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# Palladium(II) acetate catalyzed efficient synthesis of *N*-aryl-*α,β*-unsaturated amides *via* carbonylative addition of aniline derivatives to aromatic alkynes

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**A series of new *N*-aryl-*α,β*-disubstituted amides (*gem* or *E1; trans* or *E2*) were synthesized in good yields by carbonylative addition of aniline derivatives 1a–f to aromatic alkynes 2a,b catalyzed by $Pd(OAc)_2$ and 1,3-bis(diphenylphosphino)propane. The catalytic synthesis of tertiary *α,β*-unsaturated amides was also successfully achieved. Traces of products were observed in the absence of *p*-toluenesulfonic acid used as an additive. The reaction is sensitive to the type of phosphine ligand and solvent. Copyright © 2002 John Wiley & Sons, Ltd.**

**KEYWORDS:** palladium acetate; aniline derivatives; internal alkynes; carbonylative coupling; syngas; phosphine ligand; unsaturated amides

## INTRODUCTION

Transition-metal-catalyzed carbonylation of alkynes represents an important and attractive route for the production of *α,β*-unsaturated carboxylic acids and their derivatives.[1,2] Amides are an important class of compounds with wide industrial applications.[3] The classical method for the synthesis of *N*-aryl acrylamides, important intermediates for the synthesis of polymers,[4–7] is achieved by reacting aromatic amines with acyl chlorides;[8,9] however, the method has many limitations that are related to the availability and/or the reactivity and the stability of many acyl chlorides. 2-Substituted acrylamides were synthesized via palladium-catalyzed carbonylation of terminal alkynes in a strong acidic medium,[10,11] or in the presence of organic iodides.[12] Recently, Alper and coworkers have reported a selective reaction of carbon monoxide insertion into the carbon–nitrogen bond of propargyl amines and 2,3-dienylamines to form 2,4- and 2,3-dienamides and *α*-vinyl acrylamides respectively.[13,14] Recently, we have been investigating the carbonylative coupling of aniline derivatives with alkynes to exploit a straightforward route towards unsaturated amide derivatives. We have published the preliminary results of the carbonylative addition of phenylacetylene with aniline derivatives into *α,β*-unsaturated amides.[15] This reaction was further investigated in detail and also applied to aromatic internal alkynes to produce a series of new *N*-aryl-*α,β*-unsaturated amides.

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## EXPERIMENTAL

### Materials and measurements

Alkynes, aniline derivatives, palladium complexes, phosphine ligands, and *p*-toluenesulfonic acid (*p*-TsOH) are commercially available as very pure materials and were used as received without further purification.

$^1H$ NMR and $^{13}C$ NMR spectra were recorded on a Joel l500 lambda spectrometer. Chemical shifts were reported in parts per million ($\delta$) relative to tetramethylsilane (TMS) using $CDCl_3$. IR spectra were recorded on a Perkin Elmer 16F PC FT-IR spectrometer and are reported in wavenumbers ($cm^{-1}$). Gas chromatography (GC) analyses were recorded on an HP 6890 chromatograph. Thin-layer chromatography (TLC) analyses were performed on silica gel Merck 60 F254 plates (250 μm layer thickness).

### General procedure for synthesis of *N*-aryl-2,3-disubstituted acrylamides

The general procedure for the catalytic synthesis of (*E*)-*N*,2-diphenyl pentenamide (**5**, $R_2 = C_2H_5$) and (*E*)-2-ethyl-*N*,3-diphenyl propenamide (**6**, $R_2 = C_2H_5$) by the carbonylative addition of aniline (**1a**) to 1-phenyl-1-butyne (**2b**) is given below.

To a glass liner fitted in a 45 ml Parr autoclave and equipped with a stirring bar was added $Pd(OAc)_2$ (0.02 mmol), 1,3-bis(diphenylphosphine)propane (dppp; 0.04 mmol), aniline (**1a**; 2.0 mmol), 1-phenyl-1-butyne (**2b**; 2.0 mmol), *p*-TsOH (0.12 mmol) and THF (10 ml). The autoclave system was flashed, filled and vented three times with CO gas, and subsequently the system was pressurized with 300 psi CO. The mixture was stirred at 110 °C for 15 h. After cooling to room temperature the CO pressure was released and the reaction mixture was filtered through Celite and the solvent was removed under vacuum. The products **5** and **6** were separated by preparative TLC (eluant: petroleum ether/acetone 10:1). The following compound is known: **4**.[17] All other unsaturated amides were fully characterized by $^1$H and $^{13}$C NMR (500 MHz, $CDCl_3$), IR ($CHCl_3$), and GC–mass spectrometry (MS).

The reactions of carbonylative addition of aniline derivatives with internal aromatic alkynes are stereospecific, where only (*E*) isomers have been detected and identified in comparison with their carboxylic esters equivalent.[9,16,17] Compound details are given in Scheme 1.

### *N*,2-diphenyl propenamide (3)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$) 1652 (CO), 3230 (NH); $^1$H NMR $\delta$ (ppm): 5.72 (s, 1H, $=CH_2$), 6.29 (s, 1H, $=CH_2$), 7.10–7.52 (m, 11H, 10H arom. + N*H*); $^{13}$C NMR $\delta$ (ppm): 119.93, 123.36, 124.63, 128.87, 129.02, 136.67, 137.65, 145.11, 165.20; GC–MS *m/z* 223 (M$^+$).

### (*E*)-*N*,2-Diphenyl pentenamide (5)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$): 1654 (CO), 3235 (NH); $^1$H NMR $\delta$ (ppm): 1.02 (t, 3H, $CH_3CH_2$, $J$ = 7.65 Hz), 2.03 (q, 2H, $CH_2CH_3$, $J$ = 7.60 Hz); 7.05–7.49 (m, 12H, 10H arom. + NH + 1H olefinic); $^{13}$C NMR $\delta$ (ppm): 13.41, 22.90, 119.87, 124.29, 128.45, 128.89, 129.19, 129.88, 135.36, 135.55, 137.89, 144.12, 164.72; GC–MS *m/z* 251 (M$^+$).

