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(含フッ素化合物の新規合成法の開発)

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論文内容の要旨

Organofluorine chemistry has been expanding rapidly to be a promising growth area, including material sciences, agrochemicals, and pharmaceuticals. The introduction of fluorine or fluorinated functional groups into organic molecules often causes significant changes in its physical, chemical, and biological properties of original compounds, which is suitable for biasing the properties of target molecules for their demand. Among a variety of fluorine-containing functional groups, I am interested in trifluoromethylthio (SCF_3), pentafluoro- λ^6 -sulfanyl (SF_5), trifluoromethoxy (OCF_3), and fluorocarbonyl (acyl fluorides, COF) groups, due to their unique properties and reactivities. Although during the last few decades, there are many methods for the preparation of fluorine-containing organic compounds that have been developed, the methods for the preparation of the compounds having SCF_3 , SF_5 , OCF_3 , and COF groups are still challenging. In this thesis, I have developed novel methodologies for the preparation of fluorinated compounds of SCF_3 , SF_5 , OCF_3 , and COF groups.

In chapter 1, the synthesis of cyclic α - SCF_3 -ketones and lactams via deacylative trifluoromethylthiolation of cyclic 1,3-diketones, lactams, and lactones has been achieved

using CF_3 -DAST as an electrophilic trifluoromethylthiolation reagent. A wide variety of SCF_3 -lactams was synthesized in one step. Moreover, we attempted to extend this method to the corresponding pentafluorophenylthiolation of 1,3-diketones and lactams using C_6F_5 -DAST. Interestingly, lactam substrates gave the desired deacylated pentafluorophenylthiolation products by C_6F_5 -DAST, while cyclic ketone substrates furnished an α -pentafluorophenylthiolated 1,3-diketones.

In chapter 2, a catalyst-free method on the formation of aryl-tetrafluoro- λ^6 -sulfanyl chloride (SF_4Cl) from diaryl disulfide compounds by using trichloroisocyanuric acid (TCCA) and potassium fluoride (KF) under the mild condition as described. The aryl- SF_4Cl is a precursor of aryl- SF_5 , but the method for the preparation of aryl- SF_4Cl is limited. Our new method has broad applicability for the synthesis of aryl- SF_4Cl , and results proceeded well with high yields in the absence of catalysts. We also provided two-step synthesis access to complex SF_5 -substituted (hetero)aromatics and aryl tetrafluoro- λ^6 -sulfanyl alkenes. The preparation of meta- and para- SF_4Cl -substituted pyridines in the presence of TCCA was achieved for the first time.

In chapter 3, we disclose an enantioselective benzylation reaction of α - OCF_3 -indanones afforded α -benzyl- α - OCF_3 -indanones with a tetrasubstituted stereogenic carbon center in excellent yield with moderate enantioselectivity under chiral phase-transfer catalysis. The enantioselective allylation reaction of α - OCF_3 -indanones was also achieved under the same conditions to give the allylation products in moderate yield with good enantioselectivity. Cinchona alkaloid-based chiral phase transfer catalysts were observed to be helpful for this reaction, and two enantiomers of α -benzyl- α - OCF_3 -indanones and α -allyl- α - OCF_3 -indanones were accessed by using cinchonidine and cinchonine-derived catalysts.

In chapter 4, we have developed a novel, mild, and efficient method that proceeds for the synthesis of acyl fluorides (R-COF) by Pd-catalyzed cross-coupling reaction of structurally different aryl, alkenyl or heteroaryl iodides using 2-(difluoromethoxy)-5-nitropyridine. This protocol can be a powerful alternative to the existing methodologies for the synthesis of R-COF , which is a crucial intermediate in the process of pharmaceutical synthesis. This system is suitable for the late-stage direct fluorocarbonylation of a variety of substrates containing several natural products and bioactive derivatives molecules. The reaction mechanism was investigated with the assistance of ^{19}F NMR and LC-MS analysis. We also showed that acyl fluorides were used as a useful intermediate in a wide range of subsequent transformations.

In chapter 5, the summary of the thesis is described.