



nucleophilic substitution reactions. The appearance of the azide (N_3^-) group in the product indicates it needs to be added to the reaction mixture to form this specific product. You recall that nucleophiles are often delivered to reaction mixtures as ionic salts including appropriate spectator counter-cations.

Choice (D) is correct because it both includes the azide nucleophile and an appropriate counterion, sodium cation.

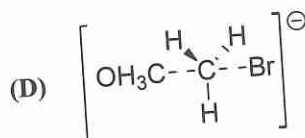
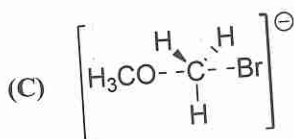
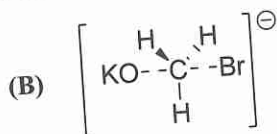
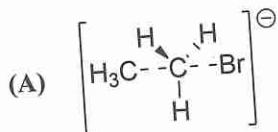
Choice (B) is not correct because iodine and nitrogen do not make an ionic bond, and therefore cannot supply the needed azide anion.

Choices (A) and (C) are not correct because they would not supply azide anion to the reaction mixture.

Practice Problems: PQ-27

SQ-9.

Which structure best depicts the transition state for the reaction of CH_3Br with CH_3OK in CH_3OH ?

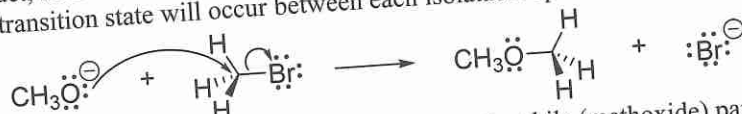


Knowledge Required: (1) Mechanism of the $\text{S}_\text{N}2$ reaction. (2) How to draw transition states.

Thinking it Through: You know that the reaction of methyl bromide (CH_3Br) with potassium methoxide (CH_3OK) is a bimolecular nucleophilic substitution ($\text{S}_\text{N}2$) reaction. You also know that the mechanism of $\text{S}_\text{N}2$ reactions proceeds through a concerted mechanism where the bond to the nucleophile is partially formed, and the bond to the leaving group is partially broken.

In addition, you know that the $\text{S}_\text{N}2$ mechanism occurs by the nucleophile attacking from the "backside" of the alkyl halide, meaning the nucleophile must approach at an angle 180° away from the leaving group. You also know that on methoxide, it is the oxygen atom that is nucleophilic and not the carbon atom.

In general, for reaction diagrams you recall that there is a transition state between each reactant-intermediate and product, so in order to identify transition states you must first draw the mechanism of the reaction. You know a transition state will occur between each isolatable species in your mechanism:



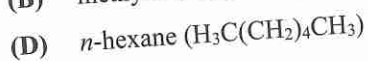
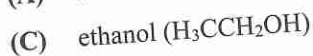
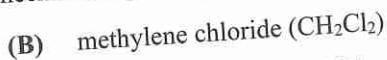
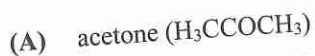
Choice (C) is correct because it shows the bond to the nucleophile (methoxide) partially formed and the bond to the leaving group (bromide) partially broken. The new bond is forming from the nucleophile's oxygen atom.

Choice (A) is not correct because the attacking nucleophile is not a methyl carbanion. Choice (B) is not correct because the attacking nucleophile is not an oxygen/potassium salt. In addition, this oxygen atom would carry a -2 charge. Choice (D) is not correct because although it shows a bond forming from the nucleophile, the atom forming the bond is a carbon, not the nucleophilic oxygen.

Practice Problems: PQ-28 and PQ-29

SQ-10.

Which solvent best promotes a unimolecular ($\text{S}_\text{N}1$) mechanistic pathway?



Knowledge Required: (1) Mechanism of unimolecular substitution ($\text{S}_\text{N}1$) pathways. (2) Solvent effects on nucleophilic substitution pathways.

Thinking it Through: You know that solvents can play a role in the kinetics of nucleophilic substitution reactions. You recall that nonpolar solvents do not allow S_N1 reactions to occur because they cannot stabilize the ionic intermediates, but polar solvents do. You also know that polar protic solvents, like water and alcohols, tend to assist with leaving group dissociation. They also solvate the ionic intermediates, so they are known to speed up unimolecular pathways like S_N1 .

