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Organic Chemistry Conceptual Study of Deoxyribonucleic Acid and Ribonucleic Acid

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ABSTRACT

I report herein the chemical behavior of the main reactive entities in the ribonucleic acid and deoxyribonucleic acid synthesis. Indeed, nitrogenous behave as nucleophiles to concede electrons to electrophiles to furnish the corresponding nucleosides. This step is the fundamental one towards the formation of nucleic acids. The following stage is the combination of nucleosides with the appropriate phosphate groups to produce the adequate nucleotides. The connection between nucleotides through phospho-ester bond formation permits to elucidate the ribonucleic acid (RNA) and deoxyribonucleic acids (DNA) synthesis. In other words, reaction sequences need nitrogenous bases, nucleosides as well as nucleotides including the enzyme, which behave as acids, bases, electrophiles or nucleophiles regarding the synthesis of these kinds of nucleic acids. The hydrolysis of these two nucleic acids can be achieved enzymatically or basically to obtain nucleosides as well as nucleotides.

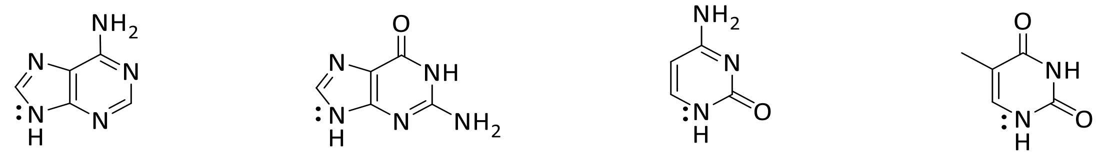
Keywords: Nitrogenous Bases, Nucleosides, Nucleotides, Ribonucleic Acid, Deoxyribonucleic Acid.

INTRODUCTION

Naturally nucleic acids refer to deoxyribonucleic acid and ribonucleic acid. Indeed, these organic compounds have functional groups such as amine group in each nitrogenous base, primary ribose hydroxyl group and phosphate group in each nucleotide. It is important to mention that these two nucleic acids utilize they functional groups as acids, bases, electrophiles or nucleophiles to react with appropriate organic reactive entities to generate the corresponding products. In this regard, the DNA synthesis illustrates the reactivity or the nucleic acid chemical behaviour. The reaction mechanisms presented in this conceptual study is an added value since they denote a comprehensive understanding of different DNA fragments connection. These kinds of reaction mechanisms could help to better understand how the DNA degradation occurs when it is exposed to a nucleophile chemical substance. In this regard, it is important to recall that a reaction mechanism means a delocalisation of electrons from an atom to another. In other words, a rich electrons atom (nucleophile) donates its electrons to a poor electrons atom (electrophile). The proposed DNA decomposition reaction mechanisms involve the action of a specific enzyme such as phosphodiesterase and a chemical substance, which reacts as a nucleophile during a base hydrolysis process.

DEOXYRIBONUCLEIC ACID NITROGENOUS BASES

Experimental observations reveal that deoxyribonucleic acid (DNA) has four nitrogenous bases named adenine (A), guanine (G), cytosine (C) and thymine.[1-2] According to their chemical structures, they are organic compounds containing nitrogen atoms rich in electrons, which define accordingly their nucleophilic ability towards electrophilic reactive entities. Because of the nucleophilic behaviour, each nitrogenous base donates its free electrons to a molecule of deoxyribose to furnish a corresponding nucleoside. In other words, the reaction consists of an addition of an intra cyclic nitrogen atom, which has a pair of free electrons, to an electron poor molecule of deoxyribose (Figure 1, Scheme 1, reaction 3).

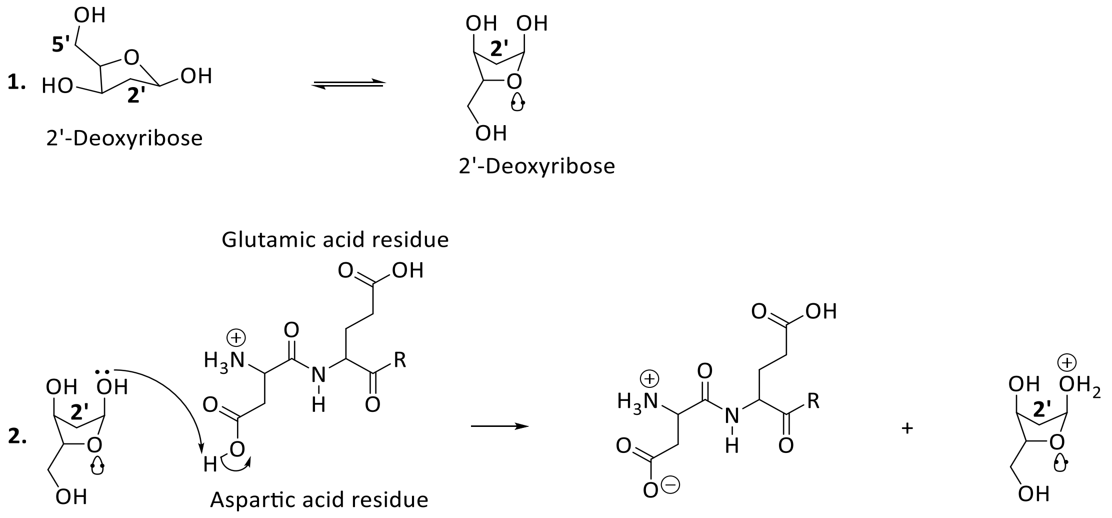


Adénine Guanine Cytosine Thymine

Figure 1

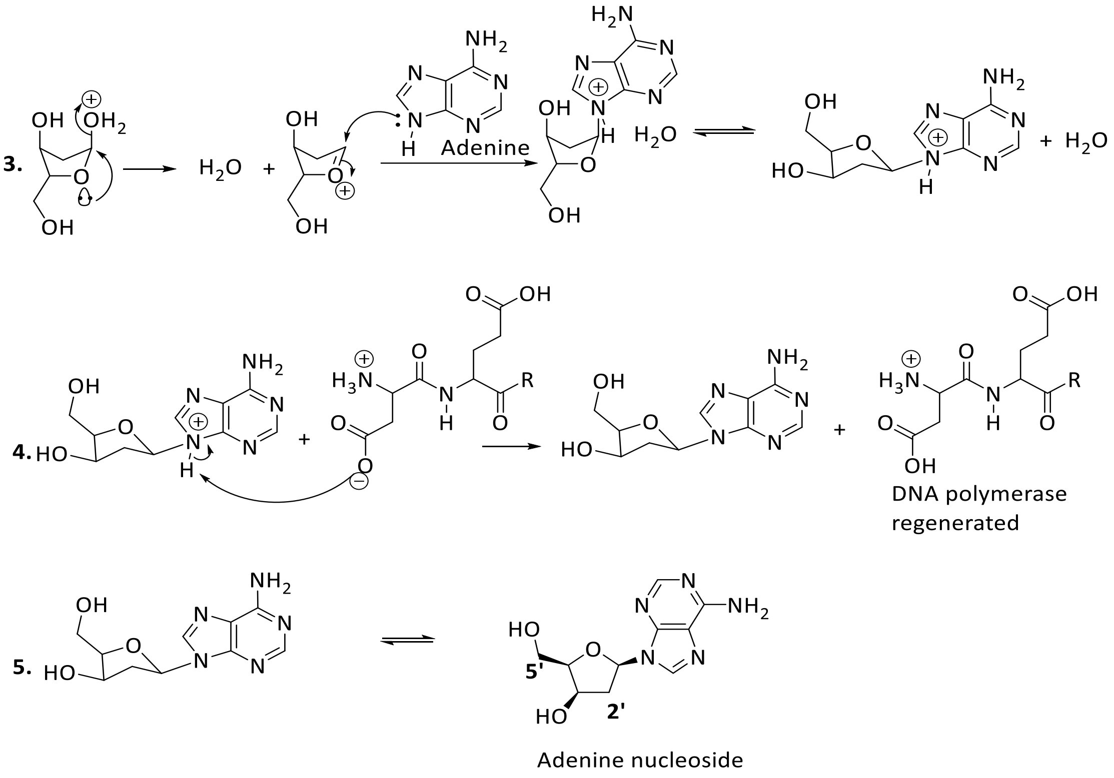
ADENINE NUCLEOSIDE SYNTHESIS

A nucleoside is a portion of a nucleotide constituted by a molecule of a sugar (ribose) attached to a nitrogenous base such as adenine base (Scheme 1, reaction 4). The nucleoside synthesis involves the enzymatic protonation of a ribose hydroxyl group to convert it as a molecule of water, a good living group, and to produce an enzymatic conjugate base as well as a carbon oxonium ion (Scheme 1, reaction 2, 3).



R = Amino acids of the DNA polymerase.

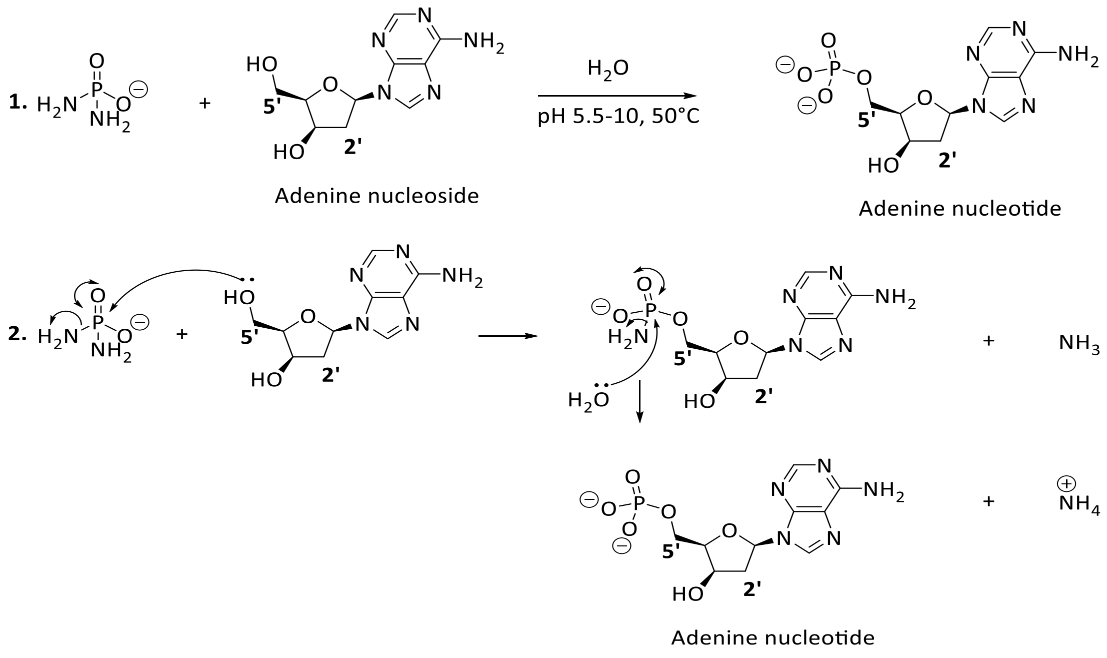
Indeed, the carbon oxonium ion bears a reactive electrophilic carbon, adjacent to the intra oxygen ion, which reacts with a nitrogen free double electron to generate a corresponding intermediate compound and a molecule of water (Scheme 1, reaction 3). In the following step, the intermediate compound donates its proton to the enzymatic conjugate base to yield a DNA polymerase and an adenine nucleoside (Scheme 1, reaction 4).



