



Pd(II)—dppb and syngas catalyze regioselective hydroesterification of terminal alkynes under neutral conditions

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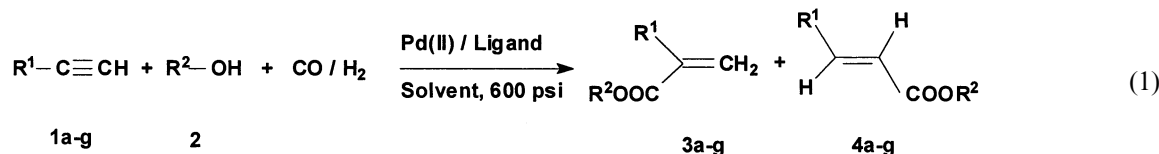
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Abstract—Palladium(II) regioselectively catalyzes the hydroesterification of terminal alkynes under syngas forming α,β -unsaturated esters **3** and **4** in excellent chemical yields under neutral conditions. The high selectivity for the linear ester **4** was obtained with a catalytic system that includes Pd(II), 1,4-bis(diphenylphosphino)butane (dppb) and CO/H₂ in CH₂Cl₂ as solvent. The control of the regioselectivity depends strongly upon the type of ligand, the solvent and the use of the syngas mixture. © 2001 Elsevier Science Ltd. All rights reserved.

The catalytic hydroesterification and hydrocarboxylation of alkynes and other π -bonded compounds are reactions with important industrial potential.^{1,2} The hydroesterification of alkynes usually leads to excellent selectivity for the branched α,β -unsaturated esters **3** or to a mixture of esters **3** and **4**. For example, the carbonylation of alkynes has been recently carried out using Pd(OAc)₂, PPh₃, *p*-TsOH, and semilabile anionic bidentate ligands such as pyridine or piperidine carboxylic acids forming the branched α,β -unsaturated esters **3** with excellent regioselectivity.³ We have previously reported the selective hydroesterification of 1-alkynes by Pd(0) or by Pd(II).⁴ The hydroesterification of propyne catalyzed by Pd(OAc)₂ in combination with 2-pyridyldiphenylphosphine (PPh₂Py) and MeSO₃H gave ester **3** with excellent selectivity (99.9%).⁵ We have recently reported a successful method for the regioselective control of the thiocarbonylation of terminal acetylenes with thiophenols.⁶ In this communication we wish to report a new catalytic system for the regioselective hydroesterification of terminal acetylenes catalyzed by Pd(II) and diphosphine ligand to afford linear α,β -unsaturated esters **4** as the major product under neutral conditions (Eq. (1)).

The hydroesterification of 1-nonyne (**1b**, R¹=C₇H₁₅) with 1-butanol (**2**, R²=C₄H₉) was carried out under syngas under pressure by changing the type of ligand, catalyst, solvent, and other parameters.⁸ The effect of varying the phosphine ligand in the presence of Pd(OAc)₂ as the catalyst in CH₂Cl₂ under 600 psi of CO/H₂ (1/1) has been carefully studied and the results are summarized in Table 1. Only traces of esters were observed with triphenylphosphine (PPh₃), diphenylphosphinomethane (dppm), or 1,2-bis(diphenylphosphino)ethane (dppe) as ligand (Table 1, entries 1–3). However, the use of 1,3-bis(diphenylphosphino)propane (dppp) increased the catalytic activity of the system but produced a 1:1 mixture of branched and linear α,β -unsaturated esters **3b** and **4b** (Table 1, entry 4). Surprisingly, replacement of dppp with 1,4-bis(diphenylphosphino)butane (dppb) increased the total yield of esters (98%) and the selectivity for the linear α,β -unsaturated ester **4b** (82%) (Table 1, entry 5). Changing the CO/H₂ ratio from 1/1 to either 5/1 or 1/5 only slightly affects the total yield of esters or the selectivity for **4b** (Table 1, entries 6 and 7). A decrease in the temperature of the reaction from 110 to 80°C significantly affected both the yield and the selectivity



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Table 1. Hydroesterification of 1-nonyne **1b** with 1-butanol catalyzed by Pd(OAc)₂ and CO/H₂ in CH₂Cl₂. Effect of varying the type of ligand^a

Run	Ligand	Total yield ^b (%)	Product distribution ^c (%)	
			3b	4b
1	PPh ₃	Traces	–	–
2	dppm	Traces	–	–
3	dppe	Traces	–	–
4	dppp	71	47	53
5	dppb	98	18	82
6 ^d	dppb	87	18	82
7 ^e	dppb	91	21	79
8 ^f	dppb	6	86	14
9 ^g	dppb	Traces	–	–
10	dpppt	77	71	29
11	dppf	94	81	19

^a Reaction conditions: Pd (0.02 mmol), ligand (0.06 mmol) except PPh₃ (0.12 mmol), 1-nonyne (2.0 mmol), 1-butanol (8.0 mmol), CH₂Cl₂ (5 ml), 600 psi (CO/H₂ = 1/1), 110°C, 20 h.

