

論文 / 著書情報
Article / Book Information

題目(和文)	フォトレドックス触媒による炭素－炭素不飽和結合のトリフルオロメチル化反応に関する研究
Title(English)	Study on Trifluoromethylation of Carbon－Carbon Unsaturated Bonds by Photoredox Catalysis
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Category(English)	Doctoral Thesis
種別(和文)	論文要旨
Type(English)	Summary

論文要旨

THESIS SUMMARY

専攻： 化学環境学 専攻
Department of
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Student's Name

申請学位(専攻分野)： 博士 (工学)
Academic Degree Requested Doctor of
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Academic Advisor(main)
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要旨 (英文 800 語程度)
Thesis Summary (approx.800 English Words)

This thesis describes the results of the study on new trifluoromethylation reactions of carbon–carbon unsaturated bonds promoted by photoredox catalysis. Trifluoromethylated compounds continue to increase their importance in the fields of the pharmaceutical, agrochemical and functional material sciences. Therefore, development of new methods for efficient and selective incorporation of a CF₃ group into diverse molecular architectures has become an important research topic in the field of synthetic organic chemistry. In particular, trifluoromethylation of carbon–carbon unsaturated bonds such as alkene, alkyne and allene to give highly functionalized trifluoromethylated compounds is valuable and greatly desired. On the other hand, photoredox catalysts such as tris(bipyridyl)ruthenium(II) ([Ru(bpy)₃]²⁺) and relevant iridium(III) complexes can perform single-electron-transfer (SET) reactions under visible-light irradiation to generate radical species. Through Chapter 2 to 5 in this thesis, the author has established four types of novel trifluoromethylation reactions of unsaturated hydrocarbons by photoredox catalysis, which involve generation of a CF₃ radical from electrophilic trifluoromethylating reagents as the key steps.

α -Trifluoromethylated ketones are versatile building blocks for a wide variety of fluorinated compounds. In general, α -CF₃-ketones are synthesized from pre-activated carbonyl compounds such as enolates. In Chapter 2 in this thesis, the author has developed a direct synthetic method for α -CF₃-ketones from alkenes by combining photoredox catalyzed trifluoromethylation and DMSO oxidation. He has found that the reaction of aromatic alkenes with electrophilic trifluoromethylating reagent such as Togni's reagent and Umemoto's reagent in DMSO in the presence of *fac*-[Ir(ppy)₃] (ppy = 2-phenylpyridyl) photocatalyst under irradiation of blue LED lamps affords the corresponding α -CF₃-ketones. The present reaction can be applied to aromatic alkenes having various functional groups and be carried out on a gram scale. He investigates the reaction mechanism through electrochemical, photochemical and NMR analyses. As a result, it has become clear that the iridium photocatalyst, which turns into a strong reducing agent when irradiated, is crucial for the direct keto-trifluoromethylation and DMSO plays key roles as a nucleophile and an oxidant.

Trifluoromethylated alkenes, especially multi-substituted CF₃-alkenes, have attracted much attention as fascinating scaffolds for pharmaceuticals, agrochemicals and fluorescent molecules. Conventional approaches to CF₃-alkenes require multiple synthetic steps or prefunctionalized substrates. In Chapter 3, the author has established highly efficient C–H trifluoromethylation of di- and trisubstituted alkenes to give tri- and tetra-substituted CF₃-alkenes, respectively. The photoreaction of 1,1-disubstituted or trisubstituted alkenes with Umemoto's reagent in the presence of the [Ru(bpy)₃](PF₆)₂ catalyst affords the corresponding

CF₃-alkenes. It is notable that the present reaction proceeds in a stereoselective manner in the case of unsymmetrical alkenes. The precursor for anti-estrogen drug, panomifene, can be synthesized stereoselectively by this reaction. Additionally, when an excess amount of Umemoto's reagent is used for 1,1-disubstituted alkenes, bis(trifluoromethyl)alkenes are obtained.

Allylic alcohols and their derivatives are highly useful building blocks for organic synthesis. Thus, allylic alcohol derivatives bearing a trifluoromethyl group are promising key intermediates for fluorinated compounds. In Chapter 4, the author has expanded the photoredox-catalyzed trifluoromethylation to another unsaturated hydrocarbon, allene. He has found the reaction of 1,1-disubstituted allenes with Umemoto's reagent in CH₂Cl₂/AcOH in the presence of [Ru(bpy)₃](PF₆)₂ catalyst under irradiation of blue LEDs affords the corresponding allylic acetates having tetrasubstituted CF₃-alkene moiety in a highly regio- and stereoselective manner. It is noteworthy that the use of AcOH as the nucleophile is crucial for the high regioselectivity. The CF₃-allylic acetate can be easily transformed into the corresponding allylic alcohol and can be subjected to palladium-catalyzed substitution reaction.

As described in Chapter 3, multi-substituted CF₃-alkenes are useful structural motifs in drugs and materials. Difunctionalization of alkynes accompanying trifluoromethylation is regarded as a straightforward approach for the synthesis of multi-substituted CF₃-alkenes. In Chapter 5, the author has developed a novel stereoselective sulfonyloxy-trifluoromethylation of internal alkynes promoted by photoredox catalysis. He has found the reaction of internal alkynes with *S*-(trifluoromethyl)diphenylsulfonium triflate in CH₂Cl₂ in the presence of [Ir(ppy)₂(dtbbpy)](PF₆) (dtbbpy = 4,4'-di-*tert*-butyl-2,2'-bipyridyl) catalyst under visible light irradiation affords the corresponding trifluoromethylated alkenyl triflates in a highly stereoselective manner. The present reaction is tolerant to aromatic alkynes having a wide variety of functional groups. Although the CF₃-alkenyl triflates derived from alkynes with an electron-donating group on benzene ring are too unstable to be isolated, it is found that CF₃-alkenyl tosylates obtained in the presence of tosylate anion turn out to be isolable. The stereoselectivity of the present reaction is attributed to the electrostatic repulsion between the CF₃ group and the triflate anion in the nucleophilic addition step to the cation intermediate. It is notable that the present reaction can be combined with well-established palladium-catalyzed cross-coupling reactions and, thus, various tetrasubstituted CF₃-alkenes are obtained in a highly stereoselective manner in a facile one-pot process.

In conclusion, the author has developed four types of trifluoromethylation reactions of carbon-carbon unsaturated bonds promoted by photoredox catalysis leading to highly functionalized CF₃-compounds. The author expects that these findings will lead to exploration of valuable compounds containing CF₃ group and discovery of new useful reactions.

備考：論文要旨は、和文 2000 字と英文 300 語を 1 部ずつ提出するか、もしくは英文 800 語を 1 部提出してください。

Note: Thesis Summary should be submitted in either a copy of 2000 Japanese Characters and 300 Words (English) or 1 copy of 800 Words (English).

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