NHC-Coordinated Cyclometalated Palladium Complex Catalyzed Addition of Arylboron Compounds to Fluorous Hemiacetals

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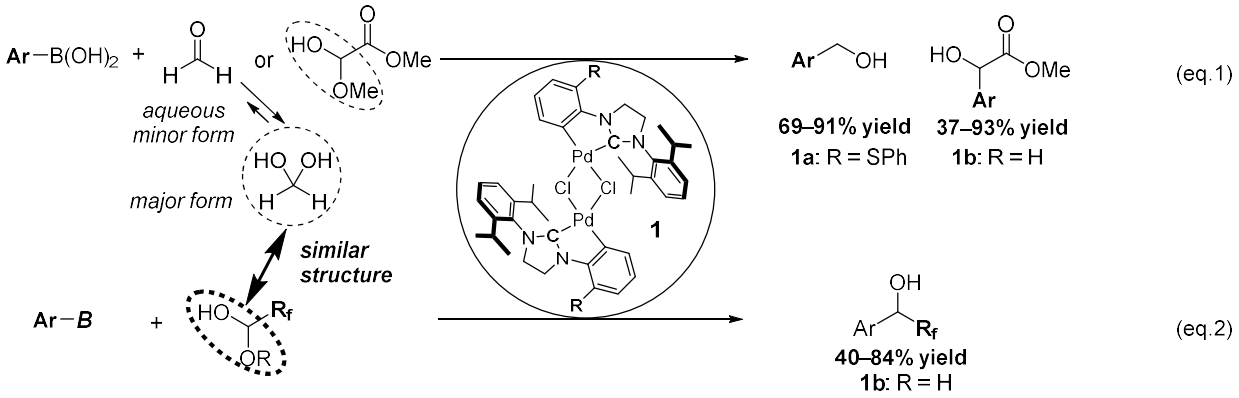
Abstract: NHC coordinated cyclometalated palladium(II) catalyzed nucleophilic addition of arylboron compounds to various fluorous hemiacetals such as 2,2,2-trifluoro-1-methoxyethanol and other fluorous silylacetals gave corresponding various functionalized secondary alcohols in good yields.

Keywords: palladium catalysis, cyclometalated palladium complex, hemiacetal, nucleophilic addition

1. Introduction

Transition-metal catalyzed nucleophilic addition of arylboron reagents to carbonyl compounds has been developed as the one of the important synthesis of benzylic alcohols as alternative methods to the classical 1,2-addition using organolithium or magnesium compounds because are tolerant to wide range of functional groups.[1] Previously, we reported that the NHC-coordinated cyclometalated palladium (II) complexes have excellent catalytic activity for the nucleophilic addition of arylboronic acids to aqueous formaldehyde (formalin) and methyl 2-hydroxy-2-methoxyacetate (Scheme 1, eq.1). [2,3] Herein, we have focused on structures of hemiacetals as a formyl synthon and examined the arylation through nucleophilic addition reaction of arylboron compounds to fluorous hemiacetals (Scheme 1, eq.2).



Scheme 1. NHC-palladacycle **1** catalyzed nucleophilic addition of arylboron reagents to hemiacetals

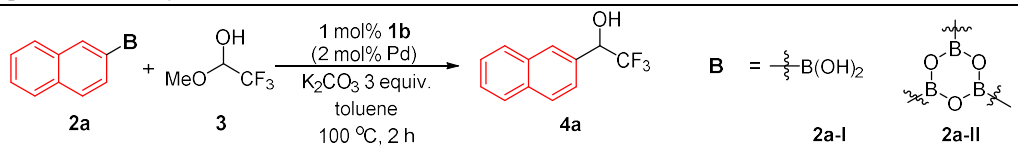
2. Experimental

General procedure: Palladium complex **1b** (0.01 mmol, 2 mol% Pd), Aryl boron compound (0.5-2.0 mmol/Ar) and K_2CO_3 (1.5 mmol) were charged in a 10 mL screw-top test tube sealed with a rubber septum. The test tube was evacuated and backfilled with argon. This sequence was repeated five times. Then solvent (1 mL) and 2,2,2-trifluoro-1-methoxyethanol (0.5 mmol) were added via the rubber septum with syringe. In an argon flow, the rubber septum was replaced with a Teflon liner screw cap. The sealed test tube was placed into an oil bath preheated at 100 °C. After the reaction mixture was stirred for 2 h, the reaction mixture was cooled to room temperature. The obtained crude was purified by passing it through a silica gel column with a hexane / ethyl acetate.

