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Electron withdrawing groups examples

Electron-donating groups on benzene, such as alkyl groups, donate electron density to the benzene ring, making it more electron-rich and increasing its reactivity towards electrophiles. In contrast, electron-withdrawing groups on benzene, such as nitro or carbonyl groups, withdraw electron density from the benzene ring, making it more electron-poor and decreasing its reactivity towards electrophiles. Overall, electron-donating groups enhance the nucleophilic nature of benzene, while electron-withdrawing groups enhance its electrophilic nature. Benzene, a six-membered ring of carbon atoms with alternating single and double bonds, is a fundamental building block in organic chemistry. The reactivity of benzene can be greatly influenced by the presence of substituents, known as electron-donating groups and electron-withdrawing groups. These substituents can either donate or withdraw electron density from the benzene ring, affecting its chemical properties. In this article, we will compare the attributes of electron-donating groups and electron-withdrawing groups on benzene.Electron-Donating GroupsElectron-donating groups are substituents that release electron density into the benzene ring through inductive or resonance effects. This results in an increase in electron density around the benzene ring, making it more nucleophilic and less electrophilic. Common examples of electron-donating groups include alkyl groups (such as methyl and ethyl), amino groups, and hydroxyl groups. These groups stabilize positive charges on the benzene ring and promote electrophilic aromatic substitution reactions.One of the key characteristics of electron-donating groups is their ability to activate the benzene ring towards electrophilic attack. This is due to the increased electron density around the ring, which makes it more reactive towards electrophiles. Electron-donating groups also enhance the ortho and para directing effects in electrophilic aromatic substitution reactions, leading to regioselective products.Another important aspect of electron-donating groups is their ability to stabilize carbocation intermediates in electrophilic aromatic substitution reactions. The electron-rich nature of these groups allows them to donate electron density to the positively charged carbon, reducing its overall positive charge and stabilizing the intermediate species.Overall, electron-donating groups enhance the reactivity of benzene towards electrophilic aromatic substitution reactions by increasing its electron density and stabilizing reaction intermediates. These groups are commonly found in organic molecules to facilitate various synthetic transformations.Electron-Withdrawing GroupsElectron-withdrawing groups are substituents that withdraw electron density from the benzene ring through inductive or resonance effects. This results in a decrease in electron density around the benzene ring, making it more electrophilic and less nucleophilic. Common examples of electron-withdrawing groups include nitro groups, carbonyl groups, and halogens. These groups destabilize negative charges on the benzene ring and promote nucleophilic aromatic substitution reactions.One of the key characteristics of electron-withdrawing groups is their ability to deactivate the benzene ring towards electrophilic attack. This is due to the decreased electron density around the ring, which makes it less reactive towards electrophiles. Electron-withdrawing groups also enhance the meta directing effects in electrophilic aromatic substitution reactions, leading to regioselective products.Another important aspect of electron-withdrawing groups is their ability to stabilize carbanion intermediates in nucleophilic aromatic substitution reactions. The electron-deficient nature of these groups allows them to accept electron density from the negatively charged carbon, reducing its overall negative charge and stabilizing the intermediate species.Overall, electron-withdrawing groups decrease the reactivity of benzene towards electrophilic aromatic substitution reactions by decreasing its electron density and destabilizing reaction intermediates. These groups are commonly used in organic synthesis to control the regioselectivity and reaction pathways of aromatic substitution reactions.ComparisonWhen comparing electron-donating and electron-withdrawing groups on benzene, several key differences can be observed. Electron-donating groups increase the electron density around the benzene ring, making it more nucleophilic and reactive towards electrophiles. In contrast, electron-withdrawing groups decrease the electron density around the benzene ring, making it more electrophilic and reactive towards nucleophiles.Electron-donating groups activate the benzene ring towards electrophilic attack, while electron-withdrawing groups deactivate the benzene ring towards electrophilic attack. This difference in reactivity can be attributed to the electron-donating or electron-withdrawing nature of the substituents, which affects the overall electron distribution in the benzene ring.Electron-donating groups stabilize positive charges on the benzene ring and promote electrophilic aromatic substitution reactions, while electron-withdrawing groups destabilize negative charges on the benzene ring and promote nucleophilic aromatic substitution reactions. These contrasting effects highlight the importance of substituent effects in controlling the reactivity of benzene in organic chemistry.Overall, electron-donating and electron-withdrawing groups play crucial roles in modulating the reactivity of benzene in various synthetic transformations. Understanding the impact of these substituents on the benzene ring is essential for designing efficient and selective organic reactions. Comparisons may contain inaccurate information about people, places, or facts. Please