



Synthesis of aromatic ketones by Suzuki–Miyaura cross-coupling of acyl chlorides with boronic acids mediated by palladium catalysts deposited over donor-functionalized silica gel



Miloslav Semler^{a,b}, Petr Štěpnička^{a,*}

^a Department of Inorganic Chemistry, Faculty of Science, Charles University in Prague, Hlavova 2030, 128 40 Prague, Czech Republic

^b J. Heyrovský Institute of Physical Chemistry, Academy of Sciences of the Czech Republic, v.v.i.; Dolejškova 3, 182 23 Prague, Czech Republic

ARTICLE INFO

Article history:

Received 27 May 2014

Received in revised form 17 June 2014

Accepted 18 June 2014

Available online 11 July 2014

Keywords:

Deposited catalysts

Palladium

Functional amides

Suzuki–Miyaura reaction

Aromatic ketones

ABSTRACT

Immobilized palladium catalysts prepared by deposition of palladium(II) acetate over silica gel functionalized with $\equiv\text{Si}(\text{CH}_2)_3\text{NHCH}_2\text{Y}$ donor groups (Y = SMe (**1**), NMe₂ (**2**), PPh₂ (**3**)) efficiently mediate cross-coupling of benzoyl chloride with benzenboronic acid and its derivatives possessing electron-donating substituents. The presence of electron-withdrawing groups at the benzene ring decreases the yield of the coupling product while aliphatic acyl chlorides such as PhCH₂CH₂COCl and *t*-BuCOCl provide the coupling products in only poor yields. The course of the coupling reaction is very sensitive to the reaction conditions, the best results being achieved with potassium carbonate sesquihydrate as the base in dry toluene. The catalysts, which serve as the source of active metal, gradually lose their activity due to metal leaching and, mainly, decomposition of the solid support presumably by the action of the strong base present in the reaction system.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

Naturally occurring and synthetic aromatic ketones are important target molecules showing interesting biological activities [1] as well as useful reaction intermediates in both laboratory and large scale syntheses [2]. Their preparation by conventional methods typically involves various oxidation processes and acylation reactions [3,4]. Alternative routes devised more recently include carbonylative cross-coupling reactions (mainly Suzuki–Miyaura) [5] and the direct Suzuki–Miyaura cross-coupling of acyl halides with boronic acids. The latter approach, reported firstly in 1997 [6,7], is particularly attractive due its relative simplicity, functional group tolerance, selectivity and the avoidance of toxic carbon monoxide and compounds possessing the environmentally persistent (hydrolytically stable) carbon–halogen bonds. On the other hand, the need for advanced and more expensive starting materials makes the coupling of acyl chlorides with boronic acids suitable mainly for the preparation of valuable fine chemicals. For instance, this method has been recently employed in the preparation of compounds active against *Trypanosoma* parasites [8], synthesis of

5-lipoxygenase activating protein (FLAP) inhibitors [9] and a selective modulator of estrogen receptor [10].

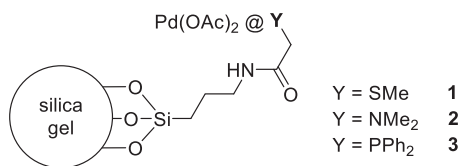
Despite the recent progress, the cross-coupling of aromatic acyl halides and arylboronic acids typically makes use of conventional homogeneous catalysts [11]. The use of deposited palladium catalysts still appears to be limited to the archetypal Pd/C system, which afforded the ketones in only moderate yields and contaminated with the corresponding biphenyls [12,13]. This led us to evaluate our recently introduced palladium catalysts immobilized over silica gel modified with donor-terminated amide pendants (Scheme 1) that have been previously employed in the Heck coupling [14] also in this reaction. Thus, this contribution reports the results achieved with catalysts **1–3** in the coupling of acyl chlorides with benzenboronic acids, paying particular attention to the influence of the reactions conditions on the course of the catalyzed process.

