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Catalytic Electrophilic Halogenation of Arenes with Electron-Withdrawing Substituents

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Brønsted Acid Catalysis Permits Electrophilic Halogenation of Electron-Deficient Arenes

Category

Organo- and Biocatalysis

Key words

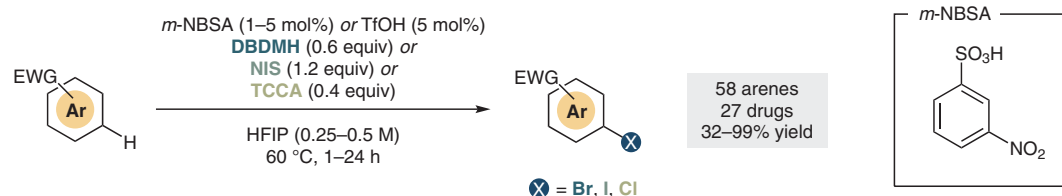
electrophilic halogenation

electron-deficient arenes

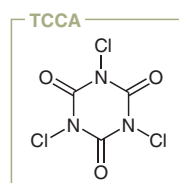
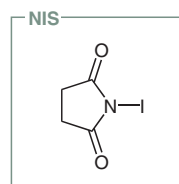
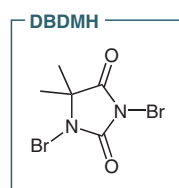
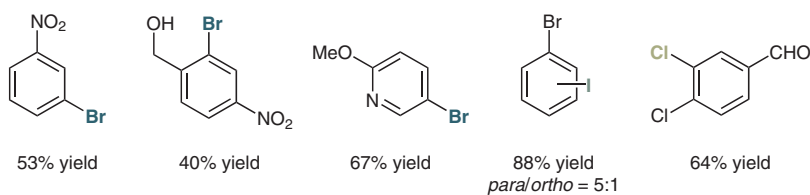
Brønsted acid catalysis

hexafluoroisopropanol

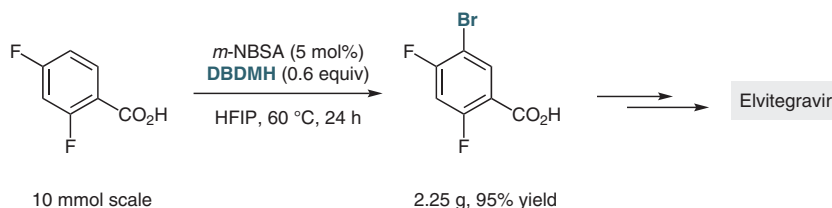
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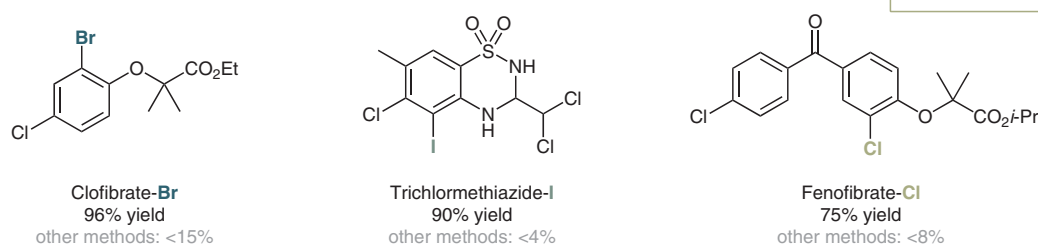
Selected examples



Application: Synthesis of Elvitegravir precursor



Late-stage halogenation of bioactive molecules



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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