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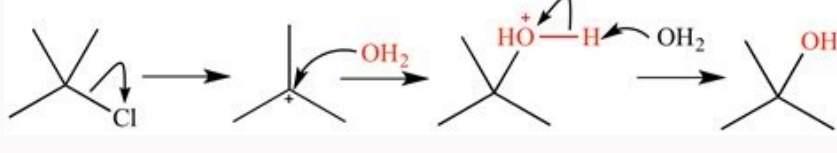
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Electrophilic substitution reaction of naphthalene pdf

Electrophilic Substitution in Naphthalene: The aromatic compounds like naphthalene, anthracene and phenanthrene are called polycyclic aromatic compounds because they contain two or more rings fused together containing one or more common carbon bonds. These compounds are cyclic, contain (4n + 2) π pi electrons, and are planar. Every carbon in the ring is sp^2 hybridized. Naphthalene is aromatic (resonance energy 61 kcal/mole) and is similar to benzene in reactions. Nitration and halogenation occur almost selectively in the α -position. The transition states for both the attack (α) and (β) have four important resonating structures as follows: The carbocation generated by the attack of nitronium ion at α -position is a hybrid of structures (I) and (II). In both these structures, the aromatic sextet is preserved. Attack at β -position generates the carbocation that is a hybrid of (III) and (IV). Here only structure (III) has an aromatic nature. Therefore, the overall energy required to attain the transition states for α -attack is less than that of β -attack. Hence nitration would occur much more rapidly at the α -position. In the case of the transition state of naphthalene, at least one ring retains its aromatic character. Since, this is not possible in benzene, the energy of the transition state for naphthalene is less than that for benzene by about 10 kcal/mole. Hence, naphthalene in general is more reactive than benzene. For example, bromination of naphthalene occurs in absence of the catalyst.



Upon nitration by nitric acid in acetic acid, naphthalene gives mainly 1-nitronaphthalene while thiophene gives 2-nitrothiophen. Make sure you also check our other amazing Article on : Theory of Orientation Nikola Stamenković, a Nataša Poklar Ulrih a and Janez Cerkovnik *b Author affiliations Electrophilic aromatic substitution (EAS) is one of the most widely researched transforms in synthetic organic chemistry. Numerous studies have been carried out to provide an understanding of the nature of its reactivity pattern. There is now a need for a concise and general, but detailed and up-to-date, overview. The basic principles behind EAS are essential to our understanding of what the

To date, textbook overviews of EAS have provided little information about the mechanistic pathways and chemical species involved. In this review, the aim is to gather and present the up-to-date information relating to reactivity in EAS, with the implication that some of the key concepts will be discussed in a scientifically concise manner. In addition, the information presented herein suggests certain new possibilities to advance EAS theory, with particular emphasis on the role of modern instrumental and theoretical techniques in EAS reactivity monitoring. This article is part of the themed collection: PCPP Perspectives This article is Open Access Please wait while we load your content... Something went wrong. Try again? First published 07 Jan 2021 This article is Open Access Phys. Chem. Chem. Phys., 2021,23, 5051-5068 N. Stamenković, N. P. Ulrih and J. Cerkovnik, Phys. Chem. Chem. Phys., 2021, 23, 5051 DOI: 10.1039/D0CP05245K This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence. You can use material from this article in other publications, without requesting further permission from the RSC, provided that the correct acknowledgement is given and it is not used for commercial purposes. To request permission to reproduce material from this article in a commercial publication, please go to the Copyright Clearance Center request page. If you are an author contributing to an RSC publication, you do not need to request permission provided correct acknowledgement is given.

