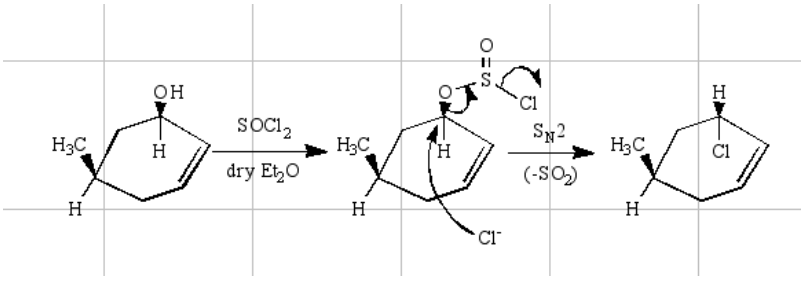
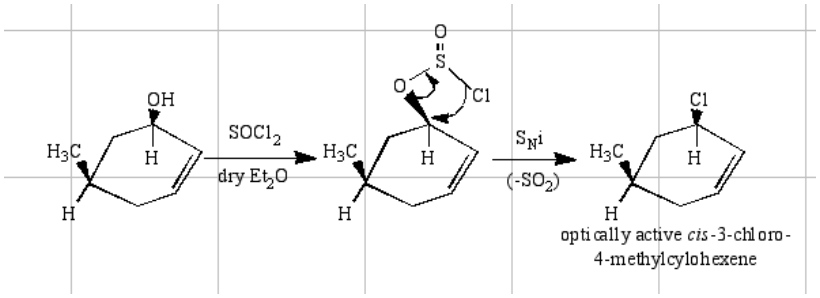
Answers to Questions

Question 1: **C**

Choice A (incorrect): As indicated below, S_N2 displacement of OS(O)Cl by Cl^- is expected to proceed with inversion of configuration at C-3, thereby affording optically active *trans*-3-chloro-5-methylcyclohexene. However, as stated in the passage, the exclusive product of this reaction was found to be the corresponding *cis* isomer (Compound 2, Figure 1).

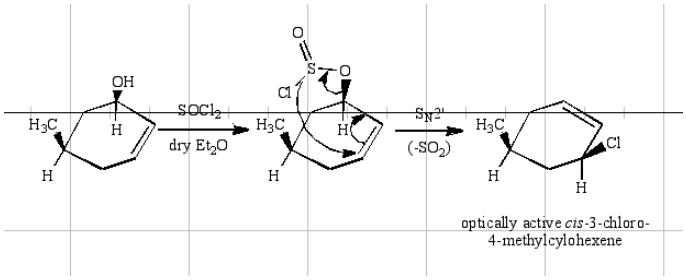


Choice B (incorrect): The mechanism of S_Ni displacement of OS(O)Cl by Cl^- with concomitant retention of configuration at C-3 is shown below:



The product formed *via* S_Ni displacement thus can be seen to possess the 3*R*, 5*R* configuration. However, as indicated in Figure 1, the absolute configuration of the reaction product, Compound 2, is 3*S*, 5*S*.

Choice C (correct response): The mechanism of S_N2' displacement of OS(O)Cl by Cl^- with concomitant allylic rearrangement is shown below:



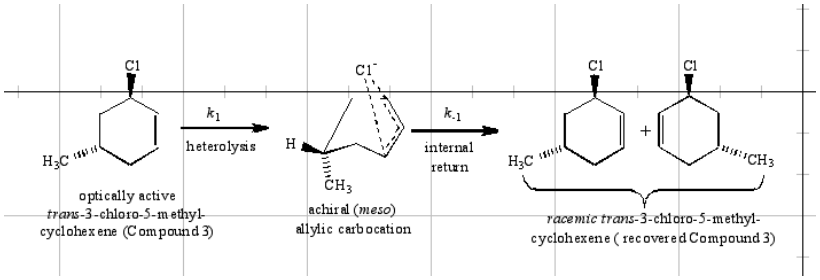
Here it can be seen that the S_N2' displacement reaction results in the formation of 3*S*-chloro-5*S*-methylcyclohexene, which corresponds to the reaction product shown in Figure 1.

