第一部份單選題及第二部份多選題考生應作答於『答案卡』

第一部份：單選題 (2 pts each)

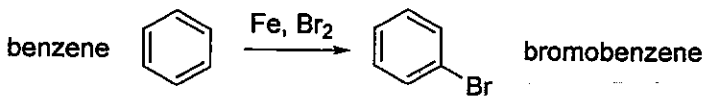
■ There are numerous isomers of hydrocarbon **A** (C_8H_{16}). Answer Question 1-3.

1. How many structural (constitutional) isomers that have a cyclopentane ring do **A** have?
   (A) 4　(B) 6　(C) 8　(D) 10　(E) 12

2. How many constitutional isomers that are straight-chain alkene and have goeometric isomers do **A** have?
   (A) 0　(B) 1　(C) 2　(D) 3　(E) 4

3. For all di-substituted cyclohexane isomers of **A**, which of the following statement is correct?
   (A) There are seven structural (constitutional) isomers.
   (B) Including all (structural + stereo) isomers, five of them are achiral.
   (C) All *trans*-isomers are more stable than their corresponding *cis*-isomers.
   (D) All of their most stable chair conformations are di-equatorial.
   (E) Including all (structural + stereo) isomers, four of them are *meso* compounds.

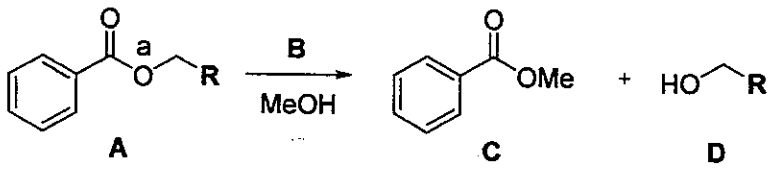
■ Bromobenzene can be prepared from benzene by the following scheme. Answer Question 4-5.



4. Which term describes this reaction most properly?
   (A) elimination　(B) addition　(C) substitution　(D) coupling　(E) radical reaction

5. How many of the following statement(s) is(are) correct?
   (a) Fe serves as the catalyst.
   (b) Bromobenzene is the sole product.
   (c) The proper molar ratio of benzene, Fe and Br_2 can be 1: 0.1: 1.
   (d) Benzene serves as the nucleophile.
   (e) The reaction undergoes the single-step mechanism.
   (A) 0　(B) 1　(C) 2　(D) 3　(E) 4

■ Compound **A** undergoes the following conversion. Answer Question 6-8.



6. Which term describes this reaction most properly?
   (A) ester formation　(B) ether formation　(C) saponification
   (D) transamidation　(E) transesterification

7. When using catalytic amount, which reagent **B** cannot facilitate the conversion?
   (A) sulfuric acid　(B) sodium methoxide　(C) sodium hydroxide
   (D) sodium benzoate　(E) sodium hydride.

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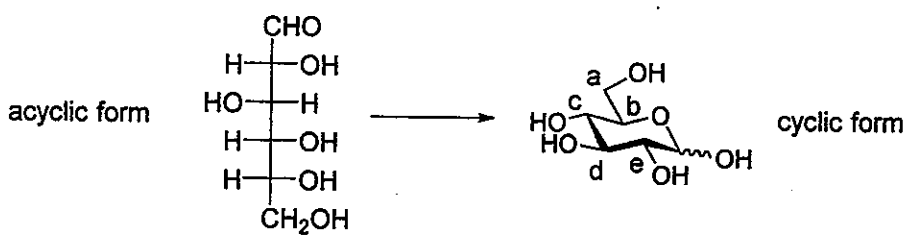
8. Which of the following statement is not correct?
(A) The oxygen O_a in **A** goes to product **C**.
(B) MeOH serves as the nucleophile.
(C) The reaction will reach equilibrium.
(D) MeOH serves as the reagent and solvent.
(E) The reaction undergoes the multi-step mechanism.

