



Nucleoside mimetics and analogues

HTS Collection &

REAL Array of new nucleoside-like molecules

Nucleoside mimetics from 2.6 M HTS Compound Collection

- **Careful Substructure Search**

Search of nucleoside core fragments and their bioisosteric heterocycles with simultaneous presence of sugar-like moiety

- **Strict MedChem Filters**

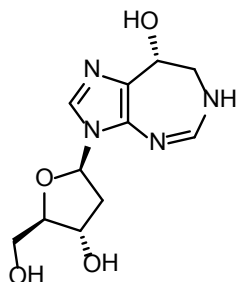
Removal of undesired functionalities, reactive groups and large aromatic fragments

- **Chemotype Control**

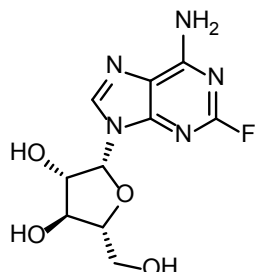
Compounds with trivial structural fragments were mostly removed.
Control of renovation of the library in accordance to new literature data.

Nucleoside analogues available from Enamine HTS Collection

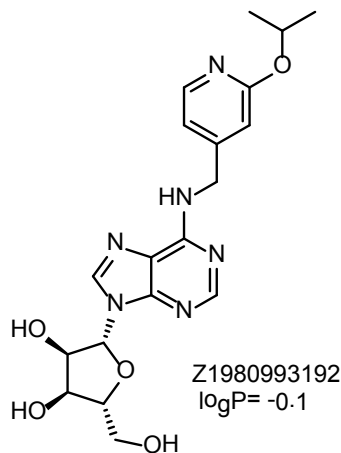
- 277 selected compounds
- off-the-shelf close analogues of natural nucleosides:



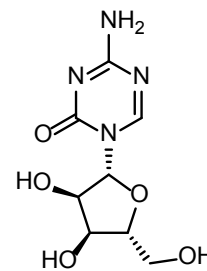
Z2216208604
logP= -2.0



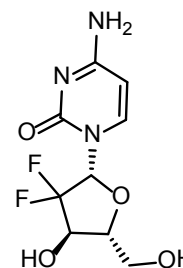
Z802671516
logP= -1.4



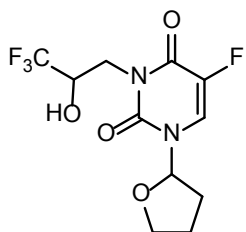
Z1980993192
logP= -0.1



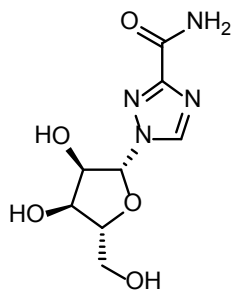
Z1522566611
logP= -3.0



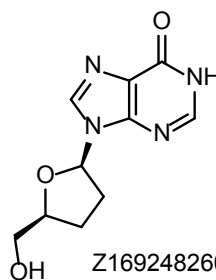
Z234896939
logP= -1.5



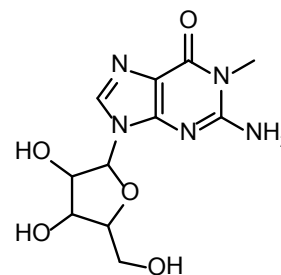
Z119992364
logP= -0.3



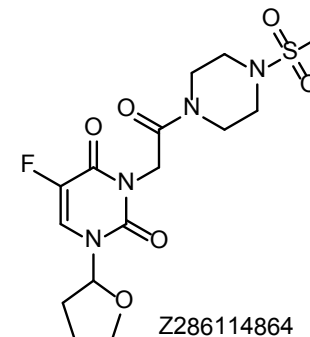
Z1522567185
logP= -2.7



Z1692482604
logP= -0.9

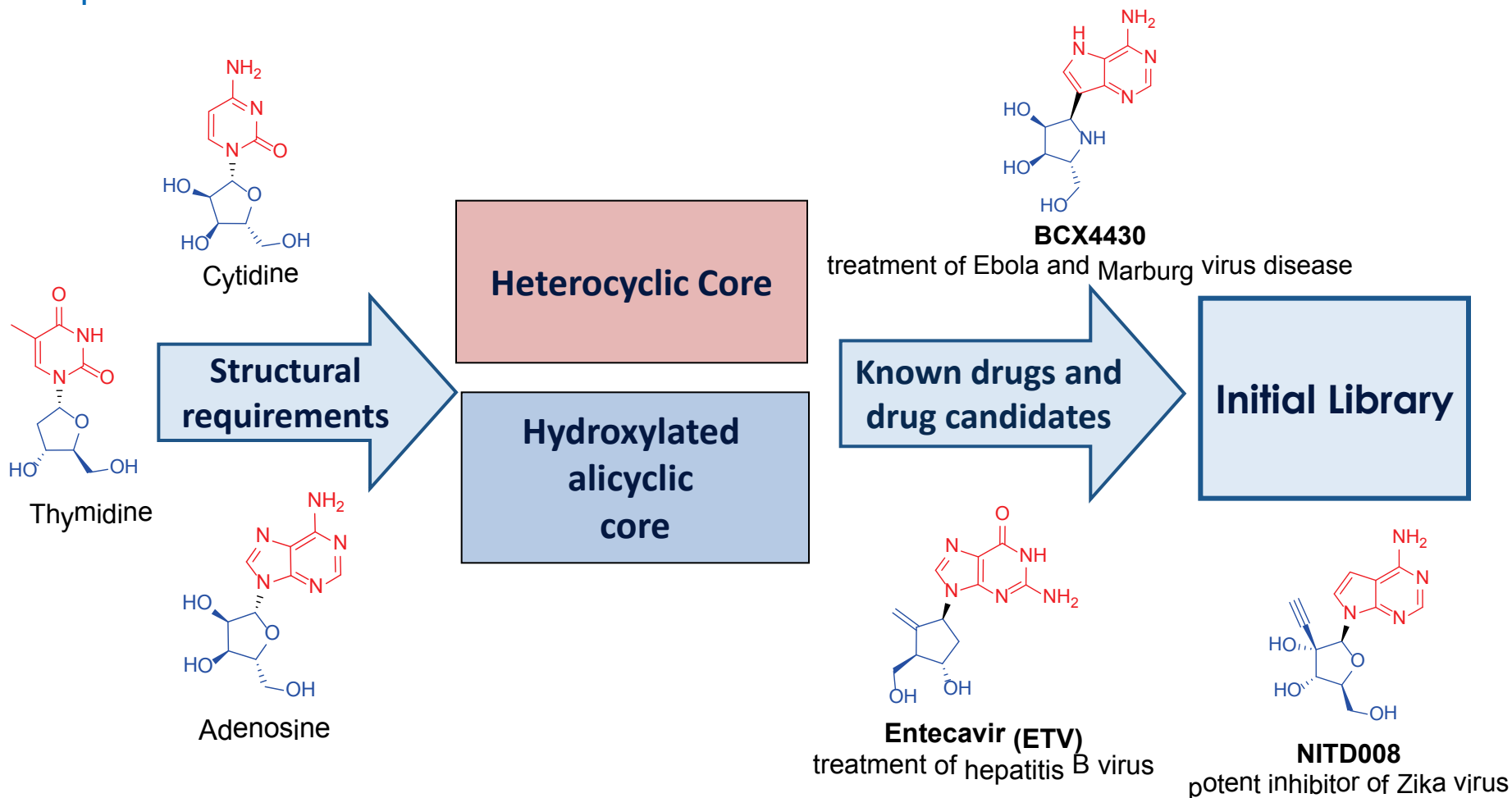


Z56786755
logP= -2.5



Z286114864
logP= -2.0

Design of REAL Nucleoside mimetics dataset



REAL structures with validated synthetic procedures

- **Combinatorial approach**

Over 100,000 Building Blocks immediately available for modification:

