

New oxazoline-containing phosphoramidite ligand for palladium-catalyzed asymmetric allylic sulfonation

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New chiral oxazoline-containing phosphoramidite was synthesized and its complex formation with rhodium(I) and palladium(II) was examined. The new ligand is a highly efficient chiral inductor (*ee* up to 92%) in palladium-catalyzed asymmetric sulfonation of 1,3-diphenylallyl acetate with sodium *p*-toluenesulfinate.

Key words: *P,N*-ligands, chiral phosphoramidites, palladium, rhodium, asymmetric allylic sulfonation.

Phosphine derivatives of chiral oxazolines represent the largest and most efficient group of *P,N*-bidentate ligands used in the modern asymmetric catalysis.^{1,2} In recent years, oxazoline-based phosphites have found application as such ligands, which have advantages due to their synthetic accessibility and pronounced π -acidity of the phosphorus center. These compounds were successfully tested in allylic alkylation, hydrosilylation, and conjugated addition of organometallic reagents to enones.^{1–3}

One approach to the design of *P,N*-bidentate derivatives of phosphorous acid involves the introduction of the (2*R*,5*S*)-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane core into these compounds.

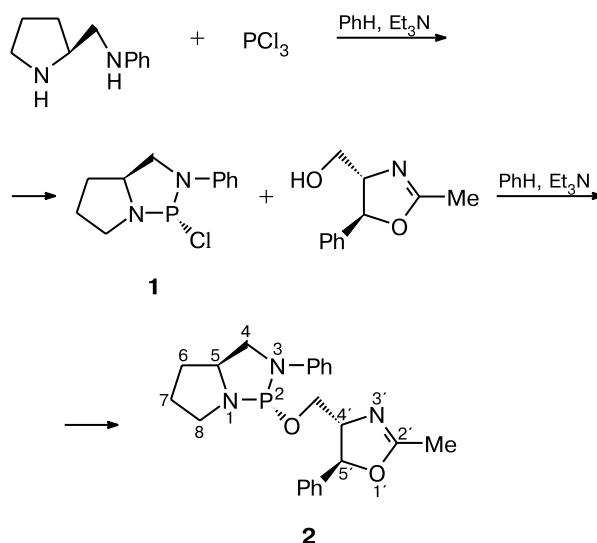
These systems have already made a considerable contribution to palladium-catalyzed amination and alkylation as well as to copper-catalyzed Diels–Alder reactions and the addition of diethylzinc to unsaturated ketones (see the study⁴ and references cited therein).

In the present study, we developed a convenient procedure for the synthesis of chiral phosphoramidite of a new type, which possesses both the above-mentioned phosphabicyclic core and oxazoline periphery. This compound proved to exhibit high asymmetrizing activity in Pd-catalyzed allylic sulfonation.

Results and Discussion

The new *P,N*-bidentate ligand was synthesized with the involvement of phosphorylating agent **1**, which was prepared by us for the first time (Scheme 1).

Scheme 1

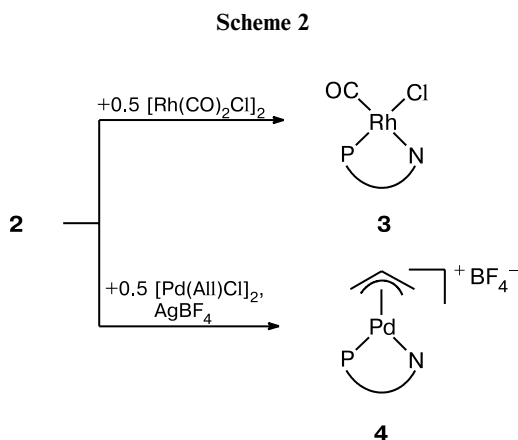


It should be noted that reagent **1** containing the chiral P atom can be readily prepared in good yield by diastereoselective phosphorylation of (*S*)-2-(anilinomethyl)pyrrolidine. The latter, in turn, is conveniently synthesized from readily accessible *L*-glutamic acid. Reagent **1** is stable on storage under a dry atmosphere, easily purified by vacuum distillation, and can be prepared in multigram amounts. Earlier, ligands with the (2*R*,5*S*)-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane core have been synthesized exclusively with the use of amides of phosphorous acid

(P(NMe₂)₃ or P(NEt₂)₃).^{4,5} In this approach, each synthetic step requires refluxing a mixture of the reagents in toluene for two hours, which could be responsible for accumulation of destruction products of phosphoramidites and isomerization of stereochemically nonrigid synthons. By contrast, compound **1** readily and efficiently performs phosphorylation under rather mild conditions (see the Experimental section).

