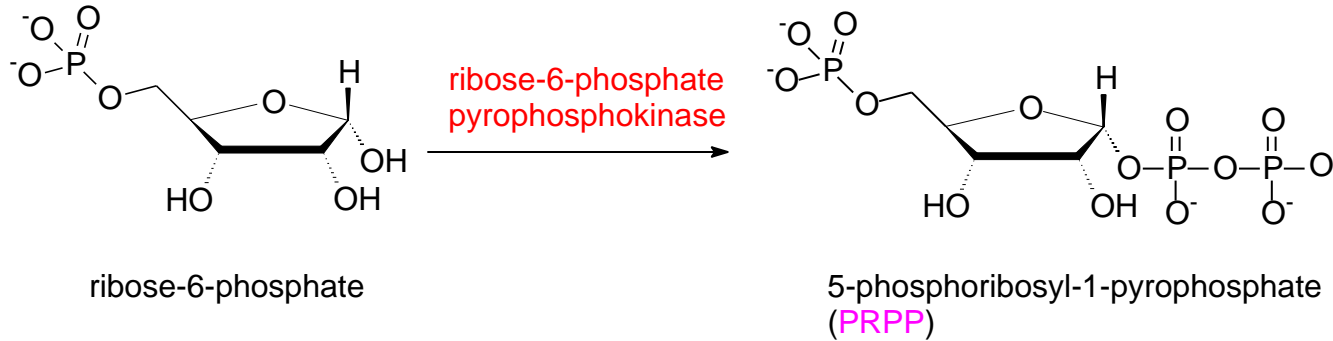


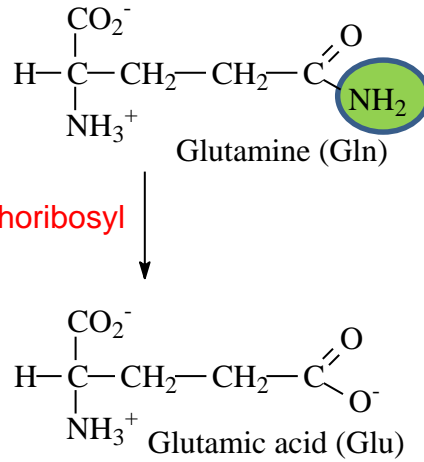
# Αντιμεταβολίτες

# Ανταγωνιστές πουρινών

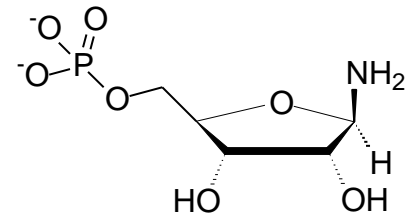
# Ανταγωνιστές πυριμιδινών



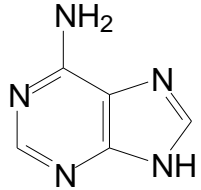
amidophosphoribosyl transferase



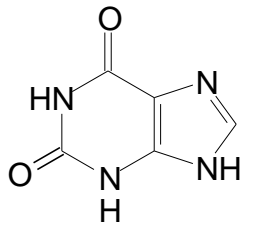
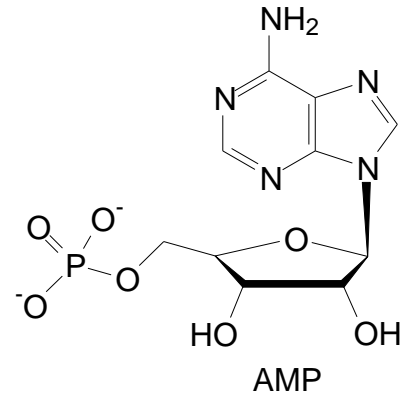
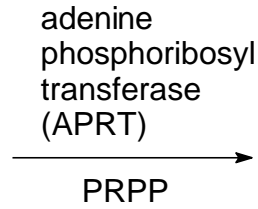
PRPP amidotransferase



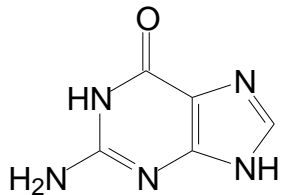
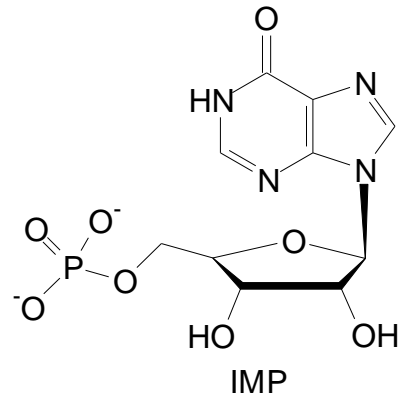
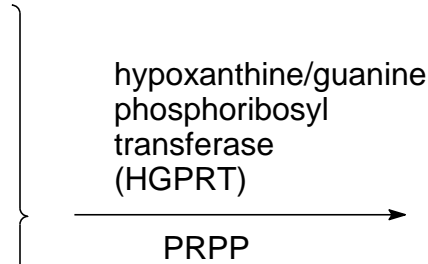
# Salvage pathways



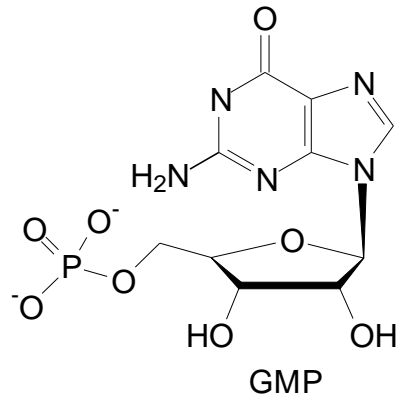
A (adenine)



H (hypoxanthine)

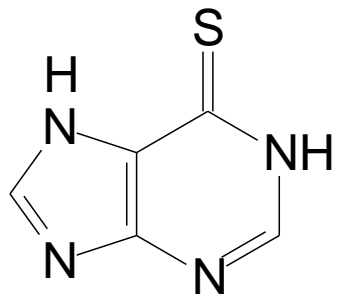


G (guanine)

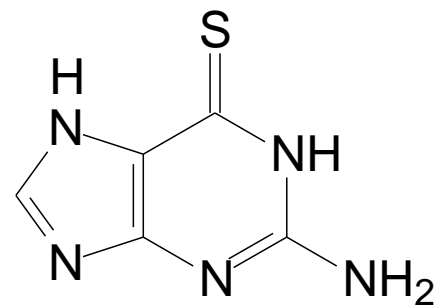


## Ανταγωνιστές πουρινών

### thiopurines

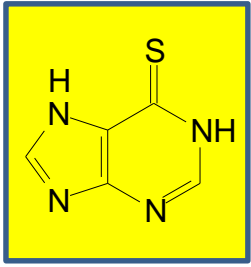
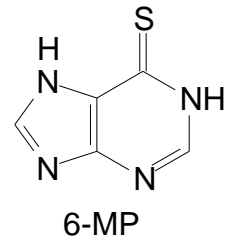


6-MP

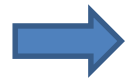
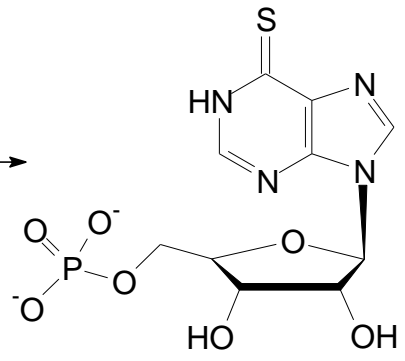


6-TG

Και τα δύο οδηγούν στο ίδιο προϊόν, δρουν συνεργιστικά έναντι L1210



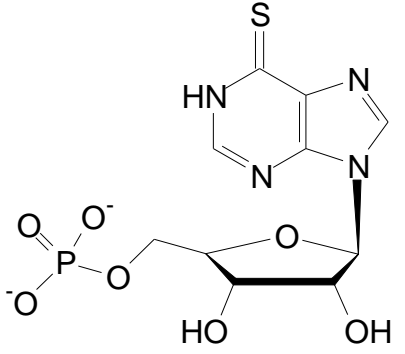
HGPRT  
PRPP



Αναστολή  
HGPRT



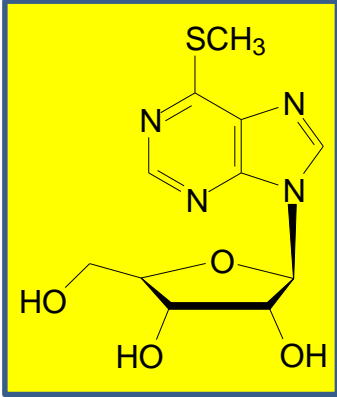
Αναστολή salvage  
pathways



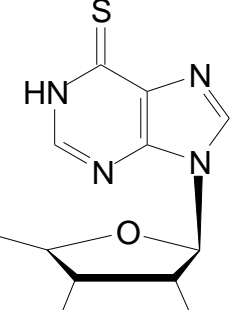
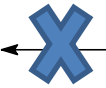
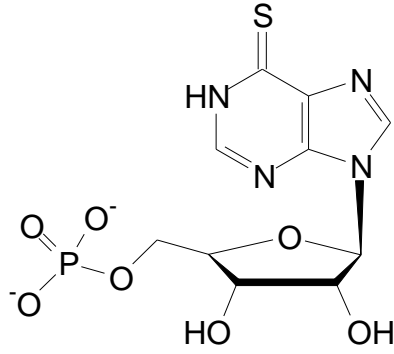
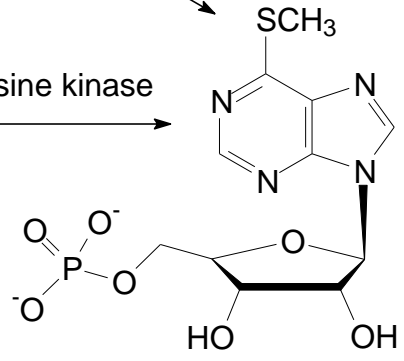
Αναστολή PRPP  
amidotransferase



