Birch Reduction: Mechanism, Localization Effects, Products and Reaction Conditions

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Abstract. Birch reduction has been a focal point of research due to its unique ability to selectively reduce aromatic compounds under mild conditions. This review paper investigates four critical aspects of Birch reduction: its mechanism, localization effects, product outcomes, and reaction conditions. In exploring these areas, the paper raises key questions concerning the nature of solvated electrons, the potential role of alkaline earth metals as novel reducing agents, and strategies for obtaining conjugated products. While recent research has leaned towards the development of novel catalysts and synthetic methods, less emphasis has been placed on understanding the intermediates involved in this reaction. This paper aims to bridge that gap by providing theoretical insights that enhance the practical application of Birch reduction. By emphasizing both the theoretical framework and its practical implications, this study seeks to advance the understanding of this reaction's fundamental processes.

Keywords: Birch reduction; localization effects; reaction conditions; benzene.

1. Introduction

Birch reduction is a widely used reaction in chemical synthesis, especially in large-scale synthesis of 1,4-cyclohexadiene. This process is usually marked by its aromatic reactants like benzene and its aliphatic products like 1,4-cyclohexadiene. Thus, birch reduction uncontroversially serves as a crucial link between aromatic compounds and non-aromatic compounds. In the reaction, alkali metals like sodium coupled with liquid ammonia and alcohols like ethanol, isopropanol, or secondary butanol are added as reaction conditions.

This reaction was first discovered in 1944 by Arthur Birch, an Australian chemist. However, as science continued developing, it was proved that not merely benzene would exhibit such properties, but other aromatic rings like furan and pyridine could also undergo such reactions. What is surprising is that chemicals without a ring, like conjugated olefins and unsaturated carbonyl compounds, permit birch reduction (conditions, of course, alterable). Among all these molecules that have the potential to do birch reduction, this article attaches more attention to benzene and its derivatives.

There is plenty of research on birch reduction, and incredible results have been achieved. These results cover many fields, including synthesis, catalysts, intermediate capture, etc. In most cases, the designation of synthesis is related to the selection of the catalyst. For example, a work offered a way to do birch reduction merely by visible light. The chemists abandoned the conventional alkali metals and found benzo[ghi]perylene imides a possible catalyst for birch reduction with the help of commercially available LED visible lights [1]. Such works are uncountable, and this article is not going to list more. The point is that birch reduction is indeed a prospective field with a relatively systematic theory structure.

This article focuses on four crucial sections of the birch reaction: mechanism, localization effects, products and reaction conditions. Some of the previous research results are cited to provide the readers with both basic concepts and more advanced findings of this reaction. This article also puts forward some questions that were previously neglected, and it gives some possible hypotheses. This article aims to cover the fundamental parts of this reaction and dig inward to figure out more unknown problems.

2. Mechanism of Birch Reduction – Benzene as an Example

As shown in Fig. 1 below, in the first step, the ammonia electron first attacks one carbon of benzene, breaking its aromaticity and forming a free radical negative ion. The conjugation system changed from six carbons to five carbons, excluding the carbon that was previously attacked. After that, alcohol is used to wash off the negative charge, leaving one free electron to delocalize among the five conjugated carbons. In steps three and four, another ammonia electron is added, while the resulting negative charge is washed off again in the same way as in step two.

In the last step, the position of the double bonds is due to resonance. The negative charge, in this case, is situated in the midst of carbon in the conjugation system. Therefore, after the protonation of ethanol, the diolefin turns out to be unconjugated.

$$\mathrm{Na} + \mathrm{NH_3(l)} \rightarrow \mathrm{Na^+} + \mathrm{e^-(NH_3)} \tag{1}$$

Note that $e^-(NH_3)$ is an ammonia electron whose standard electrode potential is approximately -2.86 V, demonstrating a strong ability to reduce [2].

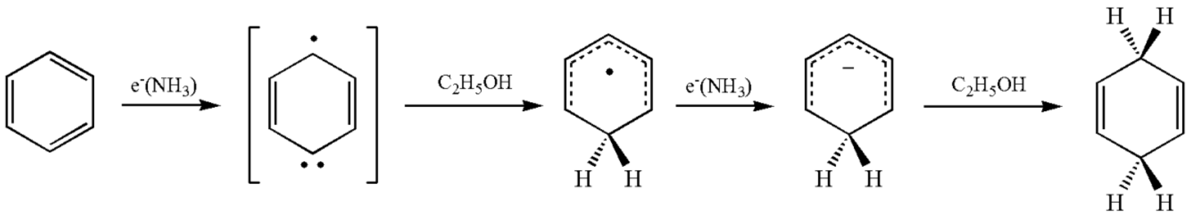

Fig. 1 The pathway of benzene's birch reduction [3].

