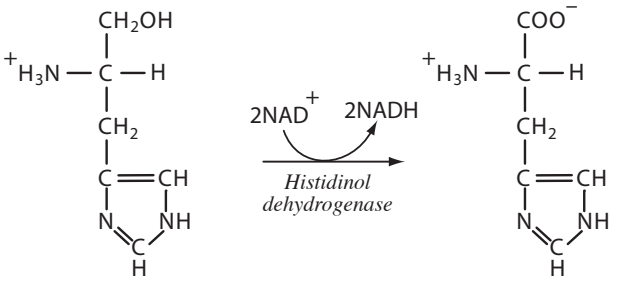
Reactions of Alcohols
Practice Items

1. Ethanol is metabolized to acetaldehyde in the cytosol of liver cells by alcohol dehydrogenase. Consumption of ethanol in excess can disregulate cellular metabolism by inhibiting gluconeogenesis and promoting fatty acid synthesis by making conditions in the cytosol too . . .

A. reducing
B. oxidizing
C. acidic
D. basic

2. Histidinol dehydrogenase is the final step in histidine biosynthesis.



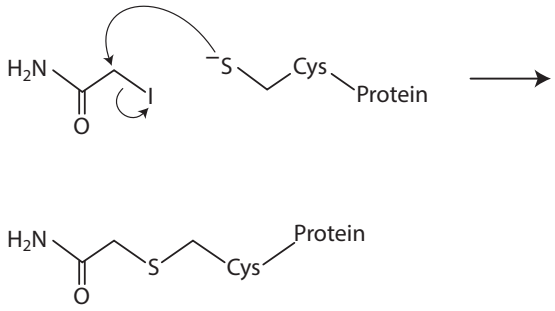
L-Histidinol Histidine

What change has occurred to the oxidation state of the hydroxyl bearing carbon of histidinol as a result of this reaction?

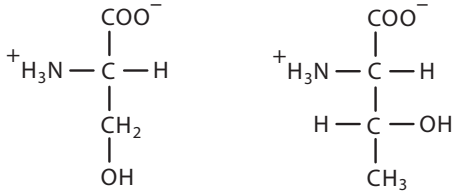
A. –1 → +3
B. 0 → +3
C. 0 → +4
D. +1 → –3

3. 2-Iodoacetamide is an alkylating agent used for peptide mapping purposes. It binds covalently with the thiol groups of cysteine residues preventing the formation of disulfide bonds. 2-Iodoacetamide may also be utilized as an irreversible inhibitor of enzymes, such as glyceraldehyde-3-phosphate dehydrogenase, that employ a reactive cysteine in their mechanism.

The figure below depicts the alkylating mechanism of 2-iodoacetamide.



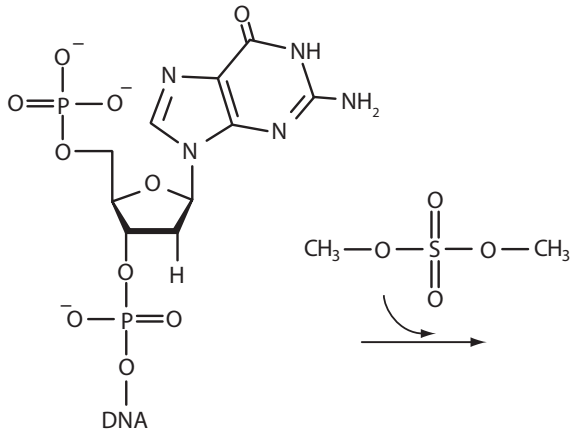
Tthe alkylation may also occur at other locations in undesireable side reactions including upon N-terminal serines or threonines with the former more apt to occur. Which of the following describes one of the reasons that serine residues are more likely to undergo alkylation than threonine residues?



Serine Threonine

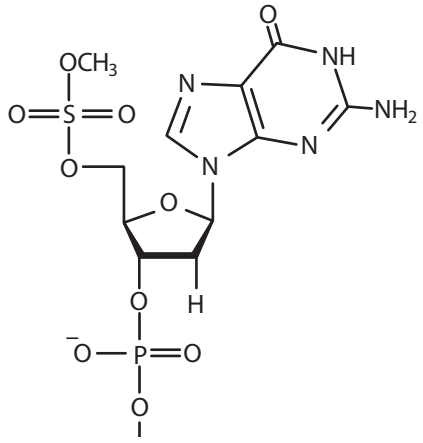
A. The hydroxyl group is a poorer leaving group from threonine than serine.
B. Carbocation formation is more likely to occur with threonine than with serine.
C. The serine hydroxyl group is less hindered than the threonine hydroxyl group.
D. The hydroxyl group of serine has a higher pK_a than that of threonine.

