Supporting Information

Visible light-induced direct alkylation of the purine C_8-H bond with ethers

Changtong Lu,[a] Gary Histand[b] and Dongen Lin*[a]

[a]Key Laboratory of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou 510641, China.
[b]The International School of Advanced Materials, School of Materials Science and Engineering, South China University of Technology, Guangzhou 510641, China.

E-mail: denlin@scut.edu.cn

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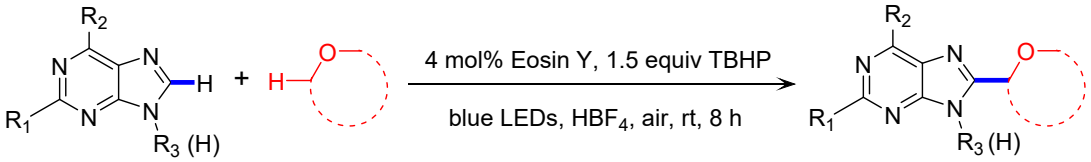
Ⅰ. General information

All reagents are purchased from the commercial suppliers for direct use without further purification. All purchased reagents are of analytical reagent grade unless otherwise noted. Purines with substitutions on C2 or C6 were obtained synthetically from 6-chloropurine and 2,6-dichloropurine using the method of Huang.[1] N7 and N9 substituted purines were synthesized from 9*H* purines according to the method of Kelley[2] and Çelik[3]. The reaction is monitored by thin-layer chromatography (TLC) using silica gel GF254 plates to observe the reaction process. Column chromatography is generally performed on silica gel (300-400 mesh) purchased from Qingdao Ocean Chemical Co. Ltd. The ^{1}H, ^{13}C and ^{19}F NMR spectra were obtained using Bruker DRX-400 or Bruker Ascend 500 spectrometers, with $CDCl_3$ or DMSO-d_6 as the solvent and TMS or a residual nondeuterated solvent peak as the internal standard. All chemical shifts (δ) are in ppm and the coupling constants (J) are in Hz. High resolution mass spectrometry (HRMS) data were recorded on an IF-TOF spectrometer. Melting points were measured using an INESA melting point WRS-2 instrument. The gas chromatography mass spectra were analyzed using the SHIMADZU model GCMS-QP5000 spectrometer. The fluorescence spectra were determined on a Hitachi Fluorescence Spectrophotometer F-7000.

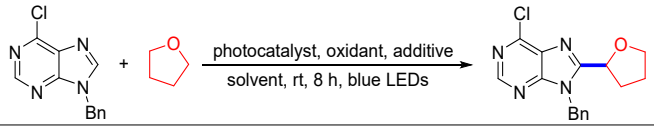
Ⅱ. General Procedure for the Visible Light-Induced Direct Alkylation of Purines



To a dried reaction tube (10 mL, borosilicate glass) equipped with a magnetic stir bar was added purine derivatives (0.15 mmol), ethers (3 mmol), Eosin Y (4 mol%), TBHP (1.5 equiv, 0.225 mmol, aq.65% in water), HBF_4 (2.0 equiv, 0.3 mmol, aq.50% in water). The reaction was stirred at room temperature and blue LEDs (450−460 nm, 20 W, SD produced by Xuzhou Ai Jia Electronic Technology Co. Ltd.) were placed 3 cm from the reaction vessel for 8 hours. After it is complete, the reaction solution is concentrated under reduced pressure and then purified by flash column chromatography on silica gel or preparative TLC on GF254 (petroleum ether/ethyl acetate or dichloromethane/methanol) to afford the 8-alkylpurines.

Ⅲ. Optimization of the reaction conditions

Table S1 Optimization of the reaction conditions[a]



entry	photocatalyst (mol%)	oxidant[b] (equiv)	additive (equiv)	solvent	yield%[c]
1	Eosin Y (4)	TBHP (1.5)	-	THF	5%
2	Eosin Y (4)	TBHP (1.5)	TFA (2)	THF	8%
3	Eosin Y (4)	TBHP (1.5)	MSA (2)	THF	45%
4	Eosin Y (4)	TBHP (1.5)	HAc (2)	THF	9%
5	Eosin Y (4)	TBHP (1.5)	Na_2CO_3 (2)	THF	N.D.
6	Eosin Y (4)	TBHP (1.5)	DABCO (2)	THF	N.D.
7	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	DCM	23%
8	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	MeCN	10%

9	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	EtOAc	64%
10	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	Acetone	86%
11	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	H_2O	18%
12	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	DMF	N.D.
13[d]	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	THF	N.D.
14[e]	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	THF	49%
15[f]	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	THF	75%
16[g]	Eosin Y (4)	TBHP (1.5)	HBF_4 (2)	THF	91%

[a]Reaction conditions: **1a** (0.15 mmol), **2a** (3 mmol), photocatalyst (4 mol%) in solvent (2.0 mL) in air at room temperature while irradiated by 20 W blue LEDs for 8 h. N.D. = not determined. [b]TBHP (65% aq. solution), DTBP (98%). [c]Determined by GC using dodecane as an internal standard. [d]In the dark. [e]Irradiated by 20 W green LEDs. [f]Irradiated by 5 W blue LEDs. [g]Under an Ar atmosphere.

Ⅳ. GC-MS of radical trapping experiment

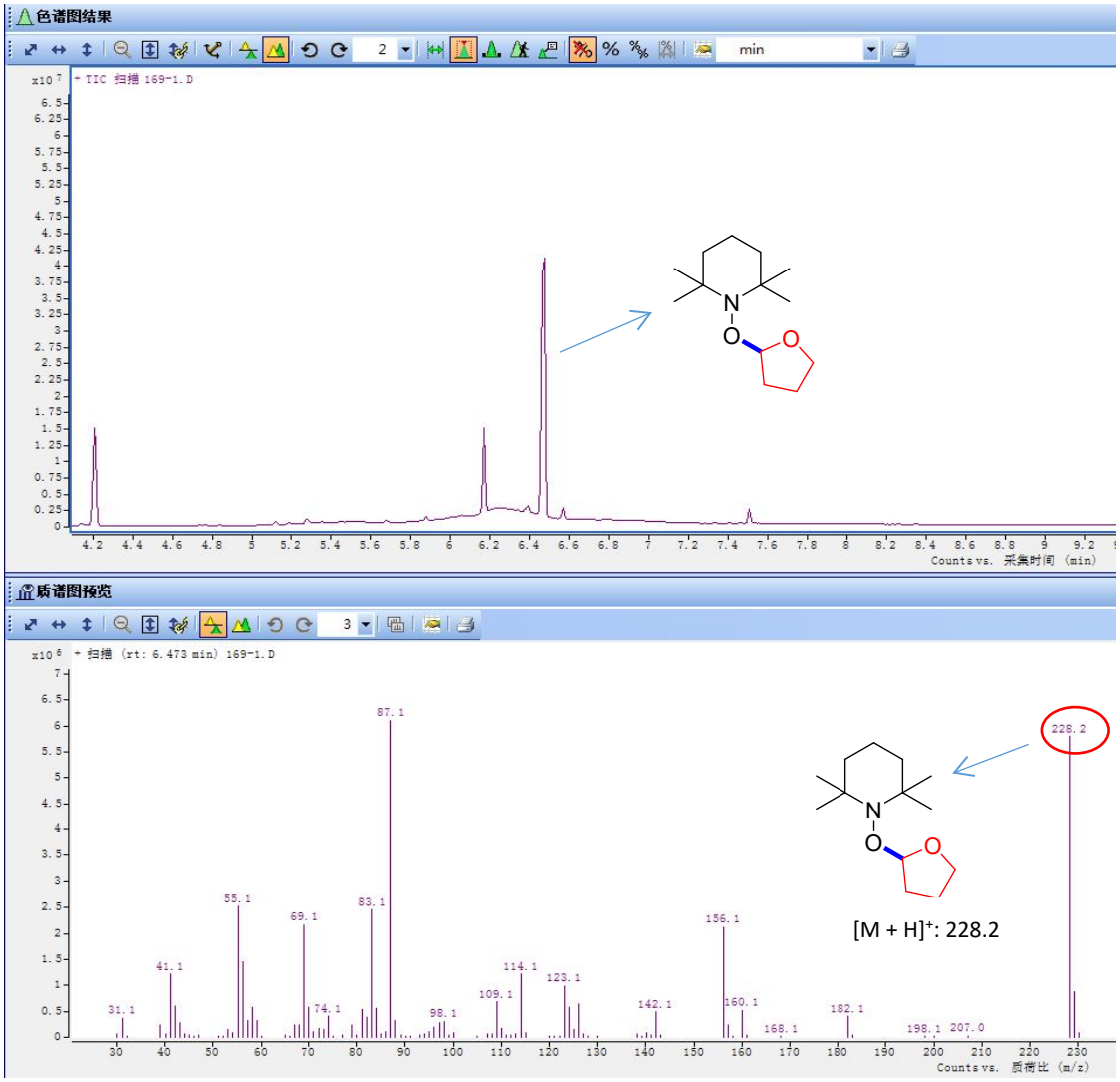


Fig. 1 GC-MS of the adduct of THF with TEMPO

Ⅴ. GC-MS of the crude product 4b

To investigate by-products in the case of free -NH purines, the crude product **4b** was analyzed by GC-MS. From the GC-MS result in Fig. 2, in addition to the expected products and sometimes unreacted starting material, there are small amounts of other side products which we think are the C8 and N9 dialkylated purines. The amount of side products is small when compared to the expected products, so no isolation was carried out.

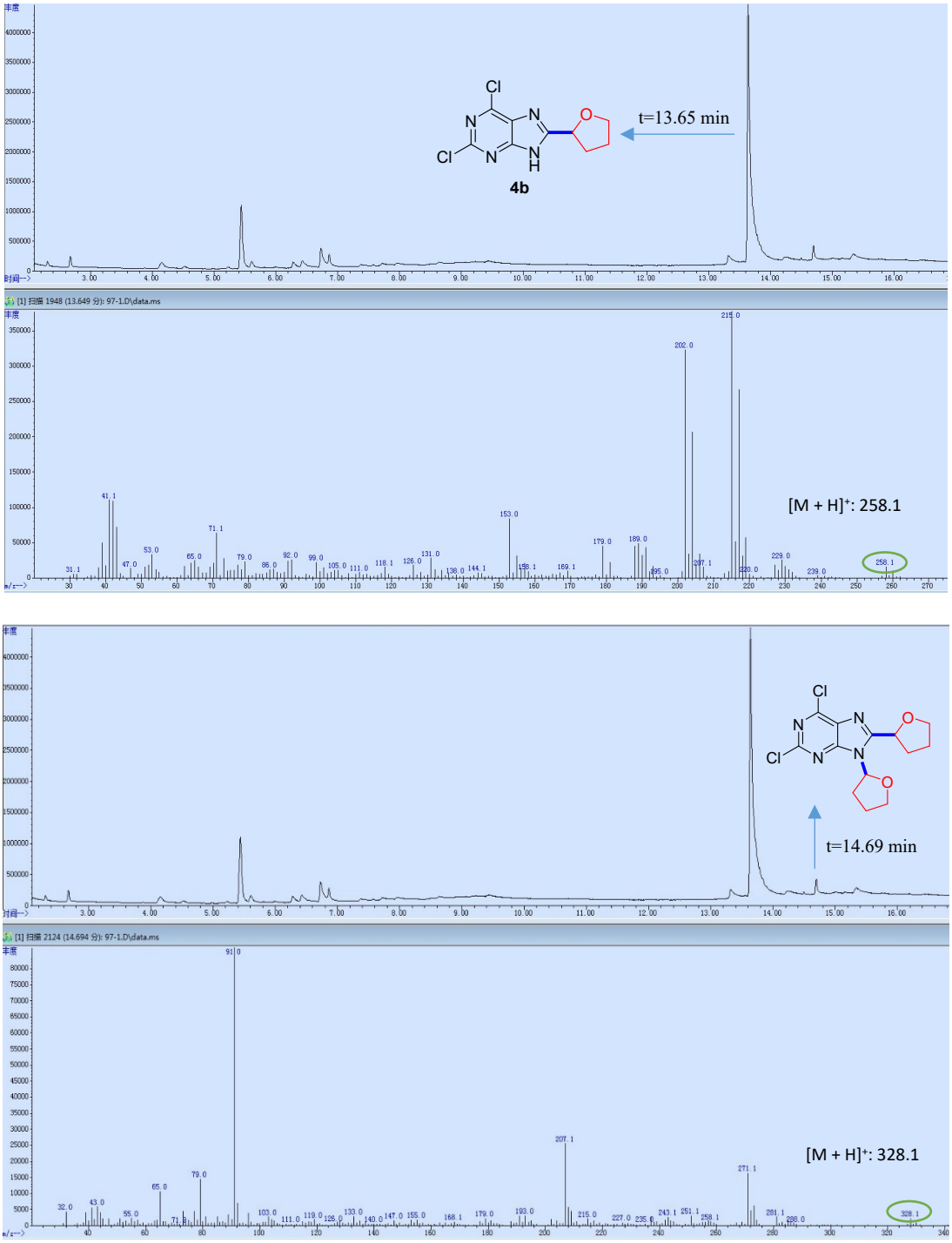


Fig. 2 GC-MS of the crude product **4b**

Ⅵ. Light on-off experiment

To investigate the effect of visible light on the reaction, a light on-off experiment with 9-benzyl-6-chloro-9*H*-purine (**1a**) and tetrahydrofuran (**2a**) was performed. In this reaction, the light source changed irradiation or darkness condition every 2 hours. The reaction was followed by GC-MS. After the first 2 hours of blue LED exposure, 45% of the expected product was obtained. However, the yield was not improved after 2 hours with the blue LEDs removed. Then the light was turned on again and after 2 hours the yield increased to 70%. No further conversion was detected when the light was turned off. The yield increased by another 14% when the light was turned on again for 2 hours. Subsequently, the yield remained constant after the light was turned off. The light on-off experiment demonstrates that visible light is an essential component of the reaction. Moreover, it also shows that the reaction is not a free radical chain reaction, but more likely proceeds through a photo-redox pathway.

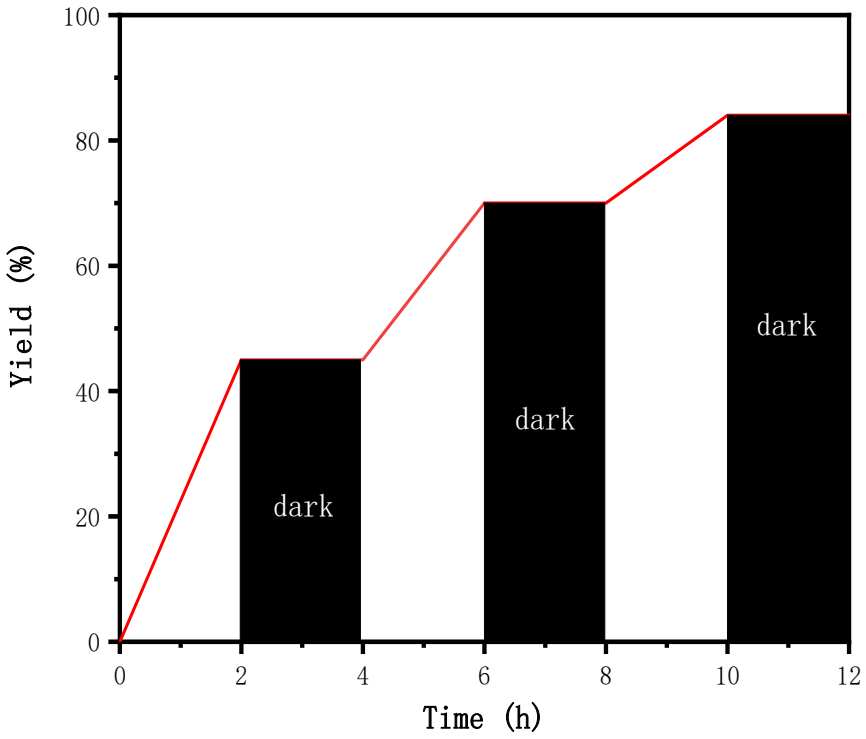


Fig. 3 Light on/off experiment

Ⅶ. Fluorescence quenching study

The fluorescence emission intensities were recorded on a Hitachi Fluorescence Spectrophotometer F-7000. The excitation wavelength was fixed at 528 nm, and the emission wavelength was measured at 558 nm (emission maximum). The solution of Eosin Y (1 μM in acetone) and various concentrations of quenchers were irradiated in a light path quartz fluorescence cuvette. Fluorescence quenching was indeed observed for Eosin Y at various concentrations of TBHP. As the TBHP concentration increases, the fluorescence intensity of the Eosin Y gradually decreases. The linear Stern-Volmer plots suggest a possible transfer of electrons between TBHP and the Eosin Y excited state.

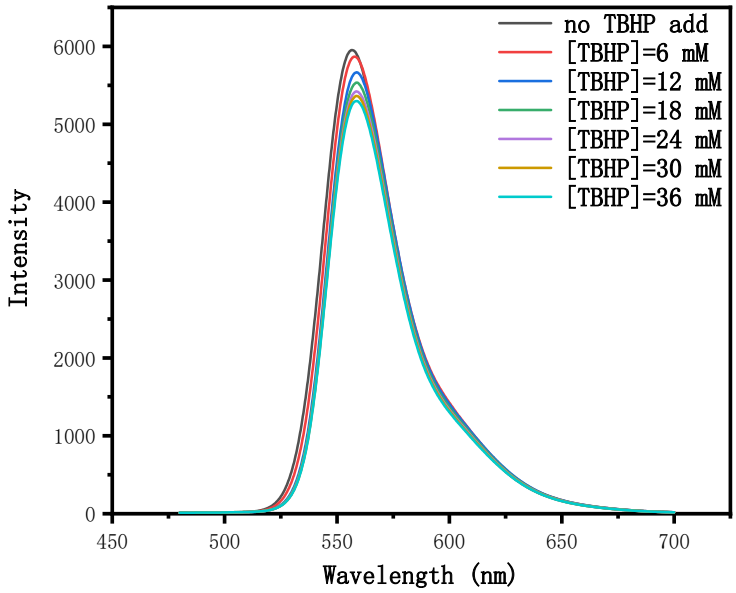


Fig. 4 Fluorescence quenching of Eosin Y with various concentrations of TBHP

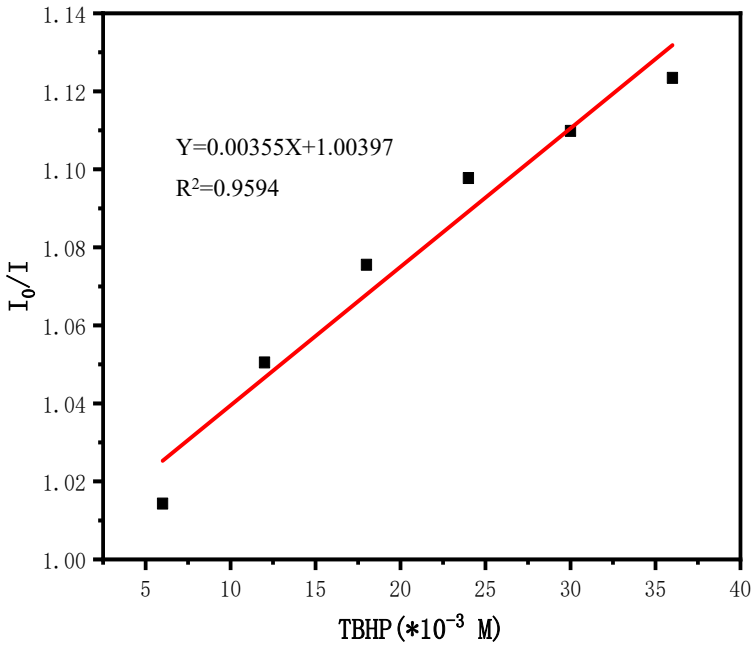


Fig. 5 Stern-Volmer plot for quenching of Eosin Y fluorescence with TBHP

Ⅷ. X-ray Crystallographic analysis for product 3c

Crystal data have been deposited to CCDC, number 2211872.

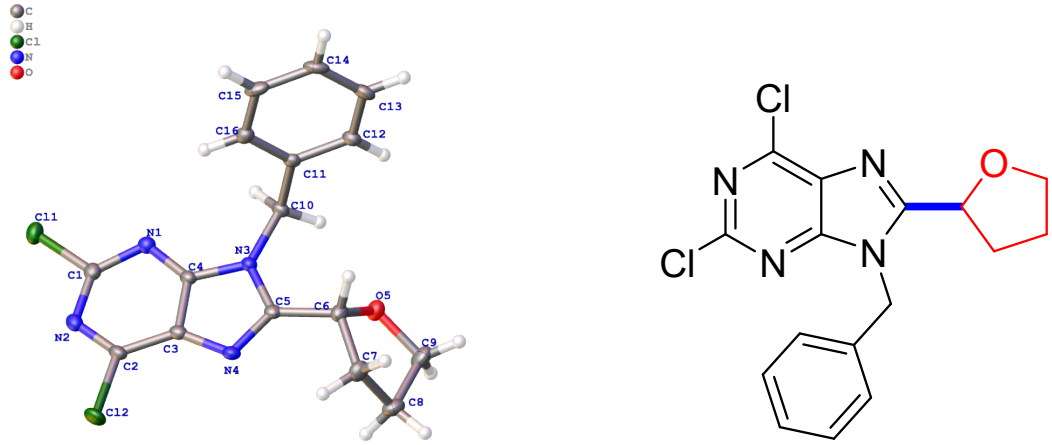


Fig. 6 The single crystal structure of **3c** (the ellipsoid contour probability level is 50%)

Crystal sample preparation: In a 1.5 mL chromatography vial, the purified sample **3c** was dissolved in dichloromethane (0.5 mL). Cyclohexane (1.0 mL) was slowly added dropwise to the vial. The solvent was allowed to evaporate naturally, and crystals were formed. The single crystals formed were analyzed by single crystal X-ray diffraction.

Table S2 Crystal data and structure refinement for 3c.

Identification code	**3c**
Empirical formula	$C_{16}H_{14}Cl_2N_4O$
Formula weight	349.21
Temperature/K	179.99(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	4.7826(9)
b/Å	16.631(3)
c/Å	19.594(2)
α/°	90
β/°	90.09(1)
γ/°	90
Volume/Å^3	1558.5(4)
Z	4
ρ_{calc}g/cm^3	1.488
μ/mm^{-1}	3.830
F(000)	720.0
Crystal size/mm^3	0.15 × 0.11 × 0.09

Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.972 to 148.236
Index ranges	-4 ≤ h ≤ 5, -20 ≤ k ≤ 19, -21 ≤ l ≤ 24
Reflections collected	5890
Independent reflections	3034 [R_{int} = 0.0540, R_{sigma} = 0.0610]
Data/restraints/parameters	3034/0/218
Goodness-of-fit on F^2	1.029
Final R indexes [I>=2σ (I)]	R_1 = 0.0796, wR_2 = 0.2037
Final R indexes [all data]	R_1 = 0.0853, wR_2 = 0.2175
Largest diff. peak/hole / e $Å^{-3}$	0.78/-0.86

Crystal structure determination of 3c

Crystal Data for $C_{16}H_{14}Cl_2N_4O$ (*M* =349.21 g/mol): monoclinic, space group $P2_1/c$ (no. 14), *a* = 4.7826(9) Å, *b* = 16.631(3) Å, *c* = 19.594(2) Å, *β* = 90.09(1) °, *V* = 1558.5(4) $Å^3$, *Z* = 4, *T* = 179.99(10) K, μ(Cu Kα) = 3.830 mm^{-1}, *Dcalc* = 1.488 g/cm^3, 5890 reflections measured (6.972° ≤ 2Θ ≤ 148.236°), 3034 unique (R_{int} = 0.0540, R_{sigma} = 0.0610) which were used in all calculations. The final R_1 was 0.0796 (I > 2σ(I)) and wR_2 was 0.2175 (all data).

Table S3 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 3c. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Cl1	11957.6(15)	1757.5(4)	2777.9(4)	39.4(3)
Cl2	5097.5(19)	2194.1(5)	4818.6(4)	46.0(3)
O5	3927(4)	5773.3(13)	3299.6(12)	37.0(5)
N1	8719(5)	3001.3(15)	2810.2(12)	29.1(5)
N2	8453(5)	2095.8(14)	3760.4(12)	32.5(5)
N3	5594(4)	4135.6(14)	2934.2(11)	24.9(5)
N4	3667(5)	3836.5(15)	3961.2(11)	28.6(5)
C1	9412(6)	2361.1(17)	3162.3(15)	30.5(6)
C2	6516(6)	2549.2(18)	4062.5(14)	30.6(6)
C3	5571(6)	3256.9(17)	3777.0(13)	27.3(6)
C4	6796(5)	3434.6(16)	3141.9(13)	25.5(5)
C5	3742(5)	4353.0(16)	3451.7(13)	25.4(5)
C6	2043(6)	5105.8(17)	3403.6(14)	30.5(6)
C7	328(7)	5290(2)	4043.3(17)	39.4(7)
C8	1928(11)	5961(3)	4376(2)	43.4(15)
C9	3213(8)	6395(2)	3767(2)	48.7(9)
C10	6177(5)	4543.3(17)	2281.3(13)	26.7(6)
C11	3898(5)	4425.2(17)	1760.4(13)	25.5(6)
C12	2706(6)	5098.0(18)	1458.0(14)	31.0(6)
C13	668(7)	5012(2)	961.9(14)	37.2(7)
C14	-160(7)	4253(2)	763.8(14)	40.2(7)

Table S3 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 3c. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
C15	1030(7)	3581(2)	1063.0(16)	38.4(7)
C16	3052(6)	3664.9(18)	1558.8(15)	32.3(6)
C17	530(60)	6223(15)	4101(15)	57(10)

Table S4 Anisotropic Displacement Parameters (Å^2×10^3) for 3c. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl1	45.1(5)	28.3(5)	44.8(5)	-2.8(3)	-1.1(3)	8.0(3)
Cl2	74.0(6)	41.0(5)	22.9(4)	12.6(3)	2.5(3)	2.5(4)
O5	48.1(11)	25.3(11)	37.4(12)	-1.2(9)	5.7(9)	0.2(8)
N1	36.4(11)	26.0(11)	24.9(11)	0.1(10)	-0.4(8)	-0.7(9)
N2	46.8(13)	24.4(12)	26.5(12)	1.4(10)	-7.8(10)	0.4(10)
N3	34.5(10)	22.0(11)	18.2(11)	1.2(8)	-1.9(8)	1.1(8)
N4	40.9(11)	28.9(12)	16.1(10)	0.1(9)	-2.4(8)	0.2(9)
C1	39.4(13)	24.8(14)	27.3(14)	-2.6(11)	-5.7(10)	0.4(10)
C2	46.9(14)	27.5(14)	17.3(12)	3.3(11)	-5.5(10)	-3.5(11)
C3	37.4(13)	26.7(14)	17.8(12)	0.2(10)	-2.7(9)	-3.8(10)
C4	36.0(12)	22.9(13)	17.7(12)	0.4(10)	-3.4(9)	-1.7(10)
C5	32.1(12)	25.6(13)	18.5(12)	-2.0(10)	-4.7(9)	-1.2(10)
C6	34.6(13)	28.6(14)	28.4(14)	-4.5(11)	-4.7(10)	4.3(10)
C7	42.6(14)	36.5(17)	39.0(16)	-5.8(14)	6.6(12)	6.5(12)
C8	57(3)	44(3)	29(2)	-11.1(19)	-1.3(18)	3(2)
C9	67(2)	32.7(17)	47(2)	-15.5(15)	3.3(16)	1.9(15)
C10	35.2(12)	25.4(13)	19.4(12)	4.4(10)	-0.1(9)	-3.0(10)
C11	34.7(12)	25.4(13)	16.2(11)	0.8(9)	3.4(9)	-1.7(9)
C12	42.5(14)	30.7(15)	19.8(12)	3.4(11)	-1.9(10)	-2.2(11)
C13	47.7(15)	44.3(19)	19.6(13)	10.7(13)	-4.1(11)	-4.8(13)
C14	49.7(16)	56(2)	14.7(12)	1.2(13)	-3.5(11)	-8.6(14)
C15	53.3(16)	39.6(18)	22.3(13)	-11.5(12)	4.8(11)	-16.7(13)
C16	43.8(14)	29.1(15)	24.2(13)	-0.9(11)	5.0(11)	-2.8(11)
C17	76(17)	40(13)	54(17)	-22(11)	30(14)	10(11)

Table S5 Bond Lengths for 3c.

Atom	Atom	Length/Å	Atom	Atom	Length/Å

Table S5 Bond Lengths for 3c.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cl1	C1	1.748(3)	C3	C4	1.407(4)
Cl2	C2	1.733(3)	C5	C6	1.496(4)
O5	C6	1.444(4)	C6	C7	1.529(4)
O5	C9	1.423(4)	C7	C8	1.502(5)
N1	C1	1.311(4)	C7	C17	1.56(2)
N1	C4	1.337(4)	C8	C9	1.524(6)
N2	C1	1.334(4)	C9	C17	1.47(2)
N2	C2	1.333(4)	C10	C11	1.506(4)
N3	C4	1.362(3)	C11	C12	1.389(4)
N3	C5	1.394(3)	C11	C16	1.385(4)
N3	C10	1.475(3)	C12	C13	1.384(4)
N4	C3	1.374(4)	C13	C14	1.378(5)
N4	C5	1.318(4)	C14	C15	1.384(5)
C2	C3	1.379(4)	C15	C16	1.378(4)

Table S6 Bond Angles for 3c.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C9	O5	C6	108.6(2)	N4	C5	N3	113.5(2)
C1	N1	C4	110.8(2)	N4	C5	C6	125.3(2)
C2	N2	C1	116.2(2)	O5	C6	C5	108.3(2)
C4	N3	C5	105.8(2)	O5	C6	C7	107.2(2)
C4	N3	C10	124.9(2)	C5	C6	C7	114.0(3)
C5	N3	C10	129.2(2)	C6	C7	C17	103.0(8)
C5	N4	C3	103.9(2)	C8	C7	C6	103.4(3)
N1	C1	Cl1	114.6(2)	C7	C8	C9	102.6(3)
N1	C1	N2	130.1(3)	O5	C9	C8	104.8(3)
N2	C1	Cl1	115.3(2)	O5	C9	C17	110.8(9)
N2	C2	Cl2	117.3(2)	N3	C10	C11	113.0(2)
N2	C2	C3	122.0(3)	C12	C11	C10	118.8(2)
C3	C2	Cl2	120.6(2)	C16	C11	C10	121.6(3)
N4	C3	C2	135.2(3)	C16	C11	C12	119.6(3)
N4	C3	C4	111.2(2)	C13	C12	C11	120.4(3)
C2	C3	C4	113.7(3)	C14	C13	C12	119.7(3)
N1	C4	N3	127.3(2)	C13	C14	C15	120.1(3)
N1	C4	C3	127.1(3)	C16	C15	C14	120.4(3)
N3	C4	C3	105.6(2)	C15	C16	C11	119.9(3)

Table S6 Bond Angles for 3c.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N3	C5	C6	121.1(2)	C9	C17	C7	102.4(13)

Table S7 Torsion Angles for 3c.

