Use of Formic or Oxalic Acid for the Regioselective Hydrocarboxylation of Alkenes and Alkynes Catalyzed by Pd/C and 1,4-Bis(diphenylphosphino)butane

B. El Ali,*,† G. Vasapollo,‡ and H. Alper*,†

Ottawa-Carleton Chemistry Institute, Department of Chemistry, University of Ottawa, Ottawa, Ontario, Canada K1N 6N5, and Centro MISO, CNR, Politecnico di Bari, Via Amendola 173, Bari, Italy

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New methodology for the hydrocarboxylation of alkenes and alkynes is of considerable interest, one focus being the search for new catalysts as well as the use of new acids as promoters.[1-11] Homogeneous catalysts have been used in most cases to effect these transformations. Heterogeneous catalysts, which offer some advantages (e.g., catalyst recovery and reuse) have not been widely investigated. In 1990 Inomata and co-workers reported that Pd/C catalyzes the carbalkoxylation of terminal olefins to mono- and diesters,[3] and Bergbreiter and co-workers[12] studied the carbonylation of some substrates with a heterogeneous Pd catalyst system whose activity is affected by the addition of ligands. Recently, we found that $Pd(OAc)_2$, in the presence of HCOOH as promoter and phosphine ligands, is an efficient catalytic system for the hydrocarboxylation of alkenes[13] and alkynes.[14] It was found that HCOOH is involved, together with CO, in the key step of the reaction mechanism as a source of "H" and "OH" in the carboxylic acid. We now wish to report that one can obtain carboxylic acids in a regioselective manner using a heterogeneous catalyst (10% or 5% Pd/C) in the presence of formic acid or oxalic acid and phosphine ligands. The heterogeneous catalysts have activity resembling that of a homogeneous catalyst.

Results and Discussion

Terminal alkenes react with formic acid or oxalic acid in the presence of 10% Pd/C and 1,4-bis(diphenylphosphino)butane (dppb) in 1,2-dimethoxyethane (DME) to give carboxylic acids (**2**, **3**) (eq 1).

$$\underset{\mathbf{1}}{\mathrm{RCH{=}CH_2}} + \mathrm{ACOOH} + \mathrm{CO} \xrightarrow[\text{DME, 6.8 atm (A = H) or 40 atm (A = COOH), 150 °C, 24 h, } -\mathrm{CO_2}]{\text{10\% Pd/C dppb}} \mathrm{RCH_2CH_2COOH} + \mathrm{RCH(COOH)CH_3} \quad (1)$$

A = H, COOH

2 **3**

The hydrocarboxylation was carried out for 24 h at 150 °C under 6.8 atm (formic acid) or 40 atm of CO (oxalic acid). The results of the reactions are summarized in Table I. All reactions gave both isomers, the linear one being the major product in all cases. The yields of the formic acid reactions are in the range of 59–80%, while oxalic acid gave acids in 54–75% yield. Palladium on carbon does not, on its own, catalyze the alkene hydrocarboxylation. However, with added dppb, Pd/C became quite an active catalyst system, and it was found that the best yields were obtained using a Pd/C/dppb ratio of 1:4.

Alkynes, **4**, react also with formic or oxalic acid in the presence of a catalytic amount of 10% Pd/C, PPh_3, and dppb at 100 °C and 100 psi pressure of CO (6.8 atm) to form the corresponding unsaturated carboxylic acids **5** and **6** (eq 2).

$$\underset{\mathbf{4}}{\mathrm{R'C{\equiv}CH}} + \mathrm{ACOOH} + \mathrm{CO} \xrightarrow[\text{DME, 6.8 atm (A = H) or 40 atm (A = COOH), 110 °C, 24 h } -\mathrm{CO_2}]{\text{10\% Pd/C, dppb, } PPh_3} \underset{\mathbf{5}}{\mathrm{R'(H)C{=}C(H)COOH}} + \underset{\mathbf{6}}{\mathrm{R'(H)C{=}C(COOH)H}} \quad (2)$$

A = H, COOH

The results of these reactions are listed in Table II. In contrast to the alkene hydrocarboxylation reaction where PPh_3 has no beneficial effect, the activity of the alkyne system increases with the addition of PPh_3 and the best yields were found using a Pd/PPh_3/dppb ratio of 1:4:2. The function of PPh_3 in the alkyne reaction is unclear.

† University of Ottawa.
‡ Politecnico di Bari.

