

オウ ケントウ

氏 名 WANG JIANDONG
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学位論文題目 含フッ素化合物の設計および合成法の開発
(Design and Synthesis of Fluorinated Compounds)

論文審査委員 主査 教授 山下 啓司
教授 柴田 哲男
教授 林 秀敏
(名古屋市立大学)

論文内容の要旨

Recently, remarkable progress in the field of organofluorine chemistry have greatly expanded organic chemists' imagination for devising new potential bioactive molecules, prompting the discovery of new pharmaceuticals and agrochemicals. And this thesis describes our contribution to the development of facile protocols for directly introducing fluorine-containing building blocks such as CF_3 , CF_2H , pentafluorophenylthio ($\text{C}_6\text{F}_5\text{S}$), pentafluorobenzenesulfonyl ($\text{C}_6\text{F}_5\text{SO}_2$) into intriguing targets. However, the notorious inertness of C-F bonds enable the widespread fluorinated compounds to be extremely long-lived and potentially toxic. Recently, the C-F bond activation, in particular, selective functionalization of C-F bond in polyfluorinated substrate to afford partially fluorinated synthetic intermediates, has gained much attention. Accordingly, the effective activation of unactivated aliphatic fluorides induced by fluorophilic main-group Lewis acids such as $\text{B}(\text{C}_6\text{F}_5)_3$, AlCl_3 , AlEt_2Cl , and silicon-based trapping reagents TMSCF_2R , has been also investigated.

Chapter 1 reveals the synthesis of pentafluorobenzenesulfonyl hypervalent iodonium ylide, which acts as electrophilic reagents for pentafluorophenylthiolation of enamines. In addition, this ylide is also proved to be a useful building block for the preparation of C₆F₅SO₂ group-containing aromatic heterocyclic skeletons such as oxazoles and furan via formal [3+2] cycloaddition in the presence of a copper catalyst.

Chapter 2 describes the direct nucleophilic trifluoromethylation of carbonyl compounds by fluoroform via improving the reactivity of anionoid trifluoromethyl species in glymes. The nucleophilicity towards ketones and aldehydes of trifluoromethyl carbanion species generated from deprotonated fluoroform by inorganic base such as *t*BuOK and KHMDS, can be controlled by tuning corresponding Lewis acidity of potassium-based countercations by using polyethers.

Chapter 3 reveals the first clear solution for C-selective difluoromethylation of β-ketoesters by using the combination of TMSCF₂Br/LiOH/CH₃(CH₂)₁₅(CH₃)₃NBr. The dual effect of the lithium counter was crucial for generating difluorocarbene by promoting α-elimination of the CF₂Br⁻ anion, thereby establishing high C/O regioselectivity.

Chapter 4 discloses the direct asymmetric difluoromethylation of aliphatic MBH-type allyl fluorides via C-F bond cleavage by using silicon reagents TMSCF₂COOEt, TMSCF₂SPh and TMSCF₂PO(OEt)₂ as nucleophiles and fluorine scavengers.

Chapter 5 is an investigation on main-group Lewis acids induced C-F bond activation of unactivated *gem*-difluorides. Accordingly, in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP), by using catalytic amount of B(C₆F₅)₃ with strong fluoro-affinity and high Lewis acidity, the aliphatic *gem*-difluorides were subjected to the C-F bond cleavage followed by cascade intramolecular Friedel-Crafts cyclization to afford substituted 2,2',3,3'-tetrahydro-1,1'-spirobiindenes. However, in the absence of hydrogen bonding donor solvents, defluorination/elimination process was preferential to provide monofluorinated alkenes. In addition, AlCl₃ also enabled the C-F cleavage of *gem*-difluoroalkanes to prepare substituted spirobiindanes in good yields, although stoichiometric amount of aluminum reagent was needed. And AlEt₂Cl can give unexpected trisubstituted vinyl chlorides via C-F bond cleavage of the same *gem*-difluorides.

Chapter 6 summarizes the complete work, which is been described in the thesis.

論文審査結果の要旨

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以上のように、本論文では含フッ素化合物の設計および合成法の開発に成功した。これらは、3編の有審査論文（うち、第1著者3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