



## Palladium catalyzed direct coupling of 5-bromo-2-furaldehyde with furfural and thiophene derivatives



Tuomo P. Kainulainen, Juha P. Heiskanen \*

Research Unit of Sustainable Chemistry, University of Oulu, PO Box 3000, FI-90014 Oulu, Finland

### ARTICLE INFO

#### Article history:

Received 8 August 2016

Revised 21 September 2016

Accepted 29 September 2016

Available online 30 September 2016

#### Keywords:

Direct coupling

Furfural

Heteroaromatic compounds

Palladium catalyst

### ABSTRACT

A direct coupling approach for the synthesis of 5,5'-bisfurfural via the coupling of 2-furaldehyde (furfural) and 5-bromo-2-furaldehyde using the air-stable catalyst Pd(OAc)<sub>2</sub> and the air-stable ligand P(*t*-Bu)<sub>3</sub>HBF<sub>4</sub> was examined. The developed procedure was used to functionalize thiophene containing moieties commonly found in organic electronics. The aromatic C–H bond activated coupling with 5-bromo-2-furaldehyde afforded novel compounds with useful 5-heteroaryl-2-furaldehyde type functionality.

© 2016 Elsevier Ltd. All rights reserved.

The movement away from fossil based sources of raw materials toward sustainable alternatives has increased, and continues to increase, the demand not only for renewable energy but also for renewable chemical feedstocks. Compounds derived from biomass that can be processed into higher value chemicals are therefore essential in reaching true sustainability. 2-Furaldehyde (furfural) is an interesting example, as it is commonly produced from monosaccharides during industrial processes which use biomass derived carbohydrates as raw materials.<sup>1</sup>

Additionally, more organic molecules and polymers that contain one or more furan rings with applications in organic solar cells (OSCs) are increasingly being reported and characterized.<sup>2</sup> The use of furan moieties can offer several advantages<sup>2g,h</sup> in addition to renewability, such as better solubility for polymeric materials in OSC applications. The replacement of thiophene or bithiophene units with furan and bifuran units as parts of conjugated systems may also be beneficial for fluorescent properties such as fluorescent quantum yield.<sup>3</sup> Moreover, the aldehyde group already present in 2-furaldehyde can be easily converted into other functional groups that are useful in solar cell applications, including octyl cyanoacetate,<sup>2d</sup> 2-cyanoacrylic acid,<sup>2e</sup> and dicyanovinyl<sup>2f</sup> moieties. The presence of an aldehyde group may also be highly desirable in the syntheses of photoswitches,<sup>4</sup> antimicrobial agents,<sup>5</sup> and fluorescent labels.<sup>6</sup>

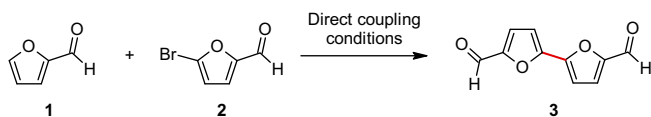
As OSCs are a promising way of producing low-cost renewable energy directly from sunlight, minimizing additional steps and

intermediates during the synthesis of the required compounds could further increase the cost-effectiveness and attractiveness of these devices. For example, in some furan containing OSC compounds,<sup>2a,e,f</sup> assembly of the target molecule has been carried out using Suzuki–Miyaura and Stille cross-coupling reactions which rely on boron, tin, and halogen containing intermediates. These intermediates have then been cross-coupled with bromo or boron derivatives of 2-furaldehyde to give the target molecules. A noteworthy fact is that 5-formyl-2-furylboronic acid, the organometallic reagent used in the Suzuki–Miyaura protocol, has proven to be a problematic coupling partner often giving coupling products in low or moderate yields with brominated heteroaromatic substrates.<sup>7</sup> By using a direct aromatic C–H activation approach the extra reaction steps to form the needed organometallic reagent are avoided. The use of expensive reagents and the amount of waste formed during the reaction is also reduced. Despite the aforementioned advantages, direct cross-coupling reactions between heteroaromatic halides and heteroaromatic C–H partners have seen limited use. Moreover, 2-furaldehyde and its brominated derivative 5-bromo-2-furaldehyde are rarely used as coupling partners with other heteroaromatic compounds in direct coupling. Examples of procedures<sup>8</sup> where 5-bromo-2-furaldehyde has been used in the direct coupling with simple heteroaromatic compounds containing only one reactive C–H bond have been reported, however, they utilize somewhat uncommon and non-commercial palladium catalysts.

Issues with the direct coupling strategy include its potentially low selectivity and yield. The regioselectivity in heteroaromatic cross-couplings is largely influenced by structure, although some

\* Corresponding author.

E-mail address: [juha.heiskanen@oulu.fi](mailto:juha.heiskanen@oulu.fi) (J.P. Heiskanen).



