

# Supplementary

## DNA repair enzymes Tyrosyl-DNA phosphodiesterases 1 and 2 inhibitors based on usnic acid as potential anticancer agents

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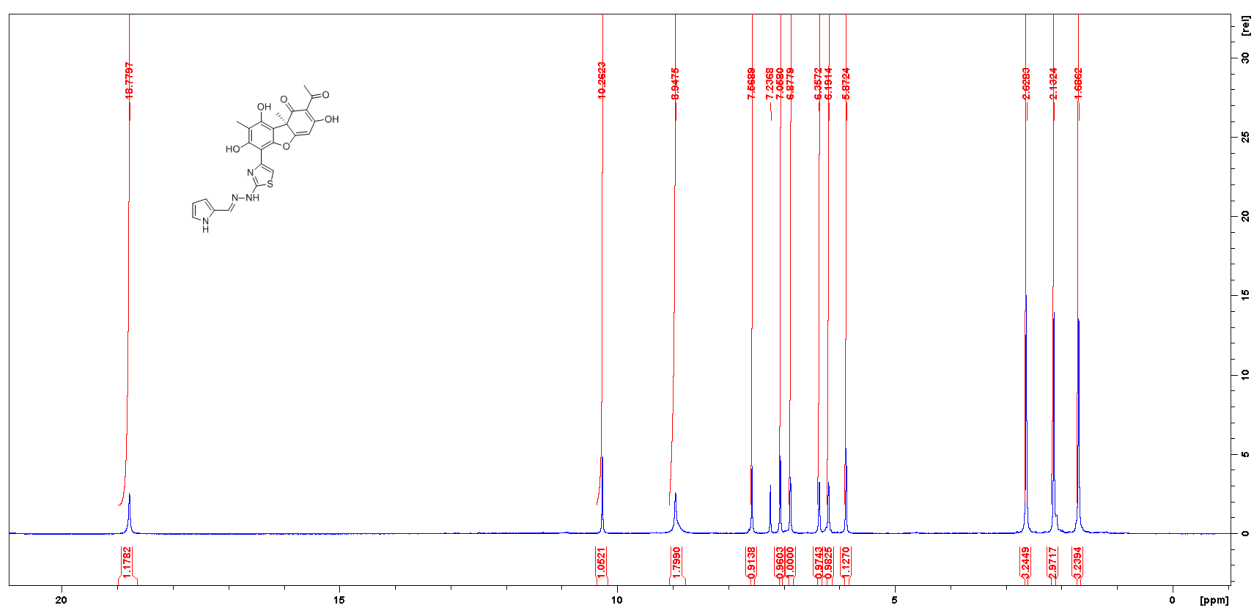


Figure S1. The  $^1\text{H}$  spectrum of compound 11a.

