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Role of the planar chirality of imine–phosphine hybrid ligands bearing chromium tricarbonyl in the palladium-catalyzed asymmetric allylic alkylation

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Abstract

Optically active Cr-complexed imine–phosphine hybrid ligands having only a planar chirality showed excellent enantioselectivity for the palladium-catalyzed allylic alkylation with predictable absolute configuration.

Keywords: planar chirality; chromium tricarbonyl; allylic alkylation.

An asymmetric C–C bond formation reaction of allylic compounds catalyzed by palladium complex has been investigated extensively.[1] To achieve high chemo-, regio-, diastereo-, and enantioselectivity, the P,N-ligands[2] have been prepared and studied because they are easily amenable by steric and electronic modification. Most of the known P,N-chiral ligands possess planar and central chirality. But efficient chiral ligands with only the planar chirality have not been developed so much.[3] Recently, planar chiral P,N-ligands bearing chromium tricarbonyl have been used[4] as chiral ligands in the catalytic asymmetric reaction. In the continuation of our efforts[5] to explore new planar chiral P,N-ligands, we present here the preparation of planar chiral imino–phosphine chromium ligands and their use in palladium-catalyzed asymmetric allylic alkylation.

The planar chiral P,N-ligands **2a**–**e** were synthesized from **1** (Eq. (1)).[6,†]

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† All the compounds have been fully characterized by ^{1}H NMR, IR, and elemental analysis (See the Supporting Information). Selected data for **2a**: Mp 56°C; IR νCO 1958, 1884 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.54 (d, 4.8 Hz, 1H), 7.43–7.12 (m, 15H), 5.94 (d, 7.0 Hz, 1H), 5.45 (t, 6.5 Hz, 1H), 5.24 (t, 6.0 Hz, 1H), 4.65 (d, 6.5 Hz, 1H), 4.40 (q, 6.6 Hz, 1H), 1.20 (d, 6.6 Hz, 3H) ppm. Anal. calcd for $C_{30}H_{24}CrNO_3P$: C, 68.05; H, 4.57; N, 2.65. Found: C, 67.68; H, 4.95; N, 2.86; $[\alpha]_D^{26}$ –84 (*c* 0.10, CH_2Cl_2).

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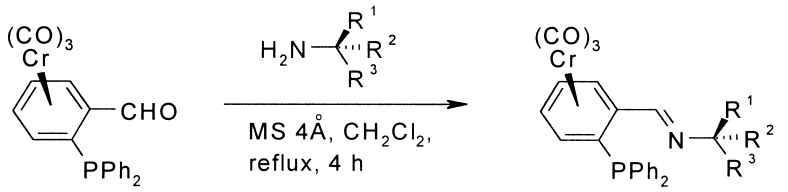
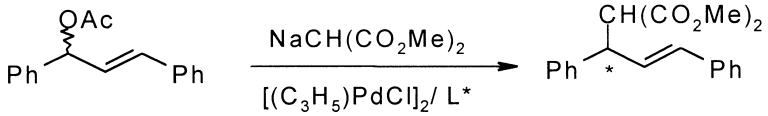


1

2a (R^1=Ph, R^2=Me, R^3=H)
2b (R^1=Me, R^2=Ph, R^3=H)
2c (R^1=R^2=R^3=Me)
2d (R^1=Ph, R^2=R^3=H)
2e (R^1=R^2=Ph, R^3=H)

The palladium-catalyzed asymmetric allylic alkylation of *rac*-1,3-diphenyl prop-2-en-1-yl acetate (**A**) with dimethyl malonate was carried out (Eq. (2)).



A

Reaction of **A** with sodium malonate in the presence of 2.4 mol% Pd(0) catalyst gave the allylic alkylation product methyl-2-carbomethoxy-3,5-diphenylpent-4-enolate in high yields.

We have screened the reaction medium using chiral ligand **2a** (entries 1–4 in Table 1). Significant solvent effects on the enantioselectivities were observed; the highest enantioselectivity (82%) was achieved in DMSO at room temperature. Thus, DMSO was chosen a reaction medium for our reactions.