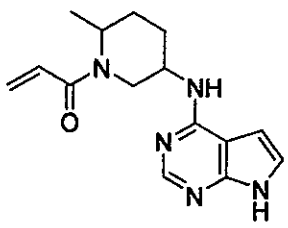
■ The acyclic form of *D*-glucose undergoes the following reaction to afford the cyclic form. Answer Question 9-10.

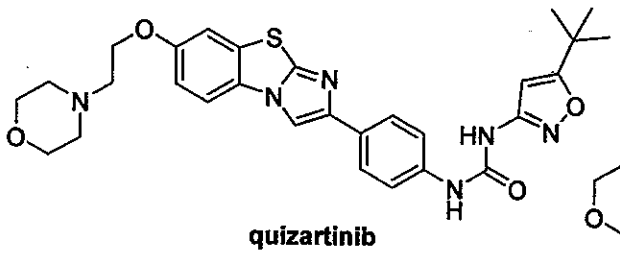


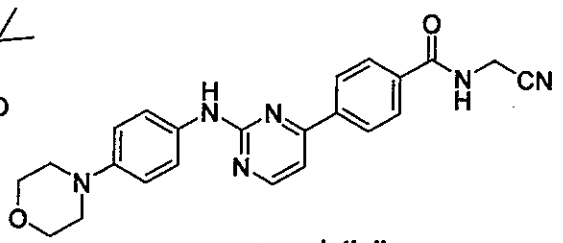
9. Which term describes this reaction most properly?
(A) hydrate formation (B) hemiacetal formation (C) acetal formation
(D) ether formation (E) ester formation

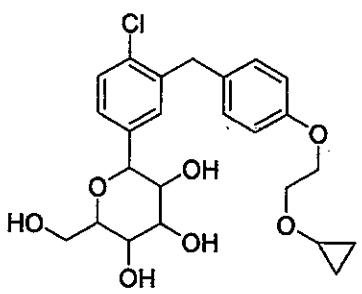
10. As depicted in the cyclic form, which carbon gives the characteristic *D* notation?
(A) C_a (B) C_b (C) C_c (D) C_d (E) C_e

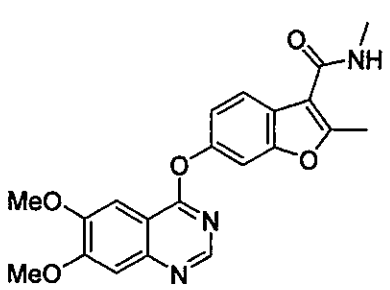
■ The U.S. Food and Drug Administration (FDA) approved 55 novel therapeutics in 2023. Structures of seven drugs are shown below. Answer Question 11-20.

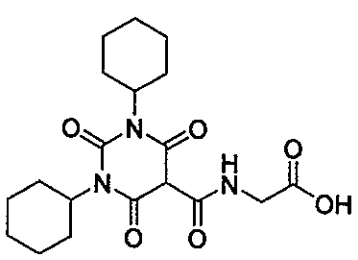

ritlecitinib

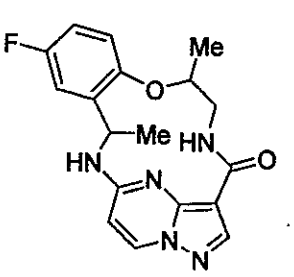

quizartinib


momelotinib


bexagliflozin


fruquintinib


daprodustat


repotrectinib

11. How many chiral centers do these seven drugs have in total?
(A) 7 (B) 8 (C) 9 (D) 10 (E) 11

12. How many functional group(s) shown below cannot be found in these seven drugs?
(a) ketone, (b) ether, (c) ester, (d) phenol, (e) alcohol, (f) acetal, (g) amine, (h) nitrile, (i) urea, (j) amide
(A) 1 (B) 2 (C) 3 (D) 4 (E) 5

