

Convenient Synthesis of Pyrrolidine by Amphiphilic Allylation

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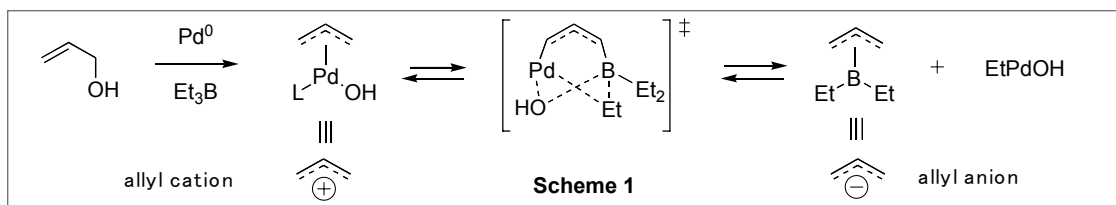
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Abstract

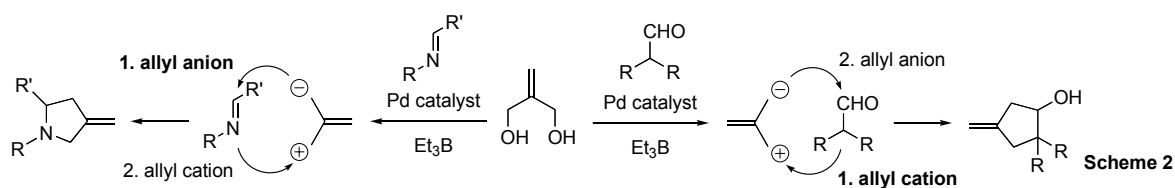
The combination of Pd(0) catalyst and triethylborane promotes the amphiphilic allylation of aldimine with 2-methylenepropane-1,3-diol in the order of nucleophilic-electrophilic attack to provide pyrrolidine in one-pot under mild conditions.

Introduction

We have developed that a combination of Pd-catalyst and Et₃B activates allyl alcohol as an allyl cation and an allyl anion species for allylic alkylations (Scheme 1). Et₃B promoted allyl alcohol to undergo the oxidative addition of a Pd(0) species via coordination to the hydroxy group to form π -allylpalladium, which serves as an allyl cation equivalent toward a variety of soft nucleophiles to cause electrophilic allylation (Tsuji-Trost type reaction).¹ In the absence of nucleophiles, π -allylpalladium is subjected to an allyl-ethyl exchange reaction, providing allyl diethylborane as an allyl anion equivalent, which reacts with benzaldehyde and aldimines to provide homoallyl alcohols and homoallylamines,² respectively (umpolung of π -allylpalladium). Furthermore, the similar catalytic system accelerates the amphiphilic allylation of alkyl aldehydes with 2-methylenepropane-1,3-diol to provide 3-methylenecyclopentanol via electrophilic–nucleophilic allylation (Scheme 2).³



Here we would like to report the sequential amphiphilic allylation of aldimines with 2-methylenepropane-1,3-diol in the order of nucleophilic-electrophilic allylation to provide 3-methylenepyrrolidines under similar catalytic system.⁴ Notably, the order of the amphiphilic allylation of aldimines is apparently opposite to that of aldehydes.

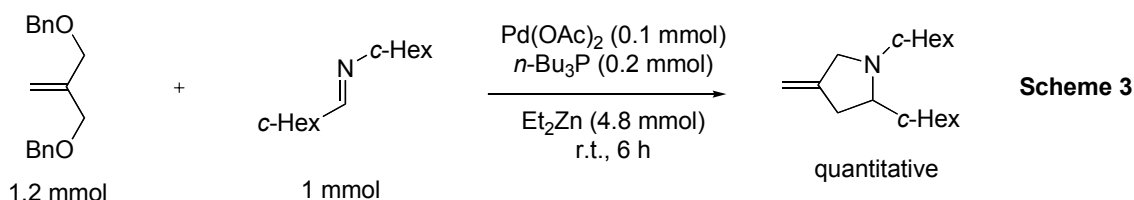


Experimental

The reaction was conducted as follows: in situ formation of aldimines prepared from aldehydes and amines via azeotropic distillation of THF-H₂O two times, and exposure of the aldimines residue to a mixture of 2-methylenepropane-1,3-diol, Pd(OAc)₂, *n*-Bu₃P, and Et₃B at 50 °C under nitrogen atmosphere.

Results and Discussions

The reaction tolerates a wide variety of aldimines generated from aromatic and aliphatic aldehydes and primary amines to provide 3-methylenepyrrolidines in high yields. Et₂Zn is also effective for the amphiphilic allylation of aldimines with 1,3-dibenzyloxy-2-methylenepropane under similar Pd catalytic system. On the contrary to the result of 2-methylenepropane-1,3-diol with Et₃B, Et₂Zn promotes the amphiphilic allylation of the aldimine composed of cyclohexanecarboxyaldehyde and cyclohexylamine to provide 3-methylenepyrrolidine at room temperature in quantitative yield (Scheme 3).



Conclusions

The catalytic system of Pd catalyst and triethylborane promotes aldimines to undergo the sequential amphiphilic allylation with 2-methylenepropane-1,3-diols. This reaction would be utilized for the efficient synthesis of physiologically active molecules, pyrrolidines and proline derivatives.

References

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