Αναστολή de novo  
σύνθεσης

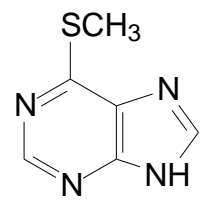


adenosine kinase

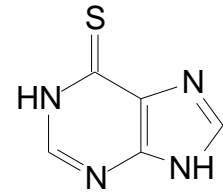


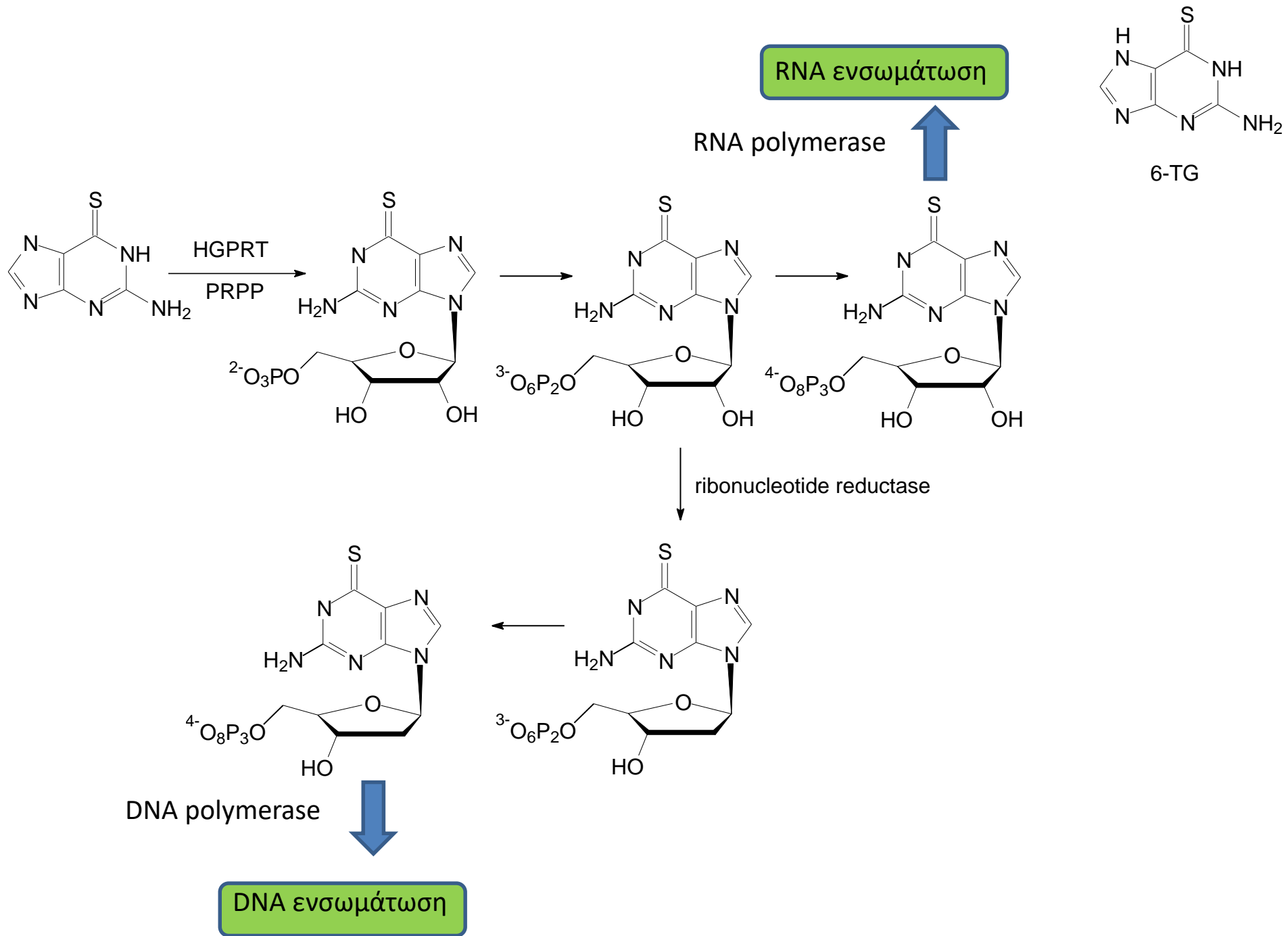
PNP

HGPRT  
PRPP



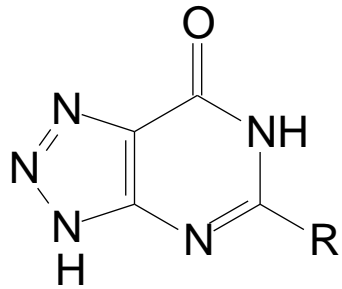
in vivo





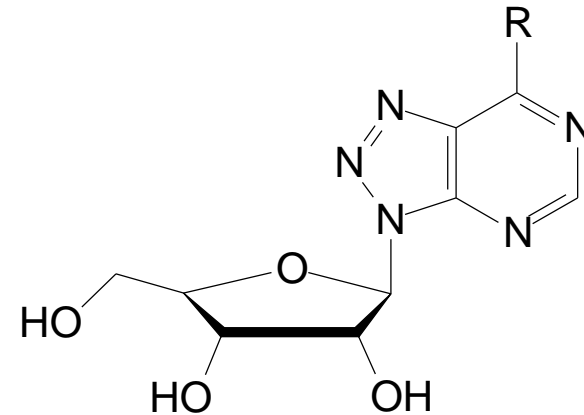
# Ανταγωνιστές πουρινών

## azapurines



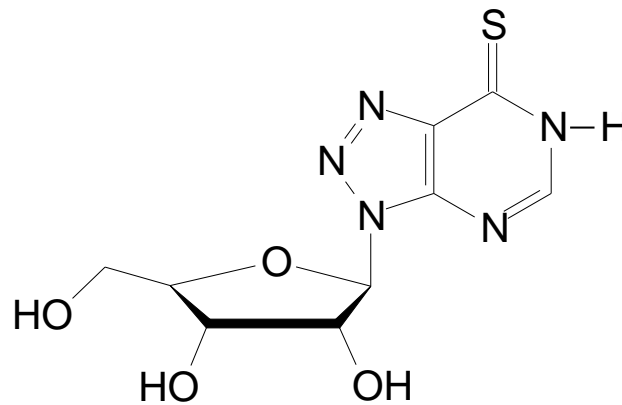
R=NH<sub>2</sub> 8-aza-G

R= H 8-azahypoxanthine



R=OH 8-azainosine

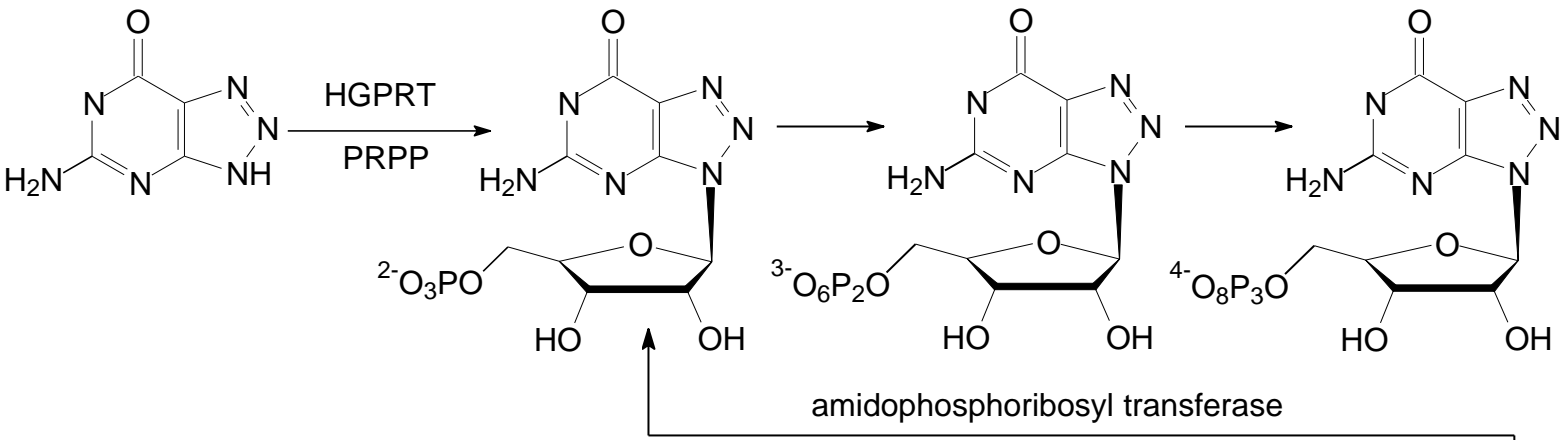
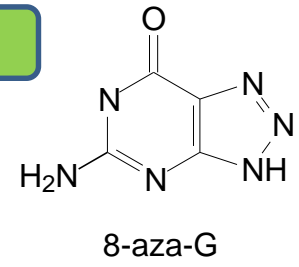
R= NH<sub>2</sub> 8-aza-A



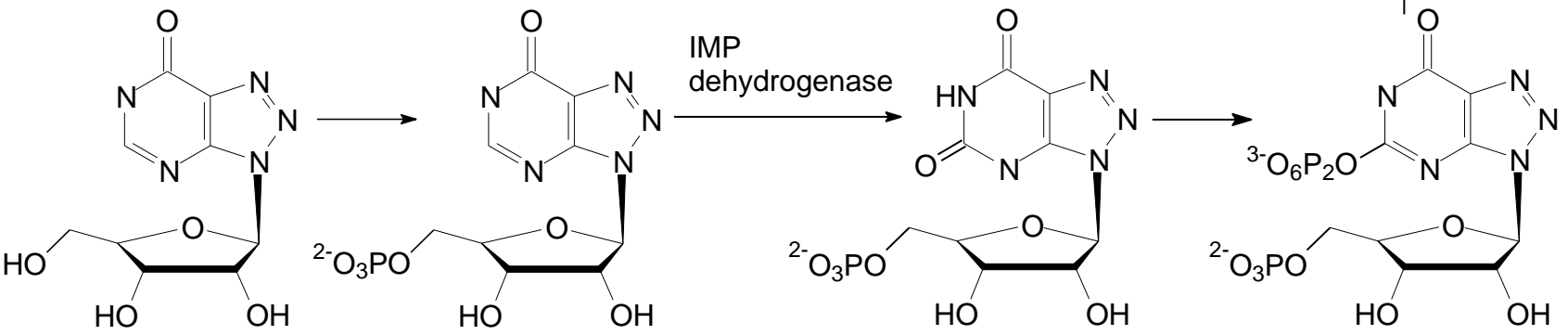
8-aza-6-thioinosine

RNA ενσωμάτωση

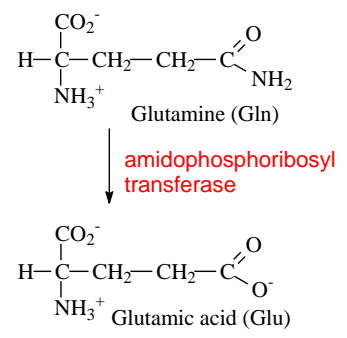
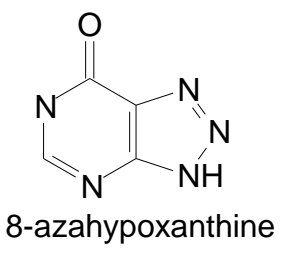
RNA polymerase