If you are the author of this article, you do not need to request permission to reproduce figures and diagrams provided correct acknowledgement is given. If you want to reproduce the whole article in a third-party commercial publication (excluding your thesis/dissertation for which permission is not required) please go to the Copyright Clearance Center request page. Read more about how to correctly acknowledge RSC content. Tweet Share Fetching data from CrossRef. This may take some time to load Loading related content Received 5th October 2020 Accepted 21st December 2020First published on 7th January 2021Electrophilic aromatic substitution (EAS) is one of the most widely researched transforms in synthetic organic chemistry. Numerous studies have been carried out to provide an understanding of the nature of its reactivity pattern. There is now a need for a concise and general, but detailed and up-to-date, overview. The basic principles behind EAS are essential to our understanding of what the mechanisms underlying EAS are. To date, textbook overviews of EAS have provided little information about the mechanistic pathways and chemical species involved. In this review, the aim is to gather and present the up-to-date information relating to reactivity in EAS, with the implication that some of the key concepts will be discussed in a scientifically concise manner. In addition, the information presented herein suggests certain new possibilities to advance EAS theory, with particular emphasis on the role of modern instrumental and theoretical techniques in EAS reactivity monitoring. Nikola Stamenković Nikola Stamenković received his BSc in chemistry from the University of Niš in 2016 and his MSc in synthetics and applied chemistry from the University of Niš, Serbia in 2018. He joined Prof. Poklar group as a PhD student in 2019. His current research focuses on the development of new methods within the theoretical reactivity concept(s) and on the reactivity and synthesis of antioxidants. Nataša Poklar Ulrih Prof. Nataša Poklar Ulrih, PhD is a full professor of biochemistry at the University of Ljubljana, Biotechnical Faculty.

Electrophilic aromatic substitution (EAS) is one of the most widely researched transforms in synthetic organic chemistry. Numerous studies have been carried out to provide an understanding of the nature of its reactivity pattern. There is now a need for a concise and general, but detailed and up-to-date, overview. The basic principles behind EAS are essential to our understanding of what the mechanisms underlying EAS are. To date, textbook overviews of EAS have provided little information about the mechanistic pathways and chemical species involved. In this review, the aim is to gather and present the up-to-date information relating to reactivity in EAS, with the implication that some of the key concepts will be discussed in a scientifically concise manner. In addition, the information presented herein suggests certain new possibilities to advance EAS theory, with particular emphasis on the role of modern instrumental and theoretical techniques in EAS reactivity monitoring. Nikola Stamenković Nikola Stamenković received his BSc in chemistry from the University of Niš in 2016 and his MSc in synthetics and applied chemistry from the University of Niš, Serbia in 2018. He joined Prof. Poklar group as a PhD student in 2019. His current research focuses on the development of new methods within the theoretical reactivity concept(s) and on the reactivity and synthesis of antioxidants. Nataša Poklar Ulrih Prof. Nataša Poklar Ulrih, PhD is a full professor of biochemistry at the University of Ljubljana, Biotechnical Faculty.

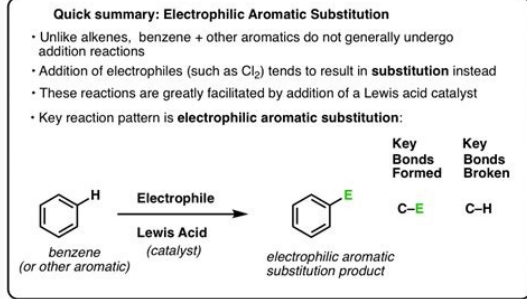


She graduated in chemistry in 1989 and received her PhD in physical chemistry from the Faculty of Chemistry, University of Ljubljana in 1994. Prof. She was a postdoctoral fellow at Rutgers (NJ, USA), a visiting professor at the University of Toronto and at the University of California, Santa Cruz (as a Fulbright scholar). She has successfully coordinated many national and international projects.

