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If you look closely at your diagram, you will notice that once benzoic acid has released its proton, the conjugate base that is formed has 6 resonance structures out of which 4 have 2 more charges that offset each other. The overall charge of benzoate anion is -1 regardless. The important part of this discussion revolves around the last 4 resonance structures. For the sake of the discussion, I will only refer to the 2 charges that offset each other. When a negative charge appears on the oxygen atom in the carboxyl group, a positive charge appears on the ring (the charge is spread across the nucleus). At this point, we see that the conjugate base is quite stable because it has 6 resonance structures. The more resonance structures the conjugate base has, the stronger the acid is. This is how the acidity of benzoic acid is explained. Now, if you placed a methoxy group in para position, it would doante electrons to the ring through a mesomeric effect. If that happens, the electron density around the nucleus increases, diminishing the positive charge. The methoxy group increases the electron density and so the positive charge on the nucleus is no longer “that positive” while the negative charge remains unaffected (“just as negative”). If the positive charge can’t properly balance the negative charge, the resonance structures involving charge separation are not advantageous to exist and so the strength of the acid decreases. This happens only if the methoxy group is situated para relative to the carboxyl group. If it is situated meta relative to the carboxyl, something interesting happens. We know that the methoxy (like the hydroxy group) exerts a -I inductive effect and a mesomeric (M) effect. That is why, if found para, it “donates” electron density through a +M effect (which manifests more than -I). When in meta, the +M effect is no longer a dominant effect and so, methoxy manifests -I effect mostly, withdrawing electron density from the nucleus. It is often said that hydroxy and methoxy groups are EDG, but only when it comes to electromeric effects. They also have -I inductive effects which makes them EWG. Overall, the presence of a EDG in ortho or para destabilises the actual negative charge of the benzoate anion, thus making it less stable. In an electron-donating group, benzoic acid's conjugate base is destabilized. It becomes less acidic as a result. In an electron-donating group, benzoic acid's conjugate base is destabilized. It becomes less acidic as a result.Electrophilic attack on the benzene ring is stopped by electron-withdrawing groups, making benzoic acids more acidic. The electron-withdrawing groups in the conjugate base of benzoic acid stabilize it. It therefore keeps its acidity.Benzene rings are activated to electrophilic attack by electron-withdrawing groups, leaving benzoic acids less acidic. Acidities of carboxylic acids can vary widely. Butanoic acid (Ka = 1.51 X 10-5) has a pH of less than 60,000 times higher than trifluoroacetic acid (Ka = 0.59). Inductive effects of substituents attached to carboxylic acids probably account for most of these vast differences in acidity. The transmission of charge by atoms within a molecule results in a permanent dipole in a bond. This effect has been experimentally observed. When halogens (such as fluorine) are present on adjacent carbons of a carboxylic acid group, the carboxylate conjugate base is stabilized and the acidity of the carboxylic acid group is increased.Fluorine atoms are more electronegative than hydrogen atoms, and therefore they have the ability to attract the electron density of covalent bonds towards themselves. As the electrons of the F-C covalent bond are drawn toward the fluorine in the fluoroacetate anion, the carbon is partially positively charged. In turn, the positively charged carbon creates a stabilizing effect by drawing electron density away from the carboxylate anion, which is then disperse to create a stable state. In addition to stabilizing carboxylate anion, carboxylic acid is made more acidic. An electron-withdrawing group for the fluorine substituent is thus being formed.Fluorine withdraws electrons from fluoroacetate anion to stabilize itSimilar effects are observed when -CH2CO2H is present with other electron-withdrawing groups. Carboxylic acids drop in pKa as their electron-withdrawing power becomes stronger. Multiplier effects compound the inductive effect, which increases the acidity of carboxylic acids. Dichloroacetic acid is a weaker acid than chloroacetic acid and trichloroacetic acid.An electrostatic potential map of acetic and trichloroacetic acids (Left) demonstrates the inductive effect of chlorine. The dark blue color of trichloroacetic acid is caused by its strong polarization of O-H bonds, thereby making it stronger than acetic acid. The amplifying effect of carboxylic acid on electron-withdrawing groups rapidly fades as the number of sigma bonds between them increases. Due to the nature of covalent bonds, ionic effects are not effectively transmitted. The chlorine's inductive effect in 4-chlorobutanoic acid is almost completely eliminated when three sigma bonds are formed, giving it a similar pKa value as unsubstituted butanoic acid. Inductively electron-donating groups (hydrocarbons) are alkyl groups. The inductive effects in this case lead to an increase in electron density on the carboxylate anion, resulting in a destabilizing effect and a decrease in acidity. Inductive effects are more readily enhanced by lengthening alkyl chains of carboxylic acids, but the effect ceases to be profound once the chain is about three carbons long.Since benzoic acid has a carboxyl group that withdraws electrons, it is a meta-directing group. Bromination of benzoic acid leads primarily to methyl bromo benzoic acid or m-bromo acid, which are similar to brominated products.ReactionReaction mechanismM-nitrobenzoic acid or meta-nitrobenzoic acid is one of the major products derived from nitrating benzoic acid. If concentrated sulfuric acid and fuming nitric acid are mixed, 3,5-dinitrobenzoic acid may form as a byproduct after nitrating concentrated sulfuric acid. An important deactivating group on benzene is its carboxylic acid group. Deactivating groups are usually meta-directing groups. By the electron donating effects of activating groups, electron density is pushed onto ortho- and para-positions, and by the electron removing effects of deactivating groups, electron density is pulled away from ortho- and para-positions. Both positions are almost unaffected by electron density shifts, though the meta-position becomes more reactive when electron density is removed from the ortho- and para-positions.Reaction mechanism Get subject wise printable pdf notesView Here Visitors are also reading: AnswerVerifiedHint: Acidity of a carboxylic acid is mainly determined by the factors like resonance and inductive effect. Here, we will see just one factor; that is how inductive effect affects the acidity of carboxylic acids. Acidity is the ability to produce $\left[{{\text{H}}^{+}} \right]$ ions and carboxylic acids have $-\text{COOH}$ groups in common. Complete answer: There are two groups under inductive effect, one electron donating groups and another is electron withdrawing groups. Electron withdrawing groups are groups which attract or displace the electrons