### (*E*)-2-Ethyl-*N*,3-diphenyl propenamide (6)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$): 1654 (CO), 3236 (NH); $^1$H NMR $\delta$ (ppm): 1.21 (t, 3H, $CH_3CH_2$, $J$ = 7.30 Hz), 2.66 (q, 2H, $CH_3CH_2$, $J$ = 7.65 Hz); 7.12–7.62 (m, 12H, 10H arom. + NH + 1H olefinic); $^{13}$C NMR $\delta$ (ppm): 13.49, 21.35, 119.98, 124.40, 128.10, 128.54, 128.92, 129.10, 132.56, 135.55, 137.89, 144.12, 167.84; GC–MS *m/z* 251 (M$^+$).

### *N*-(2,4-Dimethylphenyl)-2-phenyl propenamide (7)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$): 1670 (CO), 3238 (NH); $^1$H NMR $\delta$ (ppm): 1.99 (s, 3H, $CH_3$), 2.28 (s, 3H, $CH_3$), 5.70 (s, 1H, $=CH_2$), 6.36 (s, 1H, $=CH_2$), 6.95–7.86 (m, 9H, 8H arom. + N*H*); $^{13}$C NMR $\delta$ (ppm): 17.42, 20.84, 122.36, 123.61, 127.34, 128.46, 128.88, 131.01, 133.04, 134.82, 137.03, 144.99, 164.77; GC–MS *m/z* 251 (M$^+$).

### (*E*)-2-Ethyl-*N*-(2,4-dimethylphenyl)-2-phenyl pentenamide (9)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$): 1658 (CO), 3230 (NH); $^1$H NMR $\delta$ (ppm): 1.11 (t, 3H, $CH_3CH_2$, $J$ = 7.60 Hz), 1.88 (s, 3H, $CH_3$), 2.34 (s, 3H, $CH_3$), 2.12 (m, 2H, $CH_2CH_3$), 7.03–8.00 (m, 10H, 8H arom. + NH + 1H olefinic); $^{13}$C NMR $\delta$ (ppm): 13.14, 16.74, 20.52, 22.59, 122.36, 123.61, 127.34, 128.78, 128.88, 133.04, 134.82, 135.73, 143.25, 164.26; GC–MS *m/z* 279 (M$^+$).

### (*E*)-2-Ethyl-*N*-(2,4-dimethylphenyl)-3-phenyl propenamide (10)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$): 1652 (CO), 3234 (NH); $^1$H NMR $\delta$ (ppm): 1.15 (t, 3H, $CH_3CH_2$, $J$ = 7.35 Hz), 2.19 (s, 3H, $CH_3-$Ar), 2.23 (s, 3H, $CH_3-$Ar), 2.57 (q, 2H, $CH_2$, $J$ = 7.65 Hz), 6.95–7.82 (m, 10H, 8H arom. + NH + 1H olefinic); $^{13}$C NMR $\delta$ (ppm): 13.53, 17.80, 20.84, 21.34, 122.52, 123.84, 123.62, 127.44, 128.62, 128.40, 133.60, 134.82, 135.24, 142.62, 167.80; GC–MS *m/z* 279 (M$^+$).

### *N*-(*p*-Chlorophenyl)-2-phenyl propenamide (11)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$): 1660 (CO), 3230 (NH); $^1$H NMR $\delta$ (ppm): 5.69 (s, 1H, $=CH_2$), 6.26 (s, 1H, $=CH_2$), 7.21–7.59 (m, 9H arom.), 8.12 (s, 1H, N*H*); $^{13}$C NMR $\delta$ (ppm): 121.23, 123.83, 128.25, 128.95, 128.99, 129.02, 129.58, 136.17, 136.45, 144.77, 164.69; GC–MS *m/z* 257 (M$^+$).

### (*E*)-*N*-(*p*-Chlorophenyl)-2-phenyl pentenamide (13)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$) 1656 (CO), 3230 (NH); $^1$H NMR $\delta$ (ppm): 0.91 (t, 3H, $CH_3$, $J$ = 7.30 Hz), 1.91 (pent., 2H, $CH_2CH_3$, $J$ = 7.30 Hz), 7.01–7.49 (m, 11H, 9H arom. + NH + 1H olefinic); $^{13}$C NMR $\delta$ (ppm): 13.24, 22.78, 121.11, 127.39, 128.00, 128.72, 129.11, 130.56, 132.74, 136.29, 144.45, 164.76; GC–MS *m/z* 285 (M$^+$).

### (*E*)-2-Ethyl-*N*-(*p*-chlorophenyl)-3-phenyl propenamide (14)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$) 1658 (CO), 3234 (NH); $^1$H NMR $\delta$ (ppm): 1.06 (t, 3H, $CH_3CH_2$, $J$ = 7.65 Hz), 2.36 (q, 2H, $CH_2CH_3$, $J$ = 7.65 Hz) 7.02–7.52 (m, 11H, 9H, arom. + 1H, NH + 1H olefinic); $^{13}$C NMR $\delta$ (ppm): 13.35, 21.17, 121.21, 127.46, 128.22, 128.58, 129.70, 130.62, 132.82, 136.34, 143.42, 168.09; GC–MS *m/z* 285 (M$^+$).

### *N*-(1-Naphthyl)-2-phenyl propenamide (15)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$) 1659 (CO), 3232 (NH); $^1$H NMR $\delta$ (ppm): 5.70 (s, 1H, $=CH_2$), 6.29 (s, 1H, $=CH_2$), 7.18–8.05 (m, 8H, 7H arom. + 1H N*H*); $^{13}$C NMR $\delta$ (ppm): 120.81, 124.06, 125.77, 126.30, 126.65, 128.51, 128.81, 128.97, 129.04, 132.10, 133.99, 144.91, 165.30; GC–MS *m/z* 273 (M$^+$).

