

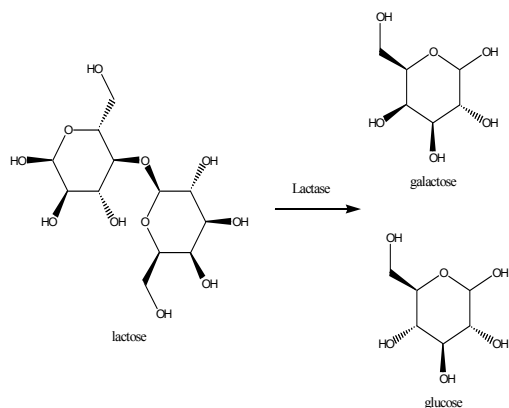
Passage I (Questions 1-4)

Cow's milk is a nutritionally complete food source which contains water, vitamins, minerals, proteins, carbohydrates, and lipids.

An important protein in milk is *casein*. This typically exists in milk as its calcium salt, *calcium caseinate*. Calcium caseinate is soluble at the normal pH of milk (6.6), but it becomes an insoluble form of casein in solutions that have a lower pH of 4.6 (the isoelectric point of calcium caseinate).

Milk contains two other important types of proteins, which can be denatured and precipitated by heat, namely *lactalbumins* and *lactoglobulins*.

Lactose (shown below), is the main carbohydrate in milk. It is a disaccharide which can be hydrolyzed with acid to give two monosaccharides, galactose and glucose. In the body, the enzyme *lactase*, digests lactose to galactose and glucose.



Adding a dilute solution of acetic acid to nonfat milk is the first step in isolating several of the components of milk. The solid material that precipitates (Solid 1) is removed. Care must be taken to avoid adding an excess of acetic acid.

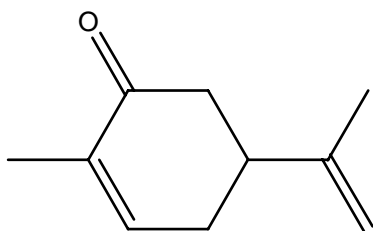
The remaining acidic solution is then treated with powdered CaCO_3 and heated to boiling, after which time another solid (Solid 2) forms. Solid 2 is removed by filtration, and hot ethanol is added to the aqueous filtrate. The solution is

allowed to cool overnight, during which time lactose crystallizes in the flask.

- The formation of curds in sour milk is most likely a result of the precipitation of:
 - casein as the pH decreases.
 - casein as the pH increases
 - lactose as the pH decreases
 - lactose as the pH increases
- In the method described in the passage, the powdered calcium carbonate is probably used to:
 - neutralize any acetic acid that may be present
 - dissolve any Solid 1 that remains
 - react with calcium caseinate to form casein
 - increase the solubility of Solid 2 in the aqueous solution
- The conversion of lactose to glucose and galactose involves the net addition to lactose of which of the following?
 - H_3O^+
 - O_2
 - H_2O
 - H_2
- The major components of Solid 2 are most likely:
 - only lactose and casein
 - casein, lactalbumins, and lactoglobulins
 - lactalbumins and the lactoglobulins
 - lactose, lactalbumins, and lactoglobulins

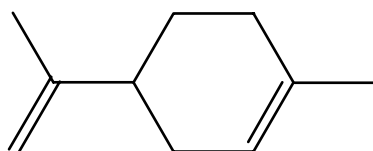
Passage II (Questions 5-9)

Carvone (shown below) can exist as one of two enantiomers. One of them, (-)-carvone is responsible for the fragrance of spearmint oil and the other, (+)-carvone, provides the characteristic odor in caraway seed oil.



carvone

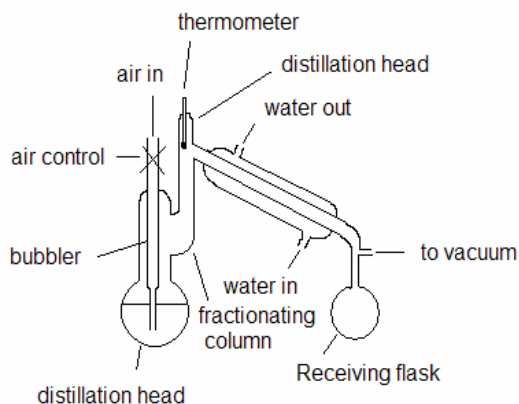
A chemist attempted to isolate (+)-carvone from caraway seed oil, which consists almost entirely of (+)-carvone and limonene (shown below).



limonene

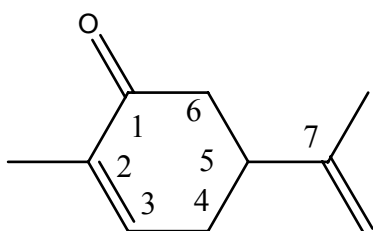
Because the two compounds have different boiling points, *vacuum fractional distillation* was chosen as the method of separation. The apparatus in Figure 1 was assembled, and a sample of caraway seed oil was placed in the distillation flask. A bubbler (or ebulliator) was lowered into the distillation flask to introduce small air bubbles into the system. The fractionating column and distillation head were wrapped with glass wool, and the apparatus was connected with thick tubing to a vacuum source.