You recall that most organic reactions require a polar solvent to dissolve the reactants: S_N1 reactions occur in polar protic solvents and S_N2 reactions occur in polar aprotic solvents. You know that in this case you do not want the solvent to interact too strongly with the nucleophile, as the nucleophile is involved in the rate-determining-step, thus a solvent with a lower dielectric constant, while still capable of dissolving the molecules, is preferred.

Choice (C) is correct because ethanol is a polar protic solvent, preferred in an S_N1 reaction.

Choices (A) and (B) are not correct because although they are polar solvents, they are aprotic. Choice (D) is not correct because hexanes are a nonpolar solvent.

Practice Problems: PQ-30

Practice Questions (PQ)

PQ-1. The effect of doubling the volume of alcohol for the reaction would be to multiply the reaction rate by a factor of



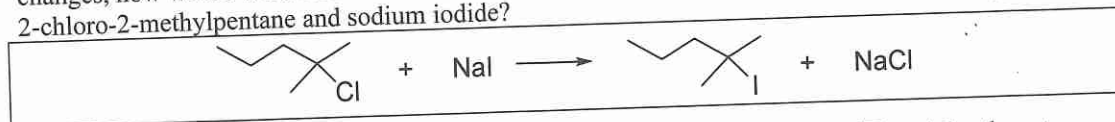
(A) $\frac{1}{4}$.

(B) $\frac{1}{2}$.

(C) 2.

(D) 4.

PQ-2. Consider the reaction of 2-chloro-2-methylpentane with sodium iodide. Assuming no other changes, how would it affect the rate if one simultaneously doubled the concentration of 2-chloro-2-methylpentane and sodium iodide?



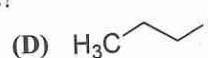
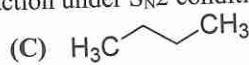
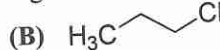
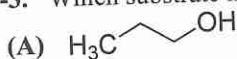
(A) no effect

(B) doubles the rate

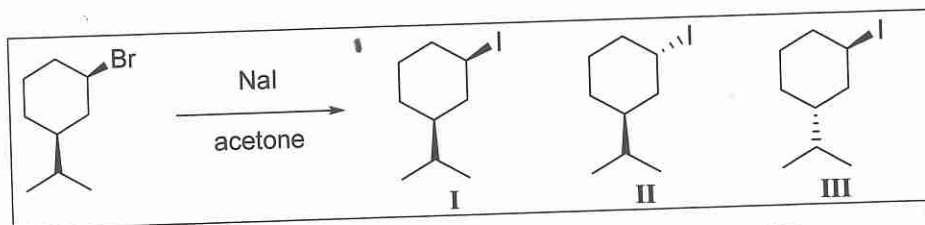
(C) quadruples the rate

(D) triples the rate

PQ-3. Which substrate has the highest relative rate of reaction under S_N2 conditions?



PQ-4. Predict the major product(s).



(A) I

(B) II

(C) III

(D) I and II

PQ-5. A bimolecular nucleophilic substitution (S_N2) is

(A) a two-step process in which a bond is broken, then a new bond is formed and there is inversion of configuration.

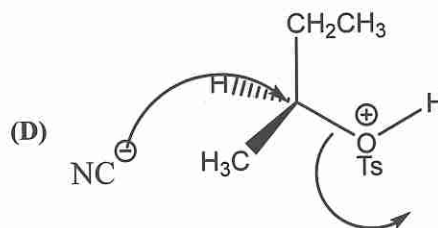
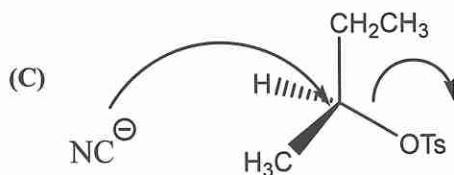
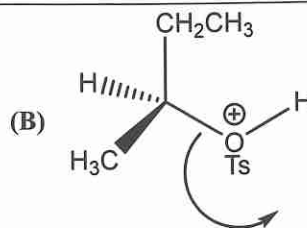
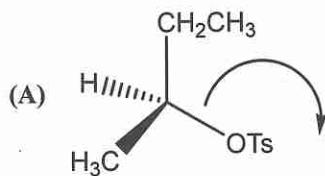
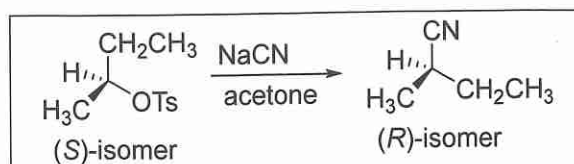
(B) a two-step process in which a bond is broken, then a new bond is formed and there is retention of configuration.

