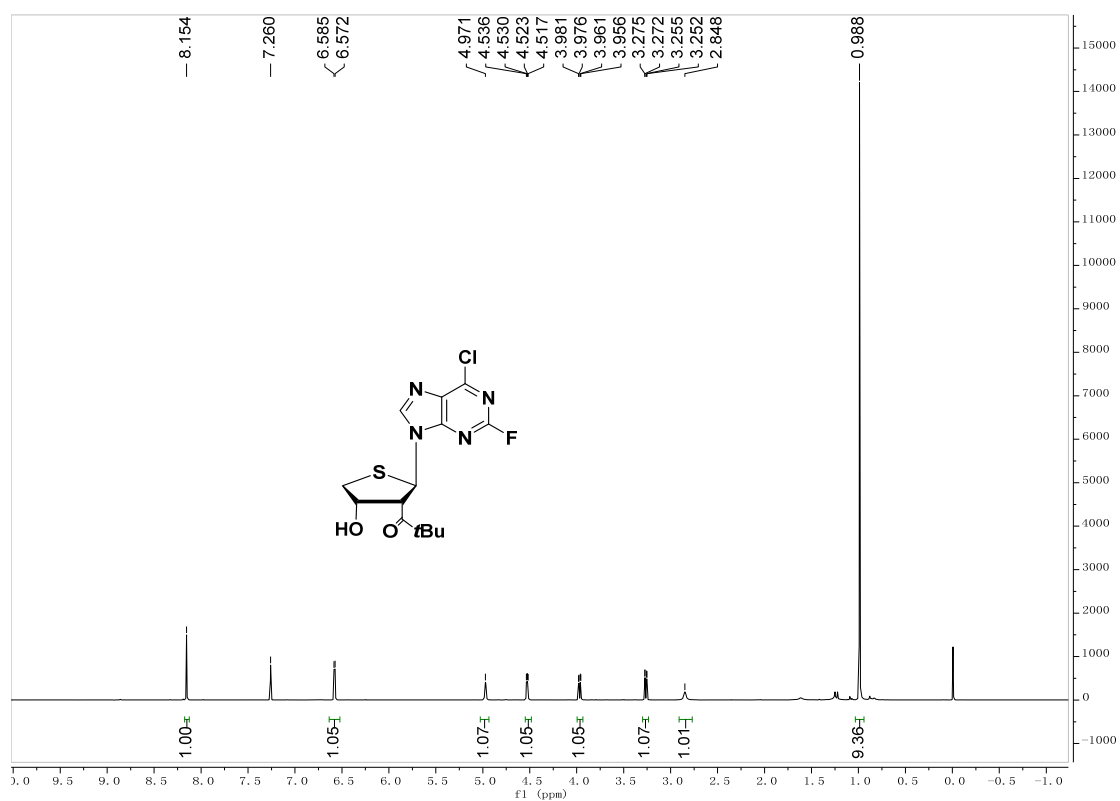
### <sup>1</sup>H NMR of 3g (400 MHz, CD<sub>3</sub>OD)



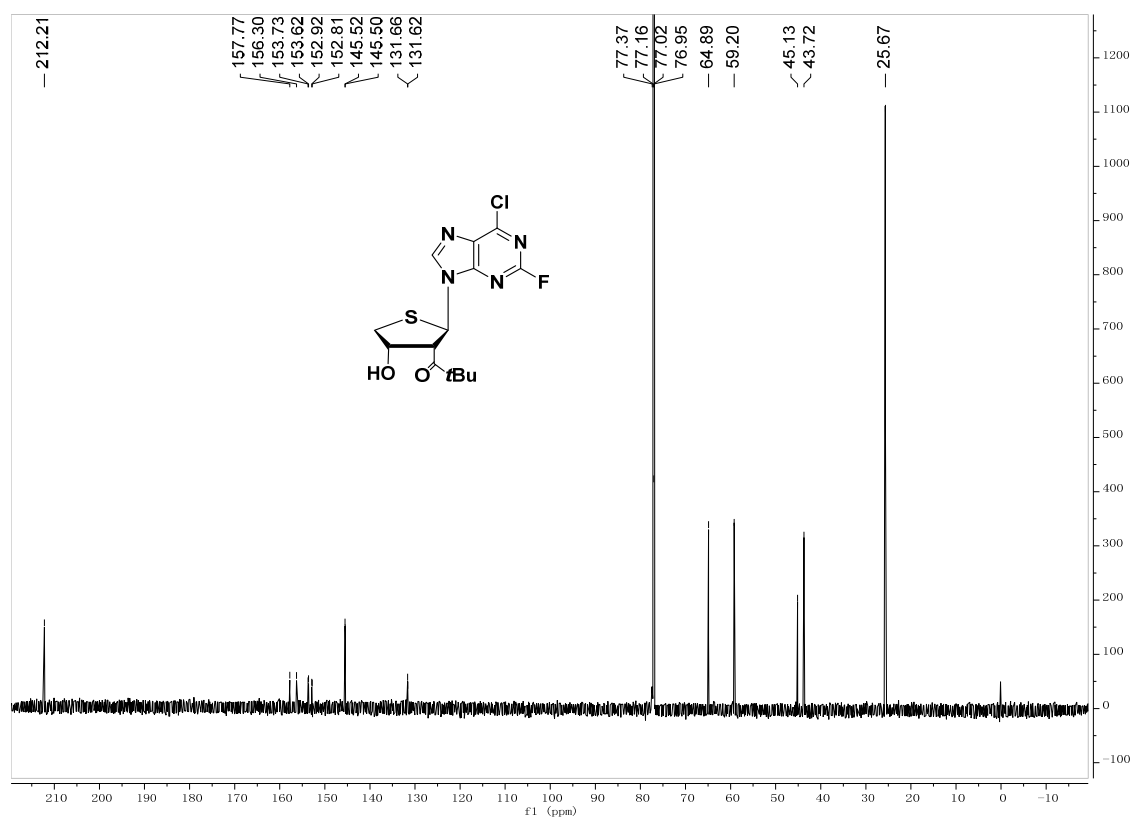
### <sup>13</sup>C NMR of 3g (100 MHz, CD<sub>3</sub>OD)



### $^1\text{H}$ NMR of 3h (600 MHz, $\text{CDCl}_3$ )

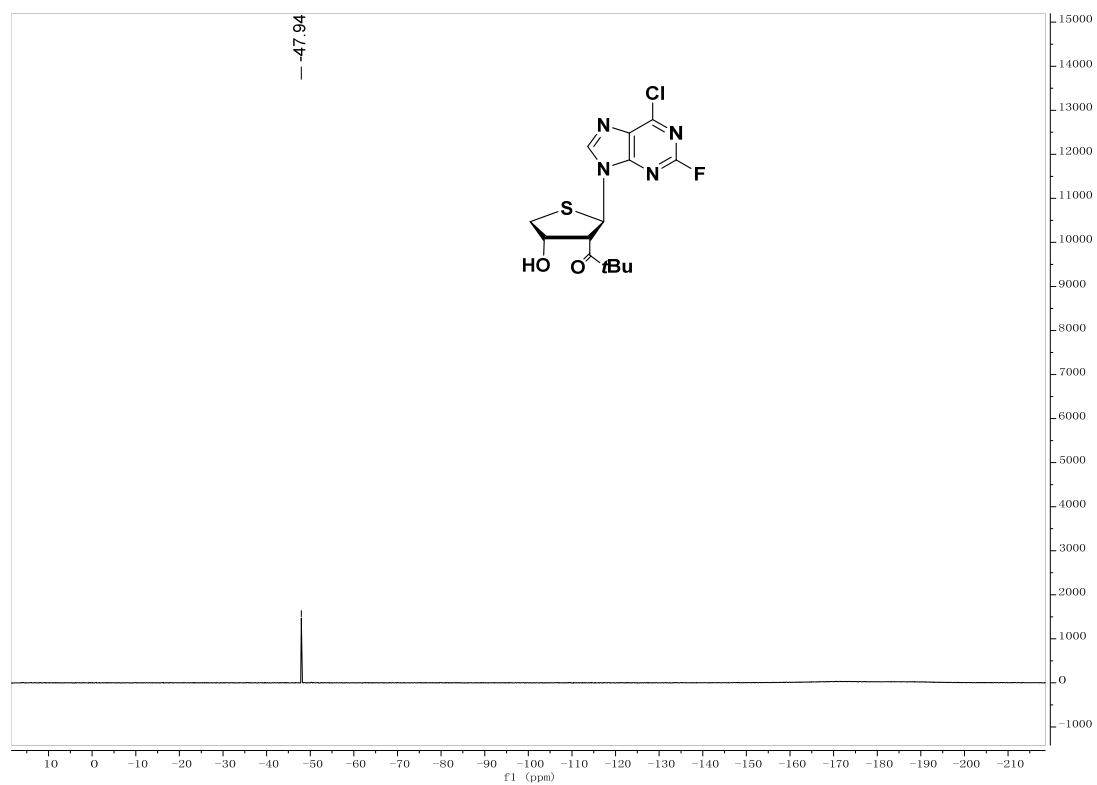


### $^{13}\text{C}$ NMR of 3h (150 MHz, $\text{CDCl}_3$ )

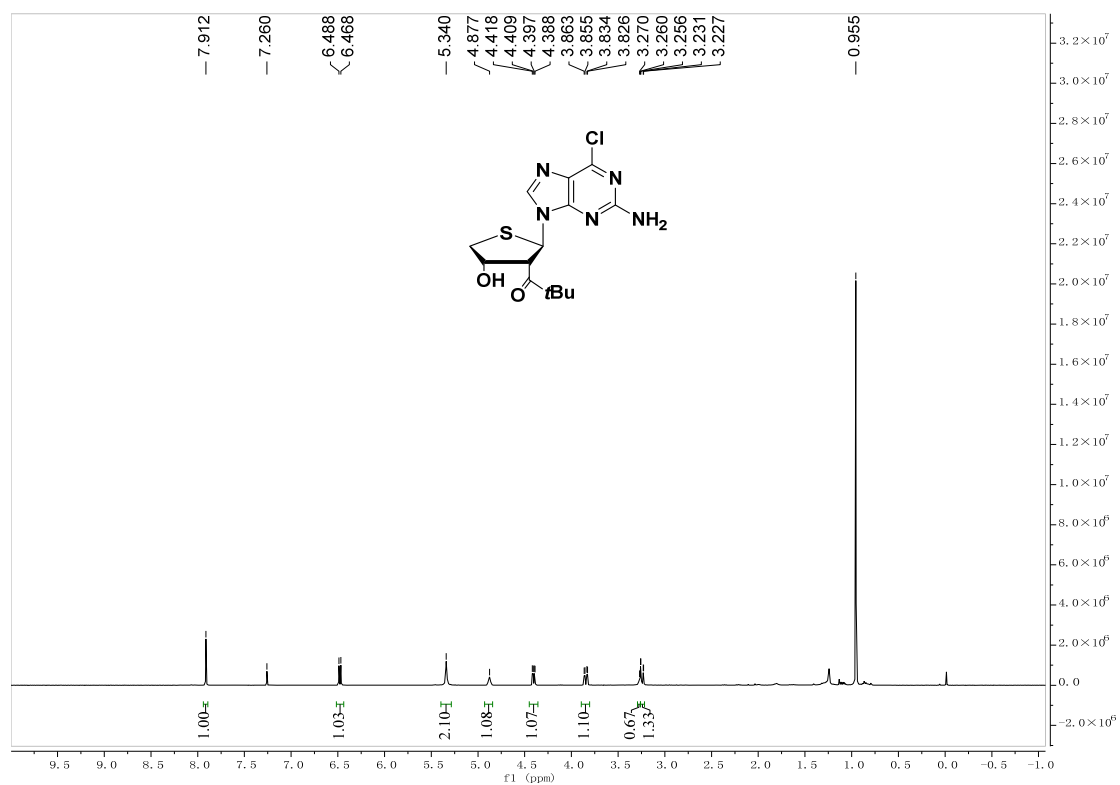




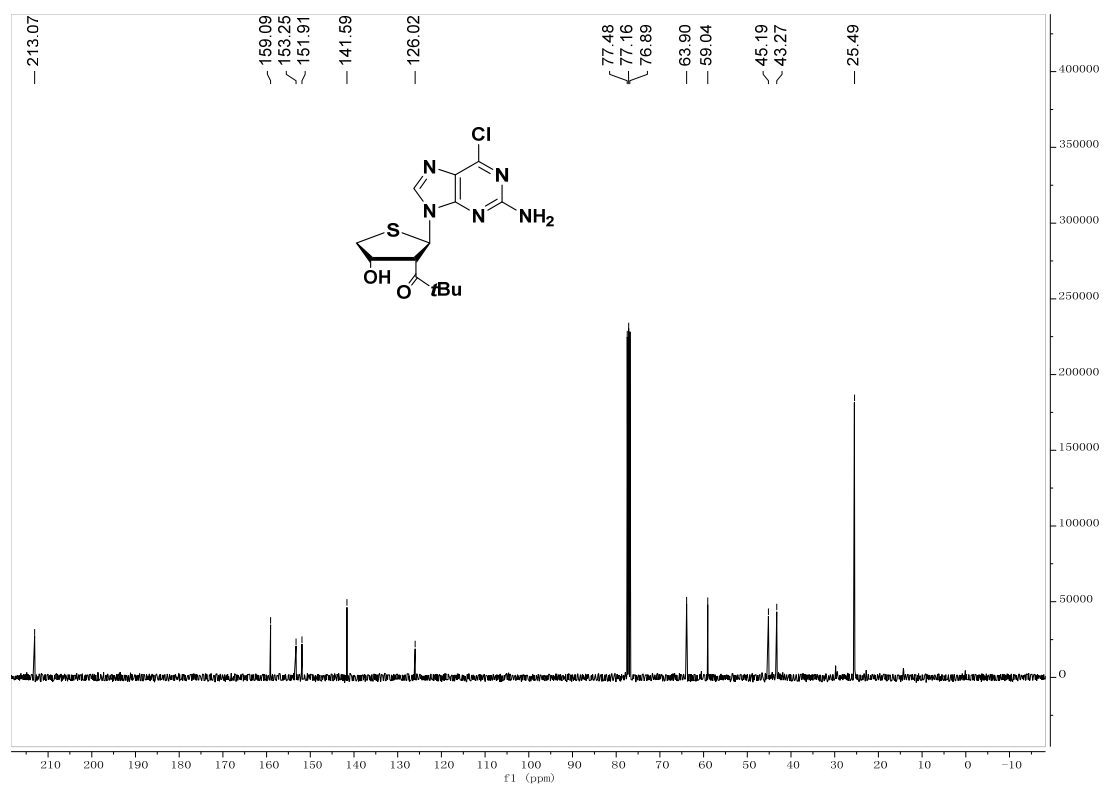
**<sup>19</sup>F NMR of 3h (565 MHz, CDCl<sub>3</sub>)**



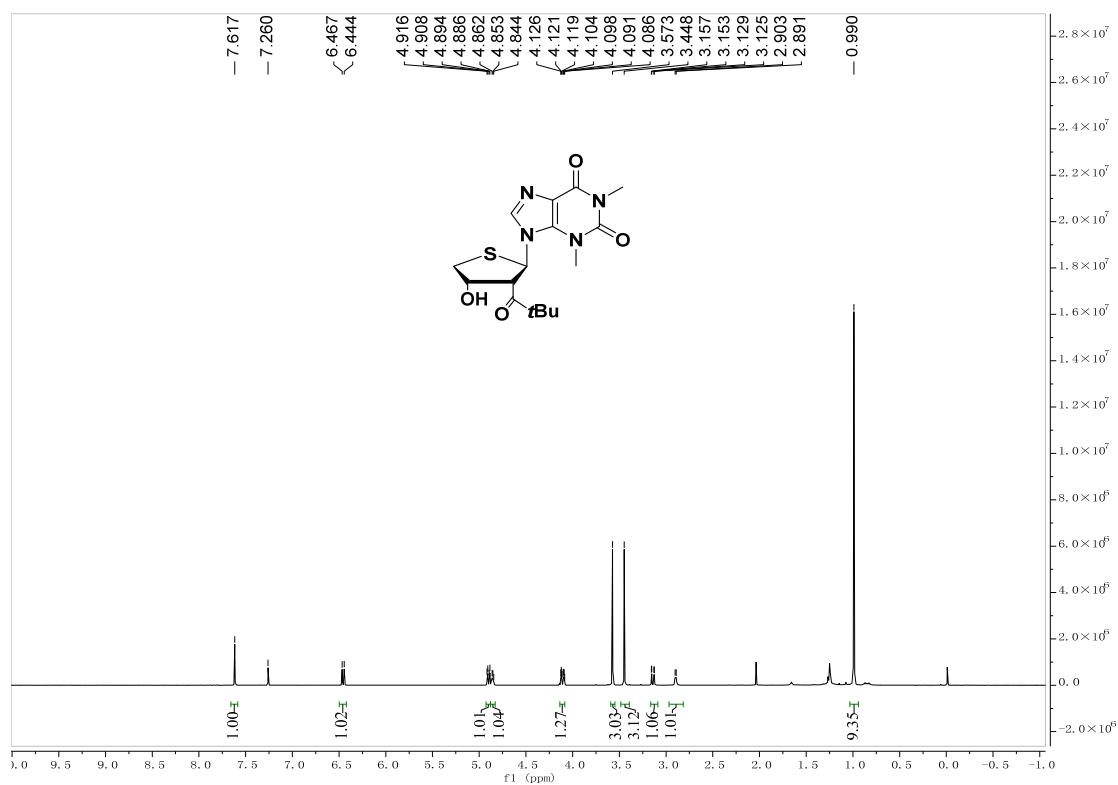
### <sup>1</sup>H NMR of 3i (400 MHz, CDCl<sub>3</sub>)



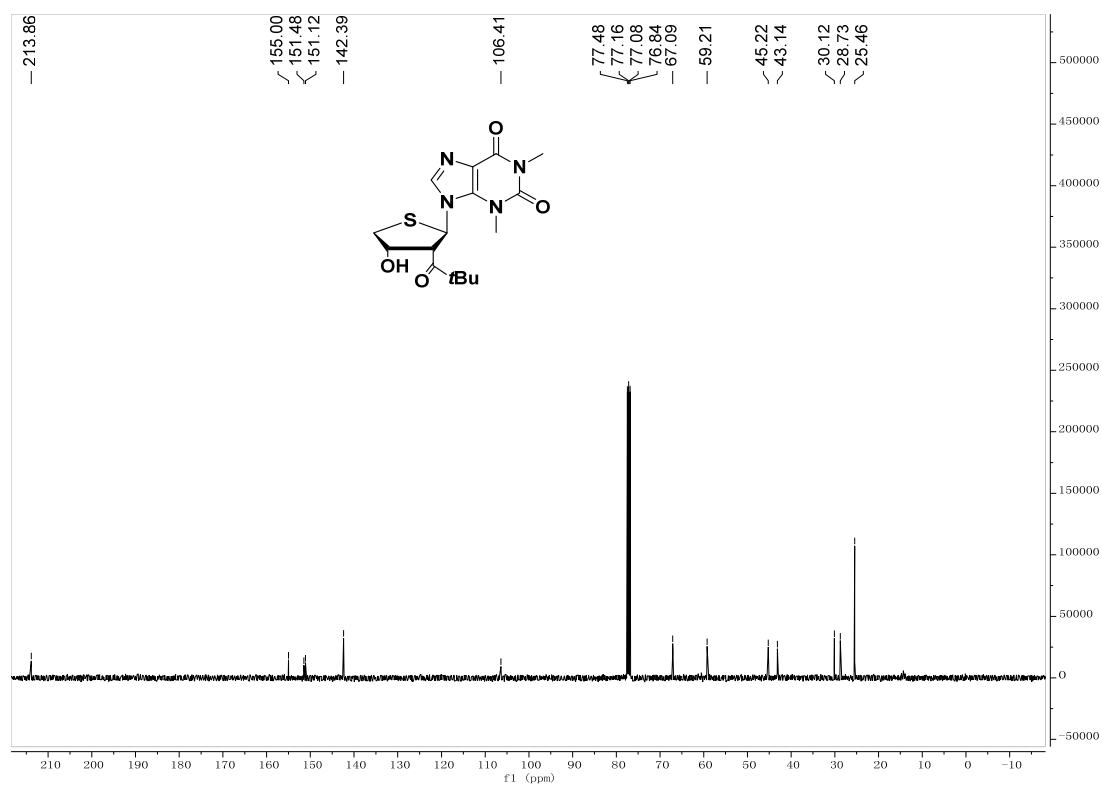
### <sup>13</sup>C NMR of 3i (100 MHz, CDCl<sub>3</sub>)



