Palladium-Catalyzed Coupling Reaction of Salicylaldehydes with Aryl Iodides *via* Cleavage of the Aldehyde C-H Bond

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It has been found that the cross-coupling reaction of salicylaldehydes with aryl iodides smoothly proceeds by using a catalyst system of $PdCl_2/LiCl$ in the presence of Na_2CO_3 as base to give the corresponding 2-aroylphenols in good yields, which appears to involve cleavage of the aldehyde C-H bond.

The activation of C-H bonds by soluble transition metal complexes has been of current interest in organomatallic chemistry.[1] Although numerous stoichiometric reactions involving C-H bond cleavage with transition metal complexes have been developed, catalytic functionalization of C-H bonds have still been less explored.[2-7] As one of the exceptional examples, rhodium-catalyzed activation of aldehydes leading to decarbonylation has been well studied.[3] A synthetic application of this reaction is the addition of the aldehyde C-H bond to alkenes as a useful route to ketones.[4] Recently, an efficient ruthenium-catalyzed addition of a C-H bond in acylarenes to alkenes has been reported, in which the C-H bond ortho to the acyl group is selectively activated.[5] A similar catalytic ortho-alkylation of the phenyl ring in 2-phenylpyridines with alkenes using a rhodium complex has also been described.[6] In the context of our study of palladium-catalyzed reactions using phenols as substrates,[8] we have found that 2-hydroxybenzaldehyde, i. e. salicylaldehyde, and its derivatives smoothly undergo cross-coupling with aryl iodides in the presence of a palladium catalyst to produce the corresponding 2-aroylphenols (Eq. 1). The arylation of olefinic, allylic, and acetylenic C-H bonds by palladium-catalyzed coupling reactions with aryl halides has been proven to be highly useful for forming C-C bonds by dehydrohalogenation.[7] However, there have so far been, to our knowledge, no examples to deal with the direct catalytic arylation of the aldehyde C-H bond using aryl halides.

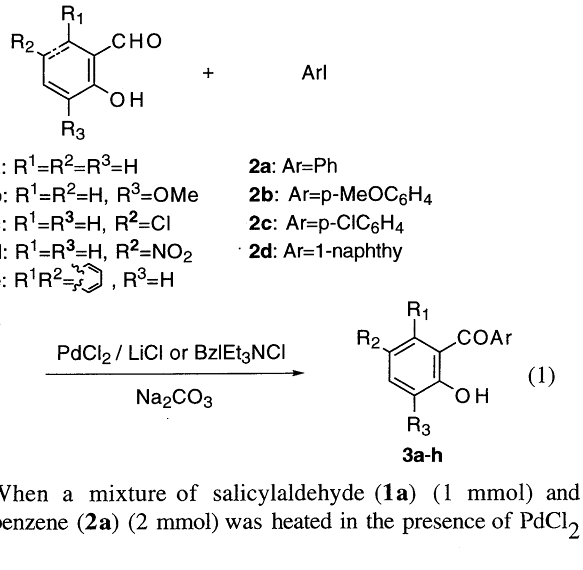
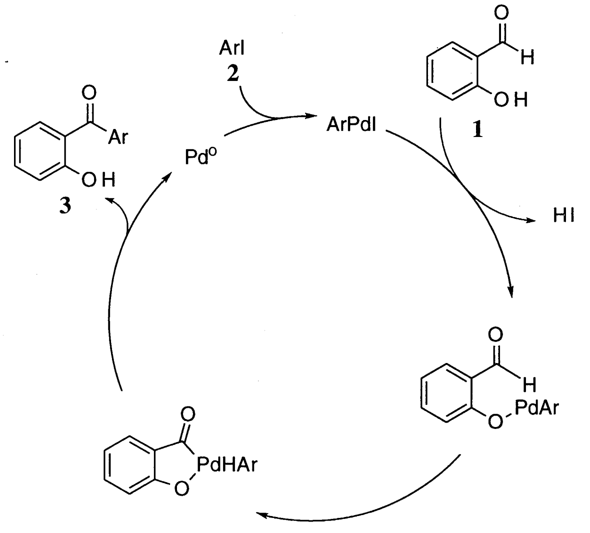


Table 1. Cross-coupling of salicylaldehyde (**1a**) with iodobenzene (**2a**)[a]

Entry	Additive (mmol)	Time/h	Yield of **3a** /%[b]
1		10	84
2	LiCl (0.2)	3.5	91
3	LiCl (1)	6	84
4	$BzlEt_3NCl$ (0.5)	15	81
5	$BzlEt_3NCl$ (1)	4	96
6[c]	LiCl (0.2)	25	93
7[d]	LiCl (0.2)	10	25