^b Isolated yield.

^c Determined by GC and ¹H NMR.

^d CO/H₂ = 1/5.

^e CO/H₂ = 5/1.

^f 80°C.

^g 1-Butanol (5 ml) was used as solvent.

of the process; only 6% of esters being obtained (Table 1, entry 8). In addition, the use of neat 1-butanol (in the absence of CH₂Cl₂) inhibited the reaction giving only traces of products (Table 1, entry 9). Other solvents such as CH₃CN, CHCl₃, toluene, THF, and DMF gave either low total yields or poor selectivity for **4b**. Surprisingly, an inversion of regioselectivity was observed with 1,5-bis(diphenylphosphino)pentane (dpppt) and 1,1'-bis(diphenylphosphino)ferrocene (dppf) as ligands (Table 1, entries 10 and 11). With these ligands, high total yields (77–94%) of the esters were maintained but good selectivity (71–81%) for the branched ester **3b** was achieved. The activity observed with dppb can be explained by the fact that this ligand is probably bidentated to palladium metal throughout the process and has the most suitable bite angle⁷ compared to other bidentate phosphine ligands.

Table 2 shows the results of hydroesterification of 1-nonyne with 1-butanol with dppb and various palladium complexes. It seems simply that all palladium(II) complexes are very active in this process, where excellent total yields (90–98%) and good to excellent selectivity for **4b** (73–82%) were obtained (Table 2, entries

Table 2. Hydroesterification of 1-nonyne **1b** with 1-butanol in the presence of dppb and CO/H₂ in CH₂Cl₂. Effect of varying the type of palladium catalyst^a

Run	Catalyst	Total yield ^b (%)	Product distribution ^c (%)	
			3b	4b
1	Pd(OAc) ₂	98	18	82
2	PdCl ₂ (PPh ₃) ₂	95	18	82
3	PdCl ₂ (PhCN) ₂	96	19	81
4	PdCl ₂	90	27	73
5	Pd/C	97	20	80
6	Pd(PPh ₃) ₄	72	58	42

^a Reaction conditions: Pd (0.02 mmol), dppb (0.6 mmol), 1-nonyne (2.0 mmol), 1-butanol (8.0 mmol), CH₂Cl₂ (5 ml), 600 psi (CO/H₂ = 1/1), 20 h.

^b Isolated yield.

^c Determined by GC and ¹H NMR.

1–4). However, palladium(0) complexes such as Pd(PPh₃)₄ gave lower total yields (72%) and low selectivity for **4b** (42%). It seems that palladium(0) is probably not the active species in this process but a Pd(II) complex is the intermediate throughout.

The results of the hydroesterification of different terminal alkynes by the catalytic system Pd(OAc)₂/dppb/1-butanol/CO/H₂ in CH₂Cl₂ at 110°C are shown in Table 3. 1-Pentyne, **1a**, also gave a high total yield (87%) and selectivity for **4a** (82%) (Table 3, entry 1). The regioselectivity of the hydroesterification is sensitive to both steric and electronic effects of the alkyne structure and to steric hindrance of the alcohol. The presence of a bulky tertiary group on alkyne favored only the formation of the linear unsaturated ester **4c** (Table 3, entry 3). The presence of a cyano, chloro or phenyl group decreased the selectivity for **4** (Table 3, entries 4–7). However, primary and secondary alcohols led to linear unsaturated esters **4** as the major product (Table 3, entries 1, 2, 8 and 9) but tertiary alcohols reacted with lower regioselectivity (Table 3, entry 10). The results with different alcohols confirm the possibility of the formation of [PdCOOR²] in the first step in the catalytic cycle, followed by the oxidative addition of the alkyne.

The hydroesterification of 1,7-octadiyne **5** (1 mmol) with methanol (4 mmol) was also carried out in the presence of the same catalytic system Pd(OAc)₂/dppb/CO/H₂ in CH₂Cl₂ at 110°C for 20 h leading to the formation of unsaturated diesters **6** (29%) and **7** (71%) in 96% total yield (Eq. (2)).

