Design and synthesis of purines analogs based on different annelated azines

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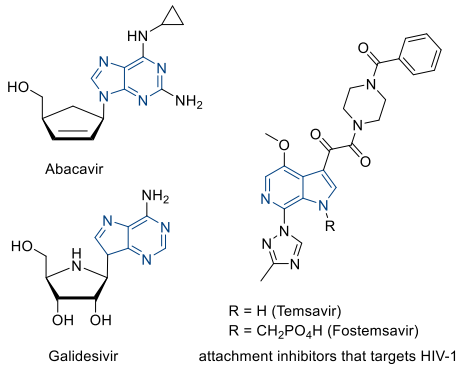
Background and aim of the project



Over the past 15 years, humanity has faced the serious problem of viral disease breakouts. Several nucleotide derivatives linked with glycosidic residue have been invented to cope with them: Remdesevir, Sofosbuvir, Abacavir and others.

Pandemic situation in the word doubled number of papers by azaindoles due to found antiviral activity of such derivatives

We tested Sonogashira products cyclization for azines as the key procedure for aza/diaza indoles

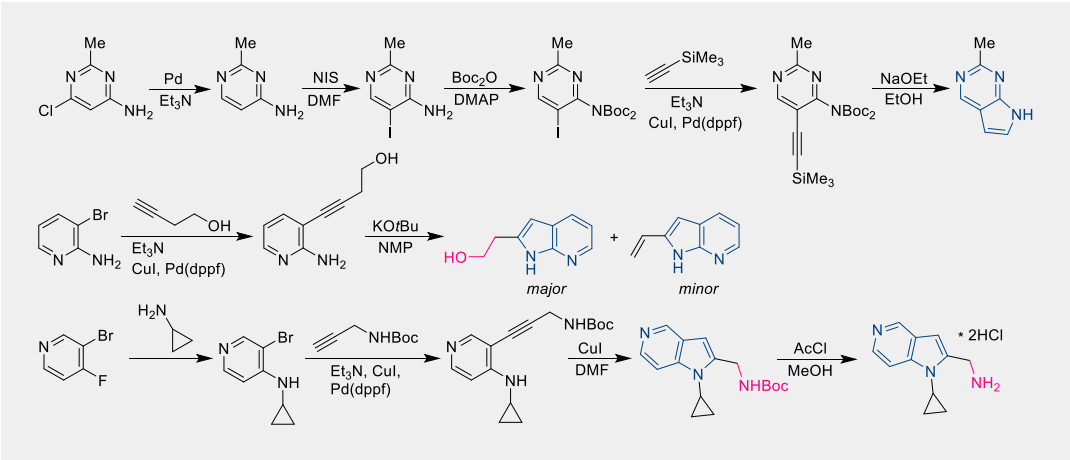
Outline of the synthetic results

Principal synthetic scheme for amino pyridine and pyrimidines

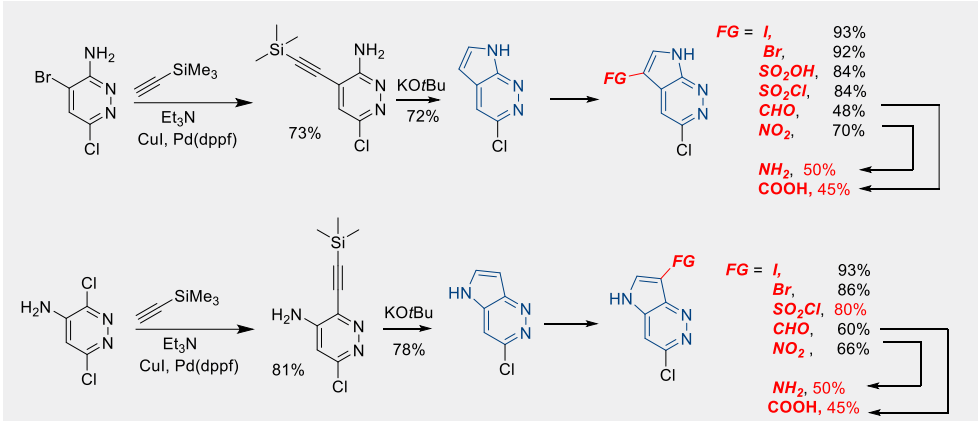
Substrate scope:

Nitrogen part: Primary, secondary and Boc protected amines

Alkynes: TMS-acetylene; homopropargyl alcohol, N-Boc-propargyl amine



Principal synthetic scheme for amino pyridazines and their modification via S_E reactions

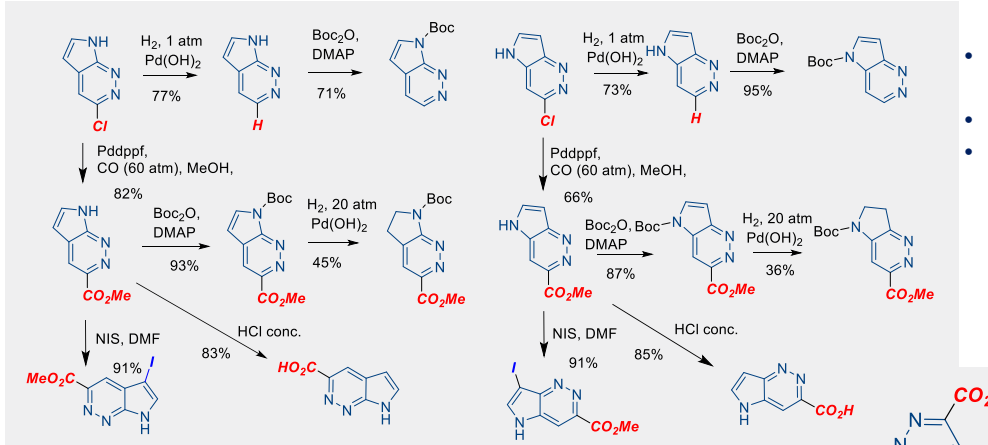


-NO_2 to NH_2 (Fe/NH_4Cl)

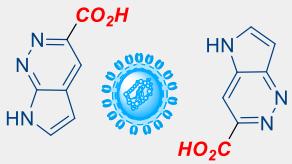
-CHO to COOH (Pinnick oxdn.)

TMSacetylene allowes preparation of both isomeric systems of heterocycles

Post-synthetic modifications



- Selective hydrogenation
- NH-protection
- Pd cat. carbonylation



Perfect precursors for antiviral drug discovery

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