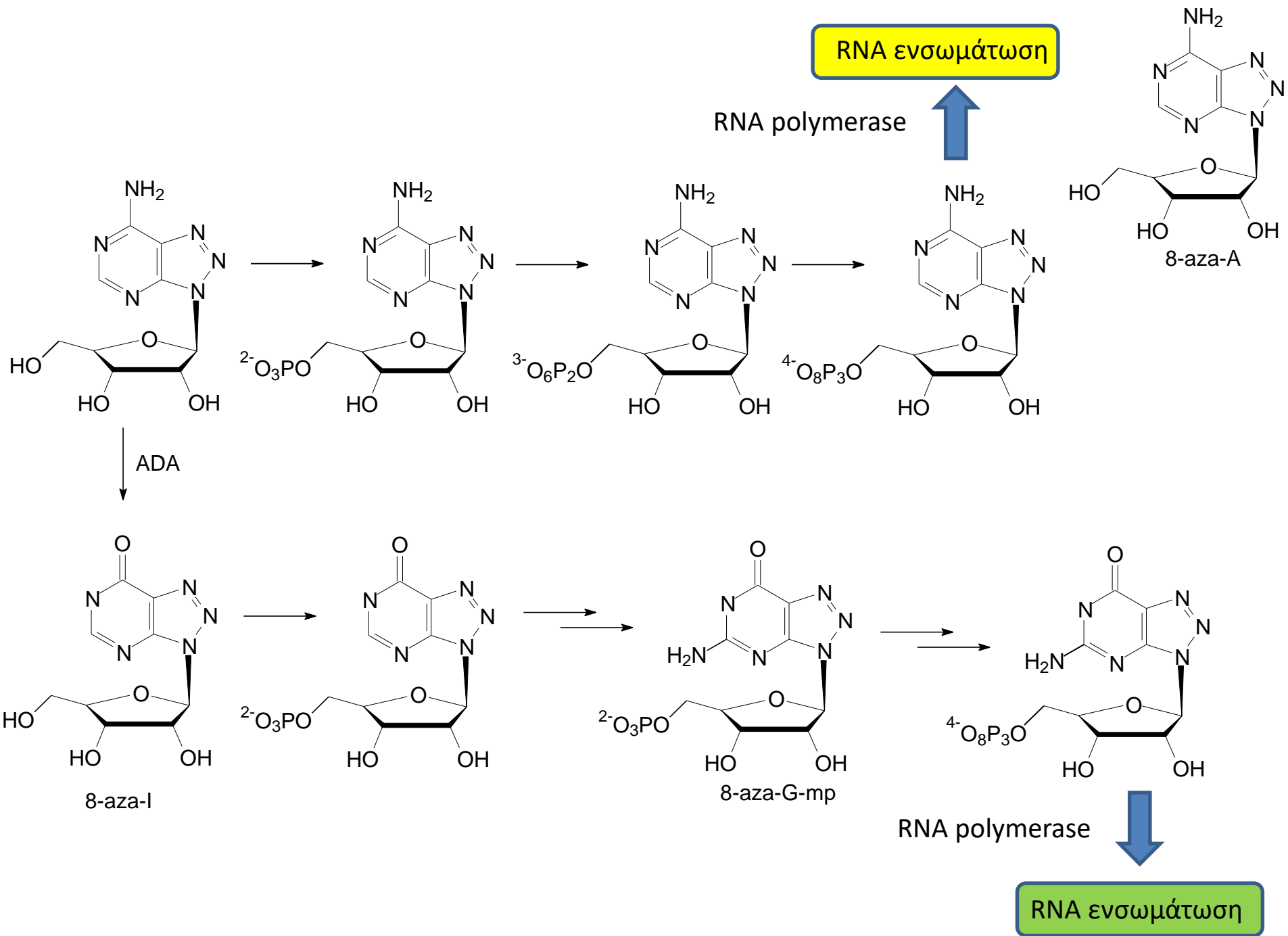


amidophosphoribosyl transferase

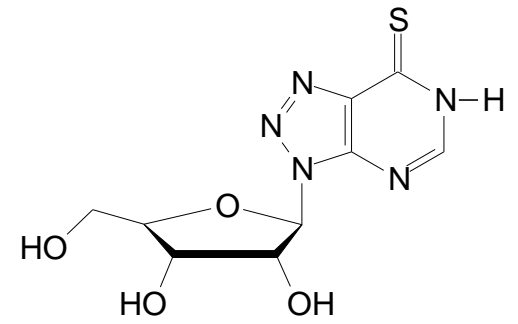


8-aza-I

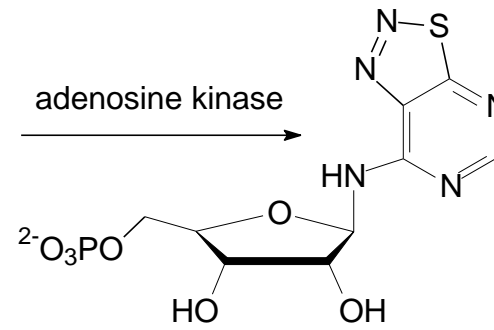
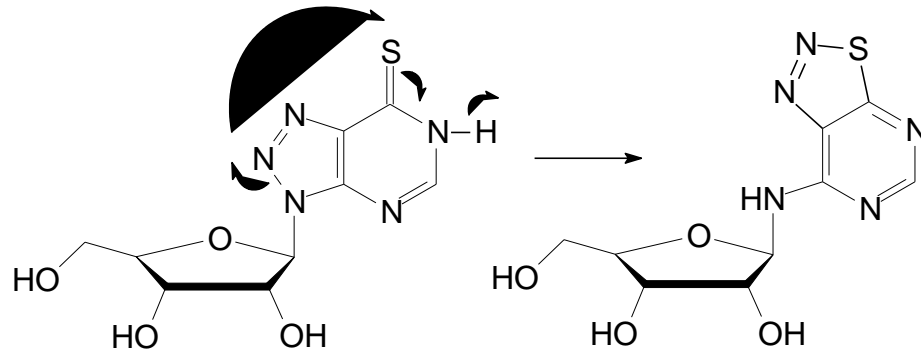




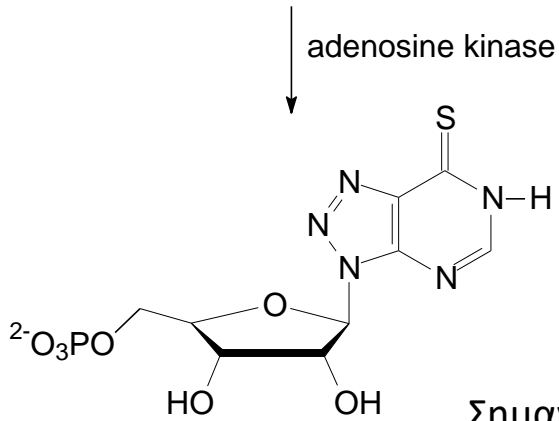




8-aza-6-thioinosine



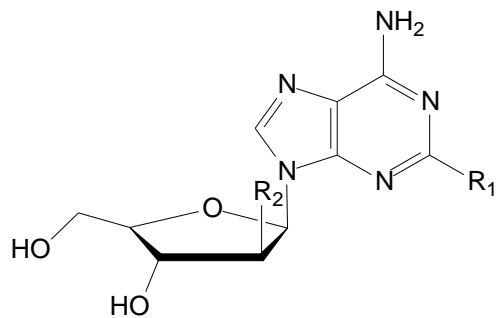
10πλάσια δραστικότητα



Σημαντική κυτταροτοξικότητα σε  
επιδερμικά καρκινικά κύτταρα

# Ανταγωνιστές πουρινών

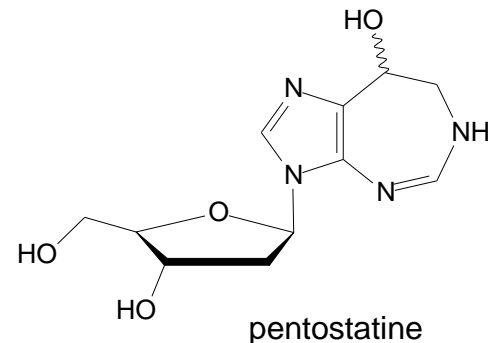
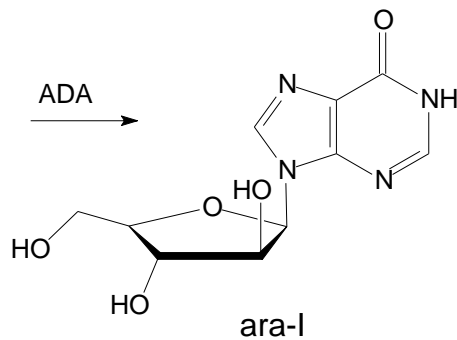
## ara-adenosine



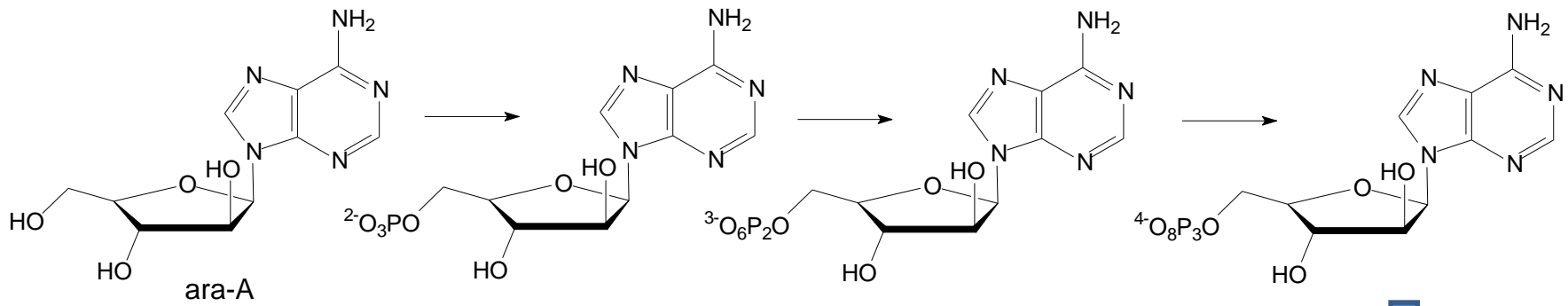
R<sub>1</sub>= H, R<sub>2</sub>= OH ara-A  
R<sub>1</sub>= F, R<sub>2</sub>=OH 2-F-ara-A  
R<sub>1</sub>= H, R<sub>2</sub>= N<sub>3</sub>

