An Exceptionally Simple Biphasic Method for the Metal Catalysed Carbonylation of Chloroarenes

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Bis(tricyclohexylphosphine)palladium dichloride is an active catalyst for the carbonylation of chloroarenes to carboxylic acids.

Catalytic cleavage of the carbon–chlorine bond in chloroarenes is still a challenging problem in organic chemistry. Unlike aromatic carbon–bromine and especially carbon–iodine bonds, which readily undergo cleavage in the presence of diverse reagents, the carbon–chlorine bond is quite inert. Being cheap, readily available in large quantities, and therefore of considerable industrial potential, chloroarenes at the same time are unreactive towards the vast majority of transition metal complexes and are usually incapable of undergoing reactions observed with the more expensive iodo- and bromo-aromatic compounds.[1] Some progress in catalytic activation and functionalization of aryl chlorides has occurred in the last few years. We have recently described highly chemoselective rhodium biphasic and phase-transfer catalysed hydrogenolysis of the chlorine–carbon bond in chloroarenes under exceptionally mild conditions.[2] Both homogeneous[3] and heterogeneous[4] palladium catalysts have been used for the carbonylation of aryl chlorides.[†] The homogeneous carbonylation reaction described by Milstein and coworkers[3] occurs under reasonable conditions (150 °C, P_{CO} = 4.8–5.5 bar, 20 h; 1 bar = 10^5 Pa), achieving catalytic turnover numbers of 70–100. However, the specific catalyst used, $Pd(dippp)_2$ [dippp = 1,3-bis(diisopropylphosphino)propane], is expensive and not readily available because of the ligand it contains. In contrast, the alkoxycarbonylation of chloroarenes described by Basset's group[4] employs unsophisticated heterogeneous palladium catalysts, but requires a higher temperature; the catalytic turnover numbers of 5–350 were obtained at 200 °C and P_{CO} = 3 bar in 50 h. In this communication we report the first example of simple and quite efficient hydroxycarbonylation of chloroarenes under mild conditions, catalysed by bis(tricyclohexylphosphine)palladium dichloride **1**. The palladium complex **1** is easily prepared in quantitative yield from $[PdCl_4]^{2-}$, and the commercially available and relatively inexpensive tricyclohexylphosphine.

Neat chloroarenes react with CO and aqueous KOH in the presence of catalytic amounts of **1** to give the corresponding carboxylic acids upon subsequent acidification. The results are presented in Table 1. The reaction occurs at *ca.* 100 °C and atmospheric pressure of CO under biphasic conditions requiring no phase-transfer catalyst (compare entries 5 and 6).[‡] It is noteworthy that palladium(0) and phase-transfer catalysed carbonylation of iodoarenes and bromoarenes is known and well documented.[9]

Since most ordinary chlorobenzenes are either liquids, or solids melting below 100 °C, they can be used for the hydroxycarbonylation under biphasic conditions without any organic solvent. This simple technique is superior to the approach employing palladium complexes of expensive sulfonated phosphines for conducting some catalytic reactions (*e.g.* coupling) in aqueous media.[10] The concentration of KOH for the hydroxycarbonylation was not optimized. Both 50 and 20% aqueous solutions of KOH were found suitable for the reaction. However, use of solid alkali is undesirable owing to its harmful effect on glass flasks at elevated temperatures.

A number of chlorobenzenes containing electron-donating (entries 3–8) and electron-withdrawing (entries 9–11) substituents have been successfully carbonylated in good yields. As seen from Table 1, electron-donating substituents activate the substrates towards carbonylation, whereas electron-withdrawing groups exert the opposite trend. No carbonylation was observed in the case of *p*-chloronitrobenzene. These observations are similar to those described by Basset and coworkers.[4]

Table 1 Biphasic carbonylation of chloroarenes catalysed by complex **1**[a]

$$ArCl + CO \xrightarrow[\text{ii, } H_3O^+]{\text{i, } \mathbf{1}\text{, aqueous KOH}} ArCO_2H$$

Entry	Ar	Reaction time/h	Isolated yield (%)[b]
1	Ph	72	8 900
2	1-$C_{10}H_7$	72	10 300
3	4-MeC_6H_4	72	11 600
4	4-MeC_6H_4	48	8 800
5	3-MeC_6H_4	48	9 000
6[c]	3-MeC_6H_4	48	8 500
7	2-MeC_6H_4	48	6 500
8	4-$MeOC_6H_4$	48	10 500
9[d]	3-$PhCOC_6H_4$	48	900
10	4-$CF_3C_6H_4$	48	500
11	4-$CF_3C_6H_4$	72	700
12	4-$NO_2C_6H_4$	24	0

[a] Reaction conditions: 40 mmol of chloroarene, 0.1 mmol of **1**, 2 g of KOH, 8 ml of water, CO (1 atm.), *ca.* 100 °C (refluxing). [b] Yield is based on **1**. [c] In the presence of 0.3 mmol of 18-crown-6 ether. [d] 10 mmol of 3-chlorobenzophenone.

Some other nickel, palladium and platinum complexes of the general formula L_2MCl_2 (M = Ni, L = PPh_3 or 1/2 $Ph_2PCH_2CH_2CH_2PPh_2$; M = Pd, L = PMe_3, PBu_3, PPh_3, 1/2 $Ph_2PCH_2CH_2PPh_2$ or $AsPh_3$; M = Pt, L = PPh_3) were explored as potential catalysts for the carbonylation of chlorobenzene. With the exception of bis(triphenylphosphine)palladium dichloride, which afforded traces of benzoic acid, the catalysts were inactive, giving palladium (or platinum, but not nickel) metal under conditions used for the carbonylation reactions catalysed by **1**.[§] Hence, the electron-rich and bulky tricyclohexylphosphine ligand plays a crucial role in the stabilization of the key catalytically active palladium species and in activation of the carbon–chlorine bond. Mechanistic studies are in progress, and will be published separately.

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[†] Nickel-,[5] cobalt-[6] and palladium-catalysed[7] carbonylation of some *activated* chloroarenes (*e.g.* 1,3,5-trichlorobenzene, chloronaphthalenes) has been reported. A *photostimulated* cobalt-catalysed carbonylation of chloroarenes is also known.[8]

[‡] The following procedure is representative: carbon monoxide was slowly bubbled through a vigorously stirred, refluxing mixture of *m*-chlorotoluene (5.1 g), water (8 ml), KOH (2 g) and **1** (0.074 g) for 48 h. Water (40 ml) was added, the aqueous layer was separated from unreacted *m*-chlorotoluene containing palladium complexes, washed with ether, acidified with 20% HCl, and extracted with ether (4 × 40 ml). The combined ether solutions were dried over $MgSO_4$, filtered, and evaporated, to give 1.22 g (8970% based on the catalyst; 22% based on *m*-chlorotoluene) of white, pure *m*-toluic acid, m.p. 106–108 °C. Unreacted *m*-chlorotoluene was recovered in 61% yield. Other chloroarenes (Table 1) were hydroxycarbonylated in a similar manner.

[§] Bis(triphenylphosphine)palladium dichloride (as well as **1**) was found to be active in the hydroxycarbonylation of aryl bromides and iodides under the same conditions.