towards it. The examples of electron withdrawing groups are $-\text{X,}-\text{C}{{\text{X}}_{3}},-\text{NH}_{3}^{+},-\text{NR}_{3}^{+},-\text{CN,}-\text{N}{{\text{O}}_{2}},-\text{CHO,}-\text{COR,}-\text{COOH,}-\text{COOR}$. Here, X refers to halogens while R refers to alkyl or aryl groups.Let us now talk about the effect of electron withdrawing groups in acidic strength:As, the electron withdrawing groups attract electrons away from other elements. So, such groups help in increasing the polarity of the $-\text{COOH}$ group. We know that oxygen is an electronegative group, so, the $-\text{OH}$ bond of $-\text{COOH}$ group will be polar or ionizable. As the electron withdrawing groups increase the polarity, it seems that electronegativity of oxygen has increased. After the release of $\left[{{\text{H}}^{+}} \right]$ from the $-\text{COOH}$ group. The compound becomes stable by the resonating structures of carboxylate ions which are stabilised by the negative charge on oxygen atoms. The placement and power of electron withdrawing groups also affect the acidity of compounds: (1) The inductive effect decreases with increasing carbon chain or increasing distance from the substituted group. So, if an electron withdrawing group is present nearer to the $-\text{COOH}$ group, the compound will be more acidic than the compound where the same electron withdrawing group is placed far from the $-\text{COOH}$ group. Like, $\text{C}{{\text{H}}_{3}}\text{ClCHCOOH}>\text{ClC}{{\text{H}}_{2}}\text{C}{{\text{H}}_{2}}\text{COOH}$ in acidic strength. (2) The power of the electron withdrawing group is also taken into account. More is the power of electron withdrawing groups, more will be the acidic strength of carboxylic acids. Like, 2-nitro ethanoic acid is more acidic than 2-chloro ethanoic acid because the –I effect of the nitro group is more than the chloro group. Note: The electron withdrawing groups increases the acidity of carboxylic acids. On the other hand, electron donating groups decrease the acidity of carboxylic acids as they decrease the polarity of $-\text{OH}$ bond of $-\text{COOH}$ group. The nearer the EWG will be placed less acidic the compound will be and if it is far, it is a little more acidic. 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. 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. I. Introduction II. Factors Affecting the Acidity of Organic Compounds II.1. Hybridisation II.2. Electronegativity and Bond Strength (Size) II.2.1. Across the Periodic Table, Acidity is Influenced by Electronegativity II.2.2. Down the Periodic Table, Acidity is Influenced by Bond Strength II.3. Inductive Effect II.3.1. Electron-withdrawing Inductive Effect II.3.2. Electron-donating Inductive Effect II.4. Resonance (Delocalisation) II.4.1. Resonance in Carboxylic Acids II.4.2. Acidity Assisted by Resonance to Benzene Ring II.4.3. Acidity Assisted by Resonance to Neighbouring Unsaturated Groups II.5. Aromaticity II.6. Solvation III. Conclusion I. Introduction Now that we have seen the pKa values of several functional group and know what they represent in general, we shall have a look at more specific compounds and trends to see what factors affect the acidity of organic compounds. As you have seen in the pKa tables, those values are approximate values for a group of compounds with the same functional group. For example, alcohols have pKa approximately 16. However, not all of them have pKa of 16, in fact only methanol does. Ethanol’s pKa is about 16.5, and t-butanol’s pKa is about 19. So what makes them different? Let’s start our discussion! *** Back to Contents *** II. Factors Affecting the Acidity of Organic Compounds You may have noticed that there are two types of acids in general: Are acids with no overall charge, such as HCl, HBr, CH3COOH, PhCOOH (benzoic acid), etc. These acids release anionic conjugate bases: negatively charged conjugate bases, such as Cl–, Br–, CH3COO–, PhCOO– (benzoate anion), etc. Are positively charged acids. Usually the acids in this class are protonated nitrogens or oxygens, such as NH4+ (ammonium ion), Et3NH+ (triethylammonium ion), C5H5NH+ (pyridinium ion), H3O+ (hydronium ion), and protonated carbonyls (R2C=OH+) and alcohols (R–OH2+). These acids release neutral conjugate bases: conjugate bases with no overall charge, such as NH3 (ammonia), Et3N (triethylamine), C5H5N (pyridine), H2O (water), and neutral carbonyls (R2C=O) and alcohols (R–OH). We have also learnt what differs strong acids to weak acids. A strong acid is an acid that releases weak (stable) conjugate base, whilst a weak acid is an acid that releases strong (unstable) conjugate base. All of these can be translated into two perspectives, depending on the acids: Neutral acids release anionic conjugate bases, which may or may not be stable. If the anionic conjugate bases are stable, then the acids are strong. If the anionic conjugate bases are unstable, then the acids are weak. Therefore, to predict the acidity of neutral acids, we have to examine the stability of their conjugate bases. Cationic acids release neutral conjugate bases. Neutral conjugate bases are generally stable. Cationic acids however, may or may not be stable. If the cationic acids are unstable, they give away their proton easily, hence they are strong acids. If the cationic acids are stable, they don’t give away their proton easily, hence they are weak acids. Therefore, to predict the acidity of cationic acids, we have to examine their own stability. That being said, factors that affect the acidity of organic compounds can simply be thought of as factors that stabilises the charged species (either the anionic conjugate base, or cationic acids). If the charged species is stable, then we have a strong acid; if not, then we have a weak acid. Therefore, the question that we need to address is: What are the factors that can make the charged species more stable? In this post, we will look at the affecting factors one by one, and prove them by comparing their pKa values. Remember: The smaller the pKa value of an acid is, the stronger the acid is, the weaker its conjugate base is. *** Back to Contents *** II.1. Hybridisation This is the most common starting point when talking about the factors affecting the acidity of organic compounds. In organic chemistry, you only get three types of hybridisation: sp3 (for single bonds), sp2 (for double bonds), and sp (for triple bonds). Let’s compare the acidity between ethane (an alkane), ethylene (an alkene), and acetylene (an alkyne). You can see that an alkene is about 7 orders of magnitude (107 times) more acidic than an alkane, and an alkyne is about 15 orders of magnitude (1015 times) more acidic than alkane! Why is this? Obviously, hybridsation. Otherwise I won’t put that example in this section! Alkyne (sp hybridisation) have more s character than alkene (sp2) and alkane (sp3). So what is this s character? Think about it like this: In sp3, you have 1 s orbital and 3 p orbitals combining (4 orbitals overall): s, p, p, p This means, the s orbital makes up about 25% (1 out of 4 orbitals) of the overall In sp2, you have 1 s orbital and 2 p orbitals combining (3 orbitals overall): s, p, p This means, the s orbital makes up about 33% (1 out of 3 orbitals) of the overall In sp, you have 1 s orbital and 1 p orbitals combining (2 orbitals overall): s, p This means, the s orbital only makes up about 50% (1 