ara-A

→  
ADA



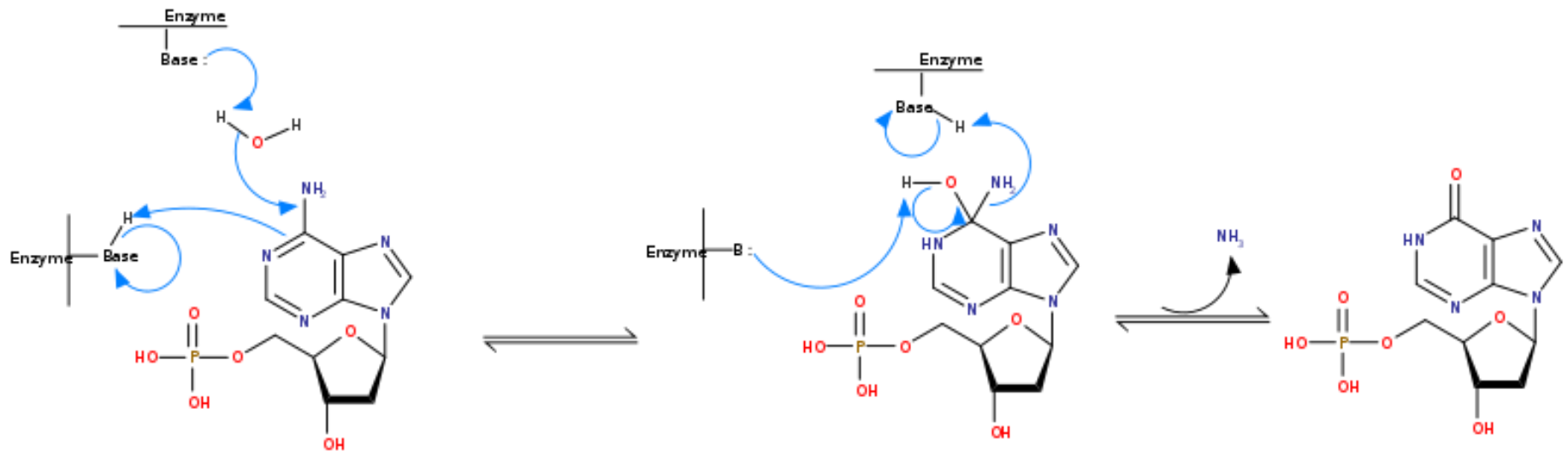
ADA inhibitor



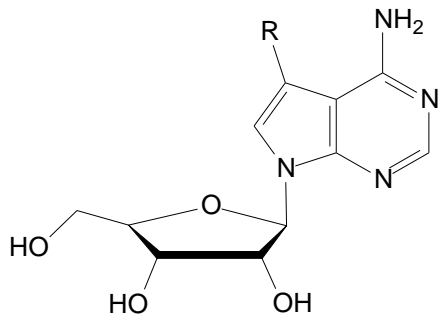
Το Ara-A αναστέλλει επιπλέον το ribonucleotide reductase, επομένως αναστέλλεται η δημιουργία 2-δεοξυνουκλεοτιδίων

αναστολέας της DNA πολυμεράσης

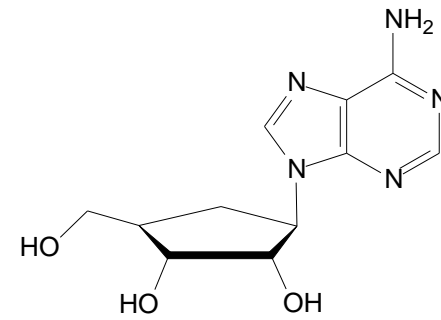
# Adenosine deaminase (ADA) mechanism



## Άλλα παράγωγα

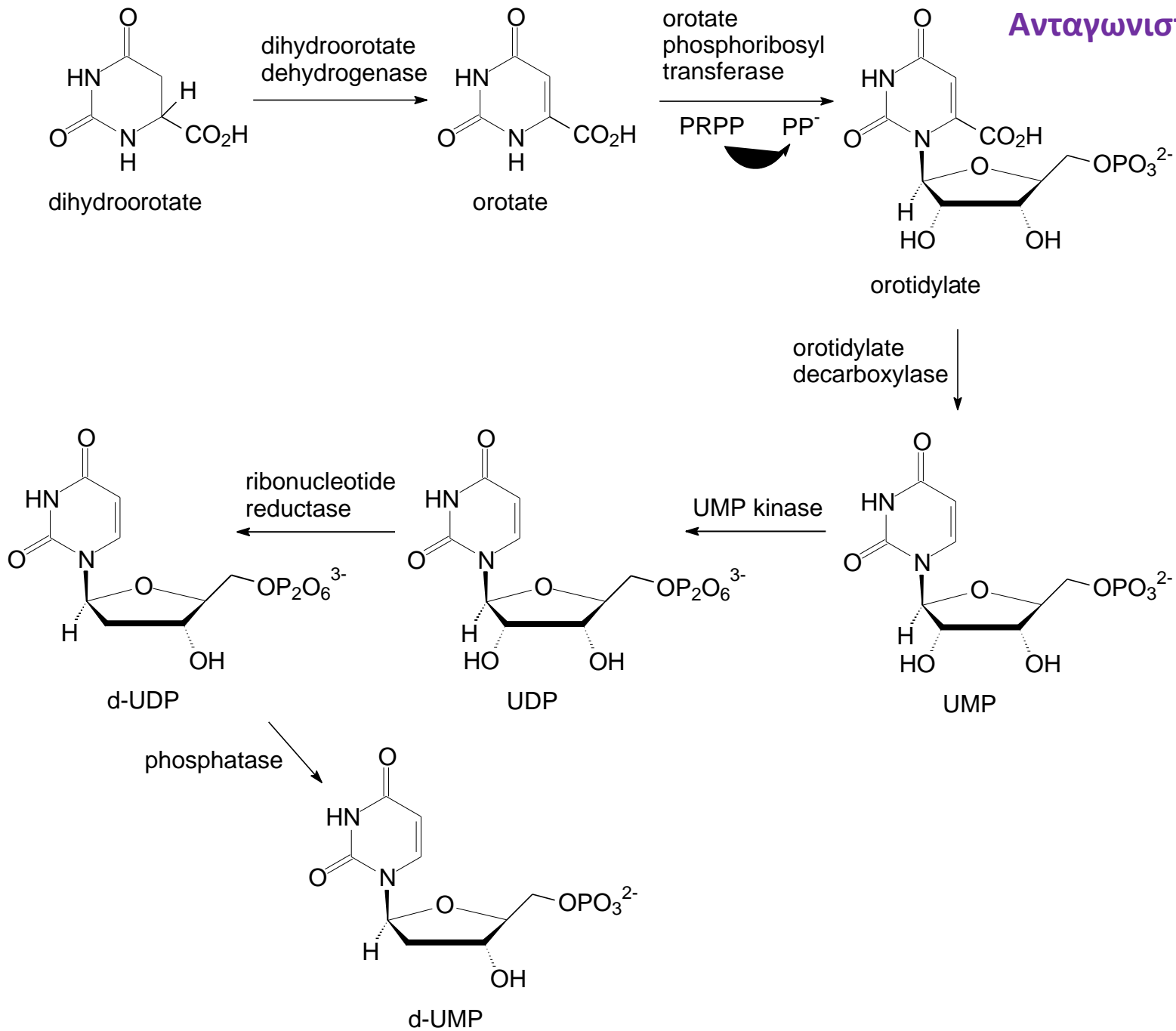


R= H      tubercidin  
R= CONH<sub>2</sub>    sangivamycin  
R= CN      toyocamycin