The contents of the distillation flask were heated, and two fractions were collected in the receiving flask.

**Figure 1** Vacuum distillation apparatus

- When the caraway seed oil is heated, which of the two components will distill first?
 - Limonene, because it has the lower boiling point
 - (+)-Carvone, because it has the lower boiling point
 - Limonene, because it has the higher boiling point
 - (+)-Carvone, because it has the higher boiling point
- The most likely function of the bubbler (ebulliator) is to:
 - provide an outlet when the system pressure becomes too high
 - promote the establishment of a high vacuum in the system
 - prevent superheating of the liquid to be distilled
 - keep the condensed vapors cool in the receiving flask

7. Which of the following experimental modifications will most likely improve the degree of separation between limonene and (+)-carvone?
- Heating the distillation flask at a slower rate
 - Using a vacuum source that can achieve a lower pressure inside the distillation apparatus
 - Cooling the condenser with ice water
 - Using a shorter fractionating column
8. Carvone is shown below with some carbon atoms labeled



carvone

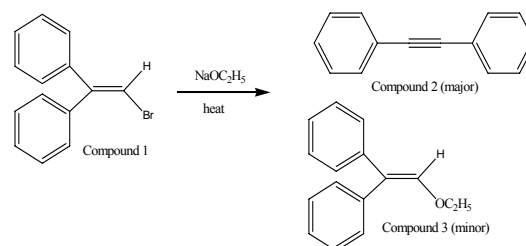
(+)-Carvone and (-)-carvone differ in the orientations of the substituents around which of the carbon atoms?

- Carbons 2, 5, and 7 only
 - Carbon 5 only
 - Carbons 2 and 5 only
 - Carbon 2 only
9. If a leak develops in the vacuum distillation apparatus, the boiling points of the two components of caraway seed oil will:
- both increase
 - both remain the same
 - both decrease
 - become more similar

Passage III (Questions 10-14)

When Compound 1 is heated with NaOEt, Compounds 2 and 3 are formed

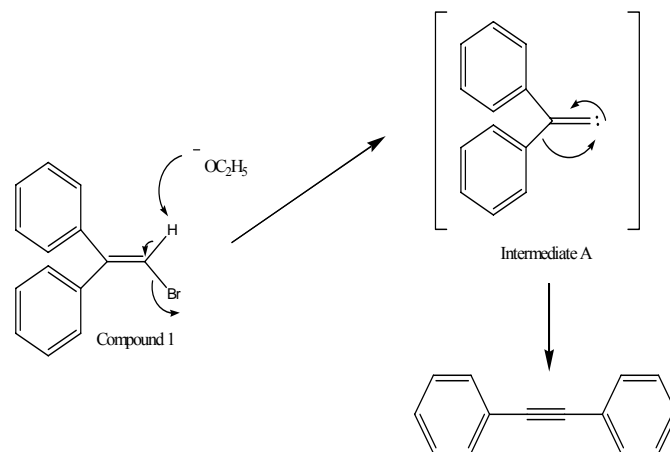
(Reaction 1).



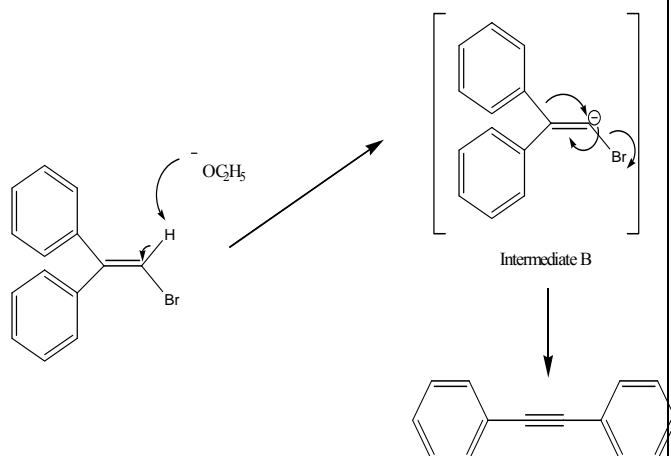
Two mechanisms were proposed for Reaction 1.

