Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 2022, **32**, 253–255

Mendeleev Communications

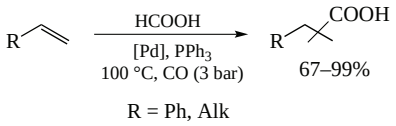
An effective Pd-catalyzed hydroxycarbonylation of olefins with CO and HCOOH

Oleg L. Eliseev,* Tatyana N. Bondarenko and Maria V. Tsapkina

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: oleg@ioc.ac.ru

DOI: 10.1016/j.mencom.2022.03.033

A new protocol for Pd-catalyzed regioselective hydroxycarbonylation of olefins with formic acid under low pressure of carbon monoxide has been developed. The same catalytic system provides good selectivity to 2-phenylpropionic acid in carbonylation of styrene and to linear acids in carbonylation of terminal alkenes. The reaction is highly susceptible to catalyst precursor and solvent nature.



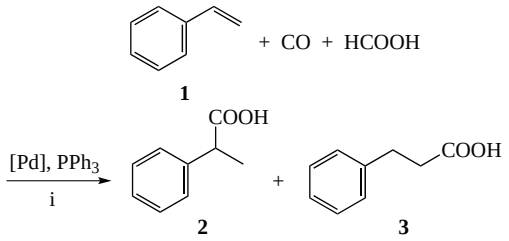
Keywords: hydroxycarbonylation, palladium, olefins, carboxylic acids, formic acid, carbon monoxide.

Carboxylic acids and their esters are valuable intermediates for organic synthesis and large volume commodity products. Among the many methods for their preparation, palladium-catalyzed carbonylation of olefins has been widely explored.[1–12] In particular, 2-arylpropionic acids are directly accessible by carbonylation of styrene derivatives. These compounds belong to the important class of non-steroidal anti-inflammatory agents, such as ibuprofen, naproxen and ketoprofen.[1,3] Another impressive example of industrial implementation is novel Lucite Alpha process for methyl methacrylate production where methoxycarbonylation of ethylene is a key step.[13] The advantages of palladium-catalyzed carbonylation of olefins are mild conditions, high chemoselectivity, 100% atom economy and good tolerance to various functional groups in substrate. However, the method usually demands high carbon monoxide pressure (20–50 bar) in the reactor. Also, strong acids, such as HCl, HF, H_2SO_4, TsOH and MesOH, are generally used as promoters[1–3,14–17] facilitating formation of catalytically active Pd-hydride species.[18–20] These acidic additives are unsuitable for some labile substrates and can cause corrosion of apparatus. Another issue is low regioselectivity when unsymmetrical olefins are used as a feed. To improve regioselectivity, special organophosphine supporting ligands have been proposed in catalyst formulation.[14,21] Both electronic and steric properties of the ligand are important for achieving high regioselectivity.[1–3,14,22,23] One of the best examples of such phosphine is bis(di-*tert*-butylphosphinomethyl)benzene (DTBPMB)[24] which provides high activity at atmospheric pressure and over 99% selectivity to linear esters in methoxycarbonylation of terminal alkenes.[18] However, the selectivity to target branched products was not as high in carbonylation of styrene and vinyl acetate. For example, branched to linear products ratio in methoxycarbonylation of styrene was 8.1[22] and in methoxycarbonylation of vinyl acetate it was 3.1[22] or 3.6.[23]

Here we report that above mentioned issues can be circumvented if formic acid is used as a nucleophile instead of water in hydroxycarbonylation of styrene and linear alkenes: high reaction rate can be achieved at CO pressure as low as 3 bar; no sophisticated ligands are needed, common PPh_3 is used; there are no strong acids in the catalyst composition; this catalytic system provides good selectivity to branched acid in carbonylation of styrene and to linear acids in carbonylation of terminal alkenes.

Hydroxycarbonylation of styrene (**1**) in the presence of HCOOH results in the formation of branched (**2**) and linear (**3**) phenylpropanoic acids (Scheme 1).† No other products were detected in the reaction mixture, with the exception of a small amount of ethylbenzene, which was observed only in high temperature runs, apparently as a result of hydrogenation of **1**.

Various catalyst precursors were initially screened in toluene solution at 100 °C under CO pressure of 10 bar (Table 1). $Pd(OAc)_2$ displayed modest activity and good selectivity to target isomer **2** (entry 1). Lower acids yield was obtained with $Pd(acac)_2$ and linear isomer **3** prevailed (entry 2). $Pd(dba)_2$ was



Scheme 1 *Reagents and conditions*: i, olefin (1.75 mmol), $Pd(OAc)_2$ (0.0175 mmol), PPh_3 (0.07 mmol), HCOOH (5.3 mmol), toluene (3 ml), CO (3 bar), 100 °C, stirring, 4 h.