2. Results and discussion

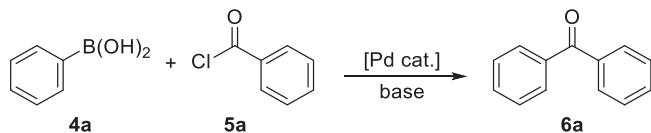
2.1. Screening experiments

Catalysts evaluated in this study are depicted in Scheme 1 and were prepared as reported earlier [14]. The initial reaction tests were performed in the reaction of benzenboronic acid **4a** with benzoyl chloride **5a** as the simplest (non-substituted) substrates

* Corresponding author. Tel.: +420 221 951 260; fax: +420 221 951 253.
E-mail address: stepnic@natur.cuni.cz (P. Štěpnička).



Scheme 1. Idealized schematic representation of the catalysts used in this study.



Scheme 2. The model coupling reaction of benzenboronic acid (**4a**) with benzoyl chloride (**5a**) to give benzophenone (**6a**).

to give the parent benzophenone **6a** (Scheme 2) with an aim of identifying factors that may possibly influence the course of this particular type of cross-coupling reaction. The reaction solvent was varied first using catalyst **3** possessing the soft phosphine donor group (1 mol.% Pd), an excess of benzoyl chloride (2.0 equiv), and caesium carbonate (1.2 equiv) as the base at 100 °C. Water and aqueous mixtures were excluded from testing in order to avoid undesired decomposition of the catalyst by hydrolysis of the siliceous support under the action of a strongly alkaline aqueous medium.

A comparison of the results achieved in different solvents (Table 1, entries 1–6) indicate the reaction to proceed best in toluene (41% after 3 h), which is indeed in line with previous reports [15,16]. Etheral solvents such as 1,4-dioxane and diethylene glycol dimethyl ether (diglyme) gave lower yields, followed by propionitrile. Finally, reactions in *N,N*-dimethylformamide (DMF) and *n*-octane representing the extreme cases as far as polarity of the solvents tested is concerned proceeded in practically negligible extent (ca. 4%).

Similarly dramatic differences were observed upon changing the base additive. Anhydrous lithium, sodium or potassium carbonate afforded much lower yields of **6a** than Cs₂CO₃ tested initially (Table 1, entries 7–10). However, addition of dibenzo-18-crown-6 as a hydrophobic macrocyclic ligand for the K⁺ ion to the reaction system containing potassium carbonate improved the conversion nearly to the level achieved with Cs₂CO₃ (Table 1, entry 11). Other simple bases such as calcium carbonate, potassium hydrogencarbonate (2.4 mmol per 1.0 mmol of **4a**) or tripotassium phosphate (2.1 mmol per 1.0 mmol of **4a**) were also unsuccessful (yields of **6a**: 3–4%; the results are not tabulated). When the amount of

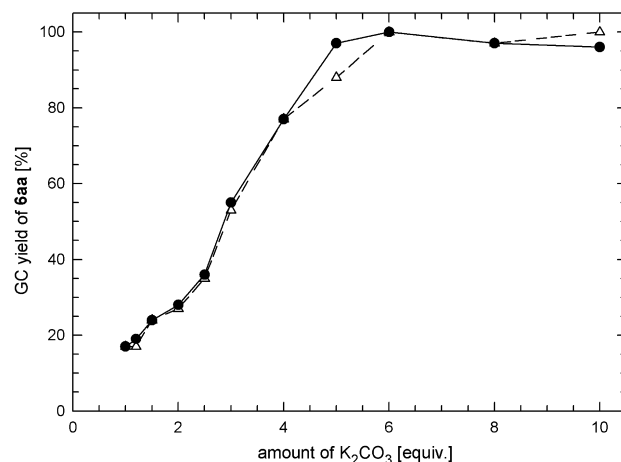


Fig. 1. Dependence of the yield of the coupling product **6a** on the amount of K₂CO₃·1.5H₂O in the reaction system. Reaction time: 30 min (empty triangles) and 3 h (filled circles). Conditions: 1.0 mmol of **4a**, 2.0 mmol of **5a** and base in 5 mL of toluene, catalyst **3** (1 mol.% Pd), 100 °C.