Choice D (incorrect) Examination of the mechanisms shown above in connection with Choices B and C indicates that both reactions lead to the formation of optically active *cis*-3-chloro-4-methylcyclohexene. However, it should be noted that the optically active products obtained *via* S_Ni or S_N2' displacement of OS(O)Cl by Cl^- are *enantiomeric*. Since the *exclusive* reaction product is shown in Figure 1 to possess the 3*S*-chloro-5*S*-methylcyclohexene configuration (Figure 1), it follows that the reaction shown in Figure 1 *may* proceed *via* S_N2'- but *not via* S_Ni - displacement of OS(O)Cl by Cl^-.

Question 2: **B**

Unimolecular heterolysis of the C-Cl bond in Compound 3 is expected to afford an allylic carbocation. This species is optically inactive by internal compensation (*meso*) and thus can only afford optically inactive products.

Nucleophilic "topside" re-capture of the intermediate allylic carbocation by Cl^- can occur at either end of the conjugated allylic system with equal probability of occurrence. Thus, “internal return” results in the formation of both enantiomers of *trans*-3-chloro-5-methylcyclohexene, a result that is consistent with information given in *Experiment 2*.



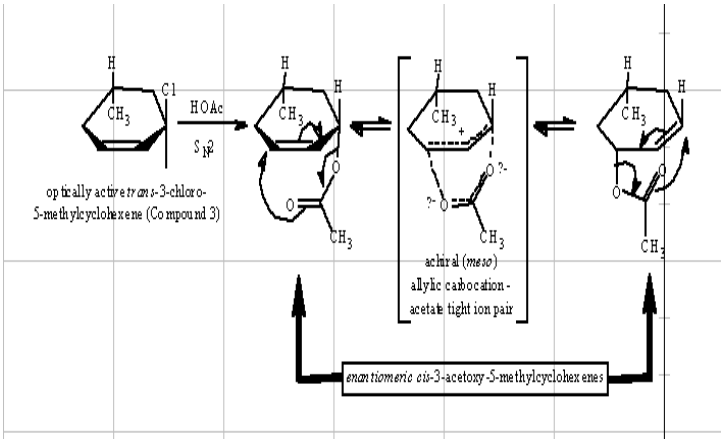
Choice A incorrectly states that heterolysis of the C-Cl bond affords a chiral carbocation.

Choice B correctly states that heterolysis of the C-Cl bond affords an achiral carbocation.

Choices C and D incorrectly suggest that acetolysis of optically active *trans*-3-chloro-5-methylcyclohexene (Compound 3) proceeds with formation of a free radical intermediate.

Question 3: **C**

The mechanism shown below accounts for the formation of racemic *cis*-3-acetoxy-5-methylcyclohexenes *via* acetolysis of optically active *trans*-3-chloro5-methylcyclohexene.

