

Tsuji–Trost N-Allylation with Allylic Acetates by Using a Cellulose–Palladium Catalyst

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Keywords: Allylic compounds / Amines / Allylation / Palladium / Heterogeneous catalysis

Allylic amines were synthesized by a simple procedure using a biodegradable and easily recyclable heterogeneous cellulose–Pd catalyst through *N*-allylation of primary and secondary amines. The scope of this protocol includes aliphatic and

Introduction

Allylic compounds such as allylic acetates, allylic alcohols, allylic halides, and allylic carbonates undergo the Tsuji–Trost reaction with various nucleophiles such as phenols, amines, and active methylene compounds in the presence of palladium to generate allylated nucleophiles.^[1] The Tsuji–Trost transformation plays an important role in the total synthesis of alkaloids such as strychnine,^[2] rosephilin,^[3] and (+)- γ -lycorane^[4] and other natural products such as hamigeran B.^[5] The preparation of allylamines by *N*-allylation of amines is an important organic transformation, as these compounds are often used in the construction of natural products and amino acids.^[6] The η^3 -allyl–Pd complex, obtained from allyl acetates, can couple with amines to produce allylamines through a mild and selective synthetic route.^[7]

At present, nonrenewable petrochemicals are the major source of polymer matrices. In view of this, an alternative ecofriendly polymer support is essential. The use of naturally abundant cellulose as a replacement may well serve the purpose. Studies on the application of cellulose and other bioderived polymers as heterogeneous supports in catalysis proved that these compounds can serve as efficient and cheap alternatives. Cellulose-supported palladium and copper particles have been used to catalyze C–C and C–N coupling reactions in various organic solvents.^[8] Earlier, a cellu-

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201201241.

benzylamines with substituted and unsubstituted allyl acetates and culminates in high yield syntheses. The highlights of the protocol include a ligand-free reaction, simple workup, and catalyst recyclability.

lose-supported Pd catalyst was used with a special phosphane ligand, tris(3-sulfophenyl)phosphane trisodium salt (TPPTS), for the *N*-allylation of cinnamyl carbonate with morpholine.^[9] Recently, we demonstrated the preparation of allyl acetates by a simple and facile Heck-type arylation reaction by using palladium supported on magnetic Fe_3O_4 .^[10]

Results and Discussion

In view of earlier success with supported palladium and the need to further investigate the application of allyl acetates, there is encouragement to explore benign supports such as cellulose. Thus, there is motivation to establish a more general and ligand-free protocol for *N*-allylation reactions by using a cellulose–Pd catalyst. Pd⁰ was immobilized on the surface of cellulose microcrystals by reducing PdCl₂ in an aqueous suspension of cellulose with the use of sodium borohydride at room temperature to afford the cellulose–Pd catalyst (Figure 1).



Figure 1. Synthesis of the cellulose-supported Pd catalyst.

Inductively coupled plasma-atomic emission spectroscopy (ICP-AES) analysis showed the weight percentage of Pd to be 9.8. The Pd catalyst was characterized by powder XRD. Immobilization of Pd^0 on the cellulose matrix was confirmed by the presence of characteristic Pd^0 signals in the spectrum (Figure 2).



SHORT COMMUNICATION



Figure 2. Powder XRD pattern for the (a) blank cellulose support and (b) cellulose–Pd catalyst.

In our continued investigations, we employed the cellulose–Pd catalyst in the *N*-allylation of amines with allylic acetates in the presence of K_2CO_3 as base. In the first attempt, a mixture of piperidine, cinnamyl acetate, K_2CO_3 , and the Pd catalyst in water was heated at reflux for 12 h. The desired product was not formed, and the full amount of cinnamyl acetate underwent hydrolysis to produce allyl alcohol. To optimize the reaction conditions, a series of experiments was carried out (Table 1).

Table 1. Standardization of reaction condition.[a]

Ph 🧹	OAc + cellulose-		Ph
	3a N K ₂ CO ₃ , sol H 4a 15 h	vent	5a
Entry	Solvent	<i>T</i> [°C]	Yield [%]
1	H ₂ O	100	0
2	THF	66	10
3	DMF	90	41
4	DMF	110	87
5	CH ₃ CN	82	35
6	toluene	100	16
7	toluene (cellulose–Pd ^{II})	100	9
8	DMF (MW, 200 W, 15 min)	100	23
9	CH ₃ CN (MW, 200 W, 15 min)	80	20
10	toluene (MW, 280 W, 15 min)	92	15

[a] Reaction conditions: Allyl acetate (1.0 mmol), amine (1.2 mmol), cellulose–Pd (50 mg), and potassium carbonate (2.0 mmol) in solvent (3 mL) subjected to the listed conditions.