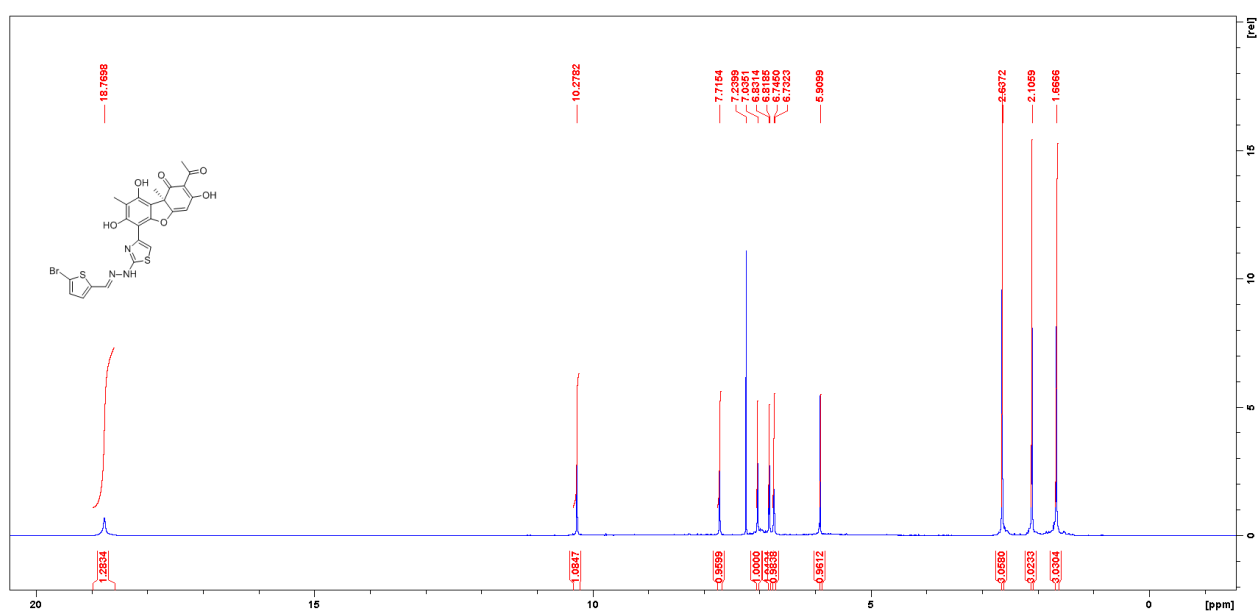
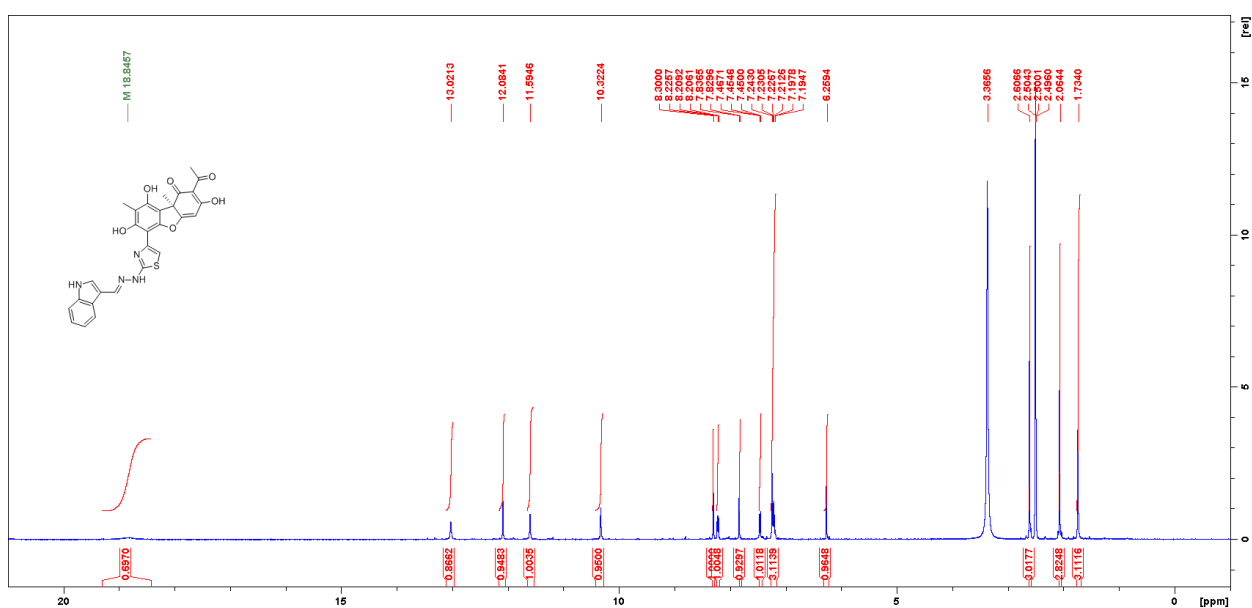
