Palladium-Catalyzed Carbonylation of Allyl Alcohols in the Presence of Phenols

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Received December 20, 1996

Palladium-catalyzed carbonylation of allylic compounds is one of the most promising methods for the preparation of synthetically useful β , γ -unsaturated carboxylic acid derivatives.¹ Effective methods for the reaction of allylic carbonates,² esters,³ halides,⁴ amines,⁵ and ethers⁶ under reasonably mild conditions have so far been developed. However, carbonylation of allyl alcohols has been less explored in spite of the ready availability of the starting materials, as the reaction requires a high pressure of carbon monoxide.7 Recently, we have shown that allyl alcohols can be carbonylated efficiently in the presence of titanium(IV) alkoxides and lithium chloride under medium CO pressure (25 atm) to give alkyl 3-butenoates.8 Meanwhile, we have also reported that palladiumcatalyzed carbonylation of terminal alkynes^{9a} and aryl iodides^{9b,c} in the presence of phenols and intramolecular carbonylative cyclization of 2-hydroxybenzyl alcohols9d proceeds smoothly under considerably mild conditions. We herein demonstrate our new findings that the direct carbonylation of allyl alcohols bearing an aryl substituent at the α - or γ -position can also be attained in the presence of phenols using a palladium catalyst to afford the corresponding β , γ -unsaturated esters even under atmospheric pressure of CO (eq 1).



Results and Discussion

When a mixture of (*E*)-3-phenyl-2-buten-1-ol (**1**) (2 mmol) and phenol (**2**) (2 mmol) was heated in the presence of $Pd(OAc)_2$ (0.1 mmol) and PPh_3 (0.2 mmol) in

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benzene (5 mL) under CO (5 atm) at 100 °C for 18 h, (E)-phenyl 4-phenyl-3-butenoate (3) was produced in a yield of 24% (entry 1 in Table 1). An increase in the amount of PPh₃ to 0.4 mmol remarkably enhanced the ester yield (76%) (entry 2), and in this case alcohol 1 was completely consumed. The yield was further improved up to 80% by the use of a slight excess of 2 (2.4 mmol) (entry 4). It was observed that Pd(PPh₃)₄ was less efficient than the combination of Pd(OAc)₂ and PPh₃ (entry 5 vs 2). This may suggest that acetic acid derived from $Pd(OAc)_2$ acts as a promoter. Indeed, the reaction of $\boldsymbol{1}$ with $\boldsymbol{2}$ using Pd(PPh_3)_4 in the presence of acetic acid (0.1 mmol) gave a better yield of 3 compared with that using Pd(PPh₃)₄ alone (entry 6). Interestingly, the phenoxycarbonylation of 1 was found to proceed efficiently even under atmospheric pressure of CO (entry 7). Polar solvents, DMF and 2-methoxyethyl ether, could not be used in the present reaction (entries 8 and 9). The reaction of **1** should be accompanied by the formation of water. Addition of molecular sieves (4A, 200 mg) for its removal, however, somewhat reduced the yield of **3** (entry 10)

Phenoxycarbonylation of a number of allyl alcohols was also performed using Pd(OAc)₂ and PPh₃ under CO (1 or 5 atm) in toluene or benzene (Table 2). The reaction of α - or γ -arylated allyl alcohols proceeded smoothly to give the corresponding phenyl esters selectively in fair to good yields. The reaction of 2-hexen-1-ol (**15**) or 1-hexen-3-ol (**17**) was, however, less efficient, giving a mixture of (*E*)and (*Z*)-isomers of ester **16** in low yield. The fact that **1** and **4** gave the same product as that in the case of **15** and **17** may suggest that the reaction process involves π -allylpalladium intermediates.

Meanwhile, the carbonylation of **1** using 4-methoxyand 3-chlorophenols in place of **2** also gave esters **18** and **19** in good yields (eq 2).

Ph. O H + C O + ArOH
$$\xrightarrow{Pd(OAc)_2}_{PPh_3}$$
 Ph. O Ar (2)
1 5 atm, 100 °C, 18h
% yield
Ar = 4-MeOC₆H₄ 18 70
Ar = 3-ClC₆H₄ 19 72

A probable mechanism for the formation of **3** from **1** and **2** is illustrated in Scheme 1 where neutral ligands are omitted. Alcohol **1** reacts with Pd⁰ species generated in situ in the presence of phenol (2) to afford a π -allylpalladium intermediate (I). Subsequently, insertion of CO to I followed by reductive elimination gives product **3**.¹⁰ In the early stage of the reaction of **1** under CO (1 atm) (conversion of 1 = 30%), formation of phenyl ether **20** (9%) as well as **3** (5%) was detected in the reaction medium, while the former disappeared in the end (entry 7 in Table 1). It was confirmed that treatment of ether **20** under the present carbonylation conditions gave **3** in a yield of 87%. These facts suggest that the ester 3 may be produced, at least in part, via 20. In contrast to our observation, ether 20 has recently been reported to be inactive toward carbonylation using palladium species in relatively polar solvents such as THF and CH₂Cl₂.¹¹

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⁽¹⁰⁾ However, another pathway *via* (phenoxycarbonyl)(σ -allyl)palladium intermediates cannot be excluded:⁴ (a) Milstein, D. *Organometallics* **1982**, *1*, 888. (b) Milstein, D. *Acc. Chem. Res.* **1988**, *21*, 428.

Table 1. Phenoxycarbonylation of 3-Phenyl-2-buten-1-ol $(1)^a$



^{*a*} Reaction conditions: 1 (2 mmol), 2 (2 mmol), and Pd catalyst (0.1 mmol) in benzene (5 mL) under CO (5 atm) at 100 °C for 18 h. ^{*b*} Determined by GLC analysis based on 1 used. Value in parentheses indicates yield after purification. ^{*c*} Pd(OAc)₂ (0.05 mmol) was used. ^{*d*} 2 (2.4 mmol) was used. ^{*e*} Under CO (1 atm) at 80 °C for 20 h. ^{*f*} In toluene. ^{*g*} In DMF. ^{*h*} In 2-methoxyethyl ether. ^{*i*} Molecular sieves (4A, 200 mg) was added.

The carbonylation of alcohol **1** using *n*-butanol as the nucleophile and Pd(OAc)₂ and PPh₃ under 5 atm of CO in benzene gave (*E*)-butyl 4-phenyl-3-butenoate (**21**) in a low yield (27%).¹² Thus, phenol appears to act as a good nucleophile in the reaction (cf. entry 2 in Table 1), so that it can be carried out under mild and nearly neutral conditions, as for the carbonylation of terminal alkynes.^{9a} Consistently, in the stoichiometric carbonylation of [Pd(η^3 -1-phenylallyl)(OAc)]₂ (**22**) (0.1 mmol) with phenol (1 mmol) in the presence of PPh₃ (0.2 mmol) in toluene (5 mL) under CO (1 atm) at 80 °C, ester **3** was smoothly formed (3 h, 77%; 22 h, 91%) (eq 3). By contrast, the reaction using *n*-butanol (2 mmol) gave ester **21** in a low yield (22 h, 19%).



While the exact role of acetic acid derived from $Pd(OAc)_2$ or added is not definitive at the present stage, it would promote the first step, oxidative addition of **1** to Pd^0 species (Scheme 1).⁶ On the other hand, one of the possible reasons for the less efficiency of the reaction of aliphatic allyl alcohols such as **15** and **17** seems to be attributable to involvement of a side reaction leading to the corresponding dienes, since β -hydride elemination from a π -allylpalladium species is known.¹ Indeed, in the treatment of (*E*)-2-decenol under the carbonylation conditions, 1,3-decadiene (21%) was formed along with the corresponding phenyl ester (24%).

Table 2. Phenoxycarbonylation of Allyl Alcohols^a



^{*a*} Reaction conditions: allyl alcohol^{*b*} (2 mmol), **2** (2.4 mmol), Pd(OAc)₂ (0.1 mmol), and PPh₃ (0.4 mmol) in benzene (5 mL) under CO (5 atm) at 100 °C for 18 h. ^{*b*} Unless otherwise noted, *E*:*Z* was >98:2. ^{*c*} GLC yield based on amount of allyl alcohols used. Value in parentheses indicates yield in the reaction under 1 atm of CO in toluene at 80 °C for 20 h.



Experimental Section

 1H NMR spectra were recorded at 400 MHz with CDCl₃ as solvent. MS data were obtained by EI. GLC analysis was carried out using a silicon OV-17 column (i.d. 2.6 mm \times 1.5 m) or with a CBP-1 capillary column (i.d. 0.5 mm \times 25 m).

The complexes $Pd(PPh_3)_4^{1a}$ and $[Pd(\eta^3-1-phenylallyl)(OAc)]_2$ (22)^{3b} were prepared by the methods reported previously. Allyl alcohols 4¹³ and 17¹³ and ether 20¹¹ were prepared according to the published procedures. Allyl alcohols 5, 7, 9, 11, and 13 were prepared by the reduction of the corresponding alkynols with

⁽¹¹⁾ Goux, C.; Lhoste, P.; Sinou, D.; Masdeu, A. *J. Organomet. Chem.* **1996**, *511*, 139. The origin of the observed remarkable solvent effect, however, is not definitive at the present stage. (12) Even in this case as well as in the reaction with phenols,

⁽¹²⁾ Even in this case as well as in the reaction with phenols, formation of a self-esterification product, 3-phenyl-2-butenyl 4-phenyl-3-butenoate, was not detected.

⁽¹³⁾ Hwa, J. C. H.; Sims, H. Organic Syntheses; Wiley: New York, 1973; Collect. Vol. V, p 608.

LiAlH₄.¹⁴ Other starting materials were commercially available. Solvents were purified by standard methods before use.

Catalytic Phenoxycarbonylation of Allyl Alcohols. A mixture of a substituted allyl alcohol (2 mmol), **2** (226 mg, 2.4 mmol), $Pd(OAc)_2$ (22 mg, 0.1 mmol), PPh_3 (52 mg, 0.2 mmol), and benzene (5 mL) was placed in a 50 mL stainless steel autoclave. Then, carbon monoxide (5 atm at room temperature) was charged, and the mixture was magnetically stirred at 100 °C for 18 h. In the reaction under a normal pressure of carbon monoxide, a 100 mL two-necked flask equipped with a balloon and a rubber cup was used. After cooling, the reaction mixture was poured into dilute hydrochloric acid, extracted with ether, and dried over sodium sulfate. The product was isolated by column chromatography on silica gel using hexane-methylene chloride as eluent.

(*E*)-Phenyl 4-phenyl-3-butenoate (3):¹¹ ¹H NMR δ 3.50 (dd, 2H, J = 1.5, 6.8 Hz), 6.40 (dt, 1H, J = 15.6, 6.8 Hz), 6.61 (d, 1H, J = 15.6 Hz), 7.09–7.42 (m, 10H); MS *m*/*z* 238 (M⁺).

(*E*)-Phenyl 4-(4-methoxyphenyl)-3-butenoate (6): mp 65–67 °C; ¹H NMR δ 3.47 (dd, 2H, J = 1.5, 7.3 Hz), 3.81 (s, 3H), 6.25 (dt, 1H, J = 15.6, 7.3 Hz), 6.54 (d, 1H, J = 15.6 Hz), 6.84–6.88 (m, 2H), 7.09–7.12 (m, 2H), 7.21–7.25 (m, 1H), 7.32-7.40 (m, 4H); MS m/z 268 (M⁺). Anal. Calcd for C₁₇H₁₆O₃: C, 76.10; H, 6.01. Found: C, 75.74; H, 6.07.

(*E*)-Phenyl 4-(4-methylphenyl)-3-butenoate (8): mp 34– 36 °C; ¹H NMR δ 2.34 (s, 3H), 3.48 (dd, 2H, J = 1.5, 6.8 Hz), 6.34 (dt, 1H, J = 15.6, 6.8 Hz), 6.57 (d, 1H, J = 15.6 Hz), 7.08– 7.14 (m, 4H), 7.22–7.26 (m, 1H), 7.30 (d, 2H, J = 7.8 Hz), 7.36– 7.40 (m, 2H); MS m/z 252 (M⁺). Anal. Calcd for C₁₇H₁₆O₂: C, 80.93; H, 6.39. Found: C, 80.53; H, 6.43.

(*E*)-Phenyl 4-(4-chlorophenyl)-3-butenoate (10): mp 63– 64 °C; ¹H NMR δ 3.49 (dd, 2H, J = 1.5, 7.3 Hz), 6.38 (dt, 1H, J = 15.6, 7.3 Hz), 6.56 (d, 1H, J = 15.6 Hz), 7.21–7.40 (m, 9H); MS m/z 272, 274 (M⁺). Anal. Calcd for C₁₆H₁₃O₂Cl: C, 70.46; H, 4.80; Cl, 13.00. Found: C, 70.39; H, 4.85; Cl, 13.08.

(*E*)-Phenyl 4-(2-thienyl)-3-butenoate (12): mp 54–55 °C; ¹H NMR δ 3.46 (dd, 2H, *J* = 1.5, 7.3 Hz), 6.23 (dt, 1H, *J* = 15.6,

(14) Sonogashira, K.; Tohda, Y.; Hagihara, N. Tetrahedron Lett. 1975, 16, 4467.

7.3 Hz), 6.73 (d, 1H, J = 15.6 Hz), 6.95–6.98 (m, 2H), 7.09–7.12 (m, 2H), 7.16–7.17 (m, 1H), 7.21–7.25 (m, 1H), 7.36–7.40 (m, 2H); MS m/z 244 (M⁺). Anal. Calcd for C₁₄H₁₂O₂S: C, 68.83; H, 4.95; S, 13.12. Found: C, 68.59; H, 5.02; S, 13.04.

(*E*)-Phenyl 4-(2-naphthyl)-3-butenoate (14): mp 104–105 °C; ¹H NMR δ 3.56 (dd, 2H, J= 1.5, 6.8 Hz), 6.53 (dt, 1H, J= 15.6, 6.8 Hz), 6.77 (d, 1H, J= 15.6 Hz), 7.11–7.14 (m, 2H), 7.22–7.26 (m, 1H), 7.37–7.47 (m, 4H), 7.62–7.64 (m, 1H), 7.75–7.82 (m, 4H); MS m/z 288 (M⁺). Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 82.92; H, 5.60.

Phenyl 3-heptenoate (16) (*E:Z* = 87:13):¹¹ ¹H NMR δ 0.92 (t, 3H, J = 7.3 Hz), 1.39–1.46 (m, 2H), 2.03–2.08 (m, 2H), 3.27 (dd, 2H, J = 1.0, 5.4 Hz, *E*), 3.34 (d, 2H, J = 5.4 Hz, *Z*), 5.64–5.68 (m, 2H), 7.07–7.39 (m, 5H); MS *m*/*z* 204 (M⁺).

(*E*)-(4-Methoxyphenyl) 4-phenyl-3-butenoate (18): mp 82–83 °C; ¹H NMR δ 3.48 (dd, 2H, J = 1.5, 7.3 Hz), 3.79 (s, 3H), 6.40 (dt, 1H, J = 15.6, 7.3 Hz), 6.55 (d, 1H, J = 15.6 Hz), 6.87–6.91 (m, 2H), 7.00–7.03 (m, 2H), 7.23–7.42 (m, 5H); MS m/z 268 (M⁺). Anal. Calcd for C₁₇H₁₆O₃: C, 76.10; H, 6.01. Found: C, 76.08; H, 6.01.

(*E*)-(3-Chlorophenyl) 4-phenyl-3-butenoate (19): mp 59– 60 °C; ¹H NMR δ 3.49 (dd, 2H, J = 1.5, 7.3 Hz), 6.37 (dt, 1H, J= 15.6, 7.3 Hz), 6.61 (d, 1H, J = 15.6 Hz), 7.01–7.04 (m, 1H), 7.14–7.16 (m, 1H), 7.21–7.37 (m, 5H), 7.40–7.42 (m, 2H); MS m/z 272, 274 (M⁺). Anal. Calcd for C₁₆H₁₃O₂Cl: C, 70.46; H, 4.80; Cl, 13.00. Found: C, 70.38; H, 4.83; Cl, 12.98.

(*E*)-Butyl 4-phenyl-3-butenoate (21):⁸ ¹H NMR δ 0.94 (t, 3H, J = 7.3 Hz), 1.39 (tq, 2H, J = 7.3, 7.3 Hz), 1.60–1.67 (m, 2H), 3.24 (dd, 2H, J = 1.5, 7.3 Hz), 4.12 (t, 2H, J = 6.8 Hz), 6.30 (dt, 1H, J = 15.6, 7.3 Hz), 6.49 (d, 1H, J = 15.6 Hz), 7.20–7.38 (m, 5H); MS m/z 218 (M⁺).

Stoichiometric Carbonylation of $[Pd(\eta^3-1-phenylally])-(OAc)]_2$ (22) in the Presence of PPh₃. A mixture of ROH (1 or 2 mmol), 22 (57 mg, 0.1 mmol), PPh₃ (52 mg, 0.2 mmol), bibenzyl (ca. 10 mg) as an internal standard, and toluene (5 mL) was stirred under CO (1 atm) at 80 °C. The time course of the reaction was monitored by GLC.

JO962387N