molecules

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Supplementary Materials

1,2,4-Triazolo[1,5-*a*]pyrimidines as a Novel Class of Inhibitors of the HIV-1 Reverse Transcriptase-Associated Ribonuclease H Activity

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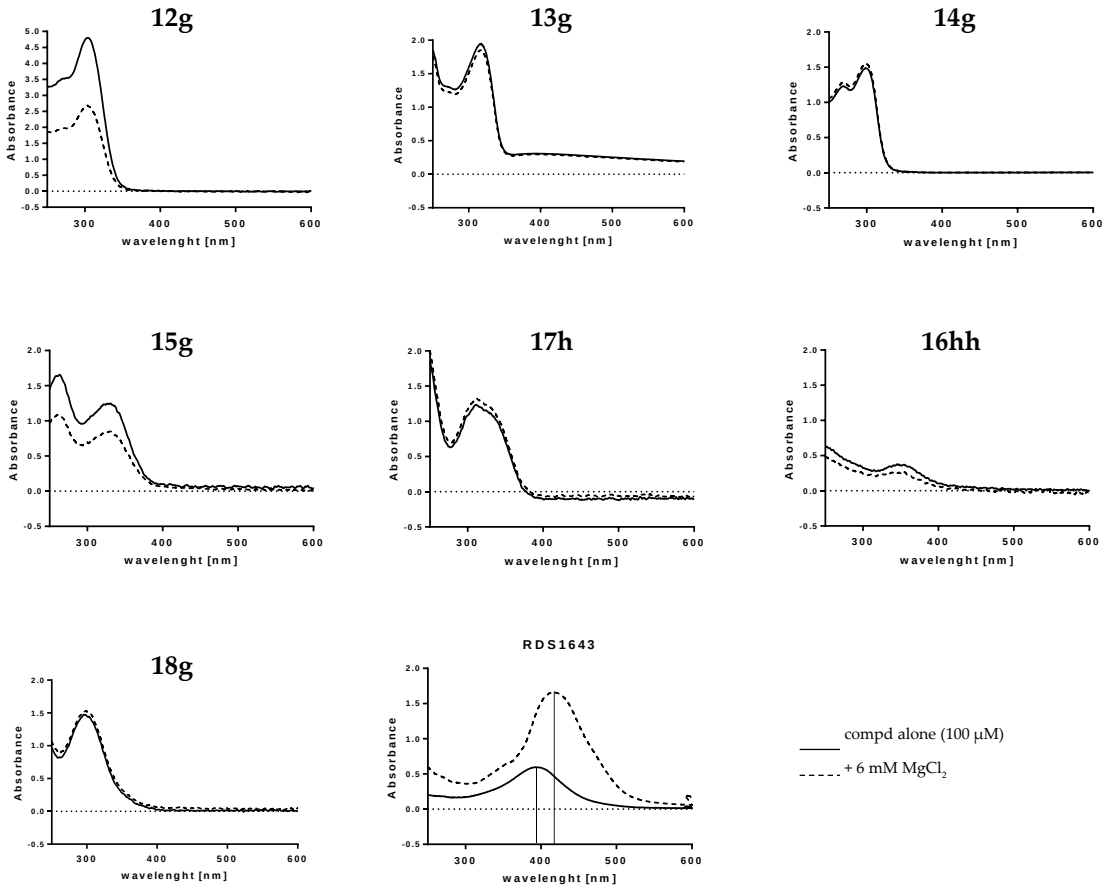

Figure S1. Effect of $MgCl_2$ on the spectrum of absorbance of compounds 12g, 13g, 14g, 15g, 16hh, 17h, and 18g. Mg^{2+} chelation UV/vis spectrum was measured with 100 µM of compound alone (unbroken line) or in the presence of 6mM $MgCl_2$ (dotted line). The active site RNHI RDS1643 [1] was used as reference compound.

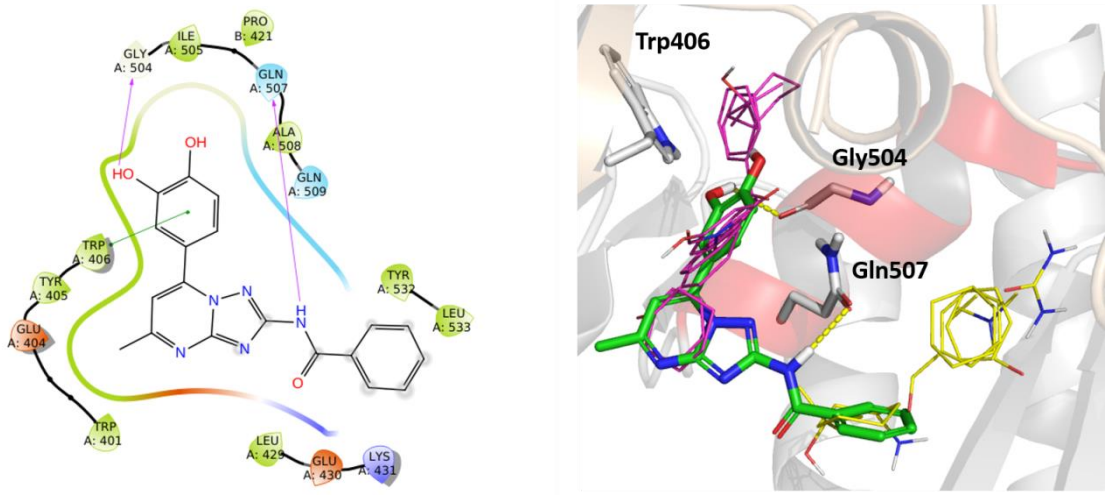

Figure S2. 2D and 3D representation of **17h** binding mode produced by docking studies on 3LP1 structure. Magenta lines, Hs1 probes; yellow lines, Hs2 probes; red cartoon, α-helix 14. Red cartoon, α-helix 14.