Ligand **2** (**L**) is stable on prolonged storage and is readily soluble in different organic solvents. This ligand contains the stereogenic phosphorus center with the (*R*) configuration, as evidenced by the characteristic^{4,5} spin-spin coupling constant (²*J*_{C(8),P} = 38.2 Hz) in its ¹³C NMR spectrum (see the Experimental section).

In the next stage of our study, we examined the complex formation with ligand **2** (Scheme 2).



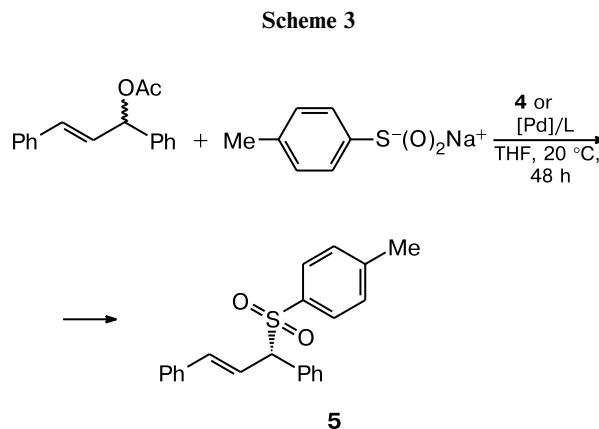
It should be noted that the reaction of ligand **2** with [Rh(CO)₂Cl]₂ proceeded nonselectively and afforded chelate compound **3** along with the *trans*-[Rh(CO)Cl(η¹-P[∘]N)] complex,* as evidenced⁴ by the presence of a doublet signal (δ_P 124.21, ¹*J*_{P,Rh} = 180.6 Hz) in the ³¹P NMR spectrum of the reaction solution in CHCl₃. The parameters of the ³¹P NMR and IR spectra of compound **3** (δ_P 119.68, ¹*J*_{P,Rh} = 242.9 Hz; ν(CO) = 2008 cm⁻¹ (CHCl₃)) indicate that oxazoline-containing phosphoramidite **2** holds an intermediate position between aminophosphines and aminophosphites in the stereochemical series of phosphorus-containing ligands.^{4,6}

By contrast, cationic palladium(II) chelate complex **4** was obtained in virtually quantitative yield. The ³¹P NMR spectrum of its solution in CDCl₃ has narrow singlets at δ_P 119.33 and 118.72 with intensities of 63 and 37% belonging to the *exo* and *endo* isomers of **4**, respectively.⁴ The FAB mass spectrum shows characteristic

* Hereinafter, the symbol «[∘]» denotes the residue of ligand **2**, which does not contain P and N atoms.

ion peaks at *m/z* (*I*_{rel} (%)) 542 [M – BF₄]⁺ (100), 396 [L + H]⁺.

Along with other Pd complexes possessing ligand **2**, complex **4** was used as the catalyst of asymmetric allylic sulfonylation (Scheme 3).



The results of the catalytic study are summarized in Table 1. It should be noted that the reactions with the use of complex **4** and the [Pd(All)Cl]₂/2L system gave virtually the same results (see Table 1, runs 1 and 2). It is reasonable to suggest that this is associated with the fact that the catalytically active metal complexes [Pd(All)(η²-P[∘]N)]⁺X⁻ (X⁻ = BF₄⁻ or Cl⁻) have similar structures. At the same time, the use of the Pd⁰ complex [Pd₂(dba)₃·CHCl₃] (dba is dibenzylideneacetone) as a precatalyst allowed us to noticeably improve the asymmetric induction (see Table 1, run 3), although the chemical yield was decreased.

