Pergamon

Tetrahedron Letters, Vol. 35, No. 12, pp. 1909-1912, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0206-D

Mono-Cr(CO)3 Complexes of Biphenyl Compounds: Cross-Coupling Reactions of (η^6-Arene)chromium Complexes with Arylmetals

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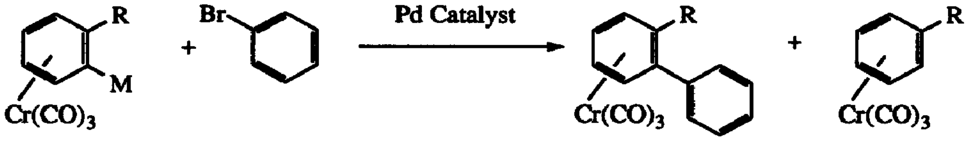
Abstract: Cross-coupling reaction of tricarbonyl(η^6-halobenzene)chromium complexes with arylmetals in the presence of palladium(0) catalyst produced mono-$Cr(CO)_3$ complexes of biphenyl compounds in good yield. Reaction of tricarbonyl(2,6-substituted 1-halobenzene)chromium complexes with *ortho*-substituted phenylboric acid gave stereoselectively cross-coupling products.

Biphenyl or binaphthyl compounds with an axial chirality are attractive compounds not only as chiral ligands in asymmetric reactions but also for the synthesis of biologically active natural products. There is a considerable current interest in the development of efficient methodologies for the asymmetric synthesis of *ortho* substituited biphenyl or binaphthalene compounds with atropisomers.[1] (η^6-Polysubstituted arene)chromium complexes can exist in two enantiomeric forms based on a planar chirality when the arene ring is substituted at *ortho-* or *meta-*position with different substituents. As part of our ongoing research interest to develop the chiral (arene)chromium complexes in organic synthesis, we require the mono-chromium complexes of biphenyl derivatives with the axial chirality. The mono-chromium complexes of *ortho* substituted biphenyl compounds with a hindered rotation about the central bond have both the axial and planar chiralities, and would be expected to act as the chiral ligand in the asymmetric reactions. Since the tricarbonylchromium complexation method of the *ortho* substituted biphenyl compounds with $Cr(CO)_6$ would afford usually a regio- and stereoisomeric mixture of the corresponding mono-chromium complexes,[2] stereoselective cross-coupling of the (arene)chromium complexes with the other arene compounds would provide an efficient method for the preparation of the (arene)chromium complexes with both the planar and axial chiralities. We wish to report our preliminary results of cross-coupling reaction of the (η^6-arene)chromium complexes with the other aryl compounds catalyzed by palladium(0).

The cross-coupling reactions of arylhalides or aryltriflates with various arylmetals catalyzed by a palladium catalyst provide the useful methods for the preparation of the biphenyl compounds.[3] For an efficient preparation of the mono-$Cr(CO)_3$ complexed biphenyl compounds, we have devised following two connecting cross-coupling methods of (arene)chromium complexes and the other aryl compounds: (A) coupling of (*arylmetal*)$Cr(CO)_3$ with arylhalide; (B) coupling of (*arylhalide*)$Cr(CO)_3$ with arylmetal. The reaction of (phenylzinc chloride)$Cr(CO)_3$ (**1**) (R=H, M=ZnCl) with bromobenzene in the presence of 5mol % $PdCl_2$(dppf) in THF gave a coupling product **3a** (R=H) as a major product along with tricarbonyl(benzene)chromium (Table 1, entry 1). With tricarbonyl(phenylboric acid)chromium, the yield of the coupling product was modest (entry

2). However, (arylmetal)chromium complexes with *o*-methoxyl substituent were reacted with bromobenzene catalyzed by the palladium(0) to give a de-metallation product, (anisole)$Cr(CO)_3$, as major product (entries 3~4). Since the corresponding chromium free arylmetals yield the coupling products in good yield under the similar conditions,[3] the extremely low yields of the coupling product of (*o*-methoxyphenyl metal)chromium complexes with bromobenzene would be attributed to a lower nucleophilicity of the tricarbonyl(arylmetal)-chromium in the transmetallation step on the palladium(II) intermediate due to the stereoelectronic effects. Therefore, we have turned our attention to another type coupling reaction (method B) for the preparation of mono-$Cr(CO)_3$ complexes of *ortho* substituted biphenyl compounds (eq 2).