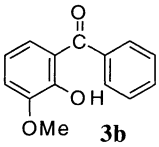
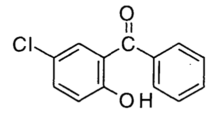
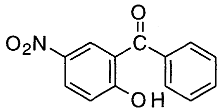
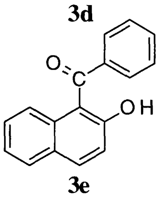
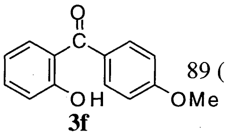
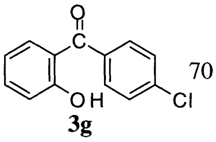
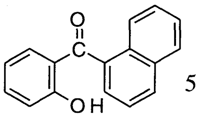
[a]Reaction conditions: **1a** (1 mmol), **2a** (2 mmol), $PdCl_2$ (0.05 mmol), Na_2CO_3 (2 mmol) in DMF (10 cm^3) at 100 °C. [b]GLC yield based on amount of **1a** used. [c]$PdCl_2$ (0.025 mmol) was used. [d]Pr^i_2NEt (2 mmol) was used in place of Na_2CO_3.

When a mixture of salicylaldehyde (**1a**) (1 mmol) and iodobenzene (**2a**) (2 mmol) was heated in the presence of $PdCl_2$ (0.05 mmol) and Na_2CO_3 (2 mmol) in DMF (10 cm^3) at 100 °C for 10 h under nitrogen, 2-hydroxybenzophenone (**3a**) was produced in a yield of 84% (Entry 1 in Table 1). Addition of LiCl (0.2 mmol) remarkably promoted the reaction and enhanced the yield of **3a** (91%) (Entry 2). Further addition of LiCl detrimentally decreased the product yield (Entry 3). An ammonium chloride, $BzlEt_3NCl$, could be used in place of LiCl, although a stoichiometric amount of the chloride was required for a high yield coupling (Entry 5). Product **3a** was also efficiently



Scheme 1.

Table 2. Cross-coupling of hydroxyaldehydes **1** with aryl iodides **2**[a]

1	2	Temp. /°C	Time /h	Product[b]	Yield /%[c]
1b	**2a**	100	8	 **3b**	81 (70)
1c	**2a**	100	6	 **3c**	63 (51)
1d	**2a**	120	22	 **3d**	72 (58)
1e	**2a**	100	3	 **3e**	85 (73)
1a	**2b**	100	6	 **3f**	89 (81)
1a	**2c**	100	2	 **3g**	70 (57)
1a	**2d**	100	24	 **3h**	50 (45)

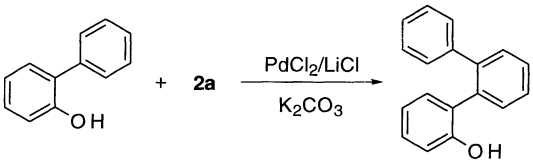
[a]Reaction conditions: **1** (1 mmol), **2** (2 mmol), $PdCl_2$ (0.05 mmol), LiCl (0.2 mmol), Na_2CO_3 (2 mmol) in DMF (10 cm^3). [b]Satisfactory spectra were obtained in measurements of ^1H NMR and MS. [c]GLC yield based on amount of **1** used. Value in parentheses indicates yield after purification.

formed using a half amount of the palladium catalyst by elongation of the reaction time (Entry 6). An organic amine base, Pr^i_2NEt, in place of Na_2CO_3 was not effective for the reaction (Entry 7). It should be noted that treatment of 2-methoxybenzaldehyde, in place of **1a**, with **2a** gave only a trace amount of the corresponding coupling product, suggesting that the phenolic function in **1** acts as a good anchor for the reaction.

Table 2 summarizes the results for the reaction of 2-hydroxybenzaldehydes (**1a**-**1d**) and 2-hydroxy-1-naphthaldehyde (**1e**) with aryl iodides (**2a**-**2d**) using $PdCl_2$, LiCl, and Na_2CO_3. It can be seen that unsymmetrical diaryl ketones (**3b**-**3h**) could be produced in fair to good yields.

A possible mechanism for the present cross-coupling of hydroxybenzaldehydes **1** with aryl iodides **2** is illustrated in Scheme 1, in which neutral ligands and substituents attached to salicylaldehyde are omitted. Oxidative addition of **2** to palladium(0) species generated *in situ* followed by reaction with **1** forms an aryl(aryloxy)palladium intermediate. Then, the second oxidative addition of the aldehyde C-H bond to the metal affords a palladium(IV) species and the subsequent two-fold reductive eliminations from it may occur to produce **3**.[9]

The above observation prompted us to investigate the activation of other kinds of C-H bonds attached to hydroxyarenes using the present catalyst system. Preliminary examinations using 2-methylphenol, 1-naphthol, and 2-phenylphenol showed that the third one was found to react with **2a** under similar conditions to give a hydroxyterphenyl as depicted in Eq. 2.



(2)

50 %

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