During the process, it is commonly acknowledged that the solvated electron superiorly fills the lowest unoccupied molecular orbital (LUMO) during the attack, but how the electron behaves when the attack is not going on is still a mystery. Whether it is free in the solvent or may form clusters is yet unknown. Though pure electrons cannot survive in liquids like water, solvated electrons act more like ions, which accept liquid environments. Therefore, the solvated electron can be free. On the other hand, if hydrogen bonds are taken into consideration, things may be different. Since nitrogen, especially free nitrogen atoms can form hydrogen bonds with hydrogen atoms, whether these solvated electrons will form clusters due to the reaction between their ligands cannot be determined. This is theoretically possible because water molecules can form clusters through electroneutral. This work can compare ammonia electrons to water molecules to some extent. One possible way to figure out how the solvated electrons act is by ${}^{15}_{7}N - NMR$. The author can interpret the NMR result of liquid ammonia wherein sodium is dissolved and then compare it with the result of pure liquid ammonia. If they turn out to be the same, then clusters are likely to form, while if they mark some different peaks, then free electrons are more likely.

3. Localization Effects and Consequential Products – Substituted Benzene

In part 2, attention is given to the benzene itself, but what if the molecule is benzene with substituents? Considering this situation, a division between substituents has to be put forward. That is, electron donor groups (EDG) and electron withdraw groups (EWG). Each of them will differently influence the location of the double bonds.

From the Fig. 2 and 3, it is clear how different substituents alter the position of double bonds in products. A notable phenomenon here is that no matter what kind of substituents the molecule possesses, one thing never changes: products are always unconjugated diolefins instead of thermodynamically more stable conjugated diolefins. Research has provided some evidence for such a seemingly weird fact.

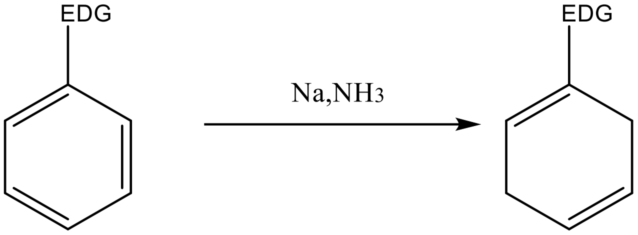

Fig. 2 EDG products (Photo credit: Original)

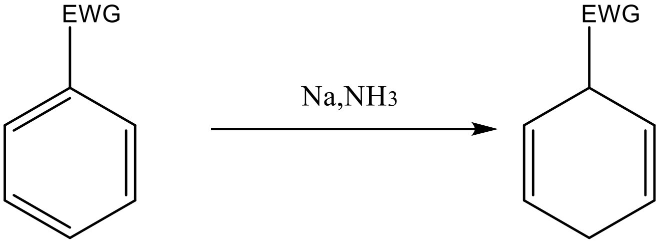

Fig. 3 EDG products (Photo credit: Original)

Pei et al. concluded Birch's work and categorized the reduction process into 3 types: ORTHO, META, and PARA (Fig. 4). According to them, when the R group is an EWG, the molecule is likely to undergo a PARA reaction; when the R group is an EDG, the reactant may undergo either ORTHO or META reaction. It can be easily found that for EWG, the mechanism is similar to that of unsubstituted benzene. This is because EWG can stabilize the negative charge of the intermediate. However, when it comes to EDG, although both ways may occur, the calculation shows that the ORTHO free radical intermediate is lower in energy compared to the META intermediate. Zimmerman H E research group also used experiments to prove that EDG does experience ORTHO more than META [4].

