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Nitroarenes are Synthesised by Oxidising Arylamines

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Abstract

Nitro compounds are a type of organic molecule that has a wide range of applications in organic synthesis, medicinal chemistry, and materials science. The direct oxidation of primary amines is an appealing alternative route among the various methodologies available for their synthesis. Efforts to develop oxidative procedures for the synthesis of nitro derivatives have spanned decades, yielding a wide range of protocols for the selective oxidative conversion of amines to nitro derivatives. This review summarises methods for the synthesis of nitroarenes via aryl amine oxidation, with a focus on recent advances in the field. The harsh reaction conditions, as well as the poor functional group tolerance and regioselectivity, are the main drawbacks of this route. Many aromatic nitro derivatives are still difficult to synthesise via this method. Alternative nitration reagents and methodologies, including transition-metal-catalyzed ipso-nitration methodologies, have emerged as powerful tools for nitroarenes synthesis.

Keywords: Anilines • Amines • Hydrogen peroxide • Sodium perborate

Introduction

Nitro compounds play a significant role in organic chemistry. Nitro derivatives are widely used in organic synthesis due to their ease of availability and ability to be converted into a wide range of functional groups. Nitroarenes are versatile building blocks that are used in the synthesis of relevant chemicals such as pharmaceuticals, dyes, materials, and perfumes. Several nitro-containing compounds, including nitroxoline, nitrofural, nitrofurantoin, and chloramphenicol, are commercially available drugs. Nitro derivatives are also important in the development of mechanistic concepts. As a result, considerable effort has gone into developing practical and convenient methodologies for their synthesis. Yan and Yang reviewed the synthesis of aromatic nitro compounds nearly ten years ago.

A silane polymer functionalized with octafluoroacetophenone was also used as a heterogeneous catalyst for the hydrogen peroxide oxidation of alkenes and aromatic amines. While pyridine derivatives yielded corresponding oxides, anilines yielded azoxyarenes or nitroarenes depending on the nature of the substituents on the aromatic ring. Aniline and alkyl- and halo-substituted anilines, in particular, yielded quantitative dimeric azoxy derivatives. When this perfluoroketone-silicate-catalyzed method was applied to electron-rich hydroxy-substituted anilines and electron-poor 3-nitroaniline, the corresponding nitroarenes were obtained selectively. Furthermore, substrates with the nitro substituent ortho to the amino group were found to be unreactive, most likely due to intramolecular hydrogen bonding between the amino and the nitro substituent.

Literature Review

The selenium-catalyzed oxidation of anilines has also been investigated in this context, allowing the development of selective procedures for the synthesis of nitroarenes, nitrosoarenes, and azoxyarenes. Indeed, a wide range of variously substituted anilines were smoothly converted into the corresponding nitroarenes 1. The methodology encompasses both electron-rich and electron-poor substrates upon reaction with hydrogen peroxide in the presence of diphenyl diselenide or benzeneseleninic acid and can be efficiently applied to the synthesis of nitroarenes on a gramme scale. Diphenyl diselenide and benzeneseleninic acid outperformed other organoselenides in terms of yield and selectivity. The reaction of aniline with hydrogen peroxide in the presence of selenium dioxide or sodium selenite, on the other hand, yielded a high yield of the corresponding azoxyarenes.

Sodium perborate has also been used as an efficient oxidant in the conversion of anilines to nitroarenes. McKillop and Tarbin reported that anilines with electron-withdrawing groups oxidise smoothly to the corresponding nitro derivatives in acetic acid at 50-55°C when reacting with sodium perborate. Because of the formation of over-oxidised side products, electron-rich anilines provided lower nitroarenes yields. Firouzabadi et al. devised a simple tungstophosphoric acid-catalyzed method for oxidising anilines with sodium perborate in aqueous basic media. Micelle source was cetyltrimethylammonium bromide. Notably, this methodology was particularly effective with electron-rich anilines, yielding high-yielding nitroarenes. Substrates with electron-withdrawing substituents, on the other hand, produced nitroarenes at a lower yield.

Discussion

Heteropolyoxometalates have also been used as catalysts in the oxidative conversion of amines to nitro derivatives. Ishii et al. discovered that anilines react with hydrogen peroxide in the presence of peroxotungstophosphate, which can be made by treating tungstophosphoric acid with H_2O_2 and cetylpyridinium chloride in water. Notably, the reaction temperature proved to be critical for the process's selectivity; indeed, while high temperatures provided good yields of nitroarenes, nitroso derivatives were formed when the reaction was performed at room temperature. The oxidation of aryl amines was also carried out under homogeneous conditions in the presence of a lacunary Keggin-type heteropolyanion containing tungsten and molybdenum addenda atoms.

Anilines with electron-donating groups produced higher yields of the corresponding nitro derivatives. However, aromatic substituents in the ortho position and electron-withdrawing groups in the para position resulted in significantly lower yields. The reaction mechanism is reasonable; the formation of 5 suggests that, like the related phenolic oxidation, aniline oxidation involves hydrogen atom abstraction from the amino group followed by trapping by the

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peroxy radical at the nitrogen or para position. Notably, using this methodology on aliphatic primary amines allowed them to be converted into carbonyl derivatives via oxidative removal of the amino group.

Nonetheless, despite the breadth of the developed routes, some challenges remain. More research into the synthesis of heteroaryl nitro compounds via oxidation strategies would be beneficial. Furthermore, developing selective procedures for the synthesis of amino-substituted nitroarenes is a fascinating but difficult task. The study of the regiochemistry of diamine and polyamine oxidation under various reaction conditions is thus an intriguing research topic. On the other hand, more efforts are needed to develop additional catalysed, mild, environmentally friendly protocols for the synthesis of nitro derivatives with valuable labile functional groups. The environmental sustainability of processes is likely to gain popularity. While catalyst recovery and recycling have been studied and optimised, column chromatography is frequently used to purify reaction products.

This review summarises the progress in the synthesis of nitroarenes via aryl amine oxidation. There have been reports of efficient and convenient methods for preparing variously functionalised nitroarenes. The various reaction conditions, as well as the use of various catalysts and oxidising agents, allowed for high selectivity and a fairly broad functional-group tolerance. A synthetic overview of some of the discussed methodologies is provided, with emphasis on the catalyst, the oxidant, the scope, and limitations. In the second column, promoters used in stoichiometric or superstoichiometric amounts are reported [1-5].

Conclusion

Nitro compounds are a diverse and important class of organic compounds. The development of practical and efficient methods for the synthesis of nitro compounds has sparked considerable interest due to their applications ranging from organic synthesis and materials science to medicinal chemistry and drug science. As a result, over the last few decades, a wide range of synthetic approaches have emerged. In this context, amine oxidation is a valuable alternative route to nitro derivatives. The absence of regioselectivity issues in oxidation-based methodologies is their primary advantage over some nitration strategies. On the other hand, significant historical drawbacks of oxidation-based approaches are associated with the formation of oxidised product mixtures.

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Conflict of Interest

There are no conflicts of interest by author.

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