1 2 3 4

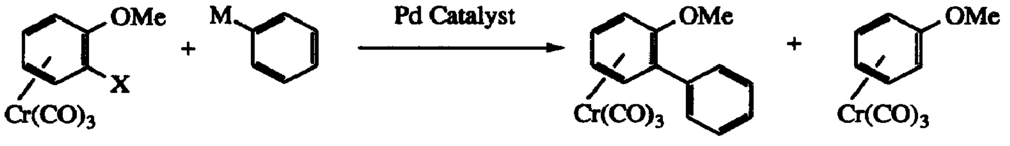
(eq 1)

Table 1 Cross-coupling reaction of (arylmetal)$Cr(CO)_3$ with bromobenzene

entry	complex 1	Pd catalyst	reaction conditions	yield 3 (%)	yield 4 (%)
1	R=H, M=ZnCl	$PdCl_2(dppf)$	THF/reflux/1h	55	16
2[a]	R=H, M=$B(OH)_2$	$PdCl_2(dppf)$	$MeOH/H_2O/Na_2CO_3$/reflux/2h	20	6
3	R=OMe, M=ZnCl	$Pd(PPh_3)_4$	THF/reflux/2h	0	81
4	R=OMe, M=$B(OH)_2$	$PdCl_2(dppf)$	$MeOH/H_2O/Na_2CO_3$/reflux/4h	10	76
5[b]	R=OMe, M=$SnBu_3$	$Pd(PPh_3)_4$	THF/reflux/4h	0	0

[a] Biphenyl without $Cr(CO)_3$ group was obtained in 44 % yield. [b] Starting materials were recovered.

An oxidative addition of carbon-halogen bond of the arylhalide to the palladium(0) is accerelated by a coordination of an electron-withdrawing tricarbonylchromium group to the arene ring.[4] Even chlorobenzene



5 6 7 8

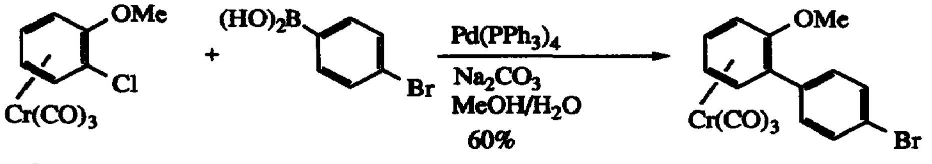
(eq 2)

Table 2 Cross-coupling reaction of (arylhalide)$Cr(CO)_3$ with phenylmetal

entry	X	M	Pd catalyst	reaction conditions	yield 7 (%)	yield 8 (%)
1	Cl	$B(OH)_2$	$PdCl_2$/dppf	$Na_2CO_3/MeOH/H_2O$/reflux/30min	70	6
2	Cl	MgBr	$Pd(PPh_3)_4$	THF/reflux/18h	53	21
3	Cl	ZnCl	$Pd(PPh_3)_4$	THF/reflux/5h	64	5
4	Br	$B(OH)_2$	$PdCl_2$/dppf	$Na_2CO_3/MeOH/H_2O$/reflux/2h	54	6
5	Br	$B(OH)_2$	$Pd(PPh_3)_4$	$Na_2CO_3/MeOH/H_2O$/reflux/30min	86	2
6	Br	MgBr	$Pd(PPh_3)_4$	THF/reflux/18h	72	5
7	Br	ZnCl	$Pd(PPh_3)_4$	THF/reflux/5h	67	1
8[a]	Br	$SnBu_3$	$Pd(PPh_3)_4$	LiCl/THF/reflux/5h	0	0

[a] Starting materials were recovered.

