Pd-Catalyzed α-Allylation of 2-Phenylpropanal and other Carbonyl Compounds with Allyl Alcohol and Allyl Acetates/Carbonates in Ionic Liquids

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Summary. The successful Pd-catalysed allylation of 2-phenylpropanal with allyl alcohol in ionic liquid is described and thus a simpler reaction composition catalytic system than in *THF* is possible. On the other hand, the Pd-catalyzed α-allylation of the same substrate with allyl acetate or allyl ethyl carbonate is proceeding nicely in ionic liquids. Allylation of different carbonyl derivatives was studied and it was found that the reaction is restricted to carbonyl derivatives from which a carbanion stabilized by an adjacent aromatic ring can be formed.

Keywords. Pd-catalyzed; Ionic liquids; α-Allylation.

Introduction

Pd-catalyzed *Tsuji-Trost* allylations of active methylene compounds are a well established method for C–C bond formation [1]. As the potential nucleophiles dialkyl malonates, β-ketoesters [2, 3], and allyl acetates or allyl carbonates are most frequently used [4, 5]. An intramolecular version of this reaction is used also for the synthesis of cyclic compounds [6]. It is also frequently performed in an asymmetric version [7–10] and we published papers on an asymmetric version of the *Tsuji-Trost* reaction in ionic liquids [11, 12].

α-Allylation of simple aldehydes and ketones has been much less studied and these carbonyl compounds in advance must be converted into their metal enolates [13, 14], or enol silyl ethers [4, 15], or enamines [16].

There are several papers on the Pd-catalyzed allylation of acetylacetone [17], β-ketoesters [18], and malonates [19] by simple allyl alcohols under drastic conditions. On the other hand, *Tamaru et al.* have found that the Pd-catalyzed allylation of methylene active compounds by allyl alcohol can be efficiently promoted by triethylborane [20]. Based on this finding they have developed also Pd-catalyzed allylation of 2-phenylpropanal by allyl alcohol [21]. The catalytic system consisted of Pd(O*Ac*)$_2$, triphenylphosphine, triethylborane, triethylamine, and LiCl. Very recently, also a paper has been published on the conversion of allyl alcohol into allyl phenyl sulfones [22]. Authors are using the same conditions as at allylation of 2-phenylpropanal [21]. Overall the very good yields were achieved after 12–15 h reaction time in *DMF* at 80°C.

The main aim of this work was to examine if allylation of aldehydes by allyl alcohol or allyl acetates/carbonates can be performed in ionic liquids.

Results and Discussion

To start our work on allylation of 2-phenylpropanal with allyl alcohol, we decided to repeat the experiment described in Ref. [21] (Scheme 1). As can be seen from entry 2 in Table 1 we achieved the same result as described. When the reaction was carried

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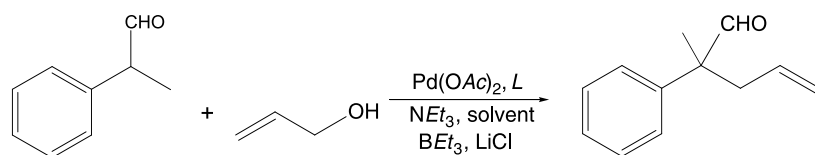
Scheme 1

Table 1. α-Allylation of 2-phenylpropanal with allyl alcohol

Entry	L	Solvent	Time/ h	T/°C	Yield/ %
1	PPh₃	*THF*	12	50	87[a]
2	PPh₃	*THF*	12	50	86
3	PPh₃	[*bmim*]PF₆	12	50	59
4	PPh₃	[*bmim*]PF₆	36	RT	50
5	PPh₃, without LiCl	[*bmim*]PF₆	36	RT	52
6	PPh₃, without B*Et*₃	[*bmim*]PF₆	36	RT	26

[a] This yield was described in [21]

out in [*bmim*]PF₆ a much lower yield was achieved. Then attempts were made to simplify the composition of the reaction mixture (entries 4, 5). We found that reaction proceeded also without addition of LiCl, but reaction without Et_3B gave much lower yield, which is in accord with Ref. [20].