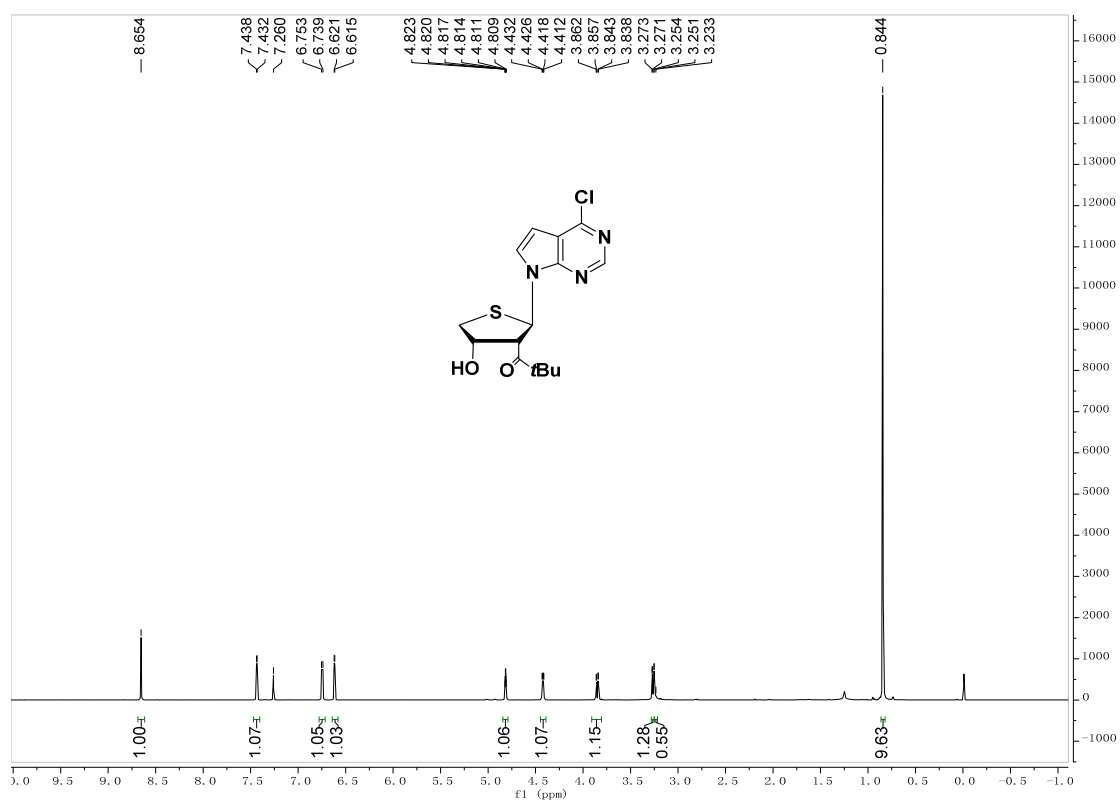
### <sup>1</sup>H NMR of 3j (400 MHz, CDCl<sub>3</sub>)



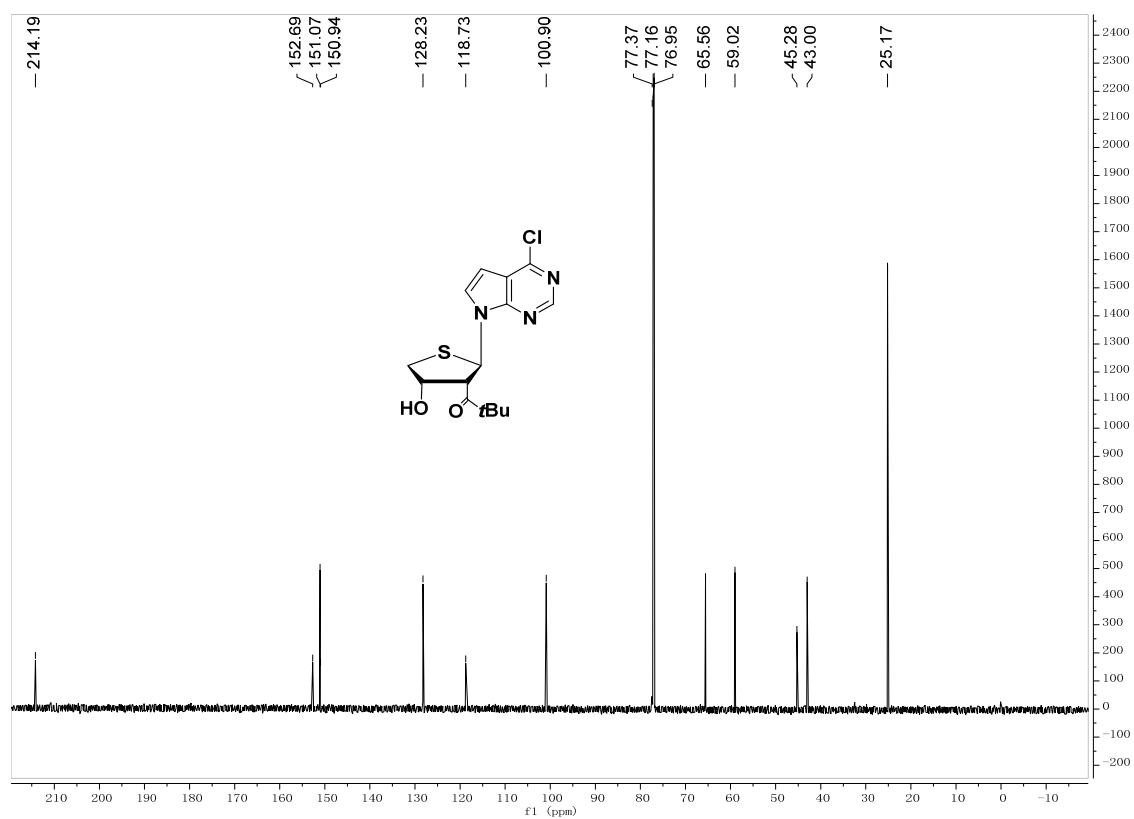
### <sup>13</sup>C NMR of 3j (100 MHz, CDCl<sub>3</sub>)



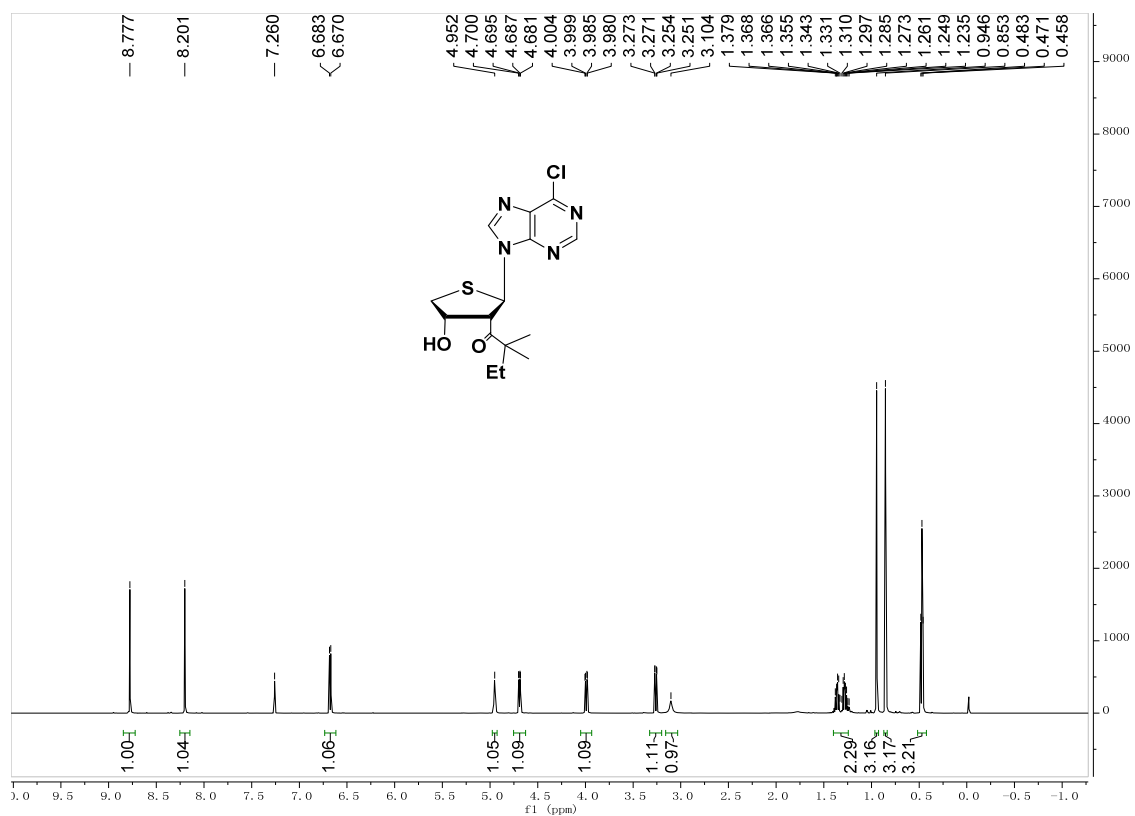
### $^1\text{H}$ NMR of 3k (600 MHz, $\text{CDCl}_3$ )



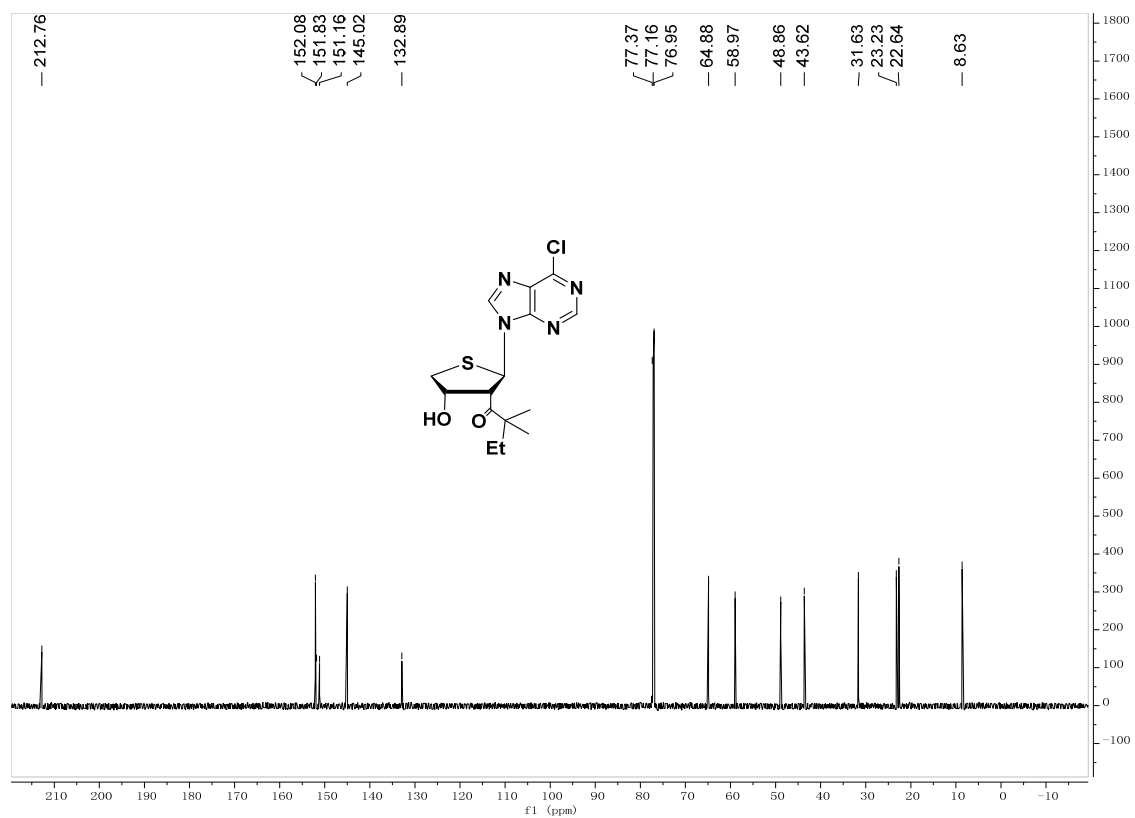
### $^{13}\text{C}$ NMR of 3k (150 MHz, $\text{CDCl}_3$ )



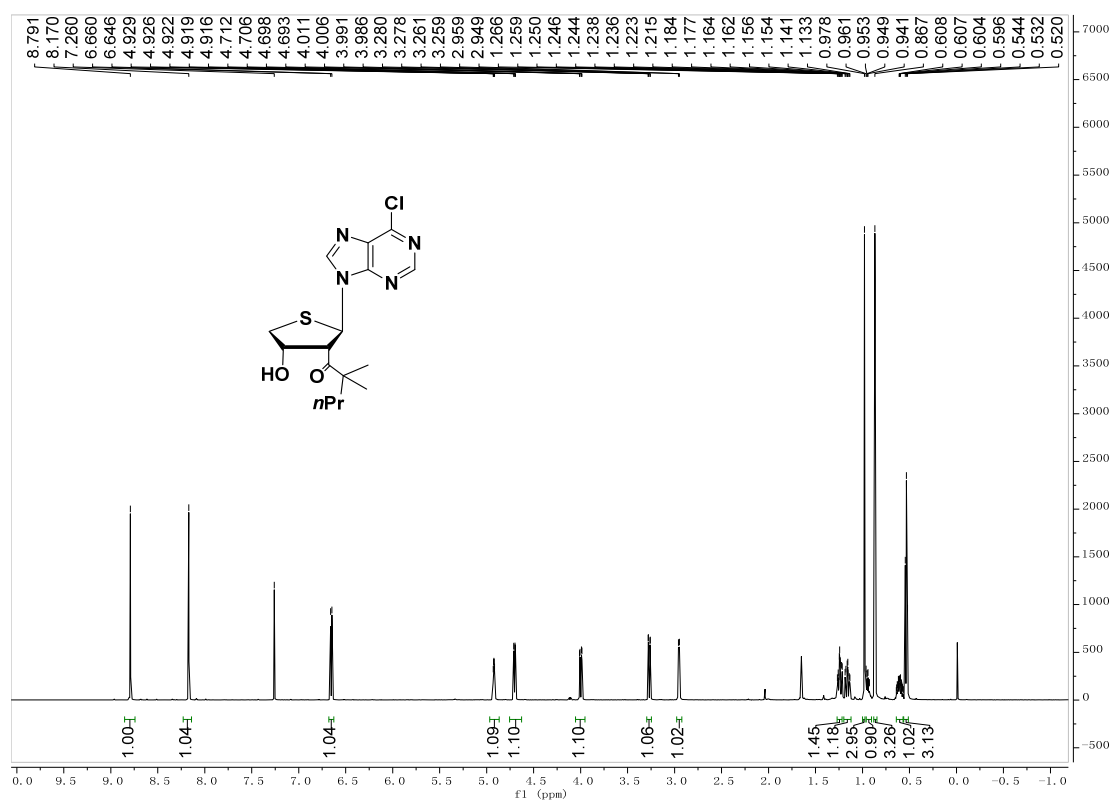
### <sup>1</sup>H NMR of 3I (600 MHz, CDCl<sub>3</sub>)



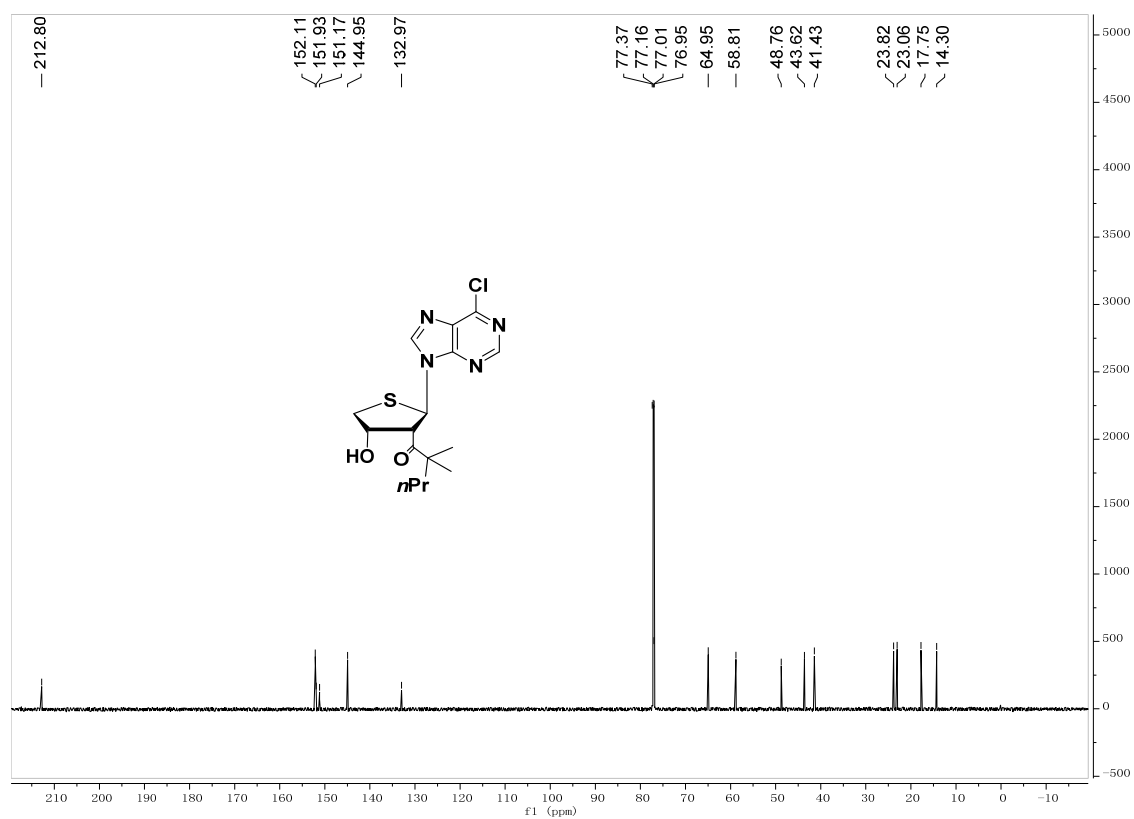
### <sup>13</sup>C NMR of 3I (150 MHz, CDCl<sub>3</sub>)