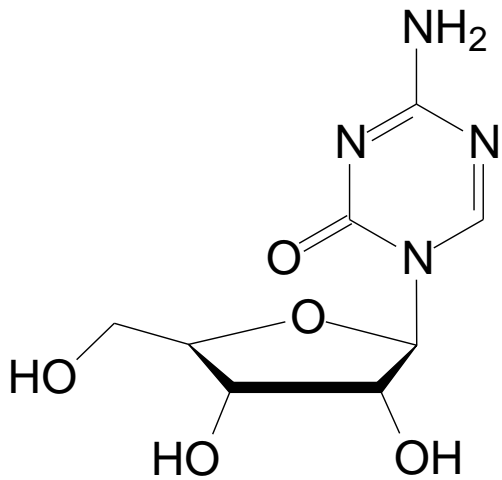
aristeromycin

# Ανταγωνιστές πυριμιδινών

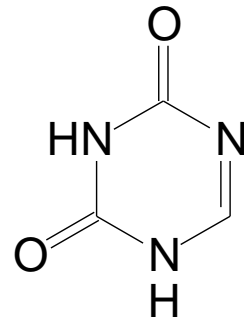


## Ανταγωνιστές πυριμιδινών

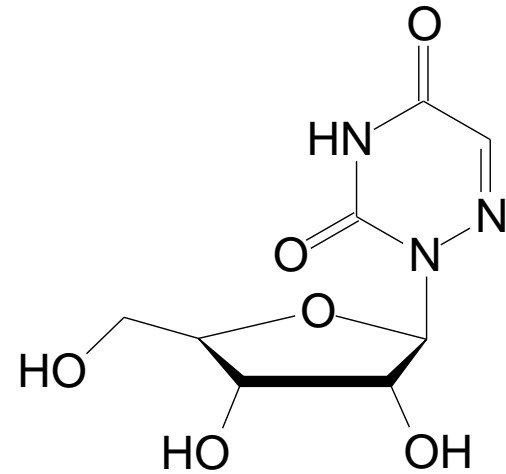
### azapyrimidines



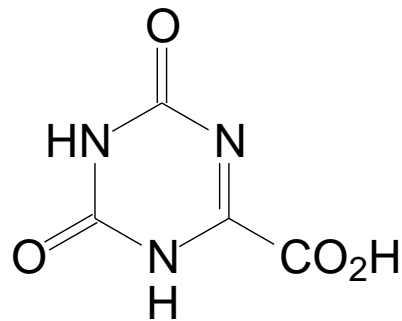
5-azaC



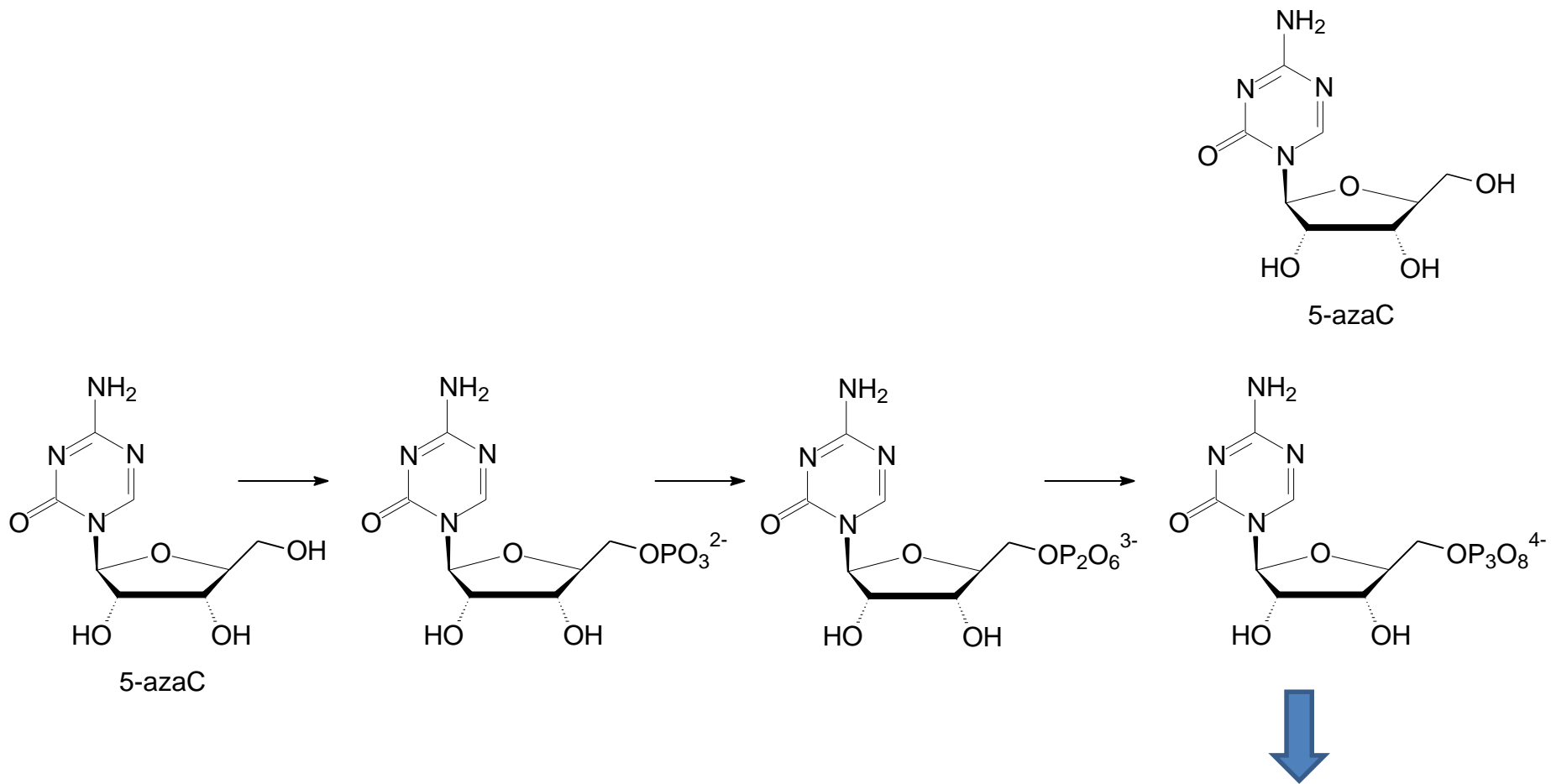
5-azaU



6-azaU



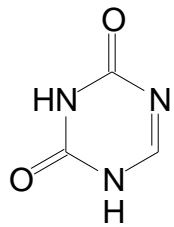
5-azaorotic acid



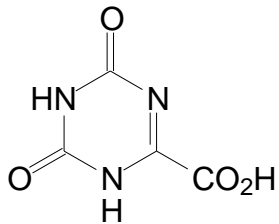
❖ Αναστέλλει τη σύνθεση m-RNA

❖ Ενσωματώνεται σε t-RNA και προκαλεί λάθος μετάφραση

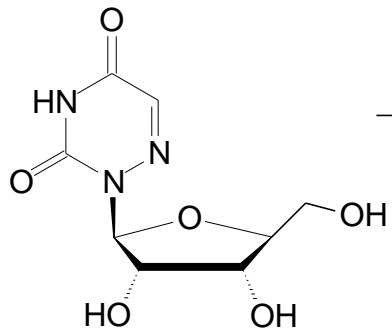
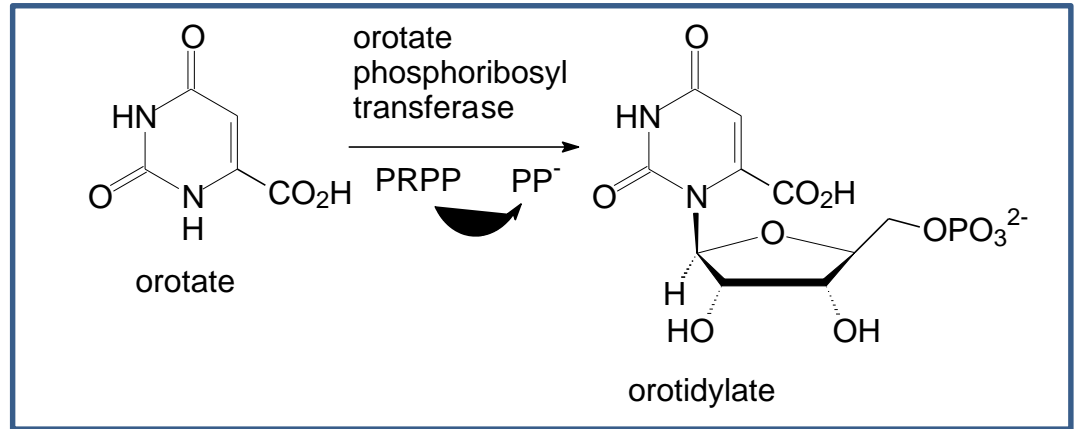
## Αναστολείς του orotate phosphoribosyl transferase



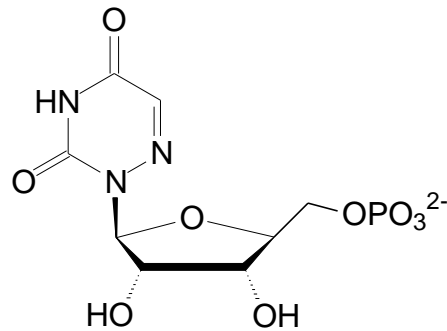
5-azaU



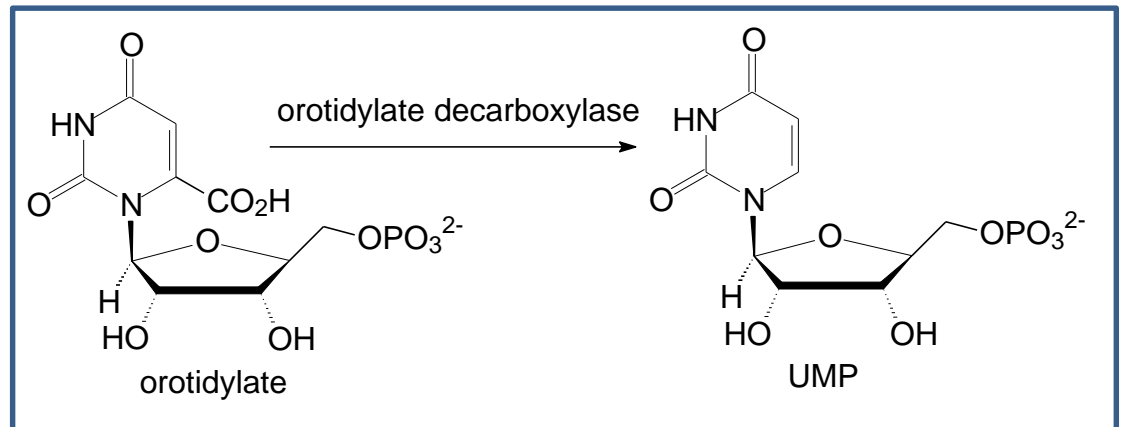
5-azaorotic acid



6-azaU

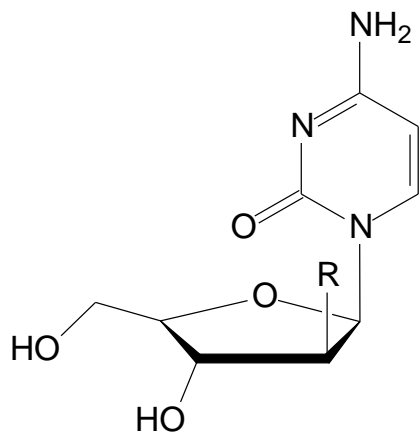


## Αναστολέας του orotidylate decarboxylase





## Ανταγωνιστές πυριμιδινών

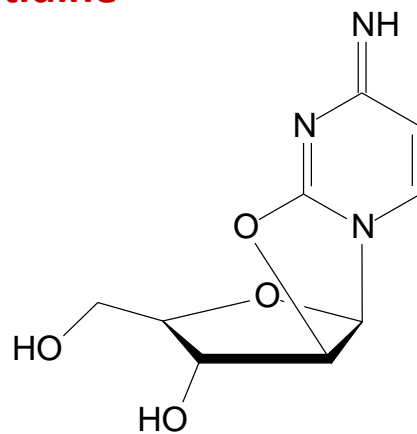


R= OH ara-C

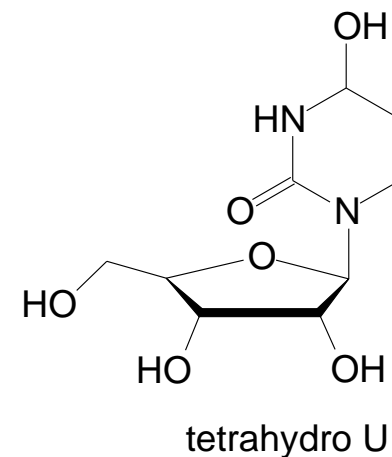
R= N<sub>3</sub>

R= NH<sub>2</sub>

## ara-cytidine



anhydro-araC

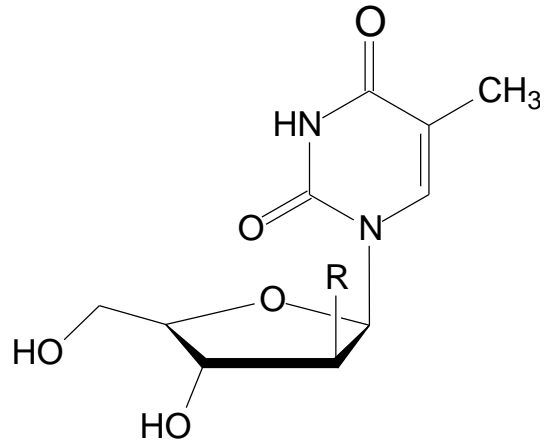


tetrahydro U

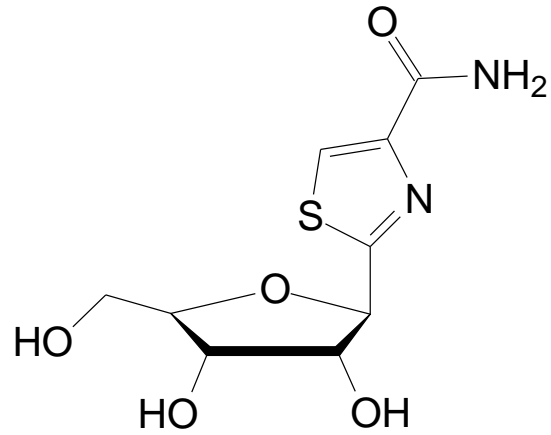
Αναγνωρίζεται και μετατρέπεται προς ara-CTP, που είναι υπόστρωμα του DNA polymerase και **ενσωματώνεται στο DNA, αλλά και στο RNA**