Her research interests mainly include the interactions of small molecules with biological macromolecules. She has published more than 120 peer-reviewed articles and two patents. Janez Cerkovnik Prof. Janez Cerkovnik, PhD is Professor of Organic Chemistry at the University of Ljubljana, Faculty of Chemistry and Chemical Technology. He graduated in chemistry in 1987 and received his PhD in organic chemistry from the University of Ljubljana in 1993 on reactive intermediates formed during low temperature ozonation of organosilicon compounds. He was a postdoctoral research associate with Professor Gary H. Posner at Johns Hopkins University (Baltimore, MD, USA). His research interests mainly include the study of mechanisms of reactions with oxygen, ozone, hydrogen peroxide and hydrogen trioxide as oxidants. Introduction to electrophilic aromatic substitution Electrophilic aromatic substitution (EAS) is one of the most researched and common reactions in organic chemistry today. Furthermore, EAS is one of the most useful reactions in the field of synthesis of aromatic compounds. The first report of the EAS reaction that yielded products like those that we know today dates back to the late 19th century, by Henry Armstrong,1 in which, the reaction was characterized as a general type of substitution that was different from those that took place at the C(sp3) reactive site. As such, Armstrong set out certain postulates of this hitherto unknown reaction, with his definition of the reaction intermediate, the (reaction) complex, and the concept of a transition state.

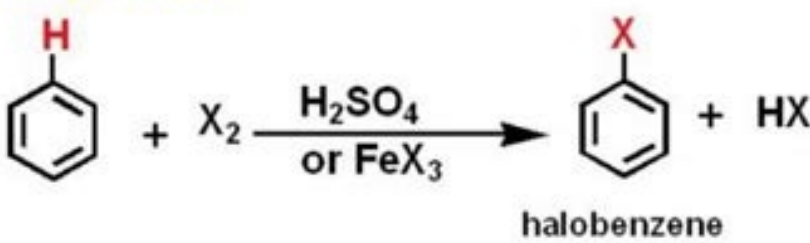


Of course, at that time, these terms were poor in information regarding their significance for this type of newly discovered reaction.

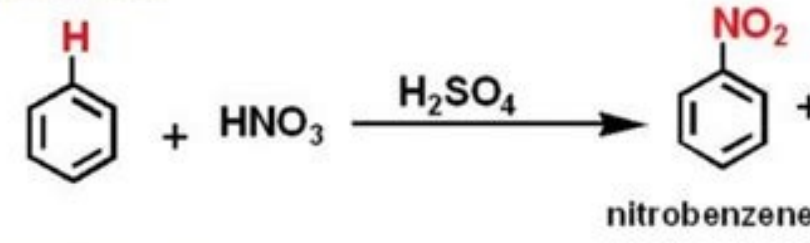


Thus, it was that, with the further development of organic and synthetic organic chemistry, these terms were theoretically and experimentally defined and determined, and introduced into theory as valid terms. In the middle of the 20th century, Wheland further explored and deepened the concept of the Armstrong (reaction) complex in EAS, and named it the σ -complex. Indeed, today, the σ -complex is also known as the Wheland complex, as it was first defined by Wheland.2 It is also important to note that today the term 'Wheland intermediate' is used in the same way as 'Wheland complex', as synonymous with the term σ -complex.

