CURRENT ADVANCEMENTS IN ULLMAN-TYPE CROSS-COUPLING REACTIONS CATALYZED BY COPPER

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Abstract

A breakthrough in cross-coupling chemistry, the copper-catalyzed Ulmann reaction provides a reliable and effective way to obtain biaryl compounds, which are essential for the synthesis of complex molecules with a wide range of uses. The Ulmann reaction, which is catalyzed by copper and is a fundamental mechanism in modern organic synthesis, offers scientists a sustainable and efficient method of obtaining biaryl compounds, a family of compounds that are essential to materials science, agrochemicals, and pharmaceuticals. The goal of this study of the literature is to provide insight into how chemical reactions evolve during organic synthesis.

Keywords: Cross-coupling, Aryl halides, Aryl metal reagents, Biaryl compounds, Copper catalysis

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Introduction

The Ulmann reaction, so called because it was first reported in 1901 by the German chemist Fritz Ulmann, has become a key step in the synthesis of organic compounds.[1] It entails the cross-coupling of aryl halides with aryl metal reagents to produce biaryl compounds, which are essential building blocks in material science, natural product synthesis, and pharmaceutical chemistry. Prior to recent developments, this transition was primarily facilitated by expensive and hazardous metals like palladium or silver, but copper, a transition metal, has shown promise as a sustainable and affordable catalyst. Because of its adaptability, gentle reaction conditions, and compatibility with different functional groups, the Ulmann reaction catalyzed by copper has attracted a lot of interest.[2] With this technology, carbon-carbon bonds may be efficiently formed, leading to the synthesis of a variety of biaryl motifs with excellent selectivity and mild reaction conditions. In addition, copper's low toxicity and abundance make it a desirable substitute for other transition metals, supporting the ideas of green chemistry.[3] All things considered, the Ulmann reaction catalyzed by copper is a fundamental process in contemporary organic synthesis that provides chemists with an environmentally friendly and effective means of obtaining biaryl compounds, a crucial class of compounds having numerous uses in the fields of materials science, agrochemicals, and medicines.[4] This transformational reaction holds promise for future advances in synthetic chemistry and the creation of new functional materials and bioactive molecules through ongoing innovation and study.

Literature Review

This review of the literature attempts to give a thorough overview of the Ulmann reaction, which is catalyzed by copper, taking into account current developments in the reaction's evolution. In order to clarify the importance of copper catalysis in facilitating the successful synthesis of biaryl compounds, this review synthesizes the vast amount of knowledge that has been gathered in this subject.[5]

Copper Nanoparticles Catalysis

The Ulmann reaction has attracted interest in the use of copper nanoparticles as catalysts because of their large surface area, reactivity, and recyclable nature. By providing enhanced catalytic efficiency and selectivity, these nanoparticles make it possible to couple a variety of aryl halides with metal reagents.[6]

Copper(I) Complexes with Novel Ligands

An improvement in catalytic performance in the Ulmann reaction has resulted from the development of new ligands for copper(I) complexes. In order to maximize catalytic activity, regioselectivity, and tolerance towards functional groups, ligand design strategies concentrate on fine-tuning steric and electronic characteristics.[7]

Dual Catalysis Approaches

Innovative dual catalysis approaches in the Ulmann reaction have been made possible by the combination of copper catalysis with other catalytic systems, such as photoredox or electrocatalysis. These synergistic systems increase the range of transformations that are possible and provide complementary reactivity.[8]

Flow Chemistry

The incorporation of the Ulmann reaction into continuous flow systems has become a potent approach for scaling up and intensifying processes. The exact control of reaction parameters made possible by flow chemistry improves the safety, reproducibility, and efficiency of the reaction.[9]

Bioorthogonal Ulmann Reactions

Site-selective alteration of biomolecules under physiological conditions is made possible by the development of bioorthogonal Ulmann reactions. These techniques enable applications in chemical biology and drug discovery by selectively coupling aryl halides with biofunctionalized metal reagents via bioconjugation procedures.[10]

Copper-Catalyzed Aryl Amination

Direct C-N bond creation is made possible by extending the Ulmann reaction to copper-catalyzed aryl amination. These techniques provide effective access to a variety of derivatives of aniline, which are important intermediates in the synthesis of agrochemicals and pharmaceuticals.[11]

Tandem and Cascade Reactions

The Ulmann reaction has led to the development of tandem and cascade reactions, which facilitate the efficient synthesis of intricate molecular structures. Rapid synthesis of heterocyclic molecules and densely functionalized biaryl scaffolds is made possible by sequential transformations.[12]

Asymmetric Ulmann Reactions

Chiral ligands and catalytic systems have been used to create enantioselective Ulmann reaction variations.These techniques make it possible to synthesize enantioenriched biaryl compounds, which may find use in medicinal chemistry and asymmetric synthesis.[13]

