Supporting Information

$K_2S_2O_8$-enabled one-pot deaminative C-N bond formation for the synthesis of fused benzimidazopurines and benzimidazoquinazolines

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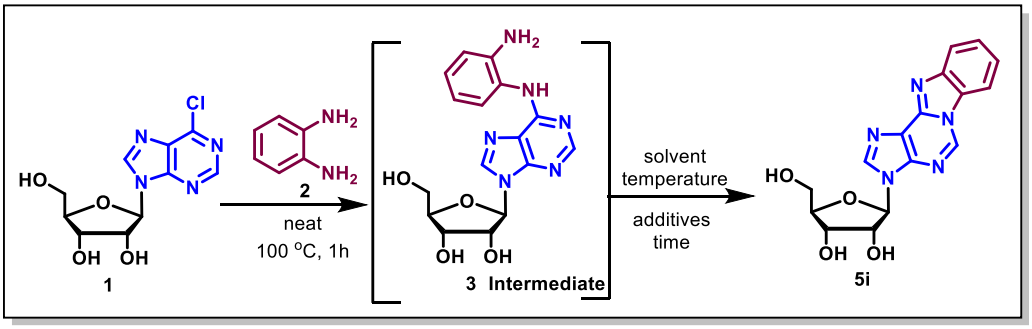
1. General information

All chemicals and solvents were purchased from commercial suppliers and used without further purification. All reactions requiring an inert atmosphere were performed using dry, freshly distilled solvents. Reaction progress was monitored by analytical thin-layer chromatography (TLC), with visualization under UV light or by staining with *p*-anisaldehyde charring solution. Solvents were removed under reduced pressure using a rotary evaporator. Column chromatography was performed using silica gel (100-200 mesh) as the stationary phase, with hexane, ethyl acetate, dichloromethane, and methanol employed as eluents. Yields of isolated compounds are reported. Melting points were determined without correction using a Buchi M-560 apparatus. NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer, including ^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), and ^{19}F NMR (377 MHz).

2. Optimization of reaction conditions

Table S1 Optimization of the reaction conditions[a]



entry	solvent	additive	t (°C)	time (h)	yield[b] (%)
1	-	$K_2S_2O_8$	110	12	-
2	DMF	$K_2S_2O_8$	110	12	70
3	DMSO	$K_2S_2O_8$	110	12	75
4	**DMA**	**$K_2S_2O_8$**	**110**	**0.5**	**85**
5	1,4-dioxane	$K_2S_2O_8$	100	12	trace
6	CH_3CN	$K_2S_2O_8$	80	3	80
7	Toluene	$K_2S_2O_8$	110	12	-
8	DMA	$Na_2S_2O_5$	110	12	70
9	DMA	Na_2SO_3	110	12	-
10	DMA	PIDA	110	12	-
11	DMA	BQ	110	12	-
12	DMA	$KMnO_4$	110	12	-
13	DMA	-	110	12	-

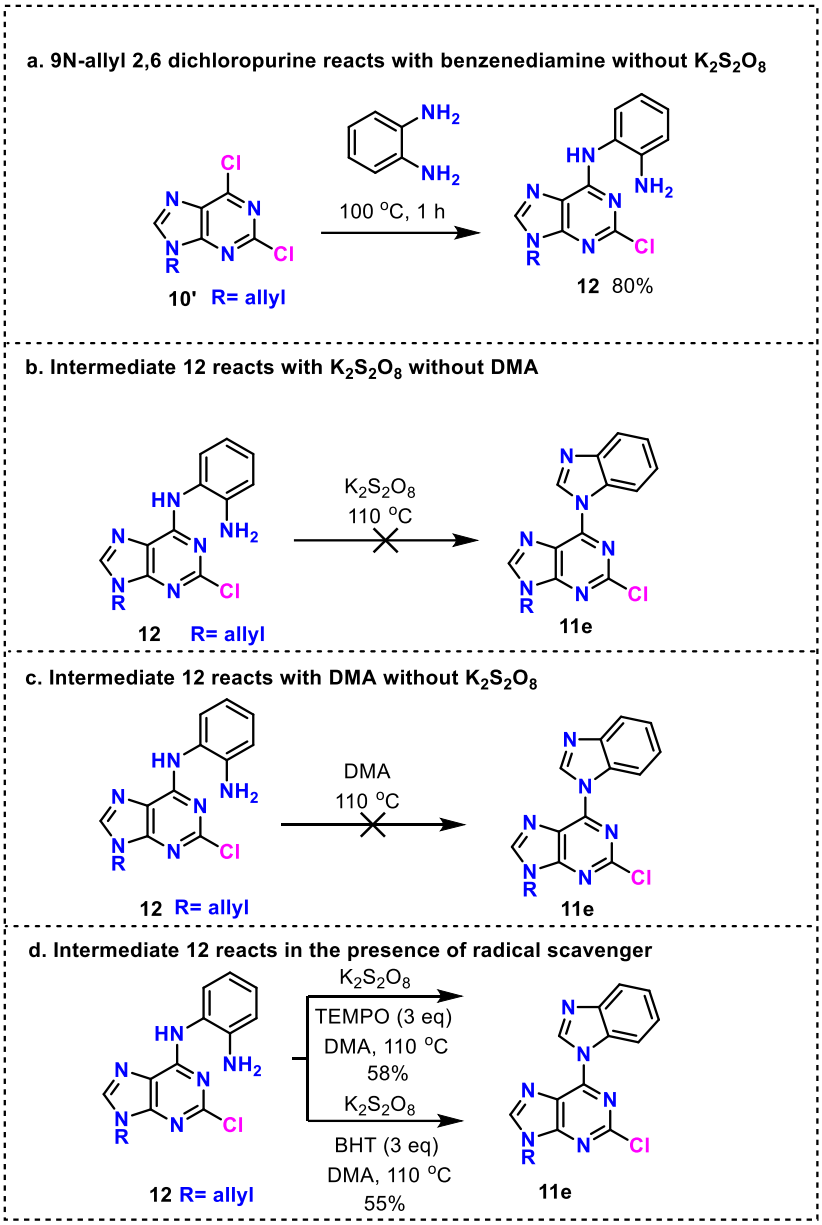
14	DMA	$K_2S_2O_8$	80	3	70
15	DMA	$K_2S_2O_8$	rt	12	-

[a]Reaction conditions: **1** (1 eq), **2** (1.5 eq), $K_2S_2O_8$ (2 eq), DMA (2 ml), 110 °C, 0.5 h, [b]Isolated yield

Encouraged by our previous research works on modified nucleosides, we began our studies using 6-chloropurine nucleoside **1** and benzene-1,2-diamine **2** as model substrates (Table S1). Initially the reaction was conducted under neat condition at 100 °C, intermediate **3** was obtained within 1 h; however, the subsequent addition of $K_2S_2O_8$ at the same temperature failed to deliver the desired product **5i**. Conducting the reaction with isolated intermediate **3** in DMF at 110 °C in the presence of $K_2S_2O_8$, afforded **5i** in 70% yield. Subsequently, carrying out the reaction in DMSO under the same condition ($K_2S_2O_8$, 110 °C) improved the yield to 75% (entries 1-3, Table S1). Gratifyingly, when the reaction was conducted in DMA with $K_2S_2O_8$ at 110 °C, the target compound **5i** was obtained in 85% yield within just 0.5 h (entry 4, Table S1). Further, solvent screening revealed that acetonitrile provided a comparable 80% yield, although the reaction required more than 3 h to reach completion, while 1,4-dioxane resulted in only trace product formation, and toluene failed to deliver any detectable product **5i** (entries 5-7, Table S1). Among the solvents evaluated, DMA emerged as optimal, providing the highest yield of the desired product within a significantly shorter reaction time. Subsequent screening of various oxidants, including Na_2SO_3, PIDA, benzoquinone, and $KMnO_4$, at 110 °C in DMA did not afford the desired product **5i**. In comparison, $Na_2S_2O_5$ delivered a moderate yield of 70% after 12 h (entries 8-12, Table S1). Moreover, conducting the reaction with intermediate **3** in DMA at 110 °C in the absence of $K_2S_2O_8$ resulted in no product formation (entry 13, Table S1). These observations underscore the essential role of $K_2S_2O_8$ in facilitating the C-N bond formation. To further optimize the reaction temperature, the transformation was performed in DMA using $K_2S_2O_8$ at 80 °C, affording product **5i** in a diminished yield of 70% after 3 h. Notably, the reaction conducted at room temperature failed to yield the cyclized product **5i** (entries 14-15, Table S1). Ultimately, the optimal condition was identified as using $K_2S_2O_8$ in DMA at 110 °C, enabling an efficient synthesis of purine-fused polycyclic nucleosides.

3. Control experiments

(A)

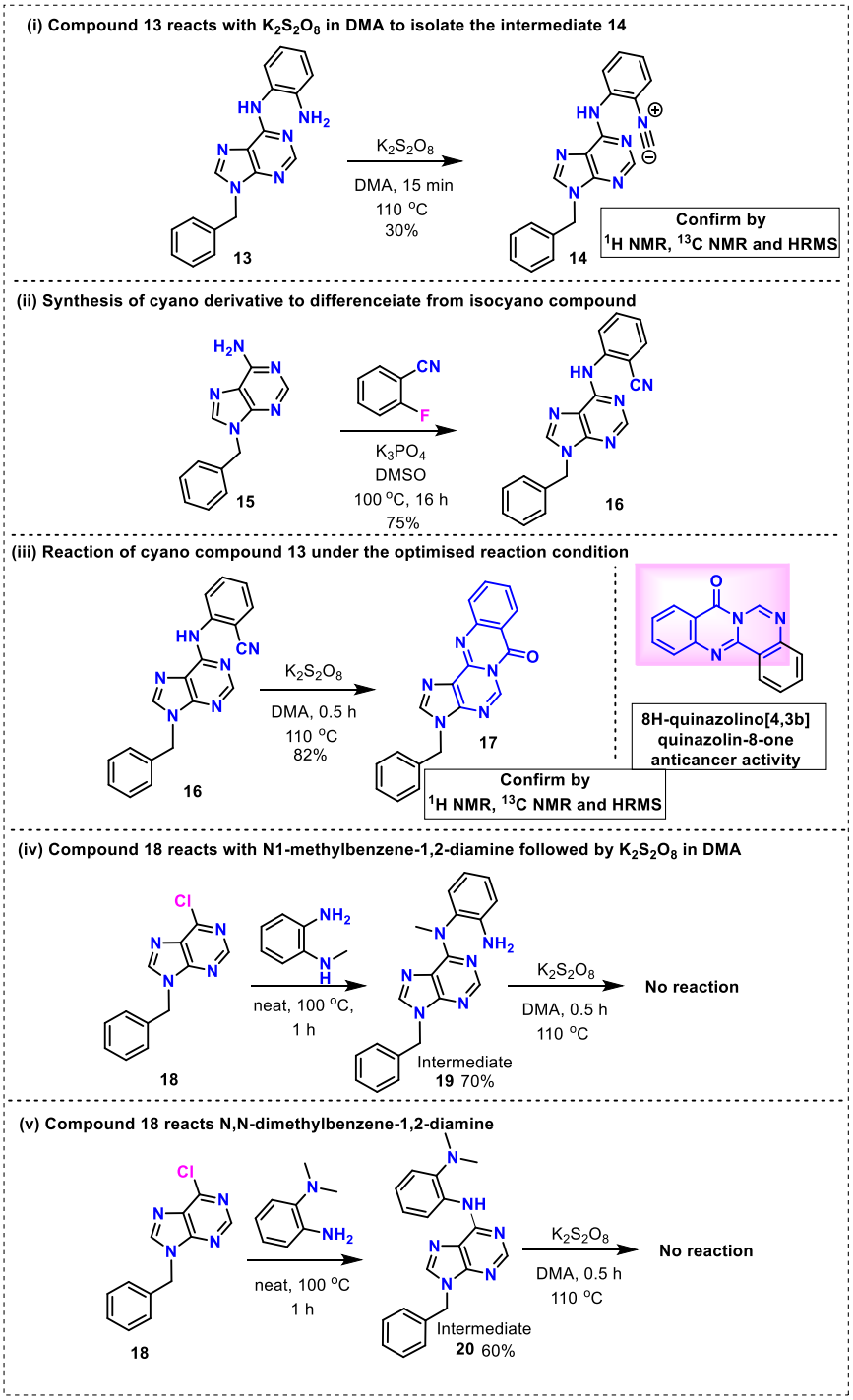


Scheme S1 Control experiments

To gain deeper insight into the reaction mechanism underlying the synthesis of benzimidazole attached purine derivatives, a series of control experiments were carried out. Initially, the reaction of a 2,6-dichloropurine derivative **10′** with *o*-phenylenediamine under solvent-free condition at 100 °C led to the formation of a 6-aminopurine intermediate **12**. This result suggests that the reaction proceeds *via* initially amination, followed by intramolecular cyclization to form the benzimidazole core (Scheme S1). To probe the role of DMA, the reaction was performed using a 2-chloro-6-aminopurine intermediate **12** in the presence of $K_2S_2O_8$ but in the absence of DMA. No reaction occurred, suggesting that DMA plays a critical role as a methylene source required for benzimidazole ring construction. Furthermore, when

the intermediate **12** was treated with DMA in the absence of $K_2S_2O_8$, no product formation was observed, highlighting the essential oxidative role of $K_2S_2O_8$ in this transformation. Finally, to determine whether the reaction proceeds through a radical pathway, the reaction was conducted in the presence of the radical scavenger TEMPO and BHT. Notably, the desired benzimidazole product was still obtained in 55-58% yield, indicating that the reaction likely does not involve a free radical mechanism.

(B)



Scheme S2 Control experiments

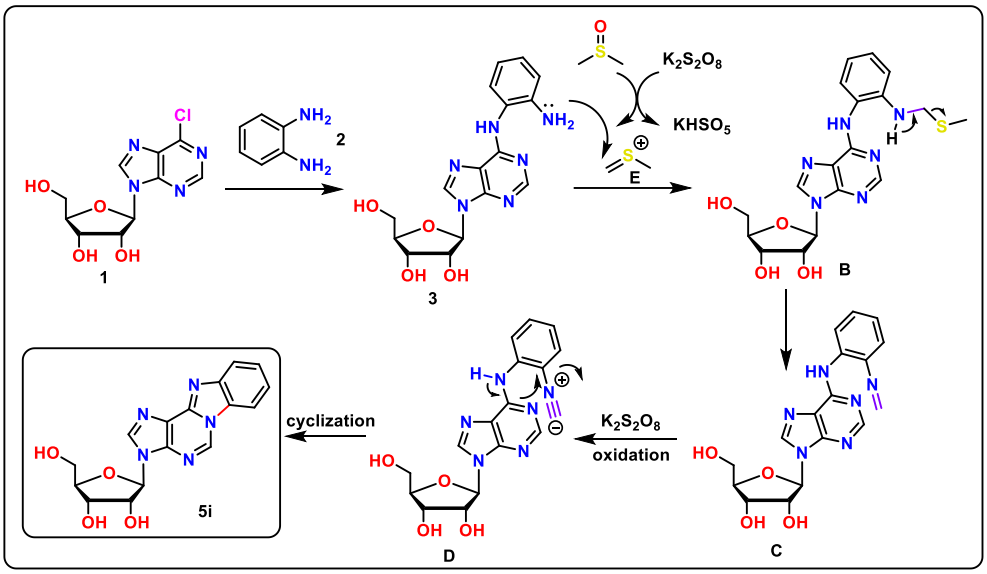
To further validate the proposed reaction mechanism and determine whether the reaction proceeds *via* intermediate **D** through an isocyanide pathway, some control experiments were conducted. When compound **13** was subjected to the optimized reaction condition ($K_2S_2O_8$ in DMA at 110 °C), a new spot appeared on TLC after 15 min. This intermediate was isolated and identified as compound **14** based on ^{1}H NMR, ^{13}C NMR, and HRMS analyses. The spectra showed the characteristic resonance of the isocyanide carbon in a slightly shielded region due to ring-current effects, confirming the in situ conversion of the amino group into the corresponding isocyanide intermediate. To distinguish intermediate compound **14** containing cyano and isocyano group, the cyano analogue **16** was independently synthesized and readily differentiated from isocyanide **14** based on its characteristic NMR features. Furthermore, subjecting cyano compound **16** to the optimized reaction condition ($K_2S_2O_8$, DMA, 110 ^{o}C) afforded quinazolinone **17**, as confirmed by NMR and HRMS analyses. This result provides strong additional evidence that the developed reaction proceeds *via* an isocyanide intermediate rather than a cyanide species. Notably, the quinazolinone framework constitutes in numerous biologically active molecules (Scheme S2).

Further some additional control experiments were conducted to gain the mechanistic insights into the cyclization process. Specifically, 6-chloropurine derivative **18** was reacted with N1-methylbenzene-1,2-diamine under neat condition in an oil bath at 100 °C for 1 h, which led to the formation of intermediate **19**. The intermediate **19** was characterized using spectroscopic techniques ^{1}H, ^{13}C NMR, and HRMS. Subsequently, DMA and $K_2S_2O_8$ were added to the same reaction vessel and the reaction mixture was stirred at 110 °C for 30 min. However, no desired cyclized product was observed. This observation strongly indicates that the free amine (N–H) group at the C-6 position of the purine is essential in facilitating the intramolecular cyclization and the subsequent aromatization step.

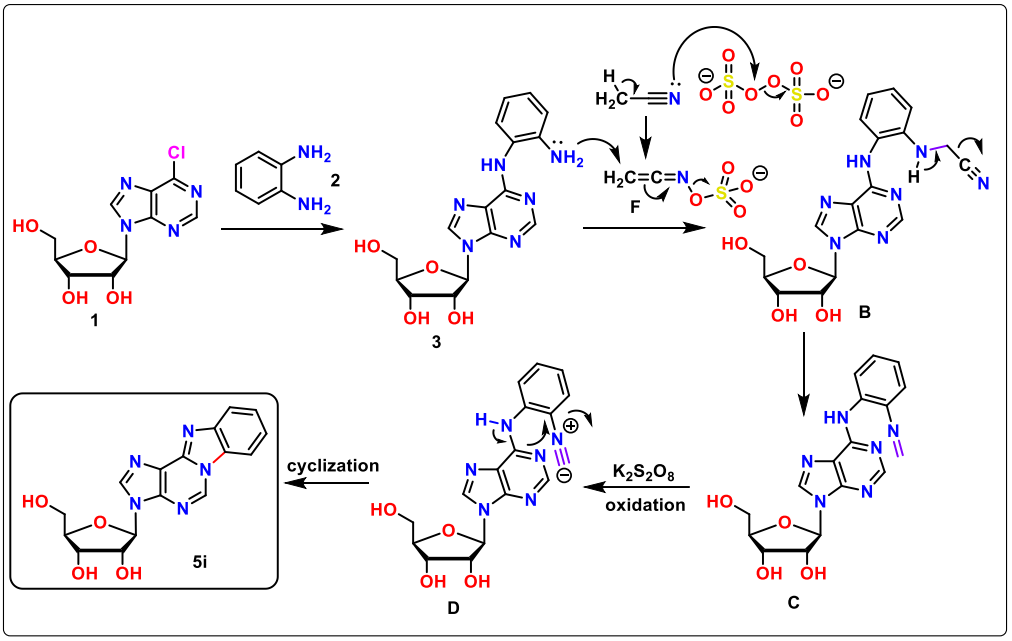
Further, we also performed another control experiment, using N,N-dimethylbenzene-1,2-diamine as per standard reaction condition instead of benzene-1,2-diamine. Under identical condition, 6-chloropurine derivative **18** reacted with N,N-dimethylbenzene-1,2-diamine to afford intermediate **20**. The intermediate **20** was characterized using spectroscopic techniques ^{1}H, ^{13}C NMR, and HRMS. Subsequently, treatment with DMA and $K_2S_2O_8$ at 110 °C for 30 min did not lead desired cyclized product. These results clearly indicate that the presence of a free amino ($–NH_2$) group of benzene-1,2-diamine is essential for the transformation.

4. Plausible reaction mechanism when DMSO and CH_3CN as a solvent

During the experiment of our investigations, the reaction was found to proceed efficiently in several polar aprotic solvents, including DMA, DMSO, and CH_3CN. Among these, DMA was selected as the optimal solvent for the studies reported in the manuscript, as it consistently provided higher yields within a shorter reaction time. Nevertheless, it is noteworthy that alternative mechanistic pathways may also operate when DMSO or CH_3CN are employed as solvents. Such possibilities are reliable with reported literature precedents,[1-4] as illustrated in scheme S3 and S4.



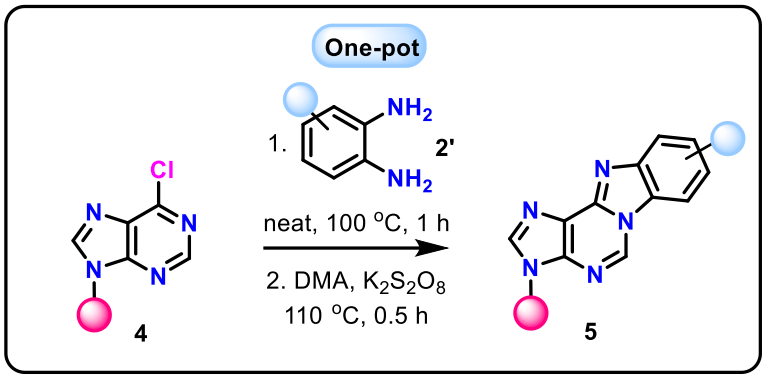
Scheme S3 Plausible reaction mechanism when DMSO as a solvent



Scheme S4 Plausible reaction mechanism when CH_3CN as a solvent

5. Experimental procedure and characterization of the products

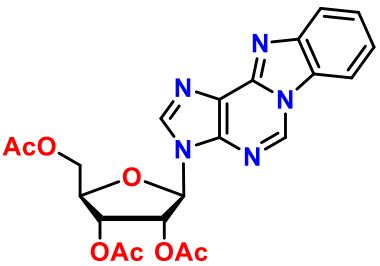
General procedure for the synthesis of Purine-fused polycyclic system (5a-t)



To a round-bottom flask, 6-chloropurine derivatives **4** (50 mg, 1 mmol) and *o*-phenylenediamine derivative **2′** (1.5 mmol) were added. The reaction mixture was stirred neat in an oil bath at 100 °C for 1 h, subsequently, DMA (2 ml) and potassium persulfate ($K_2S_2O_8$) (2 eq) were added simultaneously to the reaction mixture, and stirring was continued at 110 °C temperature for 30 minutes. Upon completion of the reaction, the mixture was extracted with ice-cold water and ethyl acetate in the presence of a brine solution. The organic layer was dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure using a rotary evaporator. The crude product was then purified by column chromatography using ethyl acetate/hexane as the eluent, affording a series of desired compounds, denoted as **5**.

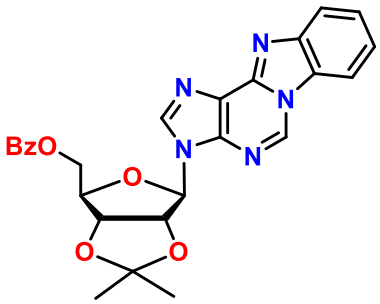
Characterization of the products

(2R,3R,4R,5R)-2-(acetoxymethyl)-5-(3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)tetrahydrofuran-3,4-diyl diacetate (5a)[5]



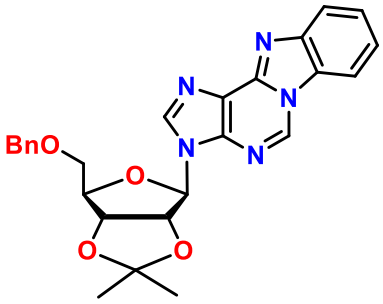
A white solid (45 mg, 80%): R_f 0.24 (Hex/EtOAc 1:4); mp > 220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 8.62 (s, 1H), 8.45 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.57 (d, J = 7.2 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 6.41 (d, J = 5.3 Hz, 1H), 6.06 (t, J = 5.6 Hz, 1H), 5.71 – 5.61 (m, 1H), 4.45 (dd, J = 8.8, 4.0 Hz, 2H), 4.31 (dd, J = 12.9, 6.5 Hz, 1H), 2.15 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.5, 169.9, 169.7, 144.4, 143.9, 141.3, 140.9, 138.7, 128.3, 126.8, 126.6, 122.9, 119.6, 112.8, 86.6, 80.0, 72.9, 70.4, 63.2, 21.0, 20.8, 20.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{22}N_5O_7$ 468.1519; Found 468.1518.

((3aR,4R,6R,6aR)-6-(3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzoate (5b)



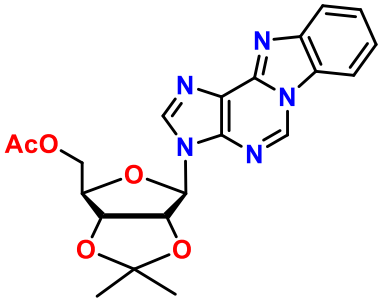
A white solid (48 mg, 85%): R_f 0.24 (Hex/EtOAc 1:4); mp > 220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.59 (s, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.30 (s, 1H), 8.08 – 8.02 (m, 2H), 7.85 (d, J = 8.1 Hz, 1H), 7.67 (t, J = 7.4 Hz, 1H), 7.58 – 7.51 (m, 3H), 7.44 (t, J = 7.7 Hz, 1H), 6.33 (s, 1H), 5.10 (q, J = 6.0 Hz, 2H), 4.92 – 4.85 (m, 1H), 4.71 – 4.63 (m, 1H), 4.54 (dd, J = 14.3, 8.4 Hz, 1H), 1.45 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.8, 144.5, 144.2, 141.8, 141.7, 138.0, 134.2, 129.9, 129.4, 129.2, 128.2, 126.4, 122.2, 121.7, 119.5, 112.7, 112.5, 103.3, 86.1, 85.1, 81.5, 46.7, 26.6, 25.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{26}H_{24}N_5O_5$ 486.1777; Found 486.1776.

3-((3aR,4R,6R,6aR)-6-((benzyloxy)methyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-3H-benzo[4,5]imidazo[2,1-i]purine (5c)



A white solid (43 mg, 76%): R_f 0.24 (Hex/EtOAc 1:4); mp > 220 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.01 (d, J = 5.9 Hz, 2H), 7.94 (d, J = 8.1 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.40 – 7.30 (m, 5H), 5.26 (s, 1H), 4.86 (s, 2H), 4.83 – 4.71 (m, 2H), 4.57 (dd, J = 13.1, 5.1 Hz, 2H), 4.41 (dd, J = 14.0, 8.5 Hz, 1H), 1.48 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 144.2, 141.2, 140.8, 136.6, 135.3, 128.6, 128.0, 127.7, 127.4, 126.4, 122.6, 122.3, 120.4, 113.0, 110.2, 108.2, 85.3, 84.9, 82.0, 70.1, 47.7, 26.4, 24.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{26}H_{26}N_5O_4$ 472.1985; Found 472.1983.

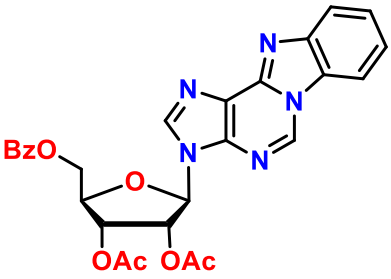
((3aR,4R,6R,6aR)-6-(3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl acetate (5d)



A white solid (48 mg, 84%): R_f 0.24 (Hex/EtOAc 1:4); mp > 220 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.04 (s, 1H), 8.04 – 7.96 (m, 2H), 7.62 (t, J = 7.7 Hz, 1H), 7.48 (t, J = 7.7 Hz, 1H), 6.32 (s, 1H), 4.92 (d, J = 5.9 Hz, 1H), 4.79 – 4.73 (m, 2H), 4.61 – 4.56 (m, 1H), 4.46 (dd, J = 14.4, 7.8 Hz, 1H), 2.19 (s, 3H), 1.51 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 141.0, 135.4, 133.1, 131.0, 127.5, 127.3, 126.6, 122.4, 120.5, 113.7, 110.1,

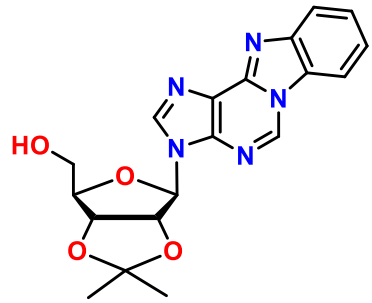
102.3, 86.7, 85.1, 83.3, 81.4, 46.7, 29.7, 26.5, 25.1, 21.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{22}N_5O_5$ 424.1621; Found 424.1608.

(2R,3R,4R,5R)-2-(3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)-5-((benzoyloxy)methyl)tetrahydrofuran-3,4-diyl diacetate (5e)



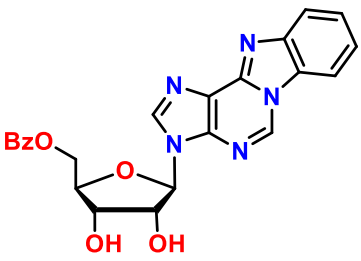
A white solid (45 mg, 82%): R_f 0.24 (Hex/EtOAc 1:4); mp > 220 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.18 (s, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.66 – 7.56 (m, 3H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.36 – 7.30 (m, 1H), 7.17 (t, *J* = 7.8 Hz, 2H), 6.35 (s, 1H), 5.45 (dd, *J* = 7.8, 4.9 Hz, 1H), 5.37 (d, *J* = 4.8 Hz, 1H), 4.85 (dd, *J* = 14.8, 3.6 Hz, 1H), 4.67 (dt, *J* = 7.7, 3.9 Hz, 1H), 4.57 (dd, *J* = 14.8, 4.1 Hz, 1H), 2.18 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 169.3, 164.1, 144.6, 143.9, 141.6, 141.5, 135.3, 133.7, 129.7, 129.1, 128.3, 127.7, 127.3, 126.4, 122.2, 120.3, 110.1, 98.3, 79.8, 74.1, 74.0, 70.6, 45.0, 20.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{24}N_5O_7$ 530.1676; Found 530.1664.

((3aR,4R,6R,6aR)-6-(3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5f)



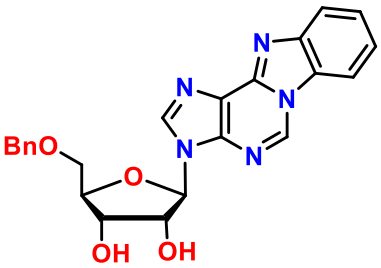
A white solid (45 mg, 78%): R_f 0.2 (Hex/EtOAc 1:4); mp 210-212 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.80 (s, 1H), 8.41 (d, *J* = 8.0 Hz, 1H), 8.39 (s, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.56 (t, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 3.9 Hz, 1H), 5.35 (d, *J* = 3.9 Hz, 1H), 4.91 (d, *J* = 5.9 Hz, 1H), 4.68 – 4.58 (m, 2H), 4.51 – 4.31 (m, 2H), 1.35 (s, 3H), 1.25 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 144.5, 144.4 142.5, 141.6, 138.1, 128.3, 126.4, 122.2, 121.8, 119.5, 112.5, 112.0, 102.8, 86.1, 84.2, 81.9, 47.8, 26.7, 25.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{20}N_5O_4$ 382.1515; Found 382.1512.

((2R,3S,4R,5R)-5-(3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl benzoate (5g)



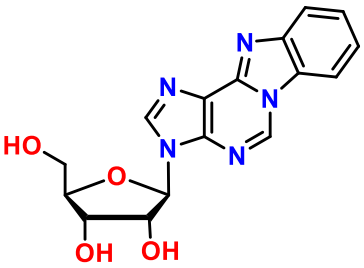
A white solid (44 mg, 77%): R_f 0.15 (Hex/EtOAc 1:4); mp 218-220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.63 (s, 1H), 8.33 (d, J = 8.0 Hz, 1H), 8.27 (s, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.64 (d, J = 7.2 Hz, 2H), 7.54 (d, J = 7.4 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.35 (t, J = 7.4 Hz, 1H), 7.22 (t, J = 7.7 Hz, 2H), 6.00 (s, 1H), 5.62 (s, 1H), 5.37 (s, 1H), 4.71 (dd, J = 14.6, 4.0 Hz, 1H), 4.55 (dd, J = 14.6, 5.2 Hz, 1H), 4.41 – 4.33 (m, 1H), 4.14 (s, 1H), 3.96 (d, J = 4.0 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.5, 144.4, 144.2, 142.7, 142.0, 137.7, 133.6, 129.3, 129.1, 128.8, 128.2, 126.3, 122.0, 121.6, 119.3, 112.4, 101.3, 81.4, 74.3, 71.5, 65.3, 45.7, 15.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{20}N_5O_5$ 446.1464; Found 446.1451.

(2R,3R,4S,5R)-2-(3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)-5-((benzyloxy)methyl)tetrahydrofuran-3,4-diol (5h)



A white solid (43 mg, 75%): R_f 0.15 (Hex/EtOAc 1:4); mp > 220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 8.41 (d, J = 8.1 Hz, 1H), 8.33 (s, 1H), 7.86 (d, J = 8.1 Hz, 1H), 7.56 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.31 – 7.20 (m, 5H), 5.76 (s, 1H), 5.22 (d, J = 4.3 Hz, 1H), 5.13 (d, J = 6.8 Hz, 1H), 4.84 (s, 1H), 4.69 – 4.62 (m, 2H), 4.46 – 4.39 (m, 2H), 4.25 (td, J = 7.2, 4.1 Hz, 1H), 4.06 (dd, J = 11.6, 7.0 Hz, 1H), 3.80 (t, J = 4.4 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 150.1, 144.5, 142.5, 141.9, 138.1, 137.9, 128.6, 128.2, 128.0, 126.4, 122.1, 119.4, 116.1, 114.1, 112.5, 111.3, 107.0, 80.7, 74.8, 72.7, 69.1, 30.8, 29.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{22}N_5O_4$ 432.1672; Found 432.1663.

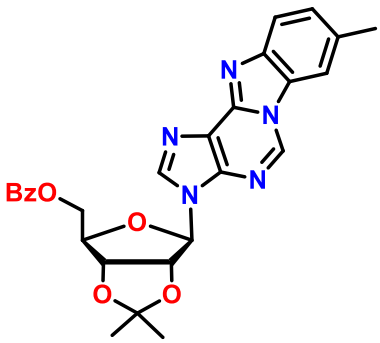
(2R,3R,4S,5R)-2-(3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)-5-(hydroxymethyl)tetrahydrofuran-3,4-diol (5i)[5]



A white solid (41 mg, 80%): R_f 0.2 (Hex/EtOAc 0:1); mp > 220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.63 (s, 1H), 8.41 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 6.09 (d, J = 5.6 Hz, 1H), 5.57 (d, J = 5.6 Hz, 1H), 5.27 (s, 1H), 5.11 (s, 1H), 4.60 (d, J = 5.1 Hz, 1H), 4.20 (s, 1H), 4.00 (d, J = 3.8 Hz, 1H), 3.71 (d, J = 11.8 Hz, 1H), 3.60 (d, J = 11.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 144.5, 144.1, 141.4, 140.5, 138.3, 128.3, 126.4,

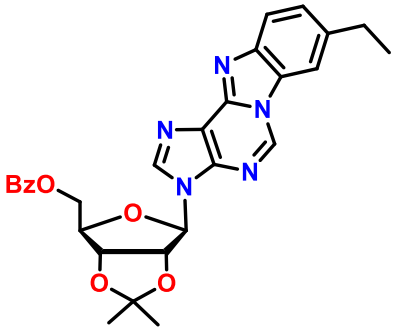
122.3, 122.2, 119.4, 112.7, 88.2, 86.1, 74.5, 70.6, 65.1, 61.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{16}N_5O_4$ 342.1202; Found 342.1192.

((3aR,4R,6R,6aR)-2,2-dimethyl-6-(8-methyl-3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzoate (5j)



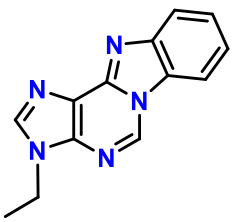
A white solid (51 mg, 88%): R_f 0.2 (Hex/EtOAc 0:1); mp > 220 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.07 (d, *J* = 6.9 Hz, 3H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.75 (s, 1H), 7.59 (d, *J* = 6.6 Hz, 1H), 7.50 (d, *J* = 7.1 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 1H), 6.57 (s, 1H), 5.01 (s, 2H), 4.77 (d, *J* = 38.2 Hz, 2H), 4.50 (s, 1H), 2.62 (s, 3H), 1.55 (s, 3H), 1.39 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 164.6, 135.3, 133.9, 133.8, 133.1, 129.7, 129.6, 129.1, 128.8, 128.8, 128.7, 128.4, 121.9, 119.4, 113.8, 110.2, 103.0, 86.7, 85.3, 81.5, 47.1, 29.7, 26.4, 25.1, 21.8. . HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{26}N_5O_5$ 500.1934; Found 500.1893.

((3aR,4R,6R,6aR)-6-(8-ethyl-3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzoate (5k)



A white solid (51 mg, 86%): *R*f 0.2 (Hex/EtOAc 0:1); mp 218- 220 °C. 1H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.06 (d, J = 7.4 Hz, 2H), 7.99 (s, 1H), 7.91 (d, J = 8.3 Hz, 1H), 7.73 (s, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.52 – 7.39 (m, 3H), 6.57 (d, J = 8.5 Hz, 1H), 4.99 (d, J = 7.2 Hz, 2H), 4.82 (dd, J = 8.0, 5.6 Hz, 1H), 4.71 (dd, J = 14.3, 5.5 Hz, 1H), 4.47 (dd, J = 14.3, 8.2 Hz, 1H), 2.90 (q, J = 7.6 Hz, 2H), 1.55 (s, 3H), 1.42 – 1.35 (m, 6H). 13C NMR (101 MHz, $CDCl_3$) δ 164.6, 142.4, 140.7, 139.3, 135.3, 133.7, 129.6, 129.6, 129.5, 129.1, 128.7, 127.5, 127.1, 119.9, 119.9, 113.8, 108.8, 103.0, 86.7, 85.3, 81.5, 46.9, 29.2, 26.4, 25.1, 16.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{28}N_5O_5$ 514.2090; Found 514.2048.

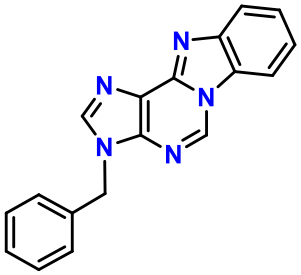
3-ethyl-3H-benzo[4,5]imidazo[2,1-i]purine (5m)[5]



A white solid (51 mg, 82%): R_f 0.20 (Hex/EtOAc 2:3); mp 216-218 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.7 8 (s, 1H), 8.40 (d, *J* = 6.9 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.56 (dd, *J* = 11.2, 4.0 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 4.39 (q, *J* = 7.3 Hz, 2H), 1.52 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101

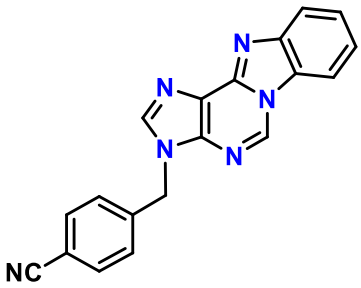
MHz, DMSO-d_6) δ 144.5, 141.5, 137.8, 128.3, 126.4, 122.1, 121.9, 119.4, 112.5, 31.3, 16.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{12}N_5$ 238.1093; Found 238.0858.

3-benzyl-3H-benzo[4,5]imidazo[2,1-i]purine (5n)[5]



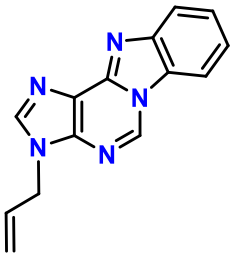
A white solid (46 mg, 75%): R_f 0.20 (Hex/EtOAc 2:3); mp 210-212 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 8.52 (s, 1H), 8.38 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.54 (dd, J = 11.3, 4.0 Hz, 1H), 7.49 – 7.23 (m, 6H), 5.59 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 144.5, 144.4, 142.0, 141.7, 138.2, 137.2, 129.2, 128.3, 128.3, 128.0, 126.4, 122.2, 122.0, 119.4, 112.5, 47.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{14}N_5$ 300.1249; Found 300.1243.

4-((3H-benzo[4,5]imidazo[2,1-i]purin-3-yl)methyl)benzonitrile (5o)



A white solid (47 mg, 78%): R_f 0.20 (Hex/EtOAc 2:3); mp > 220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.76 (s, 1H), 8.53 (s, 1H), 8.37 (d, J = 8.0 Hz, 1H), 7.85 (t, J = 7.8 Hz, 3H), 7.54 (dd, J = 14.4, 7.7 Hz, 3H), 7.47 – 7.40 (m, 1H), 5.70 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 144.5, 144.3, 142.7, 142.1, 141.6, 138.4, 133.1, 128.8, 128.3, 126.4, 122.2, 122.1, 119.5, 119.0, 112.5, 111.1, 47.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{13}N_6$ 325.1202; Found 325.1198.

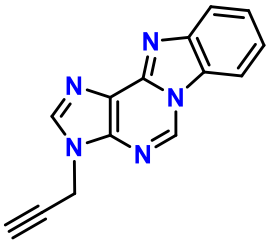
3-allyl-3H-benzo[4,5]imidazo[2,1-i]purine (5p)[5]



A white solid (52 mg, 81%): R_f 0.20 (Hex/EtOAc 2:3); mp 168-170 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 8.40 (d, J = 8.0 Hz, 1H), 8.37 (s, 1H), 7.86 (d, J = 8.1 Hz, 1H), 7.60 – 7.50 (m, 1H), 7.50 – 7.41 (m, 1H), 6.16 (ddd, J = 22.5, 10.6, 5.4 Hz, 1H), 5.26 (dd, J = 10.3, 1.3 Hz, 1H), 5.11 (dd, J = 17.1, 1.3 Hz, 1H), 5.01 (d, J = 5.4 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 144.3, 141.9, 141.6, 138.0, 133.6, 128.2, 126.5, 122.3, 119.4, 118.3, 112.5, 46.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{12}N_5$ 250.1093; Found 250.1084.

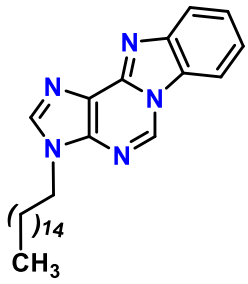
3-(prop-2-yn-1-yl)-3H-benzo[4,5]imidazo[2,1-i]purine (5q)

A white solid (51 mg, 80%): R_f 0.20 (Hex/EtOAc 2:3); mp 168-170 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.45 (s, 1H), 8.41 (d, J = 8.1 Hz, 1H), 7.86 (d, J = 8.1 Hz, 1H),



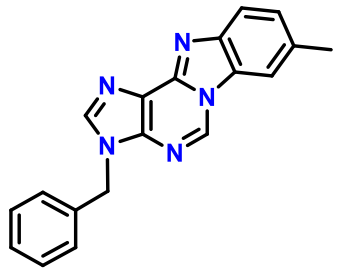
7.56 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 5.26 (d, *J* = 2.5 Hz, 2H), 3.58 (t, *J* = 2.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 144.5, 144.2, 141.4, 141.3, 138.4, 128.3, 126.5, 122.3, 121.8, 119.5, 112.6, 78.5, 76.8, 33.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{10}N_5$ 248.0936; Found 248.0929.

3-hexadecyl-3H-benzo[4,5]imidazo[2,1-i]purine (5r)



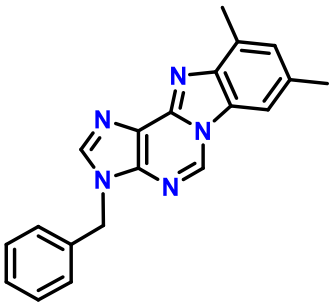
A white solid (47 mg, 72%): *R*$_f$ 0.20 (Hex/EtOAc 2:3); mp 198-200 °C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.78 (s, 1H), 8.39 (t, *J* = 4.0 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.3 Hz, 1H), 4.33 (t, *J* = 7.0 Hz, 2H), 1.90 (dd, *J* = 11.1, 4.4 Hz, 2H), 1.27 – 1.16 (m, 27H), 0.84 (t, *J* = 6.8 Hz, 3H). HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{27}H_{40}N_5$ 434.3284; Found 434.3461. ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 144.5, 144.4, 142.0, 141.7, 137.8, 128.3, 126.4, 122.1, 121.8, 119.4, 112.5, 44.1, 31.7, 30.0, 29.45, 29.41, 29.29, 29.23, 29.1, 28.8, 26.3, 22.5, 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{27}H_{40}N_5$ 434.3284; Found 434.3461.

3-benzyl-8-methyl-3H-benzo[4,5]imidazo[2,1-i]purine (5s)



A white solid (52 mg, 82%): *R*$_f$ 0.20 (Hex/EtOAc 2:3); mp 210-212 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.01 (s, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.77 (s, 1H), 7.38 (dt, *J* = 16.4, 8.8 Hz, 6H), 5.53 (s, 2H), 2.62 (s, 3H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 142.5, 141.9, 138.1, 137.1, 137.0, 132.2, 129.2, 128.4, 128.2, 128.1, 128.0, 121.4, 118.2, 112.5, 47.5, 21.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{16}N_5$ 314.1406; Found 314.1378.

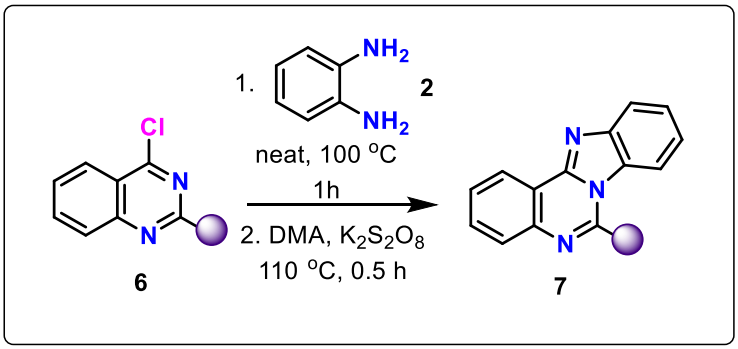
3-benzyl-8,10-dimethyl-3H-benzo[4,5]imidazo[2,1-i]purine (5t)



A white solid (55 mg, 85%): *R*$_f$ 0.20 (Hex/EtOAc 2:3); mp >200 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.02 (s, 1H), 7.60 (s, 1H), 7.37 (dd, *J* = 16.8, 7.6 Hz, 5H), 7.24 (s, 1H), 5.53 (s, 2H), 2.81 (s, 3H), 2.58 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6, 135.4, 135.2, 132.7, 129.9, 129.1, 128.7, 128.6, 127.7, 127.7,

127.0, 107.5, 48.0, 21.8, 17.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{18}N_5$ 328.1562; Found 328.1535.

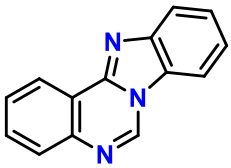
General procedure for the synthesis of quinazoline-fused polycyclic (7a-i)



To a round-bottom flask, 4-chloroquinazoline derivatives **6** (50 mg, 1 mmol) and o-phenylenediamine derivative **2** (1.5 mmol) were added. The reaction mixture was stirred neat in an oil bath at 100 °C for 1 h, Subsequently, DMA (2 ml) and $K_2S_2O_8$ (2 eq) were added simultaneously to the reaction mixture, and stirring was continued at 110 °C temperature for 30 minutes. Upon completion of the reaction, the mixture was extracted with ice-cold water and ethyl acetate in the presence of a brine solution. The organic layer was dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure using a rotary evaporator. The crude product was then purified by column chromatography using ethyl acetate/hexane as the eluent, affording a series of desired compounds, denoted as **7**.

