Theoretical study of the catalyzed formation and properties of fluorinated cyclopropanes

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As the smallest cycloalkane, the cyclopropane ring is wide spread in both natural and synthetic bioactive molecules.[1] Indeed, its introduction into molecules of biological interest can enhance its biological properties by increasing their bioavailability and metabolic stability due to its high structural rigidity.[2] The fluorine atom displays singular properties thanks to its high electronegativity and its small size. By combining the features of the fluorine atom and cyclopropanes, fluorinated cyclopropyl motifs are of very high interest for the discovery of new bioactive molecules.[3]

This work focuses on understanding the mechanisms of catalytic enantioselective cyclopropanation reaction using density functional theory (DFT, M06-L exchange-correlation functional) with an implicit solvation model (SMD). We were interested in reactions presented in the figure 1[4]. The main aim is the design of new enantioselective synthetic pathways of cyclopropane.

Two main steps were identified:

(1) The generation of the catalytic active Rh-carbene through N_2 elimination.
(2) The formation of the fluorinated cyclopropane.

This molecular modeling helps identifying the structural and electronic features that are responsible for the observed yields and selectivities.

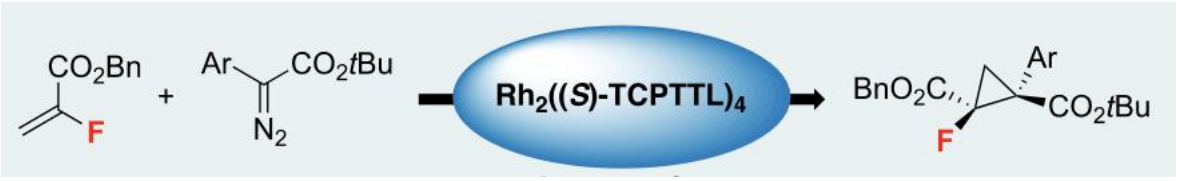

Figure 1. Catalytic Enantioselective cyclopropanation of α-Fluoroacrylates.[4]

Keywords: DFT calculations, fluorinated olefin, diazo, rhodium, cyclopropanes.

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