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Palladium-catalyzed asymmetric allylic alkylation using chiral hydrazone ligands with ferrocene skeleton

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Abstract

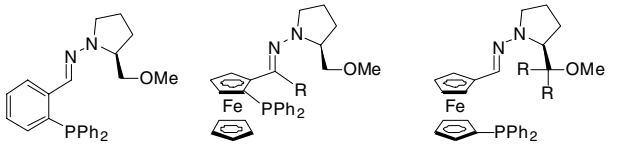
Palladium-catalyzed asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate (**4**) with a dimethyl malonate–BSA–LiOAc system has been successfully carried out in the presence of chiral phosphine–hydrazone ligands such as **3a** in good yields with good enantioselectivities (up to 84% ee).

Keywords: Palladium; Ferrocene; Hydrazone; Asymmetric catalysis; Allylic alkylation

1. Introduction

Synthesis of chiral ferrocene derivatives has attracted much interest in various research fields [1]. Chiral P,N-ligands with ferrocene skeleton have shown efficiency as catalysts for asymmetric synthesis. Palladium-catalyzed allylic substitution is a versatile and widely used process in organic synthesis [2], and the development of efficient enantioselective catalysis for this reaction is an important goal of current research in this area [3]. Chiral ferrocene ligands with planar chirality are beginning to be used in palladium-catalyzed allylic substitution [4].

We previously described palladium-catalyzed asymmetric allylic substitution using 2-diphenylphosphinobenzaldehyde SAMP hydrazone (DPPB-SAMP) (**1**) as a chiral ligand [5]. More recently, Enders and we described the synthesis of planar chiral ferrocenyl SAMP hydrazone **2** [6]. We here report on the synthesis of phosphine–chiral hydrazone ligands **3** with ferrocene skeleton without planar chirality in which the phosphine and hydrazone groups are attached to different Cp rings of ferrocene and its application to the palladium-catalyzed asymmetric allylic alkylation. Ligand **3** was formed in a seven-membered heterometallocyclic ring by chelate coordination with such metals as palladium; therefore the P–Pd–N bite angle is different between it and ligands **1** and **2**



1 **2** R = H, Ph **3** a : R = H, b = Me, c : R = Et

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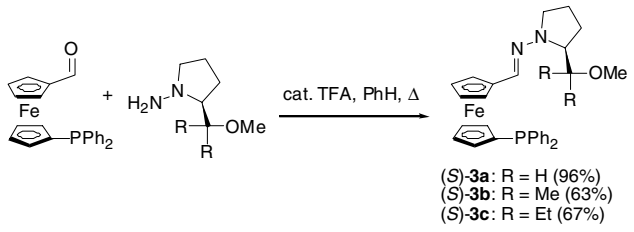
2. Results and discussion

2.1. Synthesis of the chiral hydrazone ligands

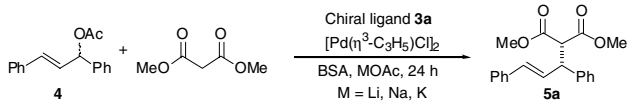
Phosphine–hydrazone ligands **3** were easily prepared from 1′-(diphenylphosphino)-1-ferrocenecarboxaldehyde [7] with SAMP ((*S*)-1-amino-2-(methoxymethyl)-pyrrolidine), SADP ((*S*)-amino-2-(1′-methoxy-1′-methylethyl)pyrrolidine), and SAEP ((*S*)-amino-2-(1′-methoxy-1′-ethylpropyl)pyrrolidine) in good yields (Scheme 1).

2.2. Palladium-catalyzed asymmetric allylic alkylation

These ligands were examined in the palladium-catalyzed asymmetric allylic alkylation of racemic 1,3-diphenyl-2-propenyl acetate (**4**) [8] with dimethyl malonate in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) [9] at room temperature (Scheme 2 in Table 1).



Scheme 1.



Scheme 2.

