Enantioselective Hydroselenation of Unsaturated Hydrocarbons

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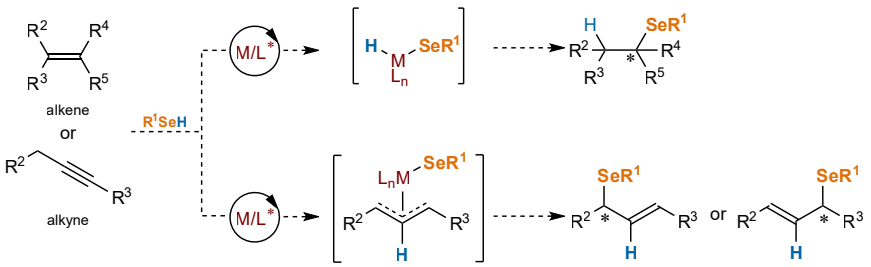
Abstract

Selenium plays a vital role as a micronutrient in various biological processes and also exhibits unique catalytic properties in synthetic chemistry. While there has been remarkable progress in achieving asymmetric hydroselenation of activated alkenes (e.g., Michael acceptors, etc.), the catalytic asymmetric hydroselenation of unactivated alkenes and alkynes remains a significant and persistent challenge (Scheme 1). A successful transformation requires a combination of highly active catalysts, precisely tuned and optimized ligands, appropriate substrates, and other conditions. With the assistance of *Science of Synthesis*, we were able to quickly obtain extensive background information and high-quality relevant literature related to this topic, thereby facilitating the efficient design of our reactions and optimization of the reaction conditions.



Scheme 1 Enantioselective Hydroselenation of Unsaturated Hydrocarbons

Discussion

Selenium is a micronutrient in the metabolic cycle of natural organisms. It has been incorporated into the design of bioactive molecules and materials. Moreover, in synthetic chemistry, selenium can provide a unique active site in chiral catalysts and ligands. Our research group is generally focused on the development of transition-metal-catalyzed methods for the asymmetric hydrochalcogenation of unsaturated hydrocarbons. In particular, our recent work has focused on the asymmetric hydroselenation of unsaturated compounds; we are interested in the stereoselective construction of new C–Se bond by novel catalytic strategies.

In the initial stage of our research, we systematically sought potential substrates, with a primary focus on alkenes and alkynes as key candidates. A comprehensive literature review and database analysis led to cyclopropenes and (2-hydroxynaphthalen-1-yl)alkynes being identified as particularly promising substrates, owing to their demonstrated reactivity profiles and synthetic versatility (Figure 1). Leveraging the powerful search capabilities of *Science of Synthesis*, we efficiently uncovered multiple established synthetic methodologies to prepare these compounds, supported by references to high-impact publications. Notably, cyclopropenes were found to be well-documented in Section 47.2[1] [approaches based on dehalogenation of cyclopropanes (Section 47.2.1.4.2) were particularly useful], while some interesting methods to prepare alkynes (from other alkynes) were extensively covered in Section 43.8.3.[2]
The information discovered in *Science of Synthesis* provided robust theoretical foundations and practical protocols for further investigation. This strategic substrate selection, informed by authoritative synthetic references, laid the groundwork for our subsequent experimental studies.

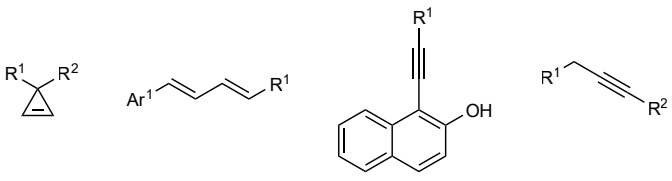


Figure 1 Unsaturated Hydrocarbon Substrates

In organic synthesis, the development of an appropriate catalytic system is paramount for achieving precise control over enantioselectivity, chemoselectivity, and regioselectivity.

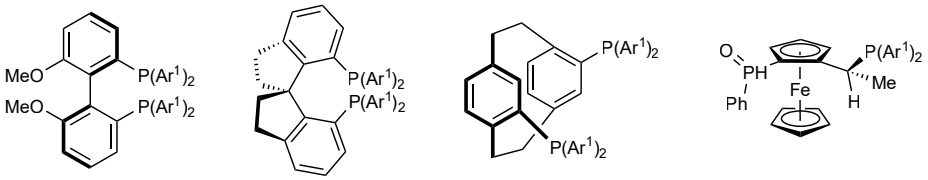


Figure 2 Various Chiral Ligand Motifs Investigated

The most critical determinant of success lies in the rational design and identification of an optimal chiral catalyst, as its structural and electronic properties directly dictate the reaction outcome. However, commercially available ligands and catalysts frequently fall short of meeting the stringent demands of asymmetric synthesis, particularly in terms of stereocontrol and substrate versatility.

To address these limitations, we leveraged the comprehensive resources of *Science of Synthesis*, which provided access to a vast repository of synthetic methodologies and high-quality literature. This enabled the systematic design of phosphine ligands with tailored steric and electronic properties (Section 31.42[3] and 42.5[4]), with well-documented synthetic protocols identified for each class of ligands investigated (Figure 2). By integrating computational modeling with experimental validation, we significantly mitigated the challenges traditionally associated with catalyst optimization, ultimately streamlining the development of new and efficient catalytic systems.

Conclusion

Science of Synthesis stands as an indispensable digital platform that has been meticulously crafted to enhance research efficiency for organic chemists. In an era where the internet floods researchers with an overwhelming volume of data, which can often be fragmented and inconsistently verified, this specialized resource acts as a curated knowledge hub. It not only synthesizes complex information into logically organized, easy-to-navigate overviews, but also rigorously maintains the highest standards of accuracy in experimental protocols. By bridging the gap between theoretical concepts and practical applications, *Science of Synthesis* empowers chemists to confidently explore synthetic methodologies, saving valuable time and minimizing trial-and-error in laboratory workflows.

References

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