

# Mechanism of the Alkoxy carbonylation of Alkynes in the Presence of the Pd(OAc)<sub>2</sub>/PPh<sub>2</sub>Py/CH<sub>3</sub>SO<sub>3</sub>H Catalytic System

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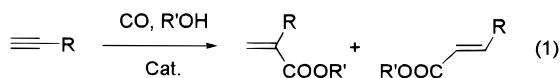
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The mechanism of the carbonylation of alkynes promoted by the Pd(OAc)<sub>2</sub>/2-pyridyldiphenylphosphine/methanesulfonic acid catalytic system has been studied. The carbonylation of 2-butyne in the presence of methanol affords stereospecifically the methyl ester of (*E*)-2-methyl-2-butenic acid, indicating that the addition of H and COOCH<sub>3</sub> moieties proceeds with *cis* stereochemistry. Experiments carried out using 1-alkynes and CH<sub>3</sub>OD reveal that the catalyst also promotes the exchange of the terminal hydrogen of the alkyne with the deuterium of the alcohol. <sup>1</sup>H NMR experiments show that upon addition of phenylacetylene to a CD<sub>2</sub>Cl<sub>2</sub> solution containing the catalyst and CH<sub>3</sub>OH a palladium complex having a 2-styryl group bound to the metal center, Pd–C(C<sub>6</sub>H<sub>5</sub>)=CH<sub>2</sub>, is formed. This species can be invoked as an intermediate to account for both the H/D exchange and the carbonylation reaction. Carbonylation of 2-butyne in the presence of a 1/1 mixture of CH<sub>3</sub>OH and CH<sub>3</sub>OD indicates that a fairly large isotope effect (*k*<sub>H</sub>/*k*<sub>D</sub> = 6.4) is operative. All these results suggest that the carbonylation of alkynes proceeds *via* the protonation of a Pd(0)–alkyne species to give a Pd–vinyl complex, followed by CO insertion and alcoholysis.

## Introduction

The alkoxy carbonylation of 1-alkynes is an important process which allows α,β-unsaturated carboxylic acids or their derivatives (eq 1) to be obtained from readily available substrates in one step.<sup>1</sup>



Recently, a novel catalytic system was developed by Drent,<sup>2</sup> who found that Pd(OAc)<sub>2</sub> in combination with 2-pyridyldiphenylphosphine (PPh<sub>2</sub>Py) and CH<sub>3</sub>SO<sub>3</sub>H gives a very active system which displays selectivities toward the formation of the 2-substituted acrylic derivatives as high as 99.95%. The high activity and selectivity of this system warrants its use not only in the synthesis of important large-scale chemical intermediates such as methacrylates<sup>2,3</sup> but also in the preparation of fine chemicals: for example, we<sup>4</sup> have taken advantage of its excellent characteristics to devise a straightforward synthesis of 2-(6-methoxy-2-naphthyl)propenoic acid, a precursor of Naproxen.

These results and some features of the catalytic system developed by Drent make mechanistic studies worthwhile: for instance, the role played by the pyridyl moiety in the ligand is outstanding since, if replaced by a phenyl group<sup>2</sup> or by a heteroaromatic ring not containing N atoms,<sup>5</sup> the catalytic activity is strongly depressed. Another puzzling feature is the role played by methanesulfonic acid in the reaction.

In principle the alkoxy carbonylation of alkynes may proceed by two mechanisms.<sup>2,6</sup> The first, reported in Scheme 1A, involves (i) formation of an (alkoxy carbonyl)palladium complex generated by the insertion of CO into a Pd–OR bond, (ii) migration of the carboalkoxy moiety on a carbon atom of the triple bond of the 1-alkyne π-coordinated to the metal center, and (iii) protonolysis of the resulting vinyl intermediate. The second (Scheme 1B) essentially involves (i) insertion of the alkyne into a Pd–H bond to give a (σ-vinyl)palladium complex and (ii) CO insertion into the Pd–C bond to afford an acylpalladium complex which upon alcoholysis yields the expected ester, regenerating the hydride.

Experimental evidence supporting the alkoxy carbonyl route<sup>6,7</sup> has been provided by Norton,<sup>8</sup> who also studied the intimate mechanism of the intramolecular addition of the COOCH<sub>3</sub> moiety to a carbon–carbon triple bond coordinated to a Pd(II) metal center.<sup>9</sup> On the other hand, evidence supporting the hypopalladation route

(1) (a) Tsuji, J. *Palladium Reagents and Catalysts*; Wiley: New York, 1996; p 471. (b) Bates, R. W. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, U.K., 1995; Vol. 3, p 349. (c) Colquhoun, H. M.; Thomson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York, 1991. (d) Bird, C. W. *Chem. Rev.* **1962**, *62*, 283.

(2) (a) Drent, E.; Arnoldy, P.; Budzelaar, P. H. M. *J. Organomet. Chem.* **1993**, *455*, 247. (b) Drent, E.; Arnoldy, P.; Budzelaar, P. H. M. *J. Organomet. Chem.* **1994**, *475*, 57.