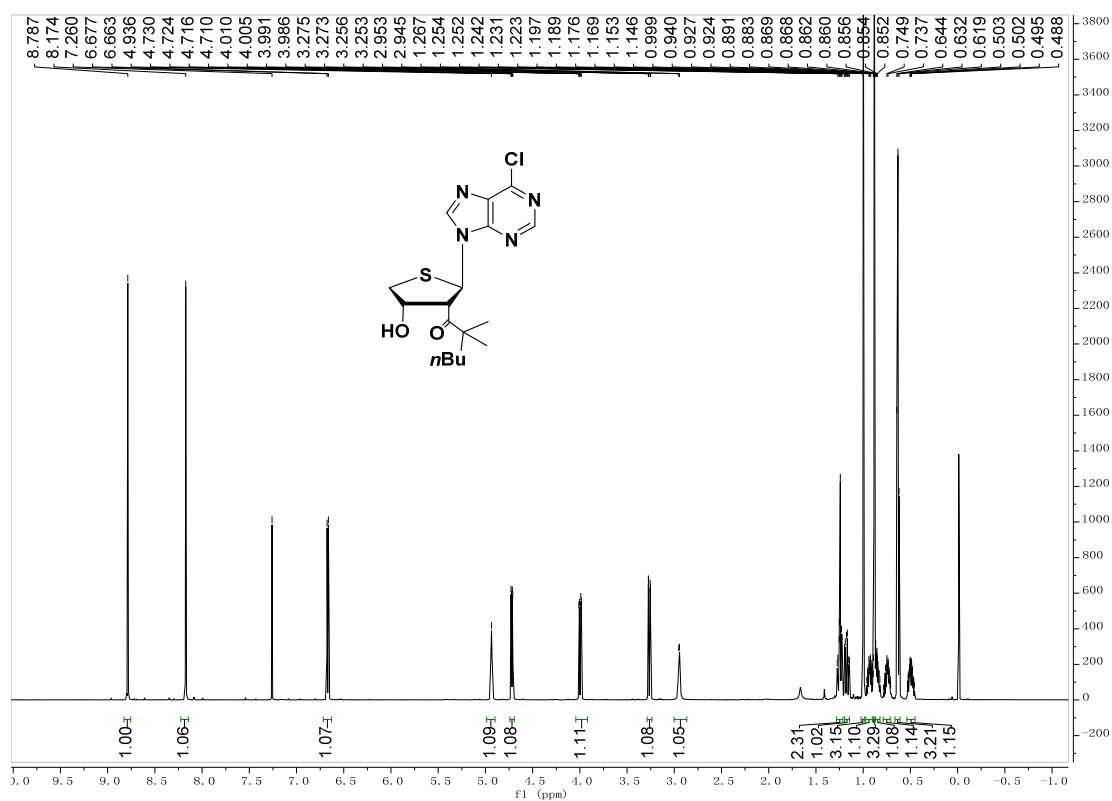
### $^1\text{H}$ NMR of 3m (600 MHz, $\text{CDCl}_3$ )



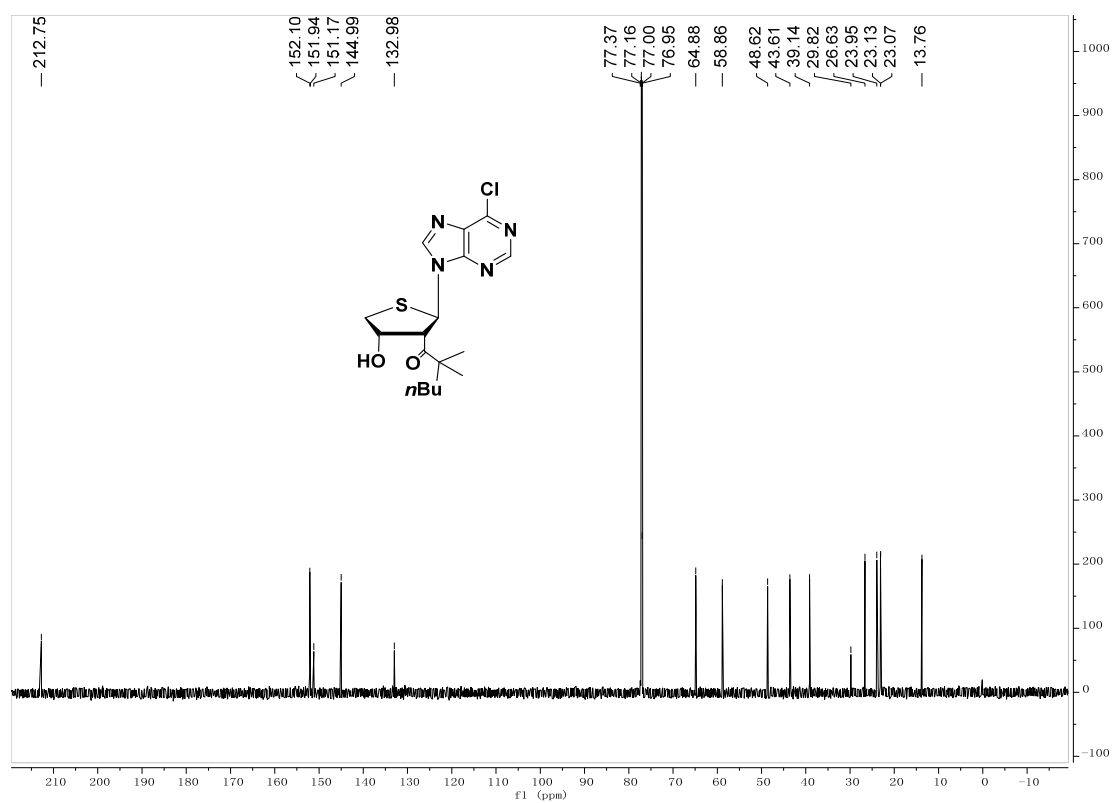
### $^{13}\text{C}$ NMR of 3m (150 MHz, $\text{CDCl}_3$ )



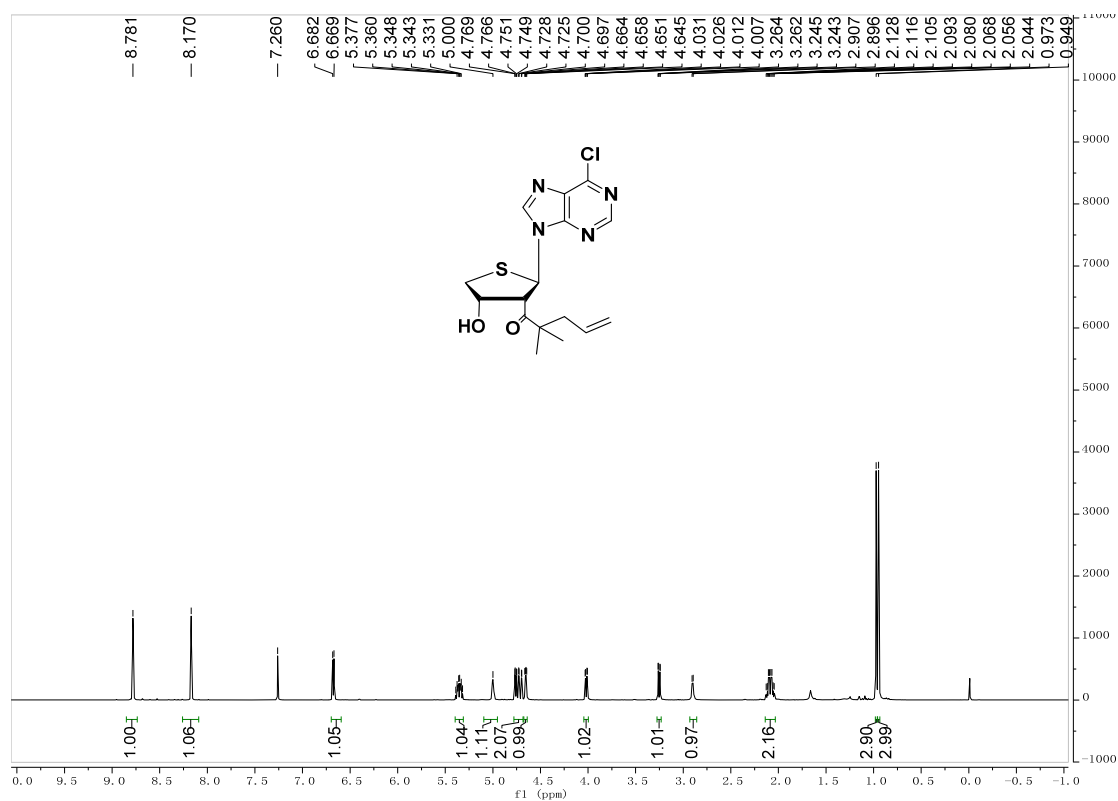
**<sup>1</sup>H NMR of 3n (600 MHz, CDCl<sub>3</sub>)**



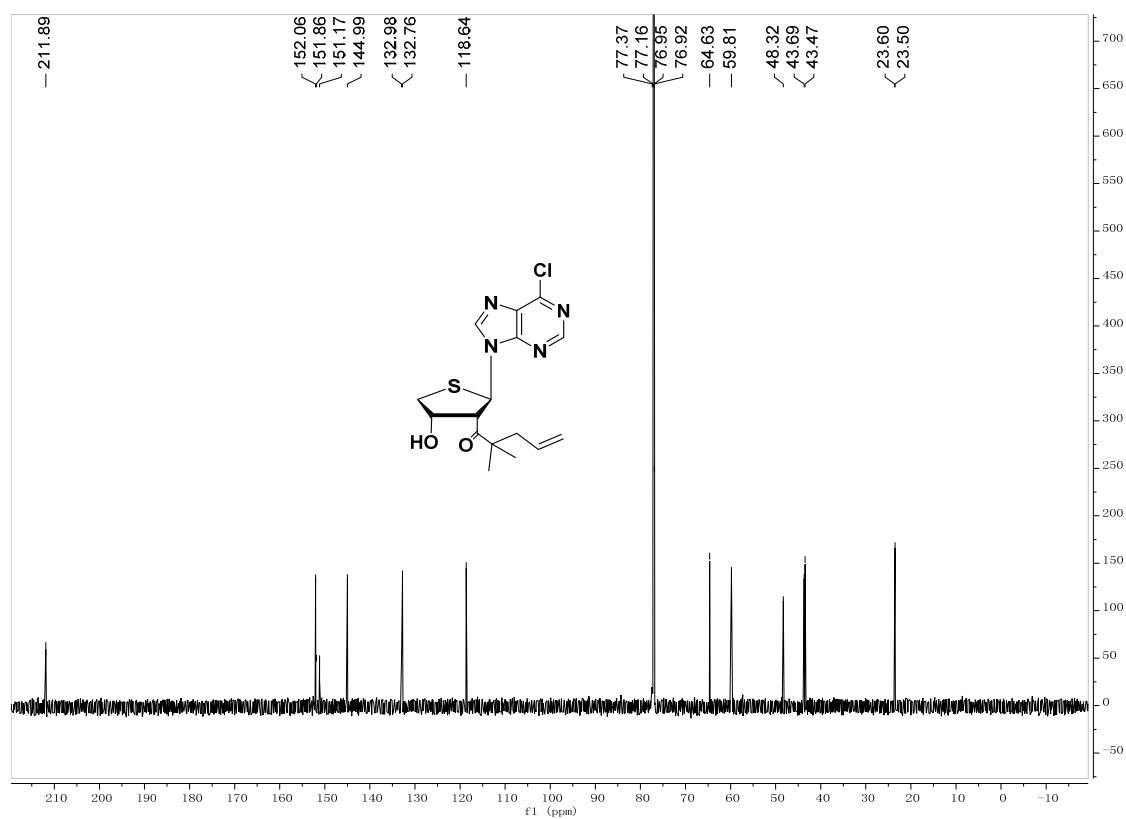
**<sup>13</sup>C NMR of 3n (150 MHz, CDCl<sub>3</sub>)**



### <sup>1</sup>H NMR of 3o (600 MHz, CDCl<sub>3</sub>)

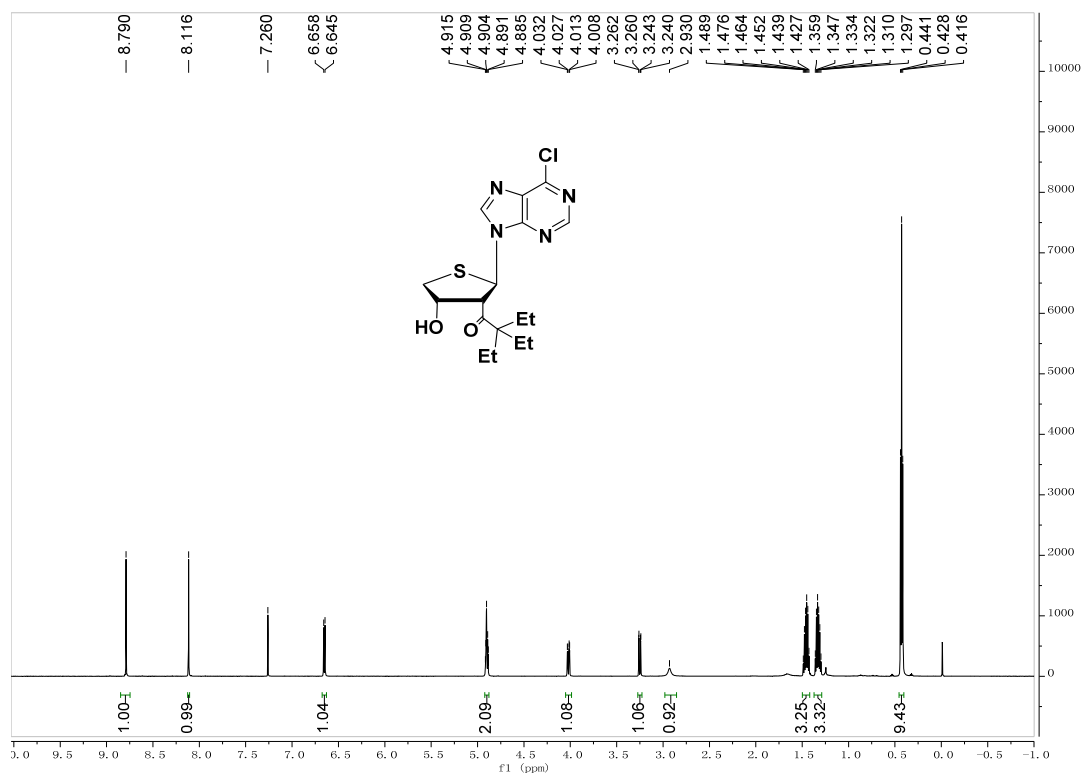


### <sup>13</sup>C NMR of 3o (150 MHz, CDCl<sub>3</sub>)

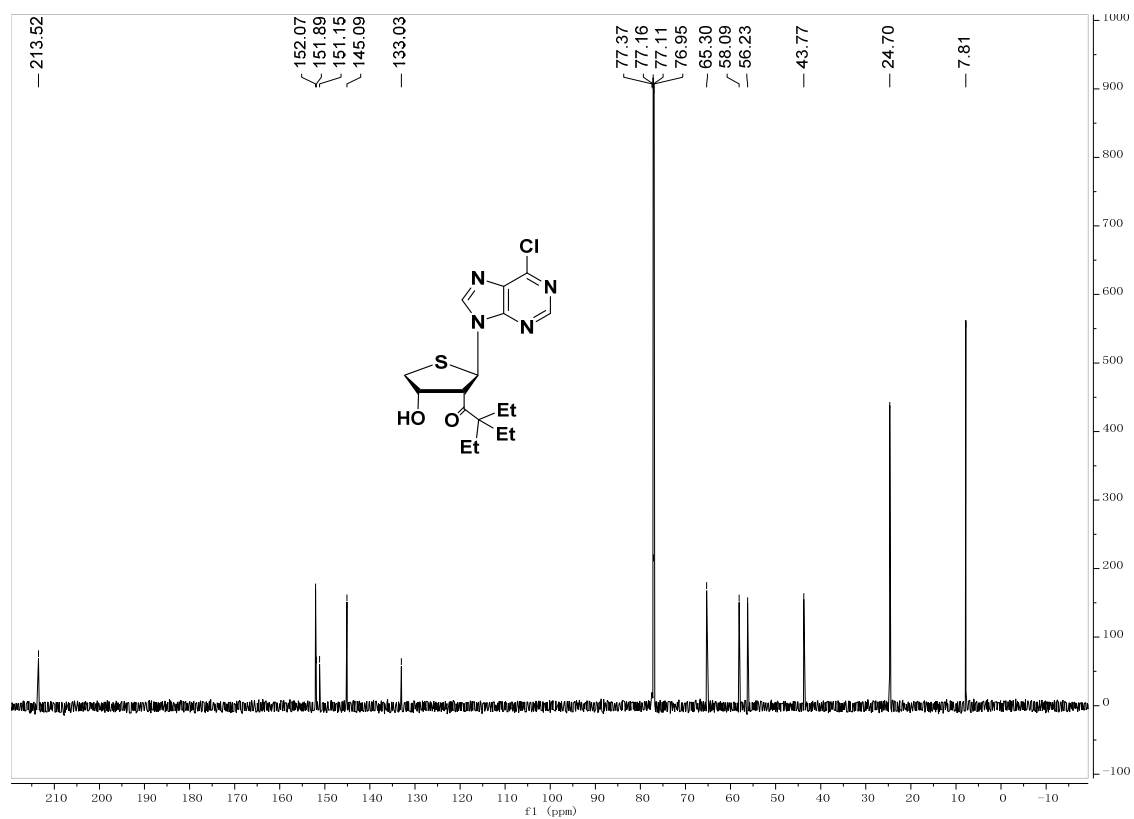




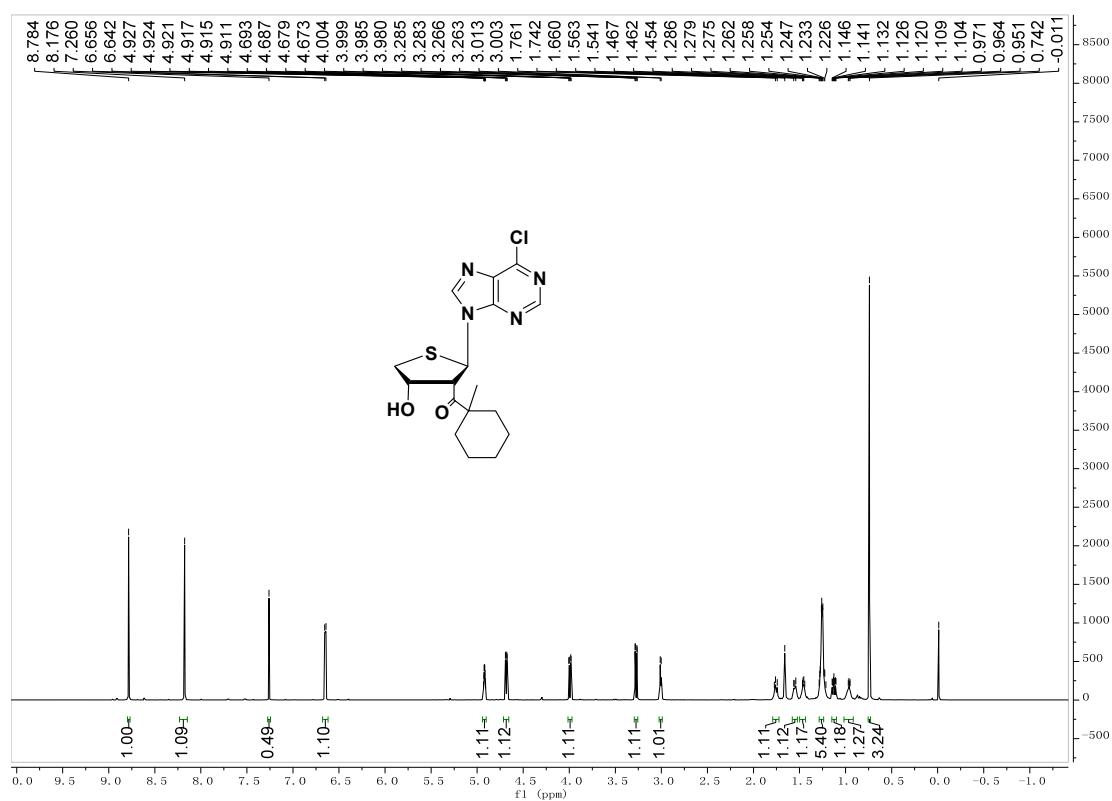
### <sup>1</sup>H NMR of 3p (600 MHz, CDCl<sub>3</sub>)