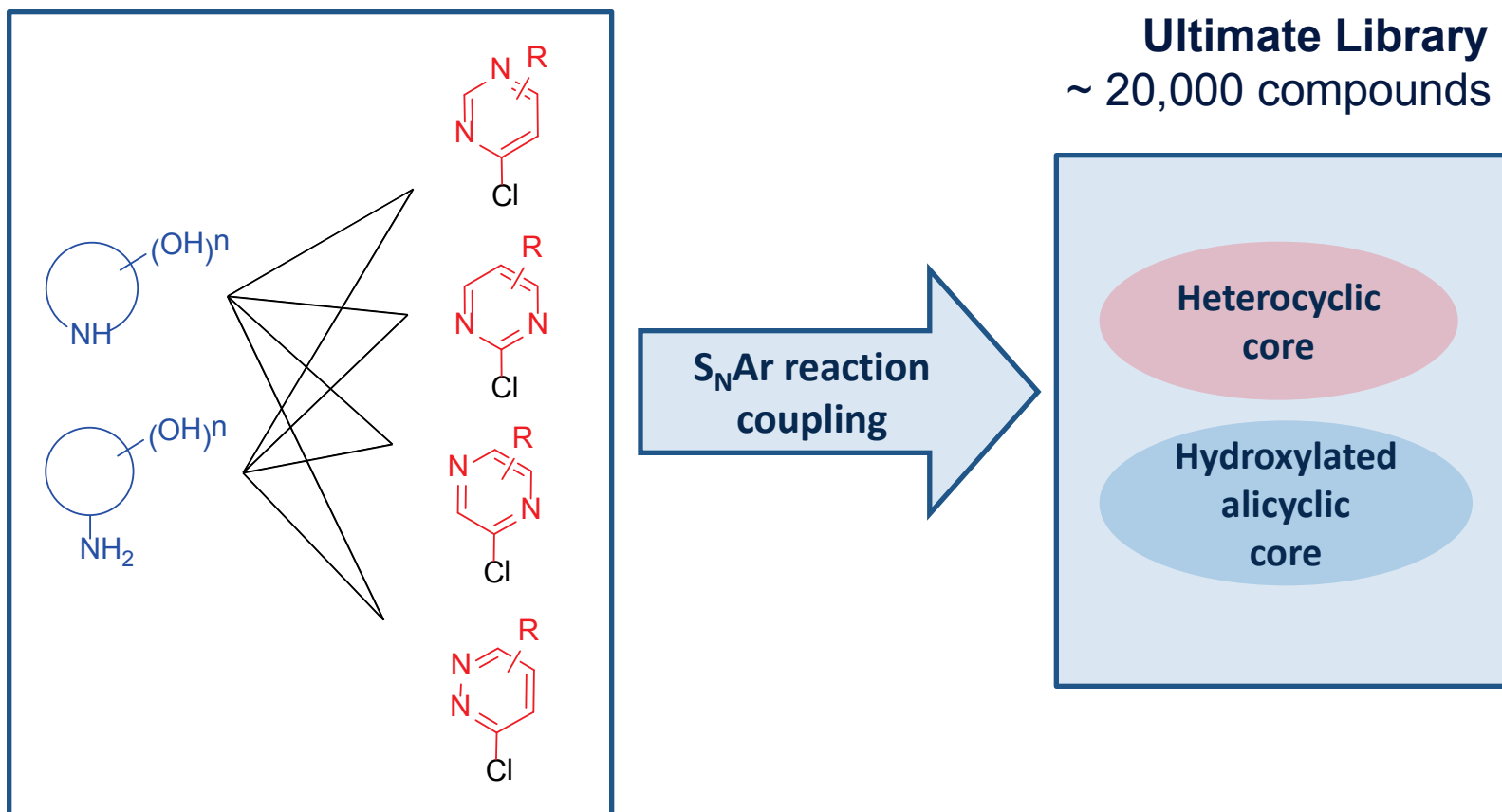
- Diazine heterocyclic cores mimic nucleobases
- alicyclic amino alcohols – sugars

