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Synthesis of allylamides from allyl halides, carbon monoxide, and titanium–nitrogen complexes prepared from molecular nitrogen

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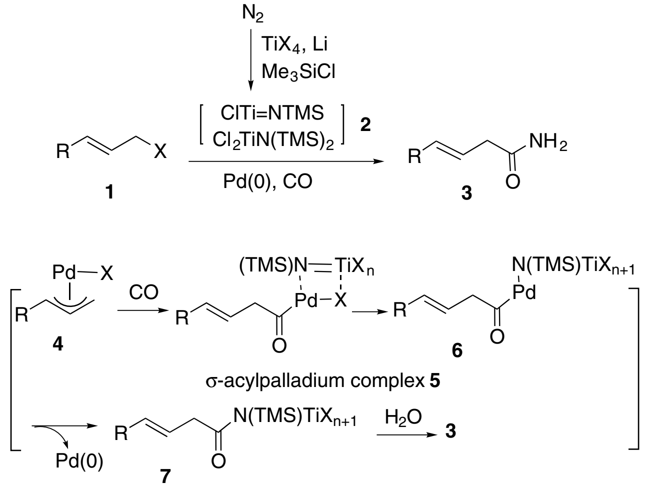
Abstract—4-Phenylbut-3-enamide could be synthesized from corresponding 3-chloroprop-2-enylbenzene, carbon monoxide (1 atm), and titanium–nitrogen complexes, prepared from Ti(O^{i}Pr)$_4$, Li, TMSCl, and molecular nitrogen (1 atm), using a palladium catalyst. The reaction proceeds via transmetalation of the titanium–nitrogen complex to an acylpalladium complex. P^{t}Bu$_3$ as a ligand of the palladium catalyst, afforded a good result, and the amounts of Li and TMSCl affected the yield of amide. When the reaction was carried out using a bidentate ligand on the palladium complex under an atmosphere of argon instead of carbon monoxide, an allylamine derivative was obtained.

Nitrogen fixation using a transition metal is a very attractive process, and the resultant nitrogen-fixation complexes should be useful in synthetic organic chemistry.[1] Titanium–nitrogen complexes, prepared from molecular nitrogen, TiX$_4$, Li, and TMSCl can be used for the synthesis of various heterocycles and nitrogen containing compounds.[2] Transmetalation of nitrogen on a titanium–nitrogen complex to transition metal complex is useful method for introducing nitrogen into an organic compound. We have already reported the synthesis of aniline derivatives from aryl halides and titanium–nitrogen complexes **2** using a palladium catalyst,[2f] and aryl amides were synthesized from aryl halide and **2** under an atmosphere of carbon monoxide using a palladium catalyst.[2i] Here we report the synthesis of 4-phenylbut-3-enamide **3**[3] from an allylic compound **1**, titanium–nitrogen complexes **2** and carbon monoxide. Our idea is shown in Scheme 1. If nitrogen from titanium–nitrogen complexes **2** can transmetalate[4] to a σ-acylpalladium complex **5** generated from a π-allylpalladium complex **4** and carbon monoxide, σ-acylpalladium amide complex **6** would be formed. Reductive elimination from **6** should give an allylamide complex **7**, which should give an amide **3** after hydrolysis.



Scheme 1. Our plan for synthesis of allylamide from CO and N$_2$.

Titanium–nitrogen complexes **2** were prepared from Ti(O^{i}Pr)$_4$ (1 equiv), Li (10 equiv), and TMSCl (10 equiv) in THF under an atmosphere of nitrogen at room temperature overnight. The solvent was changed from THF to toluene, and this toluene solution was added to a toluene solution of allyl chloride **1a** (1 equiv), Pd(OAc)$_2$ (5 mol %), PPh$_3$ (20 mol %), K$_2$CO$_3$ (3 equiv), and HMPA (2.3 equiv)[4] and then the whole solution was stirred at room temperature overnight. However, no nitrogen-fixation product was obtained after hydrolysis, and only a mixture of the dimeric compounds **8**[5] of allyl chloride **1aa** was obtained in 86% yield (Table 1, run 1). The ligand was therefore changed to P(*o*-tolyl)$_3$ and the

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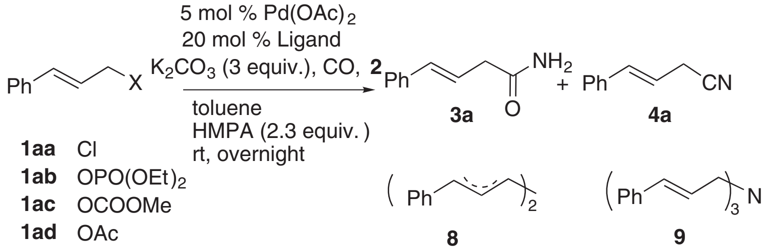
Table 1. Synthesis of allylamide from allyl chloride, **2**, and CO