Scheme 1

ADENINE NUCLEOTIDE SYNTHESIS

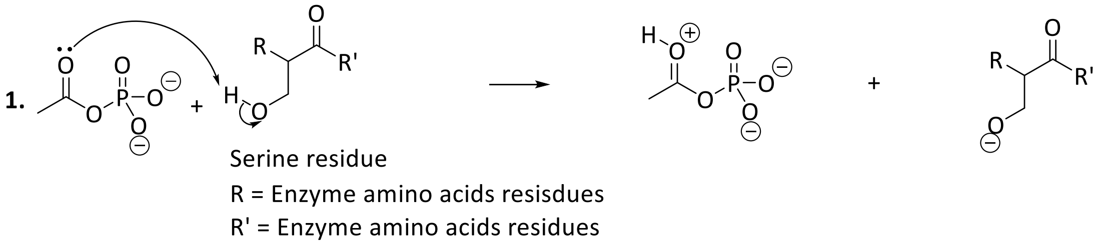
A nucleotide is a nucleoside bound to a phosphate group due to a phosphorylation reaction between a primary hydroxyl of the ribose and a diamine phosphate in an organic synthetic laboratory.[3]



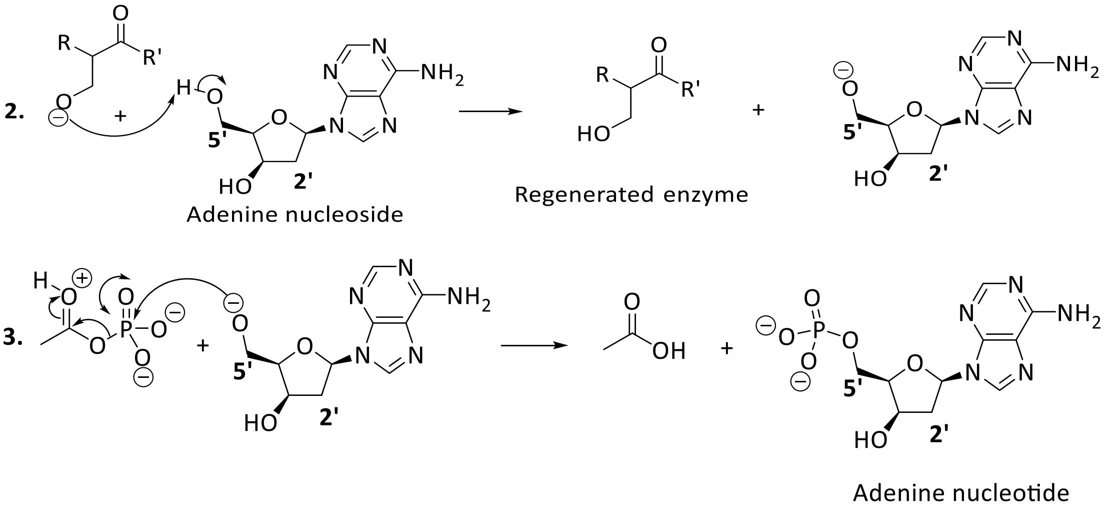
Scheme 2

Indeed, the experimental observation has revealed that diamine phosphate is generally used as a phosphorylation agent in aqueous reaction medium at 50°C pH 5.5-10 (Scheme 2).[3]

It has been reported that in nature, acetyl phosphate is used as a phosphorylating reactive chemical entity to phosphorylate nucleosides.[4] in this perspective, experimental observations have shown that the active site of an enzyme responsible for the phosphorylation reaction is mainly constituted by a serine residue (Scheme 3).[5]



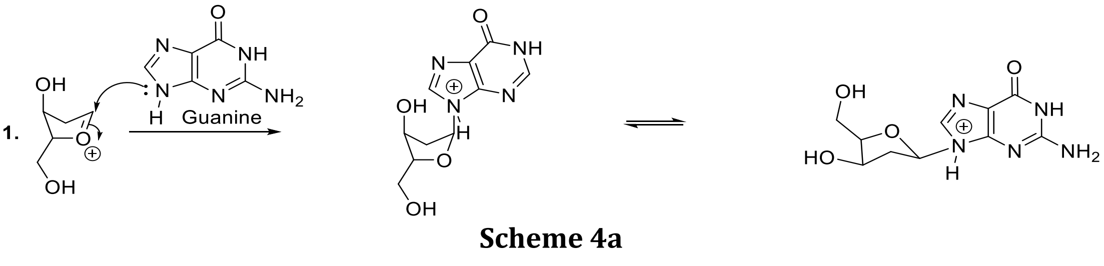
Scheme 3a



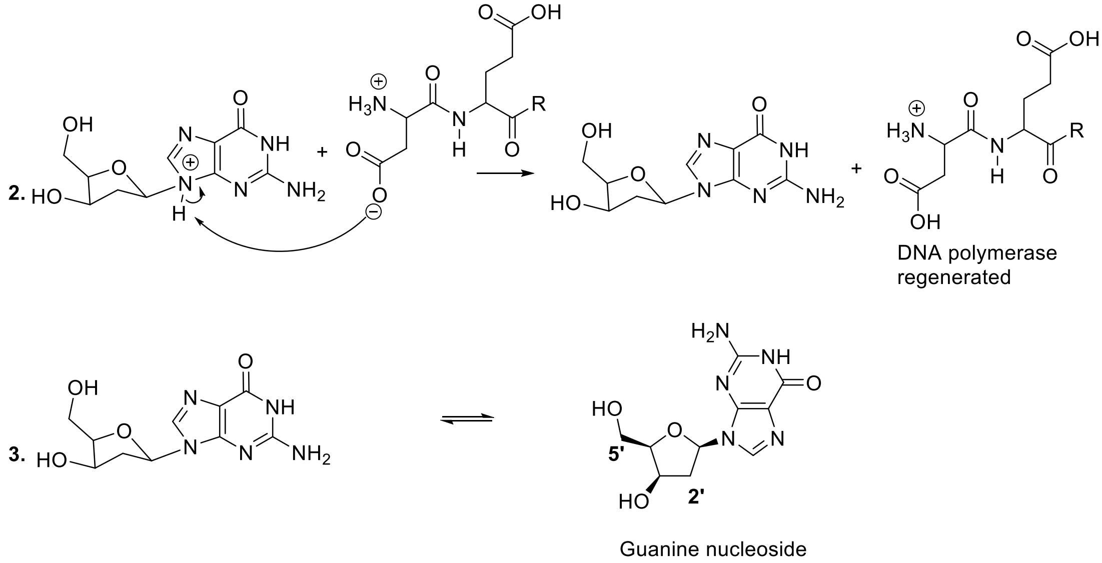
Scheme 3b

GUANINE NUCLEOSIDE SYNTHESIS

The nucleophilic addition of guanine to ribose implies the reaction between the free nitrogen double electrons and the oxonium ion electrophilic carbon to furnish the expected guanine nucleoside under the enzymatic conditions (Scheme 4). The proposed reaction mechanism shows the regeneration of the appropriate enzyme or DNA polymerase after the catalysis process (Scheme 4, reaction 2).



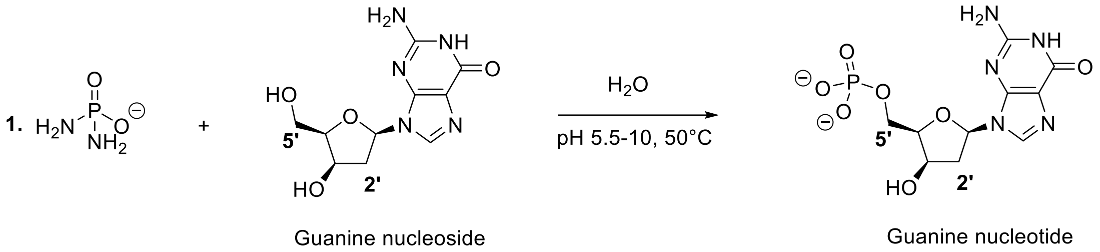
Scheme 4a



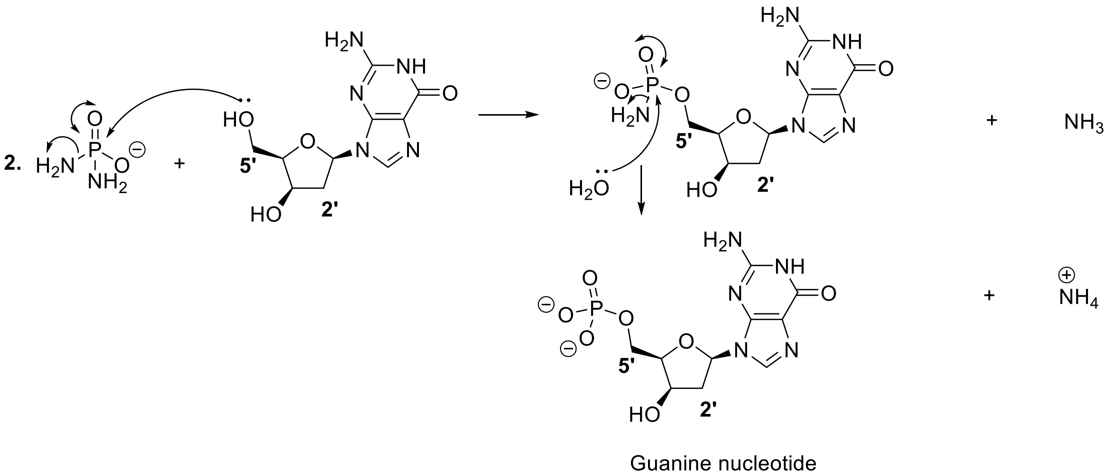
Scheme 4b

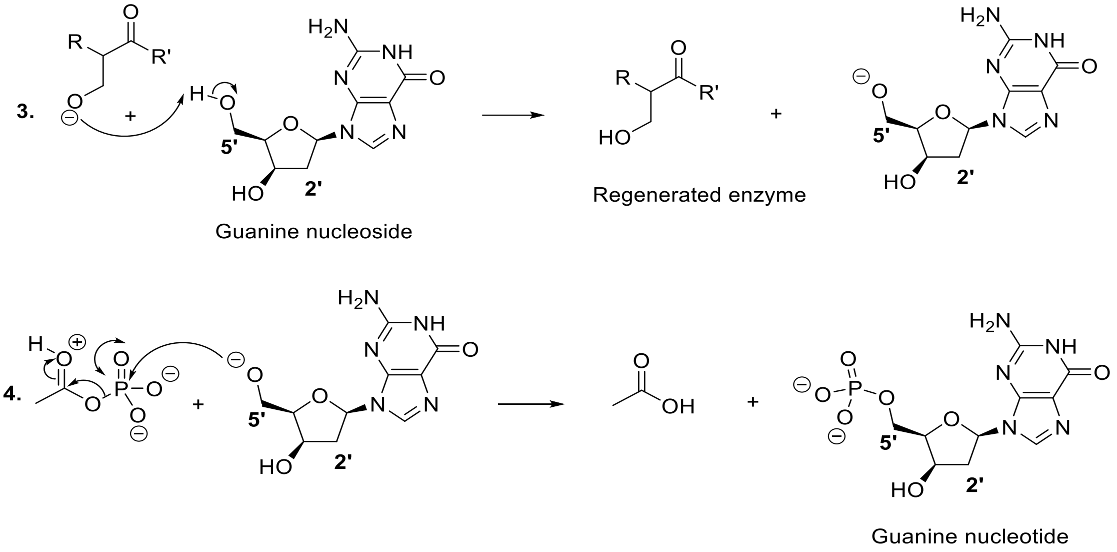
GUANINE NUCLEOTIDE SYNTHESIS

A guanine nucleotide is usually prepared using a phosphorylating reactive entity in the presence of an adequate nucleoside according the same procedure as the synthesis of an adenine nucleotide (Scheme 5, reactions 1-4).