- **Filtering of unwanted functionalities & MedChem inspection**

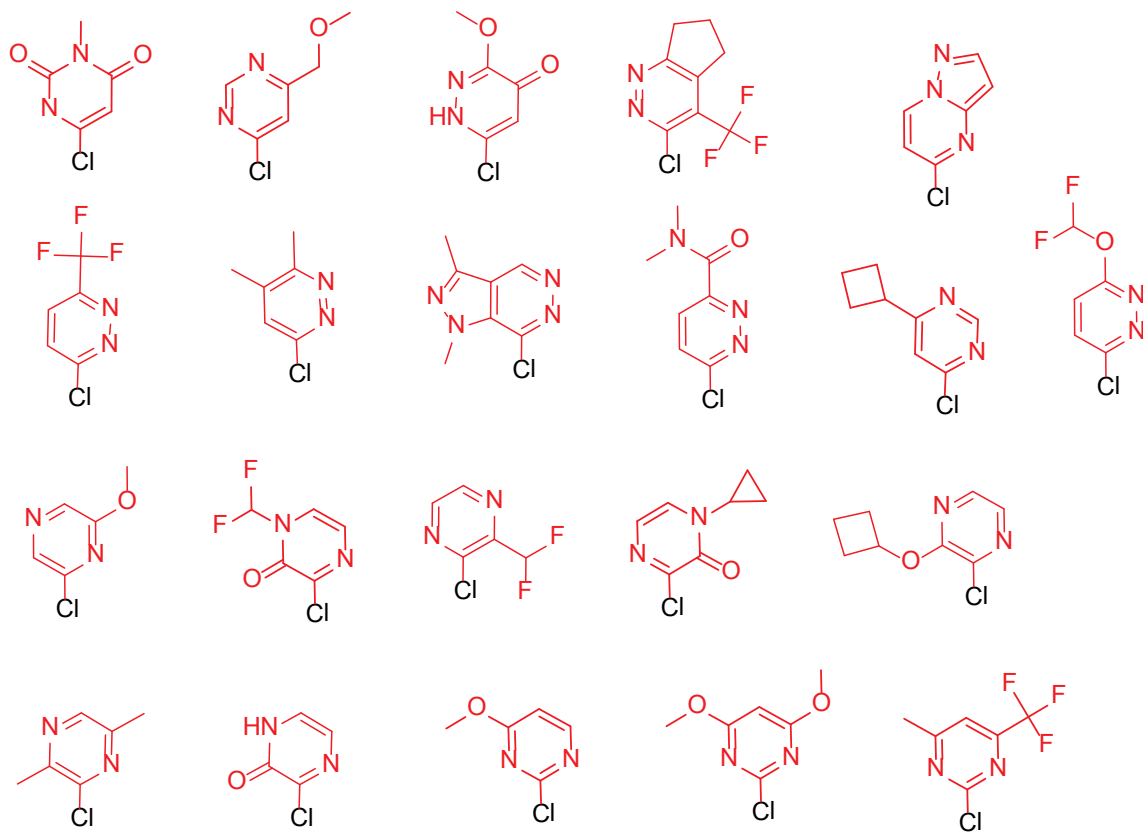
- **Automated parallel synthesis**

Implementation of well-developed reaction procedures operated by highly experienced staff