out of 2 orbitals) of the overall The Logic Box Why does having more s character means more acidic? Recall from your general chemistry or physical chemistry lectures that the s orbital is spherical around the centre of the atom (nucleus). On the other hand, each of the p orbitals (px, py, and pz) has two lobes with a node near the nucleus. A node is a part of the orbital that has no electron density. This means that: The s orbital can feel the positive charge of the nucleus better than the p orbitals (because of the nodes present in the p orbitals). A negative charge in the s orbital is able to feel the positive charge from the nucleus. The positive charge from the nucleus stabilises negative charge (opposites attract!). Therefore, a negative charge can be stabilised better by the s orbital rather than by the p orbital. This is why more s character means more negative charge stabilisation. The three examples above are neutral acids that release anionic conjugate base. The negative charge of the conjugate base is stabilised better as the s character increases. This makes sp2 hybridisation better at stabilising negative charge than sp3 hybridisation (alkene is more acidic than alkane). This also makes sp hybridisation (alkyne) the most acidic amongst the three. Of course, this is also evident in the nitrogen analogues: The three examples in the nitrogen analogues are (from left to right) amine, imine, and protonated nitrile. Amine and imine are neutral acids but protonated nitrile is a cationic acid. Therefore, the theory above can easily be applied to amine and imine, but what about protonated nitrile? Remember that the nitrile is sp hybridised, and that more s character means more negative charge stabilisation. The protonated nitrile has a positive charge and therefore gets destabilised by the s character. Because the cationic acid is destabilised, it releases its proton easily and becomes a strong acid, as shown by its pKa value. This whole theory is also evident in the oxygen analogues: Isopropanol is a neutral acid while the protonated acetone is a cationic acid. The conjugate base of isopropanol does not get much negative charge stabilisation (25% s character due to sp3 hybridisation) and therefore isopropanol is a weak acid. The protonated acetone has sp2 hybridisation, therefore its positive charge is destabilised by the s character and it becomes a strong acid. *** Back to Contents *** II.2. Electronegativity and Bond Strength (Size) Let’s first recall from your general chemistry (or high school chemistry?) lecture: Electronegativity increases from left to right Electronegativity decreases from top to bottom Atomic radius (size) decreases from left to right causing bond strength to increase Atomic radius (size) increases from top to bottom causing bond strength to decrease Consult your general chemistry textbooks if you forget about this, I will not go into too much detail here. Now, have a look at the trends in acidity within the periodic table: Some of you may ask yourself this: ‘acidity increases as electronegativity increases when we go across (left to right) the periodic table, but acidity also increases as electronegativity decreases when we go down (top to bottom) the periodic table. Why??’ Others may also ask this: ‘acidity increases as size increases when we go down (top to bottom) the periodic table, but acidity also increases as size decreases when we go across (left to right) the periodic table. Why??’ You may also ask the other way around for each case, but regardless how you ask your question, this seemingly contradictory trend can actually be explained easily: Across the periodic table, acidity is influenced by electronegativity Down the periodic table, acidity is influenced by bond strength Let’s have a look at each of the two in more detail, and let’s start with the easy one first. *** Back to Contents *** II.2.1. Across the Periodic Table, Acidity is Influenced by Electronegativity ‘As we go across the periodic table, acidity increases as electronegativity increases’ This makes sense, because the increase in electronegativity means the species is able to stabilise negative charge better. Compare the following acids from the first row: The acids are neutral acids, therefore they release anionic conjugate base. The conjugate base gets more and more stabilised by the increased electronegativity. In other words, negatively charged species gets more and more stabilised as its electronegativity increases. Therefore, the acid gets more and more stable as we go across the periodic table. The bond strength does not significantly affect the acidity when you go across the periodic table, because the elements in the same row have similar energy level and overlap of orbitals between H and the element itself. This will be clear when we talk about it in the next section. One last point to note: you’ve always been told that HF is a weak acid. Yes it is true when we compare it against HCl, HBr, or HI. But here, when we compare it to the other acids within the same row, HF is the strongest. Just look at its small pKa value compared to its neighbours. *** Back to Contents *** II.2.2. Down the Periodic Table, Acidity is Influenced by Bond Strength ‘As we go down the periodic table, acidity increases as bond strength decreases’ As you go down the periodic table, the atomic radius (size) becomes larger. This means that the orbital overlap between the element and H gets more and more ineffective. In turn, this causes the acid to release its proton more easily. Compare the following acids from the halogen group: The increase in size and the decrease in bond strength affect the acidity more than the increase in electronegativity as we go down the periodic table. Therefore HI becomes the strongest acid amongst the other acids in its group. *** Back to Contents *** II.3. Inductive Effect In the section above, we saw how electronegativity affects the acidity of the H+ directly bonded to the electronegative atom. Here, we shall see that an electronegative functional group can also affect the acidity of a H+ that is several bonds away from itself. We shall also see a non-electronegative functional group that affect the acidity of the aforementioned H+. Both of these groups affect the acidity of the H+ through the σ bonds. This effect is known as the inductive effect. There are two types of inductive effect based on the groups that exhibit the effect: Electron-withdrawing inductive effect Electron-donating inductive effect Substituted carboxylic acids are well known examples for this effect. A carboxylic acid is a neutral acid; in solution, it dissociates to give proton and carboxylate anion as its conjugate base. If the carboxylate anion can be stabilised, the carboxylic acid gets stronger. We shall use carboxylic acids as examples in this section. *** Back to Contents *** II.3.1. Electron-withdrawing Inductive Effect Electronegative functional groups affect the acidity of H+ by inductively pulling the electron density towards it through the σ bonds, therefore weaking the O–H bond in COOH and making the H+ easier to be released. They also stabilise negatively charged species, therefore the conjugate base is stabilised, making the carboxylic acid a stronger acid. This type of group is known as the electron-withdrawing group (EWG). The ‘electron-pulling through the σ bonds’ phenomenon is known as