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Substituents on a benzene ring can significantly impact the site of substitution reactions, influencing where electrophiles will attach to the ring. Electron-donating groups such as -CH3, -OH, and -NH2 increase electron density in the π system, making it more reactive and directing electrophile attack towards positions 2 and/or 4. For example, methylbenzene's methyl group is an electron donor; upon bromination, the bromine electrophile attacks at the 2 and/or 4 position, yielding products such as 2-bromomethylbenzene and 4-bromomethylbenzene. Conversely, electron-withdrawing groups like -NO2 reduce electron density, making the ring less reactive and directing electrophiles towards the 3 position, as seen in the bromination of nitrobenzene, which yields 3-bromonitrobenzene. These directing effects can be crucial for planning organic synthesis reactions. The directing properties of substituents are not always predictable; even a single substituent can have multiple effects depending on its nature and position on the ring. As the alkyl substituent in the ring increases in size, it becomes more difficult for an attack to occur at the ortho position, resulting in a decrease in the percentage of ortho isomers in the product mixture. This phenomenon is attributed to steric effects, where the larger alkyl group hinders attack at the ortho position. Moreover, the size of the electrophile also plays a role in determining the ortho/para ratio, with larger electrophiles being less able to attack at the ortho position due to steric hindrance. When drawing resonance contributors for the carbocation formed during electrophilic aromatic substitution, it is essential to consider structures where each atom has a complete octet of electrons. Halogens exhibit both inductive electron-withdrawing and resonance electron-releasing effects on the benzene ring, although the resonance effect dominates in the case of hydroxyl and amino groups. The difference in behavior during electrophilic substitutions arises from the balance between these effects, with halogens reducing overall reactivity but experiencing less reduction at ortho and para positions due to resonance. In electrophilic aromatic substitution reactions, the rate is significantly influenced by the attached groups, with electron-rich rings reacting faster. Substituents that donate electron density to the ring, such as OR and NR2, are considered activating despite their electronegativity, as they can donate a lone pair of electrons through resonance. Activating groups increase the reaction rate relative to hydrogen, while deactivating groups decrease it. The distinction between activating and deactivating groups is crucial in understanding electrophilic aromatic substitution reactions, including bromination, chlorination, nitration, sulfonylation, Friedel-Crafts alkylation, and Friedel-Crafts acylation. Not yet, so if that's the summary of what happens next, the obvious question is: how does it happen? In other words, what's the mechanism? You can't determine the mechanism by just logical thinking. Making good guesses is possible but the ultimate test is how well it fits with experiments and lab work. We give you a simplified version in an introductory course which looks obvious in retrospect but forget that there are many failures along the path to finding the correct mechanism. Measuring reaction rates can provide insights into mechanisms. By tweaking experimental conditions, we can gather useful information about how reactions operate. Changing the substrate is powerful way to probe mechanisms, for example in nitration of benzene and comparison with other substrates like toluene and trifluoromethylbenzene. The introduction of a hydrogen substitute on benzene with a highly electronegative atom such as fluorine increases the rate of nitration, whereas a deactivating group decreases it. This effect is not fully understood and is based on experimental data. The question remains why certain groups accelerate or decelerate reaction rates. Alkyl groups like CH3 are considered electron-donors due to their electronegative carbon atoms, which create partial negative charges that can be donated to adjacent atoms. In contrast, haloalkyl groups such as CF3 are electron-acceptors because the highly electronegative fluorine atoms pull electron density away from the carbon atom, resulting in a partial positive charge. These inductive effects play a crucial role in understanding the impact of alkyl groups on electrophilic aromatic substitution. The reaction rate is influenced by how quickly reactants interact with electrophiles, known as "diffusion controlled". This implies that when the reactant comes into contact with the electrophile, a reaction occurs rapidly. The -OH group plays a significant role in this process due to its high activation potential. However, it's clear that oxygen's inductive effect alone cannot explain this phenomenon. 