Air-Tolerant and Extremely Fast Lithium-Based Birch Reduction Enabled by Mechanochemistry

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Birch reduction has been widely used in organic synthesis for over half a century as a powerful method to dearomatize arenes.[1] However, the conventional Birch reduction reaction using liquid ammonia requires laborious procedures. Although several remarkable ammonia-free modifications have been reported, these solution-based protocols still require an inert atmosphere and strictly dehydrated conditions. The development of an operationally simple, efficient, and scalable protocol remains a challenge.

Based on our experiences with mechanochemical synthesis with bulk metals,[2] we hypothesized that the development of mechanochemical lithium-based Birch reduction might overcome these issues. The *in-situ* mechanical agitation provided by ball milling would accelerate the activation of bulk metal. Meanwhile, the reduced contact of the reactive organometallic species with gaseous oxygen and water under solvent-less conditions leads to significant tolerance of atmospheric conditions. In this study, we have achieved the first mechanochemical approach for lithium-based ammonium-free Birch reduction *in air* at room temperature using a ball mill. The entire synthetic procedure can be conducted under atmospheric conditions without any special precautions or elaborate synthetic techniques. Owing to the *in-situ* mechanical activation of lithium metal, the mechanochemical Birch reduction was extremely fast and completed within *one minute* for a broad range of substrates. The rapid and selective Birch reduction of bioactive targets showcased the generality of this mechanochemical protocol. The success of the gram-scale reduction within one minute implies the possibility of highly efficient scaled-up synthesis.[3]

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