

Question 1

With respect to the electrophilic aromatic substitution of benzene which of the following is **not** true?

- a) A non-aromatic intermediate is formed
- b) Benzene acts as an electrophile
- c) A proton is lost in the final step
- d) Resonance forms are important

Question 2

In the body many mono-substituted aromatic compounds are metabolised...

- a) To the *para*-fluoro compound which may be prevented by the addition of a *para*-hydroxy group
- b) By G-protein coupled receptors
- c) To less polar compounds
- d) To the *para*-hydroxy compound which may be prevented by the addition of a *para*-fluoride

Question 3

Which of the following statements is **incorrect**: aromatic compounds...

- a) Are planar
- b) Have $4n$ π -electrons
- c) Are cyclic
- d) Are generally less reactive than similarly substituted alkenes

Question 4

When considering electrophilic aromatic substitution reactions electron withdrawing substituents (e.g. nitro) are described as...

- a) *Ortho/para* directing and activating
- b) *Ortho/para* directing and deactivating
- c) *Meta* directing and activating
- d) *Meta* directing and deactivating

Question 5

The Friedel-Crafts alkylation...

- a) Works very well for primary chlorides
- b) Works very well for tertiary chlorides
- c) Works very well for acyl chlorides
- d) Works very well without a catalyst

Question 6

Salbutamol is an effective treatment for asthma; which of the following statements is **not** true:

- a) It can be synthesised from aspirin
- b) It is active at the β 2-adrenoreceptor
- c) It has a shorter duration of action than adrenaline
- d) The (R)-stereoisomer is the more active

Question 7

When considering electrophilic aromatic substitution reactions the halides are described as...

- a) *Ortho/para* directing and activating
- b) *Ortho/para* directing and deactivating
- c) *Meta* directing and activating
- d) *Meta* directing and deactivating

Question 8

When considering electrophilic aromatic substitution reactions electron donating substituents (e.g. methoxy) are described as:

- a) *Ortho/para* directing and activating
- b) *Ortho/para* directing and deactivating
- c) *Meta* directing and activating
- d) *Meta* directing and deactivating

Question 9

With respect to the electrophilic aromatic substitution of benzene which of the following is **not** true:

- a) A non-aromatic intermediate is formed
- b) Benzene acts as an electrophile
- c) A proton is lost in the final step
- d) Resonance forms are important

Question 10

Which of the following drugs does **not** contain an aromatic species? You should use this

opportunity to get some background on the well known drugs listed.

- a) Salbutamol
- b) Imatinib
- c) Valsartan
- d) Pregabalin

Question 11

Which of the following is not associated with electrophilic aromatic substitution?

- a) The formation of nitrobenzene
- b) The formation of benzyne
- c) The formation of bromobenzene
- d) The formation of benzene sulfonic acid

Answers

Q.1 b) Benzene acts as an electrophile

Feedback:

Look at the mechanism in detail and you will see that benzene reacts with an electrophilic reagent (meaning that benzene is acting in a nucleophilic manner), the reaction description (EAS) refers to the fact that benzene (or another aromatic) is being substituted by an electrophile. Check the mechanism of the reaction.

Q.2 d) To the *para*-hydroxy compound which may be prevented by the addition of a *para*-fluoride

Feedback:

The cytochrome P450 enzymes are often involved in the metabolism of aromatics. The initial product is usually an epoxide that can rearrange to form the more polar *para*-hydroxyaromatic that might be excreted directly or further conjugated to aid excretion.

Q.3 b) Have $4n$ π -electrons

Feedback:

Hückel's rule states the requirement for $4n + 2$ π -electrons.

Q.4 d) *Meta* directing and deactivating

Feedback:

In this case the resonance forms in which the carbon bearing the electron withdrawing group does not carry the positive charge in the non-aromatic intermediate is favoured - that is achieved by reaction at the meta position. The general electron withdrawing nature of the substituent means that electron density is less available for the aromatic ring to act as a nucleophile.

Q.5 b) Works very well for tertiary chlorides

Feedback:

Rearrangement is a problem for primary chlorides; the use of acyl chlorides is the Friedel-Crafts acylation reaction where a catalyst is required to aid cation formation

Q.6 c) It has a shorter duration of action than adrenaline

Feedback:

Salbutamol mimics the action of adrenaline in the lungs and does so by interacting with the β 2-adrenoreceptors which cause the dilation of the bronchial tree when activated there. One of the many problems with exploiting adrenaline as a drug is its short duration of action; salbutamol addresses this problem (and also some of the issues with side effects).

Q.7 b) *Ortho/para* directing and deactivating

Feedback:

Halides form the slightly unusual class of directing effects

Q.8 a) *Ortho/para* directing and activating

Feedback:

In the non-aromatic intermediate the electron donating group can stabilise a positive charge on the carbon that it is bonded to. Attack of the incoming electrophile at the *ortho*- or *para*-position generates resonance forms that permit the positive charge to fall on the carbon that bears the electron donating group. The availability of electron density from the electron donating group makes the aromatic system more nucleophilic in nature.

Q.9 b) Benzene acts as an electrophile

Feedback:

Look at the mechanism in detail and you will see that benzene reacts with an electrophilic reagent (meaning that benzene is acting in a

nucleophilic manner), the reaction description (EAS) refers to the fact that benzene (or another aromatic) is being substituted by an electrophile. Check the mechanism of the reaction.

Q.10 d) Pregabalin

Feedback:

Hopefully with a little background knowledge and some searching you found out that pregabalin, used to treat neuropathic pain and some seizures is not aromatic.

Q.11 b) The formation of benzyne

Feedback:

The formation of nitrobenzene, bromobenzene and benzene sulfonic acid uses classical methods of electrophilic aromatic substitution chemistry. Benzyne is an intermediate in one of the nucleophilic aromatic substitution reactions (see online material).

Q.13 Benzene sulphonic acid is:

- A . basic
- B. acidic
- C. neutral
- D. both A and B

ANSWER

Benzenesulfonic acid (conjugate base benzenesulfonate) is an organosulfur compound with the formula $C_6H_5SO_3H$. It is the simplest aromatic sulfonic acid. Its aqueous solution is strongly acidic.

Q.14. When benzene undergoes nitration using a mixture of HNO_3 and H_2SO_4 the nitrating agent in this reaction is

- A. $-NO_3$
- B. $-NO_2^+$
- C. $-NO$
- D. $-NO_2$

8. In Friedel/Crafts reaction of benzene, it is important to have a Lewis acid because the Lewis acid

- A. the neutralizes the basic reaction mixture
- B. makes the alkyl halide a better electrophile
- C. polarizes the C-X bond and thus facilitate the electrophilic attack by benzene
- D. B and C above are both correct.