Το Ara-C (όπως και το Ara-A) αναστέλλει το ribonucleotide reductase, επομένως αναστέλλεται η δημιουργία 2-δεοξυνουκλεοτιδίων

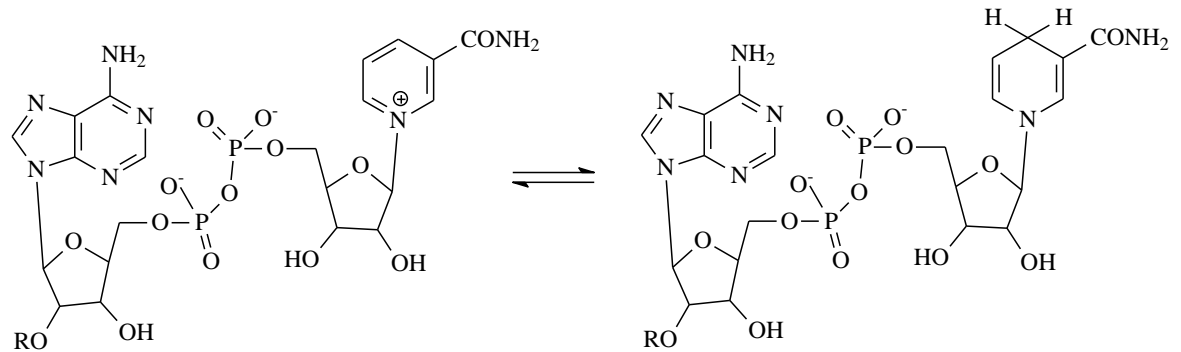
## Άλλα παράγωγα



R= OH ara-T  
R= F FMAU



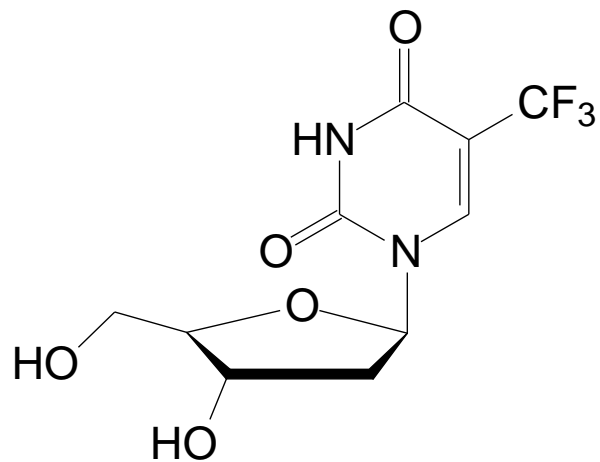
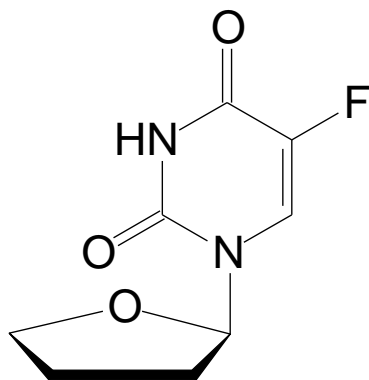
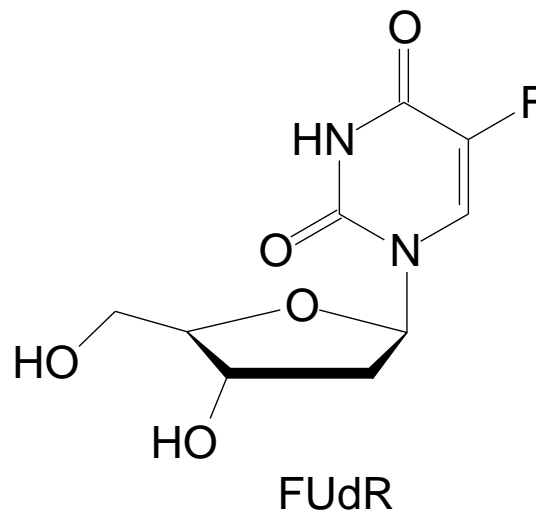
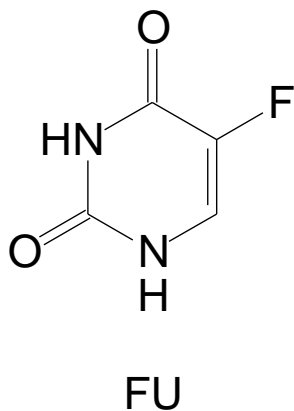
thiazofurin

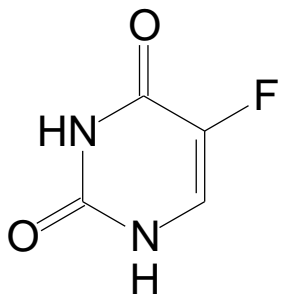


NAD, R= H  
NADP, R= PO<sub>3</sub>H<sub>2</sub>

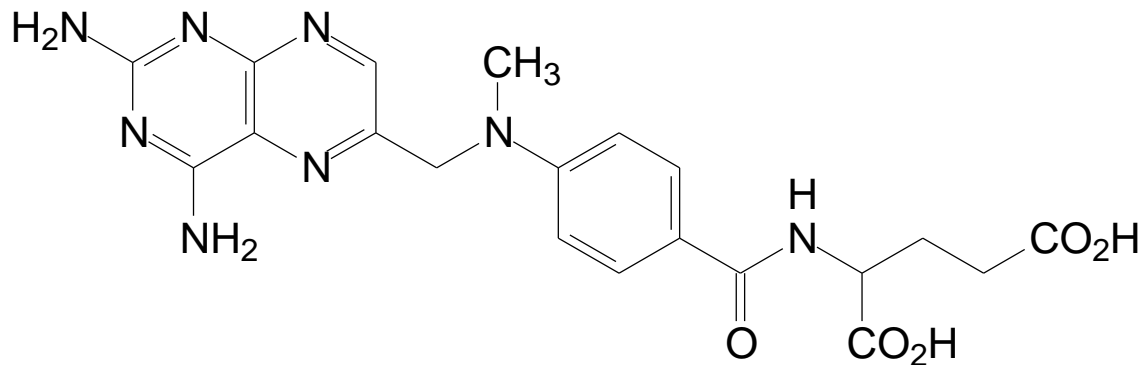
## Ανταγωνιστές πυριμιδινών

### fluoropyrimidines

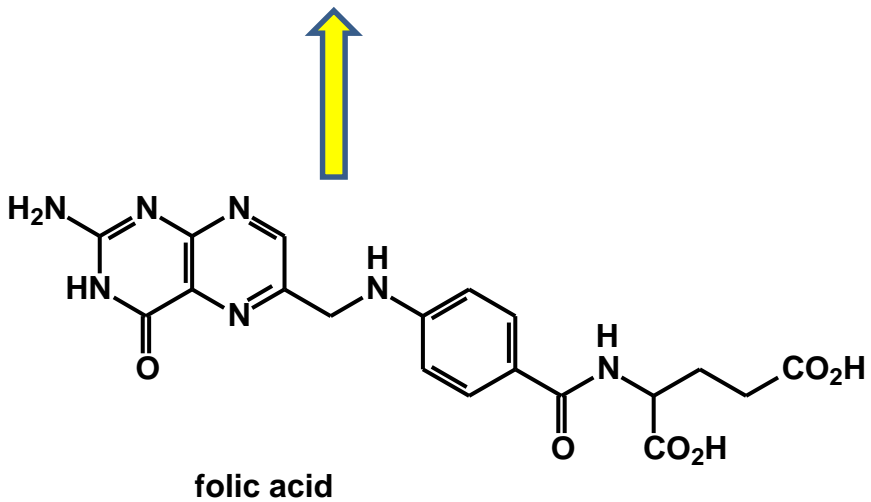
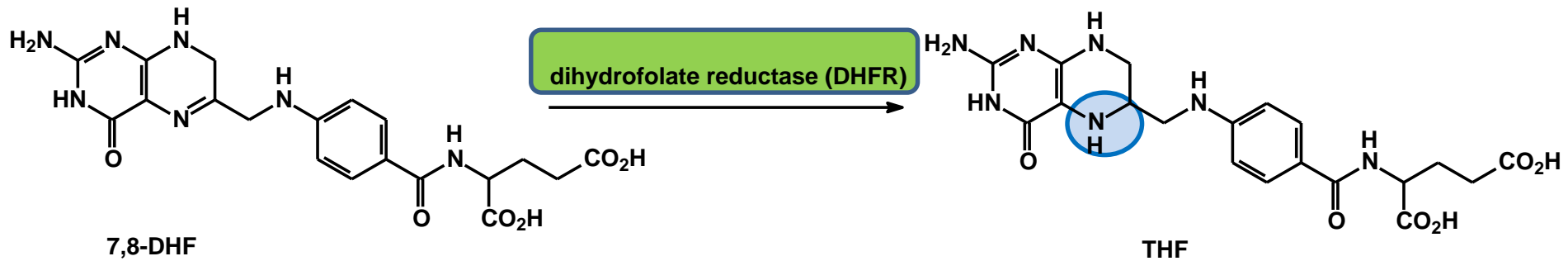
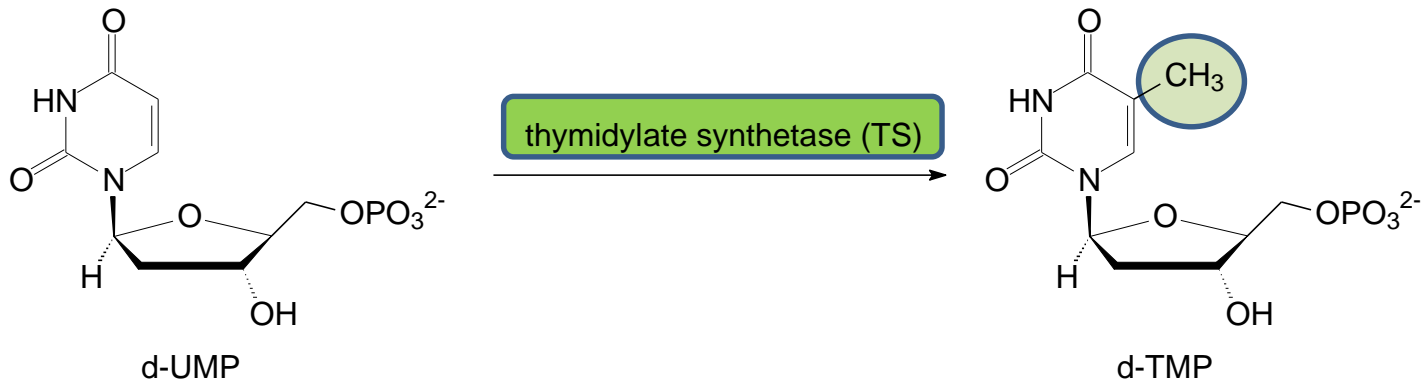