(3) Doyle, M. J.; van Gogh, J.; van Ravenswaay Claasen, J. Eur. Pat. Appl. EP-A-392,601, 1990; *Chem. Abstr.* **1991**, *114*, 102997p.

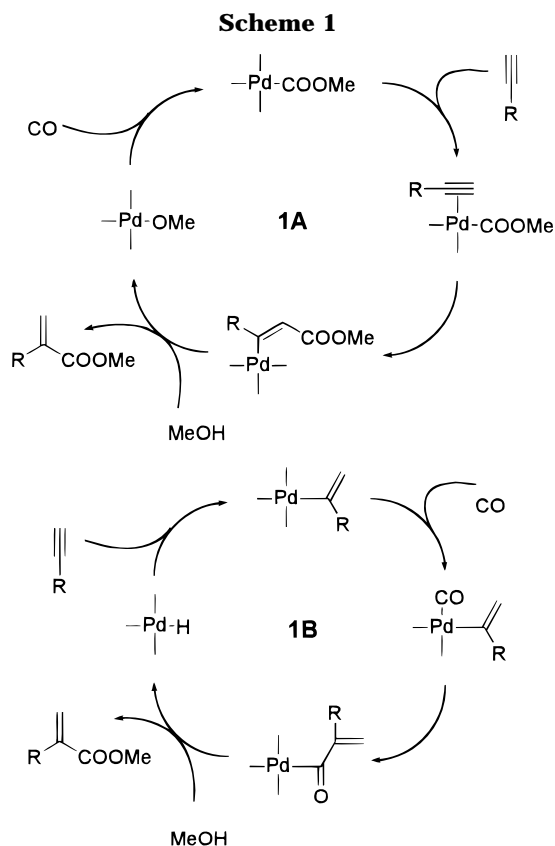
(4) Scrivanti, A.; Matteoli, U. *Tetrahedron Lett.* **1995**, *36*, 9015.

(5) Matteoli, U.; Scrivanti, A. Unpublished results.

(6) Milstein, D. *Acc. Chem. Res.* **1988**, *21*, 428.

(7) The chemistry of metal alkoxides has been reviewed: Bryndza, H. E.; Tam, W. *Chem. Rev.* **1988**, *88*, 1163.

(8) Murray, T. F.; Norton, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 4107.



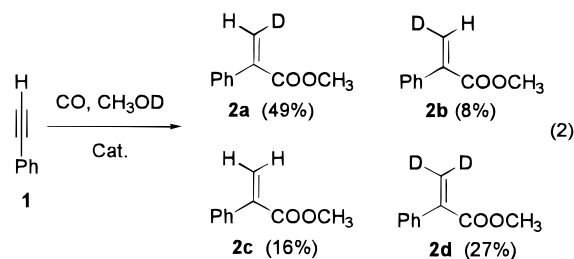
has also been found,<sup>10,11</sup> and it is likely that a number of mechanisms may operate.

Here we wish to report some results of our studies aimed at identifying the essential steps of the catalytic cycle and to understand the factors governing the chemo- and regioselectivity of the process promoted by the Drent catalyst.

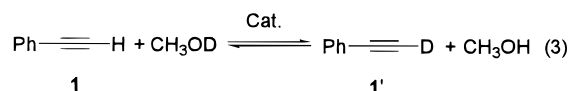
### Results and Discussion

Our initial mechanistic investigations were aimed at establishing the stereochemistry of the reaction. The carbonylation of phenylacetylene (**1**) was carried out using CH<sub>3</sub>OD in the presence of the Drent catalytic system (Pd(OAc)<sub>2</sub>/PPh<sub>2</sub>Py/CH<sub>3</sub>SO<sub>3</sub>H in the molar ratio 1/10/10, substrate/Pd = 4000/1). At 50 °C and *P*(CO) = 25 atm, complete conversion of the substrate is achieved in ca. 1 h. GLC analysis indicates that the product is a ca. 98/2 mixture of methyl 2-phenylpropenoate (**2**; methyl atropate) and methyl 3-phenylpropenoate (**3**; methyl cinnamate), respectively. <sup>1</sup>H NMR analysis indicates that **2** has the isotopomeric composition depicted in eq 2 (the isotopomeric composition of **3** was not investigated).

