

# Aminocarbonylation of phenylacetylene catalysed by palladium acetate in combination with (2-pyridyl)diphenylphosphine and methanesulfonic acid

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## Abstract

The aminocarbonylation of phenylacetylene has been studied in the presence of the catalytic system formed by palladium acetate in combination with (2-pyridyl)diphenylphosphine and methanesulfonic acid. The catalytic activity is strongly influenced by the nature of the amine: good reaction rates are achieved using amines of low basicity such as aniline. The reaction solvent influences both the activity and the selectivity of the catalyst: the highest reaction rates accompanied by complete regioselectivity towards the branched amide are obtained working in dichloromethane/*N*-methylpyrrolidinone mixtures. Also the acid to palladium molar ratio and the  $P(\text{CO})$  affect to a lower extent the process: the highest catalyst activity is obtained operating at a methanesulfonic acid/Pd molar ratio of 30:1 and at  $P(\text{CO}) = 20$  atm. © 2004 Elsevier B.V. All rights reserved.

**Keywords:** Alkynes; Carbonylation; Amides; Palladium; Aminocarbonylation

## 1. Introduction

Acrylamides are valuable monomers which are used to produce several important polymeric materials [1]. While currently the most employed process for the synthesis of acrylamide is the hydration of acrylonitrile, the synthesis of *N*-substituted acrylamides usually requires stepwise methods starting from acrylic acid or its esters [2]. An alternative method for the direct and clean synthesis of substituted acrylamides could be the carbonylation of alkynes in the presence of amines (aminocarbonylation, Scheme 1) [3].

Our interest in the synthesis of  $\alpha,\beta$ -unsaturated amides, in particular the ones deriving from 2-arylpropenoic acids (Scheme 1, R = aryl) [4] and our concern in the use of alkyne carbonylation for the synthesis of valuable fine chemicals [5] spurred us to explore the feasibility of phenylacetylene carbonylation in the presence of amines.

In the last years, a variety of new palladium-based catalytic systems active in aminocarbonylation have been described in the literature [6–12]. Among them, the most ap-

pealing appears the one formed by  $\text{Pd}(\text{OAc})_2$  in combination with (2-pyridyl)diphenylphosphine and methanesulfonic acid [11,12], a catalytic system which is also extremely active in the alkoxy carbonylation of terminal alkynes [13]. In this paper, we wish to report the results of our investigations on the carbonylation of phenylacetylene in the presence of amines and the above cited catalytic system.

## 2. Experimental

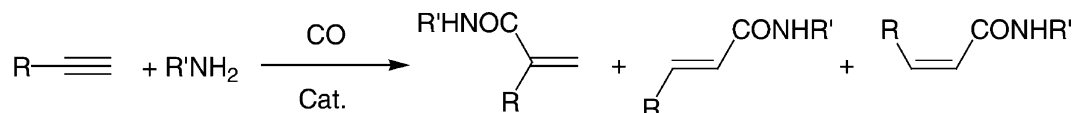
### 2.1. Materials and instruments

All the operations were carried out under argon in Schlenk-type glassware. Commercial solvents (Baker) were purified following methods described in literature [17]. Phenylacetylene, *n*-butylamine, aniline and *N*-methylpyrrolidinone were purchased from Aldrich and distilled prior to use. (2-Pyridyl)diphenylphosphine (Aldrich), methanesulfonic acid (Aldrich) and palladium acetate (Engelhard Industries) were used as received. High purity CO was purchased from SIAD.

The carbonylation experiments were carried out in a magnetically stirred stainless steel autoclave (total volume ca.

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Scheme 1. Carbonylation of terminal alkynes in the presence of amines.

150 ml). Conversion and yield of the reactions were determined by GLC on a Hewlett-Packard 5830 II series gas chromatograph, using mesitylene as internal standard. GLC-MS analyses were carried out on a HP 5830 II series gas chromatograph interfaced to a Hewlett-Packard 5971 quadrupole mass detector.

