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Catalytic Asymmetric Induction of Planar Chirality by Palladium-Catalyzed Asymmetric Cross-Coupling of a *meso* (Arene)chromium Complex

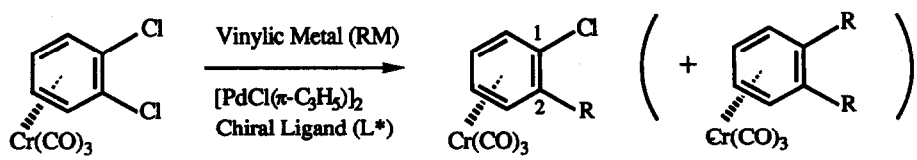
Motokazu Uemura,* Hikaru Nishimura,
Faculty of Science, Osaka City University, Sugimoto 3-3-138, Sumiyoshi-ku, Osaka 558, Japan
Tamio Hayashi*
Catalysis Research Center and Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo 060, Japan

Abstract: Asymmetric cross-coupling of tricarbonyl(*o*-dichlorobenzene)chromium with vinylic metals in the presence of a chiral palladium catalyst gave the mono-coupling products of up to 44% ee.

Tricarbonyl(η^6-arene)chromium complexes can exist as two enantiomeric forms when the phenyl ring is substituted with different groups at *ortho*- or *meta*-position. The preparation of optically pure (arene)chromium complexes has great potential for the stereoselective transformations and asymmetric syntheses.[1] The usual method for preparation of the chiral (arene)chromium complexes is the resolution via recrystallization[2] or column chromatography[3] of the diastereomers derived from racemic (arene)chromium complexes and suitable chiral reagents, the kinetic resolution by biocatalysts,[4] and the diastereoselective *ortho* lithiation.[5] However, employment of a stoichiometric amount of the chiral reagents is required for preparation of the chiral (arene)chromium complexes in these methods. In this communication, we wish to report the first catalytic asymmetric synthesis of optically active (arene)chromium complexes[6] which is achieved by asymmetric cross-coupling of a *meso* (arene)chromium complex in the presence of a chiral palladium catalyst.

An oxidative addition of C-Cl bond of the arene compounds to palladium(0) is usually difficult. However, this limiting step is favoured by the coordination of an electron-withdrawing tricarbonylchromium group to the arene ring.[7] A selective mono-substitution of one of the enantiotopic chlorine atoms of (*o*-dichlorobenzene)-chromium complex (**1**) would result in the formation of optically active (η^6-arene)chromium complexes. In this

Scheme 1



a; R= CH=CH_2 **b**; R= CMe=CH_2 **c**; R= CH=CHBu^n

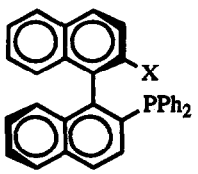
context, we have investigated the asymmetric mono-substitution reactions of the complex **1** with various vinylic metals in the presence of chiral palladium catalysts (Scheme 1).

Our preliminary results are summarized in Table 1. Reaction of **1** with tributyl(vinyl)stannane catalyzed by palladium complexes coordinated with chiral ligands BINAP[8] and PPFA[9] gave good yields of the mono-coupling product, tricarbonyl(*o*-chlorostyrene)chromium (**2a**), though in a racemic form (entries 1-2). In the presence of chiral monophosphine ligand, MeO-MOP[10], the reaction of the vinylstannane gave di-coupling product **3a** as a major product (entry 3). Since no enantioselectivity was observed in the coupling reaction with vinylstannane reagent, we have next investigated the coupling reaction with other vinylmetals. Although vinylmagnesium

