

# Cu-Catalyzed Reaction of 1,2-Dihalobenzenes with 1,3-Cyclohexanediones for the Synthesis of 3,4-Dihydrodibenzo[*b,d*]furan-1(2*H*)-ones

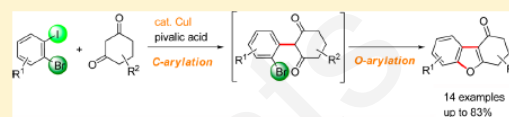
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**S** Supporting Information

**ABSTRACT:** The Cu(I)-catalyzed reaction of 1-bromo-2-iodobenzenes and other 1,2-dihalobenzenes with 1,3-cyclohexanediones in DMF at 130 °C using Cs<sub>2</sub>CO<sub>3</sub> as a base and pivalic acid as an additive selectively delivers 3,4-dihydrodibenzo[*b,d*]furan-1(2*H*)-ones with yields ranging from 47 to 83%. The highly regioselective domino process is based on an intermolecular Ullmann-type C-arylation followed by an intramolecular Ullmann-type O-arylation. Substituted products are accessible by employing substituted 1-bromo-2-iodobenzenes and substituted 1,3-cyclohexanediones as substrates. Reaction with an acyclic 1,3-diketone yields the corresponding benzo[*b*]furan.



## INTRODUCTION

Numerous molecules with a benzo[*b*]furan or a dibenzo[*b,d*]furan skeleton<sup>1</sup> have been isolated from natural sources. Typical examples include the karnatakafurans A and B from *Aspergillus karnatakaensis* Frisvad,<sup>2a</sup> achyrofuran from *Achyrocline satureioides*,<sup>2b</sup> the porric acids A–C from *Allium porrum* L,<sup>2c</sup> popolohuanone E from a Pohnpei sponge *Dysidea* sp.,<sup>2d</sup> eriobofuran from *Eriobotrya japonica* L,<sup>2e</sup> and the  $\alpha$ -,  $\beta$ -, and  $\gamma$ -pyrrofurans from *Pyrus communis* L.<sup>2f,g</sup> (Figure 1). Compounds that contain a dibenzo[*b,d*]furan structure element exhibit a wide range of biological activities including antimalarial,<sup>2a</sup> antimicrobial,<sup>2a</sup> antifungal,<sup>2c,e</sup> cytotoxic,<sup>2d</sup> antitubercular,<sup>3a,b</sup> and antimycobacterial properties.<sup>3c,d</sup>

There has been continuing interest in the development of novel synthetic methods for the efficient preparation of dibenzo[*b,d*]furans. Over the years, various routes have been reported for the synthesis of this skeleton. They include the ring closure of 2-phenoxybenzene diazonium salts which was first reported by Graebe and Ullmann,<sup>4</sup> intermolecular Diels–Alder reactions between 2- or 3-nitrobenzofurans and electron-rich dienes,<sup>5</sup> the reaction of benzofuran-3-ones with 2*H*-pyran-2-ones,<sup>6</sup> and the reaction of *o*-silyl aryltriflates with iodonium ylides.<sup>7</sup> More recently, the focus was on the development of methods based on transition-metal-catalyzed transformations. Among them are the Pd-catalyzed cyclization of 1-halo-2-phenoxybenzenes,<sup>8</sup> the Pd-catalyzed oxidative cyclization of diphenyl ethers,<sup>9</sup> the Pd- or Cu-catalyzed intramolecular O-arylation of 2-halobiphenyl-2'-ols,<sup>10</sup> the Pd- or Cu-catalyzed oxidative cyclization of 2-arylphenols,<sup>11</sup> the Pd-catalyzed intramolecular cyclization of 1-carboxyl-2-phenoxybenzenes,<sup>12</sup> and the Au-catalyzed reaction between *O*-arylhydroxylamines and 1,3-dicarbonyls.<sup>13</sup> Despite these advances, there is still a

need for new methods that avoid the use of complex substrates, expensive reagents, additives, and catalysts and allow for the straightforward synthesis of dibenzo[*b,d*]furans from readily available starting materials. Recently, we reported on Cu-catalyzed domino reactions for the synthesis of a number of carbocycles and heterocycles,<sup>14</sup> such as the reaction between 2-halobenzyl halides and amidines for the preparation of quinazolines<sup>14a</sup> and the reaction between 2-halobenzyl halides and  $\beta$ -ketoesters for the synthesis of naphthalenes and 4*H*-chromenes.<sup>14c</sup> It was assumed that the synthesis of dibenzo[*b,d*]furans could be achieved by a domino intermolecular C-arylation/intramolecular O-arylation of a 1,2-dihalobenzene and a 1,3-cyclohexanedione (I + II  $\rightarrow$  III  $\rightarrow$  IV) (Scheme 1). Needless to say, if successful, this approach could be extended to the synthesis of numerous other *O*-heterocyclic systems. The Cu-catalyzed reaction between 1,2-dihalobenzenes and 1,3-diketones has not been reported so far. However, Ma et al. have achieved the Cu-catalyzed reaction between 1,2-dihalobenzenes and  $\beta$ -ketoesters for the preparation of benzo[*b*]furans.<sup>15</sup>

In recent years, there was great interest in the transition-metal-catalyzed arylation of 1,3-dicarbonyls with aryl halides.<sup>16</sup> The Pd-catalyzed C-arylation of 1,3-dicarbonyls dates back to the 1980s<sup>17</sup> and has been further developed over the years.<sup>18</sup> Meanwhile, it is considered as a highly useful synthetic method. The only disadvantage of the Pd-catalyzed transformation is the need for expensive Pd reagents and ligands. This is the reason why there is a strong interest in replacing the Pd reagents by much cheaper Cu reagents. Early examples for the Cu-catalyzed arylation of 1,3-dicarbonyls include the reaction of

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