### (*E*)-*N*-(1-Naphthyl)-2-phenyl pentenamide (17)

Oil, IR ($CHCl_3$) $\nu$ (cm$^{-1}$) 1656 (CO), 3230 (NH); $^1$H NMR $\delta$ (ppm): 1.04 (t, 3H, $CH_3$, $J$ = 7.60 Hz), 2.06 (pent., 2H, $CH_2CH_3$, $J$ = 7.60 Hz), 7.09–8.12 (m, 14H, 12H arom. + NH + 1H olefinic); $^{13}$C NMR $\delta$ (ppm): 13.43, 22.96, 119.81, 121.09, 125.29, 125.85, 126.49, 127.39, 128.62, 129.36, 131.52, 132.55, 134.16, 135.65, 144.32, 165.03; GC–MS *m/z* 301 ($M^+$).

### (*E*)-2-Ethyl-*N*-(1-naphthyl)-3-phenyl propenamide (18)

Oil, IR ($CHCl_3$) $\nu$ ($cm^{-1}$) 1652 (CO), 3236 (NH); $^1$H NMR $\delta$ (ppm): 1.28 (t, 3H, $CH_3CH_2$, $J$ = 7.65 Hz), 2.71 (q, 2H, $CH_2CH_3$, $J$ = 7.00 Hz), 7.06–8.01 (m, 14H, 12H arom. + NH + 1H olefinic); $^{13}$C NMR $\delta$ (ppm): 13.70, 21.49, 119.51, 120.71, 121.16, 125.34, 126.82, 127.63, 128.78, 130.00, 131.62, 132.86, 134.16, 135.18, 140.44, 168.60; GC–MS *m/z* 301 ($M^+$).

### *N*-Methyl-*N*,2-diphenyl propenamide (19)

Oil, IR ($CHCl_3$) $\nu$ ($cm^{-1}$) 1663 (CO), 3240 (NH); $^1$H NMR $\delta$ (ppm): 3.42 (s, 3H, N–$CH_3$), 5.35 (s, 1H, =$CH_2$), 6.91 (s, 1H, =$CH_2$), 6.91–7.40 (m, 10 arom.); $^{13}$C NMR $\delta$ (ppm): 37.25, 126.12, 127.35, 127.96, 129.02, 129.75, 142.04, 143.72, 169.40; GC–MS *m/z* 237 ($M^+$).

### (*E*)-*N*-Methyl-*N*,2-diphenyl pentenamide (21)

Oil, IR ($CHCl_3$) $\nu$ ($cm^{-1}$) 1656 (CO); $^1$H NMR $\delta$ (ppm): 0.86 (t, 3H, $CH_2CH_3$, $J$ = 7.6 Hz), 1.98 (pent., 2H, $CH_2CH_3$, $J$ = 7.65 Hz), 3.30 (s, 3H, $NCH_3$), 6.05 (t, 1H, olefinic, $J$ = 7.65 Hz), 6.84–7.36 (m, 10H arom.); $^{13}$C NMR $\delta$ (ppm): 13.52, 21.80, 37.85, 126.53, 127.22, 128.57, 129.18, 133.00, 135.90, 138.58, 144.22, 171.76; GC–MS *m/z* 265 ($M^+$).

### (*E*)-2-Ethyl-*N*-methyl-*N*,3-diphenyl propenamide (22)

Oil, IR ($CHCl_3$) $\nu$ ($cm^{-1}$) 1656 (CO); $^1$H NMR $\delta$ (ppm): 1.06 (t, 3H, $CH_3CH_2$, $J$ = 7.35 Hz), 2.24 (q, 2H, $CH_2CH_3$, $J$ = 7.60 Hz), 3.43 (s, 3H, $NCH_3$), 6.55 (2, 1H, olefinic), 6.88–7.39 (m, 10H, arom.); $^{13}$C NMR $\delta$ (ppm): 12.77, 22.23, 37.42, 126.53, 126.42, 127.46, 128.88, 129.30, 133.96, 137.42, 139.70, 144.62, 172.16; GC–MS *m/z* 265 ($M^+$).

### *N*-Ethyl-*N*,2-diphenyl propenamide (23)

Oil, IR ($CHCl_3$) $\nu$ ($cm^{-1}$) 1665 (CO); $^1$H NMR $\delta$ (ppm): 1.18 (t, 3H, $CH_2CH_3$, $J$ = 7.0 Hz), 3.89 (q, 2H, $CH_3CH_2$, $J$ = 7.05 Hz), 5.35 (s, 1H, =$CH_2$), 5.42 (s, 1H, =$CH_2$), 6.87–7.69 (m, 11H, 10H arom. + 1N*H*); $^{13}$C NMR $\delta$ (ppm): 13.02, 44.25, 112.61, 117.52, 119.18, 126.04, 127.78, 128.18, 128.63, 128.71, 129.16, 129.40, 130.73, 137.06, 141.96, 146.04, 170.05; GC–MS *m/z* 251 ($M^+$).

### (*E*)-*N*-Ethyl-*N*,2-diphenyl pentenamide (25)

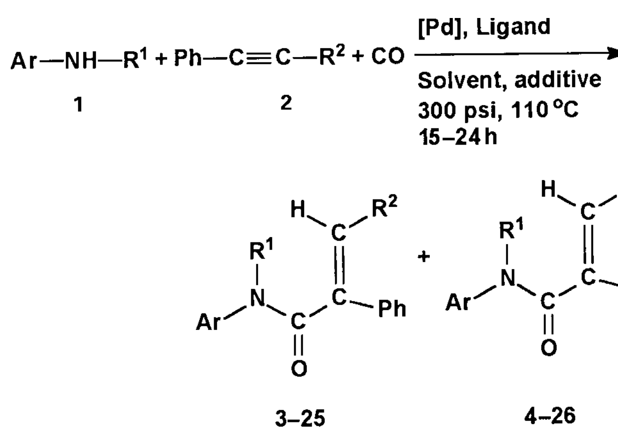
Oil, IR ($CHCl_3$) $\nu$ ($cm^{-1}$) 1652 (CO); $^1$H NMR $\delta$ (ppm): 0.86 (t, 3H, $CH_3CH_2$–C=, $J$ = 7.65 Hz), 1.09 (t, 3H, $NCH_2CH_3$, $J$ = 7.00 Hz), 1.98 (pent., 2H, =C–$CH_2CH_3$, $J$ = 7.65 Hz), 3.78 (q, 2H, $NCH_2CH_3$, $J$ = 7.15 Hz), 6.04 (t, 1H, olefinic, $J$ = 7.65 Hz), 6.78–7.34 (m, 10H, arom.); $^{13}$C NMR $\delta$ (ppm): 12.82, 13.40, 21.61, 44.58, 125.88, 126.48, 127.00, 127.55, 127.97, 128.24, 128.97, 132.59, 135.81, 137.58, 138.22, 142.30, 171.08; GC–MS *m/z* 279 ($M^+$).