6. Oxygen and Nitrogen Containing Lone Pairs Are Highly Activating When Directly Bonded To The Ring Oxygen containing hydroxyl groups are excellent pi donors because of their ability to form a pi bond with adjacent atoms through resonance. This donation effect must outweigh the electron-withdrawing inductive effects, making hydroxyl groups highly activating. Nitrogen groups, such as amines and amides, also exhibit this behavior due to their lone pairs forming pi bonds with available p-orbitals. 7. Halogens (F, Cl, Br, I) Are Deactivating Not all groups capable of pi donation are activating, however. For instance, halogens like fluorine, chlorine, bromine, and iodine tend to be deactivating due to their inductive effects outweighing any pi-donation from lone pairs. This is evident in the slower reaction rates observed with electrophilic aromatic substitution on halogenated benzenes compared to benzene itself. 8. Pi Acceptor Groups Are Strongly Deactivating Pi acceptor groups, such as nitro groups (NO2) and carbonyl groups (C=O), can accept a pi bond from the ring instead of donating it. This results in a new lone pair on an electronegative atom, leading to deactivation and slower reaction rates for electrophilic aromatic substitution. In resonance terms, a pi bond forms between the aromatic ring and the substituent, creating a positive charge on the ring. 9. A Table of Activating and Deactivating Groups A comprehensive table comparing activating and deactivating groups is presented, highlighting the importance of understanding these factors in organic chemistry, particularly for future chapters on aromatic chemistry. groups, particularly those that can donate or withdraw electrons, play a crucial role in influencing reaction rates in electrophilic aromatic substitution (EAS) reactions. The complexity of these reactions makes it challenging to rank them solely by power. However, the author suggests categorizing EAS into five main types based on the activating and deactivating effects of different functional groups. Amines (NH2, NHR, NR2), phenol (OH), and its conjugate base O– are strong activating groups due to pi-donation, while alkoxy, amide, ester groups exhibit weaker activation. Alkyl Groups with no electron-withdrawing groups are moderately activating through inductive effect, whereas halogens have a moderate deactivating influence. On the other hand, atoms with pi-bonds to electronegative groups like NO2, CN, SO3H, CHO, COR, COOH, and COOR are strongly deactivating due to their electron-withdrawing nature. Similarly, CF3, CCl3, and NR3(+) have a strong deactivating effect without any pi bonds or lone pairs. The author notes that the relationship between activating and deactivating groups can be likened to a pKa table, as both involve evaluating factors that influence acid-base properties. Ultimately, experimental measurements of reaction rates determine the position of these groups on the chart. By analyzing the electronic effects of different functional groups, researchers can infer that the rate-determining step in EAS reactions likely involves the formation of an unstable electron-poor species, such as a carbocation. Become a member to access the clickable quiz with answers on the back. The quiz provides valuable insights into organic chemistry mechanisms, specifically electrophilic aromatic substitution (EAS). Notes can be found at the end of the article. 1. [Advanced] Deuterium isotope effects are not observed in EAS reactions. This suggests that C-H bond breakage is not the rate-determining step. In other words, breaking a C-D bond is just as fast as breaking a C-H bond. 2. Carbocation intermediates have been isolated and analyzed, providing strong evidence for the proposed mechanism of EAS reactions. A particular species was observed when mesitylene reacted with ethyl fluoride and boron trifluoride at -80°C. This carbocation intermediate, also known as an arenium ion or Wheland intermediate, was isolated as a white solid with a melting point of -15°C. Note: The reason why fluorine is the most activating halogen in EAS reactions lies in its ability to form strong pi-bonds due to better overlap between its 2p orbital and the p orbital on carbon. This results in a stronger effect compared to chlorine, bromine, or iodine. Note: Some EAS reactions do exhibit very small deuterium isotope effects, but this topic will not be explored further here. The reactivity of benzene and its derivatives in nitration reactions varies significantly, with chlorobenzene and bromobenzene being around 1-3% as reactive as benzene, while ethyl benzoate is much less reactive at only 0.1-0.2%. In contrast, toluene exhibits remarkable reactivity, being 40-50 times more active than benzene. This phenomenon has been extensively