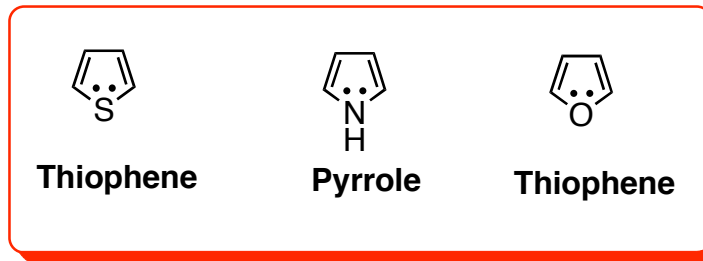


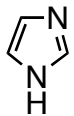
# Heterocycles (McM chapt 28)

- Monocyclic or fused rings
- Cont. one or more ring atom  $\neq$  C (normally O; N; S)
- Aromatic, partly saturated or saturated ring(s)

## 5-Membered rings (Heteroatom N, O, S)



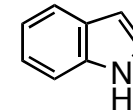
### Other examples



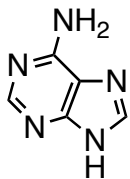
Imidazole



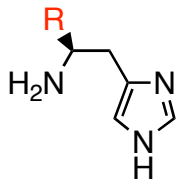
Thiazole



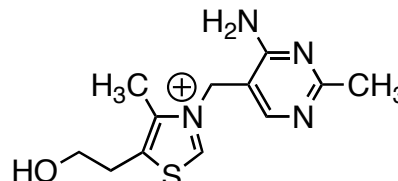
Indole



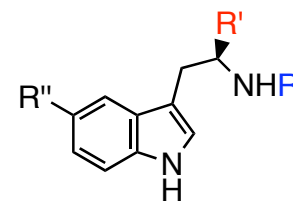
Adenine  
(purine der.)



R=CO<sub>2</sub>H: Histidine  
R=H: Histamine



Thiamin  
(Vit B1)



R=H  
R'=H  
R'''=OH } Serotonin

R=H  
R'=CO<sub>2</sub>H  
R'''=H } Tryptophane

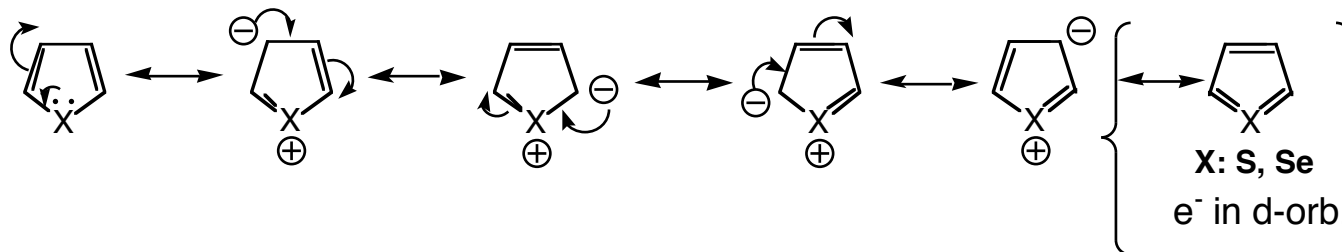
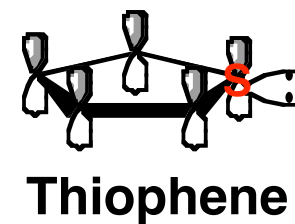
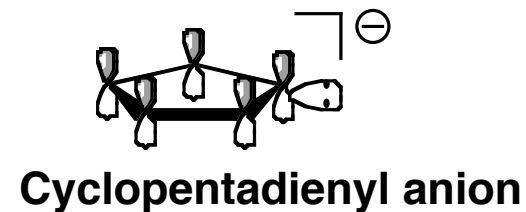
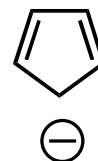
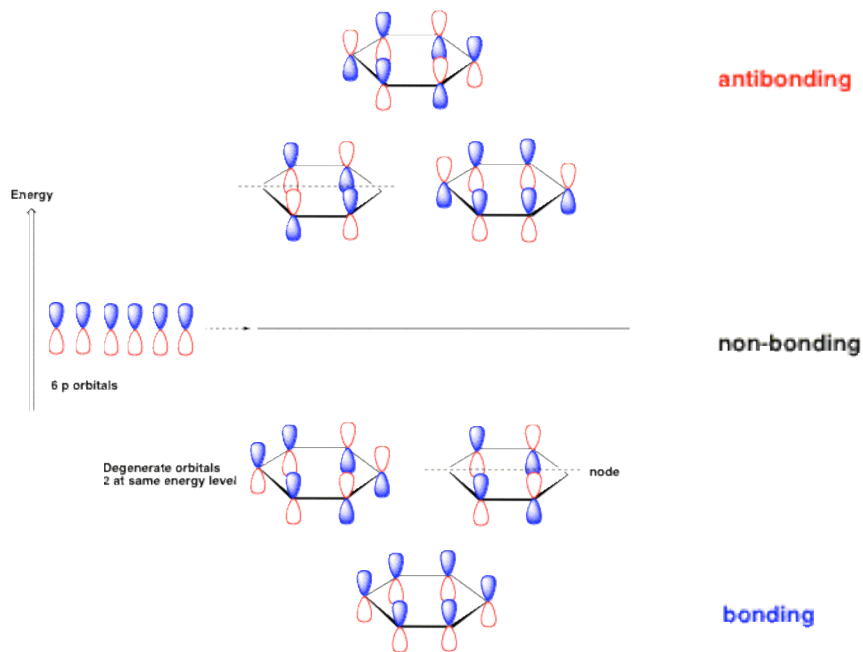
R=Ac  
R'=H  
R'''=OCH<sub>3</sub> } Melatonin

# Criteria for Aromaticity (Hückel)

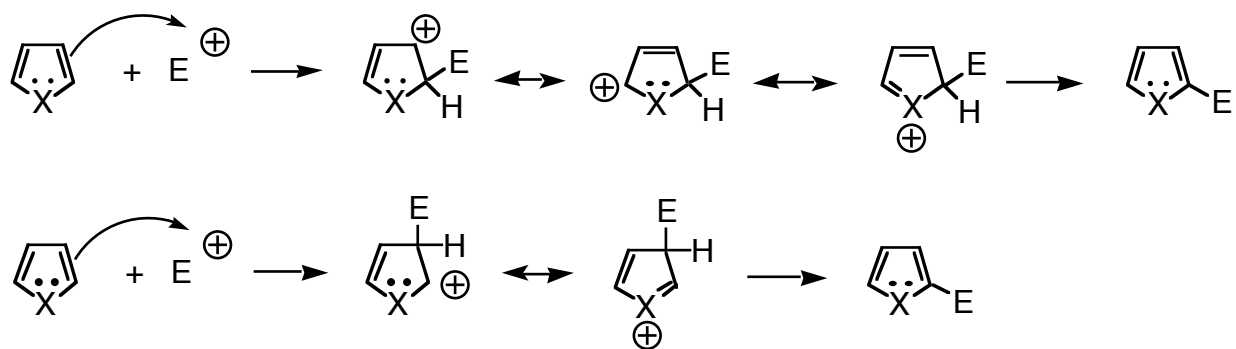
(Monocyclic) ring

Planar

No of  $\pi$ -electrons in conjugation  $4n+2$  ( $n: 0, 1, 2, \dots$ )



**5-membered rings** - electron rich - reactive i E-fil. Ar subst.

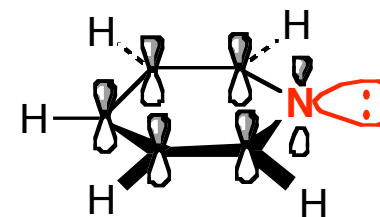
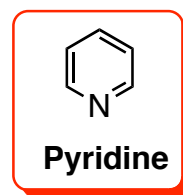


React. in  $\alpha$ -position generally preferred

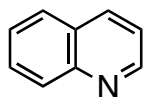
Selectivity not always good

React.: Pyrrole > thiophene > furan

# 6-Membered rings (Heteroatom N)



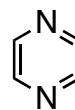
## Other examples



Quinoline



Pyrimidine

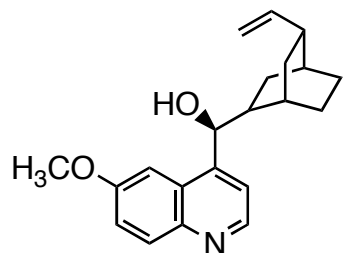


Pyrazine

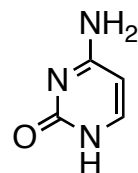


Pyridazine

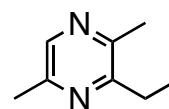
Rare in nature



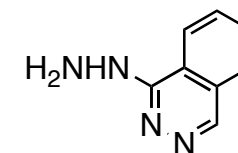
Quinine



Cytosine

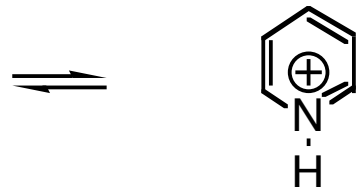
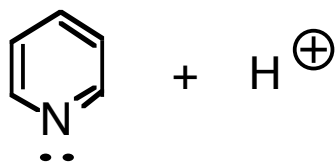


Ant pheremone

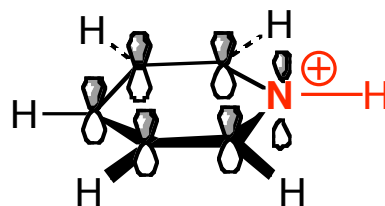
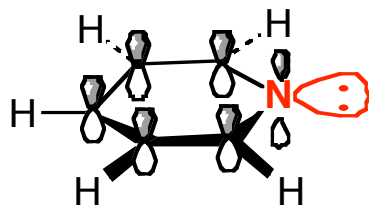