## 2.2. Carbonylation experiments

Under an inert atmosphere, a Schlenk flask was charged with 20 ml of NMP, 37.9 mg (0.144 mmol) of (2-Py)PPh<sub>2</sub>, 2.0 mg (0.009 mmol) of Pd(OAc)<sub>2</sub>, 2.550 g (25.0 mmol) of phenylacetylene, 0.837 g (9.0 mmol) of aniline, 25 mg (0.27 mmol) of CH<sub>3</sub>SO<sub>3</sub>H and 1.030 g (8.6 mmol) of mesitylene (run 3 of Table 5). The resulting solution was transferred via cannula into the autoclave, which was then pressurised with CO (20 atm). The reactor was heated at 70 °C (±1 °C) by circulating a thermostatic fluid. After 1 h, the reactor was cooled to room temperature and the residual gas vented off.

## 3. Results and discussion

In preliminary experiments, the carbonylation of phenylacetylene was carried out in the presence of *n*-butylamine. The relevant data are reported in Table 1 together with the reaction conditions.

A modest catalytic activity is observed only at 100 °C: at this temperature, the amine conversion is 51% after 65 h. The use of a GC internal standard reveals that the chemoselectivity of the reaction is not complete, the yield in amides being only 37%. The incomplete chemoselectivity is likely due to the formation of polymeric species since, besides the amides, no other products are detected by GC analysis. Quite favourably, the regioselectivity towards the branched amide is high (ca. 90%).

Table 1  
Carbonylation of phenylacetylene: influence of the amine basicity

Run	Amine	pK <sub>a</sub>	Amine (mmol)	Alkyne (mmol)	T (°C)	t (h)	Amine conversion (%)	Amide yield (%)	
								Branched	Linear <sup>a</sup>
1	<i>n</i> -Butylamine <sup>b</sup>	10.77 <sup>c</sup>	15.0	15.0	100	65	51	34	3
2	Aniline <sup>d</sup>	4.63 <sup>c</sup>	9.0	9.0	50	1	21	14	Traces

Reaction conditions: P(CO) = 20 atm, solvent = CH<sub>2</sub>Cl<sub>2</sub> (20 ml), Pd(OAc)<sub>2</sub> = 0.03 mmol, (2-Py)PPh<sub>2</sub> = 0.5 mmol, (2-Py)PPh<sub>2</sub>/Pd = 16:1, CH<sub>3</sub>SO<sub>3</sub>H = 0.72 mmol, CH<sub>3</sub>SO<sub>3</sub>H/Pd = 24:1.

<sup>a</sup> Only the *trans* isomer is obtained.

<sup>b</sup> Amine/Pd = 500:1, alkyne/amine = 1; alkyne/Pd = 500:1.

<sup>c</sup> Value from Ref. [14].

<sup>d</sup> Amine/Pd = 300:1, alkyne/amine = 1; alkyne/Pd = 300:1.

Table 2

Carbonylation of phenylacetylene: influence of the alkyne/amine molar ratio

Phenylacetylene/ aniline (mol/mol)	Aniline conversion (%) <sup>a</sup>	Branched amide yield (%)	Chemoselectivity (%) <sup>b</sup>
3/1 <sup>c</sup>	75	55	73
1/1 <sup>c</sup>	21	14	67
1/3 <sup>d</sup>	18	6	33

Reaction conditions: P(CO) = 20 atm, T = 50 °C, reaction time = 1 h, solvent = CH<sub>2</sub>Cl<sub>2</sub> (20 ml), Pd(OAc)<sub>2</sub> = 0.03 mmol, (2-Py)PPh<sub>2</sub> = 0.5 mmol, (2-Py)PPh<sub>2</sub>/Pd = 16:1, CH<sub>3</sub>SO<sub>3</sub>H = 0.72 mmol, CH<sub>3</sub>SO<sub>3</sub>H/Pd = 24:1.

