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Synthesis of novel planar chiral ferrocene and cyclopentadienyl manganese tricarbonyl derivatives and their use as chiral ligands in the palladium-catalyzed asymmetric allylic alkylation

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Abstract—We have shown that cymantrene derivatives are better P,N-chelate ligands for palladium-catalyzed allylic alkylation than ferrocenes, which have a similar pentagonal ligand structure to cymantrene derivatives. In particular, the PPh_3-substituted cymantrene gave a higher enantioselectivity (>98%).

1. Introduction

Palladium complex-catalyzed asymmetric C–C bond-forming reactions have been intensely studied.[1] The allylic alkylation reaction has been one for most popular model reactions for palladium catalyzed asymmetric C–C bond formation. As the research has ripened, many useful ligands with high selectivities have been reported. Although the 98–99% e.e. was achieved using non-metal containing ligands,[2] the ligands having a chirality based on planar chirality occupy an important position. In particular, planar chiral ligands based on ferrocene platforms were extensively studied.[3]

However, diverse non-metallocene ligands as chiral ligands are now beginning to attract the attention of chemists and were recently reviewed by Gladysz.[4] Non-metallocene ligands have some special properties compared with the chiral ligands based on the metallocene platform. Firstly, the non-metallocene ligands have different electronic properties. For example, the electron-withdrawing effect of the carbonyl group in the cymantrene-type ligand can affect the coordination mode. Secondly, the non-metallocene ligands can have different geometries including bite angles. The planar chiral ligands based on the arene chromium tricarbonyl compound have a relatively narrow bite angle compared to those based on ferrocene. Thirdly, the platform itself has a different reactivity; the ferrocene platform is relatively stable, but additional modification is difficult. However, in the case of cymantrene complexes, the carbonyl groups coordinated to the metal can easily be substituted by other ligands such as phosphines. The substitution can critically influence the steric surrounding or stability of a chiral ligand. Therefore, more effort to prepare non-metallocene ligands is needed along with a comparative study between non-metallocene ligands and metallocene ligands, which will help with the understanding of the ligand properties.

We recently developed[5] a method for the synthesis of planar chiral $CpMn(CO)_3$ compounds from planar chiral ferrocene derivatives and $(naphthalene)Mn(CO)_3^+$ cation. There have been no general methods for the synthesis of planar chiral $CpMn(CO)_3$ compounds with only one paper, describing a planar chiral $CpMn(CO)_3$ compound having both planar and central chiralities, having been reported by Helmchen et al.[6] The planar chiral ligands reported by Helmchen have one planar chirality on the cyclopentadienyl ring and two-point chirality in both the nitrogen and phosphine coordination sites. They used the compound as a P,N-chelate ligand in the Pd-catalyzed asymmetric allylic substitution and achieved a high asymmetric induction. We also reported[5] the possibility of using one of the chiral Cp manganese compounds as a source of P,N-ligands in the palladium-catalyzed allylic alkylation reaction, yielding a promising enantiomeric excess (89%). However, in order to achieve higher e.e. values, modification of the ligand was needed. With this in mind, we decided to synthesize the modified novel planar chiral ligands based on $CpMn(CO)_2L$ ($L = CO$, PPh_3) compounds and

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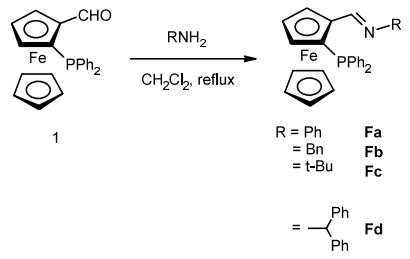


Scheme 1.

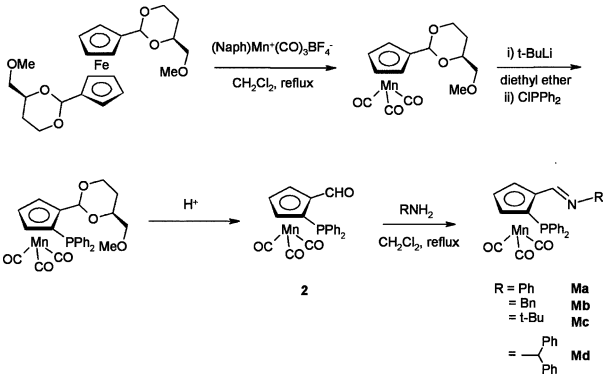
their counterparts of ferrocene platform. We investigated the enantioselectivity of the two types of ligand in the palladium catalyzed-allylic alkylation and discussed the origin of the difference in their enantioselectivity. Herein we report our results.

At first, we synthesized the planar chiral P,N-ligands based on ferrocene to compare the cymantrene-type P,N-ligands. Recently, similar ferrocenyl iminophosphine ligands were synthesized in our group.[7] However, some planar chiral P,N- ligands such as **Fa**, **Fc** and **Fd** were undeveloped and remained novel. They (**Fa**, **Fb**, **Fc** and **Fd**) were synthesized by the imination of a planar chiral aldehyde with a primary amine as shown in Scheme 1. The planar chiral aldehyde **1** was prepared by Kagan's method.[8] Among the planar chiral ferrocenes, three compounds were characterized by an X-ray diffraction study (Figure 1).[9]

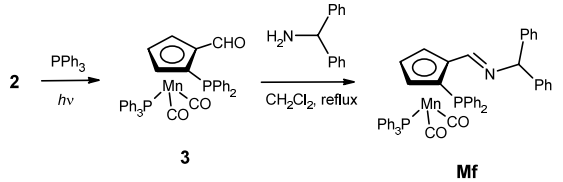
Planar chiral $CpMn(CO)_3$ compounds (**Ma**, **Mb**, **Mc**, and **Md**) were also prepared by the imination of **2** with primary amines (Scheme 2). Compound **2** has previously been reported by us.[5] Attempts to grow single crystals of **Ma**, **Mb**, **Mc**, and **Md** suitable for an X-ray diffraction study were not successful.

Substitution of one of the carbonyls by another nucleophile provides a good opportunity to modify the electronic and steric properties of the cymantrene derivatives. This modification is an important advantage of cymantrene complexes over ferrocene derivatives. Thus, we decided to synthesize **Mf** in order to obtain a better enantioselectivity.

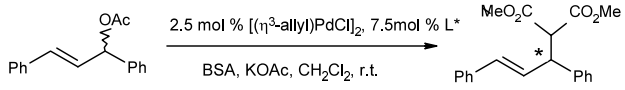
Compound **Mf** was synthesized as shown in Scheme 3. All the synthesized compounds have only a planar chirality.



Scheme 2.



Scheme 3.



Scheme 4.

To evaluate the effect of chiral ligands on the stereoselectivity of allylic alkylation, allylic substitution of *rac*-1,3-diphenyl-2-propenyl acetate was carried out in CH_2Cl_2 at 20°C in the presence of a (η^3-allyl)-palladium-ligand complex which was in situ generated by a reaction of 2.5 mol% of $[(\eta^3\text{-allyl})PdCl]_2$ with 7.5 mol% of the appropriate ligand (Scheme 4).

The nucleophile was generated from dimethyl malonate in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and a catalytic amount of KOAc. The results are summarized in Table 1.

The reactions proceeded smoothly to give high yields (86–95%). When compared to other studies, the reaction time (4 h) was relatively short. The absolute configuration of all the products was *R*, assigned by the study of the ^1H NMR spectra using a chiral europium

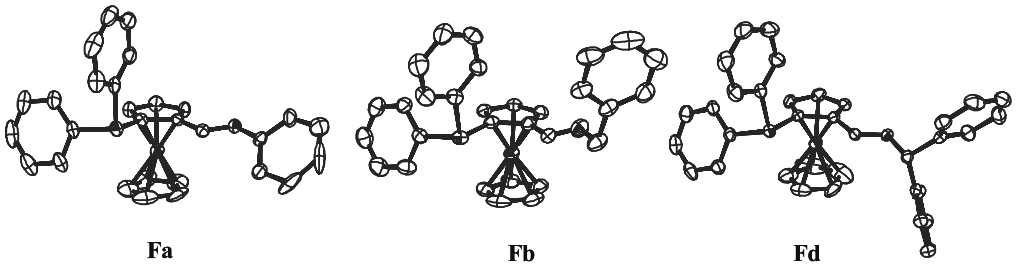


Figure 1. ORTEP drawings of chiral ligands.

Table 1. The results of allylic akylation reactions[a]

Entry	Ligand	Yield (%)[b]	E.e. (%)
1	**Fa**	98	75
2	**Fb**	93	82
3	**Fc**	95	87
4	**Fd**	86	90
5	**Ma**	93	90
6	**Mb**	90	88
7	**Mc**	94	89
8	**Md**	93	95
9	**Mf**	93	>98

[a] Reaction conditions: 2.5 mol% cat., 7.5 mol% ligand, rt, 4 h in CH_2Cl_2.
[b] Isolated yield.

complex as the shift reagent. When **Fa** was used as a ligand, the enantiomeric excess of 75% was obtained. When the R-group was changed from Ph to Bn, *t*-Bu, and -$CHPh_2$, the e.e. values increased gradually to 82, 87, and 90%.

Ma, **Mb**, and **Mc** also show similar selectivities (88–90% e.e.). However, the cymantrene derivatives generally yield better enantioselectivities than their counterpart ferrocenes do with the enantioselectivity increasing as the steric bulkiness increases. When **Mf** was used as a P,N-chelate ligand, the enantioselectivity was higher than 98%. Proton peaks due to the (*S*)-configuration were not observed in the ^{1}H NMR study (using a chiral europium shift reagent).

Contrary to our expectation, when 2-cyclohexen-1-yl acetate was used as a substrate, cymantrene ligands showed lower enantioselectivities ($\sim$38% e.e.).

Recently, we reported the synthesis of the novel planar chiral P,N-ligand **C** based on arene tricarbonyl (Chart 1).[10] The ligand **C** showed a 95% e.e. in the allylic alkylation. At first, we thought that the different selectivity might come from the different bite angle between **Fd** and **C**. **Md** and **Fd** have a very similar biting angle because they have the same ligand **L**. However, they have different selectivities, with our results suggesting that the metal tricarbonyl itself plays an important role in the enantioselectivity. In addition to the bite angle, other factors also influence the selectivity.

A recent comparison study between ferrocene and a cyclopentadienyl rhenium tricarbonyl derivatives as N,O-chelate ligands in an enantioselective phenyl transfer reaction to aldehyde has been reported.[11] Ferrocene and cyclopentadienyl rhenium tricarbonyl may have a similar biting angle. The authors reported that compared to ferrocene ligands, cyclopentadienyl rhenium tricarbonyl showed a better enantioselectivity due to an increase of Lewis acidity of the catalyst through the electron-withdrawing effect of carbonyls.

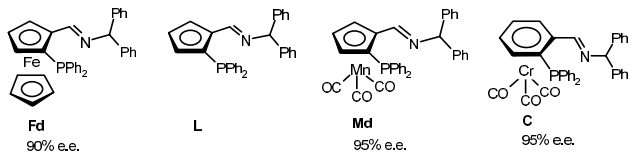


Chart 1.

In our case, we expect that the electron-withdrawing effect of carbonyls affects the electronic environment of the P- or N-atom. In addition, the steric effect exerted by metal carbonyls also plays an important role in enantioselectivity because the metal tricarbonyl is a bulkier group compared to the Cp ring in ferrocenes. As expected, when one of the carbonyls is substituted by PPh_3, the substitution reduces the electron-withdrawing effect of the carbonyls. However, higher enantioselectivity was achieved.

In conclusion, we have shown that the cymantrene derivatives are better P,N-chelate ligands for the palladium-catalyzed allylic alkylation than the ferrocenes, which have a similar pentagonal chiral ligand structure to cymantrene derivatives. In particular, the PPh_3-substituted cymantrene gave an excellent enantioselectivity. The steric effect of the metal carbonyl groups also seems to play an important role in the enantioselectivity.

2. Experimental

All reactions were conducted under nitrogen using standard Schlenk type flasks. Workup procedures were done in air. Most organic chemicals were purchased from Aldrich Chemical Co. and were used as received. ^{1}H NMR spectra were obtained on a Bruker-300 instrument. IR spectra were recorded on a Shimadzu IR-470 spectrophotometer (spectra measured as films on NaCl by evaporation of the solvent). Elemental analyses were done at the National Center for Inter-University Research Facilities, Seoul National University. Optical rotations were measured on a JASCO DIP360 instrument. HRMS measurements mass were done at Korea Basic Science Institute (DaeGu).

Compound **Mc** was synthesized by the published procedure.[5]

2.1. Synthesis of ferrocene derivatives

Fd. Compound **1** (0.050 g, 0.13 mmol), benzhydrylamine (21 μl, 0.13 mmol), molecular sieve 4 Å (0.25 g), and 10 ml of CH_2Cl_2 were put in a flame-dried Schlenk flask. The solution was heated at reflux for 18 h, filtered over a pad of Celite, concentrated by rotary evaporator, and dried in vacuo to yield **Fd** quantitatively. This compound was used in the Pd-catalyzed allylic alkylation without further purification. ^{1}H NMR ($CDCl_3$): δ 8.53 (s, 1H), 7.55–7.18 (m, 20H), 5.41 (s, 1H), 5.11 (s, 1H), 4.46 (s, 1H), 3.98 (s, 5H), 3.80 (s, 1H) ppm. Anal. calcd for $C_{36}H_{30}FeNP$: C, 76.74; H, 5.37; N, 2.49. Found: C, 76.93; H, 5.47; N, 2.50. $[\alpha]_D^{20} = 174$ (*c* 0.50, CH_2Cl_2).

Fa. ^{1}H NMR ($CDCl_3$): δ 8.58 (s, 1H), 7.51 (m, 2H), 7.35 (m, 3H), 7.25–6.99 (m, 10H), 5.19 (s, 1H), 4.55 (s, 1H), 4.09 (s, 5H), 3.90 (s, 1H) ppm. Anal. calcd for $C_{29}H_{24}FeNP$: C, 73.59; H, 5.11; N, 2.96. Found: C, 73.48; H, 5.17; N, 3.07. $[\alpha]_D^{20}=134$ (*c* 0.50, CH_2Cl_2).

Fb. ^{1}H NMR ($CDCl_3$) δ 8.55 (s, 1H), 7.56 (m, 2H), 7.40 (m, 3H), 7.25–7.12 (m, 10H), 5.10 (s, 1H), 4.65 (d, $J=13.0$ Hz, 1H), 4.54 (d, $J=13.0$ Hz, 1H), 4.11 (s, 5H), 3.85 (s, 1H) ppm. Anal. calcd for $C_{30}H_{26}FeNP$: C, 73.93; H, 5.38; N, 2.87. Found: C, 73.61; H, 5.40; N, 2.86. $[\alpha]_D^{20}=342$ (*c* 0.50, CH_2Cl_2).

Fc. ^{1}H NMR ($CDCl_3$) δ 8.38 (s, 1H), 7.54 (m, 2H), 7.40 (m, 3H), 7.26–7.16 (m, 5H), 5.06 (s, 1H), 4.44 (s, 1H), 4.08 (s, 5H), 3.80 (s, 1H), 1.14 (s, 9H) ppm. Anal. calcd for $C_{27}H_{28}FeNP$: C, 71.53; H, 6.23; N, 3.09. Found: C, 71.25; H, 6.59; N, 3.19. $[\alpha]_D^{20}=242$ (*c* 0.50, CH_2Cl_2).

2.2. Synthesis of (arene)manganese tricarbonyl derivatives

Md. Compound **2** (0.055 g, 0.13 mmol), benzhydrylamine (21 μl, 0.13 mmol), molecular sieve 4 Å (0.25 g), and 10 ml of CH_2Cl_2 were put in a flame-dried Schlenk flask. The solution was heated at reflux for 18 h, filtered over a pad of Celite, concentrated by rotary evaporator, and dried in vacuo to give **Md** quantitatively. The compound was used in the Pd-catalyzed allylic alkylation without further purification. IR ν(CO) 2024, 1941 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.14 (s, 1H), 7.43–6.96 (m, 20H), 5.54 (s, 1H), 5.36 (s, 1H), 4.60 (s, 1H), 4.29 (s, 1H) ppm. Anal. calcd for $C_{34}H_{25}MnNO_3P$: C, 70.23; H, 4.33; N, 2.41. Found: C, 70.64; H, 4.63; N, 2.43. $[\alpha]_D^{20}=-253$ (*c* 0.50, CH_2Cl_2).

Ma. IR ν(CO) 2018, 1941 cm^{-1}; ^{1}H NMR (C_6D_6) δ 8.29 (s, 1H), 7.62–6.72 (m, 15H), 5.74 (s, 1H), 4.76 (s, 1H), 4.42 (s, 1H) ppm; ^{13}C NMR (C_6D_6) 151.5, 150.1, 136.6, 134.4, 133.7, 133.5, 131.6, 131.4, 128.4, 127.9, 127.6, 127.5, 127.4, 125.0, 119.7, 100.5, 96.3, 89.2, 86.1, 79.7 ppm; HRMS *m*/*z* (EI$^+$) calcd for $C_{27}H_{19}O_3NPMn$: 491.0483, obsd. 491.0479. $[\alpha]_D^{20}=-390$ (*c* 0.25, CH_2Cl_2).