### (*E*)-*N*,2-Diethyl-*N*,3-diphenyl propenamide (26)

Oil, IR ($CHCl_3$) $\nu$ ($cm^{-1}$) 1658 (CO); $^1$H NMR $\delta$ (ppm): 1.05 (t, 3H, $CH_3CH_2$–C=, $J$ = 7.60 Hz), 1.20 (t, 3H, $NCH_2CH_3$, $J$ = 7.00 Hz), 2.22 (pent., 2H, =C–$CH_2CH_3$, $J$ = 7.35 Hz), 3.89 (q, 2H, $NCH_2CH_3$, $J$ = 7.00 Hz), 6.53 (s, 1H, olefinic), 6.81–7.42 (m, 10H arom.); $^{13}$C NMR $\delta$ (ppm): 12.56, 12.96, 22.09, 44.69, 125.82, 126.22, 127.44, 127.84, 128.66, 128.33, 132.66, 135.62, 138.22, 142.80, 171.44; GC–MS *m/z* 279 ($M^+$).

## RESULTS AND DISCUSSION

A number of aniline derivatives **1a–f** and aromatic alkynes **2a**,**b** undergo a carbonylative coupling reaction that is catalyzed by palladium complexes and phosphine ligands (Eqn. (1)). It was observed that the addition of a bidentate phosphine ligand, such as 1,4-bis(diphenylphosphino)butane (dppb) or dppp, was essential for the occurrence of the reaction of carbonylation giving high conversions and yields. In addition, no products or low yields of products of the carbonylation reaction were formed in the absence of either hydrogen or *p*-TsOH as an additive.




(1)

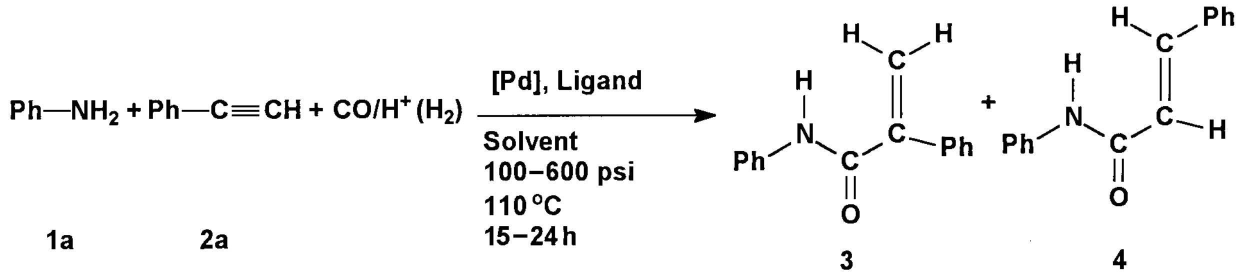
**1a**: Ar=Ph; $R^1$=H
**1b**: Ar=2,4-$(CH_3)_2$—$C_6H_3$; $R^1$=H
**1c**: Ar=*p*-Cl—$C_6H_4$; $R^1$=H
**1d**: Ar=1-naphthyl; $R^1$=H
**1e**: Ar=Ph; $R^1$=$CH_3$
**1f**: Ar=Ph; $R^1$=$CH_2CH_3$

**2a**: $R^2$=H
**2b**: $R^2$=$CH_2CH_3$

### Catalytic carbonylative addition of phenylacetylene to aniline

The reaction of carbonylative coupling of aniline (**1a**) with phenylacetylene (**2a**), adopted as a model reaction, was carried out in the presence of different palladium complexes and bidentate phosphine ligands in various solvents under

**Table 1.** Palladium(II)-catalyzed carbonylative addition of aniline (**1b**) to phenylacetylene (**2a**).[a]




| Entry | Palladium catalyst | Ligand | Gas/additive Solvent | Time (h) | Yield[b] (%) | Product distribution[c] (%) 3 | 4 |
|---|---|---|---|---|---|---|---|
| 1 | $Pd(OAc)_2$ | dppb | $CO/H_2$ $CH_2Cl_2$ | 24 | 98 | 64 | 36 |
| 2 | $Pd(OAc)_2$ | dppb | $CO/H_2$ Toluene | 24 | 90 | 67 | 33 |
| 3 | $Pd(OAc)_2$ | dppb | CO/*p*-TsOH THF | 15 | 92 | 92 | 8 |
| 4 | $Pd(OAc)_2$ | dppp | $CO/H_2$ $CH_2Cl_2$ | 24 | 17 | 90 | 10 |
| 5 | $Pd(OAc)_2$ | dppp | CO/*p*-TsOH THF | 15 | 95 | 96 | 4 |
| 6 | $Pd(OAc)_2$ | dppp | CO/*p*-TsOH Toluene | 15 | 27 | 97 | 3 |
| 7 | $PdCl_2(PPh_3)_2$ | dppb | $CO/H_2$ $CH_2Cl_2$ | 24 | 69 | 74 | 26 |
| 8 | $PdCl_2(PPh_3)_2$ | dppp | CO/*p*-TsOH THF | 15 | 15 | 98 | 2 |
| 9 | $Pd(PPh_3)_4$ | dppb | $CO/H_2$ $CH_2Cl_2$ | 15 | 97 | 67 | 33 |
| 10 | $Pd(PPh_3)_4$ | dppp | CO/*p*-TsOH THF | 15 | 90 | 97 | 3 |