Characterization of the products

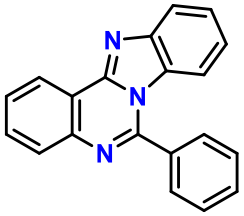
benzo[4,5]imidazo[1,2-c]quinazoline (7a)[6]



A white solid (50 mg, 65%): R_f 0.50 (Hex/EtOAc 7:3); mp >220 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.71 (dd, *J* = 7.9, 0.9 Hz, 1H), 8.06 – 7.97 (m, 3H), 7.84 – 7.79 (m, 1H), 7.73 (t, *J* = 7.2 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.3, 143.9, 142.5, 136.1, 131.8, 128.7, 128.5, 128.1, 126.2, 124.2, 123.3, 120.3, 119.3, 110.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{10}N_3$ 220.0875; Found 220.0871.

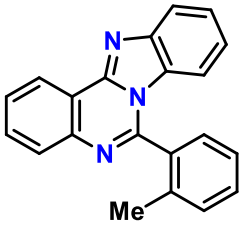
6-phenylbenzo[4,5]imidazo[1,2-c]quinazoline (7b)[6]

A white solid (43 mg, 60%): R_f 0.50 (Hex/EtOAc 7:3); mp >220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.83 (d, *J* = 8.3 Hz, 1H), 8.20 (dd, *J* = 6.7, 3.1 Hz, 2H), 8.09 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.80 – 7.49 (m, 6H), 7.40 – 7.24 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.9, 151.2,



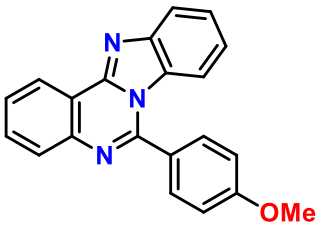
138.4, 134.9, 132.8, 131.5, 129.5, 127.7, 124.1, 120.6, 118.5, 116.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{14}N_3$ 296.1188; Found 296.1184.

6-(o-tolyl)benzo[4,5]imidazo[1,2-c]quinazoline (7c)[7]



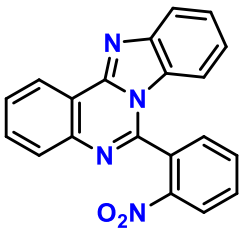
A yellow solid (33 mg, 58%): R_f 0.50 (Hex/EtOAc 7:3); mp 208-210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.08 – 7.96 (m, 2H), 7.89 – 7.79 (m, 1H), 7.79 – 7.70 (m, 1H), 7.66 – 7.59 (m, 1H), 7.58 – 7.43 (m, 4H), 7.15 – 7.06 (m, 1H), 6.31 (d, *J* = 8.4 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.4, 147.6, 144.3, 142.4, 136.5, 133.9, 131.8, 131.0, 130.9, 129.1, 128.3, 128.3, 128.2, 126.9, 125.7, 124.2, 123.1, 119.9, 118.4, 113.3, 18.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{16}N_3$ 310.1344; Found 310.1335.

6-(4-methoxyphenyl)benzo[4,5]imidazo[1,2-c]quinazoline (7d)[7]



A yellow solid (40 mg, 62%): R_f 0.50 (Hex/EtOAc 7:3); mp 200-202 °C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.94 (d, *J* = 8.3 Hz, 1H), 8.25 (d, *J* = 8.8 Hz, 2H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.90 – 7.83 (m, 1H), 7.66 – 7.59 (m, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.34 (ddd, *J* = 14.4, 9.5, 6.8 Hz, 3H), 7.27 (t, *J* = 6.6 Hz, 2H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 165.0, 162.7, 151.4, 142.3, 139.1, 133.8, 131.3, 129.7, 127.7, 127.4, 124.1, 123.3, 122.9, 120.3, 118.8, 115.9, 114.7, 112.0, 56.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{16}N_3O$ 326.1293; Found 326.1290.

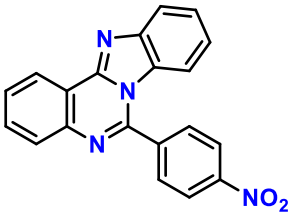
6-(2-nitrophenyl)benzo[4,5]imidazo[1,2-c]quinazoline (7e)[8]



A yellow solid (24 mg, 35%): R_f 0.50 (Hex/EtOAc 7:3); mp >220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.21 (dd, *J* = 7.9, 1.4 Hz, 1H), 8.03 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.72 (dd, *J* = 5.1, 2.8 Hz, 2H), 7.55 (dtd, *J* = 19.0, 7.4, 1.4 Hz, 2H), 7.38 (d, *J* = 2.0 Hz, 1H), 7.24 (ddd, *J* = 16.5, 8.3, 2.2 Hz, 3H), 7.18 – 7.10 (m, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.92 – 6.83 (m, 1H), 6.62 (dd, *J* = 7.6, 1.4 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.6, 147.2, 144.3, 142.2, 135.0, 134.8, 133.0, 132.2, 130.7, 127.1, 126.0, 125.0, 123.1, 122.9, 119.2, 119.2, 116.2, 112.0,

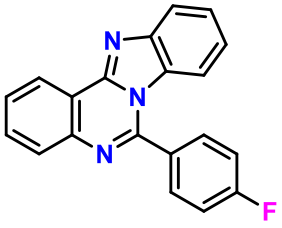
110.8, 63.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{13}N_4O_2$ 341.1039; Found 341.1031.

6-(4-nitrophenyl)benzo[4,5]imidazo[1,2-c]quinazoline (7f)[9]



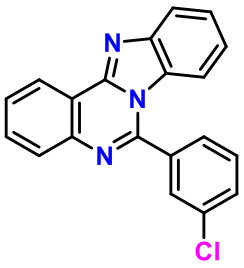
A yellow solid (28 mg, 40%): R_f 0.50 (Hex/EtOAc 7:3); mp >220 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.56 (d, *J* = 8.7 Hz, 2H), 8.03 (t, *J* = 8.9 Hz, 4H), 7.92 – 7.82 (m, 1H), 7.81 – 7.73 (m, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 147.8, 146.1, 144.4, 142.0, 140.0, 132.1, 130.0, 129.0, 128.7, 128.3, 126.0, 124.4, 124.3, 123.0, 120.5, 118.5, 113.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{13}N_4O_2$ 341.1039; Found 341.1031.

6-(4-fluorophenyl)benzo[4,5]imidazo[1,2-c]quinazoline (7g)[7]



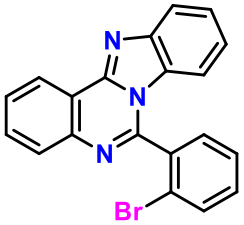
A white solid (29 mg, 45%): R_f 0.50 (Hex/EtOAc 7:3); mp 200-202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (dd, *J* = 7.9, 0.9 Hz, 1H), 8.05 (d, *J* = 8.1 Hz, 2H), 7.88 – 7.81 (m, 1H), 7.80 – 7.70 (m, 3H), 7.51 (ddd, *J* = 7.7, 5.5, 2.3 Hz, 2H), 7.40 (t, *J* = 8.9 Hz, 1H), 7.18 (dd, *J* = 11.6, 4.1 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 158.8, 147.6, 144.1, 143.7, 142.2, 133.1 (d, J = 8.0 Hz, 1C), 131.9, 130.5 (d, J = 2.0 Hz, 1C), 129.0, 128.7, 128.5 (d, J = 40.0 Hz, 1C), 125.3 (d, J = 50.0 Hz, 1C), 124.3, 123.1, 122.6 (d, J = 16.0 Hz, 1C), 120.0, 118.5, 116.6 (d, J = 20.0 Hz, 1C), 113.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -113.7 (dd, *J* = 18.8, 6.3 Hz). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{13}FN_3$ 314.1094; Found 314.1086.

6-(3-chlorophenyl)benzo[4,5]imidazo[1,2-c]quinazoline (7h)[10]



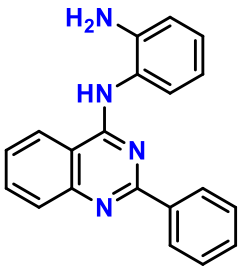
A white solid (33 mg, 48%): R_f 0.50 (Hex/EtOAc 7:3); mp >220 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.03 (dd, *J* = 8.2, 0.8 Hz, 2H), 7.87 – 7.78 (m, 2H), 7.78 – 7.70 (m, 2H), 7.68 – 7.59 (m, 2H), 7.56 – 7.48 (m, 1H), 7.19 (ddd, *J* = 8.3, 7.3, 1.1 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.1, 135.8, 135.4, 132.0, 131.2, 130.6, 128.7, 128.6, 128.2, 126.6, 125.8, 124.2, 122.8, 120.1, 114.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{13}ClN_3$ 330.0798; Found 330.0792.

6-(2-bromophenyl)benzo[4,5]imidazo[1,2-c]quinazoline (7i)[10]



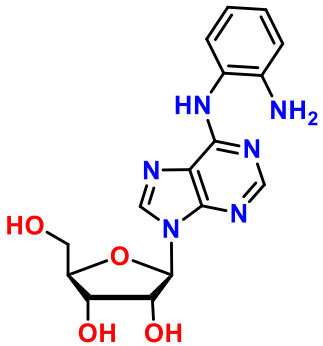
A white solid (32 mg, 42%): R_f 0.50 (Hex/EtOAc 7:3); mp >220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.65 (dd, J = 7.9, 1.1 Hz, 2H), 8.01 – 7.86 (m, 11H), 7.84 – 7.74 (m, 6H), 7.49 (t, J = 7.6 Hz, 2H), 7.23 (dd, J = 11.5, 4.1 Hz, 2H), 6.57 (d, J = 8.4 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.9, 147.8, 142.4, 133.8, 132.5, 131.2, 128.9, 128.3, 125.8, 124.8, 124.2, 123.0, 120.1, 114.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{13}BrN_3$ 374.0293; Found 374.0286.

N1-(2-phenylquinazolin-4-yl)benzene-1,2-diamine (7b′)



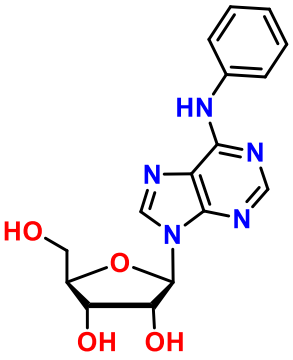
A white solid (48 mg, 75%): R_f 0.50 (Hex/EtOAc 7:3); mp 190-192 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, J = 7.9 Hz, 1H), 8.03 (t, J = 8.2 Hz, 2H), 7.86 – 7.80 (m, 1H), 7.80 – 7.65 (m, 6H), 7.49 (t, J = 7.7 Hz, 1H), 7.14 (t, J = 7.8 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 148.0, 144.3, 142.4, 134.3, 131.9, 131.0, 129.3, 129.2, 128.3, 128.3, 128.2, 125.6, 124.2, 122.6, 119.9, 118.4, 114.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{17}N_4$ 313.1453; Found 313.1443.

(2R,3R,4S,5R)-2-(6-((2-aminophenyl)amino)-9H-purin-9-yl)-5-(hydroxymethyl)tetrahydrofuran-3,4-diol (3)



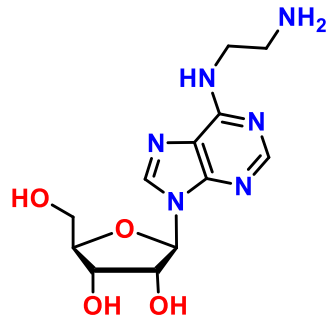
A brown solid (50 mg, 80%): R_f 0.40 (MeOH/DCM 1:9); mp 182-184 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.12 (s, 1H), 8.47 (s, 1H), 8.22 (s, 1H), 7.23 (d, J = 7.1 Hz, 1H), 6.98 (t, J = 7.6 Hz, 1H), 6.79 (d, J = 7.8 Hz, 1H), 6.61 (t, J = 7.5 Hz, 1H), 5.94 (d, J = 6.1 Hz, 1H), 5.53 – 5.45 (m, 1H), 5.44 – 5.35 (m, 1H), 5.23 (t, J = 4.1 Hz, 1H), 4.85 (s, 2H), 4.68 – 4.57 (m, 1H), 4.18 (dd, J = 7.8, 4.6 Hz, 1H), 4.03 – 3.95 (m, 1H), 3.74 – 3.67 (m, 1H), 3.60 (dd, J = 7.3, 3.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 153.9, 152.6, 149.6, 144.0, 140.7, 127.6, 126.7, 124.4, 120.6, 116.8, 116.4, 88.4, 86.3, 74.0, 71.0, 62.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{19}N_6O_4$ 359.1468; Found 359.1464.

(2R,3S,4R,5R)-2-(hydroxymethyl)-5-(6-(phenylamino)-9H-purin-9-yl)tetrahydrofuran-3,4-diol (8)[11]



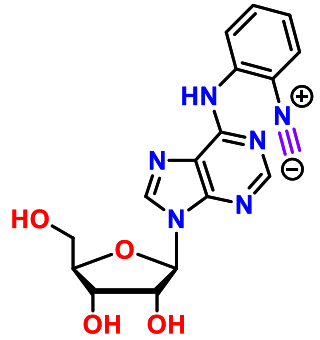
A white solid (33 mg, 55%): R_f 0.50 (MeOH/DCM 1:9); mp 186-187 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.95 (s, 1H), 8.55 (s, 1H), 8.41 (s, 1H), 7.95 (d, J = 7.9 Hz, 2H), 7.34 (t, J = 7.9 Hz, 2H), 7.06 (t, J = 7.3 Hz, 1H), 5.97 (d, J = 6.0 Hz, 1H), 5.50 (d, J = 6.1 Hz, 1H), 5.36 – 5.27 (m, 1H), 5.23 (d, J = 4.7 Hz, 1H), 4.66 (dd, J = 11.2, 5.8 Hz, 1H), 4.19 (dd, J = 8.0, 4.6 Hz, 1H), 4.01 (dd, J = 7.0, 3.7 Hz, 1H), 3.71 (dt, J = 11.8, 4.2 Hz, 1H), 3.60 (dd, J = 6.9, 3.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 152.6, 152.4, 149.8, 141.1, 139.9, 128.8, 123.2, 121.3, 120.8, 88.3, 86.3, 74.0, 71.0, 62.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{18}N_5O_4$ 344.1359; Found 344.1348.

(2R,3R,4S,5R)-2-(6-((2-aminoethyl)amino)-9H-purin-9-yl)-5-(hydroxymethyl)tetrahydrofuran-3,4-diol (9)[12]



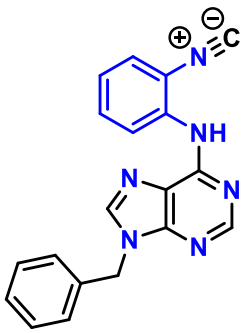
A white solid (30 mg, 55%): R_f 0.20 (MeOH/DCM 1:9); mp 90-92 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (s, 9H), 8.23 (s, 9H), 7.89 (s, 8H), 5.90 (d, J = 6.1 Hz, 11H), 4.68 – 4.55 (m, 25H), 4.16 (dd, J = 4.5, 3.2 Hz, 15H), 3.97 (d, J = 3.1 Hz, 13H), 3.77 – 3.47 (m, 42H), 2.88 (t, J = 6.4 Hz, 19H), 2.51 (s, 13H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 155.1, 152.7, 148.9, 140.3, 120.2, 88.3, 86.3, 74.0, 71.0, 62.0, 41.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{19}N_6O_4$ 311.1468; Found 311.1458.

(2R,3S,4R,5R)-2-(hydroxymethyl)-5-(6-((2-isocyanophenyl)amino)-9H-purin-9-yl)tetrahydrofuran-3,4-diol (D)



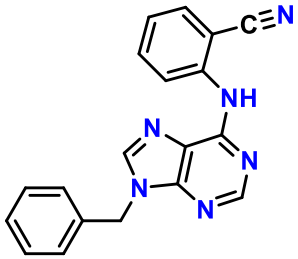
A white solid (19 mg, 30%): R_f 0.20 (Hex/EtOAc 2:3); mp 188-190 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 9.02 (s, 2H), 8.78 (d, J = 8.1 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.47 (dt, J = 14.4, 7.4 Hz, 2H), 6.14 (d, J = 5.3 Hz, 1H), 5.63 (d, J = 5.9 Hz, 1H), 5.31 (d, J = 5.0 Hz, 1H), 5.18 (s, 1H), 4.67 (d, J = 5.3 Hz, 1H), 4.24 (d, J = 4.4 Hz, 1H), 4.03 (d, J = 3.8 Hz, 1H), 3.73 (d, J = 4.3 Hz, 1H), 3.63 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d$_6$) δ 153.1, 152.5, 147.2, 145.0, 144.2, 144.0, 132.1, 125.2, 124.7, 123.0, 120.5, 116.6, 88.4, 86.2, 74.4, 70.6, 61.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{17}N_6O_4$ 369.1311; Found 369.1305.

9-benzyl-N-(2-isocyanophenyl)-9H-purin-6-amine (14)



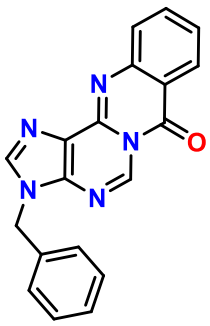
A white solid (15 mg, 30%): R_f 0.20 (Hex/EtOAc 3:2); mp 170-172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.05 (s, 1H), 9.00 (s, 1H), 8.92 (d, *J* = 7.6 Hz, 1H), 8.14 (s, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.40 (dd, *J* = 7.4, 4.4 Hz, 5H), 5.55 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 152.5, 143.8, 143.8, 143.8, 134.7, 131.7, 129.3, 128.8, 128.0, 125.2, 124.7, 122.6, 122.6, 120.0, 116.7, 47.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{15}N_6$ 327.1358; Found 327.1330.

2-((9-benzyl-9H-purin-6-yl)amino)benzonitrile (16)



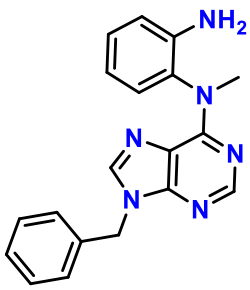
A white solid (54 mg, 75%): R_f 0.20 (Hex/EtOAc 2:3); mp 180-182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 8.6 Hz, 1H), 8.64 (s, 1H), 7.91 (d, *J* = 7.2 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 2H), 7.44 – 7.30 (m, 6H), 7.20 (t, *J* = 7.3 Hz, 1H), 5.45 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.5, 151.5, 141.4, 141.30 135.2, 133.8, 132.7, 129.2, 129.1, 128.7, 128.6, 127.8, 123.3, 121.6, 116.6, 102.9, 47.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{15}N_6$ 327.1358; Found 327.1360.

3-benzylpurino[6,1-b]quinazolin-7(3H)-one (17)



A yellowish solid (40 mg, 82%): R_f 0.10 (Hex/EtOAc 2:3); mp 202-204 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 8.49 – 8.44 (m, 1H), 8.02 – 7.94 (m, 2H), 7.90 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.0 Hz, 3H), 7.36 (d, *J* = 7.7 Hz, 2H), 5.50 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 148.3, 142.1, 140.9, 139.7, 139.6, 136.1, 134.8, 134.5, 129.2, 129.1, 128.7, 127.8, 127.7, 127.6, 125.5, 124.9, 47.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{14}N_5O$ 328.1198; Found 328.1200.

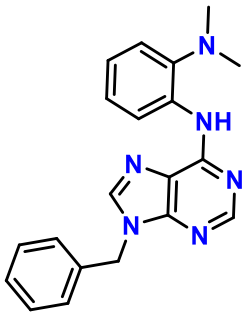
N1-(9-benzyl-9H-purin-6-yl)-N1-methylbenzene-1,2-diamine (19)



A white solid (47 mg, 70%): R_f 0.20 (Hex/EtOAc 7:3); mp 178-180 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.52 – 7.47 (m, 1H), 7.45 – 7.41 (m, 2H), 7.37 (d, *J* = 7.5 Hz, 2H), 7.30 (dd, *J* = 14.1, 7.1 Hz, 4H), 7.14 (dd, *J* = 5.9, 3.2 Hz, 2H), 6.39 (s, 2H), 5.21 (s, 2H), 4.21 (s, 3H). 13C NMR (101 MHz, DMSO d_6) δ 150.3, 143.1, 142.6, 137.3, 135.9, 131.3, 129.1,

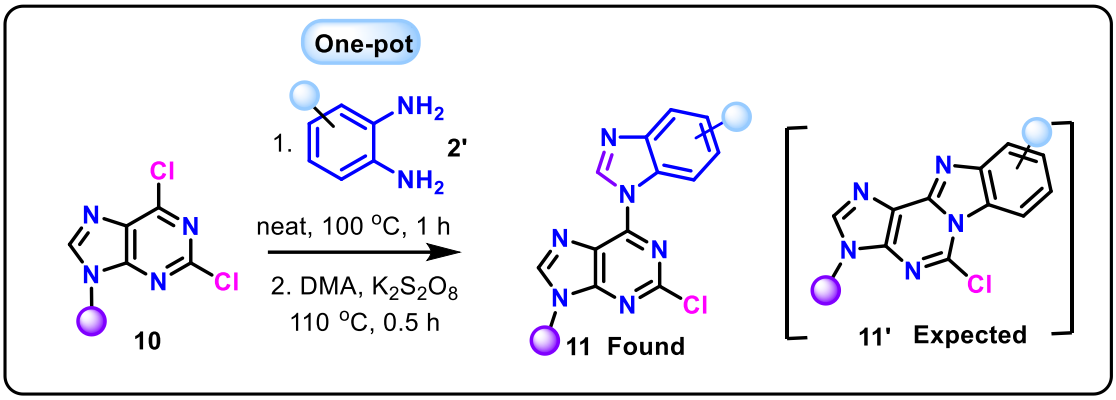
128.0, 127.7, 127.6, 121.7, 120.9, 117.3, 110.6, 109.4, 46.4, 31.9. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{19}N_6$ 331.1671; Found 331.1662.

N1-(9-benzyl-9H-purin-6-yl)-N2,N2-dimethylbenzene-1,2-diamine (20)



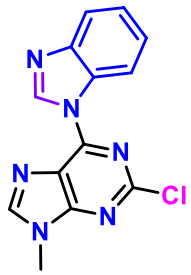
A white solid (42 mg, 60%): R_f 0.30 (Hex/EtOAc 7:3); mp 182-184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.61 (s, 1H), 7.87 (s, 1H), 7.40 – 7.32 (m, 5H), 7.25 (dd, *J* = 13.3, 7.4 Hz, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 5.44 (s, 2H), 2.79 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 152.7, 152.1, 149.7, 141.9, 140.5, 135.5, 133.6, 129.1, 128.4, 127.8, 125.1, 123.3, 120.7, 119.8, 47.3, 44.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{21}N_6$ 345.1828; Found 345.1826.

General procedure for the synthesis of benzimidazole attached purine derivatives (11a-j)



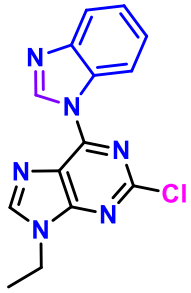
To a round-bottom flask, 2,6-dichloropurine derivatives **10** (1 mmol) and o-phenylenediamine derivative **2′** (1.5 mmol) were added. The reaction mixture was stirred neat in an oil bath at 100 °C for 1 h, subsequently, DMA (2 ml) and potassium persulfate ($K_2S_2O_8$) (2 eq) were added simultaneously to the reaction mixture, and stirring was continued at 110 °C temperature for 30 minutes. Upon completion of the reaction, the mixture was extracted with ice-cold water and ethyl acetate in the presence of a brine solution. The organic layer was dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure using a rotary evaporator. The crude product was then purified by column chromatography using ethyl acetate/hexane as the eluent, affording a series of desired compounds, denoted as **11**.

6-(1H-benzo[d]imidazol-1-yl)-2-chloro-9-methyl-9H-purine (11a)



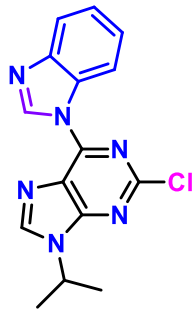
A white solid (42 mg, 60%): R_f 0.20 (Hex/EtOAc 3:2); mp 208-210 °C.^{1}H NMR (400 MHz, DMSO-d_6) δ 9.80 (s, 1H), 8.74 (s, 1H), 8.66 (s, 1H), 7.87 (s, 1H), 7.52 (d, J = 30.3 Hz, 2H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 155.0, 152.2, 148.0, 147.3, 144.0, 131.9, 131.7, 125.6, 125.1, 121.4, 120.6, 116.3, 30.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{10}ClN_6$ 285.0655; Found 285.0649.

6-(1H-benzo[d]imidazol-1-yl)-2-chloro-9-ethyl-9H-purine (11b)



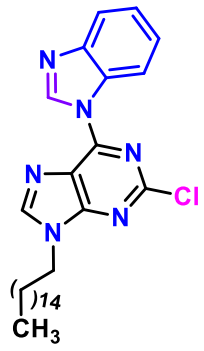
A white solid (44 mg, 65%): R_f 0.20 (Hex/EtOAc 3:2); mp 208-210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.82 (d, J = 8.1 Hz, 1H), 8.15 (s, 1H), 7.93 (d, J = 7.7 Hz, 1H), 7.51 (dt, J = 22.7, 7.3 Hz, 2H), 4.41 (q, J = 7.3 Hz, 2H), 1.67 (t, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2, 153.6, 150.1, 143.6, 125.3, 124.7, 121.6, 120.5, 116.8, 39.4, 15.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{12}ClN_6$ 299.0812; Found 299.0804.

6-(1H-benzo[d]imidazol-1-yl)-9-(tert-butyl)-2-chloro-9H-purine (11c)



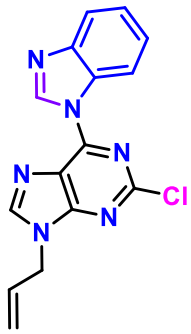
A white solid (39 mg, 58%): R_f 0.20 (Hex/EtOAc 3:2); mp 208-210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.80 (d, J = 8.0 Hz, 1H), 8.19 (s, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.59 – 7.44 (m, 2H), 5.01 (dt, J = 13.6, 6.8 Hz, 1H), 1.72 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 153.3, 147.9, 143.8, 141.8, 131.7, 125.3, 124.8, 121.8, 120.4, 116.7, 47.9, 22.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{14}ClN_6$ 313.0968; Found 313.0961.

6-(1H-benzo[d]imidazol-1-yl)-2-chloro-9-hexadecyl-9H-purine (11d)



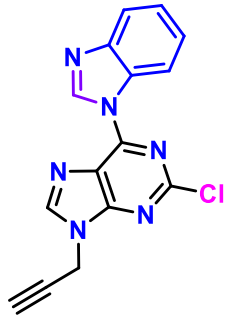
A white solid (33 mg, 56%): R_f 0.20 (Hex/EtOAc 3:2); mp 208-210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.72 (s, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.16 – 7.08 (m, 1H), 6.89 – 6.81 (m, 2H), 4.14 (t, J = 7.2 Hz, 2H), 1.90 – 1.79 (m, 2H), 1.27 (s, 24H), 0.89 (t, J = 6.8 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3, 153.6, 150.9, 141.4, 140.8, 127.2, 126.1, 124.4, 119.3, 118.8, 117.7, 44.0, 31.9, 29.9, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 29.0, 26.5, 22.7, 14.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{40}ClN_6$ 495.3003; Found 495.3010.

9-allyl-6-(1H-benzo[d]imidazol-1-yl)-2-chloro-9H-purine (11e)



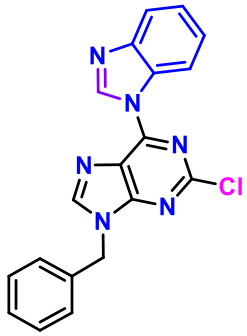
A white solid (41 mg, 62%): R_f 0.20 (Hex/EtOAc 3:2); mp 208-210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (s, 1H), 8.85 – 8.72 (m, 1H), 8.11 (s, 1H), 7.48 (dtd, *J* = 21.8, 7.4, 1.2 Hz, 2H), 6.10 (ddt, *J* = 16.2, 10.2, 5.9 Hz, 1H), 5.44 (dd, *J* = 10.2, 0.6 Hz, 1H), 5.40 – 5.28 (m, 1H), 4.93 (dt, *J* = 5.9, 1.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2, 153.8, 148.0, 144.0, 143.9, 143.7, 131.7, 130.8, 125.3, 124.8, 121.3, 120.5, 120.3, 116.6, 46.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{12}ClN_6$ 311.0812; Found 311.0805.

6-(1H-benzo[d]imidazol-1-yl)-2-chloro-9-(prop-2-yn-1-yl)-9H-purine (11f)



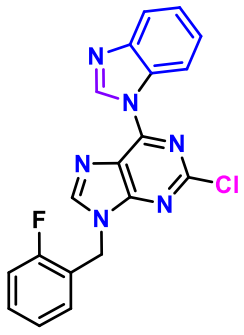
A white solid (42 mg, 64%): R_f 0.20 (Hex/EtOAc 3:2); mp 208-210 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 8.84 (s, 1H), 8.62 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 1H), 5.26 (d, *J* = 2.4 Hz, 2H), 3.63 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 154.2, 152.4, 147.7, 146.6, 144.0, 131.7, 125.6, 125.1, 121.8, 120.7, 116.4, 33.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{10}ClN_6$ 309.0655; Found 309.0650.

6-(1H-benzo[d]imidazol-1-yl)-9-benzyl-2-chloro-9H-purine (11g)



A white solid (37 mg, 58%): R_f 0.20 (Hex/EtOAc 3:2); mp 208-210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (s, 1H), 8.80 (d, *J* = 8.0 Hz, 1H), 8.05 (s, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.57 – 7.34 (m, 7H), 5.49 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 153.9, 148.1, 144.0, 143.9, 143.7, 134.3, 131.7, 129.3, 129.0, 128.1, 125.3, 124.8, 121.3, 120.5, 116.7, 47.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{14}ClN_6$ 361.0968; Found 361.0970.

6-(1H-benzo[d]imidazol-1-yl)-2-chloro-9-(2-fluorobenzyl)-9H-purine (11h)

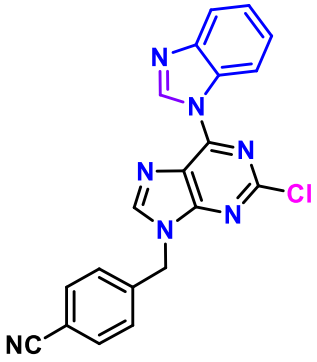


A white solid (33 mg, 52%): R_f 0.20 (Hex/EtOAc 3:2); mp 208-210 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 8.86 (s, 1H), 8.62 (d, *J* = 7.9 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.45 (dd, *J* = 14.0, 7.1 Hz, 2H), 7.36 (d, *J* = 7.1 Hz, 1H), 7.24 (dd, *J* = 16.0, 8.5 Hz, 1H), 5.64 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.7, 159.0, 154.7, 152.4, 147.4 (d, J = 35.0 Hz, 1C), 143.9 (d, J = 8.0 Hz, 1C), 131.4 (d, J = 8.0 Hz, 1C), 131.0, 130.6,125.2 (t, J = 45.0 Hz, 1C), 123.1, 122.9, 121.8,

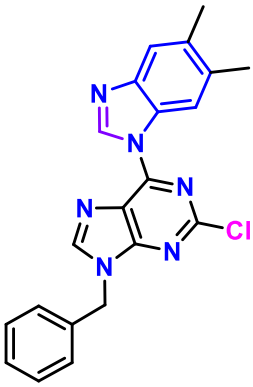
120.6, 116.3 (d, J = 16.0 Hz, 1C), 116.03, 41.8.^{19}F NMR (377 MHz, DMSO) δ -117.5 (s). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{13}ClFN_6$ 379.0874; Found 379.0866.

4-((6-(1H-benzo[d]imidazol-1-yl)-2-chloro-9H-purin-9-yl)methyl)benzonitrile (11i)

A white solid (34 mg, 55%): R_f 0.20 (Hex/EtOAc 3:2); mp 208-210 °C.^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 8.91 (s, 1H), 8.63 (d, J = 8.1 Hz, 1H), 7.87 (t, J = 6.7 Hz, 3H), 7.59 – 7.51 (m, 3H), 7.48 (d, J = 7.6 Hz, 1H), 5.69 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 154.7, 152.4, 147.7, 147.3, 144.0, 141.7, 133.2, 131.7, 128.8, 125.6, 125.5, 125.2, 125.0, 121.9, 120.6, 119.0, 116.3, 111.3, 46.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{13}ClN_7$ 386.0921; Found 386.0914.

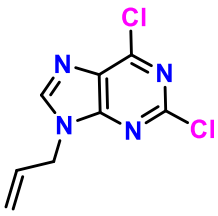


9-benzyl-2-chloro-6-(5,6-dimethyl-1H-benzo[d]imidazol-1-yl)-9H-purine (11j)



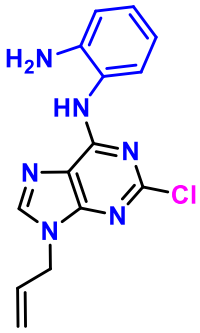
A white solid (48 mg, 70%): R_f 0.20 (Hex/EtOAc 3:2); mp 218-220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.65 (s, 1H), 8.87 (s, 1H), 8.35 (s, 1H), 7.58 (s, 1H), 7.40 (s, 1H), 7.39 (s, 3H), 7.34 (dd, J = 8.9, 4.5 Hz, 1H), 5.56 (s, 2H), 2.40 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 154.6, 152.4, 147.7, 147.1, 143.2, 142.5, 136.3, 134.1, 133.6, 130.1, 129.3, 128.6, 128.1, 121.7, 120.6, 116.5, 47.3, 20.9, 20.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{18}ClN_6$ 389.1281; Found 389.1248.

9-allyl-2,6-dichloro-9H-purine (10′)



A colourless liquid (39 mg, 65%): R_f 0.30 (Hex/EtOAc 3:2); mp 160-162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 6.05 (ddt, J = 16.3, 10.3, 5.9 Hz, 1H), 5.42 (d, J = 10.2 Hz, 1H), 5.31 (d, J = 17.0 Hz, 1H), 4.89 (d, J = 5.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 151.8, 145.5, 130.6, 130.4, 120.5, 46.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_8H_7Cl_2N_4$ 229.0048; Found 229.0042.

N1-(9-allyl-2-chloro-9H-purin-6-yl)benzene-1,2-diamine (12)



A grey solid (52 mg, 80%): R_f 0.30 (Hex/EtOAc 2:3); mp 182-184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.73 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.18 – 7.04 (m, 1H), 6.97 – 6.75 (m, 2H), 6.11 – 5.89 (m, 1H), 5.39 – 5.28 (m, 1H), 5.23 (d, *J* = 17.1 Hz, 1H), 4.77 (d, *J* = 5.8 Hz, 2H), 3.44 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 153.6, 141.3, 140.8, 131.4, 127.3, 126.0, 124.4, 119.4, 119.4, 118.8, 117.7, 45.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{14}ClN_6$ 301.0968; Found 301.0961.

6. References

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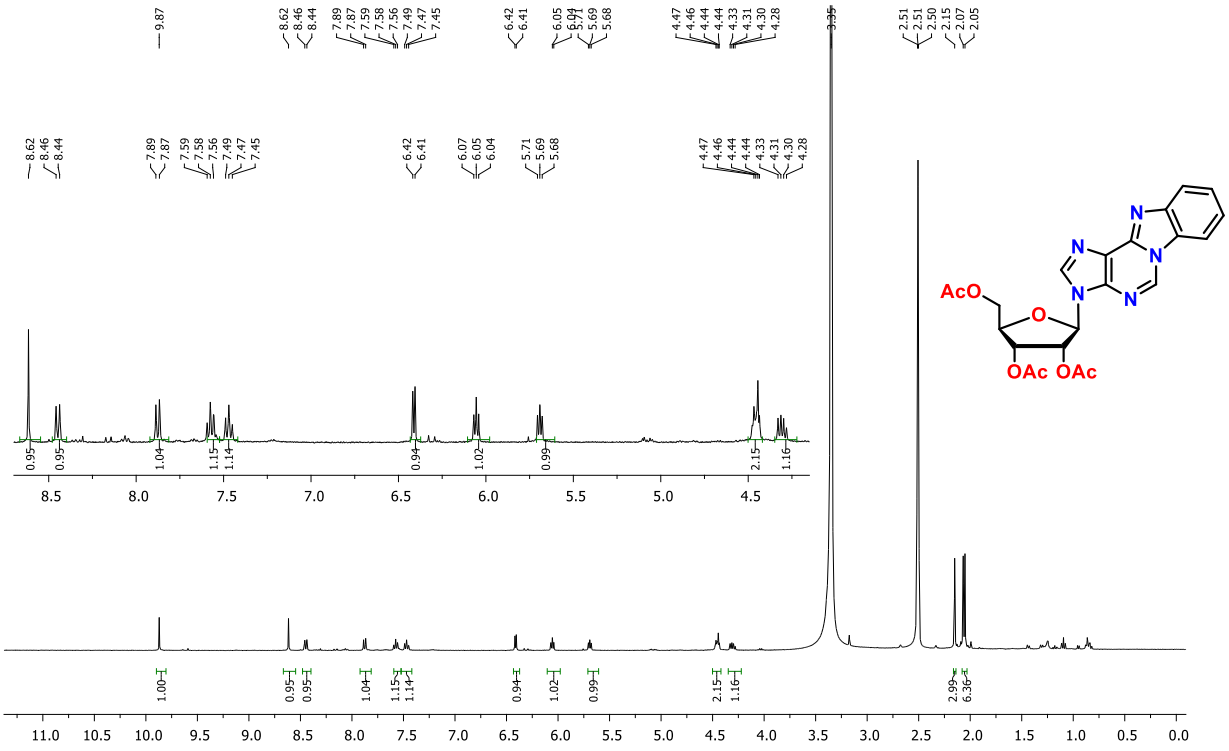
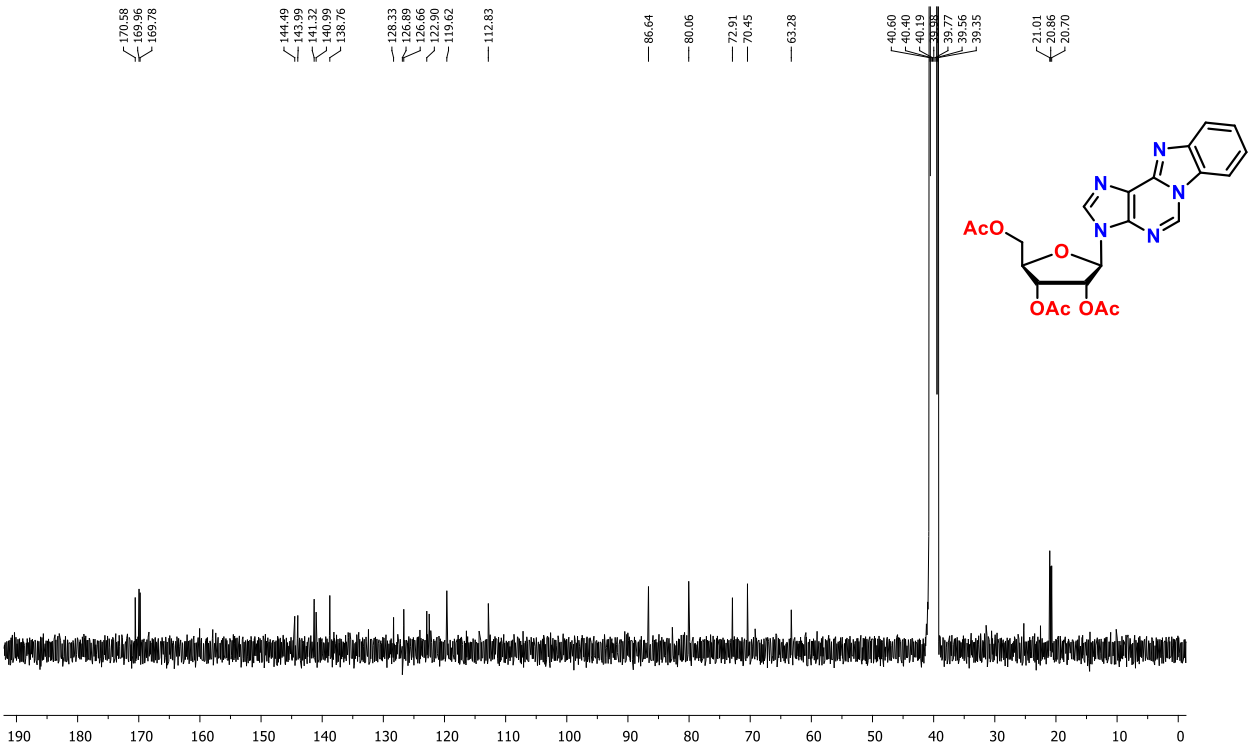
7. ^{1}H-NMR, ^{13}C-NMR, and ^{19}F-NMR spectra

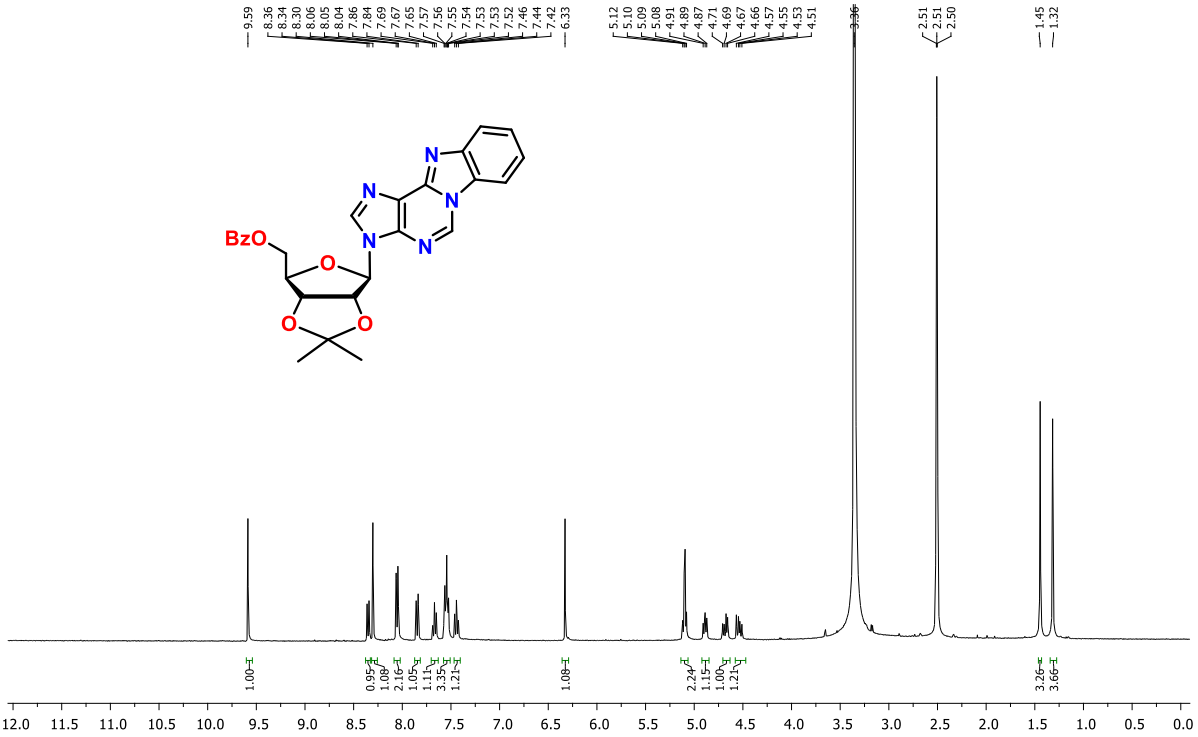
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound (5a)



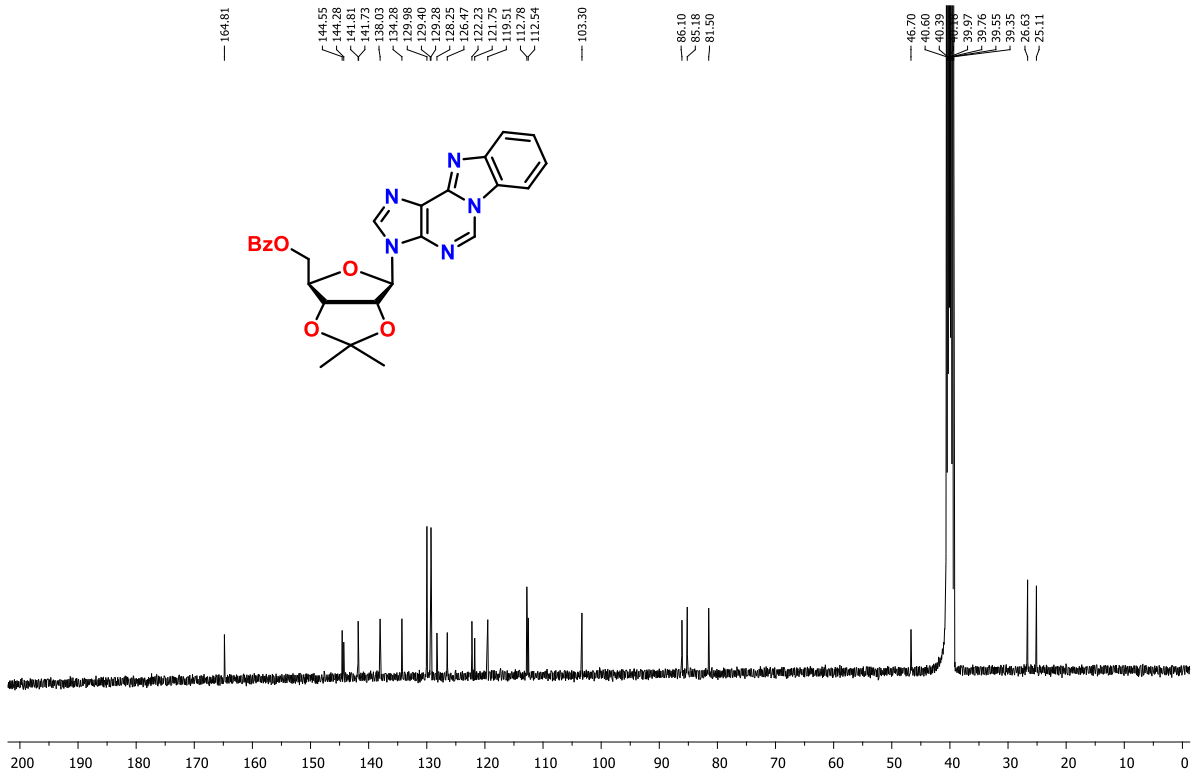
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5a)



