Room-temperature Suzuki-Miyaura reactions mediated by native and derivatized β–cyclodextrins

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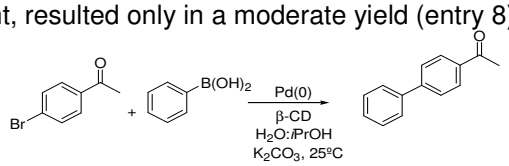
INTRODUCTION

Suzuki-Miyaura reactions provide a simple and effective synthetic route to biaryls by using a wide range of palladium catalysts[1,2]. Our group has recently showed that 2-hydroxypropyl-α-cyclodextrin is an effective green reductant/capping agent for the preparation of Pd nanoparticles[3] with good catalytic activity in C-C cross-couplings in water. In this work, we present our findings concerning the effect of different β-CDs on the room-temperature Suzuki-Miyaura reaction between phenylboronic acid and 4-bromoacetophenone in the isopropyl alcohol-water system. The results suggest that the nature of the substituents and CD concentration play a role in the catalysis.

RESULTS AND DISCUSSION

As expected, the attempt to render the model reaction (Scheme 1) selective in neat water at room-temperature (in the absence of native β-CD) led to a low yield of 4-phenylacetophenone by using Na_2PdCl_4 (1 mol%, entry 1).Through a tentative choice, the addition of 10% isopropyl alcohol provided only a moderate yield of the product (entry 2). Following this, we carried out a screening using different β-CD concentrations. Entries 5 and 6 gave the best results, even though biphenyl was observed as by-product (< 15%). Interestingly, by applying 2-hydroxypropyl-β-CD (β-HPCD, entry 7) provided the desired product with total product selectivity. Surprisingly, the use of RAME-β–CD (randomly methylated), a well-reported mass-transfer/capping agent, resulted only in a moderate yield (entry 8).



Scheme 1. The Suzuki-Miyaura reaction model.

These previous results suggest that the type of CD along with the Pd:CD molar ratio has a decisive influence on the yield/selectivity of the reaction, probably as a consequence of the nanoparticle formation. The synthetic scope involving different aryl bromides/boronic acids are under investigation.

Table 1. Suzuki reaction between 4-bromoacetophenone and phenylboronic acid.

Entry	Solvent	Pd:βCD	Yield[a] (%)
1	H_2O	-	24
2	H_2O:*i*-PrOH (90%:10%)	-	68
3	H_2O:*i*-PrOH (90%:10%)	10:1	57
4	H_2O:*i*-PrOH (90%:10%)	2:1	71
5	H_2O:*i*-PrOH (90%:10%)	1:2	86[b]
6	H_2O:*i*-PrOH (90%:10%)	1:10	82
7	H_2O:*i*-PrOH (90%:10%)	1:10	85[(c)]
8	H_2O:*i*-PrOH (90%:10%)	1:10	53[(d,e)]

[a]Measured by GC-MS after 24h. [b]10% biphenyl as by-product. [c]β-HPCD. [d]RAME-β-CD. [e]5% biphenyl as by-product.

CONCLUSION

The use of β-CDs as supramolecular carriers provides an alternative route to perform Suzuki-Miyaura reactions under exceptionally mild conditions (aqueous medium and room-temperature).

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