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New chiral phosphinoimidazolidine ligand in palladium-catalyzed asymmetric allylic substitution

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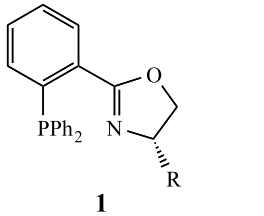
Abstract—Chiral phosphinoimidazolidine **3** was used as an excellent ligand in Pd-catalyzed asymmetric allylic alkylation of racemic 1,3-diphenyl-2-propenyl acetate **5** with dimethyl malonate. Outstanding enantioselectivity of up to 99% and remarkable catalytic activity were observed. The ligand was also found to be effective in the asymmetric allylic amination of **5** with benzylamine.

Pd-catalyzed asymmetric allylic substitution has received considerable attention as a useful asymmetric carbon–carbon and carbon–heteroatom forming process, in which racemic or achiral allylic substrate can be converted to an optically active product in the presence of a palladium complex of chiral ligand.[1,2] Development of new chiral ligands is an important chapter of current research in this area. Among numerous reported ligands, phosphorus–nitrogen heterodonor ligands are particularly effective in the asymmetric allylic alkylation due to their different electronic properties (*trans effect*).[3,4] Phosphinooxazolines **1** represent one of the most useful and versatile ligands in this area.[3] Generally, most of the phosphorus–nitrogen ligands possess an sp^2 nitrogen donor. We were interested in phosphorus–nitrogen ligands bearing an sp^3 nitrogen donor. Recently, we have found that phosphinooxazolidines **2** can act as excellent chiral ligands for the asymmetric catalysis.[5] Introduction of the oxazolidine moiety might open up a path to the development of different kinds of chiral ligands. Encouraged by the results, we have designed imidazolidine systems bearing double sp^3 nitrogens. We herein present semi-C_2-symmetrical phosphinoimidazolidine **3** as a highly efficient ligand which has the first application to the Pd-catalyzed asymmetric allylic substitution.



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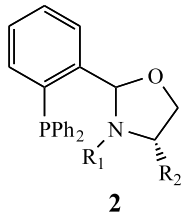

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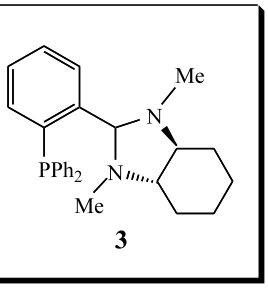

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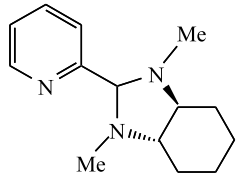

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The phosphinoimidazolidine **3**[6] was easily prepared through condensation of commercially available 2-(diphenyl-phosphino)benzaldehyde and (1*S*,2*S*)-*N*,*N*′-dimethylcyclo-hexane-1,2-diamine[7] in refluxing benzene over 12 h in nearly quantitative yield. Pyridinylimidazolidine **4** was also prepared by the same method. The catalytic properties of the palladium complexes formed in situ from these ligands and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ were investigated in the asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate **5** with dimethyl malonate.[8] *N*,*O*-Bis-(trimethylsilyl) acetamide (BSA) combined with a small amount of KOAc, NaOAc or LiOAc was used as base. The data obtained are summarized in

Keywords: asymmetric catalysis; allylic substitution; imidazolidine ligand; Pd catalyst.

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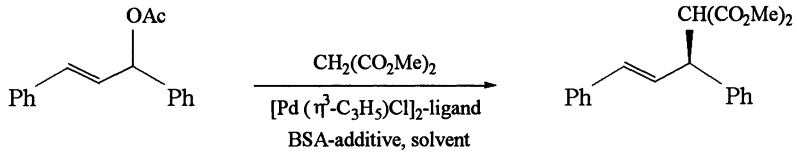
Table 1. Palladium-catalyzed asymmetric allylic alkylation of **5** with dimethyl malonate[a]