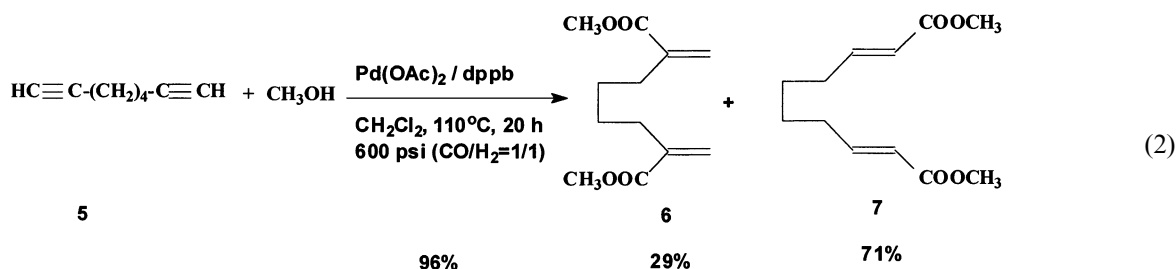


Table 3. Hydroesterification of different alkynes in the presence of the catalytic system Pd(OAc)₂/dppb/CO/H₂ in CH₂Cl₂^a

Run	Alkyne, 1 R ¹	Alcohol, 2	Total yield ^b (%)	Product distribution ^c (%)	
				3	4
1	CH ₃ CH ₂ CH ₂ 1a	CH ₃ CH ₂ CH ₂ CH ₂ OH	87	18 3a	82 4a
2	CH ₃ (CH ₂) ₅ CH ₂ 1b	CH ₃ CH ₂ CH ₂ CH ₂ OH	98	18 3b	82 4b
3	(CH ₃) ₃ C 1c	CH ₃ CH ₂ CH ₂ CH ₂ OH	85	0 3c	100 4c
4	CNCH ₂ CH ₂ CH ₂ 1d	CH ₃ CH ₂ CH ₂ CH ₂ OH	70	35 3d	65 4d
5	ClCH ₂ CH ₂ CH ₂ 1e	CH ₃ CH ₂ CH ₂ CH ₂ OH	67	27 3e	73 4e
6	PhCH ₂ 1f	CH ₃ CH ₂ CH ₂ CH ₂ OH	98	42 3f	58 4f
7	Ph 1g	CH ₃ CH ₂ CH ₂ CH ₂ OH	93	67 3g	33 4g
8	CH ₃ (CH ₂) ₅ CH ₂ 1b	CH ₃ OH	91	20 3b	80 4b
9	CH ₃ (CH ₂) ₅ CH ₂ 1b	(CH ₃) ₂ CHOH	95	25 3b	75 4b
10	CH ₃ (CH ₂) ₅ CH ₂ 1b	(CH ₃) ₃ COH	96	43 3b	57 4b

^a Reaction conditions: Pd (0.02 mmol), dppb (0.6 mmol), alkyne (2.0 mmol), alcohol (8.0 mmol), CH₂Cl₂ (5 ml), 600 psi (CO/H₂ = 1/1), 20 h.^b Isolated yield.^c Determined by GC and ¹H NMR.

In conclusion, the regioselective hydroesterification of terminal alkynes with various alcohols can be achieved under neutral conditions by using the simple catalytic system Pd(OAc)₂/dppb/CO/H₂. This method provides a significant improvement over the present systems described in the literature. Mechanistic studies and the application of this catalytic system to other important mono- and dialkynes with various alcohols and diols are in progress.

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- Typical experimental procedure for the hydroesterification of 1-alkynes with alcohols: A mixture of 2.0 mmol of 1-nonyne **1b**, 2.0 mmol of 1-butanol, 0.020 mmol of Pd(OAc)₂, and 0.08 mmol of dppb was dissolved in 10 ml of CH₂Cl₂ and placed in a 45 ml autoclave. The autoclave was purged, pressurized (600 psi of CO+H₂) and then heated (110°C). After 20 h the reaction was cooled to room temperature, filtered through Celite and concentrated by rotary evaporation. The esters **3b** and **4b** were identified by GC and ¹H and ¹³C NMR. All esters **3**, **4**, **6** and **7** were clearly identified and characterized by GC–MS and ¹H and ¹³C NMR.