**Scheme 1.** Direct coupling route to 5,5'-bisfurfural.

degree of control can be achieved with carefully controlled reaction conditions.<sup>9</sup> Still, direct cross-coupling typically has given lower yields when compared<sup>10</sup> to more common procedures, such as the Suzuki–Miyaura reaction. This can be somewhat mitigated if a multi-step synthesis of the organometallic reagent is required, which potentially lowers the total yield of the desired coupling product.<sup>11</sup>

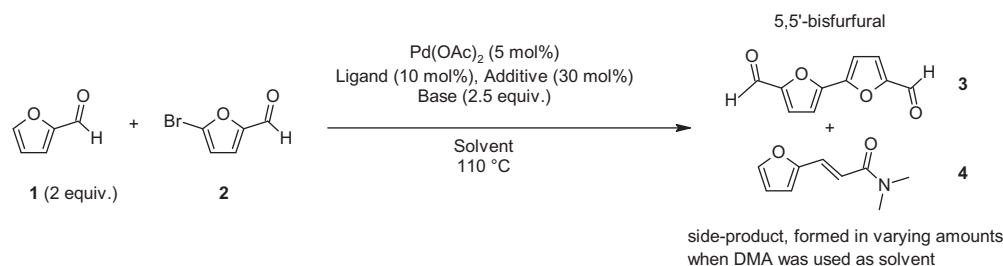
In this work, a Pd-catalyzed C–H activation route to 5-heteroaryl-2-furaldehydes was examined. Initially, the direct coupling between 2-furaldehyde (**1**) and 5-bromo-2-furaldehyde (**2**) was investigated (Scheme 1). While 2-furaldehyde is a well-known

compound, the closely related dimer 5,5'-bisfurfural (**3**) has remained somewhat obscure. Over the years it has been synthesized using various methods such as palladium-catalyzed direct coupling<sup>12</sup> between compounds **1** and **2** and a photochemical process<sup>13</sup> involving compound **2** and an excess of compound **1**. Compound **3** can also be synthesized using the palladium-catalyzed aerobic oxidative dimerization of compound **1** under a high-pressure oxygen atmosphere.<sup>14</sup> However, the palladium mediated homocoupling of compound **1** is extremely inefficient under normal atmospheric conditions.<sup>15</sup>

First, direct coupling conditions closely related to those used by McClure and co-workers<sup>12</sup> were employed. When the phosphine ligand PCy<sub>3</sub> was used as its air-stable tetrafluoroborate salt (PCy<sub>3</sub>-HBF<sub>4</sub>), low yields resulted. A different reaction system consisting of catalyst, ligand, base, and acid without additives such as Bu<sub>4</sub>NBr was then assembled and optimized (Table 1). P(*t*-Bu)<sub>3</sub>HBF<sub>4</sub> gave the highest yield of all examined phosphine ligands (entries 1–8).

It was found that the base had to be chosen carefully. In the presence of some bases, only trace amounts of desired product **3**

**Table 1**  
Optimization for the synthesis of 5,5'-bisfurfural (**3**)



Entry	Catalyst	Ligand	Base	Additive	Solvent	Yield <b>3</b> (%) <sup>a</sup>
1	Pd(OAc) <sub>2</sub>	—	K <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	6
2	Pd(OAc) <sub>2</sub>	JohnPhos	K <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	23
3	Pd(OAc) <sub>2</sub>	Xantphos (5 mol %)	K <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	23
4	Pd(OAc) <sub>2</sub>	P( <i>o</i> -tolyl) <sub>3</sub>	K <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	26
5	Pd(OAc) <sub>2</sub>	PCy <sub>3</sub> HBF <sub>4</sub>	K <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	29
6	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>2</sub> MeHBF <sub>4</sub>	K <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	36
7	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	K <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	40
8	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>2</sub> (neopentyl)HBF <sub>4</sub>	K <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	20
9	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	K <sub>2</sub> CO <sub>3</sub>	PivOH (20 mol %)	DMA	34
10	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	K <sub>2</sub> CO <sub>3</sub>	PivOH (40 mol %)	DMA	39
11	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	K <sub>2</sub> CO <sub>3</sub>	TFA	DMA	20
12	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	Propanoic acid	DMA	21
13	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	Hexanoic acid	DMA	26
14	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	Octanoic acid	DMA	20
15 <sup>b</sup>	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Li <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	Trace <sup>d</sup>
16 <sup>bc</sup>	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Li <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	29
17	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	45
18	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	CS <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	Trace <sup>e</sup>
19	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	KOAc	PivOH	DMA	33
20	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	K <sub>3</sub> PO <sub>4</sub>	PivOH	DMA	Trace <sup>e</sup>
21	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	<i>t</i> -BuOK	PivOH	DMA	Trace <sup>e</sup>
22	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	PivOH	NMP	38
23	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	PivOH	DMF	21
24	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	PivOH	1,4-Dioxane	14 <sup>d</sup>
25	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	PivOH	DMA–toluene (1:1)	12 <sup>d</sup>
26	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	PivOH	DMA–1,4-dioxane (1:1)	27
27 <sup>f</sup>	Pd(OAc) <sub>2</sub>	P( <i>t</i> -Bu) <sub>3</sub> HBF <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	PivOH	DMA	10 <sup>d</sup>

Reaction conditions: compound **1** (2 equiv), catalyst (5 mol %), ligand (10 mol %), base (2.5 equiv), additive (30 mol %), 110 °C, 20–24 h, initial solvent volume (7.5 mL), solvent (1.5 mL) containing compound **2** (1 equiv) added by syringe pump (75 μL/h). Reactions were monitored by TLC.

<sup>a</sup> Isolated yield of compound **3**.

<sup>b</sup> Reaction temperature 150 °C.

<sup>c</sup> Compound **2** fully added to the reaction mixture at the start of the reaction.

<sup>d</sup> Compound **2** not fully converted.

<sup>e</sup> Formation of compound **4**.

<sup>f</sup> Reaction was performed without compound **1**.

Download English Version:

<https://daneshyari.com/en/article/5258311>

Download Persian Version:

<https://daneshyari.com/article/5258311>

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