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
Cl2	C2	C3	N4	3.1(5)	C4	N3	C5	C6	179.4(2)
Cl2	C2	C3	C4	-175.9(2)	C4	N3	C10	C11	103.2(3)
O5	C6	C7	C8	-15.3(4)	C5	N3	C4	N1	-179.8(3)
O5	C6	C7	C17	22.4(15)	C5	N3	C4	C3	0.7(3)
O5	C9	C17	C7	24(2)	C5	N3	C10	C11	-75.4(3)
N2	C2	C3	N4	-179.6(3)	C5	N4	C3	C2	-179.3(3)
N2	C2	C3	C4	1.3(4)	C5	N4	C3	C4	-0.2(3)
N3	C5	C6	O5	-55.4(3)	C5	C6	C7	C8	104.6(4)
N3	C5	C6	C7	-174.7(2)	C5	C6	C7	C17	142.3(15)
N3	C10	C11	C12	126.1(3)	C6	O5	C9	C8	28.2(4)
N3	C10	C11	C16	-56.5(3)	C6	O5	C9	C17	-10.9(17)
N4	C3	C4	N1	-179.8(2)	C6	C7	C8	C9	31.0(4)
N4	C3	C4	N3	-0.4(3)	C6	C7	C17	C9	-28(2)
N4	C5	C6	O5	125.0(3)	C7	C8	C9	O5	-37.0(4)
N4	C5	C6	C7	5.7(4)	C9	O5	C6	C5	-131.7(3)
C1	N1	C4	N3	179.8(2)	C9	O5	C6	C7	-8.2(3)
C1	N1	C4	C3	-0.8(4)	C10	N3	C4	N1	1.3(4)
C1	N2	C2	Cl2	176.7(2)	C10	N3	C4	C3	-178.1(2)
C1	N2	C2	C3	-0.6(4)	C10	N3	C5	N4	177.9(2)
C2	N2	C1	Cl1	179.8(2)	C10	N3	C5	C6	-1.8(4)
C2	N2	C1	N1	-1.2(4)	C10	C11	C12	C13	178.0(2)
C2	C3	C4	N1	-0.5(4)	C10	C11	C16	C15	-177.7(2)
C2	C3	C4	N3	178.9(2)	C11	C12	C13	C14	-0.6(4)
C3	N4	C5	N3	0.7(3)	C12	C11	C16	C15	-0.3(4)
C3	N4	C5	C6	-179.7(2)	C12	C13	C14	C15	0.4(4)
C4	N1	C1	Cl1	-179.18(18)	C13	C14	C15	C16	-0.2(4)
C4	N1	C1	N2	1.8(4)	C14	C15	C16	C11	0.1(4)
C4	N3	C5	N4	-0.9(3)	C16	C11	C12	C13	0.5(4)

Table S8 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 3c.

Atom	*x*	*y*	*z*	U(eq)

Table S8 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 3c.

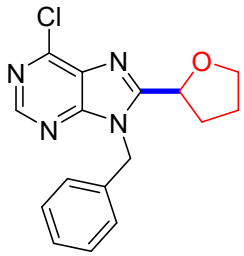
Atom	*x*	*y*	*z*	U(eq)
H6	780.29	5065.17	3011.16	37
H7AA	-1551.63	5459.17	3925.26	47
H7AB	221.87	4824.01	4340.14	47
H7BC	1122.75	5030.25	4441.93	47
H7BD	-1596.6	5116.86	3989.67	47
H8A	3360.67	5753.88	4678.99	52
H8B	694.22	6312.83	4630.86	52
H9AA	1880.02	6764.35	3564.79	58
H9AB	4862.76	6693.71	3903.75	58
H9BC	3091.15	6903.05	3525.72	58
H9BD	4665.74	6442.52	4110.21	58
H10A	7921.97	4340	2097.19	32
H10B	6409.59	5114.22	2364.89	32
H12	3280.87	5609.3	1589.46	37
H13	-139.31	5463.6	763.32	45
H14	-1519.72	4192.68	428.5	48
H15	461.51	3070.49	928.52	46
H16	3847.86	3211.66	1757.77	39
H17A	-1008.79	6483.28	3864.4	68
H17B	537.96	6395.41	4573.71	68

Table S9 Atomic Occupancy for 3c.

Atom	*Occupancy*	Atom	*Occupancy*	Atom	*Occupancy*
H7AA	0.822(16)	H7AB	0.822(16)	H7BC	0.178(16)
H7BD	0.178(16)	C8	0.822(16)	H8A	0.822(16)
H8B	0.822(16)	H9AA	0.822(16)	H9AB	0.822(16)
H9BC	0.178(16)	H9BD	0.178(16)	C17	0.178(16)
H17A	0.178(16)	H17B	0.178(16)		

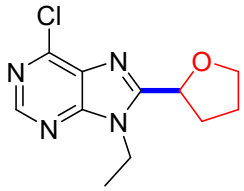
Ⅸ. Characterization data for the synthesized products

9-benzyl-6-chloro-8-(tetrahydrofuran-2-yl)-9*H*-purine (3a)



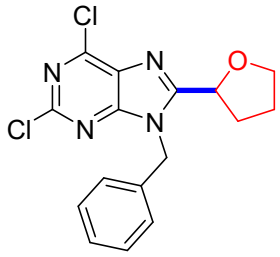
Yellow oily liquid (43.4 mg); 92% yield (eluent: petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.74 (s, 1H), 7.33–7.27 (m, 3H), 7.25–7.18 (m, 2H), 5.76 (d, *J* = 15.5 Hz, 1H), 5.60 (d, *J* = 15.4 Hz, 1H), 5.05 (dd, *J* = 7.5, 5.9 Hz, 1H), 3.97–3.87 (m, 2H), 2.80–2.70 (m, 1H), 2.30–2.20 (m, 1H), 2.14–1.98 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.02, 153.82, 151.87, 150.29, 135.55, 130.37, 128.93, 128.22, 127.33, 73.92, 69.13, 46.77, 29.13, 25.80; HRMS (ESI) calcd for $C_{16}H_{16}N_4OCl$, $[M + H]^+$: 315.1013, found: 315.1012.

6-chloro-9-ethyl-8-(tetrahydrofuran-2-yl)-9*H*-purine (3b)



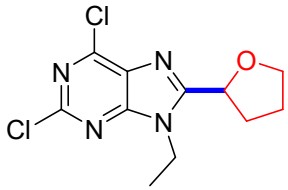
Pale yellow solid (34.2 mg); 90% yield (eluent: petroleum ether/ethyl acetate = 5:1); mp: 86.3–86.7℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.68 (s, 1H), 5.25–5.17 (m, 1H), 4.50–4.40 (m, 2H), 3.94 (h, *J* = 8.2 Hz, 2H), 2.88–2.79 (m, 1H), 2.43–2.33 (m, 1H), 2.22–2.13 (m, 1H), 2.12–2.05 (m, 1H), 1.48 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.61, 153.32, 151.45, 150.04, 130.57, 73.70, 69.14, 39.12, 29.34, 25.97, 15.18; HRMS (ESI) calcd for $C_{11}H_{14}N_4OCl$, $[M + H]^+$: 253.0856, found: 253.0864.

9-benzyl-2,6-dichloro-8-(tetrahydrofuran-2-yl)-9*H*-purine (3c)



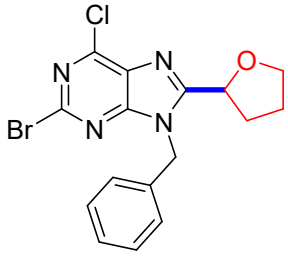
White solid (48.2 mg); 92% yield (eluent: petroleum ether/ethyl acetate = 5:1); mp: 118.2–119.1℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32–7.25 (m, 3H), 7.22–7.18 (m, 2H), 5.69 (d, *J* = 15.4 Hz, 1H), 5.54 (d, *J* = 15.4 Hz, 1H), 4.98 (dd, *J* = 7.5, 5.9 Hz, 1H), 3.94–3.84 (m, 2H), 2.76–2.63 (m, 1H), 2.25–2.16 (m, 1H), 2.11–1.95 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.88, 155.11, 152.66, 150.90, 135.05, 129.43, 128.99, 128.38, 127.45, 73.80, 69.19, 46.95, 29.02, 25.76; HRMS (ESI) calcd for $C_{16}H_{15}N_4OCl_2$, $[M + H]^+$: 349.0623, found: 349.0616.

2,6-dichloro-9-ethyl-8-(tetrahydrofuran-2-yl)-9*H*-purine (3d)



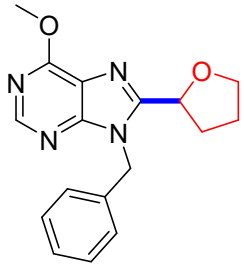
Pale yellow solid (39.2 mg); 91% yield (eluent: petroleum ether/ethyl acetate = 5:1); mp: 106.9–107.1℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.17 (dd, *J* = 7.5, 6.0 Hz, 1H), 4.47–4.36 (m, 2H), 3.98–3.88 (m, 2H), 2.86–2.77 (m, 1H), 2.42–2.33 (m, 1H), 2.22–2.13 (m, 1H), 2.10–2.02 (m, 1H), 1.47 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.47, 154.69, 152.31, 150.72, 129.68, 73.64, 69.21, 39.34, 29.28, 25.93, 15.15; HRMS (ESI) calcd for $C_{11}H_{13}N_4OCl_2$, $[M + H]^+$: 287.0466, found: 287.0469.

9-benzyl-2-bromo-6-chloro-8-(tetrahydrofuran-2-yl)-9*H*-purine (3e)



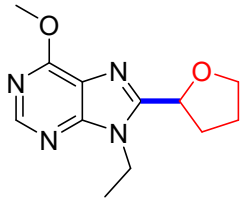
White solid (50.3 mg); 85% yield (eluent: petroleum ether/ethyl acetate = 7:1); mp: 137.9–138.6℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.27–7.19 (m, 3H), 7.17–7.10 (m, 2H), 5.62 (dd, *J* = 15.4, 6.0 Hz, 1H), 5.47 (dd, *J* = 15.4, 3.3 Hz, 1H), 4.90 (dd, *J* = 7.5, 5.7 Hz, 1H), 3.82 (dt, *J* = 14.1, 7.4 Hz, 2H), 2.69–2.58 (m, 1H), 2.19–2.09 (m, 1H), 2.04–1.96 (m, 1H), 1.96–1.87 (m, 1H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 157.65, 155.06, 150.62, 142.78, 135.07, 129.81, 128.98, 128.37, 127.46, 73.81, 69.17, 46.97, 29.03, 25.74; HRMS (ESI) calcd for $C_{16}H_{15}N_4OClBr$, $[M + H]^+$: 393.0118, found: 393.0120.

9-benzyl-6-methoxy-8-(tetrahydrofuran-2-yl)-9*H*-purine (3f)



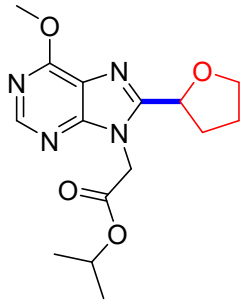
White solid (41.4 mg); 89% yield (eluent: petroleum ether/ethyl acetate = 4:1); mp: 90.8–91.8℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.56 (s, 1H), 7.31–7.26 (m, 3H), 7.24–7.16 (m, 2H), 5.74 (d, *J* = 15.6 Hz, 1H), 5.56 (d, *J* = 15.6 Hz, 1H), 5.01 (dd, *J* = 7.4, 5.8 Hz, 1H), 4.20 (s, 3H), 3.94–3.82 (m, 2H), 2.88–2.78 (m, 1H), 2.23–2.07 (m, 2H), 2.01–1.92 (m, 1H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.76, 153.97, 153.58, 152.09, 136.18, 128.81, 127.92, 127.18, 119.99, 73.63, 68.85, 54.18, 46.30, 28.73, 25.88; HRMS (ESI) calcd for $C_{17}H_{19}N_4O_2$, $[M + H]^+$: 311.1508, found: 311.1511.

9-ethyl-6-methoxy-8-(tetrahydrofuran-2-yl)-9*H*-purine (3g)



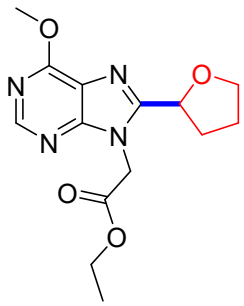
Pale yellow solid (33.5 mg); 90% yield (eluent: petroleum ether/ethyl acetate = 4:1); mp: 89.1–89.9℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.49 (s, 1H), 5.16 (dd, *J* = 7.5, 5.9 Hz, 1H), 4.45–4.36 (m, 2H), 4.15 (s, 3H), 3.95–3.83 (m, 2H), 2.95–2.85 (m, 1H), 2.33–2.25 (m, 1H), 2.19–2.11 (m, 1H), 2.06–1.98 (m, 1H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.62, 153.40, 153.06, 151.66, 120.18, 73.34, 68.85, 54.06, 38.58, 28.89, 26.02, 15.34; HRMS (ESI) calcd for $C_{12}H_{17}N_4O_2$, $[M + H]^+$: 249.1352, found: 249.1351.

isopropyl-2-(6-methoxy-8-(tetrahydrofuran-2-yl)-9*H*-purin-9-yl)acetate (3h)



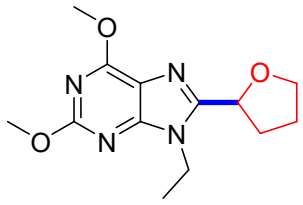
Pale yellow solid (40.5 mg); 84% yield (eluent: petroleum ether/ethyl acetate = 3:1); mp: 98.2–98.6℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.44 (s, 1H), 5.14–5.09 (m, 1H), 5.08 (s, 2H), 5.03–4.98 (m, 1H), 4.12 (s, 3H), 3.85–3.79 (m, 1H), 3.74–3.69 (m, 1H), 2.86–2.77 (m, 1H), 2.32–2.24 (m, 1H), 2.04–1.91 (m, 2H), 1.19 (d, *J* = 6.3 Hz, 6H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.07, 160.57, 153.85, 153.53, 151.90, 119.88, 74.43, 69.74, 68.82, 54.16, 44.62, 29.08, 25.61, 21.67; HRMS (ESI) calcd for $C_{15}H_{21}N_4O_4$, $[M + H]^+$: 321.1563, found: 321.1566.

ethyl-2-(6-methoxy-8-(tetrahydrofuran-2-yl)-9*H*-purin-9-yl)acetate (3i)



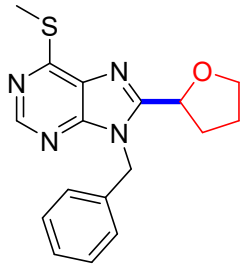
White solid (38.1 mg); 83% yield (eluent: petroleum ether/ethyl acetate = 3:1); mp: 108.1–109.4℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.47 (s, 1H), 5.15 (s, 3H), 4.23–4.17 (m, 2H), 4.15 (s, 3H), 3.88–3.83 (m, 1H), 3.78–3.72 (m, 1H), 2.90–2.82 (m, 1H), 2.34–2.27 (m, 1H), 2.06–1.95 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.59, 160.63, 153.87, 153.52, 151.96, 119.95, 74.44, 68.87, 61.86, 54.17, 44.43, 29.08, 25.64, 14.09; HRMS (ESI) calcd for $C_{14}H_{19}N_4O_4$, $[M + H]^+$: 307.1406, found: 307.1413.

9-ethyl-2,6-dimethoxy-8-(tetrahydrofuran-2-yl)-9*H*-purine (3j)



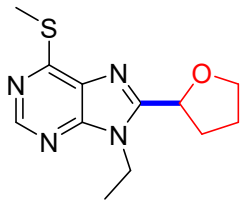
White solid (36.7 mg); 88% yield (eluent: petroleum ether/ethyl acetate = 3:1); mp: 72.0–72.6℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.11 (dd, *J* = 7.4, 6.0 Hz, 1H), 4.37–4.25 (m, 2H), 4.13 (s, 3H), 4.01 (s, 3H), 3.93–3.82 (m, 2H), 2.94–2.83 (m, 1H), 2.30–2.11 (m, 2H), 2.05–1.96 (m, 1H), 1.43 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.61, 161.44, 155.04, 151.48, 115.85, 73.35, 68.72, 54.94, 54.10, 38.31, 28.71, 26.04, 15.15, HRMS (ESI) calcd for $C_{13}H_{19}N_4O_3$, [M + H]$^+$: 279.1457, found: 279.1462.

9-benzyl-6-(methylthio)-8-(tetrahydrofuran-2-yl)-9*H*-purine (3k)



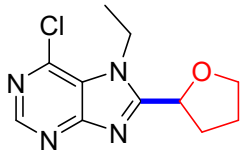
White solid (39.1 mg); 80% yield (eluent: petroleum ether/ethyl acetate = 3:1); mp: 105.9–106.7℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.69 (s, 1H), 7.27–7.19 (m, 3H), 7.17–7.11 (m, 2H), 5.68 (d, *J* = 15.6 Hz, 1H), 5.51 (d, *J* = 15.6 Hz, 1H), 4.96 (dd, *J* = 7.4, 6.0 Hz, 1H), 3.89–3.79 (m, 2H), 2.74–2.64 (m, 4H), 2.19–2.00 (m, 2H), 1.96–1.88 (m, 1H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.75, 154.04, 151.94, 150.31, 136.15, 130.24, 128.80, 127.92, 127.16, 73.94, 68.92, 46.17, 29.03, 25.80, 11.85; HRMS (ESI) calcd for $C_{17}H_{18}N_4OSNa$, [M + Na]$^+$: 349.1099, found: 349.1098.

9-ethyl-6-(methylthio)-8-(tetrahydrofuran-2-yl)-9*H*-purine (3l)



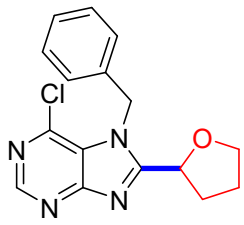
Pale yellow solid (32.1 mg); 81% yield (eluent: petroleum ether/ethyl acetate = 3:1); mp: 86.2–86.9℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.71 (s, 1H), 5.20 (dd, *J* = 7.4, 6.2 Hz, 1H), 4.48–4.38 (m, 2H), 3.98–3.91 (m, 2H), 2.90–2.81 (m, 1H), 2.73 (s, 3H), 2.40–2.31 (m, 1H), 2.23–2.16 (m, 1H), 2.12–2.03 (m, 1H), 1.48 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.55, 153.60, 151.56, 149.77, 130.50, 73.77, 68.96, 38.52, 29.29, 25.99, 15.33, 11.80; HRMS (ESI) calcd for $C_{12}H_{17}N_4OS$, [M + H]$^+$: 265.1123, found: 265.1124.

6-chloro-7-ethyl-8-(tetrahydrofuran-2-yl)-7*H*-purine (3m)



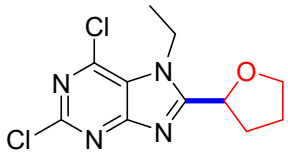
Yellow oily liquid (28.7 mg); 76% yield (eluent: petroleum ether/ethyl acetate = 2:3); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.82 (s, 1H), 5.24 (dd, *J* = 7.6, 5.3 Hz, 1H), 4.76–4.57 (m, 2H), 3.99–3.90 (m, 2H), 3.00–2.90 (m, 1H), 2.42–2.33 (m, 1H), 2.27–2.20 (m, 1H), 2.12–2.04 (m, 1H), 1.54 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.65, 160.03, 152.12, 142.15, 123.67, 72.98, 69.28, 41.00, 29.42, 25.92, 17.14; HRMS (ESI) calcd for $C_{11}H_{13}N_4OClNa$, [M + Na]$^+$: 275.0676, found: 275.0681.

7-benzyl-6-chloro-8-(tetrahydrofuran-2-yl)-7*H*-purine (3n)



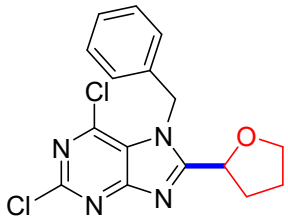
Yellow oily liquid (33.4 mg); 71% yield (eluent: petroleum ether/ethyl acetate = 2:3); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.81 (s, 1H), 7.32–7.24 (m, 3H), 7.00–6.94 (m, 2H), 5.97 (d, *J* = 16.8 Hz, 1H), 5.85 (d, *J* = 16.8 Hz, 1H), 5.07 (dd, *J* = 7.5, 5.2 Hz, 1H), 3.90–3.84 (m, 2H), 2.88–2.79 (m, 1H), 2.26–2.11 (m, 2H), 2.02–1.95 (m, 1H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.91, 160.56, 152.34, 142.46, 136.03, 129.06, 128.08, 125.84, 124.10, 73.20, 69.33, 48.58, 29.40, 25.81; HRMS (ESI) calcd for $C_{16}H_{16}N_4OCl$, [M + H]$^+$: 315.1013, found: 315.1022.

2,6-dichloro-7-ethyl-8-(tetrahydrofuran-2-yl)-7*H*-purine (3o)



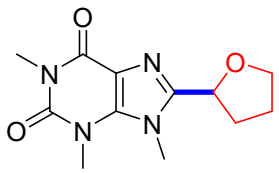
Pale yellow solid (32.2 mg); 75% yield (eluent: petroleum ether/ethyl acetate = 3:1); mp: 66.3–67.4℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.18 (dd, *J* = 7.6, 5.2 Hz, 1H), 4.67–4.49 (m, 2H), 3.92–3.82 (m, 2H), 2.84–2.75 (m, 1H), 2.36–2.27 (m, 1H), 2.18–1.98 (m, 2H), 1.48 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.19, 161.70, 152.44, 142.67, 122.79, 72.88, 69.32, 41.24, 29.41, 25.82, 17.04; HRMS (ESI) calcd for $C_{11}H_{13}N_4OCl_2$, $[M + H]^+$: 287.0466, found: 287.0469.

7-benzyl-2,6-dichloro-8-(tetrahydrofuran-2-yl)-7*H*-purine (3p)



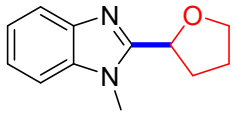
Yellow oily liquid (37.6 mg); 72% yield (eluent: petroleum ether/ethyl acetate = 4:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34–7.25 (m, 3H), 7.01–6.95 (m, 2H), 5.90 (q, *J* = 16.8 Hz, 2H), 5.10 (dd, *J* = 7.6, 5.2 Hz, 1H), 3.88 (td, *J* = 6.8, 1.5 Hz, 2H), 2.83–2.73 (m, 1H), 2.30–2.21 (m, 1H), 2.17–2.09 (m, 1H), 2.05–1.95 (m, 1H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.55, 162.20, 152.85, 143.11, 135.67, 129.11, 128.19, 125.87, 123.27, 73.11, 69.43, 48.78, 29.51, 25.76; HRMS (ESI) calcd for $C_{16}H_{15}N_4OCl_2$, $[M + H]^+$: 349.0623, found: 349.0625.

1,3,9-trimethyl-8-(tetrahydrofuran-2-yl)-3,9-dihydro-1*H*-purine-2,6-dione (3q)



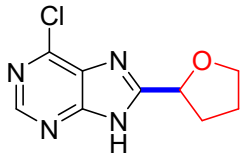
White solid (29.3 mg); 74% yield (eluent: petroleum ether/ethyl acetate = 2:1); mp: 123.8–124.2℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.01 (t, *J* = 6.9 Hz, 1H), 4.02 (s, 3H), 3.97–3.87 (m, 2H), 3.54 (s, 3H), 3.37 (s, 3H), 2.61–2.52 (m, 1H), 2.31–2.22 (m, 1H), 2.19–2.10 (m, 1H), 2.06–2.00 (m, 1H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.47, 152.37, 151.69, 147.33, 108.33, 72.61, 68.90, 32.22, 29.69, 29.58, 27.85, 25.93; HRMS (ESI) calcd for $C_{12}H_{17}N_4O_3$, $[M + H]^+$: 265.1301, found: 265.1306.

1-methyl-2-(tetrahydrofuran-2-yl)-1*H*-benzo[d]imidazole (3r)



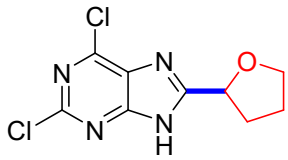
White solid (25.5 mg); 84% yield (eluent: petroleum ether/ethyl acetate = 3:2); mp: 103.5–104.4℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (dd, *J* = 6.4, 1.9 Hz, 1H), 7.34–7.23 (m, 3H), 5.19 (dd, *J* = 7.4, 6.3 Hz, 1H), 3.97–3.92 (m, 2H), 3.84 (s, 3H), 2.85–2.76 (m, 1H), 2.39–2.31 (m, 1H), 2.24–2.15 (m, 1H), 2.11–2.01 (m, 1H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.60, 141.96, 136.49, 122.69, 121.96, 119.84, 109.18, 73.58, 68.72, 30.21, 29.33, 26.07; HRMS (ESI) calcd for $C_{12}H_{15}N_2O$, $[M + H]^+$: 203.1184, found: 203.1190.

6-chloro-8-(tetrahydrofuran-2-yl)-9*H*-purine (4a)



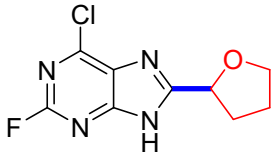
Yellow oily liquid (20.8 mg); 62% yield (eluent: dichloromethane/methanol = 30:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.63 (s, 1H), 8.81 (s, 1H), 5.32 (dd, *J* = 7.9, 5.9 Hz, 1H), 4.14–4.03 (m, 2H), 2.66–2.56 (m, 1H), 2.43–2.33 (m, 1H), 2.15–2.06 (m, 1H), 2.02–1.97 (m, 1H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.36, 152.64, 150.86, 150.09, 132.66, 75.43, 69.55, 32.13, 25.85; HRMS (ESI) calcd for $C_9H_{10}N_4OCl$, $[M + H]^+$: 225.0543, found: 225.0544.

2,6-dichloro-8-(tetrahydrofuran-2-yl)-9*H*-purine (4b)



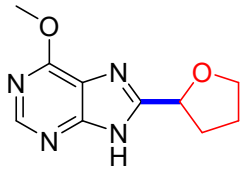
Pale yellow solid (27.1 mg); 70% yield (eluent: petroleum ether/ethyl acetate = 3:1); mp: 134.7–135.1℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.99 (s, 1H), 5.28 (dd, *J* = 7.8, 6.0 Hz, 1H), 4.06–3.96 (m, 2H), 2.58–2.50 (m, 1H), 2.45–2.35 (m, 1H), 2.12–2.00 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.10, 153.99, 152.25, 150.29, 131.01, 75.02, 69.64, 31.83, 25.82; HRMS (ESI) calcd for $C_9H_8N_4OCl_2Na$, [M + Na]$^+$: 280.9973, found: 280.9978.

6-chloro-2-fluoro-8-(tetrahydrofuran-2-yl)-9*H*-purine (4c)



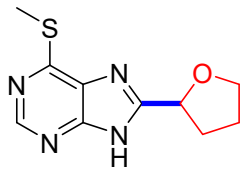
Pale yellow solid (25.1 mg); 69% yield (eluent: petroleum ether/ethyl acetate = 3:1); mp: 138.0–138.6℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 12.50 (s, 1H), 5.25 (t, *J* = 7.1 Hz, 1H), 4.05–3.86 (m, 2H), 2.56–2.45 (m, 1H), 2.39–2.28 (m, 1H), 2.09–1.95 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 160.20, 156.80 (d, $^{1}J_{C\text{-}F}$ = 219.2 Hz), 154.46 (d, $^{3}J_{C\text{-}F}$ = 15.8 Hz), 151.11 (d, $^{3}J_{C\text{-}F}$ = 17.2 Hz), 130.57, 75.04, 69.60, 31.95, 25.78; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -50.57; HRMS (ESI) calcd for $C_9H_8N_4OFClNa$, [M + Na]$^+$: 265.0268, found: 265.0266.

6-methoxy-8-(tetrahydrofuran-2-yl)-9*H*-purine (4d)



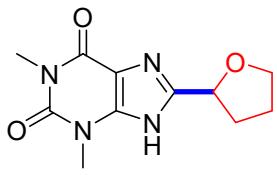
Pale yellow solid (22.1 mg); 67% yield (eluent: dichloromethane/methanol = 30:1); mp: 152.0–153.1℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.14 (s, 1H), 8.57 (s, 1H), 5.23 (dd, *J* = 7.7, 5.8 Hz, 1H), 4.14 (s, 3H), 4.07–3.96 (m, 2H), 2.51–2.32 (m, 2H), 2.05–1.90 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.48, 156.66, 152.97, 150.93, 121.89, 75.47, 69.16, 54.10, 31.79, 25.72; HRMS (ESI) calcd for $C_{10}H_{12}N_4O_2Na$, [M + Na]$^+$: 243.0858, found: 243.0865.

6-(methylthio)-8-(tetrahydrofuran-2-yl)-9*H*-purine (4e)



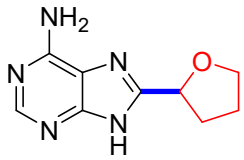
Pale yellow solid (23.4 mg); 66% yield (eluent: petroleum ether/ethyl acetate = 3:2); mp: 192.7–193.1℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.17 (s, 1H), 8.76 (s, 1H), 5.28 (dd, *J* = 7.8, 5.9 Hz, 1H), 4.13–4.00 (m, 2H), 2.71 (s, 3H), 2.57–2.48 (m, 1H), 2.38–2.29 (m, 1H), 2.09–1.92 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.53, 157.57, 150.60, 148.97, 132.21, 75.56, 69.33, 32.26, 25.80, 11.82; HRMS (ESI) calcd for $C_{10}H_{12}N_4ONaS$, [M + Na]$^+$: 259.0630, found: 259.0630.

1,3-dimethyl-8-(tetrahydrofuran-2-yl)-3,9-dihydro-1*H*-purine-2,6-dione (4f)



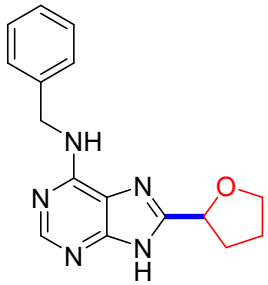
White solid (22.9 mg); 61% yield (eluent: dichloromethane/methanol = 30:1); mp: 239.2–239.5℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.73 (s, 1H), 5.11 (dd, *J* = 7.7, 5.7 Hz, 1H), 4.13–4.11 (m, 1H), 3.98–3.91 (m, 1H), 3.59 (s, 3H), 3.45 (s, 3H), 2.50–2.36 (m, 1H), 2.26–2.18 (m, 1H), 2.07–1.96 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.71, 155.49, 151.78, 149.26, 106.72, 74.94, 69.39, 32.21, 30.24, 28.39, 25.76; HRMS (ESI) calcd for $C_{11}H_{15}N_4O_3$, [M + H]$^+$: 251.1144, found: 251.1147.

8-(tetrahydrofuran-2-yl)-9*H*-purin-6-amine (4g)



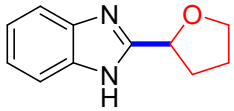
Pale yellow solid (12.6 mg); 41% yield (eluent: dichloromethane/methanol = 25:1); mp: 278.8–280.4℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (s, 1H), 7.07 (s, 2H), 5.02 (t, J = 6.9 Hz, 1H), 4.00–3.94 (m, 1H), 3.86–3.80 (m, 1H), 2.34–2.25 (m, 1H), 2.21–2.12 (m, 1H), 2.02–1.91 (m, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 152.62, 75.00, 68.70, 31.63, 25.95; HRMS (ESI) calcd for $C_9H_{12}N_5O$, $[M + H]^+$: 206.1042, found: 206.1044.

N-benzyl-8-(tetrahydrofuran-2-yl)-9*H*-purin-6-amine (4h)



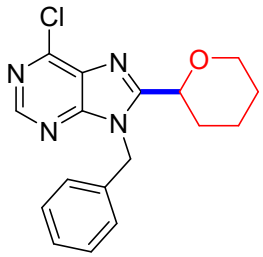
White solid (14.6 mg); 33% yield (eluent: dichloromethane/methanol = 30:1); mp: 166.5–167.3℃; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.93 (s, 1H), 8.18 (s, 1H), 7.50–7.24 (m, 5H), 7.21 (t, J = 7.3 Hz, 1H), 5.04 (s, 1H), 4.72 (s, 2H), 4.00–3.93 (m, 1H), 3.87–3.80 (m, 1H), 2.33–2.15 (m, 2H), 2.01–1.91 (m, 2H); 13C NMR (126 MHz, DMSO-d_6) δ 154.42, 152.78, 152.62, 150.94, 140.82, 128.58, 127.67, 126.96, 119.15, 75.00, 68.66, 43.36, 31.49, 26.00; HRMS (ESI) calcd for $C_{16}H_{18}N_5O$, $[M + H]^+$: 296.1511, found: 296.1514.

