

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

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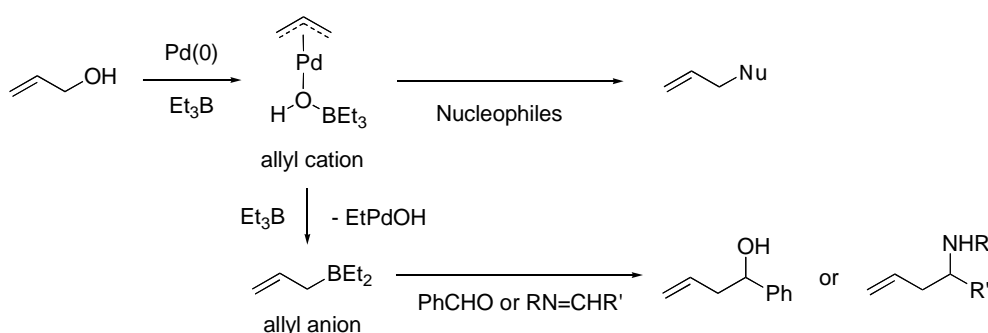
Key Words; Palladium, Triethylborane, Aldimine, Pyrrolidine, Amphiphilic Allylation

Abstract

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

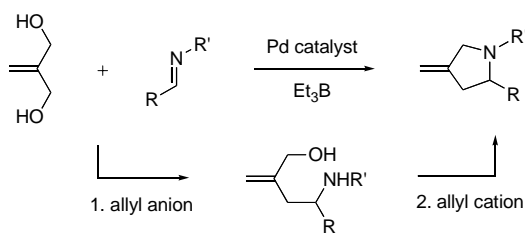
Introduction

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).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 or aldimines to provide homoallyl alcohols² or homoallylamines,³ respectively (umpolung of π -allylpalladium) (Scheme 1). 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.



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.



Scheme 2

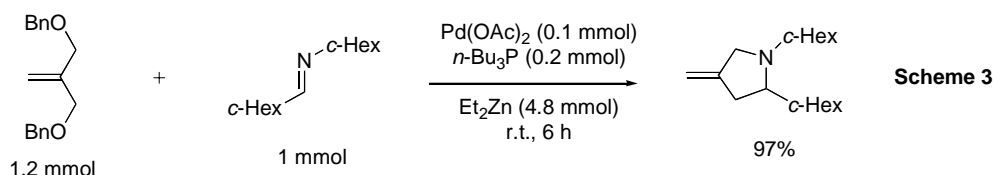
Table 1. Pd/Et₃B Promoted Allylation with 2-Methylenepropanediol

run	R	R'	yield of pyrrolidine (%)
1	Ph	<i>p</i> -Anis	80
2	Ph	Bn	71
3	<i>c</i> -Hex	<i>p</i> -Anis	68
4	<i>c</i> -Hex	<i>c</i> -Hex	0

1) Aldehyde (1 mmol) and amine (1.05 mmol) in THF (1 mL) at 75 °C for 0.5 h, then removal by distillation, addition of THF (1 mL) and distillation two additional times. 2) Pd(OAc)₂ (0.1 mmol), *n*-Bu₃P (0.2 mmol), 2-methylenepropan-1,3-diol (1.2 mmol), Et₃B (4.8 mmol) at 50 °C for 18 h.

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 cyclohexancarboxyaldehyde and cyclohexylamine to provide 3-methylenepyrrolidine at room temperature in quantitative yield (Scheme 3).



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

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