(C) a one-step process with inversion of configuration.

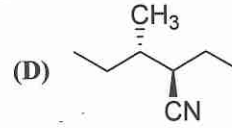
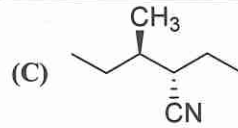
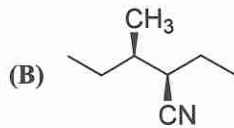
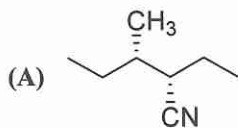
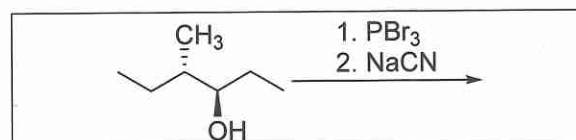
(D) a one-step process with retention of configuration.



PQ-6. What is the rate determining step of this reaction?



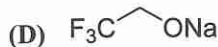
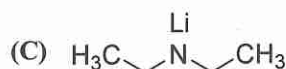
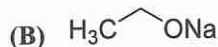
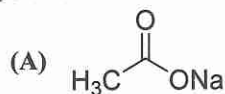
PQ-7. What is the major product?



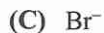
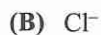
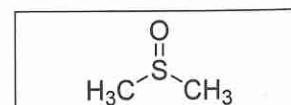
PQ-8. Consider the substitution reaction that takes place when (R)-3-bromo-3-methylhexane is treated with methanol. What would be true?

- (A) The reaction would take place only with inversion of configuration at the stereogenic center.
 (B) The reaction would take place only with retention of configuration at the stereogenic center.
 (C) The reaction would take place with racemization.
 (D) The alkyl halide does not possess a stereogenic center.

PQ-9. What is the *weakest* nucleophile?

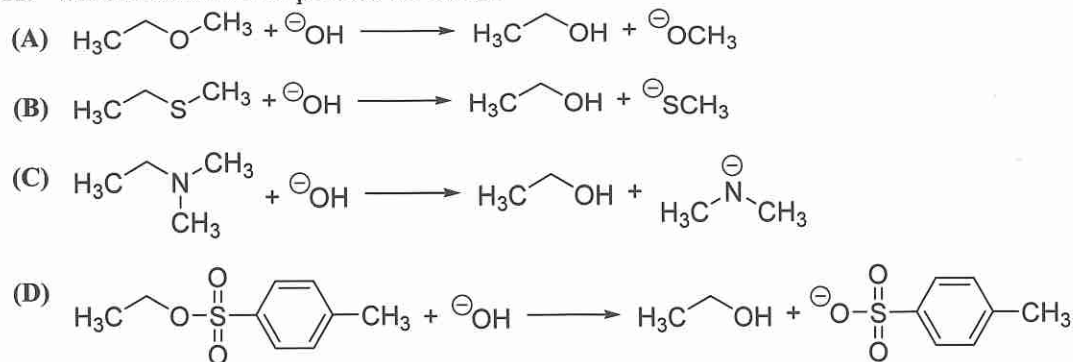


PQ-10. What is the strongest nucleophile when dimethyl sulfoxide (DMSO) is used as a solvent in an $\text{S}_{\text{N}}2$ reaction?

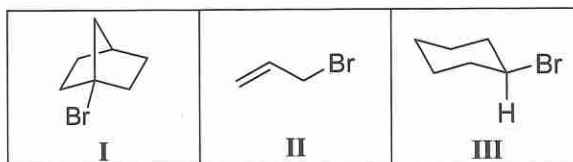




PQ-11. Which reaction would proceed the fastest?



PQ-12. What is the order from slowest to fastest for the rates of the $\text{S}_\text{N}2$ reactions of these alkyl bromides with $\text{CH}_3\text{S}^-/\text{DMSO}$?