Run		Ligand	Li (mol equiv)	TMSCl (equiv)	HMPA	Yield (%)		
						3a	**4a**	**8**
1	**1aa**	$\mathrm{PPh_3}$	10	10	+	—	—	86
2	**1aa**	P(*o*-tolyl)$_3$	10	10	+	4	7	18
3	**1aa**	P^{n}Bu$_3$	10	10	+	—	—	—
4	**1aa**	P^{t}Bu$_3$	10	10	+	47	6	45
5	**1aa**	BINAP	10	10	+	—	—	63[a]
6	**1aa**	P^{t}Bu$_3$	10	10	−	16	6	49
7[b]	**1aa**	P^{t}Bu$_3$	10	10	+	15	4	36
8	**1aa**	P^{t}Bu$_3$	5	6	+	52	3	17
9	**1aa**	P^{t}Bu$_3$	4	6	+	58	3	11
10	**1aa**	P^{t}Bu$_3$	3	6	+	44	5	11
11	**1ab**	P^{t}Bu$_3$	4	6	+	59	—	—
12	**1ac**	P^{t}Bu$_3$	4	6	+	12[c]	—	—
13	**1ad**	P^{t}Bu$_3$	4	6	+	3[d]	—	—

[a] Compound **9** was obtained in 37% yield.

[b] In the absence of $\mathrm{K_2CO_3}$.

[c] Compound **1ac** was recovered in 88% yield.

[d] Compound **1ad** was recovered in 78% yield.

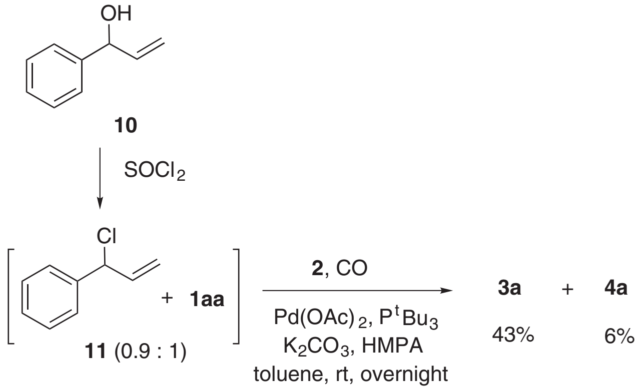
reaction was carried out under the same reaction conditions. We were very pleased to find that the desired amide **3a** was obtained, although the yield was only 4%, along with 4-phenylbut-3-enenitrile **4a** in 7% yield (run 2). Nitrile **4a** should be obtained from titaniumamide complex **7** as a result of deoxygenation of amide carbonyl oxygen by titanium metal.[2i] Various ligands were examined and the results are shown in Table 1.

Although the use of P^{n}Bu$_3$ did not give amide **3a** (run 3), Pd(OAc)$_2$–P^{t}Bu$_3$ afforded the desired compound **3a** in 47% yield along with nitrile **4a** in 6% yield (run 4). It was interesting that the use of a bidentate ligand did not afford the desired compound and only tertiary allylamine **9** was afforded in 37% yield along with **8** in 63% yield (run 5). In the absence of HMPA as an additive or in the absence of $\mathrm{K_2CO_3}$ as a base, the yields of **3a** and **4a** were decreased to 22% and 19%, respectively (runs 6 and 7). In these reactions, a large amount of dimeric compounds **8** was formed. Although the reason for the formation of **8** is not clear, it was thought that **8** is formed by an excess amount of Li. In the nitrogen-fixation reaction, excess amounts of Li and TMSCl were required to obtain a high yield of the nitrogen-fixation product.[2a] Recently, appropriate amounts of Li and TMSCl for the generation of titanium–nitrogen complexes **2** have been examined on the basis of the proposed reaction course, and 4 mol equiv of Li and 6 equiv of TMSCl gave the best result for the synthesis of an indole derivative.[2k] Thus, the reaction was carried out using this improved procedure. As a result, the desired amide **3a** was obtained in 58% yield along with **4a** in 3% yield (run 9). Either greater or smaller amounts of Li resulted in decrease in the yields of **3a** (runs 8 and 10). As a leaving group, allylphosphonate **1ab** afforded the desired product **3a** in 59% yield (run 11), but the use of allyl carbonate **1ac** and the use of allyl acetate **1ad** gave **3a** in only 12% and 3% yields, respectively (runs 12 and 13).