As the yield of allylation of 2-phenylpropanal with allyl alcohol was low, we decided to examine if it is not possible to perform its allylation with another allylation agent, namely allyl acetate and allyl ethyl carbonate (Scheme 2, Table 2). From the results given in Table 2 one can see that the reaction in [*bmim*]PF₆ was proceeding nicely, in particular, when triethylamine was used as the base. Practically equal results were achieved in an allylation with allyl acetate and allyl ethyl carbonate. Triethylamine proved to be a more efficient base than potassium carbonate. In our recent work [23] we have proved that *Michael* addition of C-nucleophiles can be performed in ionic liquids without addition of an external base. For that reason experiments without

addition of base were performed (entries 7, 8) and it was proven that allylation in an ionic liquid can be performed without addition of any base while no reaction was observed in *THF*.

Our next aim was to test the effect of the [Pd]-source and ligand on the reaction course (Scheme 3). Results are given in Table 3.

First of all it is necessary to point out that practically all reactions were proceeding with a full conversion of the starting aldehyde. The isolated yields of the products were very sensitive both to the [Pd]-source as well as the ligand. Lower isolated yields were caused by formation of several, not identified, side products. The best yields were achieved with PdCl₂(PPh₃)₂ and Pd₂(*dba*)₃ CHCl₃ as the [Pd]-source (entries 2, 5). The reaction was very clean using P(*o*-tolyl)₃ and P(2-furyl)₃ as the ligands (entries 6, 10). We were curious also if the structure of ionic liquid would have some effect on the reaction (Scheme 4) course and the corresponding results are collected in Table 4.

From the results given in Table 4 it follows that reaction proceeded very well in all ionic liquids, but the most clean results were achieved using MERCK's [*n-BuMePyrr*](C₂F₅)₃PF₃ ionic liquid.

From the results given in Tables 2–4 it is possible to conclude that allylation of 2-phenylpropanal in ionic liquid is possible without its interconversion to its metal enolates or trimethylsilyl enolate. We decided therefore to examine if allylation of other weak acidic substrates could undergo similar allylation. Attempts were made on the allylation of cyclohexanecarboxaldehyde, isobutyrylaldehyde, 2,6-dimethylcyclohexane-1-one, cyclohex-2-en-1-one, as well as with ethyl phenylacetate, but prac-
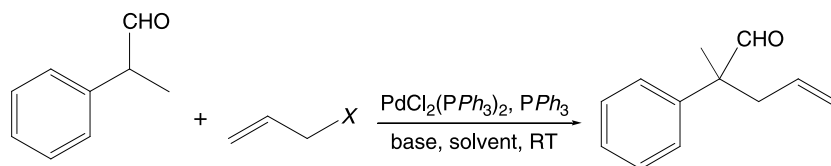
Scheme 2

**Table 2.** Effect of leaving group and base on the α-allylation of 2-phenylpropanal

Entry	X	Solvent	Base	Time/ h	Yield/ %
1	OCOCH$_3$	*THF*	K$_2$CO$_3$	20	34
2	OCOCH$_3$	[*bmim*]PF$_6$	K$_2$CO$_3$	20	69
3	OCOCH$_3$	[*bmim*]PF$_6$	*Et$_3$N*	5	83
4	O*Ts*	[*bmim*]PF$_6$	*Et$_3$N*	5	51
5	OCOO*Et*	[*bmim*]PF$_6$	*Et$_3$N*	5	85
6	Br	[*bmim*]PF$_6$	*Et$_3$N*	5	0
7	OCOO*Et*	[*bmim*]PF$_6$	–	5	63
8	OCOO*Et*	*THF*	–	5	0

tically no product was isolated even when we prolonged the reaction time or rised the temperature. We assumed that this could be connected with the low acidity of the substrate, and therefore in attempts to react with isobutyraldehyde we changed the base for potassium carbonate or *BSA*/LiO*Ac*. However, it provided no result on the reaction course.

We do not have any explanation for this fact at the moment.