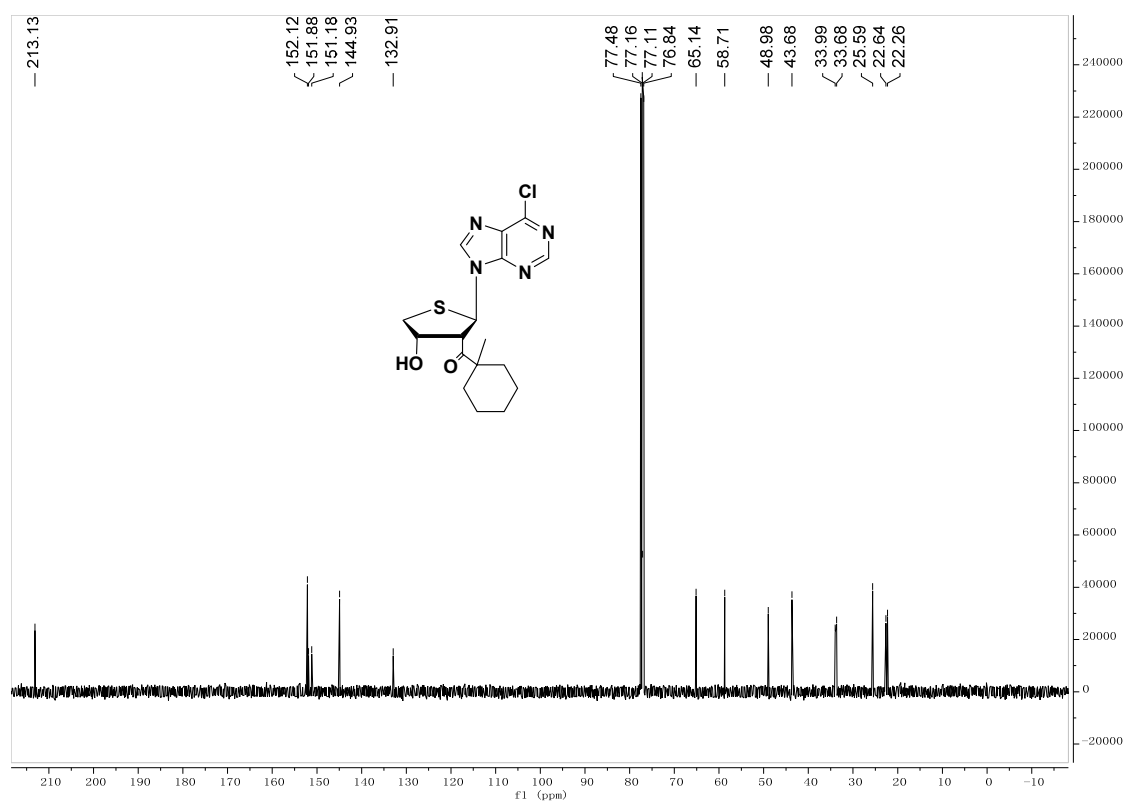
### <sup>13</sup>C NMR of 3p (150 MHz, CDCl<sub>3</sub>)



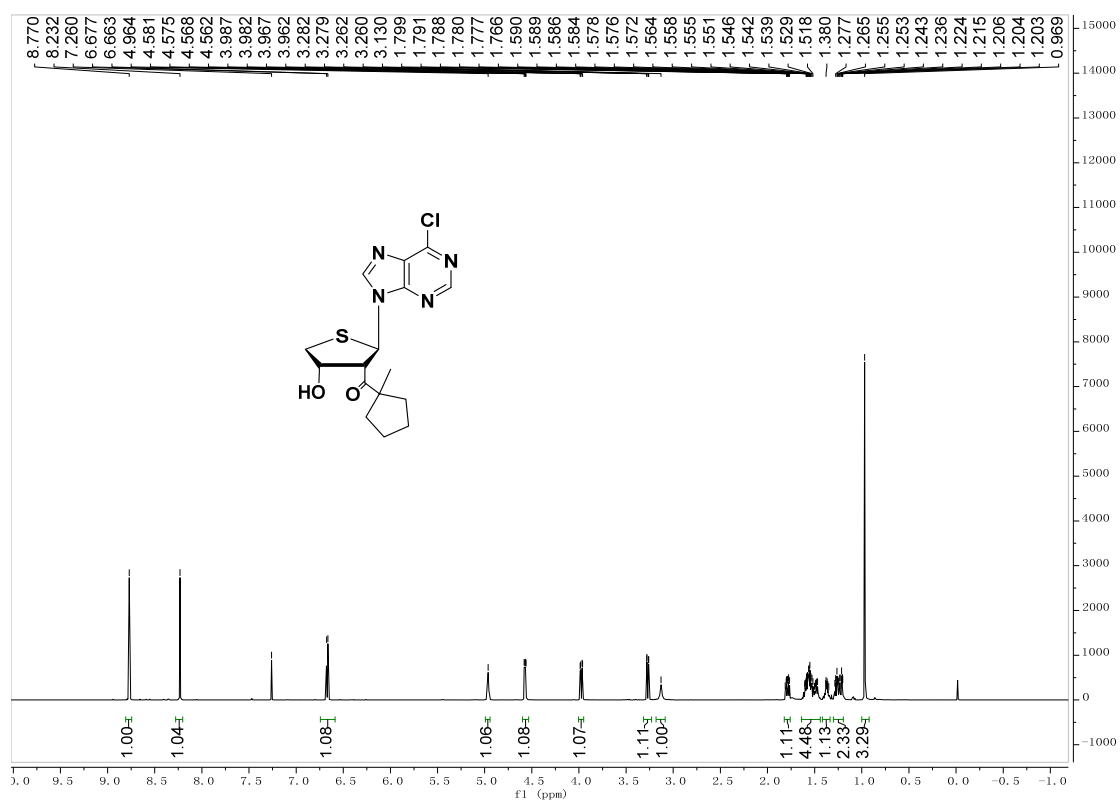
### <sup>1</sup>H NMR of 3q (600 MHz, CDCl<sub>3</sub>)



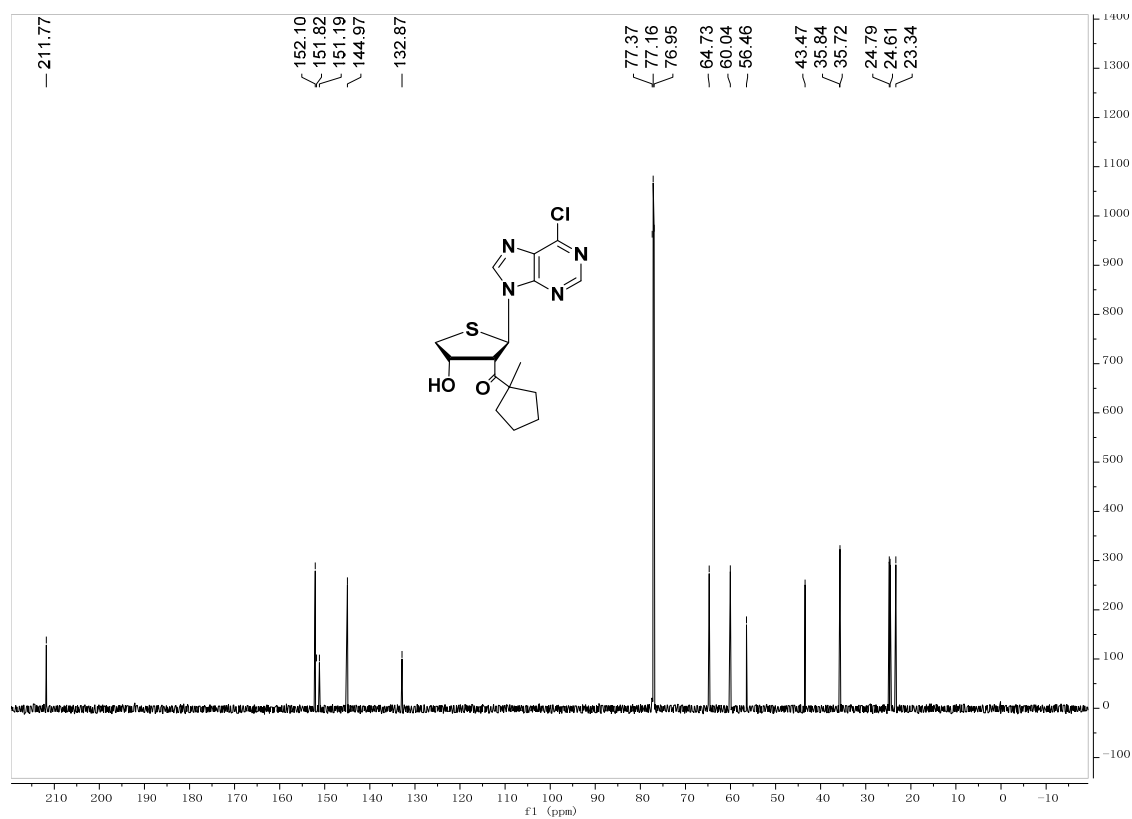
### <sup>13</sup>C NMR of 3q (100 MHz, CDCl<sub>3</sub>)



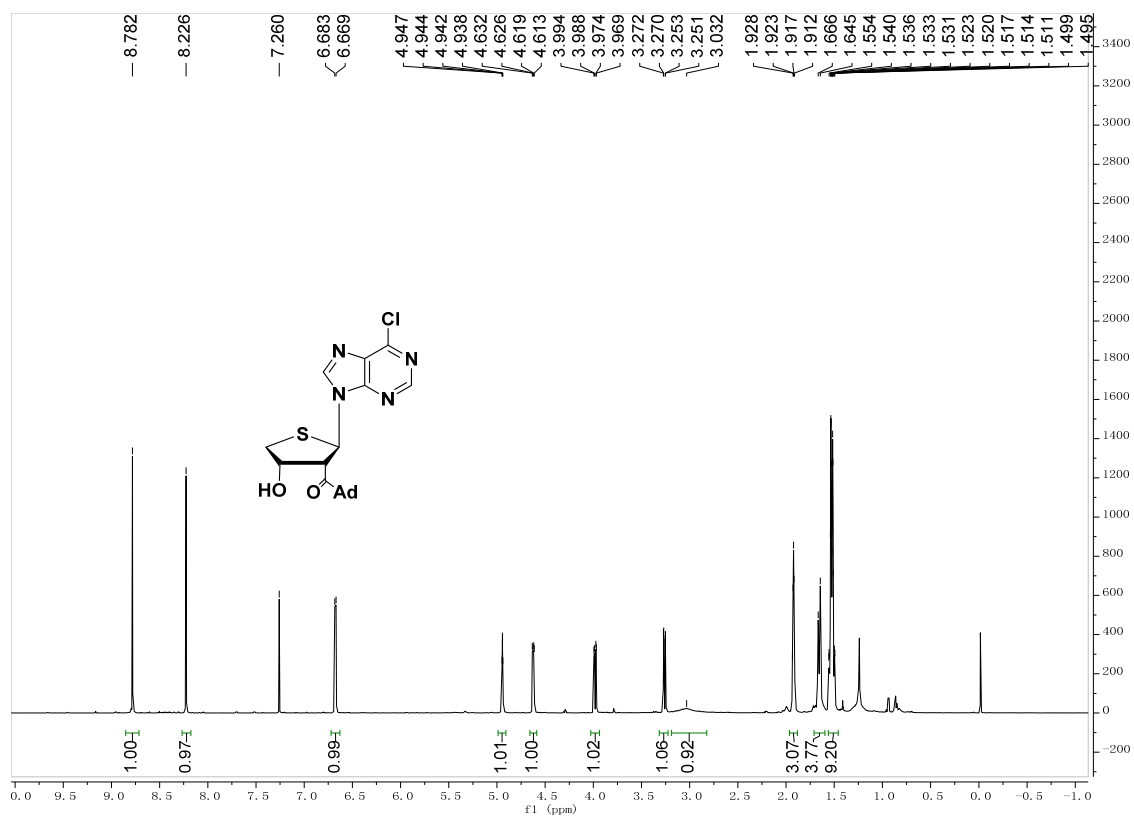
### $^1\text{H}$ NMR of 3r (600 MHz, $\text{CDCl}_3$ )



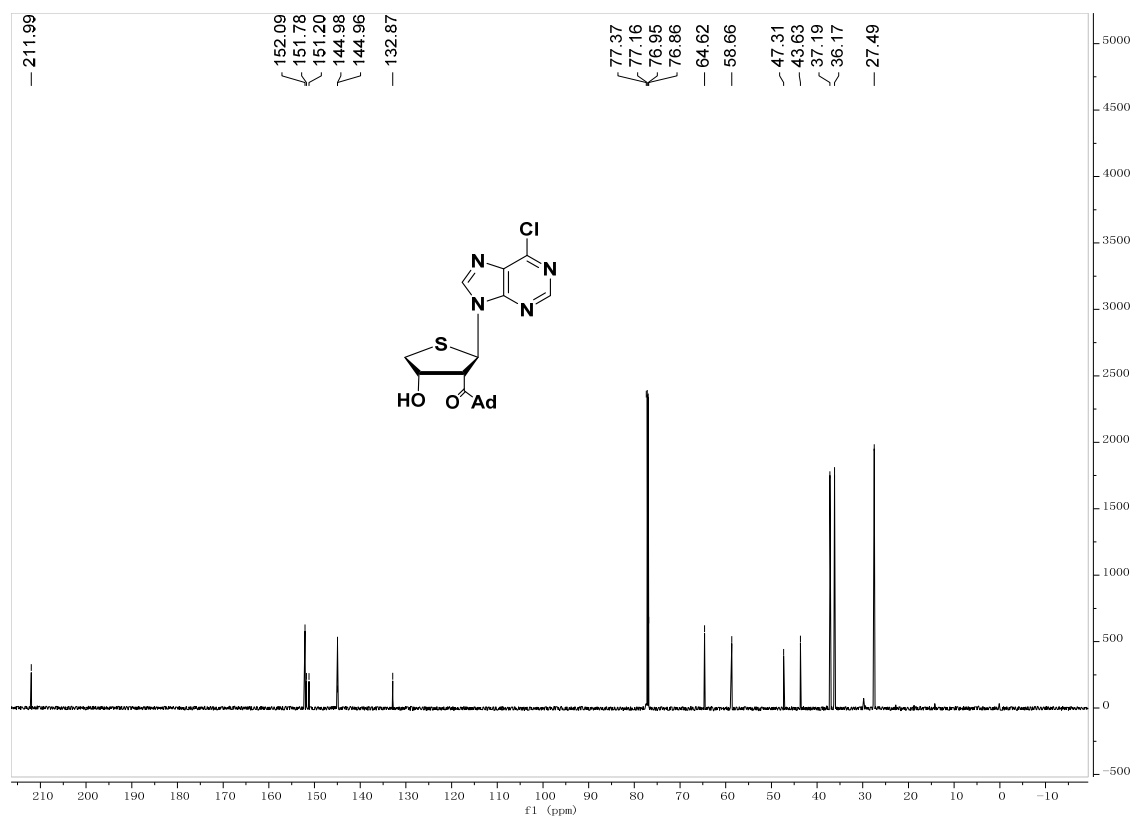
### $^{13}\text{C}$ NMR of 3r (150 MHz, $\text{CDCl}_3$ )



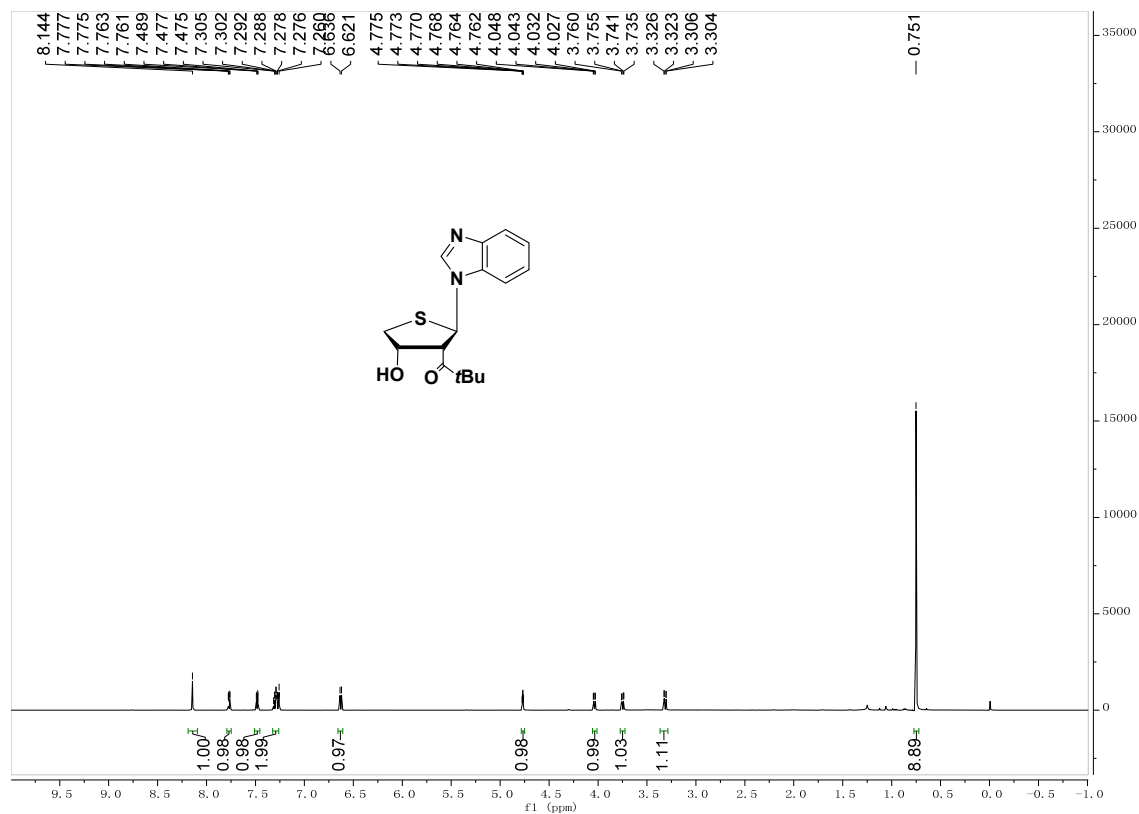
### $^1\text{H}$ NMR of **3s** (600 MHz, $\text{CDCl}_3$ )



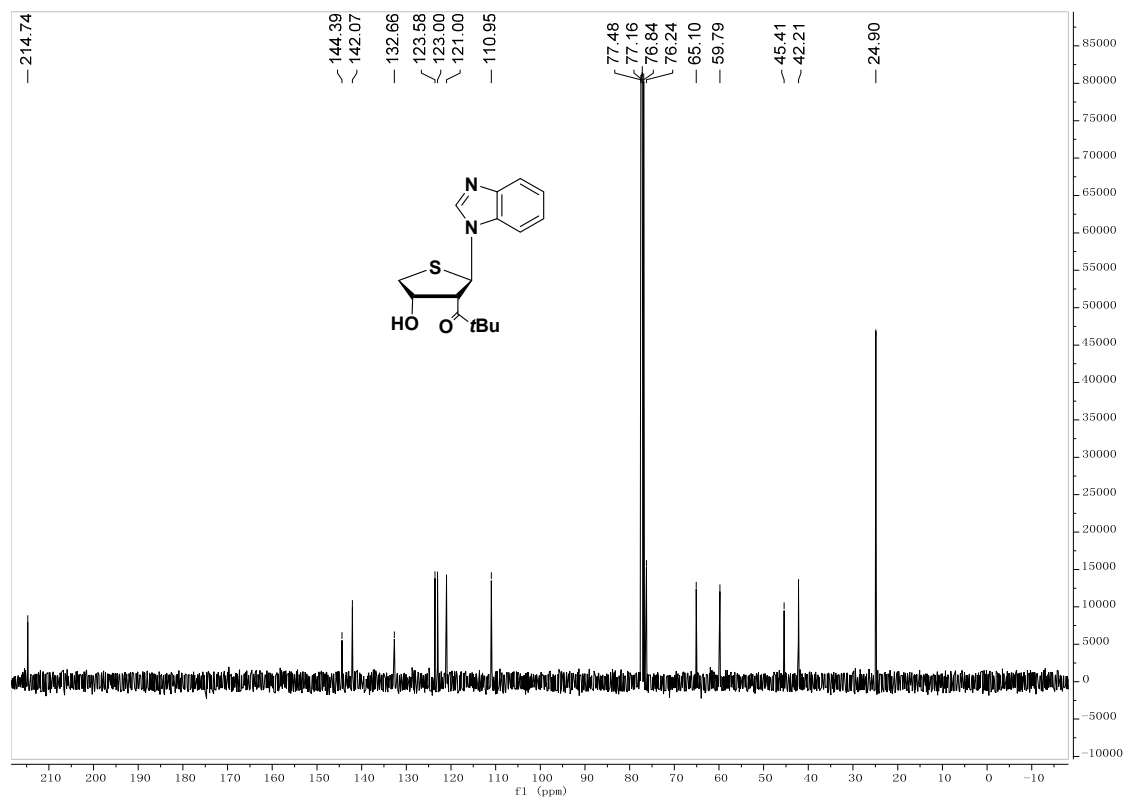
### $^{13}\text{C}$ NMR of **3s** (150 MHz, $\text{CDCl}_3$ )



