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New Chiral Phosphinooxazolidine Ligands for Palladium-Catalyzed Asymmetric Allylic Substitution

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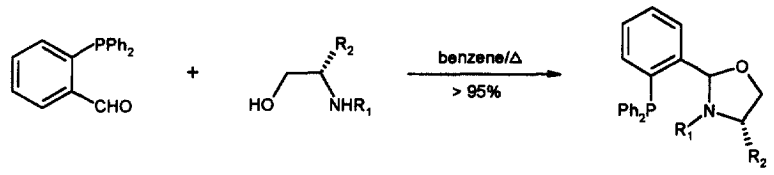
Abstract: New chiral phosphinooxazolidines were prepared and examined as chiral ligands in Pd-catalyzed asymmetric allylic substitution reaction of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate or benzylamine. Enantioselectivity up to 98% was observed.

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.



1a : R_1 = Me, R_2 = *i*-Pr
1b : R_1 = Bu, R_2 = *i*-Pr
2 : R_1 = Me, R_2 = Ph

Phosphinooxazolidines **1** and **2** were readily prepared by the reaction of commercially available 2-(diphenylphosphino)benzaldehyde and the corresponding (*S*)-*N*-alkylamino alcohols in refluxing benzene.[3] The formation of oxazolidine ring proceeded diastereoselectively, in which **1a** and **1b** 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 ^{1}H NMR spectral data[4] and the previous studies[3]. 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 **1a** afforded the alkylation product of with 98%

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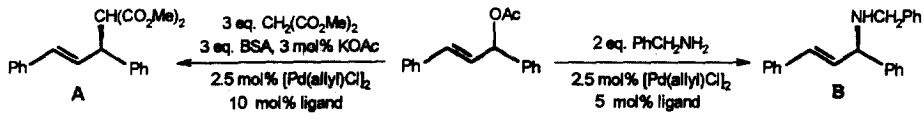
Table 1. Asymmetric Pd-catalyzed allylic substitution of 1,3-diphenyl-2-propenyl acetate



Entry	Ligand	Solvent	Temp.(℃)	Time(h)	Yield(%)[a]	%ee[b] (Confg.[c])
1	1a	THF	22	0.5	98	96(S)
2	1a	THF	10	0.5	98	98
3	1a	THF	0	1.0	97	98
4	1a	CH_2Cl_2	0	0.8	97	96
5	1b	THF	10	1.5	94	97(S)
6	1b	CH_2Cl_2	0	2.0	95	96
7	2	THF	22	1.5	94	94(S)
8	1a	THF	30	12.0	51	60(R)

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 asymmeric Pd-catalyzed allylic substitution. Further synthesis of chiral oxazolidines and their application to asymmetric catalysis are underway in our laboratory.

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References and Notes

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4. Selected data for **1a**: MS (EI) *m/z* 389 (M^+); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.94-6.93 (m, Ar), 6.02 (d, $^4J_{PH'}$ 4.5 Hz, OC*H'*N) + 5.61 (d, $^4J_{PH}$ 6.3 Hz, OC*H*N), 3.87 (dd, *J* 13.3, 7.9 Hz, OC*H*$_2$CH), 3.84 (dd, *J* 13.2, 7.9 Hz, OC*H*$_2$CH), 2.57 (ddd, *J* 13.8, 7.4, 2.4 Hz, CH_2CHN), 2.03 (s, NC*H*$_3$), 1.92(m, CHC*H*CH$_3$), 1.01 (d, *J* 6.8 Hz, CHC*H*$_3$) + 0.77 (d, *J* 6.6 Hz, CHC*H'*$_3$), 0.96 (d, *J* 6.9 Hz, CHC*H*$_3$)+ 0.61 (d, *J* 6.5 Hz, 3H, CHC*H'*$_3$). H' corresponds to minor diastereomer.
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