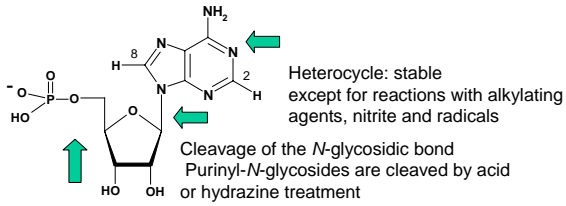


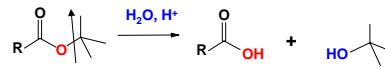
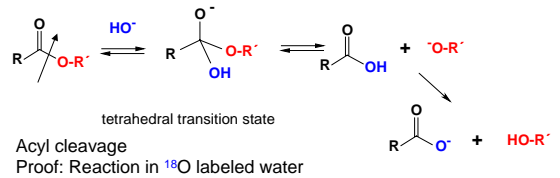
#### 4. Chemical stability of nucleic acids



Cleavage of the phosphodiester linkage:  
RNA: hydrolyzed by 0.3 M KOH  
DNA: stable

#### Chemical hydrolysis of phosphoesters

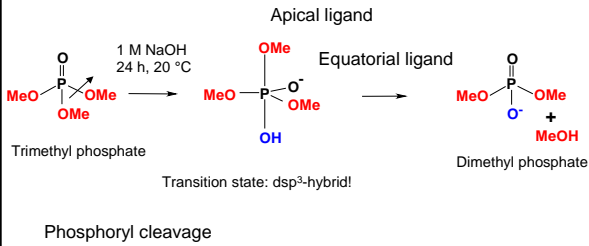
Comparison: Ester hydrolysis of carboxylic acid



Alkyl cleavage in specific cases only

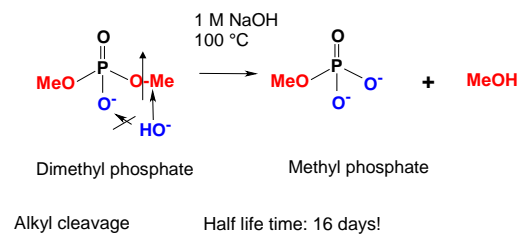
#### Chemical hydrolysis of phosphoesters

1. Phosphotriester



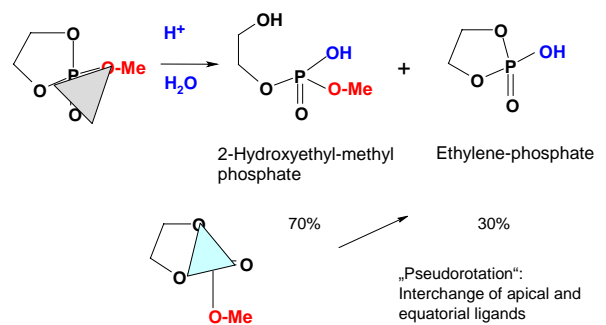
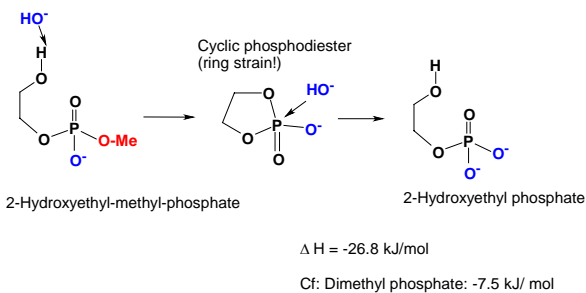
#### Chemical hydrolysis of phosphoesters

2. Phosphodiester



#### Chemical hydrolysis of phosphoesters

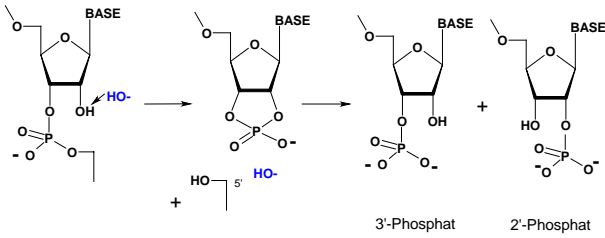
2. Phosphodiester



Leaving group may only be displaced from an apical position (longest bond)

### Alkaline hydrolysis of DNA and RNA

DNA: stable (1 h at 100 °C, 1 M NaOH)  
 RNA: hydrolyzed at RT in 0.1 M NaOH



### Enzymatic hydrolysis of RNA

#### Ribonucleases

Non-specific cleavage or specific cleavage of bases

Ribonuclease A: Pyrimidin-Nucleotides (C,U)

Ribonuclease T<sub>1</sub> (*Aspergillus oryzae*): Guanine (in *syn*-conformation)

Ribonuclease P (Ribozymes)

