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New Chiral Phosphinooxazolidine Ligands for Palladium-Catalyzed Asymmetric Allylic Substitution

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Abstract: New chiral phosphinooxazolidines were prepared and examined as chiral ligands in Pd-catalyzed asymmetric allylic substitution reaction of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate or benzylamine. Enantioselectivity up to 98% was observed. © 1999 Elsevier Science Ltd. All rights reserved.

During the last decade various chiral ligands have been developed for Pd-catalyzed asymmetric allylic substitution.¹ In particular, chiral oxazolines are widely recognized to be very effective ligands in the reaction.² However, to the best of our knowledge, the structurally-similar oxazolidine ligands have never been involved in this area. With the aim of exploiting the less popular oxazolidines, we synthesized chiral phosphinooxazolidines, starting from optically active amino alcohols. Herein we wish to describe the first application of the oxazolidines as ligands to the Pd-catalyzed asymmetric allylic substitution.



Phosphinooxazolidines 1 and 2 were readily prepared by the reaction of commercially available 2-(diphenylphosphino) benzaldehyde and the corresponding (S)-N-alkylamino in refluxing benzene.³ The formation of oxazolidine ring proceeded alcohols diastereoselectively, in which la and lb were obtained as an unseparable, ca. 10:1 diastereomeric mixture in each case and 2 was in fact diastereomerically pure within NMR detection limits. (2S,4S)-cis-Oxazolidines were assigned to be major diastereomers on a combination of the ¹H NMR spectral data⁴ and the previous studies³. Similarly to the reported procedures^{2b,5}, the allylic substitutions of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate/N,O-bis(trimethylsilyl) acetamide (BSA)-KOAc or benzylamine were performed in the presence of π -allylpalladium chloride dimer and the ligands. As shown in Table 1, the reaction with dimethyl malonate proceeded remarkably well both in terms of enantioselectivity and reactivity. The ligand la afforded the alkylation product of with 98%

	O ₂ Me) ₂ 3 eq. CH ₂ (CO ₂ Me) ₂ 3 eq. BSA, 3 mol% KOAc ³ = 2.5 mol% iPd(allvi)ClL		Ph	2 eq. Ph		Ph B
A	10	10 mol% ligand		5 m	ol% ligand	
Entry	Ligand	Solvent	Temp.(℃)	Time(h)	Yield(%) ^a	%ee ^b (Confg. ^c)
1	1 a	THF	22	0.5	98	96(S)
2	1 a	THF	10	0.5	98	98
3	1 a	THF	0	1.0	97	98
4	1 a	CH ₂ Cl ₂	0	0.8	97	96
5	1 b	THF	10	1.5	94	97(S)
6	1 b	CH ₂ Cl ₂	0	2.0	95	96
7	2	THF	22	1.5	94	94(S)
8	<u>la</u>	THF	30	12.0	51	60(R)

Table 1. Asymmetric Pd-catalyzed allylic substitution of 1,3-diphenyl-2-propenyl acetate

Entry 1-7: for reaction with dimethyl malonate, entry 8: for reaction with benzylamine. a) Isolated yields. b) Determined by HPLC with chiralcel OD column (25cm x 0.46cm): A: 1% 2-propanol in hexane, flow rate=0.5mL/min, $t_R(min)=25.6(R)$, 27.5(S); B: 0.5% 2-propanol in hexane, flow rate=0.5mL/min, $t_R(min)=23.8(R)$, 25.3(S). c) Assigned by comparison of its sign of the optical rotation with literature data.

ee (entry 2-3). In comparison, moderate enantioselectivity was observed in the amination with benzylamine (entry 8).

In conclusion, we have developed a new class of chiral ligands, phosphinooxazolidines, for the asymmetric Pd-catalyzed allylic substitution. Further synthesis of chiral oxazolidines and their application to asymmetric catalysis are underway in our laboratory.

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- 4. Selected data for la: MS (EI) m/z 389 (M⁺); ¹H-NMR (250 MHz, CDCl₃) δ 7.94-6.93 (m, Ar), 6.02 (d, ⁴J_{PH} 4.5 Hz, OCH'N) + 5.61 (d, ⁴J_{PH} 6.3 Hz, OCHN), 3.87 (dd, J 13.3, 7.9 Hz, OCH₂CH), 3.84 (dd, J 13.2, 7.9 Hz, OCH₂CH), 2.57 (ddd, J 13.8, 7.4, 2.4 Hz, CH₂CHN), 2.03 (s, NCH₃), 1.92(m, CHCHCH₃), 1.01 (d, J 6.8 Hz, CHCH₃) + 0.77 (d, J 6.6 Hz, CHCH'₃), 0.96 (d, J 6.9 Hz, CHCH₃)+ 0.61 (d, J 6.5 Hz, 3H, CHCH'₃). H' corresponds to minor diastereomer.
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