Hydralazine  
Antihypertensive drug

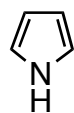
## Pyridine as a base



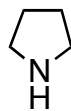
**pKa: 5.2**



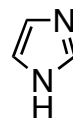
**sp<sub>2</sub> N less basic than sp<sub>3</sub>**



**pKa 0.4**



**pKa 11.3**



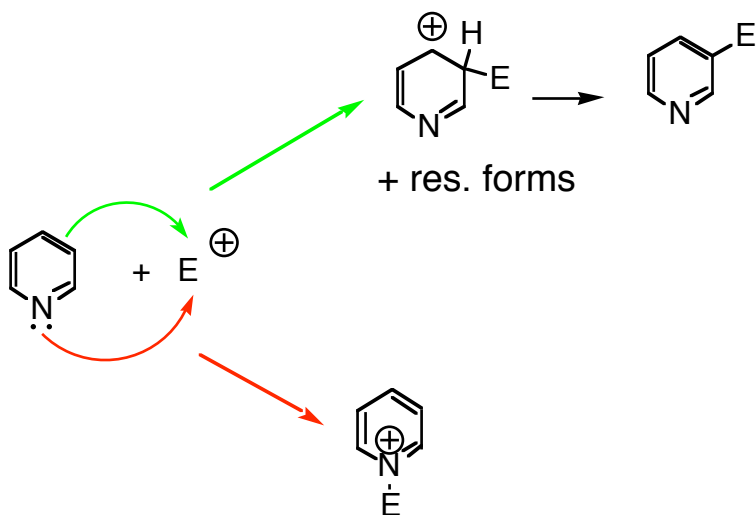
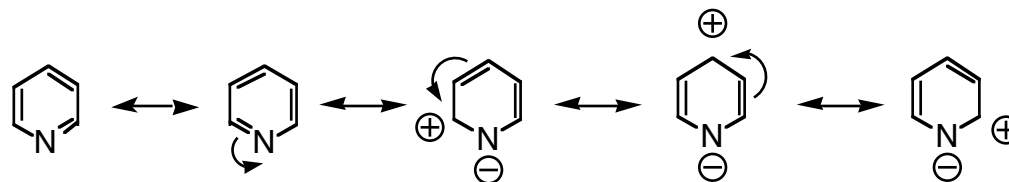
**pKa 7.1  
(≈amidine)**



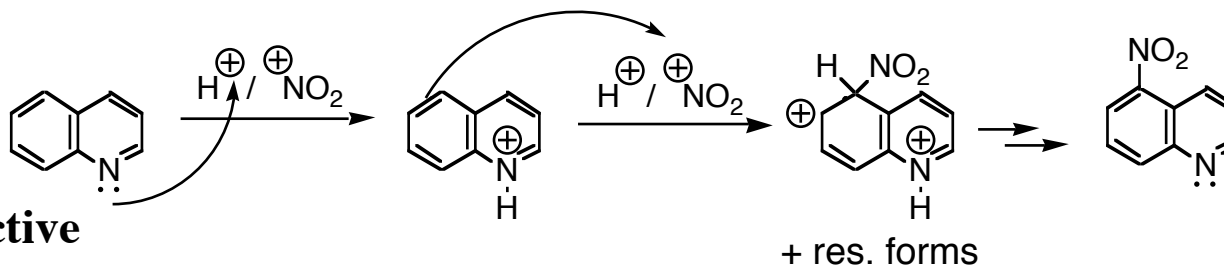
**pKa 2.5**

# Electrophilic Reaction on Carbon: E-phil. Ar. Subs.

**6-membered rings** - electron deficient - ↓ reactivity

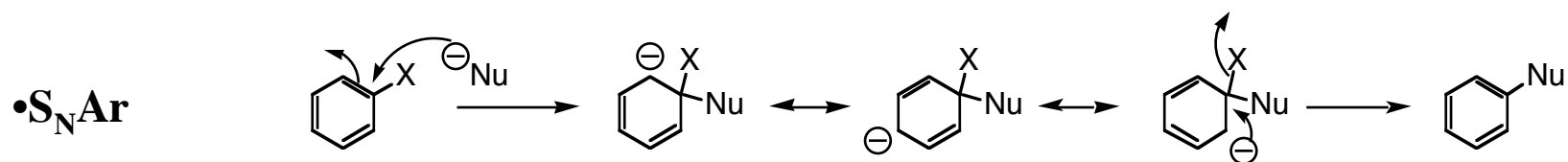


- Both C and N may react
- 3/5 pos. most reactive C
- Diazines less reactive
- Sulfonation, Nitration, halogenation
- Not FC react.



**Benzo ring most reactive**  
**Much slower react. than naphthalene**

# Nucleophilic Aromatic Substitution



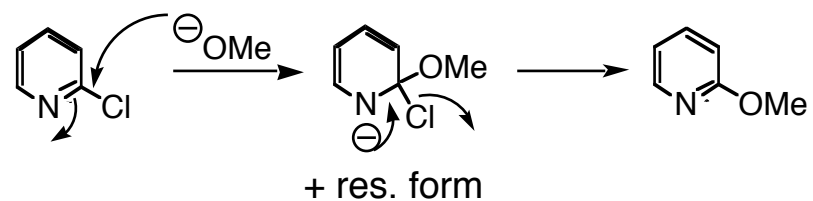
• **S<sub>N</sub>1: Via aryl cation**

• **Benzyne**

• **SRN1: Involves radicals**

• **VNS: Vicarious nucl. Subst.**

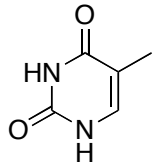
**6-membered rings** - electron deficient - reactive in Nu-fil. Ar subst.



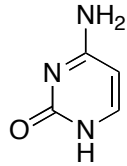
2 / 4 Pos. reactive; electron def. C, neg. charge partly on N in intermed  
3 / 5-Pos. much less reactive (benzenoid pos.)

