Formylation of Aryl Chlorides catalysed by a Palladium Complex

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The complex (dippp)$_2$Pd [dippp = 1,3-bis(di-isopropylphosphino)propane] is an efficient, unique catalyst for direct formylation of aryl chlorides to aldehydes with CO and sodium formate.

Formylation of aryl halides to aldehydes with dihydrogen, CO, and a base is catalysed by palladium complexes at elevated pressure.[1—3] Much lower pressure is required if dihydrogen is replaced by a hydrogen donor, such as a silyl hydride or a formate salt.[4] A serious limitation of these synthetically useful reactions, which hinders industrial utilization, is the fact that aryl chlorides, which are much more attractive as starting materials than aryl bromides and iodides, are not reactive. Activation of aryl chlorides towards Pd-catalysed formylation by prior stoicheiometric formation of their chromium tricarbonyl complexes was recently described.[5] Undoubtedly, a method for direct catalytic formylation of aryl chlorides to aldehydes under mild pressure would be of considerable interest. We report here that this is possible with the complex (dippp)$_2$Pd [dippp = 1,3-bis(di-isopropylphosphino)propane] (**1**) as catalyst.

A likely reason for the lack of reactivity of aryl chlorides in catalytic carbonylation to aldehydes is their much lower tendency to undergo oxidative addition to Pd(0) compared with aryl bromides and iodides.[6] In our attempts to increase the rate of this step without adversely affecting other steps in the catalytic cycle, we discovered that the new, electron-rich, chelate-stabilized complex (dippp)$_2$Pd(0) (**1**)† catalyses the carbonylation of aryl chlorides to aldehydes in high yields (equation 1). For convenience, the Pd(0) complex can be generated *in situ* under reducing reaction conditions by use of Pd(OAc)$_2$ + 2dippp.

$$\mathrm{ArCl + CO + HCO_2Na \rightarrow ArCHO + NaCl + CO_2} \quad (1)$$

A typical example is as follows: Sodium formate (20 mmol) is added to a solution of (**1**) (0.1 mmol) and chlorobenzene (10 mmol) in 3 ml of dry dimethylformamide (DMF) under nitrogen. The solution is charged with 80 psi of CO and stirred at 150 °C for 20 h. After cooling to room temperature, the gas is slowly released through an aqueous solution of BaO, resulting in formation of a precipitate of BaCO$_3$ (10 mmol). GC analysis of the reaction mixture reveals complete disappearance of chlorobenzene to yield benzaldehyde (95% yield) and benzene (5% yield). Addition of water, extraction with ether, and solvent evaporation yields almost pure benzaldehyde (90% yield).

Since the formylation process does not result in a significant pressure change, a pressure increase is indicative of dehalogenation to the arene; a good fit is obtained between yields of the arene calculated from pressure increase and solution GC.

Aryl chloride formylation experiments utilizing (**1**), isolated or generated *in situ*, are summarized in Table 1. For comparison, results of experiments with the complexes of other phosphine ligands are also listed. Some interesting

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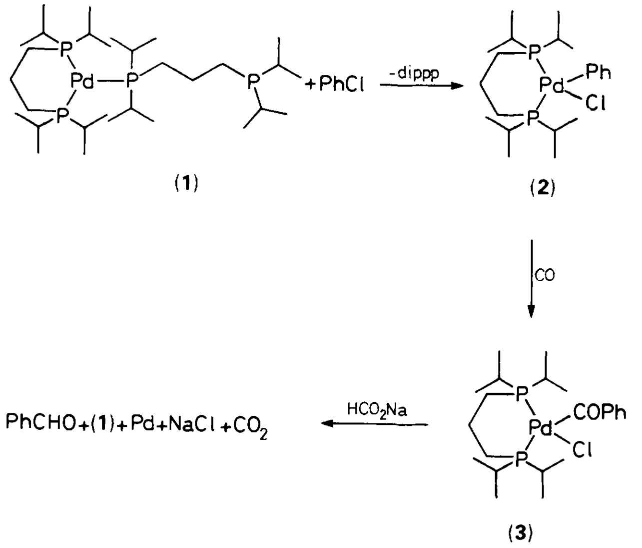
† Details on the preparation, characterization, and dynamic behaviour of this complex will be published elsewhere.



Scheme 1

observations emerge: (a) the formylation reaction is specific to the dippp ligand; (b) an *ortho* substituent significantly reduces reaction rate; (c) complexes of smaller or larger chelate sizes catalyse dehalogenation rather than formylation (Pd-complex catalysed dehalogenation of aryl bromides and iodides was reported before as a reaction of some synthetic interest, although aryl chlorides were inactive[7]); (d) same chelate size as dippp but lower basicity [dppp = $Ph_2P(CH_2)_3PPh_2$] results in very little reaction; (e) complexes of mono-dentate phosphines are inactive; (f) a ratio Pd/dippp of 1 : 2 is required.

Experiments of mechanistic relevance are as follows (Scheme 1). Firstly, chlorobenzene undergoes oxidative addition to (**1**) to yield complex (**2**).† This reaction is very slow at 50 °C, requiring days for completion. Secondly, (**2**) undergoes facile carbonylation (50 psi, 25 °C) yielding complex (**3**),† which can be obtained directly from (**1**) by oxidative addition of benzoyl chloride. Thirdly, heating of (**3**) with sodium formate in tetrahydrofuran (THF) at 100 °C results in the formation of benzaldehyde, (**1**) and Pd metal. In the presence of an extra mole of dippp, Pd does not precipitate.

Although it is premature to draw conclusions about the mechanistic detail at this stage, it seems that (a) the carbonylation step is the fastest. (b) Since some dehalogenation leading to the arene is observed, the overall halide metathesis process is probably not much slower than the carbonylation step, indicating that the oxidative addition step is probably the slowest. Rate retardation by an arene *ortho* substituent is also compatible with this. (c) Since complexes of other basic chelating phosphines (dippe, dippb) catalyse mainly dehalogenation to the arene, a process that requires aryl chloride oxidative addition and halide metathesis, it is likely that the dippp ligand is unique in promoting the carbonylation step. (d) Lack of any catalysis with dppp or monodentate phosphines suggests that, in these cases, oxidative addition (under CO) is very difficult.

Table 1. Formylation of aryl chlorides catalysed by $Pd(OAc)_2$ + 2L.[a]

Ar	L[b]	ArCHO/%	ArH/%	ArCl/%
Ph	dippp[c]	95(90[d])	5	0
Ph	dippp	93	5	0
Ph	dippp[e]	22	0	75
4-MeC_6H_4	dippp	88[d]	4	0
2-MeC_6H_4	dippp	20	0	80
4-$MeOC_6H_4$	dippp	85[d]	3	0
Ph	dippe	1	72	25
Ph	dippb	4	60	35
Ph	dppp	3	0	95
Ph	2PPh_3	0	0	100
Ph	2PMe_3	0	0	100

[a] *Conditions* as described in text. [b] dippe = $Pr^i_2P(CH_2)_2PPr^i_2$; dippb = $Pr^i_2P(CH_2)_4PPr^i_2$; dppp = $Ph_2P(CH_2)_3PPh_2$. [c] Preformed (**1**) was used. [d] Isolated yield. [e] Ratio Pd/L 1 : 1

We are actively pursuing mechanistic understanding of this process and are exploring its implication to other relevant aryl chloride activation processes.

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