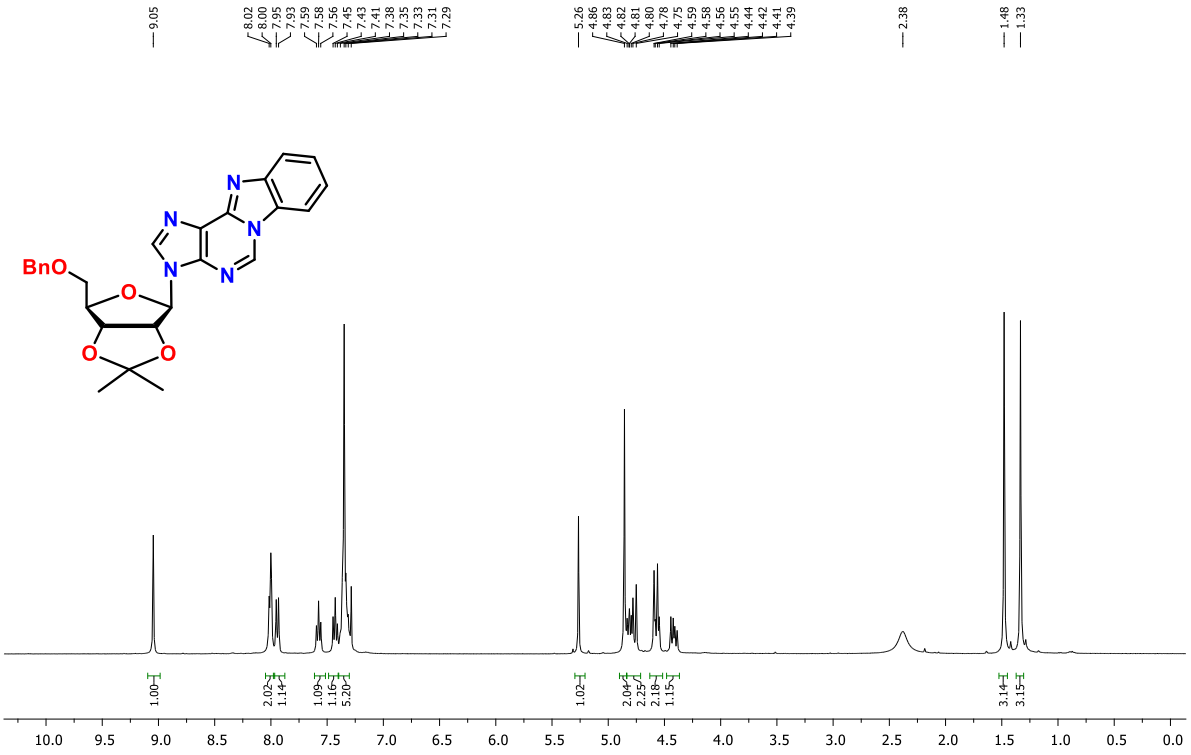
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5b)



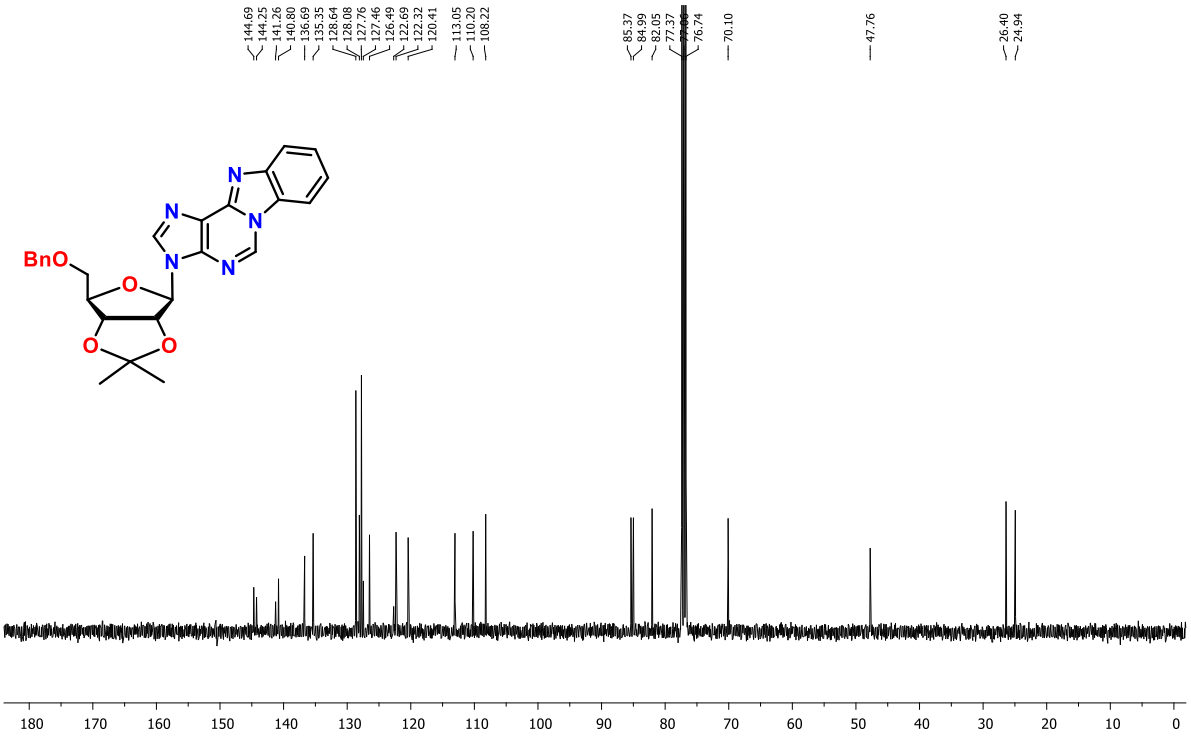
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5b)



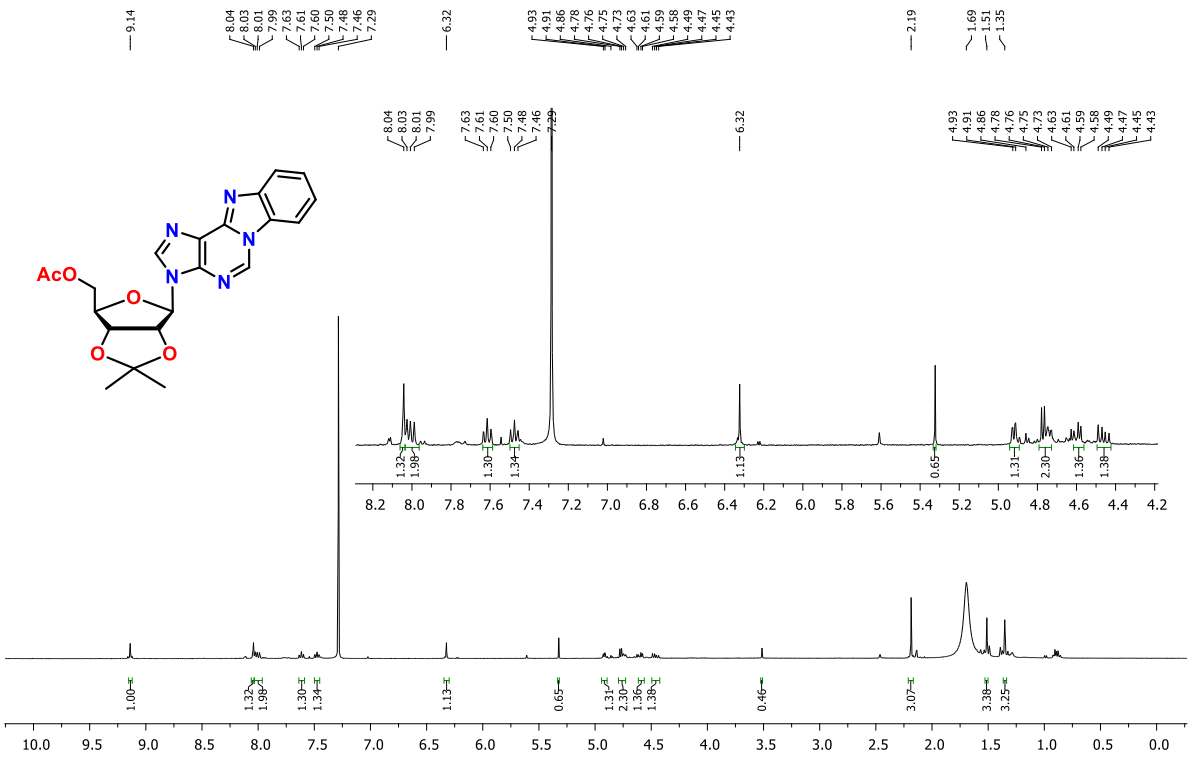
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (5c)



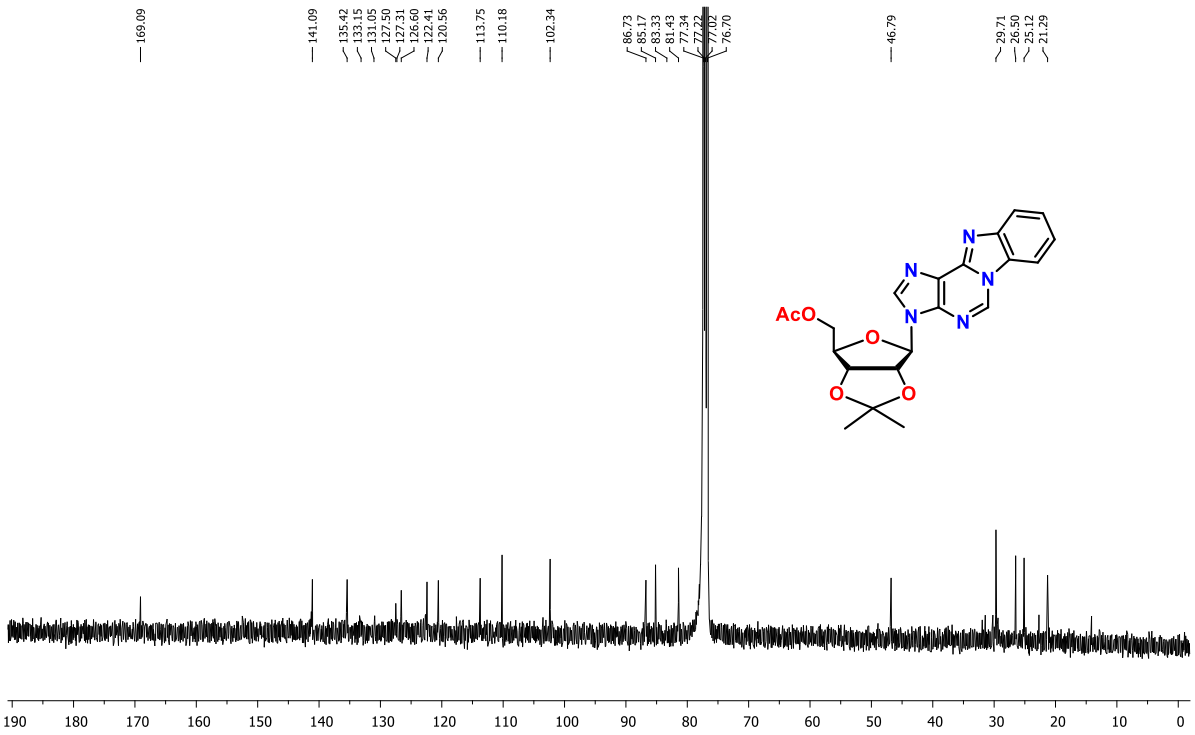
^{13}C NMR (101 MHz, $CDCl_3$) spectrum of compound (5c)



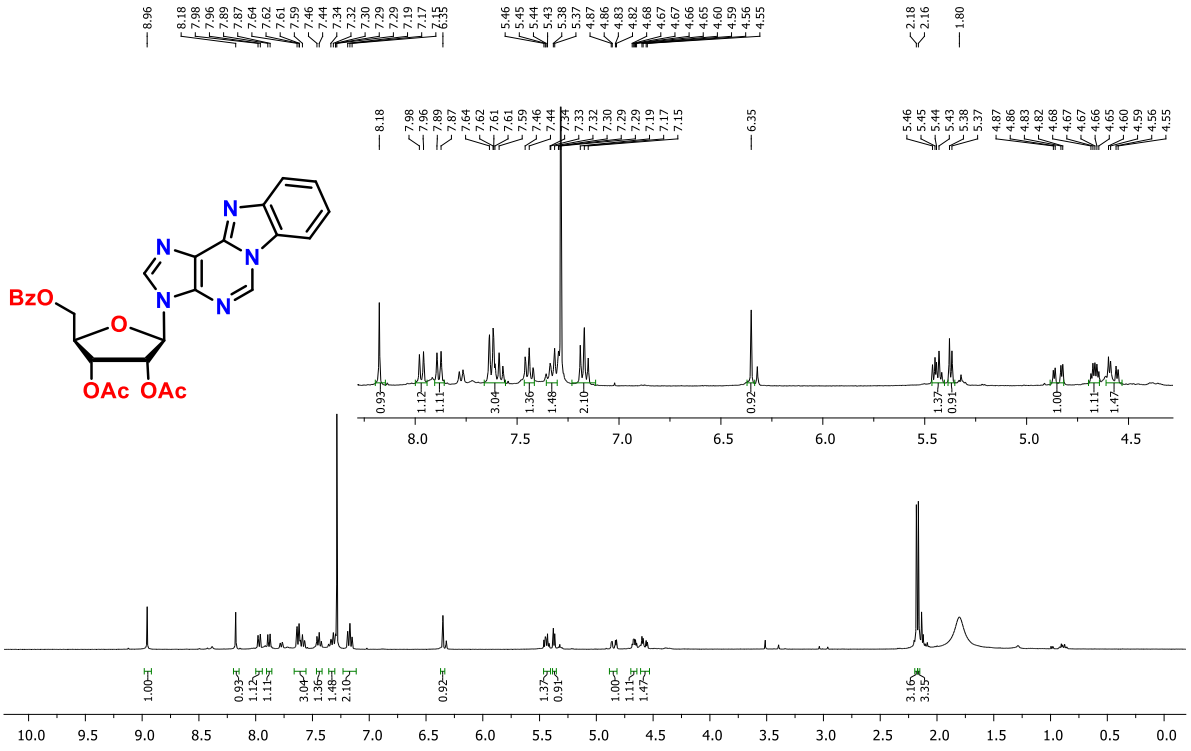
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (5d)



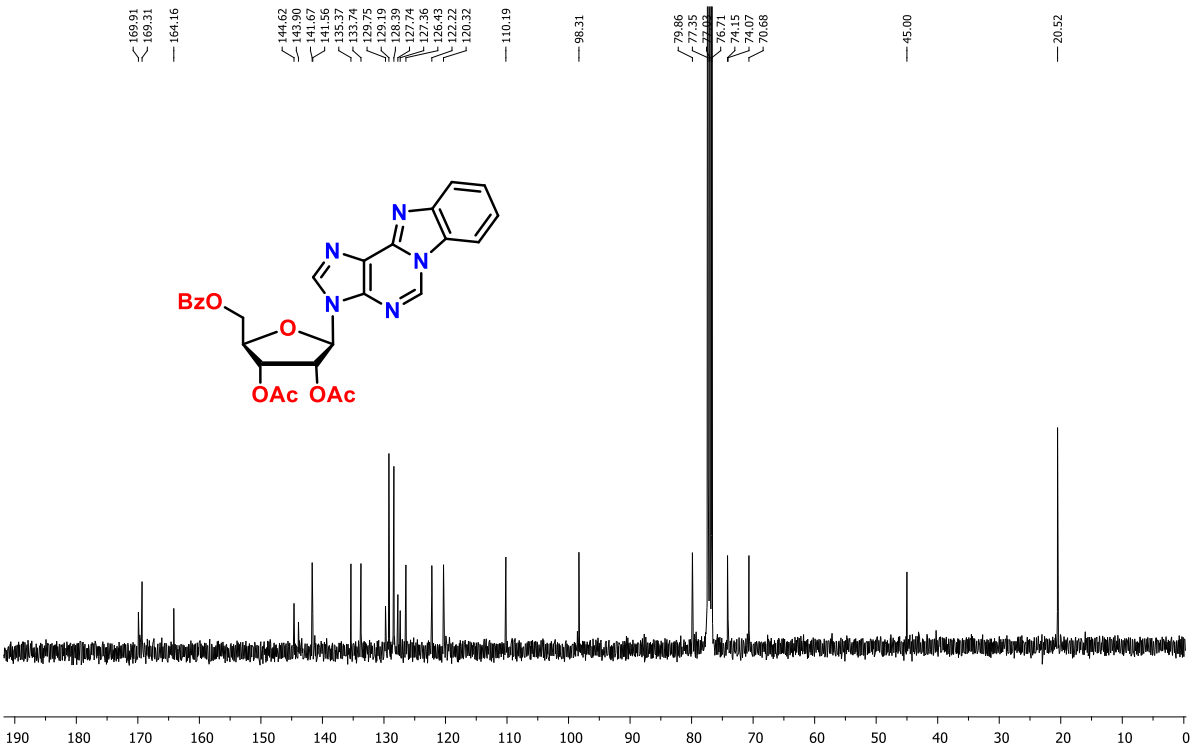
^{13}C NMR (101 MHz, $CDCl_3$) spectrum of compound (5d)



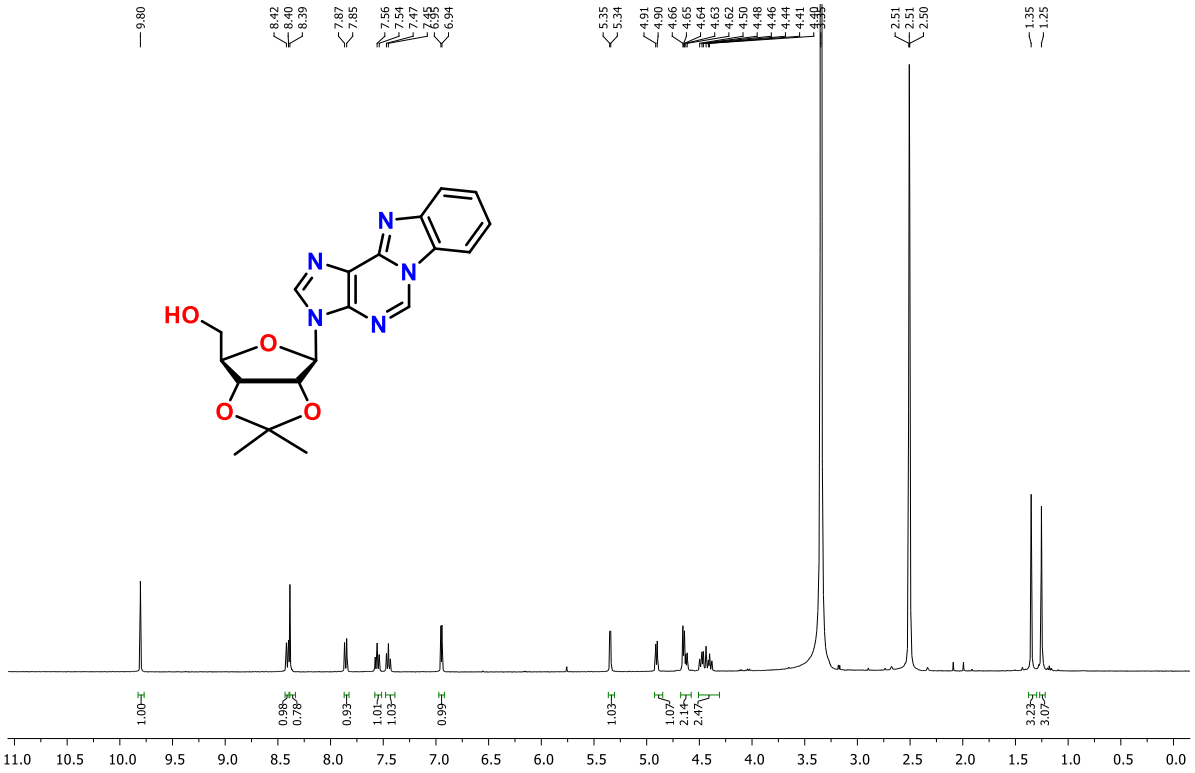
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (5e)



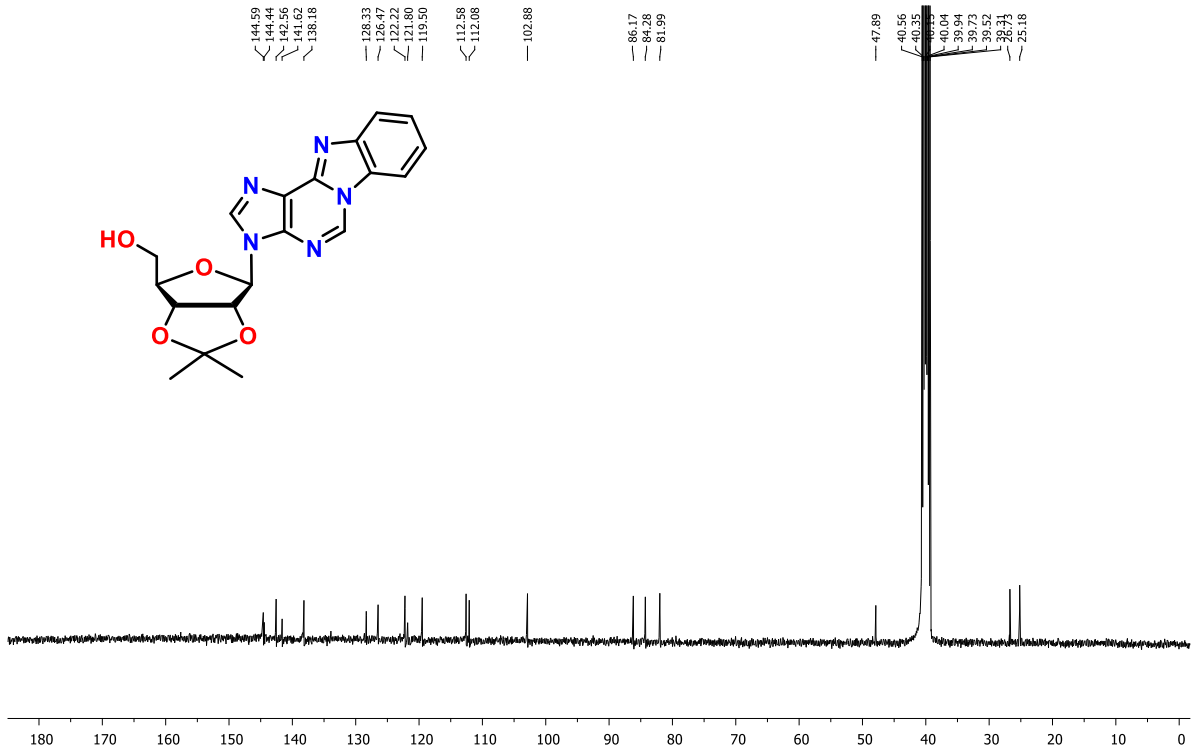
^{13}C NMR (101 MHz, $CDCl_3$) spectrum of compound (5e)



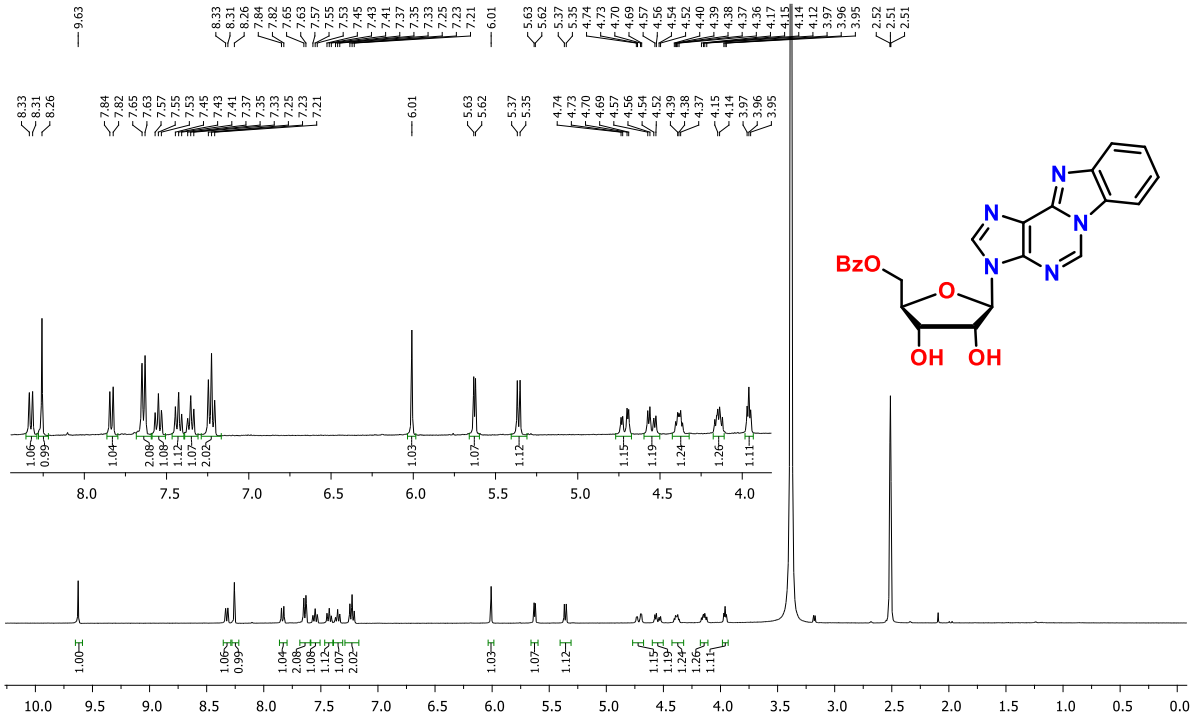
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5f)



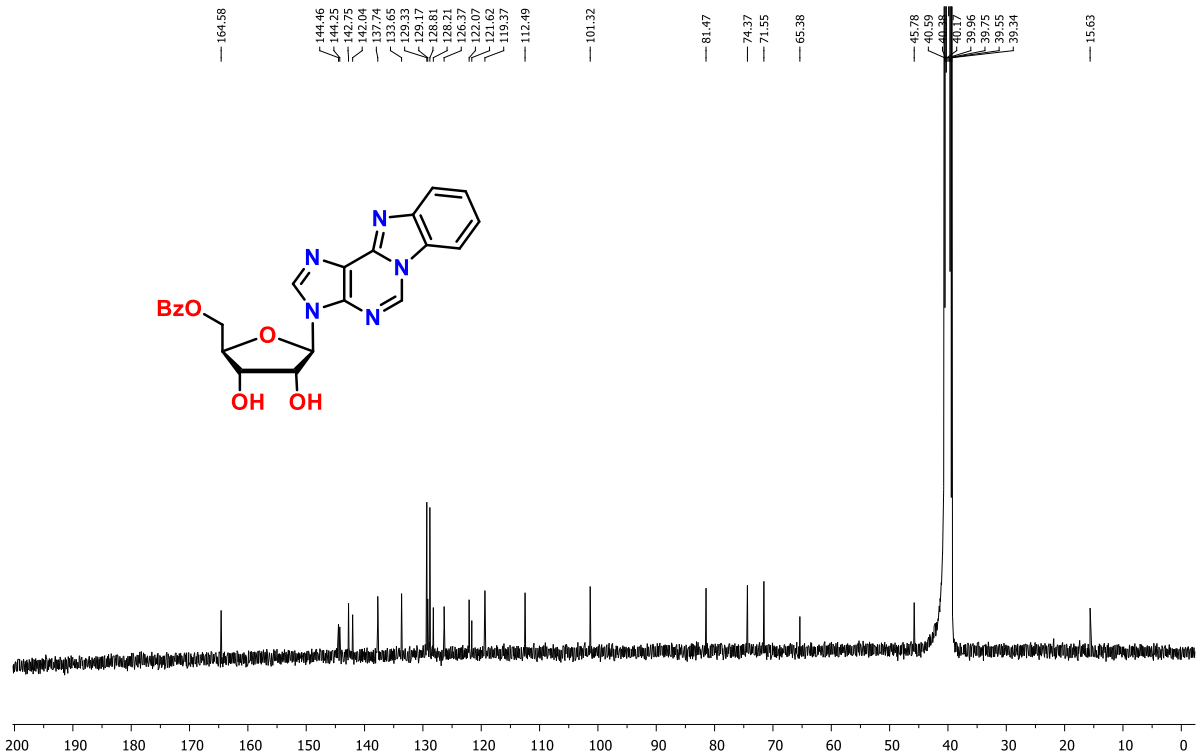
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5f)



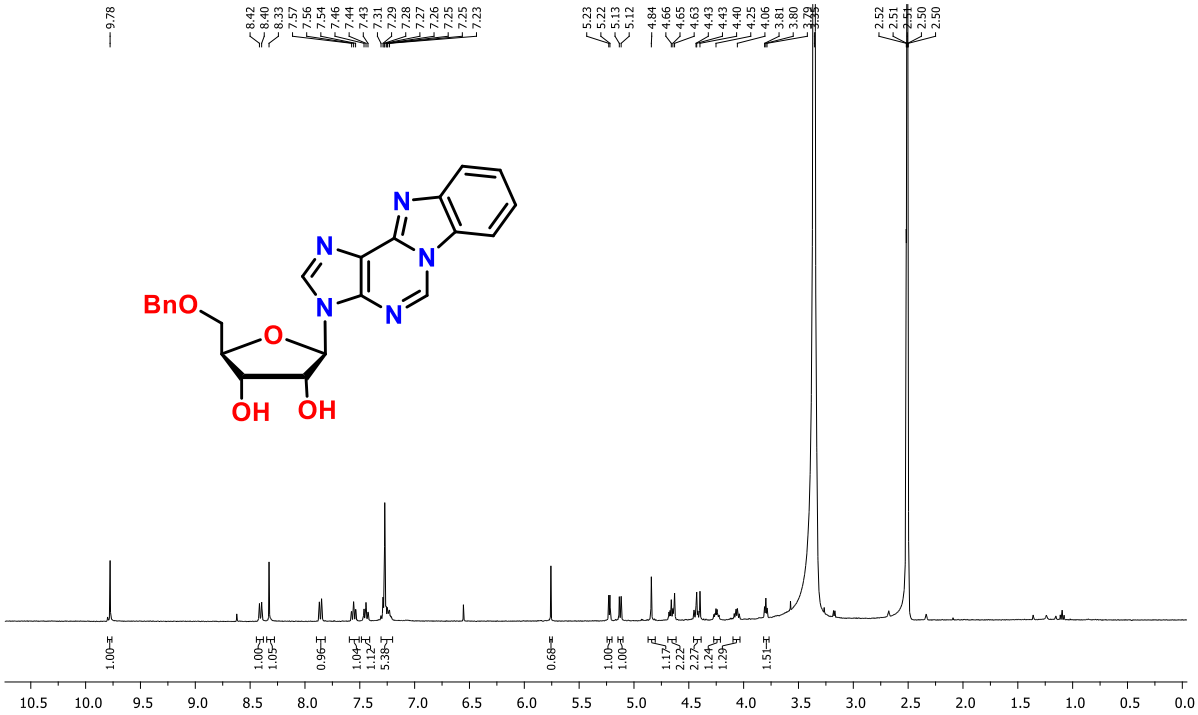
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5g)



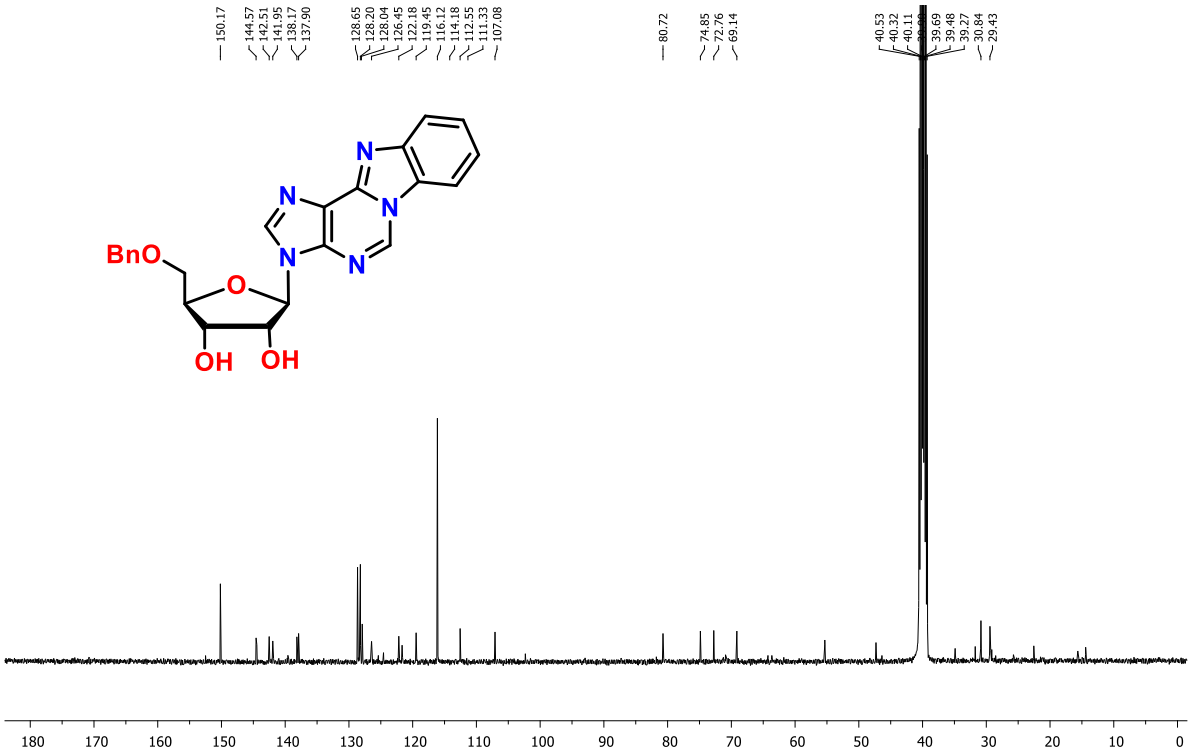
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5g)



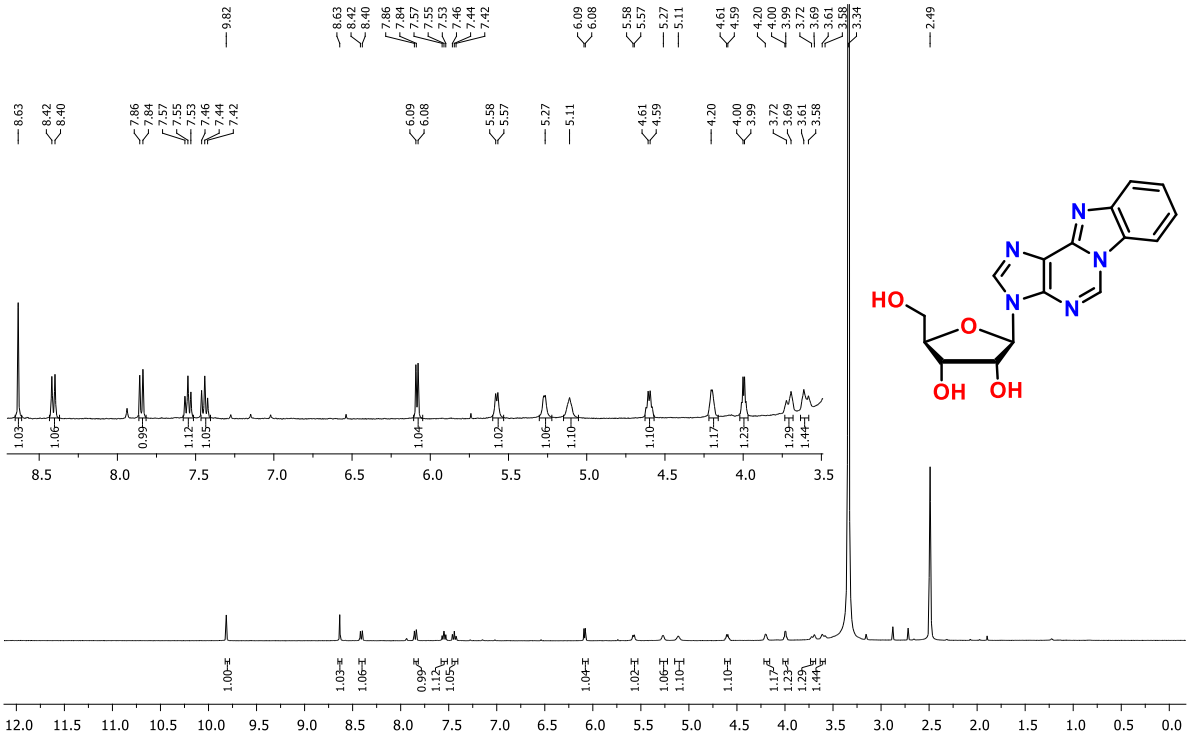
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5h)



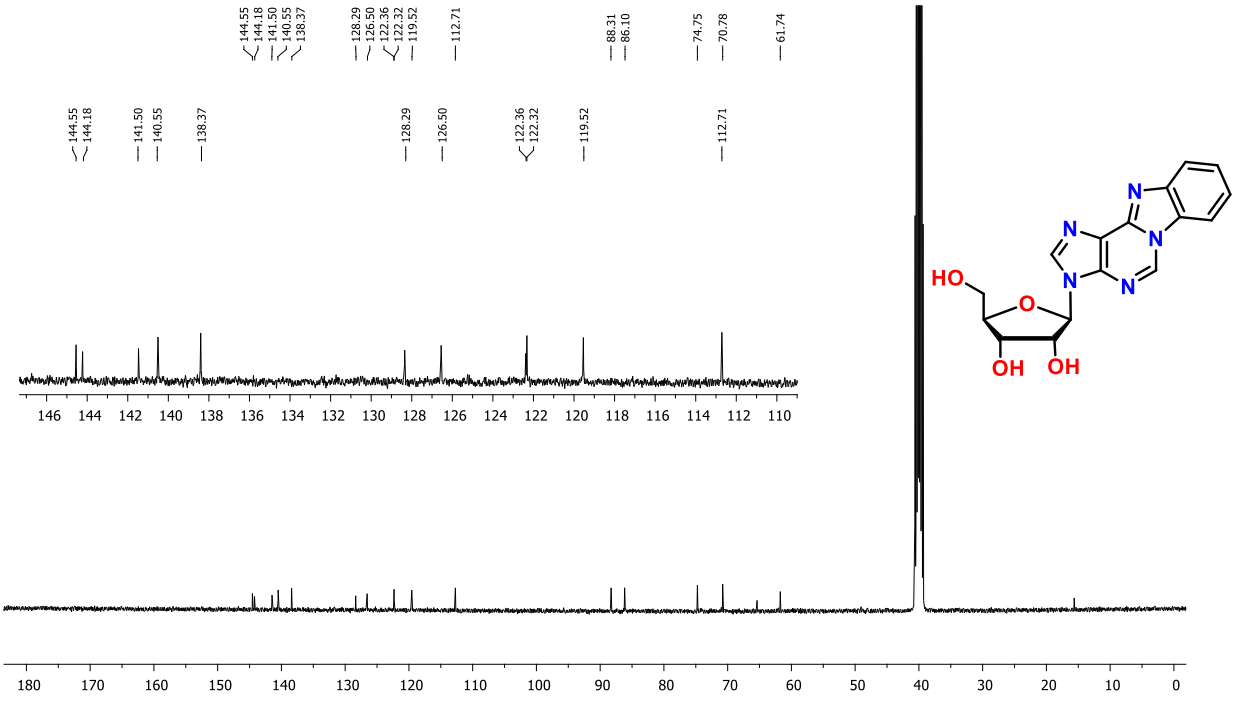
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5h)



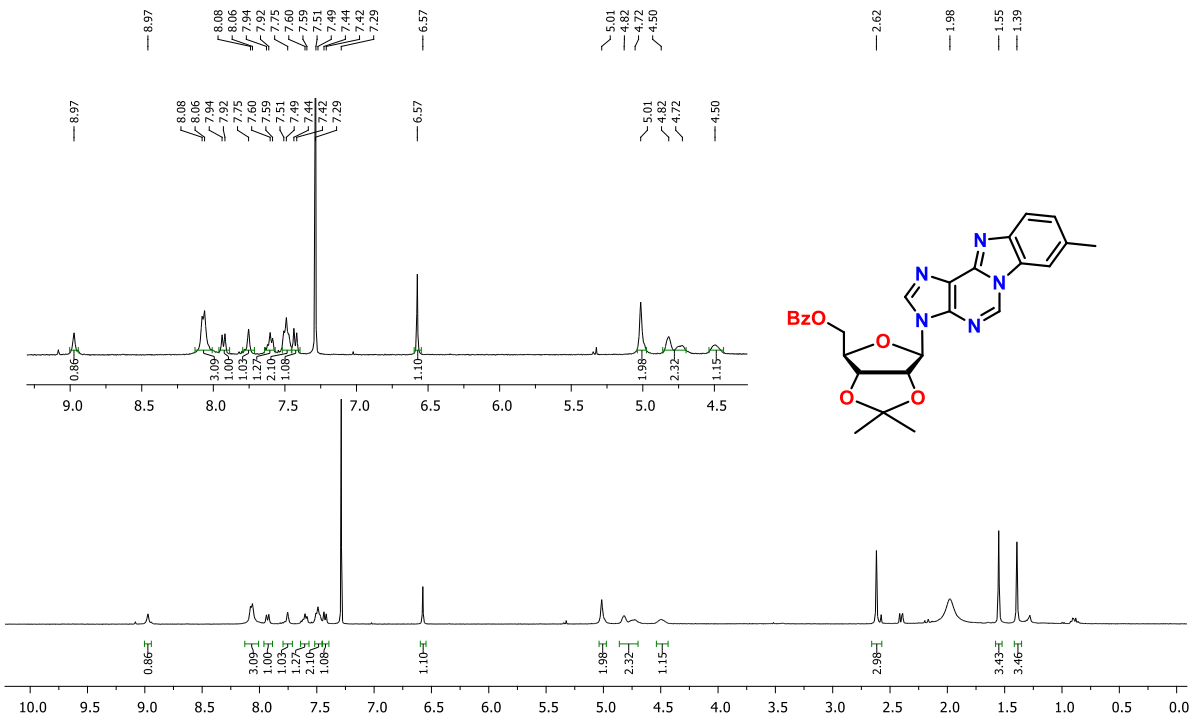
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5i)



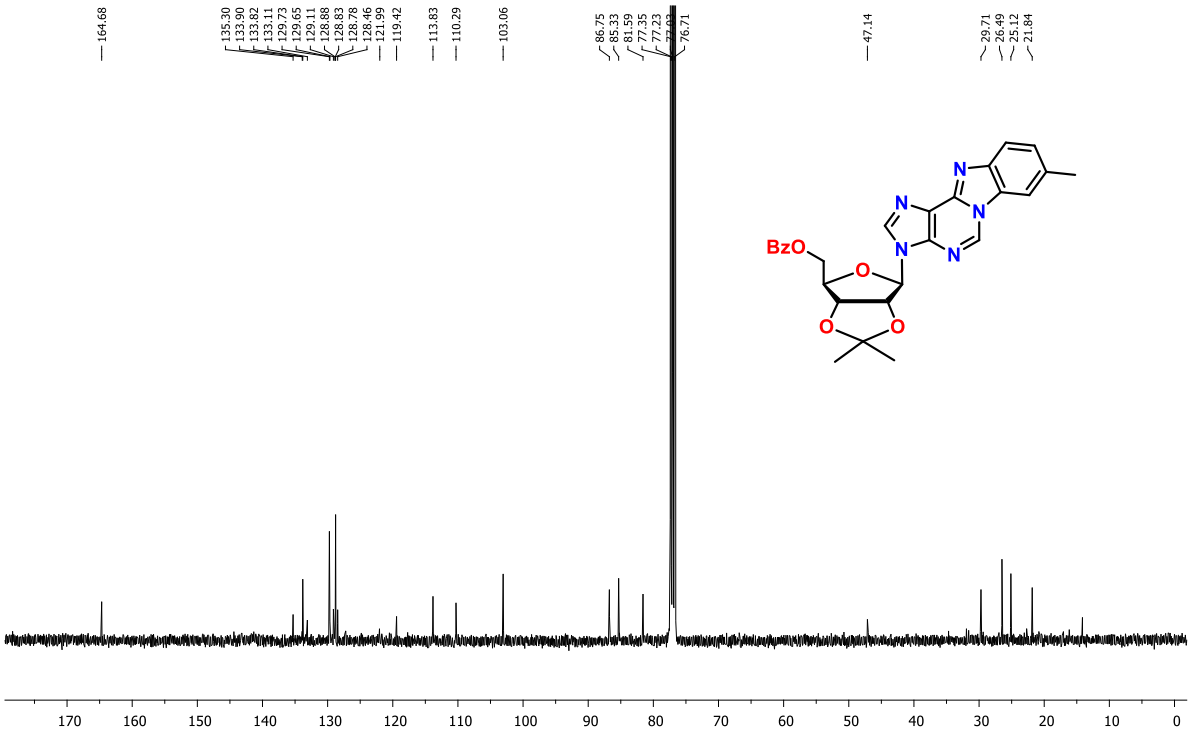
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5i)



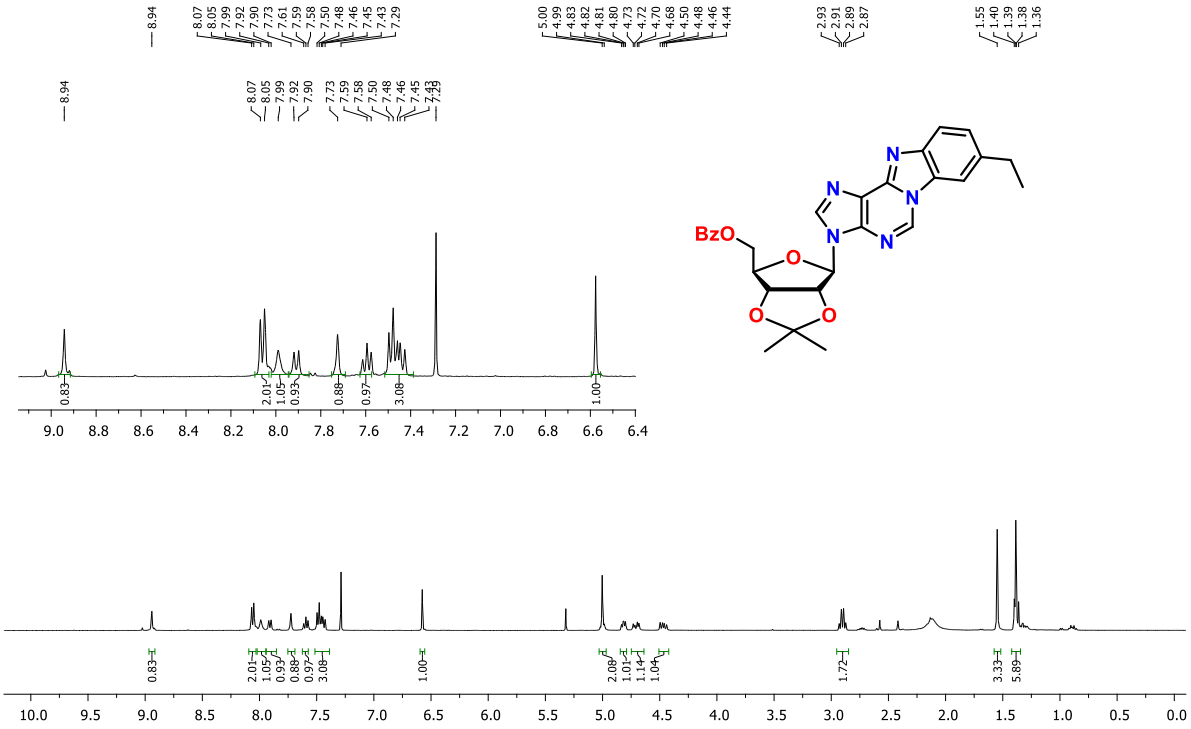
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (5j)