Scheme 5a

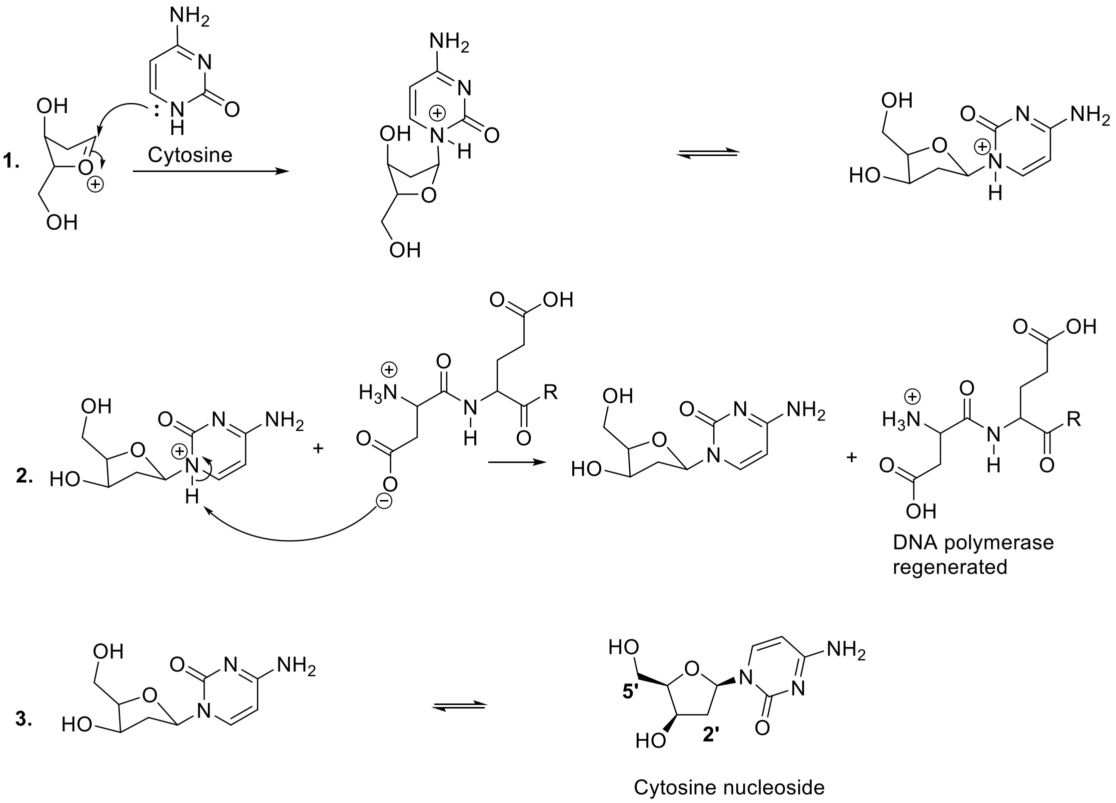




Scheme 5b

CYTOSINE NUCLEOSIDE SYNTHESIS

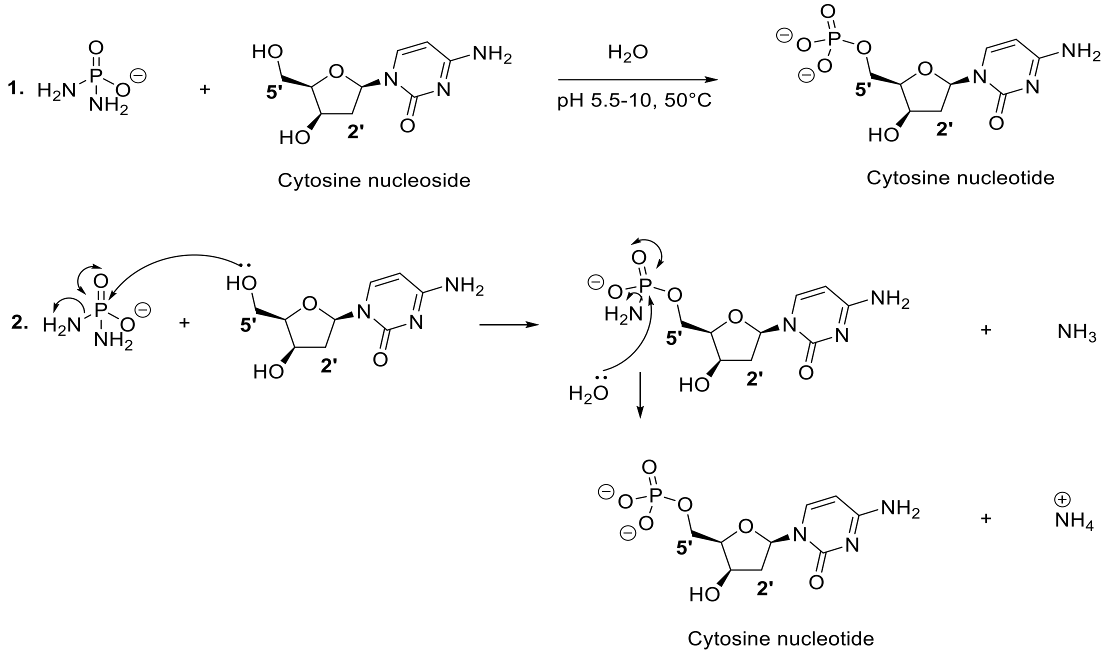
In the construction of a cytosine nucleoside, nitrogenous cytosine base acts as a nucleophile, which donates its electrons to a ribose oxonium ion (Scheme 6, reaction 1). During the following step the generated intermediate product is deprotonated with the aid of the enzyme aspartate residue to produce the expected cytosine nucleoside as well as the enzyme DNA polymerase (Scheme 6).



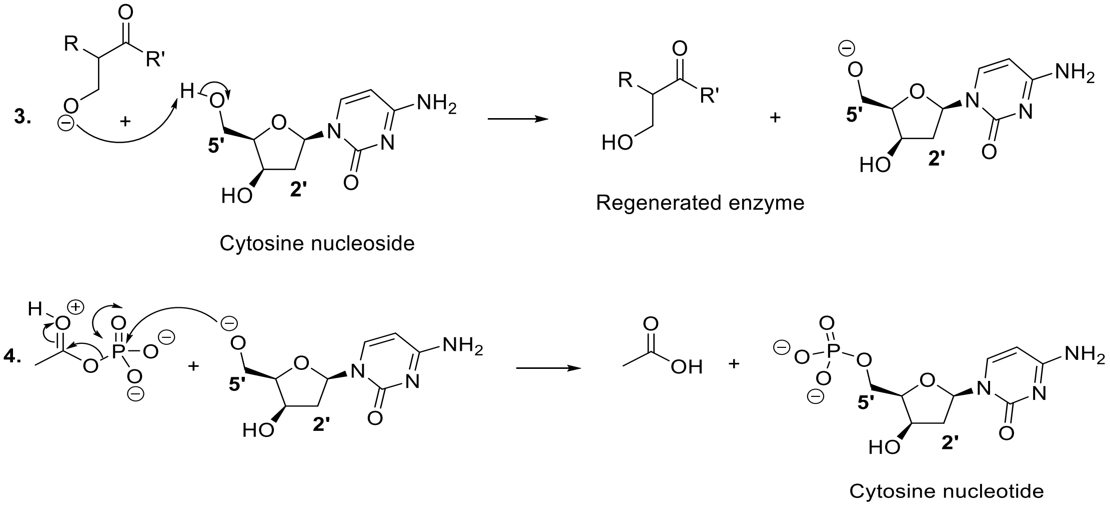
Scheme 6

CYTOSINE NUCLEOTIDE SYNTHESIS

The cytosine nucleotide synthesis signifies that the addition of a ribose primary hydroxyl group to a diamine phosphate ejects an amine leaving group as an ammoniac molecule and the formation of an intermediate compound (Scheme 7, reaction 2).



The resulting intermediate compound reacts with a molecule of water to displace an amine group as an ammonium molecule and the desired cytosine nucleotide (Scheme 7, reaction 2). Throughout the final step, the enzyme aspartate residue accepts a cytosine nucleoside proton to achieve a regenerated enzyme and a cytosine nucleophile conjugate base (Scheme 7, reaction 3). In the same regard, an appropriate phosphorylation process that occurred in living beings takes place in the presence of an acyl phosphate reactive molecule or acyl phosphate phosphorylating chemical entity (Scheme 7, reaction 4).

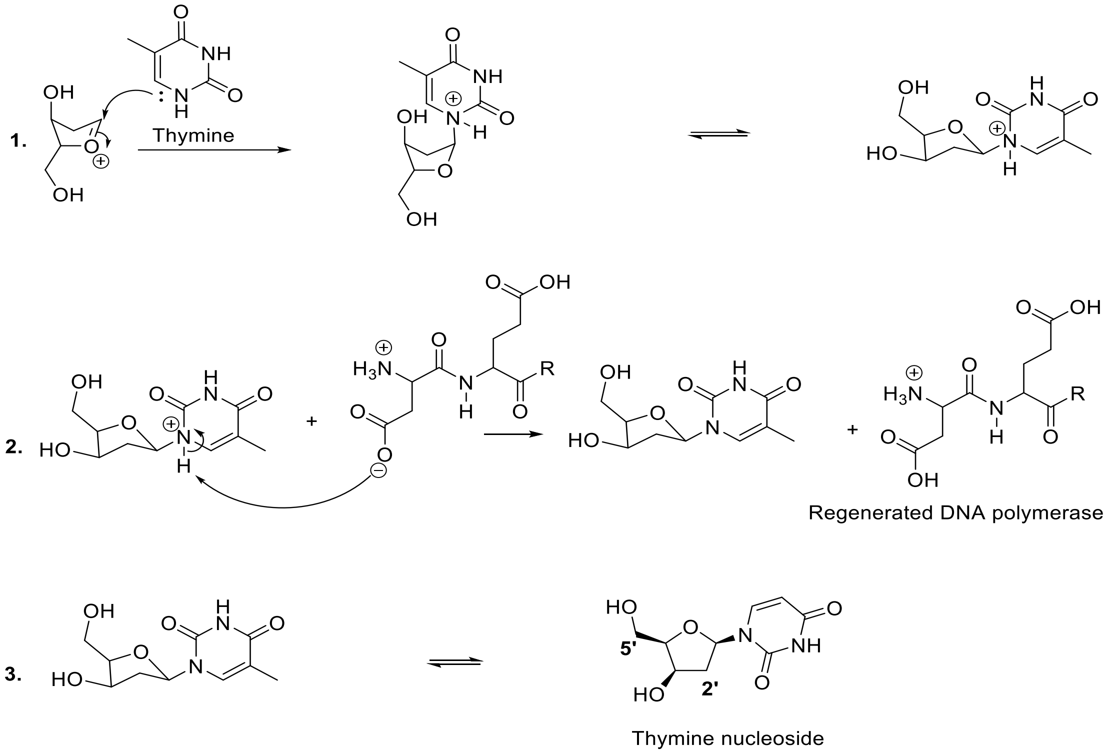


Scheme 7

Throughout the course of this kind of phosphorylation pathway, a cytosine nucleoside conjugate base reacts with an acyl phosphate to release an acetic acid molecule as well as a cytosine nucleotide (Scheme 7, reaction 4).

THYMINE NUCLEOSIDE SYNTHESIS

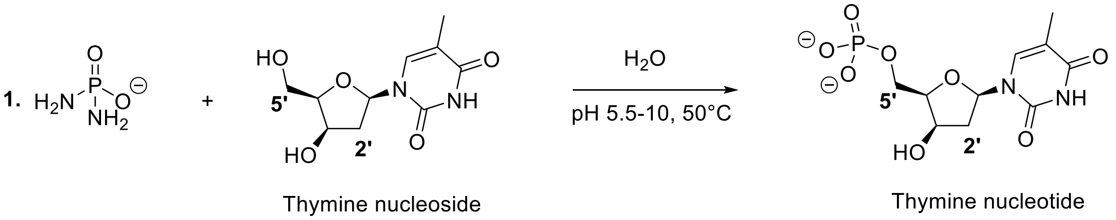
The thymine nucleophilic addition to a ribose oxonium ion yields an intermediate compound, which releases a proton to enzyme aspartate residue. This step affords a corresponding thymine nucleoside along with a regenerated DNA polymerase (Scheme 8).



