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## Diaryl Sulfones Through Oxidative Coupling of Catechols and Arylsulfinic Acids

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*A simple and efficient method for the synthesis of diaryl sulfones using the coupling reaction of in-situ generated o-benzoquinones, promoted by potassium ferricyanide, and arylsulfinic acids has been developed. High product yields, a short reaction time, and mild reaction conditions are important features of this method.*

**Keywords** Catechols; diaryl sulfones; o-benzoquinones; oxidative coupling; potassium ferricyanide

## INTRODUCTION

Organosulfones are important intermediates in organic synthesis<sup>1</sup> because of their chemical properties<sup>2</sup> and biological activities.<sup>3</sup> Diaryl sulfones are important synthetic targets, and widely used synthons for synthetic organic chemists due to diaryl sulfones' many industrial applications.<sup>4</sup> These are useful in the practice of medicinal chemistry because the sulfone functional group is found in numerous drugs, including the recently developed selective COX-2 inhibitor Vioxx.<sup>5</sup> Diphenyl sulfone is used as an intermediate for the synthesis of 4,4'-diamino-diphenyl sulfone (DAPSONE), which is effective for leprosy treatment.<sup>6</sup> Recently, diaryl has been shown to inhibit HIV-1 reverse transcriptase and represents an emerging class of substances able to address toxicity and resistance problems of nucleoside inhibitors.<sup>7</sup>

Sulfones are generally prepared by the oxidation of corresponding sulfides and sulfoxides or by a displacement reaction of sodium arenesulfinate with an appropriate alkyl halide.<sup>8</sup> The electrophilic aromatic substitution of arenes with arenesulfonic acids in the presence of

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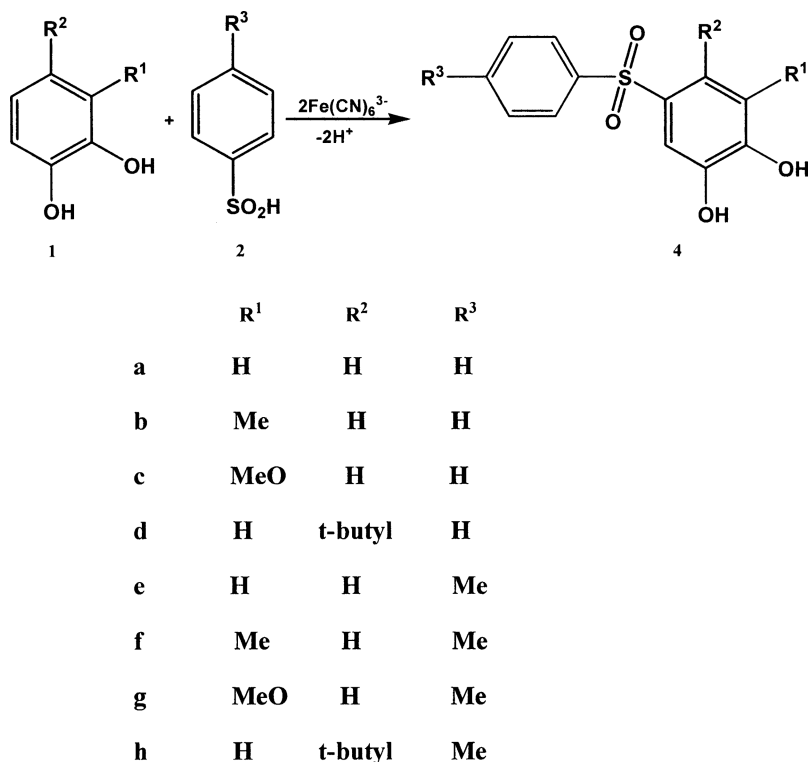
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strong acids<sup>9</sup> or with arenesulfonyl halides<sup>10</sup> and the reaction of organo-magnesium halides<sup>11</sup> or organolithium compounds<sup>12</sup> with sulfonate esters are known procedures for their preparation. Some metal halides,<sup>1a</sup> zeolites,<sup>13</sup> Bronsted acids,<sup>14</sup> bismuth triflate,<sup>15</sup> indium triflate,<sup>16</sup> and Fe (III)-exchanged montmorillonite clay<sup>17</sup> have been successfully used for the catalytic sulfonylation of arenes. Lithium perchlorate<sup>18</sup> and sodium perchlorate<sup>19</sup> have been used as efficient catalysts under neutral conditions. More recently, sulfones were prepared from sulfinic acid salts and aryl iodides using copper<sup>20</sup> and palladium catalysts.<sup>21</sup> Each of the previously discussed methods has its own merit, while some of these methods are plagued by limitations. Most methods require drastic conditions. The electrophilic approach required strong protic or Lewis acids and suffered from the formation of mixtures of isomeric products and inefficiency with arenes bearing strongly electron-withdrawing substituents. Consequently, there is an opportunity for further development toward mild conditions, increased variation of the substituents in the components, and better yields.