Next, to determine whether this reaction proceeds via the formation of a π-allylpalladium complex **4**, the reaction was carried out using allyl chloride **11**. Thus, allyl chloride **11** was prepared from allyl alcohol **10** and $\mathrm{SOCl_2}$, and it was obtained as an inseparable mixture of **11** and **1aa** (the ratio of **11** to **1aa** being 0.9–1).[6] When a toluene solution of titanium–nitrogen complexes **2** and a mixture of **11** and **1aa** was stirred in the presence of Pd(OAc)$_2$, P^{t}Bu$_3$, $\mathrm{K_2CO_3}$, and HMPA under an atmosphere of carbon monoxide at room temperature overnight, allylamide **3a** was obtained in 43% yield along with allyl cyanide **4a** in 6% yield. This result indicates that amide **3a** is formed via the same π-allylpalladium complex **4** from both **1aa** and **11** (Scheme 2).

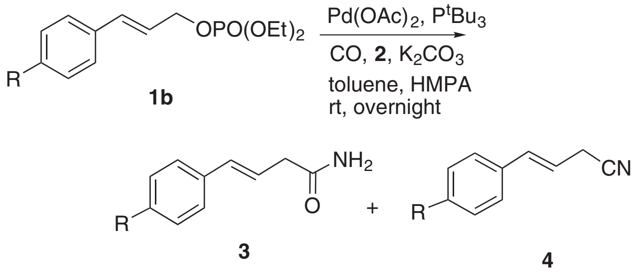
Various allyl phosphonates **1b** were treated in a similar manner and the desired amides **3** and nitrile **4** were obtained in good to moderate yields (Table 2).

When the reaction was carried out using BINAP as a ligand, a tertiary allylamine derivative **9** was obtained in 37% yield (Table 1, run 5). This indicates that when a bidentate ligand is used in this reaction, transmetalation occurs from the σ-allylpalladium complex **12** to give an



Scheme 2. Reaction of allyl chloride **11** and **2**.

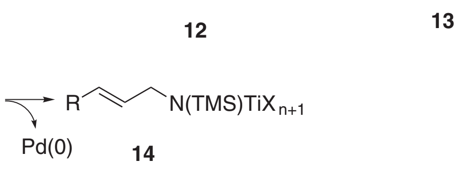
Table 2. Synthesis of various amides and nitriles



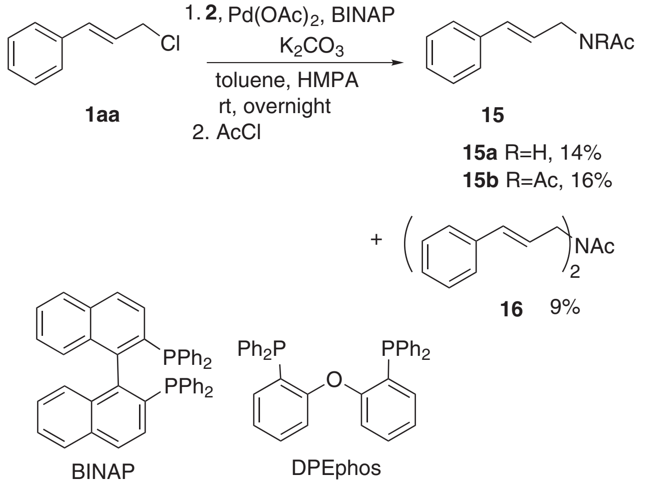
Run	R		Yield	
			3 (%)	**4** (%)
1	H	**1ab**	**3a** 59	—
2	Me	**1bb**	**3b** 35	**4b** 6
3	F	**1cb**	**3c** 51	**4c** 3
4	CF_3	**1db**	**3d** 51	—

σ-allylpalladium amide complex **13** and then reductive elimination occurs to give **14** (Scheme 3).

Thus, if a bidentate ligand is used for this reaction in the absence of carbon monoxide, an allylamine derivative should be obtained. When a toluene solution of **1aa** was stirred in the presence of **2**, a catalytic amount of $Pd(OAc)_2$, BINAP, K_2CO_3, and HMPA under an atmosphere of argon gas at room temperature overnight and then acetyl chloride was added,[7] allylamine derivatives **15a**,**b** and **16** were obtained in 14%, 16%, and 9% yields, respectively (Scheme 4).



Scheme 3. Formation of allylamine derivative.



Scheme 4. Synthesis of allylamine from **2**.

Various ligands were examined and the use of the DPEphos[8] afforded the desired amine derivatives **15a** and **15b** in 30% yields along with **16** in 10% yield, but the use of the monodentate ligand (PPh_3) did not give the desired compound.

Little is known about the synthesis of primary amide from allyl halide using palladium-catalyzed carbonylation, because NH_3 must be used as an amine for that purpose. Thus, this method using palladium-catalyzed carbonylation followed by transmetalation with titanium–nitrogen complex should be useful for synthesis of primary amide.

Further studies are in progress.

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