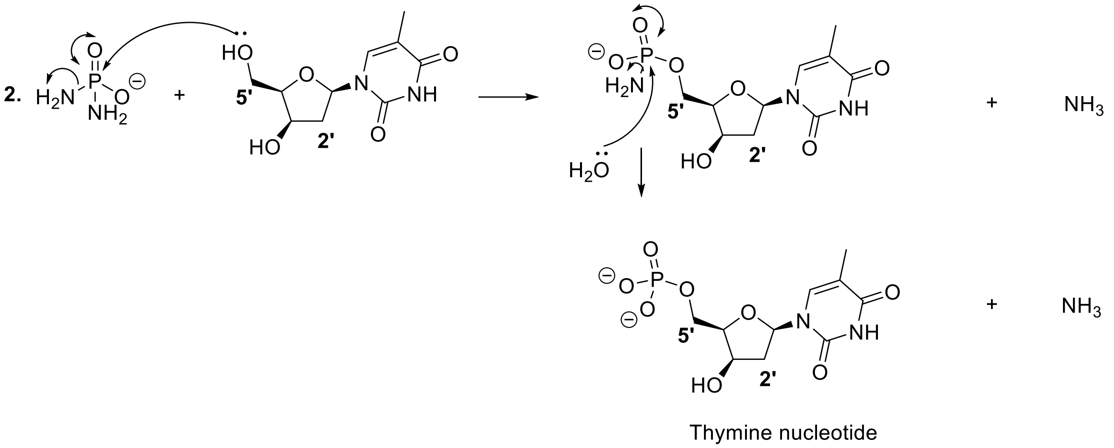
Scheme 8

THYMINE NUCLEOTIDE SYNTHESIS

Nucleophilic substitution of a diamine phosphate amine group by a ribose primary alcohol furnishes a corresponding intermediate product and an ammoniac molecule (Scheme 9, reaction 1). This step is followed by the removal of the remaining group amine to generate a desired thymine nucleotide and an ammoniac molecule as a second byproduct (Scheme 9, reaction 2).

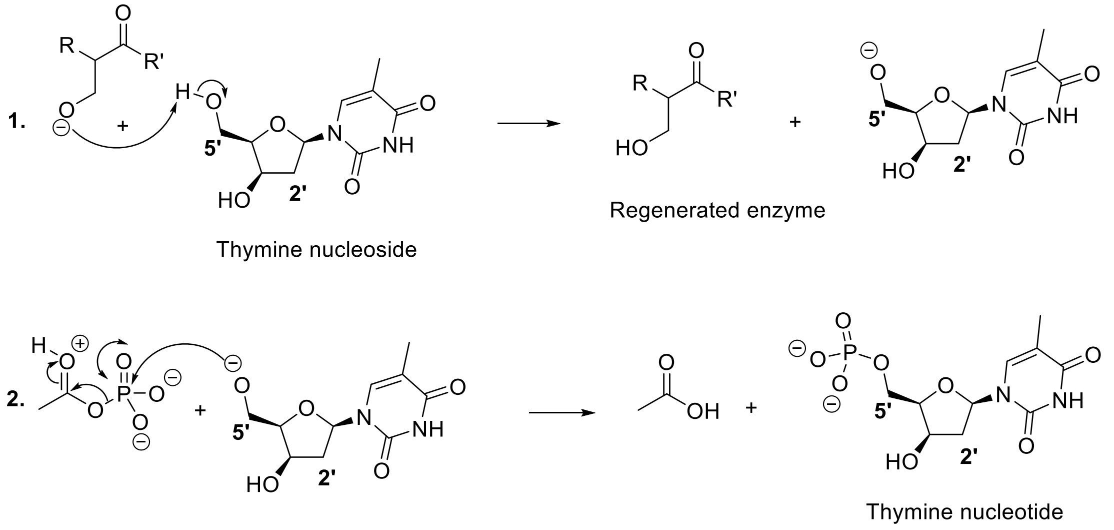


Scheme 9a



Scheme 9b

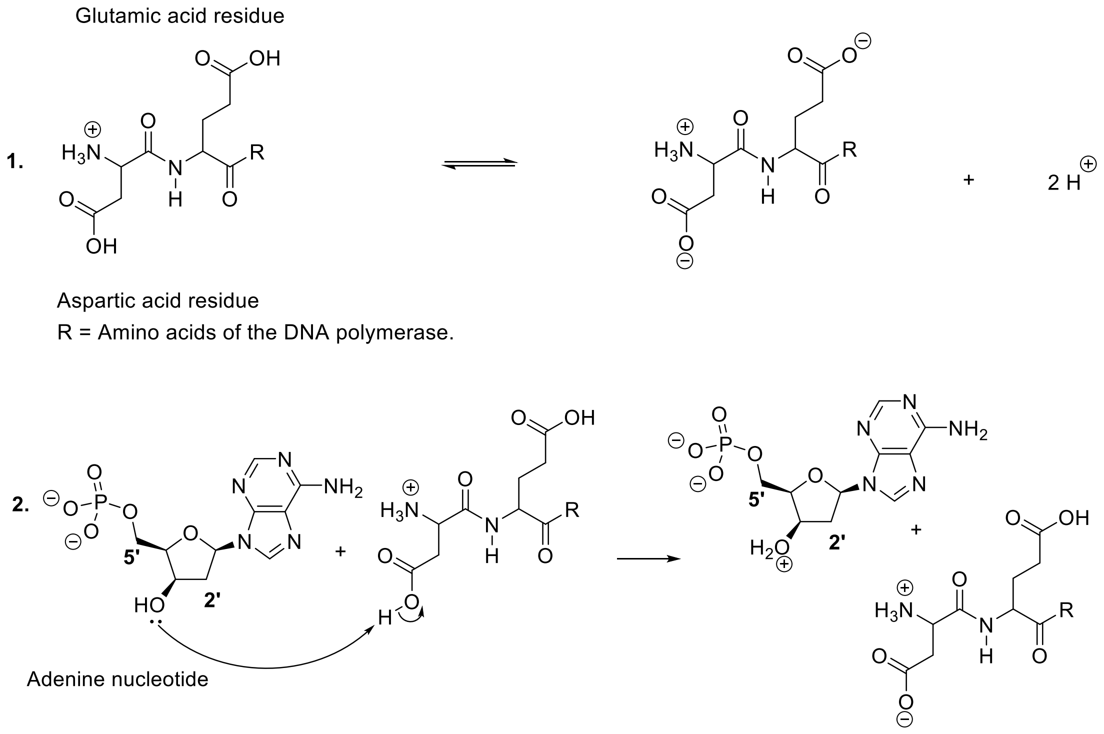
Naturally, a thymine nucleotide is also set up enzymatically. Definitely, the enzyme aspartate residue accepts a proton from a thymine nucleoside primary hydroxyl group to produce a regenerated enzyme and a nucleoside conjugate base (Scheme 10, reaction 1). This one reacts with an acyl phosphate to remove a protonated acetate leaving group to provide the expected thymine nucleotide and an acetic acid (Scheme 10, reaction 2).



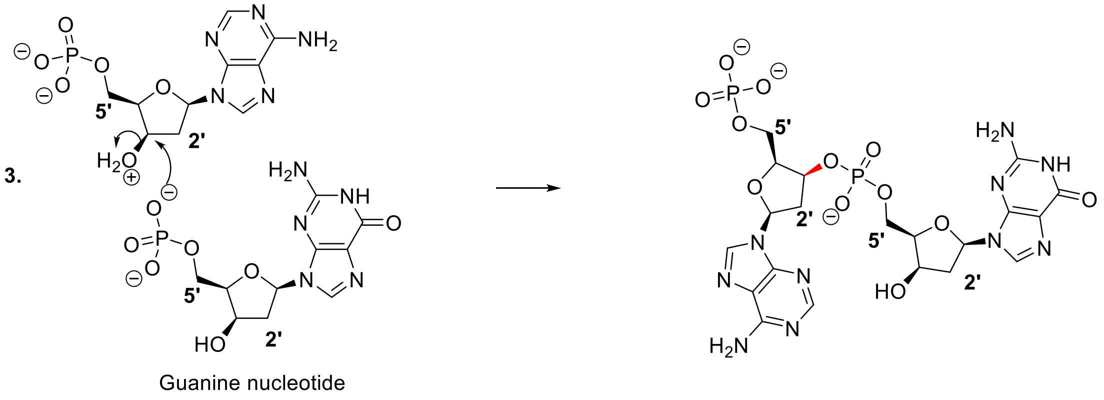
Scheme 10

DEOXYRIBONUCLEIC ACID SYNTHESIS

Deoxyribonucleic acid (DNA) polymerase is a versatile enzyme, which usually catalyzes a DNA compound from nucleotides. Indeed, adenine nucleotide is connected to guanine nucleotide through an esterification reaction or the substitution of the protonated ribose hydroxyl group by a phosphate group to generate a corresponding phospho-ester product. In other words, the ribose hydroxyl group accepts the enzyme aspartic acid residue proton to produce a hydronium ion, which is removed by an adenine nucleotide phosphate group to furnish a phospho-ester compound. This later will react with cytosine nucleotide to yield another corresponding phospho-ester product, which will combine again with thymine nucleotide to finalize the DNA structure (Scheme 11, reactions 1-7). It has been revealed that aspartic acid and glutamic acid residues are the roots for DNA polymerase catalytic activity (Scheme 11). In the same line, chemical constituents such as NADH, and hydrochloric acid found into the cytosol, a liquid portion of the cellular cytoplasm, play a fundamental role in the microbial metabolic processes.[6]



Scheme 11a



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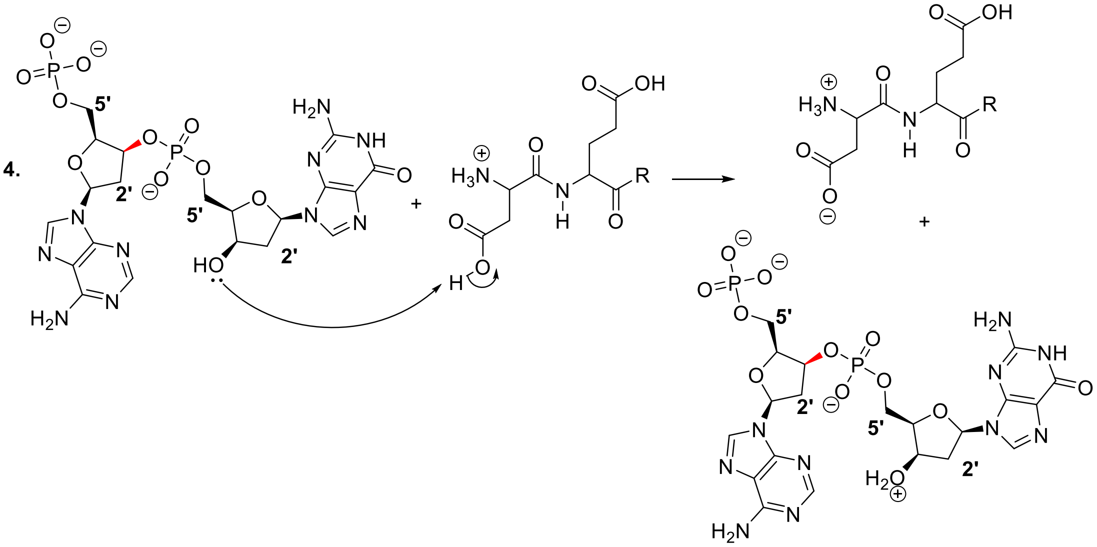
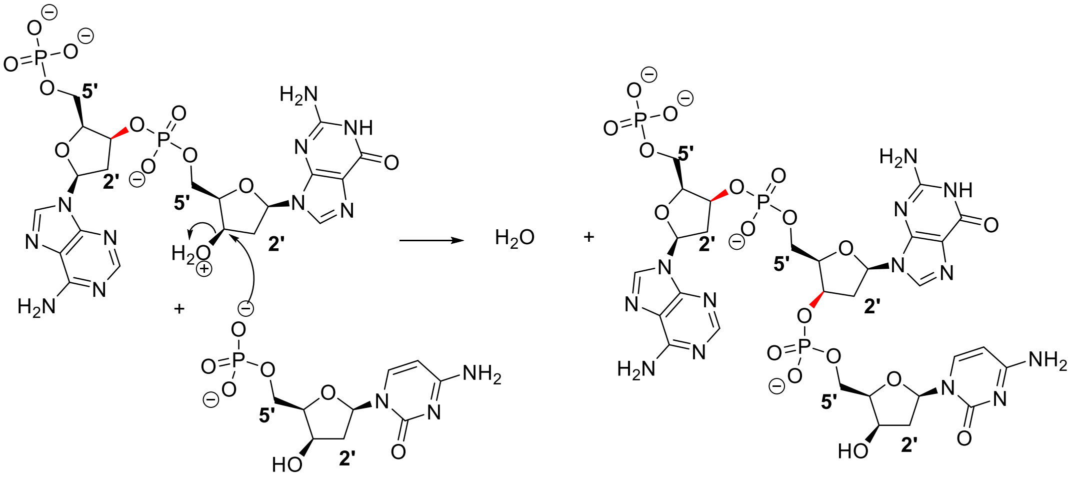
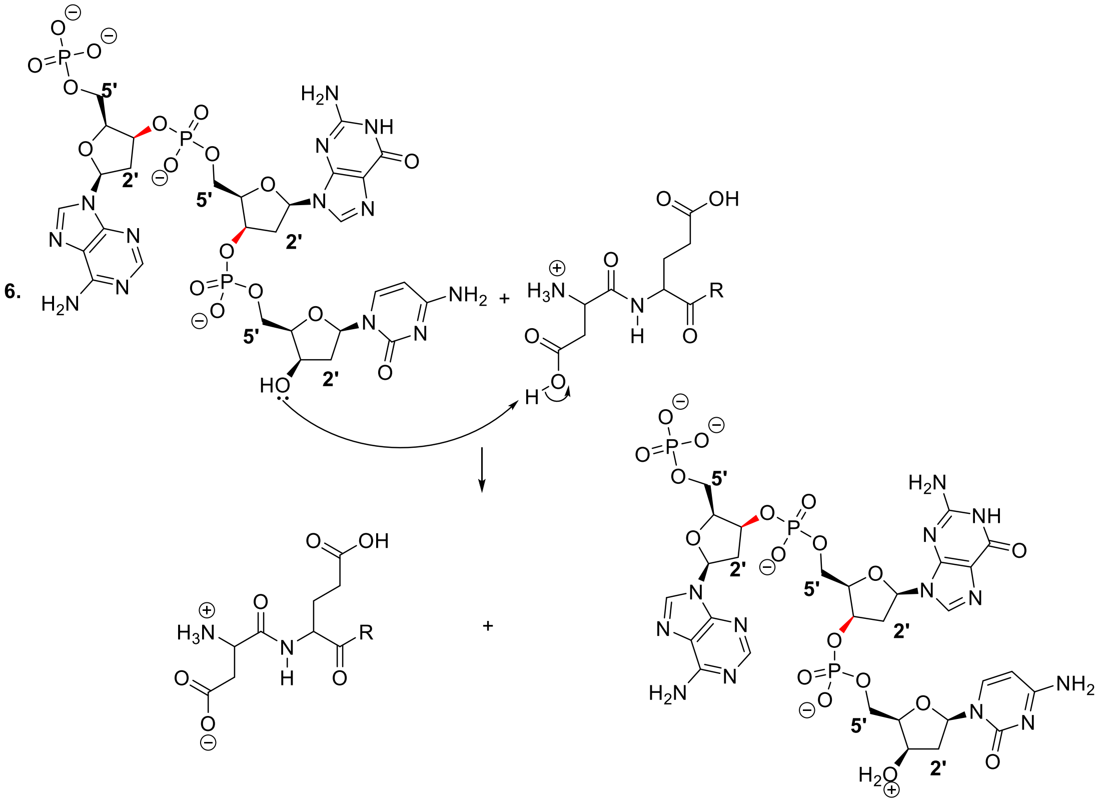


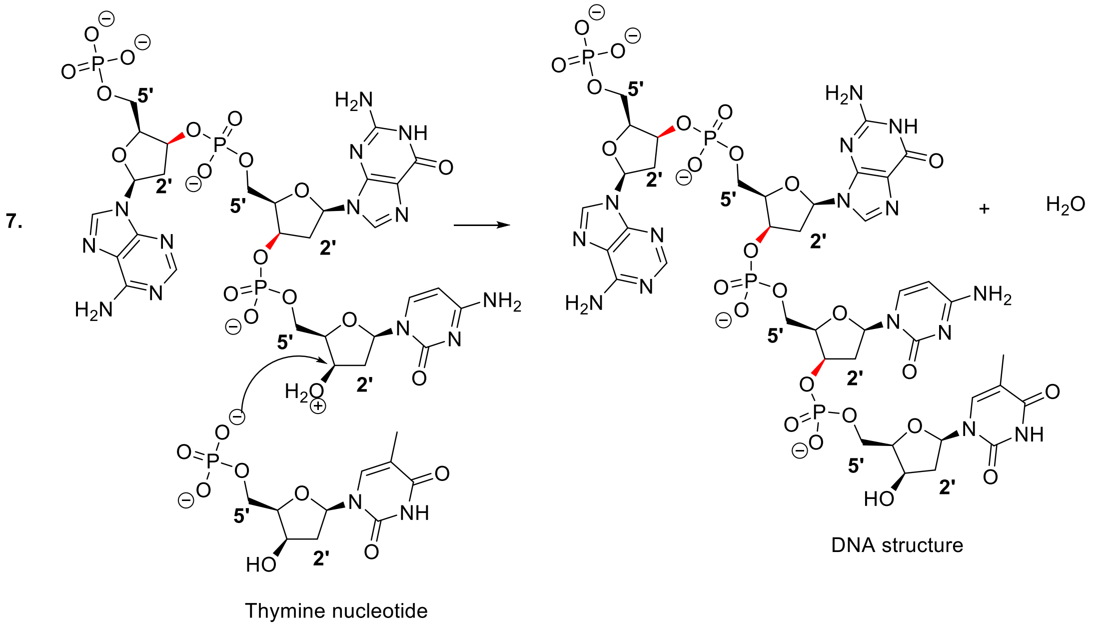
Scheme 11b

5.





Scheme 11c



Scheme 11d

URACIL NUCLEOTIDE SYNTHESIS

It should be recalled that ribonucleic acid (RNA) bears four nitrogenous bases as DNA, except that thymine is replaced by uracil. Therefore, the ribonucleic acid nitrogenous bases became adenine (A), guanine (G), cytosine (C) and uracil (U) (Figure 2).

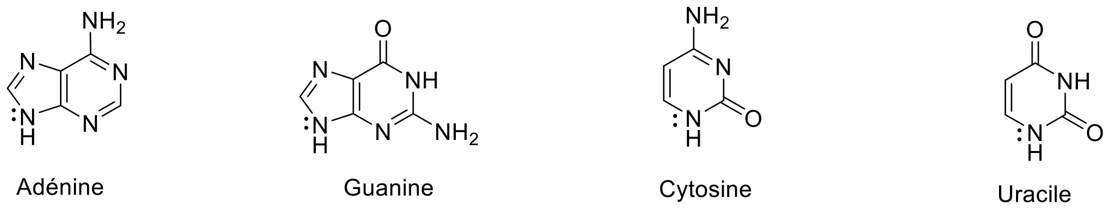
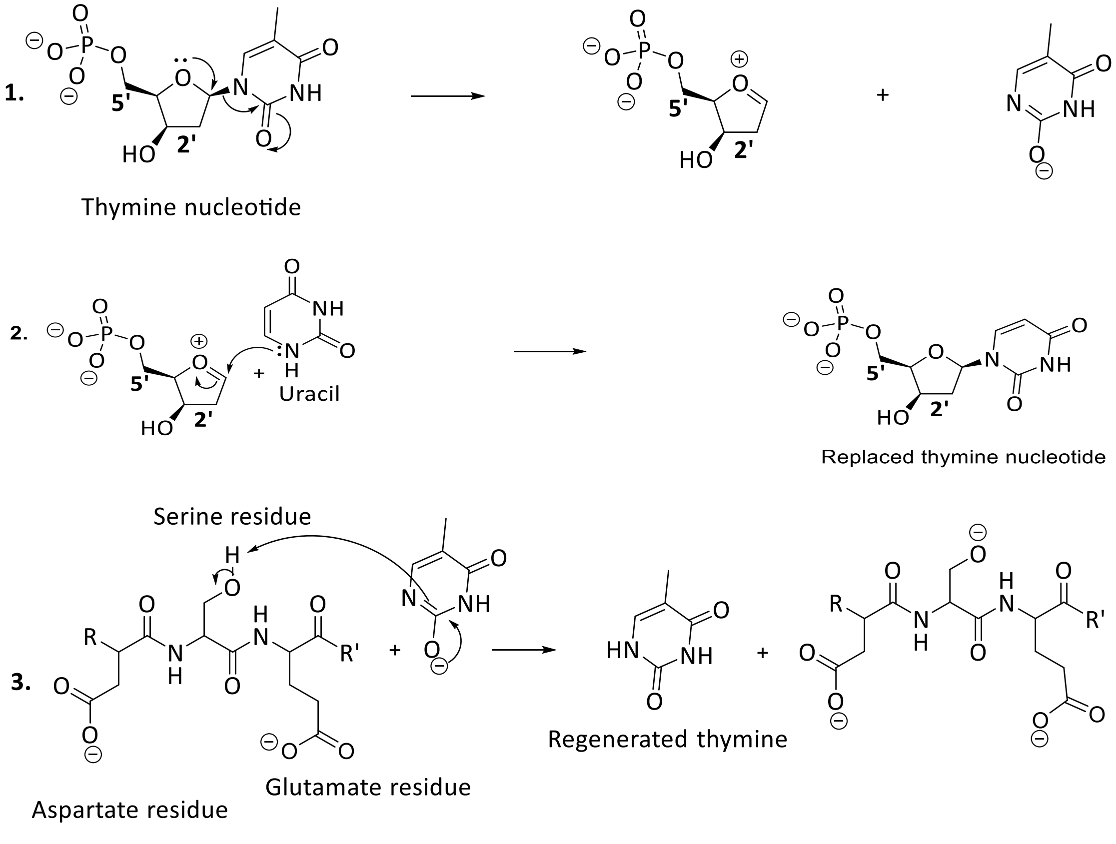
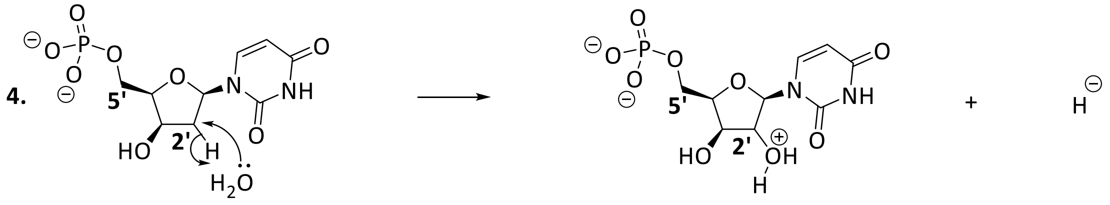

Adénine Guanine Cytosine Uracile

Figure 2

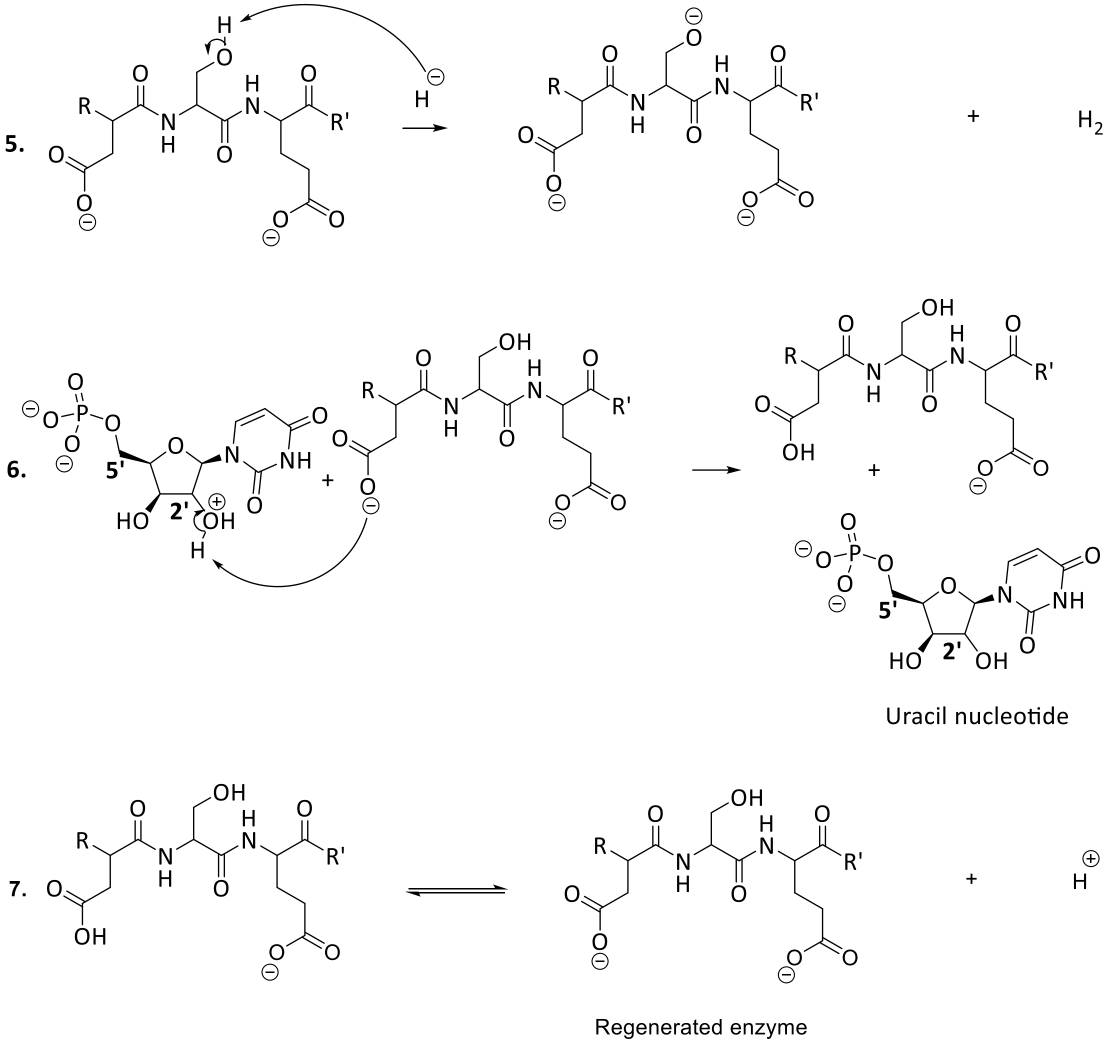
Regarding uracil nucleotide synthesis, the first step is the conversion of thymine nucleotide to produce uracil nucleotide (Scheme 12). This reaction sequence is facilitated by the delocalisation of free double electrons upon the ribose intra cyclic oxygen to afford the corresponding carbon oxonium ion and thymine enolate (Scheme 12, reaction 1). The following reaction is the nucleophilic addition of uracil to an adequate electrophile to generate a replaced thymine nucleotide bearing an uracil moiety (Scheme 12, reaction 2). This intermediate product can now react with a molecule of water to eject a hydride ion to the enzyme advantage. In other words, the hydride ion will be trapped by the enzyme serine residue to induce the resulting hydrogen molecule, and a hydroxylated intermediate compound, which will be deprotonated by the enzyme to furnish the desired uracil nucleotide (Scheme 12, reactions 4-6). In this perspective, it has been reported that the hydrolase catalytic centre, which catalyzes the deoxyribose hydroxylation reaction contains naturally aspartate, serine and glutamate residues.[7]



R = Hydrolase aminoacids
R' = Hydrolase aminoacids



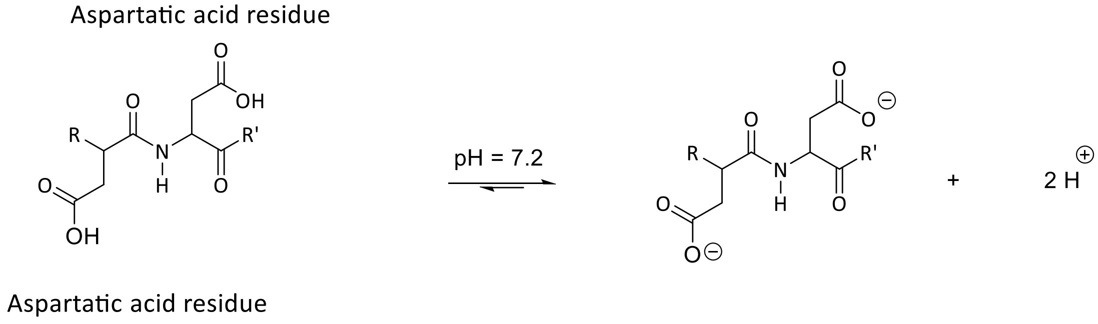
Scheme 12a



Scheme 12b

RIBONUCLEIC ACID SYNTHESIS

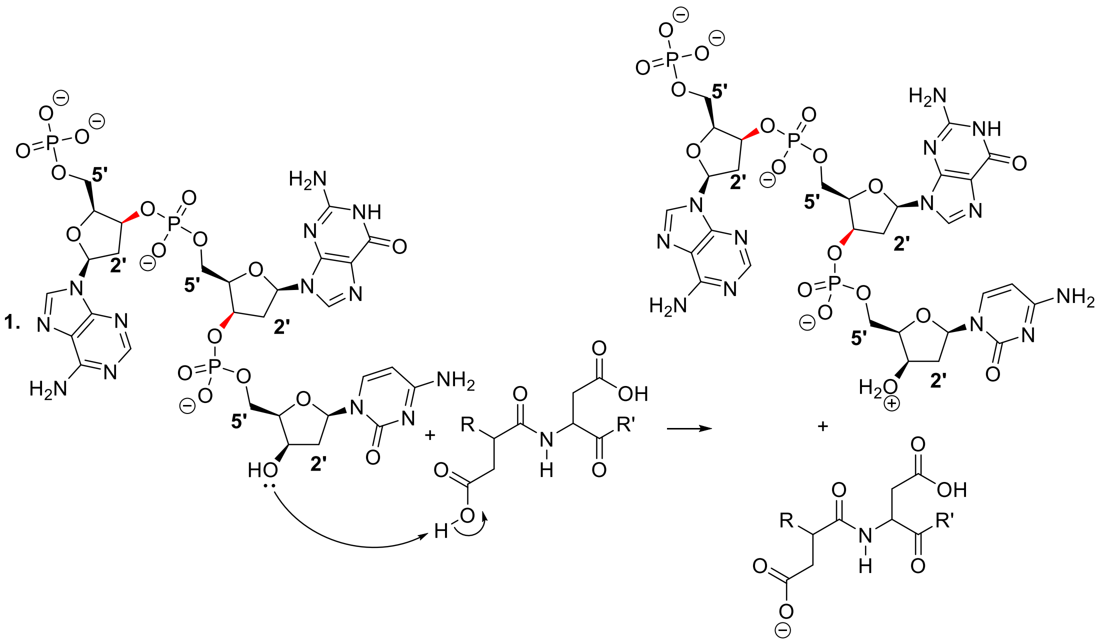
It has been reported that two Aspartate residues are among the bacteriophage RNA polymerase catalytic site (Scheme 13).[8] Because of the basic characteristic of the physiological medium, the aspartic acid carboxylic groups easily dissociate to furnish the corresponding conjugate bases (Scheme 13). It is important to mention that, according to the experimental observations, the Human physiological pH is about 7.4. [9]



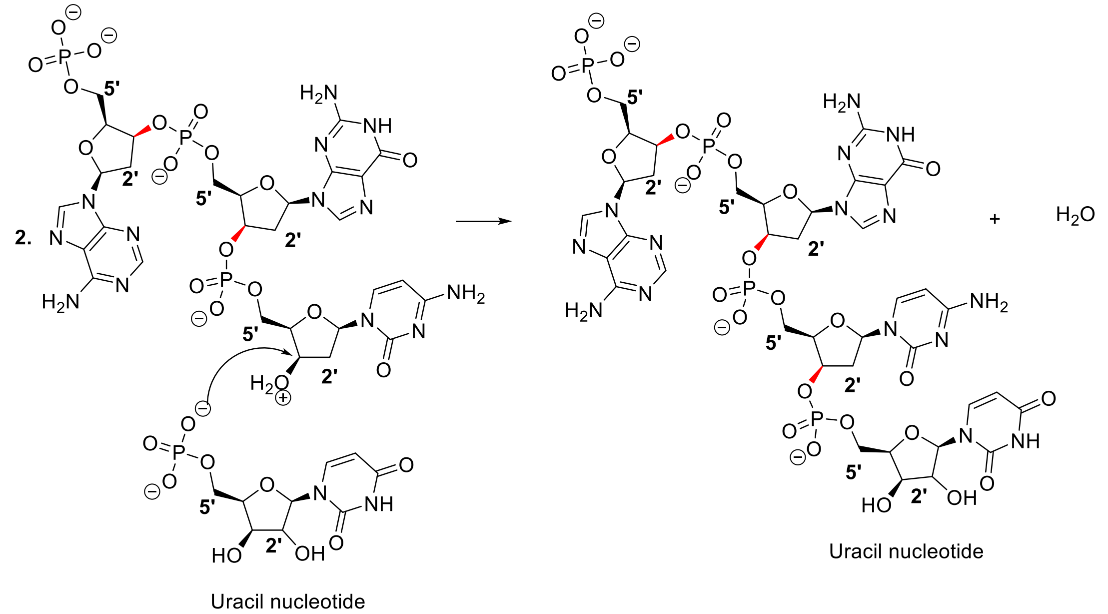
R = Amino acid residues of the RNA polymerase
R' = Amino acid residues of the RNA polymerase

Scheme 13

To perform the RNA synthesis, the first reaction sequence is to substitute a deoxyribose hydroxyl group of the cytosine nucleotide by uracil nucleotide (Scheme 14, reactions 1-2). This substitution reaction permits to generate a corresponding intermediate compound, which will be hydroxylated in the second reaction stage to overcome the RNA synthesis (Scheme 12b).

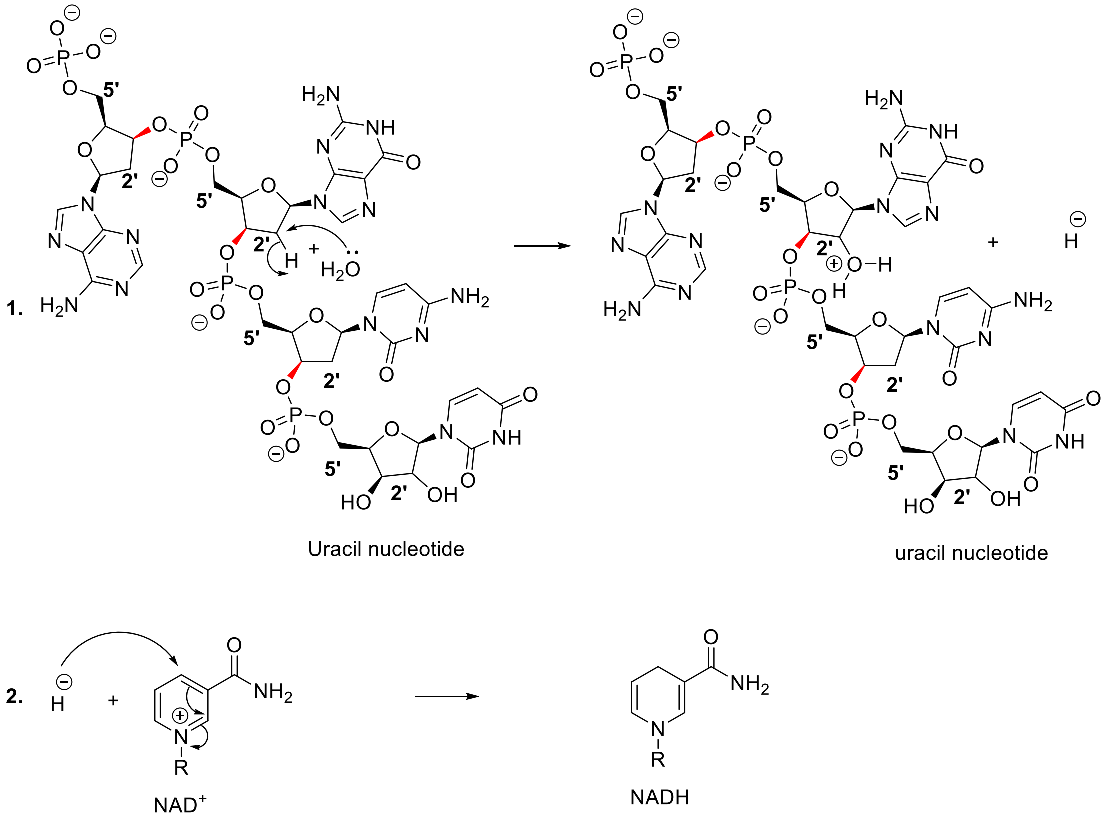


Scheme 14a

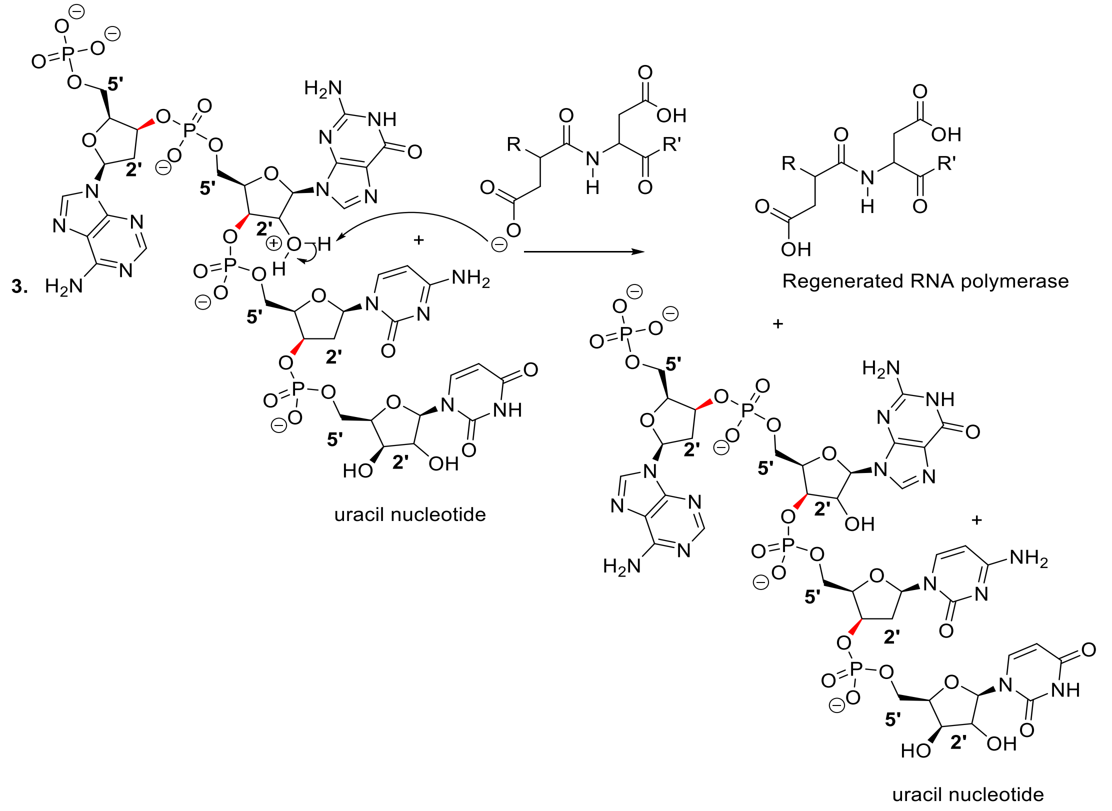


Scheme 14b

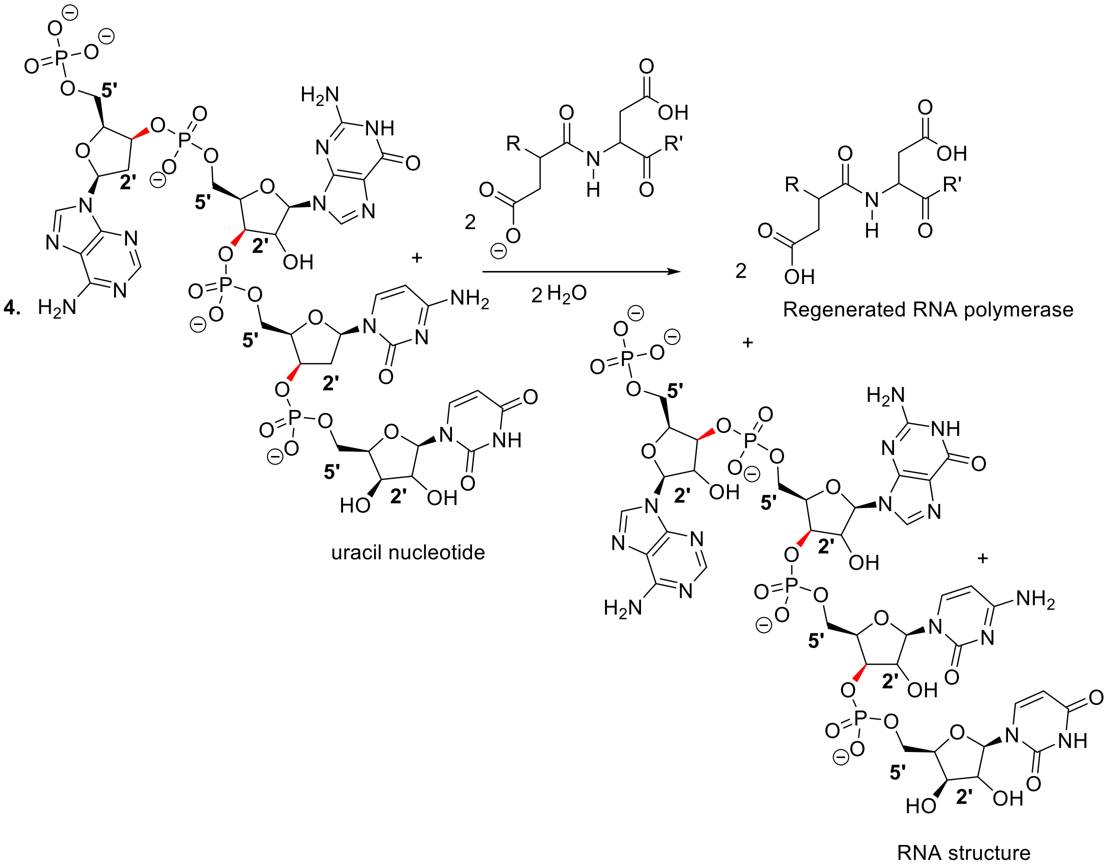
The following step is the hydroxylation of the deoxyribose carbon atom **2'** of the DNA nucleotides to produce RNA nucleotides (Scheme 15). In this perspective, the addition of 3 molecules of water to carbons 2' will eject 3 hydride ions, which will be captured by 3 molecules of NAD⁺ (nicotinamide adenine dinucleotide oxidized form) coenzyme to yield a corresponding product as well as NADH (nicotinamide adenine dinucleotide hydrogenated or reduced form) (Scheme 15). To finalize the RNA synthesis process, the RNA polymerase carboxylate group will remove water protons to regenerate this enzyme including the RNA structure (Scheme 15c).



Scheme 15a



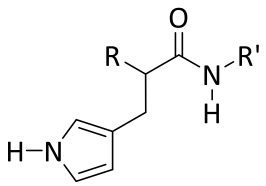
Scheme 15b



Scheme 15c

ENZYMATIC NUCLEIC ACID HYDROLYSIS

The hydrolysis of nucleotide phosphodiester bonds is essentially degraded by phosphodiesterase.[9] In this regard, the enzymatic hydrolysis is either an acid hydrolysis or a basic hydrolysis due to the chemical behaviour of the catalytic amino acid residues of the enzyme. Indeed, the amino acid residues into the enzyme catalytic site may behave as acids or bases since they can release protons or accept them depending on the reaction medium conditions. In this perspective, it has been reported that histidine residue is the Snake venom phosphodiesterase catalytic root (Figure 3).[11]