The formation of both the monodeuterated stereoisomers **2a** and **2b** may be easily accounted for by admitting that the reaction is not stereospecific. In contrast, the formation of the perprotio isotopomer **2c** and that of the dideuterated methyl atropate **2d** is difficult to



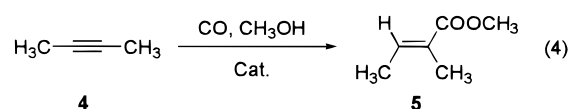
explain; therefore, we were prompted to investigate if the substrate or the product of the reaction can undergo exchange of their hydrogen atoms for deuterium when treated with CH<sub>3</sub>OD under the same conditions used for the carbonylation reaction. The experiments demonstrated that no deuterium is incorporated in a sample of perprotio methyl atropate **2c** even after prolonged treatment with CH<sub>3</sub>OD in the presence of the catalyst. Instead, when phenylacetylene was treated with CH<sub>3</sub>OD at 50 °C under an inert atmosphere in the presence of the catalyst, we observed that the terminal hydrogen of the alkyne rapidly exchanges with deuterium (eq 3).



This H/D exchange reaction is not peculiar to phenylacetylene, since it also occurs with aliphatic alkynes such as propyne and 1-heptyne; moreover, it proceeds rapidly even at room temperature and can be easily monitored by <sup>1</sup>H and <sup>2</sup>D NMR spectroscopy. To the best of our knowledge no examples of such catalytic activation of the terminal C–H bond of 1-alkynes have been reported with palladium; a similar exchange has been previously found to occur in the presence of silver trifluoromethanesulfonate.<sup>12</sup>

The detected H/D exchange allows us to readily account for the results obtained in the carbonylation of **1** in the presence of CH<sub>3</sub>OD: it appears that the dideuterioisotopomer **2d** is formed by the addition of CO and CH<sub>3</sub>OD to monodeuteriophenylacetylene, instead **2c** arises from the reaction of non-deuterated phenylacetylene with CO and CH<sub>3</sub>OH.

To avoid the intricacies caused by the hydrogen/deuterium exchange, the stereochemistry of the reaction was reinvestigated using 2-butyne (**4**) as substrate in the presence of CH<sub>3</sub>OH under the same conditions used for phenylacetylene carbonylation (eq 4) (Experimental Section).



GC–MS and <sup>1</sup>H NMR analyses demonstrated that the reaction affords stereospecifically the methyl ester of (*E*)-2-methyl-2-butenic acid (**5**; methyl tiglate), indicating that the addition of H and COOCH<sub>3</sub> to the triple bond proceeds with *cis* stereochemistry. Such stereochemistry agrees with both mechanisms of Scheme 1: as a matter of fact, Norton<sup>8,9</sup> observed that the addition of the COOCH<sub>3</sub> moiety to the C–C triple bond occurs

(9) Samsel, E. G.; Norton, J. R. *J. Am. Chem. Soc.* **1984**, *106*, 5505.

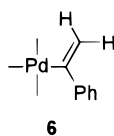
(10) Two recent reviews on the chemistry of the Pd–H moiety: (a) Takacs, J. M. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, U.K., 1995; Vol. 3, p 46. (b) Grushin, V. V. *Chem. Rev.* **1996**, *96*, 2011.

(11) (a) Zargarian, D.; Alper, H. *Organometallics* **1993**, *12*, 712. (b) Tsuji, J. *Acc. Chem. Res.* **1969**, *2*, 144.

(12) Lewandos, G. S.; Maki, J. W.; Ginnebaugh, J. P. *Organometallics* **1982**, *1*, 1700.

with *cis* stereochemistry, and in most cases<sup>13,14</sup> the insertion of an alkyne into a Pd–H bond also proceeds with *cis* stereochemistry even if exceptions are known.<sup>15</sup>

Direct experimental evidence supporting the involvement of a Pd–vinyl complex in both the alkoxy-carbonylation and the H/D exchange was obtained by <sup>1</sup>H NMR spectroscopy. As a matter of fact, the <sup>1</sup>H NMR spectrum of a CD<sub>2</sub>Cl<sub>2</sub> solution prepared by adding phenylacetylene and CH<sub>3</sub>OH to the catalytic system (Experimental Section) displays, in addition to the signals due to the alkyne, methanol, and catalyst components, a pair of doublets (*J*(H–H) = 0.9 Hz) centered at 5.74 and 6.00 ppm, respectively. Irradiation of the signal at 6.00 ppm causes the signal at 5.74 ppm to collapse to a singlet. The chemical shifts and the value of the coupling constant (0.9 Hz) are diagnostic and indicate the presence of a CH<sub>2</sub> group of a vinyl moiety. Thus, these signals can be rationalized only by admitting the presence of a Pd–vinyl species of the type



When the above CD<sub>2</sub>Cl<sub>2</sub> solution is treated with CO at atmospheric pressure, its color changes from orange to red even if no new resonances appear in the spectrum. However, the <sup>1</sup>H NMR spectrum recorded 14 h after the CO addition displays, along with the signals of **6**, those relevant to the vinylic protons of methyl atropate (**2**). Twenty-four hours later the signals of **6** have disappeared and only those due to methyl atropate are present in the vinylic region of the <sup>1</sup>H NMR spectrum.

In our opinion, these findings and the fact that Drent's catalytic system is completely chemoselective and almost regiospecific leave no doubt as to the involvement of the vinyl complex **6** in the catalytic cycle of the carbonylation reaction.