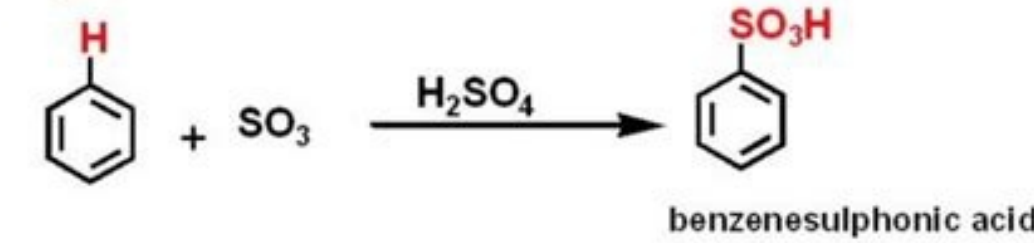
a) Halogenation



b) Nitration



c) Sulphonation



Historically, the transition state has been studied by many well-known scientists, with Hammett, Cram, and Curtin, to name but a few, who have made solid contributions to the development of the theory and concept of the transition state. Basic postulates of substitution as a transform in retrosynthetic analysis Substitution is one of the oldest reactions in both organic and inorganic chemistry, and over time, it has become an extremely important form of transformation. With the introduction of the concept of retrosynthetic analysis into the theory of synthetic organic chemistry by Corey, the concept of transformation was changed into that of transform.3 Thus, a transform relates to any type of reaction in the synthesis of a compound. In this regard, substitution is defined, in modern chemical science, as a type of transform, which implies that in such a type of reaction there is a reactant. A 'reactant' is a term that is used to describe a chemical species that is introduced into a reaction and is responsible for its initiation. What characterizes the substitution reaction (as well as many other reactions) are the physico-chemical parameters that define its course. Most often, these involve the concepts of enthalpy change, entropy, and Gibbs free energy (i.e., ΔH , ΔS , and ΔG , respectively); however, there are also the concepts of energy barrier, collision factor, Gibbs free transitional state energy, and dihedral and nucleophilic attack angles (E_a , f , ΔG^\ddagger , α_d , and α_{nuc} , respectively). In addition to these, there are other computer theoretical parameters that are more complex both in their definition and in their calculation. All of these physico-chemical parameters are equally important in considering and determining the mechanism of any particular type of reaction, including the substitution reaction.

The reactivity of benzene was tested in two different ways to determine its true reactivity. The dilemmas that arose at the time were concerned with the presence of double bonds, which were speculated to react separately as well as to react independently of each other, depending on the conditions. To perform the reaction on one double bond, the chemoselectively, the conditions of the reaction system had to be adjusted so that the amount of the electrophile was a little less than the unit amount of the particular double bond on the benzene nucleus (<0.33 eq.), while the catalysts were in much larger amounts. The first way that benzene can react is by electrophilizing the unit double bond of the benzene nucleus, without any further chemical modification of the aromatic nucleus itself. This implies a key concept when considering the mechanism of this reaction – the loss of aromaticity of the aromatic compound! The loss of aromaticity here refers to the formation of the C(sp3) sites and also to the destabilization of the molecular system. Therefore, this aromatic compound would no longer be aromatic, nor would it have a system of conjugated double bonds.4a–c An example of an addition reaction to a benzene reaction follows on from an alkene addition reaction (Scheme 3). Therefore, the general characteristics of the mechanism that characterizes the addition reaction to alkenes would also characterize the addition reaction to benzene.

Scheme 3 The reaction of benzene with HBr through a transient state during protonation of the benzene nucleus. The newly formed C(sp3) site is indicated, as an intermediate center that indicates the loss of aromaticity during this reaction. Scheme 3 indicates three aspects: the appearance of an anti-aromatic reactive species that has a carbocationic site in the α -position; the formation of a C(sp3) site that has highly acidic H-atoms; and the transition state (Scheme 3, TS), where the electrostatic potential map indicates the possibility of the formation of nonplanar polarization of the observed double bond.5 Nonplanar polarization of a single double bond is a phenomenon that accompanies the formation of a C(sp3) site on such a compound. To explain this polarization, analogous allenic or other nonaccumulated diene protonated systems can be considered, where their orbital image indicates the presence of an orbital outside one plane (Fig. 1), which can partially 'support' the existence of the phenomena of nonplanar proton abstraction in such a transition state.6 The transition state in Scheme 3 is characterized by the 'capturing' of protons from the HBr molecules, where nonplanar double-bond polarization leads to polarization of the π -electron cloud of benzene, and the generation of a carbanion reactive orbital, which is planar with the rest of the π -electron cloud in the molecule at the moment of its generation.

