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Acid Scavengers for Selective and Efficient Cleavage of Aryl Alkyl Ethers by Lewis Acids

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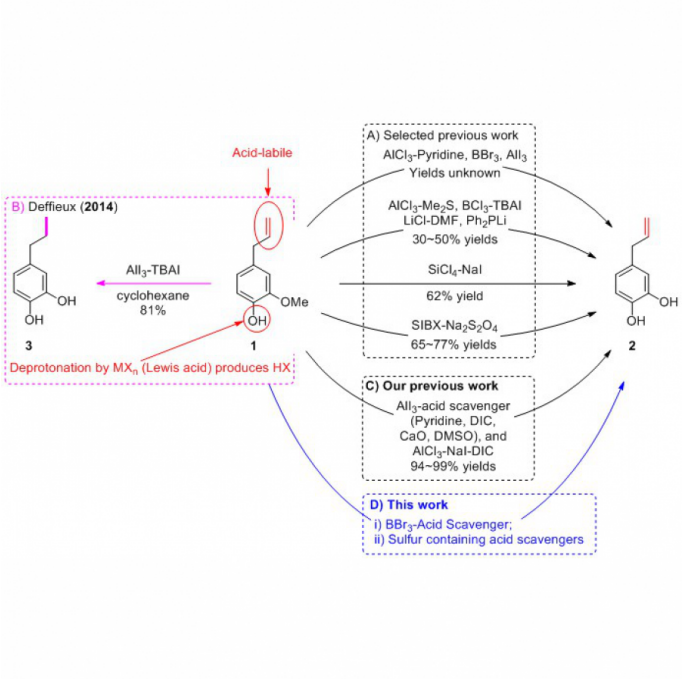
PURPOSE OF THE ABSTRACT

Cleavage of ethers is an important functional group transformation in organic and pharmaceutical industries.[1] Commonly used reagents such as HX, AlX3 and BX3 (X=Cl, Br and I) are sometimes inefficient or ineffective[2] for this reaction when the substrate contains acid-labile functional groups. For example, the reported cleavages of eugenol by AlCl3-pyridine, AlCl3-Me2S, BBr3, AlI3, Ph2PLi, BCl3-nBu4NI and SnCl4-NaI afforded hydroxychavicol in merely poor to moderate yields (Figure 1A). The demethylation by AlI3-nBu4NI was demonstrated to be ineffective that afforded 4-propylcatechol as the sole product in very good yield[2] due to the co-existence of an allyl group and a phenolic hydroxyl group (Figure 1B). Hence, an efficient and selective ether cleavage protocol is of significance to facilitate such transformations.

To this end, we have recently developed a method for the cleavage of aryl alkyl ethers with aluminum triiodide-Lewis base binary reagent system using the demethylation of eugenol as a model reaction (Figure 1C).[3] The Lewis base is used as an acid scavenger as well as a ligand to tune the reactivity of the Lewis acid.

Our new progress is reported (Figure 1D) featuring the application of several sulfur-containing reagents as acid scavengers (Figure 2). The yields are good for a foray of substrates, and the chemoselectivity is high for the discrimination of ether and ester C-O bonds. The reaction mechanism of the method is investigated, along with the exploration of scope and limitations.

FIGURES



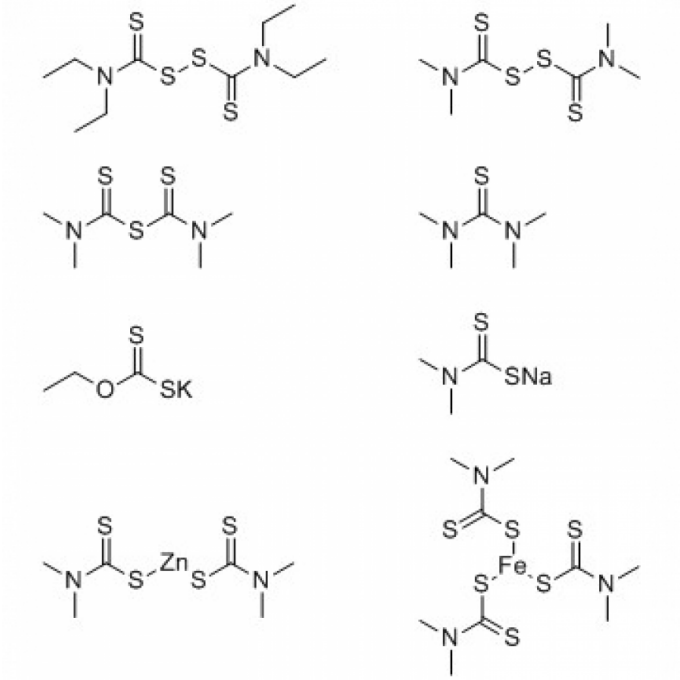


FIGURE 1

Lewis acid-mediated ether cleavage

Selected methods for the demethylation of eugenol, a naturally occuring catechol monomethyl ether

FIGURE 2

Investigated sulfur-containing acid scavengers

For the improvement of cleaving aryl alkyl ethers

KEYWORDS

o-Hydroxyphenyl alkyl ether | Demethylation | Aluminum triiodide | Acid scavenger

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