We have not been able to fully characterize **6**. As a matter of fact, only a fraction (ca. 15%) of the starting Pd(OAc)<sub>2</sub> is converted into **6** (as calculated by comparing the integration of the vinylic resonances with those relevant to the acetate groups); therefore, other palladium species must be present in solution alongside **6**. Accordingly, the low-temperature <sup>31</sup>P NMR shows a set of singlets (Experimental Section) which we were unable to reasonably assign also taking into account that PPh<sub>2</sub>-Py can give rise to polynuclear species.<sup>16</sup> Moreover, in the <sup>1</sup>H NMR the methylene protons of **6** do not show couplings with phosphorus even down to –60 °C.

An attempt to get more information on the nature of **6** by <sup>13</sup>C NMR also failed, since the spectral region between 120 and 140 ppm is crowded by a large number of signals which are mainly due to the phosphine ligands.

It is also interesting to note that the <sup>1</sup>H NMR experiments (confirmed by GC–MS) show that the acetate groups of Pd(OAc)<sub>2</sub> react with methanol to afford methyl acetate. Thus, it is likely that under catalytic

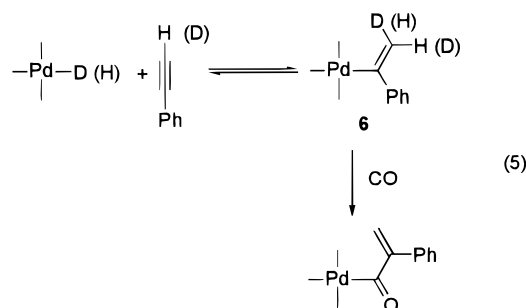
**Table 1. Influence of *P*(CO) on the Isotomeric Composition of Methyl Atropate Formed in the Carbonylation of Phenylacetylene with CH<sub>3</sub>OD<sup>a</sup>**

<i>P</i> (CO) (atm)	methyl atropate yield (%)	isotomeric composition of methyl atropate (%)			
		<b>2a</b>	<b>2b</b>	<b>2c</b>	<b>2d</b>
25	84.5	49.2	7.9	16.1	26.8
10	58.1	39.1	8.6	19.9	32.4
5	56.9	22.1	21.5	20.5	35.9

<sup>a</sup> Reaction conditions: Pd(OAc)<sub>2</sub>, 13 × 10<sup>–3</sup> mmol; PPh<sub>2</sub>Py, 13 × 10<sup>–2</sup> mmol; CH<sub>3</sub>SO<sub>3</sub>H, 13 × 10<sup>–2</sup> mmol; phenylacetylene, 26 mmol; substrate/Pd = 2000; CH<sub>3</sub>OD, 100 mmol; *T* = 50 °C.

conditions, i.e. in the presence of a large excess of alcohol, the species acting as counterion is the methanesulfonate group.

The simultaneous occurrence of both the alkoxy-carbonylation of alkynes and the hydrogen/deuterium exchange could be rationalized by the sequence of reactions depicted in eq 5: the reversible formation of **6** accounts for the H/D exchange,<sup>17</sup> while its reaction with carbon monoxide brings on the formation of the carbonylation product.



If this hypothesis is correct, the rate of H/D exchange which occurs along with the carbonylation of the substrate should be affected by *P*(CO). Thus, we carried out the carbonylation of phenylacetylene in the presence of CH<sub>3</sub>OD at different *P*(CO) values, taking care to avoid that the H/D exchange can take place before the carbonylation (Experimental Section). The relevant data are reported in Table 1. It appears that as *P*(CO) decreases the carbonylation rate decreases; in the meanwhile the H/D exchange is enhanced, as indicated by the increased yield in the isotomers **2b–d**, which should not be formed in the absence of an exchange. Thus, these data give experimental support to our hypothesis. In addition, the large effect played by the CO pressure on the carbonylation reaction indicates that the insertion of CO into the Pd–C bond of the vinyl moiety is the rate-determining step of the catalytic cycle, in keeping with the results of the NMR experiments.

Having shown that a Pd–vinyl complex is involved in the reaction, it is necessary now to discuss the mechanism leading to its formation.

As depicted in Scheme 1 and eq 5, **6** can be formed by the insertion of the alkyne into a Pd–H bond. This reaction is well-known;<sup>10,13–15</sup> however, it is not able to explain some aspects of the carbonylation.

(i) To account for the hydrogen/deuterium exchange, the formation of the vinyl complex **6** must be reversible,

(17) Lewandos in ref 12 proposed the reversible formation of a vinyl species to account for the H/D exchange observed to occur with 1-alkynes in the presence of silver triflate.

