Simple and Efficient Palladium-Catalyzed Carbonylation of Iodoxyarenes in Water under Mild Conditions

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Summary: Iodoxyarenes ($ArIO_2$) readily react with CO (1 atm) in water, in the presence of $Na_2[PdCl_4]$ (0.1%) and Na_2CO_3 at 40–50 °C, to give the corresponding carboxylic acids, ArCOOH, in 55–89% isolated yield. Particularly attractive features of the reaction are that, unlike most iodoarenes, $ArIO_2$ can be carbonylated in aqueous media without any organic solvents, due to their solubility in water and high reactivity.

In recent years, considerable interest has developed in performing various transition metal catalyzed organic reactions in aqueous media, totally avoiding the use of organic solvents.[1-4] One of the main problems with replacement of organic solvents by the most economic and safe solvent, water, is the insolubility of most organic substrates. For instance, Bumagin, Nikitin, and Beletskaya[3] have recently shown that water-soluble potassium iodobenzoates and iodophenolates can be efficiently carbonylated in *neat* water to give the corresponding dicarboxylic and hydroxybenzoic acids in high yield. At the same time, for the successful carbonylation of water-insoluble iodoarenes, under similarly mild conditions (20–50 °C, 1 atm of CO, 1% of $K_2[PdCl_4]$), aqueous DMF must be used as a solvent instead of water[3] or one can employ a higher temperature (100 °C) and triphenylphosphinepalladium complexes.[4] It seemed conceivable to us that the poor reactivity of water-insoluble iodoarenes toward Pd-catalyzed carbonylation in water could be enhanced by converting them to the corresponding water-soluble and more electrophilic iodoxyarenes, $ArIO_2$. Various compounds of polyvalent iodine are widely used in synthesis.[5] Noncatalytic[6] and palladium-catalyzed[7] carbonylation of diaryliodonium salts have been described in the literature. In the present paper, we wish to report the *first* example of the carbonylation of the pentavalent iodine compounds, $ArIO_2$, which is efficiently performed in water under very mild conditions.

Iodoxybenzene readily reacts with carbon monoxide in the presence of Na_2CO_3 and catalytic amounts of $Na_2[PdCl_4]$ to give benzoic acid in 71–77% isolated yield (eq 1). Reaction 1 occurs in water under mild conditions (40 °C and 1 atm of CO) with only 0.1 mol % of the palladium complex. The reaction is complete in 6.5 h or less, at which point a colorless solution forms and palladium black precipitates. No reaction was observed in the absence of the palladium complex. Under the same conditions, the reaction between iodobenzene and CO was very sluggish (6% conversion to benzoic acid), with Pd metal deposition within a few minutes after starting the reaction.

$$PhIO_2 + CO \xrightarrow[40\ °C,\ 1\ atm,\ 6.5\ h]{H_2O,\ Na_2CO_3,\ Na_2[PdCl_4]\ (0.1\%)} PhCOONa \quad (1)$$

A number of iodoxyarenes containing various substituents on the aromatic ring have been successfully carbonylated in water under similar conditions (see Table I).[8] All reactions were conducted using 0.1 mol % of the Pd catalyst, since the yield of benzoic acid in the reaction of $PhIO_2$ did not improve substantially upon increasing the amount of the $Na_2[PdCl_4]$ to 0.5% (entries 1 and 2). Depending on the nature and position of the substituent, 100% conversion of $ArIO_2$ was achieved in 3–10 h. The main competing process is the reduction of $ArIO_2$ to ArI. The latter (8–25% yield) can be easily separated from the desired product (carboxylic acid) by washing the reaction mixture with ether prior to acidification. Evaporation of the ether extract gives pure iodoarene which can be recycled, i.e., again oxidized and subsequently used for the carbonylation.

The oxidation of iodoarenes to iodoxyarenes is best achieved by stirring with sodium hypochlorite (commercially available laundry bleach), slightly acidified with acetic acid.[10] This method is not only inexpensive but also very efficient as it affords iodoxyarenes in 80–95%

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[8] General Procedure for the Palladium-Catalyzed Hydroxycarbonylation of Iodoxyarenes. Carbon monoxide was slowly bubbled through a stirred mixture of iodoxyarene, Na_2CO_3, water, and a 0.01 M aqueous solution of $Na_2[PdCl_4]$ (0.2 mL) until all of the solids dissolved, whereupon a colorless solution formed, and palladium metal precipitated[9] (see Table I for specifics). The resulting solution was washed with ether or petroleum ether in order to remove byproducts (iodoarenes), acidified with 20% HCl, and extracted with ether (3 × 30–50 mL). The combined ether extracts were dried over anhydrous $MgSO_4$ and filtered, and the filtrate was concentrated by rotary evaporation. The residual acids were purified by vacuum sublimation and found to be identical (^1H NMR, mass spectra, and melting points) to authentic samples. The mixtures of bromobenzoic acids with isophthalic or terephthalic acid (Table I, entries 10 and 11) were not extracted with ether, but instead filtered off, washed with water, dried under vaccum, and analyzed by ^1H NMR spectroscopy.

[9] In the carbonylation of *p*-iodoxynitrobenzene, it is difficult to determine when 100% conversion is achieved. A relatively clear reaction mixture does not form in this case due to the formation of solid, water-insoluble *p*-iodonitrobenzene (ca. 20%).

