

コウ チュウエン

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学位論文題目 Development of Novel Synthetic Methods for Fluoroalkylthio Compounds  
(フルオロアルキルチオ化合物を合成するための新手法の開発)

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## 論文内容の要旨

Fluorine and sulfur have become crucial elements in the fields of agrichemicals, pharmaceuticals and material sciences. In the last two decades, fluoroalkylthio (R<sub>F</sub>S) units have gained special attention as a potential functional group to improve and/or alter the physical and biological properties of original compounds. This thesis describes our investigation in the preparation of fluoroalkylthio (R<sub>F</sub>S) units containing compounds. We has developed the first general method for trifluoromethylthiolation of pyrroles and aryl amines under mild reaction condition with a trifluoromethanesulfonyl hypervalent iodonium ylide. Later, we disclosed a diazo-triflone for effective trifluoromethylthiolation of varies of nucleophiles. These two reagents were found not only as reagent for trifluoromethylthiolation, but also as attractive building blocks for triflones. Finally, we have developed a new protocol for direct electrophilic difluoromethylthiolation of nucleophiles.

In chapter 1, a method of copper-catalyzed regioselective trifluoromethylthiolation of pyrroles and aryl amines by trifluoromethanesulfonyl hypervalent iodonium ylide under mild condition was described. A variety of pyrroles and aryl amines could be transformed to the corresponding products in moderate to excellent yields. The combination of CuF<sub>2</sub> and NMP is critical to obtain high yields.

In chapter 2, 2-diazo-1-phenyl-2-((trifluoromethyl)sulfonyl)ethan-1-one (diazo-triflone) was revealed as an effective electrophilic trifluoromethylthiolation reagent under copper catalysis. A broad set of enamines, indoles, β-keto esters, pyrroles, and anilines were nicely transformed into corresponding trifluoromethylthio (SCF<sub>3</sub>) compounds in good to high yields by diazo-triflone under copper-catalysis via an electrophilic-type reaction. A coupling-type of trifluoromethylthiolation reaction of aryl iodides was also realized by diazo-triflone under copper catalysis in acceptable yields.

In chapter 3, synthesis of biologically attractive triflones has been achieved using electrophilic trifluoromethylthiolation reagents as building blocks, and not as reagents. Trifluoromethanesulfonyl hypervalent iodonium ylide and its diazo-analogue were found to be useful triflone-containing building blocks, depending on reaction conditions. A variety of triflones including vinyl-triflone, amide-, ester- and enol-triflones, and oxazole-triflone were synthesized in one step. Moreover, pharmaceutically attractive multi-substituted β-lactam-triflones were synthesized for the first time by diazo-triflone with imines under catalyst-free heating conditions through a Staudinger [2+2] cycloaddition reaction.

In chapter 4, a novel HF<sub>2</sub>CSO<sub>2</sub>Na/Ph<sub>2</sub>PCl system was described for direct C-H difluoromethylthiolation. Phenols and naphthols could smoothly transformed to the corresponding SCF<sub>2</sub>H-compounds in good yields with our system under mild conditions. Other Csp<sup>2</sup> and Csp<sup>3</sup> nucleophiles such as indoles, pyrroles, pyrazoles, enamines, ketones and β-keto esters were also transformed to corresponding SCF<sub>2</sub>H-products in good yields. This system is effective for the late-stage direct C-H difluoromethylthiolation of a number of natural products and pharmaceutically attractive molecules without any pre-treatment of the substrates. The reaction mechanism was investigated with the assistance of <sup>19</sup>F NMR and GC(LC)-MS analysis.

In chapter 5, summary of the thesis was described.

## 論文審査結果の要旨

Fluorine and sulfur have become crucial elements in the fields of agrichemicals, pharmaceuticals and material sciences. In the last two decades, fluoroalkylthio (R<sub>F</sub>S) units have gained special attention as a potential functional group to improve and/or alter the physical and biological properties of original compounds. This thesis describes our investigation in the preparation of fluoroalkylthio (R<sub>F</sub>S) units containing compounds. We have developed the first general method for trifluoromethylthiolation of pyrroles and aryl amines under mild reaction condition with a trifluoromethanesulfonyl hypervalent iodonium ylide. Later, we disclosed a diazo-triflone for effective trifluoromethylthiolation of various nucleophiles. These two reagents were found not only as reagent for trifluoromethylthiolation, but also as attractive building blocks for triflones. Finally, we have developed a new protocol for direct electrophilic difluoromethylthiolation of nucleophiles.

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以上のように、本論文ではフルオロアルキルチオ化合物を合成するための新手法の開発に成功した。これらは、6編の有審査論文（うち、第1著者6編）としてまとめられている。よって、本論文は、学位論文として十分価値あるものと認められる。