anhydrous caesium carbonate was increased to 2.2, 3.2 and 4.2 equiv., the yield of the coupling product decreased to 24, 19 and 19%, respectively (reaction time was maintained at 3 h). Finally, lowering the amount of the base to a half (0.6 equiv. Cs₂CO₃) had a similar effect (10% yield of **6a** after 3 h; results not given in the Table).

Considering the documented positive influence of water of hydration on the course of the coupling of acyl chlorides with boronic acids [16], we next turned to potassium carbonate sesquihydrate (K₂CO₃·1.5H₂O) as a well-defined and cheap hydrated base (Table 1, entries 11 and 12). The results for a series of experiments performed in the presence of increasing amounts of this base summarized in Fig. 1 reveal a steady increase in the yield of the coupling product until ca. 5 equiv. of this base in the testing reaction mixture, resulting in practically complete conversions of **4a** to **6a**. This trend is maintained also at relatively shorter reaction times (see kinetic profiles for 30 min reaction time in Fig. 1). Apparently, the hydrated solid (insoluble) base does not release excessive amounts of water to the hydrophobic solvent that could possibly accelerate the unwanted hydrolysis of the acid chloride. On the other hand, the accessible water can increase the equilibrium concentration of OH⁻ ions in the reaction mixture and thus facilitate conversion of the starting boronic acid to the respective borate [RB(OH)₃]⁻, which then faster transmetallates the palladium intermediate resulting by the preceding oxidative addition of the acyl chloride [17].

Table 1
Summary of the optimization experiments performed for the reaction of **4a** with **5a**.^a

Entry	Catalyst (% Pd)	Solvent	Base (amount) ^b	T (°C)	Time (h)	GC yield of 6a (%)
1	3 (1.0)	DMF	Cs ₂ CO ₃ (1.2)	100	3	4
2	3 (1.0)	Propionitrile	Cs ₂ CO ₃ (1.2)	100	3	19
3	3 (1.0)	Dioxane	Cs ₂ CO ₃ (1.2)	100	3	25
4	3 (1.0)	Diglyme	Cs ₂ CO ₃ (1.2)	100	3	27
5	3 (1.0)	Toluene	Cs ₂ CO ₃ (1.2)	100	3	41
6	3 (1.0)	<i>n</i> -Octane	Cs ₂ CO ₃ (1.2)	100	3	4
7	3 (1.0)	Toluene	Li ₂ CO ₃ (1.2)	100	3	3
8	3 (1.0)	Toluene	Na ₂ CO ₃ (1.2)	100	3	5
9	3 (1.0)	Toluene	K ₂ CO ₃ (1.2)	100	3	5
10	3 (1.0)	Toluene	K ₂ CO ₃ (4.0)	100	3	13
11	3 (1.0)	Toluene	K ₂ CO ₃ (1.2) ^c	100	3	38
12	3 (1.0)	Toluene	K ₂ CO ₃ ·1.5H ₂ O (1.2)	100	3	19
13	3 (1.0)	Toluene	K ₂ CO ₃ ·1.5H ₂ O (6.0)	100	3	quant.

^a Conditions: 1.0 mmol of **4a**, 2.0 mmol of **5a**, base in 5 mL of solvent.

^b Amount of base = mmol of base per 1.0 mmol of boronic acid.

^c Dibenzo-18-crown-6 was added (12 mg or 33 μmol per 1.0 mmol of **4a**).

Download English Version:

<https://daneshyari.com/en/article/54365>

Download Persian Version:

<https://daneshyari.com/article/54365>

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