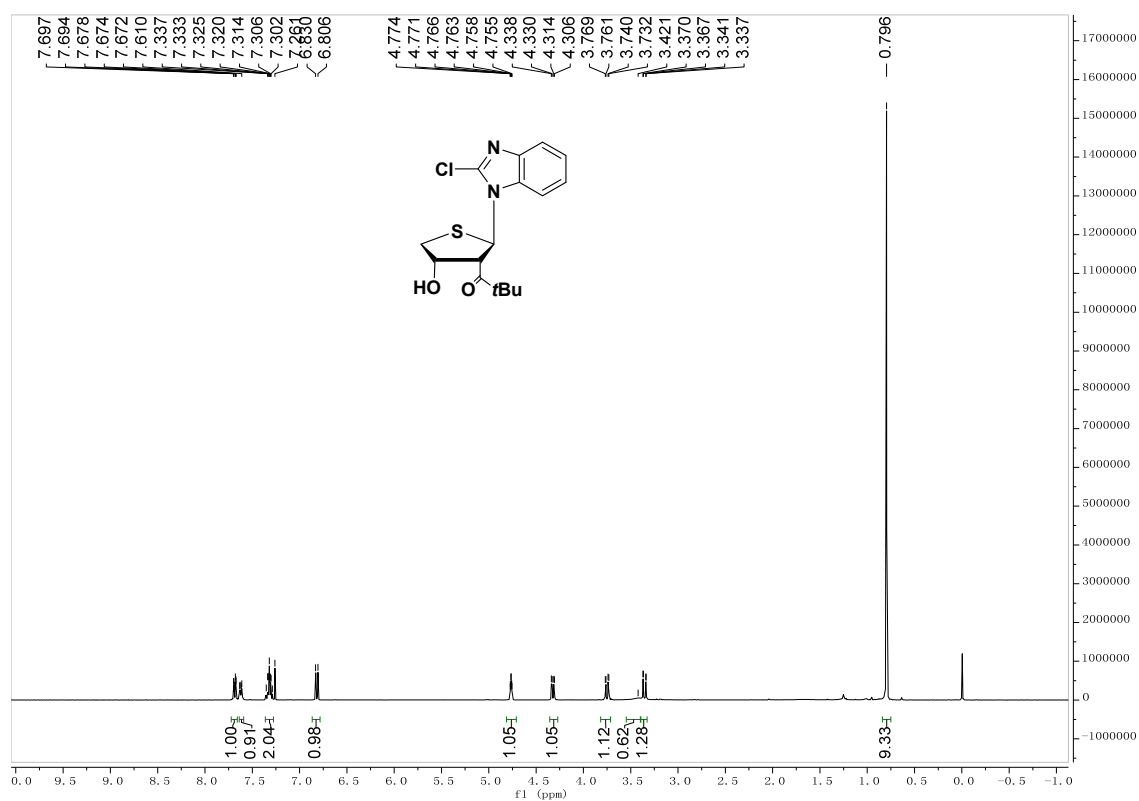
### $^1\text{H}$ NMR of 3t (600 MHz, $\text{CDCl}_3$ )



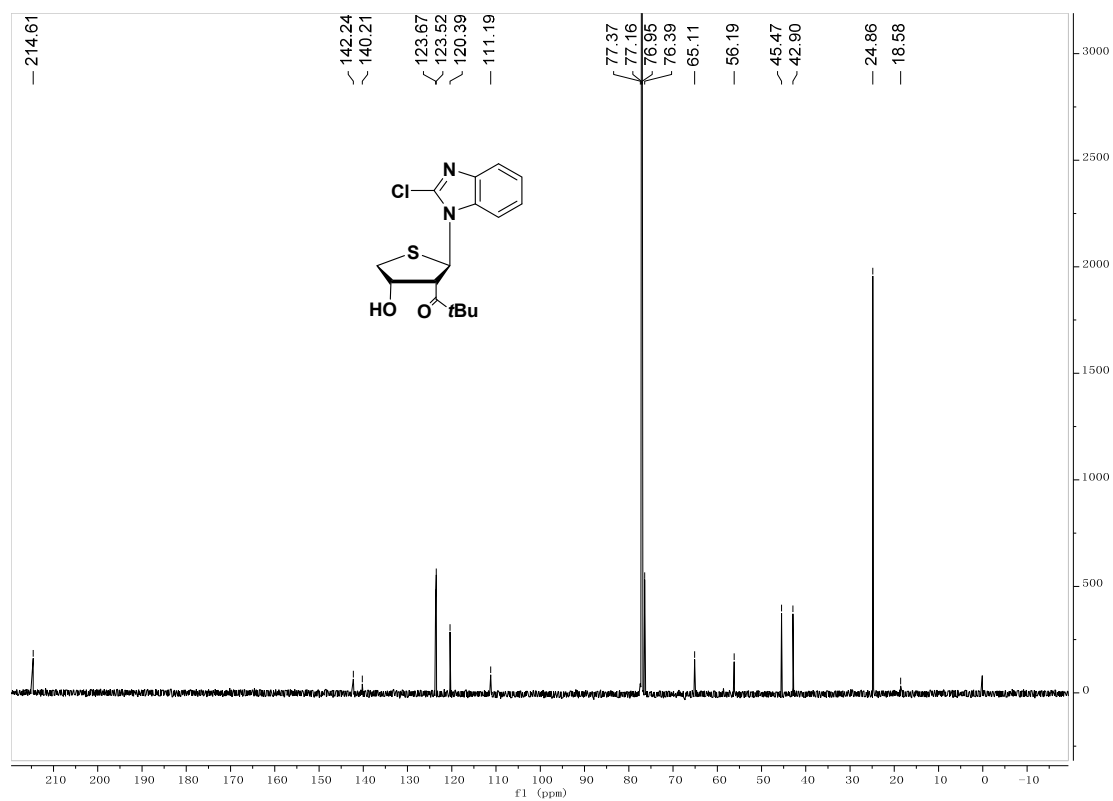
### $^{13}\text{C}$ NMR of 3t (100 MHz, $\text{CDCl}_3$ )



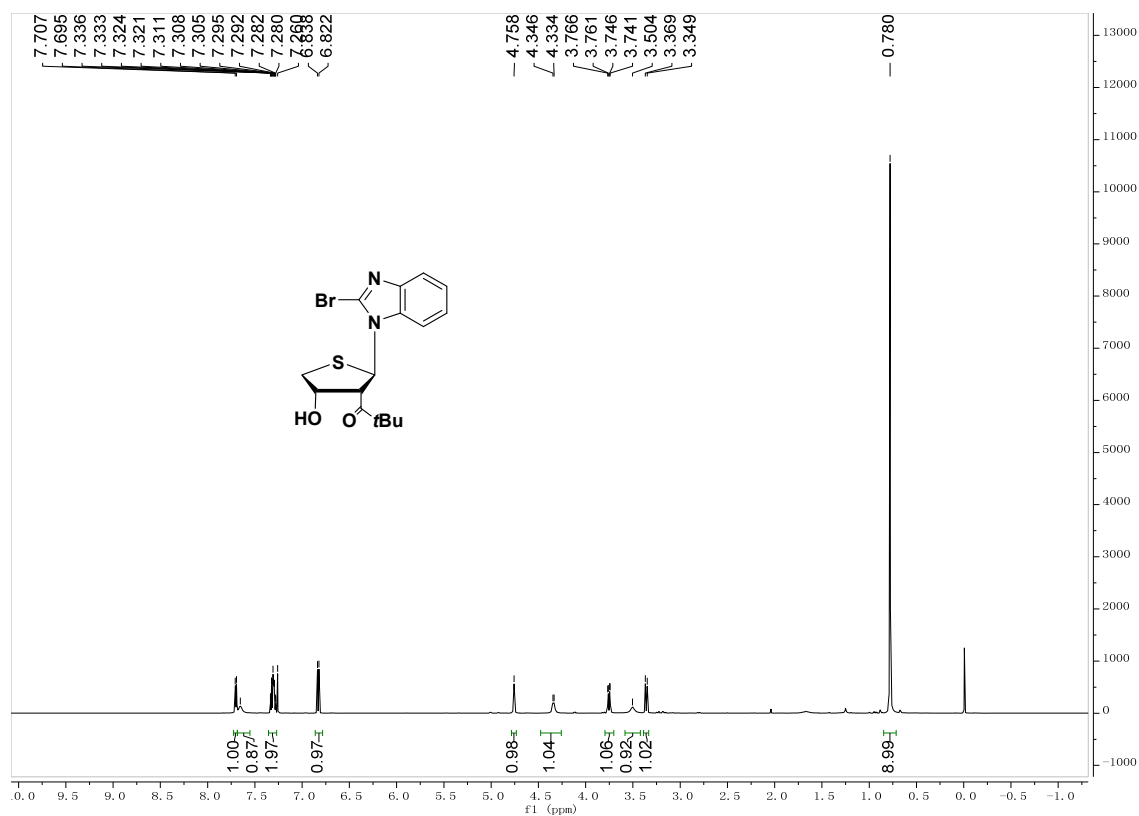
### <sup>1</sup>H NMR of 3u (400 MHz, CDCl<sub>3</sub>)



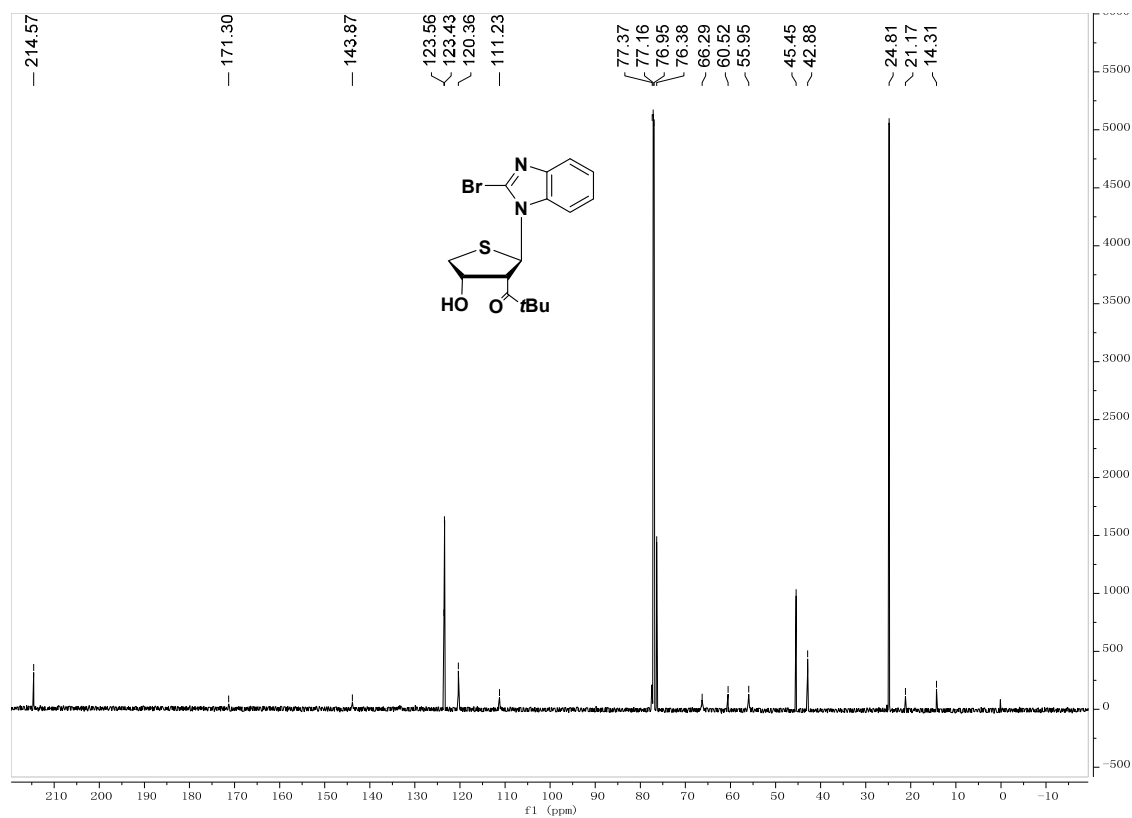
### <sup>13</sup>C NMR of 3u (150 MHz, CDCl<sub>3</sub>)



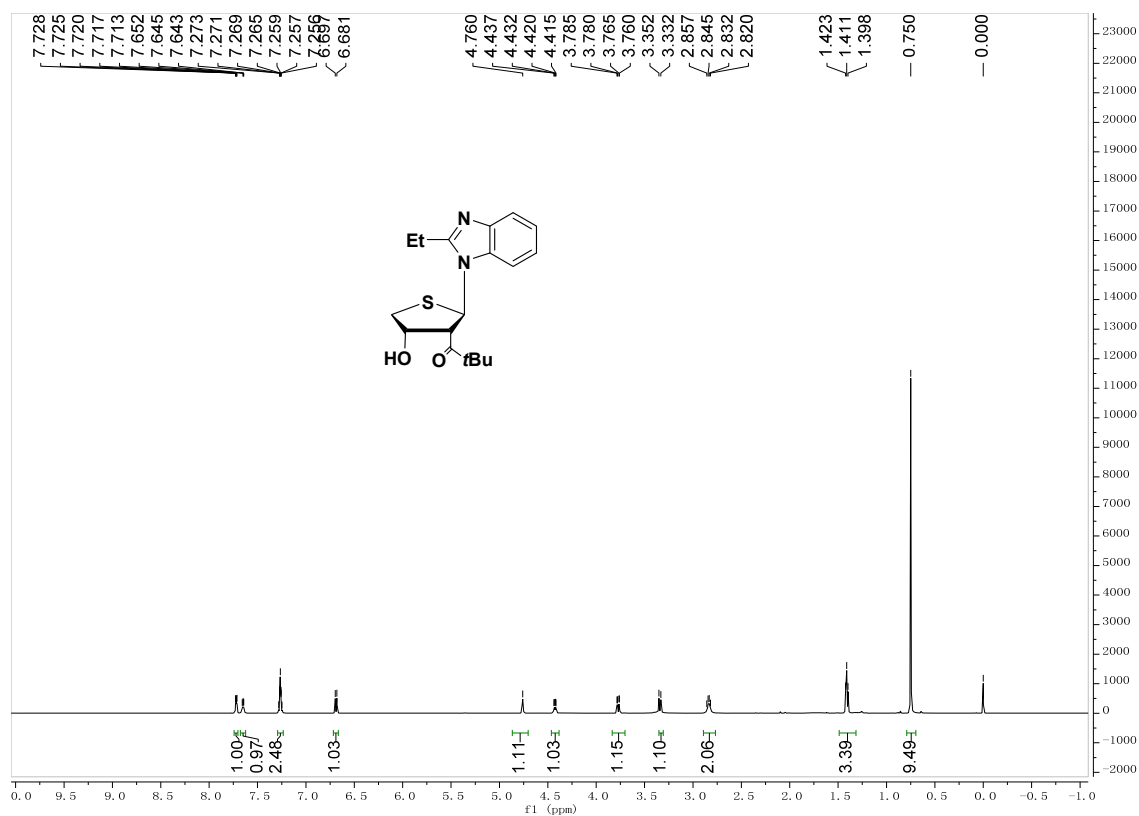
### <sup>1</sup>H NMR of 3v (600 MHz, CDCl<sub>3</sub>)



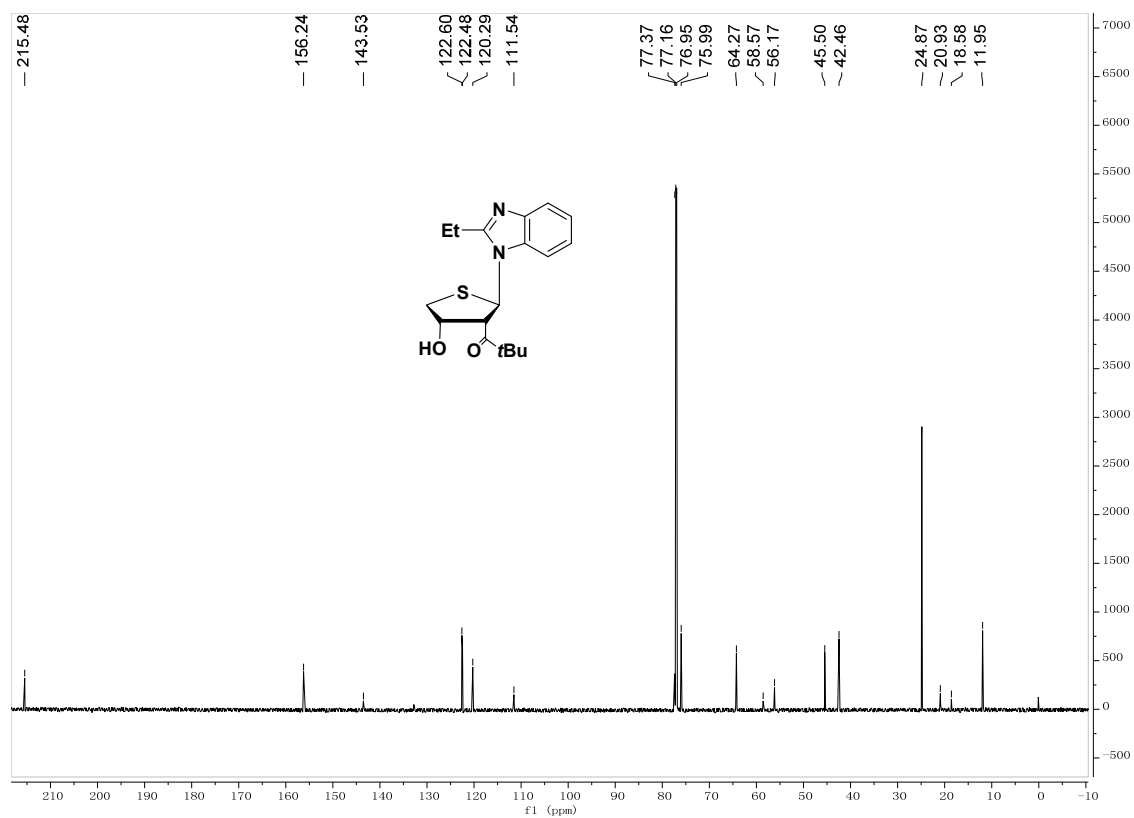
### <sup>13</sup>C NMR of 3v (150 MHz, CDCl<sub>3</sub>)