report any issues. Electron-withdrawing groups (EWGs) are functional groups that decrease the electron density of a molecule. They are commonly used to modify the reactivity of organic compounds in chemical reactions. Key entities related to EWGs include their inductive effect, resonance effect, electronegativity, and various examples. Understanding the electron-withdrawing capabilities of different functional groups is crucial for predicting the behavior of molecules and designing synthetic strategies in organic chemistry. Define electron-withdrawing groups and their role in influencing molecular reactivity. Electron-Withdrawing Groups: The Coolest Kids on the Chemistry Block Imagine molecules as tiny magnets, with different parts pulling and pushing electron clouds around. Some molecules have this superpower to suck electrons away from others, and these are called electron-withdrawing groups. They’re like the cool kids on the chemistry block, influencing how molecules react and behave. The Power of Electron-Withdrawing Groups These magnetic molecules can do some pretty awesome tricks. They: Make reactions smoother: They’re like catalysts, helping electrophilic additions (when one molecule adds to another) go down easier. Pump up acidity: They make their neighbors (protons) more acidic, like a mean mom yelling at her kids. Stabilize the bad boys: They’re friends with carbocations (molecules with a positive charge on a carbon atom), helping them chill out and stay stable. Meet the Electron-Withdrawing VIPs There are a bunch of these cool electron-withdrawing groups, each with its own style: Halogens: These guys are like the bullies of the molecular world, stealing electrons like it’s their job. Nitro: They’re like the nitroglycerin of electron-withdrawing groups, making molecules super reactive. Carbonyl: These are the kingpins of electron withdrawal, making their neighbors as sour as a lemon. Cyano: They’re the sneaky ones, stealing electrons through a back door. Sulfonyl: These guys are like the heavyweights, seriously withdrawing electrons with their size and power. How Do They Do It? These electron-withdrawing groups have two main ways of flexing their power: Inductive Effect: They pass on their electron-sucking ability through the chain of atoms, like a domino effect. Resonance Effect: They share electrons through special bonds, creating areas of positive charge that attract electrons away. Sometimes, groups use both effects, like a double dose of electron withdrawal. Nitro, carbonyl, and cyano groups are the masters of this tag team. So next time you’re dealing with molecules, remember the electron-withdrawing groups. They’re the ones pulling the strings, making reactions hotter, protons sourer, and carbocations happier. They’re the rockstars of chemistry, and they’re here to shake things up! All Hail the Electron-Withdrawing Kings and Queens In the realm of organic chemistry, we encounter these remarkable characters known as electron-withdrawing groups (EWGs). These mighty influencers have a knack for tugging electrons away from their unsuspecting neighbors, leaving a trail of fascinating reactivity patterns in their wake. Electrophilic Addition: A Boost from the Sidelines Imagine a scene straight out of a sports match. An electrophile, the eager ball carrier, needs a little help to score a touchdown. Enter our EWGs, the enthusiastic cheerleaders on the sidelines. They cheer so loudly that the electrophile gains a surge of confidence, lunging forward to seize the electrons and complete the addition. Acidity Enhanced: Proton Power Unleashed Acids, the sourpusses of chemistry, love nothing more than shedding protons. And wouldn’t you know it, EWGs are the perfect proton pushers. They create an electron-deficient zone next door to protons, making them more tempted to break free and dance away. Carbocation Stabilization: A Haven in the Storm Carbocations, the troublemakers of organic chemistry, are notoriously unstable rebels. But our heroic EWGs step in as peacemakers, stabilizing these unruly ions by dispersing their positive charge. It’s like they put the carbocations on a comfy couch, offering them some much-needed support. List and briefly describe common electron-withdrawing groups such as halogens, nitro groups, carbonyl groups, cyano groups, and sulfonyl groups. Electron-Withdrawing Groups: The Unsung Heroes of Chemistry Imagine atoms as tiny magnets, with electrons swirling around like little tornadoes. Electrons are negatively charged, so they stay far away from other negative charges. This is where electron-withdrawing groups come into play. They’re like tiny magnets with a positive charge that suck the electrons away from their neighbors. How Electron-Withdrawing Groups Rock Your Molecules These groups have a profound impact on how molecules behave. They make them more reactive by attracting electrons and creating positive charges. This means they’re more likely to react with other molecules, like when a hungry tiger pounces on a juicy antelope. Electron-withdrawing groups also make nearby protons (acidic hydrogen atoms) more acidic. Think of it like the “Bully of Chemistry.” They steal electrons from the protons, leaving them feeling exposed and vulnerable. As a result, these protons are more likely to jump off the molecule, like a kid getting picked on in the schoolyard. Common Electron-Withdrawing Groups: The Superstars of Chemistry Let’s meet some of the most common electron-withdrawing groups: Halogens (e.g., fluorine, chlorine, bromine, iodine): These guys are like the “Chuck Norris” of electron-withdrawing groups, with some of the strongest inductive effects. They’re like magnets that snatch electrons with lightning speed. Nitro groups (-NO2): These groups are like tiny fireworks, with their ability to create positive charges on the carbon atoms next to them. It’s like they’re setting off electron explosions! Carbonyl