† *General procedure for the hydoxycarbonylation*. Reagents were placed into 50 ml autoclave equipped with magnetic stirrer and glass liner. The reactor was flushed with CO three times and pressurized to 3 bar. Reaction was performed at 100 °C under stirring (600 rpm) for 4 h. Increasing the speed to 800 rpm gave no increase in substrate conversion, indicating a kinetic control of the reaction under these conditions. Then the reactor was allowed to cool to room temperature and the mixture was analyzed chromatographically using *n*-nonane as an internal standard. Prior to GLC analysis, carboxylic acids were converted into the corresponding methyl esters by treating the sample with ethereal solution of diazomethane. For identification, carboxylic acids were separated *via* sodium salts and analyzed by ^{1}H NMR spectroscopy.

Table 1 Screening of reaction conditions in styrene hydroxycarbonylation.[a]

Entry	[Pd]	Solvent	*T*/°C	Acids yield (%)	**2**/**3** ratio
1	$Pd(OAc)_2$	toluene	100	34.6	7.1
2	$Pd(acac)_2$	toluene	100	20.6	0.44
3	$Pd(dba)_2$	toluene	100	5.9	28.5
4	$PdCl_2$	toluene	100	88.4	0.77
5[b]	$PdCl_2(PPh_3)_2$	toluene	100	86.5	0.68
6	$Pd(OAc)_2$	toluene	80	18.5	8.5
7	$Pd(OAc)_2$	toluene	120	21.4	6.13
8	$Pd(OAc)_2$	MEK	100	0	–
9	$Pd(OAc)_2$	1,4-dioxane	100	1.2	0
10	$Pd(OAc)_2$	CH_2Cl_2	100	41.3	0.56
11	$Pd(OAc)_2$	MeCN	100	3.2	1.0
12	$Pd(OAc)_2$	MeOH	100	29.5	0.73
13[c]	$Pd(OAc)_2$	toluene	100	16.0	13.55

[a] Styrene (0.2 ml, 1.75 mmol), [Pd] (0.0175 mmol), PPh_3 (18.3 mg, 0.07 mmol), HCOOH (0.2 ml, 5.3 mmol), solvent (3 ml), 10 bar, 4 h. [b] 0.035 mmol PPh_3 loaded; [c] 5.6 mmol H_2O added.

practically inactive (entry 3). $PdCl_2$ and $PdCl_2(PPh_3)_2$ were the most active catalysts, though their regioselectivity was low (entries 4, 5). Then we continued with $Pd(OAc)_2$ as the most promising precursor. The reaction temperature of 100 °C was found to be the optimal one. Both decreasing and increasing temperature reduced the yield, while **2**/**3** ratio differed slightly. Moreover, 3% ethylbenzene yield was obtained at 120 °C (entry 7). It has been shown that solvent is an important factor affecting both activity and selectivity of the catalyst. The use of toluene allowed us to reach the highest acids yield while other solvents tested, such as methanol, 1,4-dioxane, acetonitrile, dichloromethane and methyl ethyl ketone (MEK), gave lower or even negligible values of the yield (entries 8–12). Nucleophilic solvents probably act here as ligands preventing styrene from entering the coordination sphere of palladium, thus hampering the reaction. Moreover, complexation of solvent molecules to palladium atom could affect an electron density on it and space available for other ligands. Both factors could change catalyst regioselectivity.

Toluene was chosen as the optimal reaction medium. Since general hydroxycarbonylation procedure involves the use of water as co-reagent, we explored the catalyst performance in the presence of water (0.1 ml). Unexpectedly, the acids yield decreased notably, albeit selectivity to **2** increased (entry 13).

Further we studied the effect of CO pressure on the reaction indexes. In sharp contrast with traditional carbonylation with water or alcohols as nucleophiles, the highest yield was obtained at low pressure of 3 bar. The yield gradually declined when pressure increased up to 20 bar and then it slightly increased again. Regioselectivity was less dependent on the pressure, though a slight increase in **2**/**3** molar ratio was definitely expressed (Figure 1).

After the reaction, Pd black was formed on the bottom of the liner in almost all experiments, thus indicating decomposition of catalytically active complexes. A tentative reason of

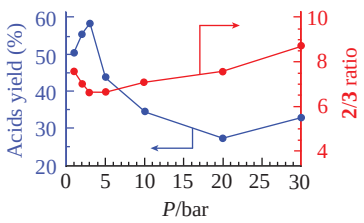


Figure 1 Effect of CO pressure on acids yield and **2**/**3** molar ratio. Reaction conditions correspond to entry 1, Table 1.

