Supporting Information

Discovery of novel PDE9A inhibitors with antioxidant activity for treatment of Alzheimer's disease

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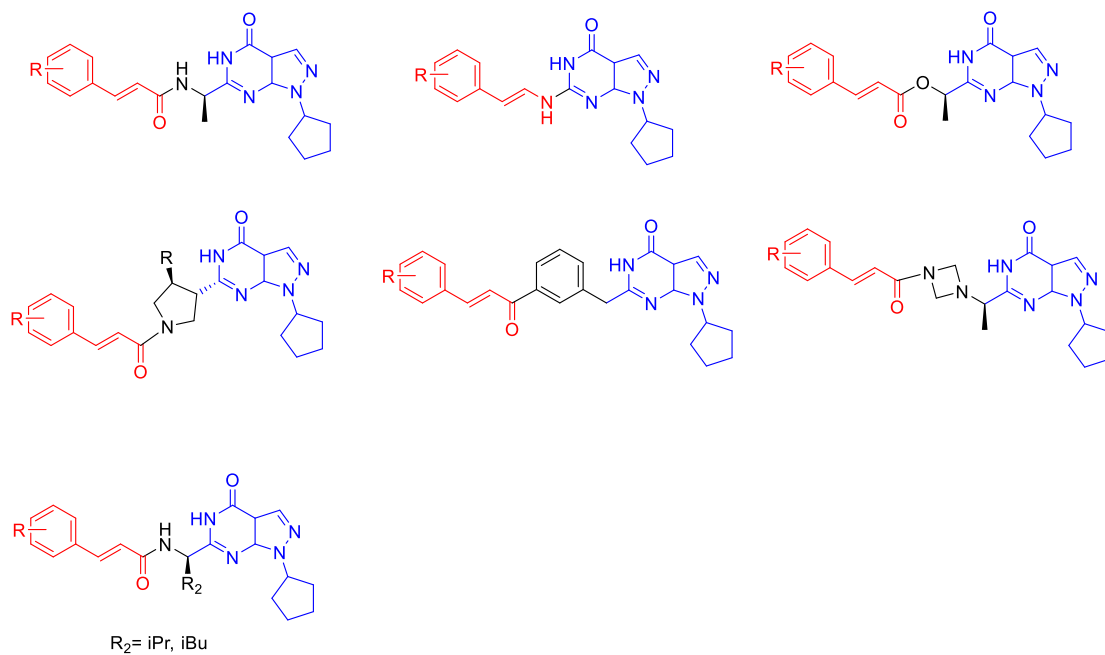
Content

Figure S1: Designed compounds with different linkers.

Table S1. The Docking Score values and IC_{50} of compounds **1a-1l**, **2**, and **3**.

Compound	Docking Score[a]	$IC_{50}\pm$ SD (nM)[b]
3	3.7284	>500[c]
1e	5.6790	>200[c]
1a	5.8646	126 ± 15
1l	6.2419	57±4
1k	6.3890	130±6
1d	6.7393	83± 11
1b	6.9738	64± 2
1j	7.0099	186±7
1h	7.1075	56±7
2	7.1897	25±4
1f	7.2400	190±7
1c	7.2997	65± 4
1i	7.8117	133±22
1g	8.6352	63± 3

[a] Docking Score values are given by the total_score of Surflex-Dock method embedded in Tripos Sybyl 2.0.

[b] IC_{50} values are given as the mean of three independent determinations.

[c] The IC_{50} values of **1e** and **3** are treated as 200 and 500 nM for the correlation with Docking Score values.

$$y = -79.11 x + 664.77$$
$$R_2 = 0.577$$

Fig. S2. The correlation between Docking Score values and IC_{50} values of compound **1a-1l**, **2**, and **3**.

Figure S3: Binding modes of compound **1a, 1c, 1d** and **1e.**

Figure S4: Binding modes of compounds **1b, 1j, 1k** and **1l**.

