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Palladium-Catalyzed Carbonylation of Benzyl Alcohol and Its Analogs Promoted by HI in Aqueous Systems

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Abstract: Carbonylation of benzyl alcohol catalyzed by a palladium(0) complex and promoted by hydrogen iodide gives phenylacetic acid in excellent yields in aqueous systems. The catalysis is proposed to proceed through a benzylpalladium species formed by the oxidative addition of benzyl iodide, produced *in situ* by the interaction of benzyl alcohol with HI, to a Pd(0) species. Application of the carbonylation process to other arylmethanol analogs provided convenient means to prepare 3-isochromanone, 1,4-benzenediacetic acid, 2-hydroxybenzeneacetic acid and 2-naphthaleneacetic acid.
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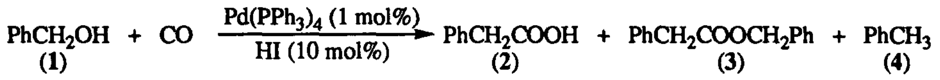
Palladium-catalyzed carbonylation of aryl halides has been extensively used in organic synthesis.[1] The corresponding catalytic carbonylation of arylalkyl halides is attracting increasing attention.[1a-c,2] However, a disadvantage of the process using the organic halides to prepare carboxylic acids and derivatives is that the halide employed has to be eventually removed as a salt with a base. This is not environmentally favorable nor preferable from the economic viewpoint. Thus development of a process without using an organic halide is desirable.[3] Successful carbonylation of arylethanol derivatives catalyzed by palladium complexes to give carboxylic acids has been reported.[4,5] In contrast, catalytic carbonylation of arylmethanols has been less explored and only *para*-hydroxy substituted benzyl alcohols have been successfully carbonylated, whereas other *meta*- and *ortho*-substituted benzyl alcohols as well as non-substituted benzyl alcohol have been reported to give only trace amounts of phenylacetic acid derivatives.[6] Palladium-catalyzed carbonylation of systems containing naphthols and aldehydes has been recently reported to give lactones in a process presumably involving the carbonylation of naphthalenemethanols formed *in situ*.[7] In the present communication, we report the successful direct carbonylation of benzyl alcohol to phenylacetic acid catalyzed by palladium complexes. The process is promoted by HI in aqueous solution as well as in water-containing systems, but not promoted by HCl as recently reported.[6]

In a typical experiment, phenylacetic acid (**2**) was produced in excellent yields when a mixture of $Pd(PPh_3)_4$ (0.05 mmol), benzyl alcohol (**1**, 5 mmol), and HI (66 μL of an aqueous solution containing 57% HI, 0.5 mmol) was heated under CO in acetone/H_2O (2/0.1 mL) or in H_2O (2 mL) containing *n*-Bu_4NBr (10 mol%) (Table 1).

Addition of HI as a co-catalyst is essential for producing **2**. Other protic acids such as HCl and HBF_4 were ineffective as promoters (Entries 7, 8 and 11, Table 1). The suitable amount of HI added is 10 mol% of **1** and decreasing or increasing HI caused a decrease in the yield of **2** (Entries 1-3). Addition of LiI instead of HI did not give any carbonylation product (Entry 6). Water is essential to promote the carbonylation and addition of Molecular Sieves 4A inhibited the formation of **2** (Entry 4). For the carbonylation of **1** in water, addition of *n*-Bu_4NBr is required (Entry 5). A Pd(II) complex such as $PdCl_2(PPh_3)_2$ can also be used as a catalyst precursor as well as a Pd(0) complex in the presence of either HI or LiI (Entries 9-10), whereas addition of $HNEt_2$ in the presence of LiI blocked the reaction (Entry 12). It is probable that the Pd(II) complex is reduced under the present conditions containing CO and water to give a Pd(0) species with liberation of a proton.[8]

Table 1. Carbonylation of Benzyl Alcohol[a]



$$\underset{(1)}{PhCH_2OH} + CO \xrightarrow[HI\ (10\ mol\%)]{Pd(PPh_3)_4\ (1\ mol\%)} \underset{(2)}{PhCH_2COOH} + \underset{(3)}{PhCH_2COOCH_2Ph} + \underset{(4)}{PhCH_3}$$