Table 1
Pd-catalyzed allylic alkylation

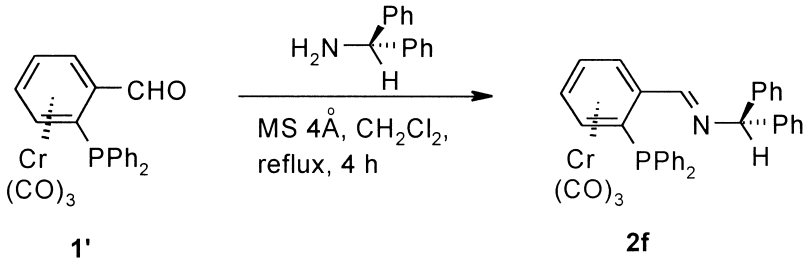
Entry	L*	Solvent	Time (h)	Temp.	Yield (%)[a]	*ee* (%)[b]
1	2a	DMF	4	0°C	64	57(*S*)
2	2a	CH_3CN	5	0°C	86	70(*S*)
3	2a	NMP	4	0°C	48	76(*S*)
4	2a	DMSO	5	r.t.	68	82(*S*)
5	2b	DMSO	6	r.t.	74	85(*S*)
6	2c	DMSO	7	r.t.	71	79(*S*)
7	2d	DMSO	6	r.t.	82	91(*S*)
8	2e	DMSO	6	r.t.	93	>98(*S*)
9	2f	DMSO	6	r.t.	85	95(*R*)

[a] Isolated yield.
[b] The *ee* values were determined by ^{1}H NMR using chiral shift reagent, $Eu(hfc)_3$.

We next investigated the ligand effect by employing **2b–e** as a ligand (entries 5–8 in Table 1). All of the ligands showed good to excellent enantioselectivities. It is noticeable that the change of the central chirality in the imine (entry 4 versus 5 in Table 1) does not affect the absolute configuration

and enantioselectivity of the reaction. This observation was quite exceptional because it is widely accepted[6] that the absolute configuration is governed mainly by the central chirality, but not by the planar chirality. Interestingly, subjecting **2c** having no central chirality to the same reaction condition provided the *S* configuration product with 79% ee. This observation suggests that the central chirality may play no role in our reaction. Furthermore, for the chiral ligands **2d** and **e** having no central chirality, as the steric bulkiness increases, the ee values were promoted to 91 and >98%, respectively. Thus, it seems that the ee value is dependent upon the steric bulkiness on the imino group, but not the central chirality.

To investigate the effect of planar chirality on the absolute configuration of the product, an (*S*)-planar chiral enantiomer **2f** was synthesized (Eq. (3))[7,‡] and subjected to palladium-catalyzed allylic substitution.



(3)

After the reaction, an *R* configuration product was obtained with 95% ee. Thus, the absolute configuration is controlled only by the planar chirality.

Generally, the palladium-catalyzed allylic alkylation would proceed through the major diastereomer at equilibrium.[8] In the reaction, two diastereomeric allylpalladium complexes, the *exo–syn–syn* and the *endo–syn–syn* isomer, can be considered as π-allyl intermediate. However, for the CD_2Cl_2 solution of palladium complex derived from **2c** only one isomer with the ^{31}P NMR chemical shift of 30.04 ppm was observed. The ^1H NMR NOE study between allyl protons and methyl protons of the *tert*-butyl imine verifies that the major isomer is the *exo–syn–syn* one (Fig. 1).

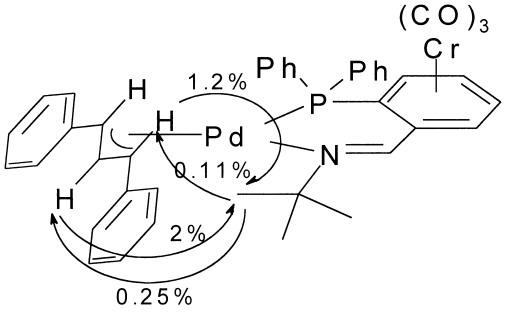


Figure 1. NOE connectivity between allyl and *tert*-butyl protons

‡ Selected data for **2f**: mp 148°C. Anal. calcd for $C_{35}H_{26}CrNO_3P$: C, 71.06; H, 4.43; N, 2.37. Found: C, 71.32; H, 4.65; N, 2.42; $[\alpha]_D^{25}$ +144 (*c* 0.10, CH_2Cl_2).