the electron-withdrawing inductive effect, also known as the ‘–I effect’. Have a look at the acetic acid derivatives below. The electronegativity of the chlorine atom pulls electron density away from the acidic H towards itself, making chloroacetic acid about 4 orders of magnitude (104 times) more acidic than normal acetic acid! This shows the inductive effect that chlorine has. More EWGs means more acidic As the number of chlorine atom increases, the inductive effect becomes stronger. Hence, trichloroacetic acid is a stronger acid than dichloroacetic acid, which in turn is a stronger acid than (mono)chloroacetic acid. All of them are more acidic compared to unsubstituted acetic acid. The addition of one chlorine atom to the acetic acid increases the acidity by 1.88 orders of magnitude (about 76x). Addition of another chlorine atom increases it further by about 1.57 orders of magnitude (about 37x), and addition of the last one increases it again by 0.64 orders of magnitude (about 4x). More electronegative EWGs means more acidic The electronegativity of the EWG itself also influences the inductive effect. Compare the acidity of trichloroacetic acid (TCA) and trifluoroacetic acid (TFA) below: Fluorine is more electronegative than chlorine, therefore its inductive effect is greater than that of chlorine, causing the pKa of TFA to be smaller than TCA. This means that TFA is more acidic than TCA by 0.9 order of magnitude (about 8x). Closer EWG means more acidic One last thing, distance matters. The closer the EWG is to the COOH, the stronger the inductive effect is, and the more acidic the acid is. You can see from the picture above that: 4-Chlorobutanoic acid is about 2x more acidic than unsubstituted butanoic acid. 3-Chlorobutanoic acid is about 3x more acidic than 4-chlorobutanoic acid. 2-chlorobutanoic acid is about 15x more acidic than 3-chlorobutanoic acid. The chlorine atom in 2-chlorobutanoic acid is one atom closer to the carboxylic group than the chlorine atom in 3-chlorobutanoic acid. Look how dramatically the acidity increases! *** Back to Contents *** II.3.2. Electron-donating Inductive Effect Alkyl functional group affects the acidity of H+ by inductively pushing the electron density away from it through the σ bonds, therefore strengthening the O–H bond in COOH and making the H+ more difficult to be released. They also stabilise positively charged species, therefore the conjugate base is destabilised, making the carboxylic acid a weaker acid. This type of group is known as the electron-donating group (EDG). The ‘electron-pushing through the σ bonds’ phenomenon is known as the electron-donating inductive effect, sometimes written as ‘+I effect’. Have a look at the acetic acid derivatives below. The methyl groups push electron density away from themselves towards the acidic H. It destabilises the anionic conjugate bases, making pivalic acid (2,2-dimethylpropanoic acid) the least acidic and formic acid the most acidic in the series of carboxylic acid above. Similar effect is also observed in alcohols: Larger number of methyl groups (EDGs) increases the electron density near the acidic H and therefore making the alcohol less acidic. This causes the t-butanol to have to largest pKa value in the series above. *** Back to Contents *** II.4. Resonance (Delocalisation) We have learnt from basic structural organic chemistry that resonance can greatly stabilise charged species. Because the acidity of organic compounds is influenced by the stability of charged species, resonance plays an important role in determining the acidity of various compounds. Similar to the inductive effect, there are functional groups that are electron-withdrawing and electron-donating through resonance. Through resonance, EWGs increases the acidity of a compound and EDGs decreases the acidity. *** Back to Contents *** II.4.1. Resonance in Carboxylic Acids The dissociation of carboxylic acid is stabilised by the resonance within the COO group. This resonance stabilises the carboxylate anion (conjugate base of carboxylic acid), making carboxylic acids acidic. We can compare the pKas of ethanol and acetic acid to see how the resonance increases the acidity of carboxylic acids: The resonance stabilises the anionic conjugate base so much so that it increases the acidity of acetic acid by about 11 orders of magnitude! *** Back to Contents *** II.4.2. Acidity Assisted by Resonance to Benzene Ring When a benzene ring is attached to the carboxylic group, resonance of the carboxylate group with the ring increases its acidity. Compare acetic acid to benzoic acid: Resonance with the benzene ring does not only increase the acidity of carboxylic acids but also other functional groups such as alcohol, thiol, and amine. First, we compare a non-conjugated alcohol (methanol) with a conjugated alcohol (phenol): The negative charge in the phenoxide anion (anionic conjugate base of phenol) is stabilised by delocalisation to the aromatic ring, whilst there is no conjugate base stabilisation in methanol. This makes phenol more acidic than methanol. This also applies to other similar compounds such as thiols (methanethiol and thiophenol): … and between methanamine and aniline too: You can observe something interesting when comparing neutral and protonated aniline (anilinium cation): In neutral aniline, the free electron pair of the nitrogen delocalises to the benzene ring, giving stability. Protonation of the aniline nitrogen takes away the conjugation, making the anilinium (which is a cationic acid) unstable. Instability of a cationic acid makes a strong acid. This, in conjunction with the stabilisation of aniline as a conjugate base, makes anilinium a strong acid, as proved by its smaller pKa value of 4.6, compared to aniline’s 28. Of course, you observe the same thing in neutral and protonated phenol: Protonation of the phenol oxygen takes away the conjugation that phenol had. This makes the protonated phenol (a cationic acid) unstable, hence making it a stronger acid than neutral phenol by 17 orders of magnitude! *** Back to Contents *** II.4.3. Acidity Assisted by Resonance to Neighbouring Unsaturated Groups Hydrogens bonded to a carbon adjacent to one or more unsaturated groups are acidic. This carbon is known as the α-carbon, whilst its hydrogen is known as the α-hydrogen. Deprotonation of α-hydrogens results in the formation of carbanion, called the α-carbanion. Overall, this type of acid is known as carbon acid. The reason α-hydrogens are acidic is because their conjugate bases are stabilised through conjugation with the unsaturated groups. For example, in butanone: You’ll probably realise that the carboxylic acid family (acids, esters, and amides) give larger pKa, meaning they are less acidic than aldehydes/ketones. The reason for this is because the OR and NR2 groups in the carboxylic acid family is more involved in resonance with the carbonyl group. Because of this, the α-carbanion has to ‘compete’ and ‘share’ the resonance with the carbonyl group. This makes the α-hydrogen of the carboxylic acid family more acidic than the aldehydes/ketones. In aldehydes/ketones, the the α-carbanion has carbonyl group only for itself, making the resonance stabilision better. This makes their α-hydrogens more acidic. The α-hydrogen is even more acidic if it’s flanked by two adjacent unsaturated groups. The figure below shows the comparison of pKas