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Theoretical Study on Selectivity Trends in (*N*-heterocyclic carbene)-Pd Catalyzed Heck reactions: Exploring Density Functionals Methods and Models

Vitor H. Menezes da Silva (PG)[1], Ana. P. de Lima Batista (PQ)[1,2], Oscar Navarro (PQ)[3], Ataualpa A. C. Braga (PQ)[1]

[1]Departamento de Química Fundamental, Instituto de Química, Universidade de São Paulo, Av. Prof. Lineu Prestes, 748, São Paulo, SP 05508-000, Brazil
[2]Departamento de Química, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP 14040-901, Brazil
[3]Division of Biomaterials and Biomechanics, Department of Restorative Dentistry, School of Dentistry, Oregon Health & Science University, 2730 SW Moody Ave, Portland, Oregon 97239

Abstract: In the present work, we investigated the use of different sizes of molecular systems and several DFs in predicting the regioselectivity of the N-Heterocyclic carbene (NHC)-Pd catalyzed Heck coupling involving phenyl bromide and styrene.[1] The density functional theory (DFT) results were compared to wave-function (WF) methods DLPNO-CCSD(T), MP2-DLPNO, and experimental data. The migratory insertion (MI) step was considered as selectivity-determining step of the overall reaction. [2,3] In small model, the transition states (TSs), in which methyl groups were used as substituents in the NHC ligand, all tested density functionals (DFs) were capable to predict the selectivity found in the experimental studies: the linear coupling product. In those systems, the electronic effects of the ligand were prominent compared to the non-covalent interactions (NCI). When crowded NHC ligand was used, in which the methyl groups were replaced by the bulkier 2,6-diisopropylphenyl substituents, dispersion-corrected DFs were required for describing the correct regioselectivity trend.[4] TPSS-D3, x B97X-D, M06-L, and BP86-D3 are consistent DF approaches to predict the regioselectivity trend observed in this NHC-Pd catalyzed Heck reaction, independently of the size of the basis set. In addition, the NCI analysis revealed the role of weak interactions in stabilizing the MI TSs.[5] The main weak interaction responsible for the stabilization of the TSs was found between the NHC moiety and the phenyl rings. In more realistic systems, the weak interaction between the chlorine auxiliary ligand and the 2,6- diisopropylphenyl substituents was responsible for further stabilization of the **rTS1** (Figure 1). TS. Therefore, the attractive dispersion forces should be correctly described to achieve reliable theoretical predictions of the regioselectivity concerning crowded NHC-based palladium catalysts. The present study validated a simpler and feasible computational protocol able to predict the regioselectivity of the current reaction.

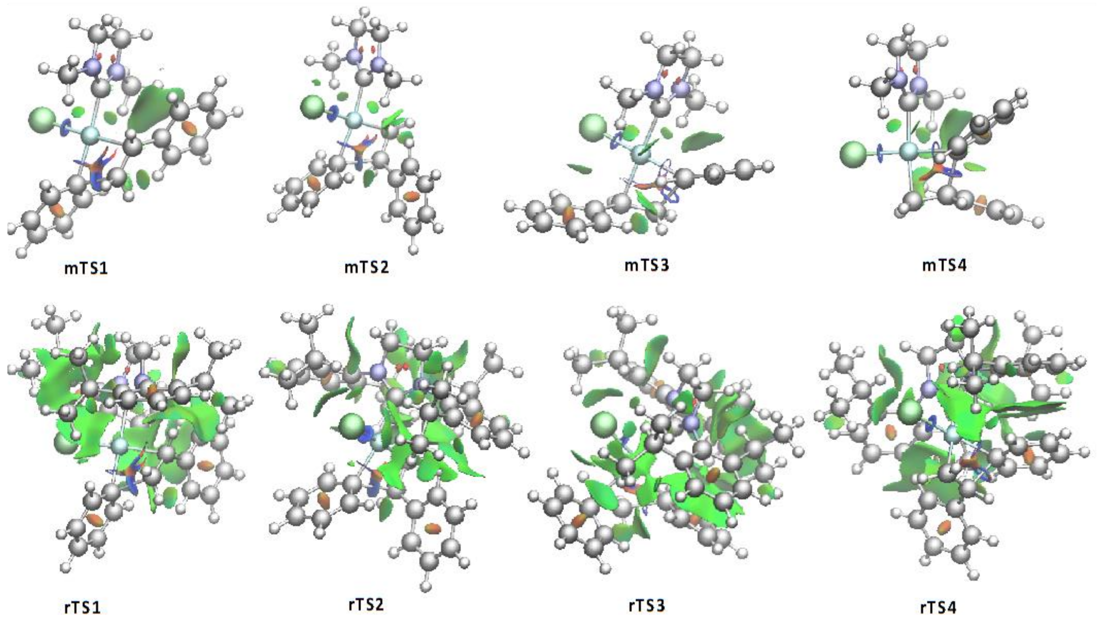

Figure 1. The optimized geometry of MI transition states analyzed to predict the regioselectivity of (NHC)-Pd catalyzed Heck coupling reaction. The model (above) and real (below) ligands were used in present work. NCI analysis using its color scale: green area translates into weak non-covalent interactions among atoms or groups of atoms, red regions depict strong nonbonded overlaps, and blue areas represent strong attractive interactions.

Key-words: N-heterocyclic carbene ligands, Heck reactions, selectivity, non-covalent interactions, DFT methods.

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