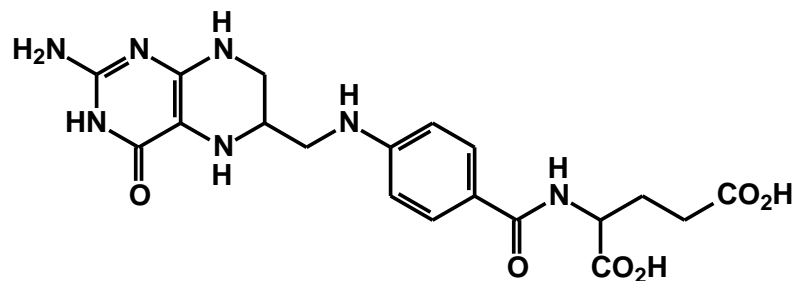


FU

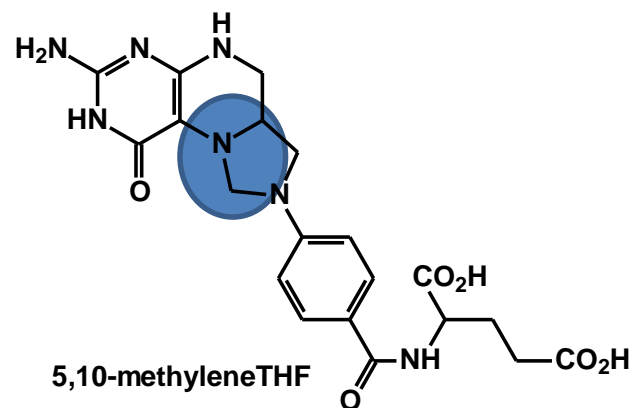
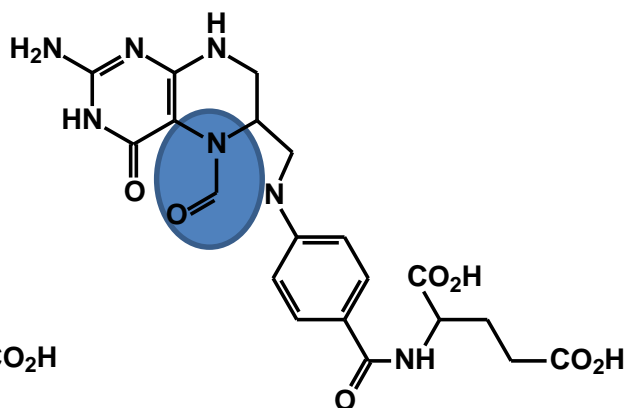
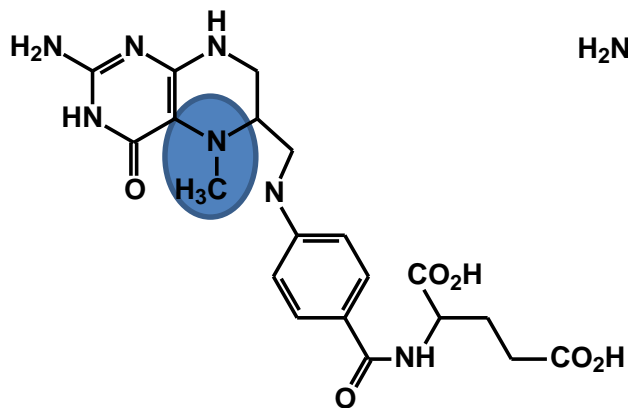


methotrexate



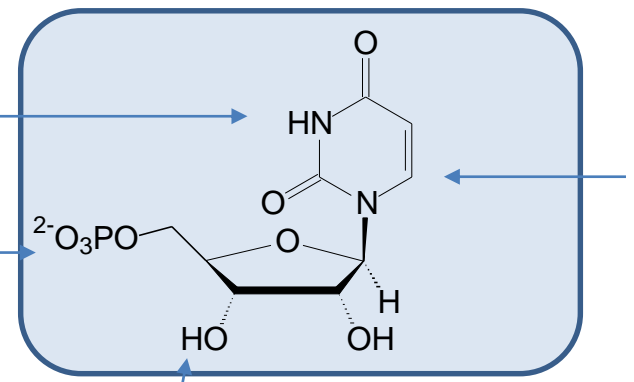


THF

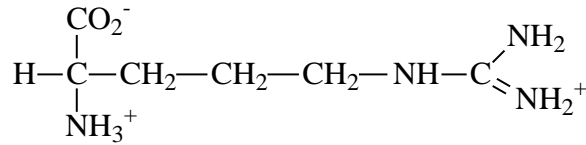


5,10-methyleneTHF

# Thymidilate synthase key residues

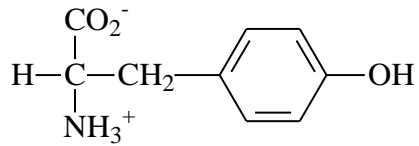


Arg 23



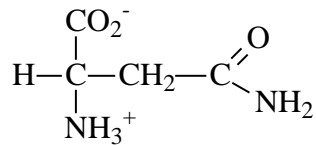
5'-phosphate

Tyr 261



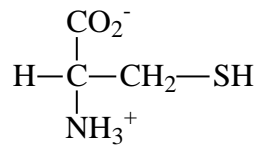
3'-OH

Asn 229



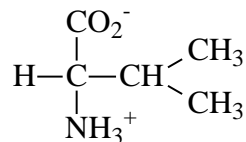
N<sub>3</sub>-H

Cys 198



C<sub>6</sub> of dUMP

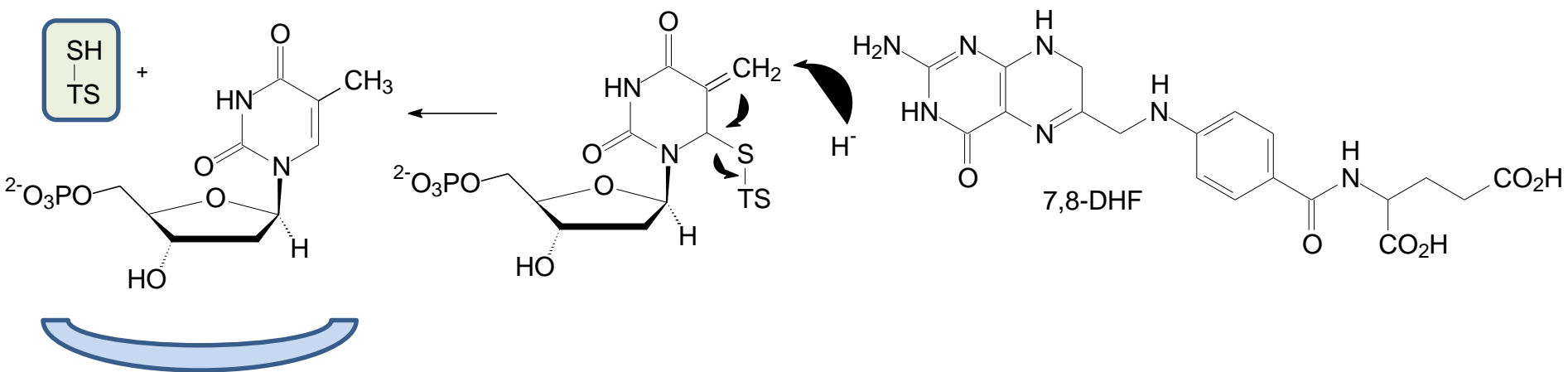
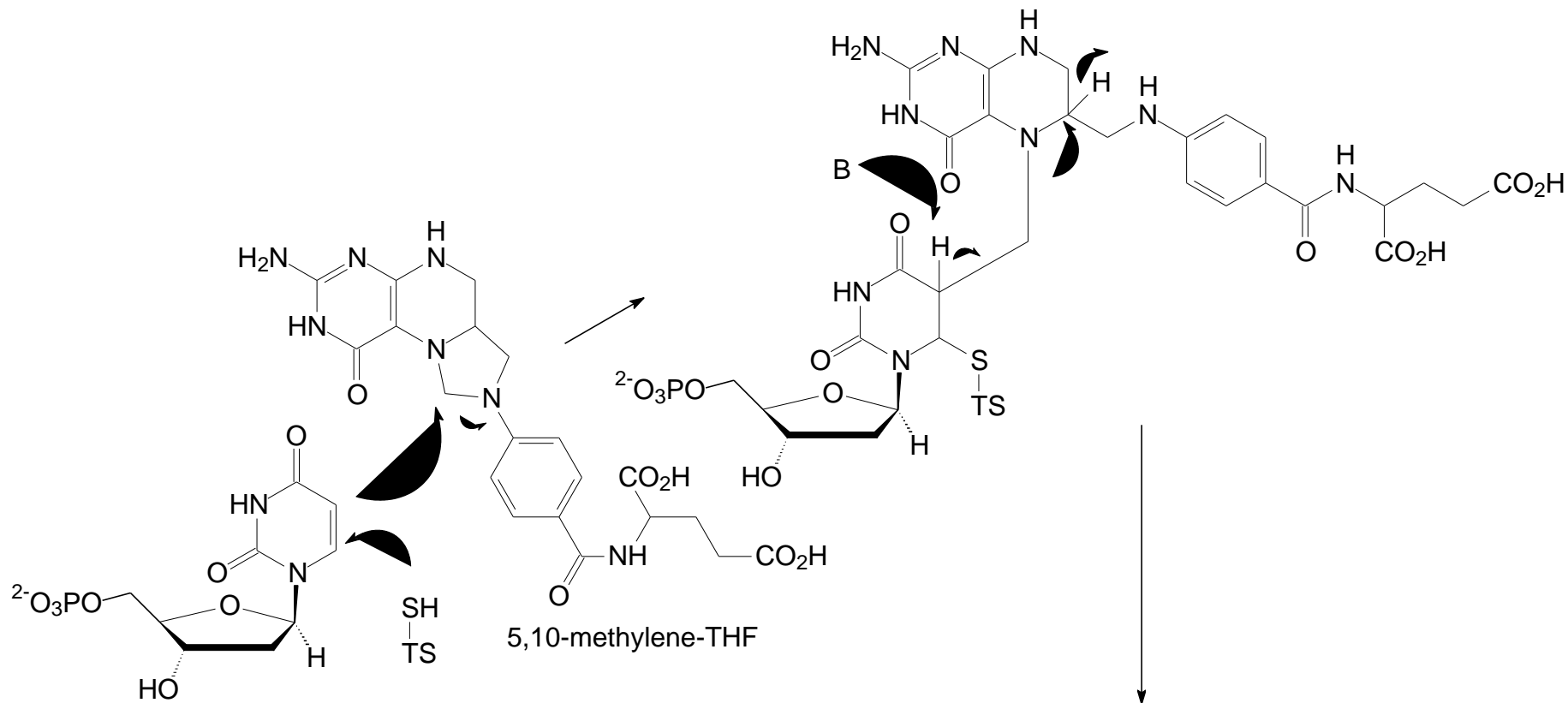
Val 316

