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Research Seminar

When: October 21, 2022
Time: 4:00 p.m.
Location: CBLL-16

Development of A Novel Fluorinating Agent and Its Applications

Abstract:

Fluorinated organic compounds are arising attraction in pharmaceutical[1], agrochemical[2], and functional material[3] fields. Fluorine atom possesses unique properties such as the highest electronegativity, the smallest size after a hydrogen atom, weak polarizability, and strong C–F bond strength. Therefore, introducing a fluorine atom into a selected position of an organic compound can produce dramatic effects on its physical, chemical, and biological properties. For example, medications which contain fluorine can be expected to display higher selectivity and efficacy. Fluorination of carbanions is pivotal for the synthesis of a slew of fluorinated compounds. Despite the existence of a vast number of electrophilic fluorinating agents[4], the fluorination of highly basic carbanions such as organo lithiums is still problematic, mainly because of the many undesired reactive sites present in the reagents themselves. Thus, we developed a novel fluorinating agent, *N*-fluoro-*N*-(*tert*-butyl)-*tert*-butanesulfonamide (NFBB)[5], consisting of the smallest fluorination core, -SO_2NF-, sandwiched between two bulky inert *tert*-butyl groups. NFBB can fluorinate highly basic (hetero)aryl and alkenyl lithium species in unprecedented high yields. With NFBB, we also discovered a conceptually new self-sustaining fluorination methodology toward active methylene compounds. Instead of requiring equimolar amounts of strong bases or environmentally unfriendly metals, our self-sustaining fluorination-deprotonation reaction cycle needed only a catalytic amount of weak base, Cs_2CO_3. NFBB was prepared in excellent yield using *N*-fluorobenzenesulfonimide (NFSI) under conditions that are well suited for laboratory preparation. It was also prepared in good conversion yield using F_2/N_2—an industry preferred fluorine source. NFBB is stable, easy-to-handle, and purified by simple distillation (bp 61.5~62 ^oC/9.5~10.1 mmHg). Its easy preparation and purification make NFBB a chemical suitable for large scale production in a factory. This presentation will showcase the development of NFBB and its application to the efficient preparation of many useful fluorinated compounds.

References:

1. Inoue, M.; Sumii, Y.; Shibata, N. *ACS Omega*. **2020**, *5*, 10633-10640.
2. Fujiwara, T.; O'Hagan, D. *J. Fluorine Chem.* **2014**, *167*, 16-29.
3. Harsanyi, A.; Sandford, G. *Green Chem.* **2015**, *17*, 2081-2086.
4. Umemoto, T.; Yang, Y.; Hammond, G. B. *Beilstein J. Org. Chem*. **2021**, *17*, 1752-1813.
5. Yang, Y.; Hammond, G. B.; Umemoto, T. *Angew. Chem. Int. Ed*. **2022**, e202211688.