4. Below is the first step in the chemical cleavage method of DNA sequencing developed by Maxam and Gilbert.

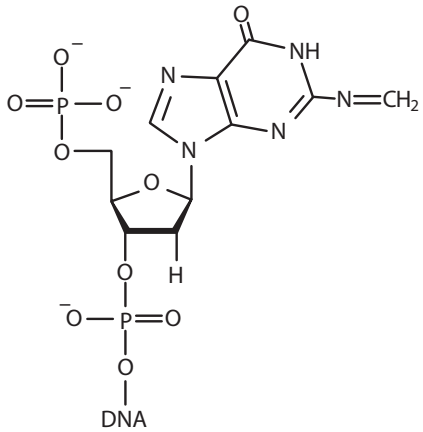


Which of the following structures represents the product of this reaction?

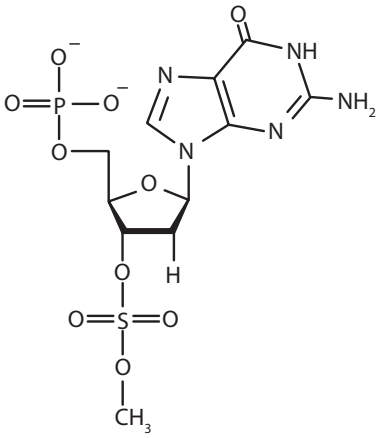
A.



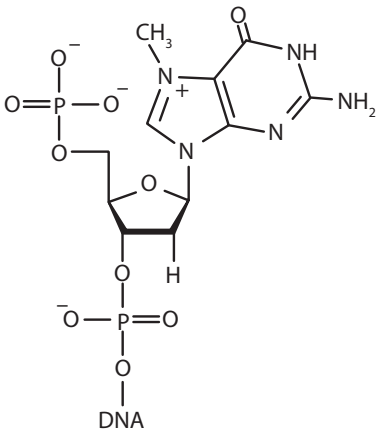
B.



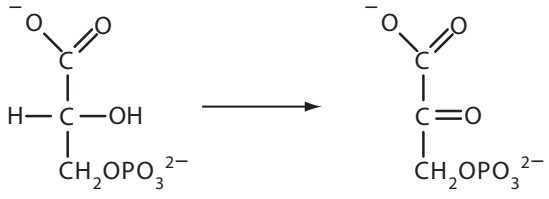
C.



D.



5. 3-phosphoglycerate dehydrogenase is a step in serine biosynthesis.

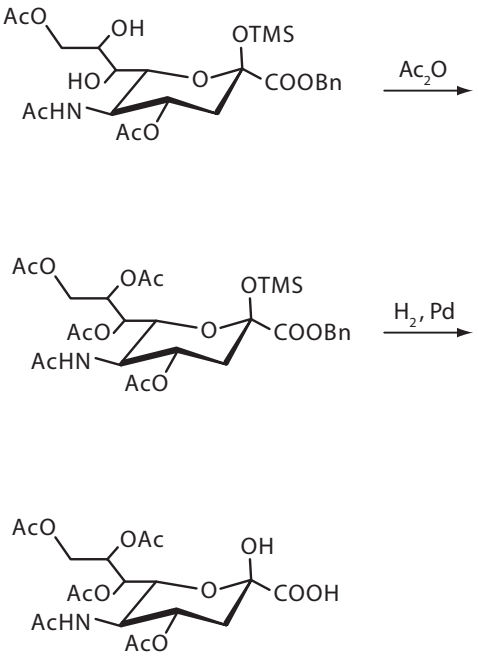


What change has occurred to the oxidation state of the hydroxyl bearing carbon of 3-phosphoglycerate as a result of this reaction?

A. −1 → +2
B. 0 → +2
C. 0 → +4
D. +1 → +2

6. Because postglycosylation acetylation of sialic acid is important to virus pathogenesis and mammalian immune response, the structural and functional understanding of these analogues is an area of active reasearch. Techniques for benchtop synthesis would afford the corresponding sialic acid analogues as useful research tools. This is one of the applications that make methodologies for selective modification of carbohydrate alcohols important synthetic tools in organic chemistry.

The figure below shows the final steps in a synthetic route to 5-N-Acetyl-4,7,8,9-tetra-O-acetylneuraminic acid.