groups (C=O): These groups have a double bond between carbon and oxygen, which makes the carbon atom electron-deficient. They’re like the “thirsty boy” of electron-withdrawing groups, always looking to grab electrons from their neighbors. Cyano groups (-CN): These groups are like the “stealthy ninjas” of electron-withdrawing groups, using their lone pair of electrons to create positive charges on nearby atoms. Sulfonyl groups (-SO2-): These groups are like the “heavyweights” of electron-withdrawing groups, with a strong inductive effect due to the presence of multiple electronegative oxygen atoms. They’re like sumo wrestlers, pushing electron density away from them with brute force. Electrifying Electron-Withdrawing Groups: The Molecular Shape-Shifters Picture this: you’re at the grocery store, trying to decide between two bags of chips. One bag has a crisp, golden glow, promising a burst of flavor. The other bag looks like it’s been through a war zone, crumpled and sad. Which one do you choose? It’s the same with molecules. They have their own unique personalities, and some are more reactive than others. Electron-withdrawing groups are like molecular bullies, snatching electrons away from their neighbors and making them more reactive. How Do They Work Their Magic? Electron-withdrawing groups are like energy vampires, siphoning electrons through special bonds called sigma bonds. Imagine sigma bonds as invisible wires connecting atoms. When an electron-withdrawing group moves into the neighborhood, it acts like a magnet, pulling electrons towards itself. This leaves the atoms next door feeling a little lonely and exposed. They become more eager to react with other molecules, like a shy kid suddenly eager to make friends. The Power Trio: Inductive, Resonance, and Mesomeric Effects There are three main ways electron-withdrawing groups exert their influence: Inductive Effect: The bully reaches out with its negative aura, creating a ripple effect where electrons are pushed away from neighboring atoms. Resonance Effect: The bully uses its electron-sucking power to create new positive charge centers within the molecule. This is like the bully’s “evil lair” where electrons are trapped and tormented. Mesomeric Effect: This is the bully’s sneaky sidekick, using lone pairs of electrons to create even more positive charge centers. It’s like the bully’s attack dog, barking at electrons and scaring them away. Examples of These Molecular Bullies Here are some common examples of electron-withdrawing groups: Halogens (like chlorine and iodine) Nitro groups (NO2) Carbonyl groups (C=O) Cyano groups (CN) Sulfonyl groups (SO2) These groups are like the ultimate bullies on the molecular playground, making their neighbors cry and desperate for attention. They’re the reason why some molecules are so reactive and others are the equivalent of couch potatoes. Electron-Withdrawing Groups: The Chemistry Cop Who Tightens the Screws You know those electron-withdrawing groups? They’re like the chemistry cops of the molecular world, patrolling around, ready to nab those sneaky electrons. They’re always on the lookout for molecules that are a little too relaxed, with their electrons hanging out like rebels without a cause. One of their favorite tricks is to use resonance. This is like a special dance party where electrons can move around to different positions, creating different shapes for the molecule. When electron-withdrawing groups get involved, they can push electrons away from certain atoms, creating areas that are electron-deficient, or positive. It’s like they’re saying, “Hey, buddy! Your electrons are getting a little too cozy. We’re going to show you who’s boss!” So, if you’re working with molecules that have electron-withdrawing groups, keep an eye out for areas where electrons might be scarce. These positive areas can make the molecule more reactive, like attracting other electrons or donating protons (like the sourpuss of the chemistry world). Delving into the Mysteries of Electron-Withdrawing Groups Imagine a molecular battleground, where tiny particles called electrons play a pivotal role in determining the outcome. Electron-withdrawing groups, like the Darth Vaders of the molecular world, wield their power to weaken electrons and boost reactivity. Understanding the Dark Side of Molecules Electron-withdrawing groups are like villains that steal electrons from nearby atoms. Their greedy nature makes the surrounding area electron-poor, increasing the vulnerability of molecules to electrophilic attacks. These groups also make protons more acidic, like sour lemons, and help stabilize unstable carbocations, like bandaging a wounded warrior. Meet the Notorious Gang of Electron-Withdrawing Groups The molecular underworld is teeming with electron-withdrawing groups, each with its own sinister specialty: Halogens (F, Cl, Br, I): These evil twins wreak havoc by pulling electrons towards them with their strong electronegativity. Nitro groups (NO2): Think of nitro groups as explosives that blast electrons away, leaving a trail of electron-poor devastation. Carbonyl groups (C=O): These double agents use their resonance magic to create multiple areas of positive charge, making molecules more vulnerable to attack. Cyano groups (CN): Cyano groups are like toxic gas, releasing their deadly electron-withdrawing power into the molecular environment. Sulfonyl groups (SO2): These ruthless dictators suppress electrons with their ruthless electronegativity, leaving victims weak and undefended. Unveiling the Dark Arts: Inductive and Resonance Effects Electron-withdrawing groups exert their influence through two diabolical mechanisms: inductive effect and resonance effect. Inductive Effect: This is like a chain reaction, where electron-withdrawing groups suck electrons from adjacent atoms, creating a ripple effect of electron deficiency. Resonance Effect: Picture an intricate dance of