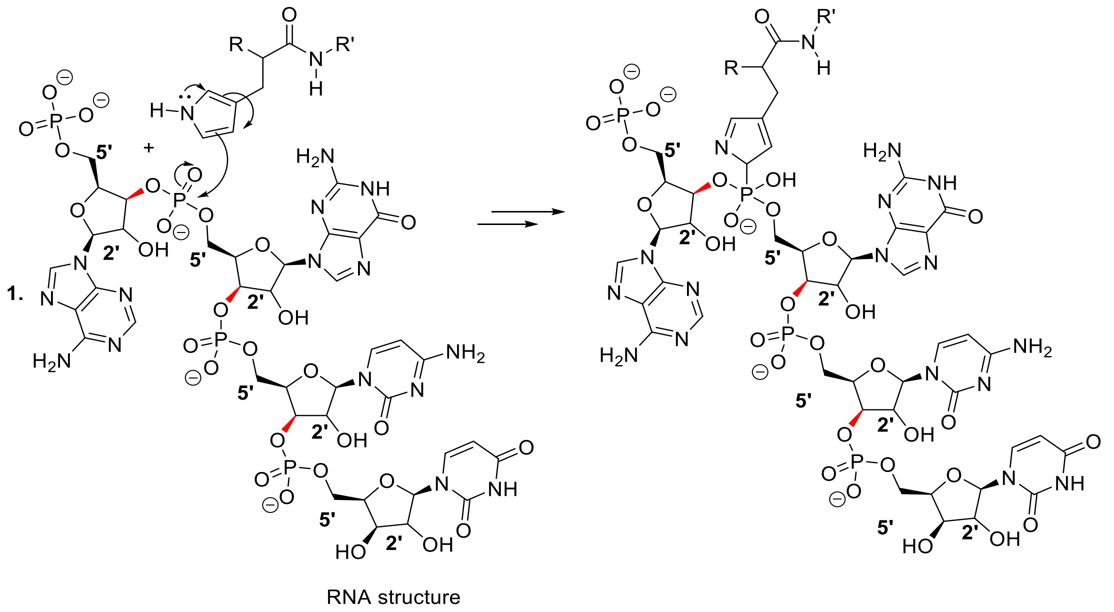


Histidine residue

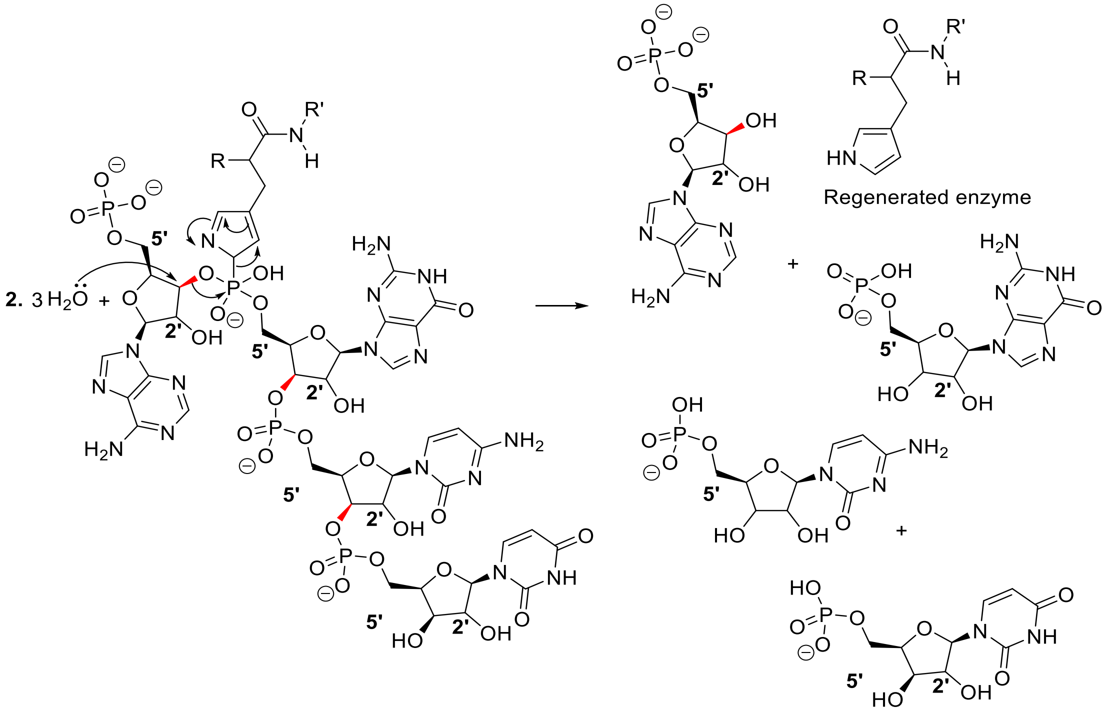
R = Amino acid residues of phosphodiesterase
R' = Amino acid residues of phosphodiesterase

Figure 3

The nucleic hydrolysis mechanism is the same for ribonucleic acid and for deoxyribonucleic acid since the nucleotides into the two acids are connected by phosphodiesters bonds. In other words, the type of mechanism implies the nucleophilic addition of the enzyme to the substrate (RNA) to yield the corresponding intermediate product (Scheme 16, reaction 1). Then, 3 molecules of water react therefore with this intermediate product to decompose the substrate or disconnect the targeted phospho-esters bonds to produce the expected nucleotides as well as the phosphodiesterase (Scheme 16, reaction 2).

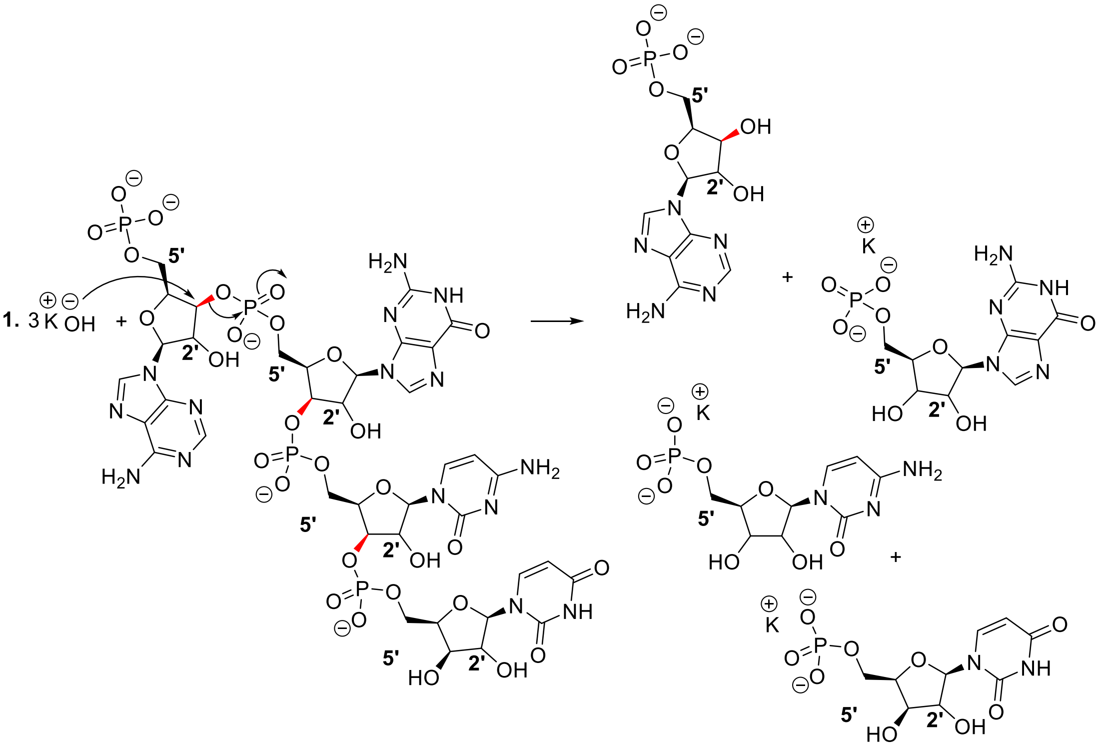


Scheme 16a

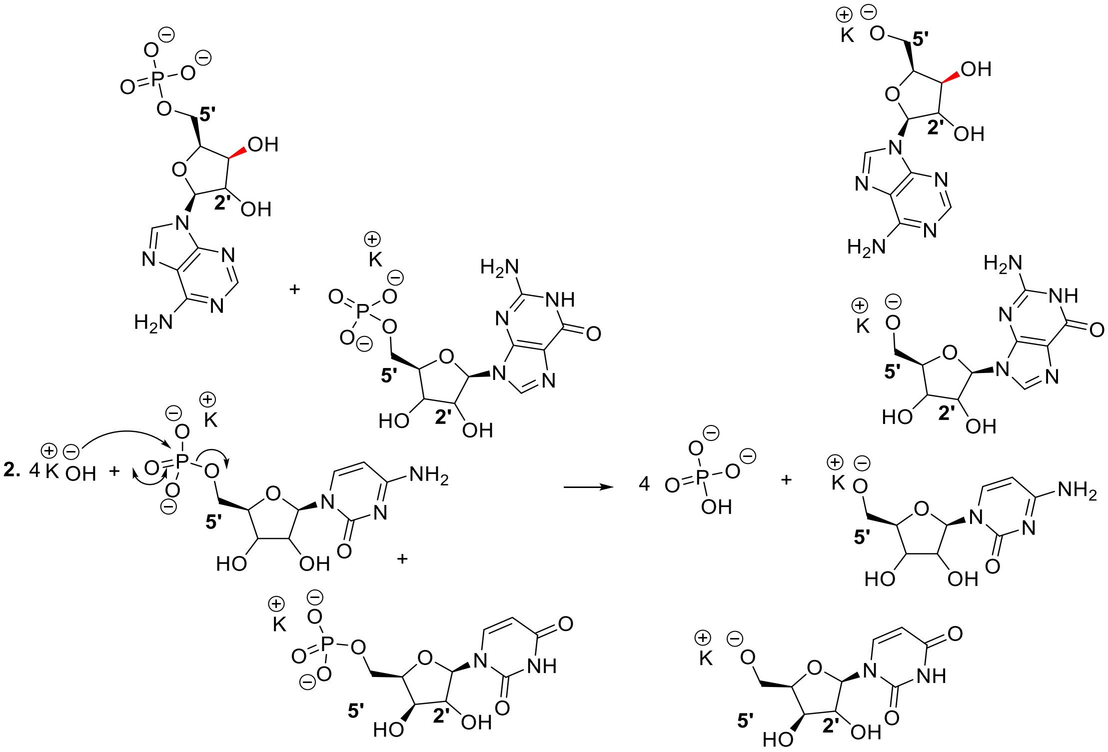


Scheme 16b

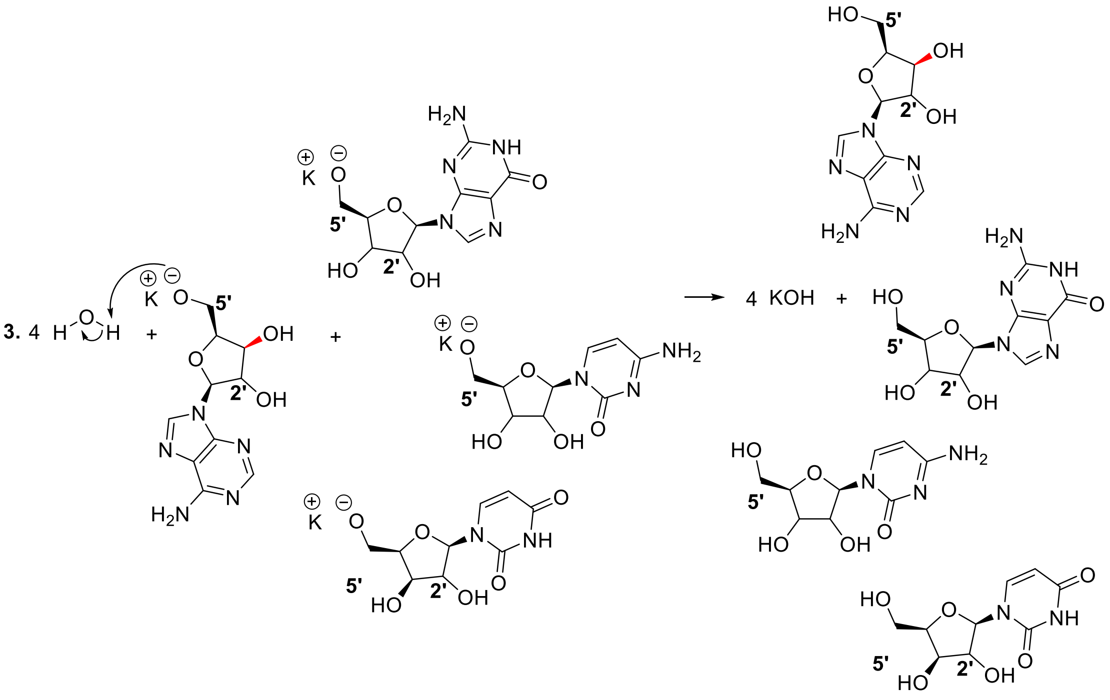
Scientific observations have revealed that nucleosides and nucleotides were isolated from plant nucleic acids in using a base hydrolysis approach such as potassium hydroxide.[12]



Scheme 17a



Scheme 17b



Scheme 17c

In this condition, the nucleophile is a hydroxide ion from the potassium hydroxide dissociation (Scheme 17, reaction 1). The nucleophilic addition to ribose moiety allows to release phosphate groups and to install hydroxide groups to ribose moieties (Scheme 17, reaction 1). In other words, the corresponding nucleotides are therefore produced (Scheme 17, reaction 1). In the following stages, the obtained nucleotides are decomposed as well to furnish the corresponding nucleosides and the potassium hydroxide regeneration because during a base hydrolysis process, the base or potassium hydroxide acts as a catalyst (Scheme 17, reactions 2-3).

CONCLUSION

This conceptual study has demonstrated the detailed reaction mechanisms leading to the chemical or enzymatic synthesis of ribonucleic acid and deoxyribonucleic acid. This conceptual has also displays the enzymatic hydrolysis of the nucleic acids as well as their base hydrolysis. In other words, the nucleic acid sequencing or decomposition is achieved enzymatically because the nature has provided specific enzymes to some creatures such as the Snake venom phosphodiesterase capable to destroy the human nucleic acids. In this approach, the nucleic acid hydrolysis is also carried out into an organic chemistry laboratory due to the ability of a human being who has imitated the nature in order to create reaction conditions suitable to organic reactions realization in an appropriate organic chemistry laboratory.

Conflict of Interest Statement

I declare that I do not have a conflict of interest regarding the publication of this paper.

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