Rhodium-Catalyzed Oxidative Amidation of Sterically Hindered Aldehydes and Alcohols

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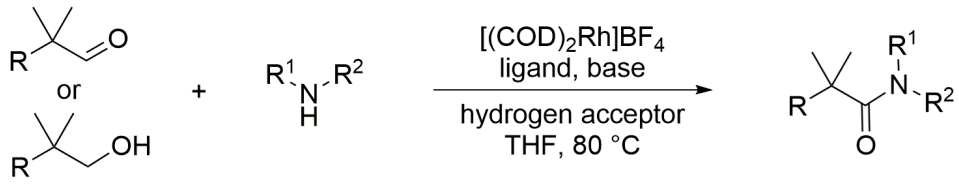
Amides are one of the most important functional groups in organic chemistry, commonly found in natural products, pharmaceuticals and agrochemicals. Amide synthesis has been traditionally accomplished via the coupling of carboxylic acids and amines, using highly reactive acid chlorides, anhydrides, or coupling reagents. This method, while effective, generates large amounts of high molecular waste. In recent years, metal-catalyzed oxidative amidation of aldehydes and alcohols has emerged as a powerful alternative to traditional methods. However, sterically hindered substrates have proven to be particularly challenging while less nucleophilic amines, such as anilines, give significantly diminished yields. These issues have been addressed with the development of a rhodium-catalyzed oxidative amidation of sterically hindered aldehydes and alcohols for the synthesis of amides containing a quaternary carbon at the alpha position. A variety of amine nucleophiles, both aliphatic and aromatic, are employed.



Small Molecule Channels Restore Physiology in Yeast by Collaborating with Endogenous Ion Pumps to Promote Potassium Uptake

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Human diseases caused by dysfunctional or missing protein ion channels have life-threatening consequences for patients. These diseases known as channelopathies impair the physiological functions of different organs, tissues, and body systems. To date, more than 30 channelopathies are incurable, demonstrating the need for new therapeutic strategies. We asked whether imperfect small molecule ion channel mimics could restore physiology in protein-ion-channel-deficient cells. We hypothesize that ion-channel-forming small molecules could work in collaboration with cellular networks of proteins involved in promoting physiological transmembrane ion gradients, to restore physiology in protein deficient Saccharomyces cerevisiae (S.cerevisiae). Here we show that ion-channel-forming small molecules vigorously and sustainably rescue growth in potassium transporter deficient S.cerevisiae. Furthermore, we demonstrate that imperfect small molecule ion channel mimics are sufficient to promote potassium uptake in a dose- and time-dependent manner. Our findings help lay the foundation for the utilization of imperfect small molecule mimics as a viable new strategy for the treatment of diseases caused by dysfunctional or missing proteins.