3. Results and discussion

Initially, we examined the correlation of the yield of 2,2,2-trifluoro-1-(naphthalen-2-yl)ethan-1-ol **4a** on the ratio of 2-naphtyl boron compounds **2a** to 2,2,2-trifluoro-1-methoxyethanol **3** in **1b** catalyzed reaction (Table 1). The catalytic reaction of **2a-I** and one molecular equivalent amount of **3** provided the corresponding alcohol **4a** in 30% yield (entry 1). By increasing the used amount of **3**, the yield was greatly decreased (entry 2). On the other hand, the yield was raised to 39% by increasing the used amount of 2-naphtylboronic acid **2a-I** (entry 3). Additionally, the yield improved significantly by using tri(2-naphtyl)boroxin **2a-II** instead of **2a-I** (entries 4 and 5).

Table 1. The dependence of the yield of **4** on the used amount of **2** and **3**

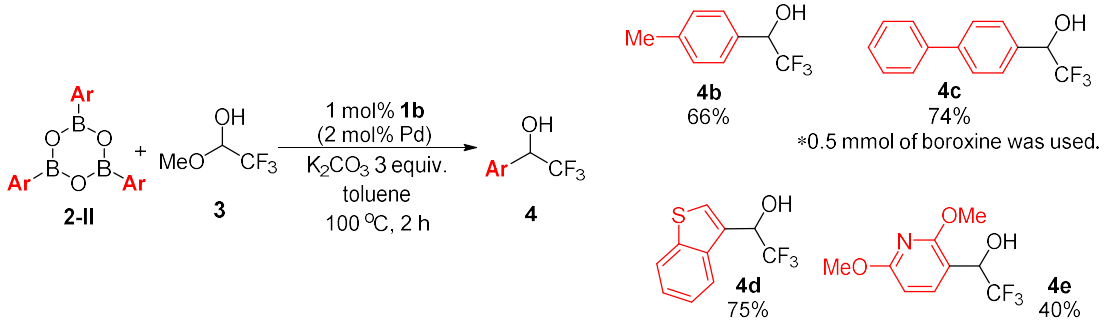


2a 3 4a 2a-I 2a-II

Entry	Compound **2**	Compound **3**	Yield[a]
1	0.5mmol (**2a-I**)	0.5 mmol	30%
2		1.5 mmol	Trace
3	2.0 mmol (**2a-I**)	0.5mmol	39%
4	0.33 mmol (**2a-II**)		68%
5	0.67 mmol (**2a-II**)		84%

a) Isolated yield.

On the basis of the results, we synthesized various 1-(hetero)aryl-2,2,2-trifluoroethanols using the **1b** catalyzed reaction of 2,2,2-trifluoro-1-methoxyethanol **3** and arylboroxins (**Figure 1**). Weaker electron donating groups such as methyl or phenyl groups substituted triarylboroxins were converted to the corresponding alcohols in good yields (**4b** and **4c**). Additionally, hetero-arylboroxins such as tri(3-benzothiophenyl)boroxin was gave the desired products in 75% but tri(2,6-methoxy-3-pyridyl)boroxin was lower reactivity (**4d** and **4e**).



2-II 3 4

Figure 1. Substrate scope of arylboroxin

4. Conclusions

In conclusion, we developed the palladium catalyzed arylation of 2,2,2-trifluoro-1-methoxyethanol using aryl- and hetero-arylboroxin to give corresponding various functionalized β-fluoro secondary alcohols in good yields.

References

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