# Nucleosides, Nucleotides, Nucleic acids (DNA; RNA)

## DNA bases



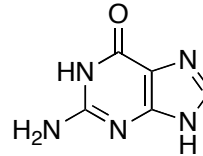
Thymin



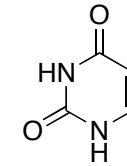
Cytosin



Adenine



Guanine



Uracil

## RNA bases

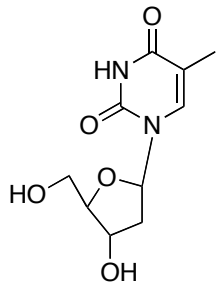
Cytosin

Adenine

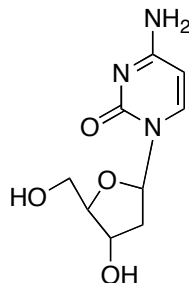
Guanine

## DNA Nucleosides

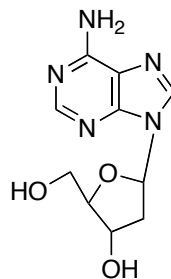
Thymidine



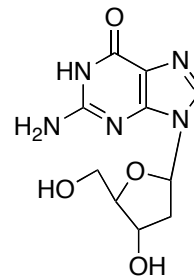
Deoxycytosine



Deoxyadenosine

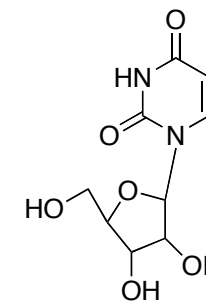


Deoxyguanosine



## RNA Nucleosides

Uridine



Cytosine

Adenosine

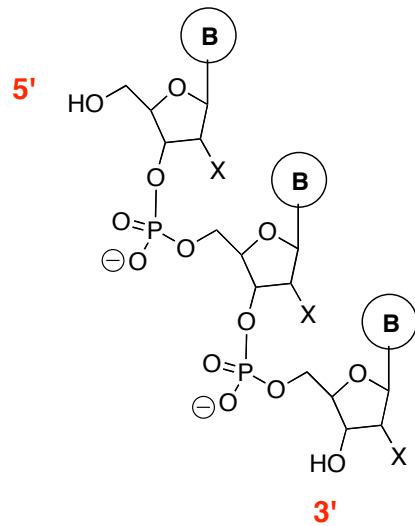
Guanosine

## 2-Deoxyribosides

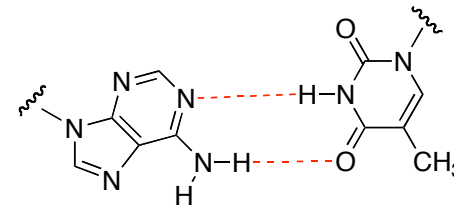
## Ribosides



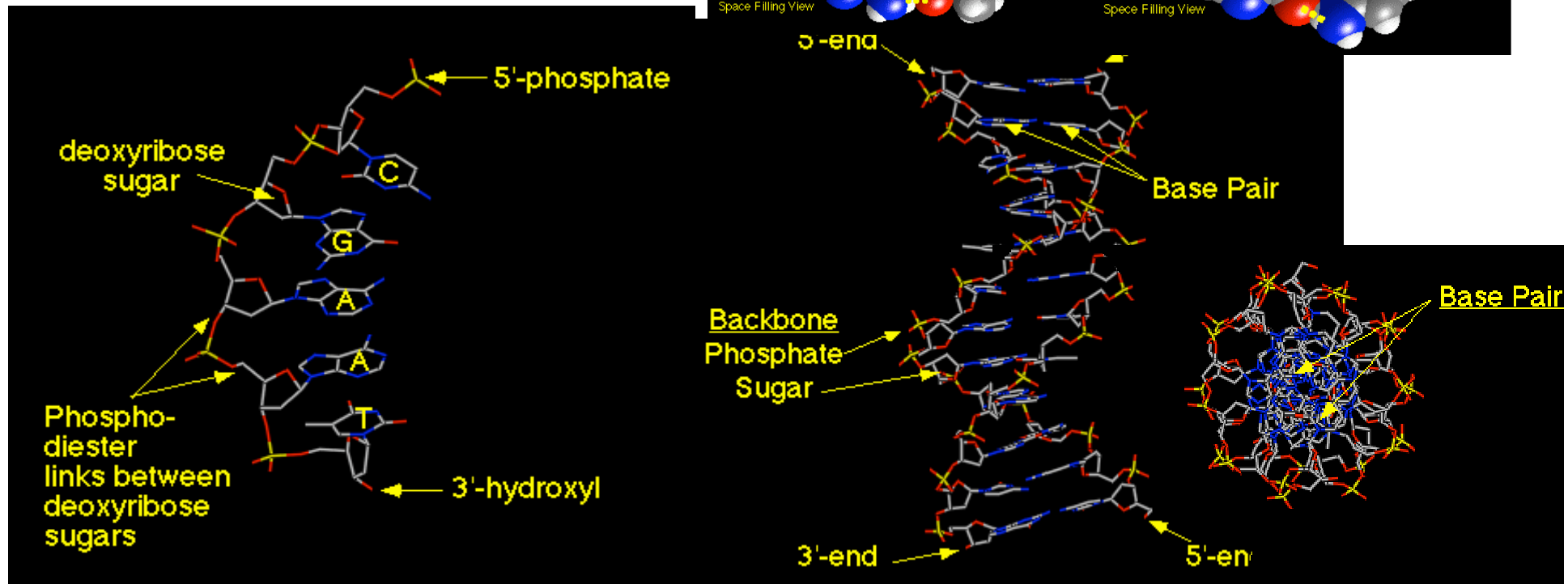
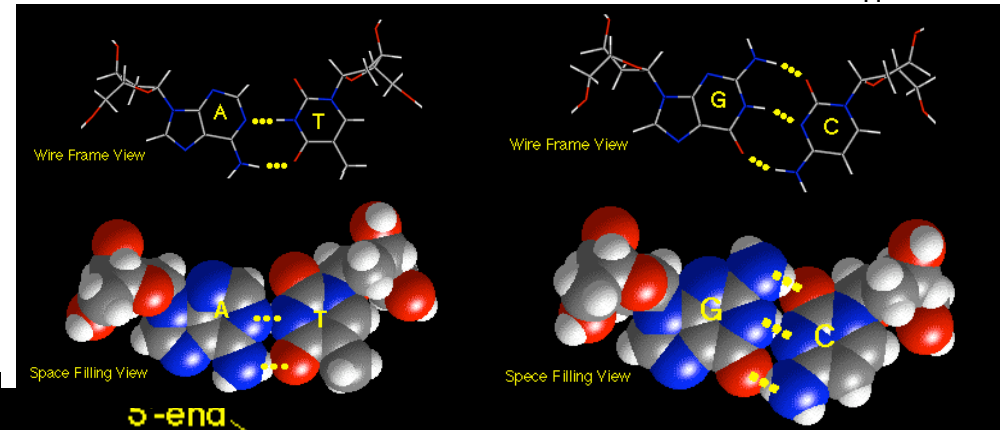
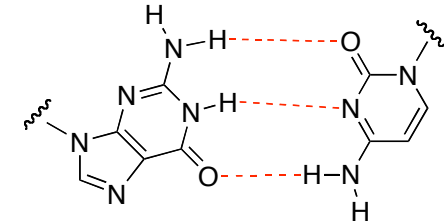
# Nucleotides



## A-T and G-C Base pairs



## Double $\alpha$ -helix (DNA)

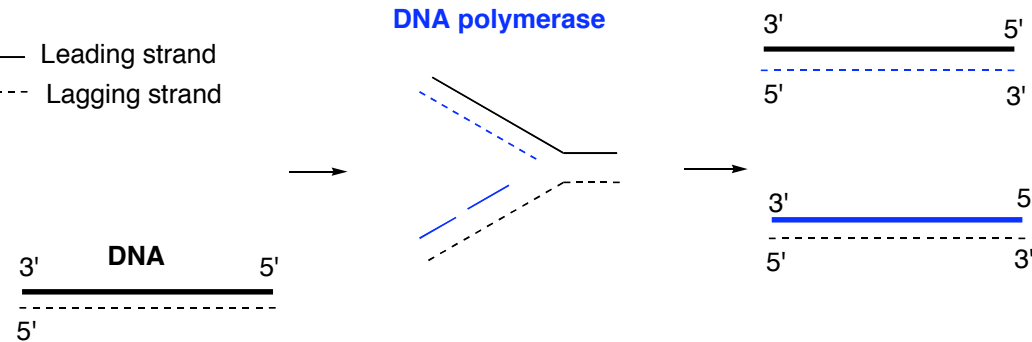


# Nucleotide sequence in DNA - genetic information

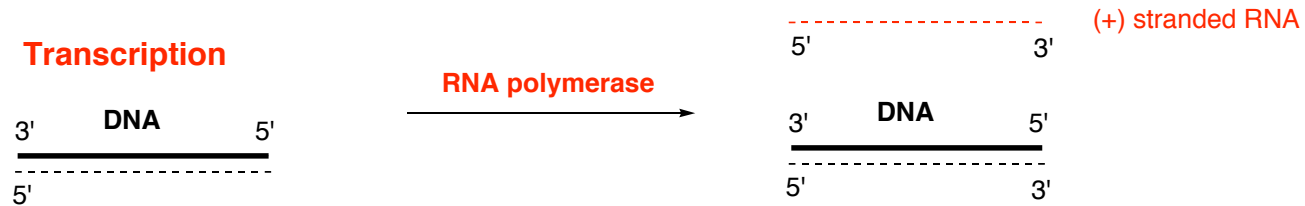
## Prokaryotes and eukaryotes

### Replication

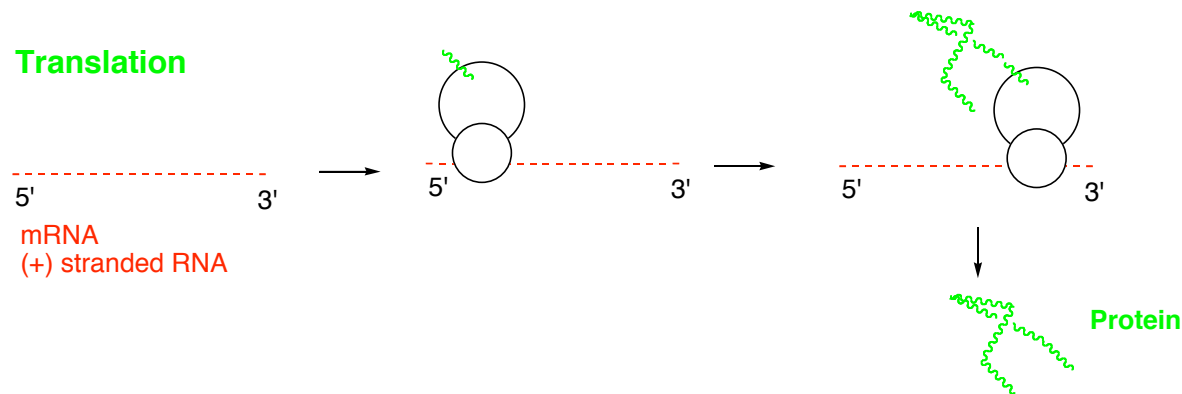
— Leading strand  
- - - Lagging strand



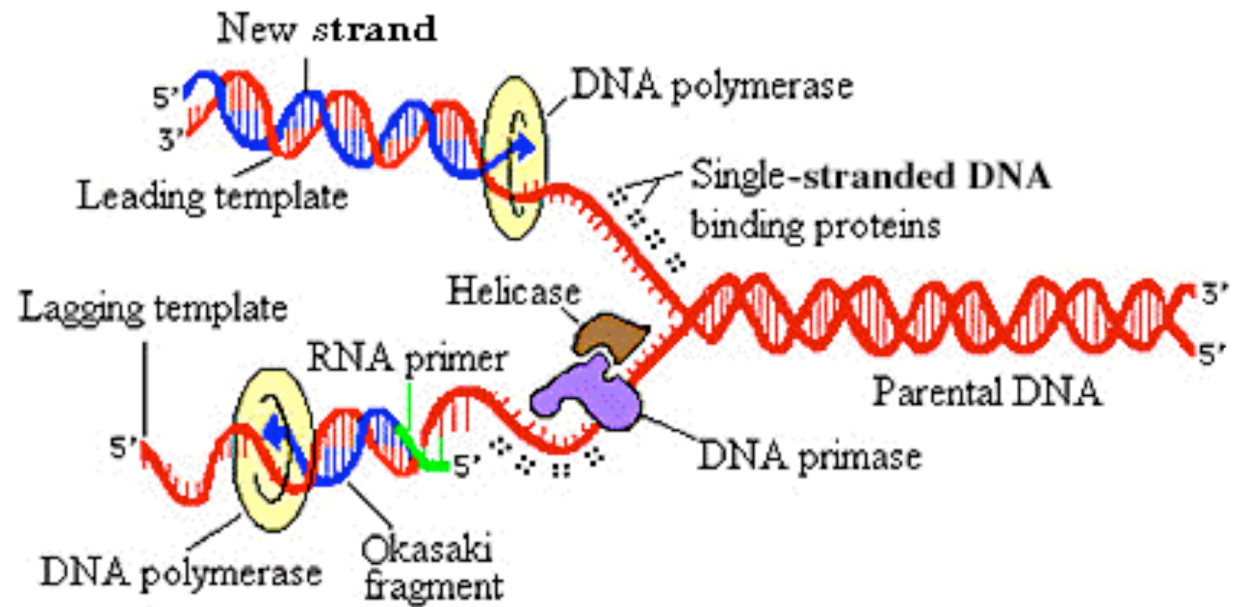
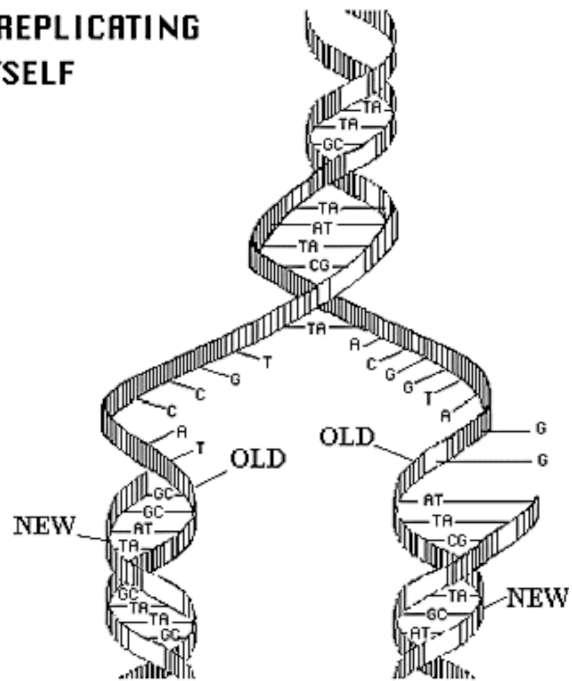
### Transcription