Design of REAL Nucleoside mimetics dataset

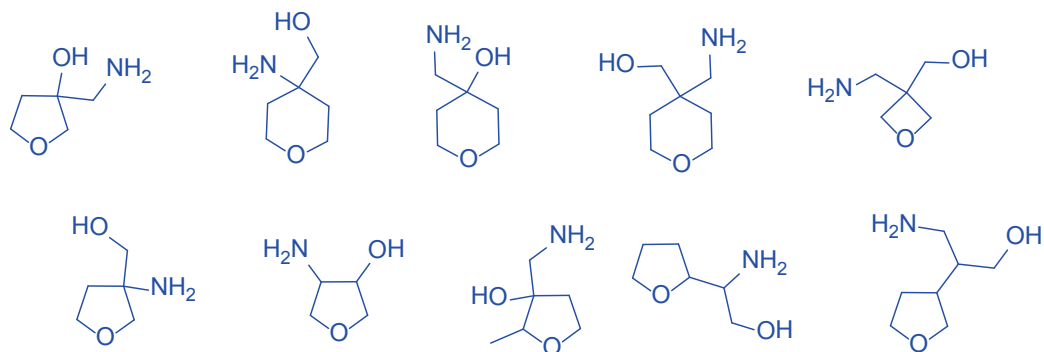


Stock available Heterocyclic Cores: Cytidine, Thymidine, Uridine mimetics

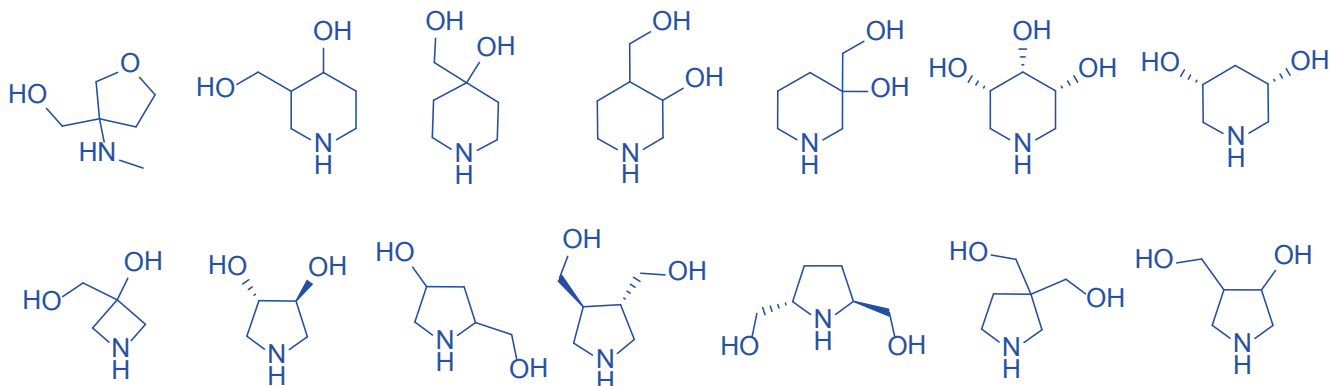


Hydroxylated Aliphatic Cores

Primary amines

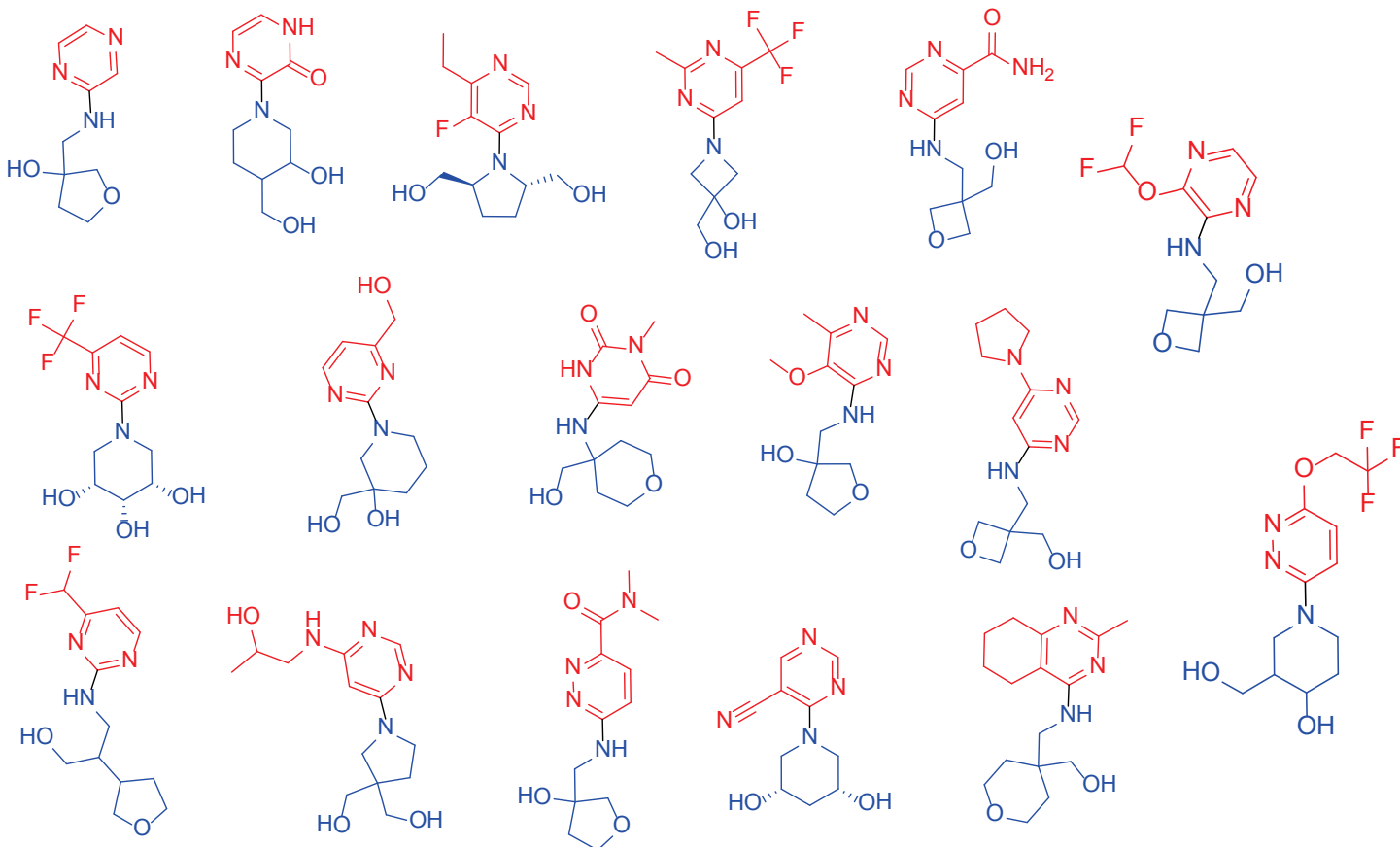


Secondary amines



