Studies on the use of Poliethyleneglicol (PEG) in Heck Oxyarylation Reaction for the Synthesis of Deoxy Pterocarpans and Analogs

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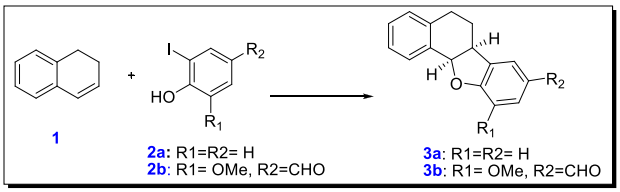
INTRODUCTION

The oxyarylation of olefins by *ortho*-iodophenols have been employed in our laboratory in the synthesis of natural pterocarpans and their analogs.[1] Recently, cross coupling reactions catalyzed by the *in situ* formation of nanoparticles of palladium in PEG were described in the literature.[2] However, so far the use of PEG in the oxa-Heck reaction was not reported. Herein we describe preliminary results on the oxyarylation employing PEG as the solvent as well as the additive, using the reaction of dihydronaphthalen (**1**) and **2a**,**b** as examples. .

RESULTS AND DISCUSSION

The reactions studied are shown in Scheme 1.



Scheme 1: Oxyarylation of dihydronaphtalene with *o*-iodophenols

Palladium acetate and an oxime-palladacycle were employed as the source of palladium (**Figure 1**).

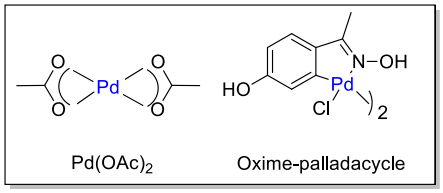


Figure 1. Sources of palladium used.

The reactions were submitted to PEG's possessing different molecular weight, as PEG-400 and PEG-2000, at 140°C. The reaction times varied from 40 minutes to 3 hours. In one set of reactions, $Pd(OAc)_2$ (10 mol%) was used as a precatalyst in the presence of Ag_2CO_3 (1.1 equiv) as the base in PEG-400 (**Conditions A**) and PEG-2000 as the solvent (**Conditions B**), while in the another set of experiments an oxime-based palladacycle (2 mol% Pd) was used as a precatalyst, in the presence of Cy_2NH (2 equiv) as the base in PEG-400 as the (**Conditions C**) and PEG-2000 as the solvent (**Conditions D**). The best results were obtained in the reactions with PEG 2000. The oxyarylation of the olefin with the *o*-iodophenol (**2a**) in **conditions B** and **D** showed excellent results (entries 2 and 4), leading to the target products in 87% and 80% yields, respectively.

Table 1. Conditions and yields for palladium catalyzed reaction of **1** and **2**

Entry	Cond	Ar	Prod	time	Yield (%)
1	A	**2a**	**3a**	2h	40
2	B	**2a**	**3a**	40 min	87
3	C	**2a**	**3a**	20h	-
4	D	**2a**	**3a**	3h	80
5	A	**2b**	**3b**	1h	45
6	B	**2b**	**3b**	30 min	51
7	C	**2b**	**3b**	1h	23
8	D	**2b**	**3b**	30 min	47

Condition A: $Pd(OAc)_2$ 10mol%, Ag_2CO_3 (1.1 eq.), PEG-400, 120ºC; **Condition B**: $Pd(OAc)_2$ 10mol%, Ag_2CO_3 (1.1 eq.), PEG-2000,140ºC; **Condition C**: Palladacycle 1mol% (2mol%-Pd), Cy_2NH (2 equiv.), PEG-400, 140ºC, **Condition D**: Palladacycle 1 mol% (2mol%-Pd), Cy_2NH (2 equiv.), PEG-2000, 140ºC

CONCLUSION

The system PEG2000-Pd was shown to be very active in the oxa-Heck reaction, mainly by the use of the oxime-palladacycle (2 mol%-Pd) as the catalyst instead $Pd(OAc)_2$ (10 mol%-Pd). Also, due to lower time reactions and improved yields, the reactions performed in PEG2000-palladacycle were shown to be advantageous when compared with reactions in the absence of PEG.[1] In addition, the condition reactions are very attractive because PEG2000 is a green solvent and in conditions D the use of Ag_2CO_3 is not required.

ACKNOWLEDGEMENTS

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