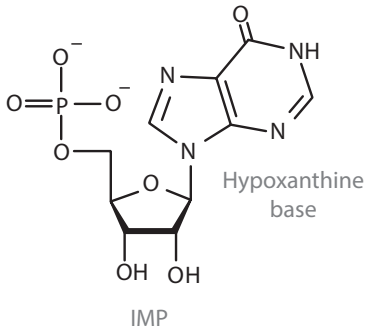


OTMS in the figure above represents . . .

A. **a** silyl ether
B. **a** sulfonic ester
C. **a** mercaptan
D. **a** purine

The following passage pertains to questions 7 - 9.

Bioynthesis of both of the purine ribonucleotides found in RNA, AMP and GMP, begins with a common pathway – the synthesis of inosine monophosphate from the starting material α-ribose-5-phosphate. α-Ribose-5-phosphate is a product of the pentose phosphate pathway.

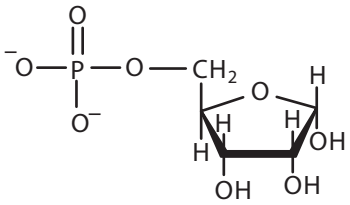


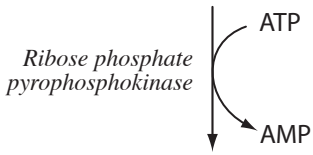
IMP

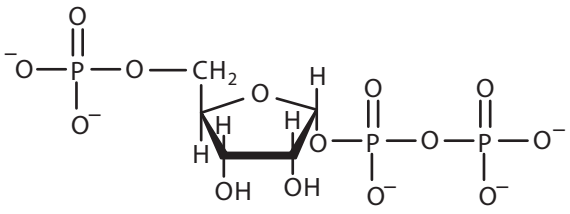
The pathway from α-ribose-5-phosphate to IMP is comprised of 11 steps. The first two steps are shown in the figure at right.

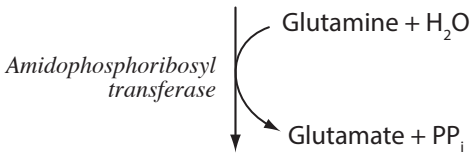
In the first step of IMP synthesis, ribose phosphate pyrophosphokinase reacts α-ribose-5-phosphate with ATP to form 5-phosphoribosyl-α-pyrophosphate (PRPP). A pyrophosphoryl group is transfered to the C1 carbon of ribose-5-phosphate.

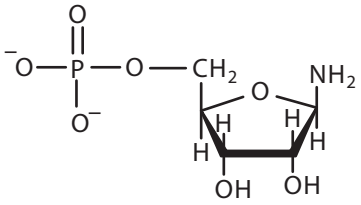
In the second step, amidophosphoribosyl transferase catalyzes the conversion of 5-phosphoribosyl-α-pyrophosphate (PRPP) into 5-phosphoribosyl-β-amine (PRA), using the amine group from a glutamine sidechain. Amidophosphoribosyl transferase possesses two catalytic domains: a glutaminase domain that produces ammonia from glutamine by hydrolysis and a phosphoribosyltransferase domain that binds the ammonia to ribose-5-phosphate. Besides having their respective catalytic abilities, the two domains coordinate with one another to ensure that all the ammonia produced from glutamine is transferred to PRPP and no other nucleophile than ammonia attacks PRPP. This is achieved mainly by blocking formation of ammonia until PRPP is bound and channelling the ammonia to the PRTase active site.

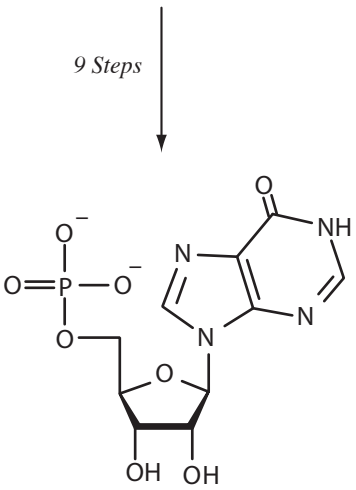












7. A researcher carried out the phosphate pyrophosphokinase reaction with [1-^{18}O]ribose-5-phosphate and ATP in the reaction vessel. The reaction was run to completion. The PRPP product was isolated successfully and mass spectroscopy carried out. The mass spectrum fingerprint of the PRPP obtained showed

A. pure ^{18}O labeled PRPP
B. pure unlabeled PRPP
C. a mxture of labeled and unlabeled PRPP in 1:1 ratio
D. a mixture with unlabeled PRPP predominating

8. The role ATP plays in 'activating' ribose-5-phosphate in purine biosynthesis is most like a common benchtop purpose of which reagent?