Using 4 mol% of SAMP hydrazone (*S*)-**3a** and lithium acetate in acetonitrile (Entry 1), the product **5a** was obtained in 92% yield and 73% ee. When THF was used instead of acetonitrile, the enantioselectivity of **5a** increased to 84% ee (Entry 2). Changing the solvent to other ether type solvents, toluene and α,α,α-trifluorotoluene decrease the enantioselectivities in comparison with THF (Entries 3–6). Sodium acetate or potassium acetate was used instead of lithium acetate in THF, the yield and enantioselectivity of **5a** were decreased (Entries 7 and 8 versus Entry 2 in Table 1). Thus, an optimized result was realized when the reaction was carried out in the presence of lithium acetate in THF. We next investigated the effect of temperature on this reaction (Entries 9 and 10 versus Entry 2 in Table 1). The enantioselectivity and yield were dependent on the reaction temperature; the best result was obtained at room temperature (Entry 2 in Table 1).

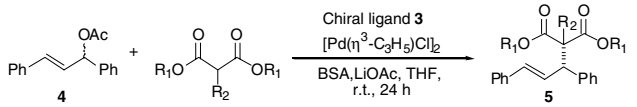
Under such conditions, SADP hydrazone ((*S*)-**3b**) and SAEP hydrazone ((*S*)-**3c**) were used instead of (*S*)-**3a**, and the enantioselectivity of **5a** decreased (Entries 2 and 3 versus Entry 1 in Table 2). Similar tendency appeared to the case of using ligand **1** [5] and **2** (R = H) [a,b]. Product **5b** was formed with the (*R*)-(+)-enantiomer predominating, as determined from the sign of the optical rotation [10]. We next investigated the palladium-catalyzed asymmetric allylic alkylation of similar active methylene compounds using **3a** as a ligand (Scheme 2, Table 2). The reaction with diethyl malonate (**5b**) instead of **5b** resulted in the corresponding product in good yield with good enantioselectivity (Entry 4). But when using diethyl methylmalonate, the reaction resulted in corresponding product **5c** in moderate enantioselectivity (Entry 5). The enantioselectivities obtained with ligands **3** for the same palladium-catalyzed asymmetric allylic alkylation with 1,3-diphenyl-2-propenyl acetate were not better than those obtained with ligand **1** or **2**.

Table 1
Asymmetric allylic alkylation catalyzed by palladium complexes with chiral hydrazone ligand **3a**[a]

Entry	Base	Solvent	Temperature (°C)	Yield[b] (%)	ee[c] (%)
1	LiOAc	MeCN	r.t.	92	73
2	LiOAc	THF	r.t.	82	84
3	LiOAc	Ether	r.t.	65	67
4	LiOAc	CPME[d]	r.t.	99	67
5	LiOAc	PhMe	r.t.	78	66
6	LiOAc	$PhCF_3$	r.t.	96	62
7	NaOAc	THF	r.t.	78	79
8	KOAc	THF	r.t.	81	78
9	LiOAc	THF	50	93	68
10	LiOAc	THF	0	41	82

[a] Molar ratio : $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.02 eq.), ligand **3a** (0.04 equiv.), dimethyl malonate (3.0 equiv.), BSA (3.0 equiv.), MOAc (0.02 equiv.).
[b] Isolated yields.
[c] The ee values were determined by HPLC analysis using a chiral column (chiralcel OD (hexane:*i*-PrOH = 99:1)).
[d] Cyclopentyl methyl ether.

Table 2
Palladium-catalyzed asymmetric allylic alkylation using (*S*)-**3**[a]



a : R_1 = Me, R_2 = H
b : R_1 = Et, R_2 = H
c : R_1 = Et, R_2 = Me

Entry	Ligand	R_1	R_2	Yield[b] (%)	ee[c] (%)
1	**3a**	Me	H	82(**5a**)	84
2	**3b**	Me	H	74(**5a**)	83
3	**3c**	Me	H	62(**5a**)	73
4	**3a**	Et	H	75(**5b**)	83
5	**3a**	Et	Me	69(**5c**)	55

[a] Molar ratio: $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.02 equiv.), ligand **3** (0.04 equiv.), malonate (3.0 equiv.), BSA (3.0 equiv.), MOAc (0.02 equiv.).
[b] Isolated yields.
[c] The ee values were determined by HPLC analysis using a chiral column (chiralcel OD (hexane:*i*-PrOH = 99:1)).

3. Conclusion

We have prepared new phosphine–chiral hydrazone ligands with ferrocene skeleton without planar chirality easily from 1′-(diphenylphosphino)-1-ferrocenecarboxaldehyde and chiral hydrazines such as SAMP. These ligands such as (*S*)-**3a** can be used in palladium-catalyzed asymmetric allylic alkylation with good enantiomeric excess.