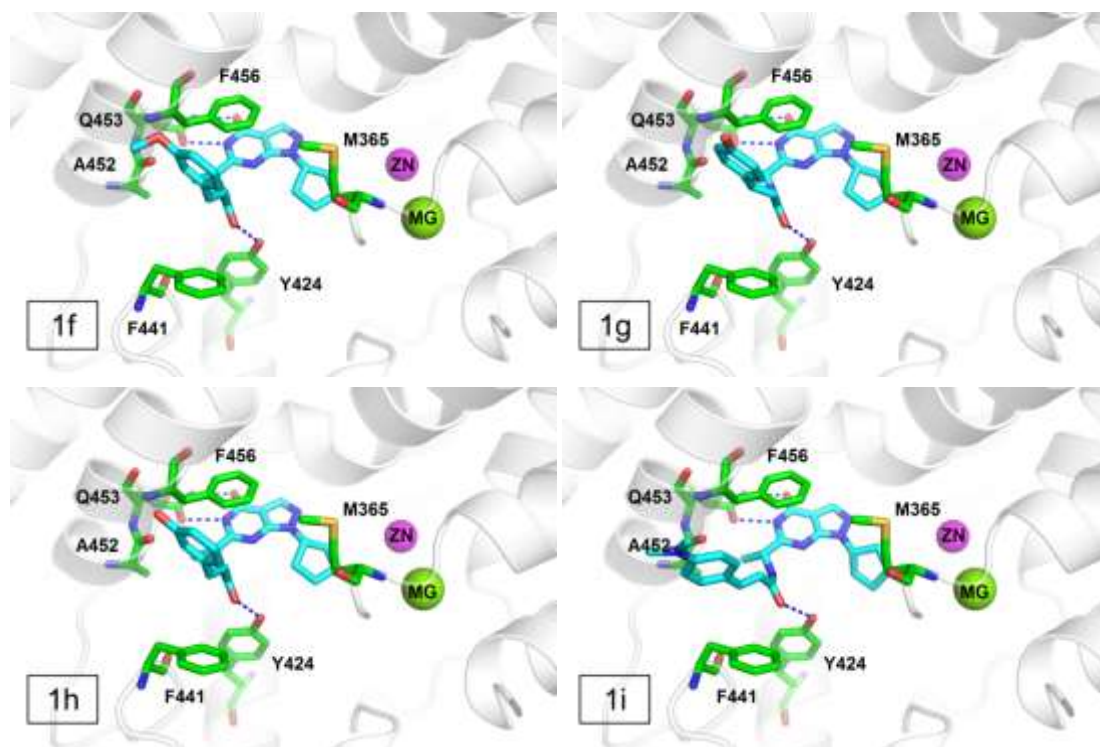**Figure S5:** Binding modes of compounds **1f, 1g, 1h** and **1i.**
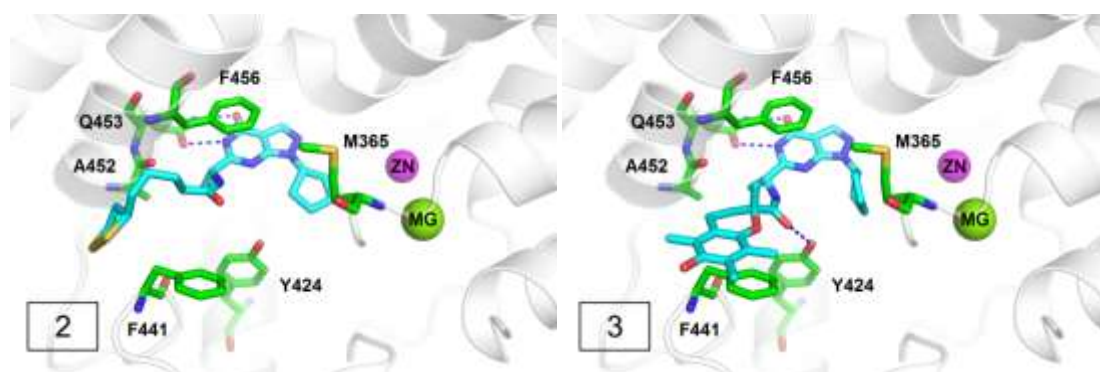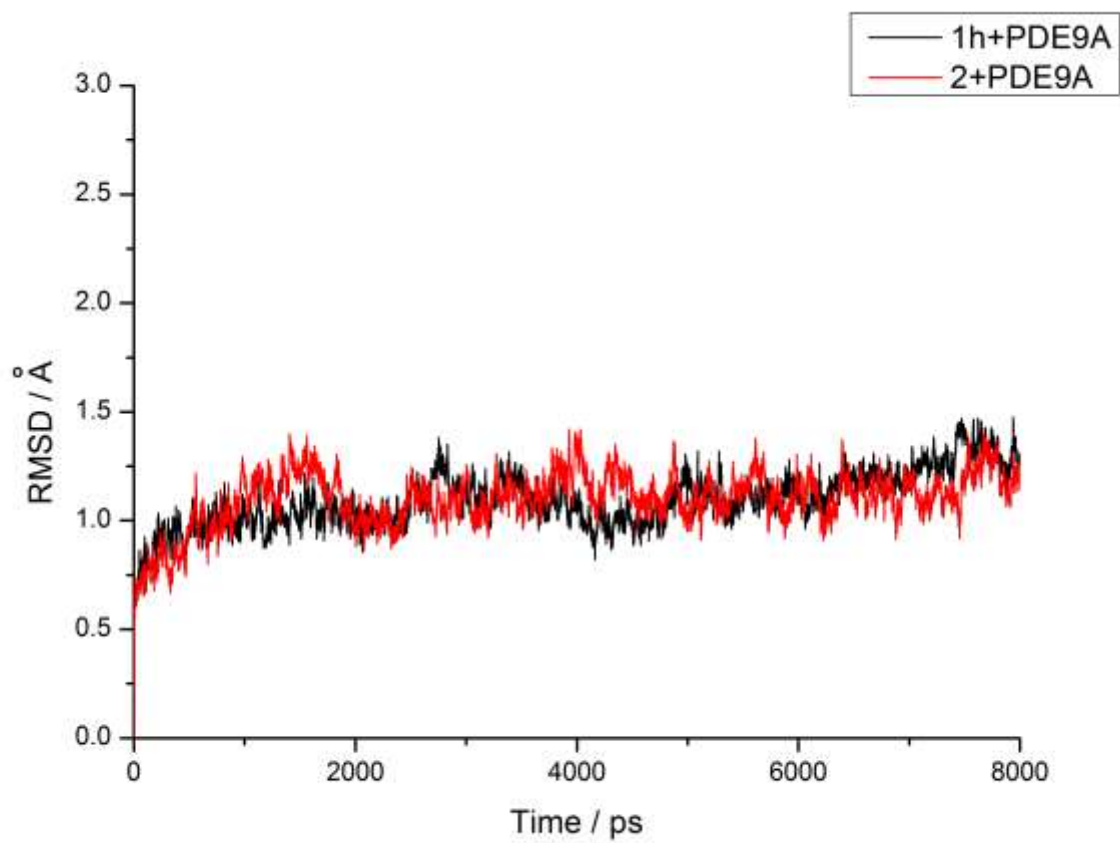