According to the relevant data on the characterization of this transient state, the most approximate theoretical studies at the MP2 level were performed on the superacid system C6H6-HBr-AlBr3, which showed that the newly generated C(sp3) site is still planar, while the reactive carbon orbital (the highest occupied molecular orbital; HOMO) is at an angle ($\alpha(\text{HOMO})$ of approximately $90^\circ < \alpha(\text{HOMO}) \leq 109.28^\circ (\pm 3.00^\circ)$ relative to the proton position.7,21 This explains the appearance of a nonplanar transition state during the protonation of benzene molecules (Fig. 2). In favor of this, the sample of naphthalene protonation (i.e., the simplest molecule in the group of polycyclic aromatic hydrocarbons) under superacid conditions produces the protonated naphthyl cation, where the C(sp3) site is generated at the C-1 position.8 Fig. 1 Orbital view of 1,3-dienyl-2-cation. The arrows indicate orbitals that are out of plane and also where nonplanar polarization has taken place.6 Fig. 2 Interaction of benzene with hydrobromic acid: (a) formation of the (angular) π -complex;3d (b) orbital representation of the π -orbital in benzene; (c) simplified π - π -model of polarization ($n = 1, 2$) of one part of the π -electron cloud of benzene during the formation of the π -complex (the carbanionic highest occupied molecular orbital (HOMO) is planar at this moment);6,9d and (d) angular deformation of the HOMO during the formation of the σ -complex and free p-orbital formation. During the formation of the intermediate species from the indicated transition state, the carbocationic species is unstable for two reasons: the carbocation drastically lowers the energy of the electrophilic orbital (i.e., as the lowest unoccupied molecular orbital [LUMO]; Scheme 3, the site adjacent to that marked by the sphere), and there is the absence of a nonnucleophilic counterion (i.e., the presence of a bromide ion).

The estimated acidity of this arenium ion is about -2.9 in ionic liquid systems9a (the extrapolated acidity of this species in an aqueous system is -24).9b,c which indicates that the bromide can have both nucleophilic and basic characteristics in further reactions. The further course of the reaction is such that the feedback reaction is favored, and that the aromatic nucleus and the molecules of hydrobromic acid are regenerated, notwithstanding the greatly increased electrophilicity of the carbanion of the protonated benzene. The problem of reversibility of the reaction can be solved by using a catalytic system or by an increase in temperature in the presence of an aprotic polar solvent (most frequently, MeCN, DCM [DCE], and THF). Both solutions are operational, bearing in mind that in the experimental sense each has its own convenience. The catalytic system establishes a favorable two-component entropic system, in which alternating and mutual stabilization of the proton and the nucleophilic acid residue occurs (here as the bromide ion). In addition, the catalytic system conditions the angular deformation of the carbanionic orbital in the transition state, which promotes additional stabilization of the catalyst-benzene relationship. On the other hand, an increase in temperature to reflux temperatures (i.e., $65\text{--}85^\circ\text{C}$) in the presence of an aprotic polar solvent reduces the level of proton stabilization, while it also favors stabilization of the nucleophilic acid residue. This thus reduces the total proton acidity, while the nucleophilic character of the acid residue remains slightly altered, but is still favorable for nucleophilic attack. As part of the further discussions of the mechanism of EAS, it is important to note the importance of the structure indicated in Scheme 3 using an asterisk. The transition state provides an insight into the orbital arrangement and reactivity of the proton, as an electrophile, but this structure provides an insight into the reactivity of the benzene nucleus during the EAS reaction. When talking about the reactivity of EAS, it is important to consider the term σ -complex. In the literature, and as indicated above, the σ -complex is also referred to as the Wheland complex or the Wheland intermediate. For σ -complex, it is important to emphasize the characteristic and subtle relationship between the intensity of the electrophilicity and the acidity of the benzene nucleus, as mentioned in the example above. Further disintegration of this complex will strictly depend not only on the conditions in which the reaction takes place, but also on the types and relationships of the participants in the reaction. The existence of nucleophilic species with a possible basic character will show in experimental and theoretical terms that the reaction takes place in the direction of proton abstraction from this complex. However, it must also be said that, as learnt over the last few years, the electrophilicity of the nonaromatic benzene nucleus can be controlled. The difference in Gibbs free energy (ΔG^\ddagger) of the addition product represents an excellent benchmark when estimating the outcome of an EAS reaction or addition to the benzene nucleus.

