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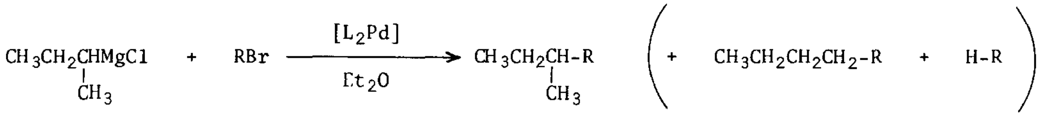
DICHLORO[1,1'-BIS(DIPHENYLPHOSPHINO)FERROCENE]PALLADIUM(II): AN EFFECTIVE CATALYST FOR CROSS-COUPLING REACTION OF A SECONDARY ALKYL GRIGNARD REAGENT WITH ORGANIC HALIDES

Tamio Hayashi, Mitsuo Konishi, and Makoto Kumada*

Department of Synthetic Chemistry, Kyoto University, Kyoto 606, Japan

Summary: Dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) was found to be an effective catalyst for the cross-coupling reaction of *sec*-butylmagnesium chloride with bromobenzene, β-bromostyrene, and 2-bromopropene to give the corresponding *sec*-butyl derivatives in exceedingly high yields.

Phosphine-palladium complexes are known[1] to catalyze the cross-coupling reaction of aromatic and alkenyl halides with organometallics, such as Grignard reagents,[2] organo-zinc,[3,2e] -aluminum,[4,2e] and -zirconium[5] compounds. Of the palladium complexes, tetrakis(triphenylphosphine)palladium(0) has received the most extensive study and proved to be an effective catalyst. The organometallics successfully used for the palladium catalyzed reaction have unfortunately been limited to aryl, alkenyl, alkynyl, and benzyl derivatives, and the reaction with alkyl derivatives containing β-hydrogenes has not been made promising with a few exceptions,[2c,f] probably because an alkylpalladium species generated in the catalytic cycle (*vide infra*) are prone to undergo β-hydride elimination giving an alkene and palladium hydride.[6] We now wish to report that selective and high-yield cross-coupling of *sec*-alkyl and *n*-alkyl Grignard reagents with organic halides can be accomplished by the use of Pd(dppf)Cl_2[7] as a catalyst, where dppf stands for 1,1'-bis(diphenylphosphino)ferrocene.[8]

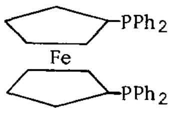


$$\underset{\underset{CH_3}{|}}{CH_3CH_2CHMgCl} + RBr \xrightarrow[Et_2O]{[L_2Pd]} \underset{\underset{CH_3}{|}}{CH_3CH_2CH\text{-}R} \left(+ CH_3CH_2CH_2CH_2\text{-}R + H\text{-}R \right) \quad (1)$$

1 3 4 5

2a: R = Ph-
2b: R = (*E*)-PhCH=CH-
2c: R = CH_2=CMe-

L_2 =



dppf

$L_2 = Ph_2P[CH_2]_nPPh_2$

n = 2: dppe
n = 3: dppp
n = 4: dppb

L_2 = 2 PPh_3

Table 1. Cross-Coupling of *sec*-Butylmagnesium Chloride(1) with Organic Halides(2) Catalyzed by Palladium Complexes.[a]

Catalyst	Halide(2) (RBr)	Reaction Conditions		Yield (%)[b]		
		Temp	Time (hr)	*sec*-BuR(3)	*n*-BuR(4)	
$Pd(dppf)Cl_2$	PhBr(2a)	r.t.	1	95 (80)[c]	0	(0)[d]
$Pd(dppf)Cl_2$[e]		r.t.	24	0	92	(2)[d]
$Pd(PPh_3)_4$		r.t.	24	4	6	(31)[d]
$Pd(PPh_3)_2Cl_2$		r.t.	24	5	6	(9)[d]
$Pd(dppe)Cl_2$		r.t.	48	0	0	(96)[d]
$Pd(dppe)Cl_2$		reflux	8	4	1	(30)[d]
$Pd(dppp)Cl_2$		r.t.	24	43	19	(23)[d]
$Pd(dppb)Cl_2$		r.t.	8	51	25	(1)[d]
$Pd(dppf)Cl_2$	(*E*)-PhCH=CHBr(2b)[f]	0°C	2	97 (78)[c]	0	(0)[g]
$Pd(dppf)Cl_2$[h]		r.t.	24	93	0	(0)[g]
$Pd(dppf)Cl_2$[e]		r.t.	20	0	90	
$Pd(PPh_3)_4$		0°C	3	33	36	(4)[g]
$Pd(dppe)Cl_2$		0°C	5	3	3	(38)[g]
$Pd(dppp)Cl_2$		0°C	5.5	76	5	(6)[g]
$Pd(dppb)Cl_2$		0°C	3.5	53	25	(8)[g]
$Pd(dppf)Cl_2$	$CH_2=CMeBr$(2c)	0°C	8	80	0	

[a] 1/2 = 1.5; catalyst/2 = 10^{-2}, unless otherwise noted. [b] Determined by glpc using an internal standard. [c] Isolated yield. [d] Recovered bromobenzene (%). [e] *n*-Butylmagnesium chloride was used instead of *sec*-butylmagnesium chloride. [f] The coupling products, *sec*-butyl- and *n*-butylstyrene have *E* configuration (>99%). [g] Yield (%) of styrene. [h] Catalyst/2b = 10^{-4}.