Figure S6: Binding modes of compound**s 2 and 3.**

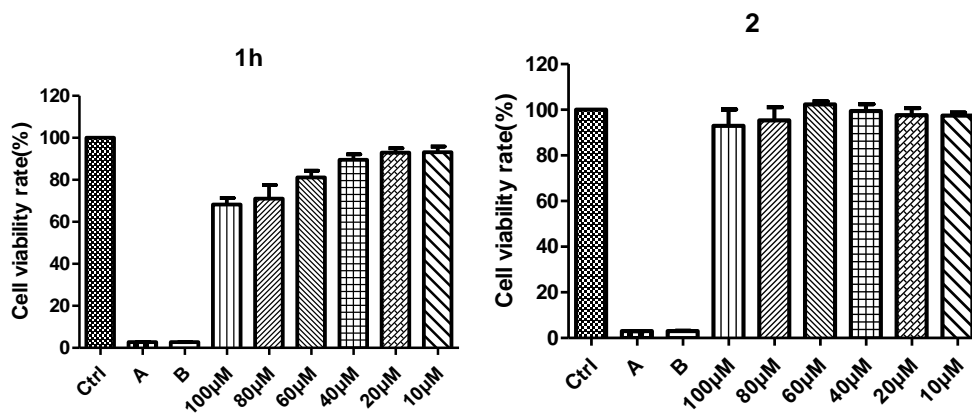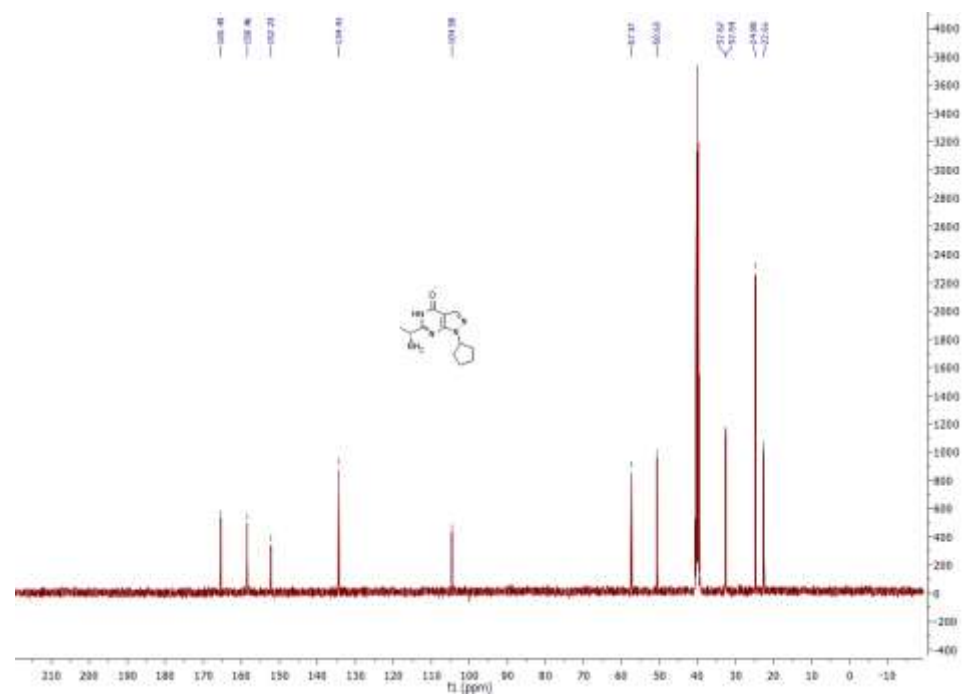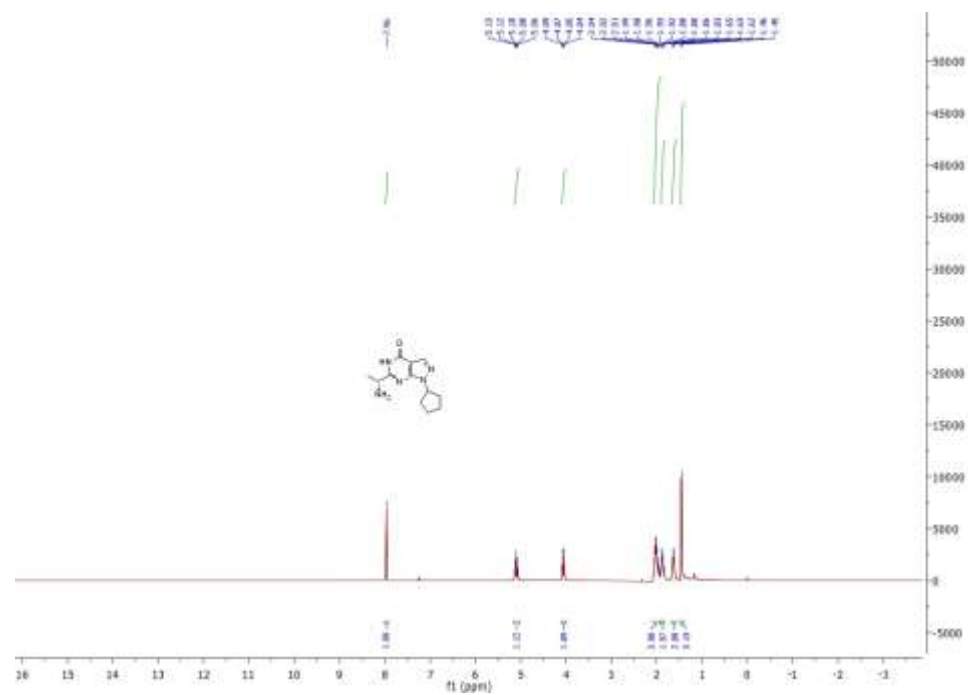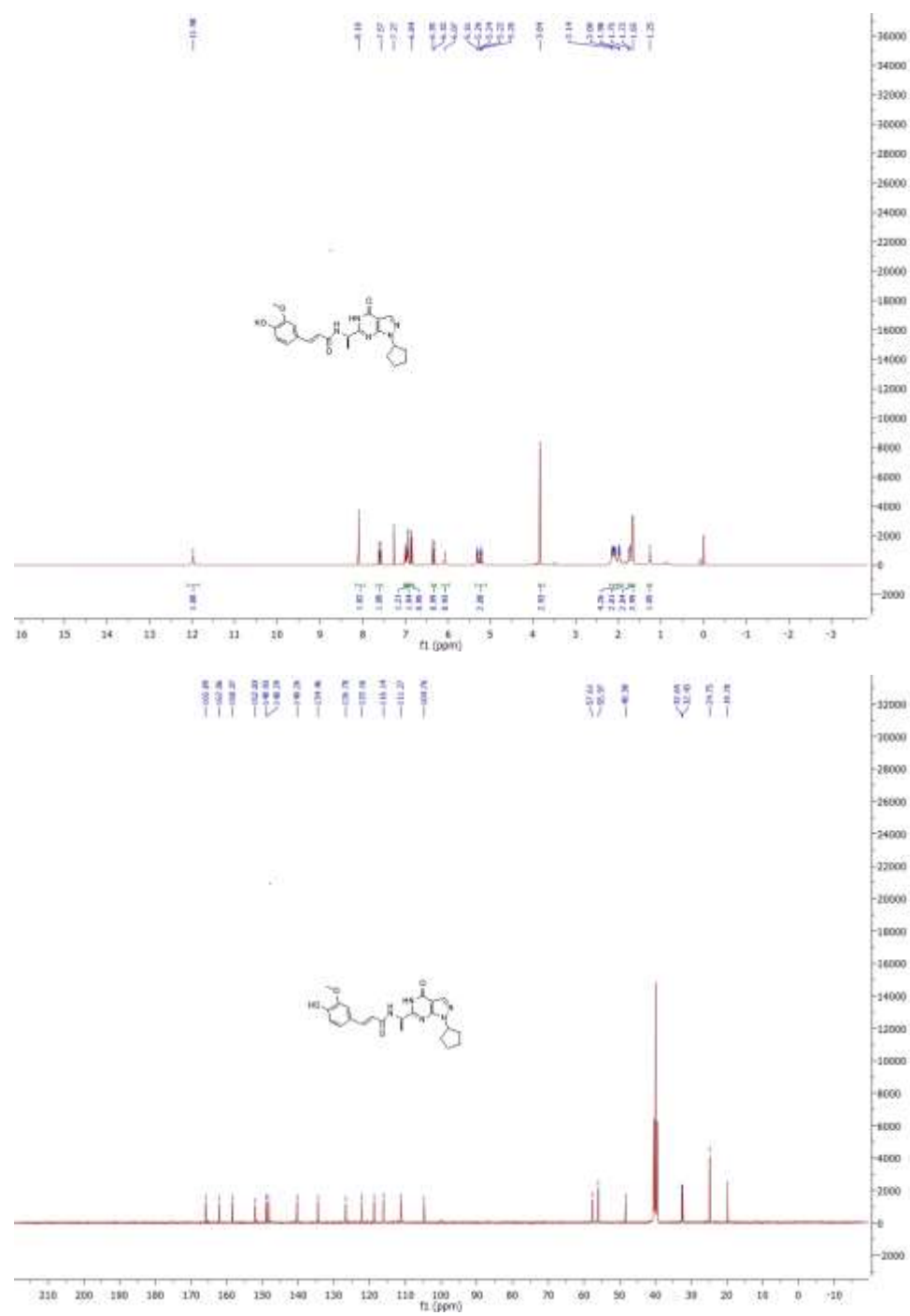**Figure S7:** The RMSD plots of compounds **1h** and **2.**