Ligand **2** provides a high degree of enantioselectivity. Thus, the reactions with the use of the oxazoline-based phosphine—[Pd(PPh₃)₄] system increased *ee* to 93%,⁷ whereas bis(diphenylphosphinite) complexes based on the known stereoselective reagent TADDOL allowed one to obtain *ee* of at most 68%.⁸ It should be emphasized that phosphoramidite **2** has advantages, such as a simple procedure for its preparation from readily available reagents and chemical stability, particularly, with respect to oxidative effects.

Table 1. Results of catalytic allylic sulfonylation of 1,3-diphenylallyl acetate using Pd complexes with ligand **2**

Run	Catalytic system	Yield of 5	<i>ee</i>
		(%)	
1	Complex 4	58	77 (<i>S</i>)
2	[Pd(All)Cl] ₂ /2L	66	82 (<i>S</i>)
3	[Pd ₂ (dba) ₃ •CHCl ₃]/2L	33	92 (<i>S</i>)

Experimental

The ^{31}P and ^{13}C NMR spectra were recorded on a Bruker AMX-400 instrument (161.98 and 100.61 MHz) with respect to 85% H_3PO_4 in D_2O and CDCl_3 (δ_{C} 76.91), respectively. The assignments of the signals of compounds **1** and **2** in the ^{13}C NMR spectra were made with the use of the DEPT technique and data published in the literature.^{4,5} The mass spectra (EI, 70 eV) were measured on a Varian MAT-311 instrument. The plasma-desorption (PD) ionization mass spectra were obtained on an MSVKh instrument with the use of ^{252}Cf fission fragments. The fast atom bombardment (FAB) ionization mass spectra were recorded on an AMD-402 instrument. The optical yield of compound **5** was determined by HPLC on a Varian 5000 chromatograph equipped with an (R, R) WHELK-01 chiral column (hexane— Pr^iOH (4 : 1) as the eluent, 1 mL min^{-1} , absorption detection at $\lambda = 254\text{ nm}$) according to recommendations of the study.⁸

The starting substrate (1,3-diphenylallyl acetate) was synthesized according to a known procedure.⁹ Sodium *p*-toluenesulfinate (Acros Organic) used as a nucleophile was dried *in vacuo* (2 h, 80 °C, 1 Torr). The spectroscopic and physico-chemical characteristics of product **5** are identical with those published in the literature.^{7,8}

All reactions were carried out under an atmosphere of dry argon in anhydrous solvents. Phosphorus trichloride was distilled immediately before use. (*S*)-2-(Anilinomethyl)pyrrolidine, which was synthesized according to a known procedure,⁵ was subjected to azeotropic drying with benzene and vacuum distillation (1 Torr) immediately before use. (4*S*,5*S*)-(–)-2-Methyl-4-hydroxymethyl-5-phenyl-2-oxazoline (Fluka) was dried *in vacuo* (2 h, 1 Torr) before use. The starting $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ and $[\text{Pd}(\text{All})\text{Cl}]_2$ complexes were prepared according to known procedures.^{9,10}

(2*R*,5*S*)-2-Chloro-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane (1). Phosphorus trichloride (0.36 mL, 4.1 mmol) and Et_3N (1.12 mL, 8.2 mmol) were dissolved in benzene (40 mL). Then a solution of (*S*)-2-(anilinomethyl)pyrrolidine (0.722 g, 4.1 mmol) in benzene (20 mL) was slowly added dropwise with vigorous stirring and cooling to 0 °C. The resulting solution was heated with vigorous stirring and then cooled to 20 °C, $\text{Et}_3\text{N} \cdot \text{HCl}$ was filtered off, and the filtrate was concentrated *in vacuo* (40 Torr). The residue was evacuated (10 Torr) for 30 min (the residue solidified as large beige crystals). The product was distilled *in vacuo* (1 Torr). The yield was 0.70 g (71%), a white crystalline powder, m.p. 110–111 °C, b.p. 156–158 °C (1 Torr). Found (%): C, 55.27; H, 5.58; N, 11.95. $\text{C}_{11}\text{H}_{14}\text{ClN}_2\text{P}$. Calculated (%): C, 54.90; H, 5.86; N, 11.64. ^{31}P NMR (CDCl_3), δ : 153.66. ^{13}C NMR (CDCl_3), δ : 27.48 (s, C(7)); 30.83 (s, C(6)); 44.08 (s, C(8)); 52.22 (s, C(4)); 65.97 (s, C(5)); 116.96–142.74 (C_{Ph}). MS (EI), m/z (I_{rel} (%)): 240, 242 $[\text{M}]^+$ (56), 205 $[\text{M} - \text{Cl}]^+$ (100), 307 $[\text{M} - \text{PCl}]^+$ (12).

