SYNTHESIS OF MODIFIED T-1106-5´-TRIPHOSPHATES AS POTENTIAL INHIBITOR OF THE SARS-COV-2 RDRP

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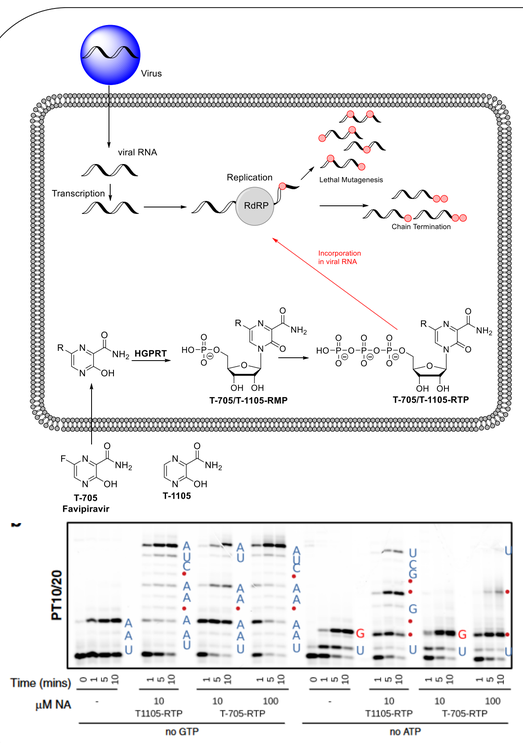
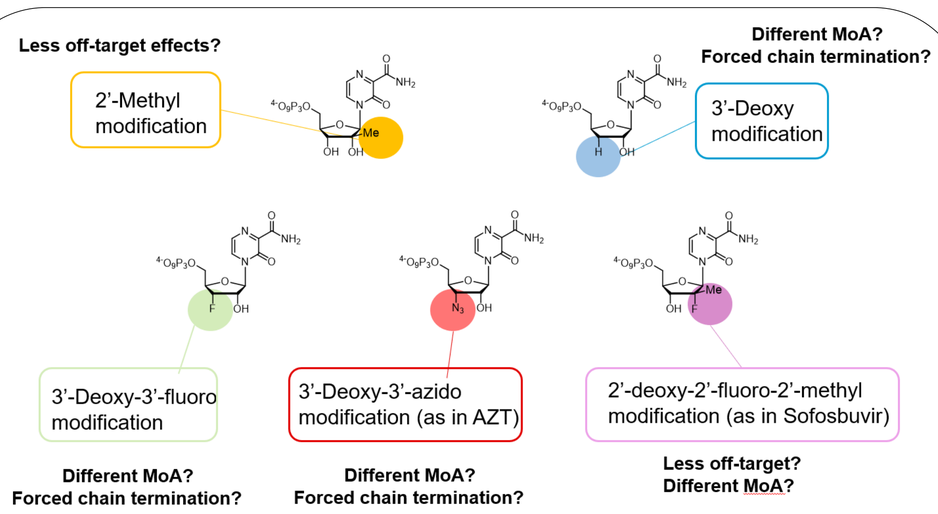
Background