<sup>a</sup> Conversion of the limiting reagent.

<sup>b</sup> Mol of amide formed divided by mol of converted limiting reagent × 100.

<sup>c</sup> Aniline = 9.0 mmol.

<sup>d</sup> Aniline = 27.0 mmol.

These modest results, probably due to the high basicity of *n*-butylamine which depresses the promoting effect of the acid cocatalyst, prompted us to carry out a further set of experiments in the presence of aniline (run 2 of Table 1). Indeed, with this amine of moderate basicity, the carbonylation of phenylacetylene proceeds with appreciable reaction rates even at 50 °C. Moreover, even if the chemoselectivity of the reaction is not complete, the regioselectivity towards the branched amide is almost total.

In order to achieve a deeper insight on the factors affecting the catalytic activity, we have carried out a systematic analysis of the effects brought about by the catalyst composition and the reaction conditions.

First, some experiments at different phenylacetylene/aniline molar ratios were carried out. From the relevant data (Table 2), it appears that there is no significant difference in reaction rate working with a 1:1 molar ratio of the two reactants or with an excess of amine (runs 2 and 3); by contrast, a considerable increase in catalytic activity is

Table 3  
Carbonylation of phenylacetylene: influence of the solvent

Solvent	<i>T</i> (°C)	<i>t</i> (h)	Aniline conversion (%)	Branched amide yield (%)	Chemoselectivity (%)
THF	50	20	16	5	31
Acetone	50	1	40	17	42
Dichloromethane	50	1	75	59	78
Dichloromethane	70	1	100	74	74
NMP	50	20	18	18	100
NMP	70	2	100	99	99

Reaction conditions:  $P(\text{CO}) = 20$  atm, solvent = 20 ml, phenylacetylene = 25.0 mmol, amine = 9.0 mmol,  $\text{Pd}(\text{OAc})_2 = 0.03$  mmol,  $(2\text{-Py})\text{PPh}_2 = 0.5$  mmol,  $(2\text{-Py})\text{PPh}_2/\text{Pd} = 16:1$ ,  $\text{CH}_3\text{SO}_3\text{H} = 0.72$  mmol,  $\text{CH}_3\text{SO}_3\text{H}/\text{Pd} = 24:1$ , aniline/Pd = 300:1.

obtained when an excess of phenylacetylene is used (run 1). This result is not surprising since kinetic measurements indicate that the reaction rate of the strictly related alkyne alkoxy carbonylation is first order in alkyne concentration [13]. It is interesting to note that in all the experiments of Table 2 total regioselectivity towards the branched isomer is obtained and that the use of an excess of aniline causes a substantial decrease of the chemoselectivity.

The data reported in Table 3 highlight the role played by the reaction solvent. At 50 °C, in tetrahydrofuran both the activity and selectivity of the catalyst are very low. The use of acetone strongly increases the reaction rate, but does not significantly change the chemoselectivity. Further improvement in both the rate and the chemoselectivity of the reaction is obtained in dichloromethane. In this solvent an increase of the temperature up to 70 °C allows to obtain complete conversion of aniline without any loss in chemo- and regioselectivity. The major drawback associated to the use of dichloromethane remains the incomplete chemoselectivity. *N*-Methylpyrrolidinone (NMP) appears to be the most suitable solvent: in fact, it allows to obtain complete chemo- and regioselectivity in the desired branched amide. Also the reaction rate, which at 50 °C is very low, at 70 °C becomes very good affording total substrate conversion in 2 h. Probably, in this solvent it is necessary to go beyond a threshold temperature (approximately 60 °C) in order to achieve high activity. The higher catalytic efficiency achieved in NMP is not easily accounted for, but it can be tentatively attributed to its highly polar character.

According to these findings, a further set of experiments was carried out in NMP to evaluate the influence of the carbon monoxide pressure.