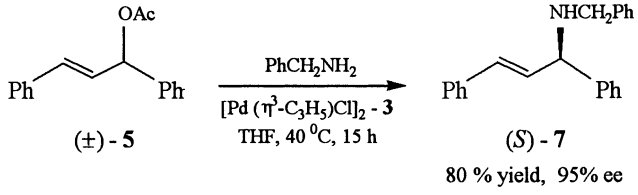


(±) - **5** (*S*) - **6**

Entry	Ligand (mol%)[b]	Solvent	Additive	Temp. (°C)	Time (h)	Yield (%)[c]	Ee (%)[d]
1	**3** (4.4)	THF	KOAc	20	0.4	97	97
2	**3** (2.2)	THF	KOAc	10	0.7	95	97
3[e]	**3** (2.2)	THF	KOAc	10	1.5	90	97
4	**3** (4.4)	THF	KOAc	0	0.9	96	96
5	**3** (4.4)	CH_2Cl_2	KOAc	10	0.7	96	95
6	**3** (2.2)	THF	NaOAc	20	0.7	97	96
7	**3** (4.4)	THF	NaOAc	10	0.8	96	97
8	**3** (4.4)	CH_2Cl_2	NaOAc	10	1	92	95
9	**3** (4.4)	CH_2Cl_2	NaOAc	20	0.7	96	94
10	**3** (2.2)	THF	LiOAc	20	0.8	97	95
11	**3** (2.2)	THF	LiOAc	10	1	95	99
12[e]	**3** (1.1)	THF	LiOAc	10	1	94	98
13	**3** (2.2)	THF	LiOAc	0	1.5	90	96
14	**3** (2.2)	CH_2Cl_2	LiOAc	10	3	70	95
15	**4** (2.2)	THF	LiOAc	20	20	35	33
16	**4** (10)	THF	LiOAc	20	20	62	32

[a] BSA (3 equiv.), dimethyl malonate (3 equiv.) and 4 mol% additive were used unless noted otherwise.
[b] Entries 1–15: ligand/$[Pd(\eta^3\text{-}C_3H_5)Cl]_2 = 2.2$, entry 16: ligand/$[Pd(\eta^3\text{-}C_3H_5)Cl]_2 = 4$.
[c] Isolated yield.
[d] Determined by HPLC with a chiralcel OD-H column. Absolute configuration was assigned by the sign of the optical rotation and the elution order from a Daicel chiralcel column.
[e] BSA (2 equiv.) and dimethyl malonate (2 equiv.) were used.

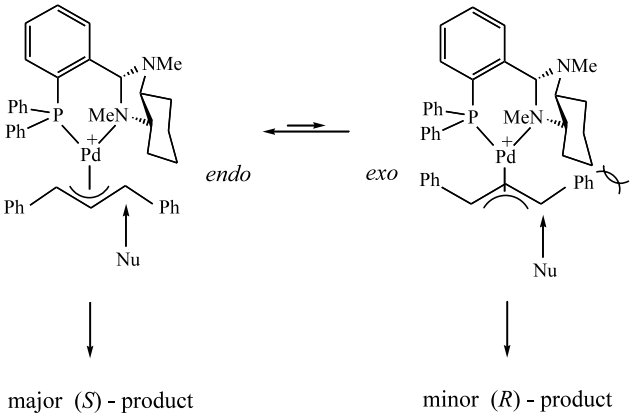
Table 1. The reaction proceeded remarkably well both in terms of enantioselectivity and reactivity. Optimum results were obtained when the reaction was performed at 10°C in THF. Use of THF is more desirable than CH_2Cl_2 in this system. Additive source seems to have little influence on the ee. BSA–LiOAc gave somewhat better enantioselectivity. Under these conditions, ligand **3** afforded the substitution product (*S*)-**6** with up to 99% ee (entry 11). The results are comparable to those of phosphinooxazolines **1** and phosphinooxazolidines **2**. It is noteworthy that nearly complete conversion and high ee were achieved with only 0.5 mol% $Pd[(\eta^3\text{-}C_3H_5)Cl]_2$ and 1.1 mol% **3** in 1 h (entry 12). In contrast, chiral *N*,*N*-homodonor ligand **4** gave low asymmetric induction and modest reactivity (entry 15 and 16). Next, the asymmetric allylic amination[9] of 1,3-diphenyl-2-propenyl acetate **5** with benzylamine was performed at 40°C in the presence of 2 mol% $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and 4.4 mol% **3**. High enantioselectivity of 95% ee was observed for the generation of (*S*)-**7**. The enantioselectivity was better than with phosphinooxazolines **1**[9b] and phosphinooxazolidines **2**.[5] The asymmetric induction by ligand **3** can be briefly explained as follows. Presumably, the nucleophilic substitution proceeds through the less sterically-hindered *endo*-π-allylpalladium complex as a major intermediate (Scheme 1). In the case of *exo*-π-allyl complex, severe repulsive interaction would be generated between the imidazolidine ring and the phenyl group in the substrate. The nucleophilic attack occurs preferentially at the allyl



(±) - **5** (*S*) - **7**

80 % yield, 95% ee

terminus *trans* to the phosphorus which is the better π-acceptor. Therefore, the (*S*)-isomer is formed as the major product, in accordance with the experimental results.



Scheme 1.

In conclusion, we have demonstrated that chiral phosphinoimidazolidine could be used as a highly efficient ligand in the asymmetric Pd-catalyzed allylic substitution. The results described above show the considerable potential of such ligands in asymmetric catalysis. Further synthesis of chiral imidazolidines and their application are underway in our laboratory.

Acknowledgements

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References

1. For recent reviews: (a) Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 497–526; (b) Trost, B. M.; van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395–422; (c) Ghosh, A. K.; Mathivanan, P.; Cappiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1–45; (d) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336–345.
2. Pfaltz, A.; Lautens, M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Yamamoto, H., Eds.; Springer: Heidelberg, 1999; Vol. 2, pp. 833–884.
3. (a) von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566–568; (b) Sprinz, J.; Helmchen, G. *Tetrahedron Lett.* **1993**, *34*, 1769–1772; (c) Dawson, G. J.; Frost, C. G.; Williams, J. M. J.; Coote, S. J. *Tetrahedron Lett* **1993**, *34*, 3149–3150; (d) Kudis, S.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3047–3050.
4. (a) Ahn, K. H.; Cho, C.-W.; Park, J.; Lee, S. *Tetrahedron: Asymmetry* **1997**, *8*, 1179–1185; (b) Sudo, A.; Yoshida, H.; Saigo, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3205–3208; (c) Pretot, R.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 323–325; (d) Imai, Y.; Zhang, W.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *Tetrahedron Lett.* **1998**, *39*, 4343–4346; (e) Hashimoto, Y.; Horie, Y.; Hayashi, M.; Saigo, K. *Tetrahedron: Asymmetry* **2000**, *11*, 2205; (f) Mino, T.; Tanaka, Y.-i.; Akita, K.; Anada, K.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2001**, *12*, 1677–1682; (g) Saitoh, A.; Achiwa, K.; Tanaka, K.; Morimoto, T. *J. Org. Chem.* **2000**, *65*, 4227–4240; (h) Fukuta, T.; Takehara, A.; Iwao, M. *Tetrahedron: Asymmetry* **2001**, *12*, 2793–2799; (i) Ito, K.; Kashiwagi, R.; Hayashi, S.; Uchida, T.; Katsuki, T. *Synlett* **2001**, *12*, 284–286; (j) Anderson, J. C.; Cubbon, R. J.; Harling, J. D. *Tetrahedron: Asymmetry* **2001**, *12*, 923–935.
5. Jin, M.-J.; Jung, J.-A.; Kim, S.-H. *Tetrahedron Lett.* **1999**, *40*, 5197–5198.
6. Synthesis of **3**: To a solution of 2-(diphenylphosphino)-benzaldehyde (290 mg, 1 mmol) in degassed benzene (5 mL), (1*S*,2*S*)-*N*,*N*′-dimethyl-cyclohexane-1,2-diamine (149 mg, 1.05 mmol) was added. The mixture was stirred at 75°C for 12 h, then concentrated under reduced pressure. The crude product was purified by short flash chromatography on silica gel pretreated with triethylamine (5% EtOAc–5% Et_3N/hexane) to yield **3** (405 mg) as a colorless glass: yield 96%; $[\alpha]_D^{20} = -59.3$ (*c* 1.5, C_6H_6); MS (EI) *m*/*e* 415 (M^+); ^1H NMR δ ($CDCl_3$, 400 MHz) 7.64 (m, 1H), 7.35–7.18 (m, 12H), 6.94 (m, 1H), 6.02 (d, $^4J_{PH}$ 4.5 Hz, 1H), 2.58 (m, 1H), 2.08 (s, 3H), 2.02 (m, 1H), 1.86 (m, 2H), 1.83 (s, 3H), 1.78 (m, 2H), 1.26 (br s, 4H). Anal. calcd for $C_{27}H_{31}N_2P$: C, 78.23; H, 7.54; N, 6.76. Found: C, 78.07; H, 7.61; N, 6.84%.
7. Alexakis, A.; Mutti, S.; Mangeney, P. *J. Org. Chem.* **1992**, *57*, 1224–1237.
8. A representative procedure for allylic alkylation: In a Schlenk tube the ligand **3** (4.6 mg, 0.011 mmol, 2.2 mol%) and allylpalladium chloride dimer (1.9 mg, 0.0052 mmol, 1.0 mol%) were dissolved in THF (0.7 mL) and the mixture was stirred at room temperature for 20 min. To this solution 1,3-diphenyl-2-propenyl acetate (130 mg, 0.52 mmol) in THF (1.6 mL), dimethyl malonate (206 mg, 1.56 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (317 mg, 1.56 mmol) and LiOAc (1.4 mg, 0.02 mmol) were successively added. The mixture was stirred at a given temperature. After the reaction was complete, the reaction mixture was diluted with ether (15 mL), washed with cold saturated aqueous ammonium chloride solution (10 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (15% EtOAc/hexane). The enantiomeric excess was determined by HPLC analysis (chiralcel OD-H column; flow rate, 0.5 mL/min; hexane:isopropanol = 99:1, $t_r = 23.4$ min, $t_s = 25.0$ min).
9. (a) Hayashi, T.; Yamamodo, A.; Ito, Y.; Nishioka, E.; Miura, H.; Yanagi, K. *J. Am. Chem. Soc.* **1989**, *111*, 6301–6311; (b) von Matt, P.; Loiseleur, O.; Koch, G.; Pfaltz, A. *Tetrahedron: Asymmetry* **1994**, *5*, 573–584; (c) Yonehara, K.; Hashizume, T.; Mori, K.; Ohe, K.; Uerura, S. *J. Org. Chem* **1999**, *64*, 9374–9380.