

Supplementary

Usnic acid derivatives inhibit DNA repair enzymes Tyrosyl-DNA phosphodiesterases 1 and 2 and act as potential anticancer agents

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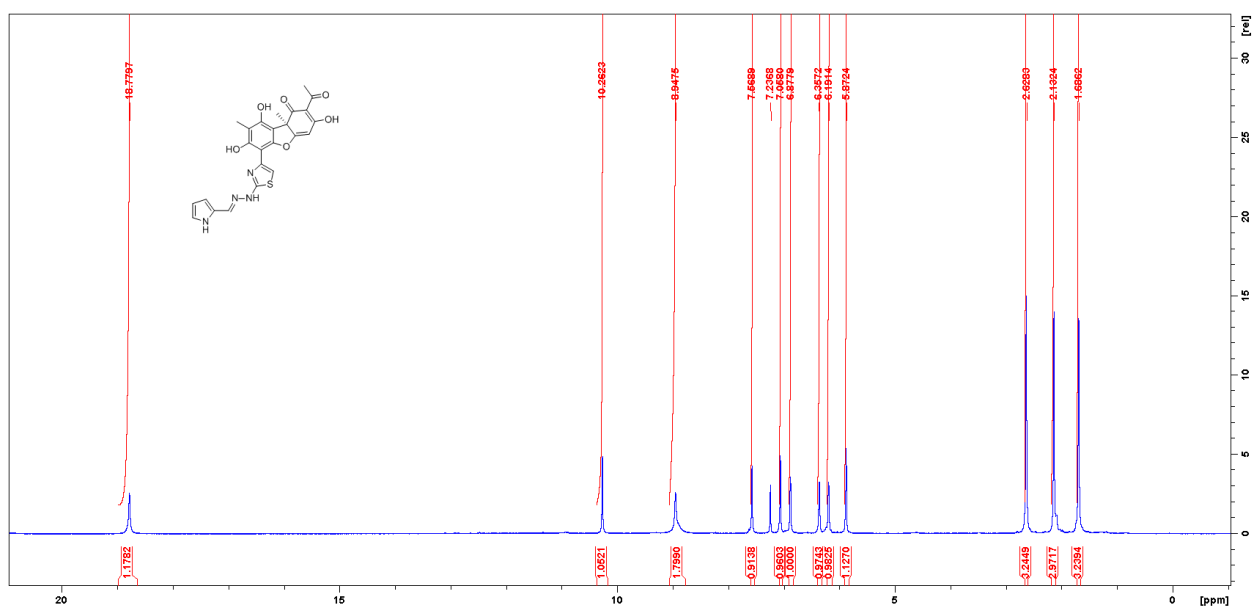


Figure S1. The ^1H spectrum of compound 11a.