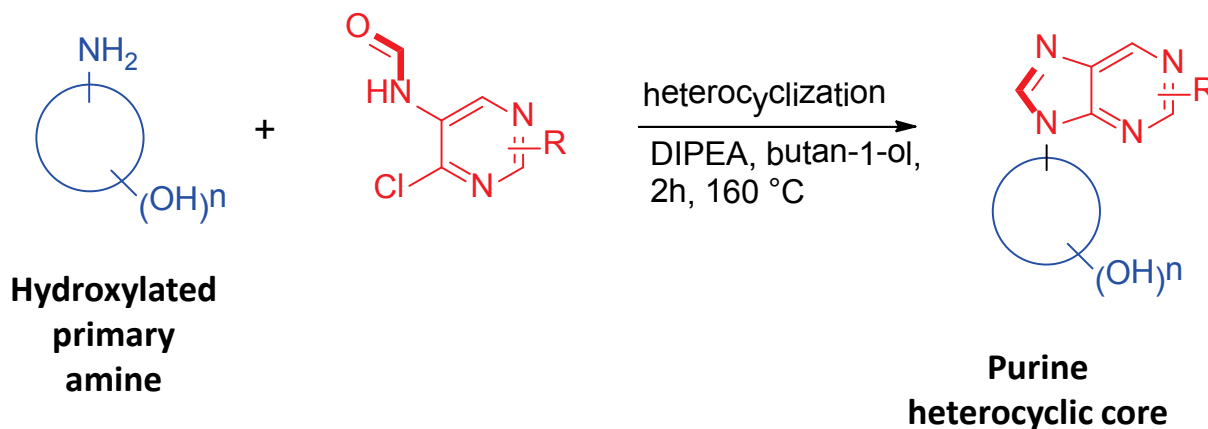
REAL Nucleosides: Cytidine, Thymidine, Uridine mimetics

Representative examples

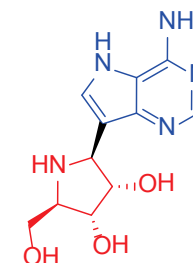


Total number of compounds: **6,800**

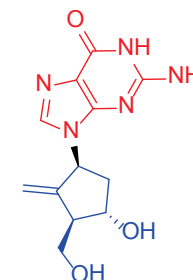
REAL Nucleosides: Adenosine, Guanosine mimetics Synthesis



examples:



BCX4430

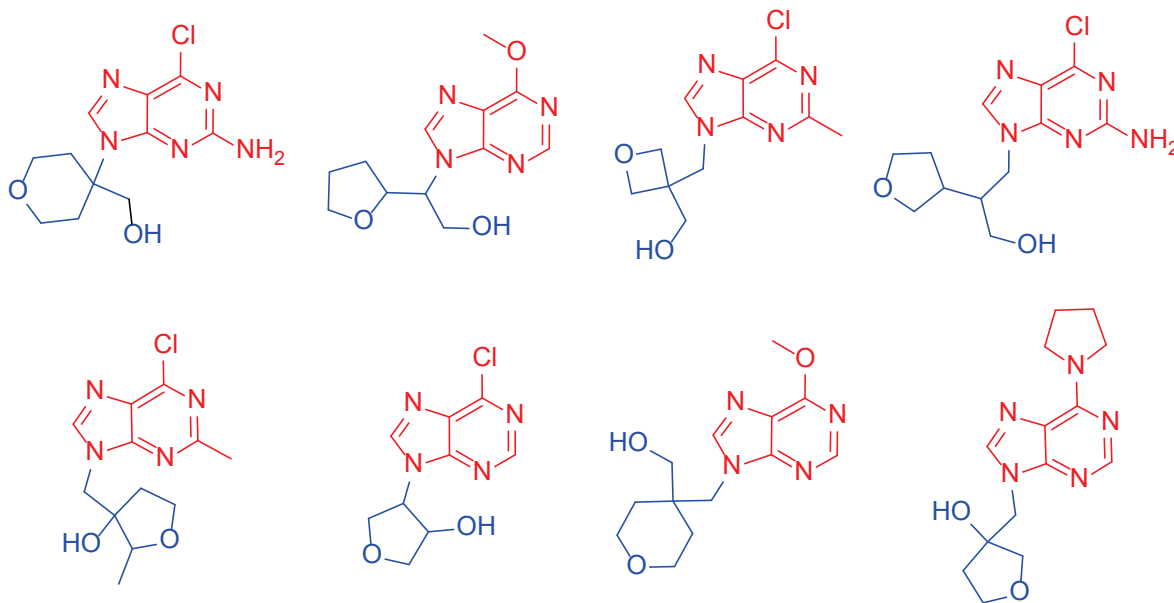


Entecavir (ETV)

1. Bioorganic and Medicinal Chemistry; vol. 23; nb. 1; (2015); p. 184 – 191
2. Bioorganic and Medicinal Chemistry Letters; **vol.** 26; nb. 11; (2016); p. 2706 – 2712
3. Archiv der Pharmazie; **vol.** 347; nb. 7; (2014); p. 478 - 485