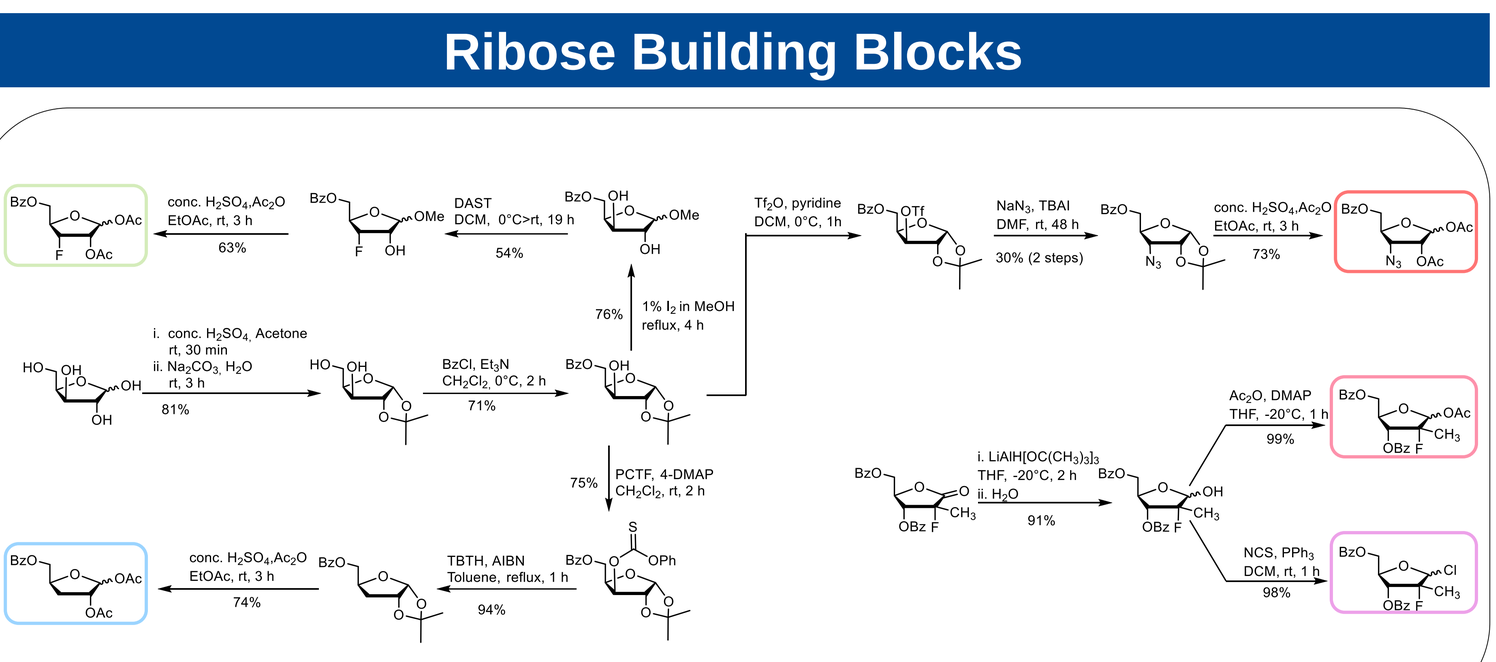
- Nucleosides were succesfully used in the past to treat viral infections by inhibiting the viral RdRp.
- Previous studies have shown that the nucleoside analogue T-1106-5´-Triphsophate is rapidly incorporated into the viral genome by the SARS-CoV-2 RdRp.
- The incorporation of T-1106 triggers C-to-U and G-to-A transition mutations.
- Transition mutations are causing an antiviral effect through lethal mutagenesis.

Objectives

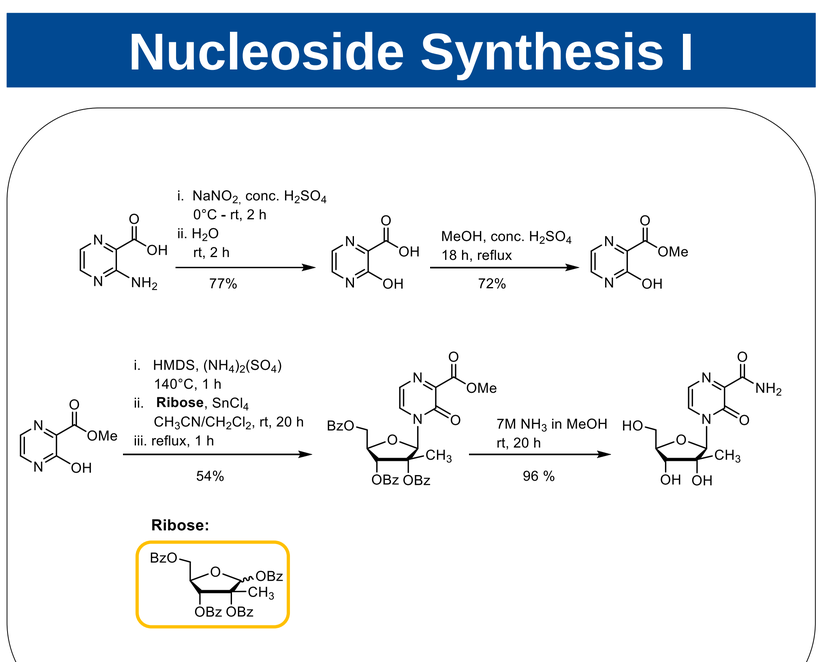


- Modified T-1106 triphosphates might show different mechanistic regarding polymerase inhibition, or different *in vivo* properties that could enhanced the antiviral potency compared to T-1106.
- Establishing a reliable route for the synthesis of modified T-1106-5´-Triphosphates.

