Synthesis of Deuterated Alcohols via Hydrogen Transfer Process Catalyzed by Iridium Complexes

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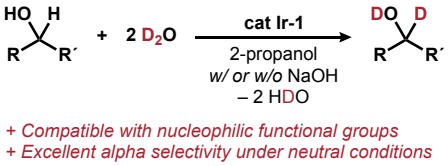
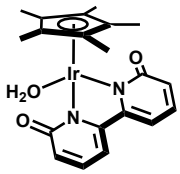
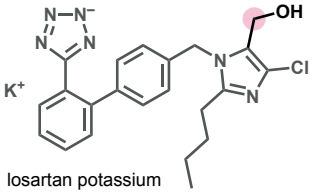
Deuterium incorporation at the α-position of hydroxyl groups is an attractive strategy to improve the stability of drugs, as the alcohol moiety in pharmaceuticals is often susceptible to metabolism. While several transition-metal catalysts for the deuteration of alcohols have been reported,[1] many of these catalysts tend to be deactivated by nucleophilic functional groups such as imidazole and tetrazole. Thus, chemoselective α-deuteration of highly functionalized alcohols remains a significant challenge.

We herein report the α-selective, iridium(III)-bipyridonate-catalyzed deuteration of alcohols using deuterium oxide (D_2O) as the primary deuterium source. We chose an iridium−bipyridonate complex (**Ir-1**) for the direct deuteration of alcohols through hydrogen transfer process because **Ir-1** is known as a structurally robust, excellent catalyst for reversible dehydrogenation of alcohols, as demonstrated by Fujita and coworkers.[2] Unlike known catalytic systems, the present deuteration method enabled the direct, chemoselective deuteration of primary and secondary alcohols under basic or neutral conditions without being affected by coordinative functional groups. Successful substrates for deuterium labelling include the pharmaceuticals losartan potassium, rapidosept, guaifenesin, and diprophylline.





Ir-1



losartan potassium

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