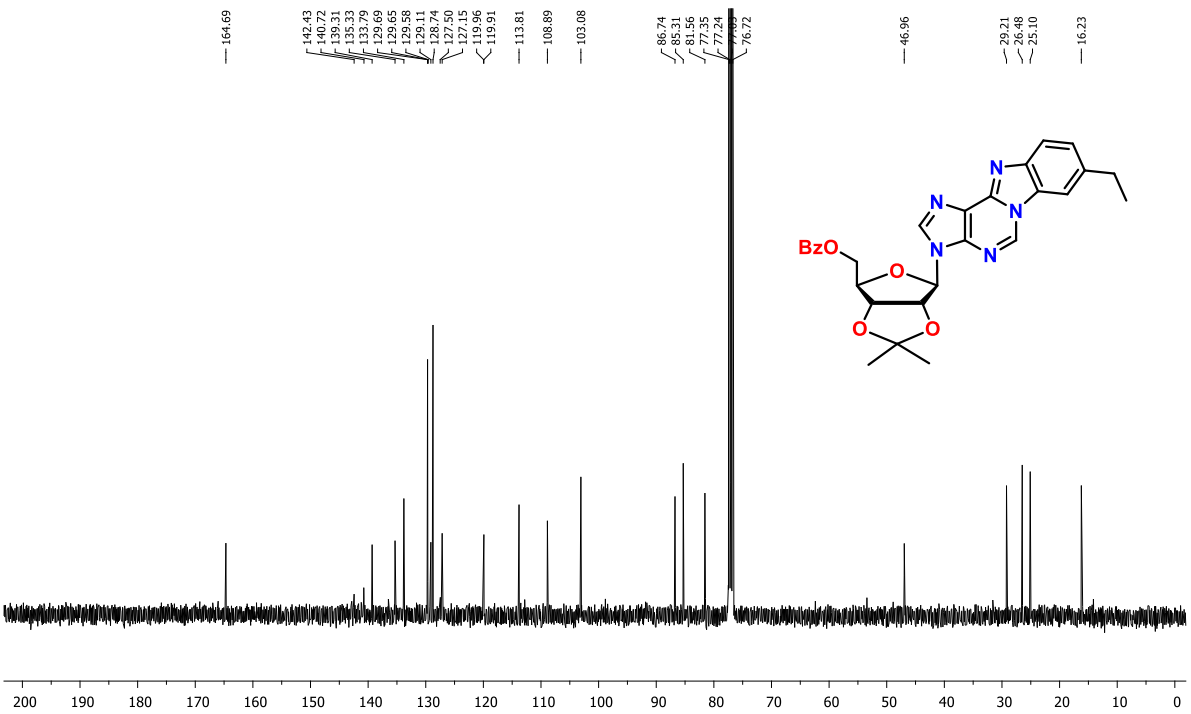
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (5j)



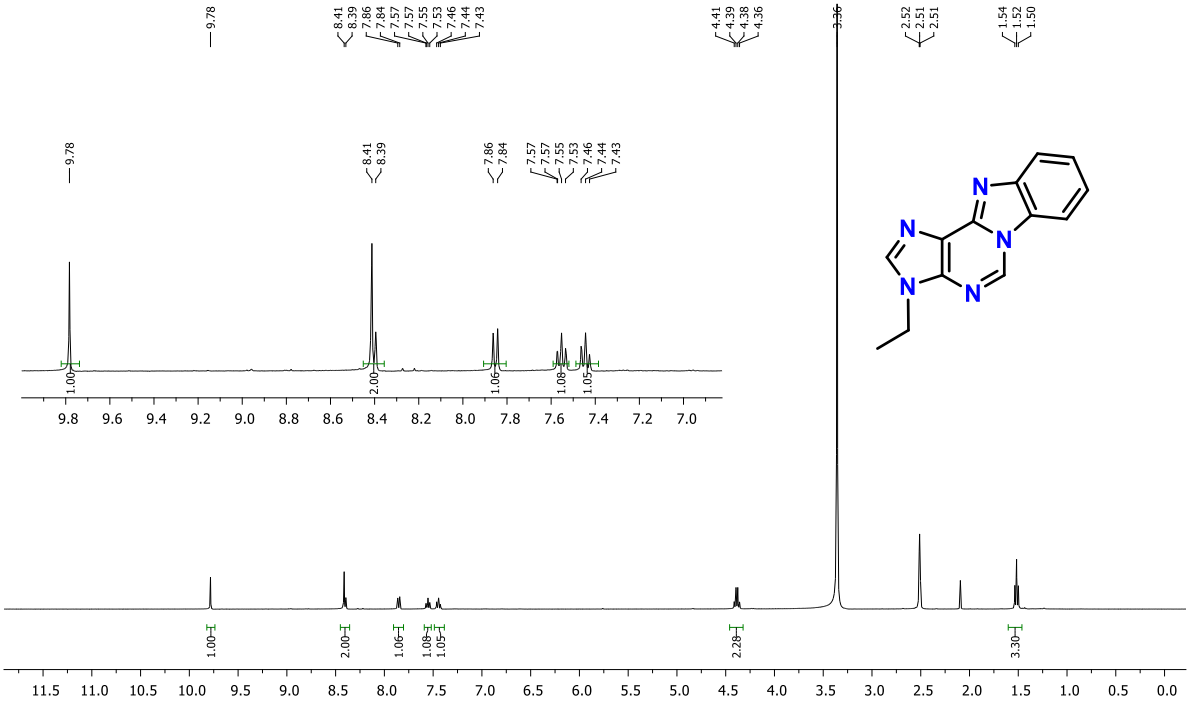
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (5k)



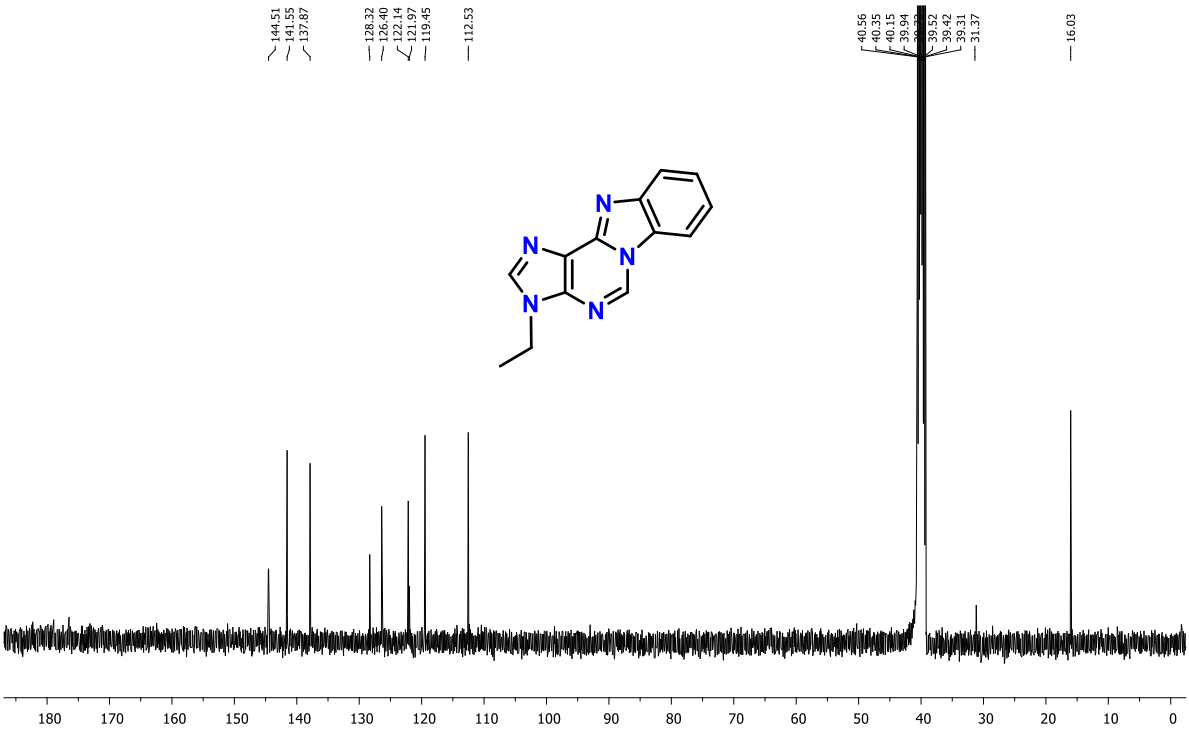
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (5k)



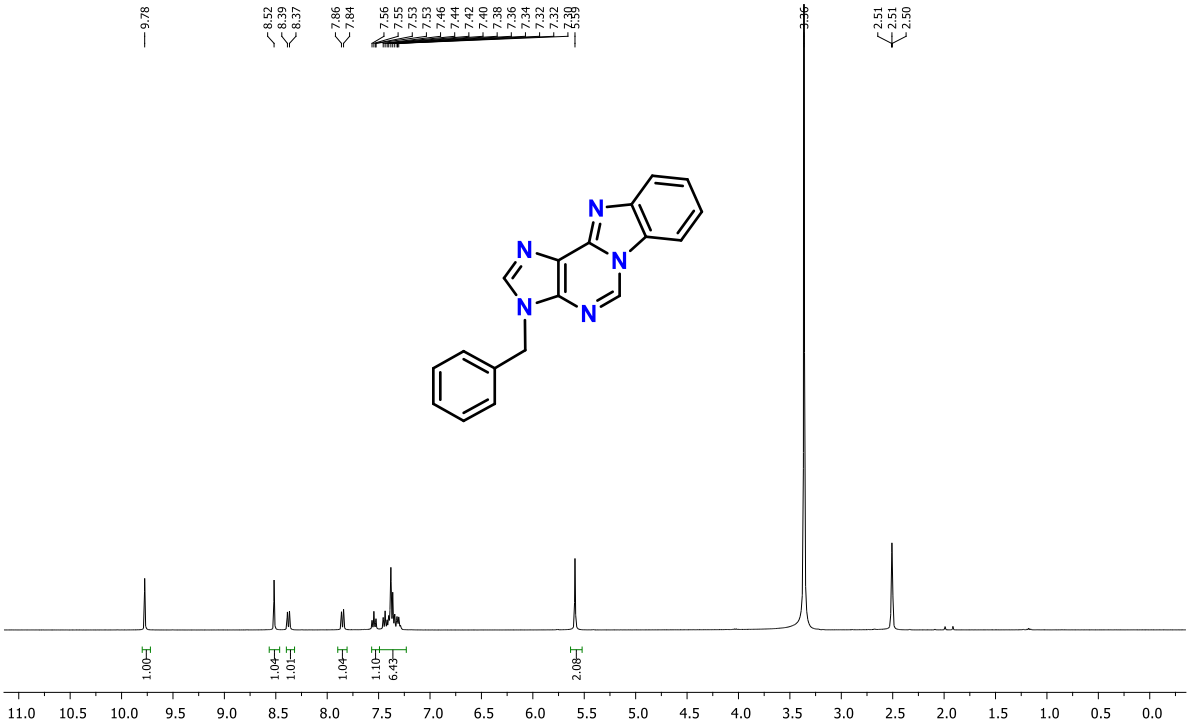
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5m)



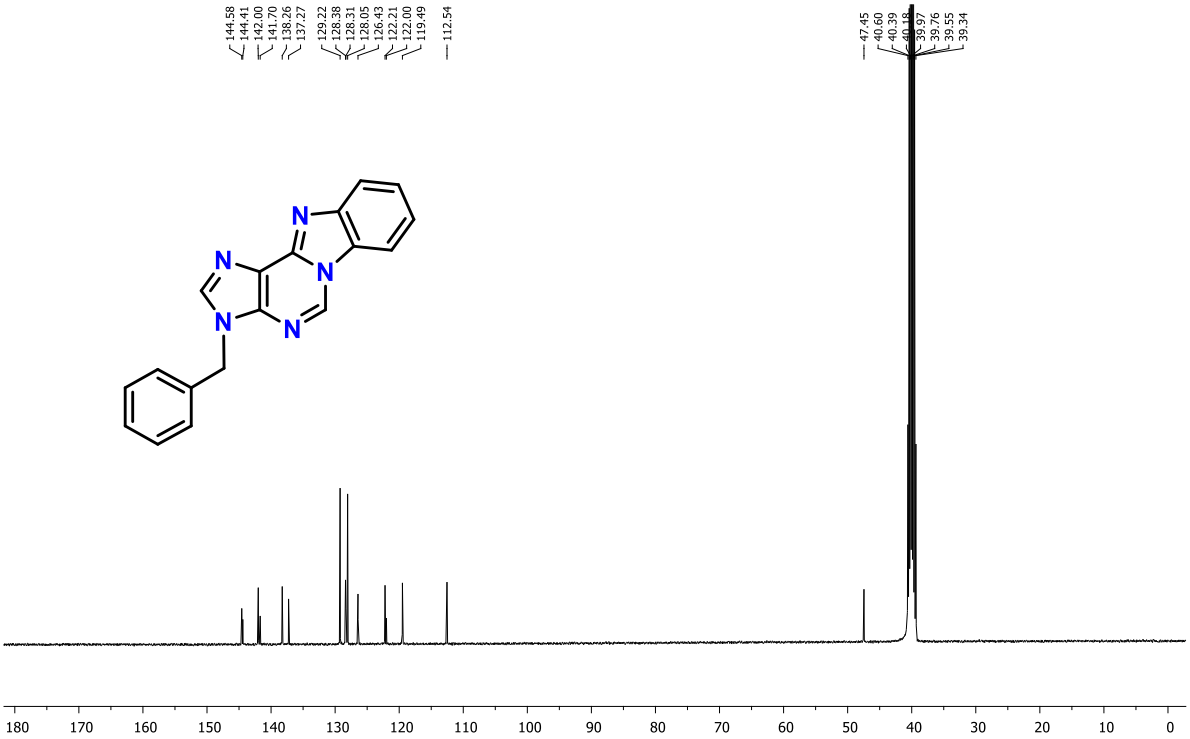
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5m)



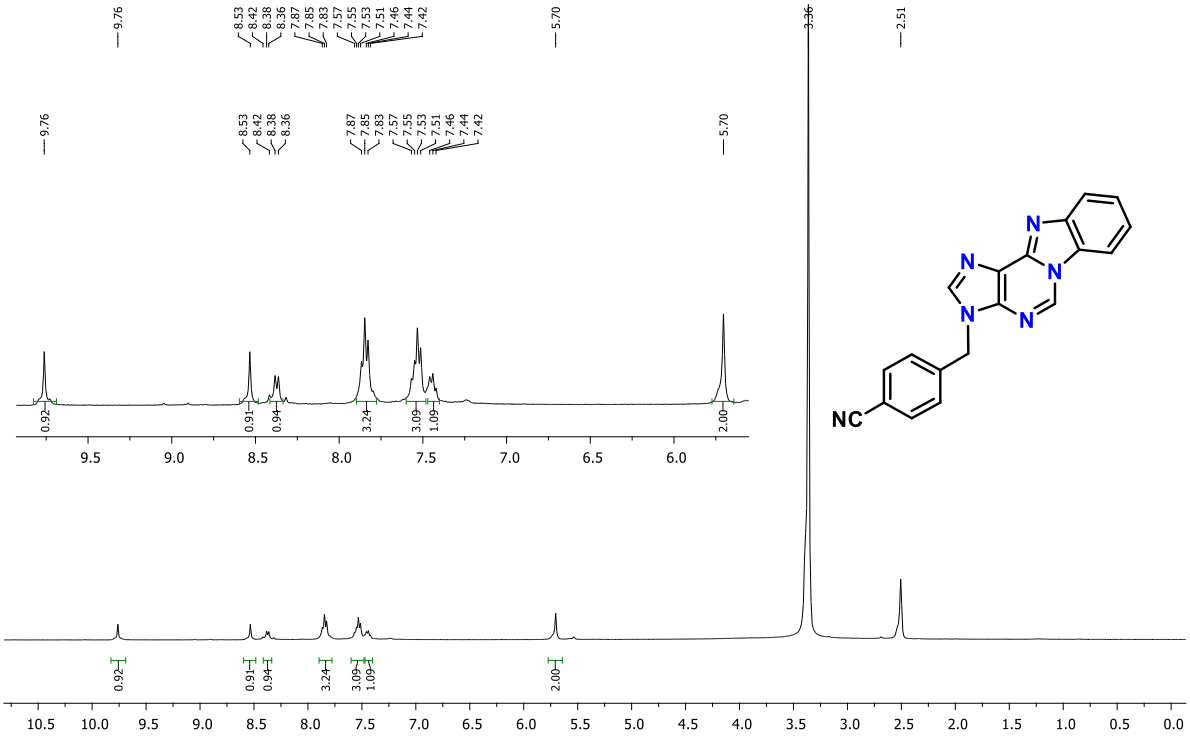
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5n)



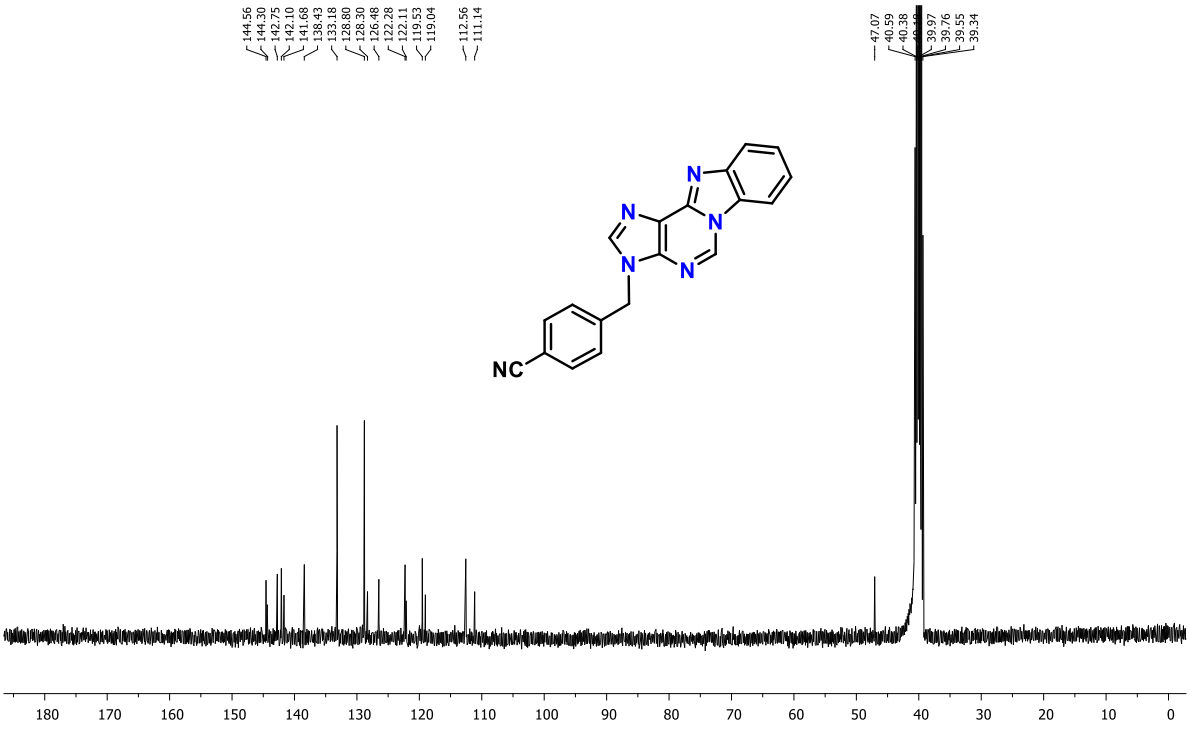
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5n)



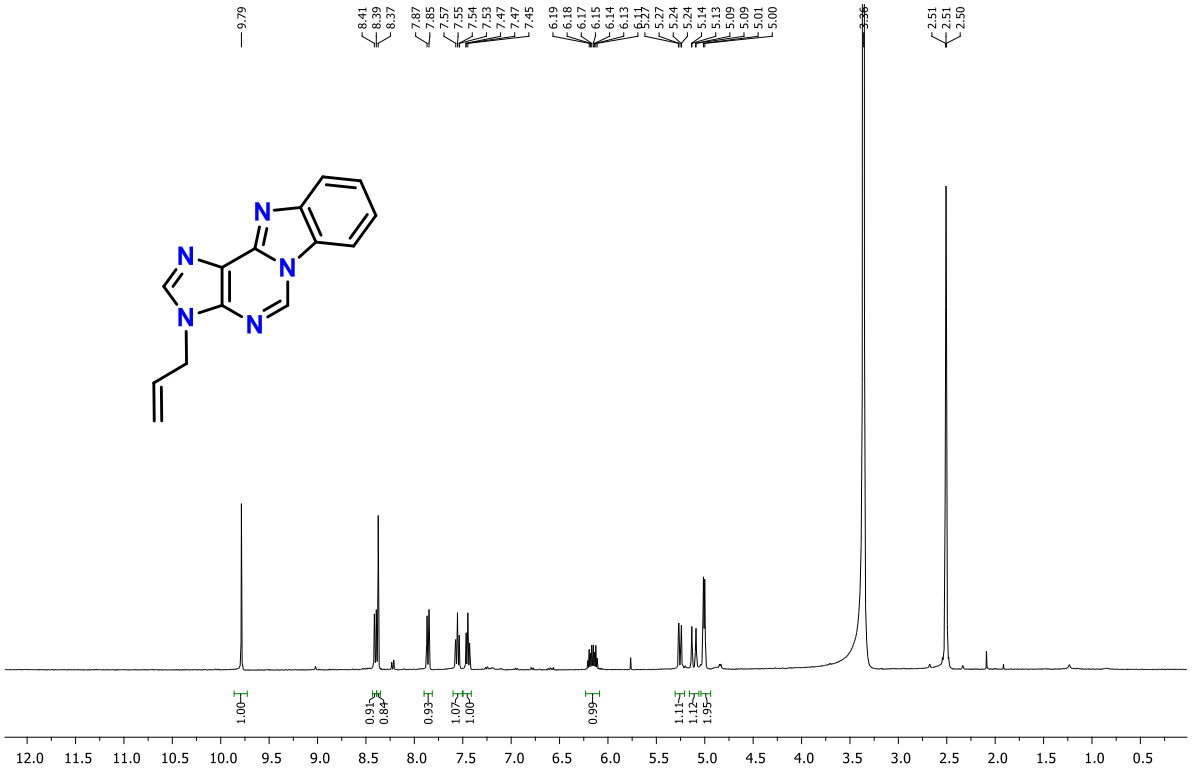
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5o)



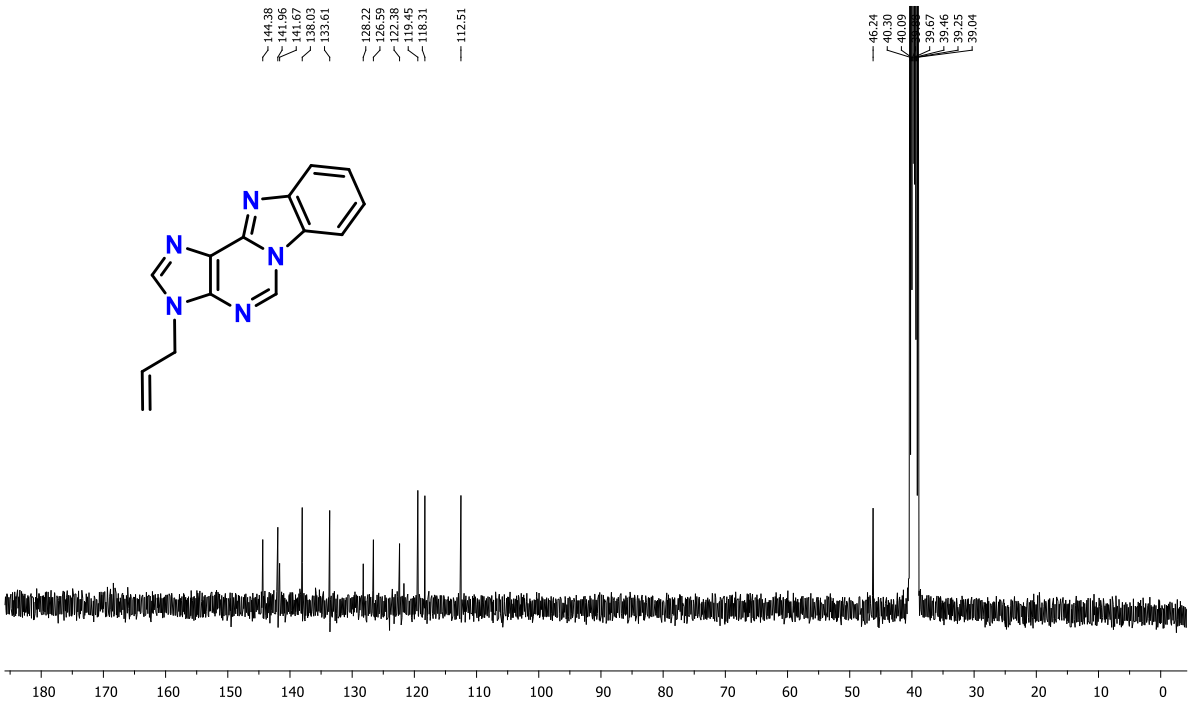
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5o)



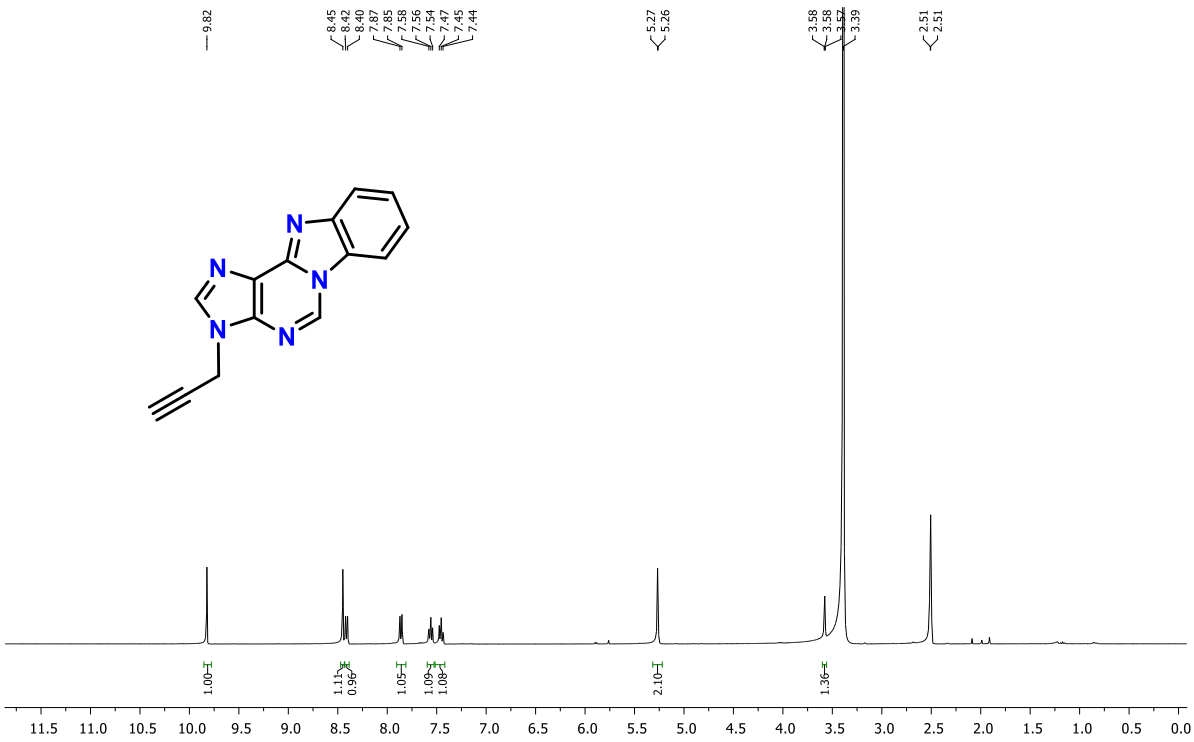
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5p)



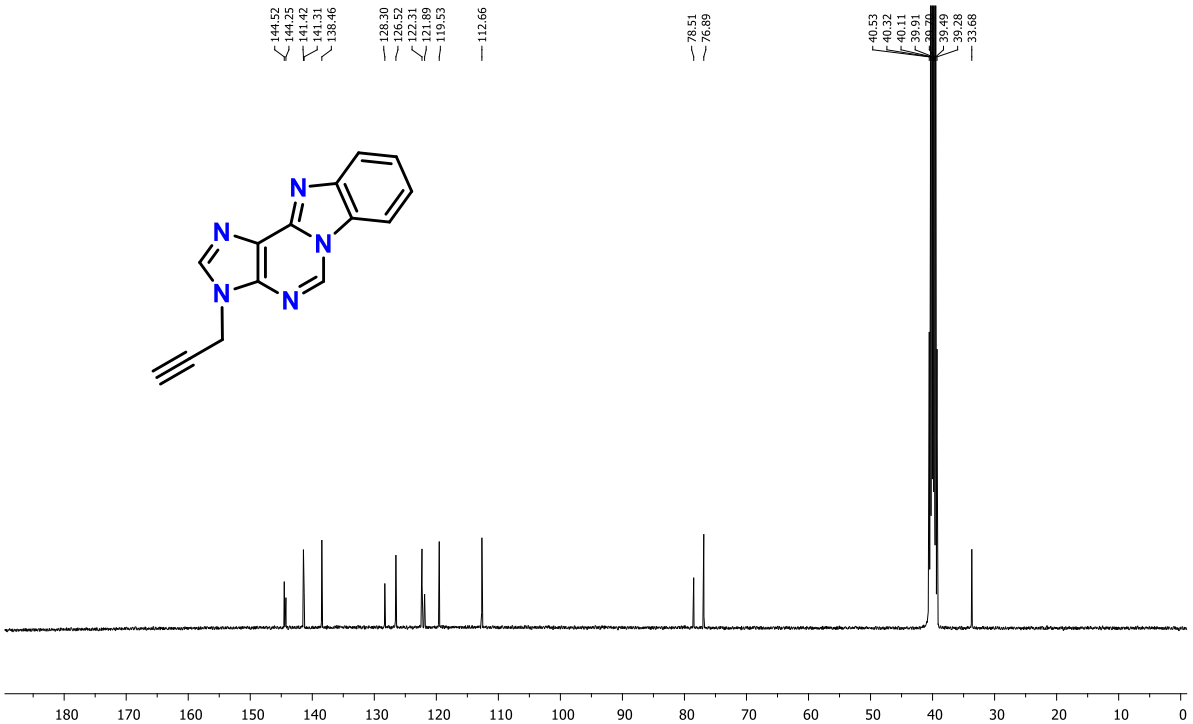
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5p)



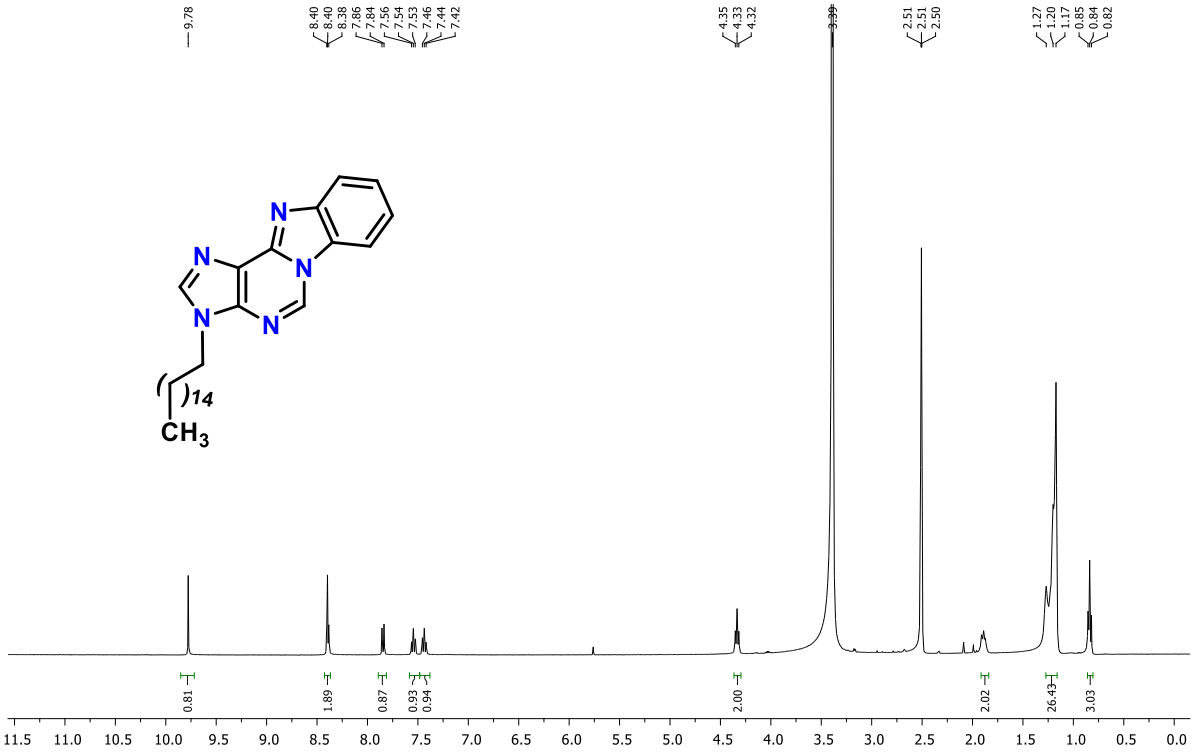
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5q)



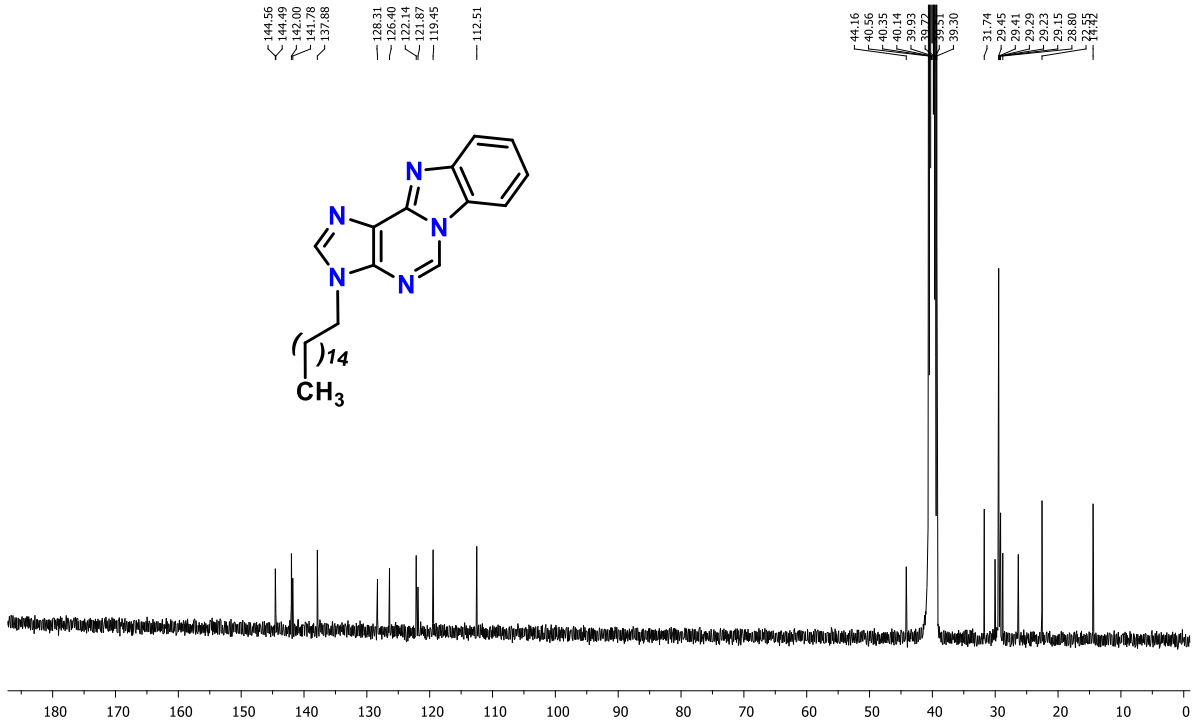
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5q)



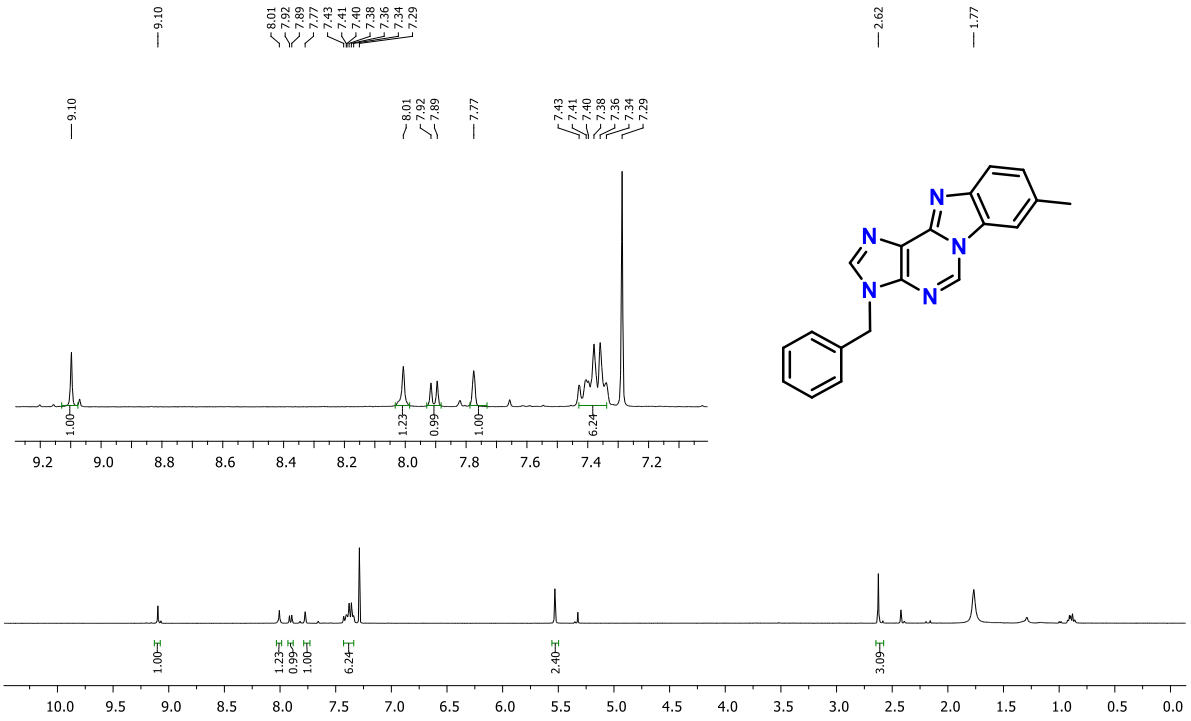
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (5r)



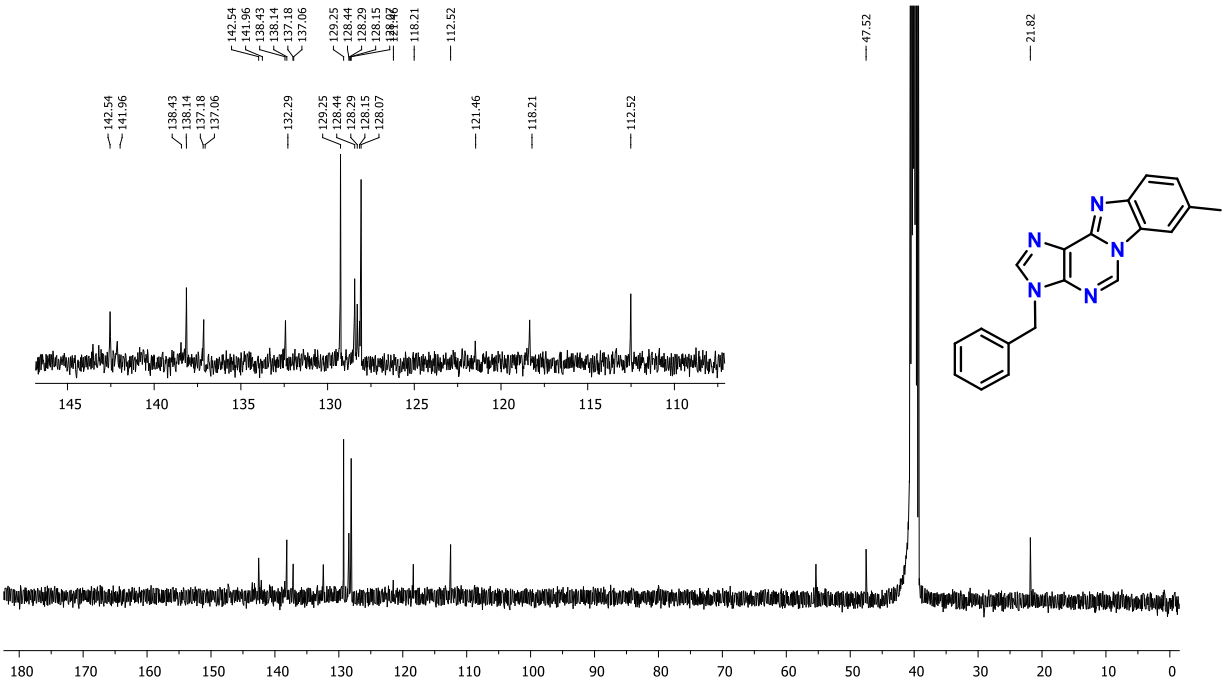
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5r)



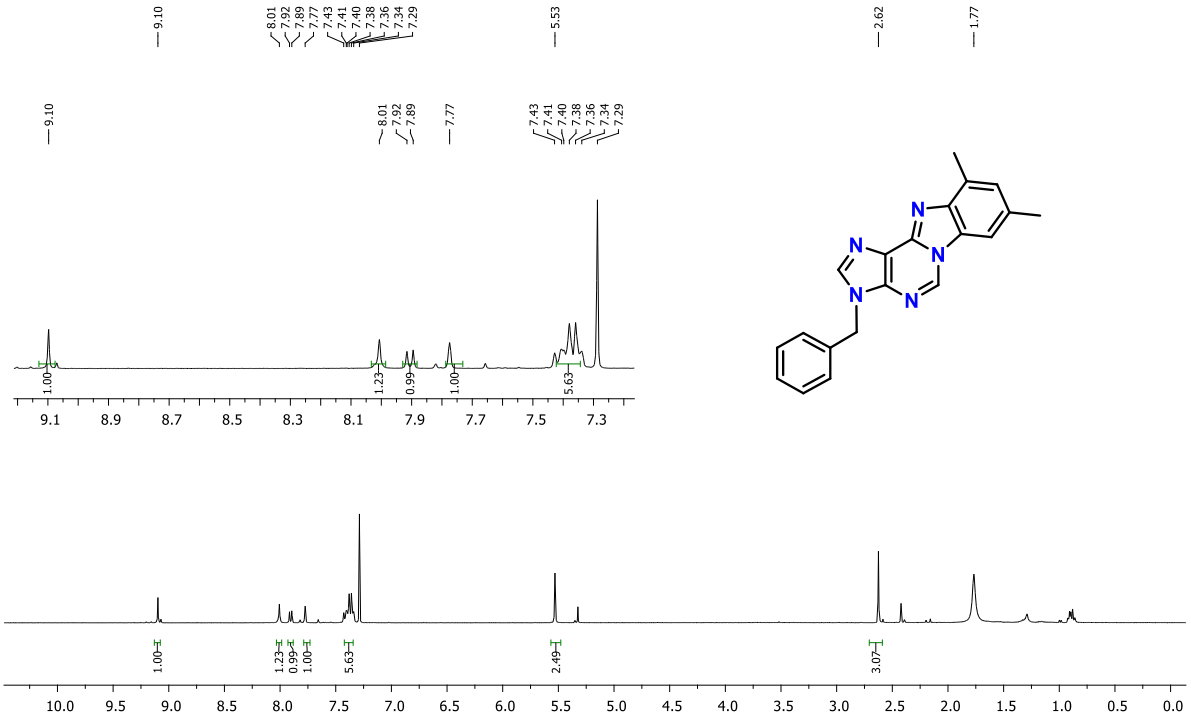
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (5s)



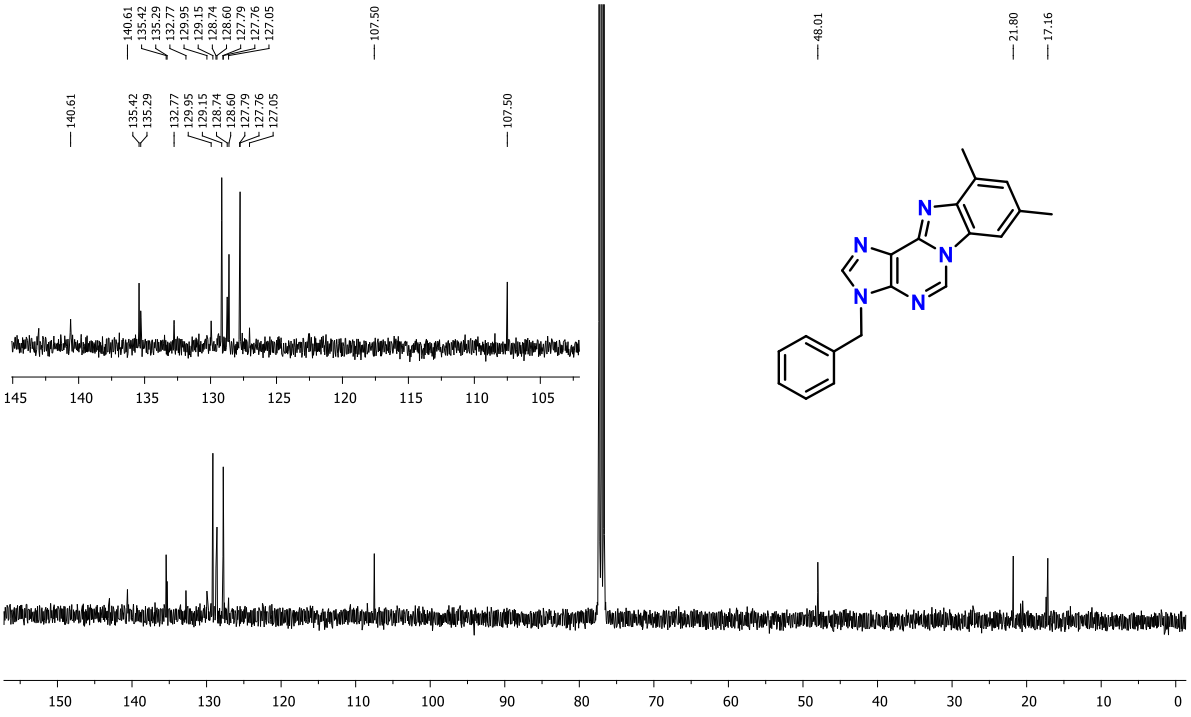
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (5s)