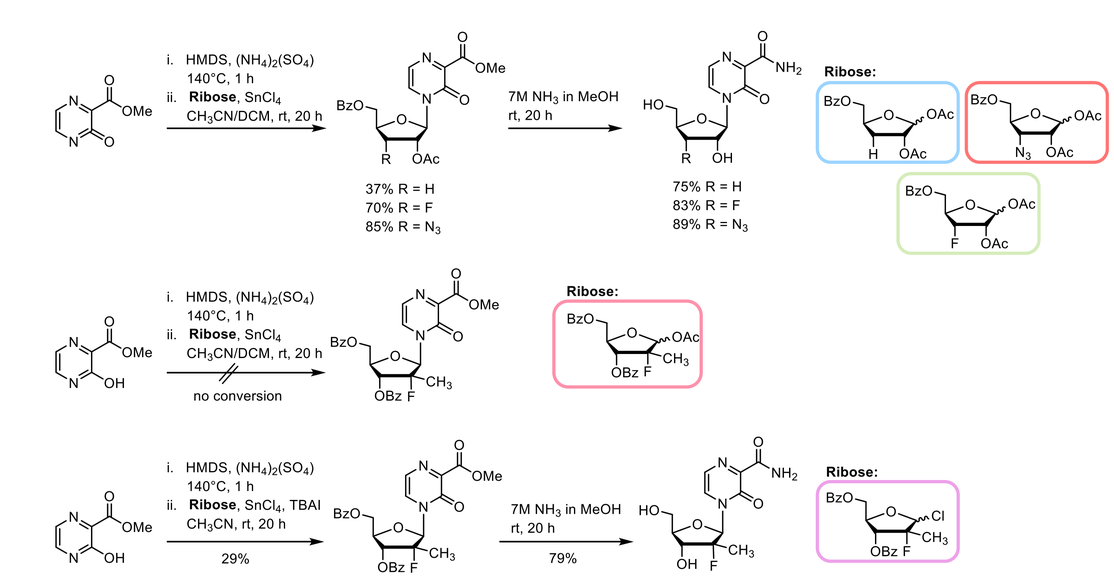
Ribose Building Blocks



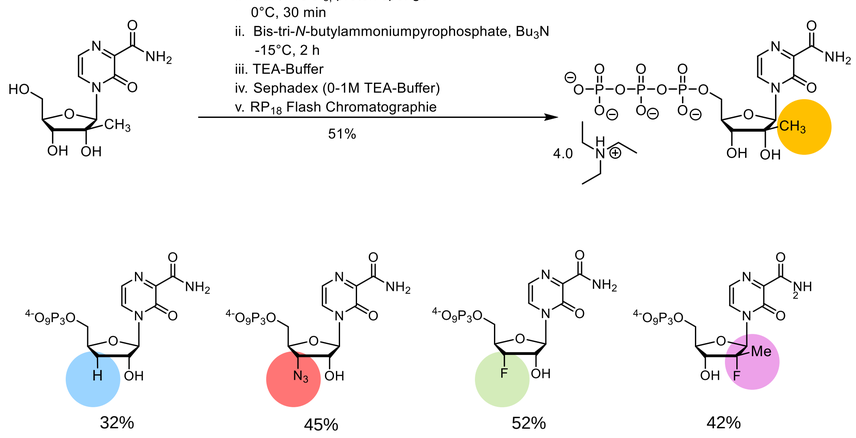
Nucleoside Synthesis I



Nucleoside Synthesis II



Triphosphate Synthesis



Conclusion

- Successful synthesis of five different modified T-1106-5´-Triphosphates via a reliable and efficient synthetic route.
- The Triphosphates are currently part of antiviral assays.

Collaboration & Funding

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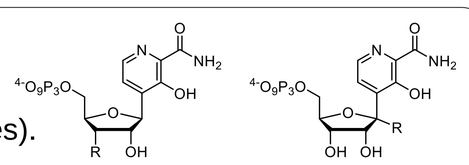
Future Perspectives

- Synthesis of Prodrugs.
- Synthesis of new modifications (C-Nucleosides).



References

[1] Shannon, A., Selisko, B., Le, NTT. et al. Rapid incorporation of Favipiravir by the fast and permissive viral RNA polymerase complex results in SARS-CoV-2 lethal mutagenesis. *Nat Commun* **11**, 4682 (2020).
[2] Huchting, Johanna, et al. Synthesis of T-705-Ribonucleoside and T-705-Ribonucleotide and Studies of Chemical Stability. *ChemMedChem* **12**,652-659, (2017).