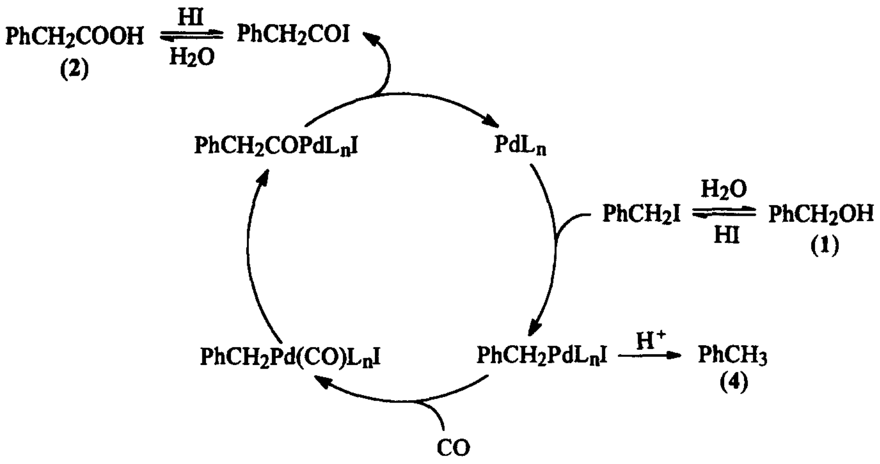
Entry	T (°C)	P (atm)	Time (h)	Solvents	Promoter (mol%)	Products (%)[b] 2	3	4	1 (%)[b]
1[c]	90	90	44	acetone/H_2O	HI (10)	90	3	6	0
2	90	90	44	as above	HI (5)	24	58	7	7
3[c]	90	90	46	as above	HI (50)	48	0	27	0
4[d]	90	100	65	acetone	HI (10)	0	18	trace	70
5[e]	110	90	43	H_2O	HI (10)	88	1	4	trace
6	100	100	46	acetone/H_2O	LiI (20)	0	0	trace	96
7	90	90	48	as above	HCl (10)	2	7	trace	88
8[f]	90	90	69	as above	$HBF_4 \cdot OMe_2$	0	0	0	40
9[g]	100	100	42	as above	HI (10)	73	10	15	trace
10[g]	100	100	42	as above	LiI (20)	35	24	4	26
11[g]	105	100	45	as above	HCl (10)	trace	trace	3	95
12[g,h]	100	100	46	as above	LiI (20)	0	0	0	100

a) Reaction conditions: a mixture of $PhCH_2OH$ (5 mmol), promoter and $Pd(PPh_3)_4$ (0.05 mmol) in a solvent (2 mL) was heated. b) Determined by GC and ^1H NMR. c) A trace of 1,2-diphenylethane was detected. d) MS 4A (1.0 g) was added and 12% of $(PhCH_2)_2O$ was formed. e) *n*-Bu_4NBr (10 mol%) was added. f) 10 mol% $HBF_4 \cdot OMe_2$ was added and 58% of $(PhCH_2)_2O$ was formed. g) $PdCl_2(PPh_3)_2$ (1 mol %) was used in place of $Pd(PPh_3)_4$. h) $HNEt_2$ (10 mmol) was added.

On the basis of the experimental results, we propose a catalytic cycle for the carbonylation of benzyl alcohol as shown in Scheme 1, which is reminiscent of the Rh-catalyzed carbonylation of methanol to acetic acid.[9]

By the interaction of benzyl alcohol with HI, benzyl iodide is formed *in situ* and it oxidatively adds to a palladium(0) complex to form a benzylpalladium intermediate.[10] The latter reacts with CO to give benzyl(carbonyl)palladium complex[11] followed by CO insertion to produce a phenylacetylpalladium complex.[12] Reductive elimination of $PhCH_2COI$ and its subsequent hydrolysis or alcoholysis yield the corresponding acid **2** or ester **3** with generation of HI and a palladium(0) complex that carries the catalytic cycle. Toluene formed as the main by-product may arise by protonolysis of the benzylpalladium complex with HI.[13] Ineffectiveness of HCl *vis-à-vis* HI is noteworthy. The difference may be due to the higher reactivity of benzyl iodide than benzyl chloride (formed by the interaction of HCl with benzyl alcohol) toward a Pd(0) species.

Addition of an amine completely blocks the carbonylation, this fact suggesting that the present process differs from the base-promoted carbonylation process using organic halides.