Mechanistic Studies and Computational Design

The mechanism of the reaction and the interactions between the catalyst and the substrate have been better understood because to developments in mechanistic research and computational design. Using computational predictions to guide rational catalyst design, more selective and efficient catalytic systems can be created.[14]

Metal-Free Ulmann Reactions

Studies on Ulmann reaction methods without the use of metals provide an alternative to conventional transition metal catalysis. By using organic or organometallic nucleophiles for aryl-aryl coupling, these techniques increase the repertoire of synthetic techniques available for biaryl synthesis.[15]

Conclusion

In conclusion, the Ulmann reaction, which is catalyzed by copper, is a fundamental process in contemporary organic synthesis that provides an effective and sustainable way to create biaryl compounds. The goal of ongoing research is to increase the copper-catalyzed Ulmann reaction's efficiency and range of applications. Current research focuses on the creation of novel catalytic systems, the examination of tandem and cascade reactions, and the integration of these systems into multistep synthesis strategies. Its scope, selectivity, and usefulness have been improved recently, opening the door for its continued use in many sectors of chemical research and industry.

References

1. Lixin, D., 2018. Ullmann Reaction, A Centennial Memory and Recent Renaissance Related Formation of Carbon-Heteroatom Bond. *Progress in Chemistry*, *30*(9), p.1257.
2. Abedinifar, F., Bahadorikhalili, S., Larijani, B., Mahdavi, M. and Verpoort, F., 2022. A review on the latest progress of C-S cross-coupling in diaryl sulfide synthesis: Update from 2012 to 2021. *Applied Organometallic Chemistry*, *36*(1), p.e6482.
3. Rahman, M., Ghosh, S., Bhattacherjee, D., Zyryanov, G.V., Kumar Bagdi, A. and Hajra, A., 2022. Recent Advances in Microwave-assisted Cross-Coupling Reactions. *Asian Journal of Organic Chemistry*, *11*(8), p.e202200179.
4. Pal, A. and Gayen, K.S., 2021. The Impact of Microwave Irradiation Reaction in Medicinal Chemistry:(A Review). *Oriental Journal of Chemistry*, *37*(1).
5. Mulugeta. D. A Review on Recent Trends in Copper-Catalyzed Organic Synthesis. Journal of Chemical, Environmental and Biological Engineering. Vol. 6, No. 1, 2022, pp. 24-33.
6. Alonso, F., Moglie, Y. and Radivoy, G., 2015. Copper nanoparticles in click chemistry. *Accounts of chemical research*, *48*(9), pp.2516-2528.
7. Tubaro, C., Biffis, A., Scattolin, E. and Basato, M., 2008. Efficient catalysis of Ullmann-type arylation reactions by a novel trinuclear copper (I) complex with a chelating tricarbene ligand. *Tetrahedron*, *64*(19), pp.4187-4195.
8. Kim, U.B., Jung, D.J., Jeon, H.J., Rathwell, K. and Lee, S.G., 2020. Synergistic dual transition metal catalysis. *Chemical Reviews*, *120*(24), pp.13382-13433.
9. Resul, M.F.M.G., Rehman, A., Saleem, F., Usman, M., Fernández, A.M.L., Eze, V.C. and Harvey, A.P., 2023. Recent advances in catalytic and non-catalytic epoxidation of terpenes: a pathway to bio-based polymers from waste biomass. *RSC advances*, *13*(47), pp.32940-32971.
10. Shao, Z., Zhang, C., Zhu, X., Wang, Y., Xu, W., Chen, Y., Wang, X., Zhu, H. and Liang, Y., 2019. Design of a 1, 8-naphthalimide-based OFF-ON type bioorthogonal reagent for fluorescent imaging in live cells. *Chinese Chemical Letters*, *30*(12), pp.2169-2172.
11. Monnier, F. and Taillefer, M., 2013. Copper-catalyzed C (aryl)–N bond formation. *Amination and Formation of sp2 CN Bonds*, pp.173-204.
12. Climent, M.J., Corma, A., Iborra, S. and Sabater, M.J., 2014. Heterogeneous catalysis for tandem reactions. *ACS Catalysis*, *4*(3), pp.870-891.
13. Berthod, M., Mignani, G. and Lemaire, M., 2004. New perfluoroalkylated BINAP usable as a ligand in homogeneous and supercritical carbon dioxide asymmetric hydrogenation. *Tetrahedron: Asymmetry*, *15*(7), pp.1121-1126.
14. Fey, N. and Lynam, J.M., 2022. Computational mechanistic study in organometallic catalysis: Why prediction is still a challenge. *Wiley Interdisciplinary Reviews: Computational Molecular Science*, *12*(4), p.e1590.
15. Fabre, I., 2017. *Experimental and theoretical mechanistic studies of transition-metal free and copper-catalyzed reactions* (Doctoral dissertation, Université Paris sciences et lettres).