### <sup>1</sup>H NMR of 3w (600 MHz, CDCl<sub>3</sub>)

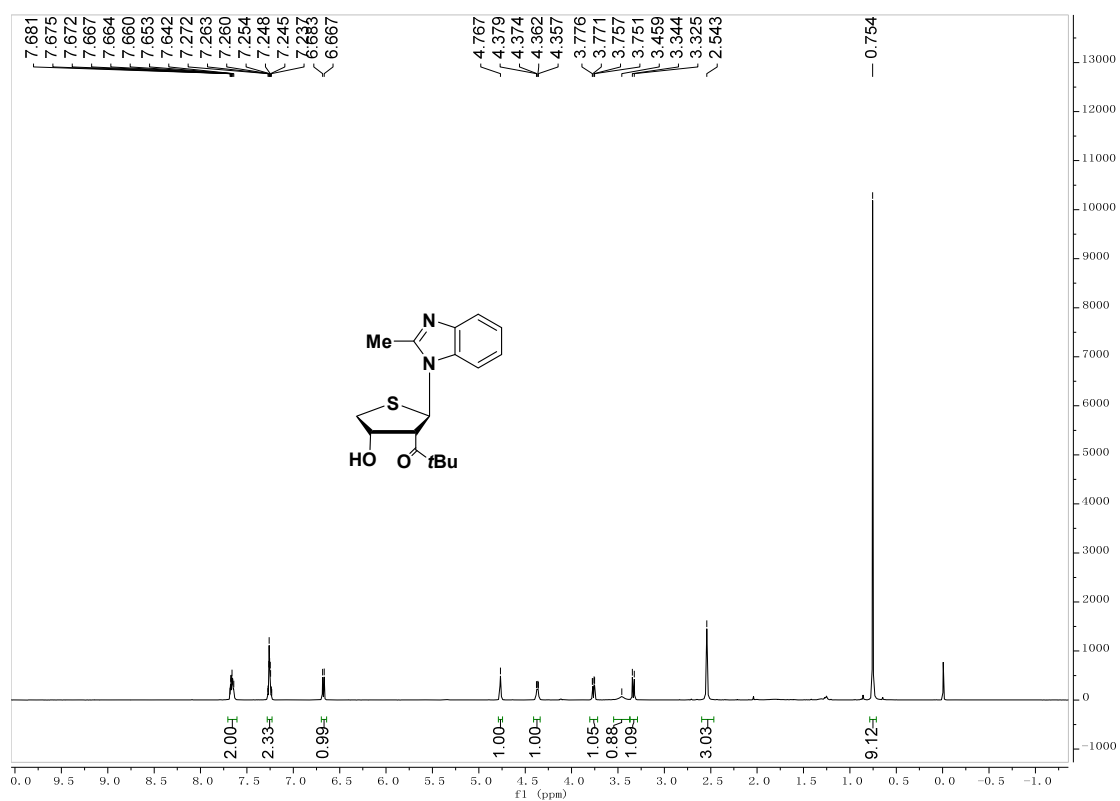


### <sup>13</sup>C NMR of 3w (150 MHz, CDCl<sub>3</sub>)

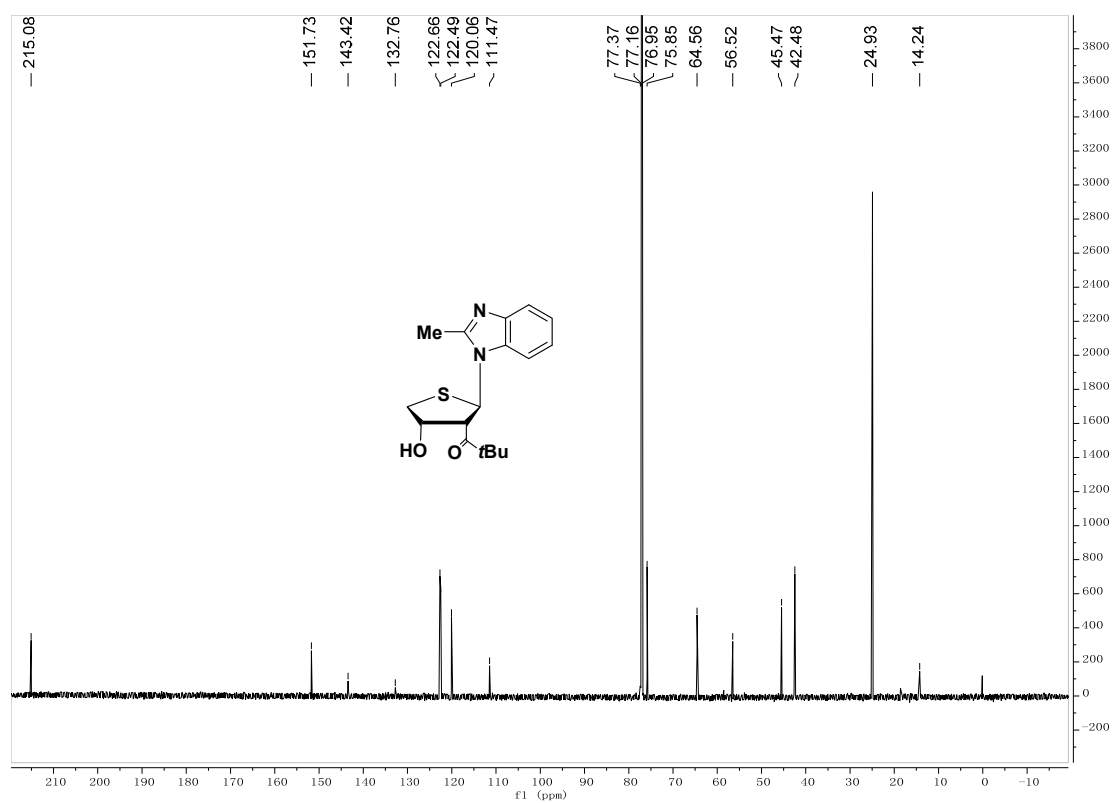




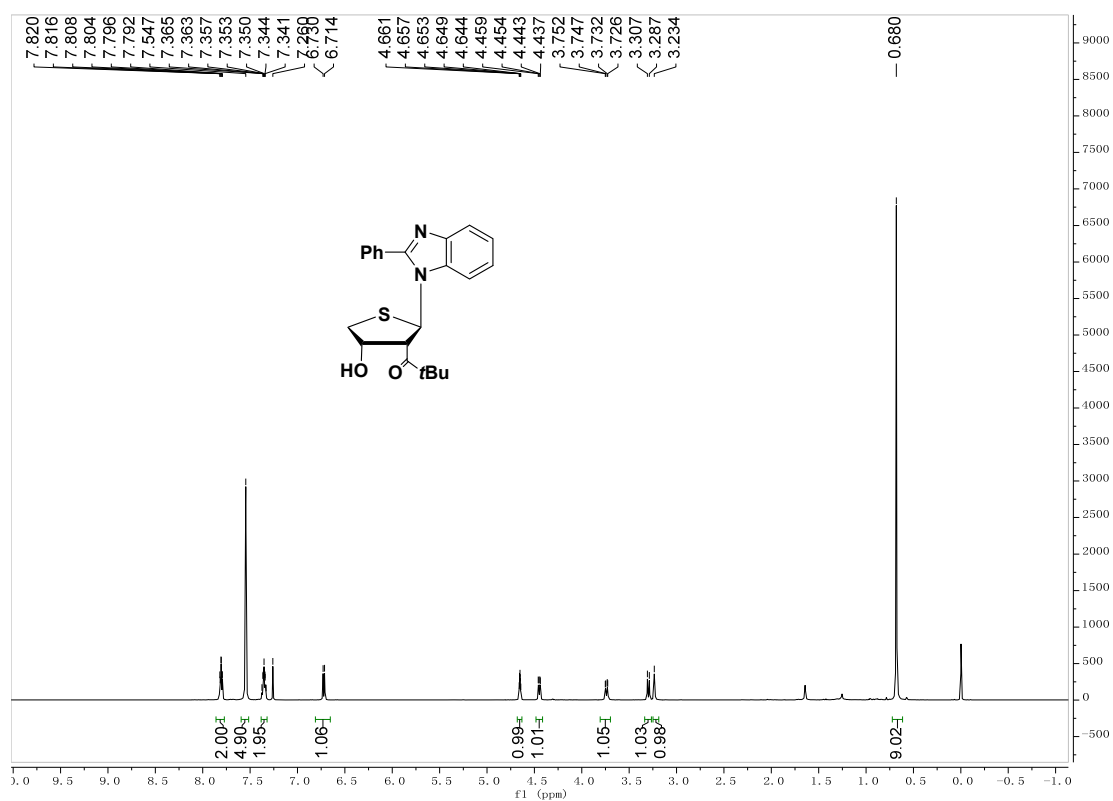
### <sup>1</sup>H NMR of 3x (600 MHz, CDCl<sub>3</sub>)



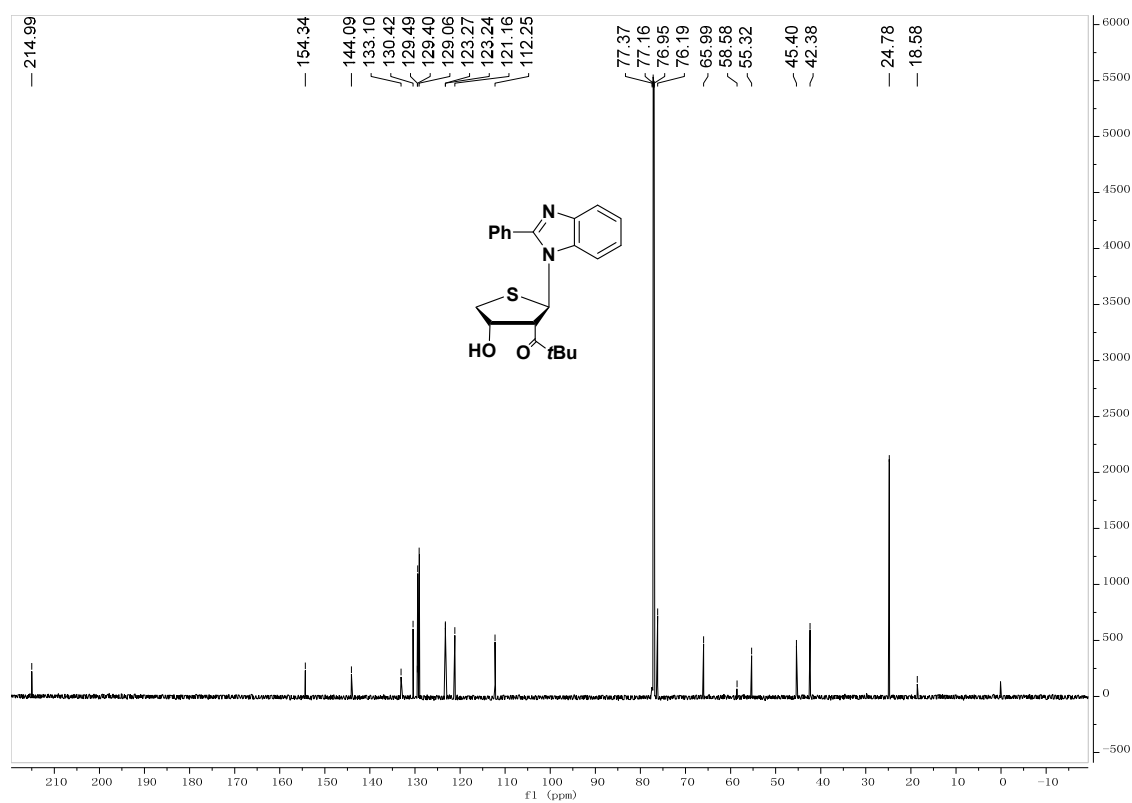
### <sup>13</sup>C NMR of 3x (150 MHz, CDCl<sub>3</sub>)



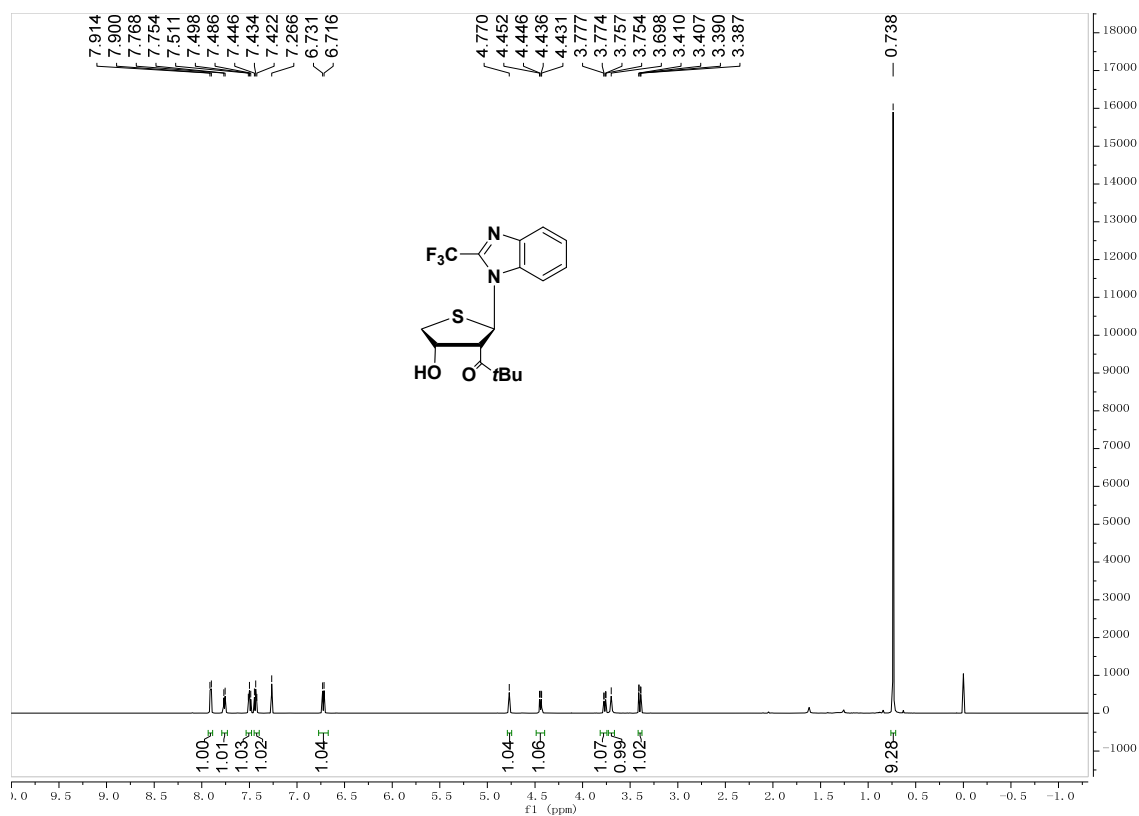
**<sup>1</sup>H NMR of 3y (600 MHz, CDCl<sub>3</sub>)**



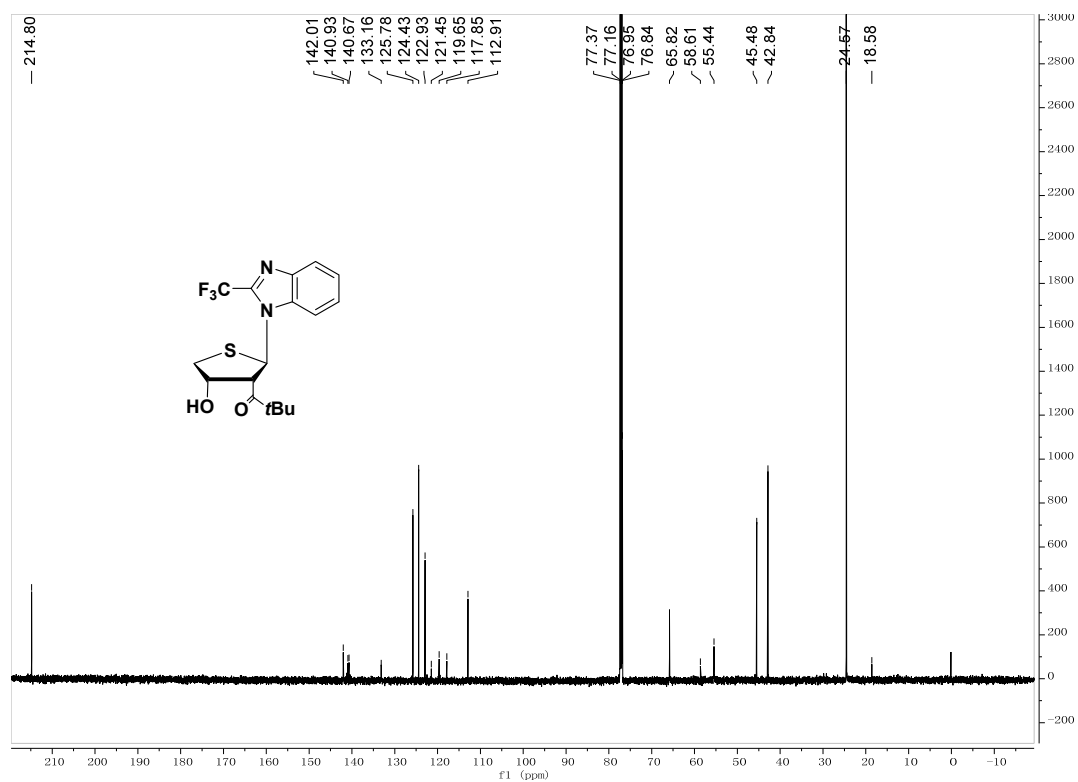
**<sup>13</sup>C NMR of 3y (150 MHz, CDCl<sub>3</sub>)**



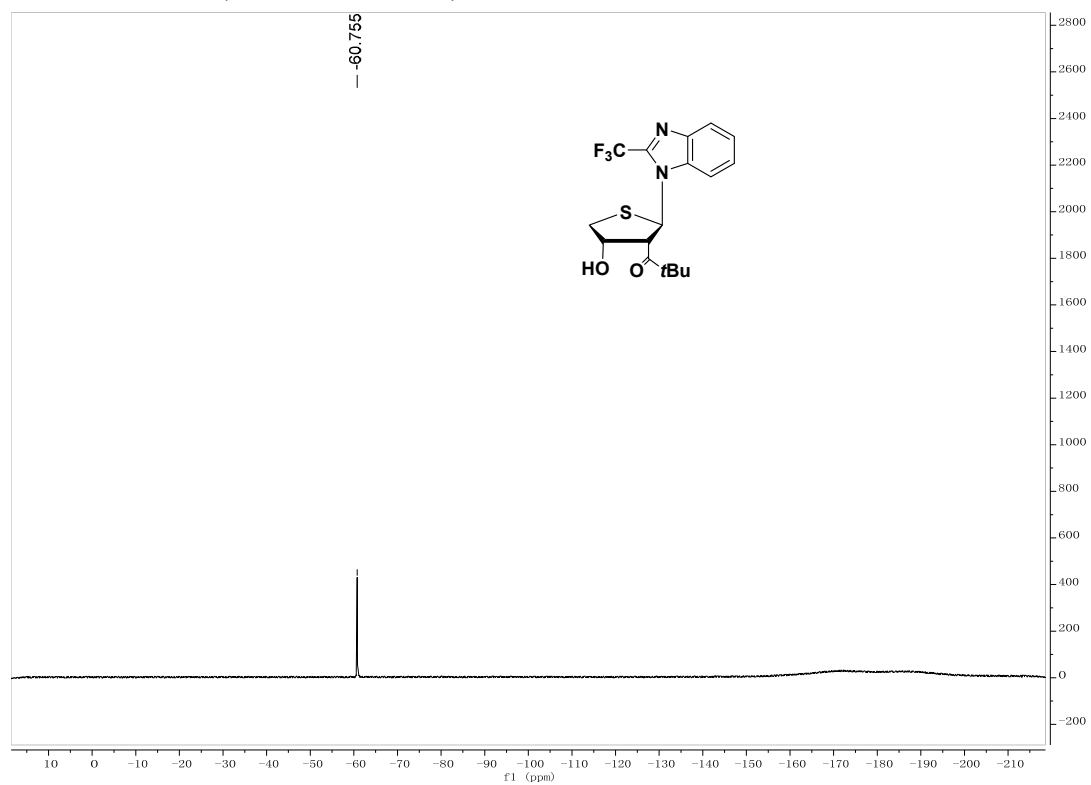
### $^1\text{H}$ NMR of **3z** (600 MHz, $\text{CDCl}_3$ )



