

Enantioselective synthesis of tertiary allylic alcohols through a Heck-Matsuda desymmetrization of substituted cyclopenten-1-ols.

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Abstract

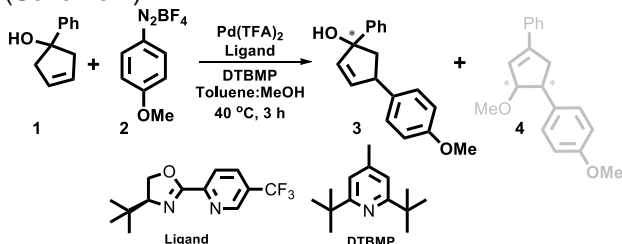
The Heck-Matsuda reaction of substituted cyclopenten-1-ols using chiral *N,N*-ligands provided tertiary allylic alcohols in good yields and high enantioselectivity by means of a desymmetrization strategy.

Introduction

Enantioenriched tertiary alcohols are ubiquitous structural motifs in natural products and pharmaceutical compounds. Their synthesis is still challenging and impressive research efforts have been dedicated towards this objective.¹ In recent years, the Heck-Matsuda reaction has gained increased recognition with the discovery of its enantioselective variant.² Recently, Correia and co-workers demonstrated the synthetic potential of the Heck-Matsuda desymmetrization strategy for the construction of arylated five-membered carbocyclic scaffolds starting from 3-cyclopenten-1-ol.³ Herein, we disclose our findings related to the preparation of enantioenriched tertiary alcohols through a desymmetrization strategy.

Results and Discussion

We commenced our studies performing some standard Heck-Matsuda reactions with cycloalkenol **1** (Scheme 1).



Scheme 1. EHM of cyclopenten-1-ol derivative.

The applied conditions furnished product **4** as the major product in 81% yield. We then decided to investigate new conditions that could furnish the Heck adduct **3** exclusively. We first evaluated different inorganic bases instead of the conventional DTBMP.

Table 1. Evaluation of the base

Base	% 3	% 4
1.1 eq. DTBMP + 1 eq. KHCO ₃	40%	-
1.1 eq. DTBMP + 1 eq. K ₂ CO ₃	20%	-
1.1 eq. DTBMP + 1 eq. Li ₂ CO ₃	35%	20%
1.1 eq. DTBMP + 1 eq. ZnCO ₃	-	52
2 eq. KHCO ₃	74	-
4 eq. KHCO ₃	82	-
6 eq. KHCO ₃	86	-

To expand the synthetic potential of the Heck arylation, its scope was evaluated using several aryldiazonium salts containing electron donating (EDG) or electron withdrawing (EWG) groups in different substitution patterns (Figure 1).

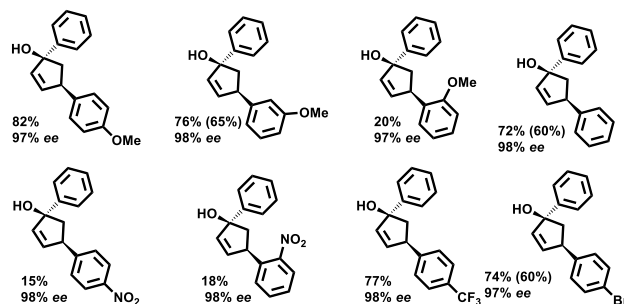


Figure 1. Reaction scope.

Conclusion

In conclusion, we have developed an efficient method to prepare tertiary alcohols through the desymmetrization Heck-Matsuda reaction. Allylic tertiary alcohols were prepared in good yields and high ee's.

Acknowledgments

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³ Angnes, R. A.; Oliveira, J. M.; Oliveira, C. C.; Martins, N. C.; Correia, C. R. D. *Chem. Eur. J.* **2014**, 20, 13117.