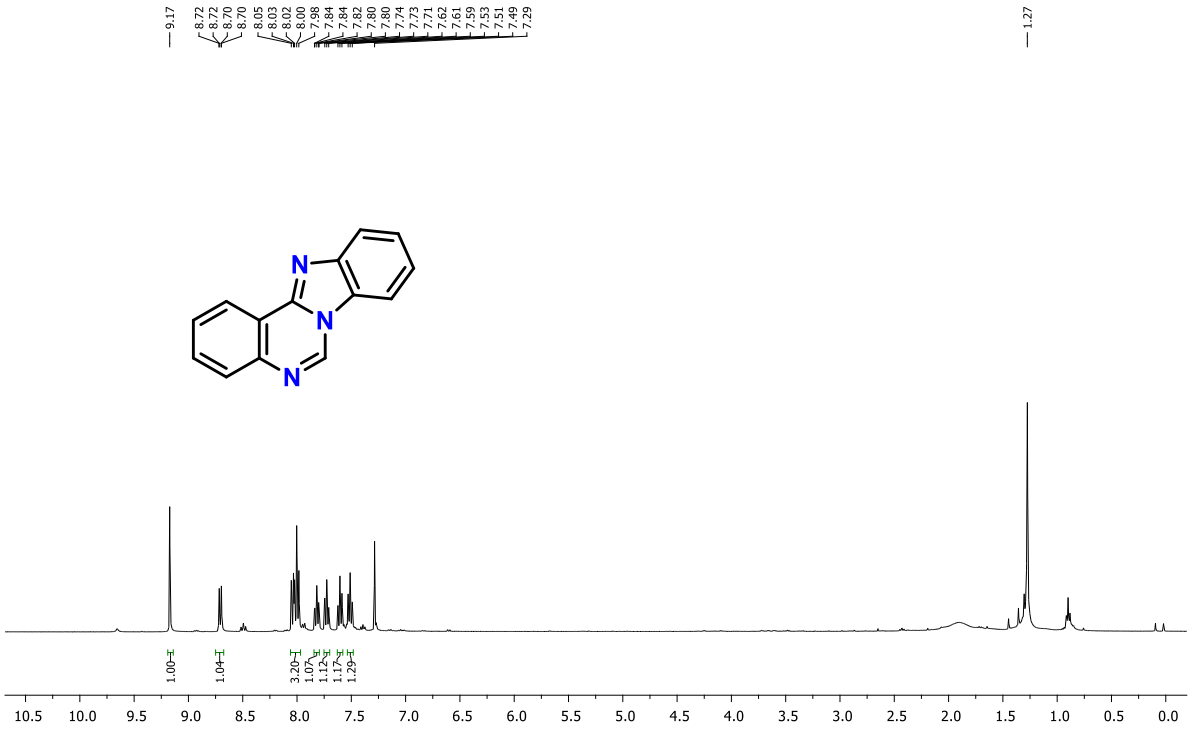
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (5t)



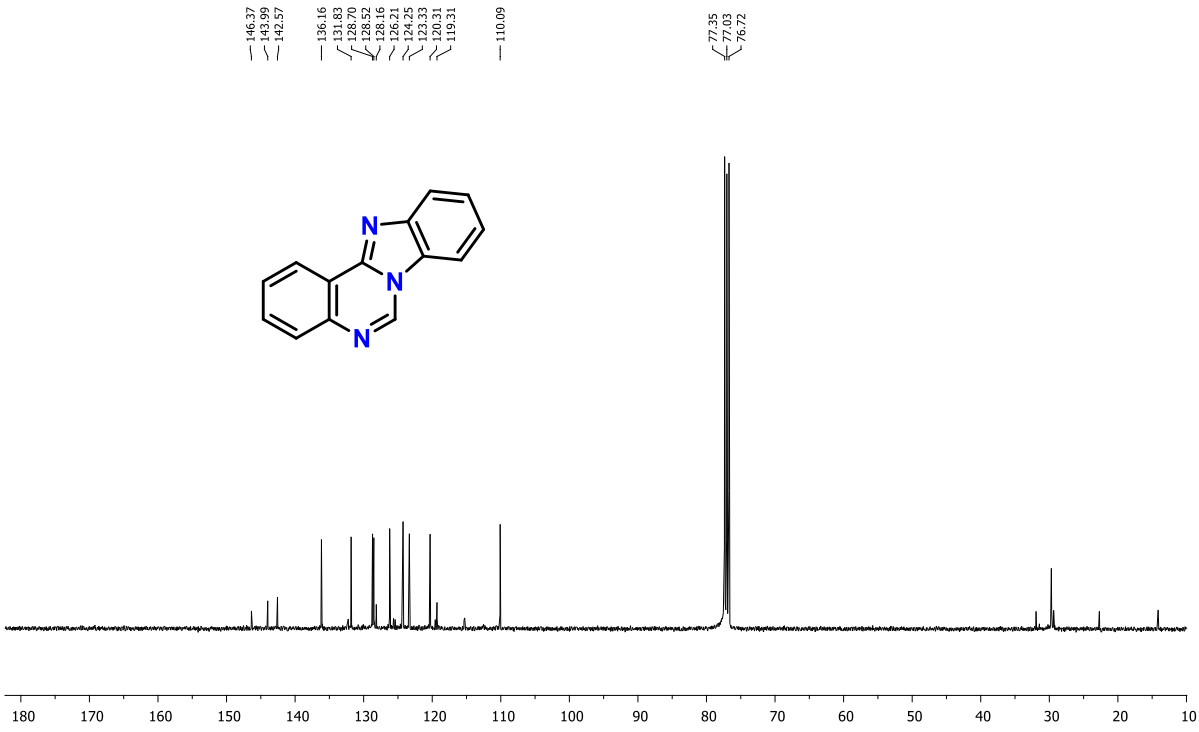
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (5t)



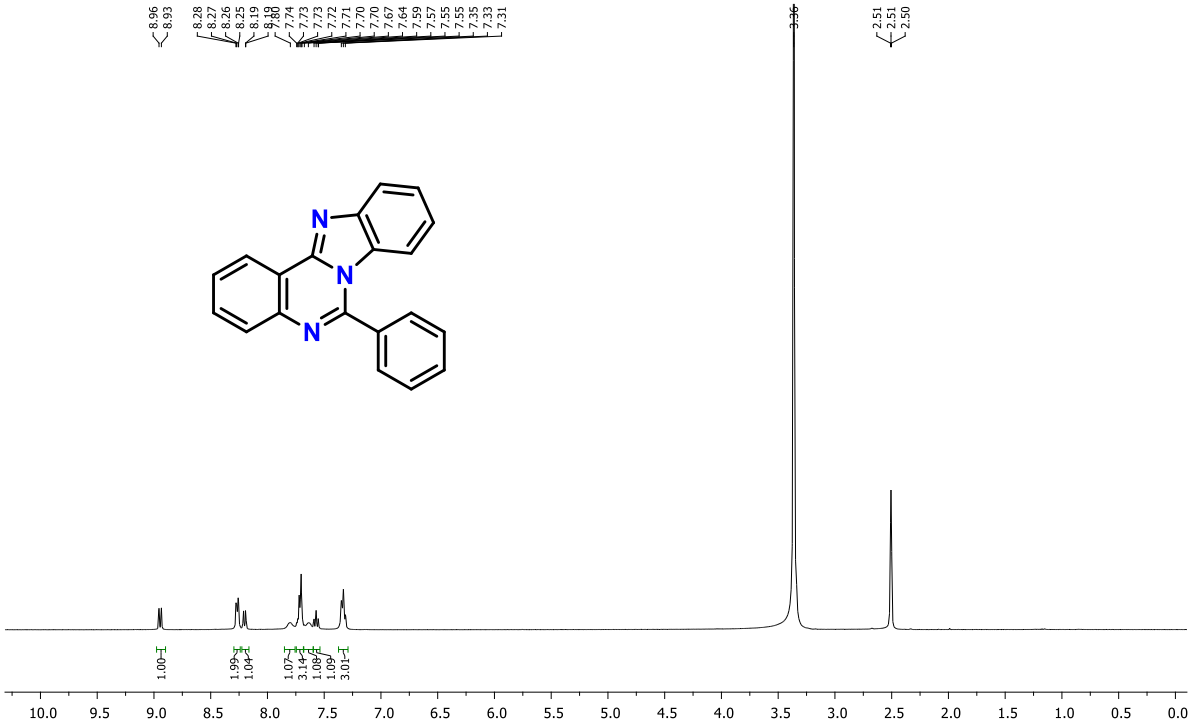
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (7a)



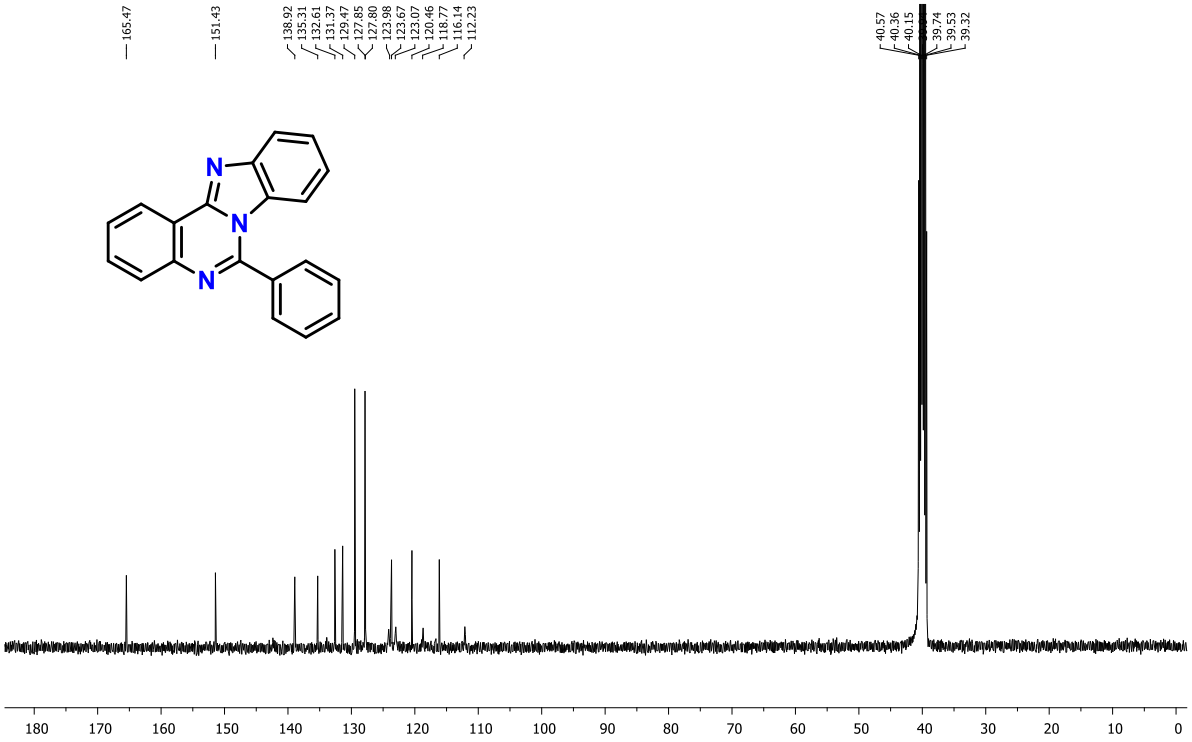
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (7a)



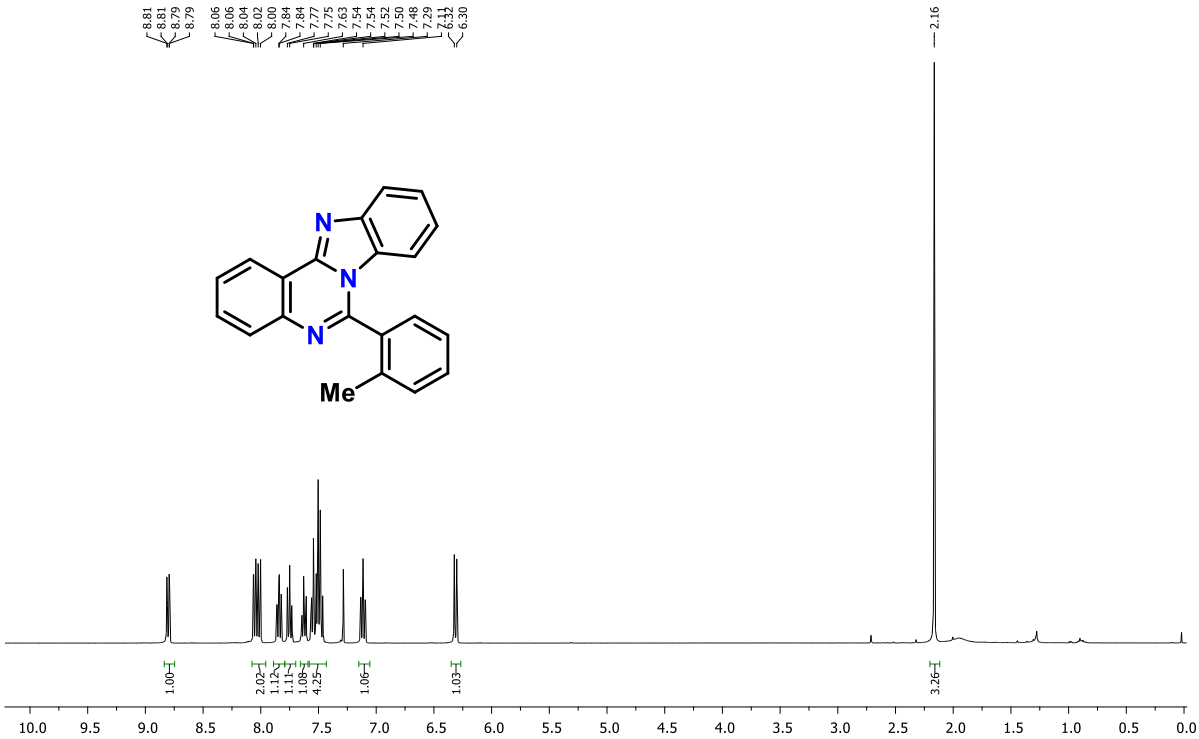
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (7b)



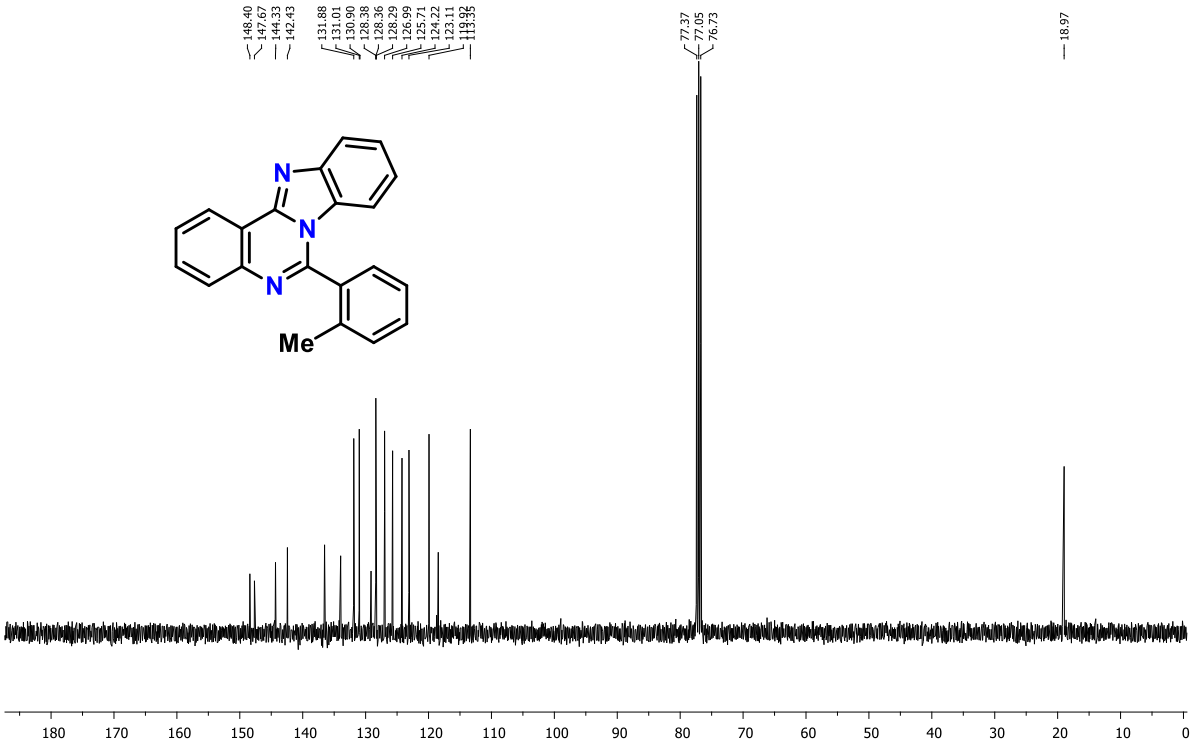
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (7b)



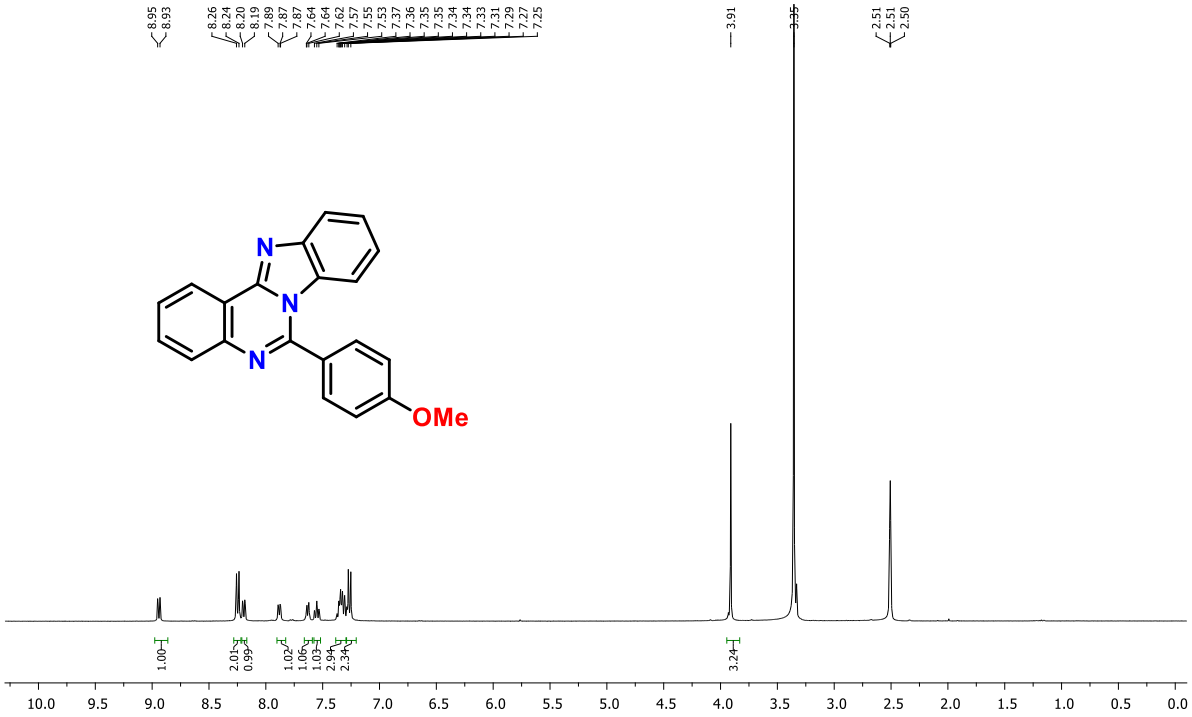
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (7c)



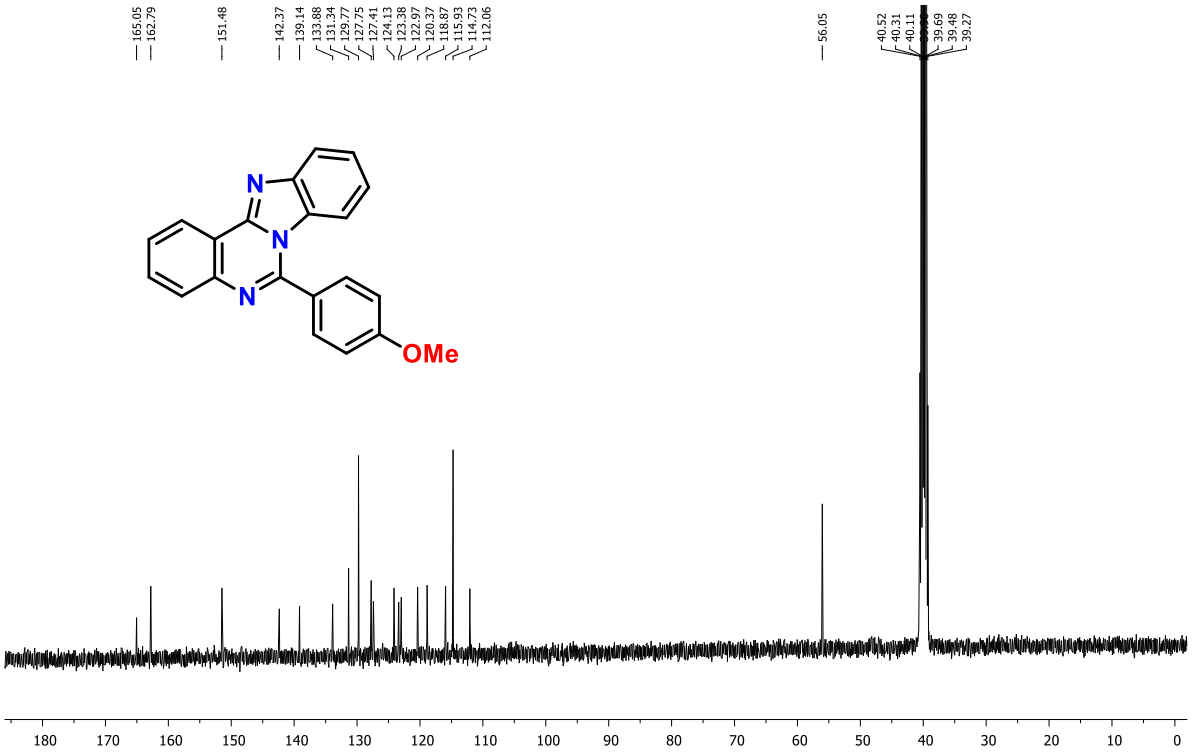
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (7c)



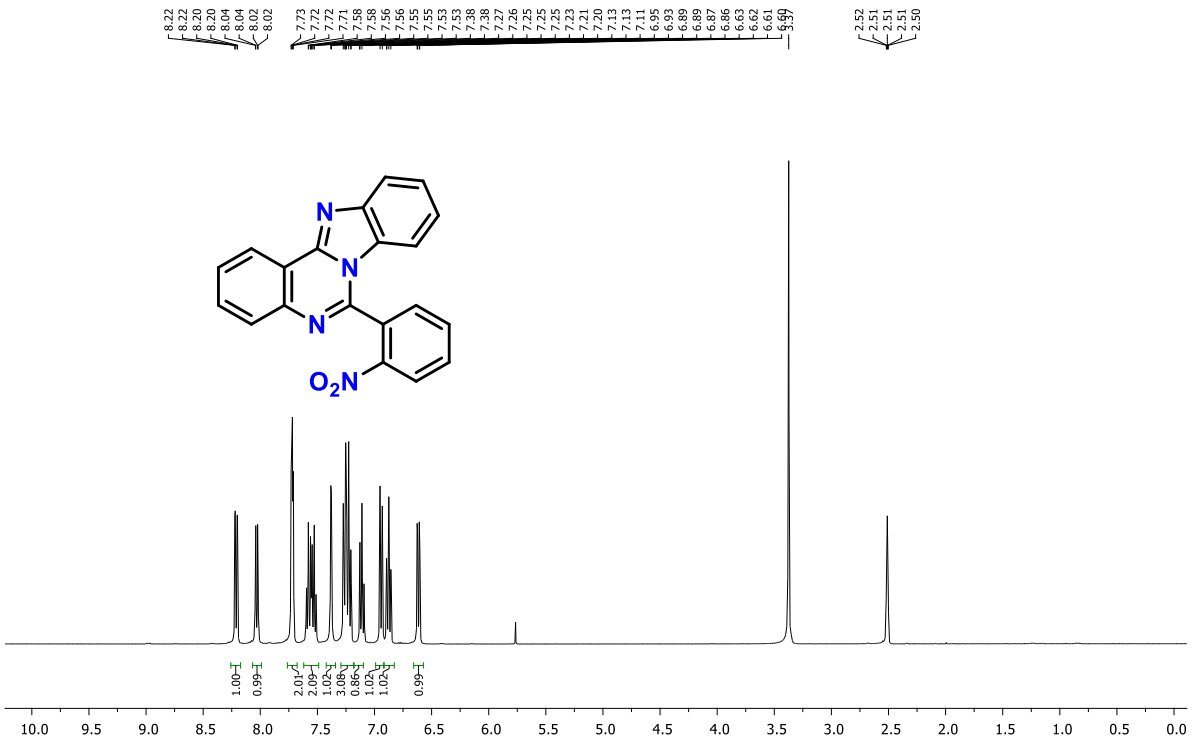
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (7d)



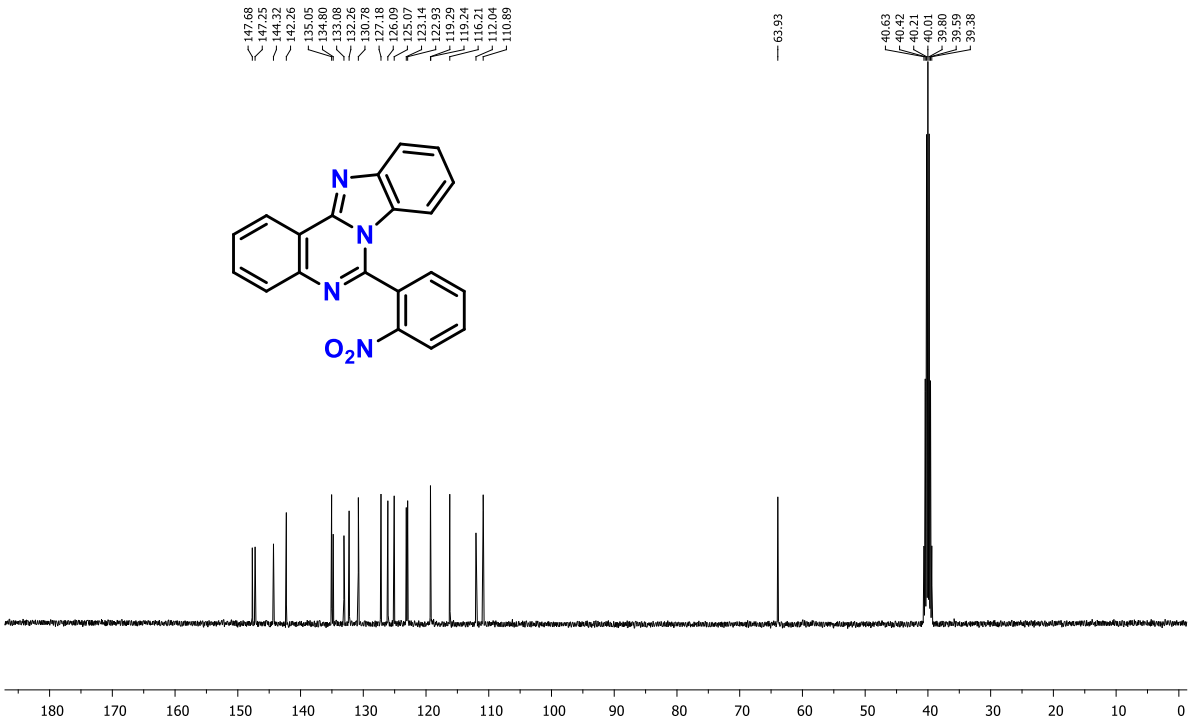
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (7d)



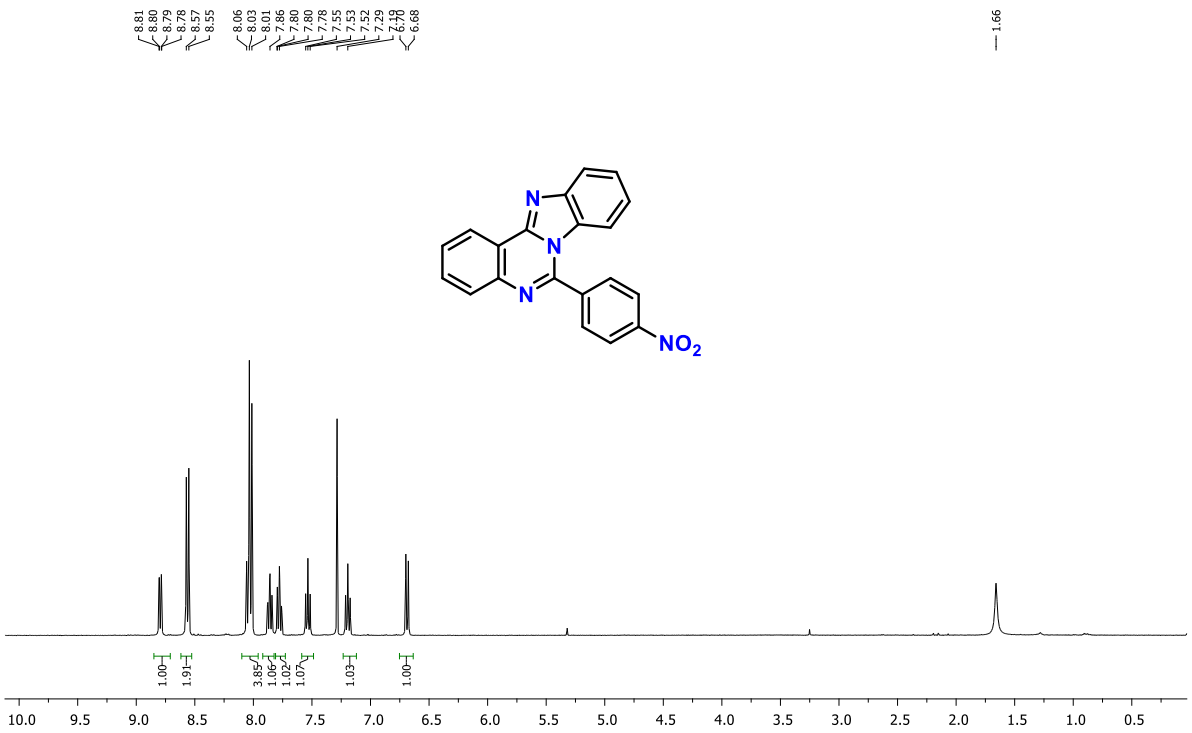
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (7e)



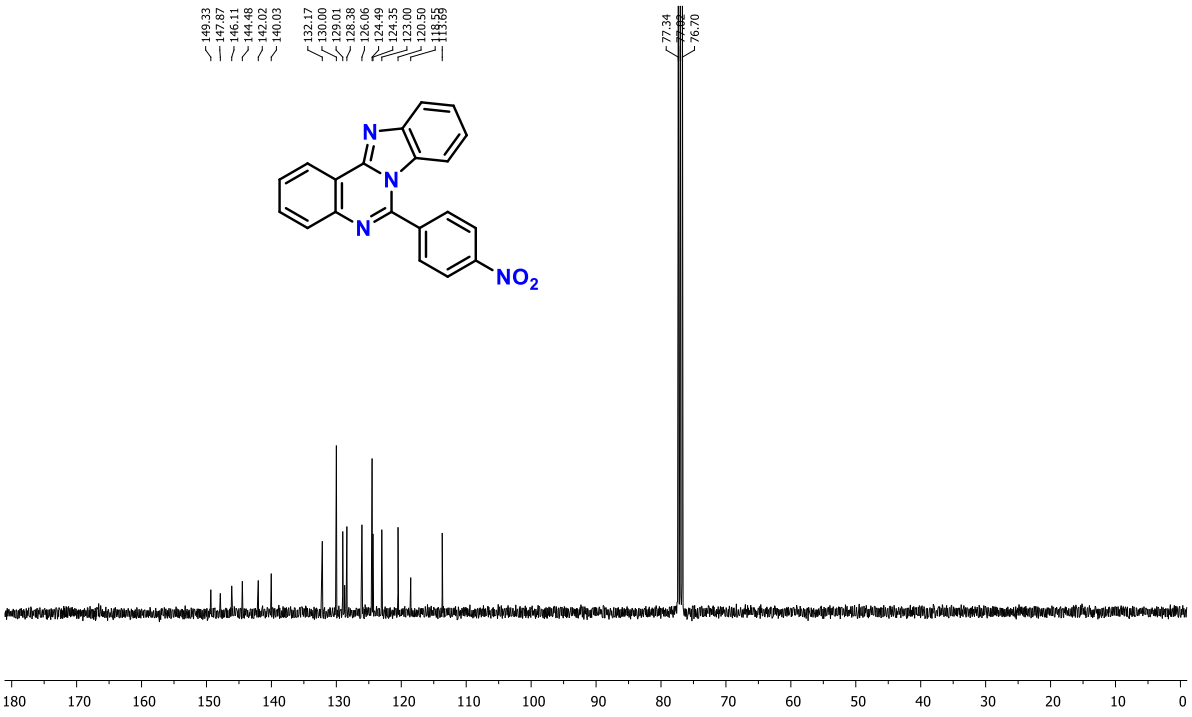
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (7e)



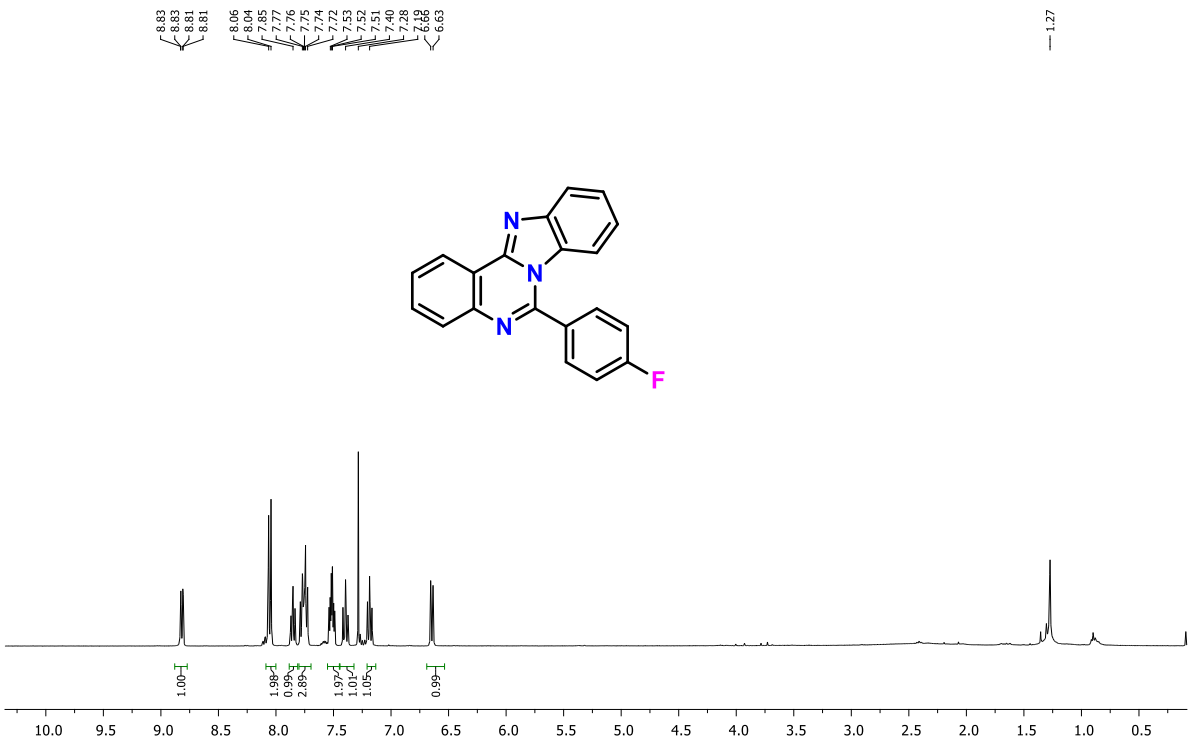
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (7f)



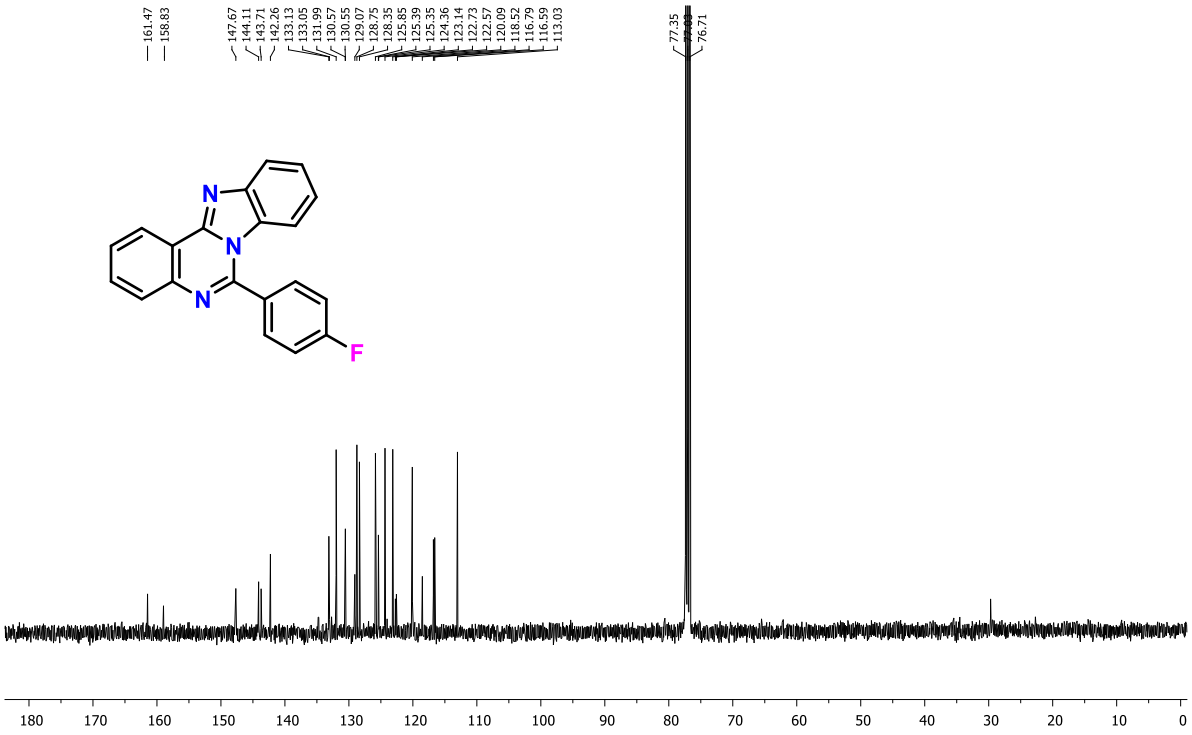
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (7f)



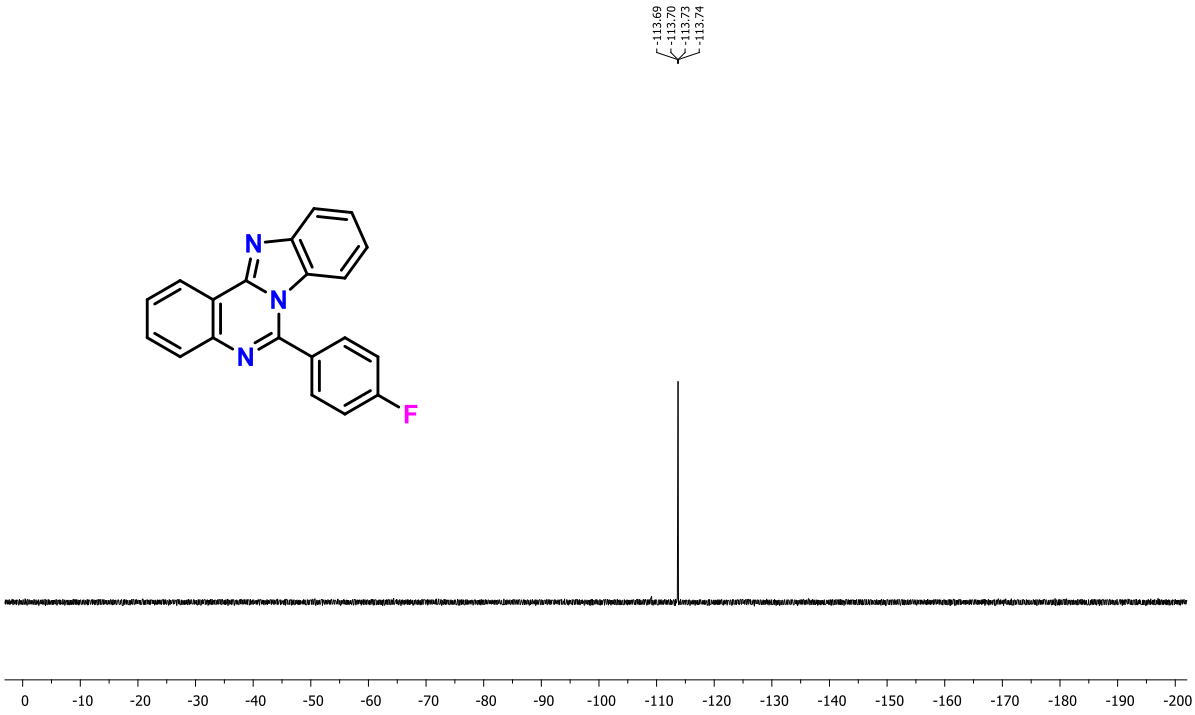
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (7g)



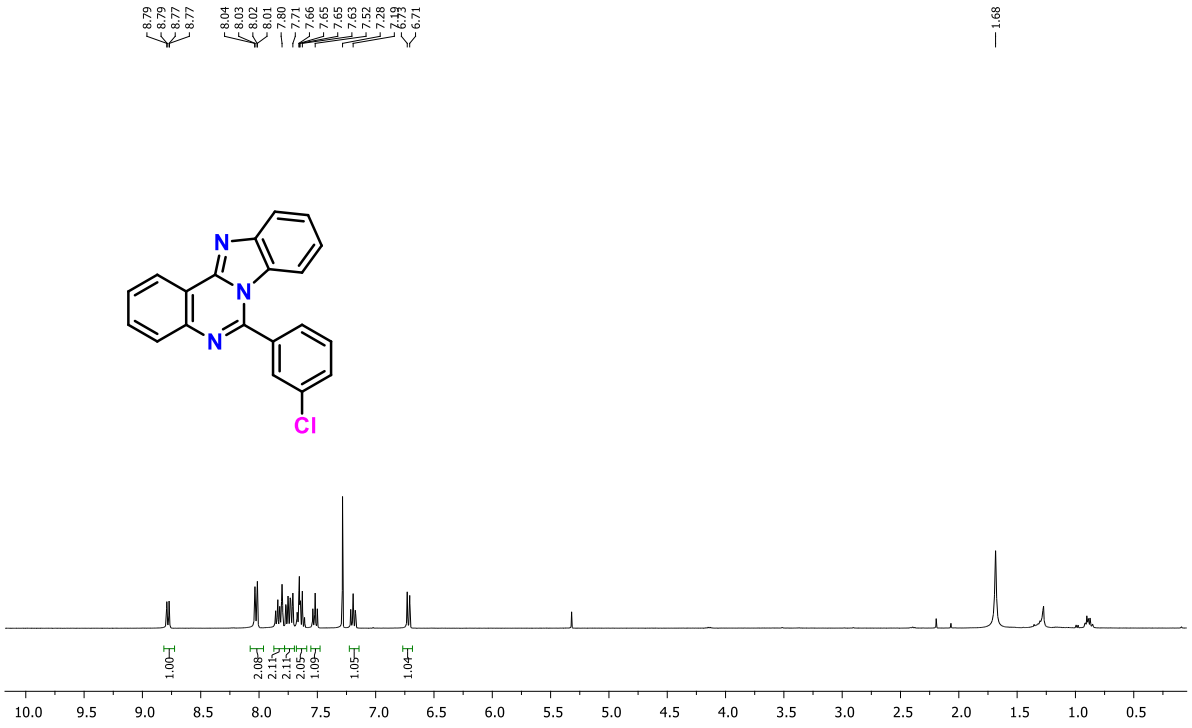
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (7g)



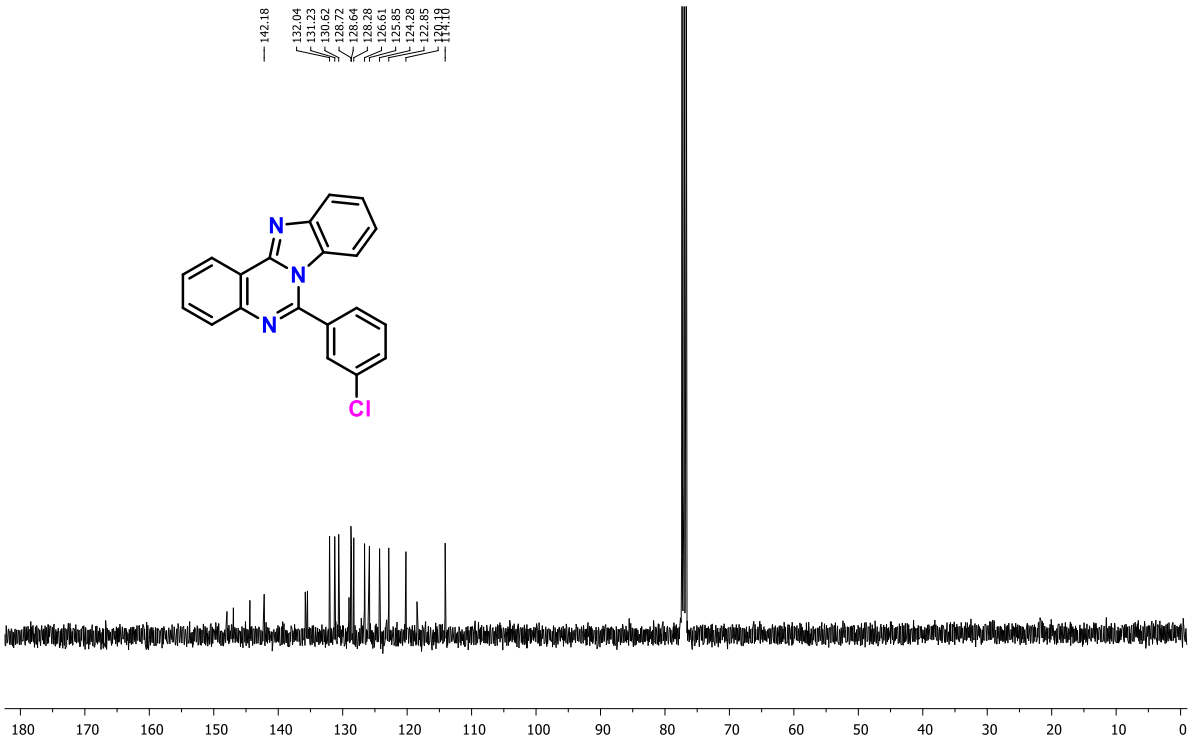
^{19}F NMR (377 MHz, $CDCl_3$) spectrum of compound (7g)



