Organic synthesis, Pharmaceutical chemistry

Short-step synthesis of cyclopentadiene derivatives catalyzed by niobium complexes

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Abstract

We have developed a new niobium complex-catalyzed reaction, providing a short-step synthesis of cyclopentadiene, an important organic compound widely used in synthetic organic chemistry and coordination chemistry. This method utilizes an alkyne and a cyclopropene as the starting materials for the coupling reaction. By combining computational chemistry approaches together with the isolation of key reaction intermediates, we clarified the details of this newly developed catalytic process. Our study revealed that the reaction involves the formation of a five-membered metallacyclic complex (see figure), which results from incorporating an alkyne and a cyclopropene to the niobium center.

Background & Results

Development of new reactions that enable the synthesis of complex organic molecules from simple starting materials in short steps is an important research target in organic chemistry. Such approaches help reduce worse environmental impact by minimizing reaction waste and energy consumption associated with long reaction sequences. Catalytic reactions that operate under mild reaction conditions with high atom efficiency represent promising technologies for advancing carbon recycling from the perspective of synthetic organic chemistry. Various methods for approaching cyclopentadiene derivatives have been reported to date; however, many reactions rely on complicated starting materials or generate unnecessary byproducts, highlighting the necessity for truly atom-economical processes. Our newly developed method not only provides cyclopentadiene derivatives efficiently but also allows their use as a ligand for metal complexes. This opens new avenue to prepare a wide range of cyclopentadienyl complexes that were previously inaccessible. Furthermore, some cyclopentadiene derivatives obtained exclusively through this method can serve as novel ligands, enabling the design of metal complexes with unprecedented functions and properties.

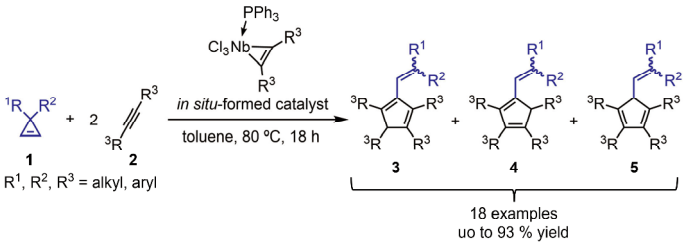
Significance of the research and Future perspective

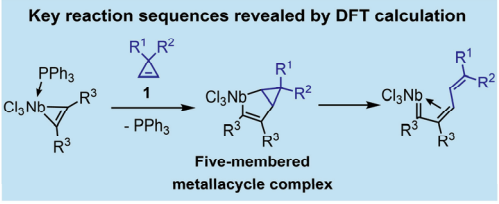
Cyclopentadiene, a five-carbon ring compound, is a valuable intermediate in synthetic organic chemistry. Its anion, the cyclopentadienyl anion, is a stable aromatic species that plays a crucial role as an anionic ligand in metal complexes. Despite its utility, conventional methods for synthesizing various cyclopentadiene derivatives often require multiple steps and frequently produce many byproducts including structural isomers. Therefore, development of a selective and short-step synthesis from simple starting materials is of great importance.

In this study, we discovered that using an alkyne and a cyclopropene as precursors, together with a low-valent niobium complex as a catalyst, enables the highly selective and atom-efficient formation of cyclopentadiene derivatives. Furthermore, we demonstrated that the resulting cyclopentadiene derivatives can be deprotonated to generate their cyclopentadienyl anions, which serve as ligands in metal complexes, as shown by the successful synthesis of ferrocene derivatives.

The key to the selectivity of this catalytic reaction lies in the formation of a five-membered metallacyclic intermediate, which occurs when the two different substrates coordinate to the niobium center. Computational studies revealed that the reaction pathway involves the insertion of cyclopropene into an alkyne-coordinated niobium secies. This step is energetically more favorable than pathways involving two alkynes or two cyclopropenes, explaining the observed high selectivity. Subsequent isomerization of this intermediate generates a β-unsaturated alkylidene species, which then incorporates another alkyne molecule to form the final cyclopentadiene product. This mechanism is consistent with experimental observations showing that when an alkyne-coordinated niobium complex is treated with cyclopropene and another alkyne, the resulting product is a cyclopentadiene derivatives derived from all three components.

Through a combination of experimental evidence and computational analysis, we elucidated the detailed mechanism of this catalytic process, clarifying the roles of each component and how the highly selective and active species is generated. This insight provides a foundation for designing new catalytic systems that enable efficient and selective transformations.





Patent

Treatise Akiyama, Takuya; Tsurugi, Hayato et al. Synthesis of multisubstituted cyclopentadiene derivatives from 3,3-disubstituted cyclopropenes and internal alkynes catalyzed by low-valent niobium complexes. Journal of the American Chemical Society. 2024, 146(49), 33338-33348. doi: 10.1021/jacs.4c06551

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Keyword homogeneous catalyst, synthetic organic chemistry, short step synthesis