Mechanism A

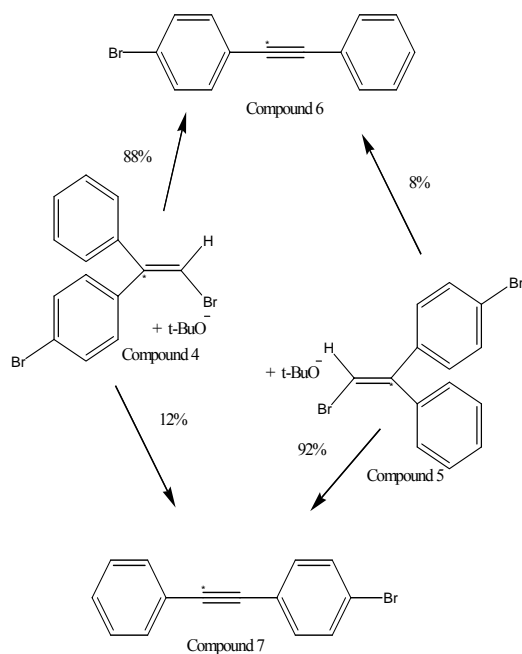
HBr is eliminated from Compound 1 to form a symmetrical vinyl carbene, Intermediate A, which then rearranges to form Compound 2.

*Mechanism B*

Ethoxide abstracts a proton from Compound 1 to produce a carbanion, Intermediate B. This then rearranges, with loss of bromide, to form Compound 2.



To distinguish between the 2 mechanisms, an isotopic labeling experiment was designed. 2 compounds (Compounds 4 and 5) were labeled with carbon-14 (^{14}C), and then each was treated with potassium *t*-butoxide (see Scheme 1). Because Compounds 4 and 5 formed varying ratios of Compounds 6 and 7, Mechanism A was ruled out.



Scheme 1 (* denotes C^{14} label)

10. Based on the results of Scheme 1, the chemists most likely ruled out Mechanism A because they assumed that a symmetrical intermediate should rearrange to form:

- A) Compound 6 only
- B) neither Compound 6 nor Compound 7
- C) equal amounts of Compounds 6 and 7
- D) Compound 7 only

11. Compound 3 most likely is formed as a result of which of the following types of reactions?

- A) Elimination
- B) Substitution
- C) Cyclization
- D) Halogenation

12. Which of the following by-products are formed in Reaction 1

- A) NaBr and EtOH
- B) Br_2 and NaOEt
- C) HBr and NaOEt
- D) EtBr and NaOH

13. Compounds 2 and 6 can be distinguished from each other by all of the following techniques EXCEPT

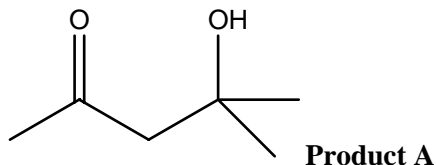
- A) gas-liquid chromatography
- B) mass spectrometry
- C) proton NMR
- D) specific rotation

14. The transformation of Compound 1 to Compound 2 involves which of the following changes in hybrid orbitals?

- A) sp^2 to sp
- B) sp^2 to sp^3
- C) sp^3 to sp^2
- D) sp to sp^3

Passage IV (Questions 15-20)

As part of an experiment, a starting material was treated with NaOH in acetone solvent ($(\text{CH}_3)_2\text{C}=\text{O}$) however, the starting material was recovered unreacted. Instead a small amount of Product A (shown below) was isolated.



It was determined that Product A resulted from the aldol self-condensation of acetone. Product A was identified based on the following observations.

Observations about Product A

1. Product A had a molecular weight of 116.
2. Elemental analysis of Product A showed only carbon, hydrogen, and oxygen in the molecule.
3. Signals in the infrared spectrum of Product A included a broad band at 3400 cm^{-1} and an intense signal at 1720 cm^{-1} .
4. Product A was a methyl ketone as it gave a positive iodoform test.
5. When Product A was treated with Br_2 in CCl_4 , the red bromine colour persisted, because no carbon-carbon double bonds were present to react with the bromine.

The structure of Product A was further confirmed when treatment with hot sulfuric acid resulted in the corresponding dehydration product, Product B.

15. What is the molecular weight of a compound that undergoes an aldol self-condensation reaction to result in a β -hydroxy ketone with a molecular weight of 144?

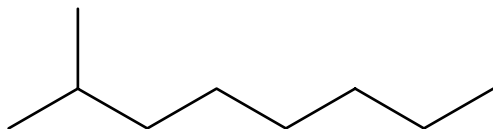
- A) 70
- B) 72
- C) 74
- D) 76

16. The aldol self-condensation of acetone is an equilibrium that favors acetone over its condensation product. Which of the following experimental modifications is most likely to shift the position of equilibrium toward Product A?