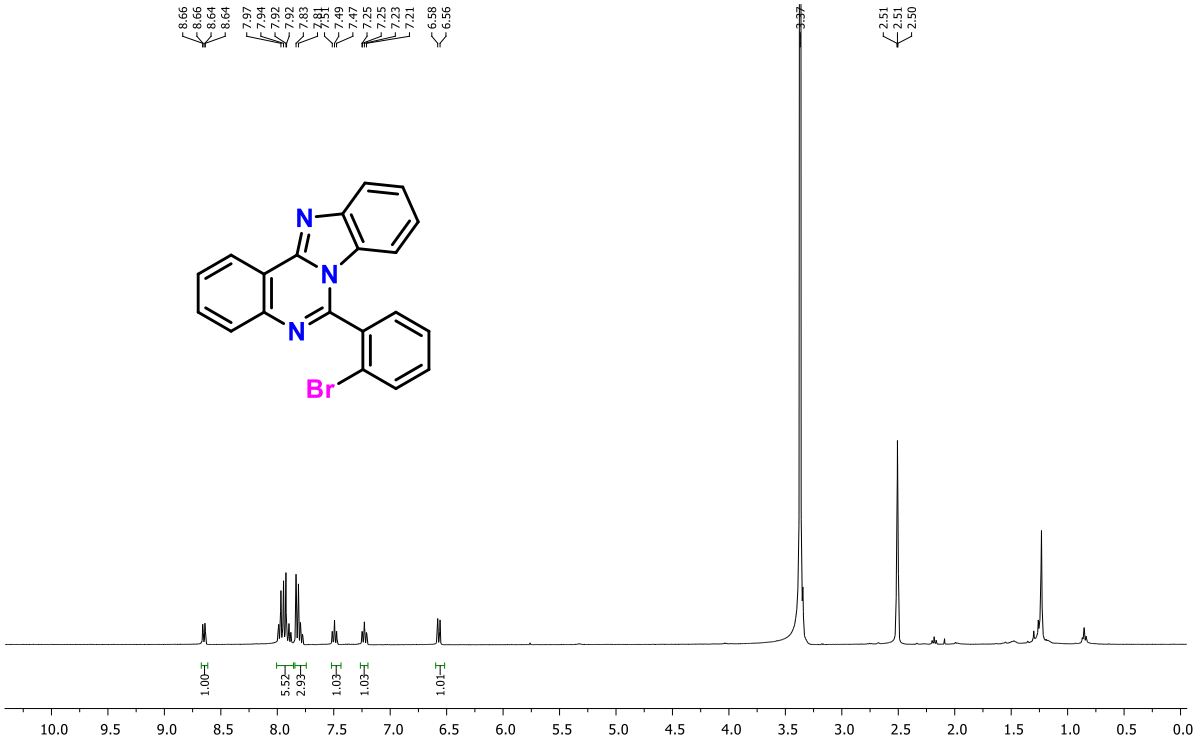
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (7h)



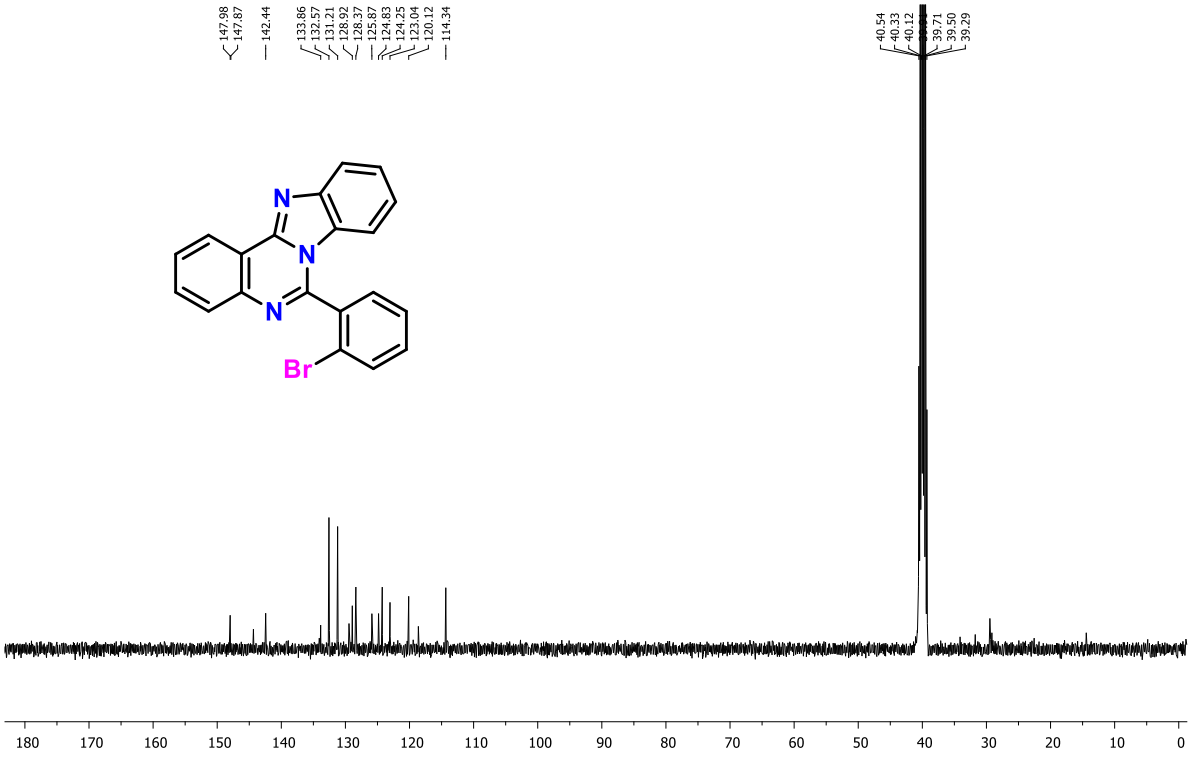
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (7h)



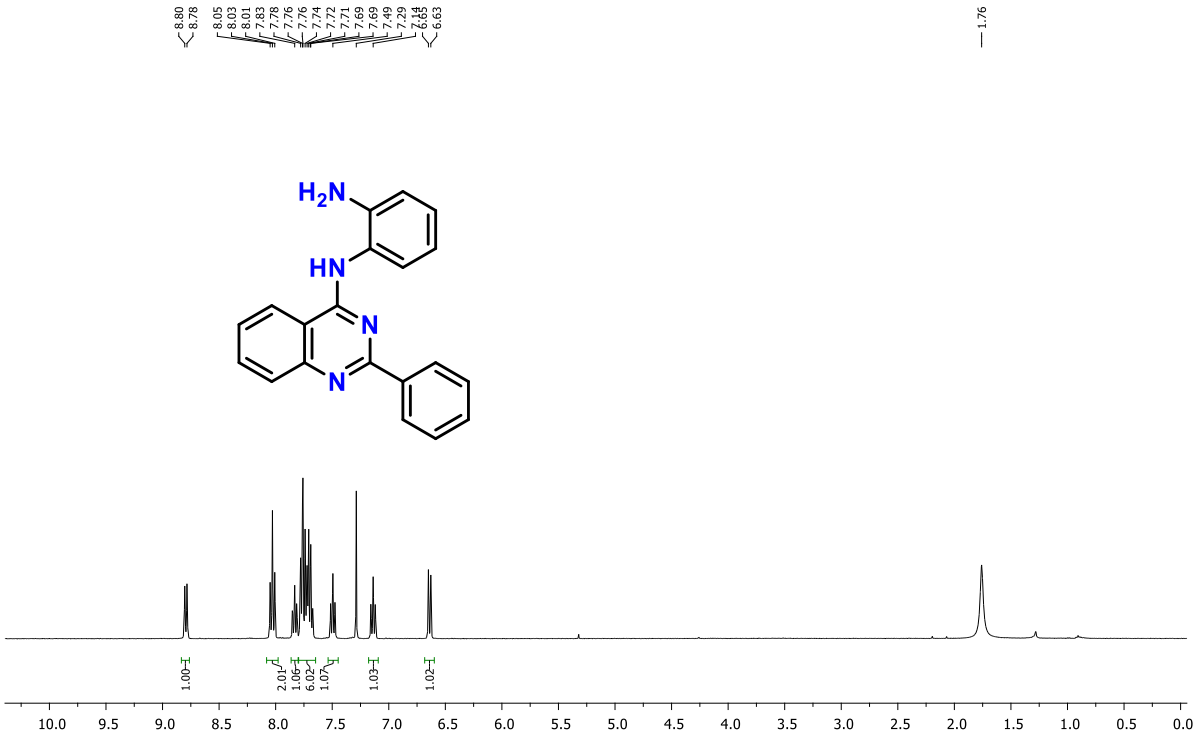
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (7i)



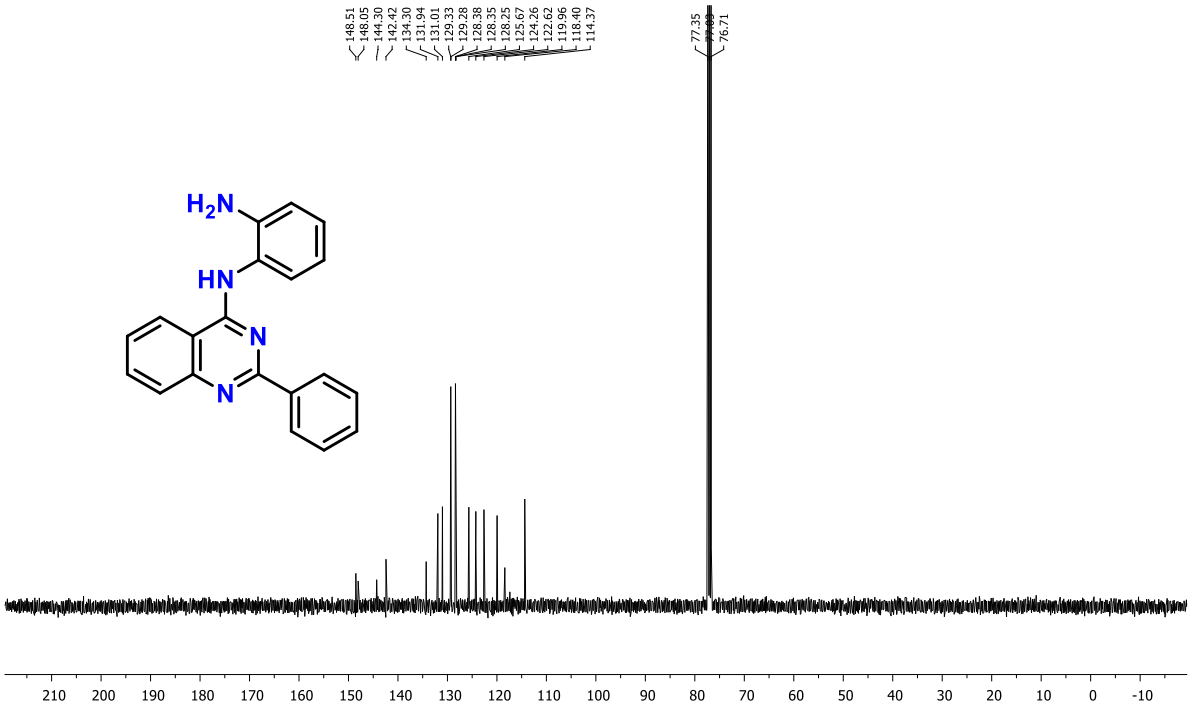
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (7i)



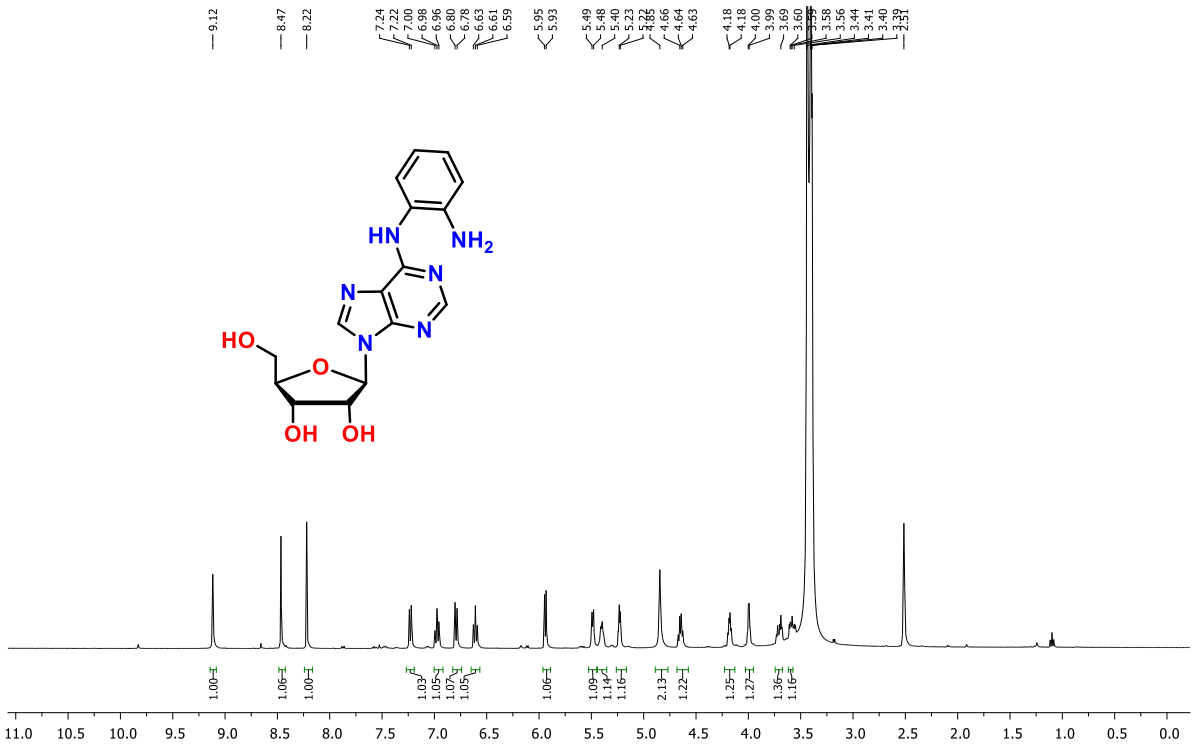
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (7b′)



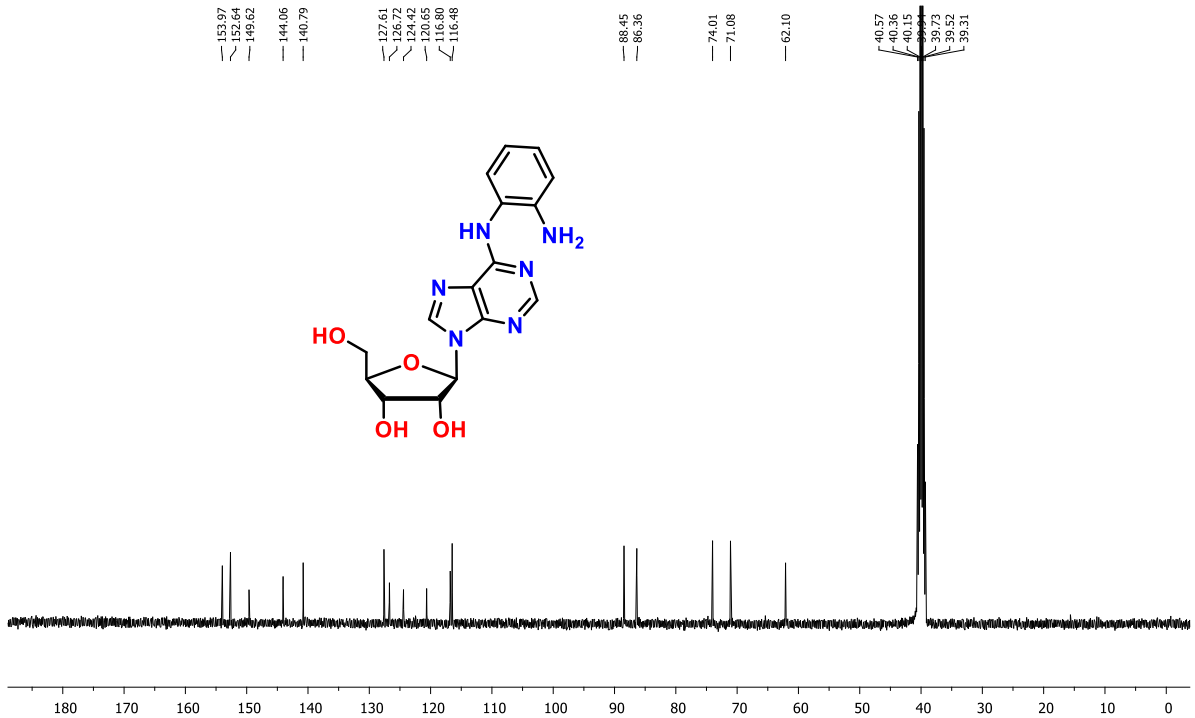
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (7b′)



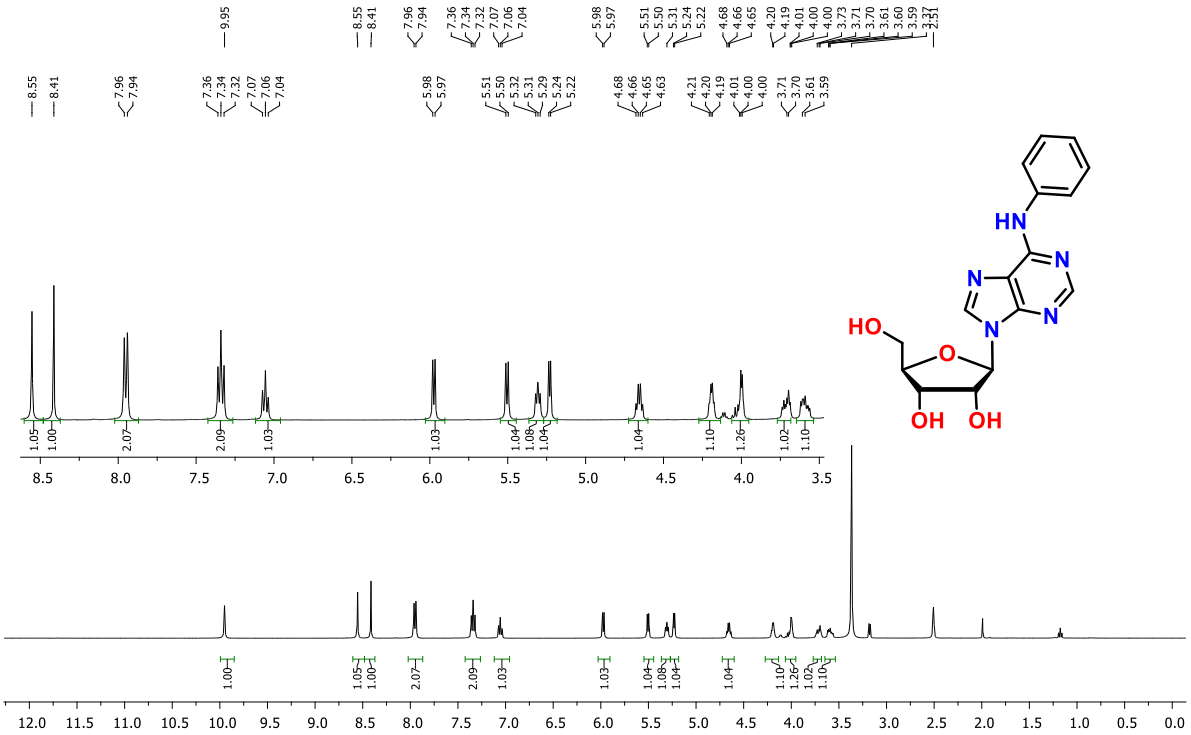
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (3)



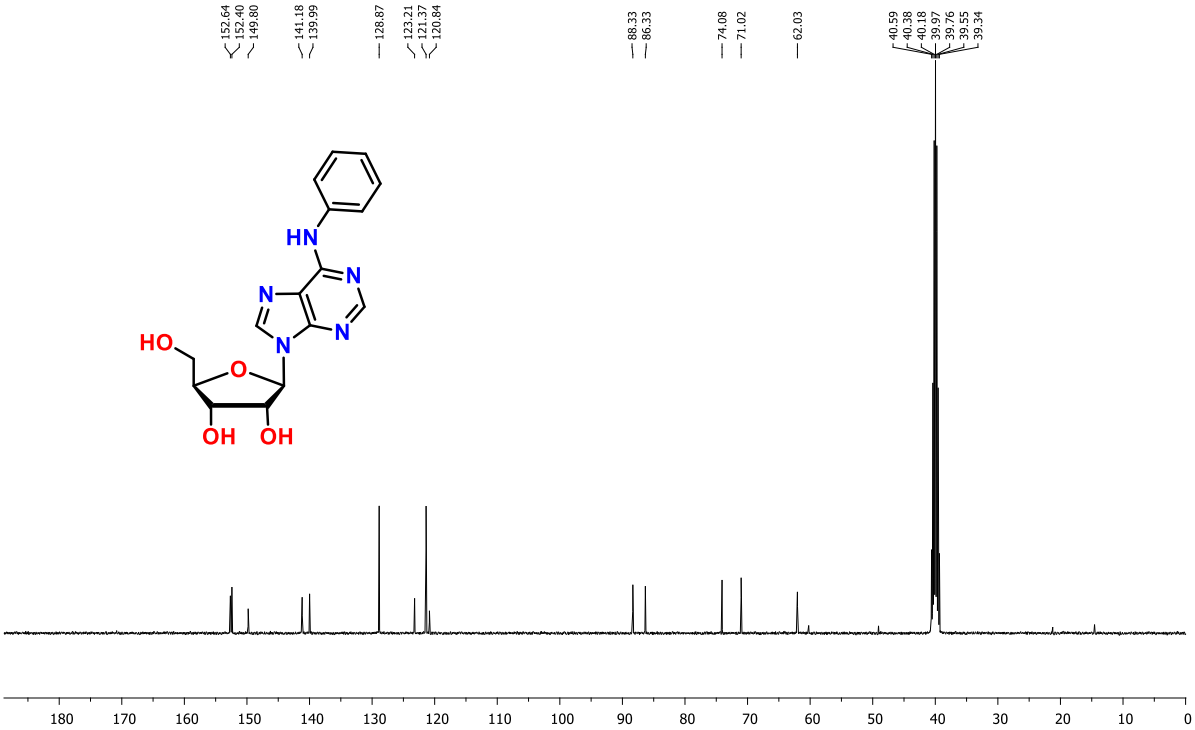
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (3)



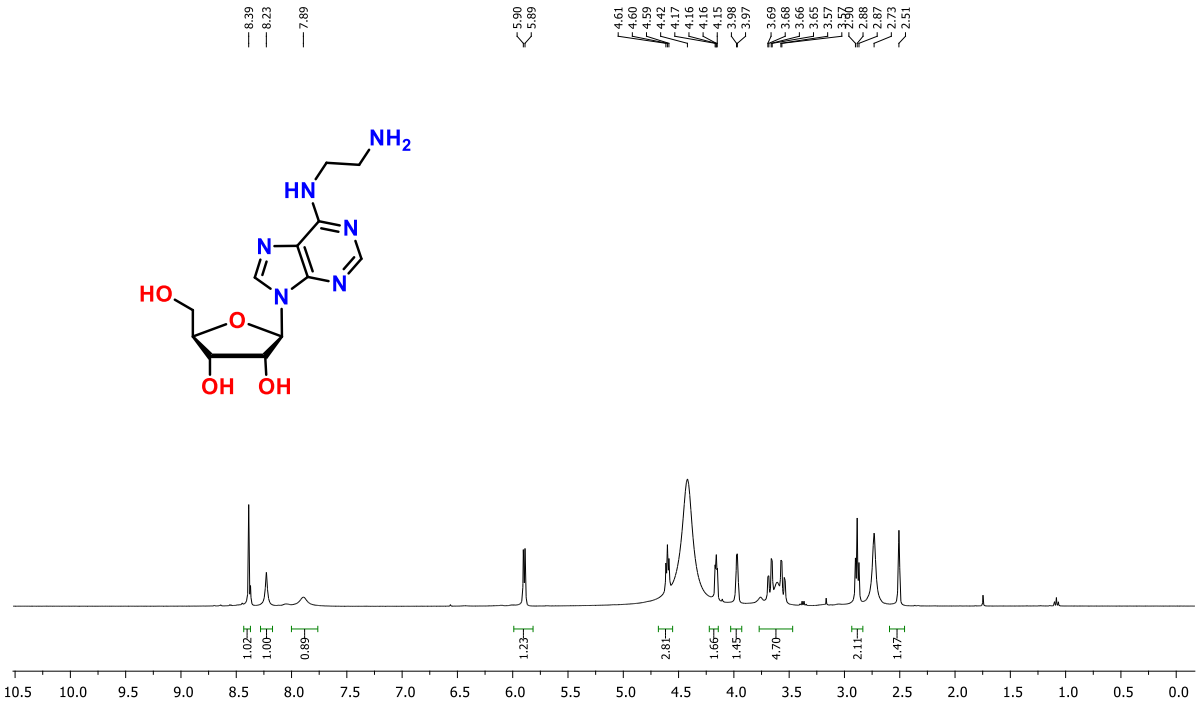
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (8)



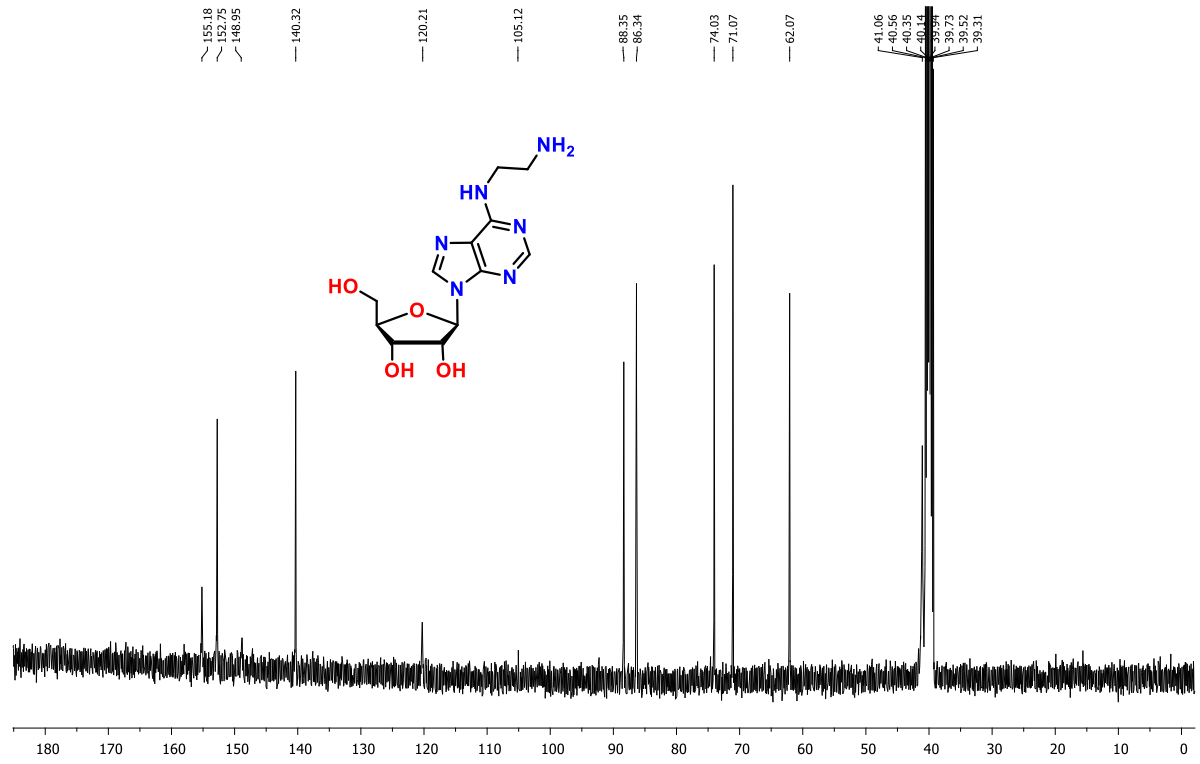
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (8)



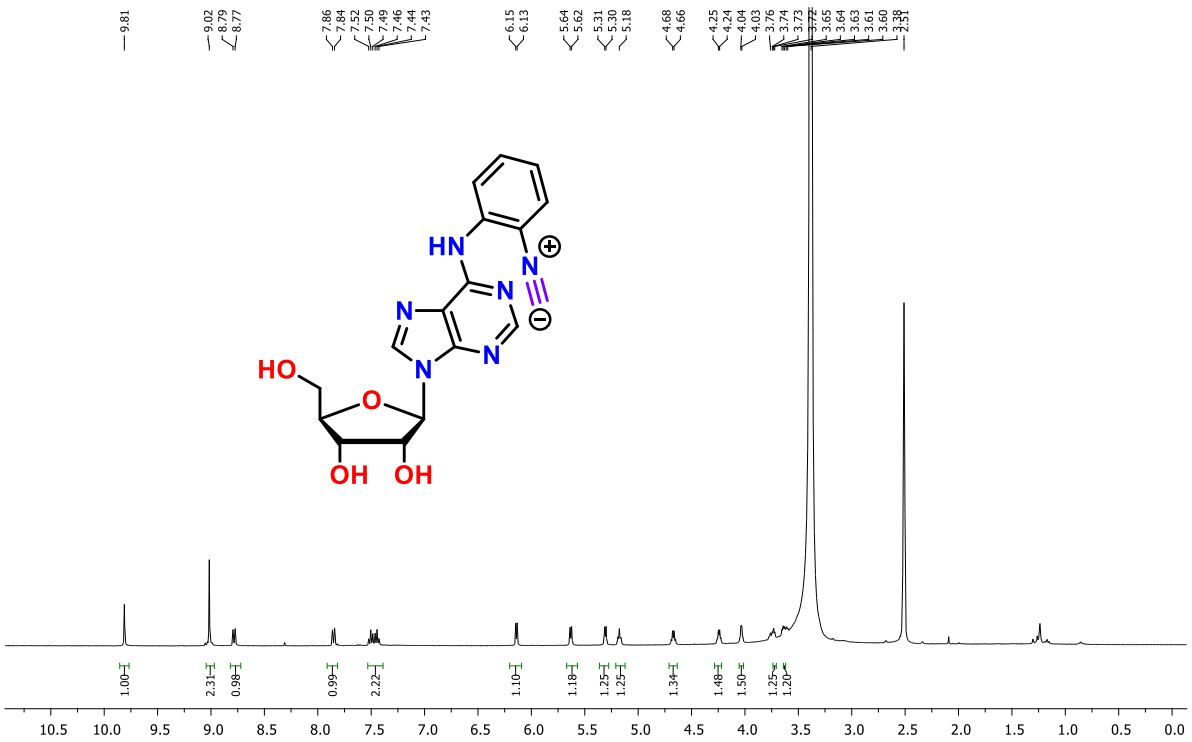
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (9)



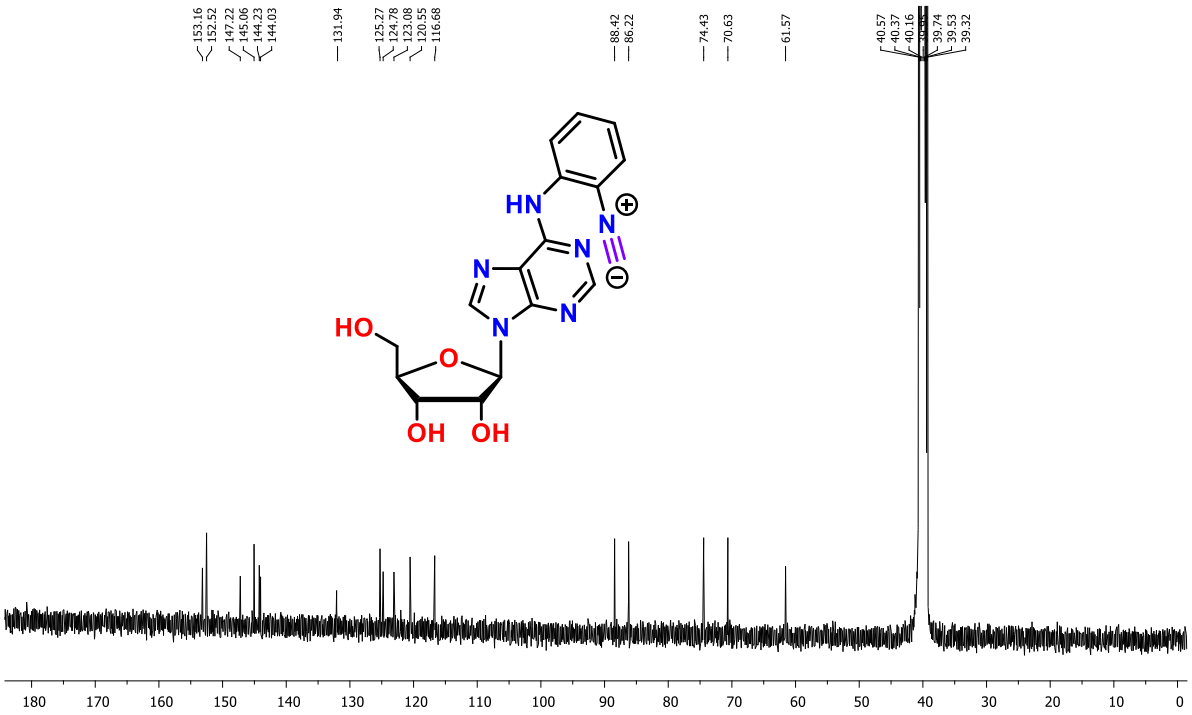
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (9)



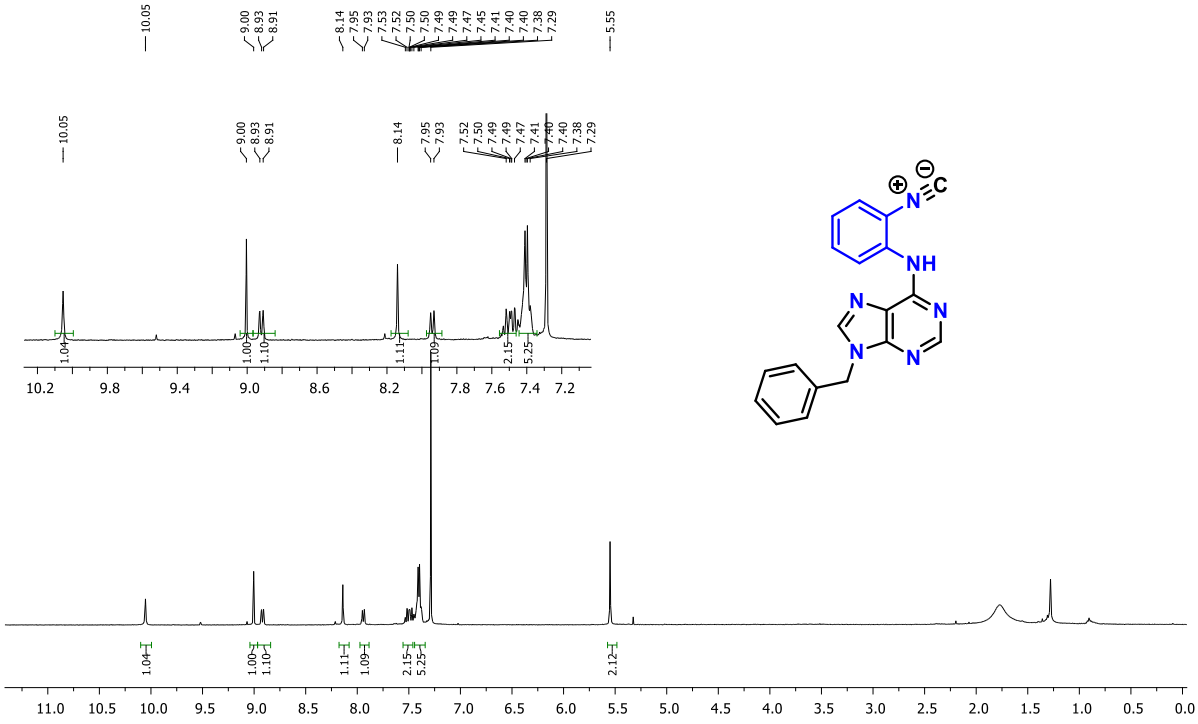
^{1}H NMR (400MHz, DMSO-d_6) spectrum of intermediate compound (D)



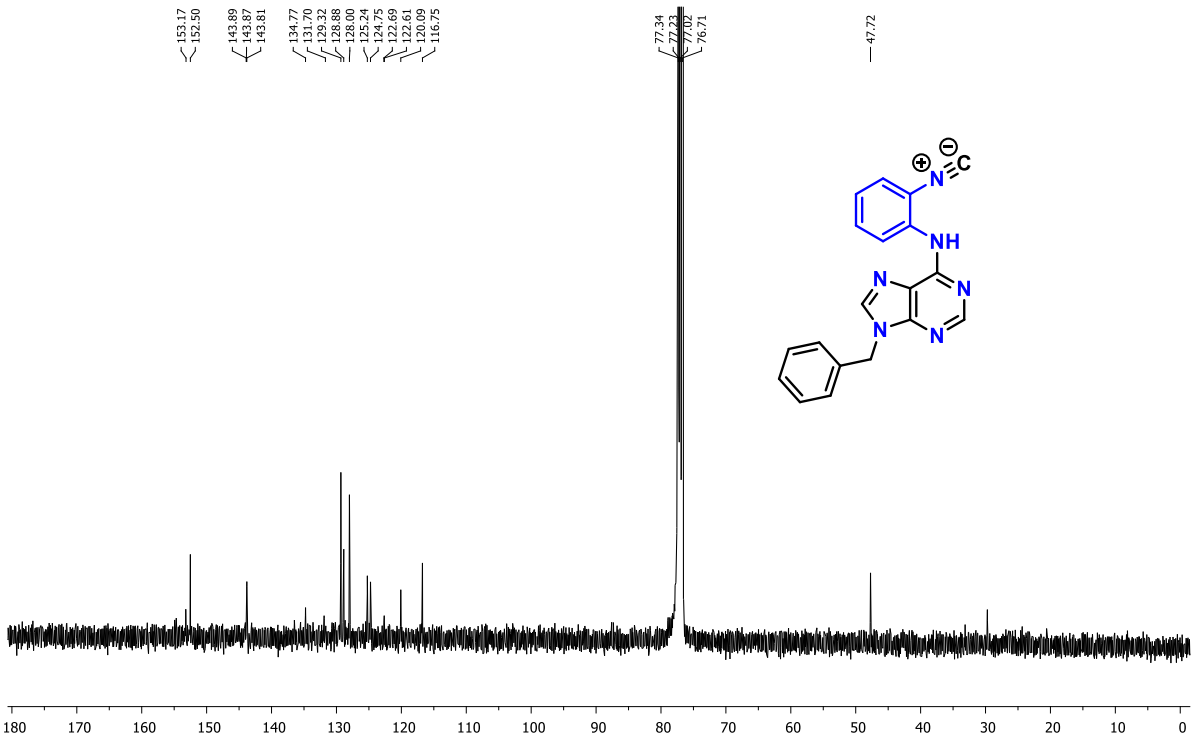
^{13}C NMR (101MHz, DMSO-d_6) spectrum of intermediate compound (D)



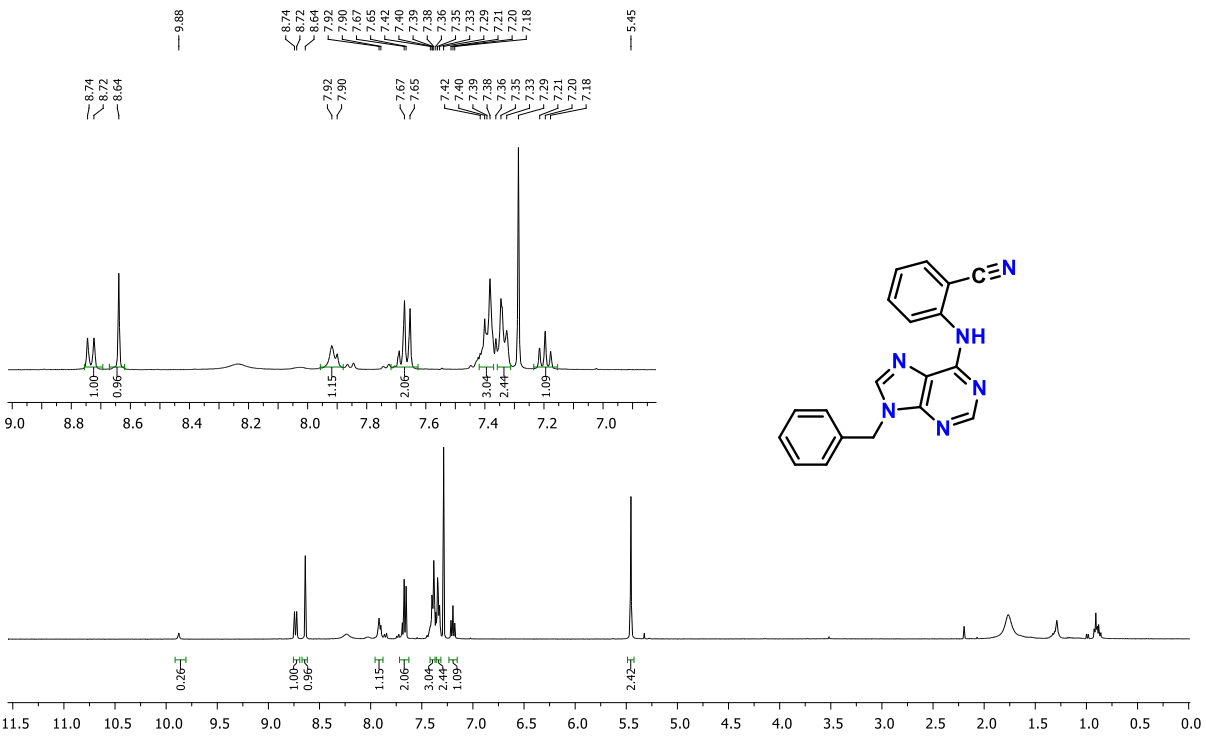
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound (14)



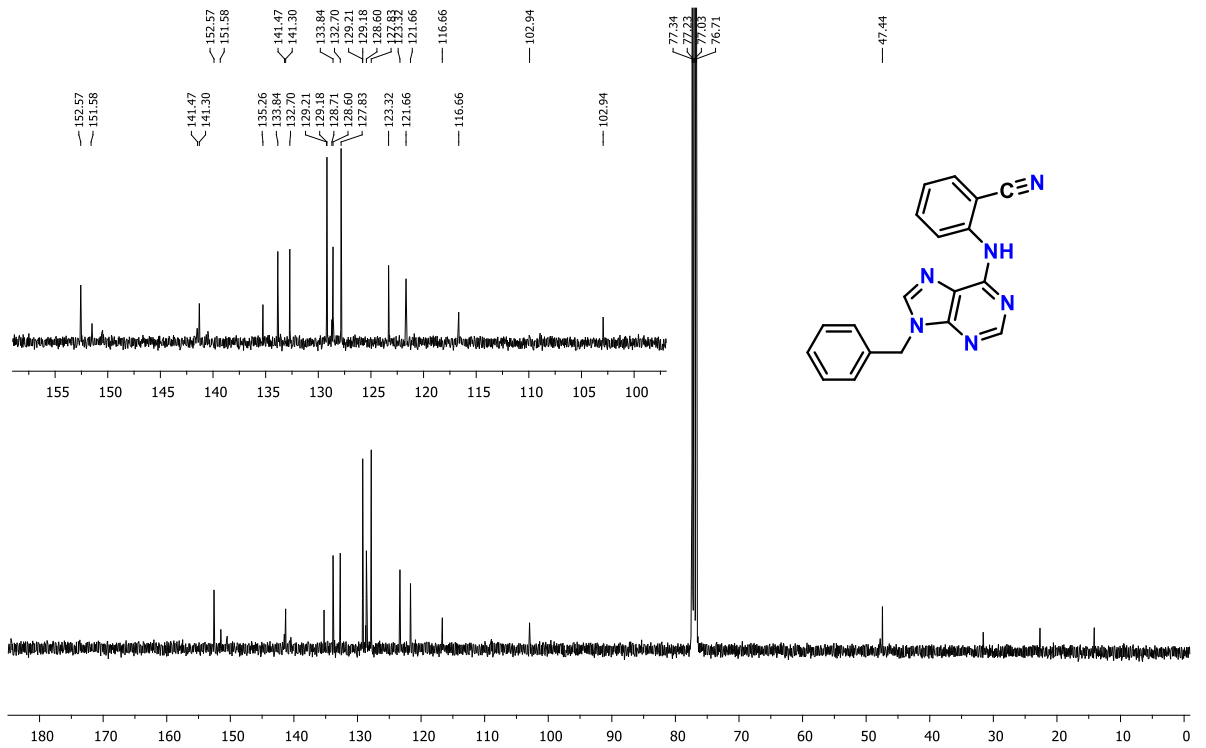
^{13}C NMR (101 MHz, $CDCl_3$) spectrum of compound (14)



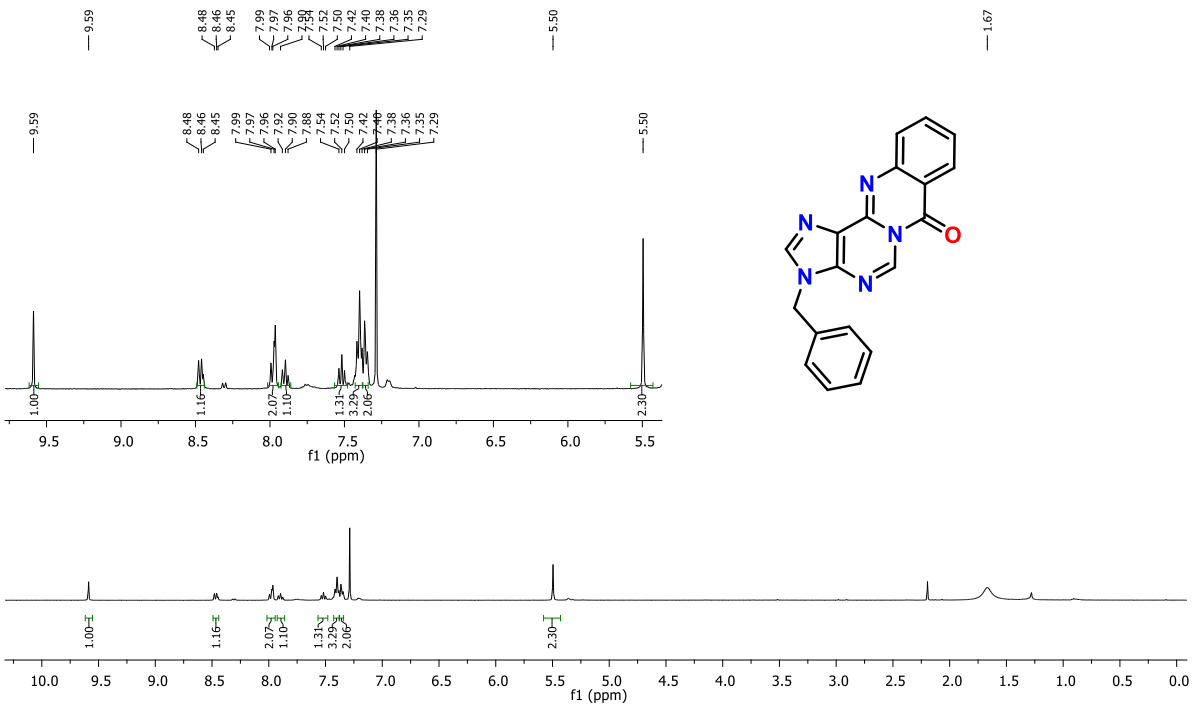
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound (16)