of (from left to right): 1,3-diester (malonate esters), dicyanomethane (malononitrile), β-keto ester, 1,3-diketone, and dinitromethane. *** Back to Contents *** II.5. Aromaticity We know that there are aromatic and anti aromatic compounds. Aromaticity stabilises compounds and therefore making acids stronger. If a compound releases an aromatic conjugate base, the aromaticity stabilises the conjugate base, which make the compound a stronger acid. If the released conjugate base is anti aromatic, the anti aromaticity destabilises the conjugate base, making the compound a weaker acid. The conjugate base of cyclopropene is anti aromatic and therefore very unstable. On the other hand, the conjugate base of cycloheptatriene is not planar, making it neither aromatic nor anti aromatic, and therefore unstable. This makes the pKa value of both compounds very large. Having an anti aromatic conjugate base, cyclopropene is therefore the most unstable of the two. Therefore, cycloheptatriene has smaller pKa than cyclopropene. On the other hand, the conjugate base of cyclopentadiene is aromatic, making it very stable and dramatically more acidic than the other two. It is about 23 orders of magnitude more acidic than cycloheptatriene and 45 orders of magnitude more acidic than cyclopropene! *** Back to Contents *** II.6. Solvation A species is considered an acid if it is able to separate its proton from its conjugate base. In order to do that, solvent plays a great role. In the absence of solvent, it is hard to separate a positive charge (proton) from a negative charge (conjugate base). This separation is greatly assisted by solvent; the solvent molecules orient themselves around the solute, separating the oppositely charged species. This process is known as solvation. Basically, it is difficult to achieve separation of proton at room temperature without the help of solvent, so the role of solvent is very crucial. In fact, all of the factors explained in Sections II.1.-II.5. are also influenced by solvation. All of the compounds used as examples in the previous sections may become more or less acidic when dissolved in different solvent. Solvent that can better stabilise the conjugate base of a neutral acid makes it a stronger acid. The ability of the solvent to stabilise the conjugate base depends on many things. One of which is the molecular structure of the acid/conjugate base itself. We’ve used these examples in Section II.3.2. previously, but they are good examples. Compare the pKa of several decreasingly-bulky alcohols and carboxylic acids: The bulkiness of the methyl groups hampers the solvation of the conjugate bases by solvent molecules. This destabilises the conjugate bases, making the compounds increasingly less acidic as bulkiness increases. Therefore, aside from the effect of EDG in those examples, solvent also affects their acidity. The solvent itself is also an important factor. The pKa values I have shown you in the pKa table are mostly measured relative to water as a solvent. The pKa of some compounds are also measured in (dimethylsulfoxide) DMSO, and as you may have guessed, their values are different to those measured in water. Here are a few examples: Acid Name Acid Formula pKa (water) pKa (DMSO) Trifluorosulfonic acid CF3SO3H –14 0.3 Hydrobromic acid HBr –9 0.9 Hydrochloric acid HCl –7 1.8 Hydrobromic acid HF 3.2 15 Acetic acid CH3COOH 4.74 12.3 Phenol C6H5OH 10 18 Methanol CH3OH 15.5 28 Water H2O 15.7 32 Ammonia NH3 38 41 You can immediately see that the pKa values in DMSO are larger than the pKa values in water. This means that in DMSO, the acids are less acidic. Some are monumentally larger (e.g. trifluorosulfonic acid is almost 14 orders of magnitude less acidic in DMSO than in water), and some are not (e.g. ammonia is only 3 orders of magnitude less acidic in DMSO than in water). As an organic solvent, DMSO is not as good as water in stabilising the anionic conjugate base. Therefore, the acids are less acidic. We will talk more about acidity, basicity, and solvent, including the levelling effect in Acid-Base VIII, Acid-Base IX, and Acid-Base X. Keep in mind that what we have talked about here is about the solvation of certain species in certain solvents. *** Back to Contents *** III. Conclusion We have seen various factors that influence the acidity of organic compounds. We have also proved the theories by looking at the pKas of the compounds we used as examples. The sp hybridisation has 50% s character, which stabilises the negative charge of a species. We get stronger acids as we go from sp3 to sp2 to sp hybridisations. As we go across the periodic table, the electronegativity effect outweighs the bond strength effect. We get stronger acids as we go from left to right due to the increase of electronegativity. As we go down the periodic table, the effect of bond strength become more significant compared to electronegativity. We get stronger acids due to the decrease in bond strength. Electronegative atoms are electron-withdrawing groups. They pull electron density towards themselves, making the conjugate base of an acid more stable, and therefore making the acid stronger. Electron-donating group pushes the electron density away from themselves, makin the conjugate base of an acid less stable, and therefore making the acid weaker. Resonance stabilises charged species. The more they’re stabilised by resonance, the more acidic they become. Aromatic conjugate bases are stable and make for stronger acids. Anti aromatic conjugate bases are unstable and make for weaker acids. Conjugated bases that can be well solvated by the solvent molecules give stronger acids. Bulkier molecuels are more difficult to be solvated and therefore less acidic. In solvents that are less good in stabilising anionic conjugate base, acids are less acidic. *** Back to Contents *** Page last updated: 06ii17 RP Other Posts in Acid, Base, and pKa Series Objectives After completing this section, you should be able to list a given series of carboxylic acids in order of increasing or decreasing acidity. explain the difference in acidity between two or more given carboxylic acids. arrange a series of substituted benzoic acids in order of increasing or decreasing acidity. determine whether a given substituted benzoic acid will be more or less acidic than benzoic acid. decide which of two or more substituted benzoic acids is the most acidic, and explain your decision on the basis of the electron-withdrawing or electron-releasing ability of the substituent. use the Ka (or pKa) of a substituted benzoic acid to predict the effect that the substituent has on the susceptibility of the benzene ring to electrophilic attack. You have already seen how the presence of an electron-withdrawing or electron-releasing group affects the stability of a positively charged carbocation. Now you see how these groups affect the stability of carboxylate anions, and in turn, determine the dissociation constant of a carboxylic acid. The resonance effect described here is undoubtedly the major contributor to the exceptional acidity of carboxylic acids. However, inductive effects also play a role. For example, alcohols have pKa's of 16 or greater but their acidity is increased by electron withdrawing substituents on the alkyl group. The following diagram illustrates this factor for several simple inorganic and organic compounds (row #1), and shows