In a typical experiment, to a mixture of bromobenzene(2a) (10 mmol) and $Pd(dppf)Cl_2$ (0.1 mmol) was added *sec*-butylmagnesium chloride(1) (15 mmol) in ether at -78°C under nitrogen. The mixture was stirred at room temperature for 1 hr, and then hydrolyzed. Analysis by glpc showed the selective production of *sec*-butylbenzene(3a) in 95% yield (80% isolated by distillation). The palladium complex, $Pd(dppf)Cl_2$, also catalyzed the reaction of 1 with (*E*)-β-bromostyrene(2b) and 2-bromopropene(2c) to produce a high yield of (*E*)-β-*sec*-butylstyrene(3b) and 2-*sec*-butylpropene(3c), respectively, with no by-products. Use of only 0.01 mol% of the catalyst gave a quite satisfactory result. The reactions of *n*-butylmagnesium chloride in the presence of $Pd(dppf)Cl_2$ gave *n*-butylated products selectively as expected.

Other phosphine-palladium complexes were checked for catalytic activity and selectivity in the coupling reactions of *sec*-butylmagnesium chloride(1). They were all much less active and less selective. Thus, tetrakis(triphenylphosphine)palladium(0) or dichlorobis(triphenylphosphine)palladium(II), which has been employed for the coupling reaction with aromatic and vinylic Grignard reagents,[2] gave only 4∿5% yield of *sec*-butylbenzene(3a), along with 6% yield of *n*-butylbenzene(4a) and a considerable amount (∿30%) of benzene(5a). Of bidentate phosphine-palladium complexes, Pd(dppe)Cl_2 was almost inactive under the present conditions; Pd(dppp)Cl_2 and Pd(dppb)Cl_2 catalyzed the coupling reaction, but it was accompanied by butyl group isomerization from secondary to primary. These results are summarized in Table 1.

As is seen from the Table, Pd(dppf)Cl_2 is the only catalyst giving exclusively *sec*-butylated derivatives(3), and other palladium complexes induced, as side reactions, isomerization of the butyl group (to form 4) and reduction of organic halides (to form 5) to some extent. In addition, the coupling reaction with Pd(dppf)Cl_2 catalyst is much faster than that with other complexes. The catalytic cycle of the palladium-catalyzed coupling reaction is assumed[2a~d] to consist of a series of two-electron oxidation and reduction of palladium via a diorganopalladium intermediate, similar to that of the well-studied nickel-catalyzed reactions.[9] The side reactions, isomerization and reduction, probably take place by a mechanism analogous to that proposed in the nickel-catalyzed Grignard coupling[10] and in arylation of olefins with organopalladium derivatives,[11] which involves σ-π interconversions of σ-alkylmetal intermediates and hydrido-olefin metal intermediates by β-hydride elimination and readdition. Accordingly, it can be said that the dppf ligand on palladium must retard the β-hydride elimination and/or accelerate the reductive elimination of coupling products from the diorganopalladium intermediate. The inefficiency of the triphenylphosphine-palladium complexes for the coupling of alkyl Grignard reagents may be attributable to the dissociation of triphenylphosphine from palladium which promotes the β-elimination by forming coordinatively unsaturated species.[12] Since bidentate phosphines are known to stabilize an alkyl-metal moiety against β-hydride elimination by inhibiting loss of one coordinated phosphine,[12a] the palladium catalysts complexed with a bidentate phosphine are expected to be more efficient than the triphenylphosphine-palladium catalyst. It is rather surprising that the dppf ligand can suppress completely the side reactions while other bidentate phosphine ligands (dppe, dppp and dppb) can not. Although the precise role of the ferrocene moiety in dppf for the coupling reaction remains to be clarified, it is likely that the delicate steric and electronic changes in phosphine ligands bring about marked differences in catalytic activity and selectivity.[13]

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(7) The palladium complex was prepared as follows: To a suspension of dichlorobis(acetonitrile)-palladium(II) (1 mmol) in 9 ml of benzene was added with stirring a solution of 1,1'-bis-(diphenylphosphino)ferrocene (1 mmol) in 9 ml of benzene. After 12 hr at room temperature, the reddish brown precipitate formed was collected by filtration, washed with benzene, and dried *in vacuo* to give Pd(dppf)Cl_2 in over 90% yield. This is pure enough for the coupling reactions. The complex can be recrystallized from chloroform/benzene, mp 265-68° (decomp.). (Found: C, 49.11; H, 3.49; Cl, 21.23. $C_{35}H_{29}Cl_5P_2FePd$ (Pd(dppf)$Cl_2 \cdot CHCl_3$) calcd.: C, 49.39; H. 3.43; Cl, 20.83%).

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