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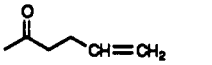
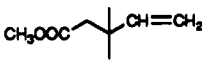
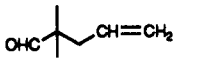
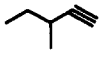
Table I. Hydrocarboxylation of Alkenes by Formic or Oxalic Acid Catalyzed by Pd/C–dppb[a]

alkene	yields[b] using formic acid (oxalic acid)	product distribution[c,d] 2	3
$C_6H_5CH{=}CH_2$	65 (65)	76 (80)[e]	24 (20)[e]
p-$CH_3C_6H_4CH{=}CH_2$	74 (73)	76 (75)[23]	24 (25)[24]
p-$ClC_6H_4CH{=}CH_2$	71 (55)	75 (82)[25]	25 (18)[25]
2,4-$Me_2C_6H_3CH{=}CH_2$	68 (65)	89 (92)[29]	11 (8)[29]
p-$CH_3OC_6H_4CH{=}CH_2$	62 (60)	68 (69)[25]	32 (31)[25]
$CH_3(CH_2)_4CH{=}CH_2$	68 (65)	79 (70)[e]	21 (30)[30]
$(CH_3)_3CCH{=}CH_2$	79 (75)	100 (100)[31]	
$CH_3(CH_2)_4C(CH_3){=}CH_2$	61 (60)	100 (100)[28]	
	78 (75)	76 (80)[27]	24 (20)
	80 (67)	100 (100)[e]	
	68 (69)	88 (88)[13]	12 (12)[13]

[a] Reaction conditions: alkene (5.0 mmol), 10% Pd/C, (0.01 mmol); HCOOH or oxalic acid (10 mmol); dppb (0.08 mmol); 5 mL of DME; 6.8 atm of CO for HCOOH (40 atm for HOOCCOOH), T = 150 °C, 24 h. [b] Isolated yields. [c] Determined by NMR spectroscopy and by comparison with authentic materials. [d] Determined by NMR spectroscopy and by comparison with literature data. [e] See Experimental Section.

Table II. Hydrocarboxylation of Alkynes by Formic or Oxalic Acid Catalyzed by Pd/C–dppb–PPh_3[a]

alkyne	yields[b] using formic acid (oxalic acid)	product distribution[c] 5	6
$CH_3(CH_2)_5C{\equiv}CH$	75 (59)	96 (90)[15]	4 (10)[15]
$C_6H_5C{\equiv}CH$	80 (82)	96 (96)[15]	4 (4)[16]
$C_6H_5CH_2CH_2C{\equiv}CH$	76 (61)	94 (90)[17]	6 (10)[17]
$(CH_3)_3CC{\equiv}CH$	71 (60)	40 (45)[21]	60 (55)[22]
$ClCH_2(CH_2)_2C{\equiv}CH$	55 (55)	75 (82)[19]	25 (8)[19]
$NCCH_2(CH_2)_2{\equiv}CH$	60 (65)	95 (86)[18]	5 (14)[18]
	82 (78)	92 (92)[d]	8 (8)[d]
	67 (61)	85 (83)[20]	15 (17)[20]

[a] Reaction conditions: alkyne (5.0 mmol); 10% Pd/C (0.02 mmol), HCOOH or oxalic acid (10 mmol), PPh_3 (0.16 mmol), dppb (0.08 mmol), DME (5 mL); 6.8 atm of CO for formic acid (40 atm for oxalic acid), T = 110 °C, 24 h. [b] Isolated yields. [c] Determined by NMR spectroscopy and by comparison with literature data. [d] See Experimental Section.

In general, the hydrocarboxylation of alkenes in the present system requires relatively mild conditions, and the product distribution is favorable for the linear acid. For alkynes, the unsaturated acid **5** is the principal regioisomer formed in most cases. It was found that this heterogeneous system (Pd/C–HCOOH or Pd/C–oxalic acid) is also compatible with other functional groups such as –CN, –Cl, double bond, –CHO, and COOH. When oxalic acid is used in place of formic acid the hydrocarboxylation reaction of alkenes and alkynes requires higher CO pressure (40 atm). However, the yields of the oxalic acid reactions are very similar to those involving formic acid, and the product distribution is also maintained.

Other bidentate ligands such as $Ph_2P(CH_2)_nPPh_2$, n = 2, 3, 5 were tested in order to determine the influence of chelation on reaction yields. Product yields decreased appreciably on substitution of dppb by other bidentate phosphine ligands. For example, hydrocarboxylation of phenylacetylene in the presence of 1,2-bis(diphenylphosphino)ethane (dppe) gave acids in 12% yield, and the yield was 15% in the case of 1,3-bis(diphenylphosphino)propane (dppp).

The mechanism of these reactions is unclear. In order to better understand this mechanism and to determine if the actual catalyst in this chemistry was a heterogeneous or homogeneous catalyst the following experiments have been carried out:

(a) Pd/C, dppb, HCOOH in DME were placed in a 45-mL autoclave. After CO was introduced at 6.8 atm, the mixture was stirred at 150 °C for 24 h. After the reaction was cooled to room temperature, the mixture was filtered to give a colorless solution and a solid material.

(b) To the solution was added $PhCH{=}CH_2$ and HCOOH. The autoclave was repressurized to 6.8 atm of CO and heated to 150 °C for 24 h. The corresponding carboxylic acids **2** and **3** were isolated in 45% yield (ratio **2**:**3** = 76:24).