how inductive electron withdrawal may also increase the acidity of carboxylic acids (rows #2 & 3). The acidic hydrogen is colored red in all examples. Water is less acidic than hydrogen peroxide because hydrogen is less electronegative than oxygen, and the covalent bond joining these atoms is polarized in the manner shown. Alcohols are slightly less acidic than water, due to the poor electronegativity of carbon, but chloral hydrate, Cl3CCH(OH)2, and 2,2,2,-trifluoroethanol are significantly more acidic than water, due to inductive electron withdrawal by the electronegative halogens (and the second oxygen in chloral hydrate). In the case of carboxylic acids, if the electrophilic character of the carbonyl carbon is decreased the acidity of the carboxylic acid will also decrease. Similarly, an increase in its electrophilicity will increase the acidity of the acid. Acetic acid is ten times weaker an acid than formic acid (first two entries in the second row), confirming the electron donating character of an alkyl group relative to hydrogen, as noted earlier in a discussion of carbocation stability. Electronegative substituents increase acidity by inductive electron withdrawal. As expected, the higher the electronegativity of the substituent the greater the increase in acidity (F > Cl > Br > I), and the closer the substituent is to the carboxyl group the greater is its effect (isomers in the 3rd row). Substituents also influence the acidity of benzoic acid derivatives, but resonance effects compete with inductive effects. The methoxy group is electron donating and the nitro group is electron withdrawing (last three entries in the table of pKa values). A fluorine atom is more electronegative than a hydrogen atom, and thus it is able to ‘induce’, or ‘pull’ the electron density of covalent bonds towards itself. In the fluoroacetate anion, the electrons in the C-F covalent bond are pulled toward the fluorine giving the carbon a partial positive charge. The positively charged carbon, in turn, draws electron density away from the carboxylate anion, dispersing the charge, and creating a stabilizing effect. Stabilizing the carboxylate anion increases the acidity of the corresponding carboxylic acid. In this context, the fluorine substituent is acting as an electron-withdrawing group. Fluoroacetate anion stabilized by electron withdrawing inductive effect of fluorine A similar effect is seen when other electron-withdrawing groups are attached to -CH2CO2H. As the power of the electron-withdrawing group becomes stronger there is a corresponding drop in the pKa of the carboxylic acid. The presence of multiple electron-withdrawing groups compounds the inductive effect and continues to increase the acidity of the carboxylic acid. Dichloroacetic is a stronger acid than chloroacetic acid, and trichloroacetic acid is even stronger. The inductive effects of chlorine be clearly seen when looking at the electrostatic potential maps of acetic acid (Left) and trichloroacetic acid (Right). The O-H bond in trichloroacetic acid is highly polarized, as shown by the dark blue color making it a much stronger acid than acetic acid. Because inductive effects are not transmitted effectively through covalent bonds, the acid-strengthening effect falls off rapidly as the number of sigma bonds between the carboxylic acid and the electron-withdrawing group increases. A distance of three sigma bonds almost completely eliminates chlorine's inductive effect in 4-chlorobutanoic acid, giving it a similar pKa value to unsubstituted butanoic acid. Alkyl groups (hydrocarbons) are inductively electron-donating. In this case, the inductive effects pushes electron density onto the carboxylate anion, producing a destabilizing effect, decreasing the acidity of the carboxylic acid. Lengthening the alkyl chain of a carboxylic acid can increase this inductive effect but it no longer decreases the acidity further after the chain is about three carbons long. The conjugate base of benzoic acid is stabilized by electron-withdrawing groups (EWG). This makes the acid more acidic by delocalizing the charge of the carboxylate ion. Electron-withdrawing groups deactivate the benzene ring to electrophilic attack and make benzoic acids more acidic. The conjugate base of benzoic acid is destabilized by electron-donating groups (EDG). This makes the acid less acidic by pushing more electron density toward the negative charge in the carboxylate. Electron-donating groups activate the benzene ring to electrophilic attack and make benzoic acids less acidic. Several examples of electron donating groups. 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Try to use the expected inductive effects of the substituents to determine the acidity rather than looking at the pKa table. Answer For the following pairs, which is expected to be the stronger acid? Explain your answer. Answer a) Consider the inductive effects of the substituents attached to the carboxylic acid. The tert-butyl group is electron-donating which should decrease the acidity of the carboxylic acid. The trimethylammonium substituent is positively charged and can be a powerful electron-withdrawing substituent. This should increase the acidity of the carboxylic acid. The compound (CH3)3NCH2CO2H is expected to be a stronger acid than (CH3)3CCH2CO2H. The acidity constants for these two compounds match the predictions. b) Having an electron-withdrawing hydroxyl group at the C-2 stabilizes the carboxylate ion of lactic acid through inductive effects. This should make lactic acid more acidic than propanoic acid. c) Due to the presence of a highly electronegative oxygen, the carbonyl group is expected to be more strongly electron-withdrawing than a carbon–carbon double bond. Thus, pyruvic acid should be a stronger acid than acrylic acid. Oxalic acid is a dicarboxylic acid with two acidic protons. The first proton is much more acidic (pKa = 1.20) than a typical carboxylic acid. However, Heptanedioic acid's first acidic proton has a pKa much closer to that of a typical carboxylic acid. Explain these differences. Answer With oxalic acid one carboxyl group acts as an inductive electron-withdrawing group which increases the acidity of the other carboxylic acid. This inductive effect is only relevant with the two carboxyl groups are separated by only a few bonds. In heptanedioic acid, the carboxyl groups are separated by five carbon which effectively negates the inductive effect. The carboxylic acid of 4-formylbenzoic acid has a pKa of 3.75. Is this molecule likely to be more reactive or less reactive than benzene toward electrophilic aromatic substitution? Answer Benzoic acid