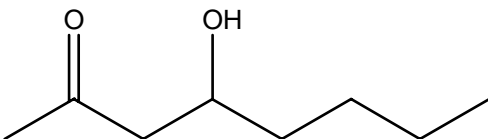
- A) Using only a catalytic amount of NaOH
- B) Using only a catalytic amount of acetone
- C) Removing Product A as it is formed
- D) Increasing the reaction temperature to the boiling point of acetone

17. Based ONLY on Observations 1 and 2 only, which of the following compounds could have been Product A?

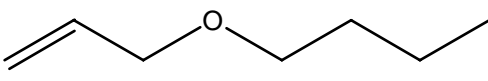
A)



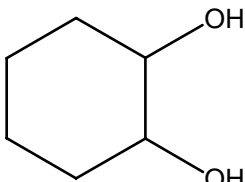
B)



C)



D)



18. If a drop of Br_2 in CCl_4 is added to Product B, the resulting solution will be:

- A) colourless, because Product B does not contain a carbon-carbon double bond
- B) colourless, because Product B contains a carbon-carbon double bond
- C) red, because Product B contains a carbon-carbon double bond
- D) red, because Product B does not contain a carbon-carbon double bond

19. A proton NMR spectrum of a sample of the isolated Product A was obtained. If the sample were contaminated with acetone, how many extra signals corresponding to the acetone would be present in the spectrum?

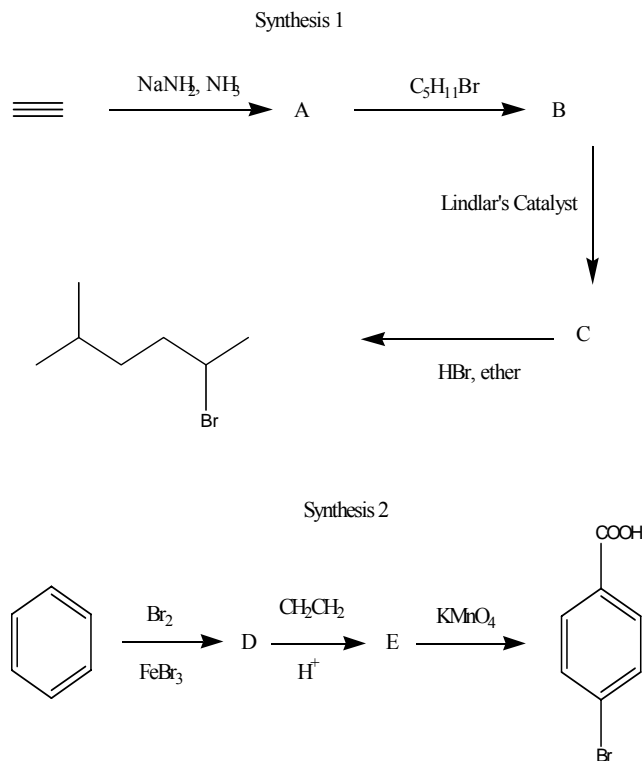
- A) 1
- B) 5
- C) 2
- D) 6

20. Which of the following compounds from the passage will give a positive iodoform test?

- A) Product A only
- B) Products A and B only
- C) Product A and acetone only
- D) Products A and B, and acetone

Passage V (Questions 21-25)

A chemist wishes to make the products shown below by the following synthetic schemes.



21. In synthesis 1 compound A is:

- A) Ethene
- B) Ethane
- C) But-1-ene
- D) Acetylide anion

22. In synthesis 1 compound B is:

- A) 5-methyl-hept-1-ene
- B) 5-methyl-hept-1-yne
- C) 5-methyl-hept-2-ene
- D) 5-methyl-hept-2-yne

23. In synthesis 1 compound C is:

- A) 2-methyl-heptane
- B) 5-methyl-hept-1-ene
- C) 5-methyl-2-bromo-hept-1-ene
- D) 5-methyl-hept-2-ene

24. In synthesis 2 compound D is:

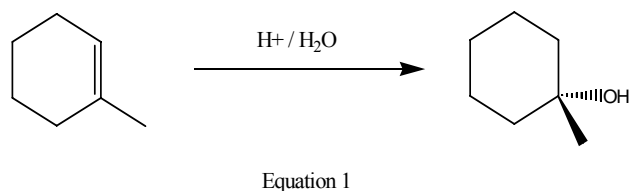
- E) 1,2-dibromobenzene
- F) 1,3-dibromobenzene
- G) Bromobenzene
- H) Bromocyclohexane

25. In synthesis 2 compound E is:

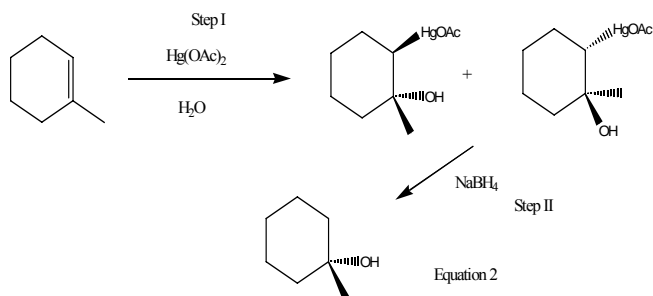
- A) p-ethylbromobenzene
- B) p-methylbromobenzene
- C) p-bromobenzaldehyde
- D) m-ethylbromobenzene

