Highly efficient and regioselective allylic amination of allylic alcohols catalyzed by [Mo₃PdS₄] cluster

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ABSTRACT

A highly efficient and regioselective allylation reaction of amines with allylic alcohols under mild conditions catalyzed by the cubane-type sulfido cluster [(Cp*Mo)₃S₄Pd(dba)][PF₆] with H₃BO₃ as an additive has been developed. A variety of amines and allylic alcohols are investigated, and in the case of allylic alcohols bearing substituents at either α- or γ-position only linear allylic amination products are obtained.

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Palladium-catalyzed allylation reaction, known as Tsuji-Trost reaction, is a powerful and well-established synthetic method for C–C and C–heteroatom bond formation.[1] General allylic substrates for this transformation are acetates, carbonates, and other related derivatives of allylic alcohols, while the allylic alcohol is seldom directly used in allylation reaction due to the inherent weak leaving capability for the OH group. Compared with allylic halides and esters, the direct use of allylic alcohol is more profitable. One reason is that the reaction of allylic alcohols forms water as a co-product whereas allylic halides and esters afford the corresponding salt wastes under basic conditions. The other one is that allylic halides and esters are derivatives of allylic alcohol. Despite the merits associated with the direct use of allylic alcohol, successful application of allylic alcohol without any activating reagents is less reported.[2] In order to promote the cleavage of C–O bond, some Lewis acids, such as As₂O₃,[3] B₂O₃,[4] BEt₃,[5] BPh₃,[6] SnCl₂,[7] Ti(OⁱPr)₄,[8] CO₂,[9] Nb(OEt)₅,[10] as additives are used.

Tamaru and co-workers[5] ever described Pd(PPh₃)₄-catalyzed allylation of amines and indoles with allylic alcohols using toxic and highly volatile triethylborane as an additive. Recently, an allylation with allylic alcohol in H₂O/AcOEt catalyzed by [Pd (η³-C₃H₅)Cl]₂/tppts was demonstrated,[11] and Lipshutz group[12] reported the amination of allylic alcohols in 2 wt % PTS/water catalyzed by [Pd(η³-C₃H₅)Cl]₂ together with HCO₂Me as additive and K₂CO₃ as base. However, both of these catalytic systems yield a mixture of linear and branched products with allylic alcohol bearing a methyl substituent at the α- or γ-position.

A series of metal-sulfur cubane-type clusters have been synthesized and investigated for various catalytic activities.[13] In particular, the cubane-type clusters with Mo₃M′S₄ core have drawn much attention because of their unique catalytic activity for intramolecular cyclization of alkynoic acids[14] and aminoalkynes[15] to enol lactones and cyclic imines, respectively. To the best of our knowledge, the allylation reaction catalyzed by the cubane-type clusters has never been documented. Herein, we wish to demonstrate for the first time an efficient allylation reaction of amines with allylic alcohols under mild conditions catalyzed by [(Cp*Mo)₃S₄Pd(dba)][PF₆][16] (Cp* = η⁵-C₅Me₅; dba = dibenzylideneacetone) (Fig. 1) with H₃BO₃ as an additive.

First we investigated the allylation of N-methylaniline using allyl alcohol in the presence of 5 mol % [(Cp*Mo)₃S₄Pd(dba)][PF₆] with boron reagents.
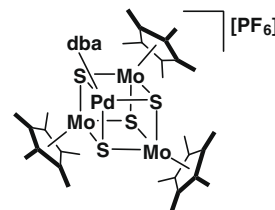
Figure 1. The structure of [(Cp*Mo)₃S₄Pd(dba)][PF₆].

