An efficient, practical and one step procedure to *trans*-3-hydroxy-4-arylpentanones core by Heck-Matsuda reaction

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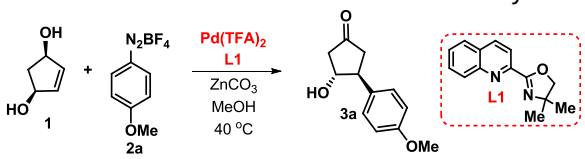
Introduction

The cyclopentane ring is a valuable and important scaffold due to its ubiquitous presence in many natural products and pharmaceuticals, such as prostaglandins and their derivatives.[1] The synthesis of prostaglandin-E remains a challenge because of an unstable β-hydroxy-ketone group and the 3,4-*anti* relationship.[2] As a synthetic method, the Heck-Matsuda reaction poses as a powerful tool to provide complex molecules in a concise manner[3] with atom economy.[4] Its byproduct is molecular nitrogen. Herein, we report on the desymmetrization of the meso *cis*-4-cyclopentene-1,3-diol (**1**) to produce *trans*-3-hydroxy-4-arylpentanones in one step by Heck-Matsuda reaction. This method has an excellent potential for the development of its asymmetric version.

Results and Discussion

We began our studies with a model reaction applying a general procedure previously established in our research group[5] using $Pd(TFA)_2$ in methanol at 40 °C. Our initial experiments focused on the feasibility of the racemic Heck arylation employing the *N,N*-QuinOX ligand **L1** and a careful evaluation the palladium catalyst loading (Table 1).

Table 1. Evaluations of the Heck-Matsuda arylation.



Entry	$Pd(TFA)_2$ (mol%)	Ligand	Time (h)	Yield (%)[a]
1	10	-	5	51
2	**10**	**L1**	**0.25**	**99**
3	5	**L1**	1	99
4	2.5	**L1**	2	98
5	1	**L1**	4	99

[a] Determined by ^{1}H NMR.

This Heck-Matsuda reaction provided the desired (±)-*trans*-3-hydroxyl-4-arylcyclopentanone in high yields and *trans*-stereoselectivity. The use of racemic quinoline oxazoline **L1** ligand furnished the best results even when employing a very small amount of 1 mol% of the palladium catalyst (entry 5). Next, we explored the scope for this new Heck-Matsuda reaction varying the electronic and substitution pattern of the arenediazonium tetrafluoroborate salts. Some selected of the Heck products are shown in Figure 1.

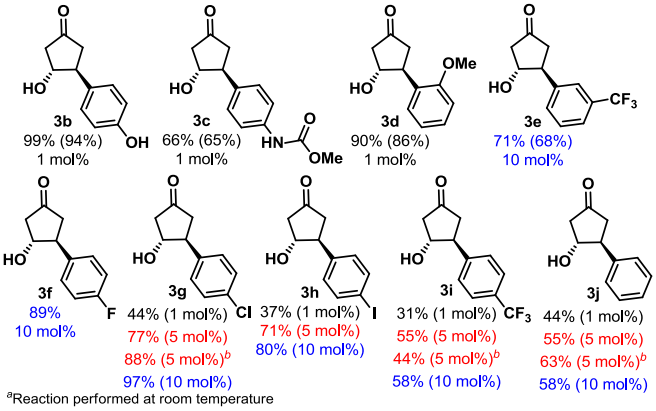


Figure 1. Heck-Matsuda scope.

Conclusions

We have developed an efficient arylation of the meso compound *cis*-4-cyclopentene-1,3-diol (**1**) by a Heck-Matsuda reaction. Our method is extremely practical, mild, can be carried out under "open vessel" conditions and is basically a one step procedure to *trans*-3-hydroxy-4-arylpentanones cores present in many bioactive compounds.

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