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Palladium-Catalyzed Carbonylation of Propargylamines. Selective Insertion of Carbon Monoxide into a Carbon−Nitrogen Bond

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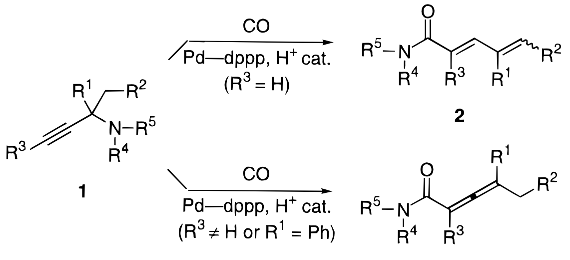
The selective insertion of carbon monoxide into an unactivated carbon−nitrogen bond of amine to form an amide provides a novel and convenient process for homologation and functionalization of nitrogen-containing organic molecules. Many attempts have been made to achieve this attractive process, and some nitrogen heterocycles have been found to undergo carbonylative ring expansion with efficiency.[1] However, the palladium-catalyzed homologation of allylamines is the only example involving an acyclic system.[2]

Propargyl alcohols and their esters have been used as reactants in a number of metal-catalyzed carbonylation reactions.[3] For example, propargyl esters such as carbonates and phosphates are readily carbonylated to give the corresponding 2,3-dienoates. We have also found that propargyl alcohols are carbonylated directly to give 2,4-dienoates[4] or furanones,[5] depending on the reaction conditions. Much less attention has been paid to the carbonylation of propargylamines, with several examples of cyclization reactions reported, including the rhodium-catalyzed hydroformylation to pyrroles[6] and silylformylation to α-(silylmethylene) β-lactams[7] as well as the palladium-catalyzed oxidative alkoxycarbonylation to 4-(alkoxycarbonyl)pyrrolidones or α-[(alkoxycarbonyl)-methylene] β-lactams.[8] We now wish to report that tris(dibenzylideneacetone)dipalladium, with added 1,3-bis(diphenylphosphino)propane (dppp) and *p*-toluenesulfonic acid, catalyzes the selective insertion of carbon monoxide into a carbon−nitrogen bond of propargylamines **1** to give the corresponding 2,4-dienamides **2** or 2,3-dienamides **3** (Scheme 1).

Scheme 1

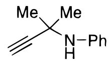
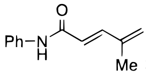
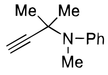
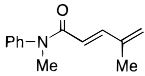
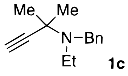
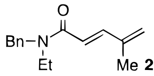
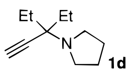
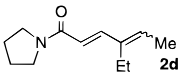
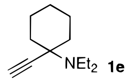
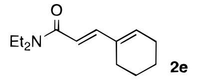
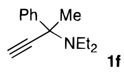
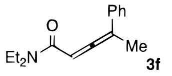
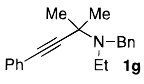
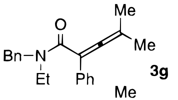
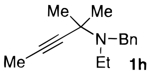
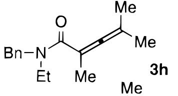
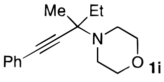
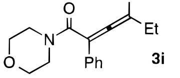


1

2

3

Table 1. Palladium-Catalyzed Carbonylation of Propargylamines to 2,4- and 2,3-Dienamides[a]

entry	propargylamine[b]	dienamide[c]	yield,[d] %
1	 1a	 2a	66
2	 1b	 2b	60
3	 1c	 2c	50
4	 1d	 2d	70[e]
5	 1e	 2e	52[f]
6	 1f	 3f	55
7	 1g	 3g	82
8	 1h	 3h	78
9	 1i	 3i	65

[a] Reaction conditions: propargylamine, $Pd_2(dba)_3{\cdot}CHCl_3$ (2 mol %), dppp (4 mol %), *p*-TsOH (4 mol %), dichloromethane, 100 °C, 6 h. [b] Propargylamines were synthesized using known methodology.[9,10] [c] Products were identified by spectroscopic methods [IR, MS, NMR (^1H, ^{13}C)]. [d] Isolated yield. [e] 60:40 (2*E*,4*E*)/(2*E*,4*Z*). [f] 48 h reaction.