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Table 1
Allylation reaction in the presence of boron reagents[a]

$$\text{allyl-OH} + \text{PhNHMe} \xrightarrow[\text{CH}_2\text{Cl}_2, \text{ reflux}]{\begin{array}{c}5 \text{ mol% } [(Cp^*Mo)_3S_4Pd(dba)][PF_6]\\ 0.5 \text{ eq. boron reagent}\end{array}} \text{Ph-N(allyl)}$$
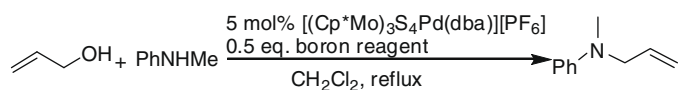
Entry	Boron reagent	Time (h)	Yield[b] (%)
1	None	12	0
2	B_2O_3	4	16
3	BEt_3	4	16
4	H_3BO_3	4	96
5[c]	H_3BO_3	12	13
6	$PhB(OH)_2$	4	96
7	$B(OMe)_3$	4	98

[a] Reaction conditions: allyl alcohol 0.4 mmol, N-methylaniline 0.4 mmol, Cat. 0.02 mmol, boron reagent 0.2 mmol, CH_2Cl_2 1 mL.
[b] Yields were determined by GC using naphthalene as an internal standard.
[c] H_3BO_3 0.12 mmol.

As shown in Table 1, using 0.5 equiv H_3BO_3, $B(OMe)_3$, and $PhB(OH)_2$ as additives, allyl alcohol and N-methylaniline were smoothly converted to N-allyl-N-methylaniline with excellent yield (96–98%) under mild conditions in 4 h, while no product could be isolated without boron additives. Decreasing the loading of H_3BO_3 to 0.3 equiv, the yield was low. BEt_3 was a useful additive for Pd(PPh$_3$)$_4$-catalyzed allylic amination of allyl alcohol,[5] while only 16% yield was obtained in our reaction under similar conditions. Additionally, B_2O_3 also had lower activity for this catalytic system. With the consideration of the stability and easy operation, we chose H_3BO_3 as additive and screened a series of Pd catalysts and other cubane-type sulfido clusters. The results are summarized in Table 2.

From Table 2, it can be seen that general Pd catalysts including Pd(dba)$_2$ (Table 2, entries 1–4) have no activity for this reaction except Pd(PPh$_3$)$_4$ which is less active than $[(Cp^*Mo)_3S_4Pd(dba)][PF_6]$. Incomplete cubane-type cluster[16] (entry 5) and other cubane-type sulfido clusters bearing Ni[14b] or Ru[16,17] do not work or only give low yield. The ligand on the Pd of cubane-type sulfido cluster also has profound effect. $[(Cp^*Mo)_3S_4Pd(dba)][PF_6]$ with dba as ligand prepared from Pd(dba)$_2$ with $[(Cp^*Mo)_3S_4][PF_6]$ has the best activity while $[(Cp^*Mo)_3S_4Pd(PPh_3)][PF_6]$[16] with PPh$_3$ as ligand has no activity (entries 6–7).

Encouraged by this result, we further investigated the allylation reaction of primary and secondary amines with allylic alcohol.[18] Besides N-methylaniline, other secondary amines (Table 3, entries 1–3) were examined and good yields were obtained. Particularly, acetanilide which has lower nucleophilicity than N-methylaniline also gave a good 72% isolated yield in 12 h.

Table 2
Catalytic activity of several Pd complexes and cubane-type sulfido clusters[a]

Entry	Cat.	Time (h)	Yield[b] (%)
1	Pd(dba)$_2$	4	0
2	Pd(PPh$_3$)$_4$	4	70
3	PdCl$_2$	4	0
4	PdCl$_2$(PPh$_3$)$_2$	4	0
5	$[(Cp^*Mo)_3S_4][PF_6]$	4	0
6	$[(Cp^*Mo)_3S_4Pd(dba)[PF_6]$	4	96
7	$[(Cp^*Mo)_3S_4Pd(PPh_3)][PF_6]$	4	0
8	$[\{(Cp^*Mo)_3S_4Ni\}_2(cod)][PF_6]_2$	4	0
9	$[\{(Cp^*Mo)_3S_4Ni\}_2(cod)][PF_6]_2$	24	26
10	$[(Cp^*Mo)_3S_4RuH_2(PPh_3)][PF_6]$	4	0
11	$(Cp^*Mo)_3S_4RuCl_3$	4	0

[a] Reaction conditions: allyl alcohol 0.4 mmol, N-methylaniline 0.4 mmol, Cat. 0.02 mmol, H_3BO_3 0.2 mmol, CH_2Cl_2 1 mL, reflux.
[b] Yields were determined by GC using naphthalene as an internal standard.

