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Ammonium iodide-promoted unprecedented arylsulfonylation of quinone with sodium arylsulfinates

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ABSTRACT

A novel ammonium iodide-promoted arylsulfonylation of quinones with sodium arylsulfinates has been explored. This reaction proceeded smoothly through unique nucleophilic addition reaction and produced the arylsulfonylation products in moderate to good yields. The reactions proceeded efficiently over a broad range of substrates with good regioselectivity and functional group tolerance.

1. Introduction

Aryl sulfone skeleton is recognized as a crucial class of scaffold in organic synthesis, medicinal chemistry, and natural products.[1] The development of facile methods for synthesis of aryl sulfones has attracted extensive attention.[2] The traditional routes to access sulfones are oxidation of sulfides and electrophilic sulfonylation of arenes, in which poor functional group compatibility and necessary strong oxidants or strong acids limit its practical application.[3] In recent years, transition metal-catalyzed aromatic C–H bond sulfonylation provided a useful tool for the synthesis of aryl sulfone.[4] However, most of these methods were limited to provide *ortho*-C-H sulfonylation with the assistance of a directing group. Direct sulfonylation *via* C–H functionalization can provide a shortcut for aryl sulfones under metal or metal-free conditions.[5] However, direct sulfonylation of an aromatic C–H bond with less reactive sodium arenesulfinates is rare under metal-free conditions.[6]

As an important cyclic compound, quinone has been found in many natural products, pharmaceuticals and functional materials.[7] Quinonyl aryl sulfone derivatives can be found to be useful skeletons in pharmaceutical as an inhibitor of β-Ketoacyl-ACP-synthase III (FabH), which is a key condensing enzyme in bacterial fatty acid biosynthesis and a part of the dissociated fatty acid synthase (FAS).[8] 2-Tosylnaphthalene-1,4-diol (**A**), 2-tosylbenzene-1,4-diol (**B**) and 2-tosylnaphthalene-1,4-diol (**C**) were identified as potent FabH inhibitors (Fig. 1). Their biological evaluation showed that the sulfonyl group and naphthalene-1,4-diol were required for activity against all enzymes.[9] Quinonyl aryl sulfones are generally prepared by oxidation of the corresponding arylthioquinones.[10] In recent years, alternative approaches have been developed for the sulfonylation of quinones using aryl sulfonyl halides or aryl sulfonic acids as sulfonylation reagents through C–H functionalization. In 2016, Wang's group reported the copper and triphenylphosphine-promoted sulfenylation of quinones using arylsulfonyl chlorides as a sulfur source with moderate to good yields (Scheme 1a).[11] Ding and co-workers described a method to prepare arylsulfonylquinones and arylsulfonyl-1,4-diols by Pd-catalyzed direct C-sulfone formation by C–S coupling of quinones with sulfonyl chloride; and Huang et al. developed an efficient method to sylfonyl quinones and sulfonyl-1,4-diols through Ir-catalyzed C–S coupling of quinones with sulfonyl chloride (Scheme 1b).[12] In 2004, Yadav's group disclosed a method of ionic liquids-promoted addition of arylsulfinic acids to quinones to produce the corresponding arylsulfonylhydroquinones, and ionic liquid plays the dual role as the solvent and the catalyst in this reaction (Scheme 1c).[13] Moreover, Bruce et al. synthesized a variety of alkyl- or