In this regard, the products of monoaddition (i.e., 5-bromocyclohexa-1,3-diene [BChex]; Fig. 3a), di-addition (i.e., 3,5-dibromocyclohex-1-ene [3,5-DBChex]; Fig. 3b), 4,5-dibromocyclohex-1-ene [4,5-DBChex]; Fig. 3c), and tri-addition (1,3,5-tribromo-cyclohexane [1,3,5-TBCy]; Fig. 3c1, 1,3,4-tribromo-cyclohexane [1,2,4-TBCy]; Fig. 3c2) are possible products in the PhH-HBr reactive system. Fig. 3 Possible products in the benzene addition reaction with HBr (above), and energy profile of the HBr addition reaction with benzene (below). AG(a1) is the Gibbs free energy value of bromobenzene (bold dashed line for its energy profile path), an EAS product (using Br2 and HBr as a catalytic system,10 as an exception from the electrophilic addition process), presented here as a comparison to the other counterparts in the electrophilic addition process. The theoretical possibility for the creation of all five of these products gives a different picture through the interpretation of the energy values of each of these possible products, as shown in Fig. 3. Namely, the di-addition and tri-addition products (i.e., 1,5-DBChex, 1,2-DBChex, 1,3,5-TBCy, 1,2,4-TBCy) have very low probabilities of formation due to the particularly high energy barriers for the alternating successive protonation-nucleophilic attack reactions that occur during the subsequent addition reactions and that are higher than those that occur during the EAS reaction. It is important to note that the electrophilicity and the acidity of the protonated addition products during di-addition and tri-addition with HBr correlate inversely with the rate of proton abstraction (kabs), such that the reverse reactions (i.e., debromination) become (slightly) less favored. In contrast, a monoaddition product (BChex) would be expected to have a very high probability of formation. However, it was first experimentally confirmed that in the PhH-HBr system the reverse reaction after protonation was favored! The reason for such a reaction course lies precisely as mentioned above, that the protonated benzene (i.e., the σ -complex) is very unstable and that proton abstraction occurs much faster than the addition of bromide to the carbocation site. Theoretically, the addition process itself can be explained whereby, although bromide would attack the carbocation site before proton abstraction and form a suitable intermediate, this intermediate would be very thermodynamically unstable and would lead to successive tandem proton abstraction and bromide departure, which would regenerate the aromatic system. The structures of all five of the products are shown in Fig. 3, while the indicated differences in reactivity are shown through the reactions in Scheme 4 and the energy profiles in Fig. 3. Scheme 4 Theoretical reactions considered for the formation of all five of the products following the addition of HBr to benzene, which depend on the amount of HBr added per 1 equivalent of benzene. The corresponding transition states and intermediates are also shown. It should be emphasized that, according to the reactivity parameter, similar processes of the hydrogenation of benzene have already been developed, and that these methodologies have been successfully applied in the laboratory and in industry (i.e. catalytic hydrogenation). In the previous example, one theoretical possibility for the reactivity of benzene (i.e., the benzene nucleus) was considered in detail, which has generally been rejected due to a lack of experimental and/or computational evidence. The second way in which aromatic nuclei can react will be discussed below, with the same PhH-HBr system taken into further consideration for reactivity. To explain the reactivity of the benzene nucleus, there is a need to first look at the terms ' π -complex' and ' σ -complex', which have already been mentioned. As a compound within this system, benzene has very unusual energy stability and thus many different ways in which it can react with reactants. The structure was discovered by the German chemist Kekulé in the 19th century whose representation is still used by the scientific community. It consists of two canonical resonance structures, which explain the unusual stability observed: a six-membered ring with (ideal) angles of $120^\circ (\pm 2^\circ)$ within which three conjugate double bonds are 'positioned'. The conjugation of the double bonds can be used to indicate and explain the unusual level of stability of this molecule. For these double bonds, experimental and computational tests have shown that they have electrons that move in the p-orbitals that are positioned to allow an uninterrupted and constant flow of electrons through this entire p-orbital system. This thus defines these double bonds as the so-called