Figure S8: Cell viability of compounds **1h** and **2.** A) without cell and compounds A) without cell but compounds were added at 100μM
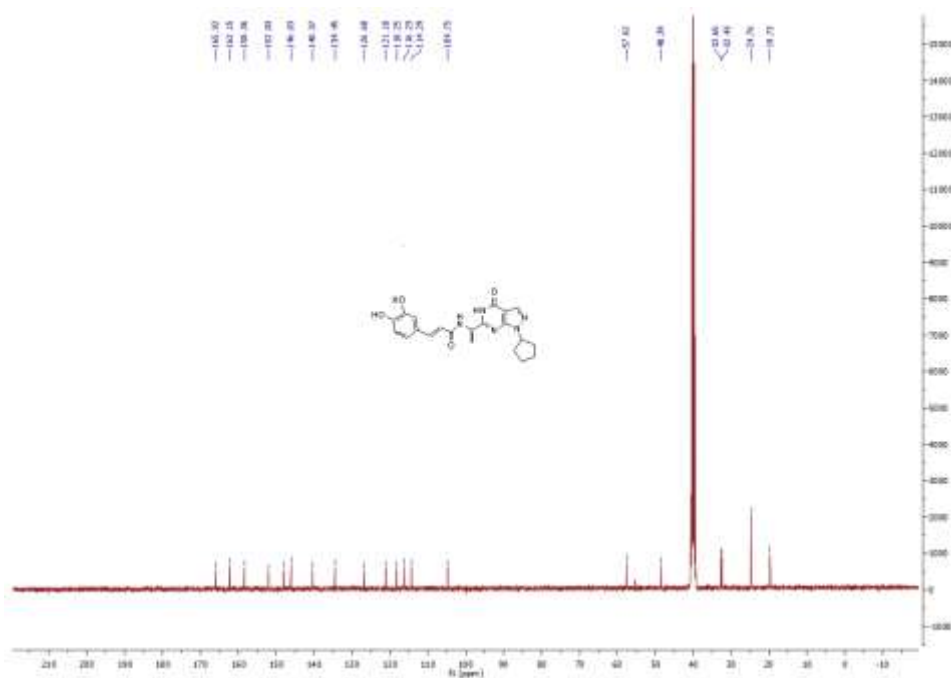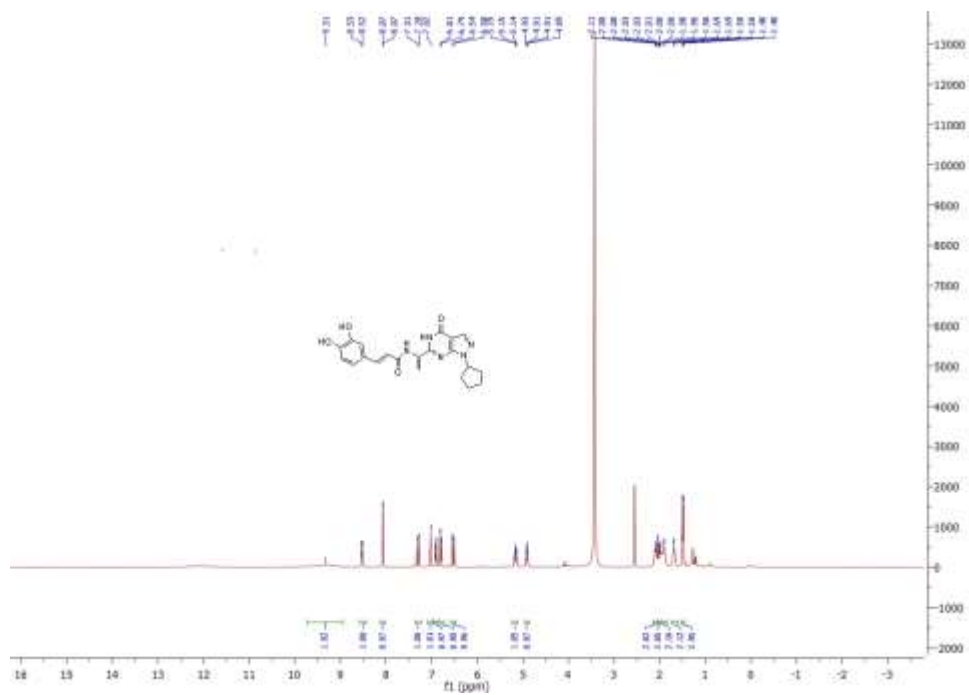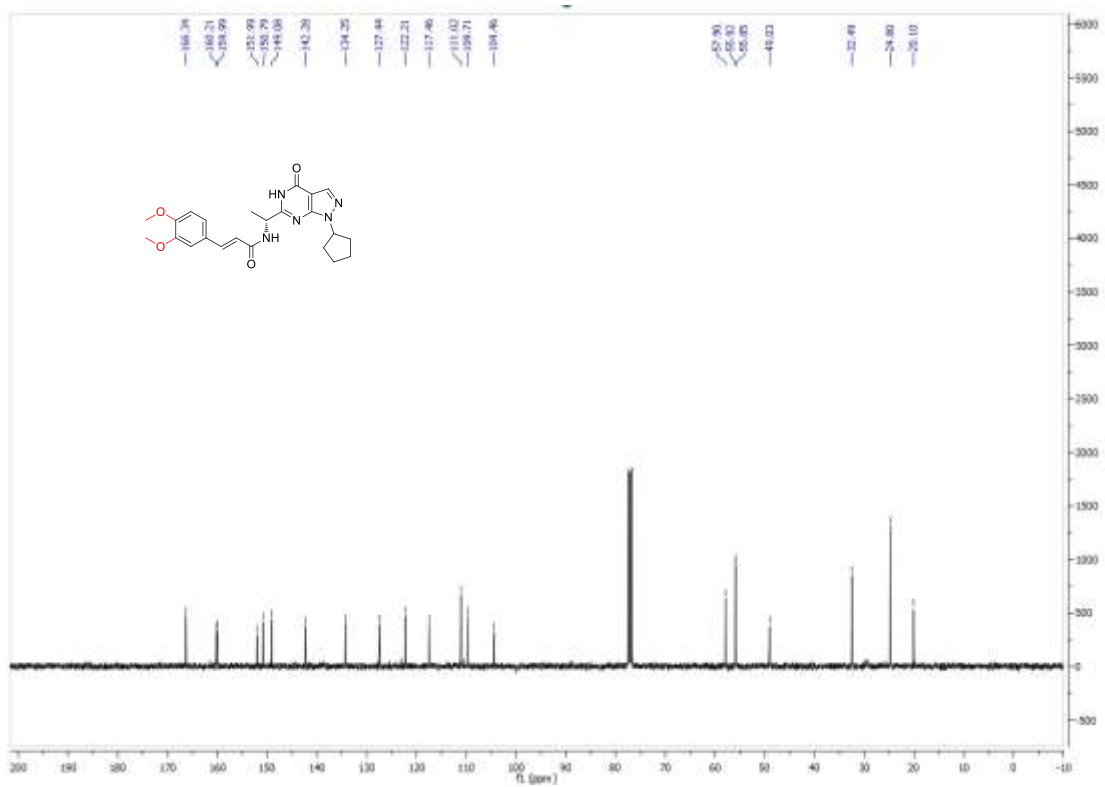
¹H and ¹³C NMR of **M-6**