electrons, where resonance structures create areas of positive charge, further weakening the surrounding electrons. The Triple Threat: Groups with Both Inductive and Resonance Powers Some electron-withdrawing groups are the ultimate villains, wielding both inductive and resonance powers. These include the notorious nitro group, the cunning carbonyl group, and the venomous cyano group. They wreak havoc on molecules, making them highly reactive and vulnerable to attack. So, there you have it, the dark secrets of electron-withdrawing groups. They are the molecular manipulators, pulling strings and influencing reactivity with their mysterious powers. By understanding their strategies, you can outwit these molecular villains and conquer the challenges of organic chemistry. Electron-Withdrawing Groups: The Good, the Bad, and the Ugly Picture this: you’ve got a molecule minding its own business, happily sharing electrons like a big, chemical family. But then, out of nowhere, an electron-withdrawing group comes along and starts snatching up all the electrons like it’s a black hole. These electron-withdrawing groups are like the mean kids on the playground who steal your lunch money. They make the molecule a lot less stable and more reactive. But hey, who needs stability, right? The Bad News: Unstable Molecules Electron-withdrawing groups make molecules behave like ticking time bombs. They pull electrons away from the rest of the molecule, creating areas of positive charge and making it more likely that the molecule will react with other chemicals. It’s like giving a hungry lion a juicy steak – it’s only a matter of time before it devours it. The Good News: Enhanced Reactivity But wait, there’s good news! This instability also makes molecules more reactive. Electron-withdrawing groups can enhance electrophilic addition, which is when an unsaturated molecule adds an electrophile (a substance that loves electrons) to itself. They can also increase the acidity of protons, making them more likely to detach themselves from the molecule. And they can even stabilize carbocations, which are positively charged carbon ions that are usually highly unstable. The Usual Suspects: Common Electron-Withdrawing Groups So, who are these electron-withdrawing meanies? Well, some of the most common ones include: Halogens (like chlorine and fluorine) Nitro groups ($-NO_2$) Carbonyl groups (C=O) Cyano groups (-CN) Sulfonyl groups ($-SO_2CF_3$) How They Do It: Inductive and Resonance Effects Electron-withdrawing groups use two main tricks to steal electrons: inductive effects and resonance effects. Inductive effects are like dominoes falling in a line. When an electron-withdrawing group attaches to a molecule, it pulls electrons away from the atoms next to it, and those atoms in turn pull electrons away from the ones next to them, and so on. Resonance effects, on the other hand, are like a game of musical chairs. Electron-withdrawing groups can create areas of positive charge by delocalizing electrons through pi bonds. This means that the electrons can move around, creating multiple resonance structures and making it more likely that the molecule will react. Examples of Both Inductive and Resonance Effects Some electron-withdrawing groups, like nitro groups, carbonyl groups, and cyano groups, can exert both inductive and resonance effects. This makes them particularly powerful at withdrawing electrons and destabilizing molecules. So, there you have it – electron-withdrawing groups: the bad boys of chemistry. They may make molecules more unstable, but they also make them more reactive, which can be useful for a variety of chemical reactions. Just remember, these groups are like handling a live wire – use them with caution, or you might get a nasty shock! Alright folks, that’s all for our electron-withdrawing groups rundown. Hopefully, you found this helpful in understanding how these groups influence chemical reactions. Remember, electron-withdrawing groups are a crucial concept in organic chemistry, and a good understanding of them can make your studies a whole lot easier. Thanks for sticking with me, and feel free to drop by again if you need a refresher or want to dive deeper into the wonderful world of chemistry. Take care, and keep those electrons in check! Last updated: February 7th, 2025 | Activating and Deactivating Groups in Electrophilic Aromatic Substitution The rate of electrophilic aromatic substitution (EAS) reactions is greatly affected by the groups attached to the ring. The more electron-rich the aromatic ring, the faster the reaction Groups that can donate electron density to the ring make EAS reactions faster. If a substituent increases the rate of reaction relative to H it is called activating. If it decreases the rate relative to H it is called deactivating. (These rates need to be measured by experiment). Important! Groups like OR and NR2 that seem like they should be deactivating because of their electronegativity are actually activating since they can donate a lone pair of electrons into the ring through resonance. There’s a lot to this post, so here’s a quick index: Table of Contents 1. Activating And Deactivating Groups Last post in this series we introduced electrophilic aromatic substitution. Here’s the general case: Why is this a substitution reaction, you ask? Because we’re forming and breaking a bond on the same carbon. We form C–E (where “E” is a generic term for “electrophilic atom”) and we break C–H. [As for the specific identity of “E”, we mentioned six key electrophilic aromatic substitution reactions in the last post (bromination, chlorination, nitration, sulfonylation, Friedel-Crafts alkylation and Friedel-Crafts acylation) that we’ll eventually dig into in detail. But not yet.] So if that’s the summary of what happens, the next obvious question is: how does it happen? In other words, what’s the mechanism? Obligatory pre-mechanism speech: You can’t