Novel Rh(I)-Catalyzed Reaction of Arylzinc Compounds with Methyl Halides

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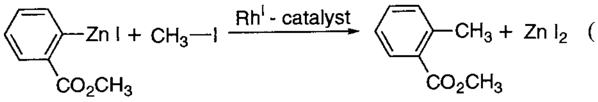
The cross-coupling reactions of arylzinc compounds with methyl iodide or substituted methyl halides like benzyl bromides took place smoothly by the catalysis of Rh(I)-dppf complex.

The utility of arylzinc compounds in organic synthesis has been recognized for a long time. Since the ionic character of C-Zn bond is relatively weak, a high degree of chemoselectivity is realized in the reactions using them as carbon nucleophiles.[1,2] Thus, Pd(0) or Ni(0)-catalyzed cross-coupling of arylzinc compounds with carbon electrophiles like aryl, alkenyl, or alkynyl halides or triflates provides one of the most general and the most valuable methods of synthesizing biaryls, and alkenyl- or alkynylarenes containing various functional groups.[3] On the other hand, similar reactions using alkyl halides as carbon electrophiles have been little investigated except for the reactions using highly reactive ones like allyl halides or benzyl halides.[4-6] At this point, we were interested in employing Rh(I) complexes in place of Pd(0) or Ni(0) complexes.[7] Although Rh(I) complexes have been scarcely applied to the catalytic cross-coupling, including one using organozinc compounds as carbon nucleophiles, it is well-known that Rh complexes like Wilkinson complex ($RhCl(PPh_3)_3$) readily insert into C-X bonds of alkyl halides to form oxidative adducts,[8-11] which are believed to be essential intermediates in the Pd(0) or Ni(0)-catalyzed cross-coupling reactions.[12] Here, we wish to report that the reactions of arylzinc compounds with alkyl halides like methyl iodide or benzyl bromides take place smoothly by the catalysis of Rh(I) complexes.

At first, to see the catalytic effect of Rh(I) complex, the reaction of 2-(methoxycarbonyl)phenylzinc iodide[13] with methyl iodide (10 equivalents) was examined in the presence of 10 mol% of various Rh(I) complexes at 35 °C under nitrogen (Eq. 1). The

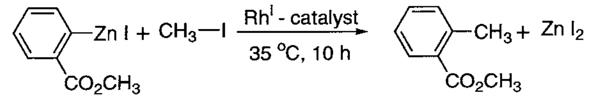


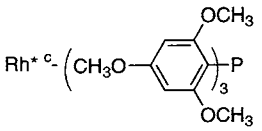
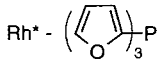
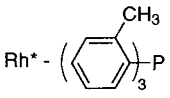
(1)

results are summarized in Table 1. Although $RhCl(PPh_3)_3$ exhibited little catalytic activity (Run 2), catalyst system composed of $[Rh(COD)Cl]_2$ and 1,1'-bis(diphenylphosphino)-ferrocene (dppf) (Run 7), exerted pronounced effects on the otherwise difficult cross-coupling.

Then, the Rh(I)-dppf catalyst was applied to the cross coupling reactions using other arylzinc compounds and/or alkyl halides. The results, summarized in Table 2, show that 1) various arylzinc compounds also underwent the coupling reactions with methyl iodide to afford the corresponding methylation products in good yields (Runs 1-6) but 2) substituents attached to methyl iodide made the reactivities of alkyl halides decrease markedly: The use of ethyl iodide did not afford the alkylation product at all (Run 8) and the use of methoxymethyl iodide afforded the alkylation product only in 44% yield (Run 9).

Table 1. Effect of Rh(I) catalyst on cross-coupling[a]



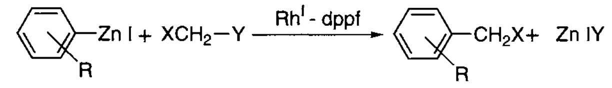
Run	Rh(I) catalyst	Yield / %[b]
1	none	< 2
2	$RhCl(PPh_3)_3$	4
3		7
4		< 2
5		6
6	Rh* - $(C_6F_5)_3P$	4
7	Rh* - dppf	74

[a] Molar ratio: Arylzinc compound / CH_3I / Rh(I) / Ligand = 1 / 10 / 0.1 / 0.3 (Runs 1-6) or 0.15 (Run 7). [b] Yields were determined by GLC.
[c] Rh* = 1 / 2 $[Rh(COD)Cl]_2$

