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Mild Iridium-Catalysed Isomerization of Epoxides. Computational Insights and Application to the Synthesis of β-Alkyl Amines

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Abstract: The isomerization of epoxides to aldehydes using the readily available Crabtree's reagent is described. The aldehydes were transformed into synthetically useful amines by a one-pot reductive amination using pyrrolidine as imine-formation catalyst. The reactions worked with low catalyst loadings in very mild conditions. The procedure is operationally simple and tolerates a wide range of functional groups. A DFT study of its mechanism is presented showing that the isomerization takes place via an iridium hydride mechanism with a low energy barrier, in agreement with the mild reaction conditions.

Keywords: iridium; epoxides; isomerization; Crabtree's catalyst; β-alkyl amines

Epoxides can be interconverted into a variety of functional groups and are thus valuable synthetic intermediates.[1] The high reactivity of the strained 3-membered ring of epoxides commonly enables a wide range of stereospecific nucleophilic ring opening reactions.[2] The isomerization into the corresponding carbonyl analogs is usually referred to as the Meinwald rearrangement.[3] Due to its excellent efficiency and atom economy, this reaction has gained relevance for the synthesis of carbonyl compounds,[4a] ring expansion reactions,[4b,c] and tandem processes.[4d,e] The Lewis acid-promoted Meinwald rearrangement has found application in fine chemistry and industrial processes.[4] However, the regiochemical outcome is a common issue since it depends on the promoter and the migratory capacity of the substituents.[5] The use of stoichiometric amounts of Lewis acids such as $BF_3{\cdot}Et_2O$,[6] lithium salts[7] and magnesium bromide[8] are the most widely used conditions. The catalytic version using copper salts,[9] indium chloride[10] or iridium chloride[11] has also been described. However, a number of limitations, namely moderate product selectivity, high temperature and catalyst loading, and toxicity of the catalysts, remain to be addressed when employing catalytic conditions.

In recent years, other alternative procedures have been reported such as the use of metal-free self-assembled organic supramolecular capsules[12] or heterogeneous mesoporous aluminosilicate materials.[13] In the organometallic field, Mazet and co-workers reported the most relevant breakthrough using novel palladium[14] and iridium[15] catalysts. However, high temperatures (85–140 °C and 100 °C respectively) were needed in both cases.

We recently reported that the readily available Crabtree's reagent[16] is an efficient catalyst for the isomerization of *N*-sulfonyl aziridines into allyl amines (Figure 1A).[17] Encouraged by this result we envisioned that this catalyst could also be used in the isomerization of epoxides. We found that, after activation,[18] Crabtree's catalyst isomerized terminal epoxides into aldehydes (Figure 1B). One of the drawbacks of this transformation was the handling of the resulting aldehydes. Therefore, we set up a one-pot