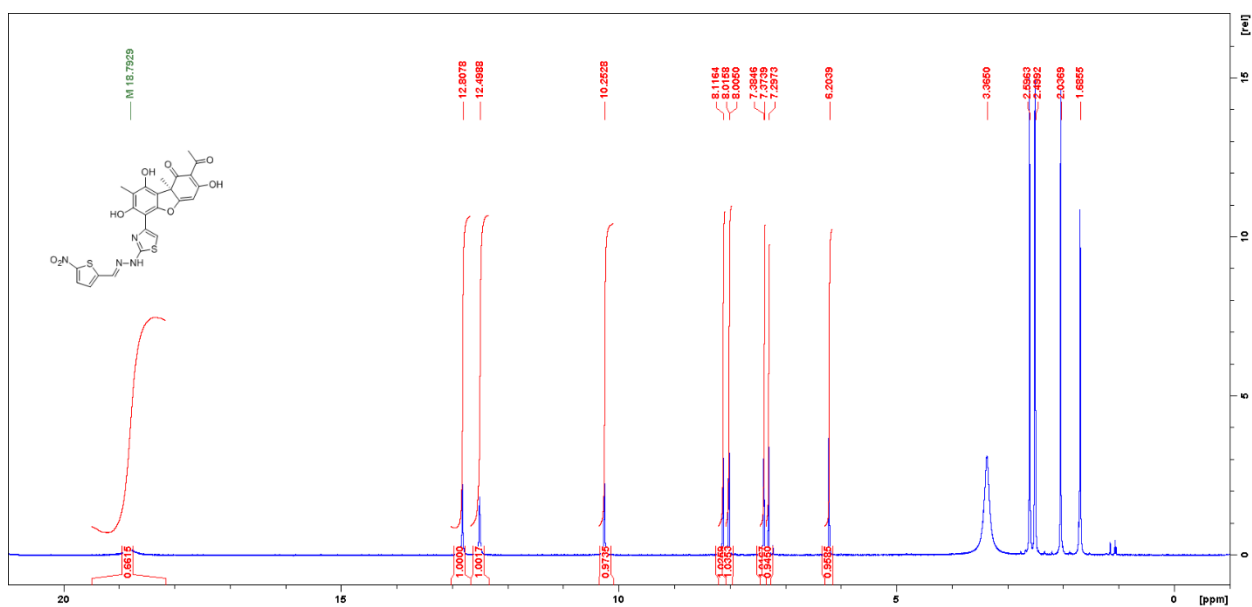