2-(tetrahydrofuran-2-yl)-1*H*-benzo[d]imidazole (4i)



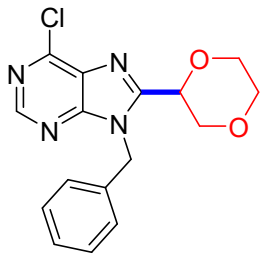
White solid (20.3 mg); 72% yield (eluent: dichloromethane/methanol = 20:1); mp: 208.6–209.1℃; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.59 (s, 2H), 7.28–7.20 (m, 2H), 5.27 (dd, J = 7.7, 5.9 Hz, 1H), 4.08–3.94 (m, 2H), 2.55–2.46 (m, 1H), 2.41–2.32 (m, 1H), 2.09–1.94 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-d) δ 156.09, 122.41, 75.36, 69.17, 31.97, 25.82; HRMS (ESI) calcd for $C_{11}H_{13}N_2O$, $[M + H]^+$: 189.1028, found: 189.1032.

9-benzyl-6-chloro-8-(tetrahydro-2H-pyran-2-yl)-9*H*-purine (5a)



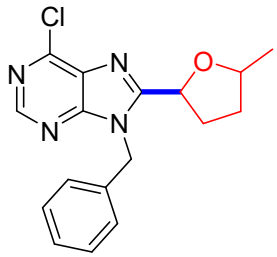
White solid (34.4 mg); 70% yield (eluent: petroleum ether/ethyl acetate = 3:1); mp: 102.7–103.4℃; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.71 (s, 1H), 7.30–7.26 (m, 3H), 7.21–7.15 (m, 2H), 5.73 (d, J = 15.3 Hz, 1H), 5.54 (d, J = 15.3 Hz, 1H), 4.53 (dd, J = 7.6, 5.5 Hz, 1H), 4.07–4.04 (m, 1H), 3.59–3.48 (m, 1H), 2.00–1.92 (m, 2H), 1.70–1.61 (m, 2H), 1.61–1.53 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-d) δ 156.41, 153.66, 151.93, 150.40, 135.71, 130.43, 128.92, 128.26, 127.52, 73.83, 68.92, 47.14, 28.88, 25.49, 22.60; HRMS (ESI) calcd for $C_{17}H_{17}N_4OClNa$, $[M + Na]^+$: 351.0989, found: 351.0993.

9-benzyl-6-chloro-8-(1,4-dioxan-2-yl)-9*H*-purine (5b)



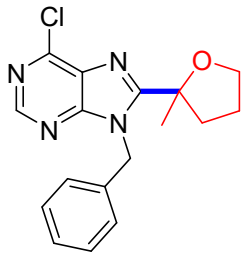
White solid (40.6 mg); 82% yield (eluent: petroleum ether/ethyl acetate = 6:1); mp: 141.3–141.6℃; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.76 (s, 1H), 7.36–7.27 (m, 3H), 7.24–7.16 (m, 2H), 5.77 (d, J = 15.3 Hz, 1H), 5.51 (d, J = 15.3 Hz, 1H), 4.71 (dd, J = 9.6, 3.0 Hz, 1H), 4.15–4.10 (m, 1H), 4.05–3.99 (m, 1H), 3.95–3.90 (m, 1H), 3.87–3.80 (m, 1H), 3.80–3.75 (m, 1H), 3.75–3.68 (m, 1H); ^{13}C NMR (101 MHz, Chloroform-d) δ 153.30, 152.83, 152.20, 150.81, 135.27, 130.36, 129.04, 128.48, 127.46, 70.97, 68.04, 66.90, 66.23, 47.06; HRMS (ESI) calcd for $C_{16}H_{15}N_4O_2NaCl$, $[M + Na]^+$: 353.0781, found: 353.0785.

9-benzyl-6-chloro-8-(5-methyltetrahydrofuran-2-yl)-9*H*-purine (5c)



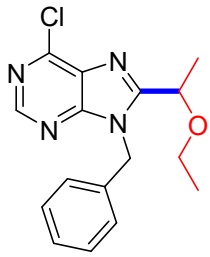
Yellow oily liquid (31.9 mg); 64% yield (eluent: petroleum ether/ethyl acetate = 15:1); a mixture of two diastereomers (dr = 55:45); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 1.7 Hz, 1H), 7.33 – 7.26 (m, 3H), 7.26 – 7.20 (m, 2H), 5.80 – 5.72 (m, 1H), 5.68 – 5.58 (m, 1H), 5.16 (t, *J* = 6.9 Hz, 1H), 5.00 (dd, *J* = 7.7, 5.8 Hz, 1H), 4.23 – 4.16 (m, 0.45H), 4.14 – 4.06 (m, 0.55H), 2.89 – 2.77 (m, 1H), 2.34 – 2.10 (m, 2H), 1.72 – 1.55 (m, 1H), 1.27 (d, *J* = 6.1 Hz, 1.6H), 1.24 (d, *J* = 6.1 Hz, 1.4H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 157.43, 157.13, 153.85, 151.83, 151.81, 150.26, 150.20, 135.61, 135.59, 130.38, 128.88, 128.84, 128.17, 128.13, 127.35, 127.34, 77.72, 76.34, 74.14, 73.35, 46.80, 46.74, 33.38, 32.82, 29.34, 29.25, 21.01, 20.66; HRMS (ESI) calcd for $C_{17}H_{17}N_4OClNa$, $[M + Na]^+$: 351.0989, found: 351.0991.

9-benzyl-6-chloro-8-(2-methyltetrahydrofuran-2-yl)-*9H*-purine (5c')



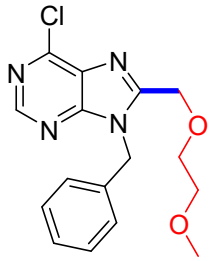
Yellow oily liquid (7.0 mg); 17% yield (eluent: petroleum ether/ethyl acetate = 15:1); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.72 (s, 1H), 7.30 – 7.25 (m, 3H), 7.17 – 7.10 (m, 2H), 5.86 – 5.77 (m, 2H), 3.93 – 3.86 (m, 1H), 3.51 – 3.43 (m, 1H), 3.19 – 3.12 (m, 1H), 2.09 – 1.95 (m, 2H), 1.87 – 1.79 (m, 1H), 1.52 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.04, 154.33, 151.67, 149.85, 136.59, 130.34, 128.61, 127.71, 126.88, 83.01, 68.94, 48.00, 38.48, 27.45, 25.48; HRMS (ESI) calcd for $C_{17}H_{17}N_4OClNa$, $[M + Na]^+$: 351.0989, found: 351.0992.

9-benzyl-6-chloro-8-(1-ethoxyethyl)-9*H*-purine (5d)



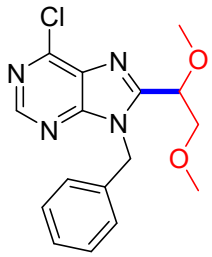
Yellow oily liquid (33.7 mg); 71% yield (eluent: petroleum ether/ethyl acetate = 4:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 7.32–7.25 (m, 3H), 7.16–7.10 (m, 2H), 5.78–5.62 (m, 2H), 4.88 (q, *J* = 6.9 Hz, 1H), 3.53–3.41 (m, 1H), 3.40–3.31 (m, 1H), 1.53 (d, *J* = 6.6 Hz, 3H), 1.09 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.82, 153.89, 151.95, 150.20, 135.57, 130.42, 128.86, 128.08, 126.79, 72.62, 64.83, 46.87, 19.06, 15.07; HRMS (ESI) calcd for $C_{16}H_{17}N_4ONaCl$, $[M + Na]^+$: 339.0989, found: 339.0992.

9-benzyl-6-chloro-8-((2-methoxyethoxy)methyl)-9*H*-purine (5e)



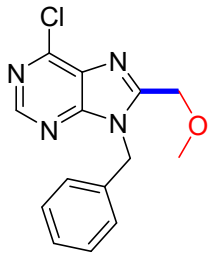
Yellow oily liquid (26.5 mg); 53% yield (eluent: petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.76 (s, 1H), 7.31–7.27 (m, 3H), 7.26–7.23 (m, 2H), 5.63 (s, 2H), 4.75 (s, 2H), 3.67–3.61 (m, 2H), 3.51–3.46 (m, 2H), 3.34 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 153.72, 153.55, 152.17, 150.51, 135.19, 130.45, 128.95, 128.35, 127.56, 71.48, 70.29, 66.39, 59.00, 46.69; HRMS (ESI) calcd for $C_{16}H_{18}N_4O_2Cl$, $[M + H]^+$: 333.1118, found: 333.1119.

9-benzyl-6-chloro-8-(1,2-dimethoxyethyl)-9*H*-purine (5e')



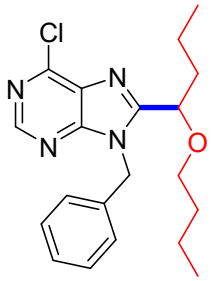
White solid (9.5 mg); 19% yield (eluent: petroleum ether/ethyl acetate = 10:1); mp: 82.9–84.2℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 7.29–7.23 (m, 3H), 7.18–7.11 (m, 2H), 5.72–5.59 (m, 2H), 4.82 (dd, *J* = 6.4, 4.8 Hz, 1H), 3.79–3.66 (m, 2H), 3.26 (s, 3H), 3.15 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.22, 153.73, 152.05, 150.44, 135.74, 130.65, 128.82, 128.12, 127.07, 77.47, 73.29, 59.30, 57.79, 47.09; HRMS (ESI) calcd for $C_{16}H_{18}N_4O_2Cl$, $[M + H]^+$: 333.1118, found: 333.1124.

9-benzyl-6-chloro-8-(methoxymethyl)-9*H*-purine (5e")



Yellow oily liquid (6.1 mg); 14% yield (eluent: petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.79 (s, 1H), 7.37–7.30 (m, 3H), 7.29–7.24 (m, 2H), 5.62 (s, 2H), 4.67 (s, 2H), 3.40 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.66, 153.52, 152.18, 150.54, 135.05, 130.48, 129.00, 128.44, 127.54, 67.63, 58.82, 46.77; HRMS (ESI) calcd for $C_{14}H_{14}N_4OCl$, $[M + H]^+$: 289.0856, found: 289.0854.

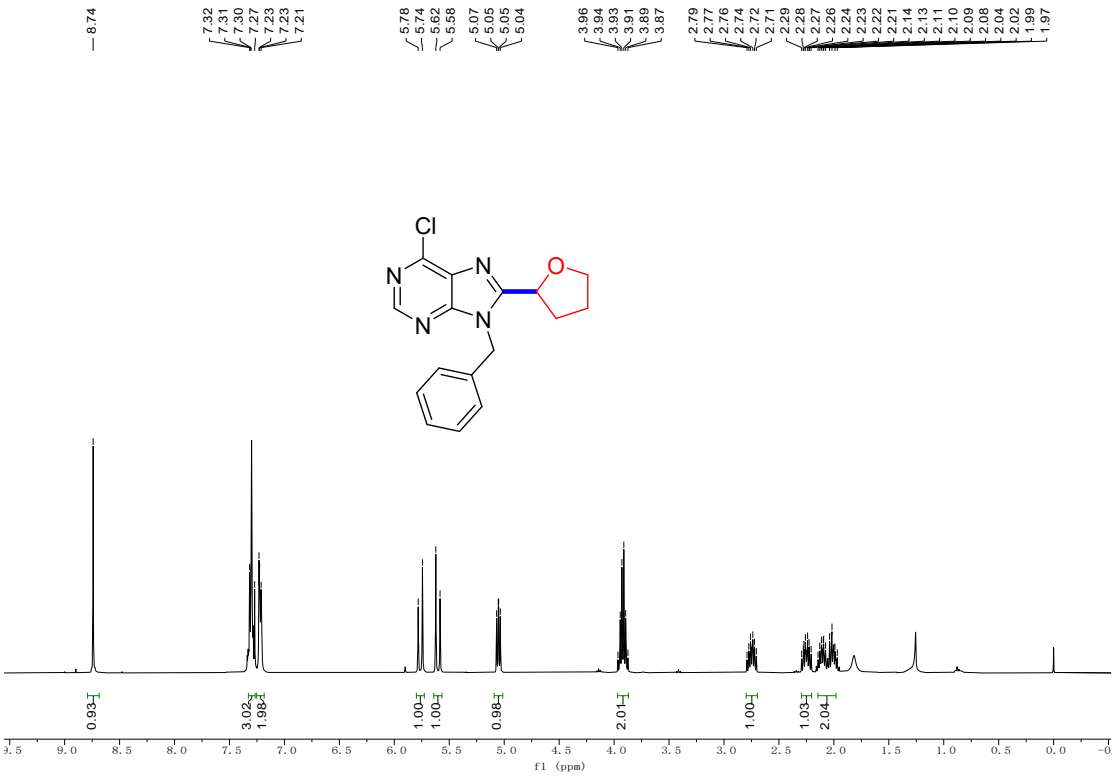
9-benzyl-8-(1-butoxybutyl)-6-chloro-9*H*-purine (5f)

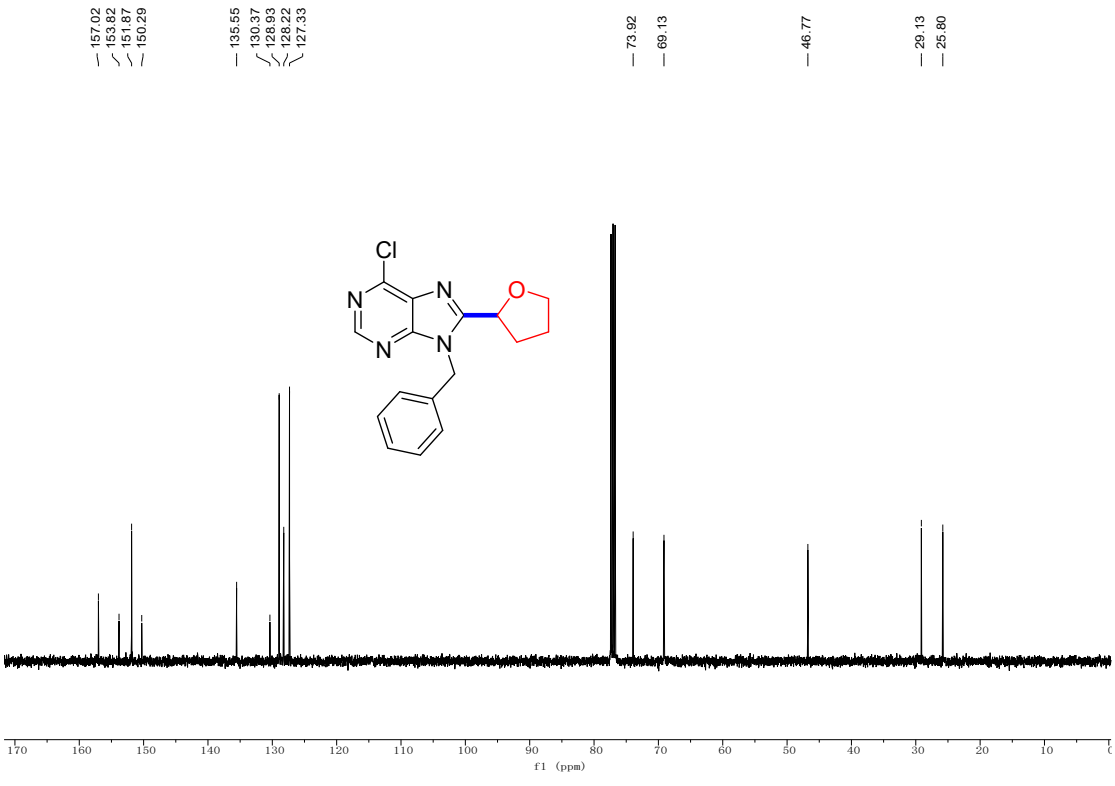


Yellow oily liquid (17.9 mg); 32% yield (eluent: petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 7.31–7.26 (m, 3H), 7.12–7.06 (m, 2H), 5.70 (d, *J* = 3.5 Hz, 2H), 4.74 (dd, *J* = 8.5, 6.1 Hz, 1H), 3.28 (q, *J* = 6.2 Hz, 2H), 1.86–1.77 (m, 1H), 1.43–1.35 (m, 2H), 1.29–1.22 (m, 4H), 0.84 (t, *J* = 7.3 Hz, 3H), 0.79 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.79, 154.00, 151.90, 150.11, 135.74, 130.54, 128.81, 128.01, 126.64, 77.55, 69.90, 46.87, 35.87, 31.55, 19.21, 18.95, 13.80, 13.55; HRMS (ESI) calcd for $C_{20}H_{25}N_4OClNa$, $[M + Na]^+$: 395.1615, found: 395.1608.

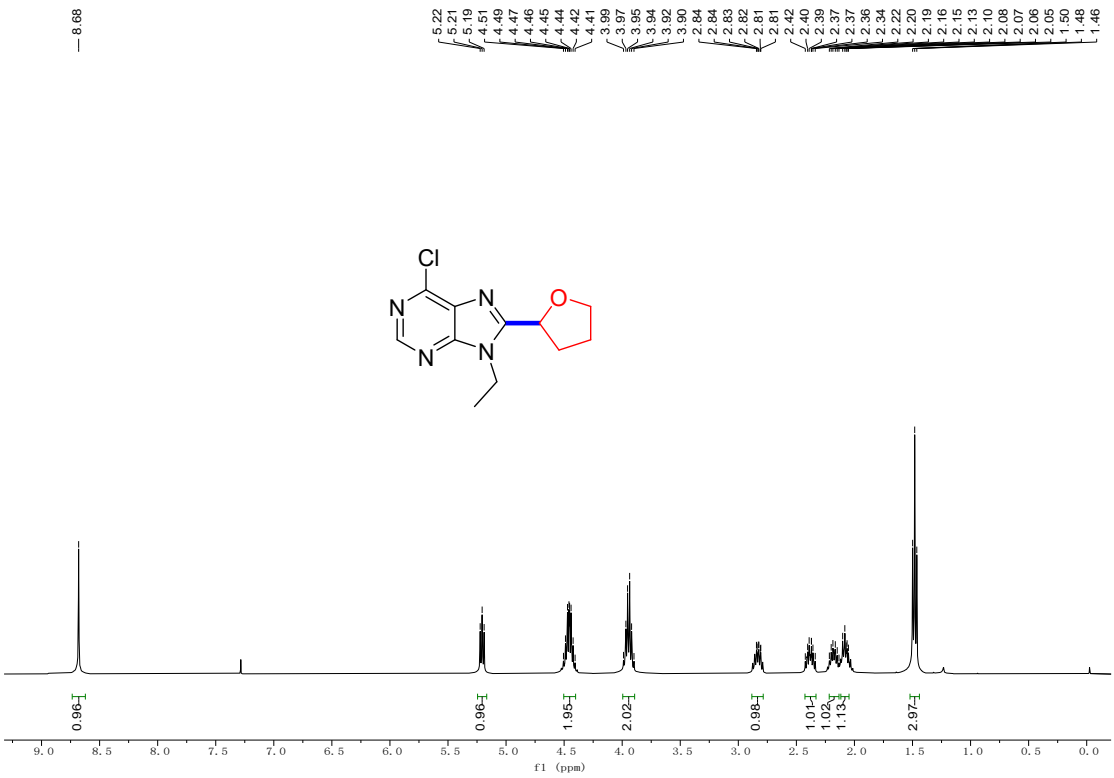
Ⅹ. NMR Spectra for all the compounds

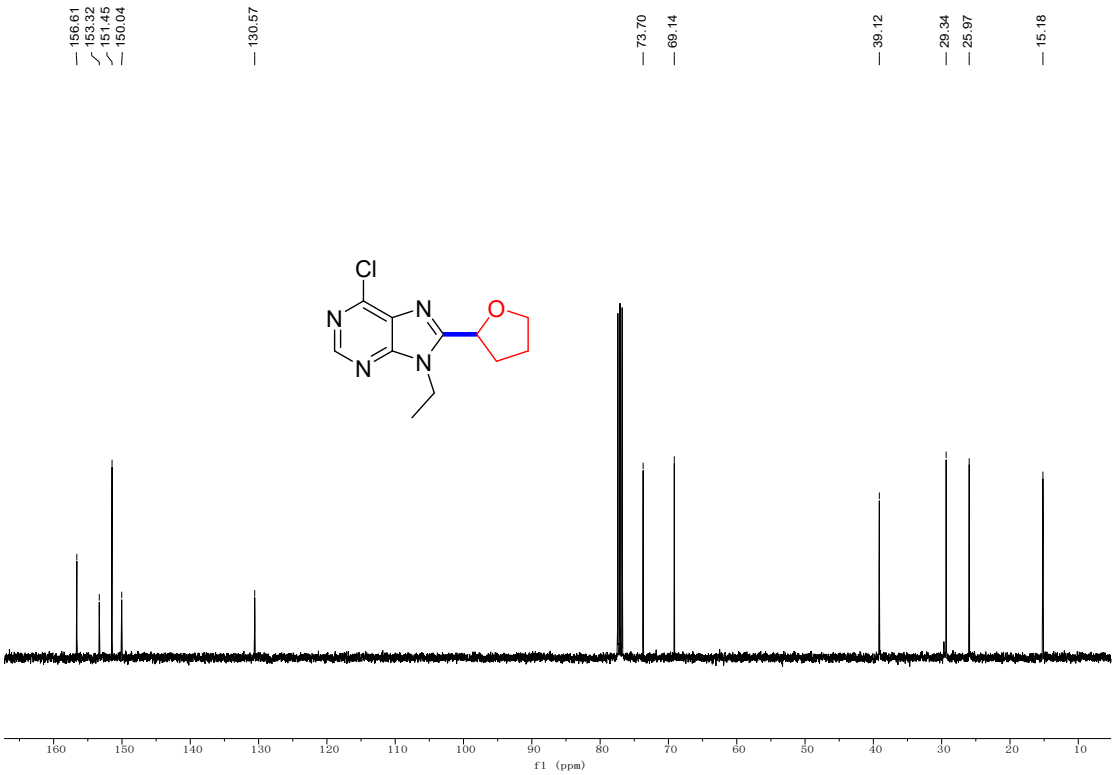
3a [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



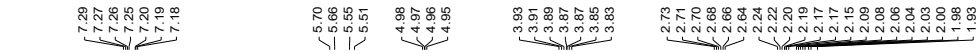


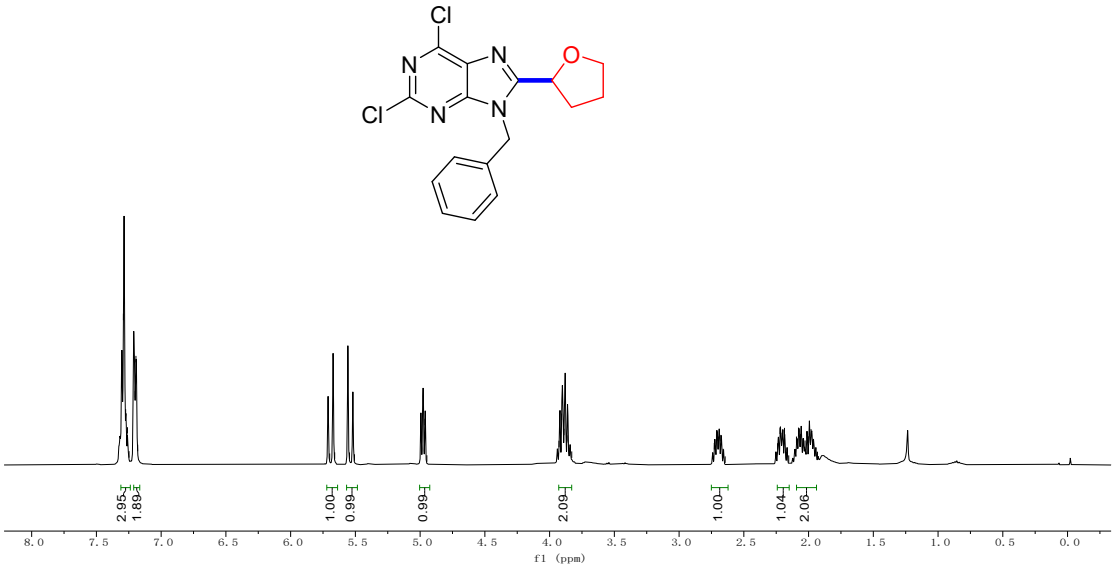
3b [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

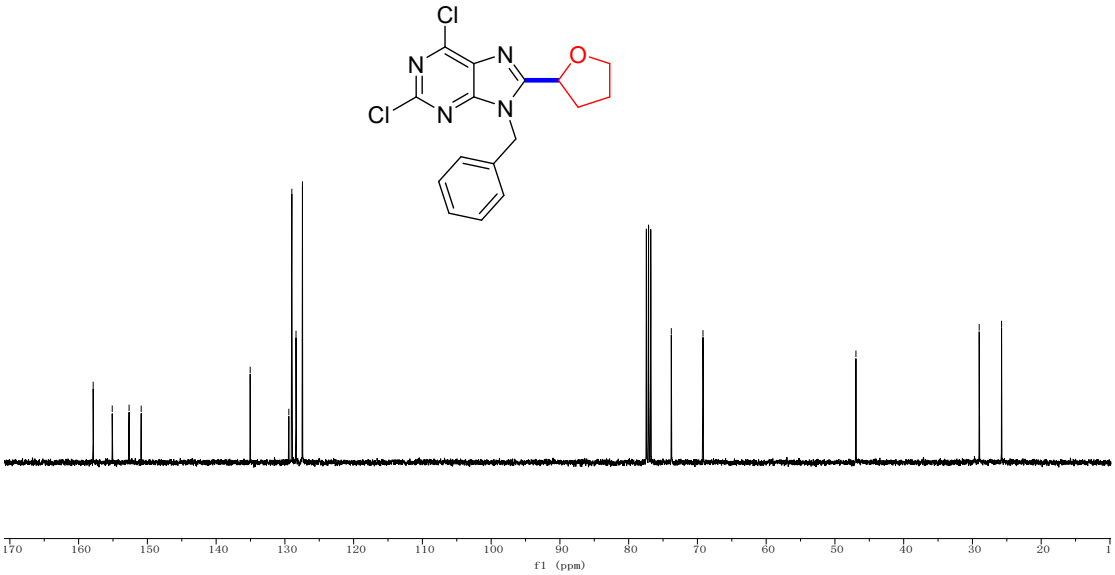




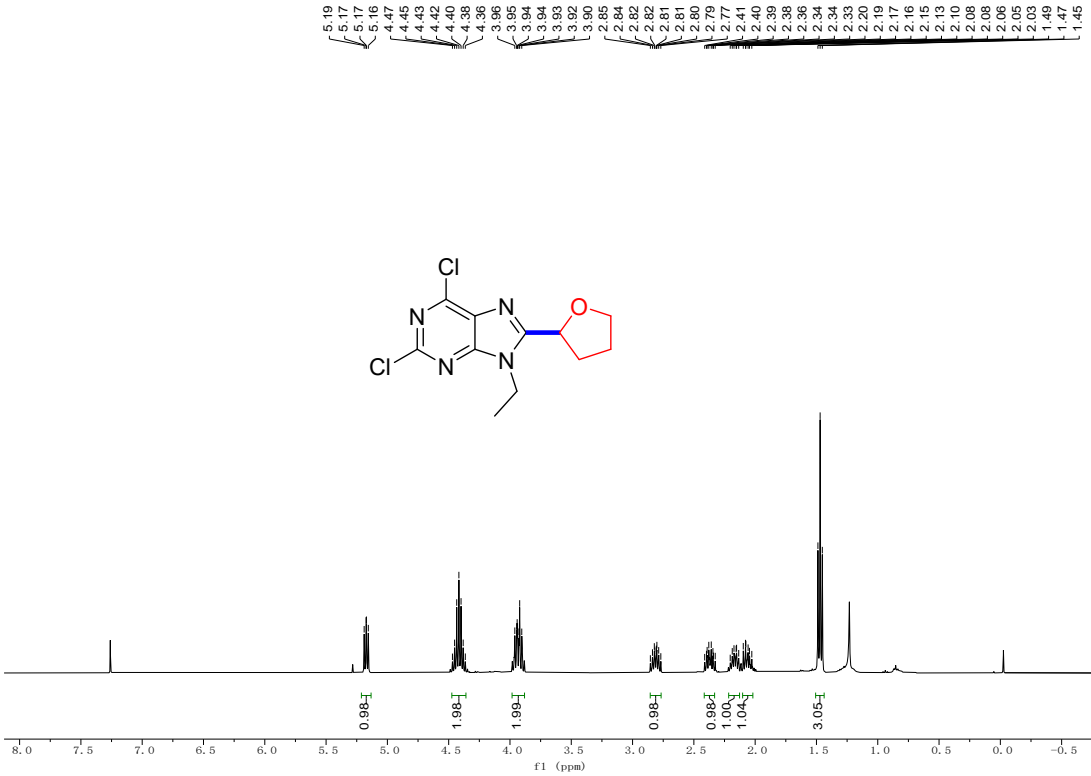
3c [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

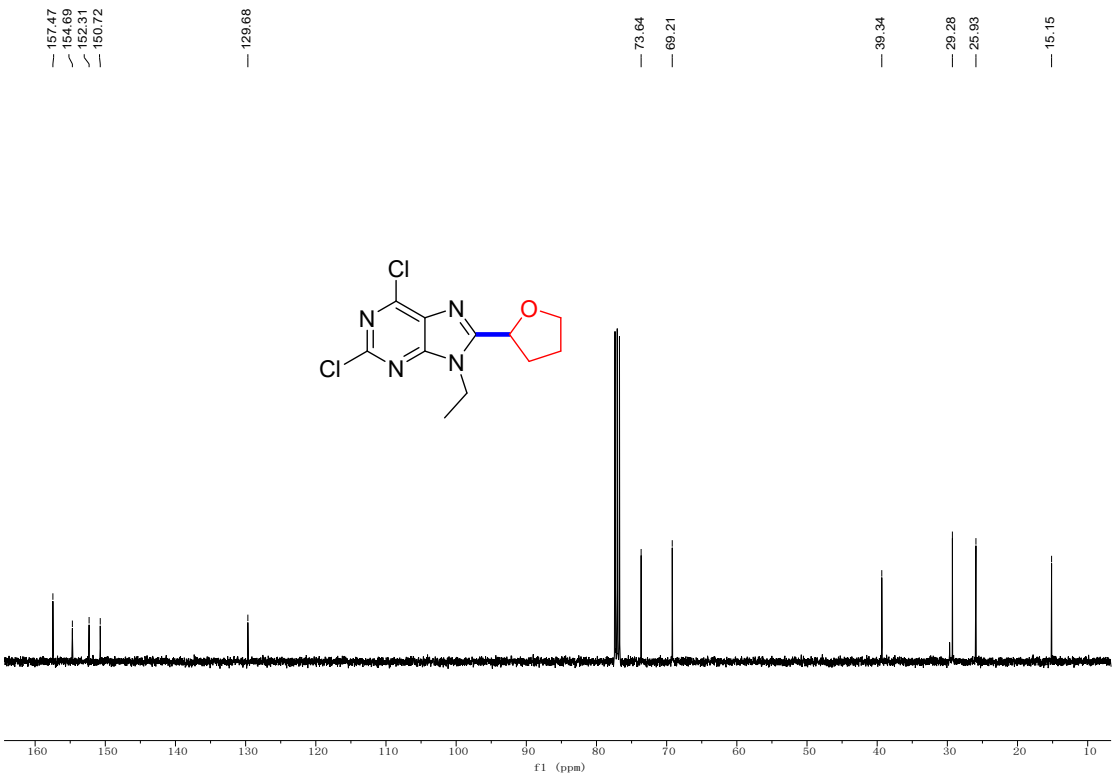




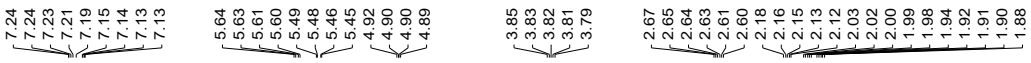


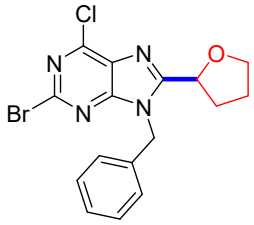
3d [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

