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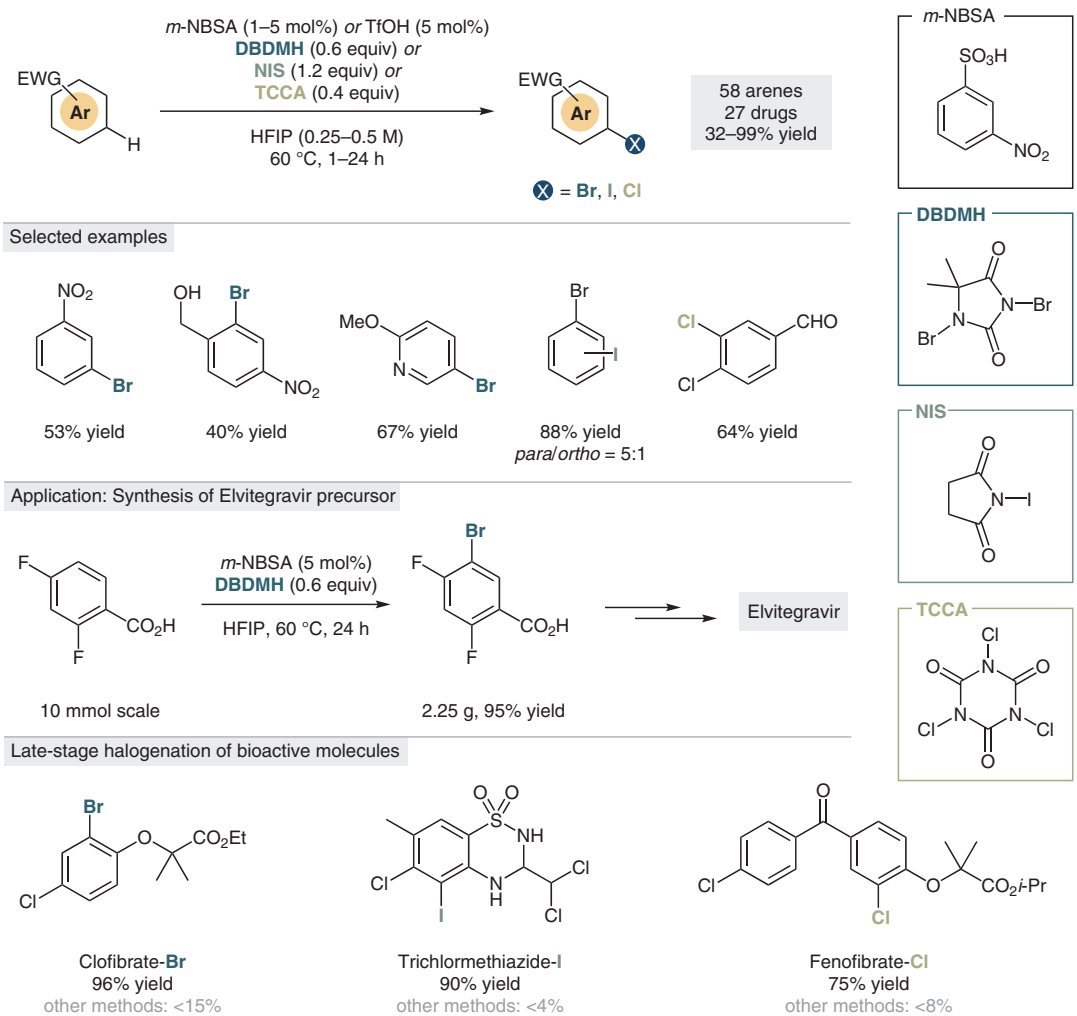
Catalytic Electrophilic Halogenation of Arenes with Electron-Withdrawing Substituents
J. Am. Chem. Soc. **2022**, 13415–13425, DOI: 10.1021/jacs.2c06440.

Brønsted Acid Catalysis Permits Electrophilic Halogenation of Electron-Deficient Arenes



Significance: Song, Jiao, and co-workers report a Brønsted acid-catalyzed electrophilic halogenation of electron-deficient arenes by using readily available halogenation reagents and 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) as a hydrogen-bond activator. Numerous sensitive electron-withdrawing substituents are tolerated under the reaction conditions, yielding various aryl halides in moderate to excellent yields.

Comment: Experimental investigations provide support for an electrophilic mechanism in which both 2-methyl-5-nitrobenzenesulfonic acid (*m*-NBSA) and HFIP synergistically activate the halogenating reagent. The authors have developed an effective halogenation system for a broad scope of challenging electron-deficient arenes with excellent functional-group tolerance. The potential of the method is demonstrated by late-stage halogenation of bioactive molecules and by a successful application in drug synthesis.

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Synfacts 2022, 18(10), 1131 Published online: 20.09.2022
DOI: 10.1055/s-0041-1738616; **Reg-No.:** B08222SF

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Category
Organo- and Biocatalysis

Key words
electrophilic halogenation
electron-deficient arenes
Brønsted acid catalysis
hexafluoroisopropanol

Synfact of the Month

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