Palladium Catalysed Coupling Reactions of Chloroaryl $Cr(CO)_3$ Complexes[1]

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Chloroaryl chromium tricarbonyl complexes undergo palladium catalysed coupling reactions with nucleophiles and palladium catalysed olefination reactions with alkenes.

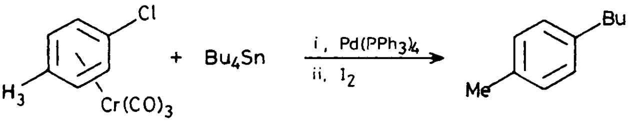
The ability to form carbon–carbon bonds between electrophiles and nucleophiles in the presence of a catalytic amount of a transition metal has proved to be useful to the synthetic organic chemist.[2] These reactions are typified by gentle reaction conditions and high reaction selectivity.

For the formation of aryl-carbon bonds using palladium catalysed coupling schemes, aryl iodides are the most commonly used electrophile owing to the ease of oxidative addition into the arene–iodine bond.[2] Aryl bromides can also be utilized, though often at comparatively higher temperatures. Aryl chlorides, however, have been shown to undergo oxidative addition only with great difficulty, the catalyst often undergoing decomposition before oxidative addition can occur.[2] Owing to the wide availability of aryl chlorides and their greater propensity to withstand the rigours of multi-step synthetic sequences, the ability to include aryl chlorides among the electrophiles amenable to palladium catalysed coupling reactions would greatly enhance the usefulness of these reactions.

Oxidative addition into aryl–electrophile bonds is similar in many ways to aromatic nucleophilic substitution reactions. Thus, it has been shown that functional groups which reduce the π-electron density of the arene act to facilitate oxidative addition. We reasoned that a species which can be put in place and removed at will, and which effectively withdraws electron density from the aromatic ring should also activate the arene toward oxidative addition.

Such a species might be the arene chromium tricarbonyl complex.[2,3] Chromium tricarbonyl complexes are known to be activated toward aromatic nucleophilic substitution reactions with sulphide[4] and alkoxide[5] anions. Even fluoroaryl chromium tricarbonyl complexes will undergo aromatic nucleophilic substitution reactions.[6] The complex is readily prepared by treatment of the arene with chromium hexacarbonyl at elevated temperatures and readily removed by one of a number of oxidative procedures.[2]

Herein, we report that chloroaryl chromium tricarbonyl complexes are capable of undergoing palladium catalysed coupling reactions.[7]† Thus, treatment of a tetrahydrofuran solution of (*p*-chlorotoluene)tricarbonylchromium (**1**) with a slight excess of tetrabutyltin in the presence of tetrakis(triphenylphosphine)palladium(0) (2 mol%) at 60 °C for 15 h, afforded a 75% yield of *p*-butyltoluene after oxidative removal of the chromium (Scheme 1).‡ Similarly, treatment of (**1**) with tributylvinyltin afforded *p*-methylstyrene.



(**1**)

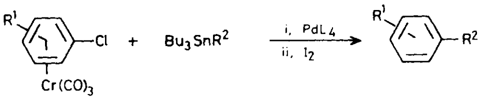
Scheme 1

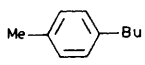
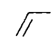
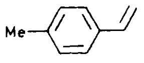
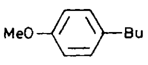
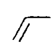
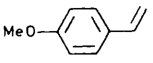
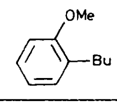
As shown in Table 1, this coupling reaction can also be applied to (*p*-chloroanisole)tricarbonylchromium. This is noteworthy because it indicates that the electron withdrawing ability of the chromium is able to activate even the electron rich anisole system.

There are few examples of the Heck olefination[8] of aryl chlorides, again owing to the difficulty of oxidative addition into the aryl carbon–chlorine bond. However, treatment of (**1**) with methyl vinyl ketone under typical Heck olefination conditions afforded the desired ester (**2**) in 58% yield (Scheme 2).

In summary, it has been shown that chloroarenes can be activated for oxidative addition by palladium catalysts through the formation of the corresponding chromium tricarbonyl

Table 1. Coupling reactions of (*p*-chloroanisole)tricarbonylchromium.



R^1	R^2	Product	Yield /%
p-Me	Bu		75
			72
p-MeO	Bu		82
			68
o-MeO	Bu		68

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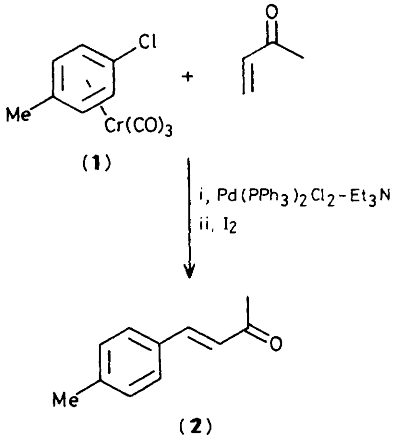
† During the course of these studies a copper–palladium catalysed coupling reaction of chloroaryl chromium tricarbonyl complexes with terminal alkynes was reported.[7]

‡ *Typical procedure*: to (*p*-chlorotoluene)tricarbonylchromium (0·125 g) under argon (1 atm) was added tetrakis(triphenylphosphine)-palladium(0) (0.035g) followed by a solution of tetrabutlytin (0.18 ml) in tetrahydrofuran (10 ml). This was subjected to three cycles of a freeze–pump–Ar purge–thaw regimen, then heated at 70 °C for 15 h. After cooling to room temperature, the mixture was treated with I_2 (0.15 g) and stirred for 6 h. The resulting slurry was separated into aqueous and organic layers and the aqueous layer was extracted once with hexanes. The combined organic layers were washed twice with a saturated solution of sodium hydrogen sulphite, twice with water, and once with a saturated solution of sodium chloride, dried over anhydrous magnesium sulphate, and filtered through silica gel. Flash chromatography (silica gel/hexanes) afforded *p*-butyltoluene as a colourless oil (0.053 g; 75% yield).



Scheme 2

complexes. These complexes may then be used in such typical palladium catalysed reactions as the coupling with nucleophiles and the Heck olefination reaction.

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