studied in the context of aromatic halogen substitution and its kinetics. A paper by Robertson et al. (1953) provides data on reaction rates for halogenation of various benzene derivatives, showcasing a wide range of activating and deactivating substituents. Notably, N,N-dimethylaniline is an extreme example, being 1018 times more reactive than benzene, while nitrobenzene exhibits the opposite effect, being 10^6 times less reactive. The influence of the methoxyl group in electrophilic aromatic substitution was examined by de la Mare and Vernon (1951). Their study found that anisole is 108 times more reactive than benzene, resulting in low o/p selectivity in reactions. This finding was further explored by Stock and Brown (1960), who conducted a rigorous study on the bromination of anisole. The researchers discovered that anisole exhibits high o/p selectivity, with bromination yielding 1.6% o- and 98.4% p-bromoanisole. The relative reactivity of anisole to benzene was measured to be 1.79 x 10^9:1.00. Additionally, the study demonstrated that s+ values (electrophilic Hammett constants) obtained through this method are comparable to those measured using other techniques. The concept of directing groups on nuclear reactivity in oriented aromatic substitutions was first introduced by Ingold et al. (1931). Their work, which focused on the nitration of toluene, introduced the term 'partial rate factor' (fp, fo, fm) to describe the impact of specific positions on a substituted benzene's reactivity compared to benzene. Table IV from this paper revealed that toluene can be anywhere from 1.2 – 10 times more reactive than benzene. Finally, Cohn et al.'s (1952) study compared the nitration of t-butylbenzene and toluene, showing that t-butylbenzene is significantly more p-directing, with 79.5% para formation compared to only 40% for toluene. These findings collectively contribute to our understanding of the complex relationships between substituents and reactivity in electrophilic aromatic substitution reactions. The transmission of polar effects through aromatic systems and the impact on nitration reactions. Steric hindrance posed by bulky groups such as t-butyl can block ortho approach. Studies have shown that polar effects play a significant role in aromatic substitutions, including nitration. A 1961 paper by Knowles and Norman presents data on the reactivity of toluene and benzene, revealing an empirical difference of 25x between the two. Toluene is found to be more reactive than benzene, while t-butylbenzene exhibits a lower reactivity profile. Bird and Ingold's work from 1938 indicates that halogenated benzenes are less reactive towards nitration, with chlorobenzene and bromobenzene exhibiting reactivity profiles around 2-3% of that of benzene. In contrast, studies have shown that the deactivating effect of a nitro group outweighs the activating influence of a methyl group in mononitrotoluenes. Brickman et al.'s work highlights the importance of substituent effects on aromatic substitution reactions. The anilinium ion's deactivation under acidic conditions is attributed to resonance effects, which lead to a lower reactivity profile compared to benzene. The paper by Brickman and Utley also explores the influence of acidity on nitration rates, suggesting that reaction proceeds via the anilinium ion in acidic media. Conversely, increasing acidity results in decreased reaction rates due to reduced availability of free aniline. A 1987 study published by Olah et al. investigates the electrophilic substitution of fluorine in benzene derivatives. The presence of the -OCF3 substituent is noted, which is less common in undergraduate chemistry courses but has applications in medicinal chemistry. The findings of this research demonstrate the intricate relationships between polar effects and aromatic substitutions, shedding light on the complex mechanisms underlying these reactions. PhOCF3 reactivity in EAS reactions is discussed by Prof. George A. Olah and his wife Judith. According to Tables VI-VIII, PhOCF3's reactivity is around 3-10% compared to benzene. The Quantum Mechanical Investigation of the Orientation of Substituents in Aromatic Molecules provides insight into the structure of arenium ions formed in EAS reactions, also known as s-complex or Wheland intermediates. Recent papers by Prof. Olah describe the isolation and characterization of intermediate ions from various electrophilic aromatic substitution reactions. These include alkylation, nitration, protonation with HBF4, and a Quantitative Treatment of Directive Effects in Aromatic Substitution.

Effect of oh on benzene ring. Effect of nitro group on benzene ring. Effect of halogens on benzene ring. Benzene ring activating groups. Effect of ch3 group on benzene ring. Effect of oh. State and explain the effect of the oh group on the reactivity of the benzene ring in phenol.