On the other hand, attempts to allylate diphenyla-cetaldehyde and diethyl phenylmalonate were successful, and high yields of the reaction products (96 and 67%; structures **2** and **3** in Fig. 1) were isolated. No allylation was going on with 2-methyl-tetraline-1-one, while the product of a bis-allylation and unreacted tetraline-2-one was isolated at reaction with tetraline-2-one (Fig. 1, **4**) (45%, with one equivalent of allyl ethyl carbonate and 86% with two equivalents of the reagent). These results point out that for a successful allylation it is necessary that a stable anion delocalised into benzene or other arene rings can be formed.

In conclusion, our study proved that the Pd-catalysed allylation of 2-penylpropanal in ionic liquids is proceeding well even with free allyl alcohol. Better yields were achieved when allyl acetate or allyl ethyl carbonate was used as the allylation agent.
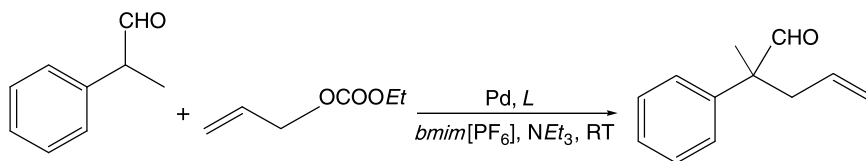
Scheme 3

Table 3. Effect of the Pd-source and ligand on the α-allylation of 2-phenylpropanal with allyl ethyl carbonate

Entry	[Pd] source (10 mol%)	L (20 mol%)	Time/h	Conversion/%	Isolated yield/%
1	Pd(O*Ac*)$_2$	P*Ph$_3$*	5	100	68
2	PdCl$_2$(P*Ph$_3$*)$_2$	P*Ph$_3$*	5	100	83
3	Pd(P*Ph$_3$*)$_4$	P*Ph$_3$*	5	100	40
4	Pd(*dppf*)$_2$	*dppf*	5	100	80
5	Pd$_2$(*dba*)$_3$ · CHCl$_3$	P*Ph$_3$*	5	100	80
6	Pd$_2$(*dba*)$_3$ · CHCl$_3$	P(o-tolyl)$_3$	5	100	83
7	Pd$_2$(*dba*)$_3$ · CHCl$_3$	P(o-tolyl)$_3$	2.5	85	70[a]
8	Pd$_2$(*dba*)$_3$ · CHCl$_3$	As*Ph$_3$*	2.5	100	50
9	Pd$_2$(*dba*)$_3$ · CHCl$_3$	*DPPF*	2.5	100	60
10	Pd$_2$(*dba*)$_3$ · CHCl$_3$	P(2-furyl)$_3$	2.5	100	96

[a] Reactions were performed with 5 mol% of [Pd] and 10 mol% of *L*
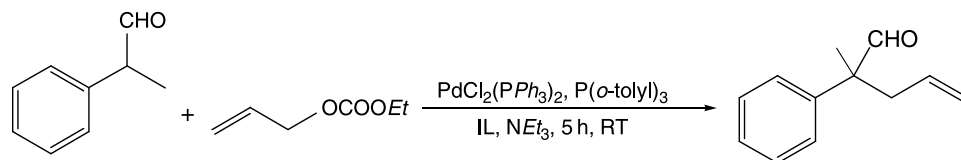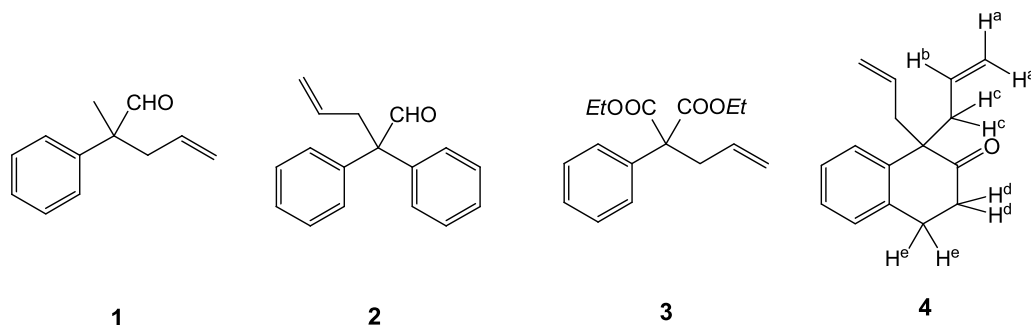