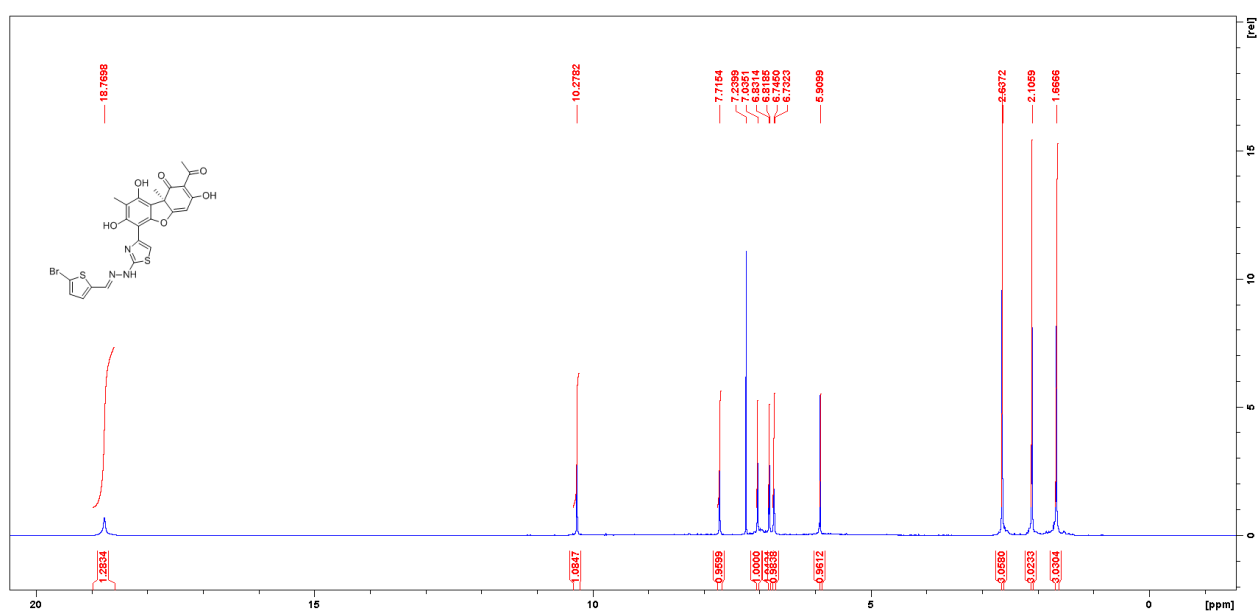
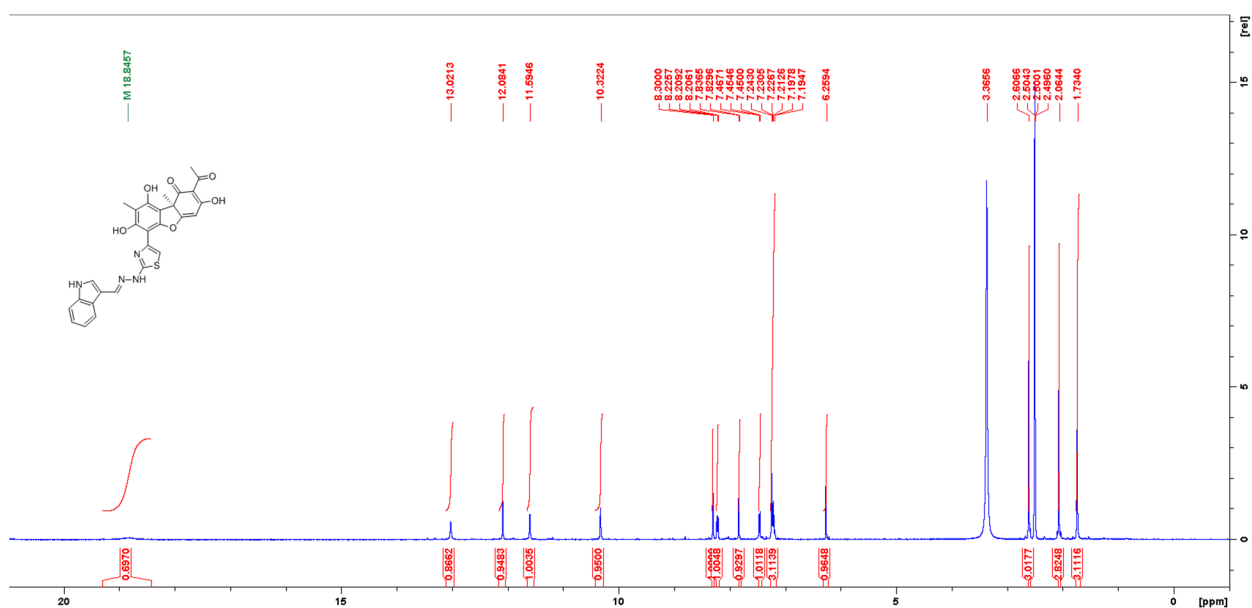