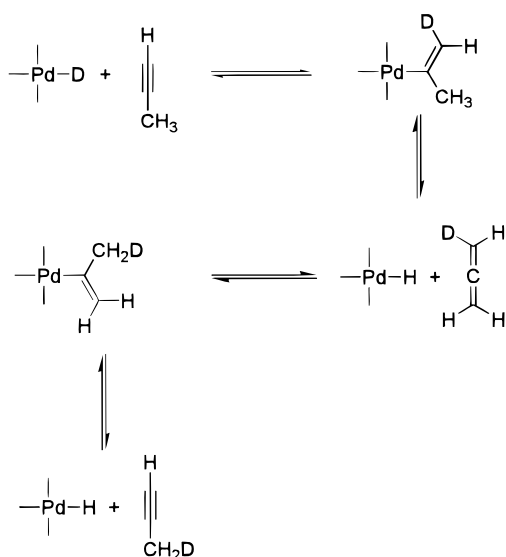
(13) Clark, H. C.; Milne, C. R. *J. Organomet. Chem.* **1978**, *161*, 51.

(14) Portnoy, M.; Milstein, D. *Organometallics* **1994**, *13*, 600.

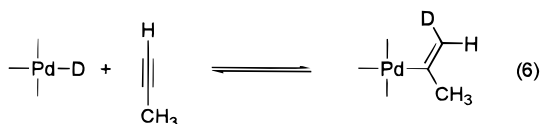
(15) Reger, D. L.; Garza, D. G. *Organometallics* **1993**, *12*, 554.

(16) Newkome, G. R. *Chem. Rev.* **1993**, *93*, 2067 and references therein.

Scheme 2



but to the best of our knowledge in the literature there is no clear-cut example of the reversibility of the insertion of an alkyne into the Pd-H bond.<sup>14</sup> Moreover, since the experiments carried out with 2-butyne (eq 4) demonstrate that the carbonylation reaction is stereospecific, a deinsertion reaction would extract the same atom which was added to the triple bond so that no hydrogen/deuterium exchange would be observed (eq 6).



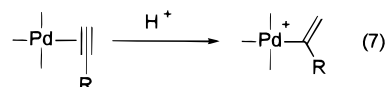
(ii) The carbonylation of propyne in the presence of CH<sub>3</sub>OD gives methyl methacrylate almost quantitatively. <sup>1</sup>H NMR analysis shows that only the vinylidene group is affected by H/D scrambling and that no deuterium is incorporated into the methyl group of the starting propyne. In our opinion, if a palladium hydride were involved in the catalytic cycle, a sequence of reactions such as those reported in Scheme 2 would take place and, therefore, some deuterium atoms would be found in the methyl group.

For example, a similar series of hydropalladations-dehydropalladations has been invoked by Trost<sup>18</sup> to account for the isomerization of alkynones to dienones catalyzed by Pd complexes. Also, Lu<sup>19</sup> resorted to a reaction scheme of this type to account for the conversion of certain propargylic acetates to allylic 1,1-diacetates.

(iii) The Pd-H moiety is able to react not only with alkynes but also with olefins; therefore, the complete chemoselectivity of the reaction remains surprising. In connection with this, it should be recalled that Pd is known to promote the carbonylation of alkenes as well as that of alkynes<sup>20</sup> and that one characteristic of the

carbonylation of the alkynes with Pd catalysts is the formation of dicarbonylation products.<sup>20</sup>

(iv) The carbonylation of 2-butyne carried out using a 1/1 mixture of CH<sub>3</sub>OH and CH<sub>3</sub>OD (Experimental Section) affords partially deuterated methyl tiglate. <sup>1</sup>H NMR analysis reveals that only 13.5% of the product is deuterated, thus indicating that a kinetic isotope effect of ca. 6.4 is operative in the formation of the vinyl intermediate. In particular, this latter result is hardly rationalized by a mechanism involving the insertion of an alkyne into a Pd-H bond.<sup>21,22</sup> Indeed, the quite large isotope effect found is consistent with a mechanism involving a rate-controlling proton-transfer step; therefore, we propose that the formation of the vinyl intermediate occurs by protonation of a Pd(0)-alkyne species as depicted in eq 7.



It is reasonable to assume that Pd(0)-alkyne species are involved in the catalytic cycle, since it has been shown that Pd(OAc)<sub>2</sub> in the presence of an excess of tertiary phosphines and protic solvents (H<sub>2</sub>O or alcohols) gives Pd(0) species<sup>23,24</sup> whose ability to coordinate alkynes is well-documented.<sup>14,25</sup> The involvement of Pd(0) species in the catalytic cycle is supported by the observation that when we used Pd<sub>2</sub>(dba)<sub>3</sub> (dba = dibenzylideneacetone) instead of Pd(OAc)<sub>2</sub> we obtained a catalytic system completely equivalent to Drent's original system. The electrophilic attack of protons on alkynes coordinated to low-valent metal centers to give vinyl complexes is a well-documented process<sup>26,27</sup> and has been previously invoked in the formation of Pd-vinyl complexes by Clark<sup>13</sup> and Alper.<sup>11</sup>

As pointed out by Henderson,<sup>26</sup> the protonation of a coordinated alkyne can occur by two different pathways: the first pathway implies the direct attack of the proton from outside the coordination sphere of the metal to give formal *trans* addition of the metal and of the proton to the triple bond (eq 8).