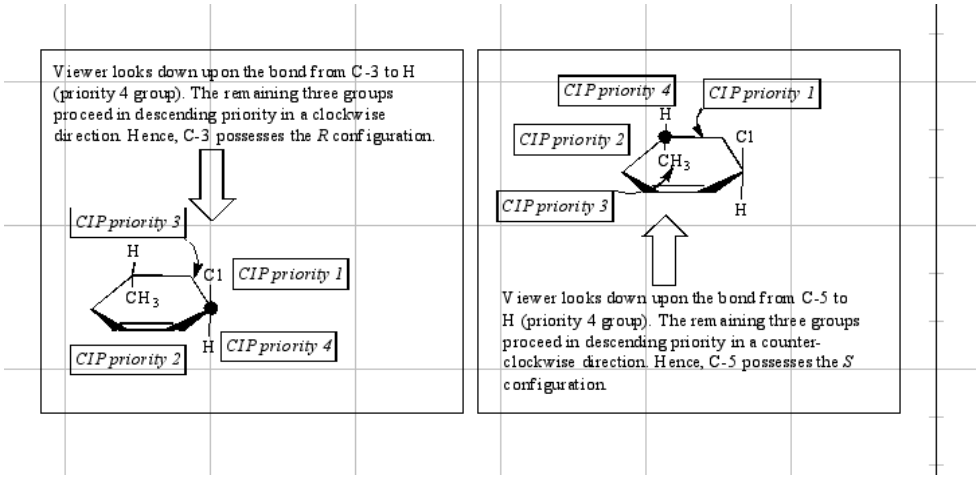


Choices A and B incorrectly suggest that a chiral intermediate is formed in this reaction.

As stated in the paragraph, "The rate of racemization of Compound 3 was found to be more than four times the corresponding rate of acetolysis". It follows that the rate of the return reaction, k_{-1}, must be greater that that of the forward reaction, k_2, that leads to products. Hence, Choice C offers the correct response to this question. Choice D incorrectly suggests that $k_2 > k_{-1}$.

Question 4. B

In the following drawings Cahn-Ingold-Prelog (CIP) sequence rules have been applied to the two chiral carbon centers in Compound 3.



It can be seen that Choice B offers the correct response to this question. Choices A, C and D offer incorrect *R/S* combinations.

Question 5. A

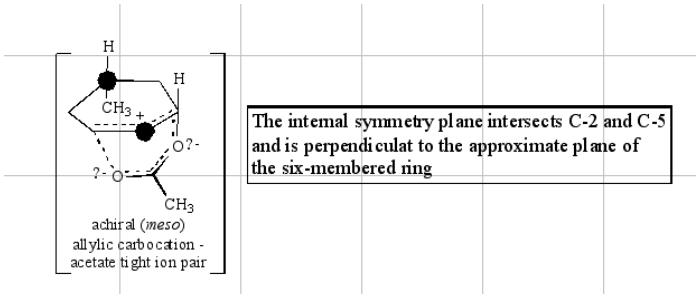
The IR absorption signals at 3060 cm^{-1} and at 1660 cm^{-1} correspond to the **=C-H** stretching vibration and **C=C** double bond stretching vibration, respectively in Compound 1. Reaction with H_2/Pd-C (catalytic hydrogenation) is expected to reduce the C=C double bond in Compound 1, thereby affording *cis*-3-methylcyclohexanol.

Since the reduction product lacks a C=C double bond, its IR spectrum is expected to be transparent in the regions 3060 cm^{-1} and at 1660 cm^{-1}. Thus, as the reaction progresses the intensity of each of the two absorption peaks of interest in Compound 1 is expected to decrease. This situation corresponds to Choice A, which offers the correct response to this question.