#### Ribonuclease A

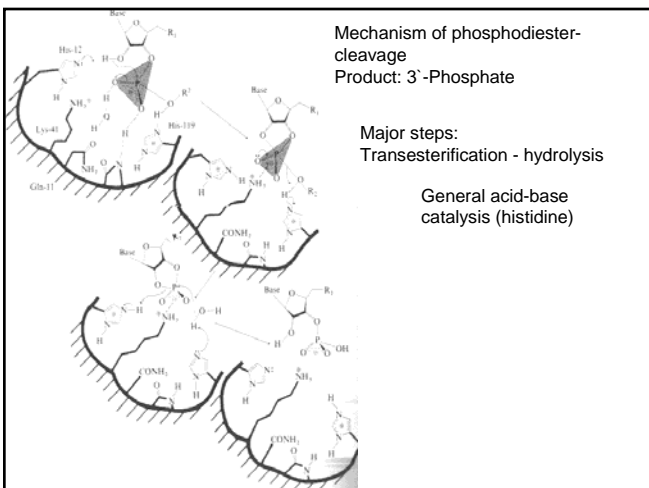
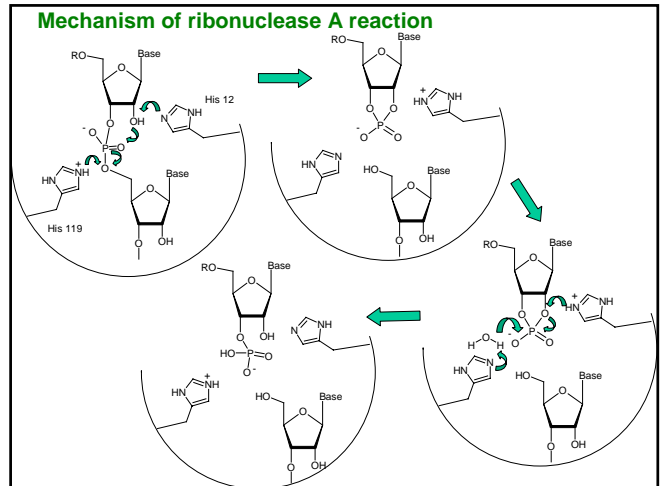
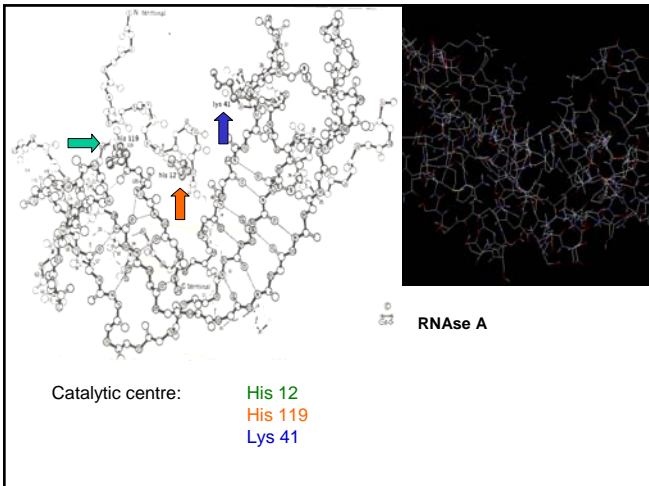
Isolation from bovine pancreas

Many crystal structures (124 entries, e.g. pdb-codes: 1AFK, 1H1H, 1QHC, 1RND)

First „NMR-structure“, 4 Nobel prizes

M: 13.680, 124 amino acids

Chemical syntheses: 1969 Merrifield (0.4 mg), 1979 Yajima (3 mg)



Ribozymes – catalytically active ribonucleic acids - metalloenzyme

Discovered in 1982

2 Groups

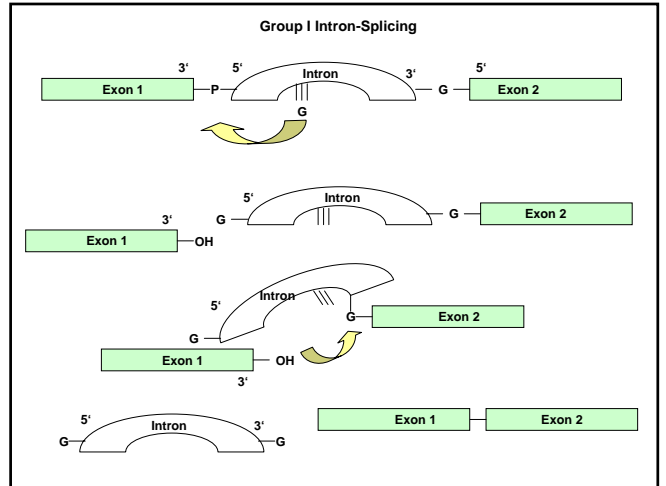
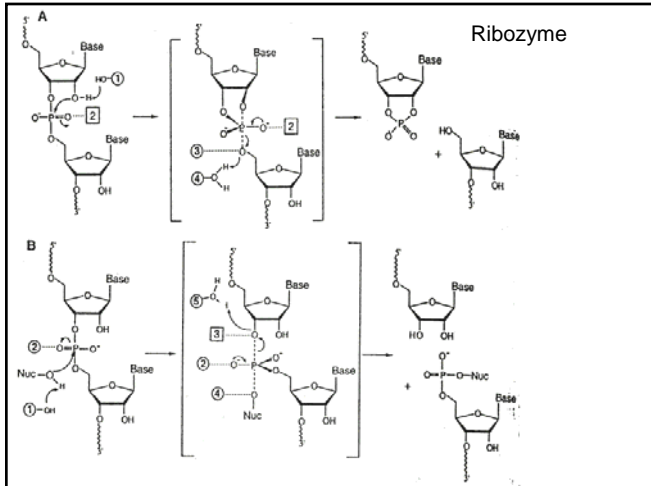
35 – 155 Nucleotides: Hammerhead, Hairpin, Hepatitis Delta  
 Formation of 2',3'-cyclo-phosphates and 5'-OH (analogous to RNase A)

100- 3000 Nucleotides: RNase P, Group I and II Introns  
 Formation of 5'-phosphate (and 3'-OH)

Self modification, except RNase P (processes t-RNA Precursor)

Reaction rate enhancement: ~ 10<sup>11</sup>

Essential: Mg<sup>2+</sup>



Magnesium:  
 Coordination of O only (Mn<sup>2+</sup> also with N)  
 6 Ligands (Ca<sup>2+</sup> > 6)

pKa of water lowered to 11.4

Smallest catalytically active RNA:  
 UUU  
 Hydrolysis of GAAA in the presence of Mn<sup>2+</sup>

Weakest codon-anticodon binding interaction