### Translation



## DNA REPLICATING ITSELF



**DNA helicases: Unwinding**

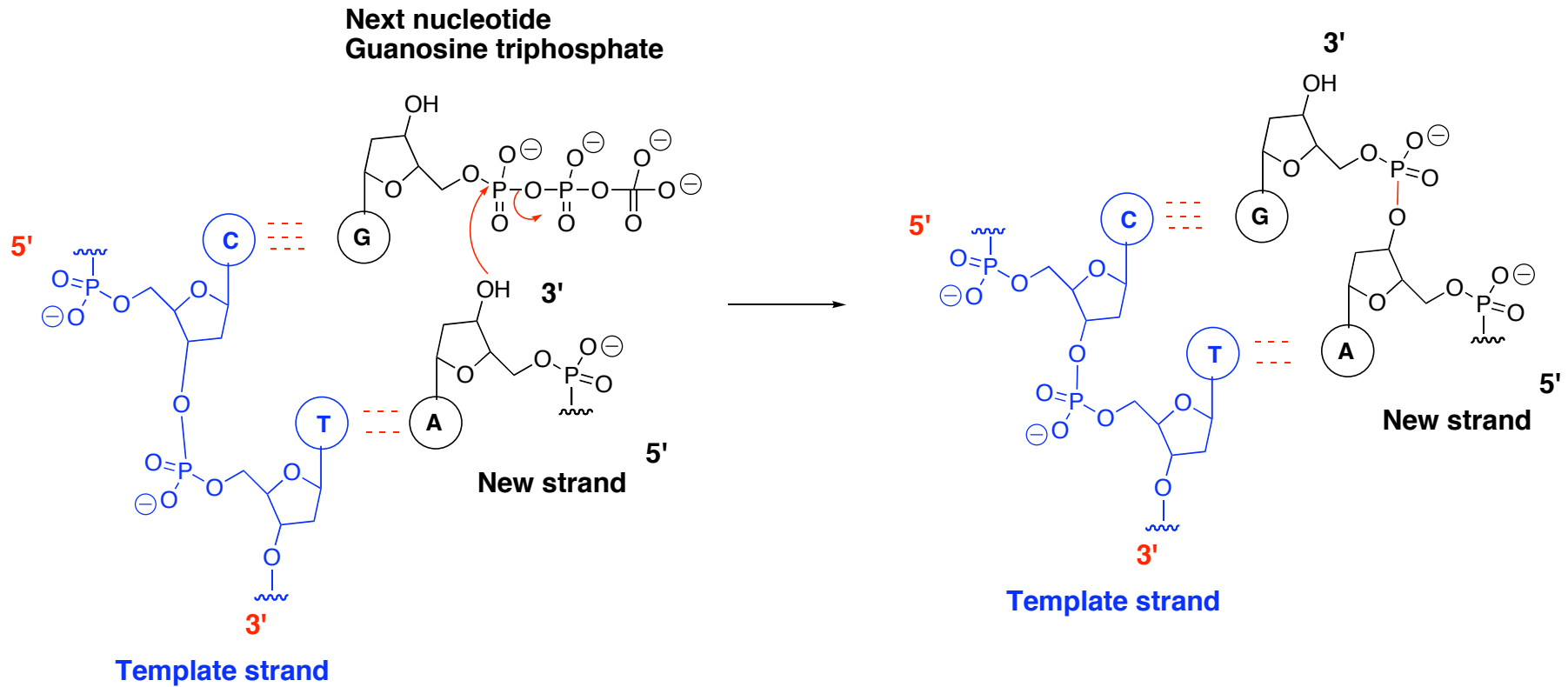
**DNA binding proteins: Prevents winding back**

**DNA primase: formation of DNA/RNA primer (from free nucleosides in cell)**

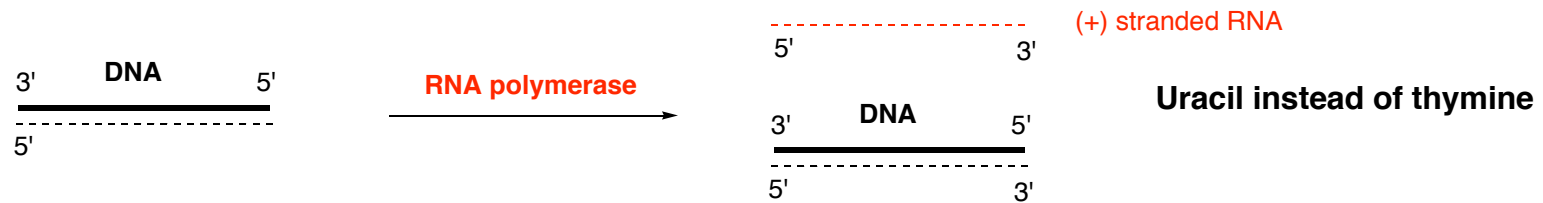
**DNA polymerase: Catalyse elongation of new strand (5' - 3')**

**Lagging strand:**

**DNA ligase: Connects Okasaki fragments**



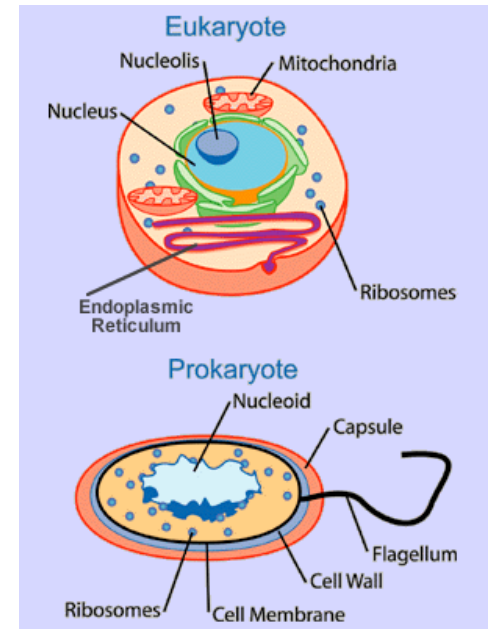
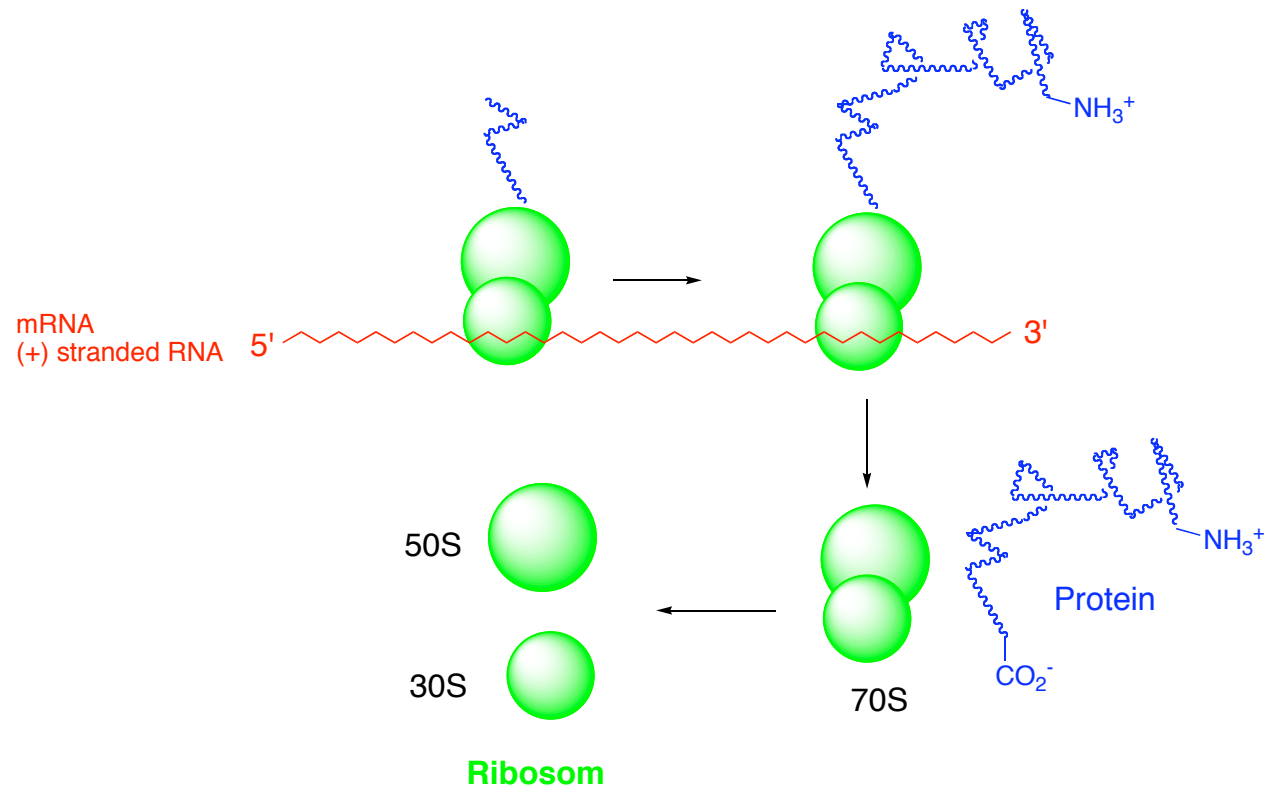
## Transcription: DNA - RNA

