

Stereospecific cyanodifunctionalization of alkenes

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Abstract

Stereospecific *syn*-oxycyanation of alkenes with *p*-toluenesulfonyl cyanide (TsCN) was achieved by utilizing a boron Lewis acid, tris(pentafluorophenyl)borane ($B(C_6F_5)_3$), as a catalyst. Furthermore, when cyanogen bromide was used as a reagent, stereospecific *syn*-bromocyanation takes place. These developed methods for the stereospecific difunctionalization of alkenes enable the efficient one-step synthesis of valuable nitriles from readily available alkenes.

Background & Results

This research significantly expands the synthetic applicability of the cyanodifunctionalization of alkenes, which was previously limited to reactions with more reactive alkynes and intramolecular reactions. Furthermore, the developed method can provide valuable synthetic intermediates, β -hydroxynitriles and β -bromonitriles, providing powerful tools for the synthesis of pharmaceuticals and functional materials.

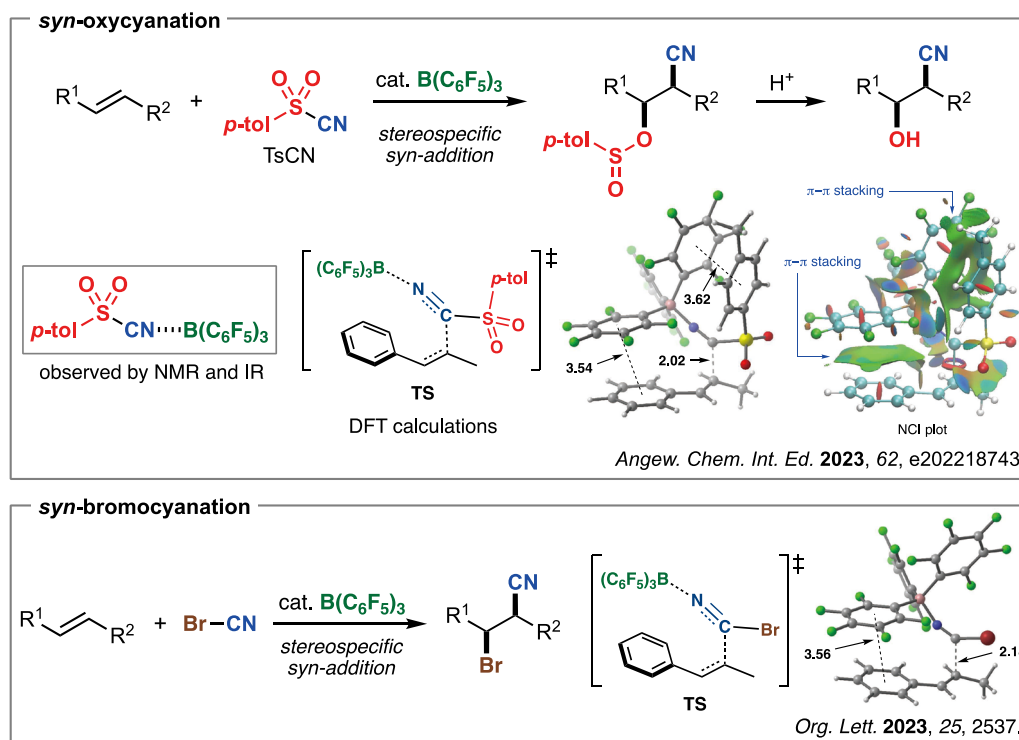
Significance of the research and Future perspective

The technique of introducing functional groups into organic compounds is an important method for synthesizing functional compounds such as pharmaceuticals and functional materials. A cyano group is a useful functional group that can be transformed

into various functional groups such as carboxyl and amino groups. Therefore, the development of the method for introducing a cyano group into organic compounds has been actively investigated. The cyanofunctionalization of carbon-carbon multiple bonds of readily available alkenes, which can be used in the one-step synthesis of functionalized compounds that would be valuable synthetic intermediates.

In this research, stereospecific *syn*-oxycyanation of alkenes with *p*-toluenesulfonyl cyanide (TsCN), providing β -hydroxynitriles, was achieved by utilizing a boron Lewis acid, tris(pentafluorophenyl) borane ($B(C_6F_5)_3$), as a catalyst. Although several methods for synthesizing β -hydroxynitriles from alkenes have been reported, they typically require multiple steps and/or harsh reaction conditions, making them less practical. The reaction developed in this study is a one-step process and surpasses conventional methods because it is applicable to a wide range of substrates with diverse functional groups. Furthermore, when cyanogen bromide was used as a reagent, stereospecific *syn*-bromocyanation takes place.

This study significantly expands the applicability of the cyanodifunctionalization of alkenes, which was previously limited to more reactive alkynes and intramolecular reactions. The developed methods allow an efficient one-step synthesis of valuable nitriles from readily available alkenes. Furthermore, the reaction mechanism of the stereospecific oxycyanation, in which $B(C_6F_5)_3$ effectively contributes to the stabilization of the transition state, was elucidated by spectroscopic analyses and DFT calculations.



Patent

Treatise

Kiyokawa, Kensuke; Ishizuka, Miu; Minakata, Satoshi. Stereospecific oxycyanation of alkenes with sulfonyl cyanide. *Angew. Chem. Int. Ed.* **2023**, *62*, e202218743. doi:10.1002/anie.202218743

Kiyokawa, Kensuke; Noguchi, Ikumi; Minakata, Satoshi et al. Tris(pentafluorophenyl)borane-catalyzed stereospecific bromocyanation of styrene derivatives with cyanogen bromide. *Org. Lett.* **2023**, *25*, 2537–2542. doi:10.1021/acs.orglett.3c00727

URL

<http://www.chem.eng.osaka-u.ac.jp/~minakata-lab/english/index.html>

Keyword

organic synthesis, catalytic reaction, functionalized compounds, nitriles