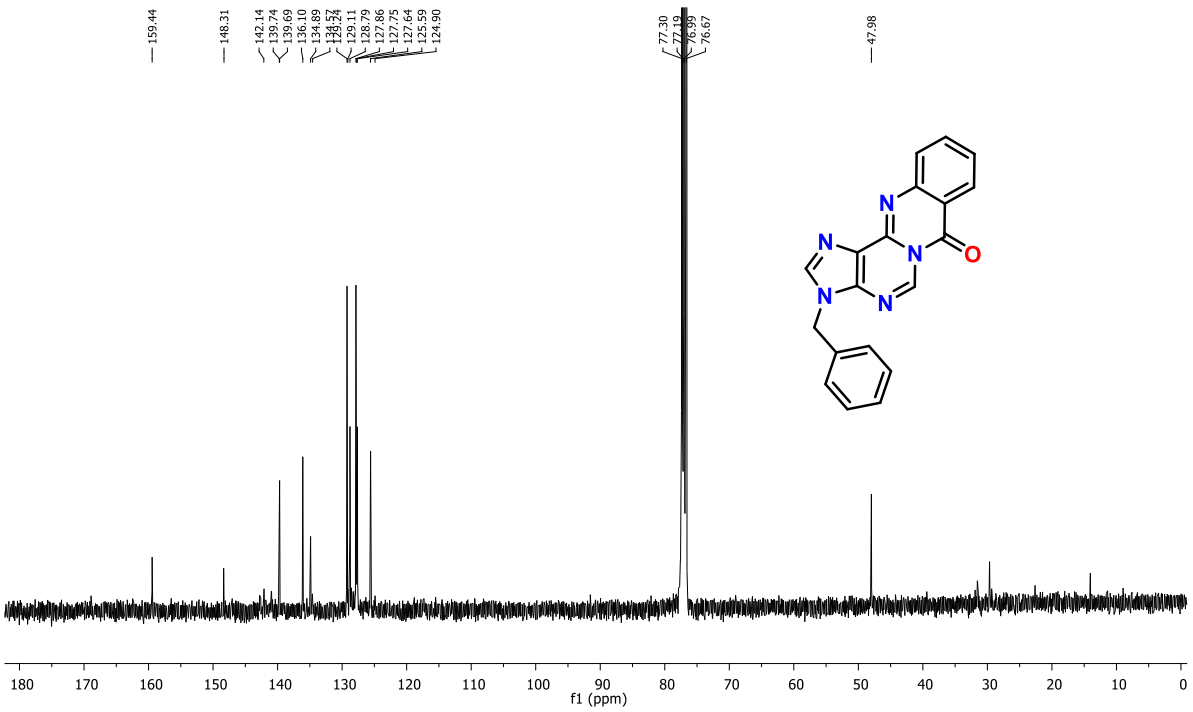
^{13}C NMR (101 MHz, $CDCl_3$) spectrum of compound (16)



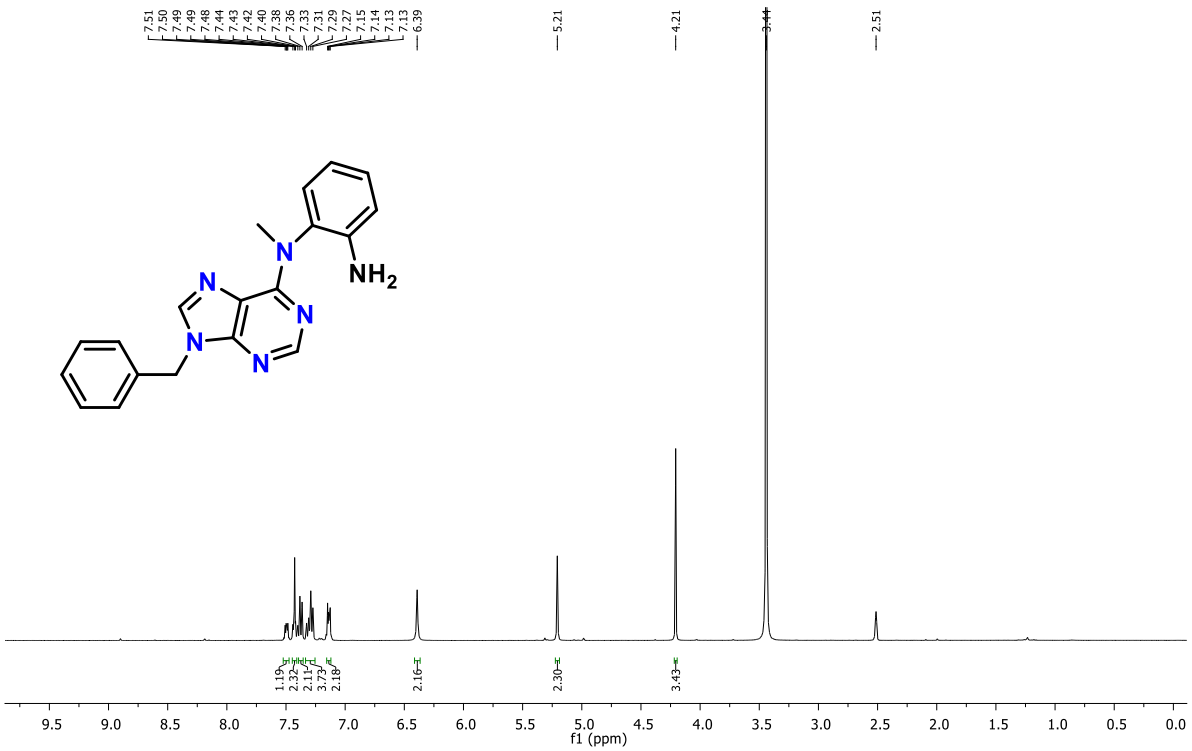
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound (17)



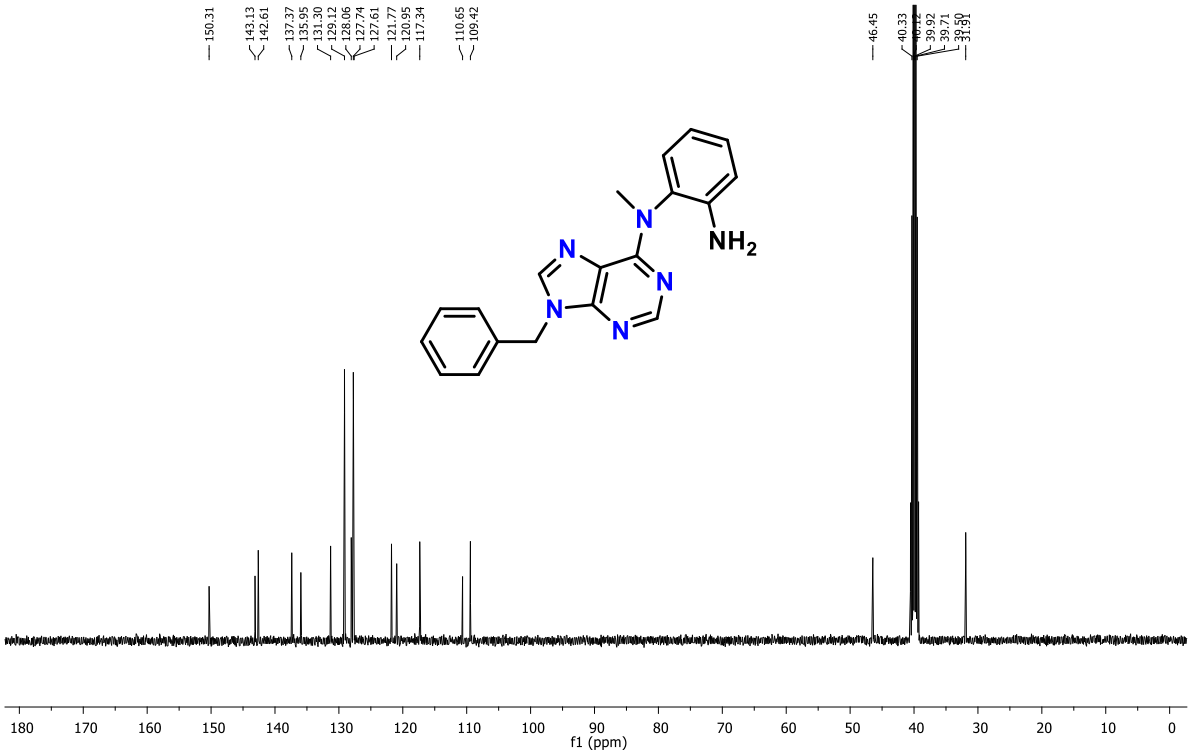
^{13}C NMR (101 MHz, $CDCl_3$) spectrum of compound (17)



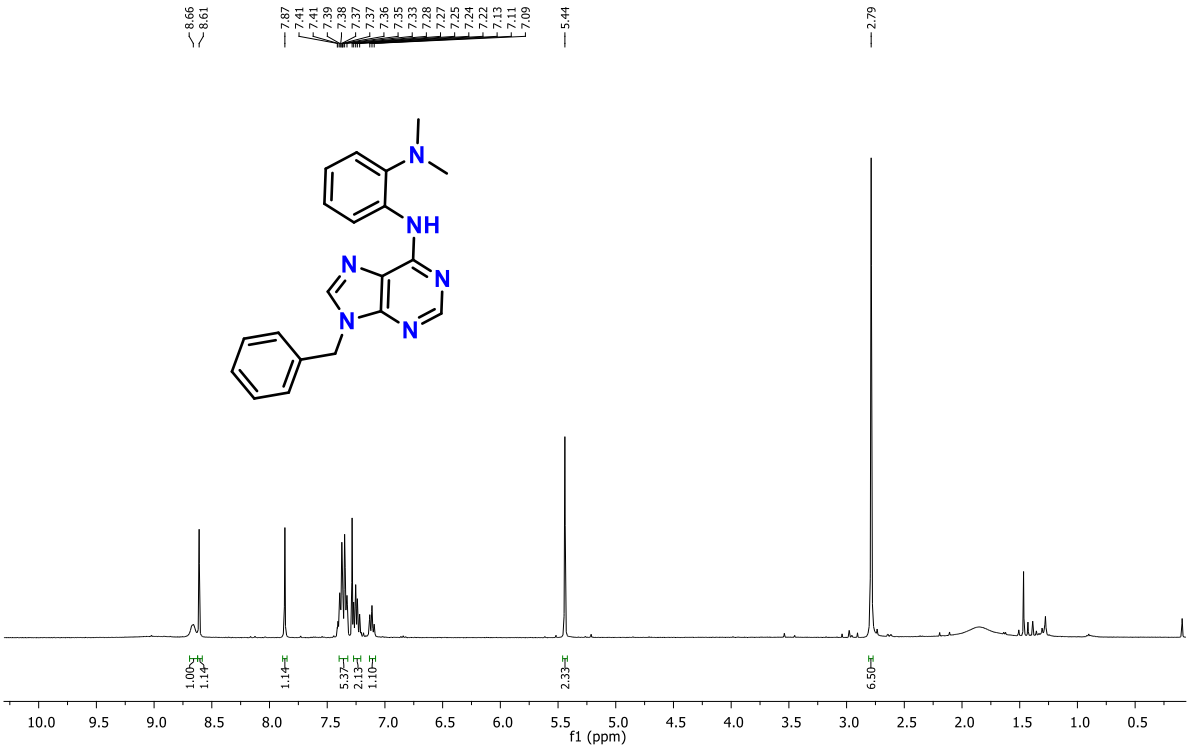
^{1}H NMR (400 MHz, DMSO-d$_6$) spectrum of compound (19)



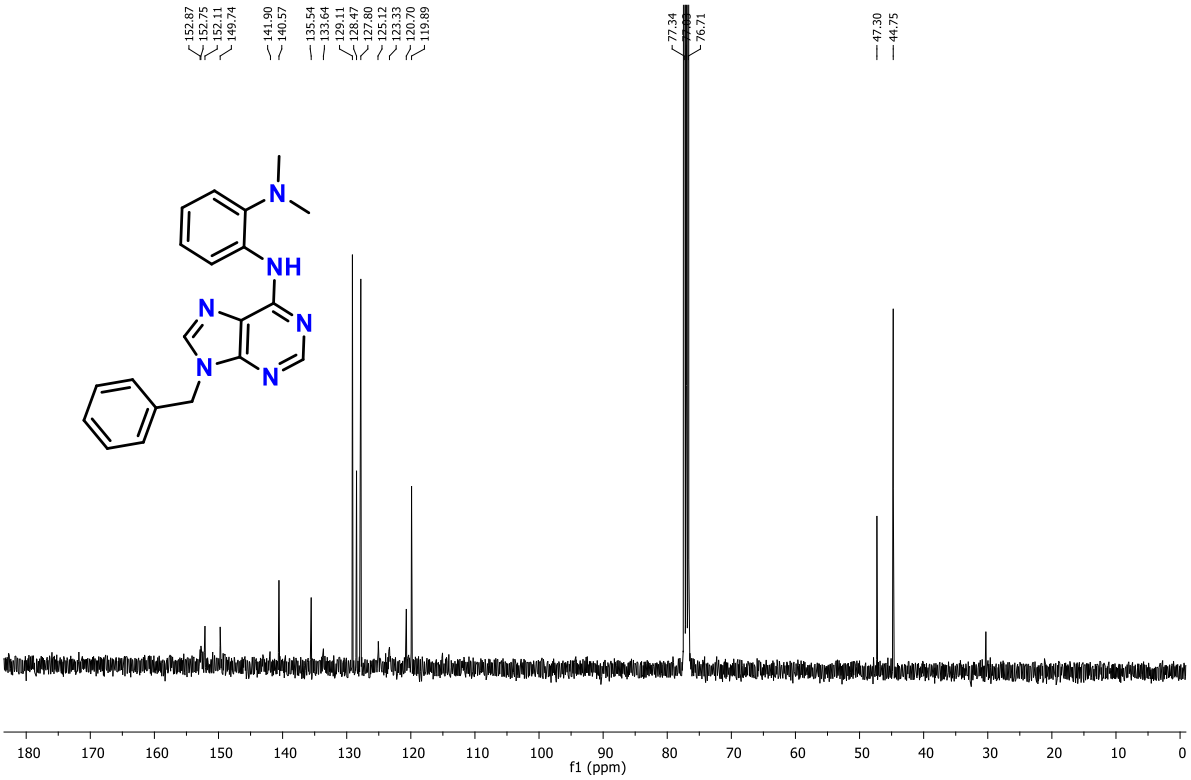
^{13}C NMR (101 MHz, DMSO-d$_6$) spectrum of compound (19)



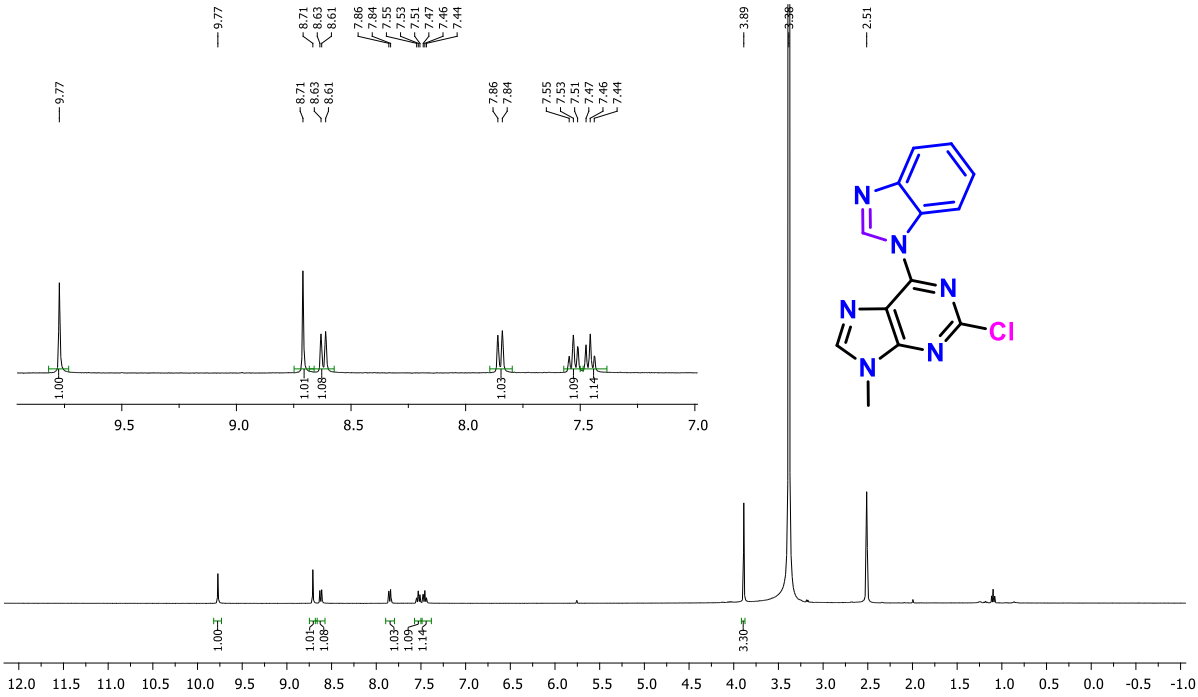
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (20)



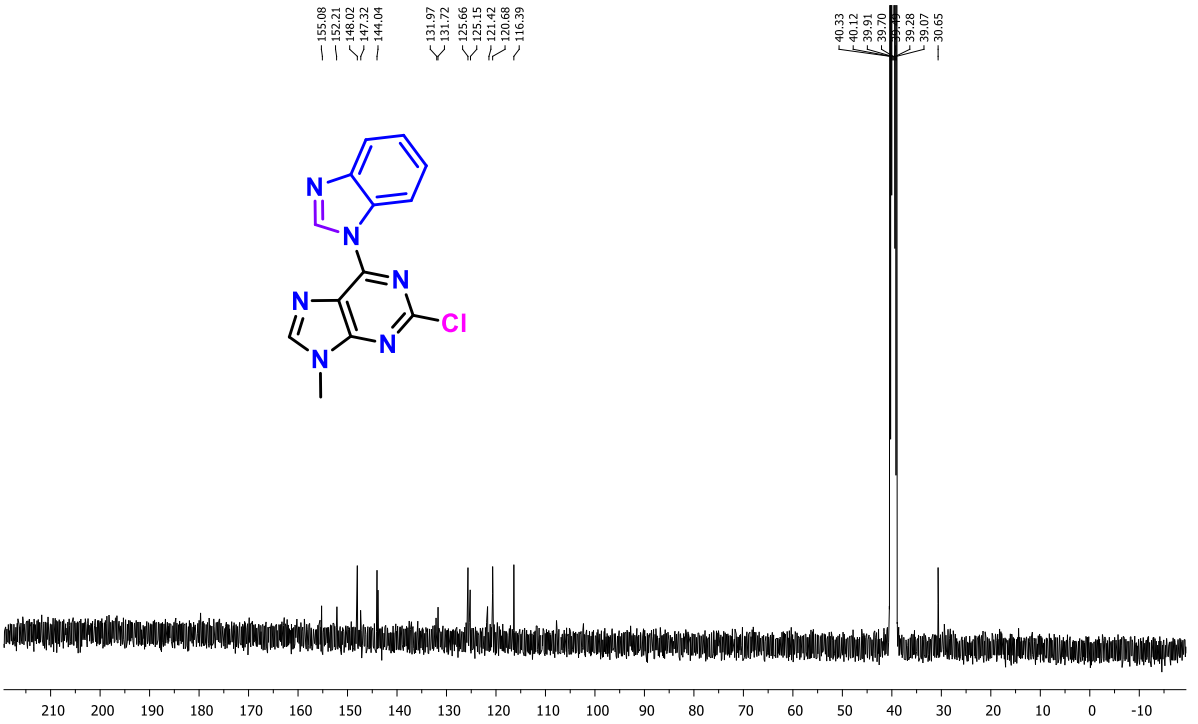
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (20)



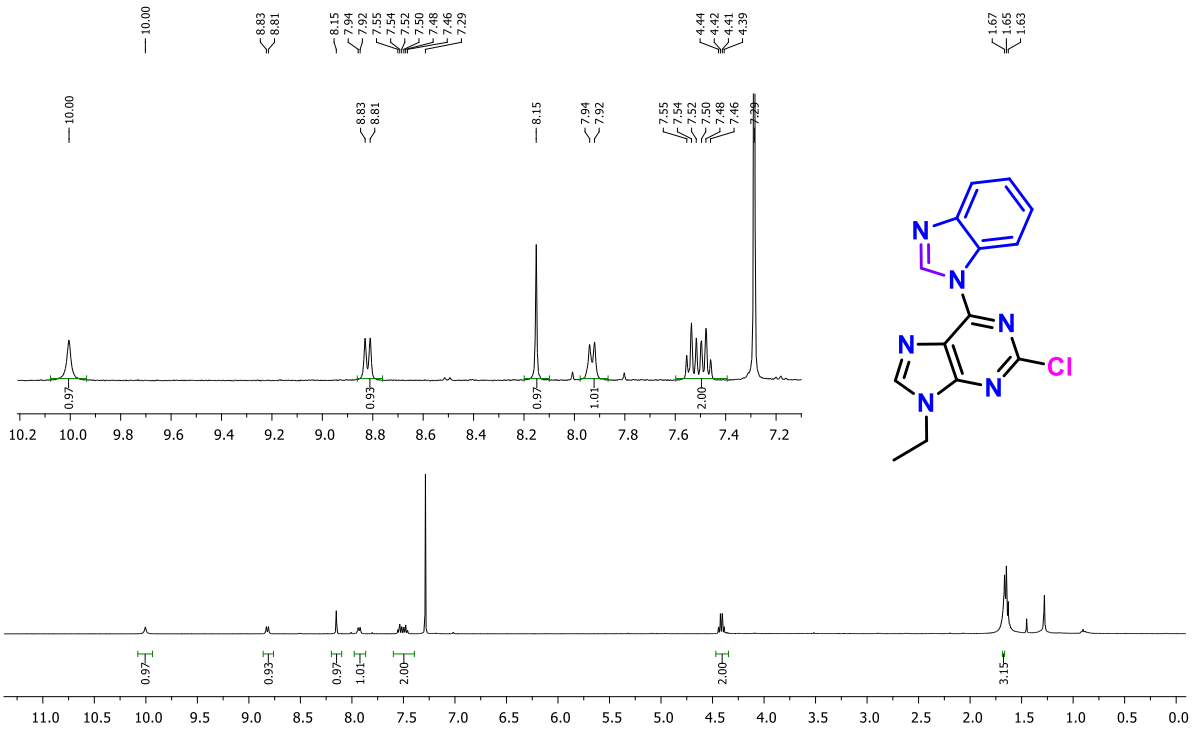
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (11a)



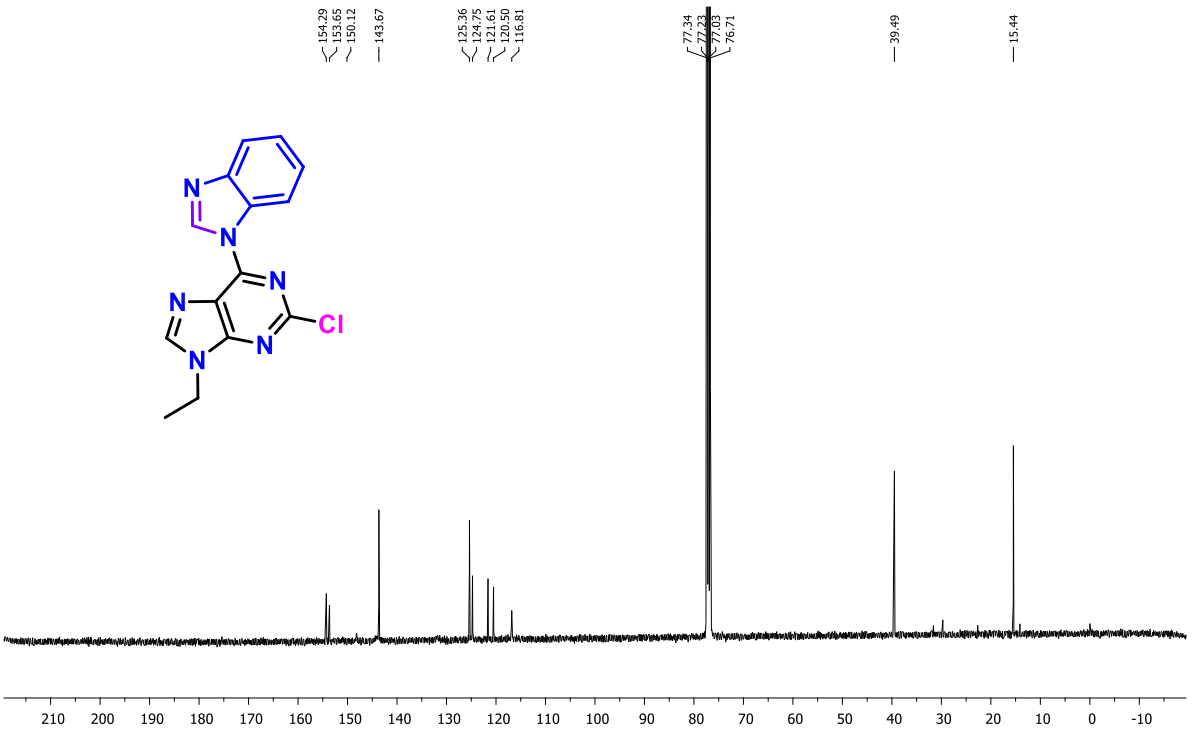
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (11a)



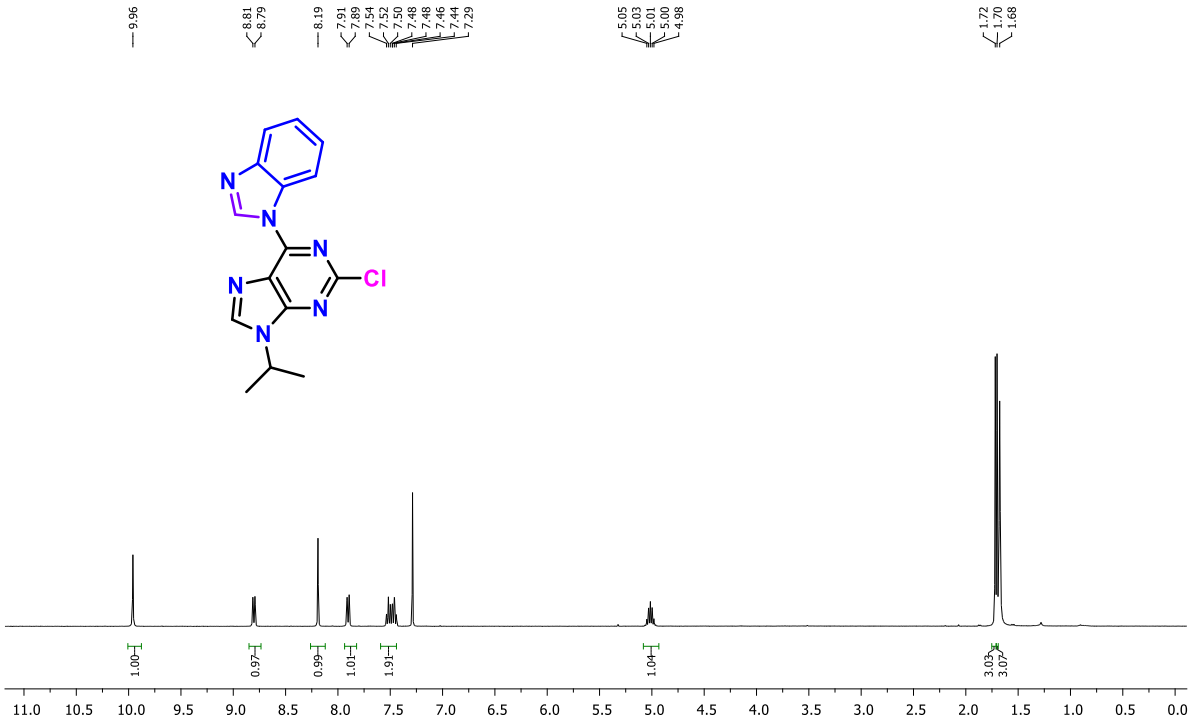
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (11b)



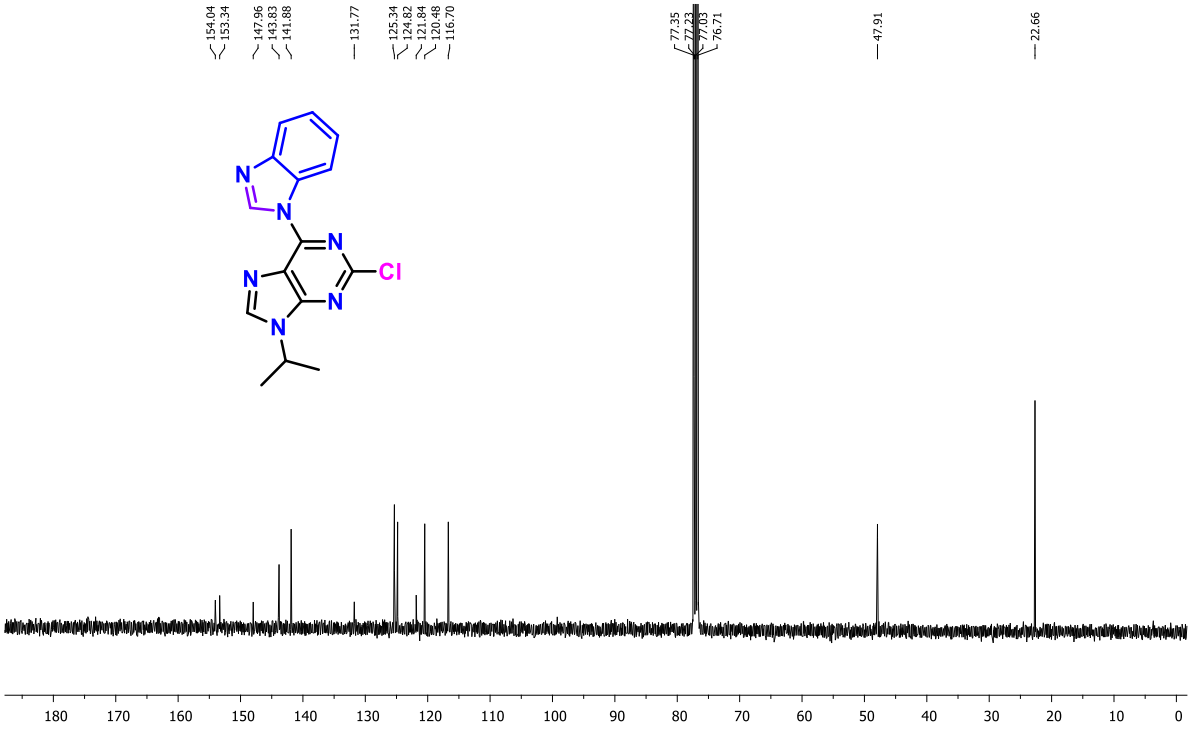
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (11b)



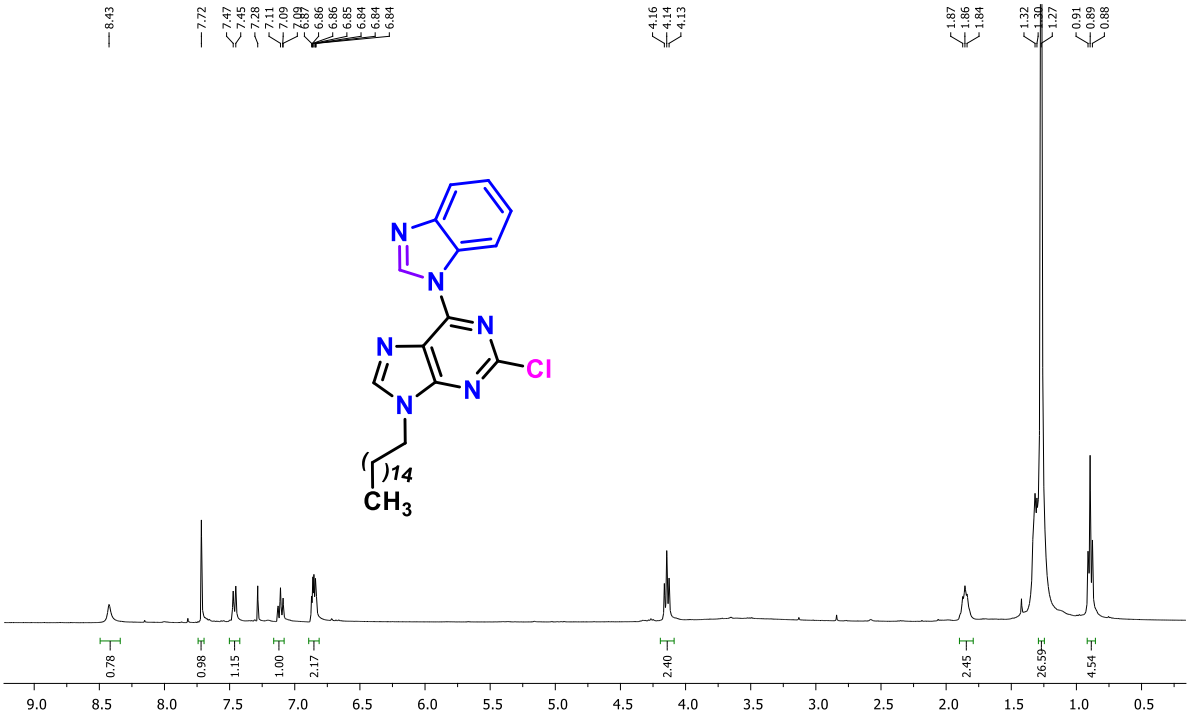
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (11c)



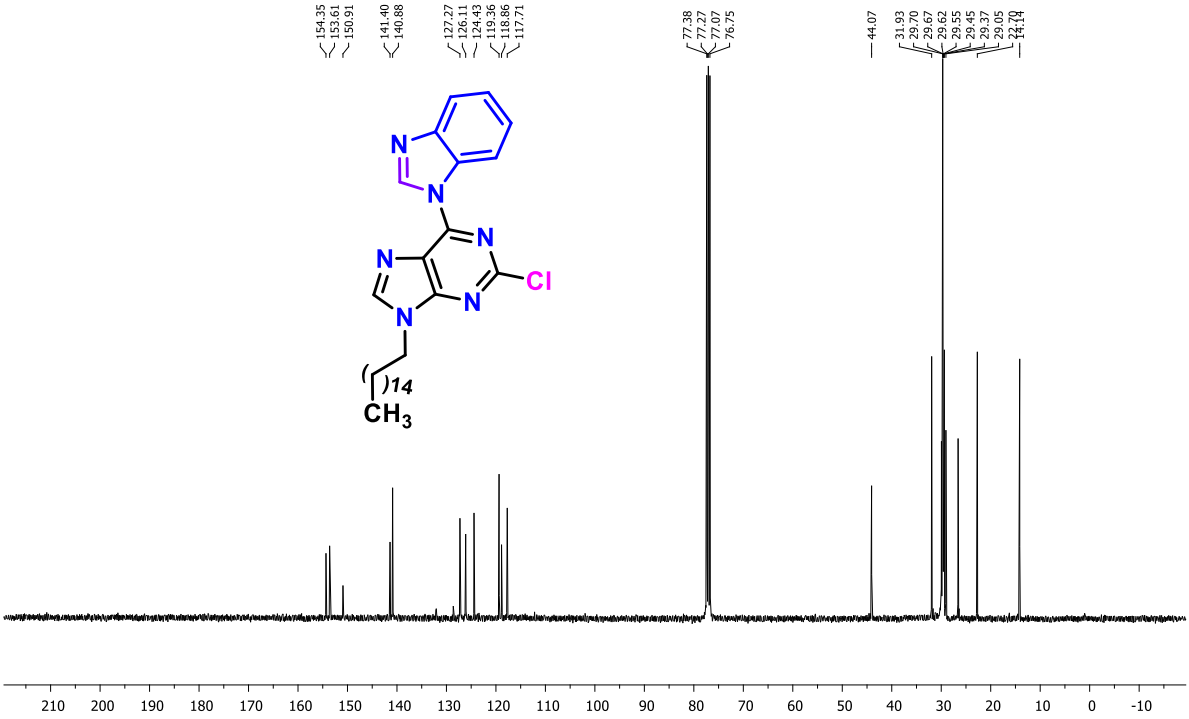
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (11c)



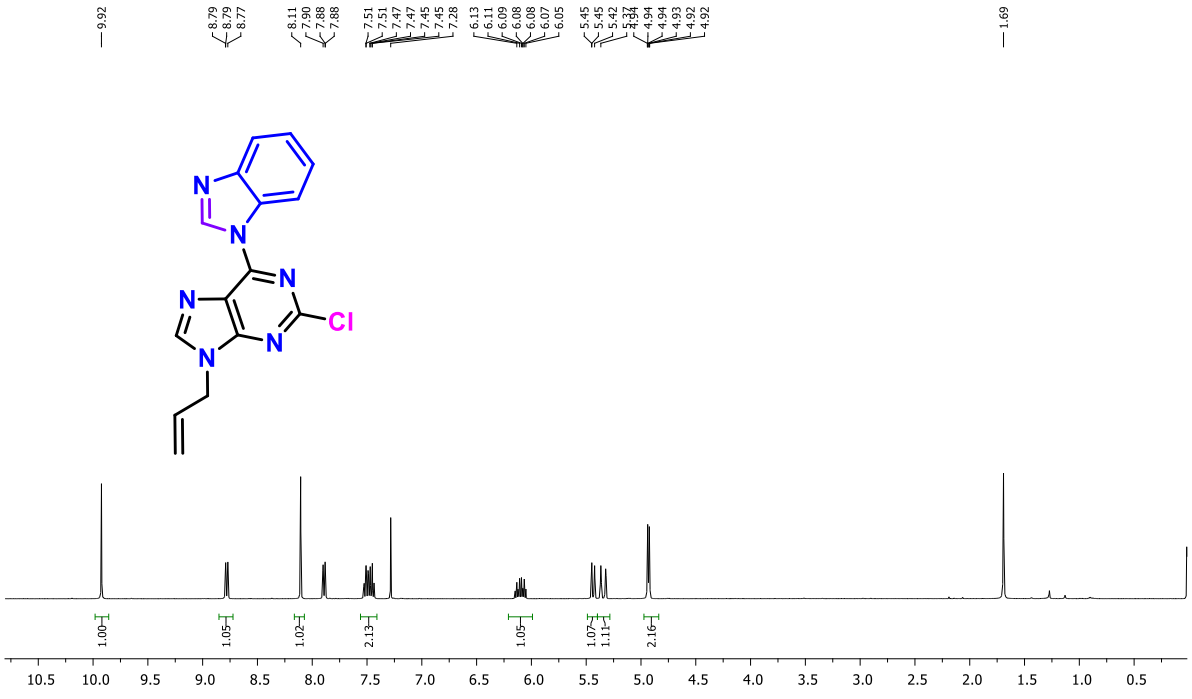
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (11d)



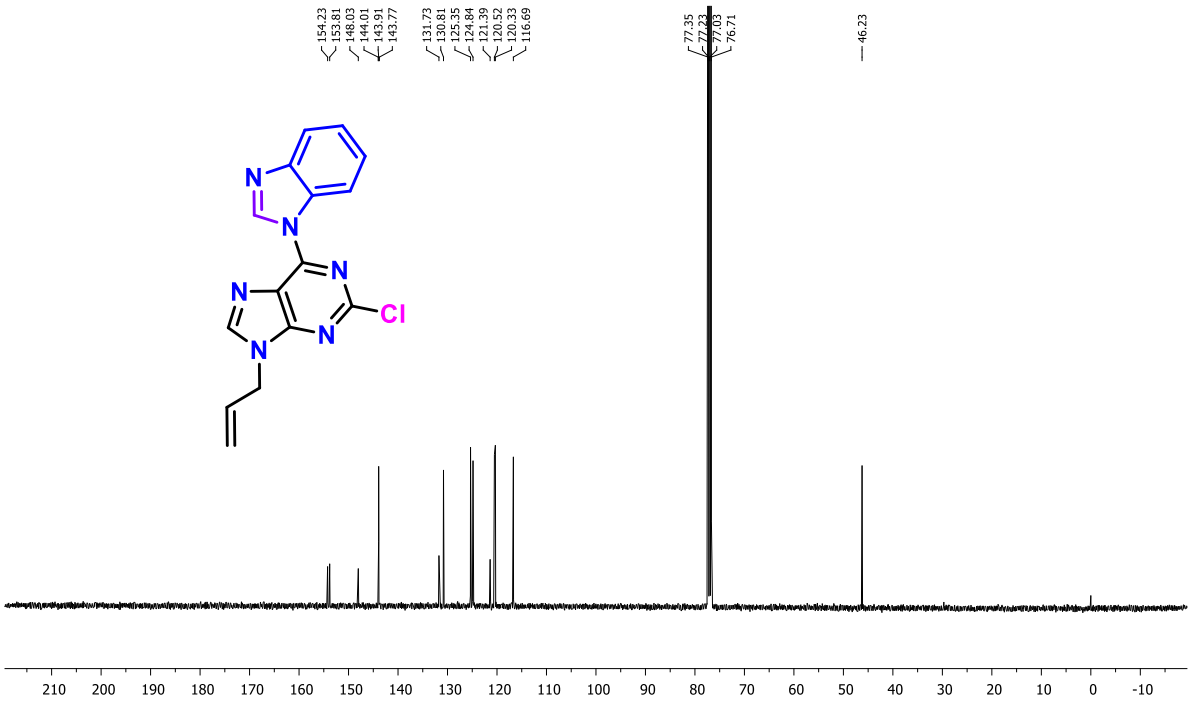
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (11d)



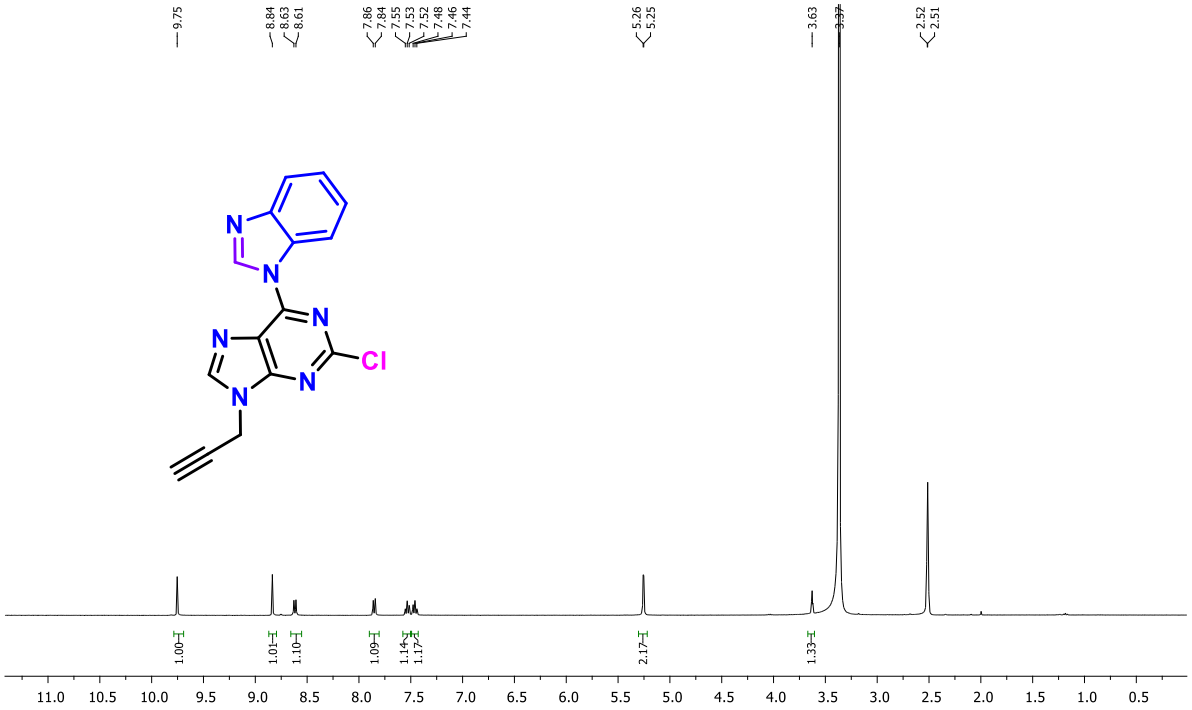
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (11e)



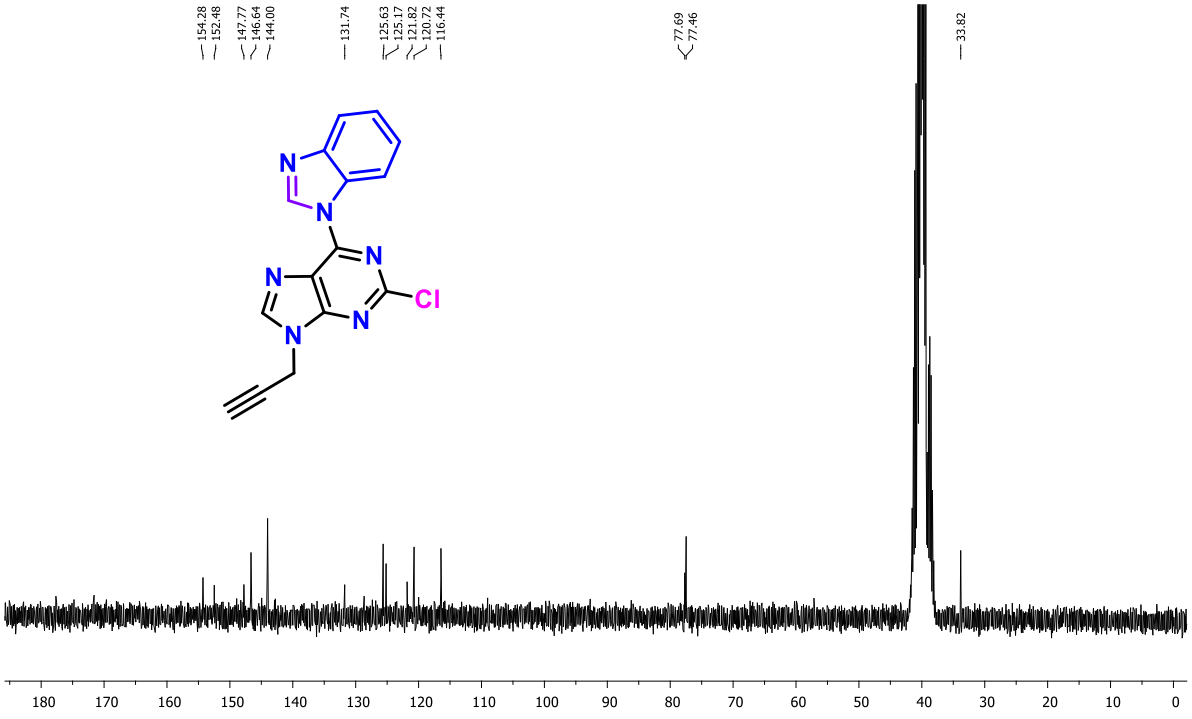
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (11e)