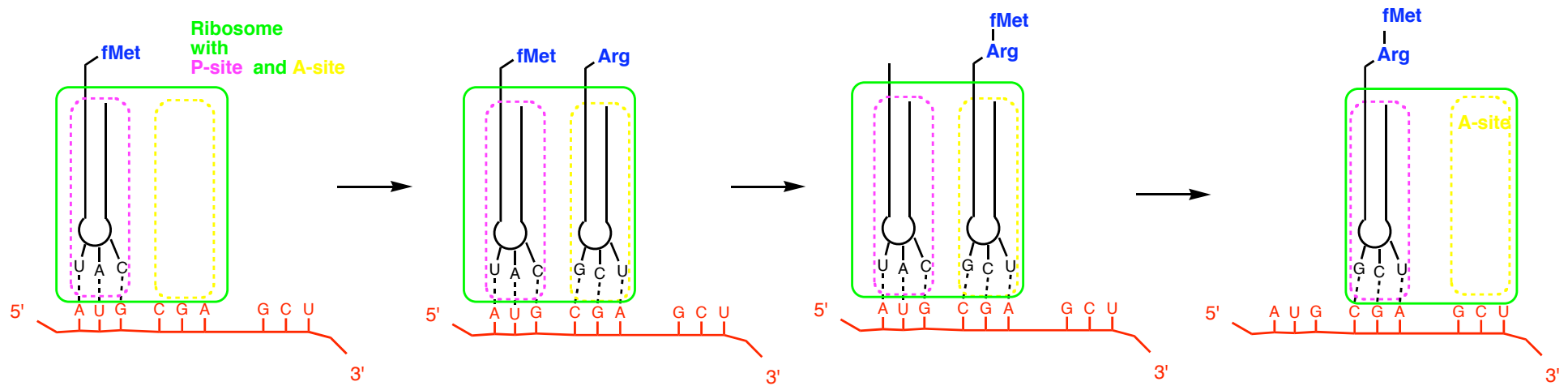
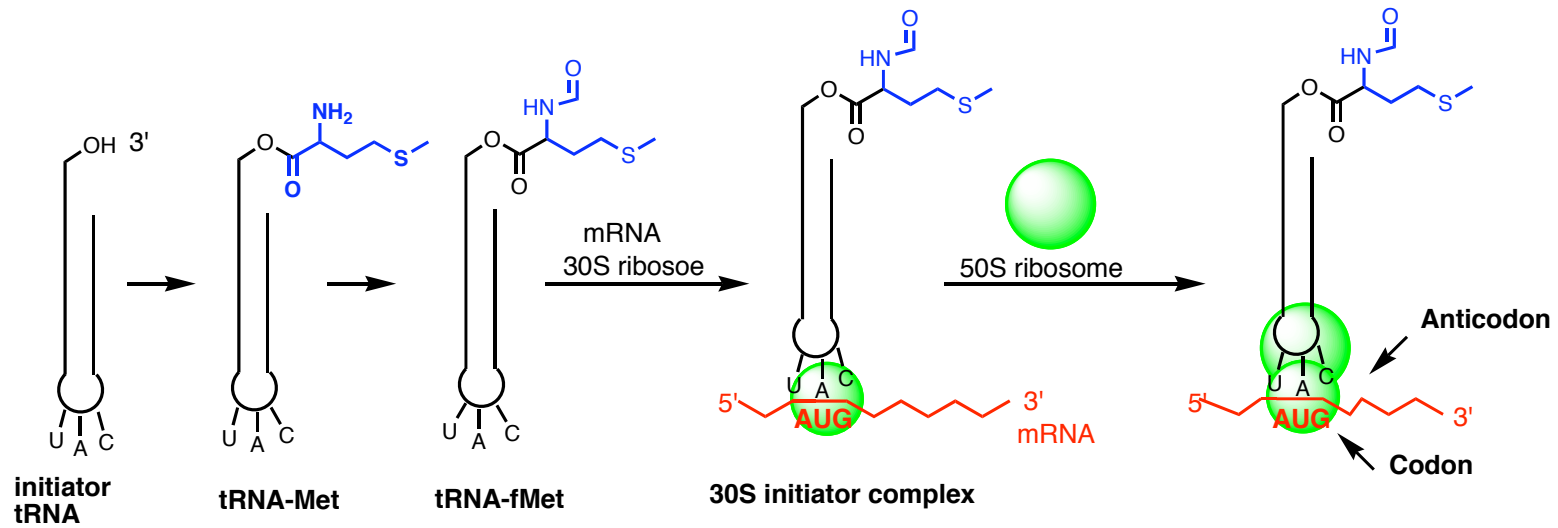


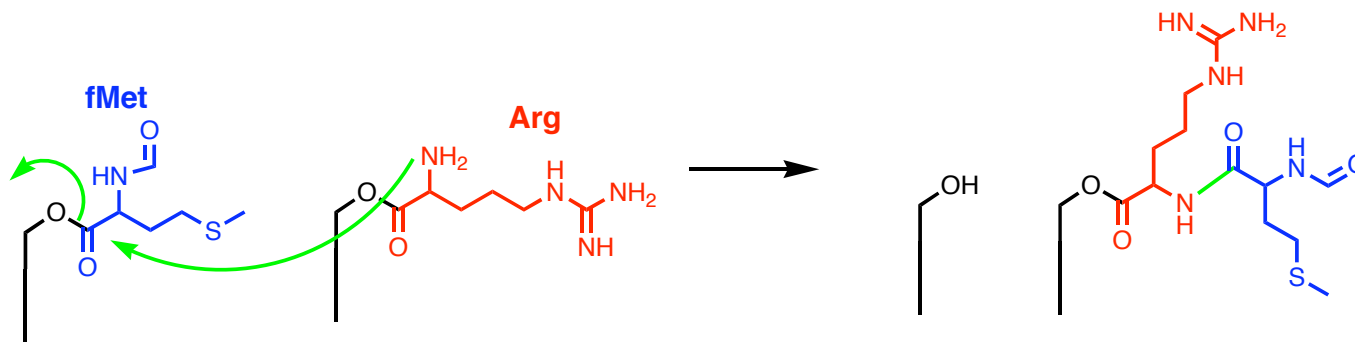
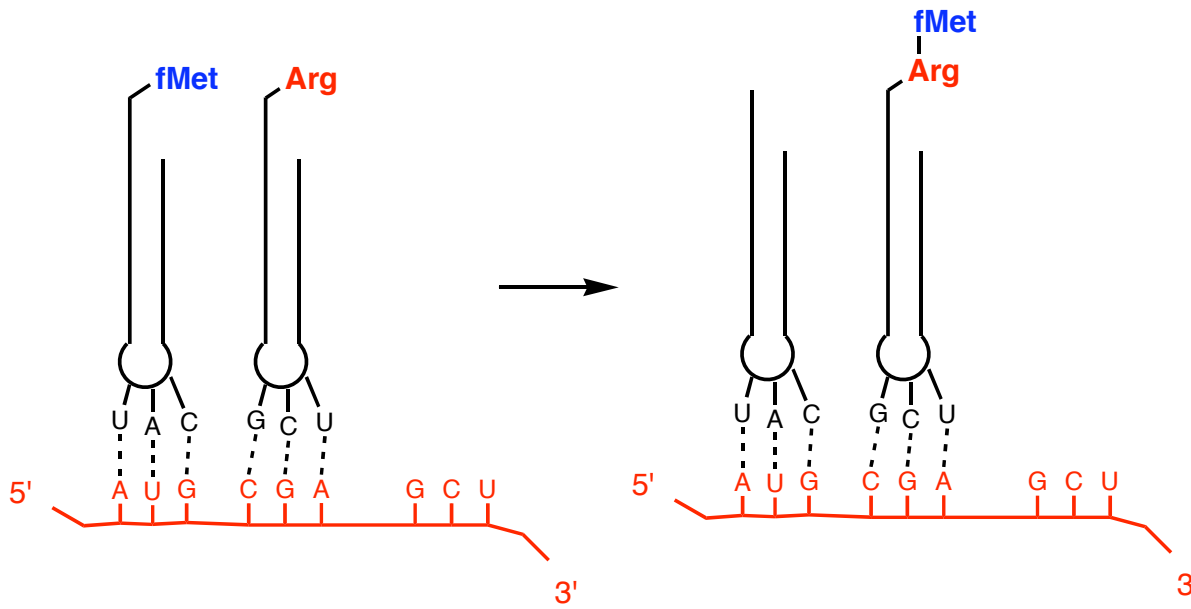
# Translation: RNA - Protein