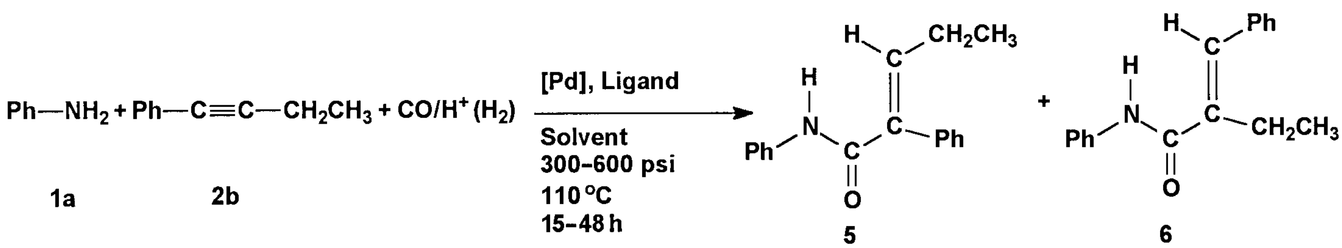
[a] Reaction conditions: [Pd], 0.02 mmol; ligand, 0.04 mmol, except for $Ph_3P$ = 0.08 mmol; aniline, 2.0 mmol; phenylacetylene, 2.0 mmol; solvent, 10 ml; *p*-TsOH, 0.12 mmol; CO, 300 psi; $H_2$, 300 psi when used; 110 °C.
[b] Isolated yield.
[c] The ratio of **3**/**4** was determined by GC and by $^1$H NMR.

$CO/H_2$ or CO/*p*-TsOH media at 110 °C (Table 1). The effect of the CO pressure and the temperature was first studied in order to determine the optimal reaction conditions. It was found that 300 psi of CO and 300 psi of $H_2$ (or 0.12 mmol *p*-TsOH when used) at 110 °C were the most suitable conditions for the reaction. The combination of $Pd(OAc)_2$ and dppb in $CH_2Cl_2$, toluene, or THF under $CO/H_2$ or CO/*p*-TsOH gave excellent total yields of $\alpha,\beta$-unsaturated amides (90–98%; Table 1, entries 1–3). However, high selectivity toward *N*,2-diphenyl propenamide (**3**) (92%) was achieved with the catalytic system including $Pd(OAc)_2$/dppb/CO/*p*-TsOH in THF as a solvent (Table 1, entry 3), whereas the replacement of dppb by dppp combined with $Pd(OAc)_2$/CO/*p*-TsOH in THF as a solvent gave excellent isolated yields (95%) of $\alpha,\beta$-unsaturated amides and exceptionally high selectivity of **3** (96%; Table 1, entry 5). The use of toluene in place of THF decreased the total yield of amides to 27% (Table 1, entry 6). In addition, the use of $CO/H_2$ in place of CO/*p*-TsOH in $CH_2Cl_2$ also gave poor yield of products (17%; Table 1, entry 4). Other bidentate and monodentate phosphine ligands, such as 1,2-bis(diphenylphosphino)ethane (dppe) or triphenylphosphine ($PPh_3$), gave low yields of products. Different palladium(II) and palladium(0) precursors, such as $PdCl_2(PPh_3)_2$ or $Pd(PPh_3)_4$, were tested in the presence of dppp or dppb in $CH_2Cl_2$ or THF under $CO/H_2$ or CO/*p*-TsOH media and gave either a low yield or a poor selectivity of the reaction of carbonylation of aniline with phenylacetylene (Table 1, entries 7–10). The analysis of the results indicated that the catalytic system $Pd(OAc)_2$/dppp combined with *p*-TsOH/CO in THF (system **A**) is more active than the same system combined with $CO/H_2$ in $CH_2Cl_2$ (system **B**). Therefore, the catalytic system $Pd(OAc)_2$/dppp/*p*-TsOH/CO in THF is the most suitable catalytic system that can be adopted in the further reactions of carbonylative coupling of phenylacetylene with various aniline derivatives.

## Catalytic carbonylative addition of 1-phenyl-1-butyne to aniline

The reaction of aniline (**1a**) with 1-phenyl-1-butyne (**2b**) catalyzed by various palladium precursors in the presence of different phosphine ligands and syngas ($CO/H_2$) or CO/*p*-

**Table 2.** Palladium(II)-catalyzed carbonylative addition of aniline (**1a**) to 1-phenyl-1-butyne (**2b**).[a]

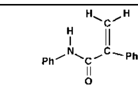
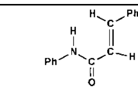
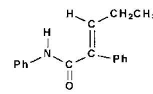
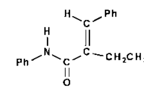
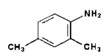
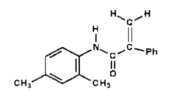
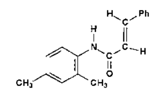
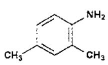
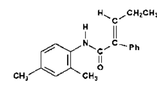
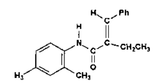
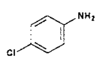
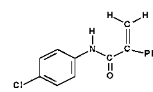
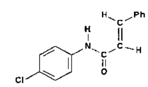
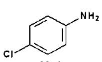
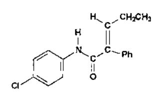
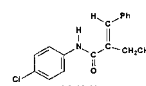
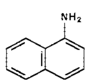
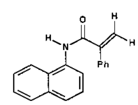
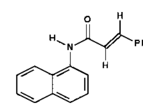
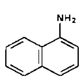
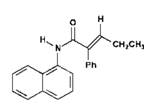
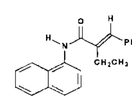
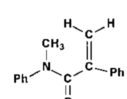
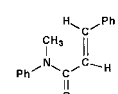
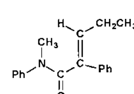
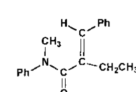
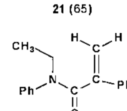
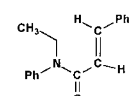
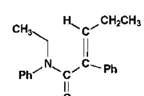
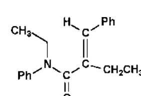