A second pathway involves the attack of the proton to the metal center followed by its transfer to the alkyne (eq 9) to give a *cis* addition product.

(21) A maximum kinetic isotope effect of ~3.6 can be estimated using the semiclassical treatment for the insertion of the alkyne into the Pd-H bond, taking  $\nu_{\text{Pd-H}} = 2100 \text{ cm}^{-1}$  and  $\nu_{\text{H}}/\nu_{\text{D}} = 1.38$  at 323 K.

(22) For a concerted mechanism a low kinetic deuterium isotope effect is expected: Nakamura, A.; Otsuka, S. *J. Mol. Catal.* **1976**, *1*, 285.

(23) Ozawa, F.; Kubo, A.; Hayashi, T. *Chem. Lett.* **1992**, 2177.

(24) Amatore, C.; Carré, E.; Jutand, A.; M'Barki, M. A. *Organometallics* **1995**, *14*, 1818.

(25) Krause, J.; Bonrath, W.; Pörschke, K. R. *Organometallics* **1992**, *11*, 1158.

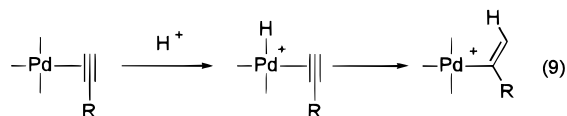
(26) Henderson, R. A.; Lowe, D. J.; Salisbury, P. *J. Organomet. Chem.* **1995**, *489*, C22.

(27) (a) Barlex, D. M.; Kemmitt, R. D. W.; Littlecott, G. W. *J. Chem. Soc., Chem. Commun.* **1969**, 613. (b) Tripathy, P. B.; Roundhill, D. M. *J. Am. Chem. Soc.* **1970**, *92*, 3825. (c) Mann, B. E.; Shaw, B. L.; Tucker, N. I. *J. Chem. Soc. A* **1971**, 2667. (d) Bennett, M. A.; Rokicki, A. *Aust. J. Chem.* **1985**, *38*, 1307.

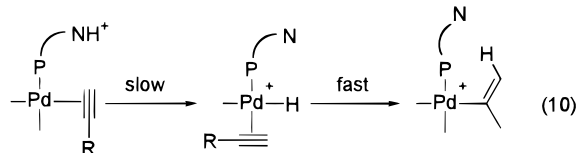
(18) Trost, B. M.; Schmidt, T. *J. Am. Chem. Soc.* **1988**, *110*, 2301.

(19) Lu, X.; Ji, J.; Ma, D.; Shen, W. *J. Org. Chem.* **1991**, *56*, 5774.

(20) Mullen, A. In *New Syntheses with Carbon Monoxide*; Falbe, J., Ed.; Springer Verlag: New York, 1980; Chapter 3, and references therein.



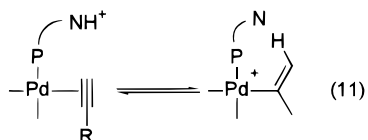
According to these considerations and the *cis* stereochemistry found for the carbonylation reaction, we propose in eq 10 a mechanism able to account for Drent's observation that the 2-pyridyl ring of the ligand is necessary to enhance the catalytic activity of the system.



In fact, a proton linked to the N atom of the 2-pyridyl ligand is placed in an ideal position to be transferred to the metal (Drent<sup>2,3</sup> already suggested that the pyridylphosphine works as a "proton messenger" in the process).

In the sequence of reactions of eq 10, the proton transfer from the protonated pyridine to palladium must be the slow step according to the kinetic isotope effect found, which is close to the maximum expected (ca. 7.0) for a reaction involving the breaking of a N–H bond.<sup>28,29</sup>

On the other hand, a route involving direct proton transfer from the protonated pyridine to the coordinated alkyne as depicted in eq 11 cannot be ruled out, since it also likely occurs with *cis* stereochemistry.



At present, we have no direct experimental evidence supporting either of the two mechanisms. However, the route in eq 11 seems to us more appealing and appropriate to explain the lack of the typical reactivity of a Pd–H moiety: i.e., the fact that no deuterium is incorporated into the methyl group of the methyl methacrylate when propyne is carbonylated in the presence of CH<sub>3</sub>OD (Scheme 2) and the fact that no double carbonylation is observed. Moreover, according to the mechanism in eq 11, the H/D exchange is easily explained by admitting that the protonation is reversible; as a matter of fact, inspection of molecular models shows that the nitrogen atom of the pyridyl ring points toward the carbon atom of the methylene group of **6**. Thus, both hydrogen atoms have roughly the same probability of being removed by the nitrogen during the deprotonation, making the H/D exchange possible.

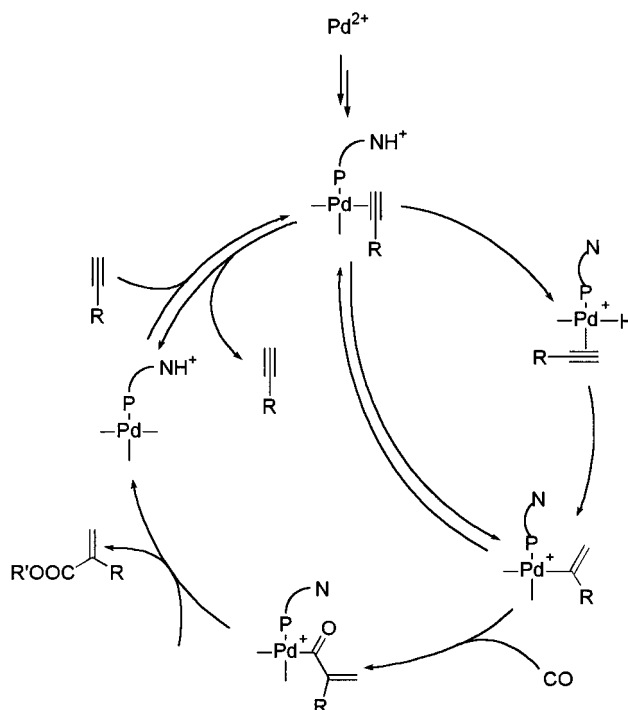
The mechanism in eq 11 is able to rationalize the complete chemoselectivity displayed by Drent's catalytic system: the carbonylation produces an alkene which is deactivated<sup>30</sup> toward electrophilic attack since it has a strong electron-withdrawing substituent. Therefore,

(28) Westheimer, F. W. *Chem. Rev.* **1961**, *61*, 265.

(29) Laidler, K. J. *Chemical Kinetics*; Harper & Row: New York, 1987; Chapter 11.

(30) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; p 747.

Scheme 3



once all the starting substrate is consumed, the reaction does not proceed further.

The mechanism proposed in eq 11 also agrees with the regioselectivity of the carbonylation: in fact, it is determined by the direction of the attack of the proton and proceeds likewise to the acid-promoted hydration of alkynes.<sup>31,32</sup> Thus, it is mainly determined by electronic factors even if steric contributions cannot be ruled out.

### Concluding Remarks

An overview of the catalytic cycle is presented in Scheme 3: the final step is the base-assisted alcoholysis<sup>33,34</sup> of the palladium acyl complex. In the present case, it can be surmised that the N atom of the pyridyl ring can also work as acceptor of the alcoholic proton, thus favoring the cleavage.

The essential features of the mechanism depicted in Scheme 3 are similar to those of other mechanisms invoking the involvement of a metal hydride. In our case, the mechanistic proposal is supported by the detection of the  $\sigma$ -vinyl intermediate **6**. This species can also be invoked to account for the H/D exchange which occurs along with the carbonylation reaction. Especially intriguing is the mechanism proposed for the formation of **6**; nevertheless, the formation of vinyl species upon protonation of coordinated alkynes has precedents in the platinum group<sup>27</sup> and is supported by the large isotope effect detected.

A mechanism involving a M–COOR species would be unable to explain the H/D exchange, and moreover, such

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a mechanism seems unlikely because of the strongly acidic character of the reaction medium.

We have no experimental data which allow us to hypothesize the exact nature of the metal complex responsible for the catalytic activity: mononuclear as well as polynuclear species could be involved, in particular if we take into account the potential bidentate nature of 2-pyridyldiphenylphosphine.<sup>16</sup>

### Experimental Section

All the operations were carried out under argon in Schlenk-type glassware. Commercial solvents (C. Erba) were purified by following methods described in the literature.<sup>35</sup> Pd(OAc)<sub>2</sub>,<sup>36</sup> Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub><sup>37</sup> (dba = dibenzylideneacetone), and 2-pyridyldiphenylphosphine<sup>38</sup> were prepared by literature methods. Methanesulfonic acid and CH<sub>3</sub>OD were purchased from Aldrich and used as received. Phenylacetylene and 2-butyne were purchased from Fluka. Propyne and carbon monoxide were obtained by SIAD. CDCl<sub>3</sub> and CD<sub>2</sub>Cl<sub>2</sub> (Aldrich) were stored over 3 Å molecular sieves. <sup>1</sup>H and <sup>31</sup>P NMR spectra were recorded on a Bruker AC 200 spectrometer operating at 200.13 and 81.01 MHz, respectively.