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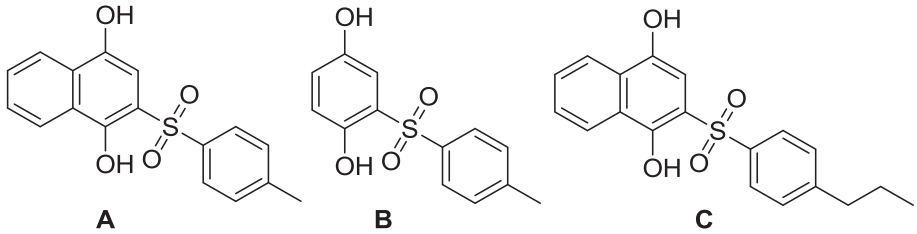
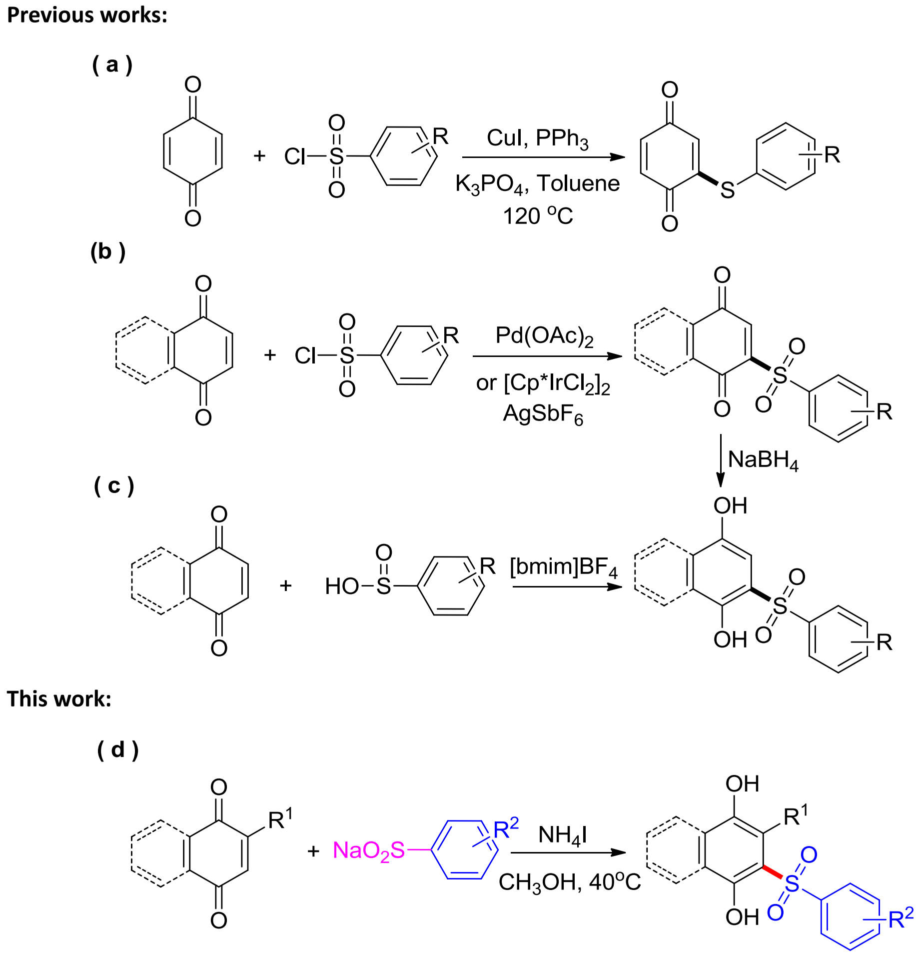


Fig. 1. Several FabH inhibitors.



Scheme 1. Synthesis of 2-arylsulfonyl benzene-1,4-diols and naphthalene-1,4-diols.

arylsulfonylhydroquinones by the nucleophilic addition of alkyl- or arylsulfinic acids to 1,4-quinones, and the reaction was conducted using a two phase dichloromethane-water system in the presence of trifluoroacetic acid.[14]

Despite these significant advances, almost all of these C–H sulfonylation methods often involved in transition-metal, acid, or base as a catalyst, and required foul-smelling, toxic, and unstable sulfur sources as starting materials, which had lower the synthetic efficiency and generality. As a consequence, it is still an attractive but challenging task to develop a metal-free, environmentally benign method for the rapid and straightforward construction of C–S bonds. Over the past few years, iodine-catalyzed systems have been proven to be powerful tools to form C–S bonds[15]; these systems have been employed in radical and ion reactions. In sharp contrast, iodide catalysts are less explored over the sulfonylation of quinones. Arylsulfinic acid sodium salts are relative stable and moisture-insensitive compared to sulfonyl chlorides. They have been widely used as arylsulfonylation reagents for preparing organosulfonyl compounds.[16] In our continued efforts on the development of new methods for the sulfonylation of quinones, herein, we report an effective route for the sulfonylation of quinones through ammonium iodide-promoted sulfonylation of quinones using sodium sulfinates as the sulfonation reagents (Scheme 1d).

2. Results and discussion

We initiated our investigation on the model reaction of *p*-benzoquinone (**1a**) with sodium benzenesulfinate (**2a**) to optimize the reaction parameters (Table 1). The C2-sulfonylation didn't take place in the absence of any catalysts in DMF at room temperature for 1.0 h (Table 1, entry 1). Inspired by iodide-induced sulfonylation reactions,[15] various additives (4.0 eq.) such as NH_4Cl, NH_4I,