¹H and ¹³C NMR of **1a**
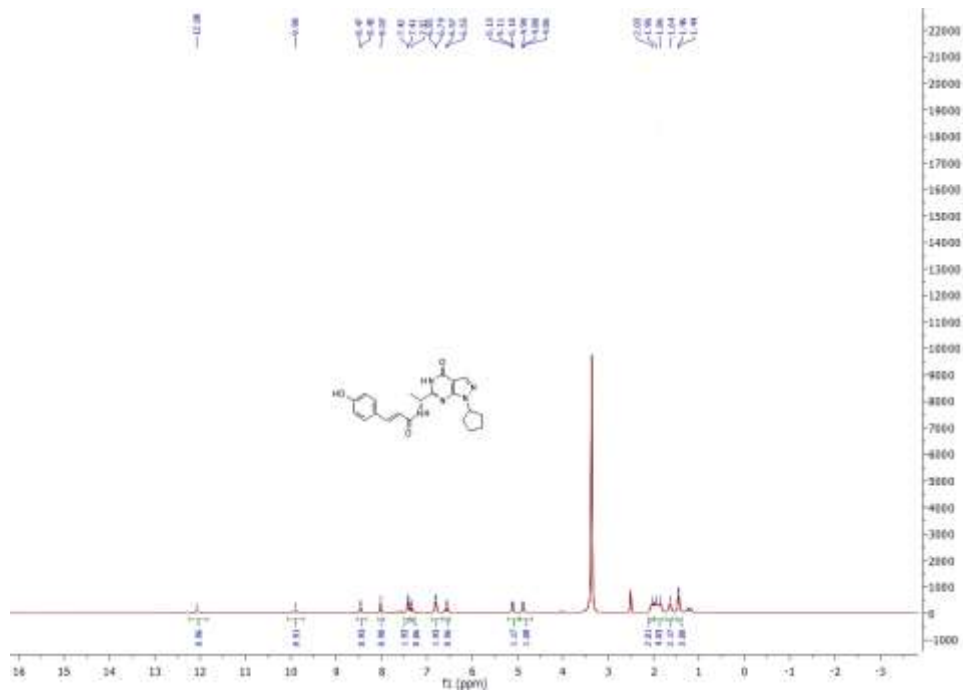
^{1}H and ^{13}C NMR of **1b**

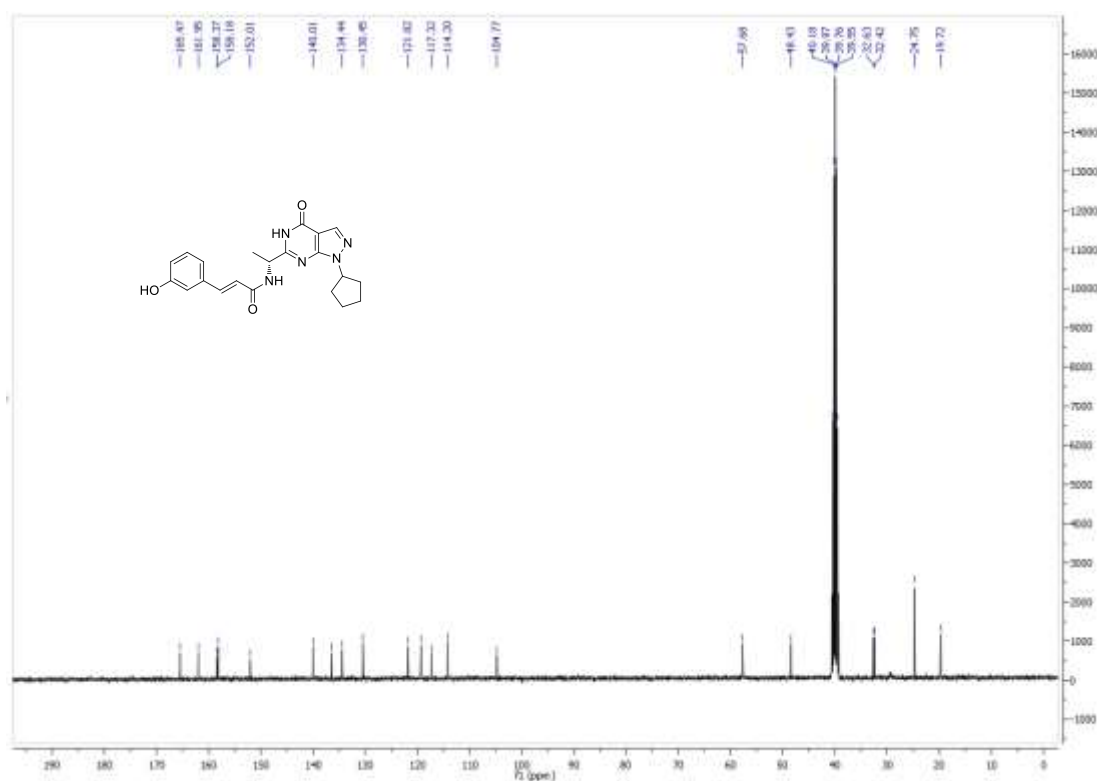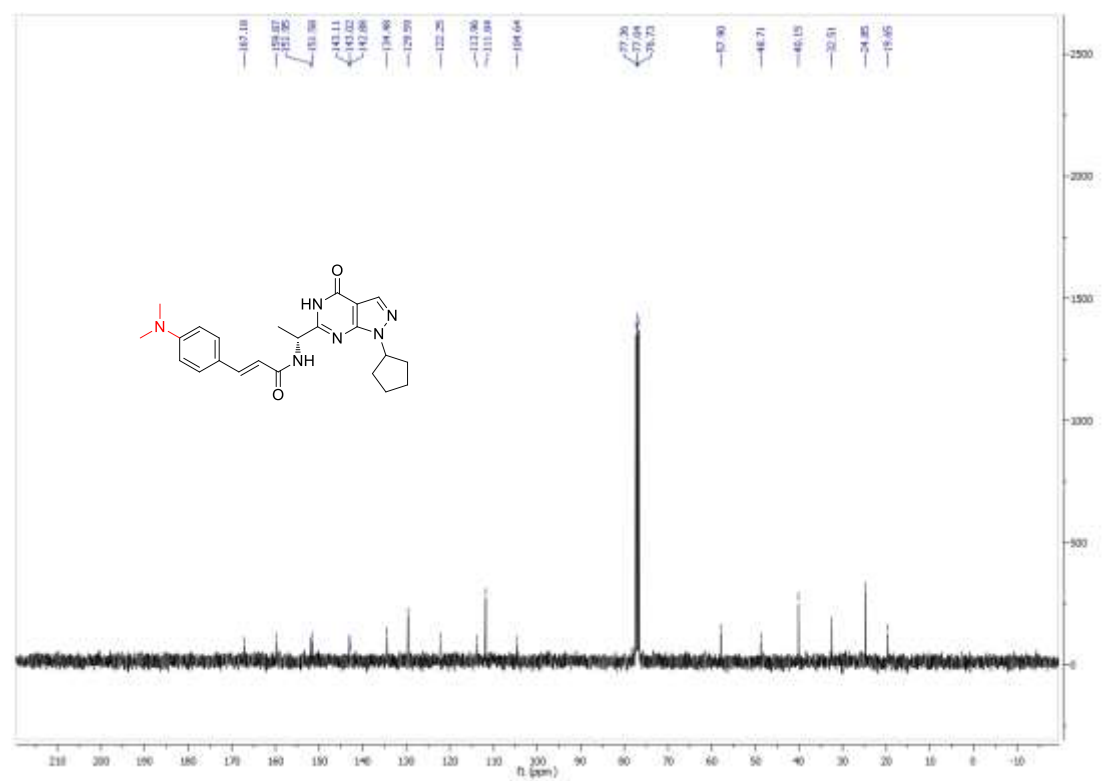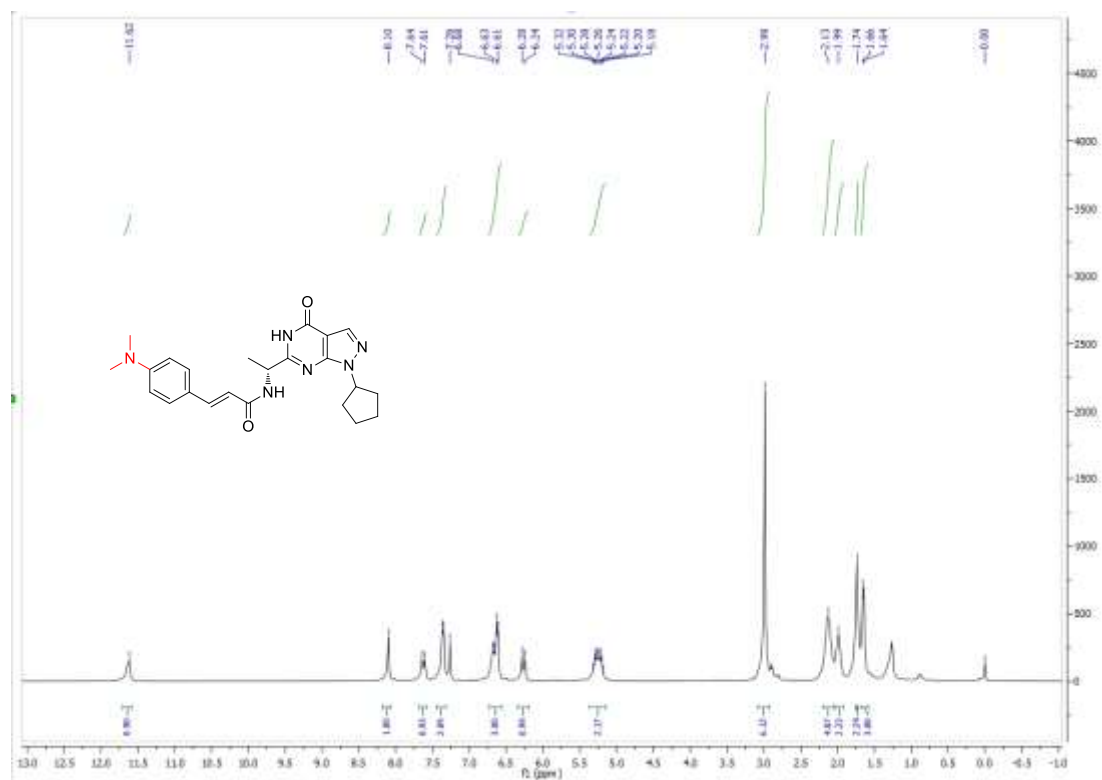^{1}H and ^{13}C NMR of **1c**