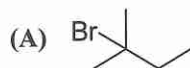
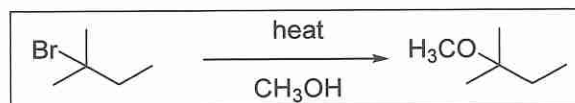
(A) $\text{III} < \text{II} < \text{I}$

(B) $\text{I} < \text{III} < \text{II}$

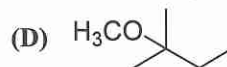
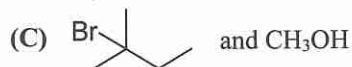
(C) $\text{II} < \text{I} < \text{III}$

(D) $\text{II} < \text{III} < \text{I}$

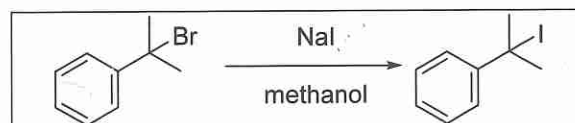
PQ-13. The rate of the reaction is dependent on the concentration of which components?



(B) CH_3OH



PQ-14. What would increase the rate of the reaction?



(A) increase the concentration of the bromide

(B) increase the concentration of NaI

(C) increase the amount of methanol

(D) add a small amount of iodide product

PQ-15. Which statement(s) is/are true regarding leaving groups?

- | |
|--|
| <p>I. Weak bases make good leaving groups.</p> <p>II. Large, polarizable anions make good leaving groups.</p> <p>III. Alkyl groups make good leaving groups.</p> <p>IV. Leaving group ability is only important for $\text{S}_\text{N}2$ reactions.</p> |
|--|

(A) I only

(B) I and II

(C) I, II, and III

(D) I, II, and IV

PQ-16. What would not act as a leaving group?

(A) Br^-

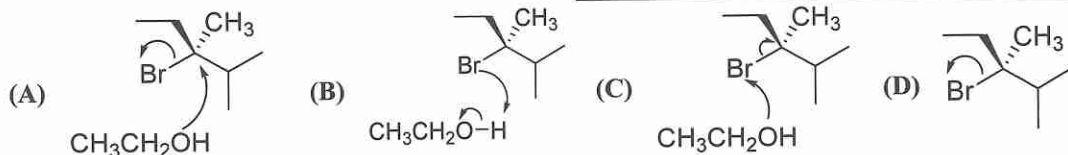
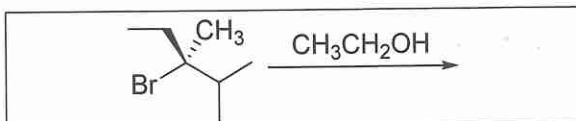
(B) TsO^-

(C) H_2O

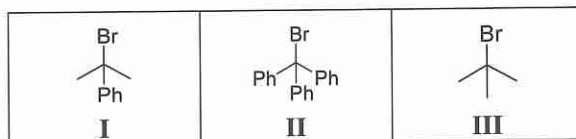
(D) $^-\text{NH}_2$



PQ-17. What is the most likely first step of this reaction's mechanism?



PQ-18. What would the relative rate (from slowest to fastest) of the solvolysis reaction be of these compounds in methanol-acetone?

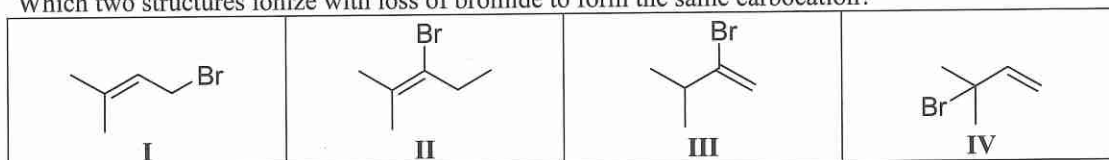


- (A) III < II < I (B) III < I < II (C) II < I < III (D) II < III < I

PQ-19. What will react fastest with NaN_3 ?

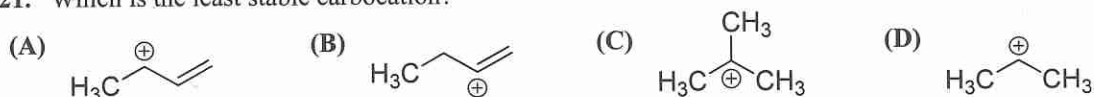


PQ-20. Which two structures ionize with loss of bromide to form the same carbocation?