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Table I. Palladium-Catalyzed Hydroxycarbonylation of Iodoxyarenes[a]

$$\mathrm{ArIO_2 + CO \xrightarrow[(2)\ H_3O^+]{(1)\ Na_2[PdCl_4],\ Na_2CO_3,\ H_2O} ArCOOH}$$

entry	Ar	*T*, °C (oil bath)	time, h	isolated yield, %
1	C_6H_5	40	6.5	71
2	C_6H_5[b]	40	4.5	77
3	2-$CH_3C_6H_4$	40	10	74
4	3-$CH_3C_6H_4$	40	4.5	77
5	4-$CH_3C_6H_4$	40	10	55
6	4-$CH_3C_6H_4$	50	6.5	51
7	4-$CH_3C_6H_4$	60	6	48
8	3-ClC_6H_4	40	4.5	88
9	4-ClC_6H_4	40	4.5	82
10	3-BrC_6H_4	40	5.5	76[c]
11	4-BrC_6H_4	40	5	61[d]
12	4-$NO_2C_6H_4$	40	5	74
13	4-$NO_2C_6H_4$	50	3	77
14	4-$CH_3OC_6H_4$	40	4	89

[a] Reaction conditions: 2 mmol of iodoxyarene, 6 mmol of Na_2CO_3, 2×10^{-3} mmol of $Na_2[PdCl_4]$, 7 mL of H_2O, CO (1 atm). [b] In the presence of 1×10^{-2} mmol of $Na_2[PdCl_4]$. [c] Isophthalic acid was also formed in 14% yield. [d] Terephthalic acid was also formed in 15% yield.

yield.[11] After isolation by simple filtration, the iodoxyarenes are pure enough for the palladium-catalyzed carbonylation. For example, no advantage was found in using water-recrystallized $PhIO_2$ for reaction 1. Iodoxyarenes are stable and convenient to work with. Their solubility in water is not very high,[12] but, as we see, quite sufficient for the hydroxycarbonylation in aqueous media.

As seen from Table I, the yields of substituted benzoic acids are mostly in the range of 71–89%, with the exception of *p*-toluic acid which is obtained from *p*-$CH_3C_6H_4IO_2$ in 55% yield (entry 5). Otherwise, no significant influence of the nature and position of the substituents on the reactivity of iodoxyarenes was observed. Interestingly, carbonylation of 3- and 4-$BrC_6H_4IO_2$ resulted in mixtures of the corresponding bromobenzoic acid with isophthalic or terephthalic acid, respectively (entries 10 and 11).

Table II. Palladium-Catalyzed Carbonylation of ArI and $ArIO_2$ in Water (1 atm of CO)[a]

substrate	$[PdCl_4]^{2-}$, %	*T*, °C	time, h	ArCOOH,[b] %	ref
4-$NO_2C_6H_4I$	1	50	5	30	3
4-$NO_2C_6H_4IO_2$	0.1	50	3	77	this work
C_6H_5I	1	40	6.5	6	this work
$C_6H_5IO_2$	0.5	40	4.5	77	this work

[a] Reaction conditions: see Table I and ref 3. [b] Isolated yield.

Therefore, unlike carbon–chlorine bonds (entries 8 and 9), the carbon–bromine bond was reactive under the reaction conditions, although its reactivity was not as high as that of the carbon–iodine bond in iodobenzoic acids and iodophenols.[3]

The difference in reactivity of iodoarenes and iodoxyarenes toward the Pd-catalyzed hydroxycarbonylation in water is illustrated by the data presented in Table II. It is clear that $ArIO_2$ undergo hydroxycarbonylation much easier than their iodoarene precursors, even at lower concentration of the catalyst. It is noteworthy that attempted carbonylation of other aromatic compounds of polyvalent iodine, such as iodosobenzene PhIO and its acetoxy and trifluoroacetoxy derivatives, $PhI(OCOCH_3)_2$ and $PhI(OCOCF_3)_2$, gave benzoic acid in only 4–6% yield (H_2O/Na_2CO_3, 0.1% of $Na_2[PdCl_4]$, 40–50 °C, 1 atm of CO, 7–20 h). Instead of carbonylation, the main reaction path of iodosobenzene and its carboxylates was reduction to iodobenzene. Iodosobenzene is about three times less soluble in water than iodoxybenzene.[13] Nevertheless, such dramatically different behavior of PhIO and $ArIO_2$ in the Pd-catalyzed reaction with CO is probably due not only to the lower solubility of iodosobenzene but also because of the principally higher polarity and reactivity of the C–I bond in the iodine(V) compounds.

In conclusion, iodoxyarenes are excellent substrates for the palladium-catalyzed hydroxycarbonylation in water under very mild conditions, in the absence of any organic solvents.

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(11) The oxidation of ArI with NaOCl/AcOH furnishes $ArIO_2$ in almost quantitative yield. The losses (5–20%) vary depending on the solubility of each particular iodoxyarene in water.[12]

(12) For instance, the solubilities of iodoxybenzene in water are [in mmol/L (°C)]: 10.1 (0); 11.6 (14); 18.3 (40); 27.8 (61); 40.0 (83); 49.7 (99).[13]

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