Carbonylation experiments were carried out in a magnetically stirred stainless steel autoclave (total volume ca. 150 mL) equipped with an auxiliary stainless steel addition funnel to charge the substrate just before the pressurization with CO. Conversion and yield of the carbonylation reactions were determined by GLC on a Hewlett-Packard 5890 II series gas chromatograph, using *p*-xylene as internal standard. GLC-MS analyses were carried out on a HP 5890 II series gas chromatograph interfaced to a Hewlett-Packard 5971 mass detector.

**Carbonylation Experiments.** In a typical experiment (Table 1) a Schlenk tube containing a magnetic bar is charged under an inert atmosphere with 36 mg (0.13 mmol) of 2-pyridyldiphenylphosphine, 2.9 mg (0.013 mmol) of Pd(OAc)<sub>2</sub>, 15 mL of dichloromethane, 4.1 mL (3.3 g, 100 mmol) of CH<sub>3</sub>OD, and 8.4 μL (12.5 mg, 0.13 mmol) of CH<sub>3</sub>SO<sub>3</sub>H. The resulting solution is transferred *via cannula* into the autoclave. Then from the addition funnel a solution of 2.86 mL (2.66 g, 26 mmol) of phenylacetylene in 3 mL of dichloromethane is forced into the reactor by a CO stream, whose pressure is then adjusted to 25 atm. The reactor is maintained at 50 °C (±0.1 °C) by circulating a thermostatic fluid. After 1 h, the residual

gas is vented off and the composition of the raw reaction mixture determined by GLC. The ester product is recovered from the reaction mixture by distillation at reduced pressure. To determine the isotopomeric composition of the ester produced, the following assignments for the <sup>1</sup>H NMR (CDCl<sub>3</sub>) are used (the <sup>1</sup>H NMR chemical shifts listed below are reported with three digits owing to the small differences in chemical shifts for the deuterio and protio compounds): **2a**, δ 3.84 (s, OCH<sub>3</sub>), 5.910 (s, vinylic proton trans to ester group), 7.3–7.5 (m, phenyl protons); **2b**, δ 3.84 (s, OCH<sub>3</sub>), 6.389 (s, vinylic proton cis to ester group), 7.3–7.5 (m, phenyl protons); **2c**, δ 3.84 (s, OCH<sub>3</sub>), 5.923 (d, *J*(H–H) = 1.2 Hz, vinylic proton trans to ester group), 6.404 (d, vinylic proton cis to ester group), 7.3–7.5 (m, phenyl protons); **2d**, δ 3.84 (s, OCH<sub>3</sub>), 7.3–7.5 (m, phenyl protons).

**2-Butyne Carbonylation.** The carbonylation of 2-butyne (0.54 g, 10 mmol) was carried out as described above for phenylacetylene using CH<sub>3</sub>OH (20 mL) both as solvent and coreagent. The reaction affords quantitatively the methyl ester of (*E*)-2-methyl-2-butenic acid, as demonstrated by GC-MS and <sup>1</sup>H NMR analysis.

**Estimation of the Isotope Effect.** The carbonylation of 2-butyne (0.54 g, 10 mmol) was carried out as described above using CH<sub>2</sub>Cl<sub>2</sub> as solvent (18 mL) and 3.2 g (100 mmol) of a 1/1 mixture of CH<sub>3</sub>OH/CH<sub>3</sub>OD. The product of the reaction was recovered by distillation under reduced pressure and its <sup>1</sup>H NMR recorded in CDCl<sub>3</sub> solution. By comparison of the resonances relevant to methyl groups vs that of the vinylic proton it appears that 13.5% of the methyl tiglate obtained is deuterated at the 2-position, therefore giving *k<sub>H</sub>/k<sub>D</sub>* = 6.4.

**Propyne Carbonylation.** The carbonylation of propyne was carried out as described for phenylacetylene, by condensing 0.5 g (12.5 mmol) of alkyne into the chilled autoclave which was previously charged with the catalyst and 3.1 mL (2.48 g, 75 mmol) of CH<sub>3</sub>OD dissolved in 15 mL of dichloromethane.

**Detection of the Intermediate 6.** In a small Schlenk flask under an inert atmosphere 1 mL of CD<sub>2</sub>Cl<sub>2</sub>, 6.7 mg of Pd(OAc)<sub>2</sub> (0.03 mmol), and 25 mg (0.09 mmol) of 2-pyridyldiphenylphosphine (P/Pd = 3) were introduced. To the resulting solution were added 7 μL (6.0 mg, 0.18 mmol) of CH<sub>3</sub>OH, 6 μL (5.1 mg, 0.05 mmol) of phenylacetylene and 6 μL (8.6 mg, 0.09 mmol) of methanesulfonic acid. The orange solution was transferred *via cannula* into a screw-cap NMR tube (Wilmad) for the spectroscopic investigations. <sup>31</sup>P NMR (CD<sub>2</sub>Cl<sub>2</sub>, 213 K): 53.9 (singlet, relative intensity 1.2), 52.6 (s, 0.4), 48.0 (s, 1), 23.6 (s, 14.8), 0.3 ppm (s, 0.85).

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