

# Synthesis and evaluation of new ligands in the enantioselective Heck-Matsuda arylation of achiral 3-cyclo-penten-1-ol.

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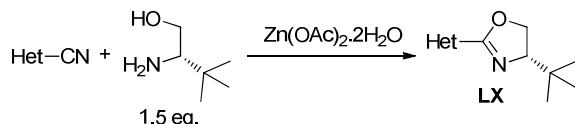
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## Introduction

In 2012 our group reported the first examples of the enantioselective Heck-Matsuda (HM).<sup>1</sup> More recently we reported on the stereo/enantioselective arylation of the achiral 3-cyclo-penten-1-ol.<sup>2</sup> Due to the importance of these Heck products we decided to design new chiral ligands for this reaction.

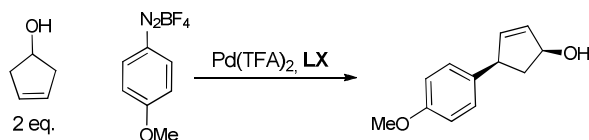
## Results and discussion

The new chiral ligands were synthesized by a modified general procedure (Scheme 1).<sup>3</sup> High yields were observed, except for **L1** (presumably due to the reactivity of the corresponding nitrile) and **L5**, which is the product of oxazoline cyclization and electrophilic aromatic substitution (Table 1).



Scheme 1: Synthesis of chiral ligands.<sup>a</sup>

The new ligands were evaluated in the enantioselective arylation of 3-cyclo-penten-1-ol (Scheme 2).<sup>2</sup> Ligands **L1**, **L2**, **L3** were less effective in the HM reaction, presumably due to electronic effects of the heteroaromatic rings. On the other hand, **L4** performed very well rivaling some previously reported results.<sup>2</sup> Despite the lower yields, **L5** was capable of delivering the Heck product in high *er* (Table 1).



Scheme 2: Evaluation of chiral ligands on the HM.<sup>b</sup>

<sup>a</sup>Zn(OAc)<sub>2</sub>·2H<sub>2</sub>O (2 mol%), Hexane (1 mol.L<sup>-1</sup>), pressure tube, 110 °C, 2 days, 2 mmol scale (except for **L1** which was performed at a 0.5 mmol scale).

<sup>b</sup>Pd(TFA)<sub>2</sub> (2.5 mol%), **LX** (3.0 mol%), 1 equiv of base, 40 °C, 0.1 mmol scale.

Table 1: Synthesis and evaluation of the new ligands **L1-L5**

Nitrile	Ligand	HM product
	 <b>L1</b> 8%	41% <i>er</i> : 55:45
	 <b>L2</b> 95%	18% <i>er</i> : 51:49
	 <b>L3</b> 96%	36% <i>er</i> : nd
	 <b>L4</b> 81%	71% <i>er</i> : 98:2
	 <b>L5</b> 5%	35% <i>er</i> : 96:4

## Conclusion

In conclusion, we synthesized and evaluated five new chiral ligands in the enantioselective HM arylation of the achiral of 3-cyclo-penten-1-ol. PyOx ligand **L4** showed the best performance combining a good yield of 71% and a high *er* of 98:02.

## Aknowlegments

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<sup>2</sup> Angnes, R. A.; Oliveira, J. M.; Oliveira, C. C.; Martins, N. C.; Correia, C. R. D. *Chem. Eur. J.* **2014**, 20, 13117.

<sup>3</sup> Costa, R. C. Estratégias assimétricas em reações de acoplamento A3, USP: São Paulo, 2013.