Table 2 Effect of PPh_3 loading on styrene hydroxycarbonylation.[a]

Entry	PPh_3/Pd molar ratio	Acids yield (%)	**2**/**3** ratio
1	4	58.2	6.67
2	6	74.5	4.52
3	8	92.9	4.60
4	10	99.5	4.24

[a] Styrene (0.2 ml, 1.75 mmol), $Pd(OAc)_2$ (0.0175 mmol), PPh_3, HCOOH (0.2 ml, 5.3 mmol), solvent (3 ml), 3 bar, 100 °C, 4 h.

moderate yields is a fast catalyst decay. To improve stability of Pd catalyst in solution, we added excess PPh_3 to the reaction mixture. Indeed, in this case, Pd black formation diminished and acids yield increased almost linearly with increasing the PPh_3 concentration. We managed to achieve complete conversion of **1** and yields of acids over 99% in 4 h run. However, **2**/**3** ratio slightly decreased with increasing the PPh_3 loading (Table 2).

With optimized reaction conditions in hand, we examined the applicability of the new protocol to terminal alkenes (Table 3). In all cases, linear fatty acids were obtained with fairly good selectivity. Their branched isomers were not only 2-methyl-substituted acids but some other isomers. They obviously arise as a result of double bond migration in the substrate followed by carbonylation of produced internal olefins, which are known to be less active then terminal alkenes owing to the steric hindrance at the double bond.[1,18] Hence, complete conversion of alkenes has not been reached in these runs. Notably, replacement of $Pd(OAc)_2$ with $PdCl_2(PPh_3)_2$ led to somewhat increase in acids yield, while linear to branched acids ratio decreased dramatically (entry 4). Thus, chloride ion reduces regioselectivity for both styrene and alkenes.

It is known that state-of-the-art catalyst $Pd_2(dba)_3$ + DTBPMB provides ~99 ratio of linear to branched (l/b) products in methoxycarbonylation of terminal alkenes.[18] However, DTBPMB is an expensive proprietary ligand, highly susceptible to oxidation. On the contrary, our catalytic system contains cheap, available and air-stable chemicals. The use of another bidentate ligand 1,2-bis{[*tert*-butyl(pyridin-2-yl)phosphanyl]methyl}benzene proposed by Beller's group[14,15] provided 2.4–2.7 l/b ratio in hydroxycarbonylation of terminal alkenes.[14]

A plausible catalytic cycle based on known 'hydride' mechanism of olefin carbonylation[1] is presented in Figure 2. Reduction of palladium acetate yields Pd^0 which may produce hydride complex by oxidative addition of HCOOH.[25] Then olefin enters Pd coordination sphere to form alkylpalladium complex which can undergo CO addition followed by migratory insertion generating acyl complex. The cycle closes by reductive elimination of mixed formyl anhydride and regeneration of Pd^0. Anhydrides are thermally unstable under acidic conditions[26] and decarbonylation affords the carboxylic acid. Figure 2 shows the formation of isomeric acid, whereas linear acid is formed similarly, but in the latter case migratory insertion of olefin yields linear alkylpalladium complex.

Table 3 Hydroxycarbonylation of terminal alkenes.[a]

Entry	Substrate	Total acids yield (%)	Linear acid yield (%)	l/b ratio
1	1-Heptene	67.1	61.1	10.2
2	1-Octene	46.6	41.5	8.1
3	1-Nonene	41.2	37.3	9.6
4[b]	1-Nonene	49.9	18.2	0.6

[a] Alkene (0.2 ml), $Pd(OAc)_2$: PPh_3 : alkene : HCOOH = 1 : 10 : 100 : 300, toluene (3 ml), 3 bar, 100 °C, 4 h. [b] 1% $PdCl_2(PPh_3)_2$ + 2% PPh_3 as a catalyst.

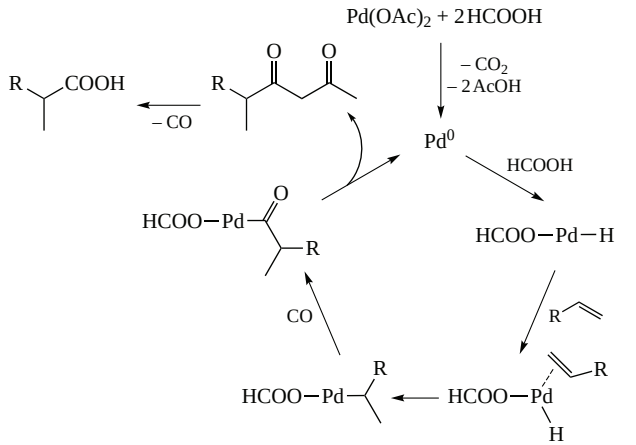


Figure 2 Plausible catalytic cycle for olefin hydroxycarbonylation with formic acid. Supporting PPh_3 ligands are omitted for clarity.