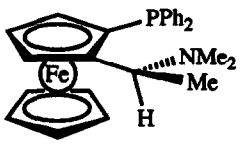
Table 1. Catalytic Asymmetric Cross-Coupling of (*o*-Dichlorobenzene)$Cr(CO)_3$ with Vinylic Metals[a]

entry	vinylic metal	ligand (L*)	°C, hrs	ratio[b] of **2** : **3** (yield[c] %)	% ee[d] of **2** (abs config)
1[e]	CH_2=CHSnBu_3	(*R*)-BINAP	40, 18	75 : 25 (80)	0
2[e]	CH_2=CHSnBu_3	(*S*)-(*R*)-PPFA	40, 18	87 : 13 (46)	0
3[e]	CH_2=CHSnBu_3	(*R*)-MeO-MOP[f]	0, 18	0 : 100 (46)	—
4[e]	CH_2=CHMgBr	(*S*)-(*R*)-PPFA	50, 48	75 : 25 (8)	—
5[e]	CH_2=CHZnCl	(*S*)-(*R*)-PPFA	40, 18	67 : 33 (56)	42 (1*S*,2*R*)
6[e]	CH_2=CHZnCl	(*R*)-MeO-MOP[f]	0, 18	24 : 76 (93)	0
7[e]	CH_2=CHZnCl	(*S*,*S*)-DIOP	40, 18	70 : 30 (33)	0
8[g]	CH_2=CHB$(OH)_2$	(*S*)-(*R*)-PPFA	23, 48	73 : 27 (59)	38 (1*S*,2*R*)
9[h]	CH_2=CHB$(OH)_2$	(*S*)-(*R*)-PPFA	22, 5	52 : 48 (67)	13 (1*S*,2*R*)
10[g]	CH_2=CHB$(OH)_2$	(*S*)-Valphos[i]	25, 48	92 : 8 (48)	10 (1*S*,2*R*)
11[g]	CH_2=CMeB$(OH)_2$	(*S*)-(*R*)-PPFA	27, 48	95 : 5 (64)	44 (1*S*,2*R*)
12[g]	CH_2=CMeB$(OH)_2$	(*R*)-BINAP	35, 48	47 : 53 (93)	25 (1*S*,2*R*)
13[g]	CH_2=CMeB$(OH)_2$	(*S*)-(*R*)-BPPFA	27, 10	91 : 9 (67)	2 (1*S*,2*R*)
14[j]	CH_2=CMeB[$O(CH_2)_3O$]	(*S*)-(*R*)-PPFA	35, 48	76 : 24 (63)	39 (1*S*,2*R*)
15[g]	CH_2=CMeZnCl	(*S*)-(*R*)-PPFA	35, 48	74 : 26 (70)	22 (1*S*,2*R*)
16[g]	(*E*)-^{n}BuCH=CH_2B$(OH)_2$	(*S*)-(*R*)-PPFA	27, 18	77 : 23 (53)	44 (1*S*,2*R*)

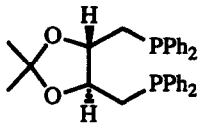
[a] Molar ratio; complex **1**/vinylic metal (RM)/chiral ligand (L*)/palladium = 1.0/3.0/0.12/0.10. [b] Ratio was determined by HPLC or ^{1}H NMR [c] Isolated yield by chromatography. [d] Enantiomeric excess was determined by HPLC (Daicel Chiralcel OD eluted with 10% isopropanol in hexane). [e] THF was used as solvent. [f] Ratio of MeO-MOP/palladium = 0.24/0.10. [g] Reaction with vinylic boric acids was carried out in the presence of 3 eq of 0.4 M TlOH in aqueous THF solution. [h] Potassium carbonate (3 eq) as base was used in a mixture of MeOH and H_2O. [i] ref. 11. [j] In the presence of 3 eq of NaOEt in ethanol.



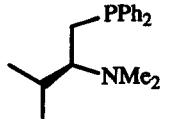
X = PPh_2 : (*R*)-BINAP
X = OMe : (*R*)-MeO-MOP