3 RNA bases coding for one AA (see Table 28.1)

Protein synthesis occurs at ribosomes

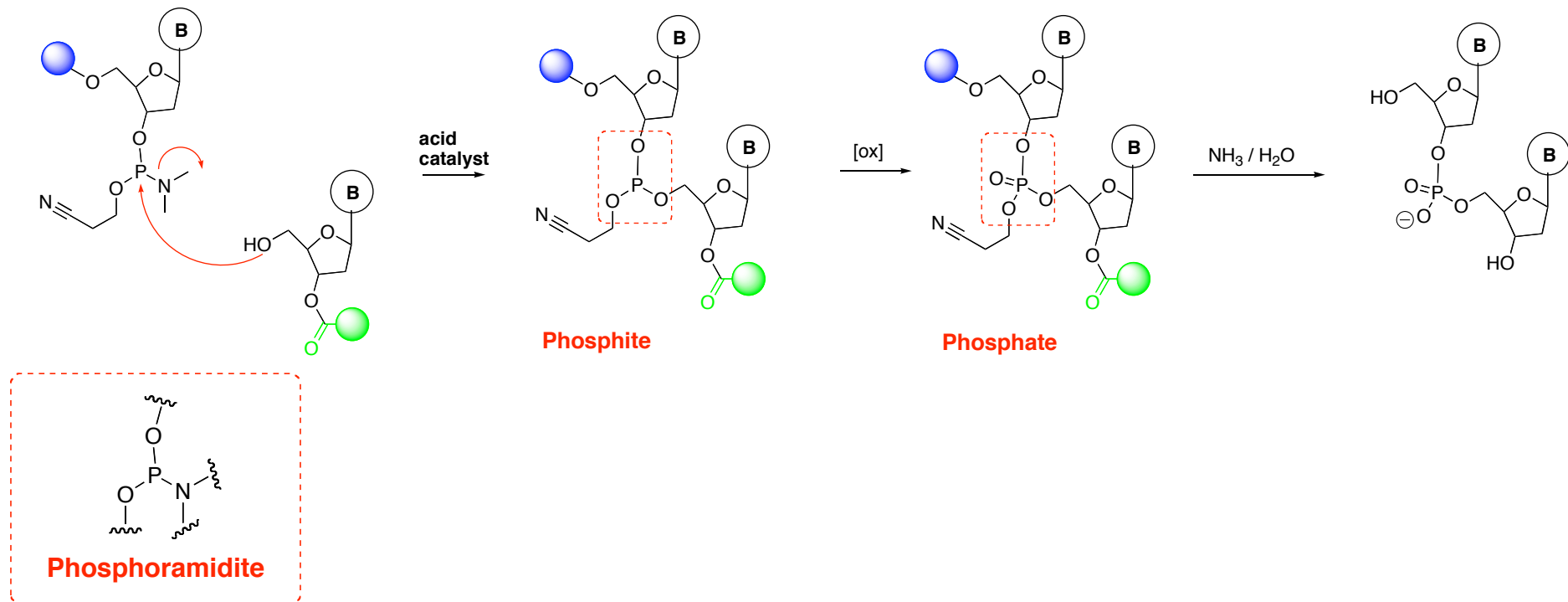






**Formyl group  
Protection of N-terminal**

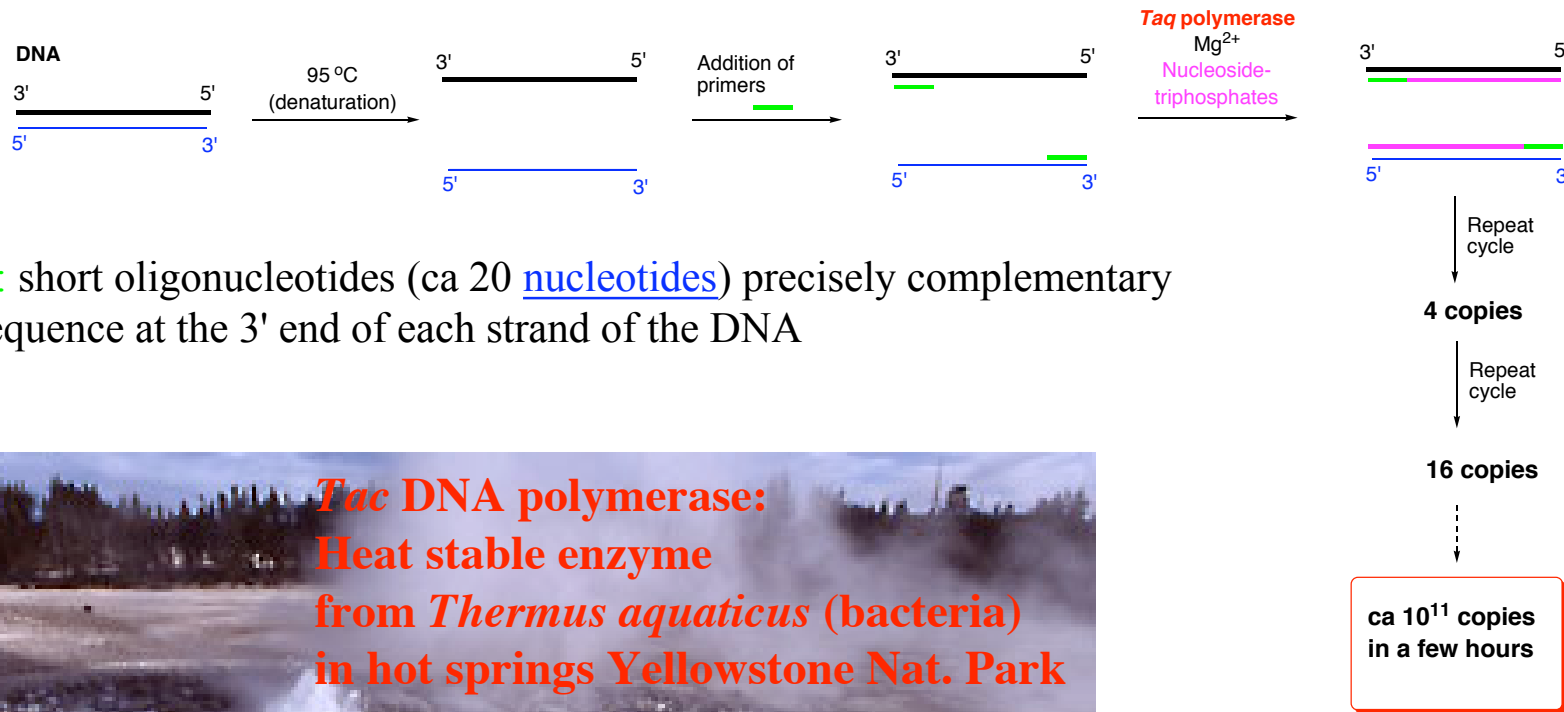
# DNA / RNA Synthesis: Protecting groups and activating groups (cf. peptide synth)





# The Polymerase Chain Reaction (PCR, 1986)

technique for quickly "cloning" (make many copies of) a particular piece of DNA in the test tube (rather than in living cells like *E. coli*).



**primers:** short oligonucleotides (ca 20 nucleotides) precisely complementary to the sequence at the 3' end of each strand of the DNA

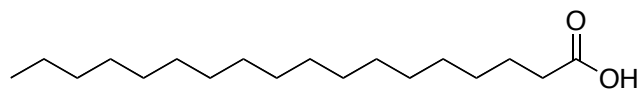


## Lipids (McM chapt 27)

Naturally occurring, lipophilic comp.

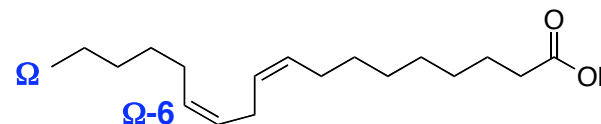
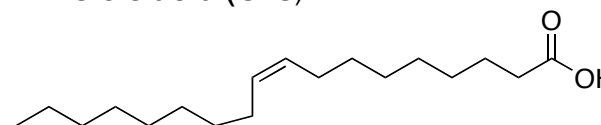
- Wax, fat oils
- Soaps
- Phospholipids
- Prostaglandins
- Terpenoids
- Steroids

Wax, fat, oils: Derivatives of fatty acids (carboxylic acids)



Ex saturated fatty acid: Stearic acid (C18)

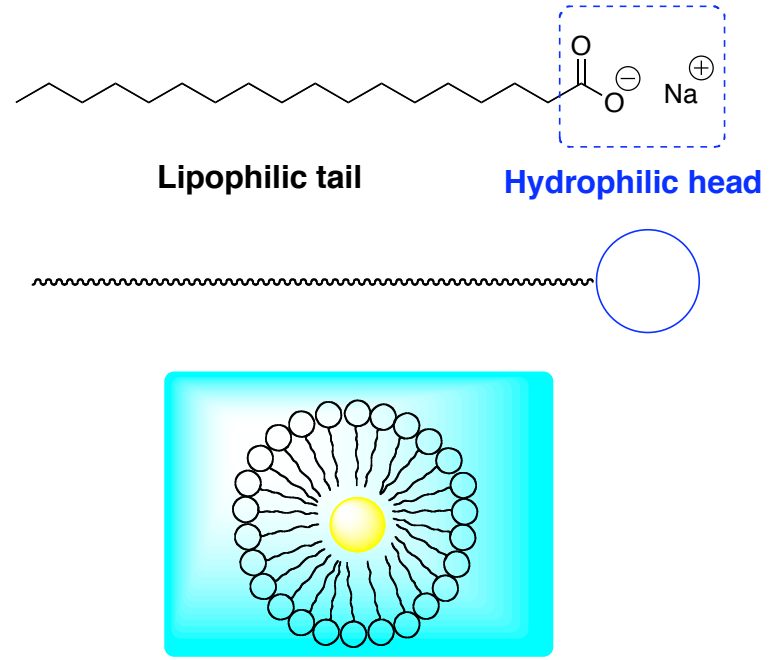
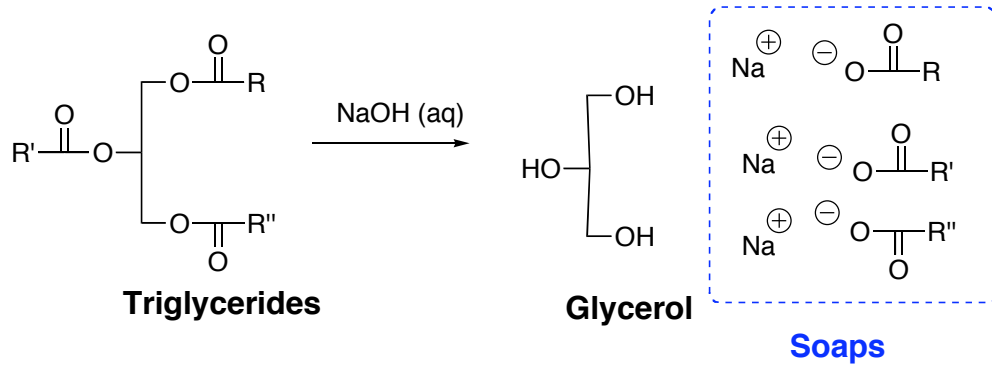
Ex unsaturated fatty acid:  
oleic acid (C18)



linoleic acid (C18)