Passage VI (Questions 26 - 29)

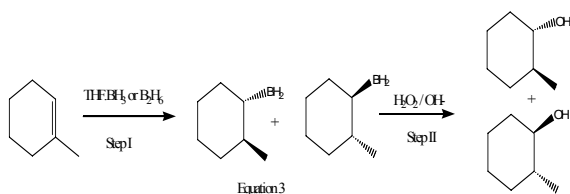
Three different methods of preparing alcohols from alkenes are shown below:



Equation 1 shows the acid catalyzed hydration of an alkene. The reaction is regioselective and not stereoselective and rearrangements may occur.



Equation 2 shows the oxymercuration/demercuration reaction. This is a two step reaction and the final alcohol is formed via the oxymercurial alcohols shown after step I. The mercury is then removed in the second step by NaBH_4 to give the alcohol product. Overall the reaction is regioselective and the first step is also stereoselective and no molecular rearrangements occur.

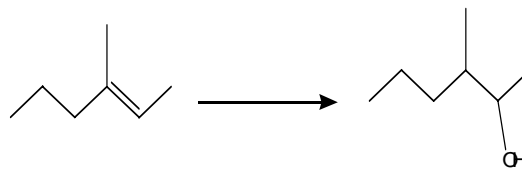


Equation 3 shows a hydroboration reaction followed by a second step to remove the boron species to give the final alcohol product. The overall reaction is regioselective and is also stereoselective in both steps. Molecular rearrangements do not take place.

26. Why can rearrangements take place in reactions of the type shown in Equation 1?

- A) Because the reaction takes place via the formation of a carbocation
- B) Because the reaction takes place via the formation of a carbanion
- C) Because the reaction takes place via an $\text{S}_{\text{N}}2$ reaction
- D) Because the reaction takes place via a radical reaction

27. Which of the following experimental methods could be used to form the alcohol from the alkene shown in the scheme below?



I Hydroboration followed by a second step as described in equation 3 above
 II Oxymercuration / demercuration as described in equation 2 above
 III Acid catalysed hydrolysis as described in equation 1 above

- A) I and II only
- B) II and III only
- C) I only
- D) III only

28. Step II in equations 2 and 3 above are respectively:

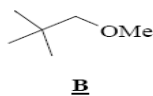
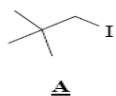
- A) An oxidation, a reduction
- B) A reduction, an oxidation
- C) A reduction, a reduction
- D) An oxidation, an oxidation

29. The IR spectra of the alcohols described in equations 1-3 all display a broad band at:

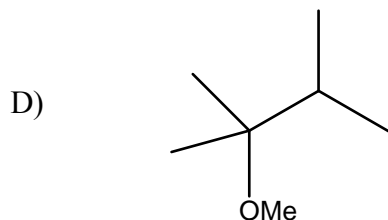
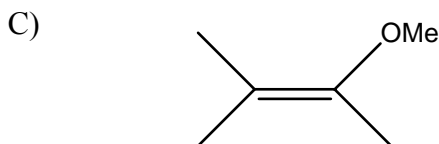
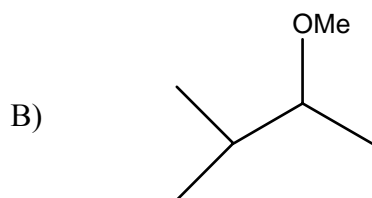
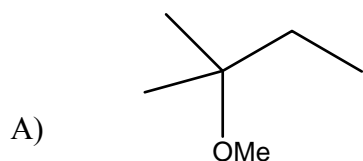
- A) 1000 cm^{-1}
- B) 2500 cm^{-1}
- C) 1500 cm^{-1}
- D) 3500 cm^{-1}

Passage VII (Questions 30 - 33)

A chemist was attempting to synthesise compound **B** from iodide **A** using MeOH as the nucleophile but the reaction was unsuccessful. Instead of obtaining the desired product **B**, an unknown molecule **C** was obtained. Molecule **C** gave 4 signals in the ^1H NMR spectrum, one singlet integrating to 6H atoms, one singlet integrating to 3H atoms, a quartet integrating to 2H atoms and a triplet integrating to 3H atoms. **C** is the product of a reaction mechanism involving a molecular rearrangement step.



30. The structure of unknown **C** is:



31. Which of the following alternative reagents (instead of MeOH) would more likely convert iodide **A** to the desired product **B**.

