

Elucidating the absolute stereochemistry of the enantioselective Heck-Matsuda arylation of 1 substituted 3-ciclopenten-1-ols by derivatization

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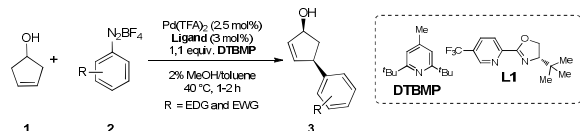
Palavras Chave: *Enantioselective, Heck-Matsuda, Arenediazonium salts, Palladium.*

Abstract

The enantioselective Heck-Matsuda arylation of 1 substituted 3-cyclopenten-1-ols was investigated. The stereochemical outcome of the Heck reaction was confirmed through chemical derivatization.

Introduction

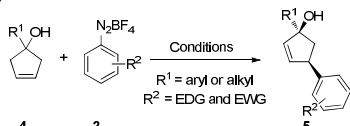
Recently we investigated the enantioselective Heck-Matsuda reaction (EHM) of 3-cyclopenten-1-ol (Scheme 1). This methodology allowed the straightforward synthesis of *cis*-aryl cyclopentenols **3**.¹



Scheme 1. Arylation of 3-cyclopentenol.

Results and discussion

To further probe the method, we envisioned the arylation of substituted 3-cyclopenten-1-ols in order to synthesize the chiral tertiary allylic alcohols **5** (Scheme 2).



Scheme 2. Synthesis of chiral tertiary allylic alcohols.

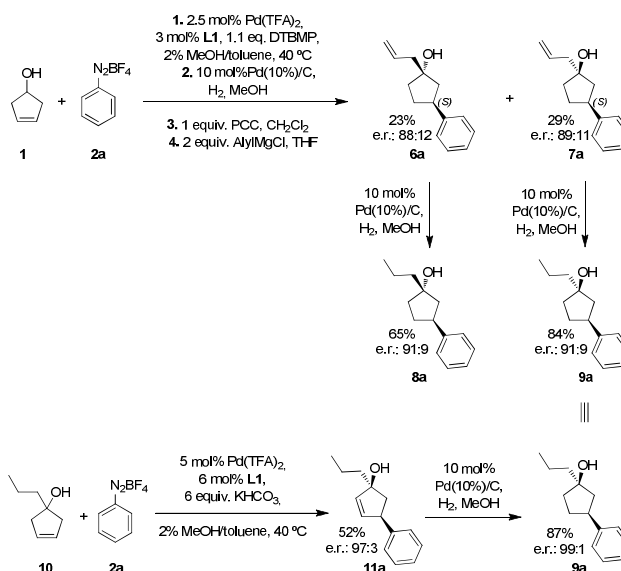
After optimizing the reaction conditions, we managed to synthesize a library of alcohols **5**. However, these new compounds were isolated as oils precluding the application of X-ray analysis. Therefore, the absolute and relative stereochemistry was obtained by chemical derivatization.

A mixture of compounds **6** and **7** was prepared through our previously described EHM arylation of **1** (Scheme 3). Consequently, both **6** and **7** have the (*S*) configuration at the benzylic center.

The absolute and relative stereochemistry of compound **6** is known in the literature;² therefore we attributed **7** to be its epimer at C-1.

Compounds **6** and **7** were then hydrogenated leading to **8** and **9** respectively, now with both compounds having established stereochemistry.

The EHM of **10** with the aryldiazonium salt **2a** lead to compound **11a**, subsequent hydrogenation gave **9a**, as the sole isomer, thus confirming the proposed absolute stereochemical outcome.



Scheme 3. Stereochemistry of the Heck adducts.

Conclusion

The arylation of C-1substituted 3-cyclopenten-1-ol derivatives using our EHM arylation procedure provides the tertiary allylic alcohols of general structure **5** having the absolute stereochemistry as displayed in compound **9a**.

Acknowledgments

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¹ Angnes, R. A.; Oliveira, J. M.; Oliveira, C. C.; Martins, N. C.; Correia, C. R. D. *Chem. Eur. J.* **2014**, *20*, 13117.

² Källström, S.; Jagt, R. B. C.; Sillanpää, R.; Feringa, B. L.; Minnaard, A. J.; Leino, R. *Eur. J. Org. Chem.* **2006**, 3826.