Palladium-catalysed Carbonylation of Allylamines

Shun-Ichi Murahashi,* Yasushi Imada, and Koichi Nishimura

Department of Chemistry, Faculty of Engineering Science, Osaka University, Machikaneyama, Toyonaka, Osaka 560, Japan

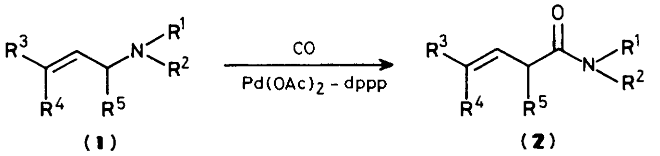
Carbonylation of allylamines proceeds smoothly in the presence of a palladium–phosphine catalyst to give β,γ-unsaturated amides in good yields.

Carbonylation is a useful process, because introduction of CO into organic substrates gives singly homologated products. Carbonylation of allylic compounds such as allyl esters[1,2] gives homoallylic compounds. During our continuing studies on the carbonylation of allylic compounds, we found that carbonylation of allylamines (**1**) proceeds efficiently in the presence of palladium–phosphine catalysts to give β,γ-unsaturated amides (**2**) selectively (Scheme 1). This is the first example of the transformation of allylamines to β,γ-unsaturated amides, which are synthetically important key intermediates.

The carbonylation of allylamine (**1a**) has been investigated in detail. The most effective catalyst was found to be a combination of $Pd(OAc)_2$ and 1,3-bis(diphenylphosphino)propane (dppp) (1:2). Other combinations of palladium complexes such as $Pd(PPh_3)_2Cl_2$, $Pd(MeCN)_2Cl_2$, $Pd(acac)_2$ (Hacac = pentanedione), and $Pd(dba)_2$ (dba = dibenzylideneacetone) and phosphine ligands such as PPh_3, Ph_2PEt, $Ph_2P(CH_2)_2PPh_2$, and $Ph_2P(CH_2)_4PPh_2$ gave poor yields of (**2a**). Toluene is the best of the solvents examined. The reaction proceeds smoothly at temperatures over 110 °C.

A typical example is the transformation of (**1d**) to (**2d**). Into a 280 ml autoclave were placed (**1d**) (25 mmol), $Pd(OAc)_2$ (1.25 mmol), dppp (2.5 mmol), and toluene (50 ml). The autoclave was charged with CO (50 kg/cm^2), and the mixture was stirred at 110 °C for 20 h. After cooling to room temperature, the mixture was extracted with ether. The ether solution was washed with 2 M HCl, saturated aqueous $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation followed by short column chromatography on silica gel (hexane–EtOAc, 9:1) gave (**2d**) in 76% yield.

Table 1 summarizes representative results. Aliphatic and aromatic allylamines can be converted into the corresponding



(**1**) (**2**)

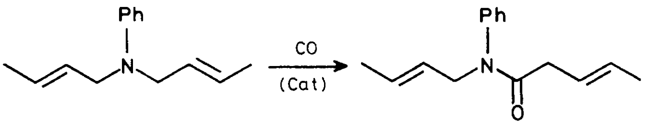
	R1	R2	R3	R4	R5
a	Et	Et	Pr	H	H
b	Bu	Bu	Me	H	H
c	Et	Et	Ph	H	H
d	Me	Ph	Pr	H	H
e	Me	CH_2Ph	Me	H	H
f	Me	CH_2Ph	H	H	Me
g	Et	Et	H	$-[CH_2]_3-$	

Scheme 1

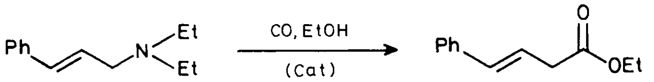
Table 1. Palladium-catalysed carbonylation of allylamines.[a]

Entry	Allylamine	Amide[b]	% Isolated yield
1	(**1a**)	(**2a**)	83
2	(**1b**)	(**2b**)	77
3	(**1c**)	(**2c**)	70
4	(**1d**)	(**2d**)	76
5	(**1e**)	(**2e**)	85
6	(**1f**)	(**2e**)	89
7	(**1g**)[c]	(**2g**)	35

[a] The reaction was carried out according to the procedure described in the text. [b] The structures of the products were determined on the basis of analytical and i.r., n.m.r., and mass spectral data. [c] The reaction was performed at 130 °C.



(1h) **(2h)**



(1c) **(3)**

(*E*)-β,γ-unsaturated amides regio- and stereo-selectively in good yields. Generally carbonylation at the secondary allylic carbon is very difficult[3] because of steric effects; however carbonylation of (**1g**) at a higher temperature (130 °C) gave (**2g**) in 35% yield along with the deamination product. The carbonylation of *N*-phenyldicrotylamine (**1h**) gave *N*-phenyl-*N*-crotylpent-3-enamide (**2h**) in 77% yield.

It is noteworthy that carbonylation of allyamines in an alcohol gives the corresponding β,γ-unsaturated acid esters. Typically, carbonylation of *N*,*N*-diethylcinnamylamine (**1c**) in ethanol under the same reaction conditions gave ethyl 3-phenylbut-2-enoate (**3**) in 71% yield.

The present reaction can be rationalized by assuming a mechanism which involves π-allylpalladium intermediate. Allylamines undergo oxidative addition to co-ordinatively unsaturated palladium–phosphine species to give π-allylpalladium complexes and amines.[4] Subsequent insertion of carbon monoxide takes place at the less hindered carbon of allyl moiety. The acylpalladium complexes thus obtained react with the amines to give the corresponding amides. It is noteworthy that both but-1-en-3-ylamine (**1e**) and but-2-en-1-ylamine (**1f**) were converted into (*E*)-pent-3-enamide (**2e**) exclusively (entries 5 and 6). This is the first demonstration of the insertion of CO into carbon–nitrogen bonds, except for the carbonylation and ring expansion reaction of aziridines.[5]

The β,γ-unsaturated amides thus obtained are versatile synthetic intermediates. Reduction of β,γ-unsaturated amides with $LiAlH_4$ in ether at room temperature gave homoallylamines in good yields. Typically, *N*,*N*-dibutylpent-3-enylamine and *N*-methyl-*N*-phenylhept-3-enylamine have been obtained from (**2b**) and (**2d**) in 95% and 85% yields, respectively. Since the starting allylamines can be readily prepared by the palladium catalysed amination of allyl esters,[6] the present reaction provides a convenient method for the preparation of homoallylic amines from allyl alcohols.

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