Mb. IR ν(CO) 2016, 1937 cm^{-1}; ^{1}H NMR (C_6D_6) δ 8.14 (s, 1H), 7.30–6.94 (m, 15H), 5.52 (s, 1H), 4.59 (s, 2H), 4.58 (s, 1H), 4.27 (s, 1H) ppm; ^{13}C NMR (C_6D_6) δ 153.2, 138.0, 136.7, 134.5, 133.8, 133.5, 131.6, 131.3, 128.4, 127.5, 125.5, 100.6, 95.0, 88.9, 86.3, 79.0, 63.4 ppm; HRMS *m*/*z* (EI$^+$) calcd for $C_{28}H_{21}O_3NPMn$: 505.0640, obsd. 505.0639. $[\alpha]_D^{20}=-558$ (*c* 0.25, CH_2Cl_2).

2.3. Synthesis of 3

Compound **2** (0.17 g, 0.41 mmol), triphenylphosphine (0.14 g, 0.53 mmol), and THF (10 ml) were put in a Schlenk flask. After the solution was exposed to ultraviolet light for 4 h at rt, it was filtered, concentrated, and chromatographed on a neutral alumina eluting with hexane and diethyl ether (v/v. 20:1). Yield: 59% (0.16 g, light-yellow solid); IR ν(CO) 1941, 1883 cm^{-1}; ^{1}H NMR (C_6D_6) δ 9.61 (s, 1H), 7.53–7.26 (m, 25H), 5.19 (s, 1H), 4.15 (s, 1H), 3.69 (s, 1H) ppm. $[\alpha]_D^{20}=-224$ (*c* 0.50, CH_2Cl_2). Anal. calcd for $C_{38}H_{29}MnO_3P_2$: C, 70.16; H, 4.49. Found: C, 70.01; H, 4.64.

2.4. Synthesis of Mf

Compound **3** (0.070 g, 0.11 mmol), benzhydrylamine (19 μl, 0.11 mmol), molecular sieve 4 Å (0.25 g), and 10 ml of CH_2Cl_2 were put in a flame-dried Schlenk flask. The solution was heated at reflux for 18 h, filtered over a pad of Celite, concentrated by rotary evaporator, and dried in vacuo to yield **Mf** quantitatively. Compound **Mf** was used without further purification. IR ν(CO) 1934, 1872 cm^{-1}; ^{1}H NMR (C_6D_6) δ 7.86 (s, 1H), 7.48–6.62 (m, 35H), 4.95 (s, 1H), 4.74 (s, 1H), 3.69 (s, 1H), 3.46 (s, 1H) ppm; ^{13}C NMR (C_6D_6) δ 153.2, 138.0, 136.7, 134.5, 133.8, 133.5, 131.6, 131.3, 128.4, 127.5, 125.5, 100.6, 95.0, 88.9, 86.3, 79.0, 63.4 ppm; HRMS *m*/*z* (FAB$^+$) calcd for $C_{51}H_{40}O_2NP_2Mn$: 816.1993, obsd. 816.1995. $[\alpha]_D^{20}=-608$ (*c* 0.25, CH_2Cl_2).

2.5. General procedures for Pd-catalyzed allylic alkylation

A solution of $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (4.0 mg, 11 μmol) and P,N-ligand (32 μmol) in 3 ml of CH_2Cl_2 was stirred at rt for 30 min. To the solution were added *rac*-1,3-diphenyl- prop-2-en-1-yl acetate (0.11 g, 0.43 mmol) and dimethyl malonate (75 μl, 0.65 mmol) in 2 ml of CH_2Cl_2. *N*,*O*-Bis(trimethylsilyl)acetamide (0.40 ml, 1.6 mmol) and KOAc (1 mg) were added to the solution. After the solution was stirred for 4h, it was evaporated to dryness and chromatographed on a silica gel column eluting with hexane and diethyl ether (v/v, 10:1).

2.6. X-Ray crystal structure determinations of Fa, Fb, and Fd

Single crystals of **Fa**, **Fb**, and **Fd** suitable for an X-ray diffraction study were grown by slow diffusion of hexane to a dichloromethane solution of **Fa**, **Fb**, and **Fd**, respectively, at room temperature. X-Ray data for single crystals were collected on an Enraf–Nonius CCD single crystal X-ray diffractometer at room temperature using graphite-mono-chromated MoKα radiation ($\lambda=$ 0.71073 A). The structures were solved by direct methods (SHELXS-97), and refined against all F^2 data (SHELXS-97). All non-hydrogen atoms were refined with anisotropic thermal parameters and the hydrogen atoms treated as idealized contributions.

Acknowledgements

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