(pKa = 4.2) has a higher pKa and is less acidic than 4-formylbenzoic acid (pKa = 3.75). This means that the formyl group is removing electrons from the aromatic ring making it deactivated toward electrophilic aromatic substitution. Contributors and Attributions Lost your password? Please enter your email address. You will receive a link and will create a new password via email. Skip to main content Reddit and its partners use cookies and similar technologies to provide you with a better experience. By accepting all cookies, you agree to our use of cookies to deliver and maintain our services and site, improve the quality of Reddit, personalize Reddit content and advertising, and measure the effectiveness of advertising. By rejecting non-essential cookies, Reddit may still use certain cookies to ensure the proper functionality of our platform. For more information, please see our Cookie Notice and our Privacy Policy. 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Objectives After completing this section, you should be able to list a given series of carboxylic acids in order of increasing or decreasing acidity. explain the difference in acidity between two or more given carboxylic acids. arrange a series of substituted benzoic acids in order of increasing or decreasing acidity. determine whether a given substituted benzoic acid will be more or less acidic than benzoic acid. decide which of two or more substituted benzoic acids is the most acidic, and explain your decision on the basis of the electron-withdrawing or electron-releasing ability of the substituent. use the Ka (or pKa) of a substituted benzoic acid to predict the effect that the substituent has on the susceptibility of the benzene ring to electrophilic attack. You have already seen how the presence of an electron-withdrawing or electron-releasing group affects the stability of a positively charged carbocation. Now you see how these groups affect the stability of carboxylate anions, and in turn, determine the dissociation constant of a carboxylic acid. The resonance effect described here is undoubtedly the major contributor to the exceptional acidity of carboxylic acids. However, inductive effects also play a role. For example, alcohols have pKa's of 16 or greater but their acidity is increased by electron withdrawing substituents on the alkyl group. The following diagram illustrates this factor for several simple inorganic and organic compounds (row #1), and shows how inductive electron withdrawal may also increase the acidity of carboxylic acids (rows #2 & 3). The acidic hydrogen is colored red in all examples. Water is less acidic than hydrogen peroxide because hydrogen is less electronegative than oxygen, and the covalent bond joining these atoms is polarized in the manner shown. Alcohols are slightly less acidic than water, due to the poor electronegativity of carbon, but chloral hydrate, Cl3CCH(OH)2, and 2,2,2,-trifluoroethanol are significantly more acidic than water, due to inductive electron withdrawal by the electronegative halogens (and the second oxygen in chloral hydrate). In the case of carboxylic acids, if the electrophilic character of the carbonyl carbon is decreased the acidity of the carboxylic acid will also decrease. Similarly, an increase in its electrophilicity will increase the acidity of the acid. Acetic acid is ten times weaker an acid than formic acid (first two entries in the second row), confirming the electron donating character of an alkyl group relative to hydrogen, as noted earlier in a discussion of carbocation stability. Electronegative substituents increase acidity by inductive electron withdrawal. As expected, the higher the electronegativity of the substituent the greater the increase in acidity (F > Cl > Br > I), and the closer the substituent is to the carboxyl group the greater is its effect (isomers in the 3rd row). Substituents also influence the acidity of benzoic acid derivatives, but resonance effects compete with inductive effects. The methoxy group is electron donating and the nitro group is electron withdrawing (last three entries in the table of pKa values). A fluorine atom is more electronegative than a hydrogen atom, and thus it is able to ‘induce’, or ‘pull’ the electron density of covalent bonds towards itself. In the fluoroacetate anion, the electrons in the C-F covalent bond are pulled toward the fluorine giving the carbon a partial positive charge. The positively charged carbon, in turn, draws electron density away from the carboxylate anion, dispersing the charge, and creating a stabilizing effect. Stabilizing the carboxylate anion increases the acidity of the corresponding carboxylic acid. In this context, the fluorine substituent is acting as an electron-withdrawing group. Fluoroacetate anion stabilized by electron withdrawing inductive effect of fluorine A similar effect is seen when other electron-withdrawing groups are attached to -CH2CO2H. As the power of the electron-withdrawing group becomes stronger there is a corresponding drop in the pKa of the carboxylic acid. The presence of multiple electron-withdrawing groups compounds the inductive effect and continues to increase the acidity of the carboxylic acid. Dichloroacetic is a stronger acid than chloroacetic acid, and trichloroacetic acid is even stronger. The inductive effects of chlorine be clearly seen when looking at the electrostatic potential maps of acetic acid (Left) and trichloroacetic acid (Right). The O-H bond in trichloroacetic acid is highly polarized, as shown by the dark blue color making it a much stronger acid than acetic acid. Because inductive effects are not transmitted effectively through covalent bonds, the acid-strengthening effect falls off rapidly as the number of sigma bonds between the carboxylic acid and the electron-withdrawing group increases. A distance of three sigma bonds almost completely eliminates chlorine's inductive effect in 4-chlorobutanoic acid, giving it a similar pKa value to unsubstituted butanoic acid. Alkyl groups (hydrocarbons) are inductively electron-donating. In this case, the inductive effects pushes electron density onto the carboxylate anion, producing a destabilizing effect, decreasing the acidity of the carboxylic acid. Lengthening the alkyl chain of a carboxylic acid can increase this inductive effect but it no longer decreases the acidity further after the chain is about three carbons long. 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Answer a) Consider the inductive effects of the substituents attached to the carboxylic acid. The tert-butyl group is electron-donating which should decrease the acidity of the carboxylic acid. The trimethylammonium substituent is positively charged and can be a powerful electron-withdrawing substituent. This should increase the acidity of the carboxylic acid. The compound (CH3)3NCH2CO2H is expected to be a stronger acid than (CH3)3CCH2CO2H. The acidity constants for these two compounds match the predictions. b) Having an electron-withdrawing hydroxyl group at the C-2 stabilizes the carboxylate ion of lactic acid through inductive effects. This should make lactic acid more acidic than propanoic acid. c) Due to the presence of a highly electronegative oxygen, the carbonyl group is expected to be more strongly electron-withdrawing than a carbon–carbon double bond. Thus, pyruvic acid should be a stronger acid than acrylic acid. Oxalic acid is a dicarboxylic acid with two acidic protons. 