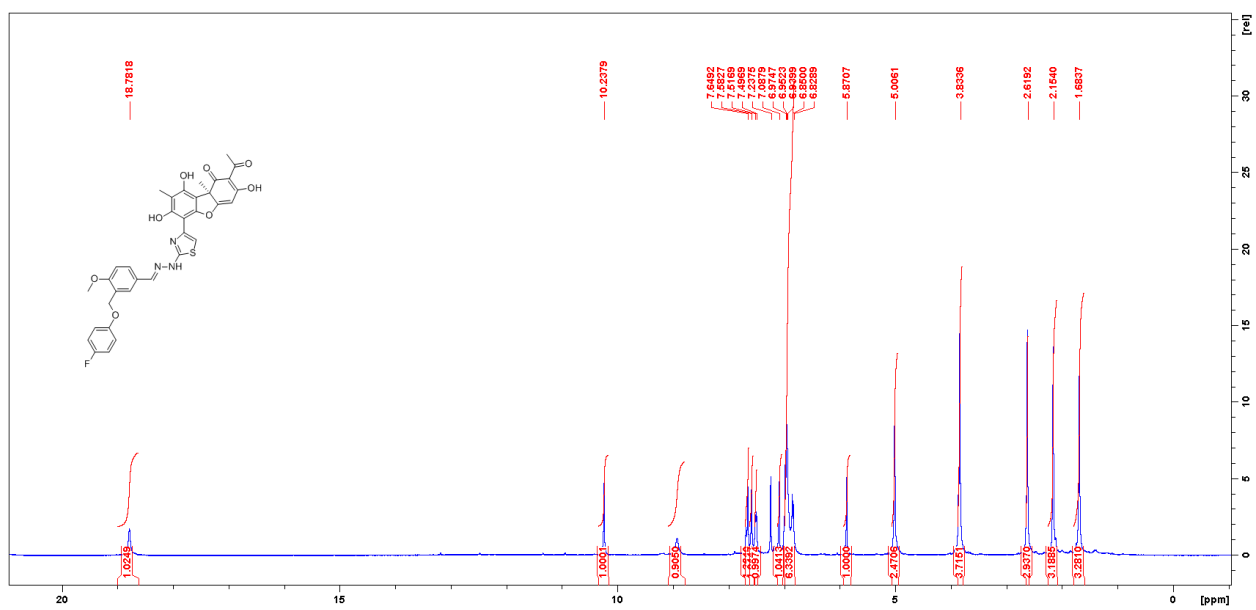
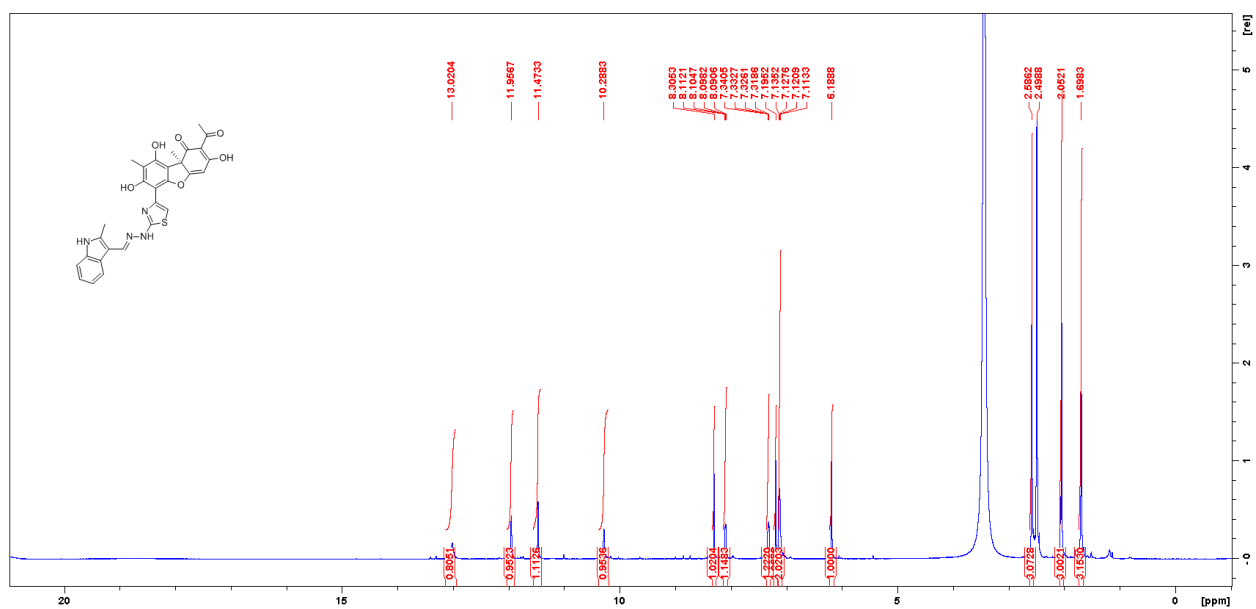