(c) The solid material from part a was added to a solution of $PhCH{=}CH_2$, HCOOH, DME, and dppb. Carbon monoxide (6.8 atm) was introduced, and the reaction mixture was heated to 150 °C for 24 h. **2** and **3** were formed in 40% yield and in the same ratio as in b.

The results obtained indicate that the phosphine ligand (dppb) may leach the metal out of the solid phase forming a catalytically active palladium phosphine species. This explanation does not rule out the possibility of occurrence of part of the reaction on the surface of the solid (a problem which is difficult to resolve). It is conceivable, taking into consideration the results of Bergbreiter's group,[5,12] that the phosphine ligand forms a colloidal phosphine–palladium species which remains on the surface of the solid phase.

Experimental Section

General. All olefins, 1,4-bis(diphenylphosphino)butane, 1,3-bis(diphenylphosphino)propane, 1,2-bis(diphenylphosphino)-ethane, palladium catalysts, HCOOH, and DME were purchased from Aldrich and were used as received. A 45-mL stainless-steel autoclave (Parr Instruments) was used for these reactions.

General Procedure for the Hydrocarboxylation of Alkynes. (a) Five mL of DME, 10 mmol of formic or oxalic acid, 42 mg (0.16 mmol) of PPh_3, 34 mg (0.08 mmol) of dppb, 22 mg (0.02 mmol) of 10% Pd/C, and 5 mmol of alkyne were put in a 45-mL autoclave. After being purged with CO, the autoclave was pressurized to 6.8 atm of CO (40 atm of CO in the case of oxalic acid) and heated at 100 °C for 24 h. After the solvent was removed, the residue was dissolved in 30 mL of ether and extracted into 2 N NaOH. The aqueous solution was neutralized and extracted with ether, dried, concentrated to remove solvent, and then distilled, affording the pure acid. Products were identified by comparison of spectral data (IR, NMR, MS) with literature results and/or authentic samples.

General Procedure for the Hydrocarboxylation of Alkenes. (b) Five mL of DME, 10 mmol of HCOOH or oxalic acid, 22 mg (0.02 mmol) of 10% Pd/C, 34 mg (0.08 mmol) of dppb, and 5 mmol of alkene were put in a 45-mL autoclave. After being purged with CO, the autoclave was pressurized to 6.8 atm of CO (40 atm of CO in the case of oxalic acid) and heated at 150 °C for 24 h. Workup was carried out using the procedure described in a.

Spectral Data for New Compounds. $CH_3OOCCH_2C(CH_3)_2(CH_2)_2COOH$. ^1H NMR: δ ($CDCl_2$) 1.0 (s, 6H, $C(CH_3)_2$–), 1.65(t, 2H, J = 8.25 Hz, CH_2CH_2COOH), 2.20 (s, 2H, CH_2

$COOCH_3$), 2.40 (t, 2H, J = 8.05 Hz, $-CH_2COOH$), 3.65 (s, 3H, $-COOCH_3$), 10.40 (br, COO*H*) ppm. GC/MS trimethylsilyl ester: $M^{\bullet+}$ = 260.

$CH_3(CH_2)_3C{\equiv}C(CH_2)_2C(COOH){=}CH_2$. ^1H NMR: δ ($CDCl_3$) 0.80 (t, 3H, J = 7.85 Hz, CH_3CH_2-), 1.30 (m, 4H, $CH_3(CH_2)_2-$), 2.05 (t, 2H, J = 7.80 Hz, $CH_2CH_2C{\equiv}C-$), 2.30 (t, 2H, J = 7.90 Hz, $CH_2CH_2C(COOH){=}CH_2$), 2.40 (t, 2H, J = 7.90 Hz, $CH_2CH_2C(COOH){=}CH_2$), 5.70 (d, 1H, J = 1.10 Hz, vinylic proton *trans* to COOH), 6.30 (d, 1H, vinylic proton *cis* to COOH), 10.70 (br, COO*H*) ppm. GC/MS trimethylsilyl ester: $M^{\bullet+}$ = 252.

$CH_3(CH_2)_3C{\equiv}C(CH_2)_2CH{=}CHCOOH$ (*trans*). ^1H NMR: δ ($CDCl_3$) 0.80 (t, 3H, J = 7.85 Hz, CH_3CH_2-), 1.30 (m, 4H, $CH_3(CH_2)_2-$), 2.05 (t, 2H, J = 7.80 Hz, $CH_2CH_2C{\equiv}C-$), 2.30 (t, 2H, J = 7.90 Hz, $CH_2CH_2CH{=}CH-$), 2.40 (m, 2H, $CH_2CH_2CH{=}CH-$), 5.85 (dt, $^3J_{H-H}$ = 15.5 and 1.60 Hz, $-CH{=}CHCOOH$), 7.05 (dt, $^3J_{H-H}$ = 15.5 and 7.0 Hz, $-CH{=}CHCOOH$), 10.70 (br, COO*H*) ppm. GC/MS triethylsilyl ester: $M^{\bullet+}$ = 252.

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