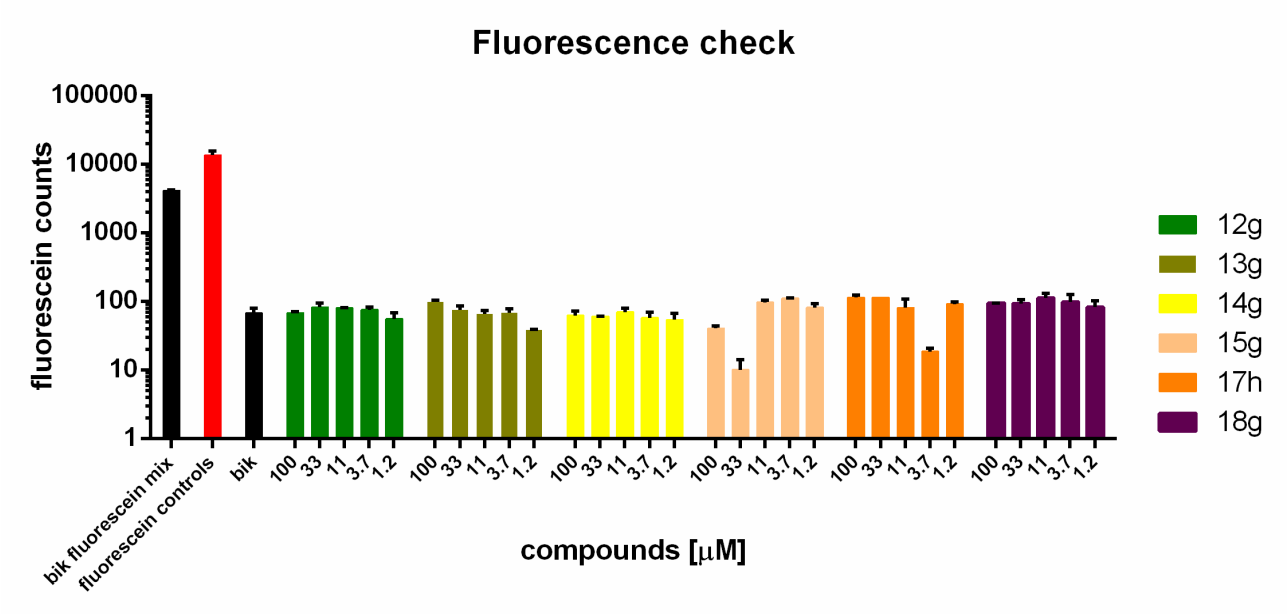

Figure S3. Effect of compounds **12g**, **13g**, **14g**, **15g**, **17h**, and **18g** on the fluorescein-based assay condition. Data are reported as the average and standard deviation of a triplicate.

Table S1. #Pprobes generated by FTMap for the analyzed crystal structures.

PDB ID	Site 1	Site 2	PDB Protein	Site 1	Site 2
5K14	20	/	**1C1B**	18	/
2YNG	9	15	**1C1C**	15	/
2YNI	10	6	**1EP4**	5	7
3QIP	15	/	**1FK9**	8	5
3LP1	20	/	**1JKH**	10	4
3MEC	7	/	**3DLE**	8	9
3MEE	19	10	**4I7F**	24	2
3LAK	11	11	**3DLG**	3	/
1RTJ	18	/	**2RKI**	16	6

Table S2. Predicted Ligand Binding Energy (LBE), predicted Ki (Ki_{pred}) and number in cluster (NiC) for docked TZPs.

Compd	3LP1			4I7F			HIV-1 RNaseH IC_{50} (μM)
	LBE (Kcal/mol)	Ki_{pred} (μM)	NiC	LBE (Kcal/mol)	Ki_{pred} (μM)	NiC	
12g	-9.07	0.23	58	-8.42	0.67	44	0.8
13g	-8.45	0.64	34	-8.54	0.55	84	3.5
15g	-9.39	0.13	61	-9.53	0.10	100	1.86
17h	-8.15	1.07	54	/	/	/	1.13
18g	-8.78	0.37	58	-9.02	0.25	68	0.41
19g	/	/	/	-8.25	0.89	65	43.1

References

1. Tramontano, E.; Esposito, F.; Badas, R.; Di Santo, R.; Costi, R.; La Colla, P. 6-[1-(4-Fluorophenyl)methyl-1*H*-pyrrol-2-yl)]-2,4-dioxo-5-hexenoic acid ethyl ester a novel diketo acid derivative which selectively inhibits the HIV-1 viral replication in cell culture and the ribonuclease H activity in vitro. *Antiviral Res.* **2005**, *65*, 117-124. doi: 10.1016/j.antiviral.2004.11.002