When *N*-(3-methyl-1-butyn-3-yl)aniline (**1a**) was treated with carbon monoxide (600 psi) and a catalytic system consisting of $Pd_2(dba)_3{\cdot}CHCl_3$, dppp, and *p*-TsOH in dichloromethane at 100 °C for 6 h, pure *N*-phenyl-4-methyl-2,4-pentadienamide (**2a**) was isolated in 66% yield by column chromatography. It is noteworthy that the stereochemistry of the α,β-double bond is exclusively *E* as confirmed by the ^1H NMR coupling constant ($^3J_{H2-H3}$ = 15.3 Hz). The reaction in the absence of *p*-TsOH gave the amide **2a** in low yield. Bidentate phosphines such as dppp and 1,4-bis(diphenylphosphino)butane were effective as added ligands, while other bidentate and monodentate phosphines, or the absence of any phosphines, showed quite low activities for the formation of **2a**. The reaction proceeds well in dichloromethane or benzene but not in THF.

The carbonylation of propargylamines proceeded smoothly to give 2,4-dienamides **2** in 50−70% yield for both secondary and tertiary acyclic propargylamines containing a terminal acetylene unit, and the results are listed in Table 1 (entries 1−4). Cyclic propargylamine **1e** also underwent carbonylation to give the cyclic dienamide **2e** (Table 1, entry 5); however, 48 h was required to complete the reaction presumably due to steric effects. In all cases, 2*E* isomers were formed exclusively. On the other hand, propargylamines bearing either a substituent at the acetylene terminus or an

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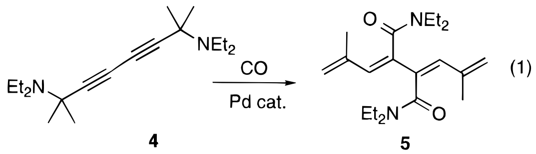
aromatic substituent at the α-position reacted under the same conditions to give 2,3-dienamides **3** in 55−82% isolated yield (Table 1, entries 6−9). The isolation of **3** may be due to the stability of allene compounds toward isomerization to 2,4-dienamides. This reaction may proceed *via* a σ-allenylpalladium intermediate.

When *N*,*N*,*N′*,*N′*-tetraethyl-2,7-dimethylocta-3,5-diyne-2,7-diamine (**4**) was treated with carbon monoxide in the presence of the same catalytic system, at 90 °C for 24 h, the novel tetraenedicarboxamide **5**, *N*,*N*,*N′*,*N′*-tetraethyl-2,3-bis(2-methyl-2-propenylidene)succinamide, was obtained in 22% isolated yield (eq 1) along with some uncharacterized polymeric materials. The presence of an *N*,*N*-diethylcarbamonyl group in the polymer was confirmed by ^{1}H and ^{13}C NMR and IR spectra, which indicates that the reaction occurs in the same way as other substrates, but the tetraenedicarboxamide undergoes facile polymerization.



The following general procedure was used: a mixture of propargylamine (1 mmol), $Pd_2(dba)_3$·$CHCl_3$ (0.02 mmol), dppp (0.04 mmol), *p*-TsOH (0.04 mmol), and dichloromethane (5 mL) was reacted in an autoclave at 600 psi of carbon monoxide at 100 °C for 6 h. After the mixture was cooled to room temperature and CO was released, the reaction mixture was percolated through Florisil with dichloromethane as an eluant to give the amide, which includes a small amount of dba. Flash column chromatography on silica gel afforded the pure amide.

In conclusion, $Pd_2(dba)_3$·$CHCl_3$, together with dppp and *p*-TsOH, catalyzes the regioselective carbonylation of propargylamines to 2,4- or 2,3-dienamides. Not only is this method attractive for the preparation of dienamides[11,12] but it also demonstrates the selective insertion of carbon monoxide into a carbon−nitrogen bond of acyclic amines.

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Supporting Information Available: General experimental procedures and characterization data for all starting materials and products; NMR (^{1}H, ^{13}C) spectra for **1b**−**d**, **1f**−**i**, **2b**−**e**, **3f**−**i**, **4**, and **5** (41 pages).

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