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13. Several monocyclic or polycyclic aromatic systems can be found in these seven drugs. How many aromatic systems contain 6π electrons in total?
(A) 6 (B) 8 (C) 10 (D) 12 (E) 14

14. How many heterocycles shown below can be found in these seven drugs?
(a) triazole, (b) pyrimidine, (c) purine, (d) piperidine, (e) morpholine, (f) pyridine, (g) pyridazine
(A) 2 (B) 3 (C) 4 (D) 5 (E) 6

15. Which of the following drug has the most basic function group?
(A) ritlecitinib (B) quizartinib (C) momelotinib (D) daprodustat (E) repotrectinib

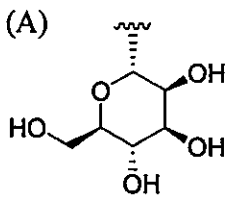
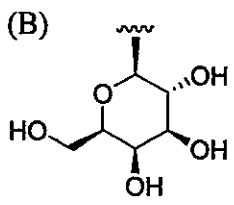
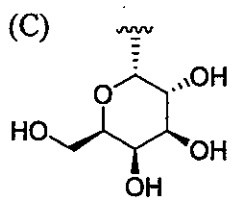
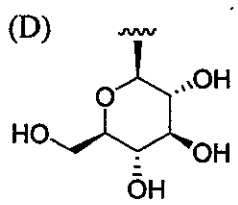
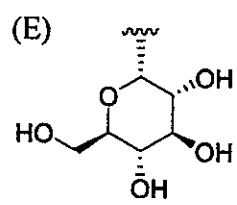
16. Which of the following drug has the most acidic function group?
(A) ritlecitinib (B) quizartinib (C) momelotinib (D) daprodustat (E) repotrectinib

17. Which of the following drug has the most acidic C-H ?
(A) ritlecitinib (B) quizartinib (C) momelotinib (D) daprodustat (E) repotrectinib

18. How many benzylic hydrogens do these seven drugs have in total?
(A) 0 (B) 1 (C) 2 (D) 3 (E) 4

19. The cysteine (Cys) residue, a thiol-containing α-amino acid, from target proteins can react with one of these drugs to form a covalent bond, that inhibits the biological activity of proteins. Which drug is it?
(A) ritlecitinib (B) momelotinib (C) bexagliflozin (D) fruquintinib (E) daprodustat

20. Bexagliflozin contains a β-*C*-*D*-glucoside moiety. Which structure shows the correct stereochemistry?

(A) 
(B) 
(C) 
(D) 
(E) 

■ Carbonyl compounds, such as aldehydes, ketones and acid carboxylic acid derivatives, are one of the most important family in organic chemistry. Nine well-known tansformations are shown below. Considering only simple carbonyl componds, answer Question 21-23.
(1) Hydrate (gem-diol) formation (2) hemiacetal formation (3) acetal formation,
(4) imine formation (5) Aldol reaction (6) ester hydrolysis
(7) amide hydrolysis (8) nitrile hydrolysis (9) Claisen condensation.

21. How many tansformations are both acid-catalytic (pH<2) and base-catalytic (pH>13)?
(A) 3 (B) 4 (C) 5 (D) 6 (E) 7

22. How many tansformations are both acid-promoted and base-promoted, and require full equivalent of acids or bases?
(A) 1 (B) 2 (C) 3 (D) 4 (E) 5

23. How many tansformations must require aldehydes or ketones as one of starting materials?
(A) 3 (B) 4 (C) 5 (D) 6 (E) 7

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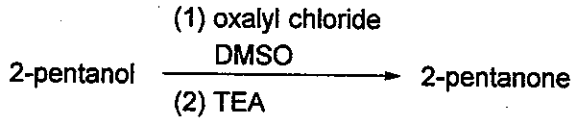
24. Which compond in the following reacton is the major oxidant?