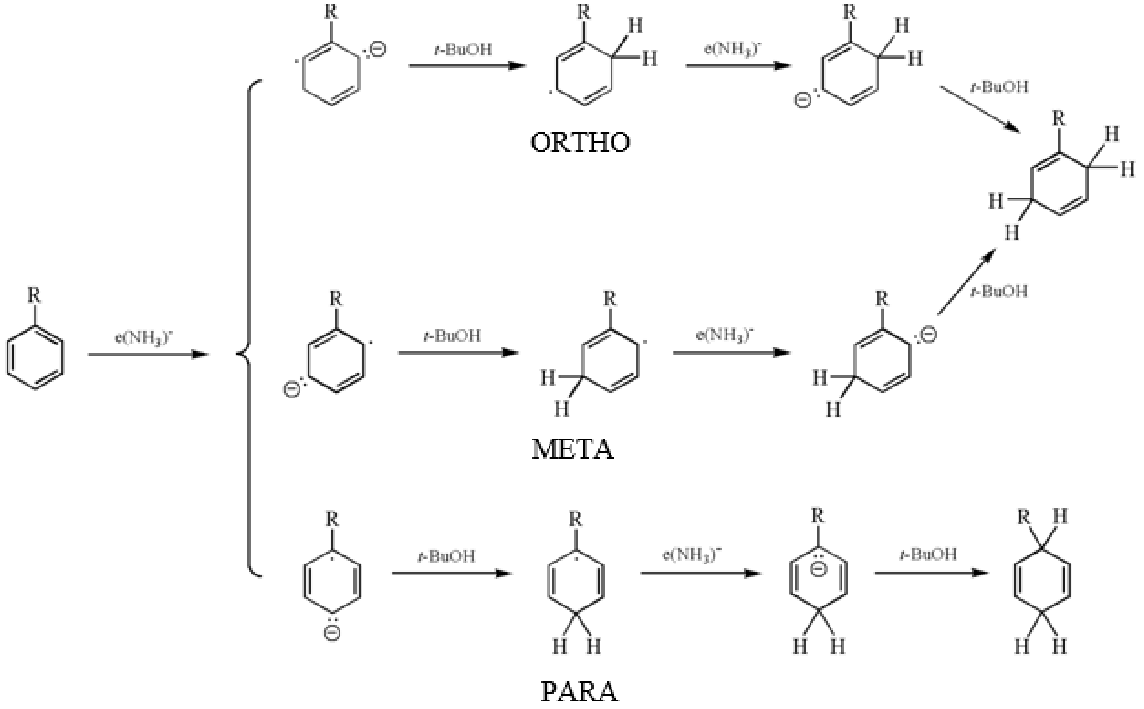

Fig. 4 Three pathways of birch reduction [2].

4. Reaction Conditions

Under many circumstances, birch reduction is realized with the help of alkali metals and liquid ammonia. However, ammonia is somewhat harmful, both to experimenters and the environment.

Therefore, some other substitute compounds are put forward. Jie An, together with his team, raised a novel way to do birch reduction without the presence of ammonia.

Sodium dispersion, as is used in the reaction above, is not only convenient for operation but is also more stable in solvents like THF or gasoline (Fig. 5) [5]. In this situation, crown ether strongly coordinates with sodium, forming a reductive electron salt, which is not the common usage of crown ethers (phase transfer catalysts) [6].

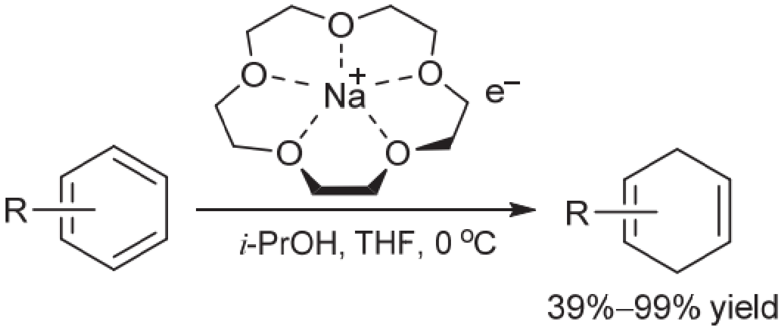

Fig. 5 Sodium dispersion as a substitute catalyst [5].

5. Possible Improvements

The above four parts superficially demonstrated different aspects of birch reduction: definition, mechanism, localization effects, and reaction conditions. Though not very comprehensive, it still implies incredible research value about birch reduction. Here, this article solely gives some more humble opinions on this topic.

First is the catalyst. Since the dissociated electron is the key in the reaction, as long as the catalyst can dissociate electrons, the catalyst would be prospective. As now the most used metals are lithium and sodium, people are wondering whether earth metals are capable of the job. This is because earth metals are more moderate compared to alkali metals of the same period. Furthermore, it is also due to the fact that earth metals' cations are smaller than alkali metals' cations. Therefore, the potential spatial obstructions may decrease. However, whether this proposal could really be applied to real life still requires some calculations. Comparing alkali metals and earth metals, things are only different when the electron is not yet solvated. Therefore, it is only necessary to look up the first and second ionization energy of the earth metals. Taking magnesium as an example, the first ionization energy is 737.7 kJ/mol, while the second ionization energy is 1450.7 kJ/mol. As for sodium, the first ionization energy is 495.8 kJ/mol [7]. From this aspect, it can be concluded that magnesium is less active in reaction than sodium. This may be a disadvantage in many reactions, but when it comes to some very sensitive reactions, moderate earth metals could show up. Especially in those reactions that release much energy and those that are too fast, earth metals can calm them down and modify the reaction rate.