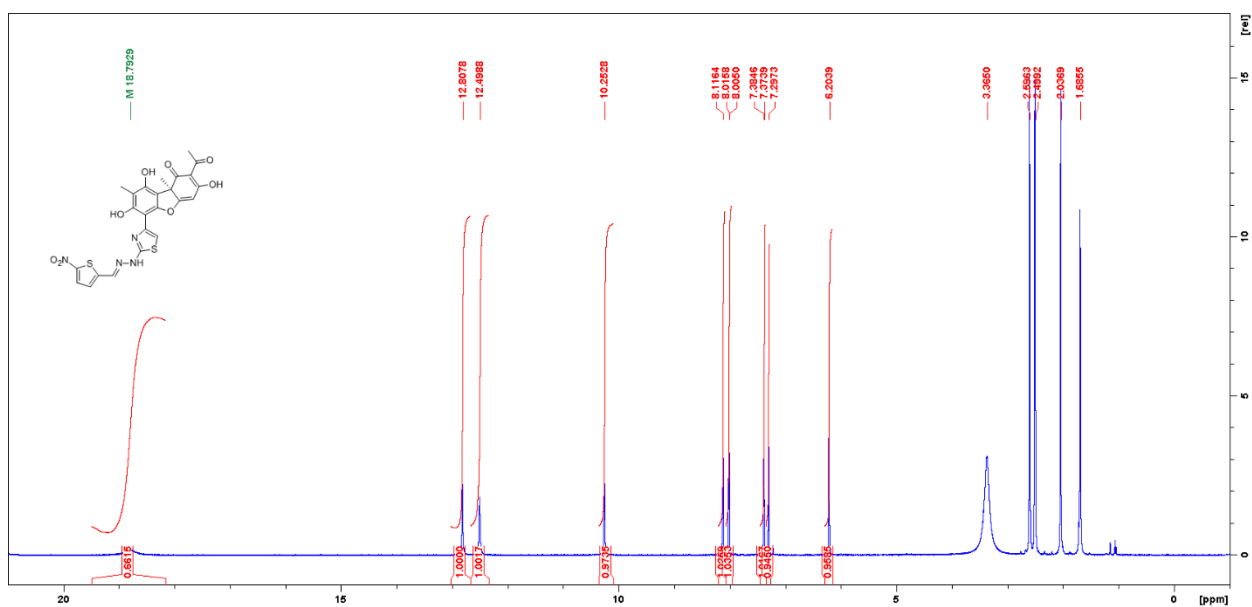