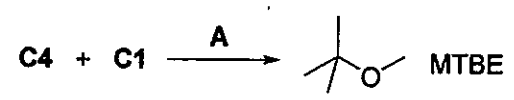


(A) 2-pentanol (B) oxalyl chloride (C) DMSO (D) TEA (E) 2-pentanone

25. When acetone is mixed with bleach (sodium hypochlorite), what major product can be produced?
(A) 3,3,3-trichloropropanal (B) trichloromethane (C) 1,3-dichloroacetone
(D) 2,2-dichloroacetic acid (E) 1,1-dichloroacetone

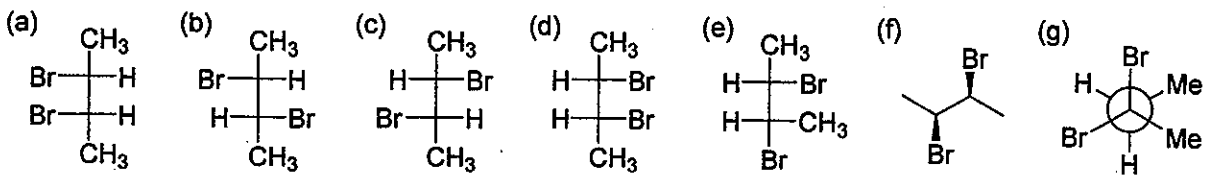
第二部份：多選題(需全部答對才得分) (2 pts each)

26. Methyl *tert*-butyl ether (MTBE) can be prepared by the following scheme, where **C4** is a four-carbon compound and **C1**is a one-carbon compound. What **C4, C1** and condition **A** can be used, respectively?



(A) isobutene, methanol, sulfuric acid
(B) potassium *tert*-butoxide, methanol, DMF
(C) *tert*-butanol, methyl iodine, triethylamine/DMF
(D) *tert*-butyl chloride, sodium methoxide, DMF
(E) potassium *tert*-butoxide, methyl *p*-toluenesulfonate, DMF

■ 2,3-Dibromobutane is the key model compound to discuss stereochemistry. Answer Question 27-29.



27. Which of the following structural representations are used?
(A) Howard projection (B) Fischer projection (C) Newman projection
(D) sawhorse projection (E) skeletal line structure

28. In the above structural model (a)-(f), which of the following statements are correct?
(A) Four structural models are chiral.
(B) The model (a) and (g) are identical.
(C) The model (b) and (c) are enantiomers.
(D) The model (d) and (f) are diastereomers.
(E) Three structural models are *meso* compounds.

29. 2,3-Dibromobutane isomers can be prepared from corresponding alkenes with bromine. Which of the following statements are correct?
(A) Alkenes serves as the nucleophile.
(B) The reaction is through radical addition.
(C) The isomer (g) can be prepared from *cis*-2-butene.
(D) The isomer (e) can be prepared from *trans*-2-butene.
(E) The reaction undergoes the multi-step mechanism.

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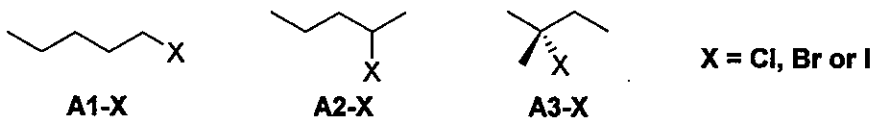
■ Alkyl halide **A-X** ($C_5H_{11}X$, X = Cl, Br or I) compounds are common starting materials in synthesis. Some isomers of **A-X**s are shown below. Answer Question 30-33.



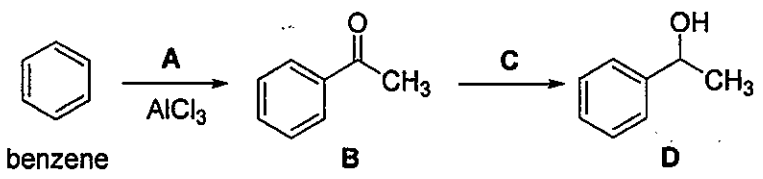
30. For all alkyl bromide **A-Br** ($C_5H_{11}Br$) compounds, which of the following statements are correct?
(A) There are eight structural (constitutional) isomers.
(B) Two structural isomers are chiral.
(C) Three structural isomers are secondary (2°) bromides.
(D) All chiral isomers are secondary (2°) bromides.
(E) All chiral carbons are tertiary (3°).