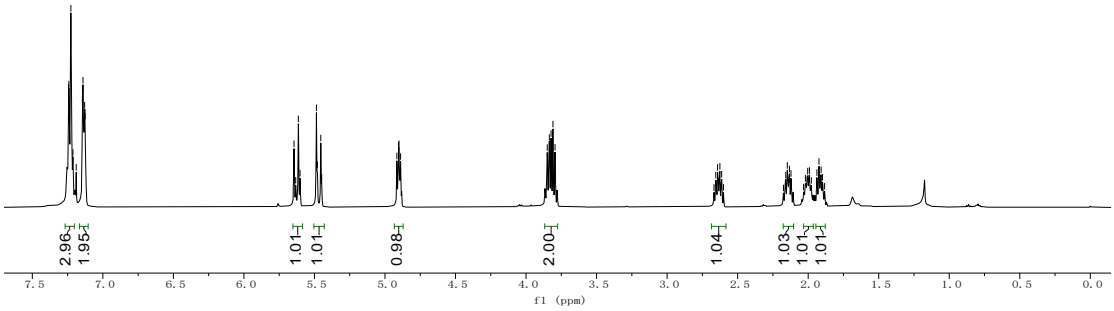


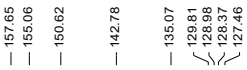


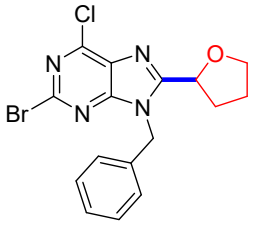
3e [^{1}H NMR (500 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)]

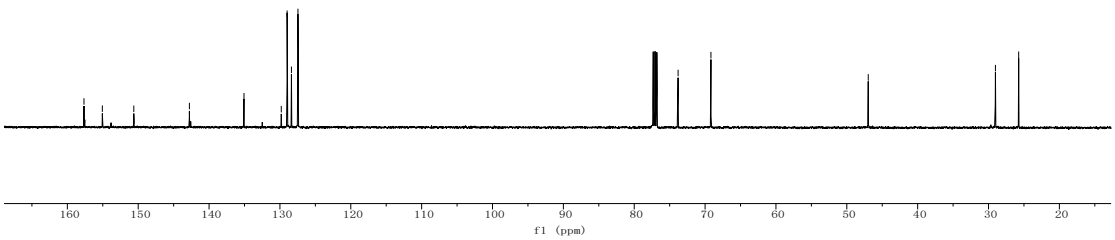




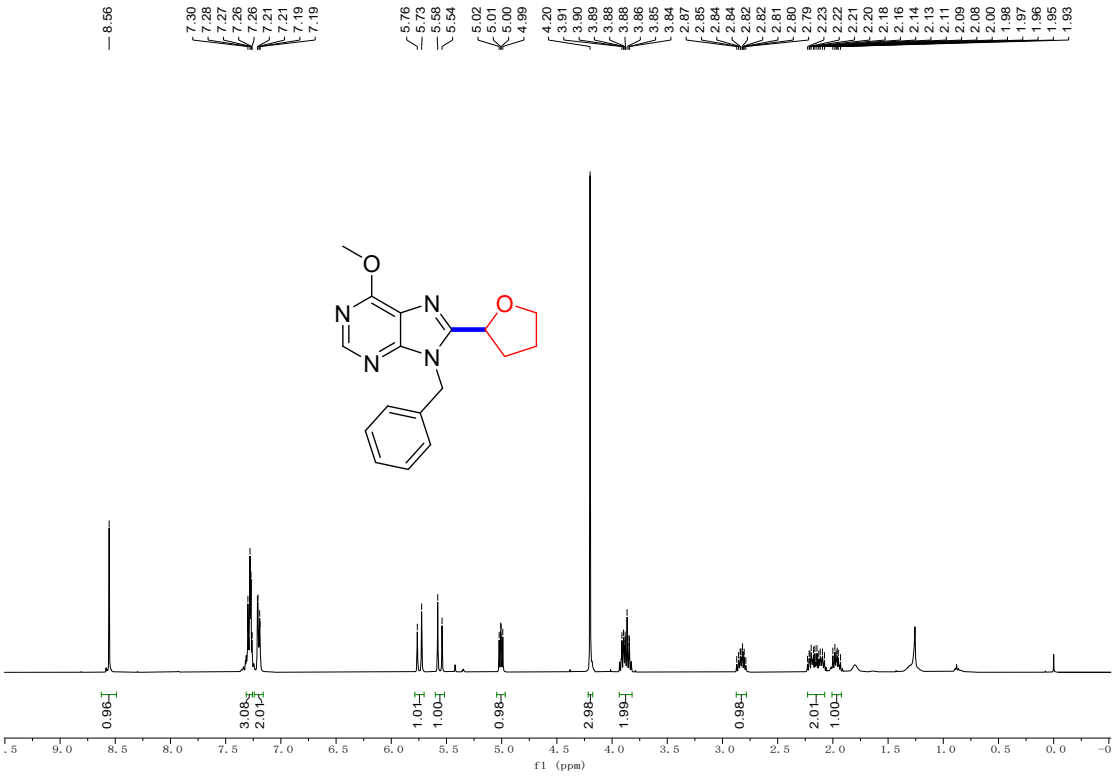


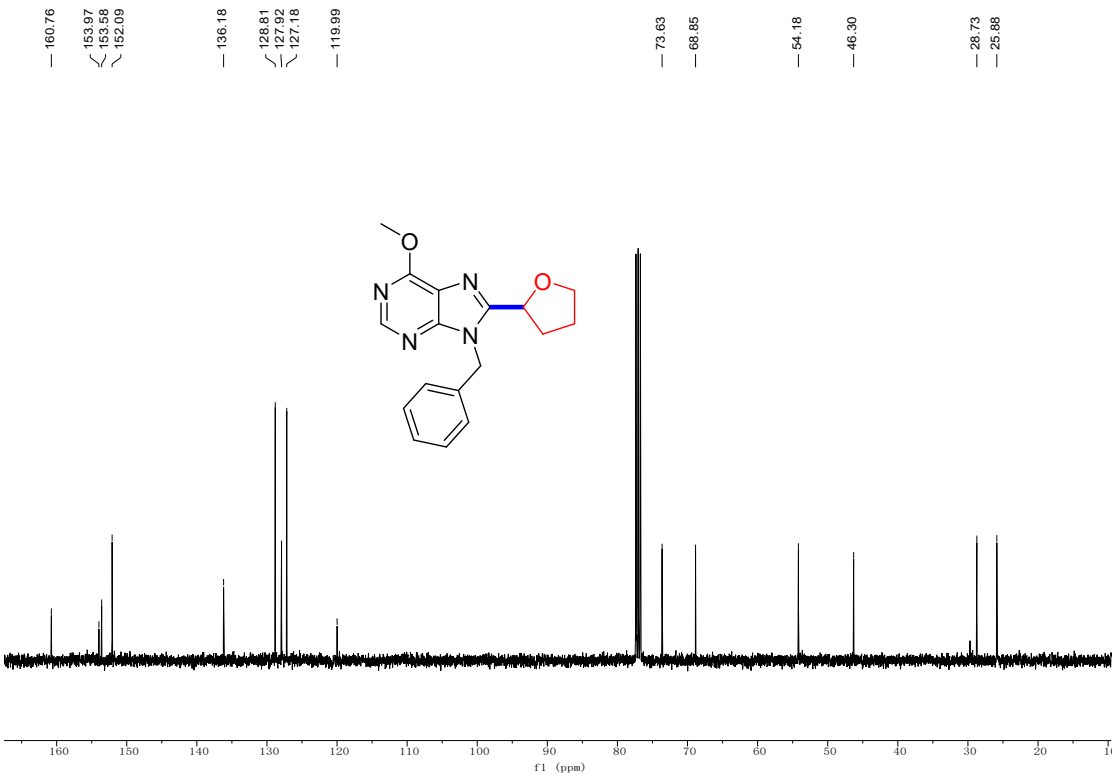




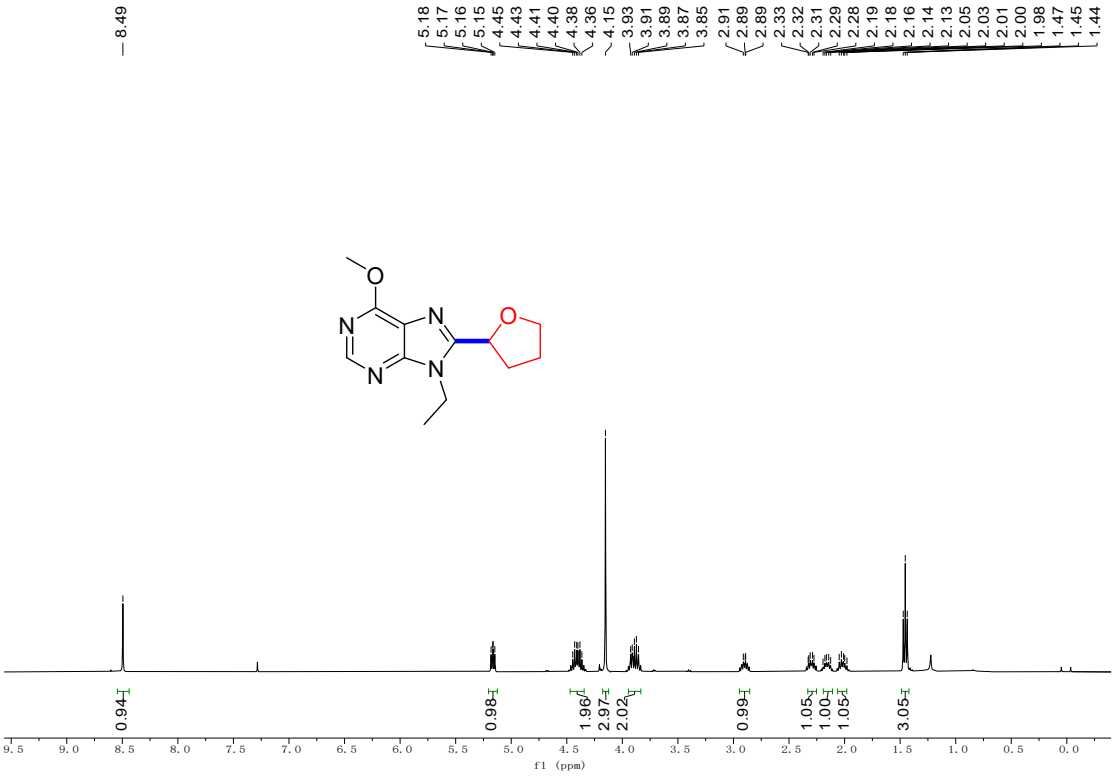


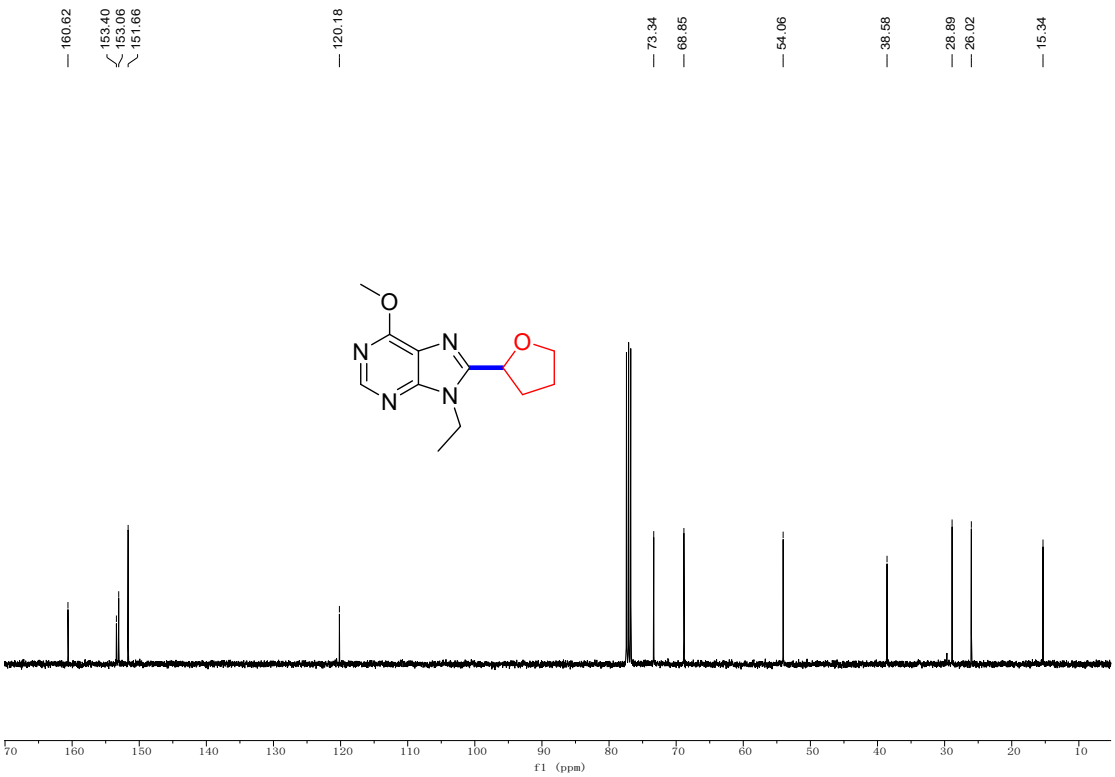
3f [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



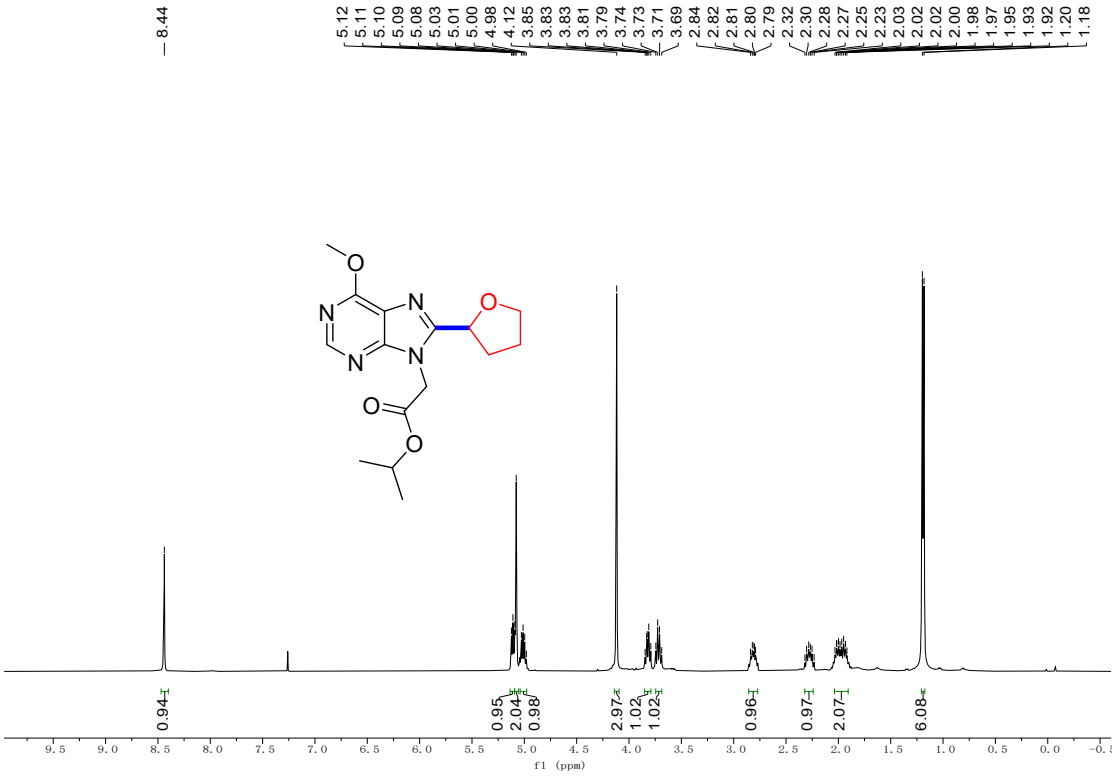


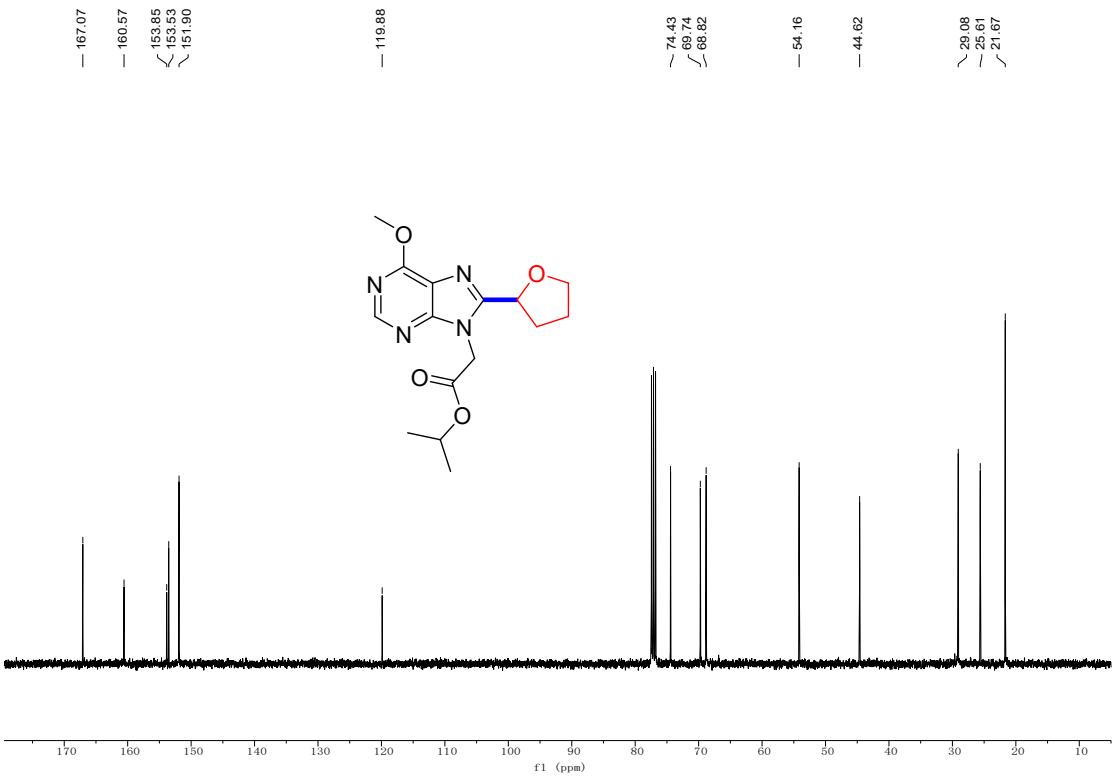
3g [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



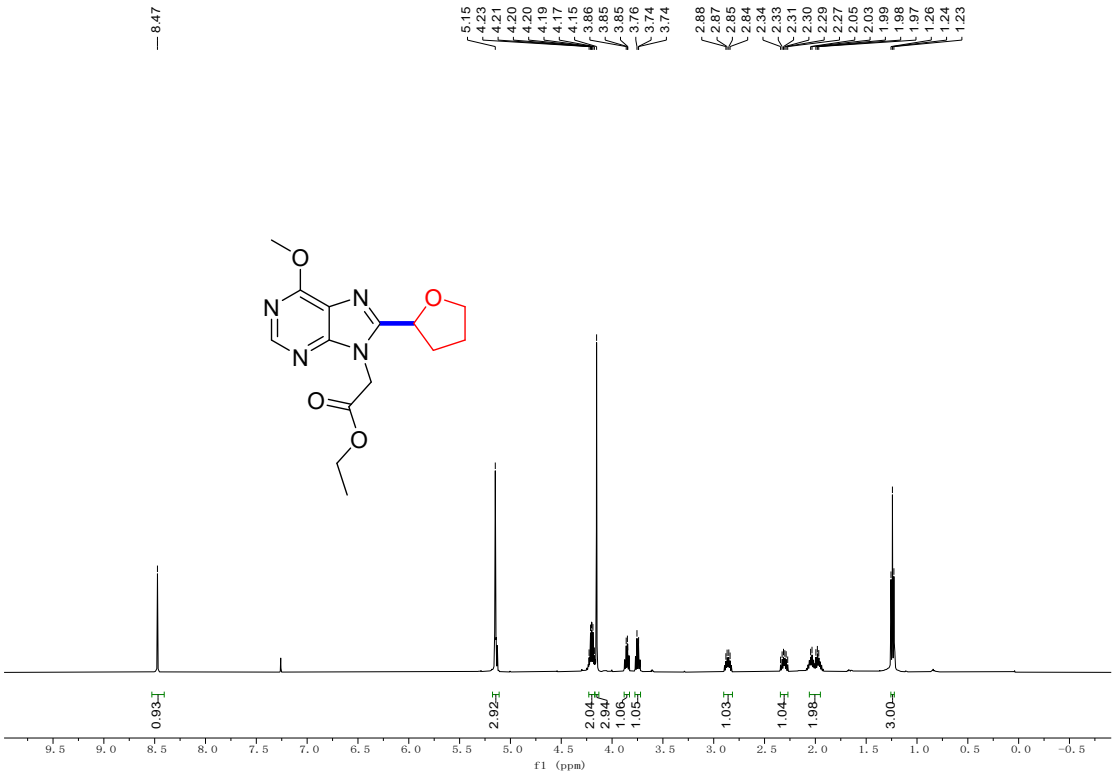


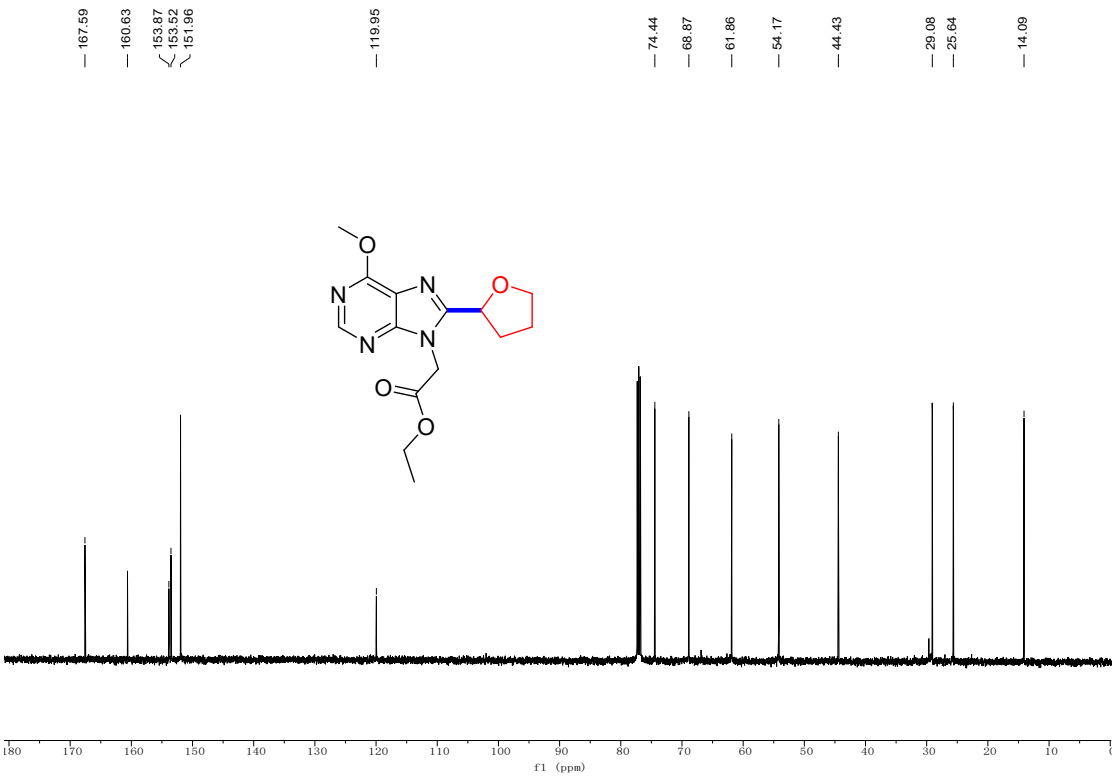
3h [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



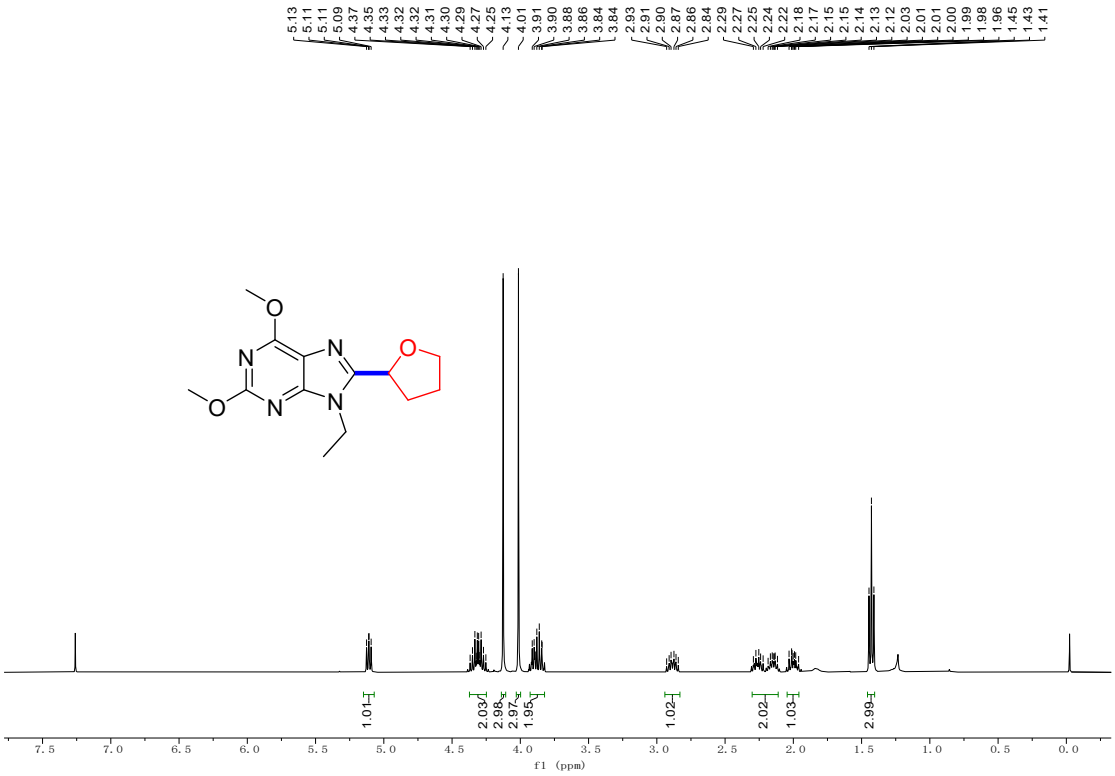


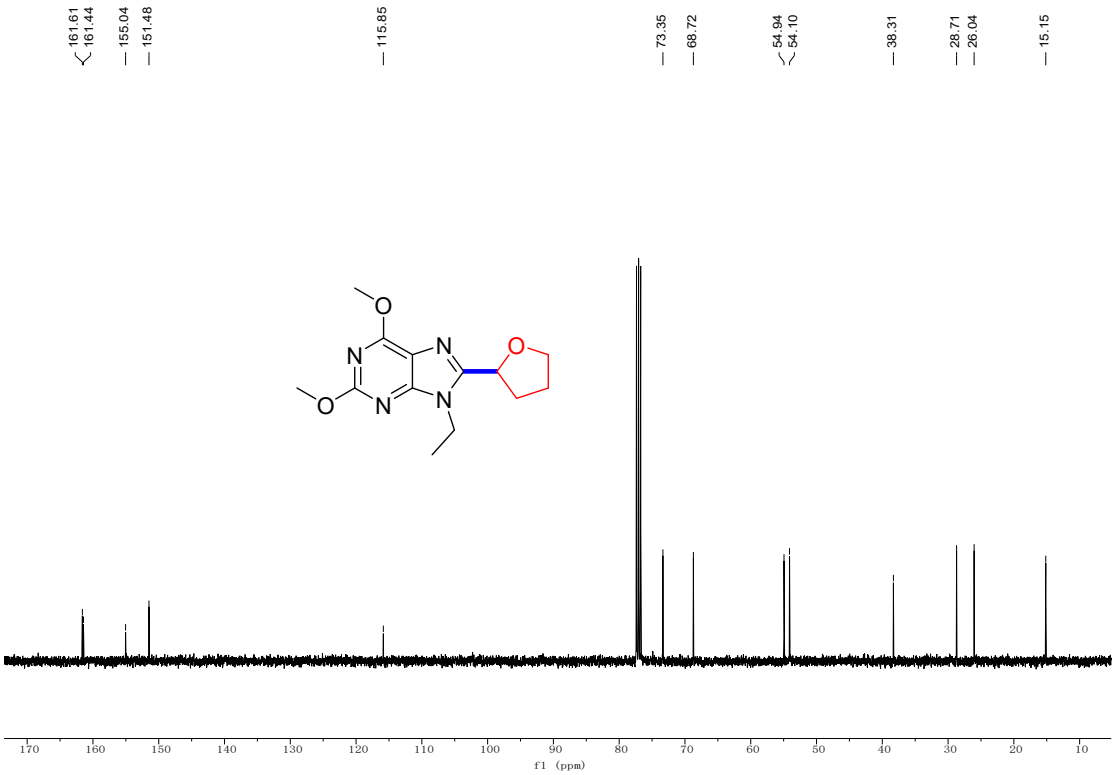
3i [^{1}H NMR (500 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)]