- A) Me-O-Me
- B) MeONa
- C) MeCOOH
- D) MeMgBr

32. Given the reaction conditions, and that you are told that a molecular rearrangement takes place in the above equation to give unwanted product **C**, the most likely mechanism characteristics of this reaction are:

- A) An $\text{S}_{\text{N}}1$ reaction involving a carbocation intermediate
- B) An $\text{S}_{\text{N}}2$ reaction involving inversion at a carbon centre
- C) A carbene intermediate involving a methyl shift
- D) A radical mechanism involving a methyl shift

33. Which of the following statements are true?

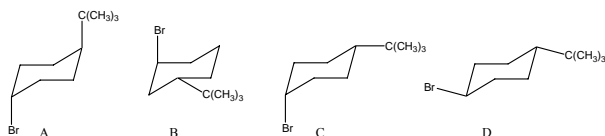
- I. An $\text{S}_{\text{N}}2$ reaction at a chiral carbon inverts the stereochemistry of that chiral centre
- II. An $\text{S}_{\text{N}}1$ reaction at a chiral carbon racemises the chirality of that centre
- III. An $\text{S}_{\text{N}}1$ reaction at a chiral carbon does not change the stereochemistry of the centre

- A) I alone
- B) II and III alone
- C) I and II alone
- D) III alone

Passage VIII (Questions 34 - 37)

The rate of the base-induced dehydrohalogenation reaction of *cis*-1-bromo-4-*tert*-butylcyclohexane is proportional to the concentration of both the bromide and the base, however that of the *trans* isomer is proportional only to the concentration of the bromide.

34. What is the structure of *cis*-1-bromo-4-*tert*-butylcyclohexane.



35. Which of the following mechanisms best accounts for the dehydrohalogenation reaction of *cis*-1-bromo-4-*tert*-butylcyclohexane.

- A) E2
- B) E1
- C) SN1
- D) SN2

36. Which of the following statements about eliminations is true?

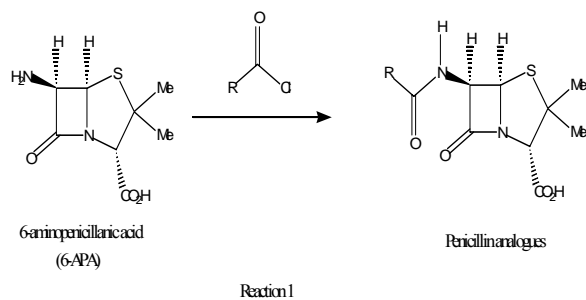
- A) E1 mechanisms are unimolecular in nature and E2 mechanisms require a *cis* configuration of the abstracted proton and leaving group.
- B) E1 mechanisms involve carbocation intermediates and E2 mechanisms require an anti-periplanar arrangement of abstracted proton and leaving group.
- C) E1 mechanisms involve carbocation intermediates and E2 reaction rates are dependent on the concentration of base only
- D) E1 reaction rates are dependent on the concentration of base only and E2 mechanisms involve radical intermediates

37. Which of the following mechanisms best accounts for the dehydrohalogenation reaction of *trans*-1-bromo-4-*tert*-butylcyclohexane.

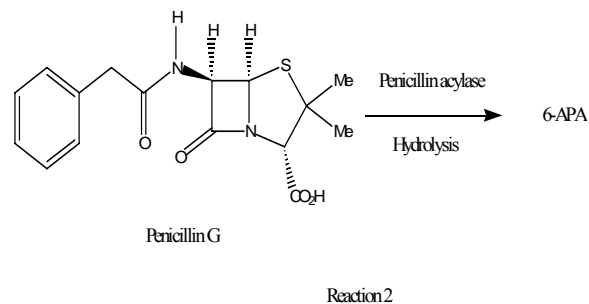
- A) E1
- B) E2
- C) S_N2
- D) Radical

Passage IX (Questions 38 - 42)

Chemists investigating the antibiotic agent, penicillin G, wished to prepare a number of analogues which might solve the problem of bacterial resistance to this class of drugs. A method of production was required which was efficient and cheap. Chemists decided to start from 6-APA and following the scheme outlined in Reaction 1, they synthesized a number of analogues with a variety of groups at R.



In order to obtain large enough amounts of 6-APA for this synthetic scheme, chemists used Penicillin G in an enzymatic cleavage reaction to form 6-APA (reaction 2).



38. In reaction 1, the compound above the reaction arrow is called an acyl chloride or an acid chloride. From the following list of syntheses of acid chlorides, select from A,B,C or D the answer which is true.