determine the mechanism of a chemical reaction merely through logical deduction from first principles. Sure, you can make guesses – even good ones! But the ultimate test of a mechanistic hypothesis is how well it fits with experiment, and that typically involves a lot of lab work. What you’re taught in an introductory course is the tippy-topmost layer of snow on the iceberg. We give you the best answer, and in retrospect it looks obvious. What you don’t see is all the failure, wrong turns, and false hypotheses that happened along the path towards determining the correct mechanism. However, the mechanisms of these reactions that you will learn about weren’t obvious to most of their discoverers, who were among the brightest and best chemists of their time. Remember that. 2. Measuring Reaction Rates Can Provide Insight Into The Mechanism As far as determining mechanisms is concerned, one of the best tools we have in our experimental arsenal is the ability to measure reaction rates. By measuring the effect that slight tweaks in the experimental conditions (e.g. structure of reactant, temperature, solvent) have upon the rate, we can gather useful insights about how a reaction operates “under the hood”. Of the parameters mentioned above, changing the substrate (reactant) is probably the most powerful way to probe a mechanism, because it allows you to tune how electron-rich (nucleophilic) or electron-poor (electrophilic) it is. Let me show you what I mean. Let’s arbitrarily pick one electrophilic aromatic substitution reaction: nitration. We know that by adding nitric acid and H2SO4, benzene can undergo nitration to form nitrobenzene (break C-H, form C-NO2) We can even measure the rate of this reaction at a given temperature, concentration, and solvent. Using the exact same experimental conditions we can then measure the rate of the reaction when toluene (methylbenzene, C6H5CH3) is used as the substrate instead of benzene. The nitration of toluene is 23 times faster than it is for benzene. [Ref 1] Using the exact same experimental conditions, we can also use trifluoromethylbenzene (C6H5CF3) as the substrate, and measure the reaction rate. The nitration of trifluoromethylbenzene is 40,000 times slower than it is for benzene (2.5 × 10-5). Bottom line: if we swap a hydrogen on benzene for a methyl group, the reaction is faster. If we swap a hydrogen for a trifluoromethyl group, the reaction is slower. This pattern turns out to be general for other electrophilic aromatic substitution reactions as well (chlorination, bromination, Friedel-Crafts, and others). 3. “Activating” and “Deactivating” Groups – A Definition Let’s call a group activating that increases the rate of an electrophilic aromatic substitution reaction, relative to hydrogen. As we just saw, CH3 is a perfect example of an activating group; when we substitute a hydrogen on benzene for CH3, the rate of nitration is increased. A deactivating group, on the other hand, decreases the rate of an electrophilic aromatic substitution reaction, relative to hydrogen. The trifluoromethyl group, CF3 , drastically decreases the rate of nitration when substituted for a hydrogen on benzene. This definition is ultimately based on experimental reaction rate data. It doesn’t tell us why each group accelerates or decreases the rate. “Activating” and “deactivating” just refers to the effect of each substituent on the rate, relative to H. OK then. So why might CH3 increase the rate of reaction, and CF3 decrease it? 4. “Sigma” (σ) donors and acceptors (otherwise known as “inductive effects”) Let’s quickly think back to what we know about alkyl groups (such as CH3) and haloalkyl groups (such as CF3), and try to address this question. In CH3, the carbon atom is more electronegative (2.5) than hydrogen (2.2). This means that the carbon attracts a bit more than an equal share of electron-density from the covalent bond with H, resulting in a partial negative charge (δ–) on carbon and a partial positive charge (δ+) on hydrogen. This partial negative charge is then available to be donated to an adjacent atom. Hence, we tend to think of CH3 as an electron-rich species; an electron–donor. In CF3 the electrons are pulled in the opposite direction. Three highly electronegative (4.0) fluorine atoms pull electron density away from the carbon atom (2.5), resulting in a partial positive charge (δ+) on carbon. Rather than donate electron density, the carbon tends to accept (pull away) electron density from adjacent atoms (this is the familiar inductive effect) We generally consider CF3 to be an electron-poor species; an electron-acceptor. Since these inductive effects operate solely through single bonds (“sigma”, or σ bonds) this behaviour is sometimes called “sigma donation” (as for CH3) or “sigma accepting” (for CF3). So it seems like a good hypothesis that activating groups are electron-donating (relative to H), and deactivating groups are electron-withdrawing (relative to H) 5. Pi (π) Donors and Acceptors (otherwise known as “Resonance”) Sigma donation and acceptance helps us to understand the effect of alkyl groups on electrophilic aromatic substitution. So what about other functional groups? What effect might, say, a hydroxyl group have on the rate of nitration? Quiz time. Do you think –OH would be activating (increase the rate) or deactivating (decrease the rate) for electrophilic aromatic substitution (such as nitration)? Guessing is OK! Based on what we just said, it’s fully understandable if you said, “deactivating”. After all, oxygen is highly electronegative (3.4) and through induction, pulls away electron density through the bond. In other words, it’s a sigma-acceptor. The fact is, however, that OH greatly accelerates the rate, orders of magnitude more than CH3 does. In fact I couldn’t find good rate data comparing OH to CH3 because in the case of -OH, the reaction is what’s called, “diffusion controlled”. That roughly means, “as soon as the reactant comes in contact with the electrophile, a reaction occurs.” In other words, the –OH group is highly activating. Clearly, something else must be going on here besides the inductive effect of oxygen! 