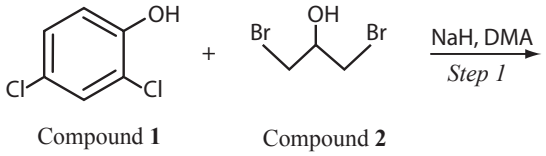
A. trimethylsilyl chloride
B. geranyl pyrophosphate
C. ***p***-toluenesulfonyl chloride
D. pyridinium chlorochromate

9. Based on reagent vs. product stereochemistry, Students A, B, C, & D debated whether the amidophosphoribosyl transferase reaction occurs via SN1 or SN2 mechanism. Student A argued that evidence for SN2 was unequivocal due to the inversion of configiburation at C1. Student B countered that SN1 mechanism might be capable of producing a stereospecific result in the biochemical context. Student C argued for competing reactions consistent with the weak nucleophile. Student D argued that neither SN1 nor SN2 would describe the mechanism but imine formation instead. Which student is correct?

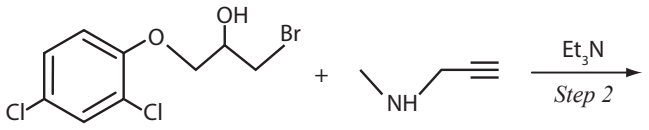
A. Student A
B. Student B
C. Student C
D. Student D

The following passage pertains to questions 10 - 14.

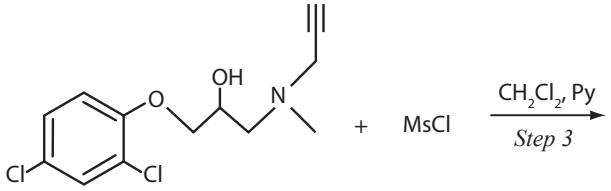
Chemists devised a synthesis of N-[3-(2',4'-dichlorophenoxy)-2-^{18}F-fluoropropyl]-N-methylpropar gylamine (^{18}F-fluoroclorgyline) as a potential positron emission tomography (PET) radiotracer for monoamine oxidase A (MAO-A).



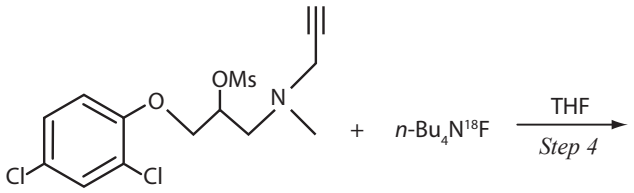
Compound **1** Compound **2**



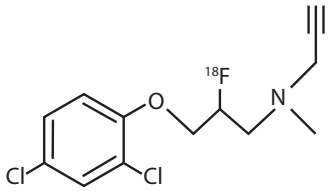
Compound **3** Compound **4**



Compound **5** Compound **6**



Compound **7** Compound **8**



18F-fluoroclorgyline

10. Which is the best description of the dimethylacetamide (DMA) solvent utilized in Step 1?

A. nonpolar
B. protic
C. aprotic
D. aromatic

11. Which step in the spathway includes the inversion of the configuration of a chiral center?

A. Step 1
B. Step 2
C. Step 3
D. Step 4

12. What is the rationale of Step 3?

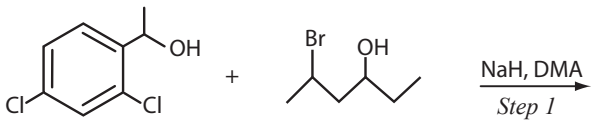
A. ensuring that synthesis is regiospecific
B. protecting the hydroxyl group from oxidation to a carbonyl group
C. preventing formation of precipitate
D. transforming the hydroxyl group into a good leaving group

13. Which of the following results from the action of NaH in Step 1?

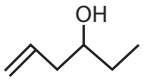
I. acid catalysis
II. activation of the nucleophile
III. stabilizing the transition state
IV. production of H_2 gas

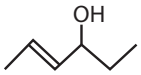
A. I only
B. I and II
C. II and IV
D. I, II, and III

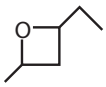
14. The alternative reagents shown below were utilized in an attempt to carry out a variation of the reaction in Step 1:



The product was quenched with acid and purified of residual 1-(2,4-dichlorophenyl)ethanol. What was the major product obtained?

A. 

B. 

C. 

D.