¹H and ¹³C NMR of **1d**

¹H and ¹³C NMR of **1e**

¹H and ¹³C NMR of **1f**
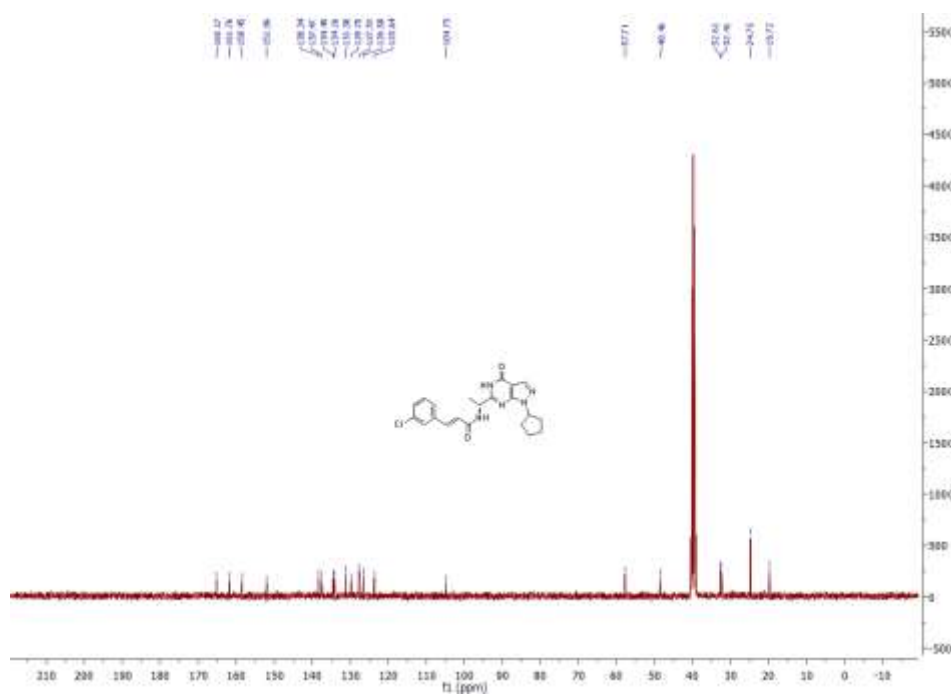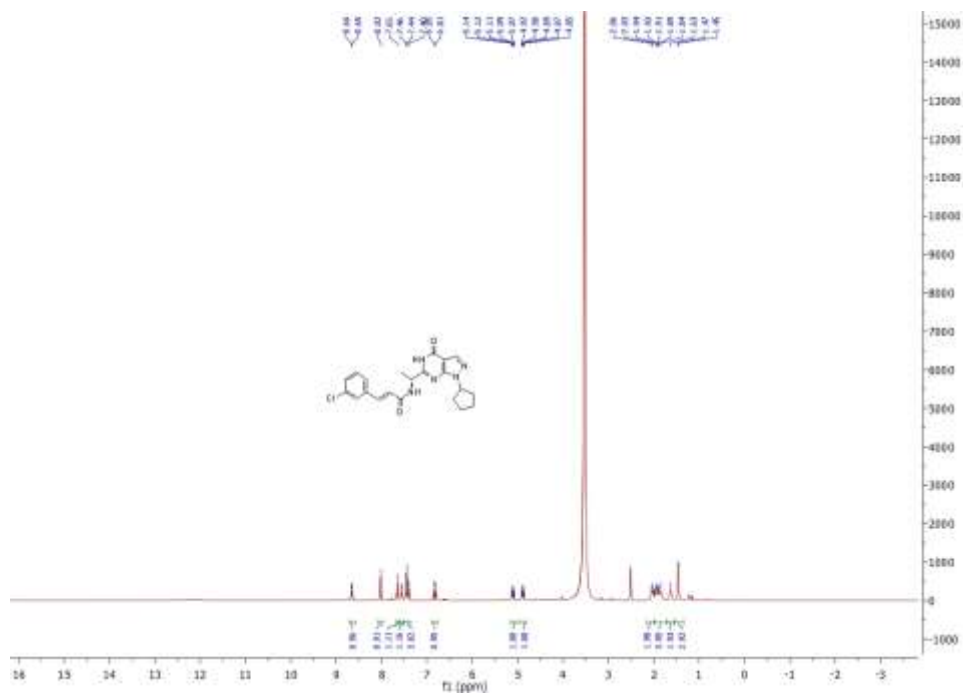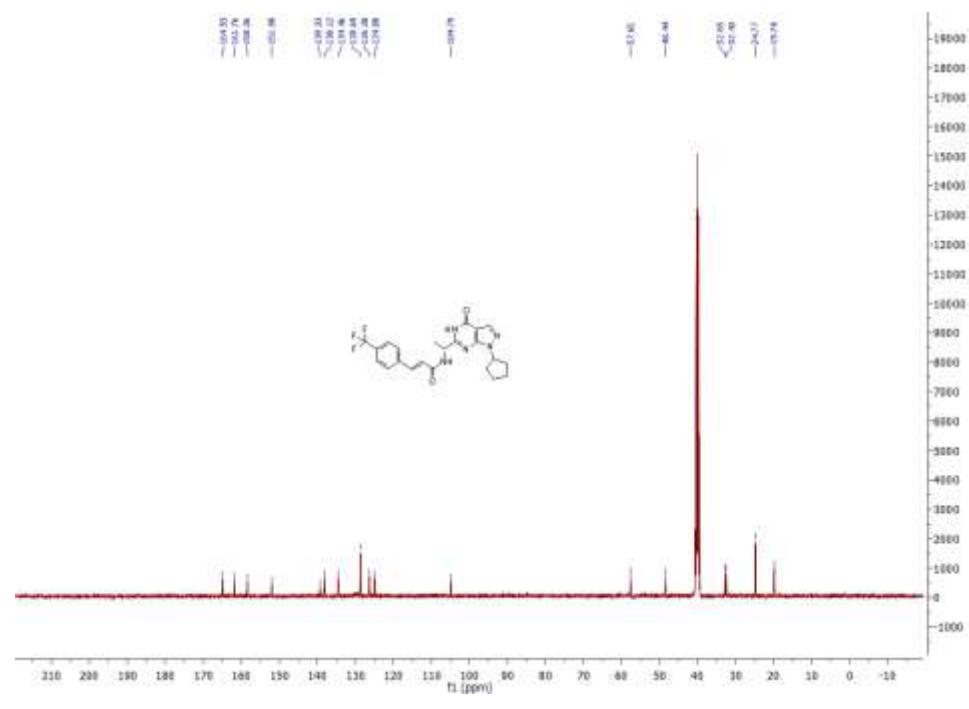