6. Oxygen And Nitrogens Containing Lone Pairs Are Highly Activating When Bonded Directly To The Ring As we saw in our chapter way back on resonance, hydroxyl groups are excellent pi donors. The lone pairs on the oxygen atom can form a pi bond with an adjacent atom containing an available p-orbital. This donation effect (or “resonance”) must outweigh electron-withdrawal via inductive effects, otherwise we’d observe that hydroxyl groups are deactivating. The same is true for nitrogen groups with lone pairs, such as amines and amides (below). [One measure of the importance of pi-donation in the activating nature of amines is seen in their behavior under strongly acidic conditions. If the nitrogen lone pair is either protonated with strong acid or undergoes a substitution reaction to form NR3+ , pi-donation is impossible and the group becomes strongly deactivating (see table below).] 7. Halogens (F, Cl, Br, I) Are Deactivating Not all groups capable of pi donation are activating groups. For example, halogens (F, Cl, Br, I) tend to be deactivating. The rates of electrophilic aromatic substitution reactions on fluorobenzene, chlorobenzene, bromobenzene, and iodobenzene are all slower than they are for benzene itself. In these cases, inductive effects (“sigma accepting”) would appear to have a greater effect on the rate than any pi-donation from the lone pairs. [pi donation < sigma acceptance]. [Why?] A good rule of thumb for pi-donation ability is the basicity of the lone pair. Amines tend to be better bases than oxygens, which are far better bases than halogens. Alright. What if electrons flow in the opposite direction? Is there an opposite of “pi donor” ? 8. Pi Acceptor Groups Are Strongly Deactivating Yes! As you may already know, the opposite of a “pi-donor” is a “pi acceptor”. Certain functional groups can accept, rather than donate, a pi bond from the ring, resulting in a new lone pair on a substituent atom. Examples are NO2, carbonyl groups (C=O), sulfonyl, cyano (CN) among others. These groups are universally deactivating, slowing the rate of electrophilic aromatic substitution. In terms of resonance, one can draw a pi bond from the aromatic ring forming a pi bond with the atom bound to the ring, resulting in formation of a new lone pair on an electronegative atom on the substituent. Note how this results in a positive charge on the ring! So how do we keep all of these factors straight? This is an example of why I say that resonance is the most important key concept to review for Org 2. In the section on aromatic chemistry it comes back with a vengeance. 9. A Table of Activating and Deactivating Groups Now seems like the right time to present a big table of activating and deactivating groups. It’s hard to rank exactly by power since the effect is averaged over several types of reactions. Oh dear, this looks like a lot to remember. How to keep it all straight? I would suggest five main “buckets”, below: Nitrogen and oxygens with lone pairs – amines (NH2, NHR, NR2), phenol (OH) and its conjugate base O– are very strong activating groups due to pi-donation (resonance). Alkoxy, amide, ester groups less strongly activating. Alkyl Groups – (with no electron withdrawing groups). Moderately activating through inductive effect. Halogens – Moderately deactivating. Electron withdrawing (highly electronegative) nature outweighs donation of electron density through a lone pair. Atoms with pi-bonds to electronegative groups – Strongly deactivating. NO2, CN, SO3H, CHO, COR, COOH, COOR, CONH2. All pi-acceptors. Electron withdrawing groups with no pi bonds or lone pairs – Strongly deactivating. CF3, CCl3, and NR3(+). Pure inductive effect. Once you remember the somewhat counterintuitive fact that O and N-bonded functional groups with lone pairs are activating, and halogens are deactivating, the rest is fairly straightforward. One final word. Our table of “activating” and “deactivating” groups turns out to be a little bit like a pKa table. How? We can evaluate several factors that have an impact on pKa, but the ultimate test of which factor is more important is experimental measurement of an equilibrium constant. Likewise, with activating and deactivating groups, we can identify factors which may or may not make a certain group activating or deactivating, but in the end, its position on the chart comes down to experimental measurements of reaction rates. Click to Flip 10. Summary: What Does This Tell Us About The Mechanism Of Electrophilic Aromatic Substitution? OK. So what does all of this tell us? Since the rate is so sensitive to whether the group is electron donating or electron withdrawing (“electronic effects”, as organic chemists might quickly summarize it) it would suggest that the rate determining step is the formation of a fairly unstable electron-poor species, such as a carbocation. Recall CH3 and CF3. You may recall that the order of carbocation stability (tertiary > secondary > primary) is due to the fact that carbocations are stabilized by adjacent alkyl groups (such as CH3), and, conversely, are destabilized by adjacent electron withdrawing groups (like CF3). Likewise, carbocations are stabilized by adjacent atoms that can donate lone pairs (e.g. O and N) through resonance, and destabilized by pi acceptors such as C=O, NO2, and so on. A likely first step would be something like this: We’ll go into the full mechanism of electrophilic aromatic substitution in the next post, but will fill in additional detail in a bonus topic below. Next Post: Electrophilic Aromatic Substitution: The Mechanism Quiz Yourself! Become a MOC member to see the clickable quiz with answers on the back. Become a MOC member to see the clickable quiz with