## RESULTS AND DISCUSSION

Previously, we have shown the oxidation of catechols to *o*-quinones in the presence of a variety of nucleophiles such as methanol,<sup>22</sup> 4-hydroxycoumarin,<sup>23</sup> 4-hydroxy-6-methyl-2-pyrone,<sup>24</sup>  $\beta$ -diketones,<sup>25</sup> and barbituric acids.<sup>26</sup> The formed *o*-quinones are quite reactive and can be attacked by nucleophiles and converted to the corresponding methoxyquinone,<sup>22</sup> coumestan,<sup>23,24</sup> benzofuran,<sup>25</sup> and pyrimidine<sup>26</sup> derivatives, respectively. The importance of sulfones has prompted us and other workers to synthesize a number of these compounds by chemical and electrochemical routes.<sup>27</sup> In order to improve synthetic procedures of these compounds, in the present work, we have performed the oxidation of catechols (**1**) in the presence of arylsulfinic acids (**2**) as possible nucleophiles in aqueous sodium acetate solution using potassium ferricyanide as oxidizing agent (Scheme 1).

A suitable oxidizing agent is a compound that can only oxidize catechols (**1**) to related *o*-benzoquinones without any effect on arylsulfinic acids (**2**). Potassium ferricyanide is a stable, easily handled and commercially available oxidizing agent. Recently, we have shown the suitability of potassium ferricyanide with an oxidation potential of 0.24 V vs. SCE for the oxidation of catechols.<sup>23c</sup> Several aqueous media with different pH were investigated during the course of this study. The best results were achieved using an acetate buffer (pH = 4.5) as a solvent. When catechols (**1**) (1 mmol) were treated with potassium ferricyanide



SCHEME 1

(2 mmol) (as dropwise) in the presence of **2** (1 mmol) in an aqueous solution containing 0.2 M sodium acetate, arylsulfonylbenzenediols (**4**) were obtained in good yields (Scheme 1). In more basic solutions, the formation of anionic forms of catechols, formed by an acid dissociation reaction, was enhanced, and the coupling of anionic forms with *o*-quinones interfered in the Michael reaction of arylsulfinic acids (**2**) with *o*-quinones. In other words, in an aqueous solution containing 0.2 M sodium acetate, any hydroxylation<sup>28</sup> or dimerization<sup>29</sup> reactions are too slow to interfere in the synthesis of **4a–h**.

Meanwhile, the oxidation of compounds **4a–h** is more difficult than the oxidation of the parent-starting molecules (**1**) by virtue of the presence of the electron-withdrawing phenylsulfonyl group on the catechol ring, and the obtained products are stable in air and can be stored for several months. As shown in Table I, the treatment of a series of catechols and arylsulfinic acids in the presence of potassium ferricyanide

**TABLE I Preparation of Diaryl Sulfones Through an Oxidative Coupling Reaction**

Entry	Catechol	Sulfinic acid ( $R^3$ )	Diaryl sulfone	Time (min)	Yield (%) <sup>a</sup>
1	1a	H	4a	15	95
2	1b	H	4b	15	90
3	1c	H	4c	20	85
4	1d	H	4d	30	80
5	1e	Me	4e	10	97
6	1f	Me	4f	10	93
7	1g	Me	4g	15	88
8	1h	Me	4h	20	85

<sup>a</sup>Isolated yields.

afforded the corresponding sulfonyl compounds (**4a–h**) in good to excellent yields.

In summary, we have introduced a facile and convenient method for the synthesis of arylsulfones using ferricyanide, an inexpensive and commercially available oxidizing agent, and water as an environmentally friendly solvent. Moreover, the ease of the procedure may find application in organic synthesis.

## EXPERIMENTAL

### General

Chemicals were purchased from Merck and Fluka. Yields refer to isolated products. All of the products were characterized by a comparison of their spectra and physical data with those obtained by the literature method.<sup>27b,c,d</sup>

### General Procedure for the Preparation of Diaryl Sulfones (**4a–h**)

To a vigorously stirred solution of acetate buffer 0.2 M, (pH = 4.5), arylsulfinic acids (**2**) (1 mmol) and potassium ferricyanide (2 mmol) were added. In a dropping funnel, a solution of catechols (**1**) (1 mmol), in relevant solution, was added dropwise to the stirred previous solution over a period of 10–30 min. The solution became dark, and some precipitates were formed. At the end of the reaction, the mixture was placed in the refrigerator overnight. The reaction mixture was filtered, and solid

materials were collected by filtration, washed copiously with water, and recrystallized from an appropriate solvent.

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