REAL Nucleosides: Adenosine, Guanosine mimetics

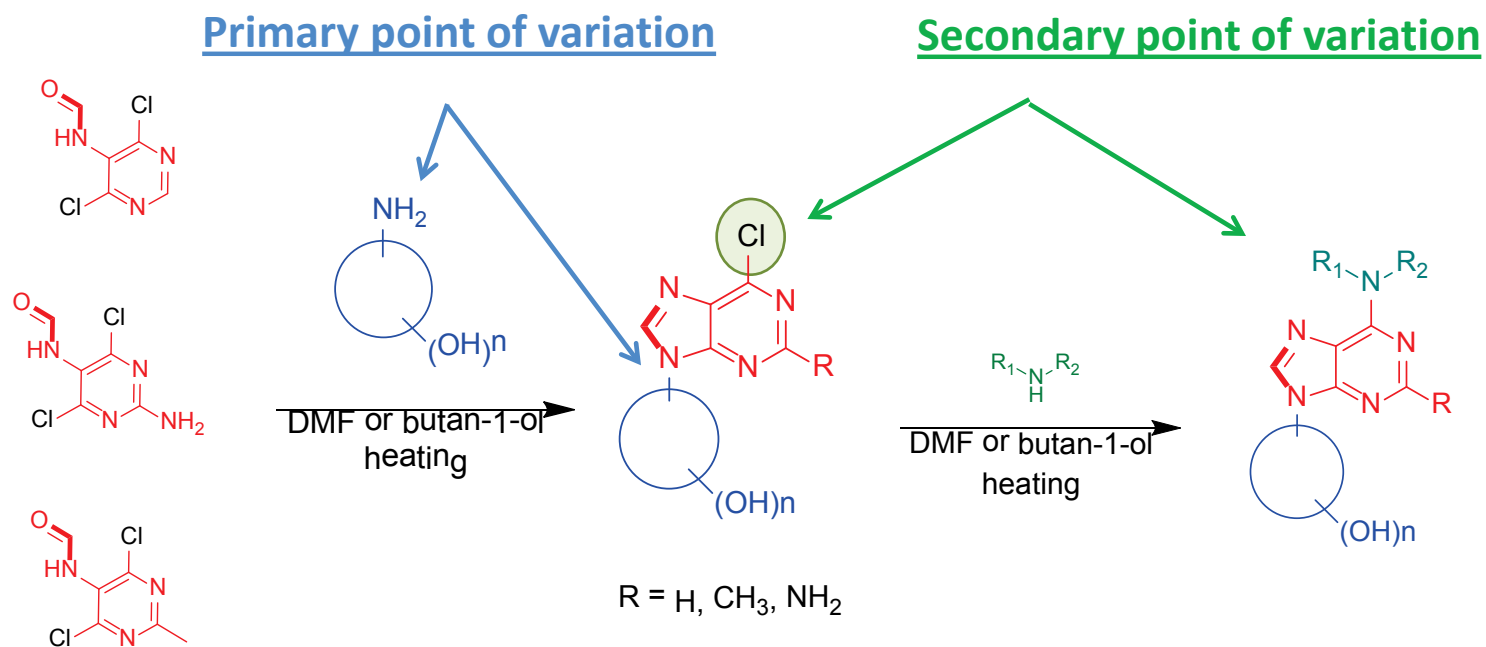
Representative examples



- over **100** compounds

Adenosine, Guanosine mimetics

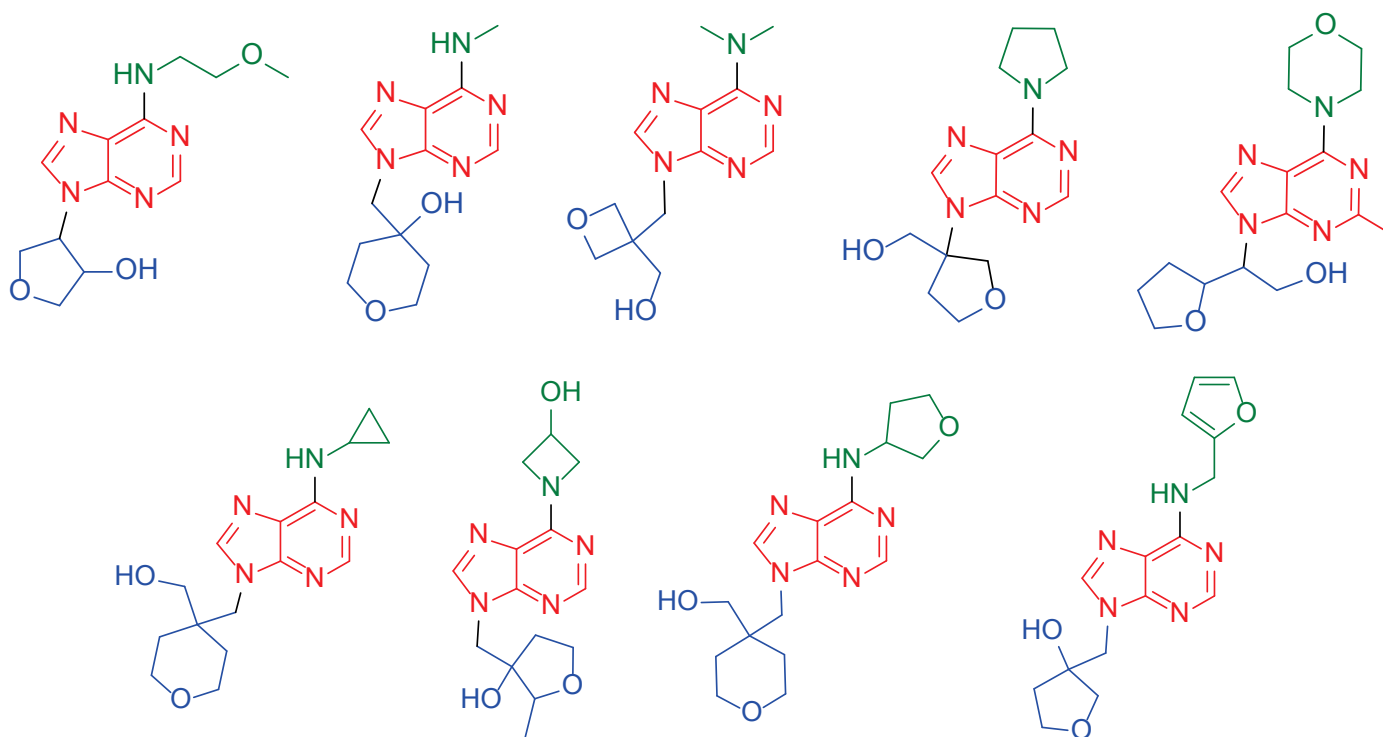
3-component reactions



- Sequential substitution of chlorine atoms allows for a sized set based on purine scaffold

Adenosine, Guanosine mimetics

Representative examples



- over **15,000** compounds are accessible through proposed 3-component reaction approach