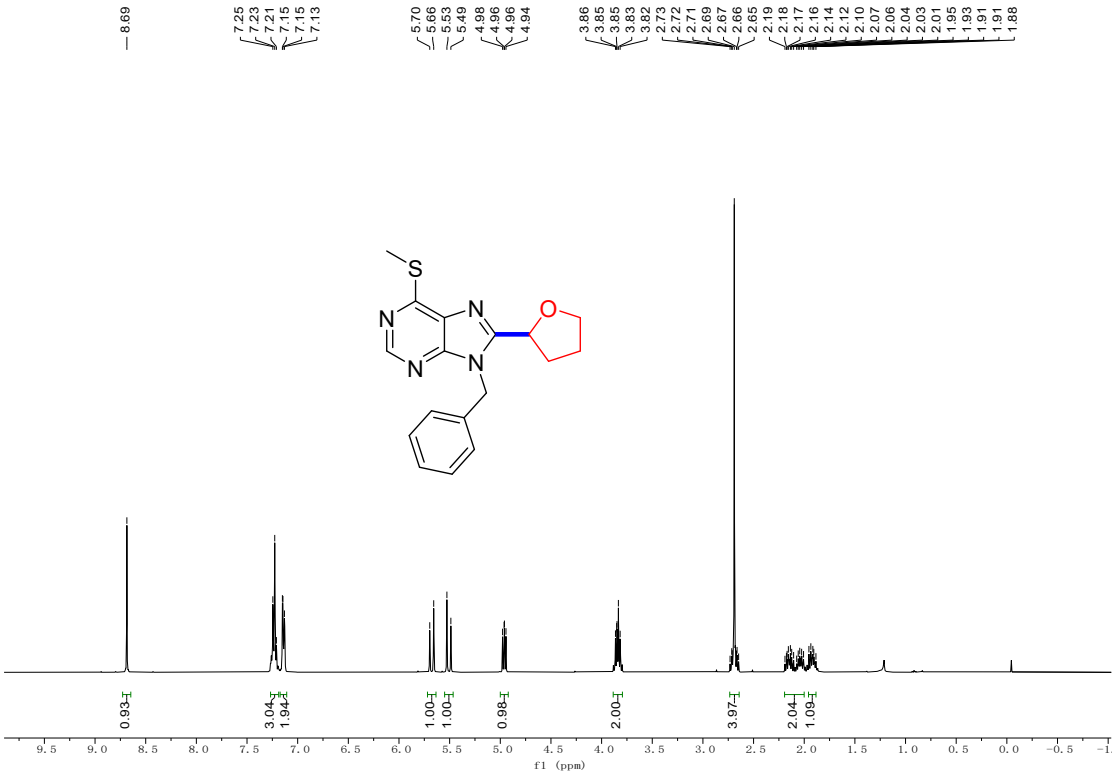


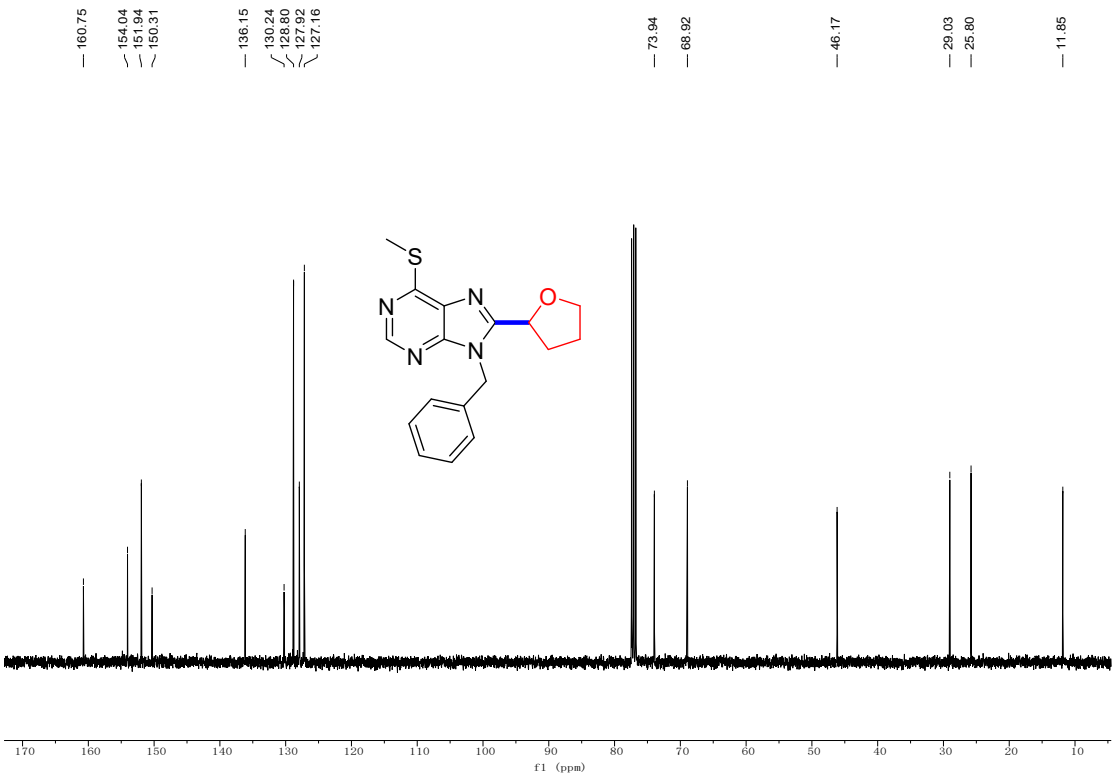
3j [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



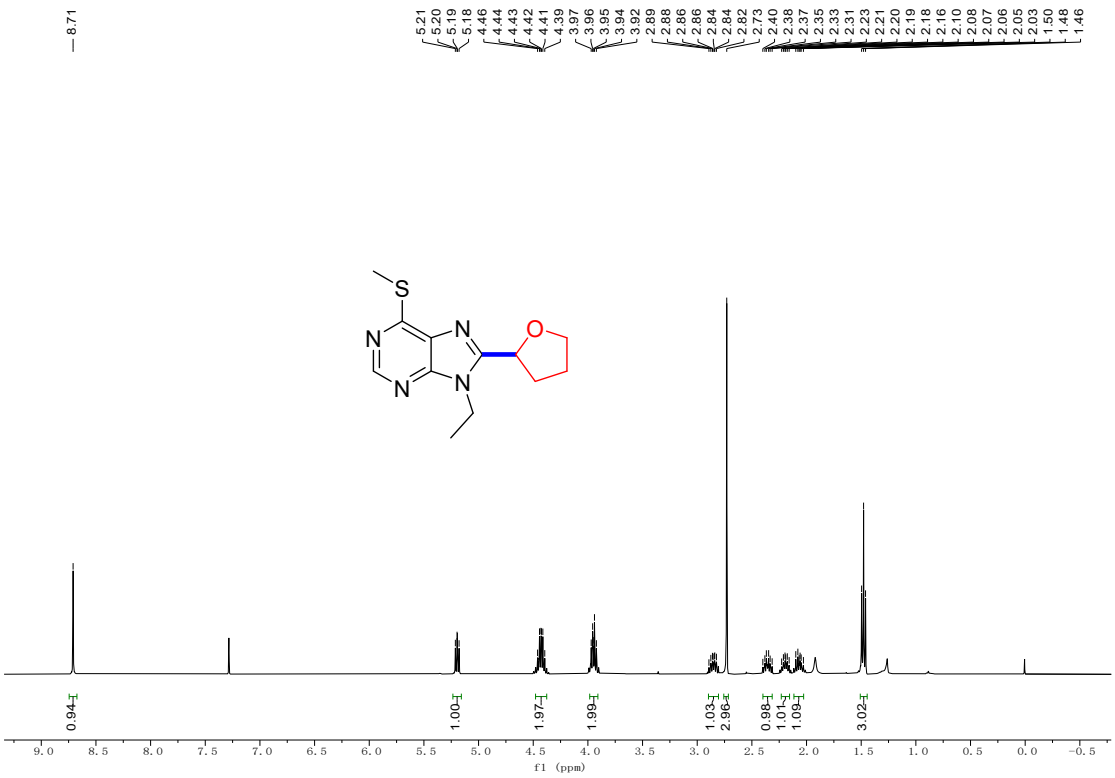


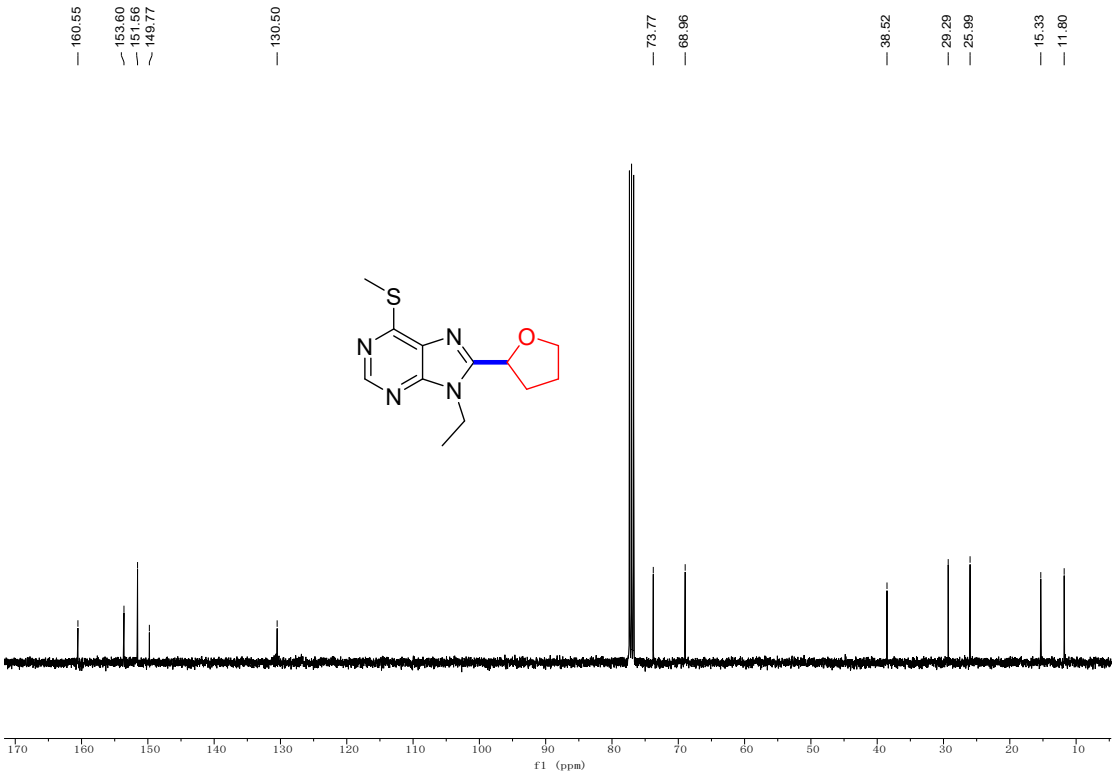
3k [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



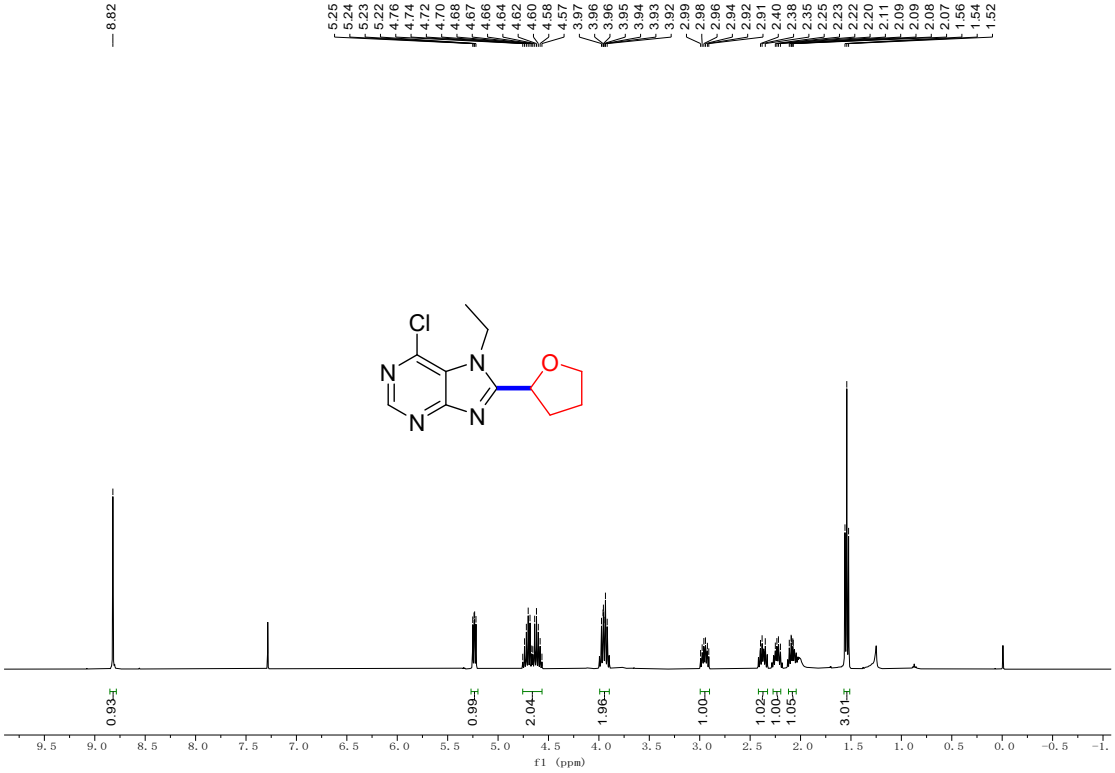


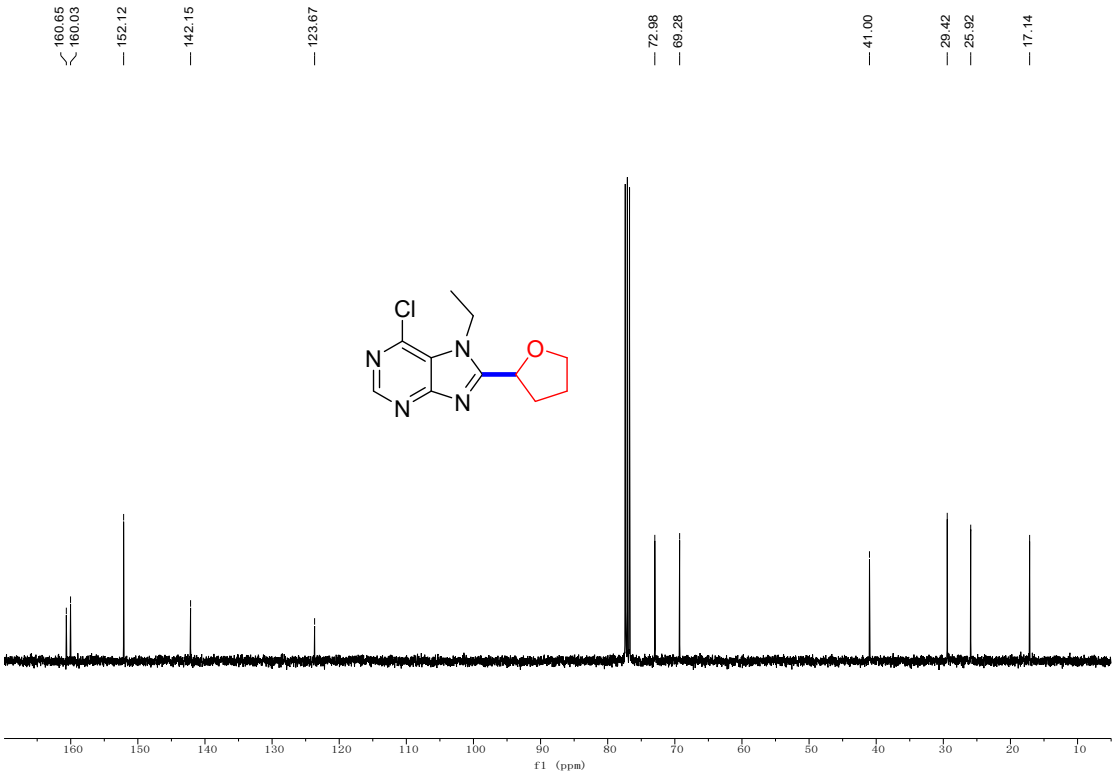
3l [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



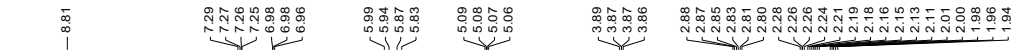


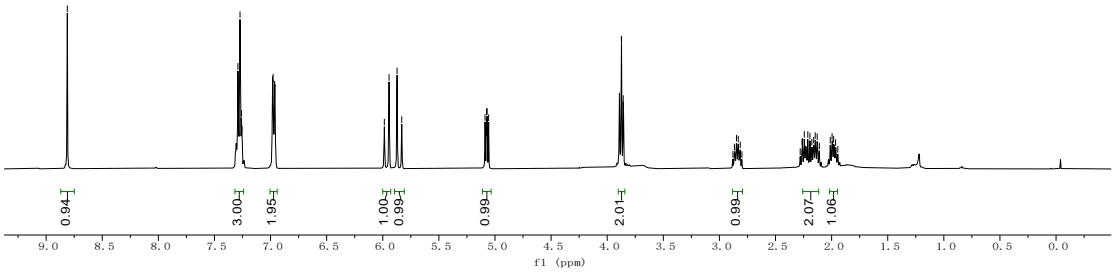
3m [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

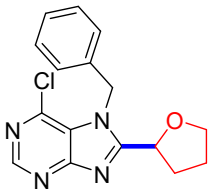




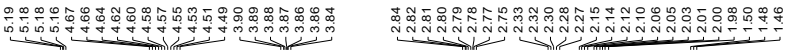
3n [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

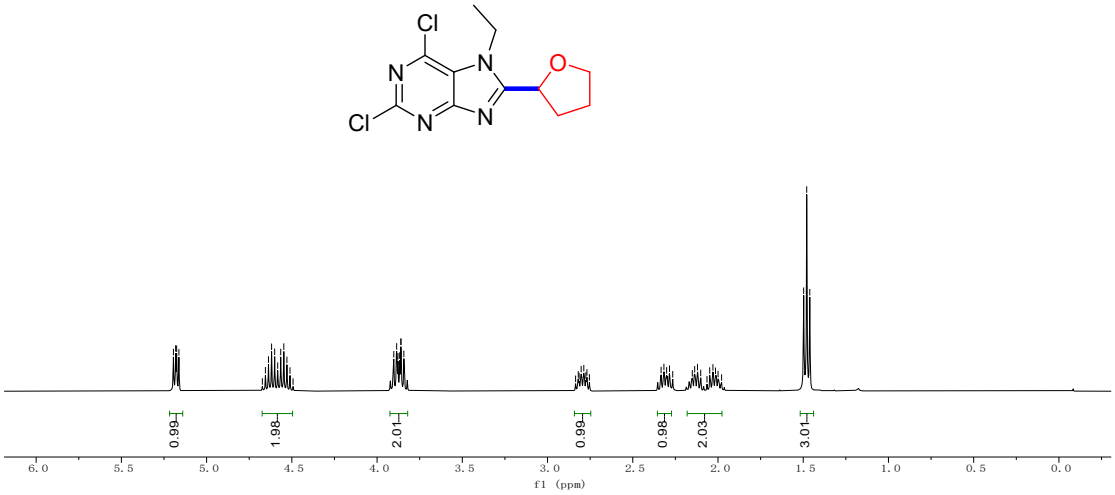


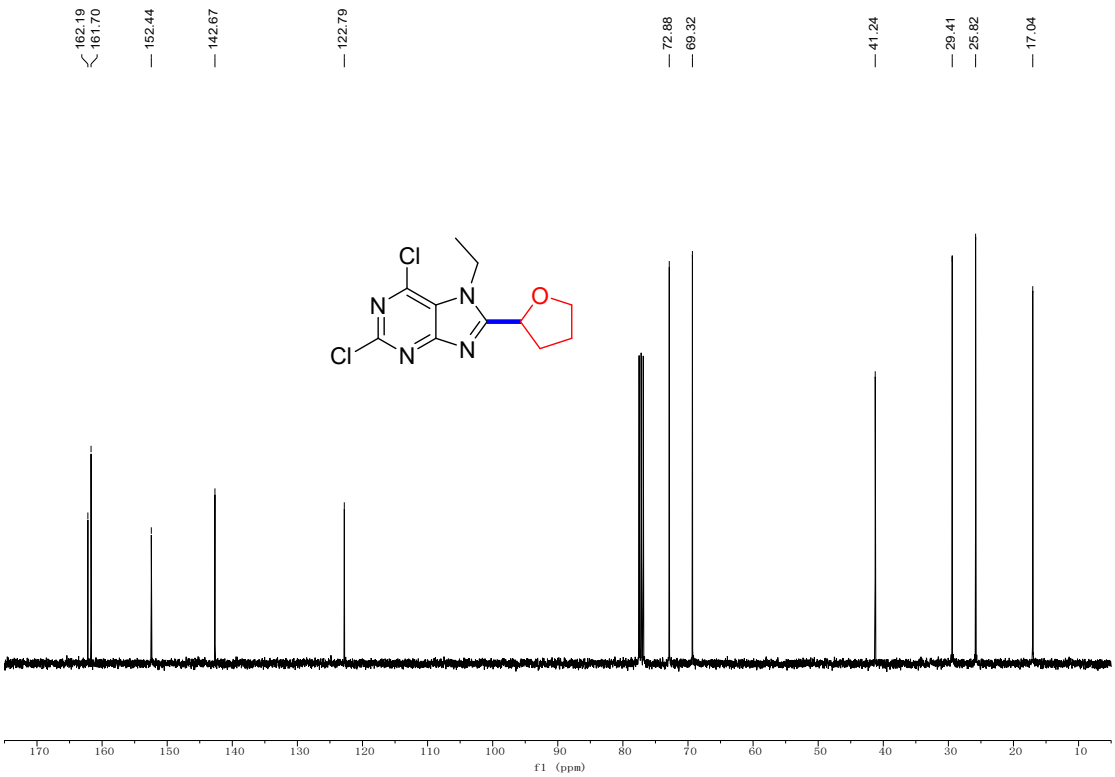




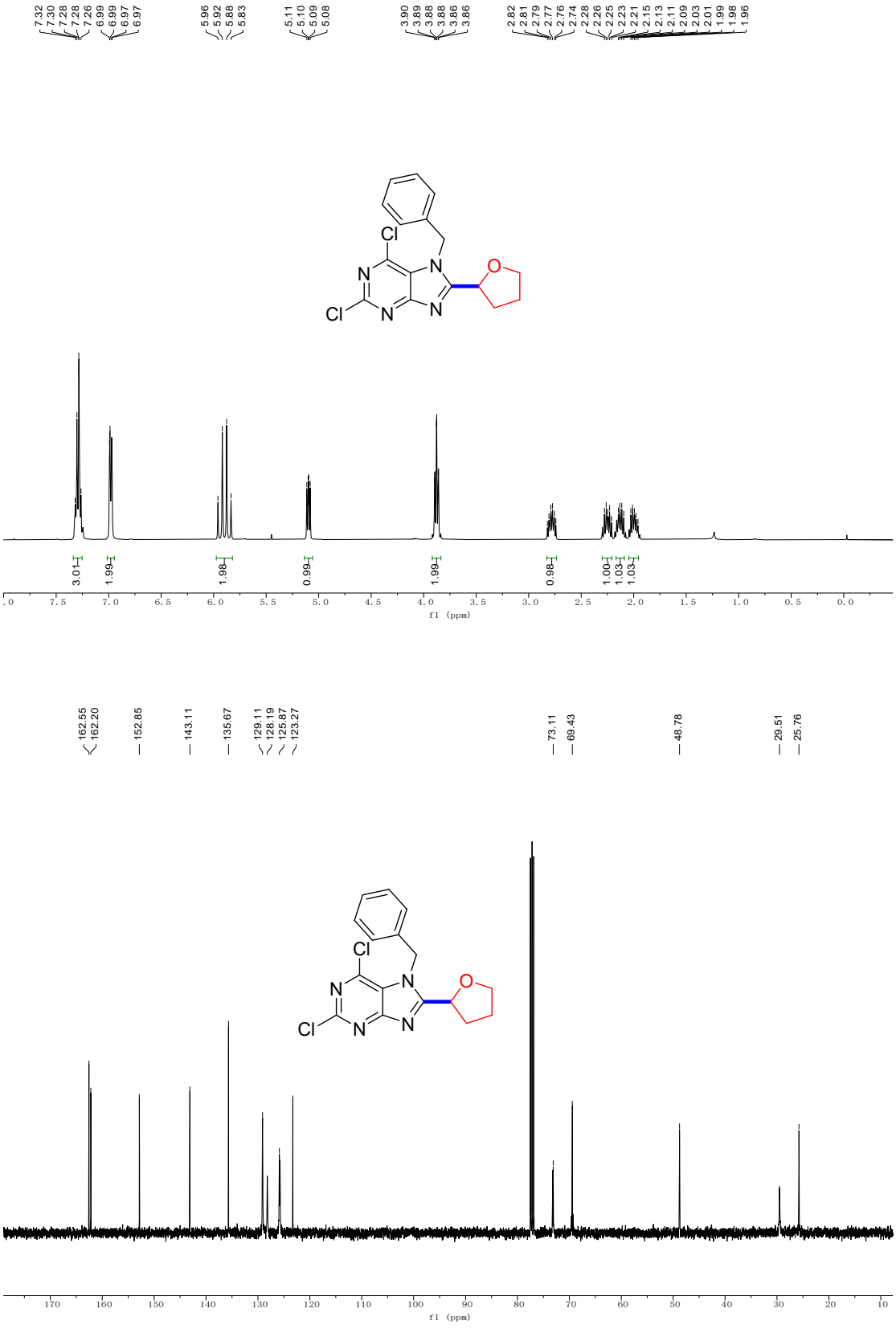
3o [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



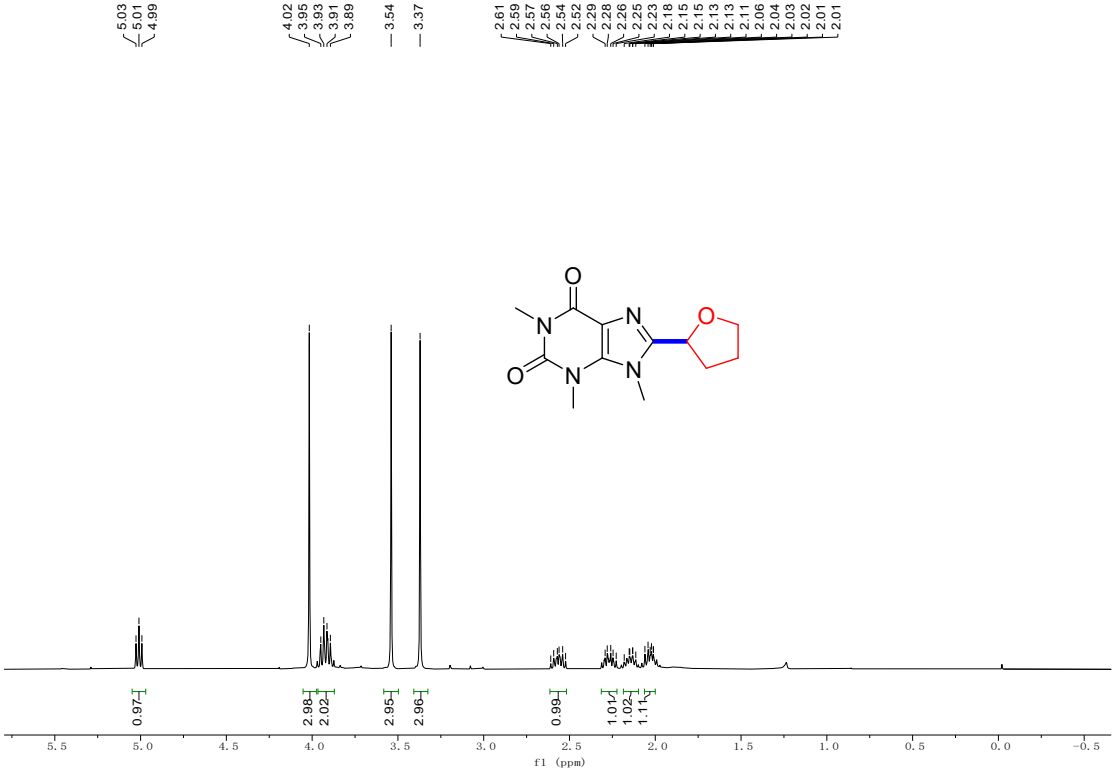


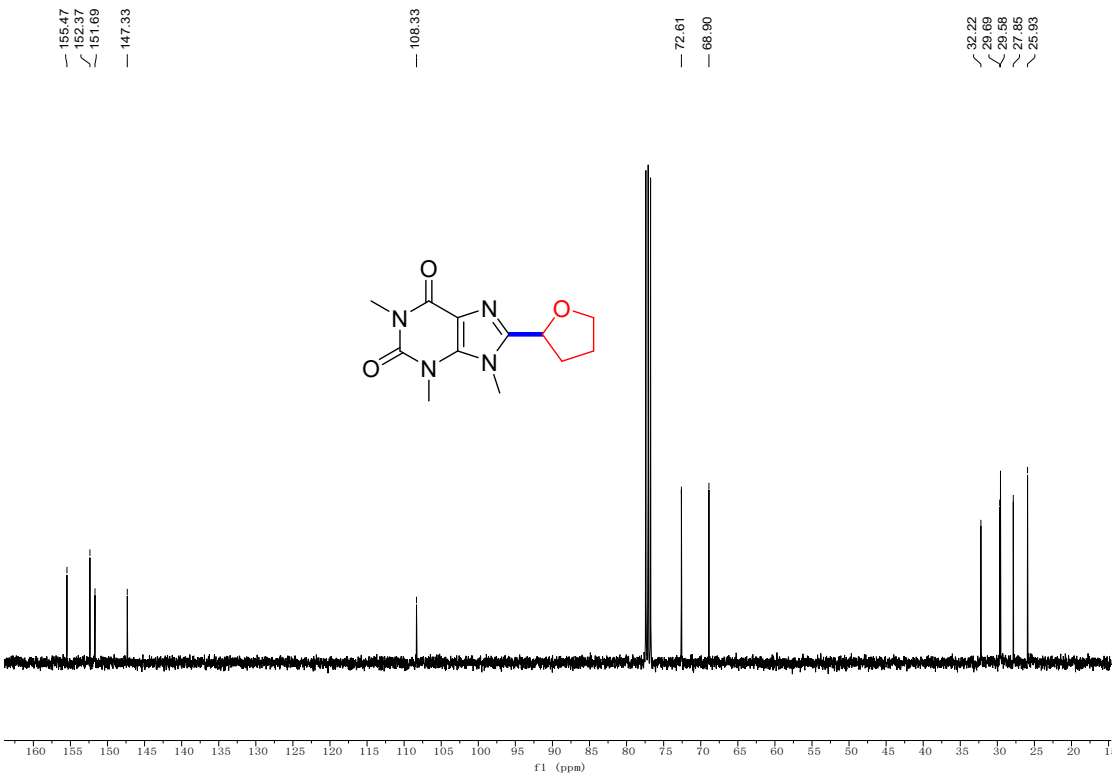


3p [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

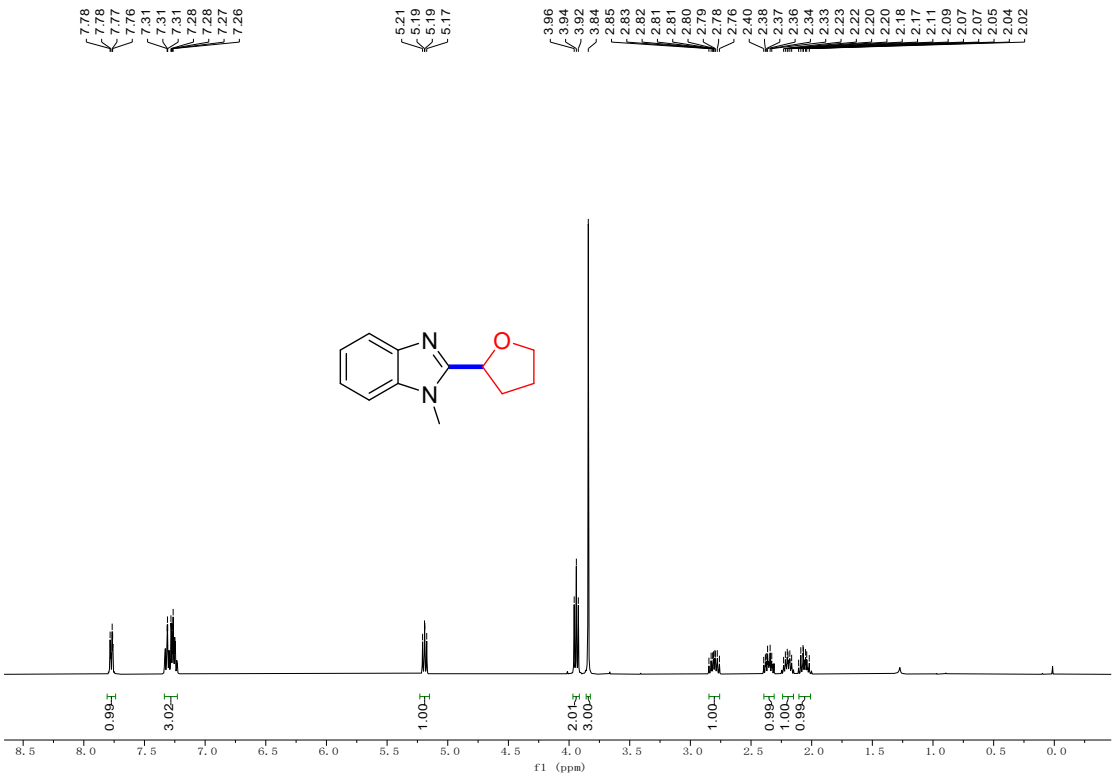


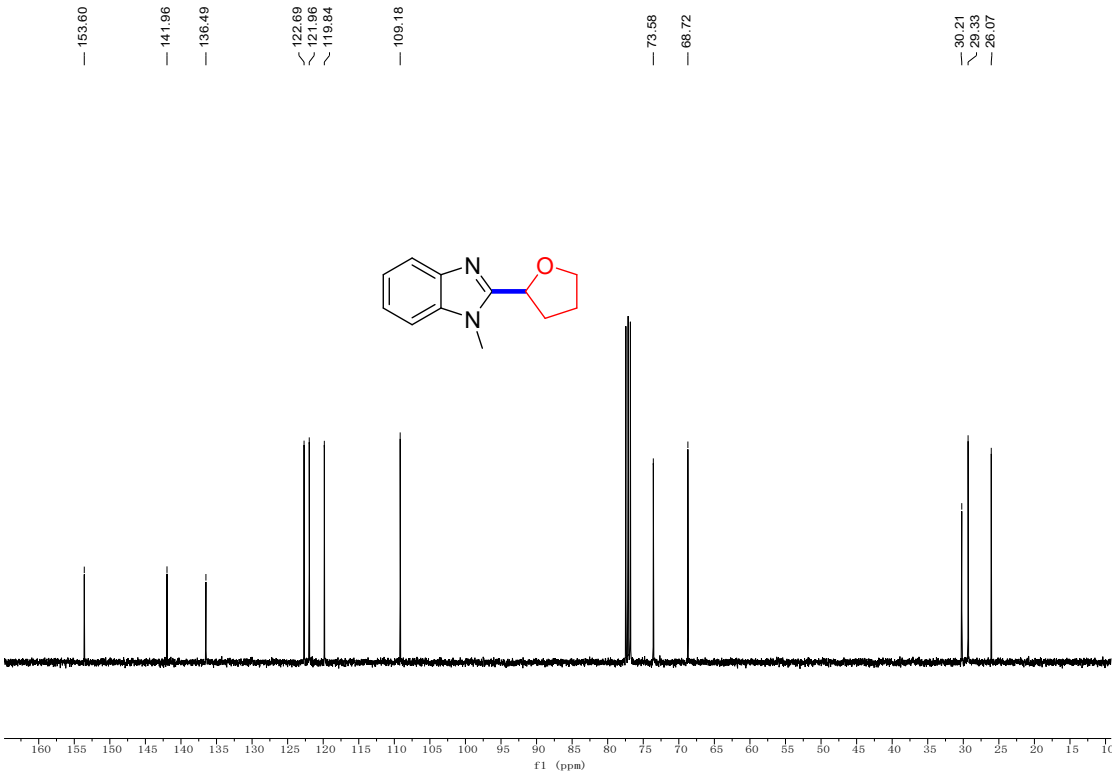
3q [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