The results, collected in Table 4, show that also the  $P(\text{CO})$  affects the catalysis. The highest reaction rates are obtained working at relatively low pressures, i.e. 20 atm, while at higher CO pressures the catalytic activity is reduced. An alike behaviour has been previously noticed when the same catalytic system is used in the alkoxy carbonylation of alkynes [15,16]: it is likely that CO competes either with the alkyne or the amine for the co-ordination to the active centre in the catalytic cycle.

Table 4  
Carbonylation of phenylacetylene: influence of  $P(\text{CO})$

$P(\text{CO})$ (atm)	Aniline conversion (%)	Branched amide yield (%)	Chemoselectivity (%)
20	100	99	99
30	95	95	99
40	63	63	100
60	26	26	100

Reaction conditions:  $T = 70$  °C, reaction time = 1 h, solvent = NMP (20 ml), phenylacetylene = 25.0 mmol, aniline = 9.0 mmol,  $\text{Pd}(\text{OAc})_2 = 0.03$  mmol,  $(2\text{-Py})\text{PPh}_2 = 0.5$  mmol,  $(2\text{-Py})\text{PPh}_2/\text{Pd} = 16:1$ , aniline/Pd = 300:1,  $\text{CH}_3\text{SO}_3\text{H} = 0.72$  mmol,  $\text{CH}_3\text{SO}_3\text{H}/\text{Pd} = 24:1$ .

To further optimise the reaction conditions, we also investigated the influence of the acid/palladium molar ratio (Table 5).

The data indicate that on increasing the acid to palladium molar ratio the catalyst activity increases reaching a maximum at an acid to palladium ratio of 30. The use of higher acid quantities results in a sharp decrease of the reaction rate. In all the reactions, the chemoselectivity remains complete.

It is interesting to note that this behaviour is different from that observed in alkoxy carbonylation where for acid to palladium molar ratios greater than 10:1 the reaction is zero order in acid concentration [13]. In aminocarbonylation, probably, the observed maximum results from a compromise between two opposite factors, i.e. the need for high acid and high free amine concentration.

The data reported in Table 3 suggest that while NMP improves the chemoselectivity, dichloromethane enhances the

Table 5  
Carbonylation of phenylacetylene: influence of acid/palladium ratio

$\text{CH}_3\text{SO}_3\text{H}/\text{Pd}$ (mol/mol)	Aniline conversion (%)	Branched amide yield (%)
10	10	10
20	20	20
25	28	28
30	44	44
40	10	10

Reaction conditions:  $P(\text{CO}) = 20$  atm,  $T = 70$  °C, reaction time = 1 h, solvent = NMP (20 ml), phenylacetylene = 25.0 mmol, aniline = 9.0 mmol,  $\text{Pd}(\text{OAc})_2 = 0.009$  mmol,  $(2\text{-Py})\text{PPh}_2 = 0.14$  mmol,  $(2\text{-Py})\text{PPh}_2/\text{Pd} = 16:1$ , aniline/Pd = 1000:1.

Table 6  
Carbonylation of phenylacetylene in CH<sub>2</sub>Cl<sub>2</sub>/NMP mixtures

CH <sub>2</sub> Cl <sub>2</sub> /NMP (vol/vol)	Aniline/Pd (mol/mol)	Aniline conversion (%)	Branched amide yield (%)
9/1	1000	100	100
9/1	4000	46	46
8/2	4000	25	25

Reaction conditions:  $P(\text{CO}) = 20 \text{ atm}$ ,  $T = 70^\circ\text{C}$ , reaction time = 1 h, solvent = 20 ml, phenylacetylene = 25.0 mmol, Pd(OAc)<sub>2</sub> = 0.009 mmol, (2-Py)PPh<sub>2</sub> = 0.14 mmol, (2-Py)PPh<sub>2</sub>/Pd = 16:1, CH<sub>3</sub>SO<sub>3</sub>H = 0.27 mmol, CH<sub>3</sub>SO<sub>3</sub>H/Pd = 30:1.

reaction rate. Thus, we have carried out a set of carbonylation experiments using dichloromethane/NMP mixtures as the reaction solvent so as to limit the use of NMP which is expensive and difficult to remove. The results, reported in Table 6, show that using dichloromethane containing small percentages of NMP it is possible to obtain a considerable enhancement of the reaction rate still retaining the high selectivity typical of NMP.

