Convenient Synthesis of Pyrrolidine by Amphiphilic Allylation

Katsumi Tohyama¹, Yumi Yamaguchi², Masanari Kimura²*
¹Graduate School of Science and Technology,
²Department of Applied Chemistry, Faculty of Engineering,
Nagasaki University, 1-14 Bunkyo-machi, Nagasaki 852-8521, Japan
*Tel: +81-95-819-2679, Fax: +81-95-819-2683, E-mail: masanari@nagasaki-u.ac.jp

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Abstract

The combination of Pd(0) catalyst and triethylborane promotes the amphiphilic allylation of aldimine with 2-methylene propane-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-allylpalldium, 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-allylpalldium 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-allylpalldium). Furthermore, the similar catalytic system accelerates the amphiphilic allylation of alkyl aldehydes with 2-methylene propane-1,3-diol to provide 3-methylene cyclopentanol via electrophilic–nucleophilic allylation (Scheme 2).³

Here we would like to report the sequential amphiphilic allylation of aldimines with 2-methylene propane-1,3-diol in the order of nucleophilic-electrophilic allylation to provide 3-methylene pyrrolidines 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-H$_2$O two times, and exposure of the aldimines residue to a mixture of 2-methylene propane-1,3-diol, Pd(OAc)$_2$, $n$-Bu$_3$P, and Et$_3$B 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-methylene pyrrolidines in high yields. Et$_2$Zn is also effective for the amphiphilic allylation of aldimines with 1,3-dibenzyl oxy-2-methylene propane under similar Pd catalytic system. On the contrary to the result of 2-methylene propane-1,3-diol with Et$_3$B, Et$_2$Zn promotes the amphiphilic allylation of the aldimine composed of cyclohexanecarboxy aldehyde and cyclohexylamine to provide 3-methylene pyrrolidine 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-methylene propane-1,3-diols. This reaction would be utilized for the efficient synthesis of physiologically active molecules, pyrrolidines and proline derivatives.

References