¹H and ¹³C NMR of **1g**
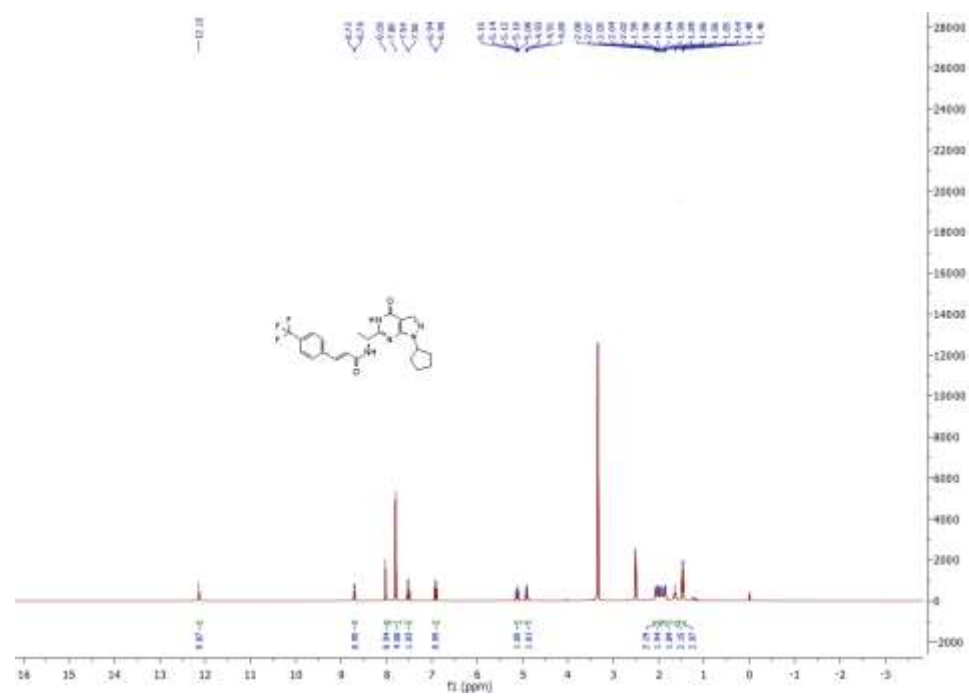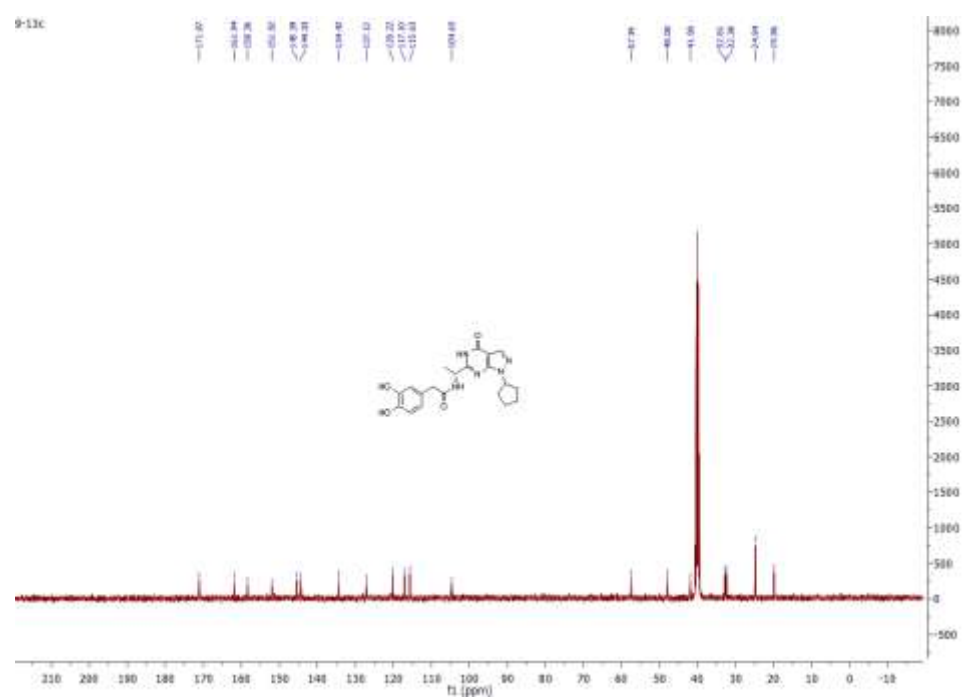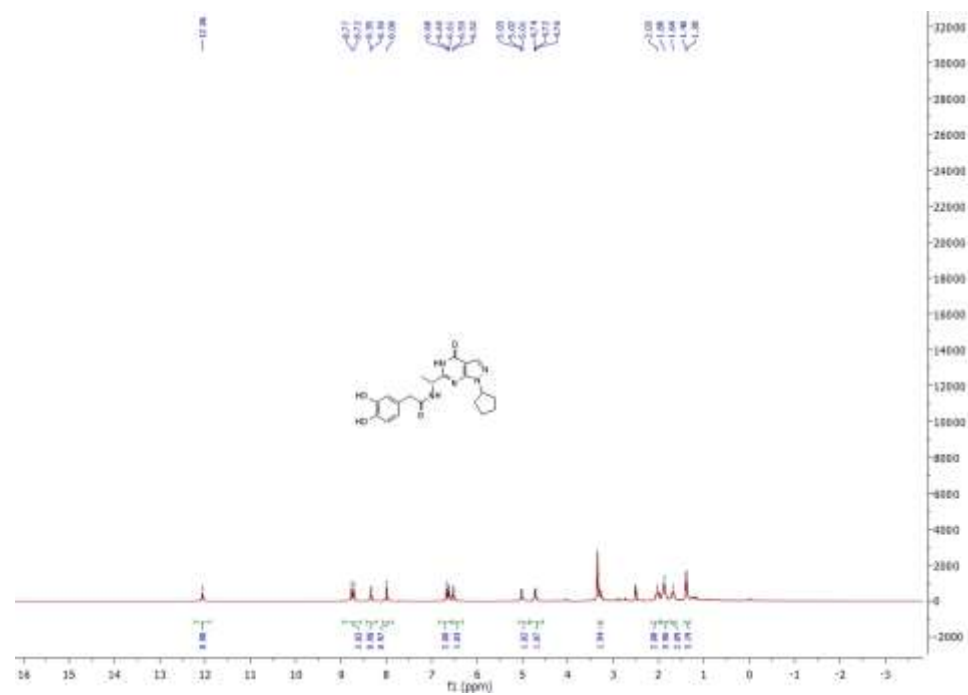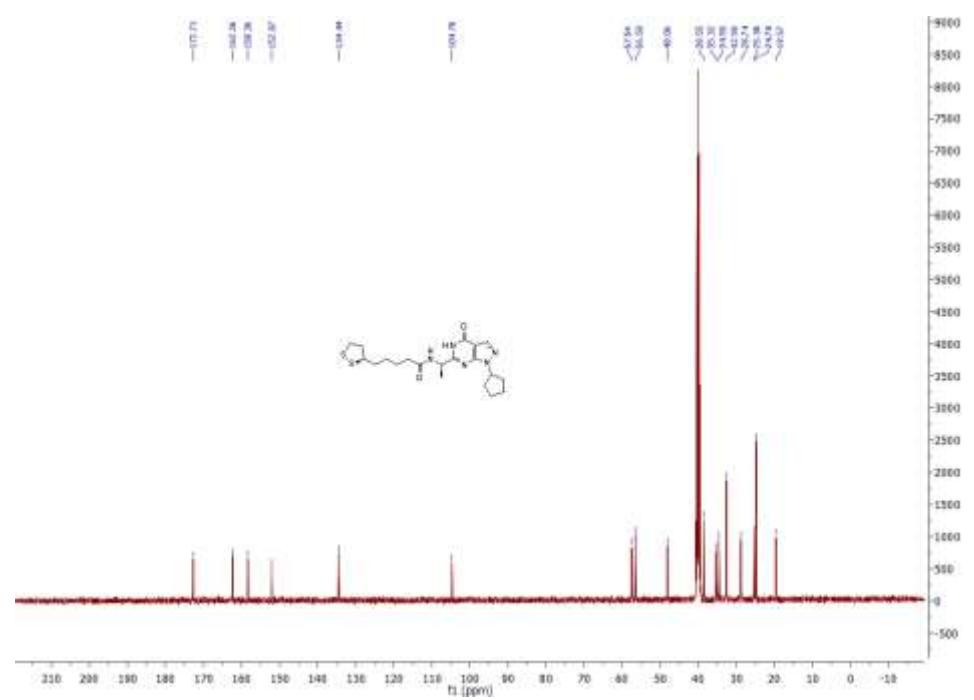
^{1}H and ^{13}C NMR of **1h**