4. Experimental

4.1. General methods

All the experiments were carried out under an argon atmosphere. IR spectra were taken on a Hitachi 260-10 spectrometer or a JASCO FT/IR-230 spectrometer. NMR spectra were recorded on a JEOL A-400 spectrometer or a Bruker DPX-300 spectrometer. Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H and ^{13}C NMR. ^{31}P NMR spectra were obtained using 85% H_3PO_4 as an external reference. Mass spectra were recorded on a JEOL JMS-HX110 or a JMS-700 or a Shimadzu GCMS-QP2000A or a Hitachi M-80B. Optical rotations were measured on a JASCO DIP-370 or a HORIBA SEPA-200. Chiral HPLC analyses were performed on a Shimadzu LC-6A system using a Chiralcel OD column (25 cm×0.46 cm) by Daicel Chemical Ind., Ltd.

4.2. Typical procedure for the preparation of 3

A mixture of 1′-(diphenylphosphino)-1-ferrocenecarboxaldehyde (0.5 mmol), chiral hydrazine (1.0 mmol), and CH_2Cl_2 (5 mL) was stirred at room temperature for 6 h under an argon atmosphere. The reaction mixture was diluted with ether and water. The organic layer was washed with brine and dried over $MgSO_4$. The filtrate was concentrated with a rotary evaporator and the residue was purified by column chromatography.

1′-(Diphenylphosphino)-1-ferrocenecarboxaldehyde SAMP hydrazone ((*S*)-**3a**): 96%; $[\alpha]_D^{20} = +227.0^\circ$ (c, 1.0, $CHCl_3$); ^1H NMR (300 Mz, $CDCl_3$) δ 1.76–2.05 (m, 4H), 2.79 (dd, 7.9 and 16.4 Hz, 1H), 3.28–3.34 (m, 1H), 3.39 (s, 3H), 3.42–3.47 (m, 2H), 3.55–3.62 (m, 1H), 4.00–4.05 (m, 2H), 4.11 (t, 1.8 Hz, 2H), 4.33 (t, 1.7 Hz, 2H), 4.38–4.42 (m, 2H), 6.86 (s, 1H), 7.28–7.40 (m, 10H); ^{13}C NMR (75 Mz, $CDCl_3$) δ 22.1, 26.6, 49.8, 59.3, 63.2, 67.2 (d, 9.7 Hz), 69.8, 72.1 (dd, 1.9 Hz), 73.6 (d, 11.0 Hz), 73.7 (d, 11 Hz), 74.6, 76.2 (d, 6.1 Hz), 84.4, 128.0, 128.1, 128.4, 132.5, 133.3 (d, 2.7 Hz), 133.6 (d, 2.7 Hz), 139.1 (d, 2.2 Hz), 139.3 (d, 2.2 Hz); ^{31}P NMR (121 Mz, $CDCl_3$) δ −16.64; FAB-MS *m*/*z* 510 (M^+, 12); HRMS (FAB) Anal. Calc. for $C_{29}H_{31}N_2OPFe(M^+)$ 510.1523, found 510.1499.

1′-(Diphenylphosphino)-1-ferrocenecarboxaldehyde SADP hydrazone ((*S*)-**3b**): 63%; $[\alpha]_D^{20} = +194.0^\circ$ (c, 1.0, $CHCl_3$); ^1H NMR (300 Mz, $CDCl_3$) δ 1.15 (s, 3H), 1.24 (s, 3H), 1.76–2.04 (m, 4H), 2.75 (dd, 8.4 and 15.8 Hz, 1H), 3.25 (s, 3H), 3.37–3.49 (m, 2H), 3.99–4.04 (m, 2H), 4.08–4.10 (m, 2H), 4.30–4.34 (m, 3H), 4.43 (d, 1.3 Hz, 1H), 6.82 (s, 1H), 7.29–7.39 (m, 10H); ^{13}C NMR (75 Mz, $CDCl_3$) δ 21.0, 23.3, 23.7, 24.7, 49.6, 51.0, 66.5, 67.5, 69.7, 69.8, 71.1, 72.1 (d, 2.2 Hz), 72.2 (d, 2.2 Hz), 73.5, 73.6 (d, 3.6 Hz), 73.8, 76.1 (d, 6.3 Hz), 77.7, 84.8, 128.0, 128.1, 128.4, 130.8, 133.4, 133.6, 139.1 (d, 2.2 Hz), 139.3 (d, 2.2 Hz); ^{31}P NMR (121 Mz, $CDCl_3$) δ −16.55; FAB-MS *m*/*z* 538 (M^+, 40); HRMS (FAB) Anal. Calc. for $C_{31}H_{35}N_2OPFe(M^+)$ 538.1836, found 538.1837.