By hybridizing all of the carbon orbitals in this ring and rearranging them, whereby the electron cloud is formed, it can be concluded that these six electrons are π -electrons. From this, it can be concluded consequently that π -electrons actually contribute to the nucleophilicity of the benzene nucleus. To activate this π -electron cloud, it is necessary that there is an electrophilic species in the reactive system that can allow substitution on this benzene ring. The proton from HBr is an electrophilic species,10 although, during the formation of the σ -complex, the newly formed species would contain two identical electrophiles. This would characterize the reaction as reversible on the basis of the identical probability of abstraction of two protons at the newly generated C(sp3) site. This leads to the conclusion that the electrophile should be a nonproton species that can react with a benzene electron cloud. This is solved by the addition of catalysts to sufficiently reduce the energy of the LUMO of the potential electrophile, thereby disturbing the stability of the π -electron cloud by reacting with a given electrophile in this catalytic system. The σ -complex thus formed can then undergo proton abstraction by the nucleophilic or basic species present in the system and shift the equilibrium toward the reaction product. When the reacting electrophile is different from the proton during the nucleophilic attack of benzene on it to obtain a substitution product, the reaction is known as EAS.4 The basic catalytic systems that are used in EAS reactions include Lewis acids,11–14 which in principle coordinate the electrophile to make it more electrophilic for the attack of the benzene nucleus. Recent research has indicated that proton catalytic systems can also efficiently undergo EAS reactions, which opens up a new field for research into the mechanism of the EAS reaction.10 Newer catalytic systems will be discussed later, and for the needs of the general mechanism of electrophilic aromatic substitution, and in relation to the aforementioned, we will use the modified system of Lewis acid-benzene (LA-E+–PhH). Electrophile-electrophile substitution – electrophile differentiation Thus far, we have been concerned specifically about the potential mechanism of addition, which in mechanistic terms has similarities with the EAS reaction, although they actually differ from each other in only one step: the differentiation of electrophiles15a during the reaction. Electrophile differentiation means that an electrophile of similar reactivity is added to a benzene nucleus, such as a proton. This has already been mentioned above in terms of the EAS response mechanism (see Section 2.1), but it is now important to clarify this. The generation of different electrophiles can undoubtedly lead to different yields and outcomes in EAS reactions on the benzene considered here. These will depend on the experimental experience and on the methodology applied during the realization (i.e., execution) of these types of synthetic transforms. Scheme 5a shows the general EAS reaction, while Scheme 5b1 and b2 show the complete mechanism of the EAS reaction.4,15b Scheme 5 General mechanisms of electrophilic aromatic substitution (EAS): (a) general response of EAS and (b1 and b2) general mechanism of EAS, in relation to reaction (a).15b We have used the PhH-HBr system mentioned above to explain the mechanism of benzene addition. However, as can be seen from Scheme 5b1 and b2, the addition of a catalyst leads the reaction in a different direction. To explain this direction, it is necessary to emphasize that both the electrophile and the catalyst are completely different from the HBr molecules. The only difference between the addition reaction and the electrophile-aromatic substitution is in the nature of the final product. Mechanistically, the reactions are very similar, but the addition reaction has a product that loses aromaticity and consequently isomerizes very quickly to an aromatic form, which is particularly favorable for the feedback reaction. Instead, the EAS reaction regenerates aromaticity and a substituted compound on the aromatic compound is obtained (as the name of the reaction itself indicates). It can be seen from Scheme 5 that the EAS reaction also goes through the formation of π -complexes and σ -complexes,16–23 which explains the gradual destabilization of the aromatic system. First, a π -complex is formed, which is thermodynamically less stable and rapidly isomerizes to the corresponding σ -complex.42 The stability of the π -complex is characterized by both the quality of the electrophile present and the coordination of the π -electron with this electrophile. This coordination is usually established slowly, so the formation of a π -complex is slow, and mobile π -electrons bind to free hybrid orbitals (if there are any). This results

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