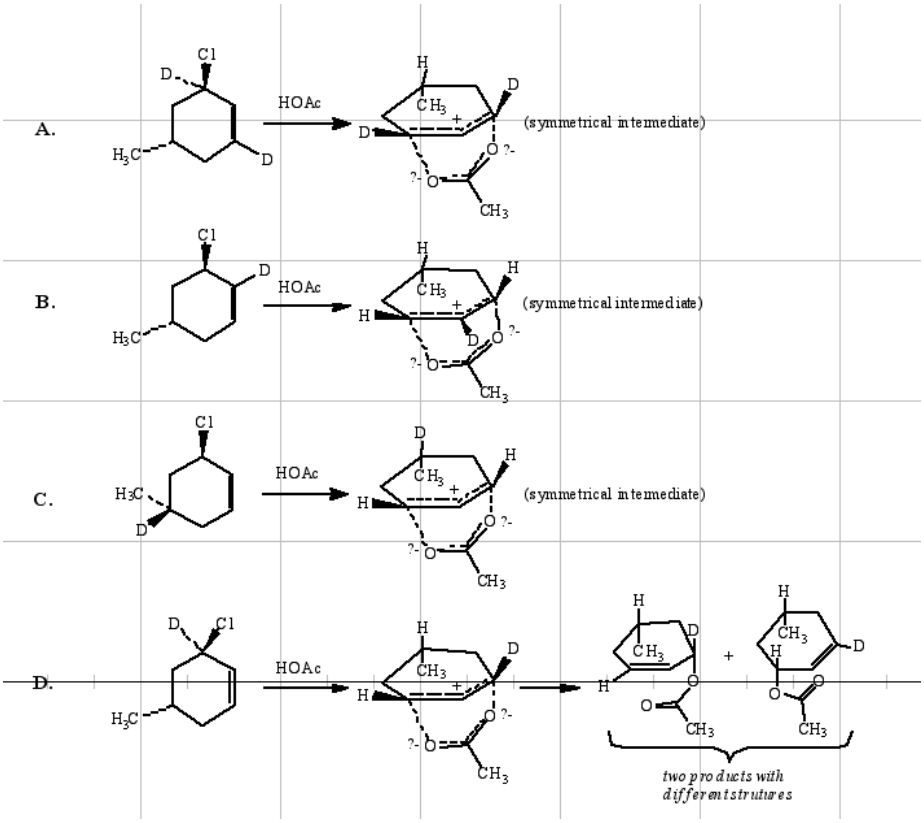
Question 6. D

Refer to the structure drawings that appear in the answer to Question 3 (*vide supra*)

An allylic cation (or allylic cation - anion tight ion pair) can be invoked as a reaction intermediate in the acetolysis of optically active *trans*-3-chloro-5-methylcyclohexene (Compound 3). It should be noted that this intermediate is achiral due to internal compensation (i. e., the allylic cation possesses an internal plane of symmetry that intersects C-2 and C-5.



Specific deuterium substitution of the starting material is only useful if the deuterium atoms are placed in positions that necessarily break the symmetry of the intermediate allylic cation. This is seen to be the situation for Choice D. Choices A, B and C each lead to the formation of a symmetrical deuterium-substituted intermediate..

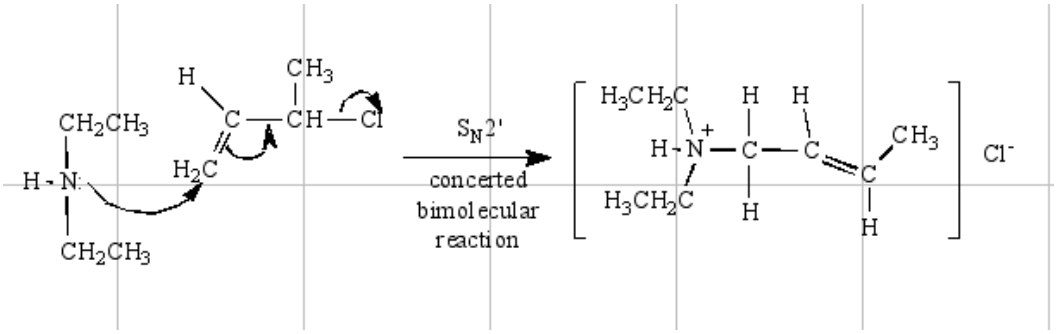


Question 7. C

Among the indicated protons in Compound 3, the vinyl protons are expected to display ^{1}H NMR absorption signals in the region δ 5-6. The -C**H**Cl proton at C-3 is expected to absorb in the region δ 3.5-4 whereas the methyl protons are expected to display absorption signals at highest field, i. e., δ 0.5-1. It follows that Choice C offers the correct response to this question.

