Sequential Amphiphilic Allylation of Aldimines with 2-Methylenepropane-1,3-diols

Masanari Kimura1*, Takato Tamaki1, Yoshinao Tamaru2

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: +81-95-819-2684, E-mail: masanari@nagasaki-u.ac.jp

Key Words; Palladium, Triethylborane, Aldimine, Pyrrolidine, Amphiphilic Allylation

Abstract
The combination of Pd catalyst and triethylborane promotes amphiphilic allylation of aldime with 2-methylenepropane-1,3-diol in the order of nucleophilic-electrophilic attack to provide pyrrolidine under mild conditions.

Introduction
We have developed the first direct allylic activation of allyl alcohol promoted by Pd-catalyst and Et3B. Et3B activates allyl alcohol toward oxidative addition of a Pd(0) species by 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). 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 or aldimes to provide homoallyl alcohols or homoallylamines, respectively (umpolung of π-allylpalladium) (Scheme 1). Here we would like to report the sequential amphiphilic allylation of aldimes with 2-methylenepropane-1,3-diol in the order of nucleophilic-electrophilic allylation to provide 3-methylenepyrrrolidines under similar catalytic system.

\[
\begin{align*}
\text{Pd(0)} & \quad \text{Et}_2\text{B} \\
\text{Et}_3\text{B} & \quad \text{OH} \\
\text{Nu} & \quad \text{PhCHO or RN=CHR'} \\
\text{Ph} & \quad \text{R'}
\end{align*}
\]
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. The representative results are summarized in Table 1 and Scheme 2.

Results and Discussions

The reaction tolerates a wide variety of aldimines, except for the combination of aliphatic aldehyde and aliphatic amines. Et₂Zn is also effective for the amphiphilic allylation of aldimines with 1,3-dibenzyloxy-2-methylenepropane in the presence of Pd catalyst under mild conditions. On the contrary to the result of 2-methylenepropane-1,3-diol with Et₃B (run 4 in Table 1), 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, pyrrolidine and proline derivatives.

References