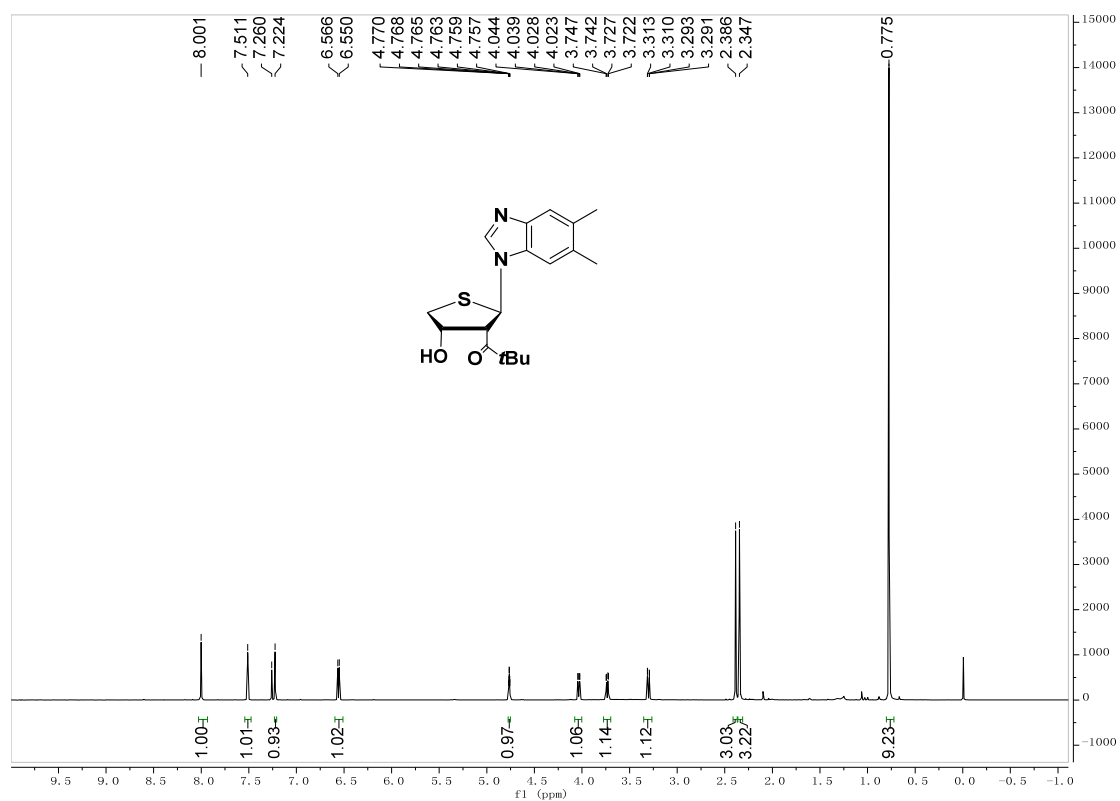
### $^{13}\text{C}$ NMR of **3z** (150 MHz, $\text{CDCl}_3$ )



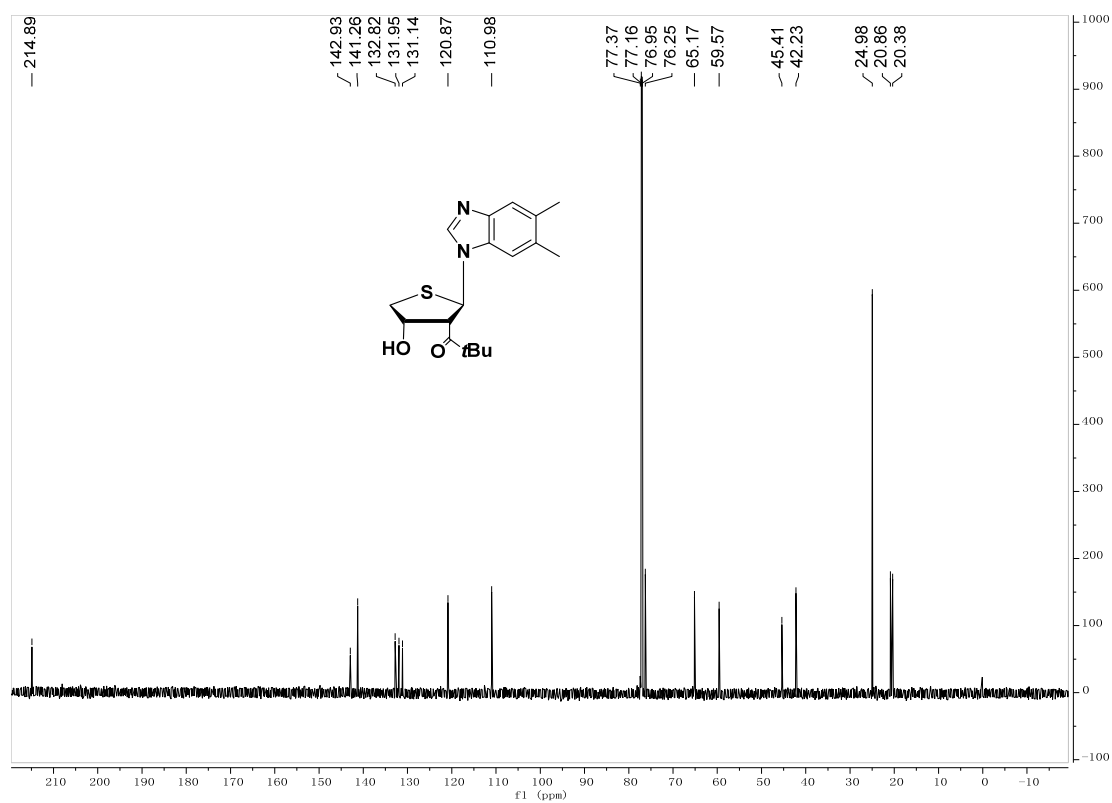
**<sup>19</sup>F NMR of 3z (565 MHz, CDCl<sub>3</sub>)**



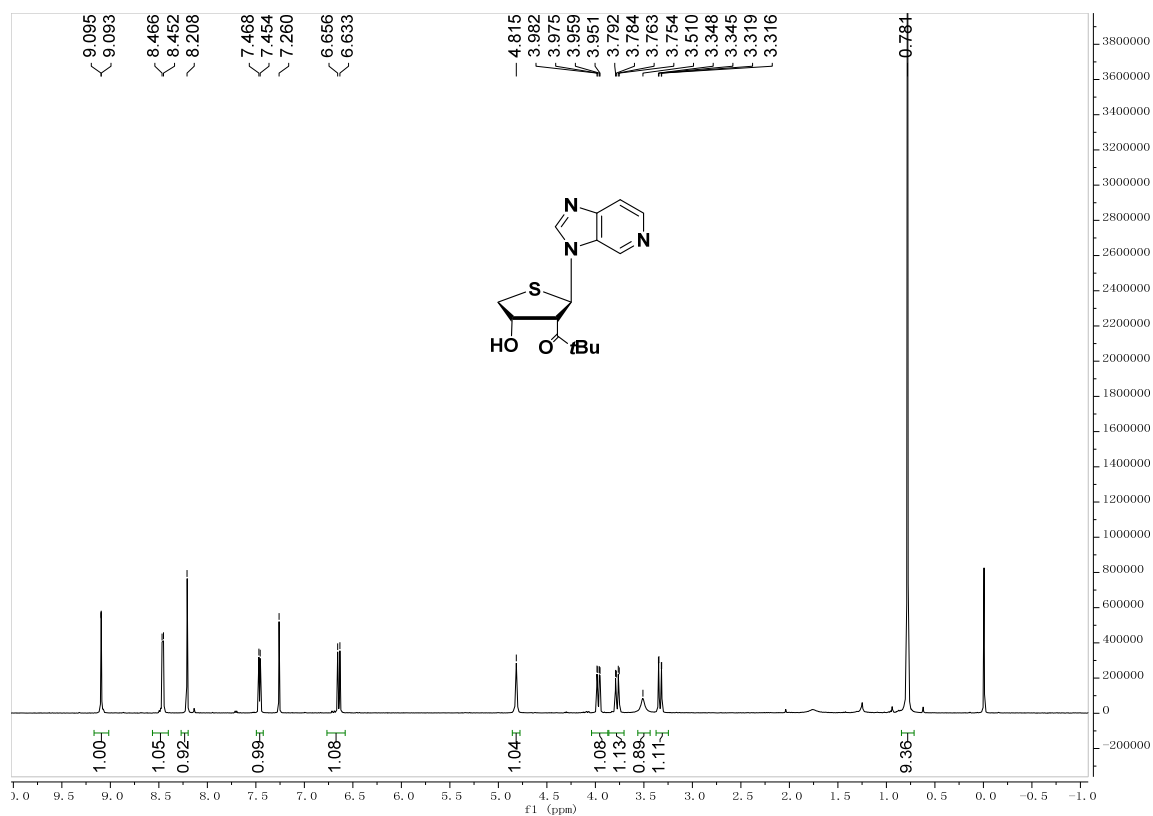
### <sup>1</sup>H NMR of 3aa (600 MHz, CDCl<sub>3</sub>)



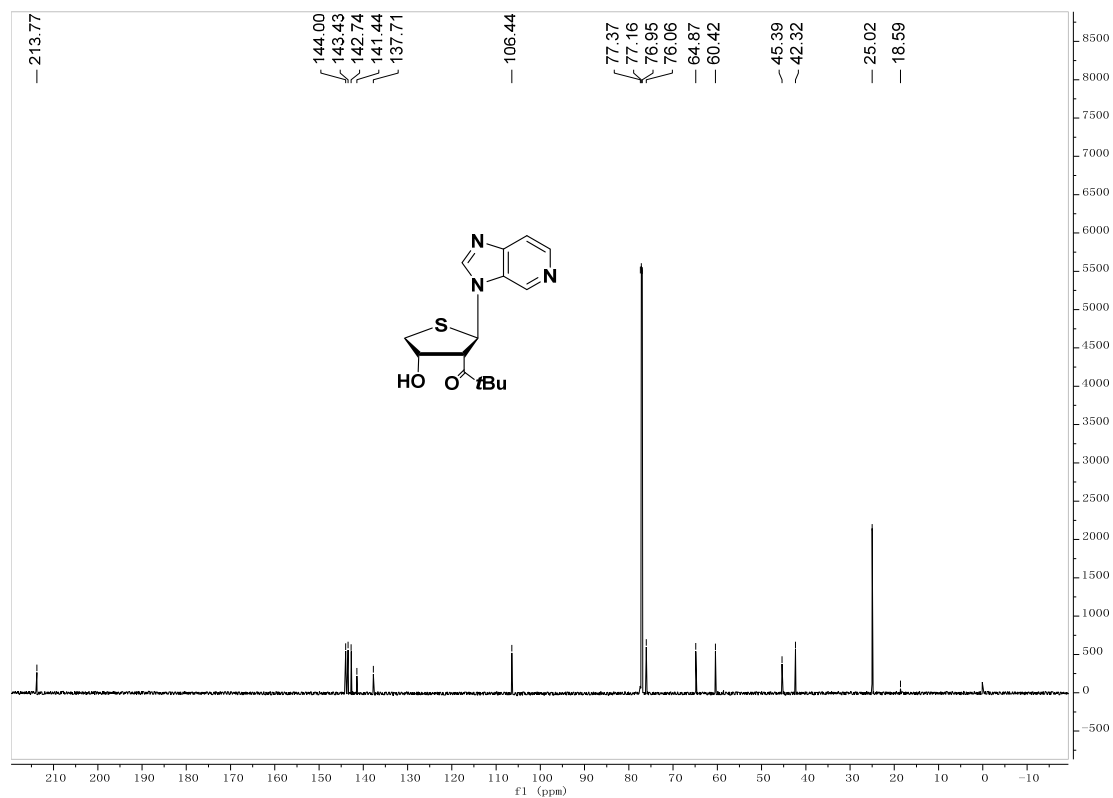
### <sup>13</sup>C NMR of 3aa (150 MHz, CDCl<sub>3</sub>)



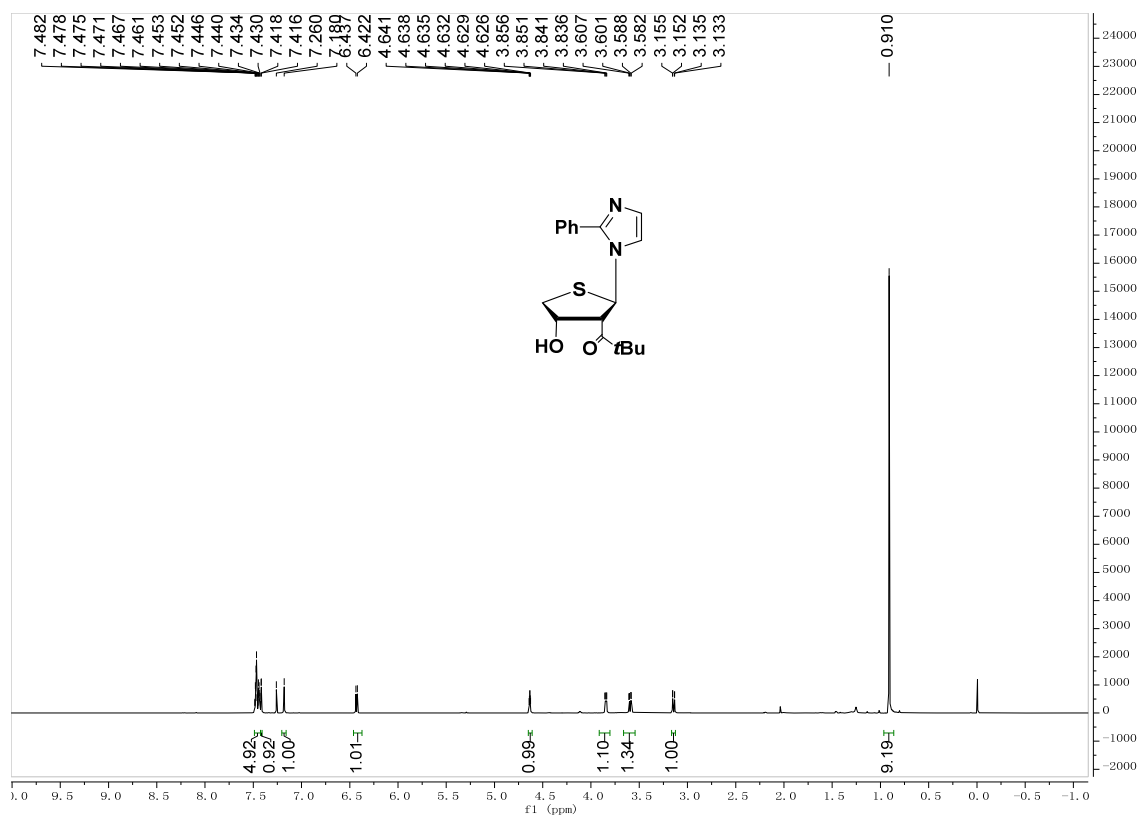
### <sup>1</sup>H NMR of 3ab (400 MHz, CDCl<sub>3</sub>)



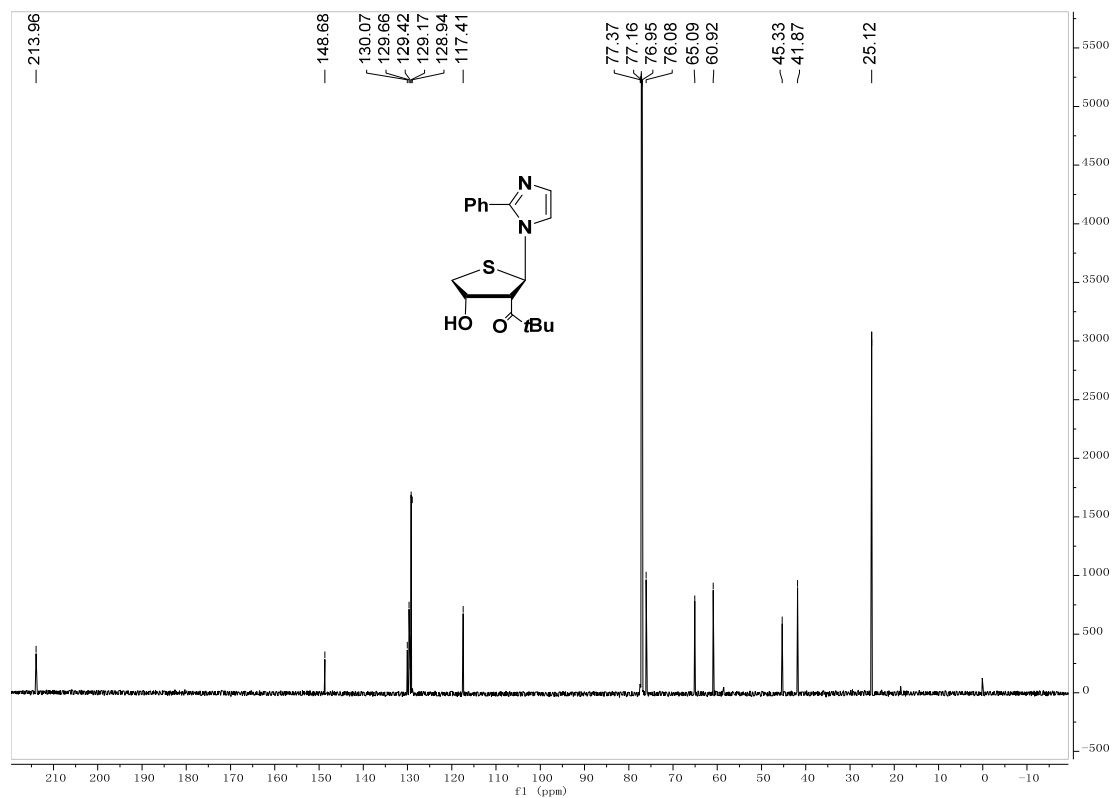
### <sup>13</sup>C NMR of 3ab (150 MHz, CDCl<sub>3</sub>)



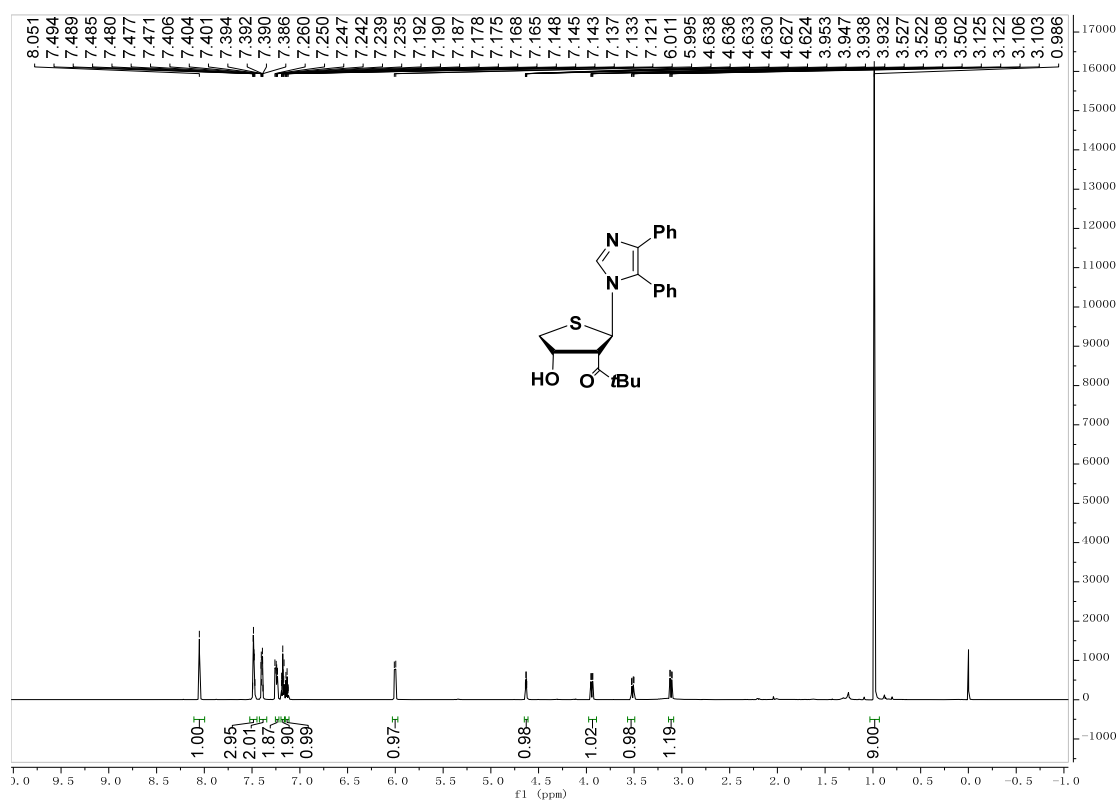
### $^1\text{H}$ NMR of **3ac** (600 MHz, $\text{CDCl}_3$ )



