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Research Seminar

When: March 4, 2021 @ 2:30 PM
Location: Microsoft TEAMS

Development and Applications of Halogenating Agents

Abstract

Organic halides are one of the most extensively utilized compounds for synthetic intermediates and useful final products in many areas such as pharmaceuticals, agrochemicals, fine chemicals, materials, polymers, and many others.[1] To meet these demands, many halogenating agents have been developed. However, these reagents still suffer from lower efficiency or selectivity, difficult handling, stability issues, or limited substrate scope. In this context we have developed several halogenating agents which have proved to be superior to the conventional halogenating agents.[2-6]

Intrigued by the idea of exploring the applications of HCl.DMPU other than chlorination, we have developed HCl.DMPU-assisted one-pot conversion of aldehydes to nitriles. This method exhibits broad substrate scope with high yields.[7] The first part of my talk will include details of this new finding.

Another crucial member of organo-halogen family is organic fluorides. Among them, trifluoromethylated compounds have recently received significant attention due to their unique properties particularly in pharmaceutical and agrochemical areas. Studies to develop effective methods to introduce a trifluoromethyl (CF3) group to an organic molecule have been actively pursued by many research groups worldwide. Electrophilic trifluoromethylating agents have lagged behind nucleophilic and radical CF3 reagents in the development because of the strong electron-withdrawing effect of CF3 group. Although Umemoto's reagents are well known,[8] electrophilic trifluoromethylating agents still possess significant drawbacks such as low-atom economy and insufficient reactivity. To address this long-standing challenge associated with the electrophilic trifluoromethylating agents, we have designed novel dithiadications-containing electrophilic trifluoromethylating agents. We expect that the novel reagents could be powerful and endowed with two transferable trifluoromethyl groups, in contrast to the existing trifluoromethylating agents which transfer only a single trifluoromethyl group, making the process of trifluoromethylation much more efficient than existing methods. The second part of my talk will discuss attempts made by us for the dithiadication-type electrophilic trifluoromethylating agents.

Among electrophilic trifluoromethylations, trifluoromethylation of secondary hydroxylamines is one of recent topics, because there have been no other methods than Togni's reagent.[9] However, Togni's reagent has a significant drawback that it is potentially explosive. Therefore, it cannot be used for large scale reactions. We are in the process of developing an efficient method for the trifluoromethylation of secondary hydroxylamines using thermal stable 2,8-difluoro- and 2,3,7,8-tetrafluoro-S-(trifluoromethyl) dibenzothiophenium triflates (Umemoto's reagents II and III),8 which can be produced by one-step method at large scale. This part will be covered at the end of my talk.

References:

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(6) Ebule, R.; Mudshinge, S.; Nantz, M. H.; Mashuta, M. S.; Hammond, G. B.; Xu, B. A 5 + 1 Protic Acid Assisted Aza-Pummerer Approach for Synthesis of 4-Chloropiperidines from Homoallylic Amines. The Journal of Organic Chemistry 2019, 84 (6), 3249.
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