| Entry | Palladium catalyst | Ligand | Additive Solvent | Pressure $CO/H_2$ (psi) | Time (h) | Yield[b] (%) | Product distribution[c] (%) 5 | 6 |
|---|---|---|---|---|---|---|---|---|
| 1 | $Pd(OAc)_2$ | dppb | $CO/H_2$ $CH_2Cl_2$ | 300/300 | 24 | 75 | 62 | 38 |
| 2 | $Pd(OAc)_2$ | dppb | CO/*p*-TsOH THF | 300/– | 15 | 86 | 55 | 45 |
| 3 | $Pd(OAc)_2$ | dppp | $CO/H_2$ $CH_2Cl_2$ | 300/300 | 25 | 5 | 63 | 37 |
| 4 | $Pd(OAc)_2$ | dppp | CO/*p*-TsOH THF | 300/– | 15 | 95 | 60 | 40 |
| 5 | $Pd(OAc)_2$ | dppe | $CO/H_2$ $CH_2Cl_2$ | 300/300 | 48 | 18 | 84 | 16 |
| 6 | $Pd(OAc)_2$ | dppe | CO/*p*-TsOH THF | 300/– | 15 | 30 | 75 | 25 |
| 7 | $Pd(OAc)_2$ | $Ph_3P$ | $CO/H_2$ $CH_2Cl_2$ | 300/300 | 48 | 58 | 86 | 14 |
| 8 | $Pd(OAc)_2$ | $Ph_3P$ | CO/*p*-TsOH THF | 300/– | 24 | 62 | 80 | 20 |
| 9 | $PdCl_2$ | dppp | CO/*p*-TsOH THF | 300/– | 15 | 10 | 68 | 32 |
| 10 | $PdCl_2(PPh_3)_2$ | dppp | CO/*p*-TsOH THF | 300/– | 15 | 12 | 70 | 30 |
| 11 | $Pd(PPh_3)_4$ | dppp | CO/*p*-TsOH THF | 300/– | 15 | 16 | 65 | 35 |

[a] Reaction conditions: Pd, 0.02 mmol; ligand, 0.04 mmol, except for $Ph_3P$ = 0.08 mmol; aniline derivative, 2.0 mmol; 1-phenyl-1-phenyl-1-butyne, 2.0 mmol; solvent, 10 ml; *p*-TsOH, 0.12 mmol when used; 110 °C.
[b] Isolated yield.
[c] The ratio of **5**/**6** was determined by GC and by $^1H$ NMR.