answers on the back. Become a MOC member to see the clickable quiz with answers on the back. Become a MOC member to see the clickable quiz with answers on the back. Notes Possibly a useful reference sheet. Adapted from Ingold’s “Structure and Mechanism in Organic Chemistry”, 2nd ed. 1. [Advanced] No deuterium isotope effect is observed in electrophilic aromatic substitution In electrophilic aromatic substitution a C-H bond is broken. One way to probe the mechanisms of reactions that involve C-H bond cleavage is to use deuterium (D) labelling. In reactions where C-H bond breakage is a rate-determining step (e.g. E2 elimination) a C-H bond can break up to 6-7 times faster than a C-D bond. This is called a deuterium isotope effect and it is measurable. Electrophilic aromatic substitution reactions have no significant deuterium isotope effects. [Note] This strongly suggests that C-H bond breakage is not the rate determining step. 2. Carbocation intermediates have been isolated that strongly support the proposed mechanism Here’s a species that’s been observed when 1,3,5-trimethylbenzene (mesitylene) is treated with ethyl fluoride and boron trifluoride at –80°C (this is a Friedel-Crafts alkylation reaction, by the way). The carbocation intermediate (called an “arenium ion” or “Wheland intermediate” was isolated as a white solid with melting point –15°C, and analyzed by NMR spectroscopy. As Eric Jacobsen might say: “mechanisms can never be proven, but….” . (this pretty much seals the deal). We’ll go into in more detail in the next post. Note 1. Reference: March, Advanced Organic Chemistry 5th ed, page 692. Note 2. Why? Interestingly, fluorine is the most activating of the halogens. The reason is likely that the overlap of the lone pair in the fluorine 2p orbital with the p orbital on carbon is much better (resulting in a stronger pi-bond) than is donation with the 3p (and higher) p orbitals of chlorine, bromine, and iodine. Note 3. Actually a white lie; some electrophilic aromatic substitution reactions do have very small deuterium isotope effects, but we’re not touching that topic, nosiree. [partitioning effects, see March’s Advanced Organic Chemistry, 5th ed., p. 679] (Advanced) References and Further Reading As mentioned, this topic is useful for all types of EAS reactions – Friedel-Crafts alkylation/acylation, halogenation, nitration, etc. —The chlorination of anilides. The directing influence of the acylamido-group Kennedy Joseph Previté Orton and Alan Edwin Bradfield J. Chem. Soc. 1927, 986-997 DOI: 10.1039/JR9270000986 An early paper discussing the ortho/para product distribution obtained by electrophilic chlorination of anilides (generally 65% para/35% ortho). Unfortunately this paper does not have data comparing the rate of chlorination to benzene. Kinetics and mechanism of some electrophilic benzene substitution reactions Alan E. Bradfield and Brynmor Jones Faraday Soc. 1941, 37, 726-743 DOI: 10.1039/TF9413700726 Table I in this paper contains partial rate factors for nitration of benzene and related compounds. Chlorobenzene and bromobenzene are around 1-3% as reactive as benzene, whereas ethyl benzoate is significantly deactivated – it is around 0.1-0.2% as reactive as benzene! Toluene is 40-50 times as reactive as benzene. The kinetics of aromatic halogen substitution. Part IX. Relative reactivities of monosubstituted benzenes P. W. Robertson, P. B. D. de la Mare, and B. E. Swedlund J. Chem. Soc. 1953, 782-788 DOI: 10.1039/JR9530000782 Pg. 783 in this paper contains data for reaction rates of halogenation of various benzene derivatives. This spans the gamut of extreme activating substituents (N,N-dimethylaniline is 1018 times more reactive than benzene!) and deactivating substituents (nitrobenzene is 10-6 times less reactive than benzene). The influence of the methoxyl group in aromatic substitution P. B. D. de la Mare and C. A. Vernon J. Chem. Soc. 1951, 1764-1767 DOI: 10.1039/JR9510001764 This paper examines the effect of -OMe in electrophilic aromatic substitution (e.g. anisole and related compounds vs. benzene). Overall, anisole is 108 times more reactive than benzene, and as a result, o/p selectivity in reactions is very low. Rates of Bromination of Anisole and Certain Derivatives. Partial Rate Factors for the Bromination Reaction. The Application of the Selectivity Relationship to the Substitution Reactions of Anisole Leon M. Stock and Herbert C. Brown Journal of the American Chemical Society 1960, 82 (8), 1942-1947 DOI: 1021/ja01493a026 This paper is a more rigorous study of the bromination of anisole by Nobel Laureate Prof. H. C. Brown. The o/p selectivity of anisole is actually rather high – bromination gives 1.6% o– and 98.4% p-bromoanisole. The relative reaction of anisole:benzene is also measured to be 1.79 x 109:1.00. This paper also shows that s+ values (electrophilic Hammett constants) measured this way are comparable to Hammett values measured through other methods, and that the Hammett values also provide a good measure of how a substituent will effect EAS reactions as well. —Influence of directing groups on nuclear reactivity in oriented aromatic substitutions. Part II. Nitration of toluene Christopher Kelk Ingold, Arthur Lapworth, Eugene Rothstein, and Denis Ward J. Chem. Soc. 1931, 1959-1982 DOI: 10.1039/JR9310001959 This is the first paper to introduce the term ‘partial rate factor’ (usually denoted by fp, fo, fm) to denote the amount by which a specific position on a substituted benzene may be more or less reactive compared to benzene. Table IV shows in this paper that toluene can be anywhere from 1.2 – 10 times more reactive than benzene. Effects of Alkyl Groups in Electrophilic Additions and Substitutions COHN, H., HUGHES, E., JONES, M. and PEELING, M. G. Nature 1952, 169, 291 DOI: 1038/169291a0 This paper has data comparing the nitration of t-butylbenzene and toluene. T-butylbenzene is much more p-directing than toluene (79.5% para for t-butylbenzene vs. 40% para for toluene), which is likely due to sterics (ortho approach is blocked by the bulkier t-butyl group). The transmission of polar effects through aromatic systems. Part II. The nitration of benzyl derivatives J. R. Knowles and R. O. C. Norman J. Chem. Soc. 1961, 2938-2947 DOI: 10.1039/JR9610002938 J. R. Knowles went on to become a Professor at Harvard, specializing in enzymology. The knowledge of kinetics that one gets from doing physical organic chemistry is applicable in a wide variety of areas! In this paper, Table 2 is interesting, and shows that the empirical reactivity difference between toluene and benzene is 25x, which is what is commonly found in textbooks today. T-butylbenzene is less reactive than toluene, but still 15x more reactive than benzene. Influence of directing groups on nuclear reactivity in oriented aromatic substitutions. Part IV. Nitration of the halogenobenzenes Marjorie L. Bird and Christopher K. Ingold J. Chem. Soc. 1938, 918 DOI: 10.1039/JR9380000918 Table I in this paper shows that overall, chlorobenzene and bromobenzene are around 2-3% as reactive as benzene towards nitration under a wide variety of conditions. Some aspects of the nitration of the mononitrotoluenes J. G. Tillett J. Chem. Soc. 1962, 5142-5148 DOI: 10.1039/JR9620005142 Pg. 5148 in this paper shows that in nitrotoluenes, the deactivating nature of nitro wins out over the activating nature of the methyl group. Interestingly, in m-nitrotoluene, the meta position to the nitro group is less reactive than the other positions, due to resonance effects. Note that these compounds are also precursors to the common explosive TNT! Substituent effects of positive poles in aromatic substitution. Part I. The nitration of the anilinium ion in 90—100% sulphuric acid Madeline Brickman and J. H. Ridd J. Chem. Soc. 1965, 6845-6851 DOI: 10.1039/JR9650006845 Substituent effects of positive poles in aromatic substitution. Part II. The nitration of N-methylated anilinium ions Madeline Brickman, J. H. P. Utley, and J. H. Ridd J. Chem. Soc. 1965, 6851-6857 DOI: 10.1039/JR9650006851 In contrast to aniline, which is very reactive in EAS compared to benzene, the anilinium ion (which is easily formed in acidic media) is deactivated. As the acidity of the medium increases, the amount of meta product obtained from nitration of aniline increases, indicating that the reaction is proceeding via the anilinium ion (PhNH3+). Reaction rates also decrease with increasing acidity, as the amount of free aniline available in the reaction gets lower and lower. Aromatic substitution. 53. Electrophilic nitration, halogenation, acylation, and alkylation of (.alpha.,.alpha.,.alpha.-trifluoromethoxy)benzene George A. Olah, Takehiko Yamato, Toshihiko Hashimoto, Joseph G. Shih, Nirupam Trivedi, Brij P. Singh, Marc Piteau, and Judith A. Olah Journal of the American Chemical Society 1987, 109 (12), 3708-3713 DOI: 10.1021/ja00246a030 The -OCF3 substituent is not commonly encountered in undergraduate chemistry courses, but is used in medicinal chemistry. This paper by Nobel Laureate Prof. George A. Olah and his wife Judith, covers the directing effects and reactivity of PhOCF3 in a variety of EAS reactions. Overall, PhOCF3 is around 3-10% as reactive as benzene in EAS (see Tables VI-VIII). A Quantum Mechanical Investigation of the Orientation of Substituents in Aromatic Molecules G. W. Wheland Journal of the American Chemical Society 1942, 64 (4), 900-908 DOI: 10.1021/ja01256a047 This discusses the structure of the arenium ion that gets formed in EAS reactions, also known as the s-complex or Wheland intermediate, after the author here who first proposed it. Isolation of the Stable Boron Trifluoride – Hydrogen Fluoride Complexes of the Methyl-benzenes ; the Onium Salt (or σ-Complex) Structure of the Friedel-Crafts Complexes OLÁH, G., KUHN, S. & PAVLÁTH, A. Nature 1956, 178, 693–694 DOI: 1038/178693b0 The Benzotrifluoride–Nitryl Fluoride–Boron Trifluoride Complex OLÁH, G., NOSZKÓ, L. & PAVLÁTH, A. Nature 1957, 179, 146–147 DOI: 1038/179146b0 Isolation of the Stable Boron Trifluoride-ethylfluoride and Boron Trifluoride-formylfluoride Complexes of the Methylbenzenes: Mechanism of the Friedel–Crafts Reactions OLÁH, G., KUHN, S. Nature 1956, 178, 1344–1345 DOI: 10.1038/1781344a0 These papers by Nobel Laureate Prof. G. A. Olah describe the isolation and characterization of the intermediate ions (‘Wheland intermediates’) from various electrophilic aromatic substitution reactions – alkylation, nitration, and even protonation (by HBF4!) A Quantitative Treatment of Directive Effects in Aromatic Substitution Leon M. Stock, Herbert C. Brown Phys. Org. Chem. 1963, 1, 35-154 DOI: 10.1016/S0065-3160(08)60277-4 This is a very comprehensive review for its time, summarizing work on directing effects in EAS (e.g. determining which groups are o/p-directing vs. meta-directing, and to what extent they direct/deactivate). Stable carbocations. CLXX. Ethylbenzenium ions and the heptaethylbenzenium ion George A. Olah, Robert J. Spear, Guisseppe Messina, and Phillip W. Westerman Journal of the American Chemical Society 1975, 97 (14), 4051-4055 DOI: 1021/ja00847a031 This paper discusses the characterization of benzenium ions, which are intermediates in EAS, and the characterization of the heptaethylbenzenium ion, which is a stable species because it lacks a proton and therefore eliminates with difficulty. The Anomalous Reactivity of Fluorobenzene in Electrophilic Aromatic Substitution and Related Phenomena Joel Rosenthal and David I. Schuster Journal of Chemical Education 2003, 80 (6), 679 DOI: 1021/ed080p679 A very interesting paper, suitable for curious undergrads, and discusses something that most practicing organic chemists will know empirically – fluorobenzene is almost as reactive as benzene in EAS or Friedel-Crafts reactions, which is counterintuitive when one considers electronic effects.