Wax: esters between fatty acid and long chain alcohol

# Fat (solid), oil (liquid) - Soaps



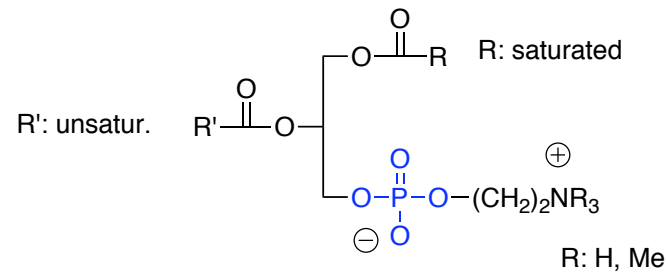
## Basic ester hydrol. - Saponifications

Ca<sup>2+</sup> - "Hard water" Ca(OCOR)<sub>2</sub> (s)

Cationic soaps

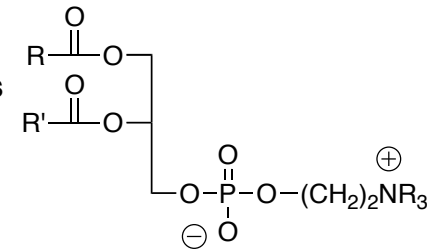
# Phospholipids

## Glycerophospholipids



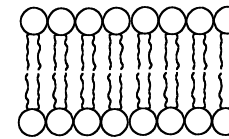
Diester Phosphoric acid

2 Lipophilic tails



Hydrophilic head

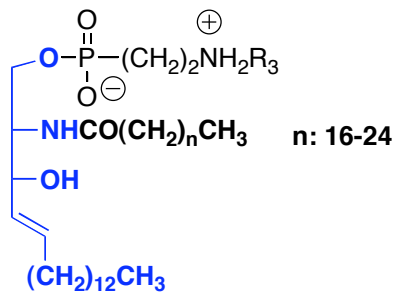
Extracellular fluid



Cell membrane  
Passive diffusion: Small, lipophilic

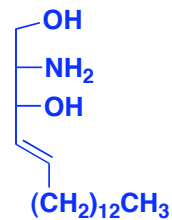
Intracellular fluid

## Sphingomyelins



coating of nerve fibers

## Sphingosine

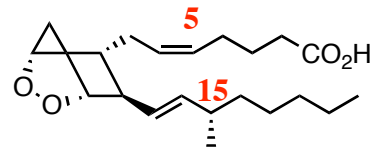


# Prostaglandins etc

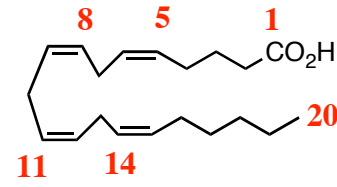
Inhib. by many pain killers



Cyclooxygenase (COX)



Prostaglandin H<sub>2</sub> (PGH<sub>2</sub>)



Arachidonic acid

Prostacyclines

Tromboxanes

Prostaglandines



Many different biolog. effects  
Inflamations, allergy response

## Subtypes COX

**COX-1:** Synth of essential prostagland.

**COX-2:** Active only under inflammations

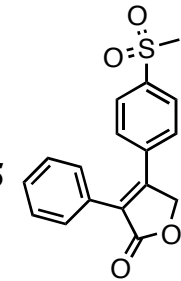
## COX2 inhibitors

Coxibes

*Rofecoxib*  
Vioxx®

COX2/COX2: 35

Avreg 2004

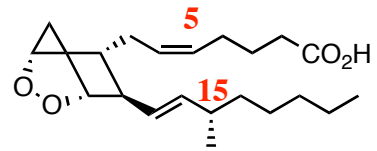


# Prostaglandins etc

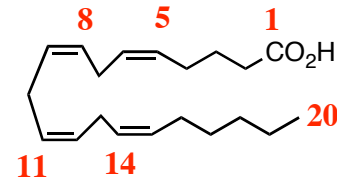
Inhib. by many pain killers



Cyclooxygenase (COX)



Prostaglandin H<sub>2</sub> (PGH<sub>2</sub>)



Arachidonic acid

Prostacyclines

Tromboxanes

Prostaglandines



Many different biolog. effects  
Inflamations, allergy response

## Subtypes COX

**COX-1:** Synth of essential prostagland.

**COX-2:** Active only under inflammations

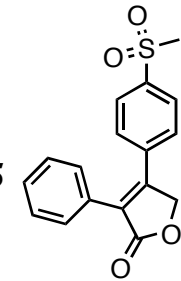
## COX2 inhibitors

Coxibes

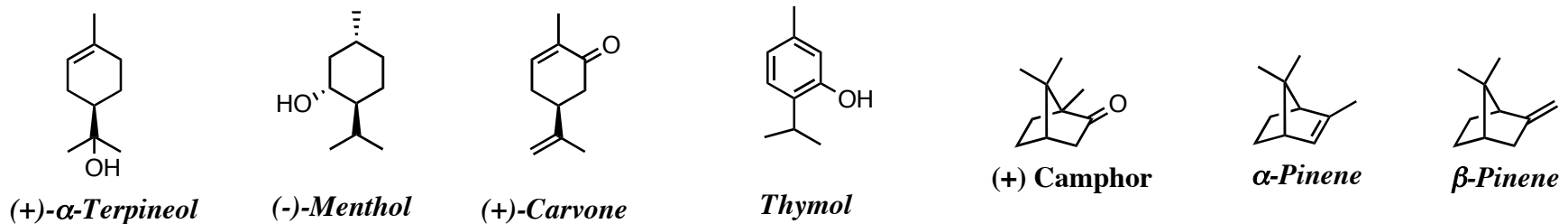
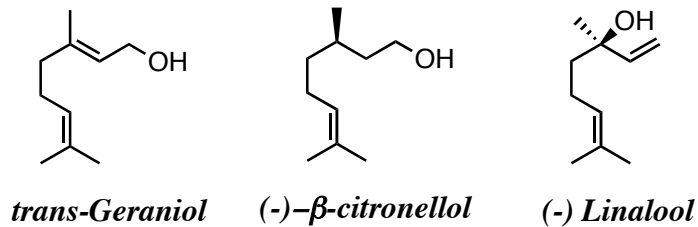
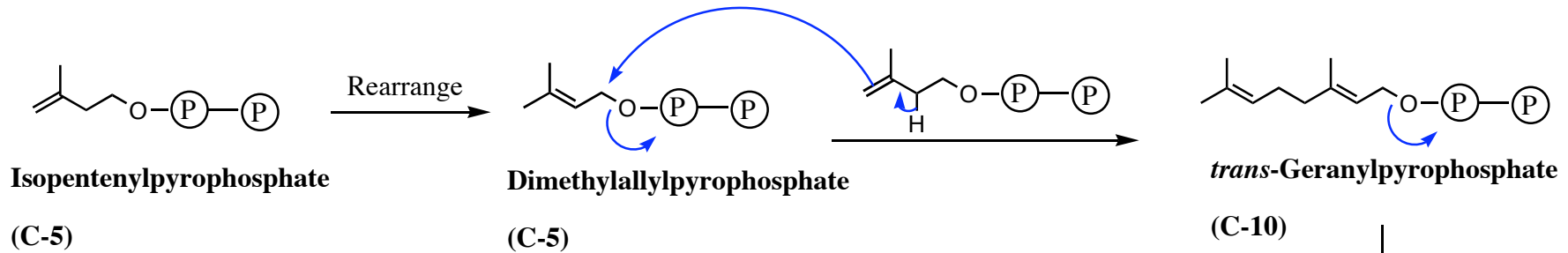
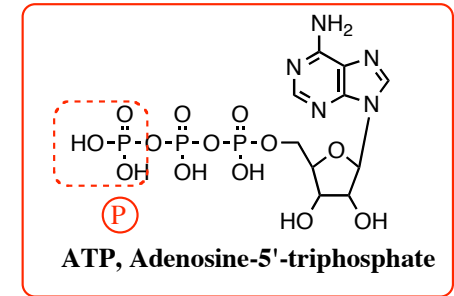
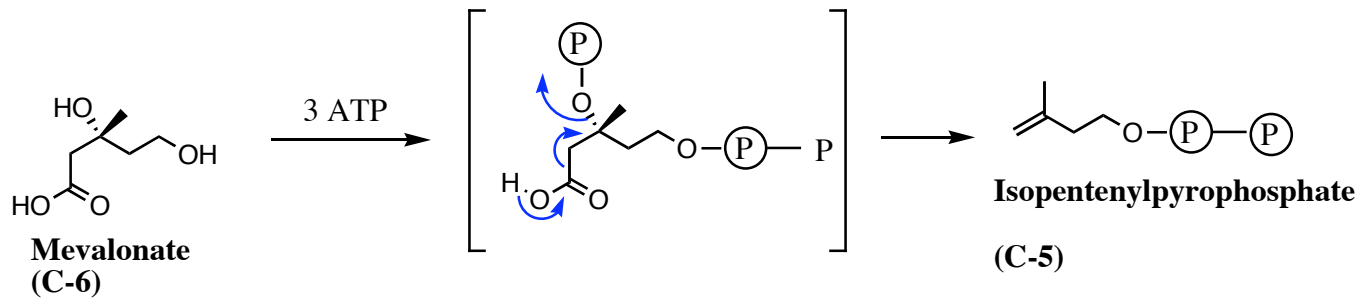
*Rofecoxib*  
Vioxx®