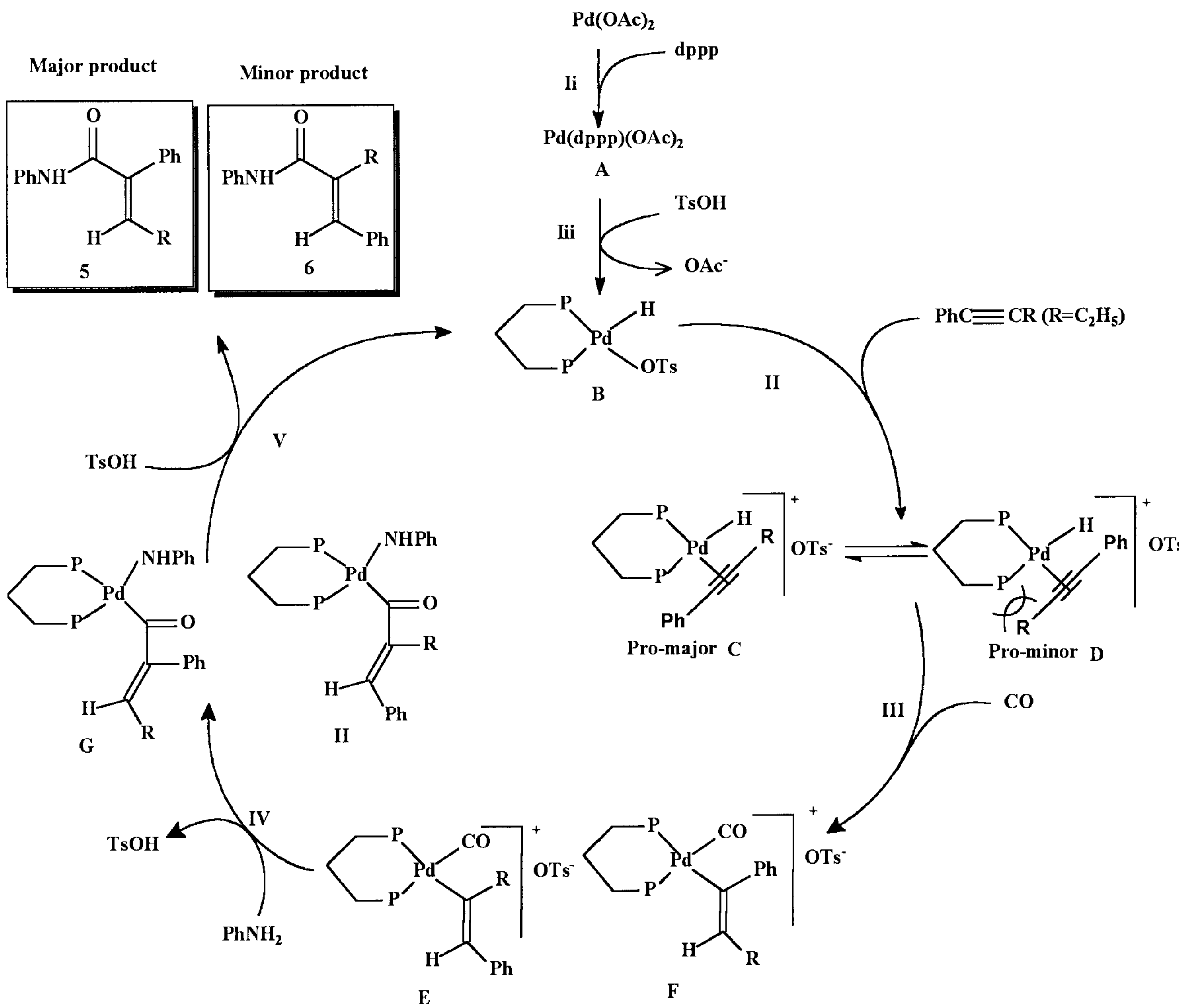
TsOH was chosen as a model reaction in the study of the carbonylative addition of aniline derivatives to aromatic internal alkynes (Table 2). The influence of the nature of the phosphine ligand was examined in the presence of $Pd(OAc)_2$ as a palladium catalyst under the following experimental conditions, which were determined in the previous section, namely: system **A**: $CO/H_2$ in $CH_2Cl_2$; system **B**: CO/*p*-TsOH. The two expected products of the reaction of carbonylation of aniline (**1a**) with 1-phenyl-1-butyne (**2b**) are (*E*)-*N*,2-diphenyl pentenamide (**5**) and (*E*)-2-ethyl-*N*,3-diphenyl propenamide (**6**). The bidentate phosphine ligands dppb, dppp, dppe were tested with $Pd(OAc)_2$ as a catalyst in this carbonylation reaction in order to determine the effect of chelation on the selectivity of the reaction. Dppb gave good yields of products (75–86%) under either conditions **A** or **B**, and the regioselectivity of the reaction was moderate with a little excess of **5** (Table 2, entries 1, 2). However, dppp gave only 5% of products under conditions **B**; but excellent yields (95%) with the ratio of products **5**/**6** equal to 60/40 under conditions **A** (Table 2, entries 3, 4). The ratio of **5**/**6** was improved to 84/16 and 75/25 by using dppe as ligand. However, the total yields were low (18–30%; Table 2, entries 5, 6). The monodentate phosphine $PPh_3$ gave higher yields (58–62%) and good selectivity of **5** (80–86%) than dppe (Table 2, entries 7, 8), but the yields were low compared with the results obtained with dppp, even at elongated reaction time (48 h). The use of other monodentate phosphine ligands, such as tri-*o*-tolylphosphine, tricyclohexylphosphine, or tributylphosphine, led to lower yields and selectivity of the reaction. In addition, the combination of dppp and $PPh_3$ in the same reaction did not improve the product distribution of **5**/**6**. Other palladium(II) and palladium(0) complexes, such as $PdCl_2$, $PdCl_2(PPh_3)_2$, and $Pd(PPh_3)_4$, have been used in the reaction of carbonylative addition of aniline (**1a**) with 1-phenyl-1-butyne (**2b**) in the presence of dppp as ligand and under the experimental conditions **B**. The yields were generally very low (10–16%; Table 2, entries 9–11), with no change in the selectivity of the reaction being observed. It seems obvious now that the combination of $Pd(OAc)_2$/dppp/CO/*p*-TsOH in THF represents an active catalytic system of the carbonylative addition of aniline derivatives to aromatic internal alkynes.

**Table 3.** Palladium(II)-catalyzed carbonylative addition of aniline derivatives (**1a–f**) to aromatic alkynes (**2a,b**).[a,b]

| Entry | Aniline derivative (**1**) | Alkyne (**2**) | Yield[c] (%) | Product distribution[d] | |
|---|---|---|---|---|---|
| | | | | *gem* or *E1* **3–25** (%) | *trans* or *E2* **4–26** (%) |
| 1 | $C_6H_5NH_2$ (**1a**) | Ph–C≡CH (**2a**) | 95 |  3 (96) |  4 (4) |
| 2 | $C_6H_5NH_2$ (**1a**) | Ph–C≡C–$CH_2CH_3$ (**2b**) | 95 |  5 (60) |  6 (40) |
| 3 |  (1b) | Ph–C≡CH (**2a**) | 98 |  7 (98) |  8 (2) |
| 4 |  (1b) | Ph–C≡C–$CH_2CH_3$ (**2b**) | 89 |  9 (65) |  10 (35) |
| 5 |  (1c) | Ph–C≡CH (**2a**) | 93 |  11 (100) |  12 (0) |
| 6 |  (1c) | Ph–C≡C–$CH_2CH_3$ (**2b**) | 85 |  13 (66) |  14 (34) |
| 7 |  (1d) | Ph–C≡CH (**2a**) | 92 |  15 (100) |  16 (0) |
| 8 |  (1d) | Ph–C≡C–$CH_2CH_3$ (**2b**) | 90 |  17 (72) |  18 (28) |
| 9 | $C_6H_5$–NH–$CH_3$ (**1e**) | Ph–C≡CH (**2a**) | 93 |  19 (98) |  20 (2) |
| 10 | $C_6H_5$–NH–$CH_3$ (**1e**) | Ph–C≡C–$CH_2CH_3$ (**2b**) | 82 |  21 (65) |  22 (35) |
| 11 | $C_6H_5$–NH–$CH_2CH_3$ (**1f**) | Ph–C≡CH (**2a**) | 95 |  23 (96) |  24 (4) |
| 12 | $C_6H_5$–NH–$CH_2CH_3$ (**1f**) | Ph–C≡C–$CH_2CH_3$ (**2b**) | 90 |  25 (72) |  26 (28) |

[a] Reaction conditions: $Pd(OAc)_2$, 0.02 mmol; dppp, 0.04 mmol; alkyne, 2.0 mmol; aniline derivative, 2.0 mmol; *p*-TsOH, 0.12 mmol; THF, 10 ml; 300 psi CO; 110 °C; 15 h.
[b] Spectra are available with the Editor as supplementary material.
[c] Isolated yields.
[d] The ratio *gem* or *E1*/*trans* or *E2* was determined by GC and $^1$H NMR.