Thus, working in a CH<sub>2</sub>Cl<sub>2</sub>/NMP 10:1 mixture (v/v) at a amine to palladium ratio of 1000, total conversion is achieved in 1 h. When the aniline/palladium ratio is 4000:1 a reaction rate of approximately 1800 mol/mol palladium per hour is achieved.

#### 4. Conclusions

The work here reported shows that palladium acetate in the presence of (2-pyridyl)diphenylphosphine and methanesulfonic acid is an efficient catalyst for the carbonylation of terminal alkynes in the presence of an amine of moderate basicity such as aniline. The reaction rate is strongly influenced by the concentration of the acid cocatalyst and the reaction parameters: In particular, the use of NMP as solvent appears to play an outstanding role allowing to obtain total chemoselectivity towards amides.

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#### References

- [1] F.C. Bucholz, Ullmann's Encyclopedia of Industrial Chemistry, Polyacrylamides and Poly(acrylic acids), 6th ed., Electronic Release, Wiley-VCH, Weinheim, 1998.
- [2] T. Ohara, T. Sato, N. Shimizu, G. Prescher, H. Schwind, O. Weiberg, K. Marten, Ullmann's Encyclopedia of Industrial Chemistry, Acrylic Acid and Derivatives, 6th ed., Electronic Release, Wiley-VCH, Weinheim, 1998.
- [3] W. Reppe, Justus Liebigs Ann. Chem. 582 (1953) 1.
- [4] U. Matteoli, C. Botteghi, F. Sbrogiò, V. Beghetto, S. Paganelli, A. Scrivanti, J. Mol. Catal. A: Chem. 143 (1999) 287.
- [5] A. Scrivanti, V. Beghetto, U. Matteoli, Adv. Synth. Catal. 344 (2002) 543.
- [6] B. El Ali, J. Tijani, A.M. El-Ghanam, Appl. Organomet. Chem. 16 (2002) 369.
- [7] B. El Ali, J. Tijani, A.M. El-Ghanam, J. Mol. Catal. A: Chem. 187 (2002) 17.
- [8] S. Torii, H. Okumoto, M. Sadakane, L.H. Xu, Chem. Lett. (1991) 1673.
- [9] B. El Ali, A. El-Ghanam, M. Fettouhi, J. Tijani, Tetrahedron Lett. 41 (2000) 5761.
- [10] K. Mori, T. Mizoroki, A. Ozaki, Chem. Lett. (1975) 39.
- [11] E. Drent, P. Arnoldy, P.H.M. Budzelaar, J. Organomet. Chem. 455 (1993) 247.
- [12] E. Drent, US Patent 5128475 (1992).
- [13] E. Drent, W.W. Jager, J.J. Keijsper, F.G.M. Niele, in: B. Cornils, W.A. Hermann (Eds.), Applied Homogeneous Catalysis with Organometallic Compounds, VCH, Weinheim, 1996 (Chapter 3.3.9).
- [14] CRC Handbook of Chemistry and Physics, 76th ed., CRC Press, Boca Raton, 1995.
- [15] A. Scrivanti, V. Beghetto, E. Campagna, M. Zanato, U. Matteoli, Organometallics 17 (1998) 630.
- [16] A. Scrivanti, V. Beghetto, M. Zanato, U. Matteoli, J. Mol. Catal. A: Chem. 160 (2000) 331.
- [17] W.L.F. Armarego, D.D. Perrin, Purification of Laboratory Chemicals, 4th ed., Butterworth-Heinemann, Oxford, 1996.