

Synthesis of 1,4-disubstitued homoallylic alcohols in one step using a nickel-catalysed three-component coupling reaction



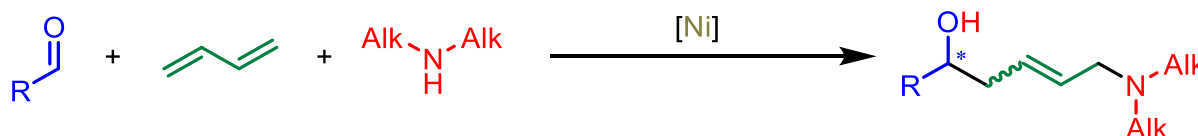
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Homoallylic alcohols represent a crucial category of compounds in organic chemistry, characterized by the presence of a hydroxyl group and a double bond that can be further transformed. Their structure makes them excellent precursors for the synthesis of more complex molecules that are of interest in the field of pharmaceutical chemistry¹. The synthesis of these compounds typically involves the reaction between a carbonyl derivative and an allylation reagent, often employing catalysis.² However, this traditional synthetic method often leads to the formation of stoichiometric amounts of salts or undesirable by-products. New synthetical approaches have been developed for the synthesis of 1,4-disubstitued homoallylic alcohols, employing transition metals oxidative coupling reaction with aldehydes and 1,3-dienes.³ In this chemistry, nickel emerges as a particularly attractive choice of metal due to its abundance and low cost compared to other precious metals such as palladium. This communication presents an unprecedented nickel-catalyzed reaction that involves a coupling step followed by the nucleophilic attack of a nucleophile such as a secondary amine (Scheme 1).



Scheme 1: Nickel-catalysed coupling reaction between an aldehyde, a 1,3-diene and a secondary amine

This reaction, carried out in a single step (one-pot), achieves a 100% atom economy. This eco-friendly approach allows for the simultaneous formation of C-C, C-N bonds and introduces an asymmetric carbon. An optimization phase was conducted to investigate the impact of various parameters (temperature, solvent, etc.) and to understand the limitations in terms of substrates, nucleophiles, dienes, and other factors.

References

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