(*S*)-(*R*)-PPFA



(*S*,*S*)-DIOP

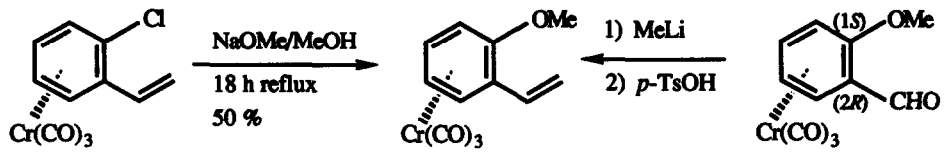


(*S*)-Valphos

bromide gave low yield of the coupling products (entry 4), the corresponding zinc reagent afforded 42% ee of (–) mono-coupling product **2a** ($[\alpha]_D^{17}$ –115.4° (*c* 0.32, EtOH)) in 44% yield catalyzed by 10 mol % of di-μ-chlorobis(π-allyl)palladium(II) and 12 mol % of (*S*)-(*R*)-PPFA in THF (entry 5). The asymmetric reaction with vinylboric acid catalyzed by the palladium in the presence of PPFA in aqueous thallium hydroxide gave 38% ee of the mono-coupling product (entry 8). Use of potassium carbonate in aqueous methanol as base resulted in lower enantioselectivity (entry 9).

The absolute configuration of mono-coupling product **2a** could be easily determined as follows (Scheme 2). Nucleophilic substitution[12] of the chlorine atom of the mono-coupling complex (–)-**2a** (40% ee) with sodium methoxide in methanol by refluxing for 18 h gave (–)-tricarbonyl(*o*-methoxystyrene)chromium **4** ($[\alpha]_D^{20}$ –122.9° (*c* 0.17, EtOH)) in 50 % yield. On the other hand, optically resolved (–)-(1*S*,2*R*)-tricarbonyl(*o*-anisaldehyde)-chromium[3b] (**5**) was converted to (–)-(*o*-methoxystyrene)chromium (**4**) ($[\alpha]_D^{20}$ –492° (*c* 0.19, EtOH)) in 75% overall yield by treatment with methyllithium followed by dehydration with *p*-toluenesulfonic acid in benzene. Therefore, the absolute configuration of the cross-coupling product **2a** was determined as (1*S*,2*R*).

Scheme 2



2a **4** **5**

Comparable enantioselectivities (44% ee) were observed in the reactions with substituted vinylboric acids (entries 11, 16).[13] The ratio of mono- to di-coupling product was improved with α-methylvinylboric acid in the presence of PPFA, probably due to stereoelectronic effects of the electron donating methyl group. Reaction with the corresponding boric ester gave similar enantioselectivity (entry 14).

Thus, we have succeeded, for the first time, in catalytic asymmetric synthesis of optically active molecules whose chirality is based on planar chirality due to 1,2-unsymmetrically substituted (η^6-arene)chromium structure. The stereochemical outcome in the present catalytic asymmetric cross-coupling reaction should be determined at the oxidative addition step where one of the enantiotopic carbon-chlorine bonds reacts selectively with a chiral palladium(0) species forming palladium-carbon bond. Essentially the same enantiomeric purity of the coupling products, **2a**, **2b**, and **2c** obtained with unsubstituted and substituted vinylic boric acids supports the stereocontrol at the oxidative addition step. The loss of enantioselectivity observed with the vinylstannane may imply that metal of the vinylation reagents also plays an important role at the oxidative addition. Further studies are in progress to resolve these mechanistic issues.

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13 Typical procedure: A solution of (*o*-dichlorobenzene)$Cr(CO)_3$ (28 mg, 0.10 mmol), α-methylvinylboric acid (26 mg, 0.30 mmol), $[PdCl(\pi\text{-}C_3H_5)]_2$ (1.8 mg, 0.010 mmol), (*S*)-(*R*)-PPFA (5.3 mg, 0.012 mmol) and thallium hydroxide (0.75 mL, 0.4 M in water, 0.30 mmol) in THF (1 mL) was degassed by three cycles of freeze/pump/thaw, and stirred at 27 °C for 48 h under argon. The reaction mixture was quenched with water and extracted with ether. The extract was washed with brine dried over $MgSO_4$ and evaporated in vacuo. The residue was purified with silica gel chromatography (ether/hexane = 1/20) to produced a mono-coupling product **2b** (18 mg, 61%); mp 61 °C ($[\alpha]_D^{20}$ –8.1° (*c* 0.32, EtOH)). The optical purity of **2b** was determined by Daicel Chiralcel OD (eluted with 10% 2-propanol in hexane; flow rate 0.5 mL/min; UV detector 254 nm; temperature 26 °C; retention times; 15.8 min for (1*R*,2*S*)-isomer, 17.3 min for (1*S*,2*R*)-isomer).

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