31. For all alkyl iodine **A-I** ($C_5H_{11}I$) compounds, which of the following statements are incorrect?
(A) **A3-I** is the poorest S_N2 substrates.
(B) All primary (1°) **A-I**s are good S_N2 substrates.
(C) **A3-I** is the best E1 substrate.
(D) All **A-I**s are E2 substrates.
(E) **A3-I** is a poor E2 substrate.

32. Both **A1-X**s and **A2-X**s can be used to prepare elimination products. Which of the following statements are correct?
(A) When **A1-X**s and **A2-X**s are reacted with NaOMe, their major elimination products are the same.
(B) When **A1-X**s and **A2-X**s are reacted with *t*-BuOK, their major elimination products are the same.
(C) When reacted with NaOMe, **A1-X**s give a better yield of elimination products than **A2-X**s.
(D) When reacted with NaOMe, the enantiomers of **A2-X**s give the same product.
(E) When **A1-X**s are reacted with NaOMe, the ranking of reaction rates is **A1-I** > **A1-Br** > **A1-Cl**.

33. **A3-X**s can be used to prepare substitution products. Which of the following statements are correct?
(A) When reacted with MeOH, the ranking of reaction rates is **A3-I** > **A3-Br** > **A3-Cl**.
(B) When reacted with 0.1 M or 0.2 M AcOH, the ranking of reaction rates is 0.1 M < 0.2 M.
(C) When reacted with MeOH or NaOMe, the yield of ether formation is MeOH > NaOMe.
(D) When reacted with MeOH, **A3-X**s give a better yield of substitution products at higher temperature.
(E) When reacted with MeOH, the ether product is racemic.

■ Compound **D** can be prepared from benzene through intermediate **B**. Answer Question 34-48.



34. Which reagent A(s) can be used in the above scheme?
(A) acetaldehyde (B) acetic chloride (C) acetic anhydride (D) acetic acid (E) ethyl choride

35. Which reagent C(s) can be used in the above scheme?
(A) Zn(Hg), HCl (B) H_2H_4, KOH (C) $NaBH_4$, EtOH (D) $LiAlH_4$, THF (E) DIBAL, THF

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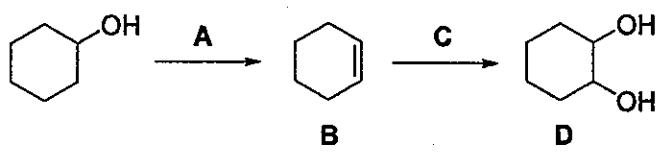
36. What other synthetic schemes can also be used to prepare **B**?
(A) (1) methyl benzoate + MeMgBr, then (2) Jones reagent
(B) phenylacetylene + $HgSO_4/H_2O$
(C) (1) phenylacetylene + excess HBr, then (2) hydrolysis
(D) (1) ethyl benzene + NBS (1 equiv.) with light, then (2) hydrolysis
(E) 2-phenyl-1-propene + O_3, then (2) Me_2S

37. What other synthetic schemes can also be used to prepare **D**?
(A) (1) benzoic acid + $LiAlH_4$ in THF, then (2) hydrolysis
(B) (1) phenylethylene + excess HBr, then (2) hydrolysis
(C) ethyl benzene + $KMnO_4$
(D) styrene + HBr/ROOR with light, then (2) hydrolysis
(E) (1) ethyl benzene + NBS with light, then (2) hydrolysis

38. Which of the following statements are correct?
(A) $AlCl_3$ serves as a catalyst.
(B) $AlCl_3$ serves as a Lewis base.
(C) More than one equiv. of $AlCl_3$ should be added.
(D) The IUPAC name of **B** is 1-phenylethan-1-one.
(E) The multi-acetylation is the major concern, yielding a *meta*-di-acetylation side product.