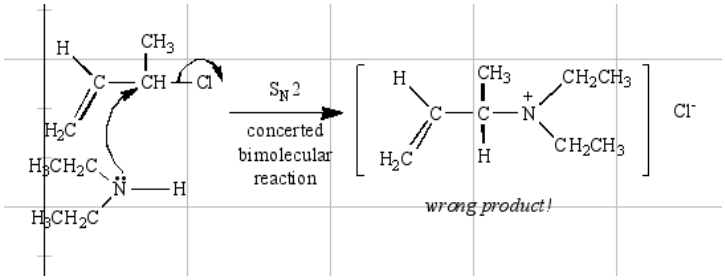
Question 8. C

As shown below, a reasonable mechanism for the reaction of interest involves S_N2' displacement of Cl^- by Et_2N: with concomitant allylic rearrangement.



This concerted bimolecular reaction proceeds with concomitant allylic rearrangement. Thus, Choice C offers the correct response to this question.

Choice A incorrectly suggests that the reaction proceeds *via* nucelophilic attack by diethylamine at the α-carbon atom in α-methylallyl chloride. This approach does not lead to the formation of Compound 5 (*vide infra*).



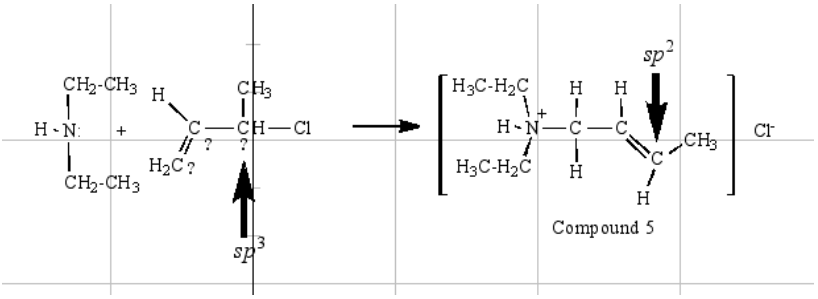
Choice B incorrectly suggests that the reaction proceeds *via* nucelophilic attack by diethylamine at the β-carbon atom in α-methylallyl chloride, which is not a reactive center in any allylic system.

Choice D incorrectly suggests that the reaction involves rate-determining S_N1 heterolysis of the C-Cl bond in α-methylallyl chloride. If this were true, then contrary to information given in the question the reaction would be unimolecular, and the rate would be independent of $[Et_2NH]$

concentration.

Question 9. D

As indicated below, the α-carbon atom in α-methylallyl chloride is sp^3 hybridized. This same carbon atom becomes sp^2 hybridized in the product (Compound 5). This change in hybridization, $sp^3 \rightarrow sp^2$, corresponds to Choice D, which offers the correct response to this Question.



Choices A and B both incorrectly invoke *sp* hybridization, does not correspond to the hybridization state of any of the atoms in either in α-methylallyl chloride or the product, Compound 5. The hybridization changes are reversed incorrectly in Choice C

Question 10. A

This question asks examinees to recognize which reagent is capable of converting the OH group in a primary alcohol into a good leaving group for participation in an S_N2 reaction.

Methanesulfonyl chloride (Choice A) is used to convert ROH into the corresponding methanesulfonyl ester, ROMs. The mesylate group (OMs) is a good leaving group in S_N2 reactions due to the weak basicity of the mesylate anion. Choice A offers the correct response to this question.

Dimethyl sulfate (Choice B) and methyl iodide (Choice C) are alkylating agents that convert alcohols into methyl ethers, $ROCH_3$. Methoxide ion is a relatively strong base; hence, methoxy groups are poor leaving groups, and thus methyl ethers cannot normally function as substrates in S_N2 reactions.

Trityl chloride (Choice D) is used to convert ROH to the corresponding trityl ether. However, the $OCPh_3$ is a poor leaving group, so trityl ethers are not suitable substrates for use in S_N2 reactions.

When trityl ethers are cleaved either *via* hydrogenolysis or by application of strong acid, it is the $O\text{-}CPh_3$ bond that is cleaved to afford a trityl cation + ROH. For this reason trityl chloride frequently is used as an alcohol OH protecting group: