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New planar chiral P,N-ligands containing tricarbonyl(arene)chromium for enantioselective asymmetric hydroboration of styrenes

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Abstract

Optically active (1,2-disubstituted arene) chromium tricarbonyl complexes **2A**–**2D** with a pyridyl and a phosphorus group in the two *ortho* benzylic positions have been stereoselectively synthesized from a commercially available (+)-(4,6-*O*-benzylidene)methyl-α-D-glucopyranoside. These chromium complexes have been used as chiral ligands in the preparation of rhodium catalysts for the hydroboration of styrene derivatives. High enantioselectivities were observed in the hydroboration of vinylarenes.

1. Introduction

We recently reported a new and easy method for the asymmetric synthesis of chiral benzaldehyde complexes modified by a sugar moiety.[1] Thus, starting from chiral (benzaldehyde) chromium tricarbonyl compound, optically active (1,2-disubstituted arene) chromium tricarbonyl complexes with a diamine and a phosphorus group in the two ortho benzylic positions have been stereoselectively synthesized and used as chiral P,N-ligands in the hydroboration of styrenes.[2] The new chiral ligands have been shown to afford moderate enantioselectivities (19–81%) at −15°C and to exhibit pronounced effects on the enantioselectivity depending on the electronic substituent on the styrene. The P,N-ligand represents a class of chiral auxiliaries that are easily tuned by steric and electronic modification.[3] As an extension of our recent work, we have prepared new planar chiral P,N-arene chromium compounds having chromium carbonyls, pyridine, and phosphorus and investigated their role as chiral ligands in the rhodium-catalyzed asymmetric hydroboration of styrenes. Herein we report the results of our investigation.

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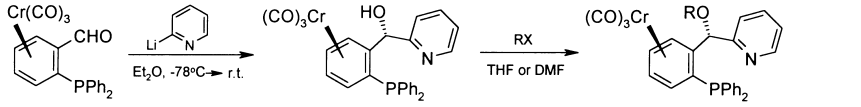
2. Results and discussion

2.1. Synthesis of planar chiral (arene)Cr(CO)$_3$ complexes

The planar chiral compounds **2A**–**2D** were synthesized from **1** (Eq. 1). Compound **1** was previously prepared by us.[2]



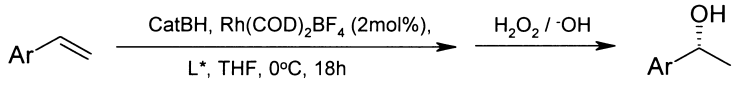
(1)

Treatment of **1** with 2-pyridine lithium at −78°C led to a diastereomeric mixture (de 31%) in 64% yield. The diastereomeric mixture was easily separated by flash column chromatography. The major (42% yield) diastereomer shown in Eq. 1 was named **2A** and used to make compounds **2B**–**2D**. Compound **2B** was prepared in 73% yield by deprotonation of **2A** in THF followed by addition of MeI. In the same way, compounds **2C** and **2D** were prepared by the addition of benzyl bromide with a catalytic amount of tetrabutylammonium iodide and 4-methoxybenzylchloride, respectively, to the deprotonated form of **2A**. From **2A**, compounds **2B**, **2C**, and **2D** were obtained in 73%, 69%, and 71% yields, respectively. The stereochemistries of **2A**–**2D** were confirmed by the X-ray crystal structure determination of **2B**. Single crystals of **2B** suitable for X-ray study were grown by slow evaporation of a solution of **2B** in CH_2Cl_2 and hexane (v/v, 1:1) at −20°C. Fig. 1 shows an X-ray crystal structure of **2B** with the atomic numbering. Crystal data and experimental details are shown in Table 1 and selected bond distances and angles are shown in Table 2.

The pyridine ring is almost upright to the plane of arene coordinated to Cr(CO)$_3$. The nitrogen atom is located 1.624(6) Å above the plane of arene, and the phosphorus atom is located 0.164(4) Å above the plane of the arene. The planes of the pyridine ring and the free arene ring (C01–C016) attached to the phosphorus are roughly parallel (the interplanar angle: 18.3(2)°) and the distance between the centroids of these two planes is 4.00 Å. The distance between P and N is 3.649(3) Å. The observed average Cr–CO bond length (1.842 Å) is shorter than the average value of 1.866 Å.[4]

2.2. Asymmetric hydroboration

Rhodium complexes with **2A**–**2D** have been examined with regard to the catalytic activity and enantioselectivity in the reaction of vinylarenes with catecholborane (Eq. 2).



L* = **2A - 2D**

(2)

The results are summarized in Table 3. Our standard reaction conditions are as follows: 1.2 equiv. catecholborane, 0.02 equiv. [Rh(COD)$_2$]BF$_4$, 0.024 equiv. of **2A**–**2D** in THF at 0°C for 18 h. Hydroboration of styrene derivatives followed by oxidation with alkaline hydrogen peroxide gives the corresponding *sec*-alcohol. To determine the enantiomeric excess (ee) values, we used (*S*)-(+)-*O*-acetyl mandelate as a chiral derivatizing reagent to convert an enantiomeric mixture to a pair of diastereomers and calculated the ee by the inspection of ^{1}H NMR spectra of diastereomers.

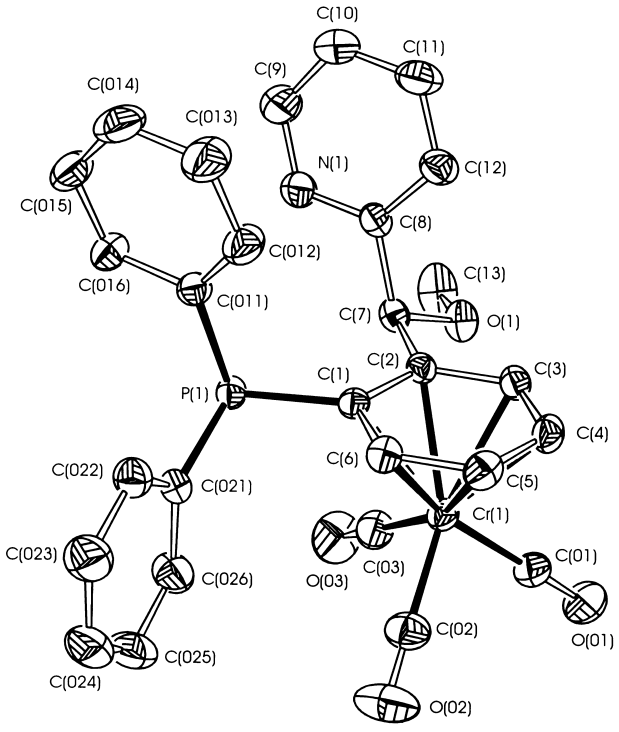


Figure 1. ORTEP drawing of **2B**, with atom-labeling scheme. Thermal ellipsoids are drawn at the 30% probability level

Initially we started to study the hydroboration of 4-methoxystyrene, which otherwise only reacts with catecholborane at elevated temperatures,[5] using **2A** as a chiral ligand (entry 1 in Table 3). The result (45% yield and 14% ee) was quite disappointing.

To improve the value of the ee, we introduced a substituent to the benzylic position of **2A** and prepared **2B**–**2D**. When 4-methoxystyrene was hydroborated using **2B** as a chiral ligand (entry 2), the ee was dramatically improved to 84% with a 72% yield. When **2C** was used as a chiral ligand (entry 3), the ee also improved to 82% with 86% yield. When **2D** was used as a chiral ligand (entry 4), the ee was improved to 61%, but the yield was only 39%. As expected, the ee increases as the steric bulk of the substituent at the benzylic position increases. However, this is not always true as seen in **2D**.

Among **2B**–**2D**, we chose **2C** as a chiral ligand in the catalytic asymmetric hydroboration of other styrene derivatives. The results are shown in entries 5–8 in Table 3. The enantioselectivity was slightly dependent on the reaction temperature: enantiopurities of 1-(4-methoxyphenyl)ethanol obtained for the hydroboration at 0°C and −15°C were 82% and 84%, respectively (entries 3 and 5). The enantioselectivity for other styrene derivatives obtained at 0°C were 73–86%. At first we expected that the electronic effect of the substituent on the styrene ring would affect the ee values. However, the ee values were not very sensitive to the electronic effect of the substituent on the styrene ring.[6] The highest ee value was obtained for 2,4-dimethylstyrene (entry 8). The difference in ee values between 2,4-dimethylstyrene and other substrates was only marginal. The steric effect of the substituent on the styrene was not great.

The reaction of 4-methoxystyrene in the presence of **2A** as a chiral ligand gives the *S* alcohol with a poor enantioselectivity, whereas reactions of styrene derivatives in the presence of **2B**–**2D** afford the *R* alcohols with high enantioselectivities formed by the opposite stereoselection. Any intermediates were not characterized. However, chiral P,N-ferrocenyl chelating ligands similar to our chiral ligands were synthesized and their rhodium and palladium complexes were structurally characterized.[3f,7] Thus, we

Table 1
Crystal data and structure refinement for **2B**

empirical formula	$C_{28}H_{22}CrNO_4P$
fromula weight	519.44
crystal system	monoclinic
space group	$P2_1$
a, Å	9.3734(10)
b, Å	12.8456(9)
c, Å	11.1662(13) Å
β, deg	107.239(9)
volume, $Å^3$	1284.1(2)
Z	2
d(calcd), Mg/m^3	1.343
tot. no. of obserns	2510
no. of unique data	2360
θ range/deg	1.91-24.97
no. parameters refined	404
final R indices[I >σ 2(I)]	R1 = 0.0267, wR2 = 0.0689
R indices (all data)	R1 = 0.0292, wR2 = 0.0708
GOF on F^2	1.072

$R1 = (\Sigma|Fo - Fc|)/\Sigma|Fo|$, $wR2 = \{\Sigma[w(Fo^2 - Fc^2)])/\Sigma[w(Fo^2)^2]\}^{1/2}$

Table 2
Selected bond lengths (Å) and angles (deg) for **2B**

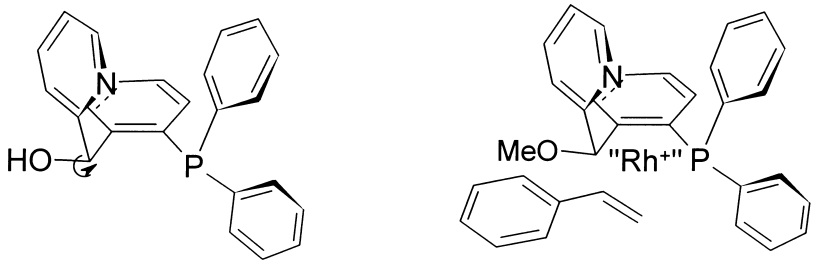
Cr-C01	1.838(3)	Cr-C1	2.214(3)	Cr-C4	2.217(3)
C1-P1	1.854(3)	C1-C2	1.436(4)	C3-C4	1.397(5)
C5-C6	1.412(5)	N1-C8	1.330(4)	N1-C9	1.342(6)
C2-C1-P	119.6(2)	C7-C8-N	116.5(3)	C1-C2-C7	121.2(3)
C2-C7-C8	110.7(2)	C011-P1-C021	101.7(1)	C2-C7-O1	108.3(2)

Table 3
Catalytic asymmetric hydroboration of styrenes

entry	Ligand	Substrate	temp (°C)	yield (%)[a]	**R** : **S**	ee (%)
1	**2A**	4-Vinylanisole	0	45	43 : 57	14
2	**2B**	4-Vinylanisole	0	72	92 : 8	84
3	**2C**	4-Vinylanisole	0	86	91 : 9	82
4	**2D**	4-Vinylanisole	0	39	80.5:19.5	61
5	**2C**	4-Vinylanisole	-15	41	92 : 8	84
6	**2C**	4-Bromostyrene	0	93	92 : 8	84
7	**2C**	3,4-Dimethoxystyrene	0	31	86.5:13.5	73
8	**2C**	2,4-Dimethylstyrene	0	56	93 : 7	86

[a] Isolated yield.

envisage that the stereochemical outcome may be related to the steric bulkiness at the benzylic position. For **2A**, there may be almost no steric restriction from the hydroxy group and the pyridyl group may be partly free to rotate (Scheme 1).



Scheme 1.

Consequently a poor stereoselectivity resulted. However, for **2B**–**2D**, there should be some steric restriction due to the substituent at the benzylic position and the pyridyl group may be fixed (Scheme 1). Thus, high stereoselectivities would be obtained.

3. Conclusion

We have demonstrated that planar chiral P,N-ligands **2A**–**2D** can be synthesized from the chiral benzaldehyde chromium complex **1** and have been used as chiral P,N-ligands in the preparation of a rhodium catalyst for the hydroboration of styrene derivatives. Good enantioselectivities were observed.

4. Experimental

All solvents were purified by standard methods, and all synthetic procedures were performed under a nitrogen atmosphere. Reagent grade chemicals were used without further purification.

Elemental analyses were carried out at the Chemical Analytic Center, College of Engineering, Seoul National University or the Chemical Analytic Center. ^{1}H NMR spectra were obtained with a Bruker 300 or a Bruker AMX-500 instrument. Infrared spectra were recorded on a Shimadzu IR-470 spectrometer. Compound **1** was prepared by the published method.[1]

4.1. Synthesis of **2A**

A solution of **1** (0.27 g, 0.63 mmol) in 10 mL of Et_2O at −78°C was transferred via cannula to the solution of 2-pyLi (generated in situ by the reaction of 2-bromopyridine (0.09 mL, 0.9 mmol) in 15 mL of Et_2O with *n*-BuLi (0.35 mL, 2.5 M in hexane, 0.9 mmol) at −78°C). The resulting solution was stirred at −78°C for 30 min and at 0°C for 30 min and quenched by sat. aq. NH_4Cl (10 mL)/Et_2O (50 mL). The ether layer was separated, dried over anhydrous $MgSO_4$, concentrated, and chromatographed on a silica gel column eluting with hexane and diethyl ether (v/v, 1:1 → 1:2). Evaporation of the solvent gave a yellow solid (0.38 g, 64%) as a mixture of two diastereomers. We named one of the diastereomers (the second eluting band) as **2A** (42% yield). The first eluting band was the other diastereomer (22% yield). Characterization of **2A**: mp 130°C (dec.); IR ν_{CO} 1954, 1874 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.23 (d, 4.3 Hz, 1H), 7.37 (m, 5H), 7.26–7.13 (m, 4H), 7.06 (t, 7.4 Hz, 2H), 6.94–6.90 (m, 2H), 6.61 (m, 1H), 5.72 (d, 6.1 Hz, 1H), 5.64 (t, 5.9 Hz, 1H), 5.09 (t, 6.1 Hz, 1H), 4.89 (d, 6.0 Hz, 1H), 3.47 (d, 5.1 Hz, 1H) ppm. Anal. calcd for $C_{27}H_{20}CrNO_4P$: C, 64.16; H, 3.99; N, 2.77. Found: C, 63.84; H, 3.99; N, 2.91. $[\alpha]_D^{27}$ +344 (c 0.1, CH_2Cl_2). Characterization of the other diastereomer: mp 150°C (dec.); IR ν_{CO} 1956, 1878 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.55 (d, 5.0 Hz, 1H), 7.78 (t, 7.6 Hz, 1H), 7.71 (d, 7.7 Hz, 1H), 7.35 (m, 10H), 7.28 (m, 1H), 6.33 (dd, 6.4, 7.4 Hz, 1H), 5.25 (m, 2H), 4.84 (d, 7.4 Hz, 1H), 4.74 (m, 2H) ppm. Anal. calcd for $C_{27}H_{20}CrNO_4P$: C, 64.16; H, 3.99; N, 2.77. Found: C, 64.04; H, 4.20; N, 2.71. $[\alpha]_D^{20}$ +210 (c 0.11, CH_2Cl_2).

4.2. Synthesis of **2B**

To a solution of **2A** (0.12 g, 0.24 mmol) in 5 mL of THF was added NaH (0.023 g, in 50% mineral oil) at room temperature. The solution was stirred for 30 min, and then MeI (0.03 mL, 0.48 mmol) was added. After the resulting solution was stirred for 2 h, the solution was quenched by addition of aq. NH_4Cl (15 mL) and Et_2O (50 mL). The ether layer was separated, dried over anhydrous $MgSO_4$, concentrated, and chromatographed on a silica gel column eluting with hexane and diethyl ether (v/v, 1:1). Evaporation of the solvent gave a yellow solid (0.09 g, 73%). Mp 145°C (dec.); IR ν_{CO} 1963, 1882 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.14 (d, 4.4 Hz, 1H), 7.30 (m, 5H), 7.21–7.09 (m, 3H), 7.02 (t, 7.5 Hz, 2H), 6.84–6.73 (m, 3H), 6.05 (d, 5.7 Hz, 1H), 5.89 (m, 1H), 5.68 (t, 12.7 Hz, 1H), 5.05 (t, 6.2 Hz, 1H), 4.81 (d, 6.2 Hz, 1H), 3.50 (s, 3H) ppm. Anal. calcd for $C_{28}H_{22}CrNO_4P$: C, 64.74; H, 4.27; N, 2.70. Found: C, 64.74; H, 4.29; N, 2.70. $[\alpha]_D^{24}$ +373 (c 0.1, CH_2Cl_2).

4.3. Synthesis of **2C**

Using the same method as the synthesis of **2B** except using tetrabutylammonium iodide (0.1 equiv.) and benzyl bromide (2 equiv.) instead of MeI, the crude product obtained was purified by chromatography on a silica gel column and eluted with hexane and diethyl ether (v/v, 1:1). Yellow solid; yield: 69%. Mp 125°C (dec.); IR ν_{CO} 1958, 1877 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.11 (d, 4.5 Hz, 1H), 7.35 (m, 10H), 7.18–7.09 (m, 3H), 7.02 (t, 6.3 Hz, 2H), 6.83 (t, 7.2 Hz, 2H), 6.75 (t, 7.2 Hz, 1H), 6.32 (d, 5.7 Hz, 1H), 6.02 (dd, 2.4, 6.1 Hz, 1H), 5.66 (t, 6.4 Hz, 1H), 5.09 (t, 6.3 Hz, 1H), 4.83 (d, 11.2 Hz, 1H), 4.80 (d, 6.1 Hz, 1H), 4.57 (d, 11.2 Hz, 1H) ppm. Anal. calcd for $C_{34}H_{26}CrNO_4P$: C, 68.57; H, 4.40; N, 2.35. Found: C, 68.56; H, 4.48; N, 2.32. $[\alpha]_D^{28}$ +281 (c 0.1, CH_2Cl_2).

4.4. Synthesis of **2D**

To the solution of **2A** (0.15 g, 0.30 mmol) in 2 mL of DMF was added NaH (25 mg, in 50% mineral oil, 5.1 mmol) at 0°C. After the solution was stirred at 0°C for 15 min, 4-methoxybenzylchloride (0.27 mL, 2.0 mmol) was added. The resulting solution was stirred at room temperature for 12 h and quenched by sat. aq. NH_4Cl (10 mL) and Et_2O (50 mL). The ether layer was separated, dried over anhydrous $MgSO_4$, concentrated, and chromatographed on a silica gel column eluting with hexane and diethyl ether (v/v, 1:1). Evaporation of the solvent gave a yellow solid (0.13 g, 71%). Mp 55–58°C; IR ν_{CO} 1963, 1883 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.11 (d, 3.3 Hz, 1H), 7.30 (m, 7H), 7.15–7.03 (m, 5H), 7.00–6.75 (m, 5H), 6.30 (d, 5.7 Hz, 1H), 6.00 (m, 1H), 5.65 (t, 6.1 Hz, 1H), 5.09 (t, 6.2 Hz, 1H), 4.79 (d, 6.4 Hz, 1H), 4.76 (d, 10.6 Hz, 1H), 4.52 (d, 10.3 Hz, 1H), 3.80 (s, 3H) ppm. Anal. calcd for $C_{35}H_{28}CrNO_5P$: C, 67.20; H, 4.51; N, 2.24. Found: C, 66.92; H, 4.46; N, 2.19. $[\alpha]_D^{24}$ +230 (c 0.1, CH_2Cl_2).

4.5. Catalytic asymmetric hydroboration

A typical procedure is given for 4-vinylanisole. A mixture of $[Rh(COD)_2]BF_4$ (7 mg, 0.017 mmol) and **2C** (12 mg, 0.20 mmol) in 3 mL of THF was stirred under nitrogen at room temperature for 1.5 h, and 4-vinylanisole (0.11 mg, 0.82 mmol) was added at 0°C. Catecholborane (0.97 mL in 1 M in THF, 0.97 mmol) was added at 0°C, and the mixture was stirred at 0°C for 18 h and then quenched with 5 mL of ethanol. To the mixture was added 5 mL of 3 M NaOH and 0.5 mL of 35% H_2O_2, and the whole was stirred at room temperature for 3 h. Extraction with Et_2O followed by chromatography on a silica gel column eluting with hexane and diethyl ether (v/v, 10:1) gave 107 mg (86%) of (*R*)-1-(4-methoxyphenyl)ethanol. The regioisomer was not detected by ^1H NMR analysis of the crude reaction mixture. To determine the enantiomeric excess (ee) values, we used (*S*)-(+)-mandelic acid as a chiral derivatizing reagent to convert the enantiomeric mixture to a pair of diastereomers and calculated the ee by the inspection of ^1H NMR spectra of diastereomers.

4.6. X-Ray crystal structure determination of **2B**

Crystals of **2B** were grown by slow evaporation of a solution of **2B** in hexane and methylene chloride (v/v, 1:1). Diffraction was measured by an Enraf–Nonius CAD4 diffractometer with an ω–2θ scan method. Unit cells were determined by centering 25 reflections in the approximate 2θ range. Other relevant experimental details are in the supporting information. The structure was solved by direct method using SHELXS-86 and refined by full-matrix least squares with SHELXL-93. All atoms were refined with anisotropic temperature factors. Further details of the crystal structure investigation are available from the author.

Acknowledgements

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