

## Accepted Manuscript

Synthesis of 2-substituted benzofuran derivatives by the palladium-catalyzed intermolecular coupling of 2-fluoroallylic acetates with phenols

Takumi Udagawa, Masaki Kogawa, Yukiko Tsuchi, Hirotaka Watanabe, Mitsuaki Yamamoto, Motoi Kawatsura

PII: S0040-4039(16)31640-9  
DOI: <http://dx.doi.org/10.1016/j.tetlet.2016.12.011>  
Reference: TETL 48423

To appear in: *Tetrahedron Letters*

Received Date: 9 November 2016  
Revised Date: 1 December 2016  
Accepted Date: 5 December 2016

Please cite this article as: Udagawa, T., Kogawa, M., Tsuchi, Y., Watanabe, H., Yamamoto, M., Kawatsura, M., Synthesis of 2-substituted benzofuran derivatives by the palladium-catalyzed intermolecular coupling of 2-fluoroallylic acetates with phenols, *Tetrahedron Letters* (2016), doi: <http://dx.doi.org/10.1016/j.tetlet.2016.12.011>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.





## Synthesis of 2-substituted benzofuran derivatives by the palladium-catalyzed intermolecular coupling of 2-fluoroallylic acetates with phenols

Takumi Udagawa, Masaki Kogawa, Yukiko Tsuchi, Hiroataka Watanabe, Mitsuaki Yamamoto, and Motoi Kawatsura\*

Department of Chemistry, College of Humanities & Sciences, Nihon University, Sakurajosui, Setagaya-ku, Tokyo 156-8550, Japan

### ARTICLE INFO

#### Article history:

Received  
Received in revised form  
Accepted  
Available online

#### Keywords:

Keyword\_1 palladium  
Keyword\_2 fluorine  
Keyword\_3 benzofuran  
Keyword\_4 C-F bond activation  
Keyword\_5 cyclization

### ABSTRACT

We investigated the intermolecular coupling reaction of 2-fluoroallylic acetates with simple phenols by the  $[\text{Pd}(\text{C}_3\text{H}_5)\text{Cl}]_2$ , DPPF, and KHMDS at 100 °C for 16 h, and succeeded in obtaining 2-substituted benzofuran derivatives in good to high yield through the C-F bond activation and intermolecular cyclization.

2009 Elsevier Ltd. All rights reserved.

Benzofuran is an important scaffold in the several biologically active organic compounds, and the development of an efficient method to construct it and its derivatives is one of the major topics in organic synthesis. Although several methods have been reported to synthesis benzofuran derivatives involving a transition metal catalyzed reaction,<sup>1</sup> most of them are achieved by the reaction of prefunctionalized substrates,<sup>2-4</sup> while there are only limited examples of the construction of benzofuran derivatives by intermolecular coupling using simple phenols and a sequential cyclization reaction.<sup>5</sup> To the best our knowledge,  $\beta$ -keto esters, alkynes, or alkenes were used as the coupling partner for the transition metal catalyzed construction of benzofuran derivatives with simple phenols. For example, Li reported the iron-catalyzed reaction of phenols and  $\beta$ -keto esters,<sup>5a</sup> and Wang reported the palladium-catalyzed construction of benzofuran derivatives from phenols and bromoalkynes.<sup>5b</sup> More recently, the palladium- or copper-catalyzed reaction of phenols with 1,2-diarylethyne was developed by Sahoo<sup>5c</sup> and Jiang.<sup>5d</sup> Furthermore, Maiti discovered the palladium-catalyzed reaction of phenols and alkenes.<sup>5e</sup> On the other hand, we have studied the palladium-catalyzed double substitution of 2-fluoroallylic esters,<sup>6</sup> and reported the double etherification with phenols.<sup>6b</sup> During the course of these studies, we found that the other palladium-catalyzed conditions provide the 2-benzyl benzofuran derivatives, therefore, we now report the palladium-catalyzed construction of 2-substituted benzofuran derivatives from phenols and 2-fluoroallylic esters.

As we previously reported,<sup>6b</sup> the  $\text{Pd}(\text{PPh}_3)_4$  catalyzed reaction of 2-fluoroallylic acetate (**1a**) with phenol (**2a**) selectively afforded the doubly etherified product **3aa** in good yield (Table 1, entry 1). However, when the reaction was conducted using  $[\text{Pd}(\text{C}_3\text{H}_5)(\text{cod})]\text{BF}_4/\text{PPh}_3$ , we observed the formation of a small amount of the benzofuran derivative **4aa** (entry 2). Based on this initial observation, we examined other reaction conditions to realize the selective formation of **4aa** in high yield. Fortunately, we found that the DPPF coordinated palladium catalyst effectively allowed the intended reaction, and changing the solvent from toluene to dioxane also increased the yield of **4aa** to a 72% NMR yield without any formation of **3aa** (entries 3 and 4). Furthermore, we confirmed that KHMDS was a better base than  $\text{Cs}_2\text{CO}_3$  (entry 5), and a higher NMR yield was attained when  $[\text{Pd}(\text{C}_3\text{H}_5)\text{Cl}]_2$  was used as the palladium precatalyst (entries 6-9). Finally, the highest yield (92% NMR yield, 89% isolated yield) was obtained when the reaction was conducted with an excess amount of phenol (entry 10).

With the optimal conditions in hand, we examined the palladium-catalyzed reaction of the 2-fluorocinnamyl acetates **1a** with several phenols, and results are summarized in Table 2. The reaction of **1a** with *p*-cresol (**2b**) provided the intended benzofuran derivative **4ab** in 72% isolated yield (Table 2, entry 1), and the reactions with phenols **2c** and **2d** also afforded **4ac** and **4ad** in acceptable yields (entries 2 and 3). The reaction with *m*-cresol (**2e**) formed a product as a mixture of two regioisomers, but we confirmed that the major product was **4ae** (entry 4). This result indicated that the cyclization occurred at the sterically less

\* Corresponding author. Tel.: +81-3-5317-9740; fax: +81-3-5317-9740; e-mail: kawatsur@chs.nihon-u.ac.jp

Download English Version:

<https://daneshyari.com/en/article/5260358>

Download Persian Version:

<https://daneshyari.com/article/5260358>

[Daneshyari.com](https://daneshyari.com)