

Aromatic electrophilic substitution (ar-se) reactions essay



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Engineering Chemistry III Prof. K. M. Muraleedharan Aromatic electrophilic substitution (Ar-SE) Reactions The special reactivity of aromatic systems towards electrophiles arises mainly from two factors: the presence of π electron density above and below the plane of the ring - making it nucleophilic, and the drive to regain the aromatic character by opting for substitution as opposed to a simple addition reaction. Preference towards addition reactions in the case of alkenes and substitution in the case of aromatic compounds becomes evident if we analyze the energy profiles of these reactions (Figures 1 and 2).

Figure 1. Indian Institute of Technology Madras Engineering Chemistry III Prof. K. M. Muraleedharan Figure 2. Note: consider all the resonance structures of the Wheland complex The mechanism of electrophilic aromatic substitution involves an initial rate determining interaction of the π system with the electrophile to give a benzenonium ion intermediate (π complex or Wheland complex), which undergoes a rapid de-protonation by the base in the second step to restore aromaticity (Figure 3). $E + H \rightarrow E^+ + H^-$ fast $E + H \rightarrow E^+ + H^-$ Figure 3.

Some common electrophilic aromatic substitution reactions are: halogenation, nitration, sulfonation, Friedel-Crafts Acylation and Friedel-Crafts alkylation. These differ only in the Indian Institute of Technology Madras Engineering Chemistry III Prof. K. M. Muraleedharan nature and mode of generation of electrophiles, but in general follow the same two-step mechanism described above. Reagent combinations that lead to the generation of electrophiles in these reactions are shown in Figure 4. Indian

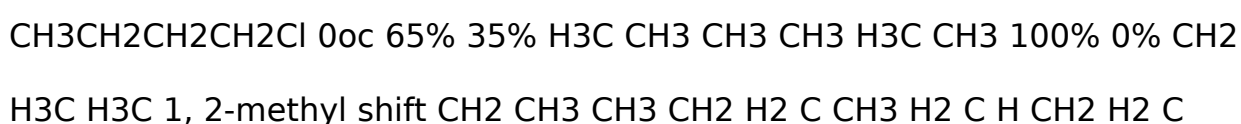
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Reaction Electrophile Generation of electrophiles $\text{Cl}_2 + \text{FeCl}_3 \rightarrow \text{Cl}_3\text{Fe} \text{ Cl Cl}$ First step Chlorination Cl^+ bromination Br^+ $\text{Br}_2 + \text{FeBr}_3 \rightarrow \text{Br}_3\text{Fe} \text{ Br Br}$ Iodination I^+ $\text{I}_2 + 2\text{Cu}^{2+} + 2\text{I}^- + 2\text{Cu}^+$ Nitration $\text{O}=\text{N}=\text{O} \text{ HO NO}_2 + \text{H OSO}_3\text{H} \text{ H}_2\text{O NO}_2 + \text{HSO}_4 \text{ O}=\text{N}=\text{O} + \text{H}_2\text{O}$ Sulfonation $\text{O S O O O HO S OH} + \text{O O H O S OH O O HO S OH}_2 \text{ O} + \text{O O S OH O O O S O Cl}$ Alkylation eg. 1 $+ \text{H}_3\text{C O HO S O} + \text{H}_2\text{O} + \text{AlCl}_3 + \text{AlCl}_4$ eg. 2 $\text{H}_3\text{C H C C H CH}_3^+ \text{ HF H}_3\text{C} ? \text{ H C C H}_2 \text{ CH}_3 + \text{F OH}$ eg. 3 $+ \text{H}_2\text{SO}_4 \text{ O} + \text{O S OH} + \text{H}_2\text{O O O}$ Acylation $\text{H}_3\text{C H}_3\text{C O Cl} + \text{AlCl}_3 \text{ H}_3\text{C AlCl}_3 \text{ O R O R O H}_3\text{C}$ acylium ion $\text{O R R O O} + \text{AlCl}_3 \text{ R O O} + \text{AlCl}_3(\text{RCO}_2) \text{ O} + \text{AlCl}_4$ Figure 4

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Muraleedharan Note: since the product of acylation is a ketone which can complex with AlCl_3 , two equivalents of the Lewis acid is necessary to bring about the conversion efficiently. The complex can later be hydrolyzed using water Among the reactions mentioned above, Friedel crafts alkylation suffers from two main draw backs: a) the possibility of multiple substitutions due to ring activation on mono-alkylation and b) the formation of products arising from rearranged electrophiles (carbocations) to more stable ones (Figure 5).

Multiple substitutions can be avoided by using a large excess of the substrate (aromatic system) to ensure the collision of the electrophile with an un-substituted substrate and not a mono-substituted one. $\text{H}_3\text{C AlCl}_3 + \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$  $\text{H}_3\text{C CH}_3 \text{ CH}_3 \text{ CH}_3 \text{ H}_3\text{C CH}_3 \text{ 100\% 0\% CH}_2 \text{ H}_3\text{C H}_3\text{C 1, 2-methyl shift CH}_2 \text{ CH}_3 \text{ CH}_3 \text{ CH}_2 \text{ H}_2 \text{ C CH}_3 \text{ H}_2 \text{ C H CH}_2 \text{ H}_2 \text{ C}$

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CH₃ CH H₂C C H₂ H₃C H₃C 1, 2-hydride shift C H₂ H₂C CH₃ H₃C CH₂Cl CH₃
 AlCl₃ CH₃ C H₃C C CH₃ H₂C + Figure 5.

