

Substrate control in an intramolecular Heck-Matsuda reaction: a DFT Study

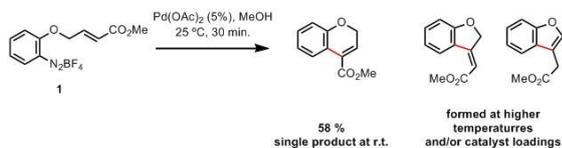
Bruno M. Servilha^a (PG), **Carlos Roque D. Correia^b** (PQ), **Ataulpa A.C. Braga^a** (PQ)

^a Instituto de Química, Universidade de São Paulo, CP 26077, CEP 05513-970, São Paulo – SP

^b Instituto de Química, Universidade de Campinas, CP 6154, CEP 13084-970, Campinas - SP

INTRODUCTION

The development of new synthetic methodologies for heterocyclic compounds is a constant issue in organic synthesis. In 2010 Correia's Group reported the first examples of intramolecular Heck-Matsuda employing *o*-diazo aryl allyl ethers as substrates. The Heck-Matsuda reaction of **1**, an allylic ester, was completely regioselective for the benzopyran product at room temperature. At higher temperatures and catalyst loadings, regioisomer mixtures were obtained (Scheme 1). We have performed DFT calculations on the migratory insertion step of this reaction in order to understand the origin of regioselectivity for the benzopyran product at milder conditions. We are considering here a cationic mechanism, with methanol as a spectator ligand.



Scheme 1 Regioselective intramolecular Heck-Matsuda reaction of allylic ester **1**

METHODS

All calculations were performed on Gaussian 09 suite of quantum chemistry programs employing the M06 functional² with the SDD pseudopotential for Pd and the 6-31+G(d,p) basis set for all other atoms. All geometries were optimized in the gas phase and characterized either as local minima or transition states. Single point energies in methanol on the gas-phase optimized structures were calculated with the SMD model. Relative energies are reported as Gibbs free energies in methanol at 298,15K

RESULTS AND DISCUSSION

The starting complexes, **2** and **3**, for the regioisomeric migratory insertion steps are essentially isoenergetic. In both compounds the palladium-aryl bond is almost perpendicular to the alkene double bond and there is a weak coordination of the sp^2 carboxyl oxygen of the ester moiety to palladium. In order to **2** adopts the structure of **TS2**, the palladium-alkene bond must

be parallel, weakening the back-bonding stabilization of this complex. On the other hand, in **TS3**, the lowest energy transition state, this weakening of the back-bonding interaction is less pronounced than in **TS2**, even though, in this structure the palladium-oxygen bond is lost.

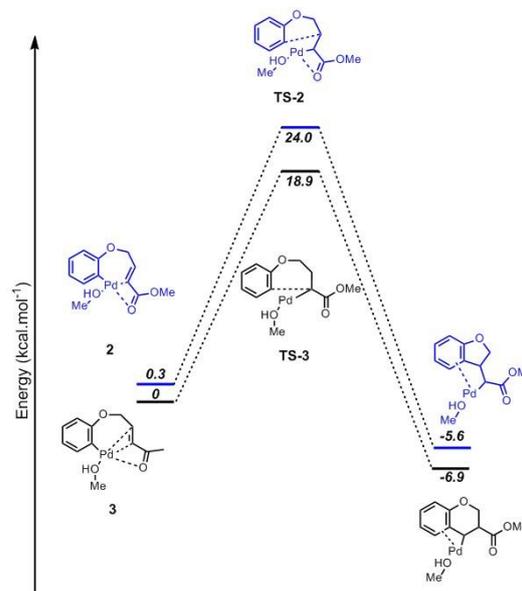


Figure 1 Energy profiles for the regioisomeric migratory insertion pathways. Relative Gibbs free energies (in methanol) are in kcal.mol^{-1} . Charges were omitted for clarity.

CONCLUSIONS

In this work DFT calculations successfully rationalized the regioselectivity in a model substrate-controlled intramolecular Heck-Matsuda reaction. Further studies regarding on the complete catalytic cycle will be reported in due course.

ACKNOWLEDGMENTS

The authors thank FAPESP (grant #2015/01491-3), CNPq and CAPES for financial support and fellowships. We also thank LCCA-USP and CENAPAD for computational facilities.

REFERENCES

- Siqueira, F.A.; Taylor, J.G.; Correia, C.R.D. *Tetrahedron Lett.* 2010, 51, 2102
- Zhao, Y. T.; Truhlar, D.G. *Theor Chem Accounts*, 2006, 120 215