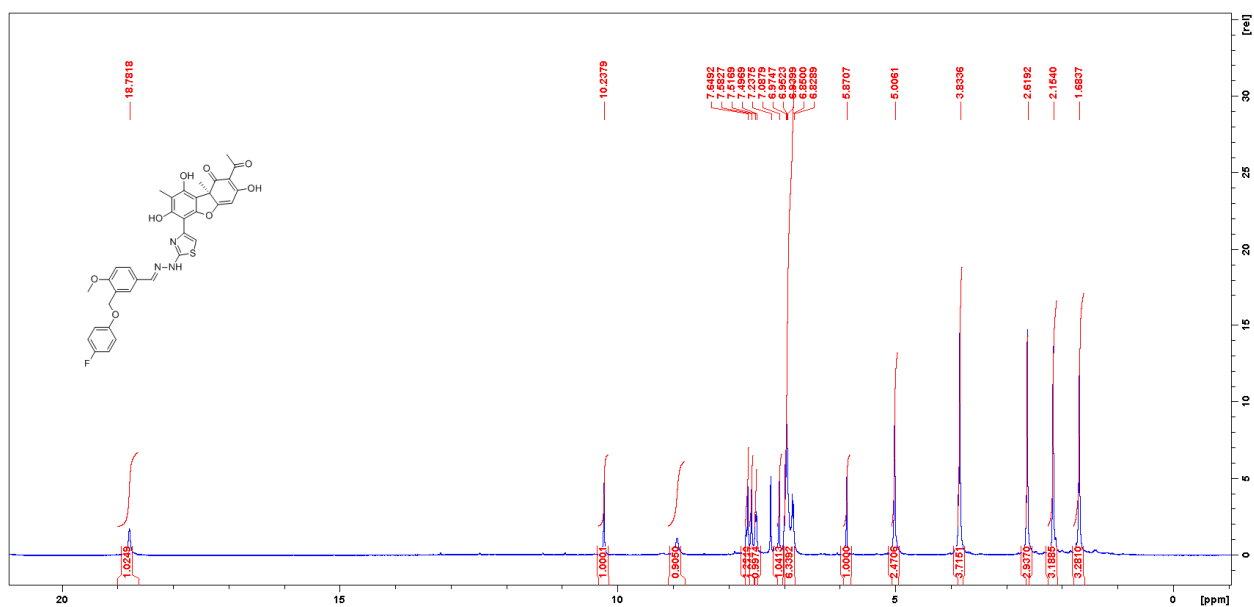
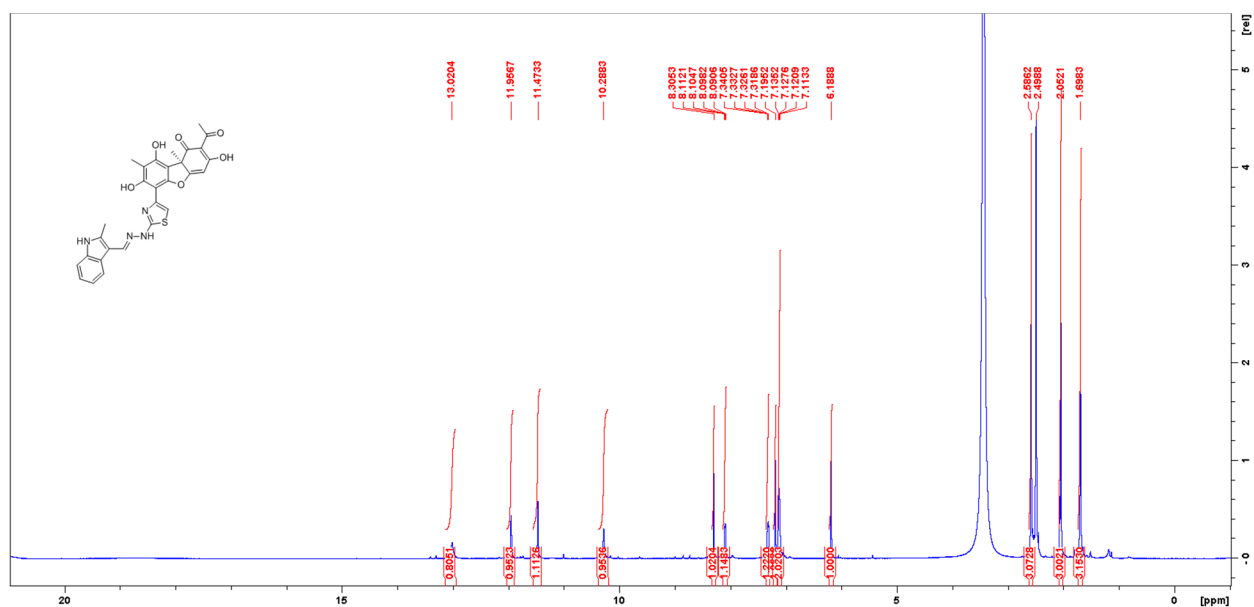