Figure S2. The  $^1\text{H}$  spectrum of compound 11b.





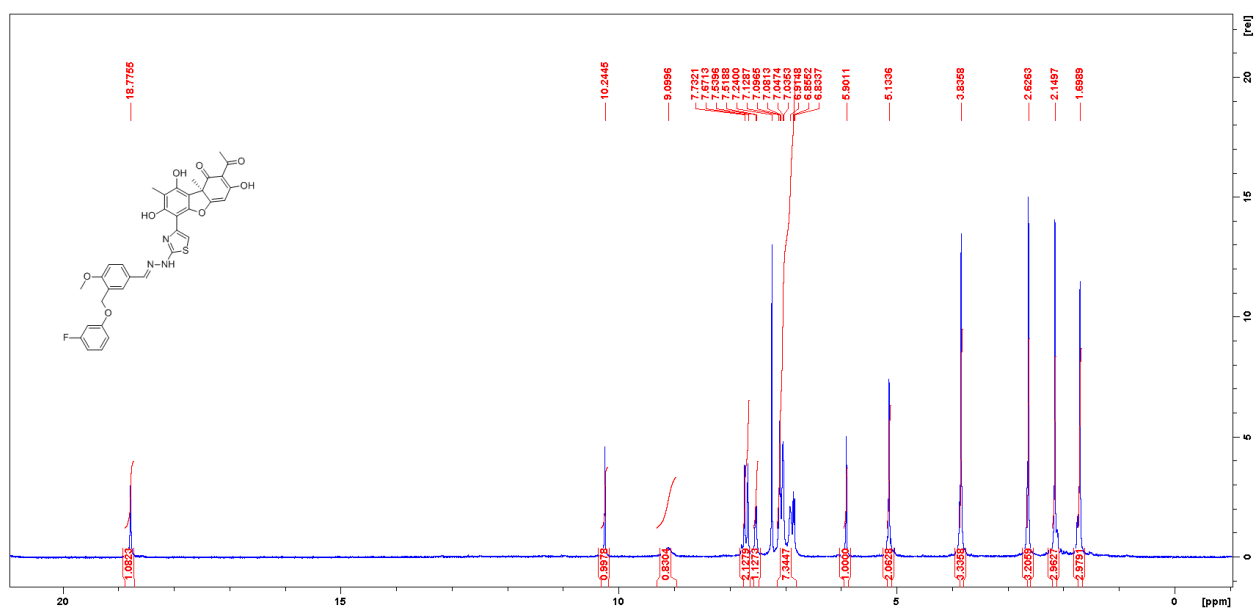


Figure S7. The <sup>1</sup>H spectrum of compound 11g.

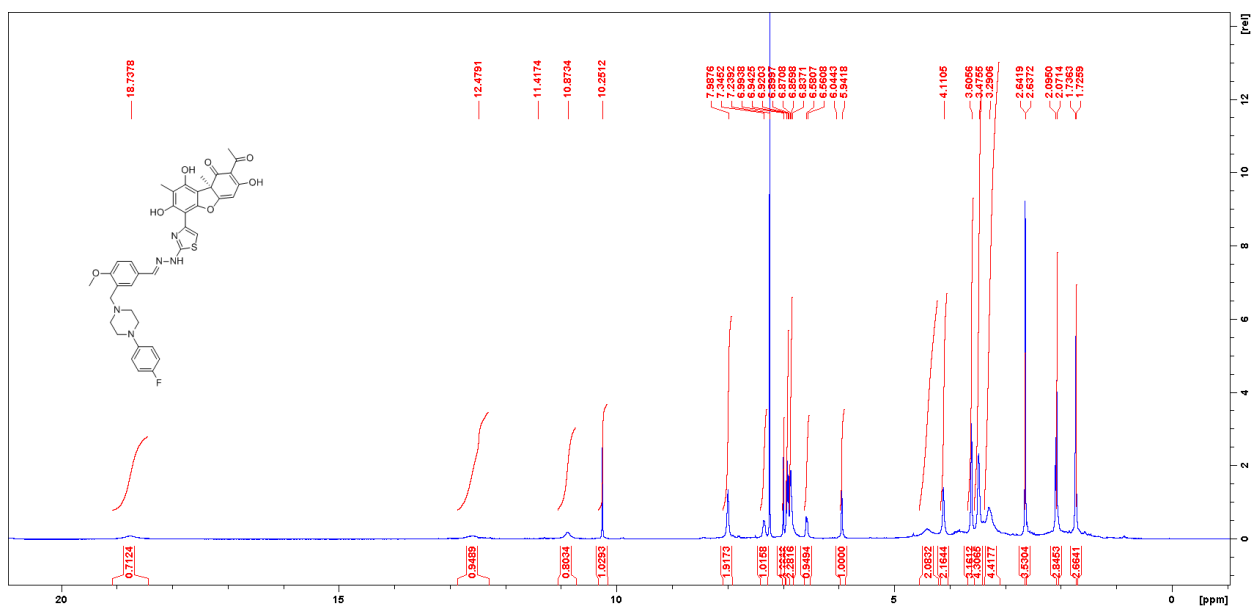
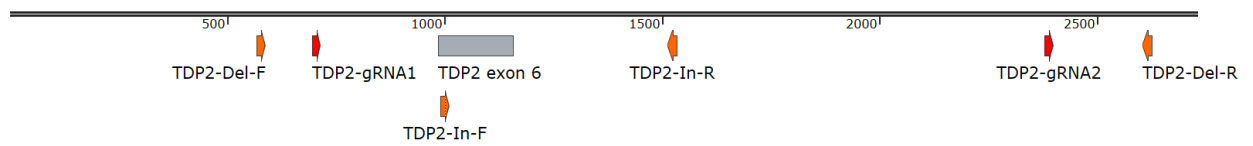
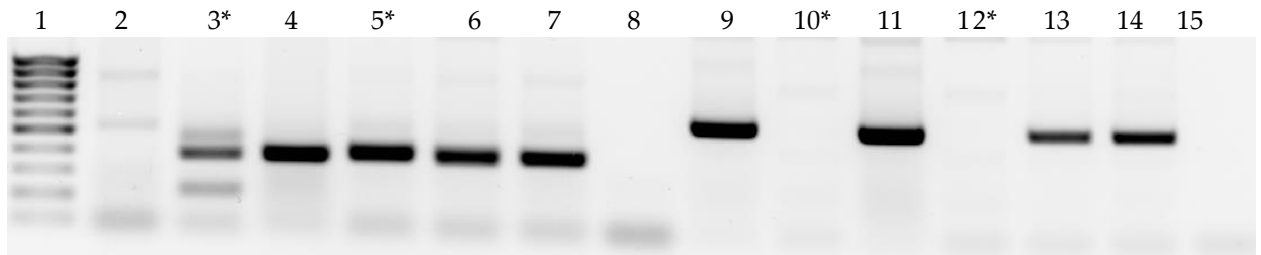