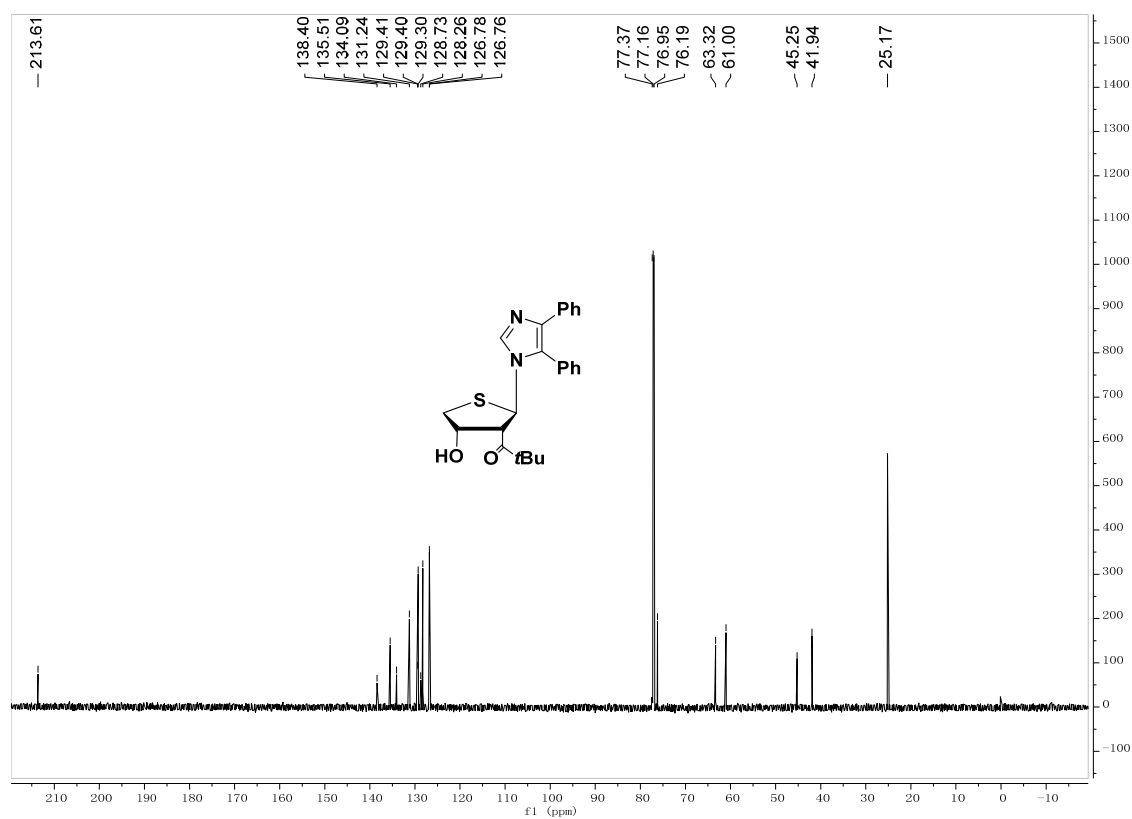
### $^{13}\text{C}$ NMR of **3ac** (150 MHz, $\text{CDCl}_3$ )



### $^1\text{H}$ NMR of 3ad (600 MHz, $\text{CDCl}_3$ )

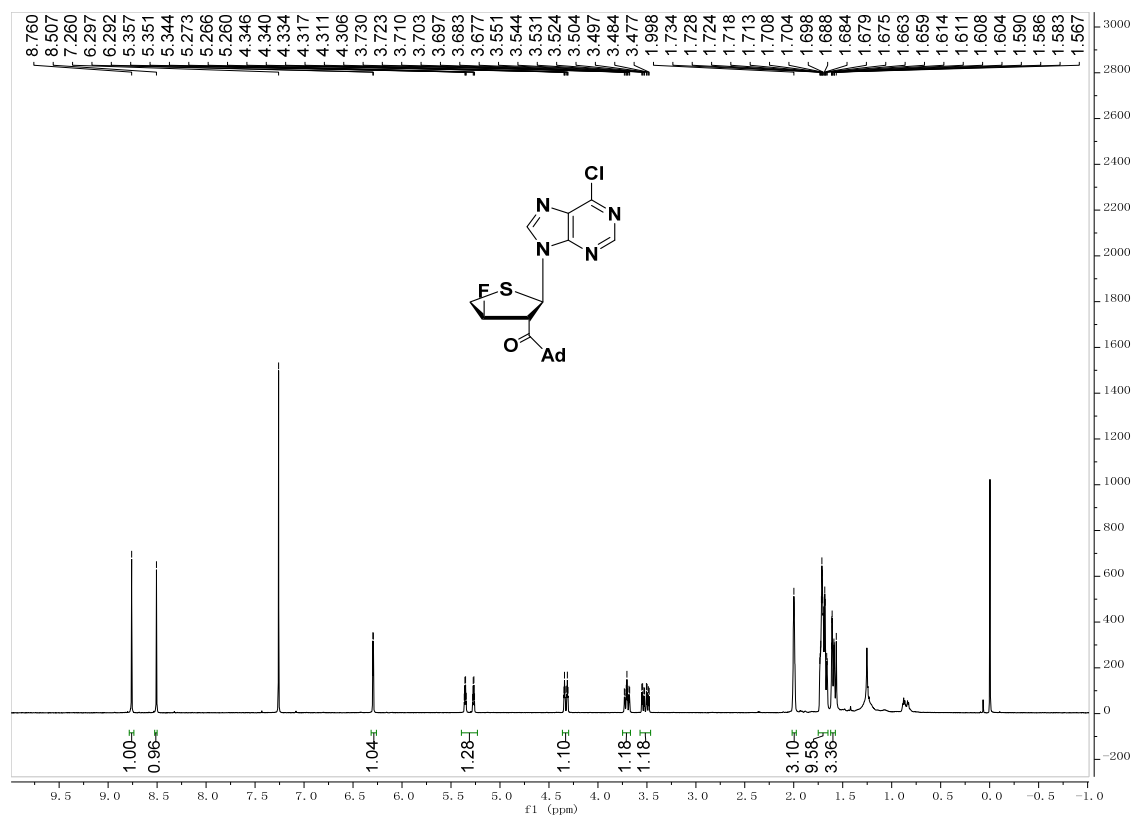


### $^{13}\text{C}$ NMR of 3ad (150 MHz, $\text{CDCl}_3$ )

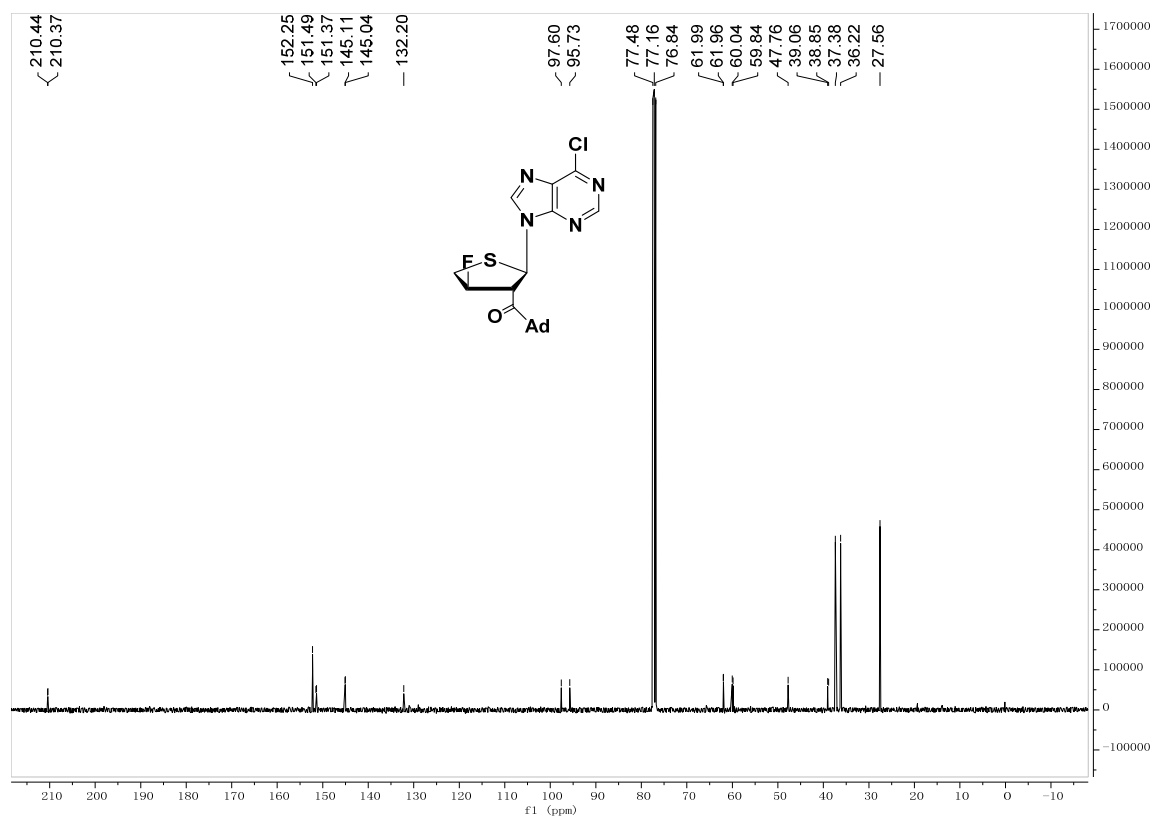




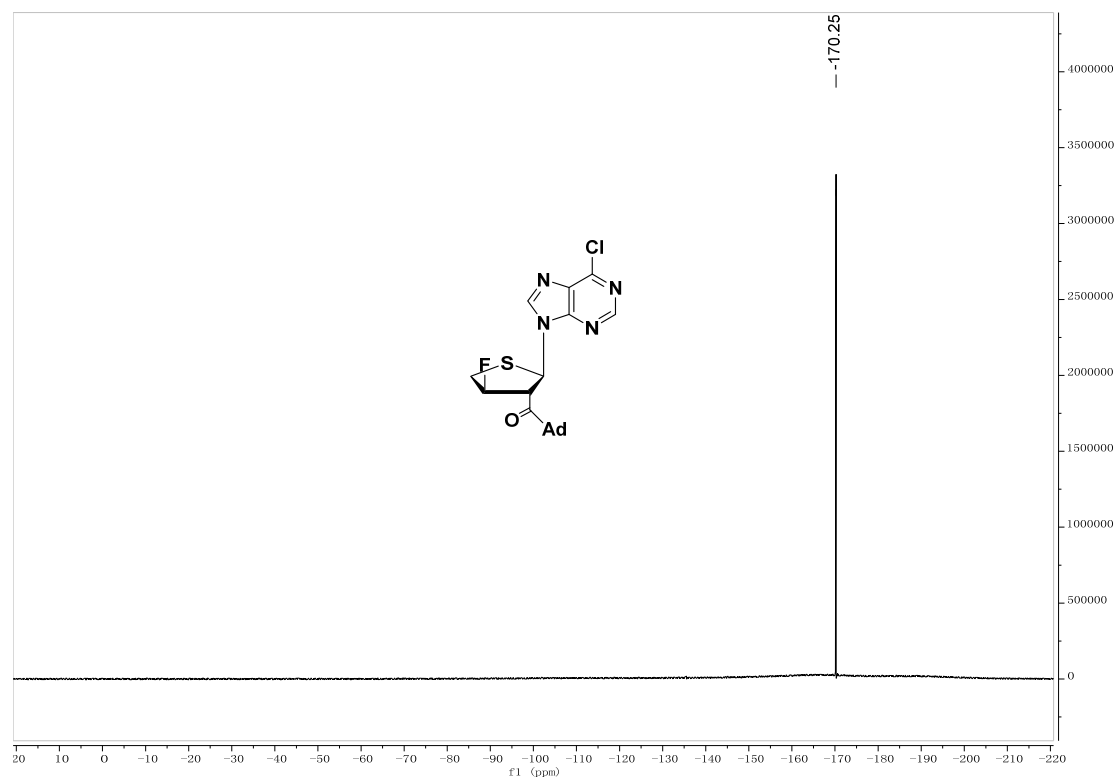
### <sup>1</sup>H NMR of 5a (400 MHz, CDCl<sub>3</sub>)



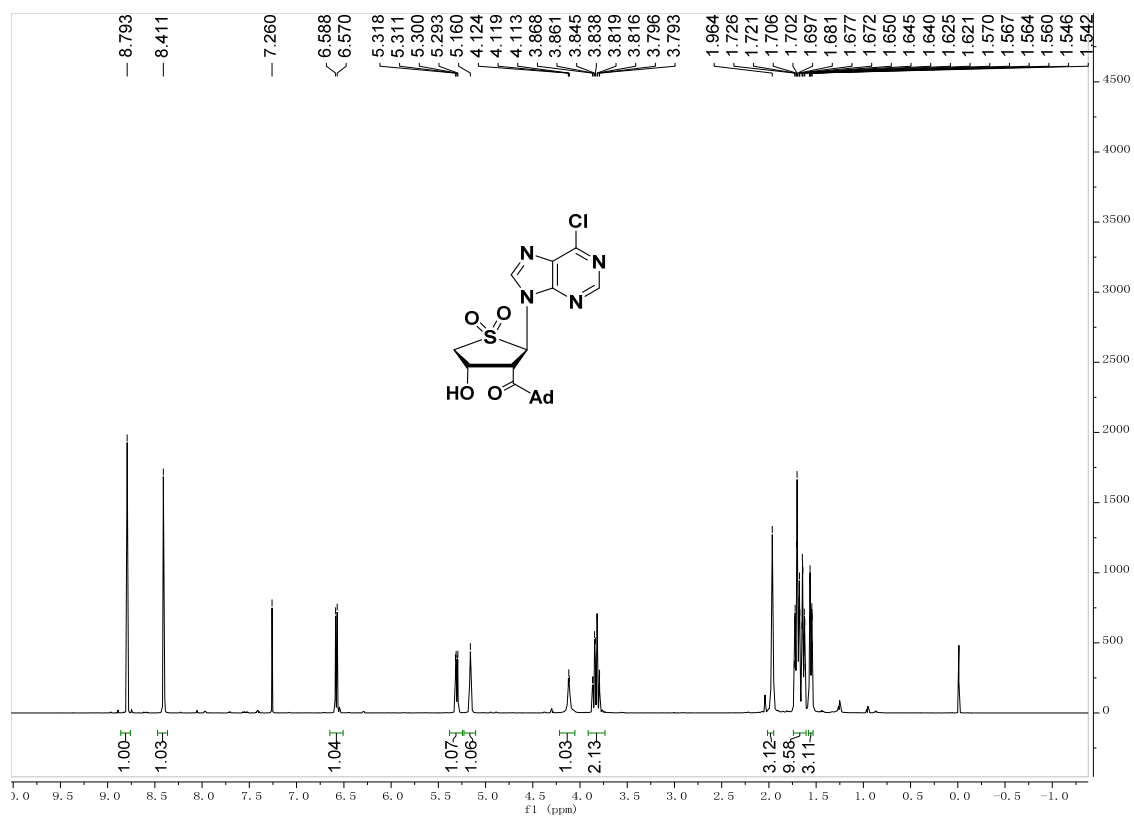
### <sup>13</sup>C NMR of 5a (100 MHz, CDCl<sub>3</sub>)



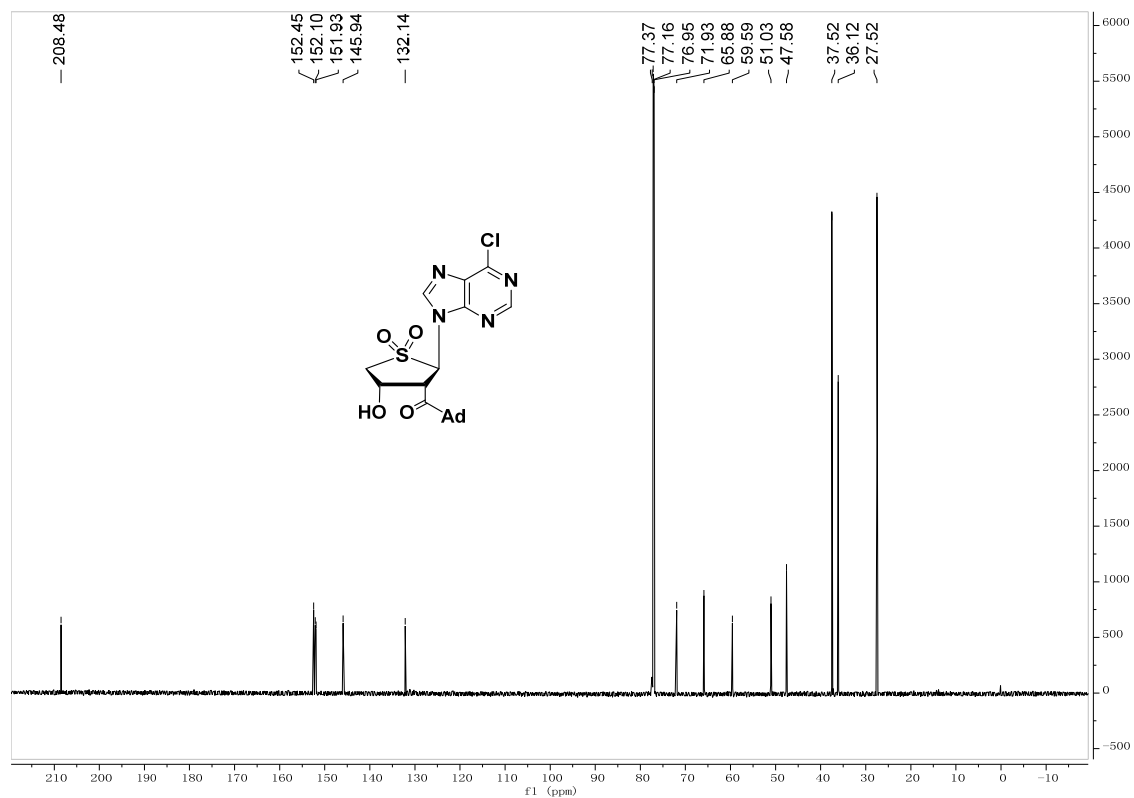
**<sup>19</sup>F NMR of 5a (376 MHz, CDCl<sub>3</sub>)**



### <sup>1</sup>H NMR of 5b (600 MHz, CDCl<sub>3</sub>)



### <sup>13</sup>C NMR of 5b (150 MHz, CDCl<sub>3</sub>)



## 8. Reference

1. Q.-L. Yang, M.-S. Xie, C. Xia, H.-L. Sun, D.-J. Zhang, K.-X. Huang, Z. Guo, G.-R. Qu and H.-M. Guo, *Chem. Commun.*, 2014, **50**, 14809-14812.
2. (a) N. Baricordi, S. Benetti, V. Bertolasi, C. De Risi, G. P. Pollini, F. Zamberlan and V. Zanirato, *Tetrahedron*, 2012, **68**, 208-213. (b) K.-X. Huang, M.-S. Xie, J.-W. Sang, G.-R. Qu and H.-M. Guo, *Org. Lett.*, 2020, **23**, 81-86.
3. M. Waser, E. D. Moher, S. S. K. Borders, M. M. Hansen, D. W. Hoard, M. E. Laurila, M. E. LeTourneau, R. D. Miller, M. L. Phillips, K. A. Sullivan, J. A. Ward, C. Xie, C. A. Bye, T. Leitner, B. Herzog-Krimbacher, M. Kordian and M. Müllner, *Org. Process Res. Dev.*, 2011, **15**, 1266-1274.