Figure S2. The ^1H spectrum of compound 11b.





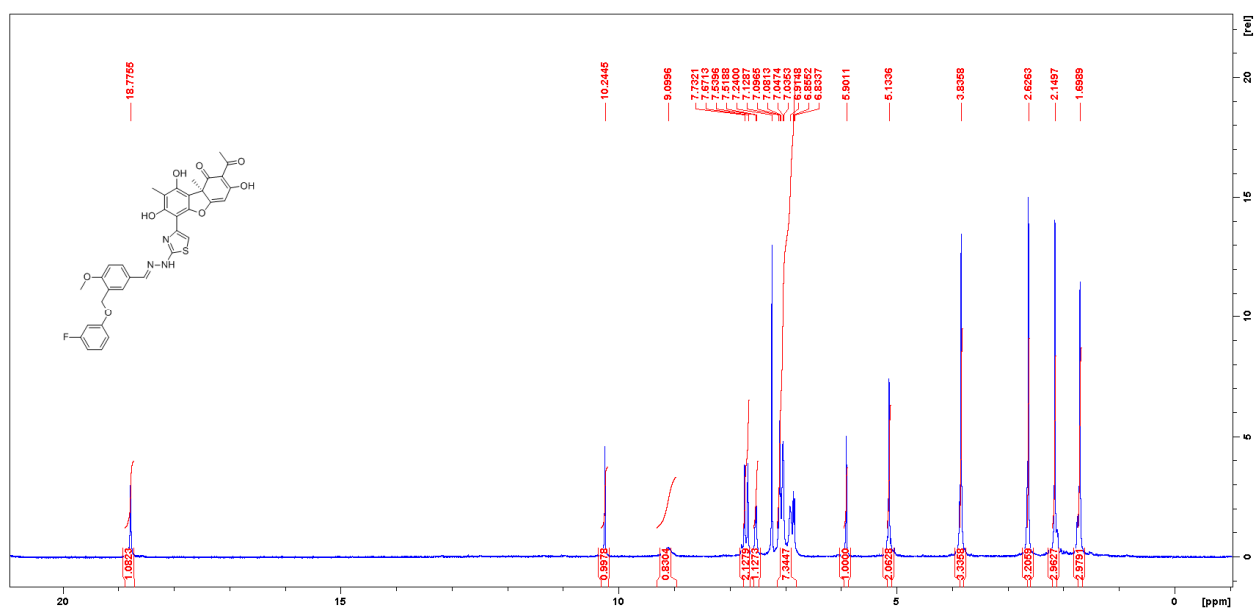


Figure S7. The ¹H spectrum of compound 11g.

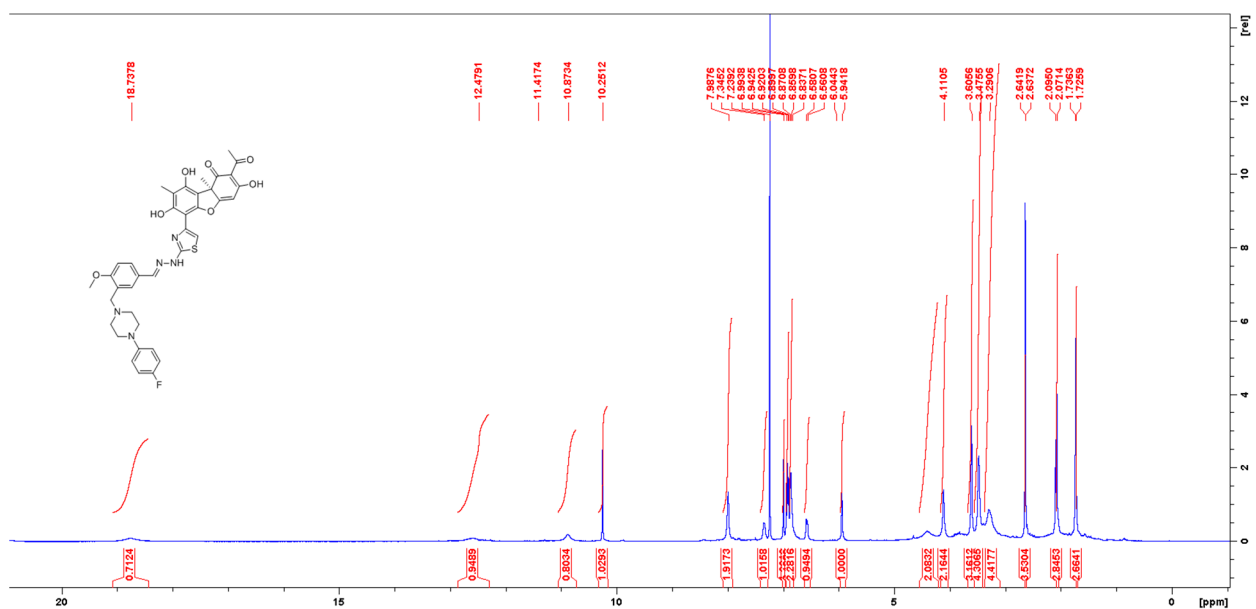
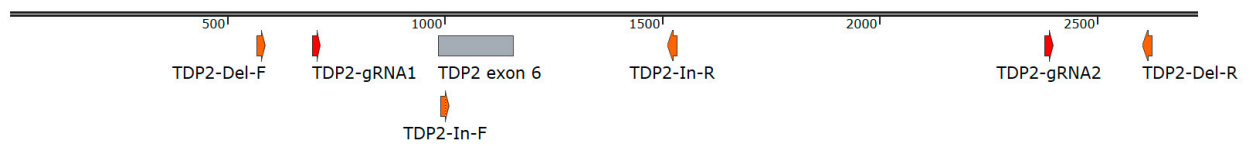