The second thing is the products. Since in part 3, the fact is mentioned that the unconjugated diolefins are not privileged in energy, an idea occurred to us: why can't the conjugated diolefins be generated by altering the reaction conditions? Although there is no clear direction to how to do this, some pioneering research has proved the possibility. In Fig. 6, a reaction that violates the conventional rule of birch reduction is shown.

Tobias et al. did the above work. The finding not only gains untraditional products of birch reduction but also guarantees the selectivity of stereochemistry. According to them, after the usage of carbonyl compounds, the products turn out to afford diastereomeric mixtures in ratios of about 4:1 [8]. Therefore, it marks a giant leap forward in the field of 1,3-cyclohexadiene synthesis. The work consists of two main parts: the birch reduction mechanism and the further synthesis using the products. The author will focus more on the birch reduction part. The reason why the products are different in different conditions has something to do with an intermediate shown in Fig. 6.

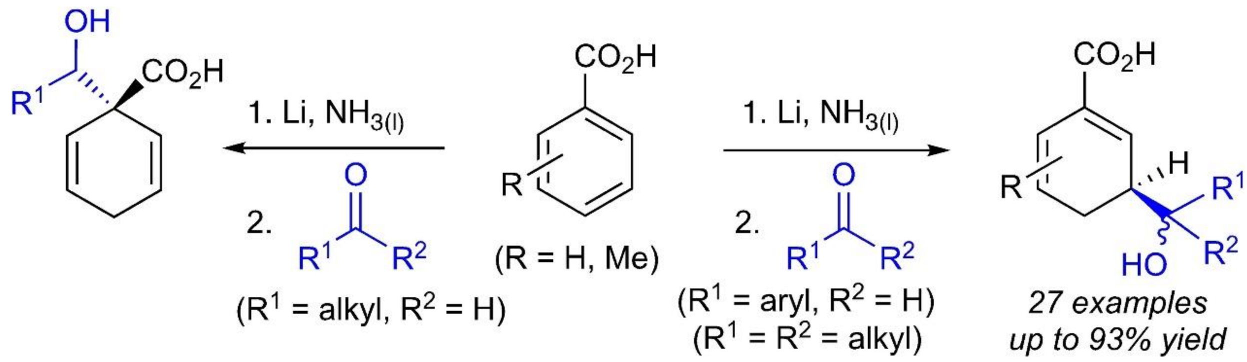

Fig. 6 Different products in different conditions [8].

Because of resonance, the double bonds in this dianion will shift their position (Fig. 7). To be more specific, after the dianion is protonated, the remaining negative charge will resonate with the double bonds and will move to the interposition of the branch. After that, more reactions will happen, but that will not influence the positional relationship (conjugated) between the two double bonds in the ring. The special branch of the ring makes the conjugation system not strained inside the ring, thus making it possible to switch the bond positions.

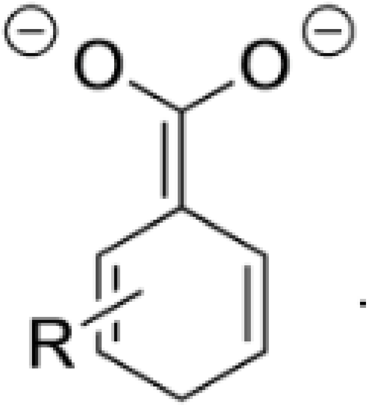

Fig. 7 The crucial intermediate dianion [8].

6. Conclusion

Based on what has been mentioned above, it can be seen that birch reduction is indeed an important reaction. This article focuses on four major parts of this reaction and puts forward both questions and possible solutions. Much previous research has been referred to, and this article analyzes the findings. The main conclusion is that there exists the possibility to monitor the behavior of solvated electrons using $^{15}_{7}N - NMR$ and that earth metals or sodium dispersions may replace current sodium and ammonia. Another conclusion concerning products is that conjugated olefins may be available via alteration in conditions.

In further research, more investigations will be made to gain more insight into birch reduction. Some possible aspects are as follows: aromatic rings besides benzene and chemicals without a ring. For rings like furan or pyridines, the attacking point is obviously different from the benzene; thus, both mechanisms and products will be completely different, not only the chemicals themselves but their properties. As for chemicals without a ring, the reduction process will turn out to be another way as well, but one thing will not change: the conjugation system will definitely be broken. It is unknown whether it will be rebuilt – it needs more interpretation in the mechanisms.

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