Since acylium ions do not undergo rearrangement, an acylation-reduction strategy can be conveniently used to introduce alkyl groups which are prone to rearrangement as demonstrated by the example below (Figure 6) Indian Institute of Technology Madras Engineering Chemistry III Prof. K. M.

Muraleedharan O + CH₃CH₂CH₂-C Cl O 1. AlCl₃ 2. H₂O C H₂ C C H₂ CH₃
 Zn(Hg), HCl ? Clemmensen reduction H₂C H₂ C C H₂ CH₃ Figure 6.

Reversibility in Ar-SE Reactions Sulfonation of aromatic compounds is reversible and generally follows the following path (Figure 7). Similar equilibration is possible with electrophilic species such as HSO₃⁺ as well.

HSO₄ + SO₃ SO₃ H SO₃ H₃O SO₃H consider all resonance forms H₂SO₄ H₂O
 Figure 7. To drive the equilibrium forward, we can use large excess of the sulfonating agent with minimum amount of water at lower temperature.

Likewise, the reverse reaction will be facilitated by using dilute acids at higher temperatures with excess of water or passing superheated steam through the reaction mixture to remove the volatile de-sulfonated product.

Indian Institute of Technology Madras Engineering Chemistry III Prof. K. M. Muraleedharan Problem: How would you bring about the following transformation CH₃ ? CH₃ D

As per the principle of microscopic reversibility, the desulfonation should follow the same path in the reverse direction and energies of transition states and intermediates should remain the same. That is, the rate determining step here would involve the loss of +SO₃H from the protonated

intermediate as shown below (Figures 8 and 9). $\text{SO}_3\text{H} + \text{H}^+ \rightarrow \text{SO}_3\text{H}_2^+$ RDS + + SO_3H consider all resonance forms Figure 8. Indian Institute of Technology Madras Engineering Chemistry III Prof. K. M. Muraleedharan RDS for the forward and reverse reactions Free Energy If Deuterium labeled SO_3D SO_3H consider all resonance $\text{SO}_3\text{H} + \text{H}^+ \rightarrow \text{SO}_3\text{H}_2^+$ + SO_3H SO_3H_2^+ + H^+ Progress of the Figure 9. Note: The energy barrier in the second step (deprotonation) would be slightly higher for deuterated benzenonium ion intermediate compared to protonated one. This leads to a moderate isotope effect, where H^+ is displaced almost twice as fast compared to D^+ from the corresponding analogs. Forward reaction in the case of protonated species becomes more feasible due to relatively lower energy barrier, where as larger fraction of deuterated ones revert back to the starting material, thus decreasing the overall rate.

Reactivity of substituted aromatics Electron donating substituents usually activate the ring towards substitution where as electron withdrawing groups deactivate it. Compounds with activating groups react faster compared to benzene where as the ones with deactivating substituents react slower. This trend can be explained if we analyze the energy profile of the reaction and compare the stabilities of Indian Institute of Technology Madras Engineering Chemistry III Prof. K. M. Muraleedharan the benzenonium ion intermediates involved (Figure 10).

Since factors that stabilize the benzenonium ion intermediate should stabilize the transition-state as well (late transition-state) the activation energy in the case of aromatics with electron donating substituents will be lower than that for benzene. Due to the same reason, activation energy for <https://assignbuster.com/aromatic-electrophilic-substitution-ar-se-reactions-essay/>

derivatives with electron withdrawing substituents will be higher than that for benzene, leading to deactivation. The effects of these groups become very prominent if they are located at ortho or para positions with respect to the incoming electrophile. O N O E H

High energy resonance form that lead to deactivation (Consider other resonance forms as well) E H E H E H OCH₃ E H OCH₃ E H E H H₃CO H₃CO E H + E⁺ E + H⁺B⁺ Stabilizing effect of e-donor groups when present at ortho or para positions Figure 10. Note: relative energies of starting materials and products are NOT clearly defined in the above figure. Only the intermediates and transition states need to be considered. Indian Institute of Technology Madras Engineering Chemistry III Prof. K. M. Muraleedharan The same concept can be extended to explain the ability of pre-existing substituents to orient the incoming electrophiles.

Typically, an electron donating group activate the ring towards substitution at ortho and para positions and electron withdrawing groups orient them to meta position. Taking benzene as the reference, it can be stated that an activating group activates all positions in the ring (ortho, meta and para), but substitution predominantly takes place at ortho and para positions as these positions are activated to a larger extent compared to meta. Similarly, an electron withdrawing group deactivates all positions in the ring (including meta), but substitution takes place at meta position as other locations in the ring are deactivated even more.

This trend becomes clear if we look at the reaction conditions and product distributions in the sets of reactions presented in Figure 11. Various

substituents and the nature of their electronic influences that lead to activation/deactivation are summarized in Figure 12. Indian Institute of Technology Madras Engineering Chemistry III Prof. K. M. Muraleedharan

~30°C H₂SO₄ 95% NO₂ (A) NO₂ + HNO₃ ~100°C NO₂ NO₂ 7% NO₂ 88%
O₂N 1% NO₂ CH₃ + HNO₃ H₂SO₄ 25°C 62% CH₃ NO₂ NO₂ 5% CH₃ CH₃
O₂N 33% (B) OCH₃ + HNO₃ Ac₂O 10°C 71% OCH₃ NO₂ NO₂