- I A carboxylic acid plus sodium chloride gives an acid chloride
- II A carboxylic acid plus thionyl chloride gives an acid chloride
- III A ketone plus lithium aluminium hydride gives an acid chloride
- IV An aldehyde plus carbon tetrachloride gives an acid chloride

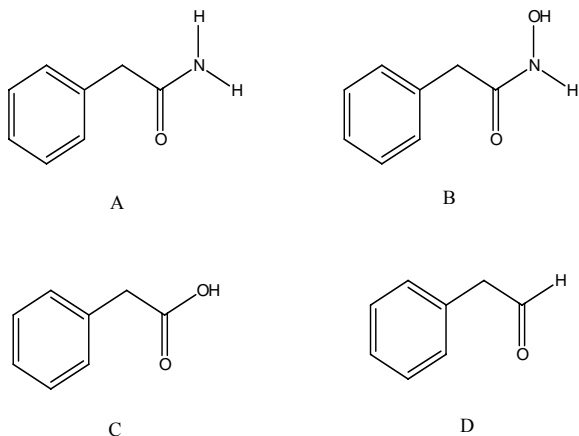
- A) I and II
- B) I, II and IV
- C) II alone
- D) IV alone

39. Acid chlorides are useful compounds in chemical syntheses. Which of the following reactions can use acid chlorides as an integral step

- I Friedel Crafts acylation
- II Friedel Crafts alkylation
- III Synthesis of esters from alcohols
- IV Synthesis of amides from amines

- E) I and II
- F) I, III and IV
- G) I and III
- H) IV alone

40. In reaction 2, the enzymatic hydrolysis of Penicillin G most likely gives 6-APA and what other compound as products?



41. Amide bonds are biologically important in such structures as peptides where they are also termed peptide bonds. When chemists want to synthesise peptides in the laboratory from two different amino acids one of the methods that can be used for small peptides utilizes various protecting groups and coupling reagents. Which of the following would be an acceptable route for the synthesis of a dipeptide by this method.

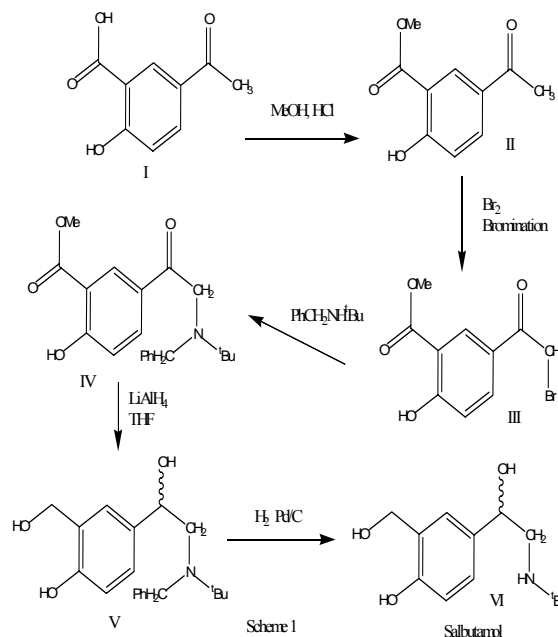
- A) Protect the free amino group of one amino acid, protect the free carboxylic acid group of the other amino acid, form the peptide bond with DCC and then deprotect the amino group and the carboxylic acid group.
- B) Protect the free amino group of one amino acid, form the peptide bond with DCC, deprotect the amino group
- C) Protect the free amino group of one amino acid, protect the free carboxylic acid group of the other amino acid, form the peptide bond with DCC.
- D) Protect the amino group which will form the peptide bond of one of the amino acids, protect the carboxylic acid group which will form the other part of the peptide bond of the other amino acid, form the peptide bond with DCC, deprotect the amino group and the carboxylic acid group

42. If we did not use protecting groups in the synthesis of a dipeptide starting from two different amino acids, and instead used an acid chloride reaction with an amine to form the amide bonds of the dipeptide, how many different products would we obtain?

- A) 1
 B) 2
 C) 3
 D) 4

Passage X (Questions 43 - 47)

Salbutamol is an important molecule used for the treatment of asthma. It is a β_2 agonist and relaxes bronchial smooth muscle resulting in dilation of the airways. In the laboratory Salbutamol can be synthesized according to the reactions shown in Scheme 1.



43. The reaction from molecule I to molecule II in Scheme 1 is:

- A) An acid catalyzed hydrolysis
- B) A base catalyzed dehydration
- C) An acid catalyzed formation of an ether
- D) An acid catalyzed esterification

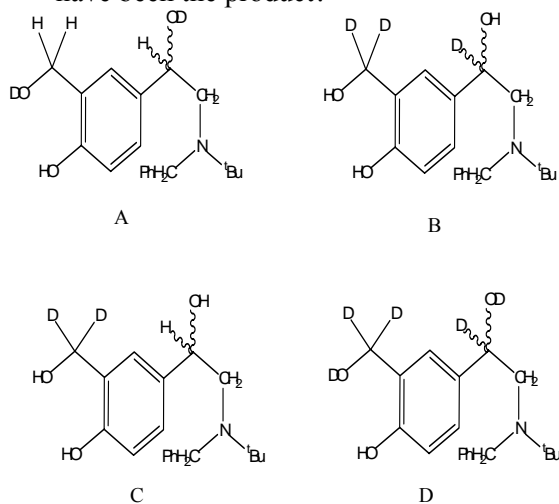
44. The transformation of molecule III to molecule IV in Scheme 1 is an example of:

- A) An E1 reaction
- B) An S_N1 reaction
- C) An E2 reaction
- D) An S_N2 reaction

45. The transformation from molecule IV to molecule V in Scheme 1 is what kind of reaction?

- A) A hydrolysis
- B) A reduction
- C) A rearrangement
- D) A de-esterification

46. If the chemist had used LiAlD₄ as the reagent in the transformation of molecule IV to molecule V instead of LiAlH₄ what would have been the product?

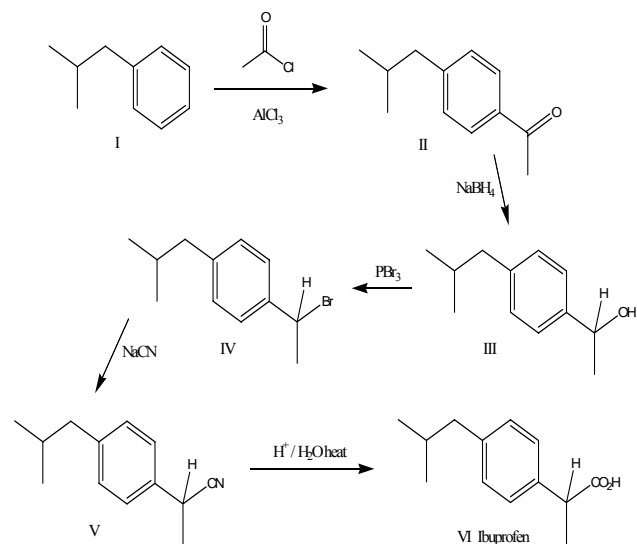


47. In the last step of the synthesis of Salbutamol shown in Scheme 1, the Pd/C is acting as a:

- A) Reagent
- B) Catalyst
- C) Radical initiator
- D) Drying agent

Passage XI (Questions 48 - 52)

Non steroidal anti-inflammatory agents (NSAIDs) are a successful class of compounds used for the treatment of pain and inflammation in a range of disorders and are especially useful in the treatment of arthritis. One such drug is Ibuprofen. In the laboratory chemists can prepare the racemic ibuprofen compound by many different routes. One such synthetic route is shown in Scheme 1 below.



48. Which of the following statements about the conversion of I to II in Scheme 1 above is true?
- A) The reaction is a Friedel Crafts alkylation and the AlCl_3 is a reagent usually present in equimolar amounts.
 - B) The reaction is a Friedel Crafts acylation and the AlCl_3 is a reagent usually present in less than equimolar amounts
 - C) The reaction is a Friedel Crafts alkylation and the AlCl_3 is a Lewis acid.
 - D) The reaction is a Friedel Crafts acylation and the AlCl_3 is a phase transfer catalyst
49. Read the following statements about molecule II in Scheme 1 above and select the answer from A,B,C or D which is true.
- i) Molecule II is derived from an electrophilic aromatic substitution reaction on molecule I
 - ii) The acyl group of molecule II is oriented para to the alkyl group of molecule I because the alkyl group is an ortho/para directing group
 - iii) Molecule II is an activated aromatic aldehyde
 - iv) The alkyl group of molecule II is usually meta directing but because of steric bulk the acyl group of molecule II has been directed to the para position.
- A) i) and iii) only
 - B) i), ii) and iv)
 - C) i) and ii) only
 - D) iii) and iv) only
50. The conversion of molecule II to molecule III in Scheme 1 is an example of a:
- A) Oxidation
 - B) Reduction
 - C) Elimination
 - D) Radical reaction
51. The conversion of IV to V in Scheme I above is an example of a nucleophilic substitution reaction. For an $\text{S}_{\text{N}}2$ reaction which of the following statements is true?:
- A) Primary alkyl halides are better substrates than secondary and $\text{S}_{\text{N}}2$ reactions at chiral centres proceed with inversion of configuration.
 - B) Tertiary alkyl halides are better substrates than primary and $\text{S}_{\text{N}}2$ reactions at chiral centres give racemates.
 - C) The rate of reaction is proportional only to the concentration of nucleophile and reactions often proceed with rearrangements.
 - D) Primary alkyl halides are better substrates than tertiary alkyl halides and the reaction rate is proportional to the concentration of nucleophile only.
52. The last step (molecule V to molecule VI) in Scheme 1 above to form Ibuprofen is called a:
- A) Wittig reaction
 - B) Elimination reaction
 - C) Acid catalyzed hydrolysis
 - D) Nitrile aldol reaction