Figure S8. The <sup>1</sup>H spectrum of compound 11h.

A



B



**Figure S9.** Scheme of protospacers (TDP2-gRNA1 and TDP2-gRNA1) and primers location in *TDP2* gene (A) and PCR analysis of CRISPR/Cas9-induced deletion (B): lanes: 1) DNA ladder Step100 (Biolabmix, Novosibirsk, Russia; 2-7) PCR analysis of HEK293FT clones genomic DNA with primers for detecting a deletions (TDP2-Del-F and TDP2-Del-R); 8) H<sub>2</sub>O with primers TDP2-Del-F and TDP2-Del-R; 9-14) PCR analysis of HEK293FT clones genomic DNA with primers for the detection of the wild-type alleles (TDP2-In-F and TDP2-In-R); 15) H<sub>2</sub>O with primers TDP2-In-F and TDP2-In-R; \* - these two cell clones were selected for further analysis.

**Table S1.** Molecular docking results

| ID ligand      | Docking score | Emodel   | IFD score | Interactions           |                                                                                                                         |
|----------------|---------------|----------|-----------|------------------------|-------------------------------------------------------------------------------------------------------------------------|
|                |               |          |           | $\pi$ - $\pi$ Stacking | Other interactions                                                                                                      |
| <b>(-)-11a</b> | -8.463        | -93.324  | -469.56   | Trp307, Tyr321         | Arg276 $\pi$ -cation<br>Ser236, Arg276, Asn274 - H-bond<br>Ley134, Trp307, Ley315, Tyr321 - hydrophobic                 |
| <b>(-)-11b</b> | -7.112        | -94.008  | -469.67   | Phe325                 | Asn274 - H-bond<br>Ley315, Tyr321 - hydrophobic                                                                         |
| <b>(-)-11c</b> | -8.033        | -108.527 | -469.14   | Trp307                 | Arg276 $\pi$ -cation<br>Arg276 - H-bond<br>Trp307, Tyr321 - hydrophobic                                                 |
| <b>(-)-11d</b> | -8.613        | -113.831 | -468.70   | Trp307, Tyr321, His323 | Arg241, Arg276 $\pi$ -cation<br>Asn274, Arg276, Asp277, Lys322 - H-bond<br>Ley134, Trp307, Ley315, Tyr321 - hydrophobic |
| <b>(-)-11e</b> | -7.524        | -98.671  | -467.97   | Trp307, Tyr321, His323 | Arg241, Arg276 $\pi$ -cation<br>Arg276, Asn274 - H-bond<br>Trp307, Ley315 - hydrophobic                                 |
| <b>(-)-11g</b> | -7.335        | -104.451 | -468.41   | Trp307, Tyr321         | Arg276 $\pi$ -cation<br>Ley315 - hydrophobic                                                                            |
| <b>(-)-11h</b> | -8.649        | -120.321 | -468.01   | Trp307, Phe325         | Arg241 $\pi$ -cation<br>Asn274, Arg276 - H-bond<br>Ley134, Trp307, Ley315 - hydrophobic                                 |