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

Rafaela C. Carmona1 (PG) e Carlos Roque D. Correia2* (PQ)

1Instituto de Química, Universidade Estadual de Campinas-Unicamp, C.P. 6154, CEP 13084-971, Campinas-SP, Brasil roque@iqm.unicamp.br

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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. The synthesis of prostaglandin-E remains a challenge because of an unstable β-hydroxy-ketone group and the 3,4-anti relationship. As a synthetic method, the Heck-Matsuda reaction poses as a powerful tool to provide complex molecules in a concise manner with atom economy. 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 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.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pd(TFA)2 (mol%)</th>
<th>Ligand</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
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<tr>
<td>1</td>
<td>10</td>
<td>-</td>
<td>5</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>L1</td>
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<tr>
<td>4</td>
<td>2.5</td>
<td>L1</td>
<td>2</td>
<td>98</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>L1</td>
<td>4</td>
<td>99</td>
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</tbody>
</table>

* Determined by 1H NMR.

This Heck-Matsuda reaction provided the desired (+)-trans-3-hydroxy-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.

Acknowledgment

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*References*