In conclusion, we have developed an effective Pd-catalyzed regioselective hydroxycarbonylation of olefins with formic acid as a co-reagent under mild reaction conditions. The advantages of the proposed method are low CO pressure and the absence of strong mineral acid in the catalyst composition.

Scientific Schools Development Program by Zelinsky Institute of Organic Chemistry is gratefully acknowledged.

References

1 G. Kiss, *Chem. Rev.*, 2001, **101**, 3435.
2 X.-F. Wu, X. Fang, L. Wu, R. Jackstell, H. Neumann and M. Beller, *Acc. Chem. Res.*, 2014, **47**, 1041.
3 A. Brennführer, H. Neumann and M. Beller, *ChemCatChem*, 2009, **1**, 28.
4 G. Cavinato and L. Toniolo, *Molecules*, 2014, **19**, 15116.
5 L. Acemoglu and J. M. J. Williams, *J. Mol. Catal. A: Chem.*, 2003, **196**, 3.
6 T. M. Konrad, J. T. Durrani, C. J. Cobley and M. L. Clarke, *Chem. Commun.*, 2013, **49**, 3306.
7 A. Ionescu, G. Laurenczy and O. F. Wendt, *Dalton Trans.*, 2006, 3934.
8 I. del Rio, N. Ruiz, C. Claver, L. A. van der Veen and P. W. N. M. van Leeuwen, *J. Mol. Catal. A: Chem.*, 2000, **161**, 39.
9 A. Lapidus, O. Eliseev, T. Bondarenko and N. Stepin, *J. Mol. Catal. A: Chem.*, 2006, **252**, 245.
10 A. Lapidus, O. Eliseev, N. Stepin and T. Bondarenko, *Russ. Chem. Bull.*, 2004, **53**, 2564 (*Izv. Akad. Nauk, Ser. Khim.*, 2004, 2458).
11 O. Eliseev, N. Stepin, T. Bondarenko and A. Lapidus, *Dokl. Chem.*, 2005, **401**, 59 (*Dokl. Akad. Nauk*, 2005, **401**, 486).
12 M. Amézquita-Valencia, G. Achonduh and H. Alper, *J. Org. Chem.*, 2015, **80**, 6419.
13 A. Tullo, *Chem. Eng. News*, 2009, **87** (42), 22.
14 R. Sang, P. Kucmierczyk, R. Dühren, R. Razzaq, K. Dong, J. Liu, R. Franke, R. Jackstell and M. Beller, *Angew. Chem., Int. Ed*., 2019, **58**, 14365.
15 K. Dong, X. Fang, S. Gülak, R. Franke, A. Spannenberg, H. Neumann, R. Jackstell and M. Beller, *Nat. Commun.*, 2017, **8**, 14117.
16 K. Dong, R. Sang, X. Fang, R. Franke, A. Spannenberg, H. Neumann, R. Jackstell and M. Beller, *Angew. Chem.*, 2017, **129**, 5351.
17 P. Roesle, C. J. Dürr, H. M. Möller, L. Cavallo, L. Caporaso and S. Mecking, *J. Am. Chem. Soc.*, 2012, **134**, 17696.
18 C. J. Rodriguez, D. F. Foster, G. R. Eastham and D. J. Cole-Hamilton, *Chem. Commun.*, 2004, 1720.
19 G. R. Eastham, B. T. Heaton, J. A. Iggo, R. P. Tooze, R. Whyman and S. Zacchini, *Chem. Commun.*, 2000, 609.
20 P. Roesle, L. Caporaso, M. Schnitte, V. Goldbach, L. Cavallo and S. Mecking, *J. Am. Chem. Soc.*, 2014, **136**, 16871.
21 A. Grabulosa, J. J. R. Frew, J. A. Fuentes, A. M. Z. Slawin and M. L. Clarke, *J. Mol. Catal. A: Chem.*, 2010, **330**, 18.
22 H. Ooka, T. Inoue, S. Itsuno and M. Tanaka, *Chem. Commun.*, 2005, 1173.
23 A. J. Rucklidge, G. E. Morris and D. J. Cole-Hamilton, *Chem. Commun.*, 2005, 1176.
24 C. J. Moulton and B. L. Shaw, *J. Chem. Soc., Chem. Commun.*, 1976, 365.
25 M. Oshima, I. Shimizu, A. Yamamoto and F. Ozawa, *Organometallics*, 1991, **10**, 1221.
26 J. M. Baird, J. R. Kern, G. R. Lee, D. J. Morgans Jr. and M. L. Sparacino, *J. Org. Chem.*, 1991, **56**, 1928.

Received: 22nd September 2021; Com. 21/6701