The KA^2 coupling under sustainable metal catalysis: assembly of tetrasubstituted propargylamines and theoretical study of the manganese-catalyzed version

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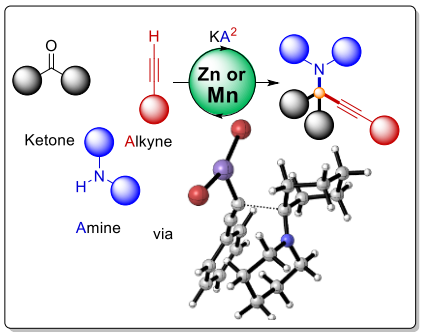
Propargylamines are a unique class of compounds, serving as versatile synthons for a variety of organic transformations and possessing intrinsic value due to the biological properties exhibited by some of them [1-3]. Recently, the KA^2 coupling reaction (Ketone-Amine-Alkyne) emerged as a highly useful tool, providing facile access to tetrasubstituted propargylamines [2,3]. In this regard, our research group has contributed by developing novel, sustainable catalytic systems for the KA^2 coupling. As demonstrated by our recent results, the "green", zinc-based protocol has a wide substrate scope, leading to the functionalization of challenging molecular scaffolds [3,4]. Additionally, the efficiency of manganese(II) in this transformation was unlocked in higher temperatures, and DFT calculations were used to rationalize the mode of action of manganese-acetylide intermediates and other key species involved, thus unravelling important aspects of this reaction for the first time (Scheme 1) [5].



Scheme 1: The KA^2 coupling reaction under zinc or manganese catalysis.

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