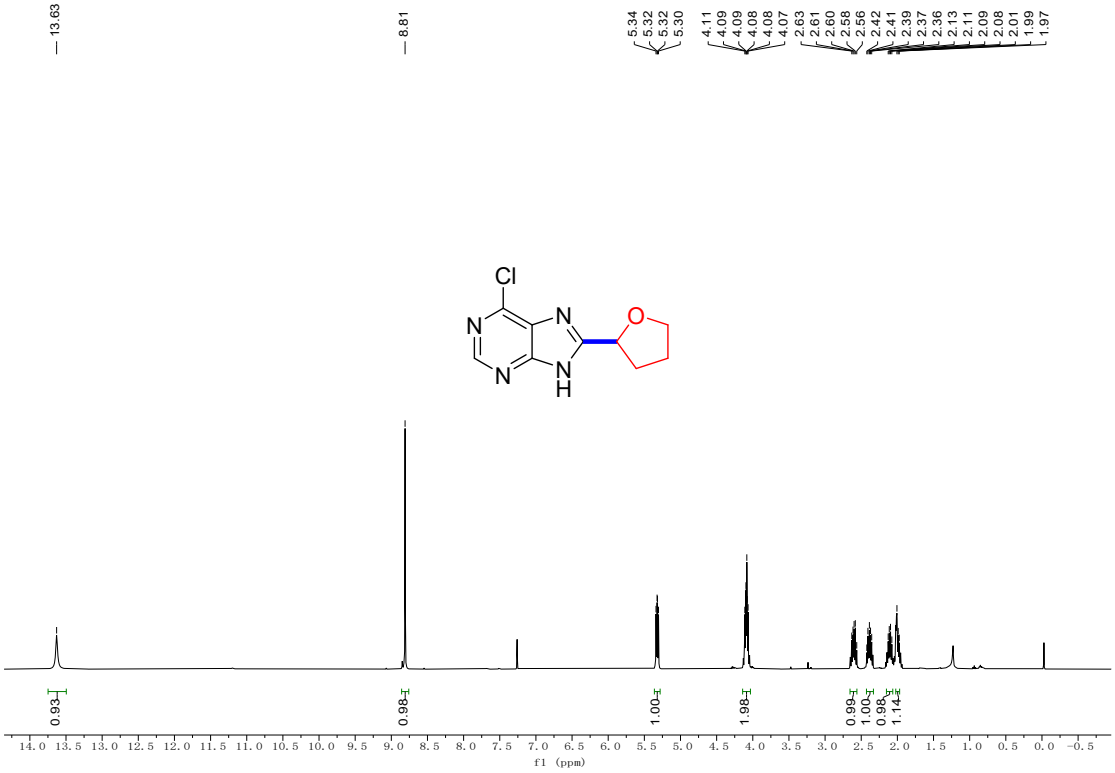


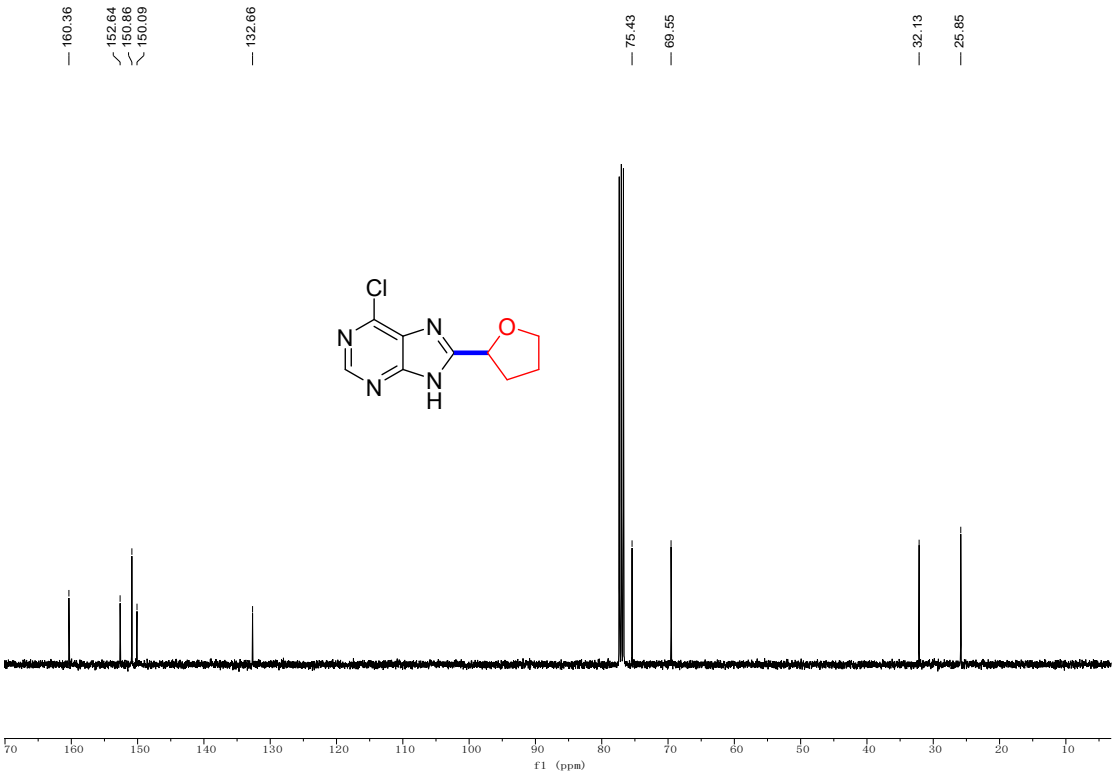
3r [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



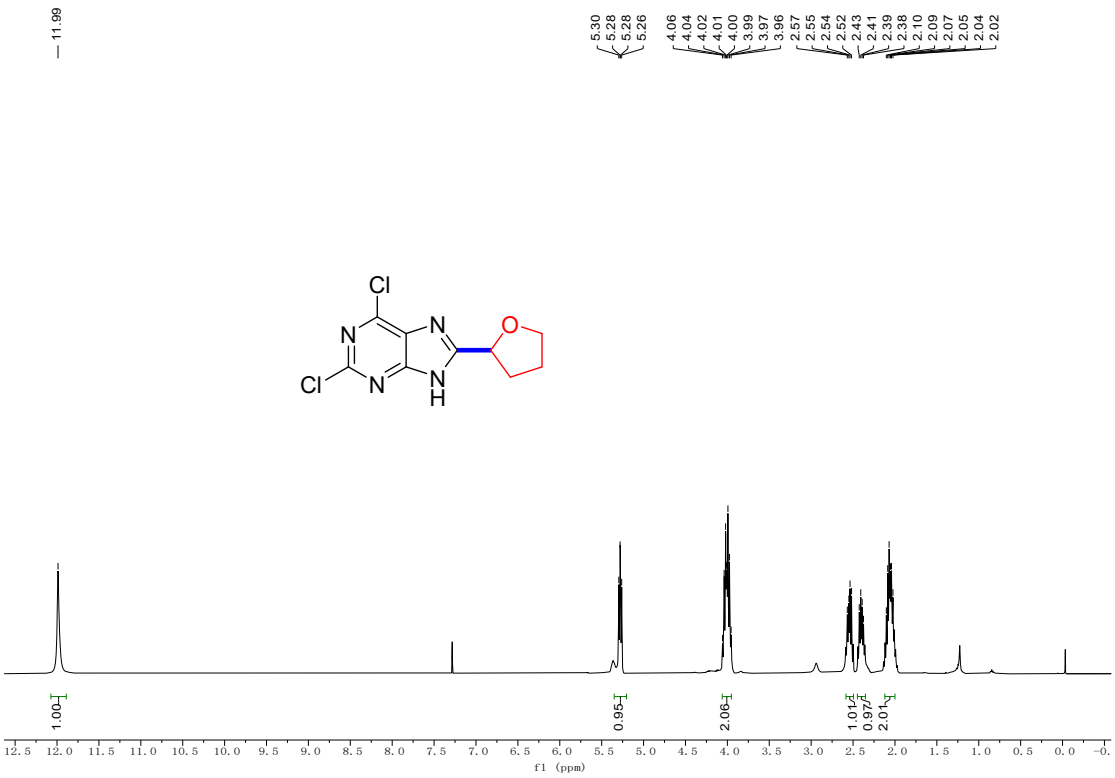


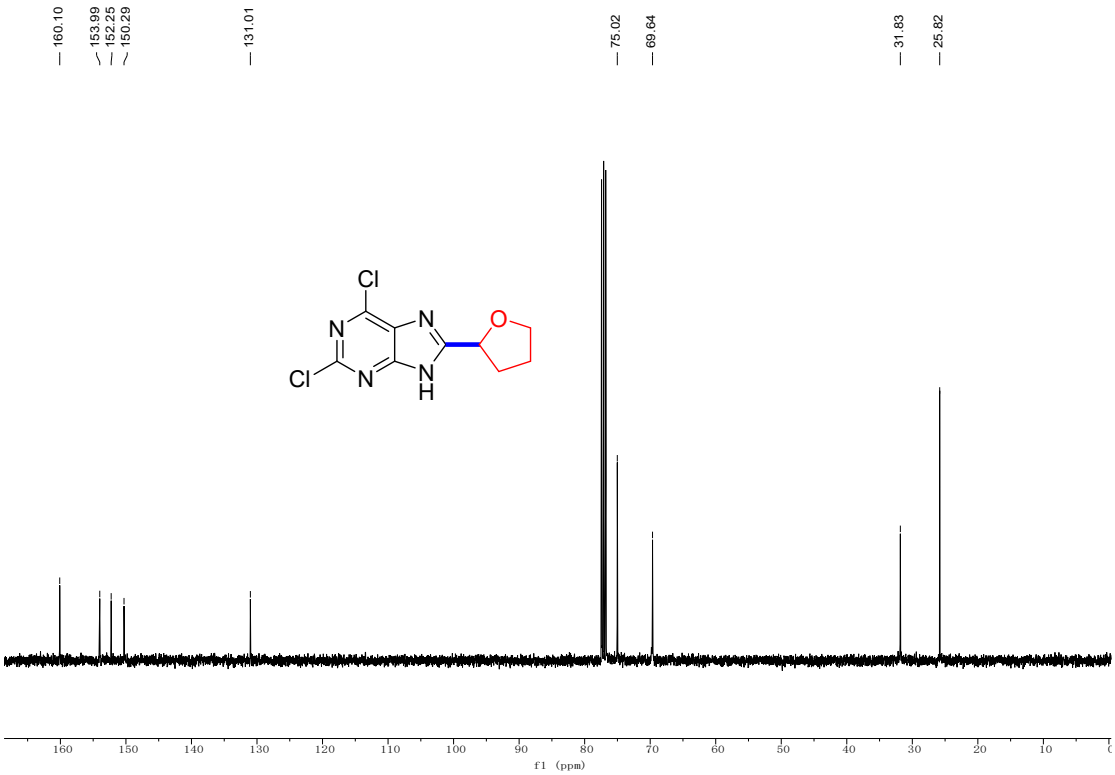
4a [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



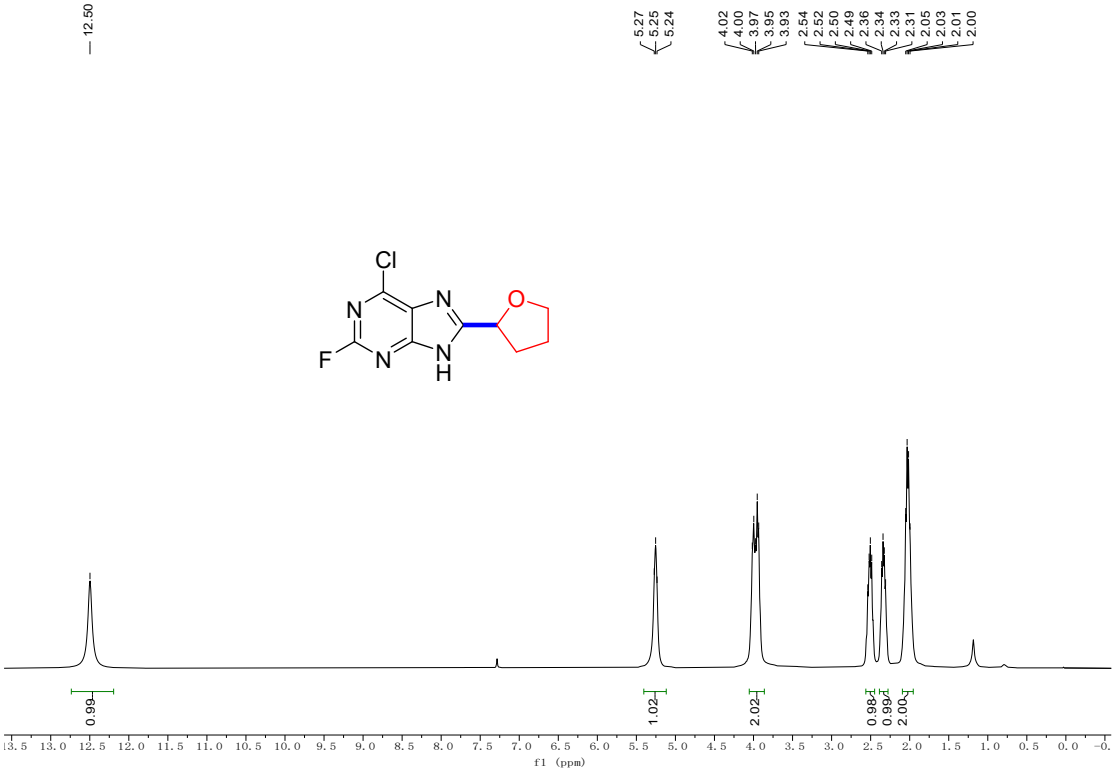


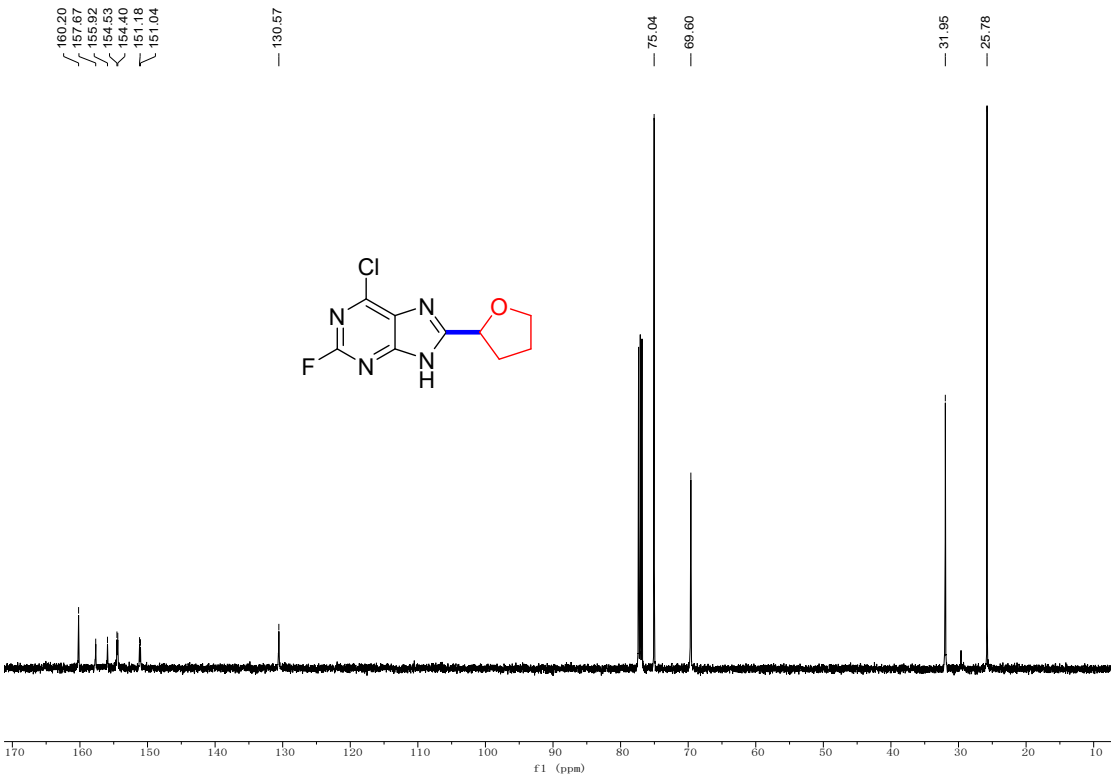
4b [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

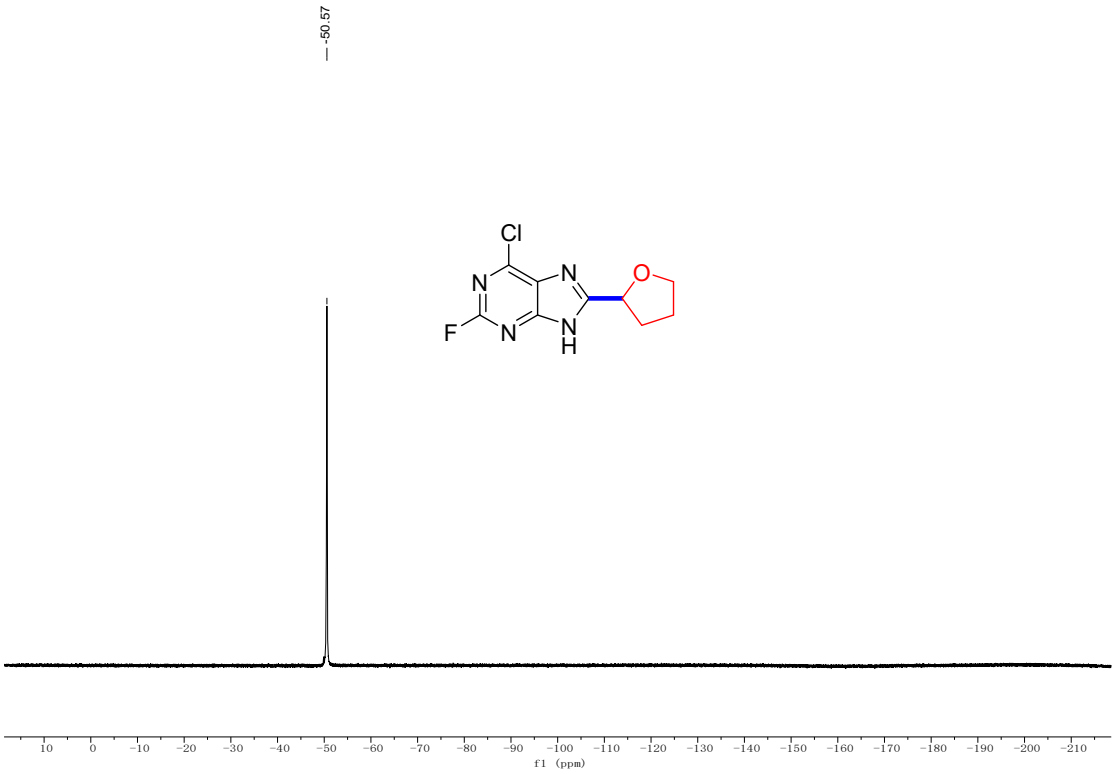




4c [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$), ^{19}F NMR (376 MHz, $CDCl_3$)]






-50.57
Cl
N
N
O
F
N
N
H
10
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−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
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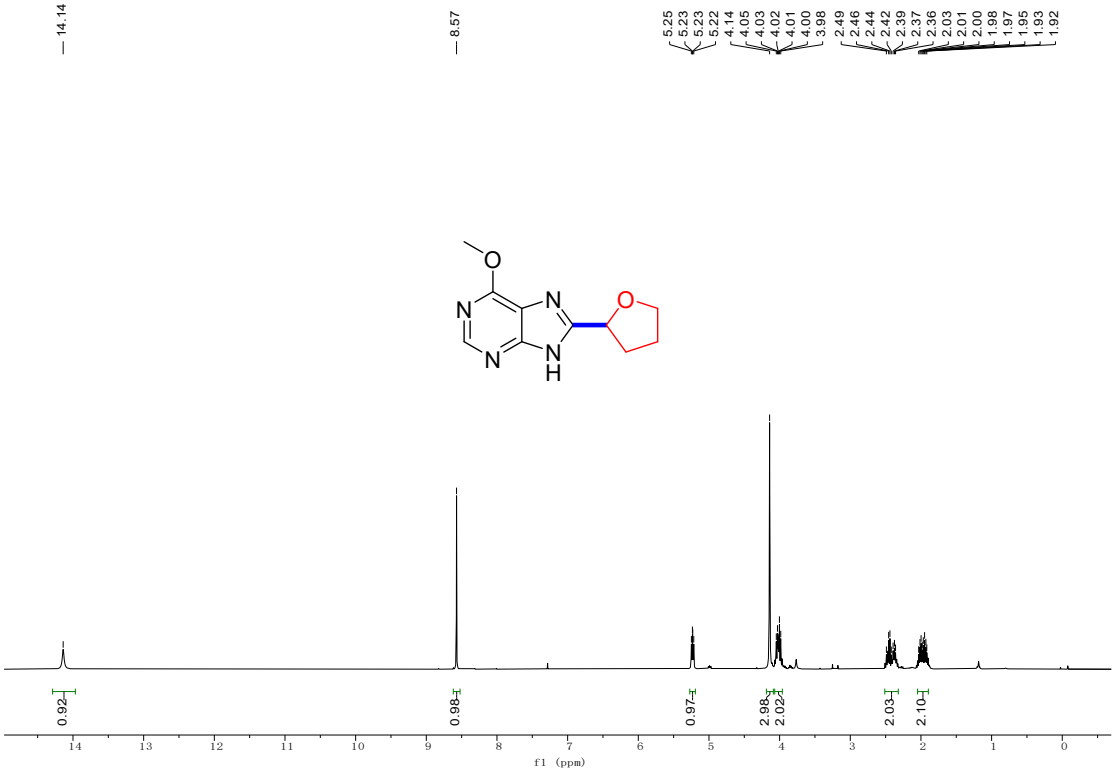
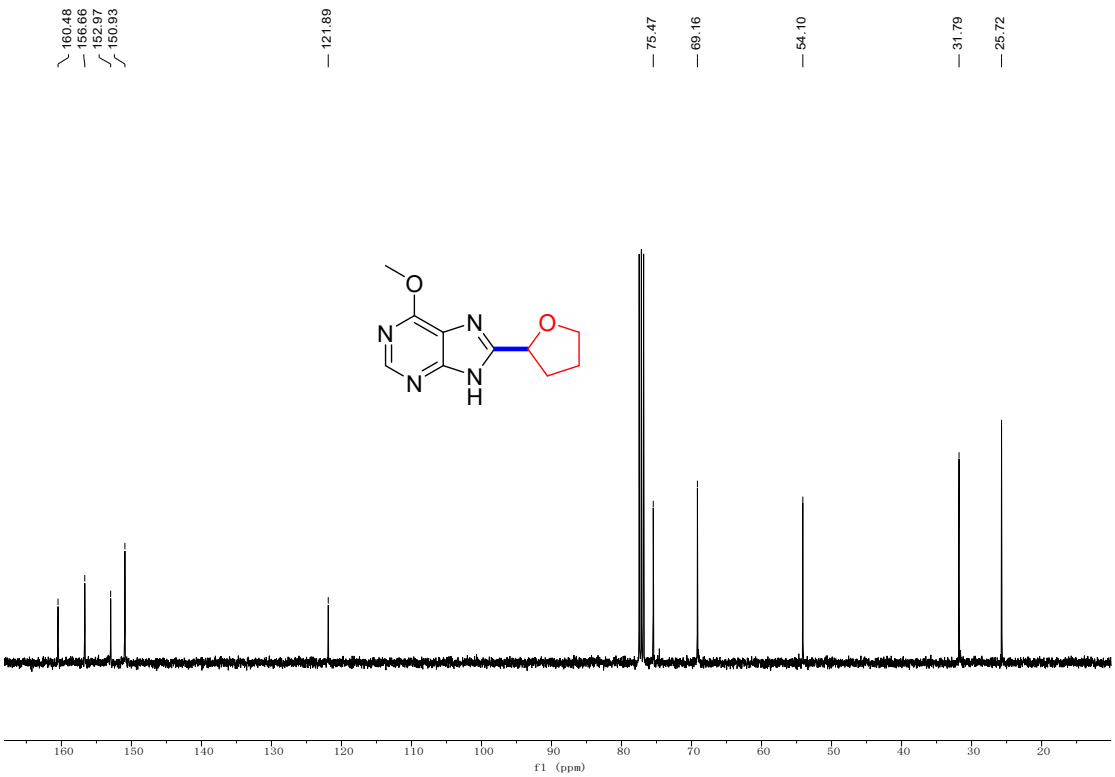
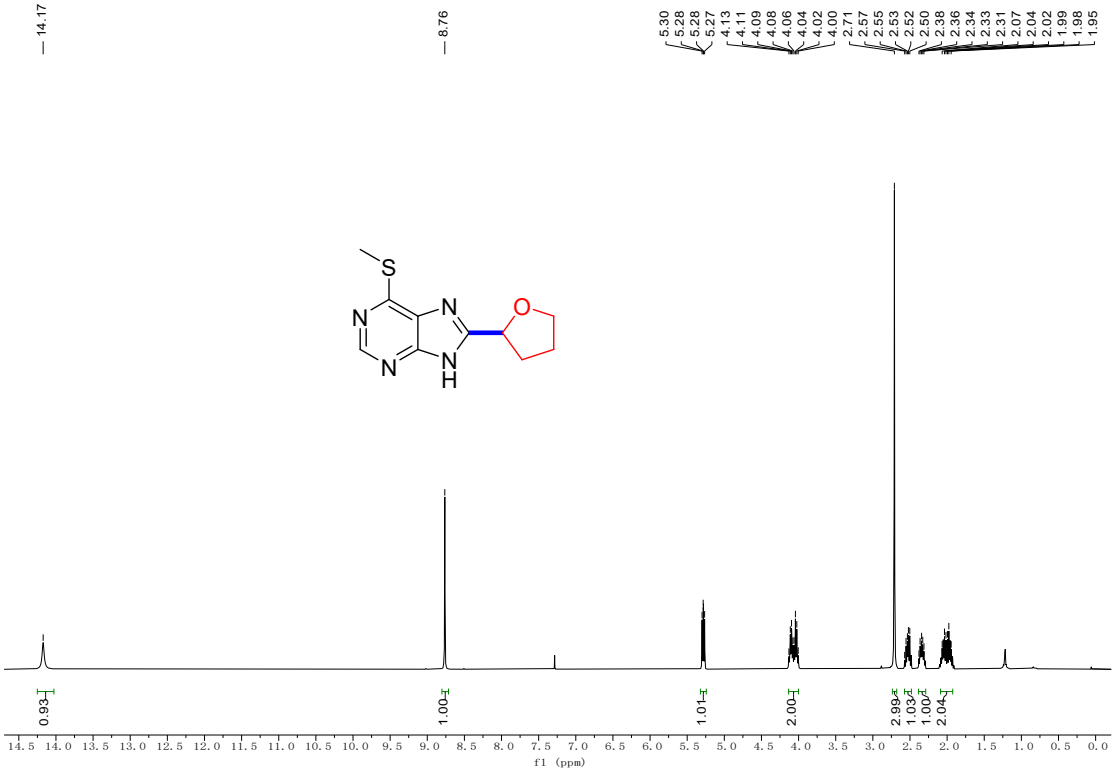
f1 (ppm)

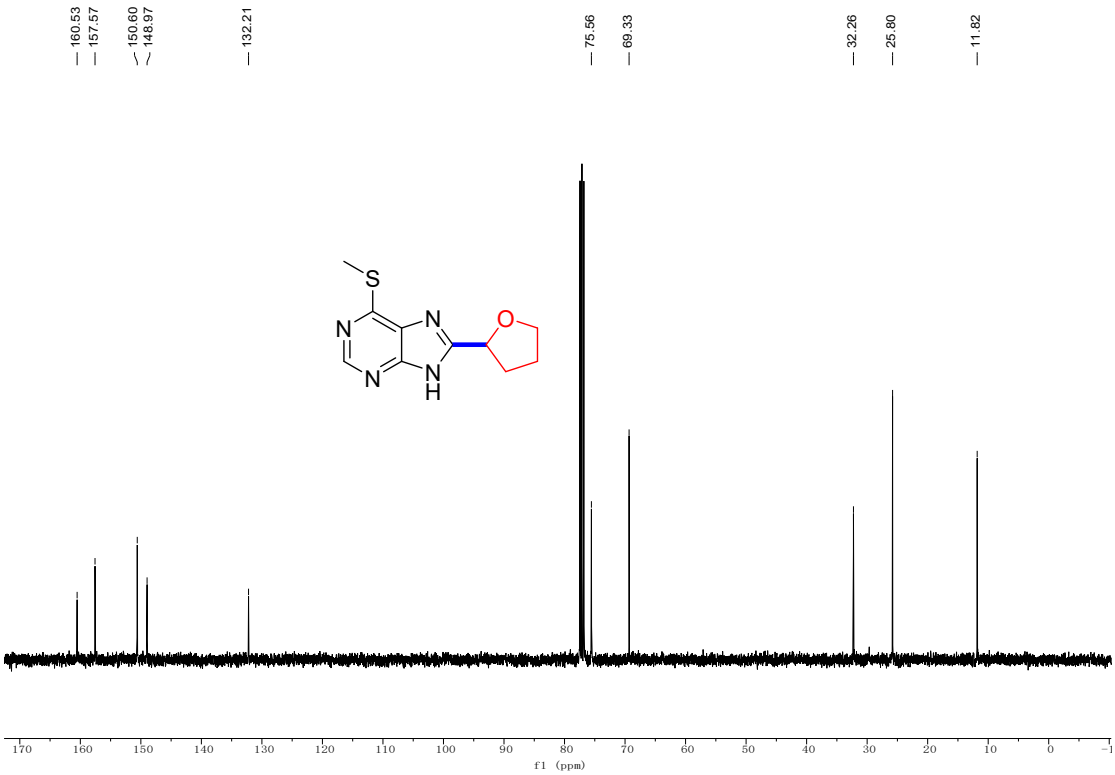
4d [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



