

## A DFT Study on the non-covalent interaction control on enantioselective Heck-Matsuda Reactions

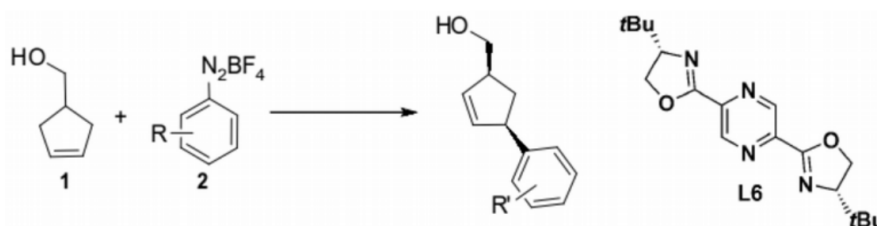
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**Abstract:** Heck-Matsuda reactions are a variant of the well-known Heck-Mizoroki reactions employing aryldiazonium salts as electrophiles.<sup>1</sup> Previously we have shown that a non-covalent interaction between a palladium center and an hydroxyl plays a pivotal role in the high enantioselectivity observed in the desymmetrization of 3-cyclopenten-1-ol.<sup>2</sup> In this work, we have employed Density Functional Theory (DFT) calculations (M06L-def2SVP(d)//M06L-6-31G(d), SDD(Pd)) on the migratory insertion step of the Heck-Matsuda desymmetrization of the analogous substrate cyclopentylmethanol, which contains an one-carbon tether between the hydroxyl group and the cyclopentane ring, in order to investigate the influence of the hydroxyl group of this substrate on the enantioselectivity of these process (Scheme 1)



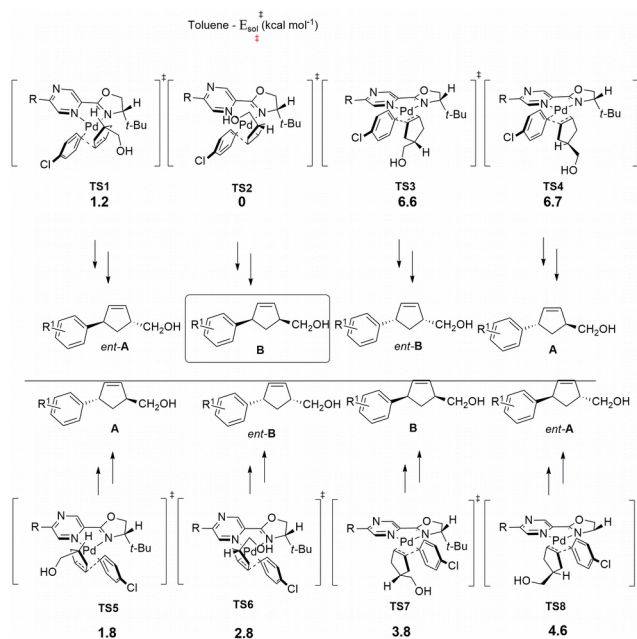
Scheme 1: Heck-Matsuda arylation of cyclopentylmethanol with ligand L6

All the eight transition states involved in this reaction were found and their potential energies are reported in Scheme 2. **TS 2**, the lowest energy transition state has the hydroxyl group oriented towards palladium, a C-H  $\pi$  interaction between the pyrazine ring of the ligand and the aryl moiety of **2**, and the tert-butyl group oriented far away from the substrates. Additionally, all the transition states with the *endo* orientation of the hydroxyl group (TS2, TS3, TS5 and TS6) also show a nonclassical C-H-O hydrogen bond between the hydroxyl group and the phenyl ring of the aryldiazonium salt substrate. Non-covalent interaction (NCI) Isosurfaces<sup>3</sup> were plotted for TS2 (Figure 1) showing these non-covalent interactions along with steric ones. Benchmark studies on these reactions will be reported in due course in order to correctly these trends in terms of Gibbs Free Energies along with novel experimental results.

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Scheme 2: Transition State Energies (kcal.mol<sup>-1</sup>) for the migratory insertion step (Single-point energies in toluene (SDD))

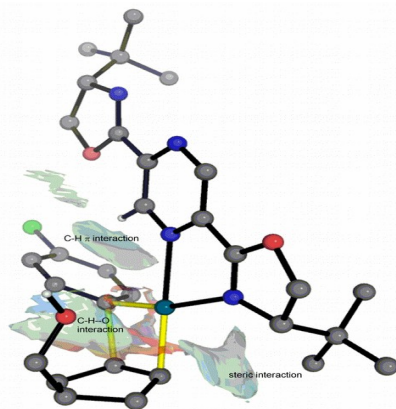


Figure 1: NCI Plot isosurface of TS 2

**Key-words:** Heck-Matsuda, Non-covalent interactions, DFT

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## References:

- [1] J. G.; Moro, A. V.; Correia, C. R. D. European J. Org. Chem. 2011, 2011 (8), 1403–1428.
- [2] De Oliveira Silva, J.; Angnes, R. A.; Menezes Da Silva, V. H.; Servilha, B. M.; Adeel, M.; Braga, A. A. C.; Aponick, A.; Correia, C. R. D. J. Org. Chem. 2016, 81 (5), 2010–2018.
- [3] Contreras-García, J.; Johnson, E.R.; Keinan S.; Chaudret, R. ; Piquemal, J-P.; Beratan, D.N.; Yang, W. J. Chem. Theory. Comput. 7 (3), 625-632.