To elucidate the stereochemical outcome, the X-ray crystal structure of palladium complex **3** prepared by the reaction of $[Pd(\eta^3\text{-PhCHCHCHPh})Cl]_2$ with **2c** was determined. The crystal structure shows the *exo–syn–syn* geometry with pseudo square-planar coordination around palladium (Fig. 2),[9,§] which is consistent with the result of the NOE study. The 1,3-diphenylallyl ligand is rotated in a clockwise manner along the Pd-allyl axis so that the terminal allyl carbon trans to phosphorus is above the P-Pd-N coordination plane. The steric effect of the *tert*-butyl group would enforce the allyl group away at one terminus and thereby the carbon atom *trans* to phosphorus could be an enhanced reaction center for nucleophilic addition since it may carry more positive charge character.[10] The nucleophilic attack results in the *S* configuration. Thus, the X-ray structure explains the absolute configuration of the product.

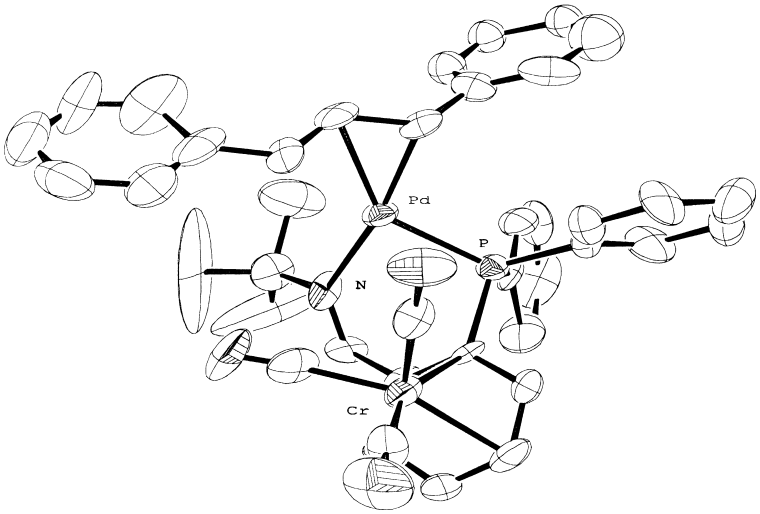


Figure 2. View of the structure of **3**. The BF_4^- ion is omitted for clarity

In conclusion, we have demonstrated that the imine–phosphine ligands with only the planar chirality can produce an excellent asymmetric environment for palladium-catalyzed allylic alkylation. Furthermore, both *R* and *S* enantiomers were obtained in excellent enantioselectivities by changing the enantiomer of the planar chiral ligand.

§ Selected data for **3**: mp 180°C (dec.); IR νCO 1968, 1916 cm^{-1}; ^1H NMR (CD_2Cl_2): δ 8.14 (d, 4.2 Hz, 1H), 7.66–6.82 (m, 20H), 6.54 (dd, 9.8, 14.4 Hz, 1H), 6.41 (dd, 9.3, 14.3 Hz, 1H), 5.83 (t, 6.0 Hz, 1H), 5.63 (m, 1H), 5.42 (t, 6.4 Hz, 1H), 4.93 (t, 6.6 Hz, 1H), 4.19 (d, 9.2 Hz, 1H), 0.85 (s, 9H) ppm. Anal. calcd for $C_{41}H_{37}BCrF_4NO_3PPd$: C, 56.74; H, 4.30; N, 1.61. Found: C, 56.52; H, 4.67; N, 1.55. Crystal data for **3**: $C_{41}H_{37}BCrF_4NO_3PPd$, $M = 867.90$, orthorhombic, $P2_12_12_1$ (No. 19), $a = 11.146(2)$, $b = 18.170(3)$, $c = 19.107(4)$ Å, $U = 3869.6(13)$ $Å^3$, $Z = 4$, $Dc = 1.490$ g cm^{-3}, λ(Mo–Kα) = 0.845 mm^{-1}, Enraf–Nonius CAD4 diffractometer, λ = 0.71073 Å. 3833 reflections measured, 3806 unique reflections used in all calculations. The structure was solved by direct methods (SHELXS-86) and refined by full-matrix least-squares (SHELXL-93) on F^2. The final $R = 0.1357$ (obsd), $wR(F^2) = 0.3411$ (obsd), $S = 1.034$ (obsd). Due to the consistently poor quality of the crystals, refinement of the structure has been unsatisfactory. A detailed discussion of the structural parameters is therefore inappropriate, but it clearly shows that the molecular structure has the *exo–syn–syn* geometry. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Center. See: Notice Authors, Issue No. 1.

Acknowledgements

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