Table 3
Catalytic allylation of allyl alcohol with amines[a]

Entry	Nucleophile	Time (h)	Product	Yield[b] (%)
1	Ph-NH-C(O)CH$_3$	12	Ph-N(allyl)-C(O)CH$_3$	72
2	Ph-NH-CH$_2$Ph	10	Ph-CH$_2$-N(Ph)(allyl)	95
3[c]	Bn$_2$NH	24	Bn$_2$N(allyl)	68
4	PhNH$_2$	8	Ph-NH-allyl **1a**	61
			Ph-N(allyl)$_2$ **1b**	15
5[d]	PhNH$_2$	8	**1a**	87
			1b	3
6[e]	ArNH$_2$	24	Ar-NH-allyl **2a**	34
			Ar-N(allyl)$_2$ **2b**	30
7[f]	ArNH$_2$	24	**2b**	86

[a] Reaction conditions: allyl alcohol 0.4 mmol, amine 0.4 mmol, $[(Cp^*Mo)_3S_4Pd(dba)][PF_6]$ 0.02 mmol, H_3BO_3 0.2 mmol, CH_2Cl_2 1 mL, reflux.
[b] Isolated yield.
[c] 1,2-Dichloroethane as solvent, 80 °C.
[d] Aniline/allyl alcohol = 2:1 (mole ratio).
[e] ArNH$_2$ = 2,4,6-trimethylaniline.
[f] ArNH$_2$ = 2,4,6-trimethylaniline, ArNH$_2$/allyl alcohol = 1:4 (mol ratio), H_3BO_3 0.4 mmol.

For the primary amines, when equivalence of aniline and allyl alcohol was applied, the ratio of the mono- and diallylation product was 80:20 (Table 3, entry 4), and with 2 equiv of aniline the selectivity of mono-alkylation was much better (96:4) (Table 3, entry 5). Ozawa et al.[19] reported that (π-allyl)palladium complexes bearing sp^2-hybridized phosphorous ligands (0.1 mol %) could catalyze the amination of allyl alcohol with 2 equiv of aniline to give 91% of mono- and 8% of diallylation product, respectively. Although the selectivity of 2,4,6-trimethylaniline was not satisfying when using equivalence of allyl alcohol, excessive allyl alcohol (4 equiv) could give diallylation product successfully.

The control of the regioselectivity of allylation with allylic alcohol is very important. Thus we examined a series of allylic alcohols bearing a methyl or a phenyl substituent at either α- or γ-position for their regioselectivity (Table 4). Those allylic alcohols all gave linear products without any detection of branched products. For example, both crotyl alcohol and 3-butene-2-ol (Table 4, entries 3–4) smoothly reacted with N-methylaniline to produce the corresponding linear product N-(2-butenyl)-N-methylaniline. These results apparently indicated that each of the two pairs of reactions proceeded via a common π-allylpalladium intermediate. 2-Methyl-3-buten-2-ol (Table 4, entry 7) with increased steric bulk at α-position led to decreased yields (40%). Elevating the reaction temperature (1,2-dichloroethane as solvent, 80 °C) or using $B(OMe)_3$ as additive could improve the yield. (Table 4, entries 8–9).

Although the reaction mechanism of the present catalytic system has not been fully elucidated, the proposed mechanism was shown in Scheme 1. The hydroxy group of allyl alcohol may coordinate to boric acid to promote the formation of π-allylpalladium intermediate. Then nucleophile attacks the intermediate to give the corresponding product. This process is analogous to Pd-catalyzed allylation reaction with BEt_3 as an additive.[5] $(Cp^*Mo)_3S_4$ fragment can be regarded as a bulky ligand to provide steric hindrance avoiding the formation of branched products.