Interestingly, reactions of benzyl bromides with arylzinc compounds took place smoothly at 80 °C and afforded the benzylation products in various yields, depending on the kind of benzyl bromides or arylzinc compounds used (Runs 10-14). Thus, for example, the reaction between 2-chlorophenylzinc iodide and benzyl bromide afforded 2-chloro-1-benzylbenzene in 74% yield, whereas the reaction between 4-ethoxycarbonylphenylzinc iodide and the same bromide afforded the desired product, ethyl 4-benzylbenzoate, in 20% yield (Runs 10,13). In the latter run, two types of homo-coupling products, ethyl 4-[4-(ethoxycarbonyl)phenyl]benzoate and 1,2-diphenylethane, were formed in 20% and 58% yield, respectively, which might be partly responsible for the reduced yield of benzylation product. In Run 14, homo-coupling products, methyl 2-[2-(methoxycarbonyl)phenyl]benzoate and methyl 4-{2-[4-(methoxycarbonyl)phenyl]ethyl}benzoate, were produced in 16% and 14 % yield, respectively.

It is to be noted that the catalytic efficiency of Rh(I) complexes in cross-coupling reaction is not limited to alkyl electrophiles. That is, the reaction between aryl iodides and arylzinc compounds was effectively catalyzed by the Rh(I)-dppf, too (Scheme 1). Thus, now we have the new choice of catalyst in undergoing the cross-coupling reaction with arylzinc compounds as carbon nucleophiles.[14]

Table 2. Rh(I)-dppf catalyzed cross-coupling of arylzinc compounds with alkyl halides[a]

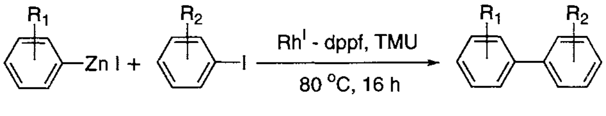


Run	R	X	Y	Yield /%[b]
1	2-CN	H	I	(71)
2	3-CO_2CH_3	H	I	(90)
3	4-$CO_2C_2H_5$	H	I	(86)
4	4-COC_6H_5	H	I	(91)
5	4-OCH_3	H	I	(77)
6	2-Cl	H	I	(77)
7	2-Cl	H	I	(64)
8	2-Cl	CH_3	I	(0)
9	2-Cl	CH_3O	I	(44)
10	2-Cl	C_6H_5	Br	74
11	2-Cl	4-CH_3O_2C-C_6H_4	Br	68
12	2-CO_2CH_3	C_6H_5	Br	53
13	4-$CO_2C_2H_5$	C_6H_5	Br	20
14	2-CO_2CH_3	4-CH_3O_2C-C_6H_4	Br	42

[a] Molar ratio: Arylzinc compound / alkyl halide / $[Rh(COD)Cl]_2$ / dppf = 1 / 10 (Runs 1-6, 8, 9) or 2 (runs 7, 10-14) / 0.05 / 0.15. Reaction temp.: 35 °C (Runs 1-9) or 80 °C (Runs 10-14). Reaction time: 16 h (Runs 1-6, 8, 9), 20 h (Run 7), or 24 h (Runs 10-14)

[b] Isolated yields. Yields in parentheses were determined by GLC.

Scheme 1.



R_1, R_2, Yield / %
o-CO_2CH_3, H, 73
p-$CO_2C_2H_5$, o-CO_2CH_3, 70
o-CN, p-Cl, 71

References and Notes

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13 Arylzinc compounds were prepared by the reaction of aryl iodides with zinc powder in 1,1,3,3-tetramethylurea (TMU) following the reported procedure. The aliquots of the resulting solutions were used in the cross-coupling reactions, after the concentrations of arylzinc compounds were determined by quenching the aliquot of the solutions with iodine; K. Takagi, *Chem. Lett.*, **1993**, 469.

14 A typical procedure is as follows: To the mixture composed of $[Rh(COD)Cl]_2$ (12.4 mg, 0.025 mmol), dppf (42 mg, 0.075 mmol), and methyl 4-(bromomethyl)benzoate (230 mg, 1 mmol), 0.83 M-TMU solution of 2-chlorophenylzinc iodide (0.60 ml, 0.5 mmol) was added at room temperature under nitrogen and the resulting solution was allowed to stirr at 80 °C for 24 h. The resultant solution was chromatographed on silica-gel column using hexane-ethyl acetate (50:1) as an eluent to afford 89 mg of methyl 4-[(2-chlorophenyl)-methyl]benzoate (68%). Mp 37.5 °C; IR ($CDCl_3$) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.88 (s, 3H), 4.13 (s, 3H), 7.14-7.99 (m, 8H). Anal. Calcd for $C_{15}H_{13}ClO_2$: C, 69.10; H, 5.03%. Found: C, 69.07; H, 5.13%.