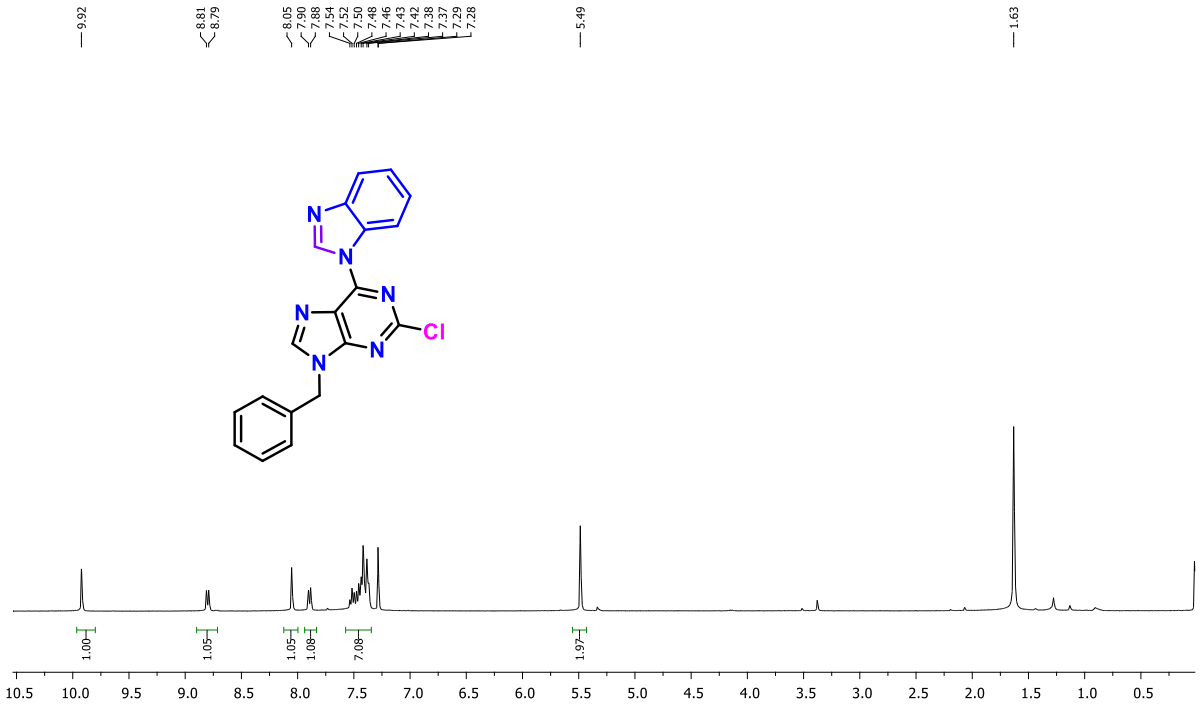
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (11f)



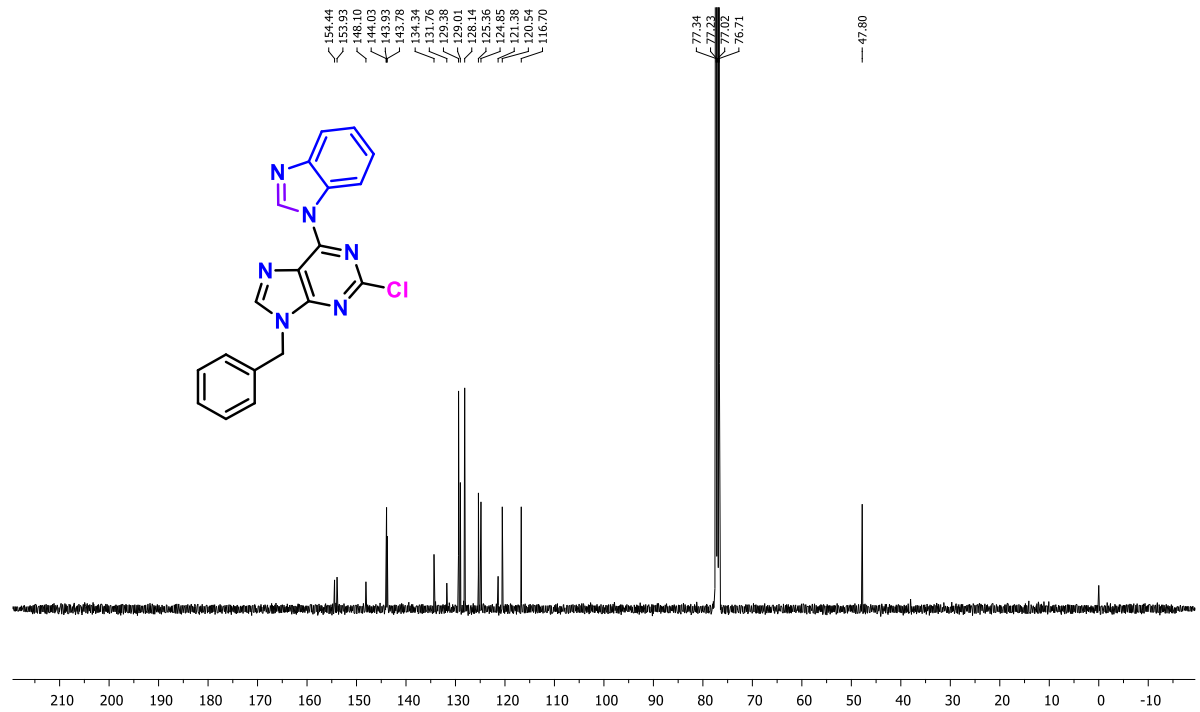
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (11f)



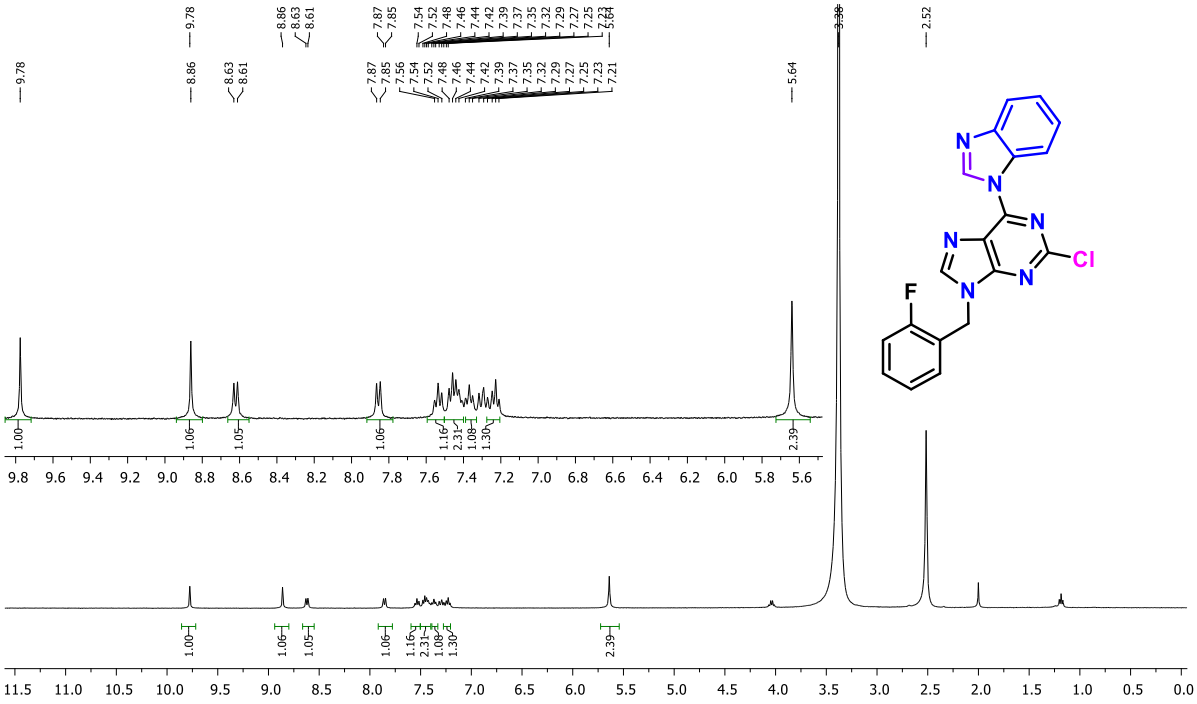
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (11g)



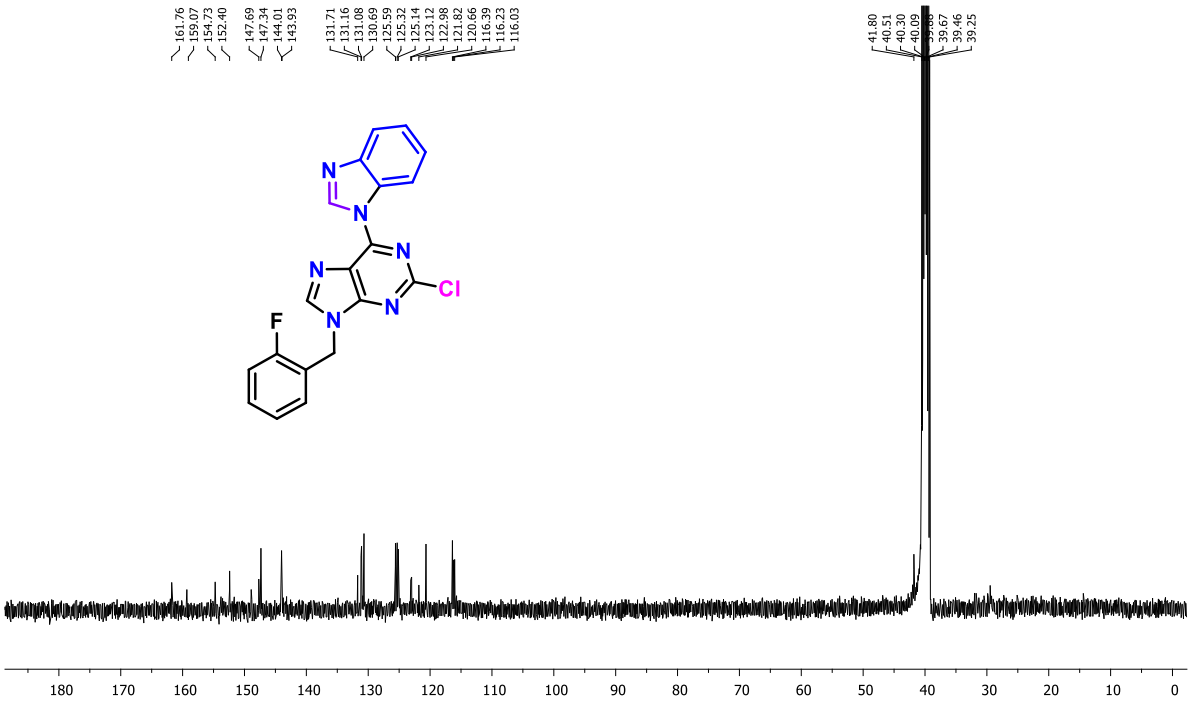
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (11g)



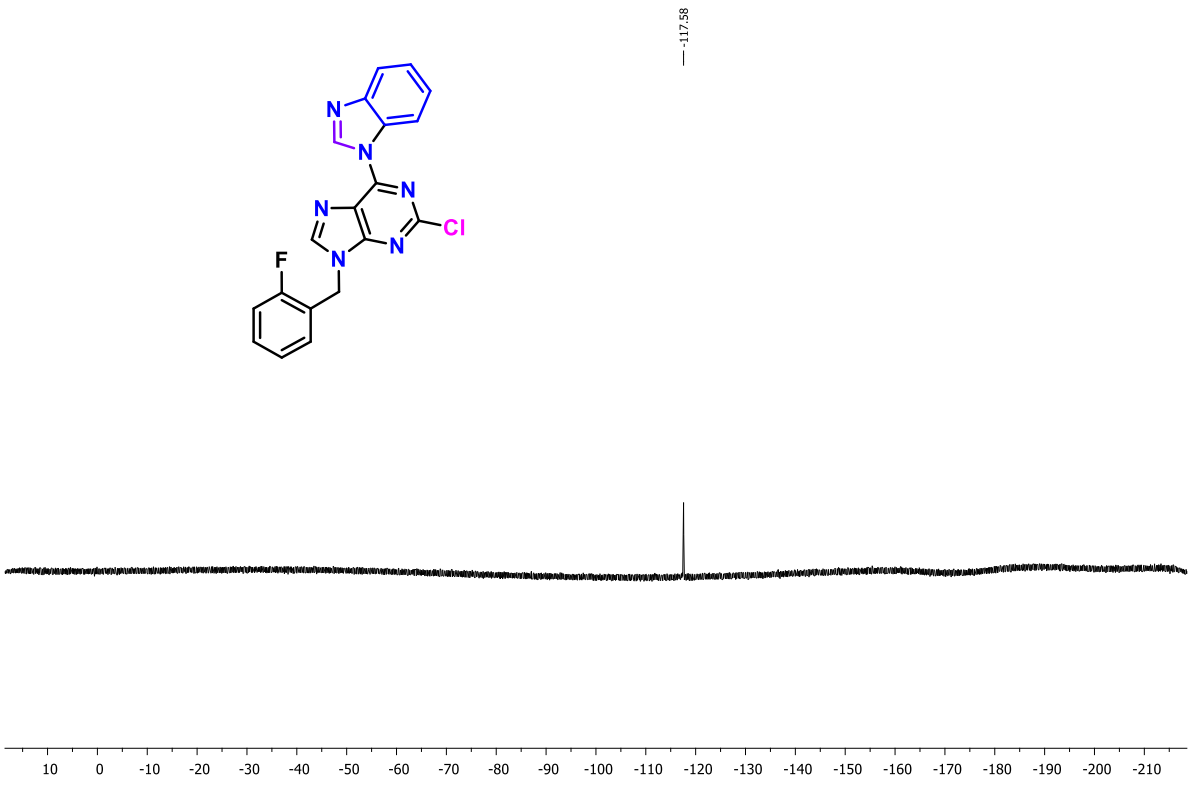
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (11h)



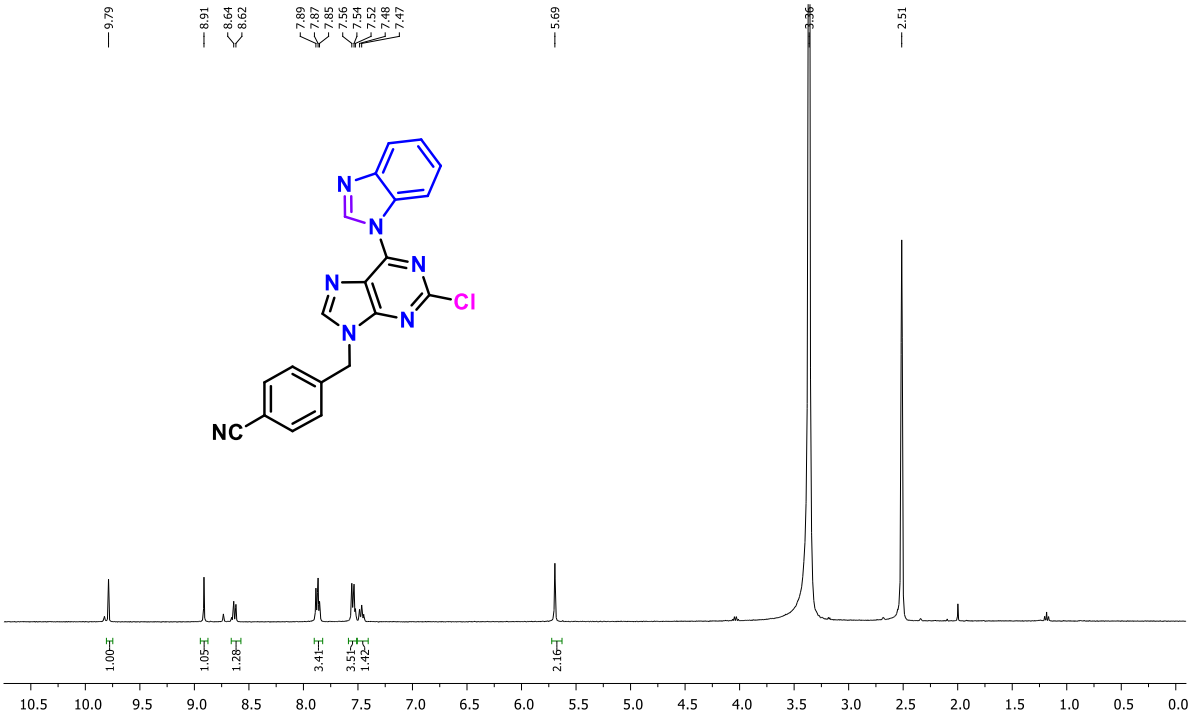
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (11h)



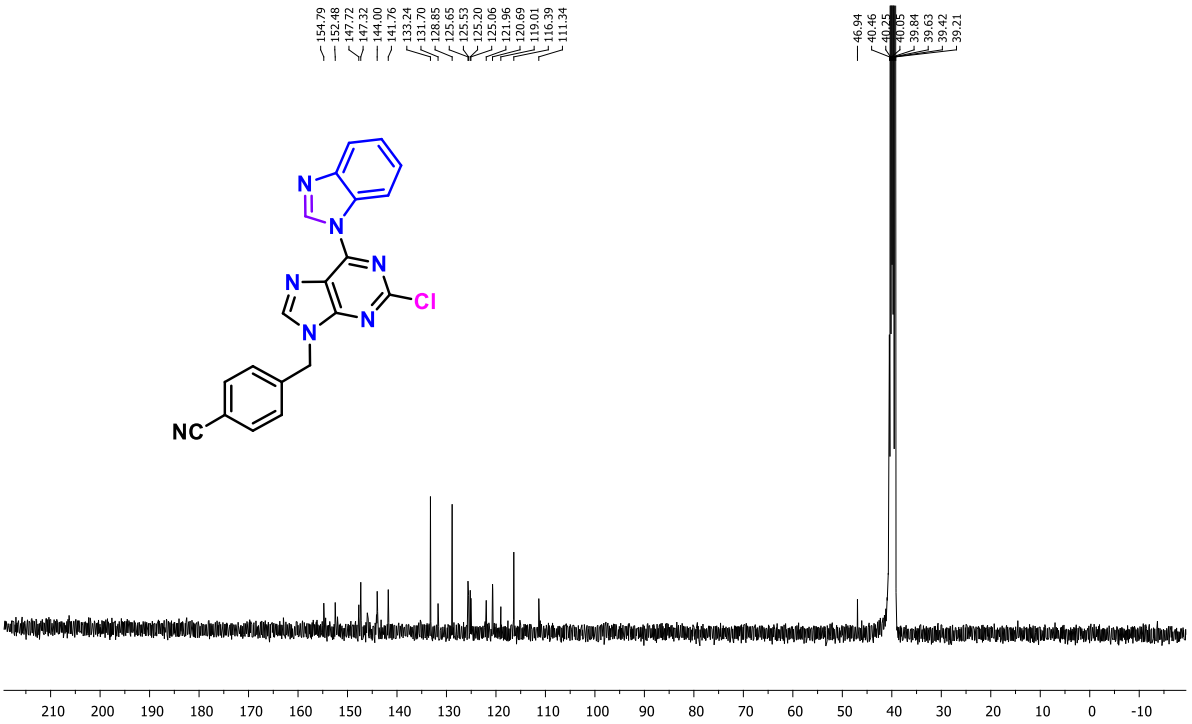
^{19}F NMR (377 MHz, DMSO-d_6) spectrum of compound (11h)



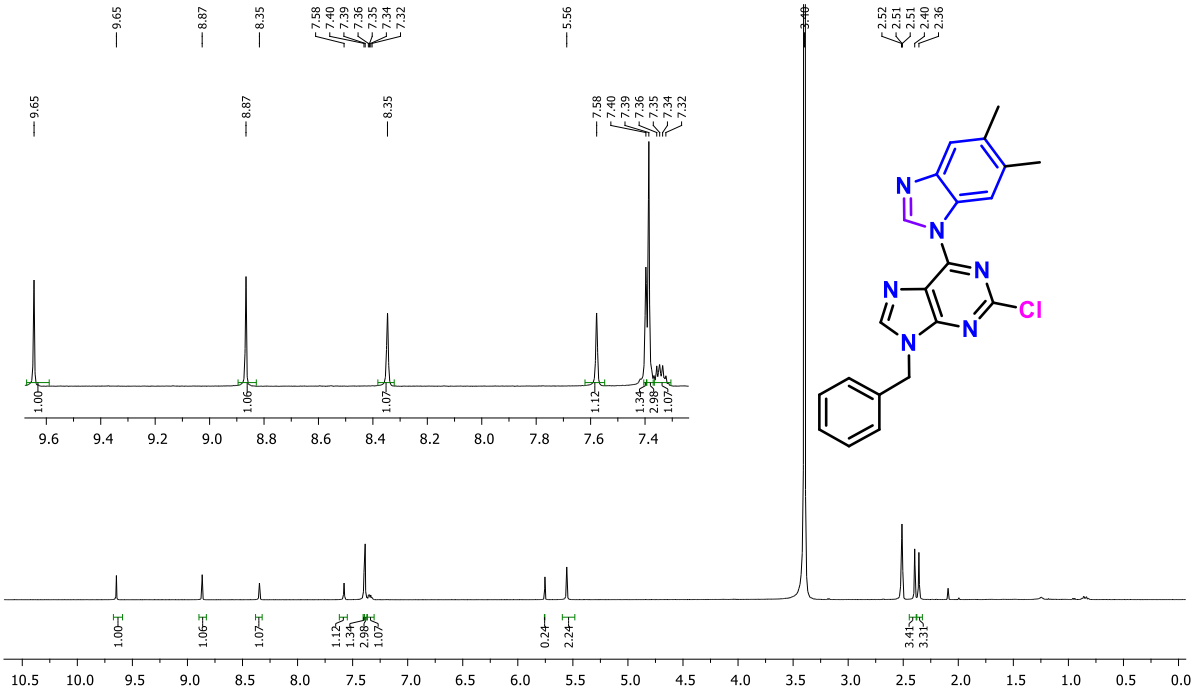
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (11i)



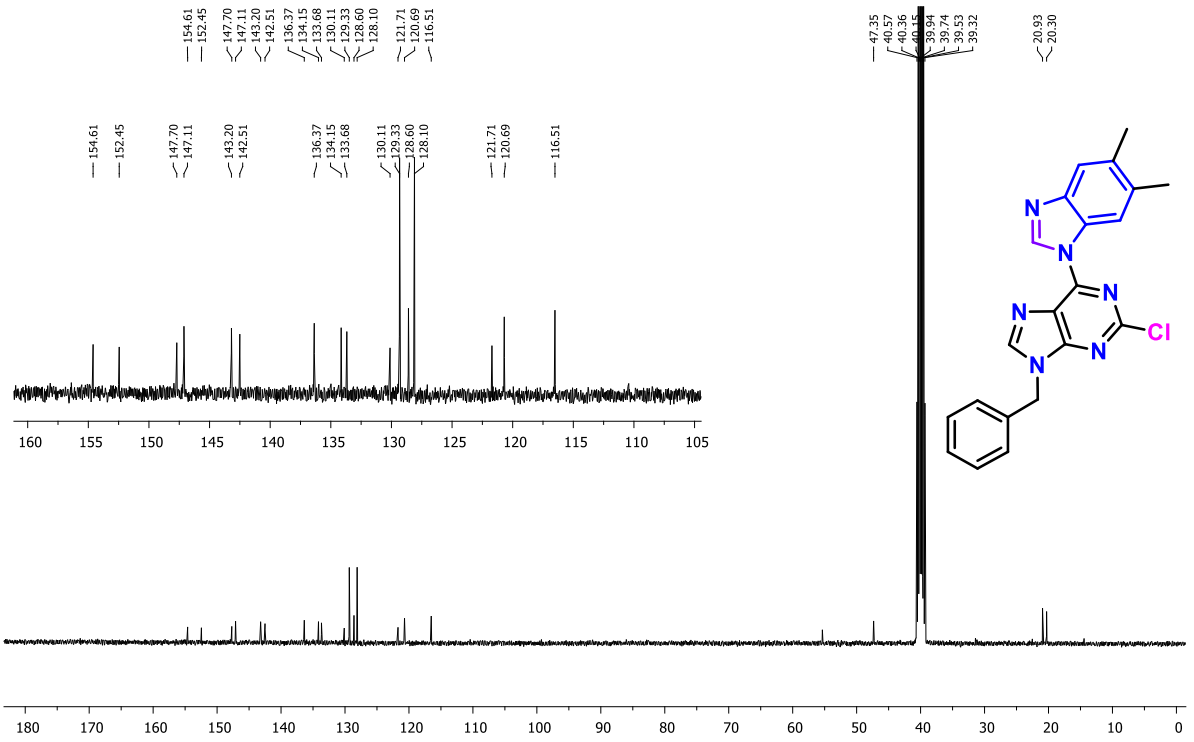
^{13}C NMR (101MHz, DMSO-d_6) spectrum of compound (11i)



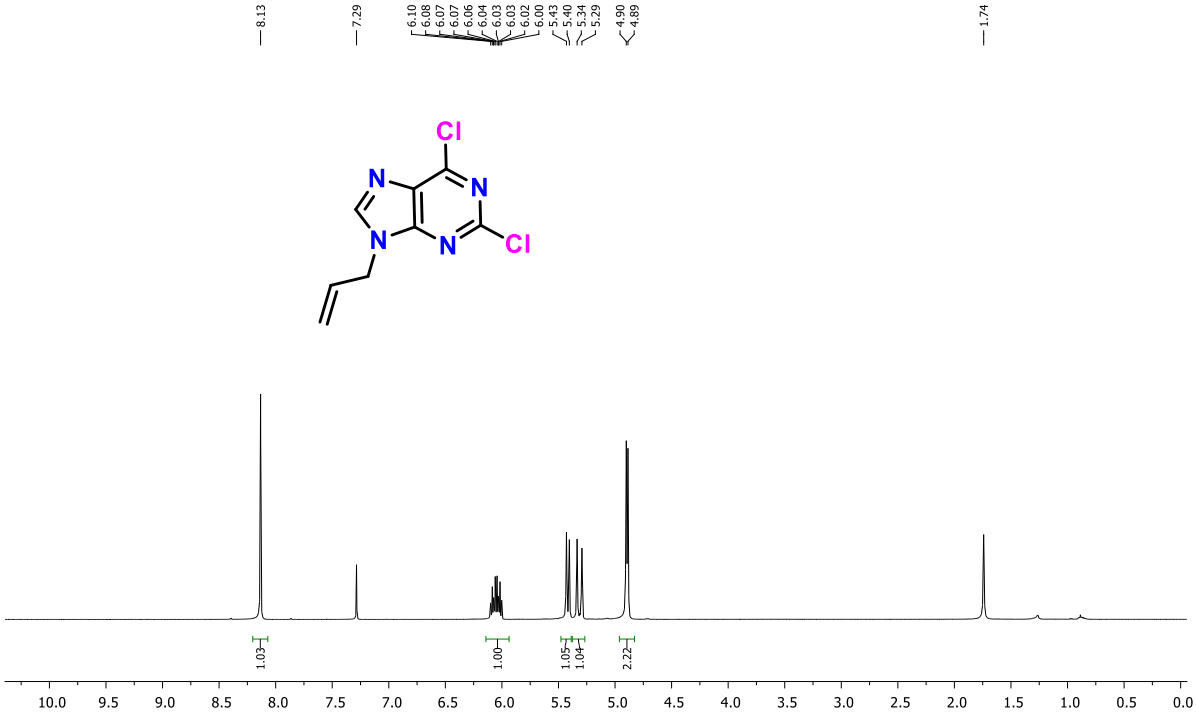
^{1}H NMR (400MHz, DMSO-d_6) spectrum of compound (11j)



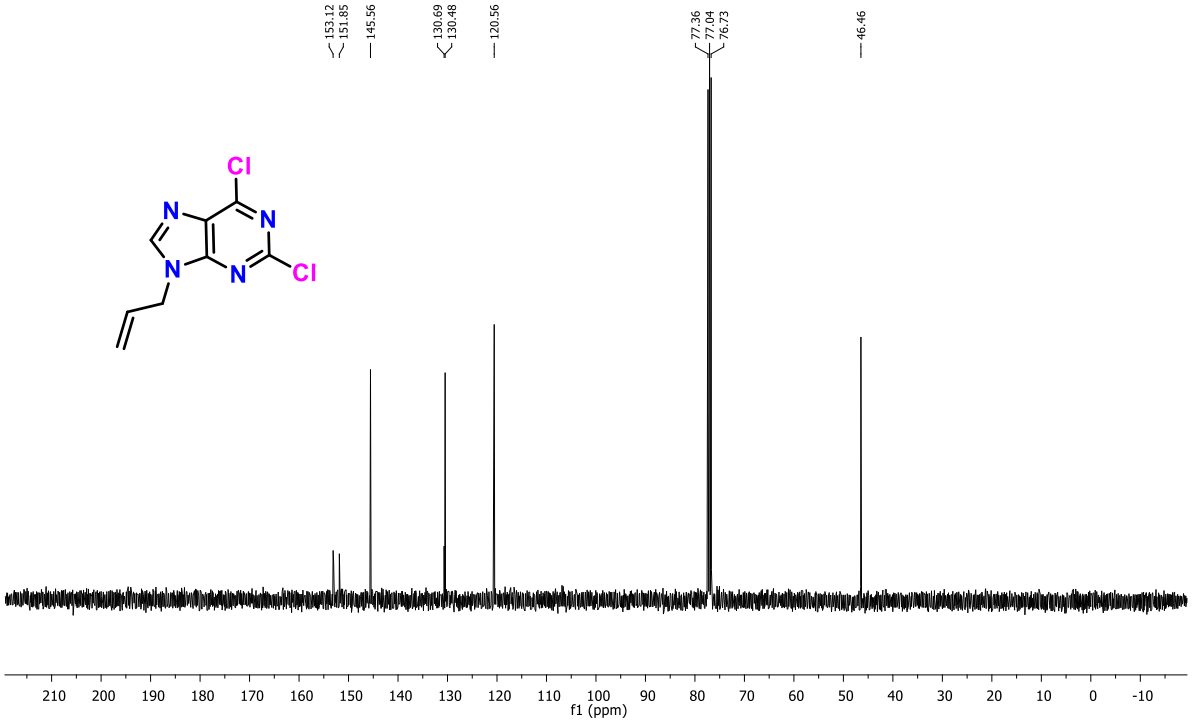
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound (11j)



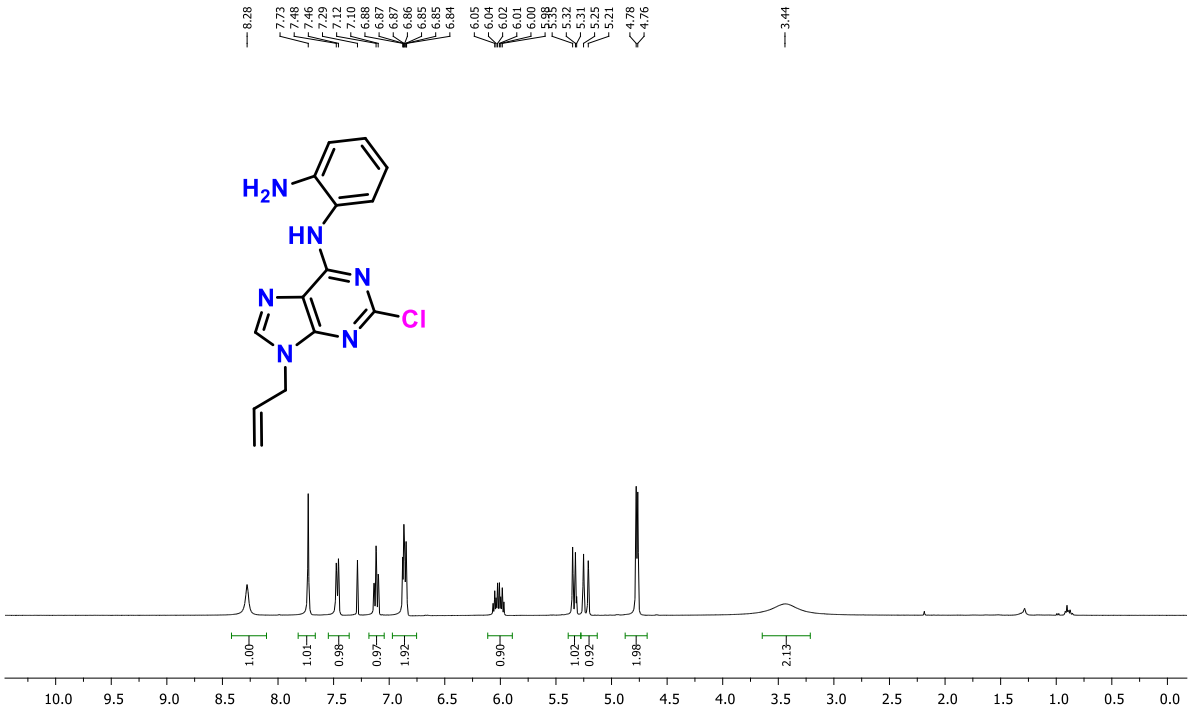
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (10′)



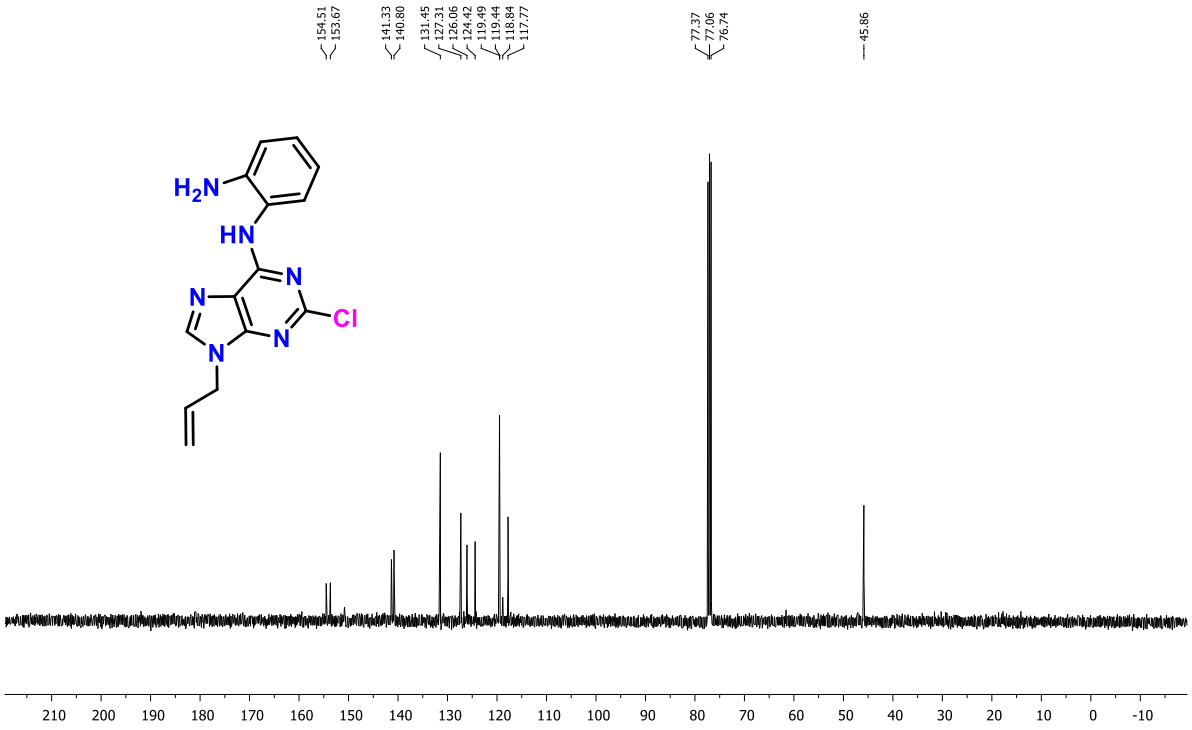
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (10′)



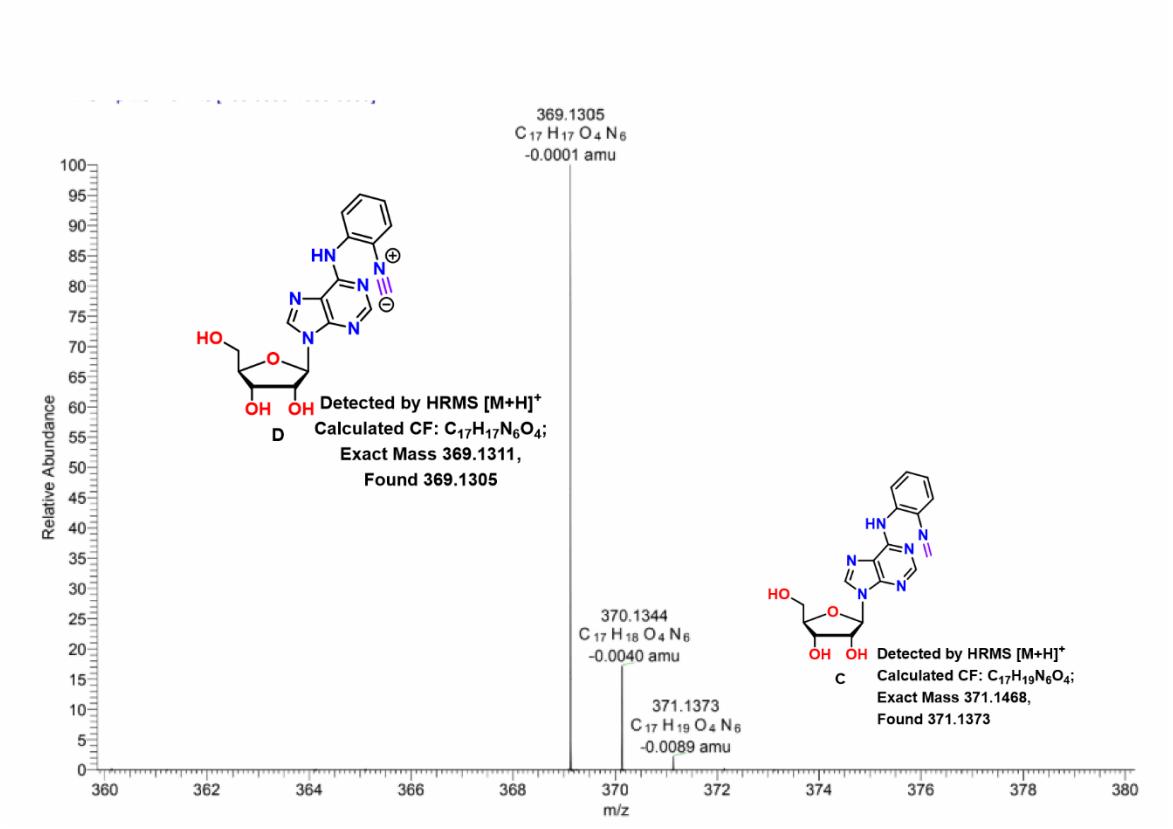
^{1}H NMR (400MHz, $CDCl_3$) spectrum of compound (12)



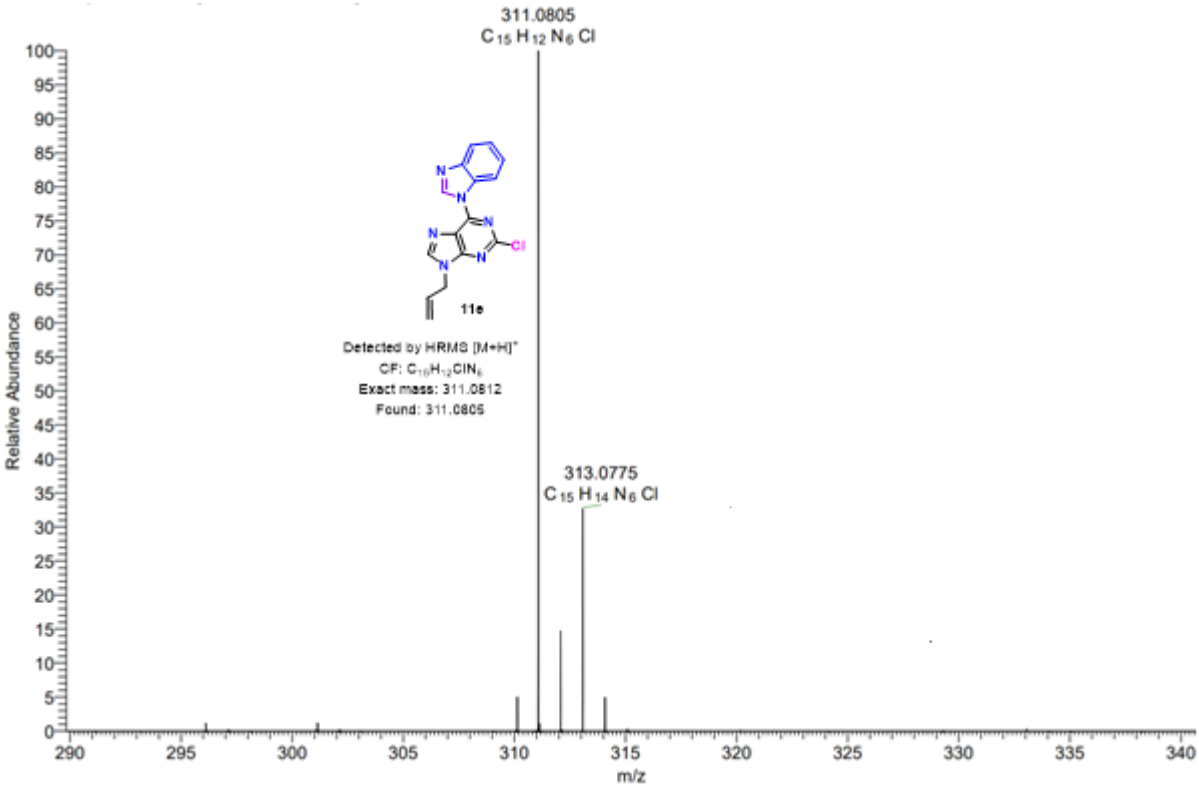
^{13}C NMR (101MHz, $CDCl_3$) spectrum of compound (12)



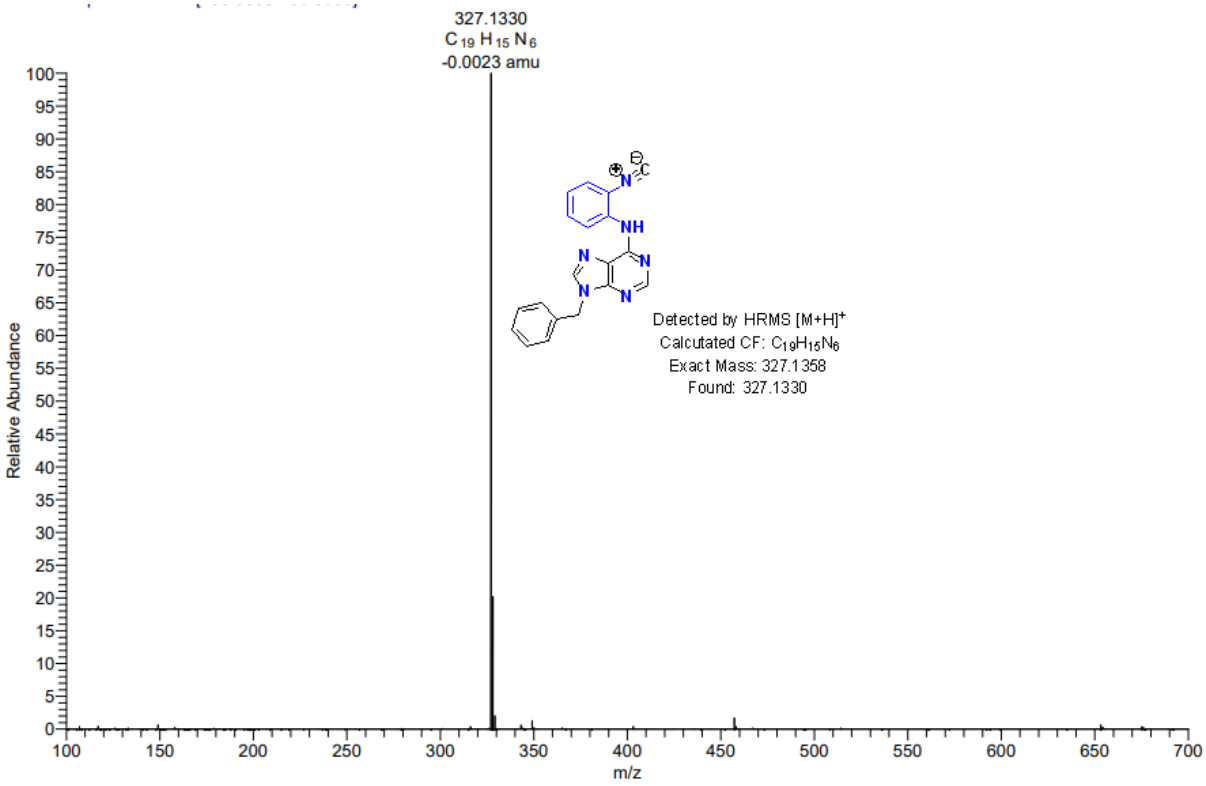
8. HRMS spectra of the intermediate C and D (Scheme 5)



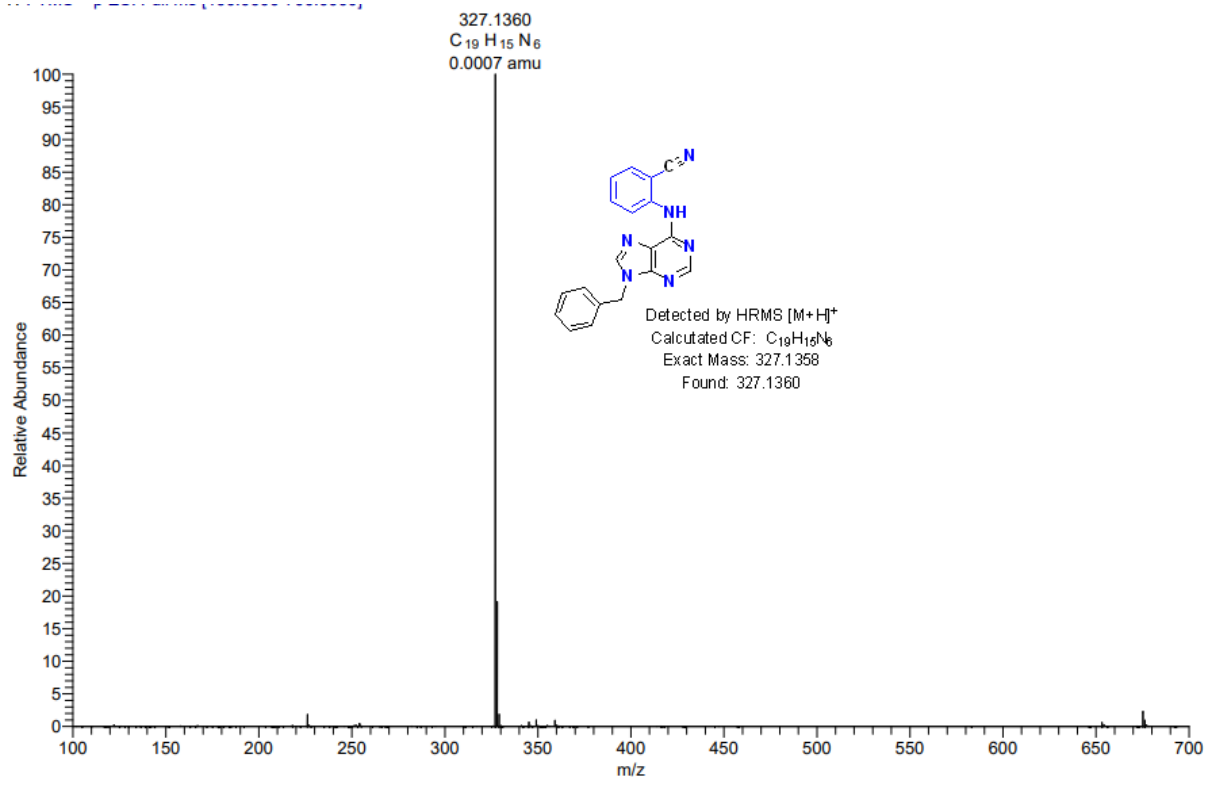
HRMS spectra of the intermediate 11e (Scheme 7)



HRMS spectra of compound 14



HRMS spectra of compound 16



HRMS spectra of compound 17