Table 4
Catalytic allylation of *N*-methylaniline with allylic alcohols[a]

Entry	Allylic alcohol	Time (h)	Product	Yield [b] (%)
1	Ph⌒⌒OH	8	Ph⌒⌒N(Ph)	95
2	(OH, Ph)	8	Ph⌒⌒N(Ph)	94
3	(OH)	12	⌒⌒N(Ph)	89 (E:Z = 7.6:1)
4	⌒⌒OH	14	⌒⌒N(Ph)	93 (E:Z = 6.2:1)
5	(OH)	12	N(Ph)	90
6	(OH)	12	⌒N(Ph)	87
7	(OH)	24	⌒N(Ph)	40
8[c]		24		79
9[d]		24		85

[a] Reaction conditions: allylic alcohol 0.4 mmol, *N*-methylaniline 0.4 mmol, [(Cp*Mo)$_3$S$_4$Pd(dba)][PF$_6$] 0.02 mmol, H$_3$BO$_3$ 0.2 mmol, CH$_2$Cl$_2$ 1 mL, reflux.
[b] Isolated yield.
[c] 1,2-Dichloroethane as solvent, 80 °C.

In summary, under mild conditions the highly efficient and regioselective allylic amination of allylic alcohols catalyzed by [(Cp*Mo)$_3$S$_4$Pd(dba)][PF$_6$] with H$_3$BO$_3$ as additive has been described. A variety of allylic alcohols and amines are investigated. The reaction proceeds with excellent regioselectivity, leading to linear product for allylic alcohols bearing a methyl or a phenyl substituent at either α- or γ-position.

Acknowledgments

References and notes

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18. *General procedure for the allylation reaction of amines with allylic alcohol*: All manipulations were carried out under Ar atmosphere by using standard Schlenk techniques. The solvents were dried by common procedures and distilled before use. *N*-Allyl-*N*-benzylphenylamine (Table 3, entry 2): [(Cp*Mo)$_3$S$_4$Pd(dba)][PF$_6$] (25 mg, 0.02 mmol) and boric acid (12 mg, 0.2 mmol) were added to a 25 mL Schlenk tube, then CH$_2$Cl$_2$ (1 mL), *N*-benzylaniline (70 mg, 0.4 mmol), and allyl alcohol (22 mg, 0.4 mmol) were added stepwise. The tube was sealed and heated to reflux until the appointed time. The products (81 mg, 95% yield) were obtained by column chromatography on silica gel (eluent: petroleum ether/EtOAc, 20:1).
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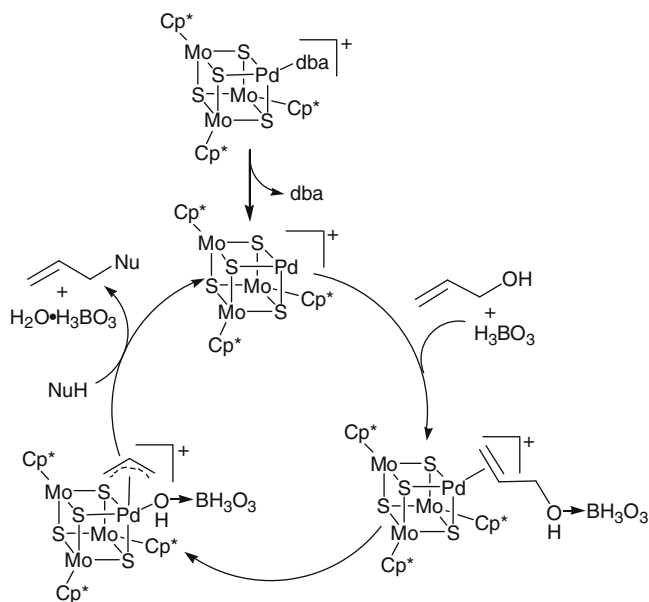
Scheme 1. Proposed mechanism for allylation reaction.