■ Compound **D** can be prepared from cyclohexanol through intermediate **B**. Answer Question 39-41.



39. Which synthetic condition **A**(s) can be used in the above scheme?
(A) Lucas' reagent
(B) (1) phosphorus tribromide, then (2) sodium acetate
(C) concentrated phosphoric acid with heating
(D) *N*,*N*′-dicyclohexylcarbodiimide (DCC)
(E) (1) concentrated hydrobromic acid, then (2) potassium *tert*-butoxide

40. Which reagent **C**(s) cannot be used in the above scheme?
(A) basic $KMnO_4$ (B) O_3 then Me_2S (C) (1) BH_3, then (2) $H_2O_2/NaOH$
(D) $NaIO_4$ (E) MCPBA, then NaOH

41. When osmium tetroxide is used as **C**, which of the following statements are correct?
(A) The most stable conformation of **B** is the chiar form.
(B) Under this condition, the major product **D** has three streoisomers.
(C) Under this condition, the major product **D** is racemic.
(D) Under this condition, the most stable conformation of **D** is chiar form.
(E) Under this condition, there are two major stable conformations of **D**.

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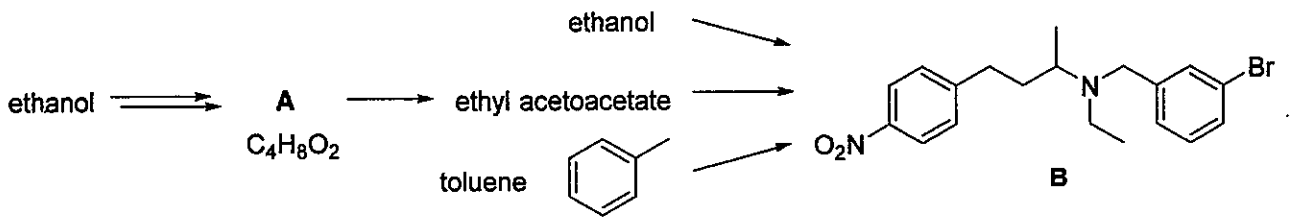
※ 注意：請於試卷內之「非選擇題作答區」作答，並應註明作答之題號。

第三部份：問答題

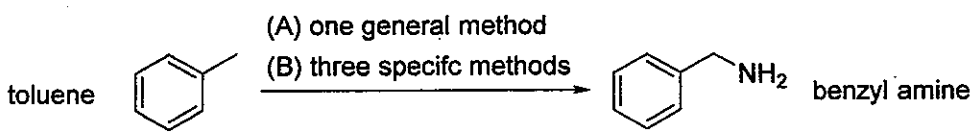
42. Use ethanol and toluene as *only* two carbon sources to prepare compound **B**. When designing the synthesis, include ethyl acetoacetate as the key intermediate.



(A) Provide reagents, schemes and intermediate compounds. (Note: You do not need to provide mechanisms) (6 pts)

(B) Provide the mechanism of preparation of ethyl acetoacetate from **A** ($C_4H_8O_2$). Indicate the driving force of the transformation. (4 pts)

43. Amines are important nitrogen-containing organic compounds. Based on numbers of substituents on nitrogen atoms, amines can be primary (1°), secondary (2°) and tertiary (3°). However, preparing one specific type of amines without contamination of other types of amines has posed a great challenge. Using toluene and benzyl amine as the starting material and the target compound, answer the following questions.



(A) Provide one general method that can prepare *any type* of amines without contamination of other types of amines. (Note: Use benzyl amine from toluene as an example) (2 pts)

(B) Provide three specific methods that *only* can synthesize primary (1°) amines. (Note: Use benzyl amine from toluene as an example) (6 pts)

試題隨卷繳回