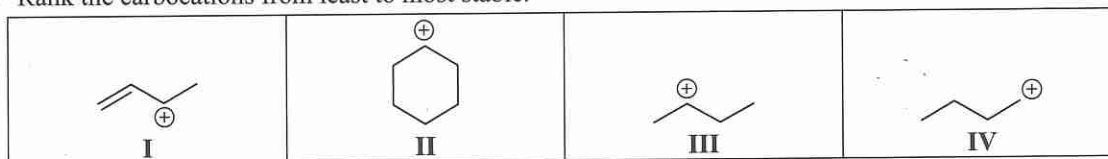


- (A) I and II (B) II and III (C) I and IV (D) III and IV

PQ-21. Which is the least stable carbocation?

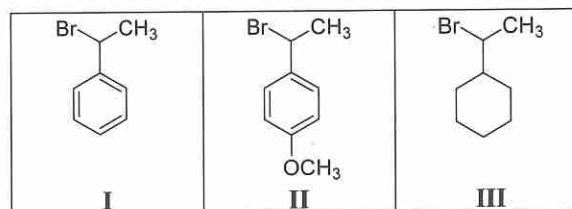


PQ-22. Rank the carbocations from least to most stable.



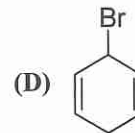
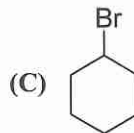
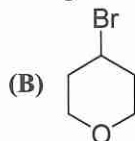
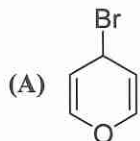
- (A) IV < III < II < I (B) II < I < IV < III (C) IV < III < I < II (D) I < IV < III < II

PQ-23. Rank the structures from slowest to fastest rate of $\text{S}_{\text{N}}1$ reaction.



- (A) I < II < III (B) III < II < I (C) III < I < II (D) II < I < III

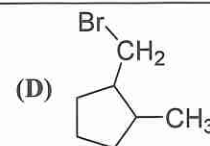
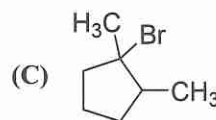
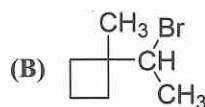
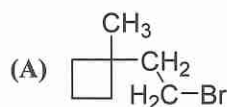
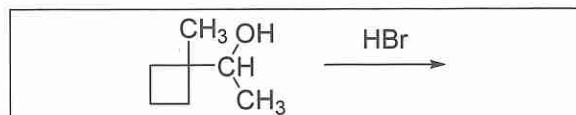
PQ-24. What will most rapidly undergo solvolysis in aqueous ethanol?



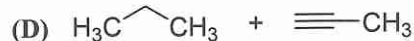
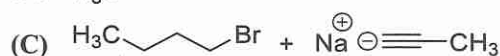
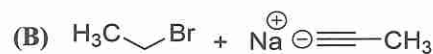
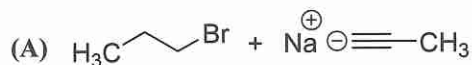
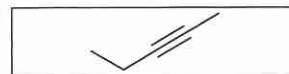
PQ-25. Why must a secondary alcohol react with a haloacid to form an alkyl halide instead of just reacting with the halide nucleophile in a polar aprotic solvent?

- (A) Halides are not strong enough nucleophiles to force this reaction.
 (B) The acid must protonate the hydroxyl group to form a reasonable leaving group.
 (C) Halides won't dissolve in polar aprotic solvents.
 (D) A secondary alcohol is less reactive than a primary alcohol in an S_N1 -like reaction.

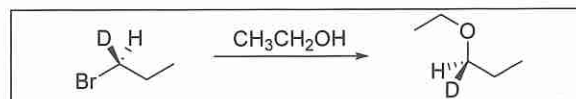
PQ-26. What is the major product of this reaction?



PQ-27. Which reagents could be used to accomplish a synthesis of this compound?



PQ-28. How many mechanistic steps are in the reaction?



(A) 1

(B) 2

(C) 3

(D) 4

PQ-29. How many transition states would appear in a reaction coordinate diagram for the reaction?



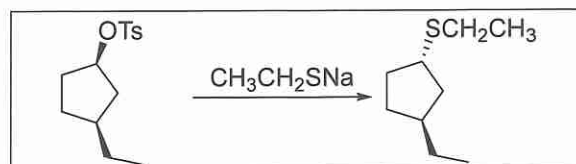
(A) 1

(B) 2

(C) 3

(D) 4

PQ-30. Which solvent will allow this reaction to occur the most rapidly?



(A) methanol

(B) acetone/water

(C) DMSO

(D) hexanes