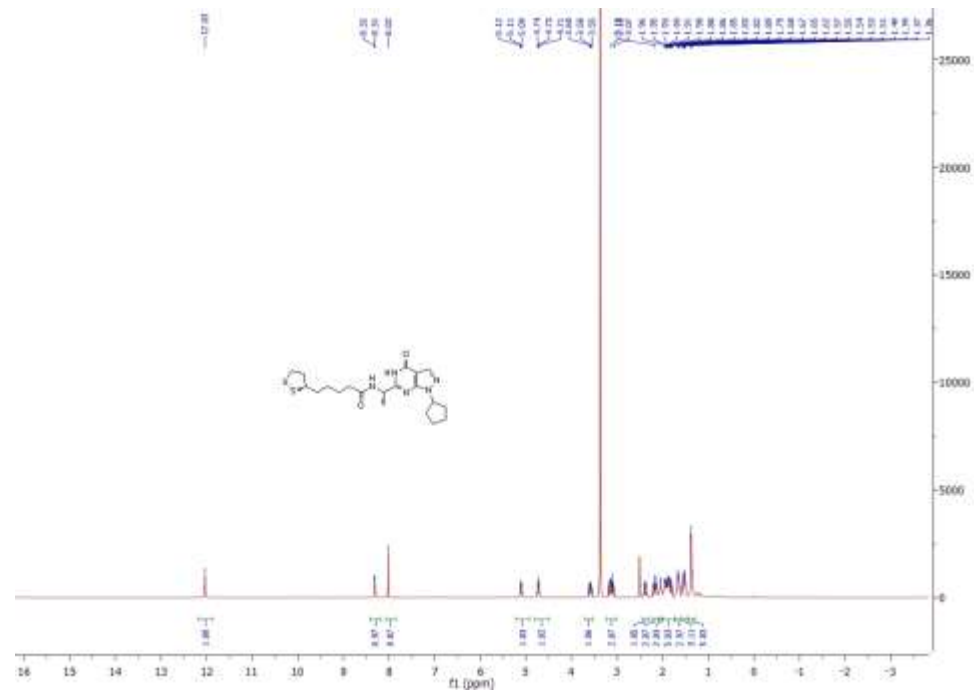^{1}H and ^{13}C NMR of **1i**

¹H and ¹³C NMR of **1j**

¹H and ¹³C NMR of **1k**

¹H and ¹³C NMR of **1l**

¹H and ¹³C NMR of **2**

¹H and ¹³C NMR of **3**