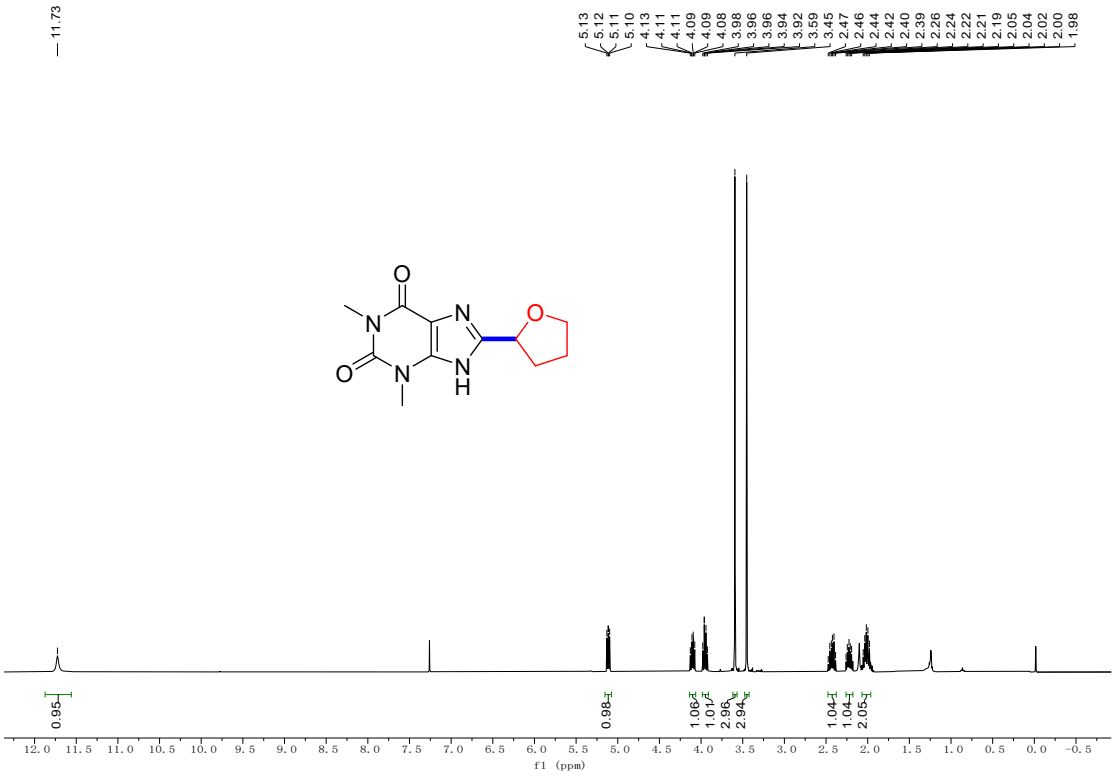


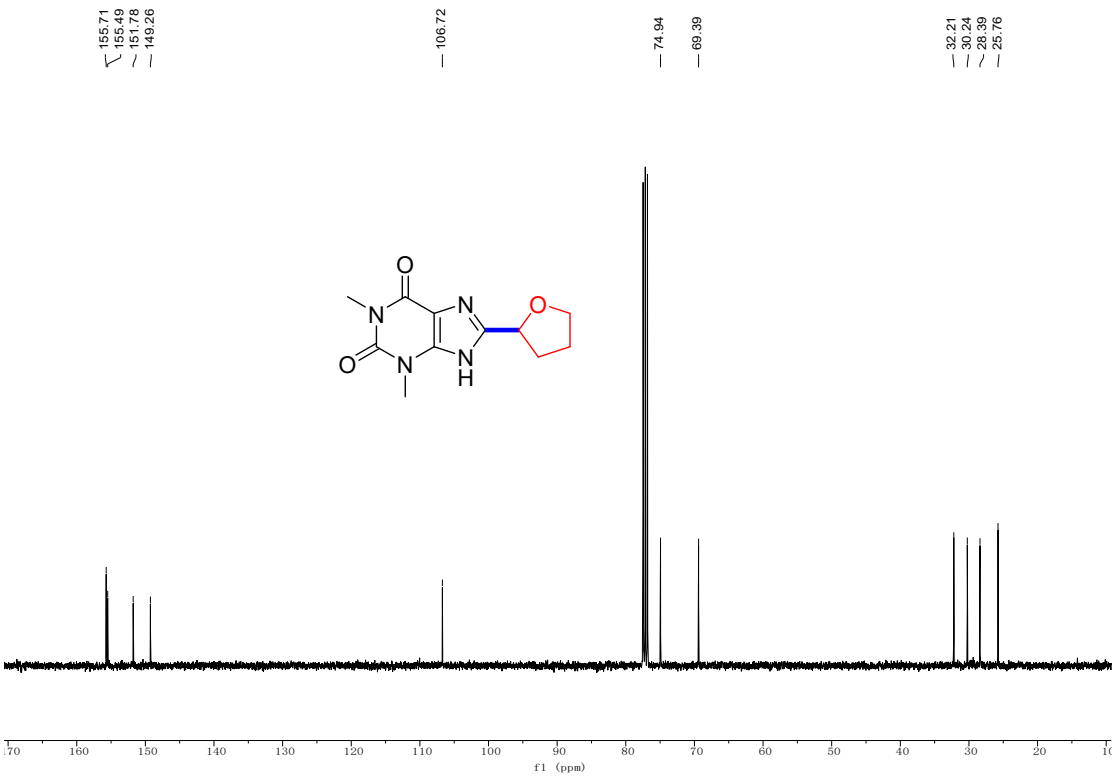
4e [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



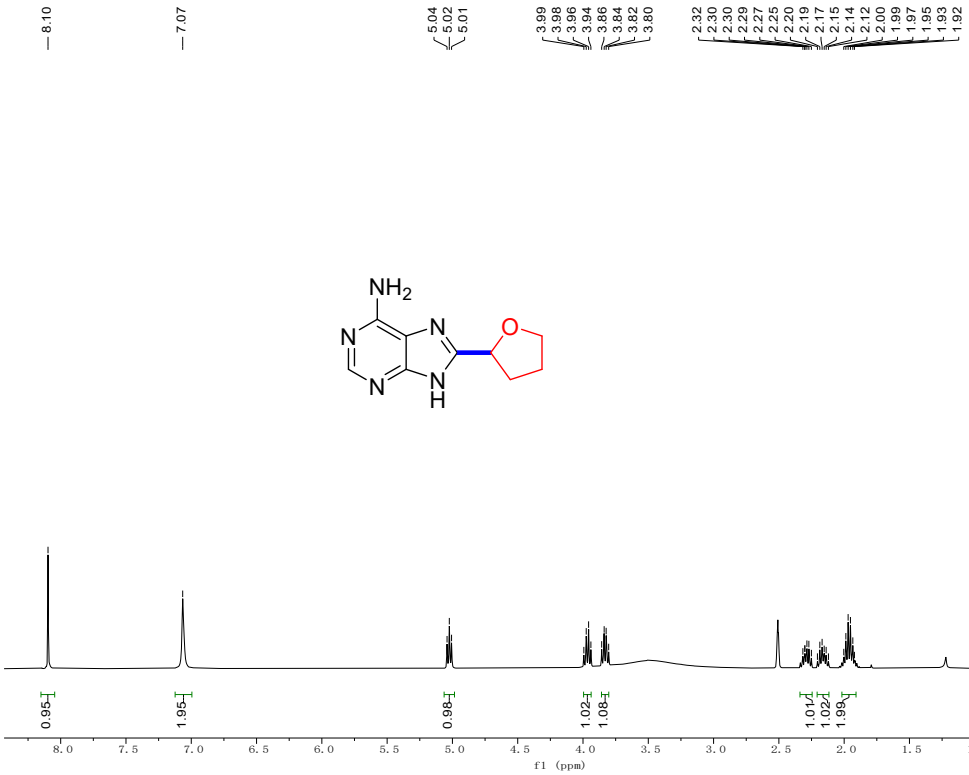


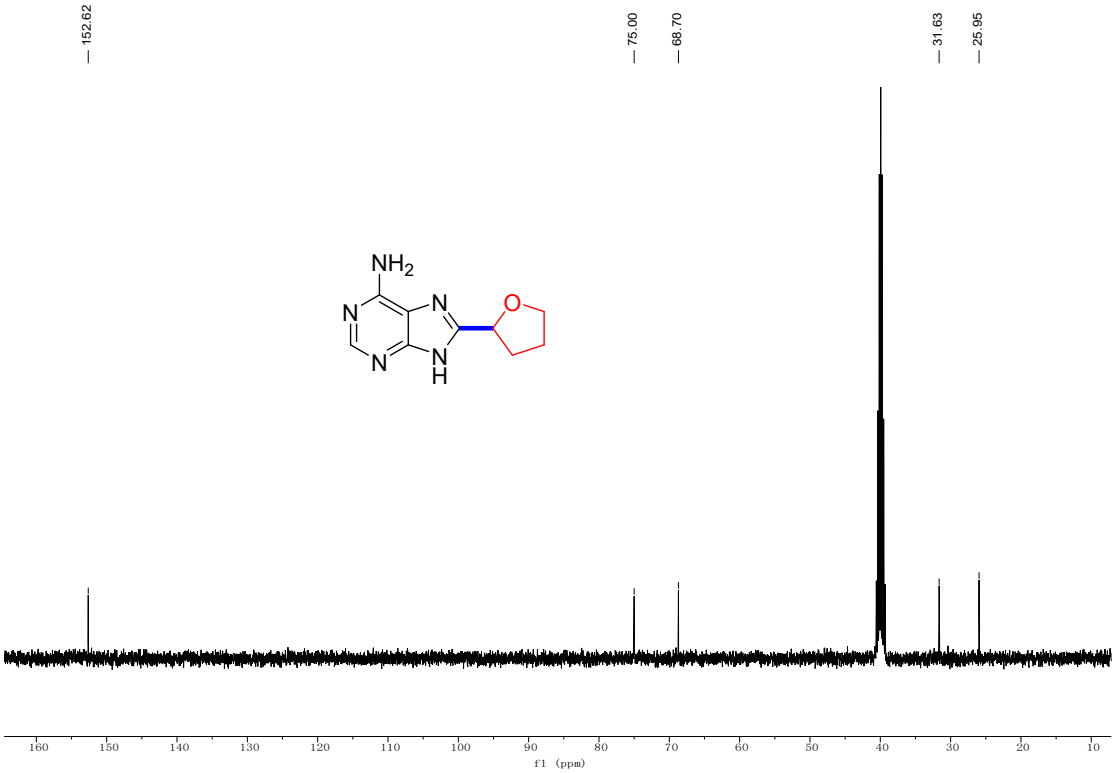
4f [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



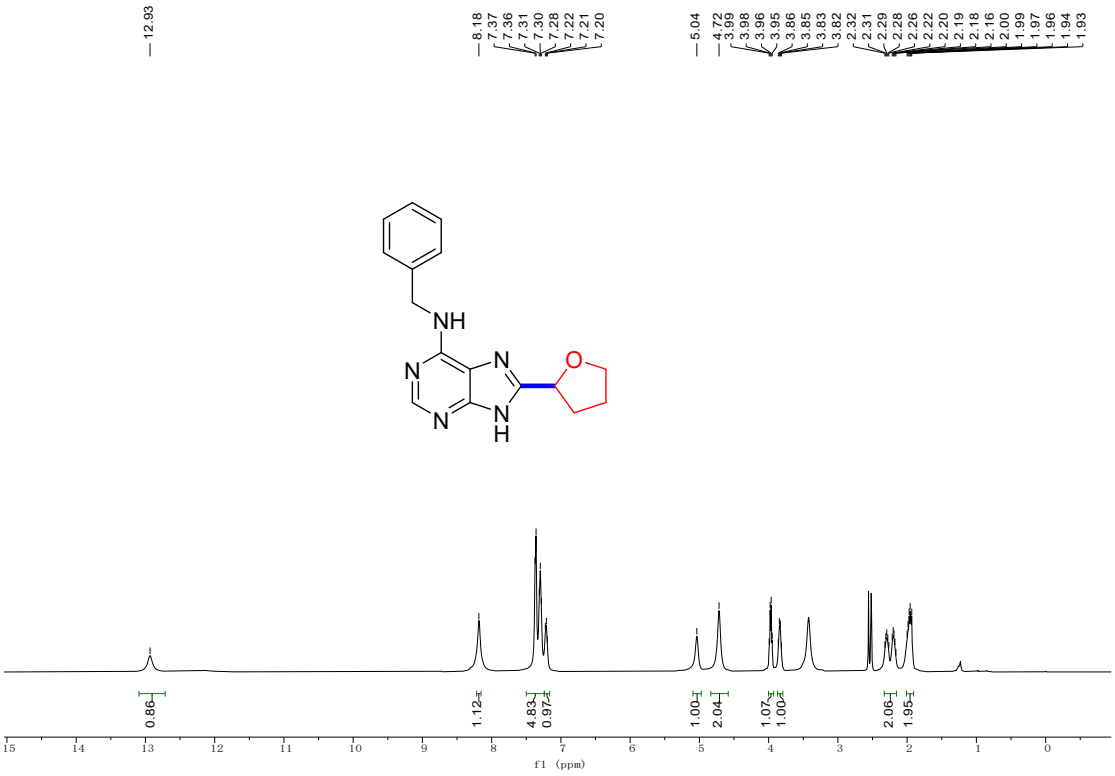


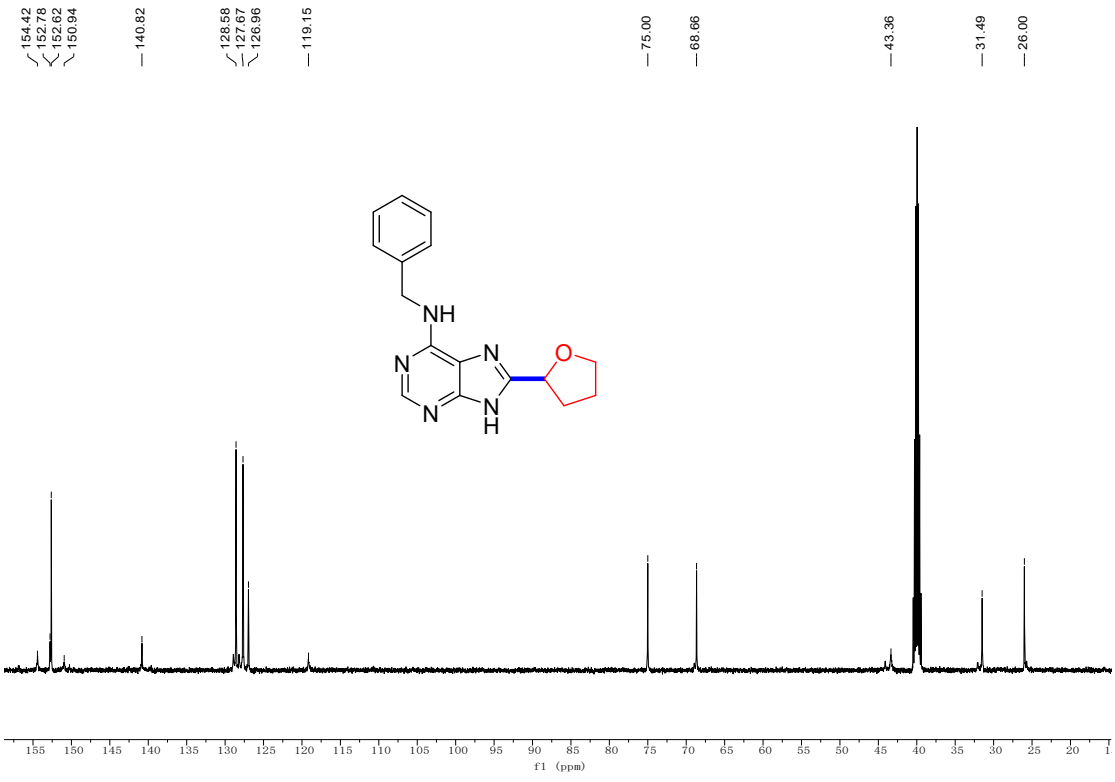
4g [^{1}H NMR (400 MHz, DMSO-d_6), ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6)]



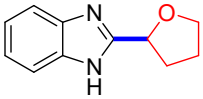


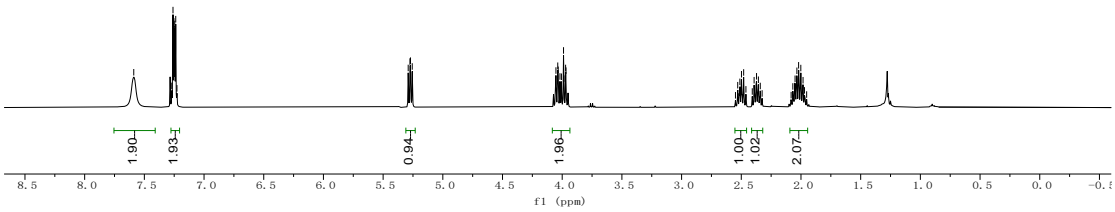
4h [^{1}H NMR (500 MHz, DMSO-d_6), ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6)]

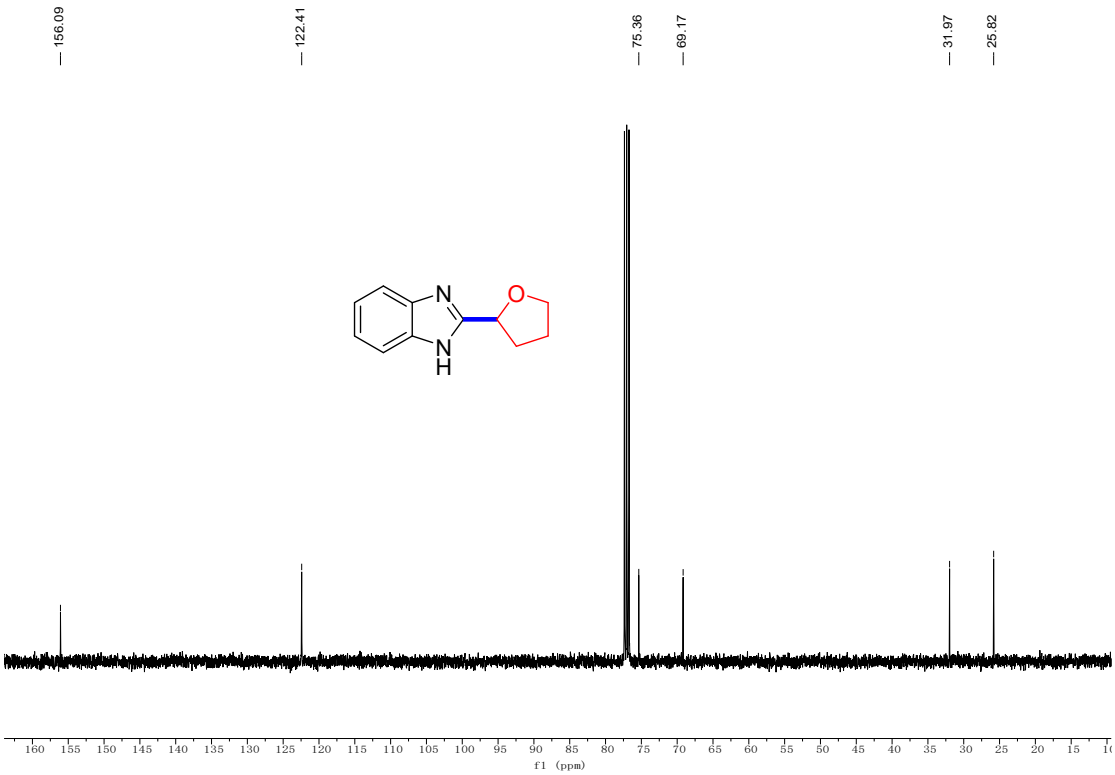




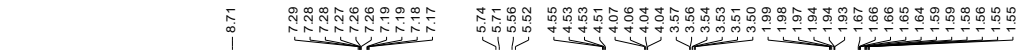
4i [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

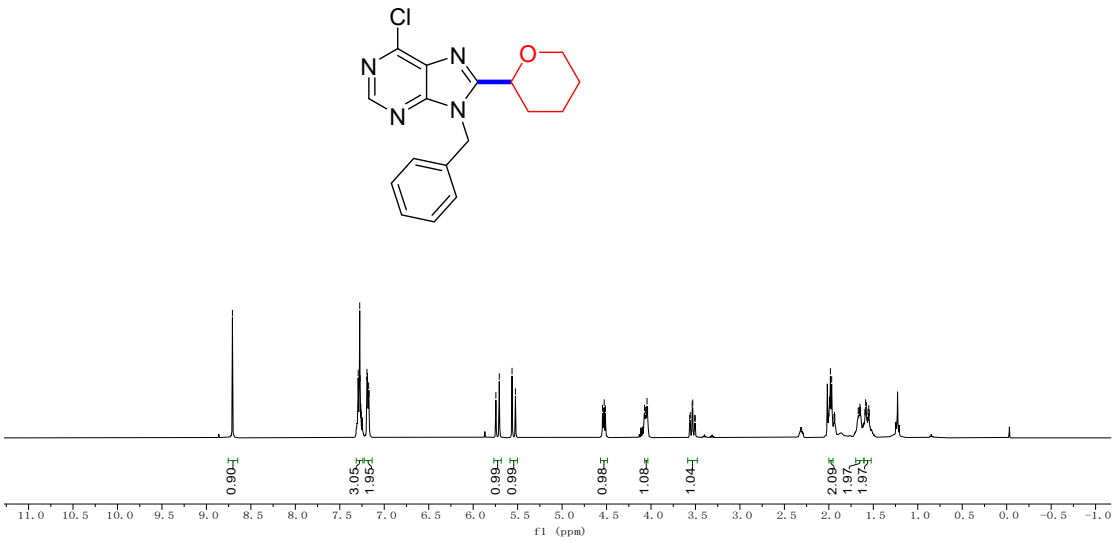


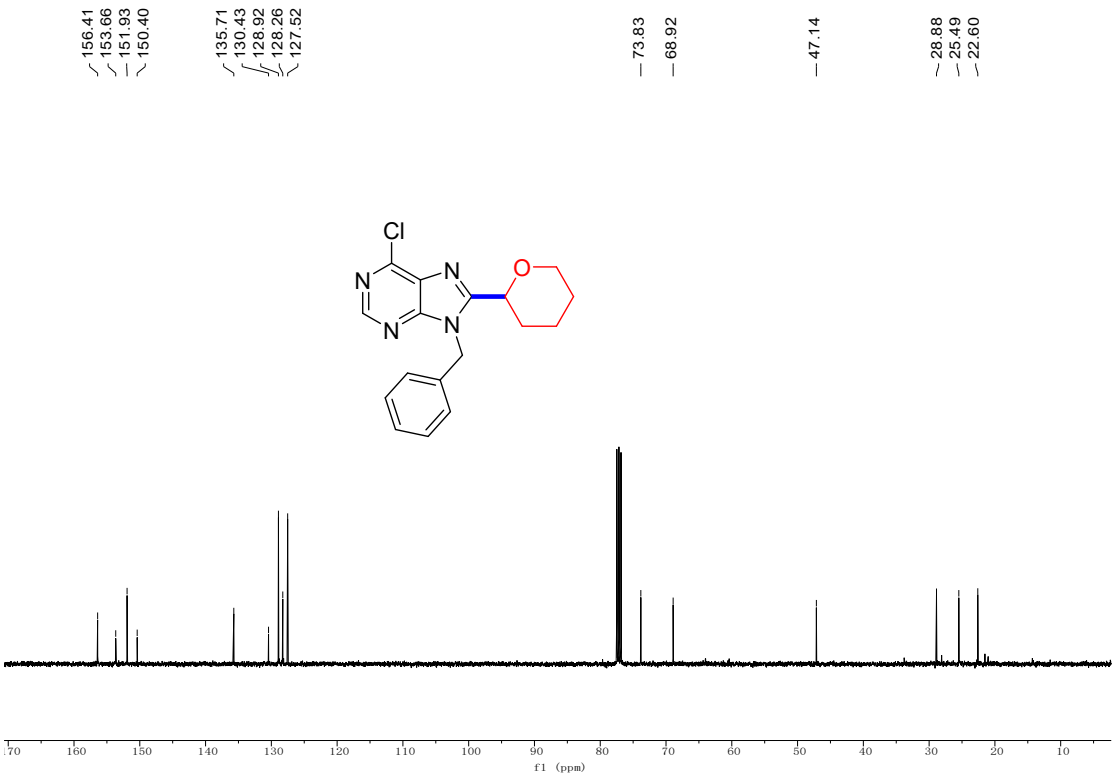




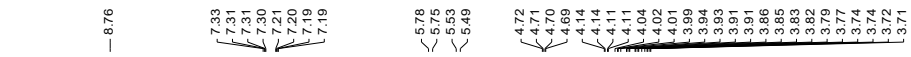
5a [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

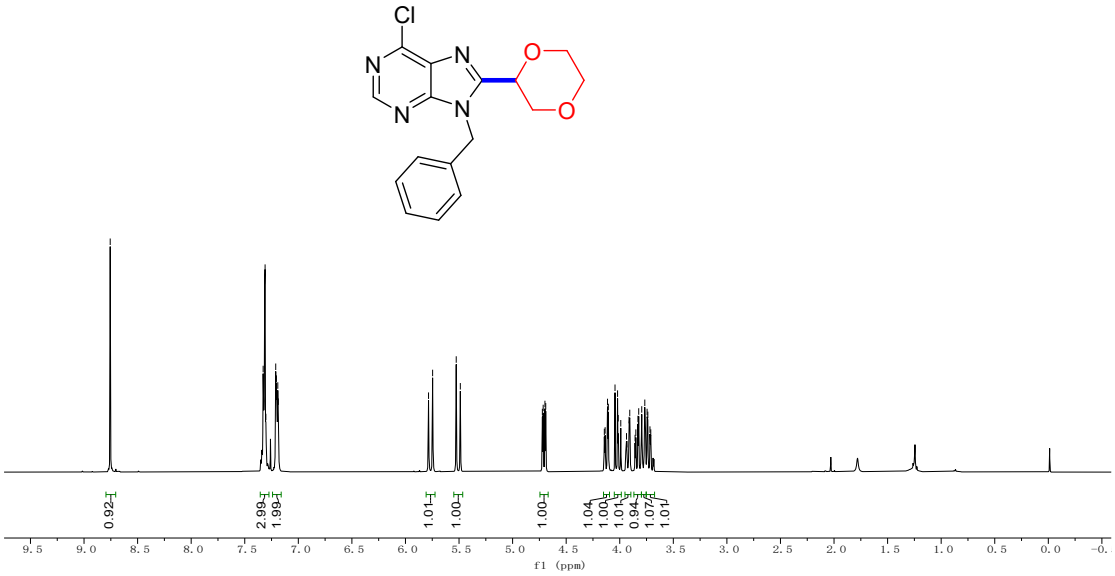


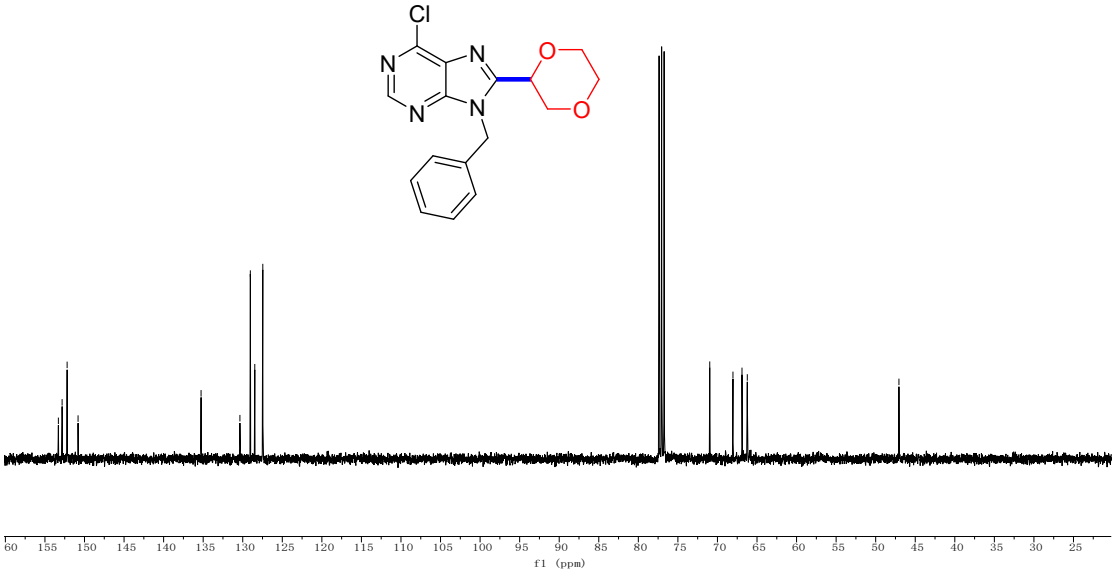




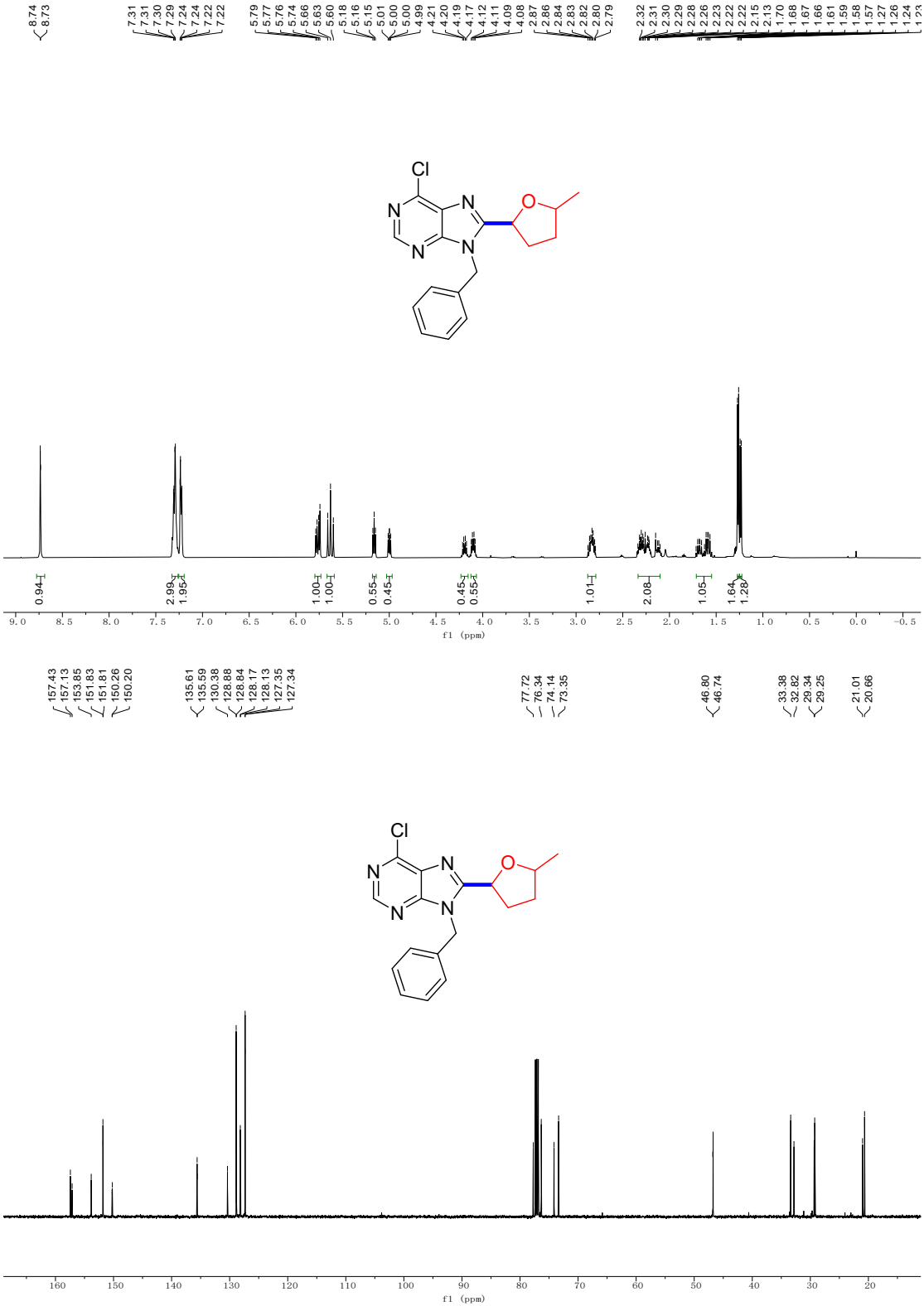
5b [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