Scheme 1.

## Catalytic carbonylative addition of aromatic alkynes to different aniline derivatives

The carbonylative addition of aniline derivatives to aromatic alkynes is more sensitive to the types of alkyne substituent than to the substituents of the aniline derivatives. The results are summarized in Table 3. In general, internal aromatic alkynes react less regioselectively than terminal aromatic alkynes. For example, the carbonylation of phenylacetylene in the presence of different aniline derivatives (Table 3, entries 1, 3, 5, 7, 9, 11) showed excellent total yields (92–100%) of *gem* and *trans* unsaturated amides with excellent selectitivities (96–100%) toward *gem* products. The carbonylation of *p*-chloroaniline (**1c**) and 1-naphthylamine (**1d**) with phenylacetylene (**2a**) led to one product of the reaction with excellent total yields (92–93%) of the corresponding *gem*-$\alpha,\beta$-unsaturated amides **11** and **15** respectively (Table 3, entries 5, 7). The results obtained with various aniline derivatives showed that the carbonylation reaction is not sensitive to the type of aniline. For instance, the *N*-substituted aniline derivatives, such as *N*-methylaniline and *N*-ethylaniline, showed high reactivity in the reaction of carbonylation with phenylacetylene (Table 3, entries 9, 11). The presence of a methyl or an ethyl group on the nitrogen of the aniline did not impose any steric demand, and also did not affect the regioselectivity of the reaction.

The carbonylation of 1-phenyl-1-butyne (**2b**), an internal aromatic alkyne, with various aniline derivatives was also investigated. The two expected products of the reaction were present in the *E* form. These products were formed by either the addition of CO to the carbon of the triple bond attached to the phenyl group (product *E1*), or *via* the addition of CO to the carbon of the triple bond attached to the alkyl group (product *E2*). The examination of different aniline derivatives **1b–f** having an electron-donating group (**1b**) or electron-withdrawing groups (**1c**,**d**) substituted on the aromatic ring and also *N*-alkyl substituted aniline derivatives (**1e**,**f**) resulted in excellent total yields (80–90%) of $\alpha,\beta$-unsaturated amides $E1 + E2$ and moderate to good selectivities (65–72%) toward the *E1* isomers (Table 3, entries 2, 4, 6, 8, 10, 12). It seems clear that the substituents of the alkynes have a determining role in the regioselectivity; hence, the steric effect around the nitrogen of the aniline and the acidity of hydrogen attached to the nitrogen atom have less effect on the selectivity of the reaction of carbonylation of aniline derivatives with phenylacetylene or with aromatic internal alkynes.

## PROPOSED MECHANISM

The mechanisms of the hydrocarboxylation and hydrocarboalkoxylation of alkenes and alkynes have been studied thoroughly in the last two decades; however, these mechanism remain elusive. It was proposed that metal-catalyzed hydrocarboalkoxylation of alkynes and alkenes can, in principle, proceed through either M—H[16,18,19] or M—COOR.[20,21] On the basis of the literature precedents and our experimental results, the following tentative hydride mechanism has been proposed for the carbonylative addition of aniline (**1a**) and 1-phenyl-1-butyne (**2a**) catalyzed by $Pd(OAc)_2$/dppp/*p*-TsOH/CO (Scheme 1). This mechanism involves the coordination of bidentate ligand dppp to $Pd(OAc)_2$ to form complex **A**, which reacts with *p*-TsOH to generate the palladium hydride complex **B** (steps **Ii** and **Iii**). The coordination of alkyne to **B** leads to two probable intermediates: pro-major and pro-minor cationic species **C** and **D** (step II). The insertion of the coordinated alkyne into the Pd—H bond accompanied with CO addition gives complexes **E** and **F** (step III). The CO insertion into the Pd—C bond followed by the coordination of aniline to the palladium center affords the acylpalladium complexes **G** and **H** (step IV). The final step of the reaction is the reductive elimination that takes place in the presence of *p*-TsOH to form the products **5** and **6** and regenerate the active catalytic species **B** (step V). The regioselectivity of the reaction is probably determined in steps II and III. The steric factor of the bidentate phosphine ligands and the presence of the phenyl group on the acetylenic bond have important influences on the selectivity of the reaction. In the case of phenylacetylene, the addition of [Pd—H] to the triple bond is mainly directed by the electronic effect of the phenyl group. However, the presence of an alkyl group on the other carbon of the triple bond activates the addition of Pd—H on this carbon. Thus, the Pd—H is most probably added to the less crowded carbon in the way that the substituents **R** would be placed away from the chelating ligand.

## CONCLUSION

The carbonylative addition of aniline derivatives to aromatic alkynes using the catalytic system $Pd(OAc)_2$/dppp/*p*-TsOH in THF provides an efficient and simple method for the synthesis of new *N*-aryl-2,3-disubstituted acrylamides. The other catalytic system formed of $Pd(OAc)_2/PPh_3$/*p*-TsOH in THF, despite the moderate total isolated yields, also represents an attractive system towards the selective synthesis of *N*-aryl-$\alpha,\beta$-disubstituted amides. These methods demonstrated the high efficiency of palladium (II) acetate associated with dppb or dppp as an active catalyst of carbonylation reaction in the synthesis of highly useful compounds such as $\alpha,\beta$-unsaturated amides. The regioselectivity of the carbonylative coupling was very sensitive to the type of alkyne. The terminal aromatic alkynes gave excellent yields and selectivity, whereas the aromatic internal alkynes gave moderate selectivity of the reaction. It is important to note that the catalytic synthesis of tertiary $\alpha,\beta$-unsaturated amides was successfully achieved in a one-step reaction. Currently, we are examining the efficiency of this catalytic system, $Pd(OAc)_2$/dppp/*p*-TsOH, in the carbonylative coupling of primary and secondary alkylamines and diamines with terminal, internal alkyl and aromatic alkynes.

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