Scheme 1. Catalytic Cycle for the Carbonylation of $PhCH_2OH$ (L = PPh_3)

The successful carbonylation of benzyl alcohol prompted us to explore the carbonylation of other alcohols. Difunctional alcohols, 1,2- and 1,4-benzenedimethanol (**5** and **12**) and 2-hydroxybenzenemethanol (**8**), also undergo direct carbonylation to give 3-isochromanone (**6**), 1,4-benzenediacetic acid (**13**) and 2-hydroxybenzeneacetic acid (**10**) in moderate to good yields, respectively, as shown in Table 2 (Entries 1-3, Table 2). The formation of **6** provides a novel method to synthesize a δ-lactone, which was previously prepared by the carbonylation of 2-bromomethylbenzyl alcohol (71% yield).[14] In addition, 2-naphthaleneacetic acid (**16**) and 3-thiopheneacetic acid (**18**) were obtained in moderate to excellent yields from the carbonylation of 2-naphthalenemethanol (**15**) and 3-thiophenemethanol (**17**), respectively (Entries 4-5, Table 2).

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9. To our knowledge, this paper provides the first example of Pd-catalyzed direct carbonylation of arylmethanols promoted by HI, whereas Rh-catalyzed carbonylation of unsubstituted methanol to acetic acid is well-known, see: Forster, D. *Adv. Organomet. Chem.* **1979**, *17*, 255.
10. Generation of $Pd(CH_2Ph)(PPh_3)_2I$ by the reaction of $Pd(PPh_3)_4$ and $PhCH_2I$ (1:1) in $CDCl_3$ has been confirmed by ^1H NMR.
11. Formation of *trans*-$[Pd(CH_2Ph)(^{13}CO)(PMe_3)_2]PF_6$ by the reaction of (η^3-benzyl)bis(trimethylphosphine)palladium(II) hexafluorophosphate and ^{13}CO in CD_2Cl_2 at -40 °C has been confirmed by ^1H, ^{13}C and ^{31}P NMR.
12. For comparison, the acyl complex, *trans*-$Pd(COCH_2Ph)(PPh_3)_2Cl$ was prepared by the reaction of $Pd(PPh_3)_4$ and $PhCH_2COCl$ and identified by ^1H, ^{13}C, ^{31}P NMR and elemental analysis.
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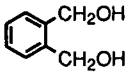
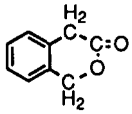
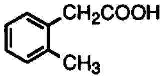
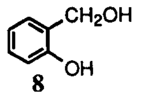
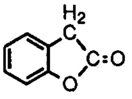
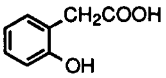
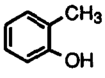
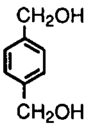
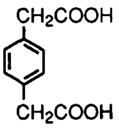
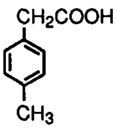
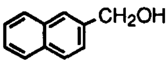
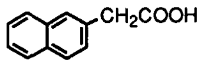
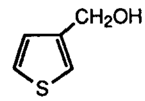
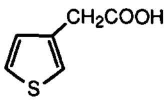
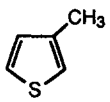
Table 2. Carbonylation of Aromatic Methanols[a]

Entry	Alcohol	Products, yield%[b] (isolated yield%)
1[c]	 **5**	 **6**, 88 (56) +  **7**, 9
2[d]	 **8**	 **9**, 9 +  **10**, 56 (36) +  **11**, 7
3[c,e]	 **12**	 **13**, (48) +  **14**, 16
4[c]	 **15**	 **16**, 97 (90)
5	 **17**	 **18**, 34 +  **19**, 11

a) Reaction conditions: a mixture of alcohol (4 mmol), HI (0.4 mmol) and $Pd(PPh_3)_4$ (0.04 mmol) in acetone/H_2O (3/0.1 mL) under CO (90 atm) was heated at 90 °C for 42 h. b) Determined by GC and ^1H NMR; c) A trace of *o*-xylene (Entry 1), *p*-xylene (Entry 3) and 2-methylnaphthalene (Entry 4) were detected. d) Dioxane/H_2O (3/0.2 mL) was used as solvent instead of acetone/H_2O and the reaction was carried out at 120 °C. e) HI (0.8 mmol) and $Pd(PPh_3)_4$ (0.08 mmol) were used.

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