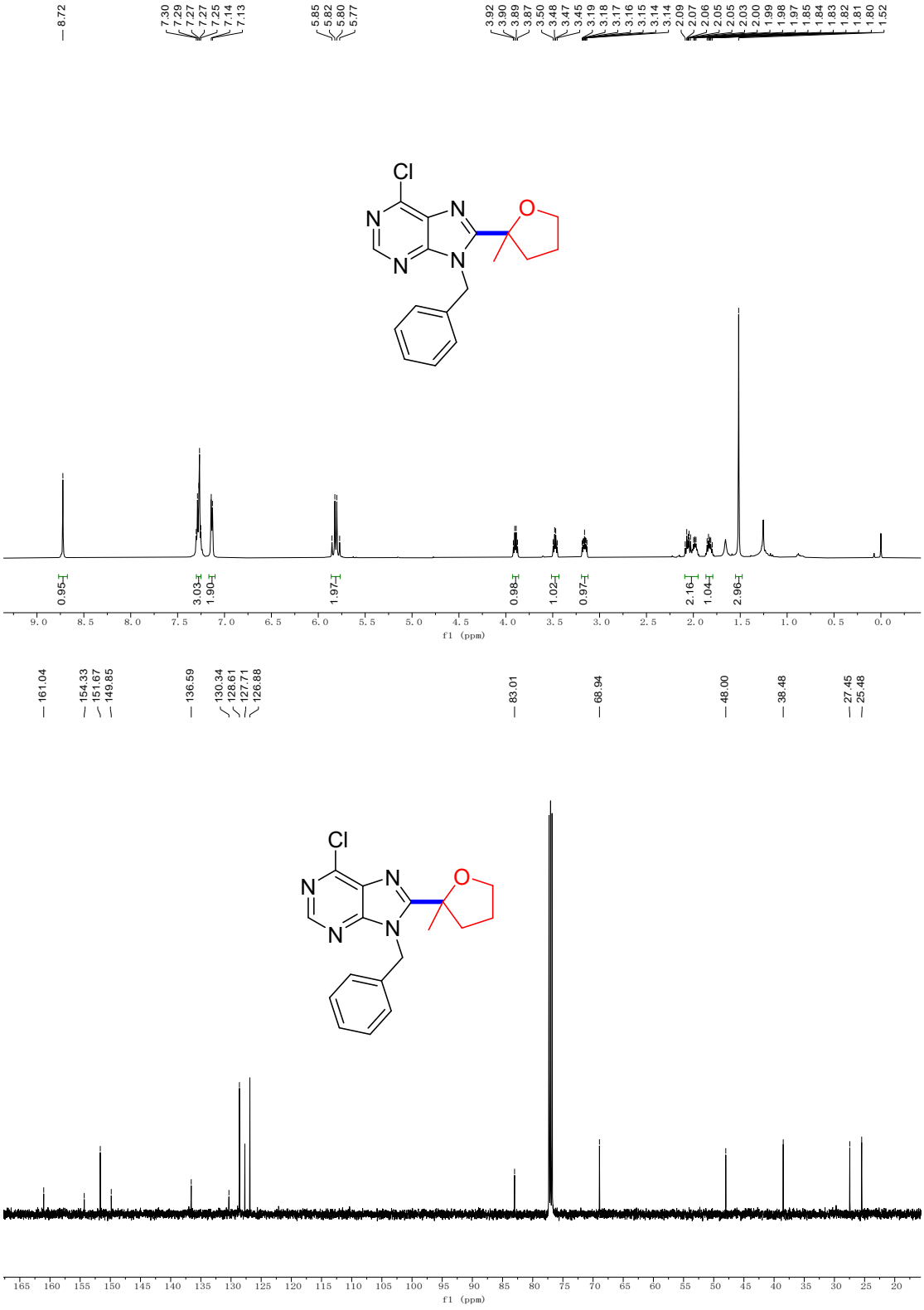




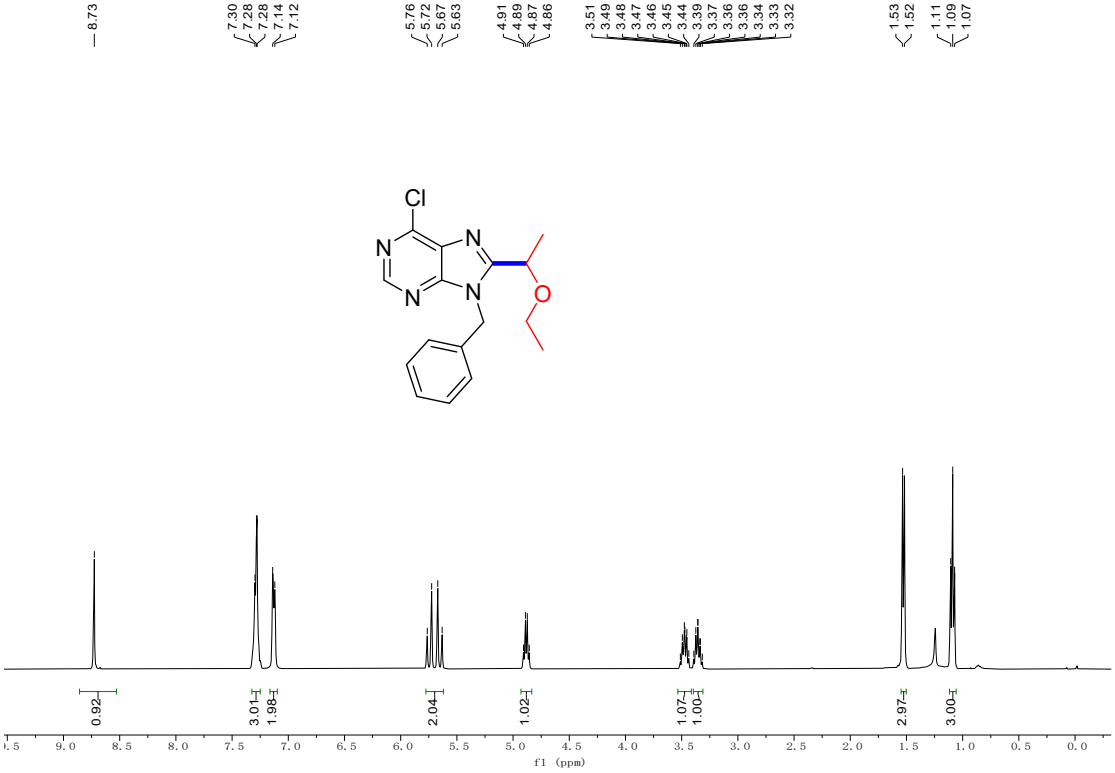
5c [^{1}H NMR (500 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)]

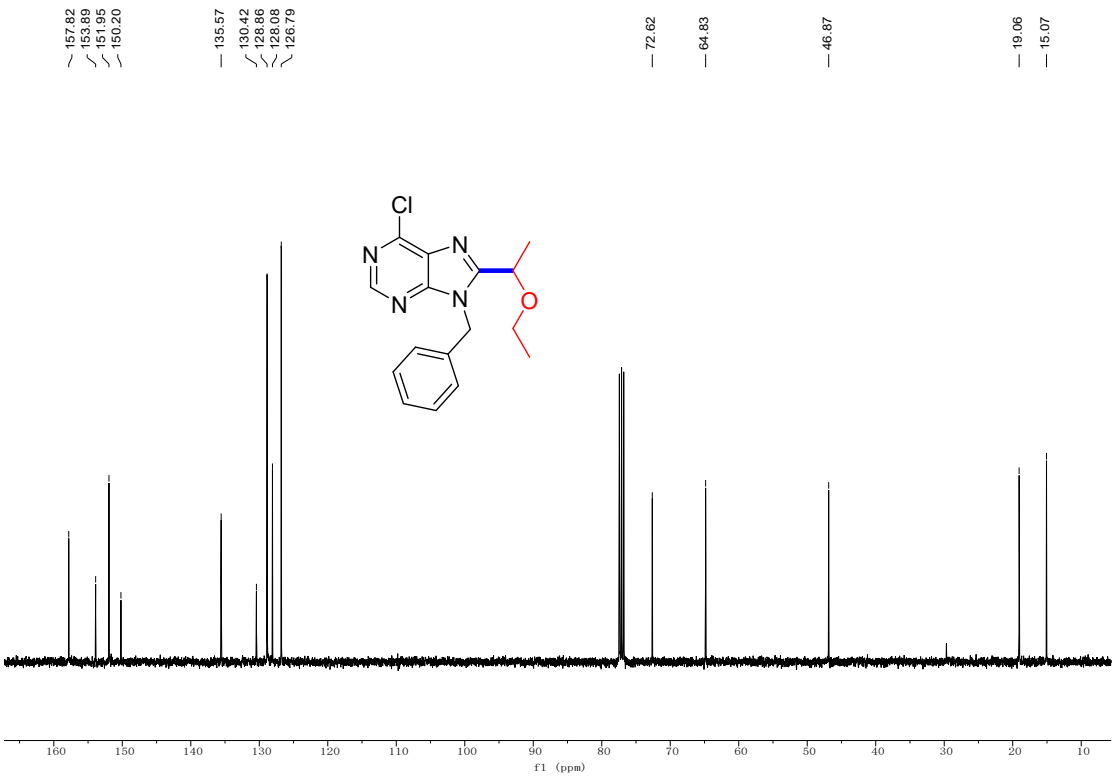


5c' [^{1}H NMR (500 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)]

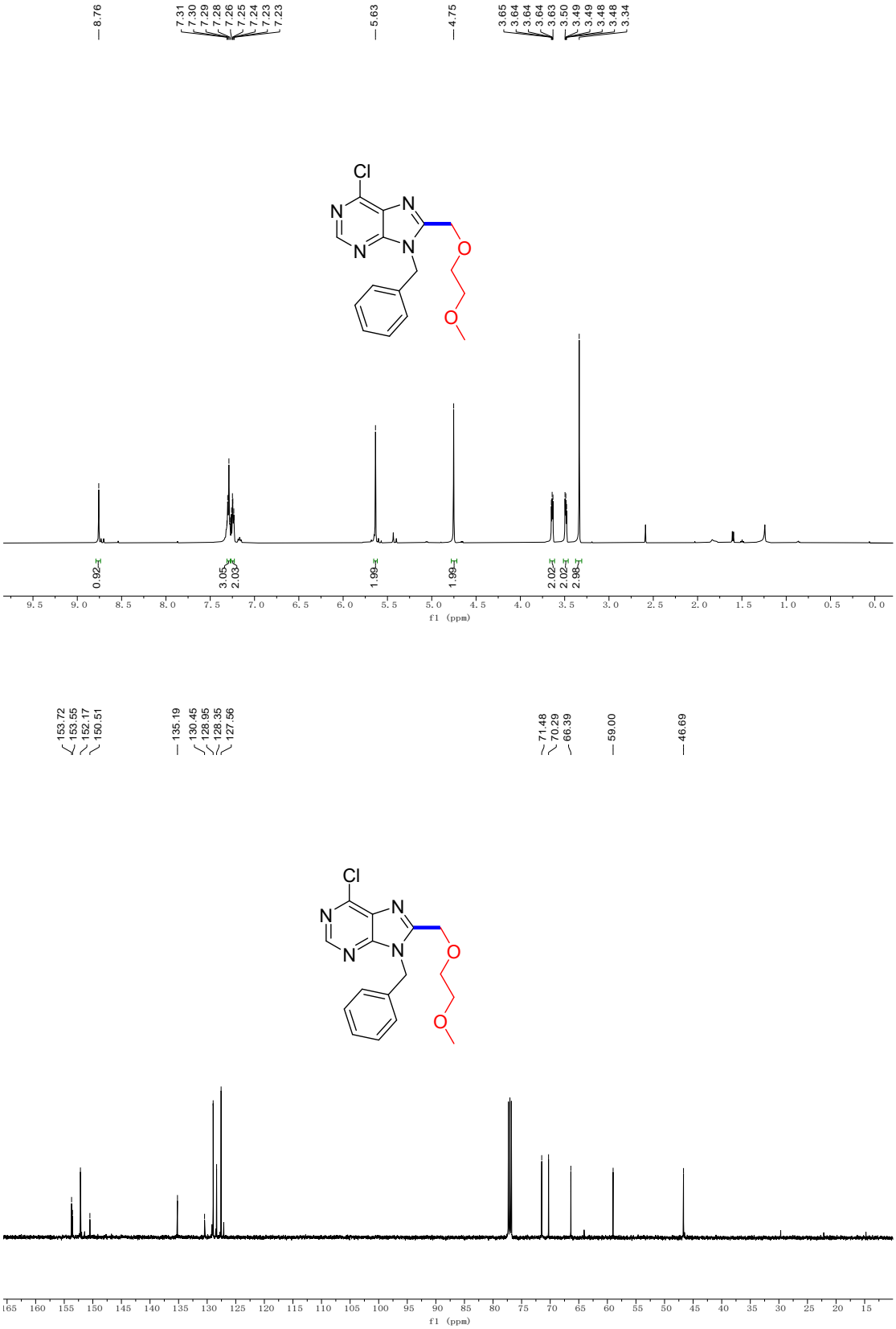


5d [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]

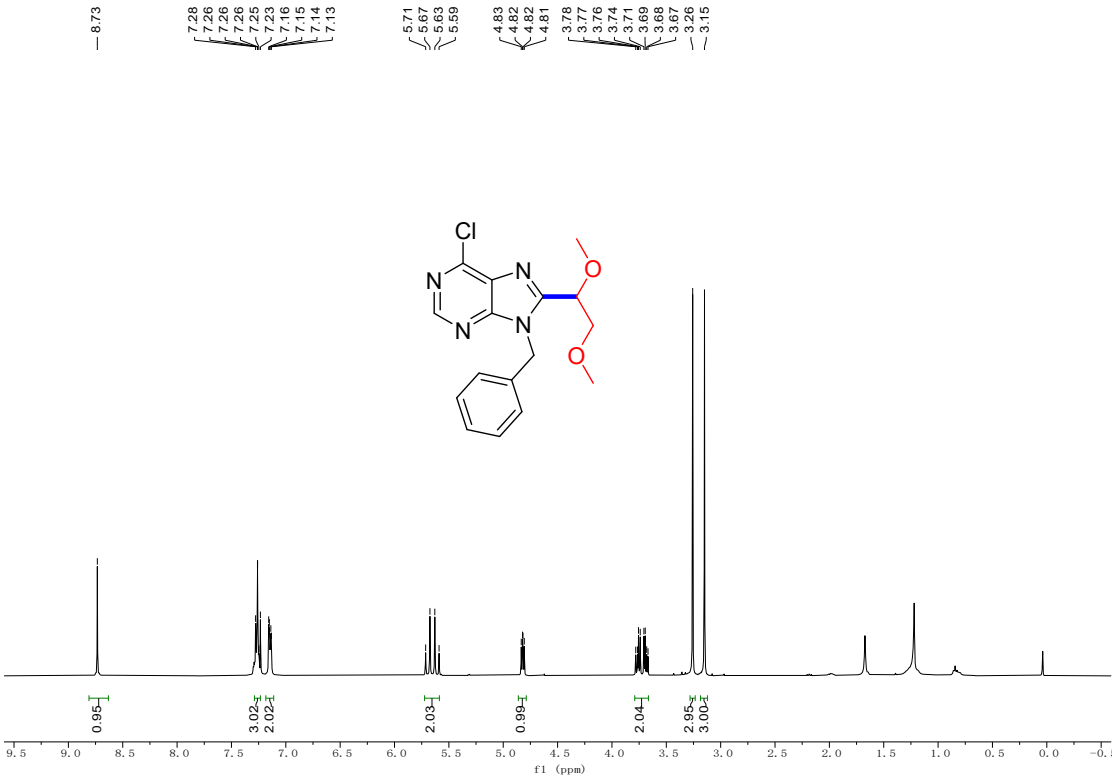


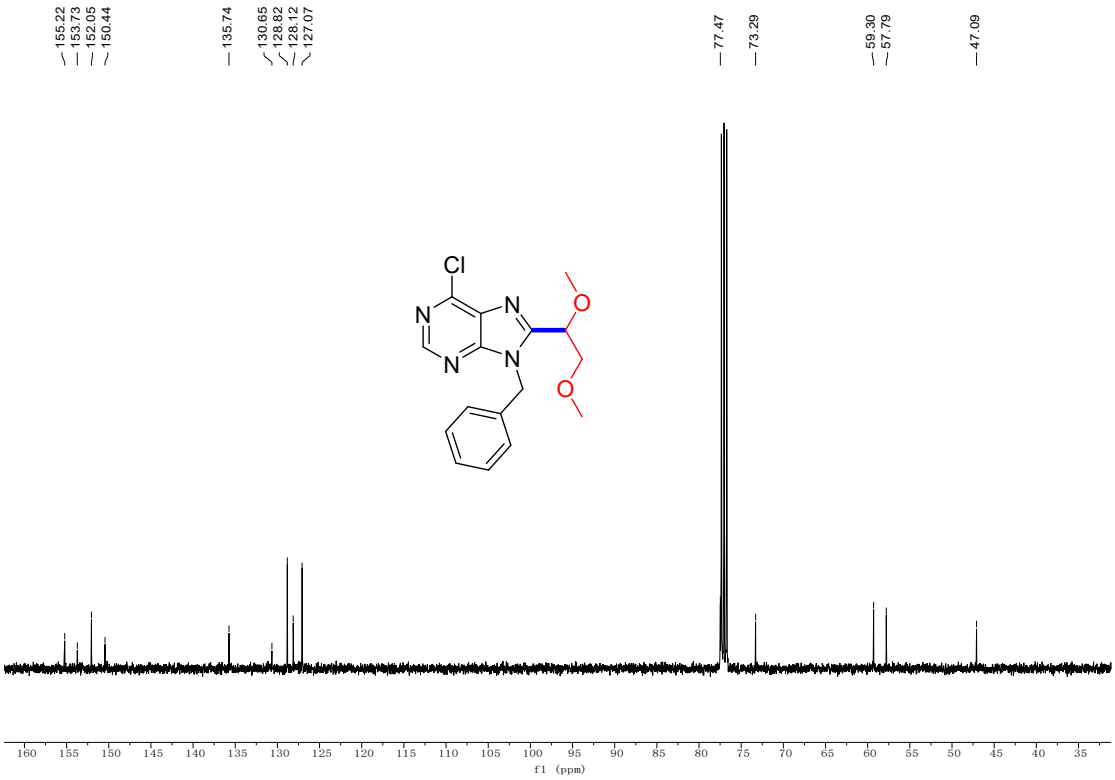


5e [^{1}H NMR (500 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)]

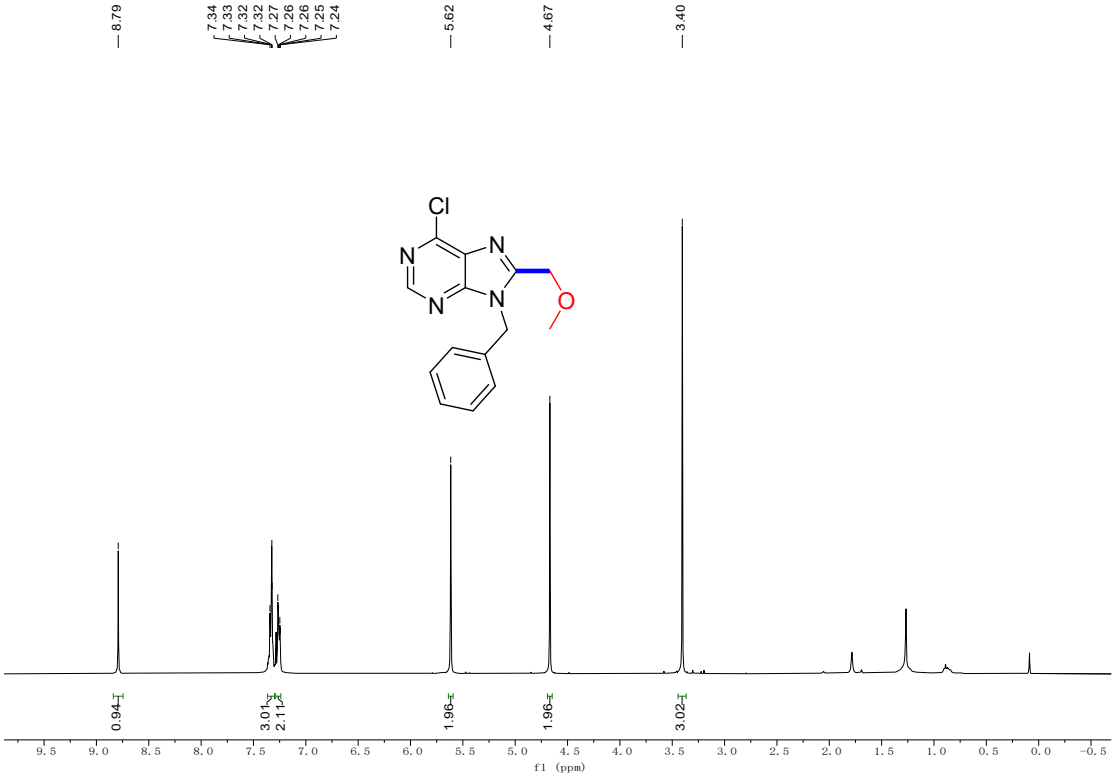


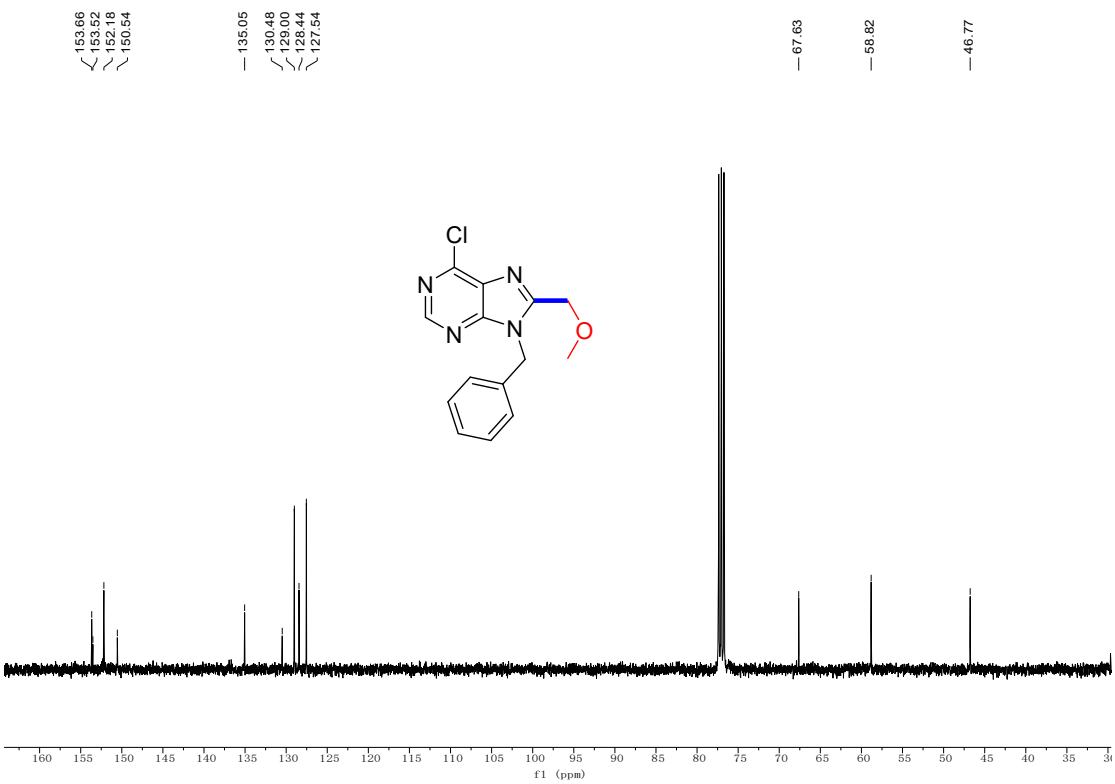
5e' [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]



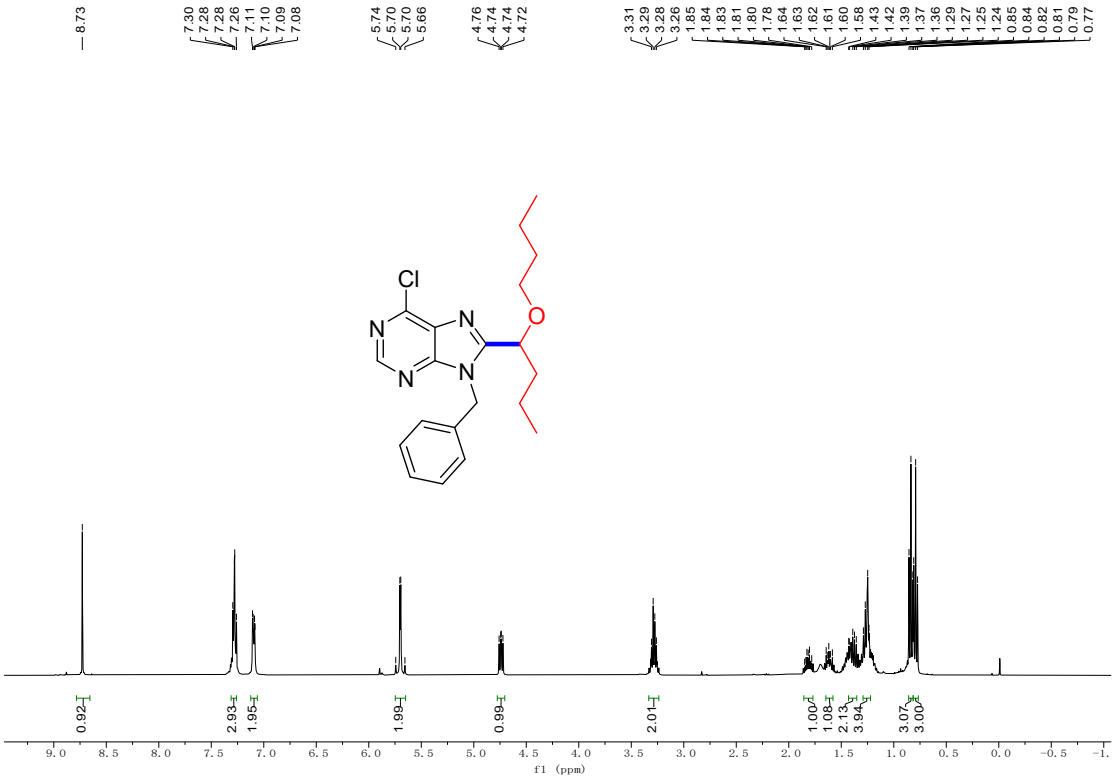


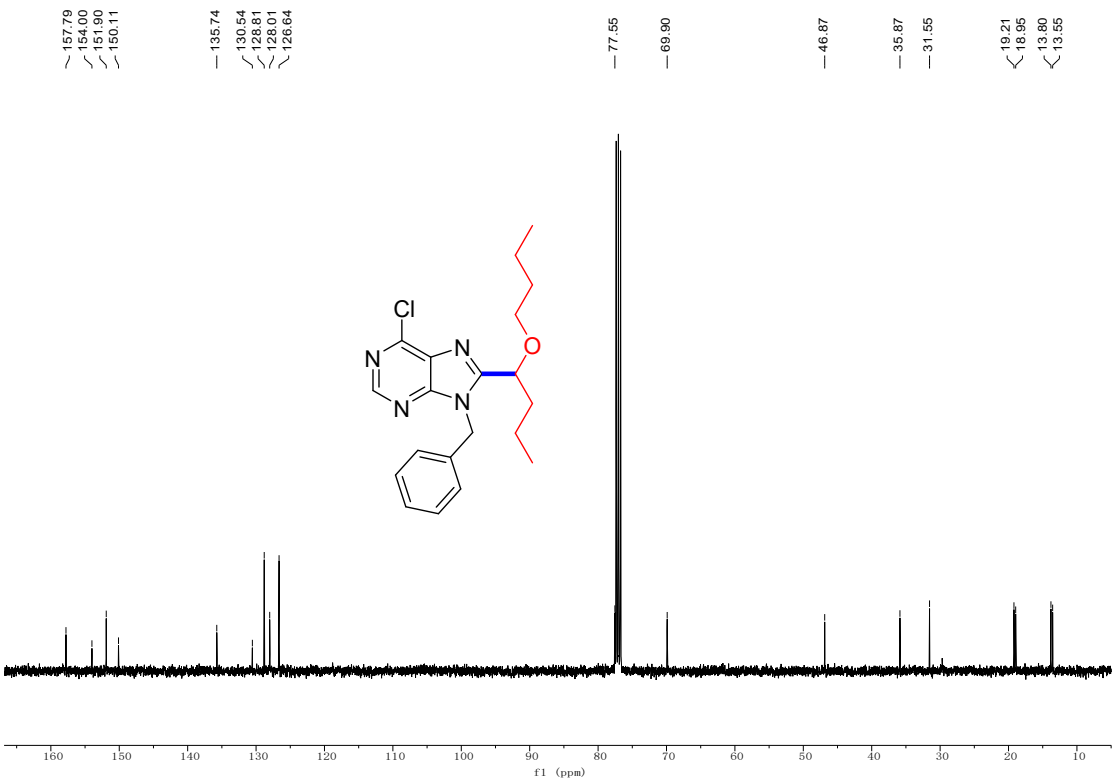
5e” [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]





5f [^{1}H NMR (400 MHz, $CDCl_3$), $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)]





Ⅺ. References

1. L. K. Huang, Y. C. Cherng, Y.-R. Cheng, J.-P. Jang, Y.-L. Chao and Y.-J. Cherng, *Tetrahedron*, 2007, **63**, 5323-5327.

2. J. L. Kelley, R. G. Davis, E. W. McLean, R. C. Glen, F. E. Soroko and B. R. Cooper, *J. Med. Chem.*, 1995, **38**, 3884-3888.

3. G. Dilek Celik, A. Disli, Y. Oner and L. Acik, *Chem. Pharm. Bull.*, 2012, **60**, 578-582.