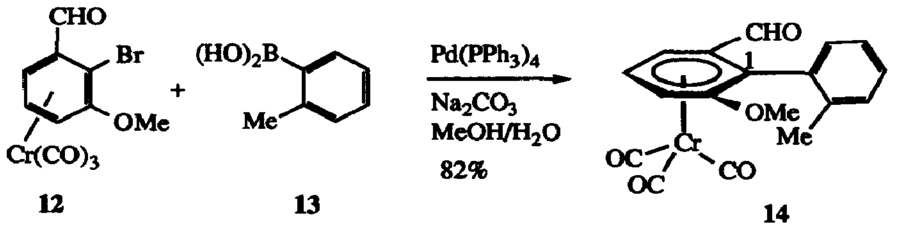
can be easily susceptible to the oxidative addition by utilizing the corresponding tricarbonylchromium complex giving the cross-coupling products. The cross-coupling reaction of the tricarbonylchromium complexes of *o*-methoxy bromobenzene or *o*-methoxy chlorobenzene with phenyl metals such as phenylboric acid, phenylmagnesium bromide and phenylzinc chloride, by the palladium(0) catalyst afforded expectedly the coupling product 7 as major product (Table 2). However, no coupling product was observed by the coupling reaction with tri-n-butyl phenylstanane (entry 8). The facile cross-coupling reaction utilizing the tricarbonylchromium complexes of halobenzene derivatives proceeds even in the reaction of (*o*-chloroanisole)$Cr(CO)_3$ with *p*-bromophenylboric acid to give a hetero-coupling product 11 in 60% yield without formation of a homo-coupling product of *p*-bromophenylboric acid (eq 3). In the oxidative addition step of the carbon-halogen bond of the arene to the palladium(0), C-Cl bond of the chromium complex 9 is preferred over C-Br bond of **10**, despite the presence of an electron-donationg methoxyl group at the *ortho* position of the chromium complex.



9 **10** **11**

(eq 3)

Since the cross-copuling reaction is achieved by reaction of tricarbonyl(*arylhalide*)chromium complexes and phenylmetals in the presence of Pd(0) catalyst in high yield, we have next investigated stereochemistry of the coupling product of the tricarbonyl(*ortho* di-substituted halobenzene)chromium complexes with *ortho* substituted arylboric acid. The palladium(0) catalyzed coupling reaction of (2-methoxy-6-formyl-bromobenzene)$Cr(CO)_3$ (**12**) with *o*-methylphenylboric acid (**13**) in the presence of aqueous sodium carbonate in MeOH at refluxing for 30 min gave a coupling product **14** in 82% yield without formation of the corresponding atropisomer[5] (eq 4). The stereochemistry of **14** was determined by X-ray crystallography[6] of the corresponding benzylacetate complex derived from **14** by reduction of the formyl group and following acetylation, and found to be (S^*,S^*)[7]-configuration. It is interesting to note that the methyl group of the complex **14** is directed toward the tricarbonylchromium group in spite of a severe steric interaction between the methyl and $Cr(CO)_3$ groups. Since the arene chromium complex **12** can be easily obtained as an optically active form,[8] a photo-oxidized chromium free *ortho* tri-substituted biphenyl compound derived from the coupling product **14** would be prepared as an enantiomerically pure coumpound. Further studies are in progress for mechanistic issue in the stereochemistry of the coupling products and synthesis of the biphenyl compounds with the axial chirality in enantiomerically pure forms.



12 **13** **14**

(eq 4)

Acknowledgement: Partial financial support for this work was provided by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan, and by a CIBA GEIGY Foundation (Japan) for the Promotion of Science.

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† Fellowships of the Japan Society for the Promotion of Science for Japanese Junior Scientists.

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5 Typical procedure: A mixture of (2-methoxy-6-formyl bromobenzene)$Cr(CO)_3$ (**12**) (103mg, 0.30mmol), *o*-methylphenylboric acid (**13**) (82mg, 0.60mmol), sodium carbonate (64mg, 0.60mmol) and $Pd(PPh_3)_4$ (34mg, 0.03mmol) in methanol (4mL) and water (0.4mL) was degassed by three cycles of freeze/pump/thaw, and stirred at 75 °C for 30 min under nitrogen. The reaction mixture was quenched with water and extracted with ether. The extract was washed with 10 % aqueous NaOH, brine and dried over $MgSO_4$ and evaporated in vauo. The residue was purified with flash SiO_2 chromatography (ether/hexane = 1/10) to produced the coupling product **14** (86mg, 82%); mp 118 °C; ^{1}H-NMR ($CDCl_3$) δ 2.62 (3H, s), 3.80 (3H, s), 5.39 (1H, d, J = 6.7Hz), 5.53 (1H, d, J = 6.1Hz), 5.79 (1H, dd, J = 6.1, 6.7Hz), 7.06 (1H, d, J = 7.3Hz), 7.17~7.23 (1H, m), 7.36 (2H, d, J = 3.7Hz), 9.48 (1H, s).

6 Results of X-ray crystallography will be published elsewhere.

7 First symbol indicates a configuration of planar chirality of the chromium complexed arene (at C-1 position) and second symbol shows the configuration of the axial chirality.

8 Optical resolution of the racemic chromium complex **12** is achieved by column chromatographical separation of diastereomers derived from (*L*)-valinol.[9]

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(*Received in Japan* 4 *November* 1993; *accepted* 8 *January* 1994)