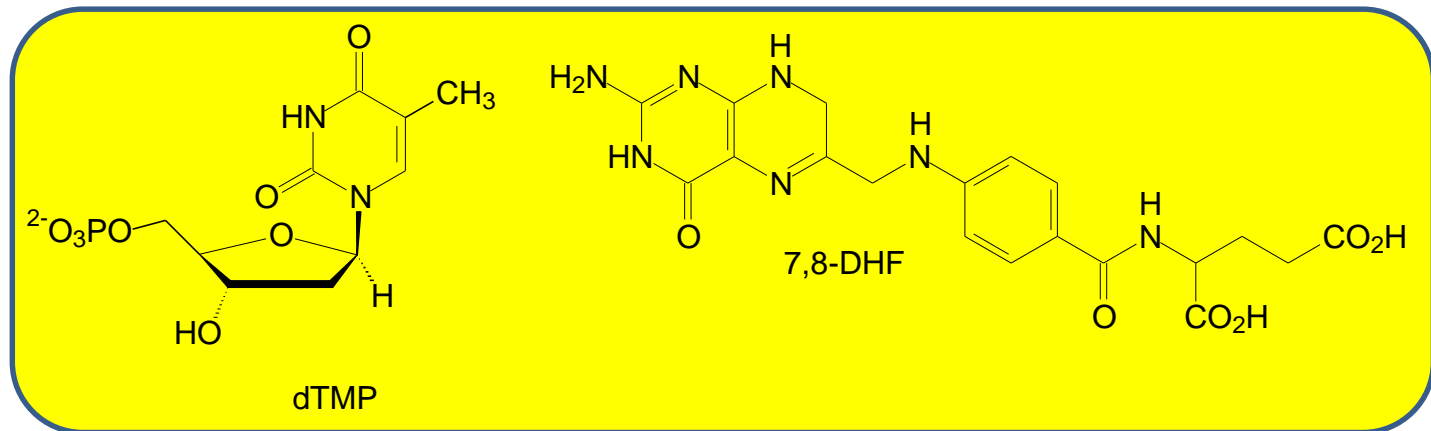
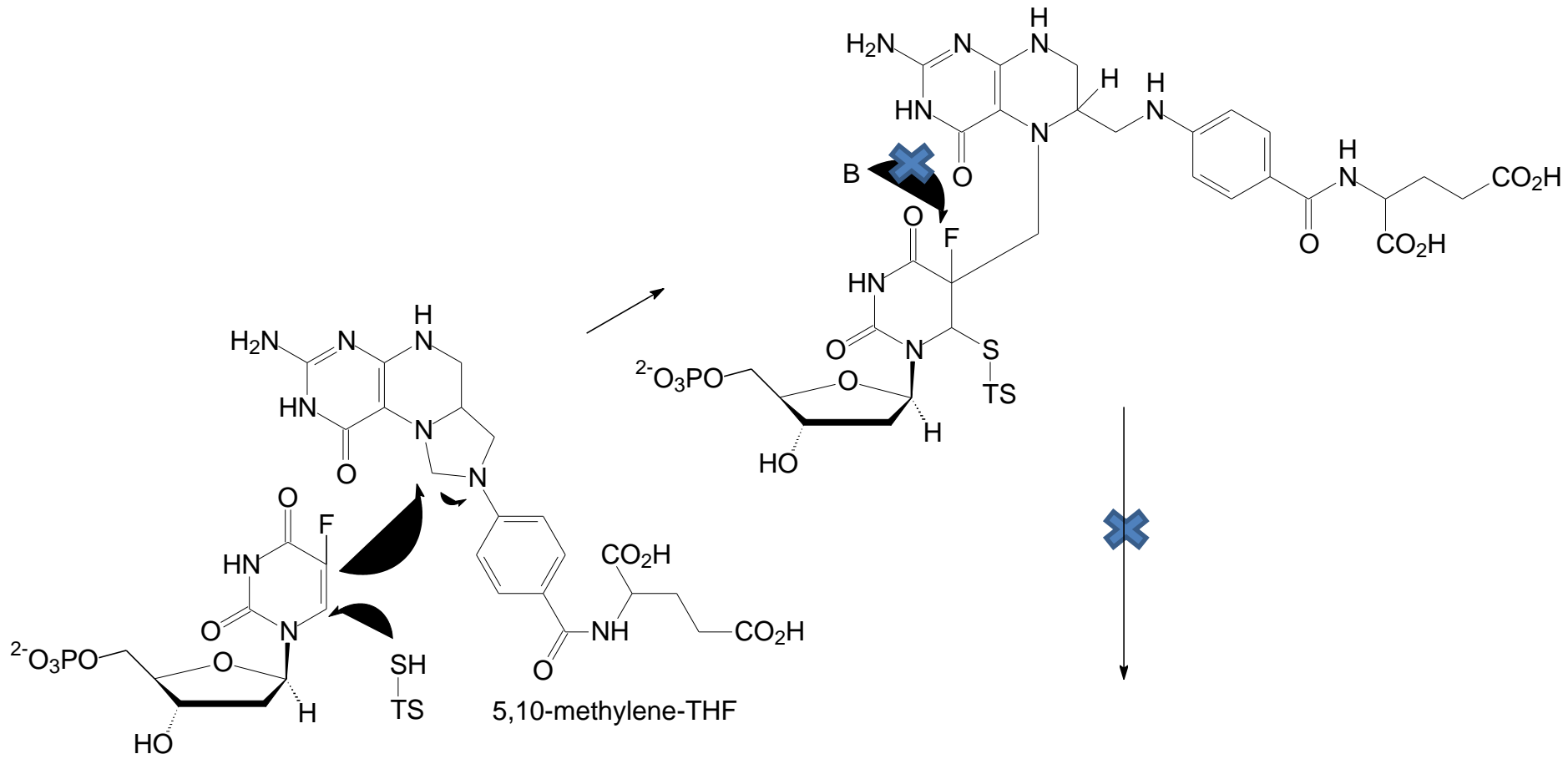


C-terminal





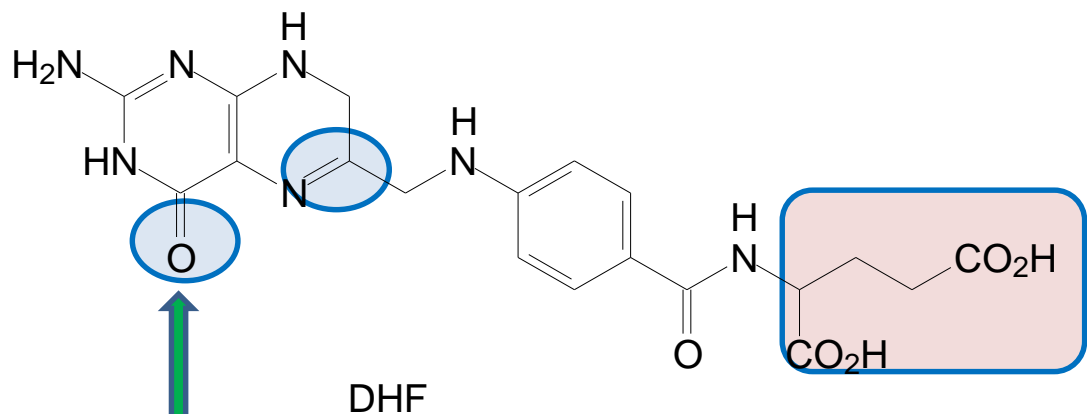
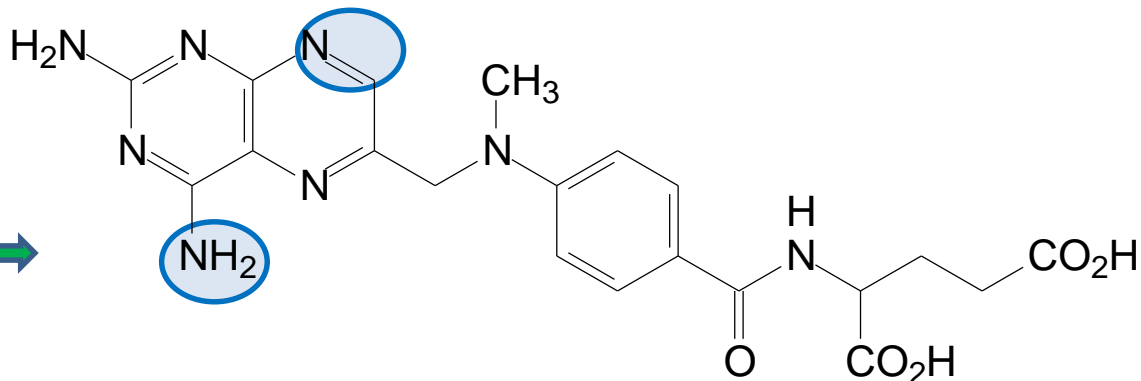




$N_1$  is the most basic N



e-donating



e-withdrawing



$N_5$  is the most basic N