1′-(Diphenylphosphino)-1-ferrocenecarboxaldehyde SAEP hydrazone ((*S*)-**3c**): 67%; $[\alpha]_D^{20} = +252^\circ$ (c, 1.0, $CHCl_3$); ^1H NMR (300 Mz, $CDCl_3$) δ 0.90 (t, 7.4 Hz, 3H), 0.93 (t, 7.4 Hz, 3H), 1.51–2.04 (m, 8H), 2.69–2.78 (m, 1H), 3.25 (s, 3H), 3.28–3.34 (m, 1H), 3.62 (dd, 3.0 and 8.9 Hz, 1H), 3.99–4.01 (m, 2H), 4.08–4.11 (m, 2H), 4.29–4.34 (m, 3H), 4.47 (dd, 1.5 and 3.3 Hz, 1H), 6.69 (s, 1H), 7.29–7.38 (m, 10H); ^{13}C NMR (75 Mz, $CDCl_3$) δ 7.77, 8.70, 23.5, 23.6, 24.4, 26.3, 50.36, 50.4 (d, 4.4 Hz), 66.2, 67.6, 68.4, 69.5, 69.7, 72.1 (d, 4.1 Hz), 72.2 (d, 3.9 Hz), 73.5, 73.7 (d, 1.5 Hz), 73.9, 76.1 (d, 6.5 Hz), 80.4, 84.9, 128.0, 128.1, 127.4 (d, 5.1 Hz), 129.5, 133.3 (d, 14.1 Hz), 133.6 (d, 14.5 Hz), 139.1 (d, 8.8 Hz), 139.2 (d, 9.8 Hz); ^{31}P NMR (121 Mz, $CDCl_3$) δ −16.58; FAB-MS *m*/*z* 566 (M^+, 15); HRMS (FAB) Anal. Calc. for $C_{33}H_{39}N_2OPFe(M^+)$ 566.2150, found 566.2113.

4.3. General procedure for the palladium-catalyzed allylic alkylation

To mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.01 mmol), chiral hydrazone **3** (0.02 mmol), and metal acetate (0.01 mmol) in a solvent (1 mL) was added BSA (1.5 mmol), racemic 1,3-diphenyl-2-propenyl acetate (**4**) (0.5 mmol), and various malonate (1.5 mmol) at room temperature under an argon atmosphere. After being stirred for 24 h, the reaction mixture was diluted with ether and water. The organic layer was washed with brine and dried over $MgSO_4$. The filtrate was concentrated with a rotary evaporator and the residue was purified by column chromatography.

References

[1] For leading references, see: (a) A. Togni, T. Hayashi (Eds.), Ferrocenes, VCH, Weinheim, 1995;
(b) C.J. Richards, A.J. Locke, Tetrahedron: Asymmetry 9 (1998) 2377.

[2] (a) J. Tsuji, I. Minami, Acc. Chem. Res. 20 (1987) 140;
(b) B.M. Trost, T.R. Verhoeven, in: G. Wilkinson, F.G.A. Stone, E.W. Abel (Eds.), Comprehensive Organometallic Chemistry, vol. 8, Pergamon Press, Oxford, 1982, p. 799;
(c) B.M. Trost, Acc. Chem. Res. 13 (1980) 385.