Scheme 4

Fig. 1. Structures of the products of α-allylations of different carbonyl compounds

Table 4. Ionic liquid α-allylation of 2-phenylpropanal with allyl ethyl carbonate[a]

Entry	Ionic liquid	Conversion/ %	Isolated yield/%
1	[*bmim*]PF$_6$	100	95
2	[*bmim*]PF$_6$	90	60[b]
3	[*emim*]SO$_4$*Et*	100	94
4	[*n*-Bu$_3$EtP](*Et*O)$_2$PO$_2$	100	95
5	[*i*-Bu$_3$MeP]*Ts*	90	81
6	[*n*-BuMePyrr](C$_2$F$_5$)$_3$PF$_3$	100	98

[a] All reactions were carried out with 10 mol% of [Pd] and 20 mol% of *L*
[b] 1st recyclation

Allylation of different carbonyl compounds with these reagents revealed that reaction in ionic liquids is possible only in the case when the reagent has just one C–H bond adjacent to the carbonyl group and the formed carbanion is conjugated to an arene ring. Bis-allylation products were isolated in the reactions with reagents having two C–H bonds adjacent to the carbonyl group.

Experimental

^{1}H NMR spectra were measured at 300 MHz, ^{13}C NMR at 75 MHz, with a Varian Mercury Plus instrument as solution in CDCl$_3$ with tetramethylsilane as internal standard. Elemental analysis was measured with a Carlo Erba Instrumentation Analyzer. Measured data for the new compound are in accord with the calculated data.

General Procedure for Allylation of Carbonyl Compounds
Palladium source (0.05 mmol of [Pd] and 0.1 mmol phosphine) were dissolved in 0.8 cm^3 ionic liquid and the solution was stirred, under N$_2$ atmosphere, at 80°C for 20 min. The solution of the pre-formed catalyst was cooled down to room temperature and then was added 0.5 mmol allyl ethyl carbonate or allyl acetate, 0.5 mmol of carbonyl compound, and

0.6 mmol of the base. The reaction mixture was stirred at room temperature for 5 h. The reaction mixture was then extracted several times with diethyl ether ([*bmim*]PF$_6$ as IL) or *n*-hexane. Extracts were dried (Na$_2$SO$_4$), filtered, and the solvent was evaporated on a RVO. The residue was purified by column chromatography on silica gel using an ethyl acetate: isohexane (1:7) mixture as the eluent.

From the reaction with 2-phenylpropanal was isolated 2-phenyl-4-butene-2-carboxaldehyde (Fig. 1, **1**), an oil, NMR spectra are identical with those described in Ref. [24].

From the reaction with diphenylacetaldehyde was isolated 2,2-diphenyl-3-propen-1-carboxaldehyde (Fig. 1, **2**), an oil, NMR spectra are identical with those described in Ref. [25].

From the reaction with diethyl phenylmalonate was isolated diethyl allylphenylmalonate (Fig. 1, **3**), an oil, NMR spectra are identical with those described in Ref. [26].

1,1-Diallyltetraline-2-one (**4**, C$_{16}$H$_{18}$O)
From the reaction with tetraline-2-one 45% of an oil could be isolated. ^{1}H NMR (CDCl$_3$, 300 MHz): $\delta = 7.35–7.14$ (m, 4H$_{Ar}$), 5.44–5.30 (m, 2H[b]), 4.94–4.85 (m, 4H[a]), 2.80 (dd, 2H[e]), 2.54 (m, 4H[c]) ppm; ^{13}C NMR (CDCl$_3$, 75 MHz): $\delta = 212.59, 138.11, 135.94, 132.33, 126.98, 125.90, 125.32, 117.26, 54.96, 44.05, 39.26, 26.82$ ppm.

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