COX2/COX2: 35

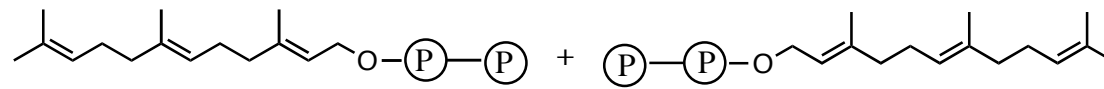
Avreg 2004



# Terpenoids

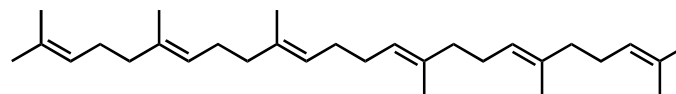


↓ ↓  
**C-10: Monoterpenes**  
**C-15: Sesquiterpenes**  
**C-20: Diterpenes**  
**C-25: Sesterterpenes**  
**C-30: Triterpenes**

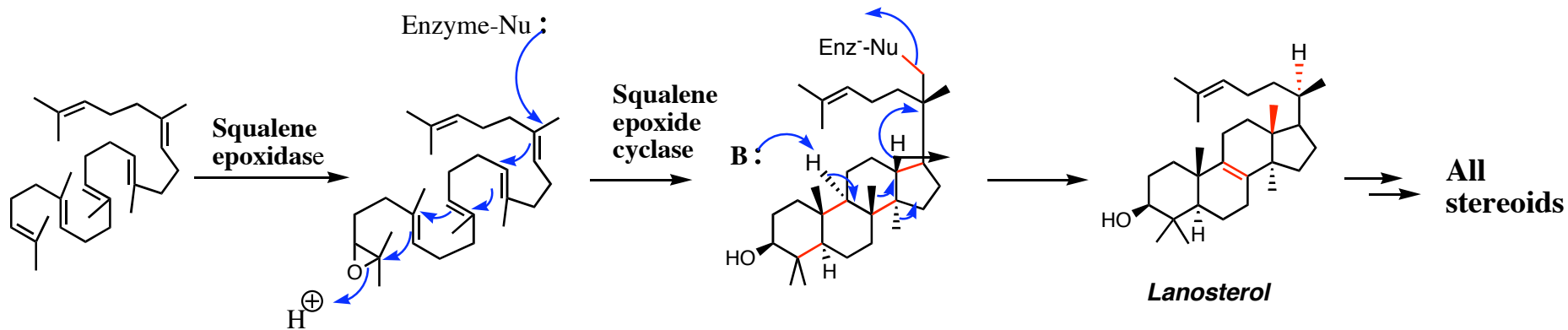


*trans, trans*-Farnesylpyrophosphate  
(C-15)

tail to tail coupling

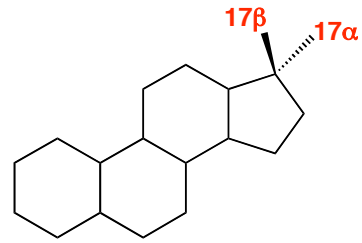
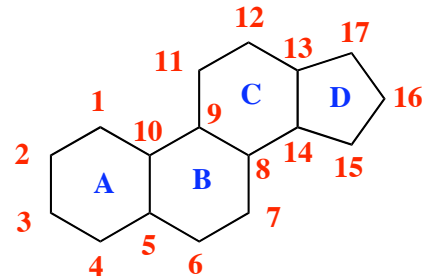


Squalene (C-30)

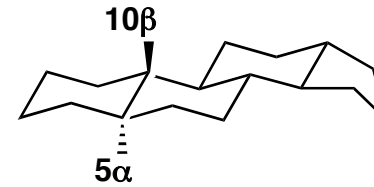
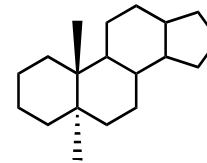




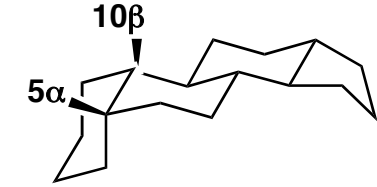
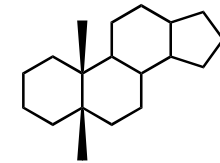
# Steroids



**A / B *trans* fused**

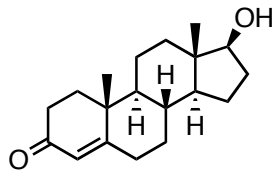


**A / B *cis* fused**



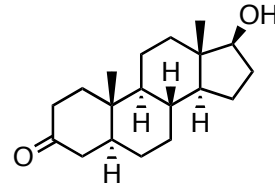
**B / C og C / D always *trans***

## Sex Hormones

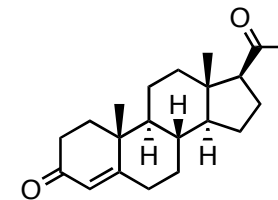


*Testosterone*

**5α-reduktase**



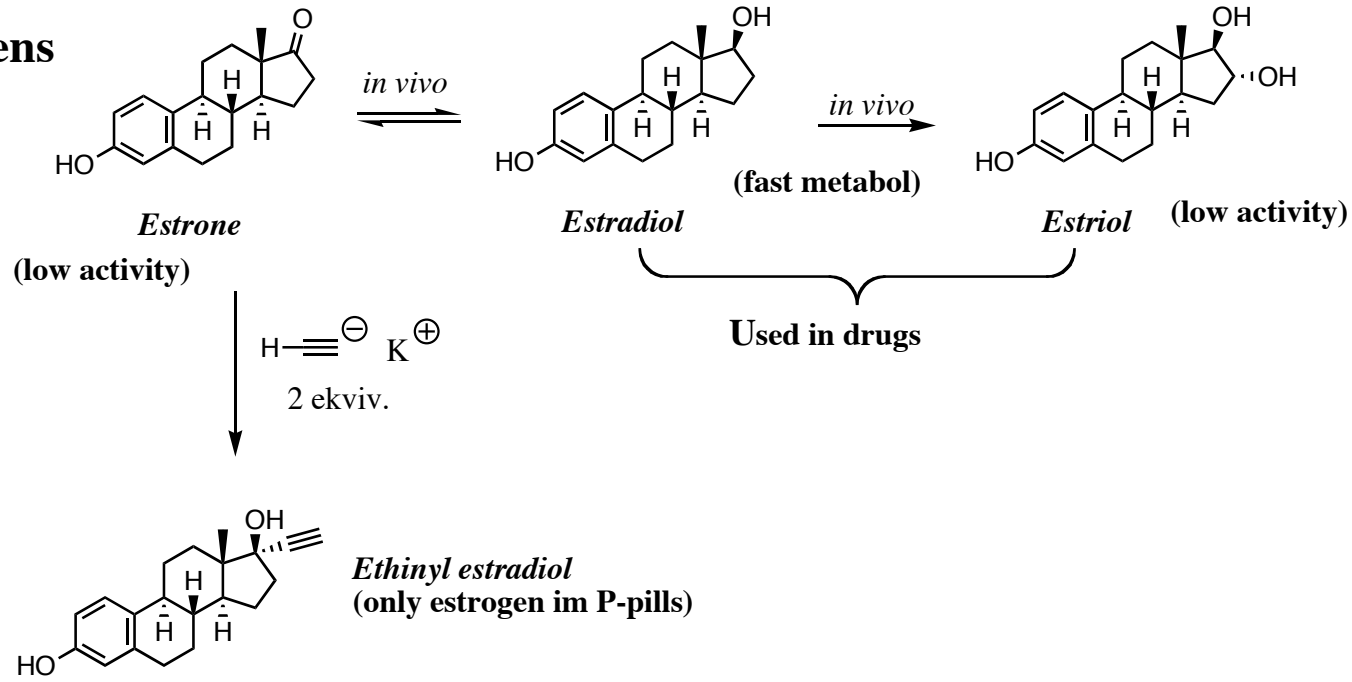
**5α-Dihydrotestosterone (5DHT)**  
**More active A-B ring *trans***  
***Cis* isomer inactive**



*Progesterone*

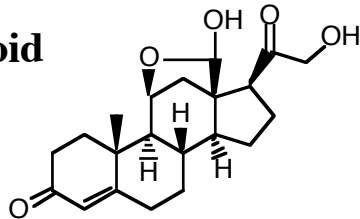
**Many semisynth drugs in use (better bioavalabil.)**

## Estrogens



## Corticosteroids

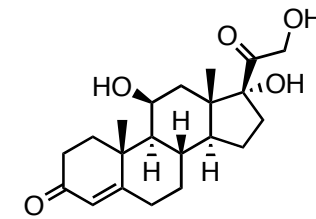
### Mineralcorticoid



*Aldosterone*

Regulation of elektrolyttic ballance  
increase re-uptake of Na (and hence H<sub>2</sub>O)

### Glucocorticoid



*Hydrokortison*

Effect on metabolism (karbohydrates, lipids, proteins)  
Antiinflammatoric

Numerous semisynth. analogs as drugs  
Various antiinflam. activity, mineralcorticoid side effects