[3] (a) B.M. Trost, Chem. Pharm. Bull. 50 (2002) 1;
(b) G. Helmchen, J. Oraganomet. Chem. 576 (1999) 203;
(c) A. Pfaltz, M. Lautens, in: E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), Comprehensive Asymmetric Catalysis, vol. 2, Springer, Tokyo, 1999, p. 833;
(d) B.M. Trost, D.L. Van Vranken, Chem. Rev. 96 (1996) 395;
(e) J.M.J. Williams, Synlett (1996) 705;
(f) A. Pfaltz, Acc. Chem. Res. 26 (1993) 339;
(g) T. Hayashi, in: I. Ojima (Ed.), Catalytic Asymmetric Synthesis, VCH Publishers, New York, 1993;
(h) G. Consiglio, R.M. Waymouth, Chem. Rev. 89 (1989) 257 and references cited therein.

[4] (a) For some recent papers on palladium-catalyzed allylic substitution, see; X. Hu, H. Chen, H. Dai, Z. Zheng, Tetrahedron: Asymmetry 14 (2003) 3415;
(b) B.F. Bonini, M. Fochi, M. Comes-Franchini, A. Ricci, L. Thija, B. Zwanenburg, Tetrahedron: Asymmetry 14 (2003) 3321;
(c) P. Barbaro, C. Bianchini, G. Claudio, A. Togni, Tetrahedron Lett. 44 (2003) 8279;
(d) J.H. Lee, S.U. Son, Y.K. Chung, Tetrahedron: Asymmetry 14 (2003) 2109;
(e) X. Hu, H. Chen, H. Dai, X. Hu, Z. Zheng, Tetrahedron: Asymmetry 14 (2003) 2073;
(f) O.G. Mancheno, J. Priego, S. Cabrera, R.G. Arrayas, T. Llamas, J.C. Carretero, J. Org. Chem. 68 (2003) 3679;
(g) T. Tu, Y.G. Zhou, X.L. Hou, L.X. Dai, X.C. Dong, Y.H. Yu, J. Sun, Organometallics 22 (2003) 1255;
(h) R.J. Kloetzing, M. Lotz, P. Knochel, Tetrahedron: Asymmetry 14 (2003) 255;
(i) X. Hu, H. Chen, X. Hu, H. Dai, C. Bai, J. Wang, Z. Zheng, Tetrahedron Lett. 43 (2002) 9179;
(j) R.M. Moreno, A. Bueno, A. Moyano, J. Organomet. Chem. 660 (2002) 62;
(k) J. Priego, O.G. Mancheno, S. Cabrera, R.G. Arrayas, T. Llamas, J.C. Carretero, Chem. Commun. (2002) 2512;
(l) A.A. Nazarov, C.G. Hartinger, V.B. Arion, G. Giester, B.K. Keppler, Tetrahedron 58 (2002) 8489;
(m) X. Hu, H. Dai, X. Hu, H. Chen, J. Wang, C. Bai, Z. Zheng, Tetrahedron: Asymmetry 13 (2002) 1687;
(n) L. Bernardi, B.F. Bonini, M. Comes-Franchini, M. Fochi G. Mazzanti, A. Ricci, G. Varchi, Eur. J. Org. Chem. (2002) 2776;
(o) S.L. You, X.L. Hou, L.X. Dai, Y.H. Yu, W. Xia, J. Org. Chem. 67 (2002) 4684.

[5] (a) T. Mino, W. Imiya, M. Yamashita, Synlett (1997) 583;
(b) T. Mino, M. Shiotsuki, N. Yamamoto, T. Suenaga, M. Sakamoto, T. Fujita, M. Yamashita, J. Org. Chem. 66 (2001) 1795.

[6] (a) T. Mino, T. Ogawa, M. Yamashita, J. Organomet. Chem. 665 (2003) 122;
(b) T. Mino, T. Ogawa, M. Yamashita, Heterocycles 55 (2001) 453;
(c) D. Enders, R. Peters, R. Lochtman, J. Runsink, Eur. J. Org. Chem. (2000) 2839.

[7] (a) P. Stepnicka, T. Base, Inorg. Chem. Commun. 4 (2001) 682;
(b) I.R. Butler, R.L. Davies, Synthesis 11 (1996) 1350;
(c) M.E. Wright, Organometallics 9 (1990) 853.

[8] P.R. Auburn, P.B. Mackenzie, B. Bosnich, J. Am. Chem. Soc. 107 (1985) 2033.

[9] B.M. Trost, D.J. Murphy, Organometallics 4 (1985) 1143.

[10] T. Hayashi, A. Yamamoto, T. Hagihara, Y. Ito, Tetrahedron Lett. 27 (1986) 191.