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This means that the formyl group is removing electrons from the aromatic ring making it deactivated toward electrophilic aromatic substitution. Contributors and Attributions The nonreactivity of Brønsted superacids' conjugate bases towards hydrogen ions is often mirrored in nonreactivity towards other Lewis Acids/electrophiles, most notably metals. This makes these substances useful as inert or noncoordinating ions, although since all are reactive towards suitably electrophilic centers, they are perhaps better understood as weakly coordinating. A number of noncoordinating anions are commonly used in synthetic and other applications. The conjugate base of perchloric acid, perchlorate, was a common noncoordinating inert anion in classical coordination chemistry and continues to be used widely in electrochemistry. In contrast, the conjugate bases of triflic acid, hexafluoroboric acid, and tetrafluoroboric acid are now more commonly used as counterions for isolating reactive cations. Even less reactive noncoordination anions include derivatives of tetraphenylborate, particularly those with electron withdrawing substituents. Other classes of noncoordinating ions include fluoroantimonate clusters, derivatives of the carborane anion (\(CB_{11}H_{11}^-\)), and fluorinated aluminum tetraalkoxides. The listing of pKa values shown previously in Table 20.3 indicates that there are substantial differences in acidity from one carboxylic acid to another. For example, trifluoroacetic acid (Ka = 0.59) is 33,000 times as strong as acetic acid (Ka = 1.75 × 10–5). How can we account for such differences? Because the dissociation of a carboxylic acid is an equilibrium process, any factor that stabilizes the carboxylate anion relative to undissociated carboxylic acid will drive the equilibrium toward increased dissociation and result in increased acidity. For instance, three electron-withdrawing fluorine atoms delocalize the negative charge in the trifluoroacetate anion, thereby stabilizing the ion and increasing the acidity of CF3CO2H. In the same way, glycolic acid (HOCH2CO2H; pKa = 3.83) is stronger than acetic acid because of the electron-withdrawing effect of the electronegative oxygen atom. Because inductive effects operate through σ bonds and are dependent on distance, the effect of halogen substitution decreases as the substituent moves farther from the carboxyl. Thus, 2-chlorobutanoic acid has pKa = 2.86, 3-chlorobutanoic acid has pKa = 4.05, and 4- chlorobutanoic acid has pKa = 4.52, similar to that of butanoic acid itself. Substituent effects on acidity are also found in substituted benzoic acids. We said during the discussion of electrophilic aromatic substitution in Section 16.4 that substituents on the aromatic ring strongly affect reactivity. Aromatic rings with electron-donating groups are activated toward further electrophilic substitution, and aromatic rings with electron- withdrawing groups are deactivated. Exactly the same effects can be observed on the acidity of substituted benzoic acids (Table 20.4). Table 20.4 Substituent Effects on the Acidity of p-Substituted Benzoic Acids Y Ka × 10–5 pKa –NO2 39 3.41 Deactivating groups –CN 28 3.55 –CHO 18 3.75 –Br 11 3.96 –Cl 10 4.0 –H 6.46 4.19 –CH3 4.3 4.34 Activating groups –OCH3 3.5 4.46 –OH 3.3 4.48 As Table 20.4 shows, an electron-donating (activating) group such as methoxy decreases acidity by destabilizing the carboxylate anion, and an electron-withdrawing (deactivating) group such as nitro increases acidity by stabilizing the carboxylate anion. Because it’s much easier to measure the acidity of a substituted benzoic acid than it is to determine the relative reactivity of an aromatic ring toward electrophilic substitution, the correlation between the two effects is useful for predicting reactivity. If we want to know the effect of a certain substituent on electrophilic reactivity, we can simply find the acidity of the corresponding benzoic acid. Worked Example 20.1 gives an illustration. Worked Example 20.1Predicting the Effect of a Substituent on the Reactivity of an Aromatic Ring toward Electrophilic SubstitutionThe pKa of p-(trifluoromethyl)benzoic acid is 3.6. Is the trifluoromethyl substituent an activating or deactivating group in electrophilic aromatic substitution? StrategyDecide whether p-(trifluoromethyl)benzoic acid is stronger or weaker than benzoic acid. A substituent that strengthens the acid is a deactivating group because it withdraws electrons, and a substituent that weakens the acid is an activating group because it donates electrons.SolutionA pKa of 3.6 means that p-(trifluoromethyl)benzoic acid is stronger than benzoic acid, whose pKa is 4.19. Thus, the trifluoromethyl substituent favors dissociation by helping stabilize the negative charge. Trifluoromethyl must therefore be an electron-withdrawing, deactivating group. Problem 20-6 Which would you expect to be a stronger acid, the lactic acid found in tired muscles or acetic acid? Explain. Problem 20-7 Dicarboxylic acids have two dissociation constants, one for the initial dissociation into a monoanion and one for the second dissociation into a dianion. For oxalic acid, HO2C–CO2H, the first ionization constant is pKa1 = 1.2 and the second ionization constant is pKa2 = 4.2. Why is the second carboxyl group far less acidic than the first? Problem 20-8 The pKa of p-cyclopropylbenzoic acid is 4.45. Is cyclopropylbenzene likely to be more reactive or less reactive than benzene toward electrophilic bromination? Explain. Problem 20-9 Rank the following compounds in order of increasing acidity. Don’t look at a table of pKa data to help with your answer. (a) Benzoic acid, p-methylbenzoic acid, p-chlorobenzoic acid (b) p-Nitrobenzoic acid, acetic acid, benzoic acid If you look closely at your diagram, you will notice that once benzoic acid has released its proton, the conjugate base that is formed has 6 resonance structures out of which 4 have 2 more charges that offset each other. The overall charge of benzoate anion is -1 regardless. The important part of this discussion revolves around the last 4 resonance structures. For the sake of the discussion, I will only refer to the 2 charges that offset each other. When a negative charge appears on the oxygen atom in the carboxyl group, a positive charge appears on the ring (the charge is spread across the nucleus). At this point, we see that the conjugate base is quite stable because it has 6 resonance structures. The more resonance structures the conjugate base has, the stronger the acid is. This is how the acidity of benzoic acid is explained. Now, if you placed a methoxy group in para position, it would doante electrons to the ring through a mesomeric effect. If that happens, the electron density around the nucleus increases, diminishing the positive charge. The methoxy group increases the electron density and so the positive charge on the nucleus is no longer “that positive” while the negative charge remains unaffected (“just as negative”). If the positive charge can’t properly balance the negative charge, the resonance structures involving charge separation are not advantageous to exist and so the strength of the acid decreases. This happens only if the methoxy group is situated para relative to the carboxyl group. If it is situated meta relative to the carboxyl, something interesting happens. We know that the methoxy (like the hydroxy group) exerts a -I inductive effect and a mesomeric (M) effect. That is why, if found para, it “donates” electron density through a +M effect (which manifests more than -I). When in meta, the +M effect is no longer a dominant effect and so, methoxy manifests -I effect mostly, withdrawing electron density from the nucleus. It is often said that hydroxy and methoxy groups are EDG, but only when it comes to electromeric effects. They also have -I inductive effects which makes them EWG. Overall, the presence of a EDG in ortho or para destabilises the actual negative charge of the benzoate anion, thus making it less stable.