Figure S8. The ¹H spectrum of compound 11h.

A



B

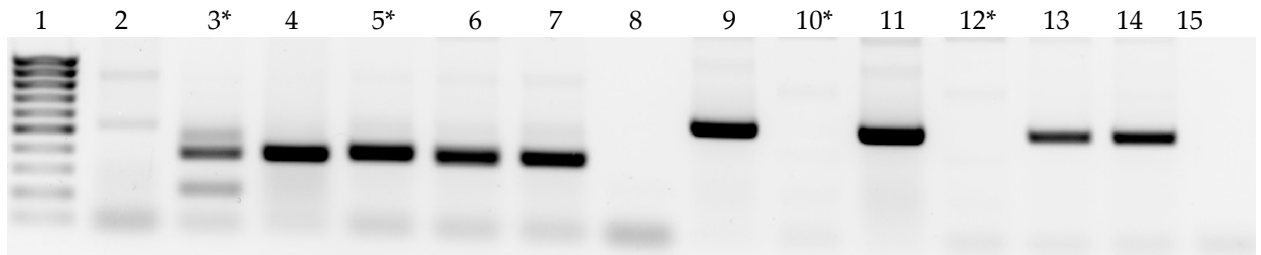


Figure S9. Scheme of protospacers (TDP2-gRNA1 and TDP2-gRNA1) and primers location in *TDP2* gene (A) and PCR analysis of CRISPR/Cas9-induced deletion (B): lanes: 1) DNA ladder Step100 (Biolabmix, Novosibirsk, Russia; 2-7) PCR analysis of HEK293FT clones genomic DNA with primers for detecting a deletions (TDP2-Del-F and TDP2-Del-R); 8) H₂O 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) H₂O 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 | |
|----------------|---------------|----------|-----------|------------------------|---|
| | | | | π - π Stacking | Other interactions |
| (-)-11a | -8.463 | -93.324 | -469.56 | Trp307, Tyr321 | Arg276 π -cation Ser236, Arg276, Asn274 - H-bond Ley134, Trp307, Ley315, Tyr321 - hydrophobic |
| (-)-11b | -7.112 | -94.008 | -469.67 | Phe325 | Asn274 - H-bond Ley315, Tyr321 - hydrophobic |
| (-)-11c | -8.033 | -108.527 | -469.14 | Trp307 | Arg276 π -cation Arg276 - H-bond Trp307, Tyr321 - hydrophobic |
| (-)-11d | -8.613 | -113.831 | -468.70 | Trp307, Tyr321, His323 | Arg241, Arg276 π -cation Asn274, Arg276, Asp277, Lys322 - H-bond Ley134, Trp307, Ley315, Tyr321 - hydrophobic |
| (-)-11e | -7.524 | -98.671 | -467.97 | Trp307, Tyr321, His323 | Arg241, Arg276 π -cation Arg276, Asn274 - H-bond Trp307, Ley315 - hydrophobic |
| (-)-11g | -7.335 | -104.451 | -468.41 | Trp307, Tyr321 | Arg276 π -cation Ley315 - hydrophobic |
| (-)-11h | -8.649 | -120.321 | -468.01 | Trp307, Phe325 | Arg241 π -cation Asn274, Arg276 - H-bond Ley134, Trp307, Ley315 - hydrophobic |