

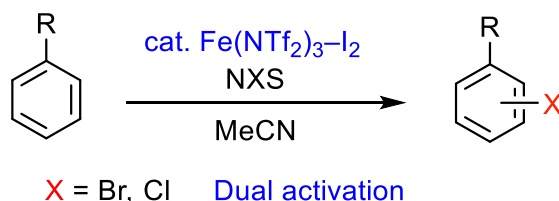
Highly regioselective halogenation of aromatics using NXS by dual activation with $\text{Fe}(\text{NTf}_2)_3$ and I_2

(Nippon Dental University) ○ Kiyoshi Tanemura

Keywords: Halogenation, Aromatic compounds, NXS, Regioselectivity, Solvent-free reactions

Halogenation of aromatic compounds is one of the most important reactions in synthetic organic chemistry. Aromatic halides are important synthetic intermediates which were used in metal-catalyzed cross-coupling reactions such as Suzuki-Miyaura cross-coupling, substitution reactions, and Grignard reactions. NBS, NCS, and NIS are particularly excellent halogenating reagents due to their ease of handling, low cost, and stable properties. We have been investigating the halogenation of aromatic compounds using NXS.¹⁾

In this report, the author reports the halogenation of various aromatic compounds catalyzed by $\text{Fe}(\text{NTf}_2)_3$ in the presence of a catalytic amount of I_2 using NBS or NCS in MeCN. Dual activation with $\text{Fe}(\text{NTf}_2)_3$ and I_2 was quite useful to accelerate the reactions. High para selectivity was realized for the substrates possessing electron-donating groups. The method was effective for the halogenation of acid-sensitive substrates such as acetals, aldehydes, epoxides and electron-deficient substrates such as halobenzenes and methyl benzoate. Solvent-free reactions were useful in the halogenation of electron-deficient compounds such as halobenzenes and methyl benzoate. BiCl_3 was especially useful for the halogenation of phenol and aniline derivatives to afford the corresponding halides in moderate to excellent yields. The procedure was effectively applied to the late-stage halogenation of drugs and natural products. One-pot bromination / Suzuki-Miyaura cross-coupling reactions gave the corresponding products in good yields without the removal of the solvent. When BiCl_3 was used as the catalyst, one-pot bromination / Sonogashira coupling reactions gave the corresponding alkynes without the removal of the solvent. The method is practical because the catalysts are cheap and the reactions can be conducted under air conditions.



- 1) a) K. Tanemura, T. Suzuki, Y. Nishida, K., Satsumabayashi, T. Horaguchi, *Chem. Lett.* **2003**, 32, 932-933. b) K. Tanemura, *Org. Biomol. Chem.* **2024**, 22, 5105-5111.