The effect of Pd^{II} was studied by immobilization of cellulose microcrystals on the surface by stirring a methanol suspension of cellulose and PdCl₂ in an aqueous ammonia solution for 15 h at room temperature. When the reaction was performed with the cellulose–Pd^{II} catalyst, a poor yield of the desired product was obtained (Table 1, entry 7). Among the various conditions explored to optimize the reaction, heating in DMF at 110 °C for 15 h produced the maximum yield (Table 1, entry 4). Using these optimized conditions, the reaction was studied for its substrate scope with different amines and allylic acetates (Table 2).

The effect of various nitrogen nucleophiles was studied. The reaction of cinnamyl acetate with piperidine, morpholine, 2-methylpiperidine, benzylamine, (S)-methylbenzylamine, and (R)-methylbenzylamine resulted in products 5a-f (Table 2, entries 1–6) in 85–95% yield, which indicates that the progress of the reaction is only minimally affected by structural and nucleophilicity effects. Phenylallyl acetates in which the phenyl group was substituted with activating and

Table 2. Synthesis of allylic amines catalyzed by cellulose-Pd⁰.





deactivating groups were employed to study the reaction scope. (*E*)-3-(4-Methoxyphenyl)allyl acetate participated in the reaction with morpholine to give allylated product **5h** in 86 % yield. (*E*)-3-(*p*-Tolyl)allyl acetate reacted efficiently with morpholine to afford **5j** in 88 % yield.

(*E*)-3-(4-Chlorophenyl)allyl acetate reacted smoothly with 1-methylpiperazine to give **5k** in 92% yield. Unsubstituted allyl acetate also participated efficiently in the reaction with piperidine and morpholine to yield **5g** and **5i** in 96 and 93% yield, respectively, which indicates that the nature of the substituent on the allyl acetate does not have a significant effect on the reaction. A branched cinnamyl acetate, 1-phenylallyl acetate, also provided linear *trans*product **5a** (Table 2, entry 12), which supports the mechanism that describes the intermediacy of a η^3 -allyl–Pd complex as the key intermediate in the reaction. The high yields of the products with various substrates indicate the broad scope of the optimized protocol. In the case of primary amines (Table 2, entries 4–6), trace amounts of diallylation products were found.

The active role of palladium in the catalytic cycle of the reaction was established by control experiments. No product formation occurred in the absence of a catalyst. The same reaction, when carried out separately in the presence of cellulose, was fruitless, but the cellulose–Pd catalyst gave good product yields, and this indicates that the reaction is catalyzed only by palladium.

Upon completion of the reaction, the catalyst was separated by filtration or centrifugation and washed with acetone followed by drying in a vacuum oven. The recovered catalyst was used over three consecutive cycles of the reaction (Table S1, Supporting Information). The amount of palladium on the cellulose was analyzed after recovering the catalyst after the fifth reaction cycle. ICP-AES analysis showed almost the same palladium concentration on the catalyst; the absence of palladium metal in the reaction solvent indicated that no metal leached into the reaction mixture. The hydroxy groups on cellulose may provide efficient binding sites that coordinate with palladium, which would thus enable efficient catalyst recycling and prevent metal leaching.

Conclusions

A simple and easy procedure for the *N*-allylation of amines was developed by using a biodegradable and easily recyclable heterogeneous cellulose-supported Pd catalyst in DMF under conventional heating. This protocol is applicable to aliphatic and benzylamines and substituted and unsubstituted allyl acetates. Highlights of this protocol include a ligand-free reaction, simple workup, and catalyst recovery and reuse.

Experimental Section

General Procedure: A mixture of allyl acetate (1.0 mmol), amine (1.2 mmol), cellulose–Pd (50 mg), and potassium carbonate (2.0 mmol) in anhydrous DMF (3 mL) was heated at 110 °C under a N₂ atmosphere for 15 h. Upon completion of the reaction, as indicated by TLC, the reaction mixture was diluted with water and centrifuged/filtered to separate the catalyst. The decanted liquid was extracted with ethyl acetate (3×10 mL); the organic layer was dried with anhydrous sodium sulfate and evaporated under reduced pressure to afford the crude product. The crude product was purified by passing through a silica gel column (ethyl acetate/hexane).

Supporting Information (see footnote on the first page of this article): Experimental procedures, ¹H NMR and ¹³C NMR spectra, and MS data.

Acknowledgments

B. R. V. and A. S. are supported by the Postgraduate Research Program at the National Risk Management Research Laboratory administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the U.S. Department of Energy and the U.S. Environmental Protection Agency.

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Received: September 18, 2012 Published Online: October 30, 2012