(2*R*,5*S*,4′*S*,5′*S*)-2-[(2′-Methyl-5′-phenyl-2′-oxazolin-4′-yl)methoxy]-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane (2). Reagent **1** (0.377 g, 1.57 mmol) and Et_3N (0.21 mL, 1.57 mmol) were dissolved in benzene (10 mL). Then (4*S*,5*S*)-(–)-2-methyl-4-hydroxymethyl-5-phenyl-2-oxazoline (0.3 g, 1.57 mmol) was added with vigorous stirring and cooling

to 0 °C. The resulting solution was stirred for 10 min, heated to 60 °C over a short period of time, and cooled to 20 °C. Then $\text{Et}_3\text{N} \cdot \text{HCl}$ was filtered off, the filtrate was concentrated *in vacuo* (40 Torr), and the residue was evacuated (2 h, 1 Torr). The yield was 0.527 g (85%), a transparent resin, $[\alpha]_{\text{D}}^{25} -204.7$ (c 0.6, CHCl_3). Found (%): C, 67.12; H, 6.51; N, 10.77. $\text{C}_{22}\text{H}_{26}\text{N}_3\text{O}_2\text{P}$. Calculated (%): C, 66.82; H, 6.63; N, 10.63. ^{31}P NMR (CDCl_3), δ : 121.67. ^{13}C NMR (CDCl_3), δ : 13.90 (s, Me); 25.91 (d, C(7), $^3J_{\text{C,P}} = 2.9\text{ Hz}$); 31.99 (s, C(6)); 48.38 (d, C(8), $^2J_{\text{C,P}} = 38.2\text{ Hz}$); 54.69 (d, C(4), $^2J_{\text{C,P}} = 7.3\text{ Hz}$); 62.62 (d, CH_2O , $^2J_{\text{C,P}} = 5.0\text{ Hz}$); 63.03 (d, C(5), $^2J_{\text{C,P}} = 8.9\text{ Hz}$); 74.74 (d, C(4′), $^3J_{\text{C,P}} = 1.9\text{ Hz}$); 83.30 (s, C(5′)); 112.07–147.51 (C_{Ph}); 165.10 (s, C(2′)). MS (EI), m/z (I_{rel} (%)): 395 $[\text{M}]^+$ (2), 237 (18), 70 $[\text{N}(\text{CH}_2)_4]^+$ (100). MS (PD), m/z (I_{rel} (%)): 395 $[\text{M}]^+$ (42), 205 (100), 70 $[\text{N}(\text{CH}_2)_4]^+$ (39).

Rhodium complex **3** was prepared and characterized by spectroscopic methods in a solution in CHCl_3 without isolation according to a procedure described earlier.⁴

{(2*R*,5*S*,4′*S*,5′*S*)-2-[(2′-Methyl-5′-phenyl-2′-oxazolin-4′-yl)methoxy]-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane}[π -allyl]palladium tetrafluoroborate (4). A solution of oxazolinophosphoramidite **2** (0.395 g, 1 mmol) in CHCl_3 (15 mL) was added dropwise with vigorous stirring to a solution of $[\text{Pd}(\text{All})\text{Cl}]_2$ (0.183 g, 0.5 mmol) in CHCl_3 (15 mL) at 20 °C for 30 min. The reaction mixture was stirred at 20 °C for 1 h and then a solution of AgBF_4 (0.195 g, 1 mmol) in THF (15 mL) was added. The reaction mixture was stirred for 1 h and the precipitate of AgCl that formed was filtered off. The filtrate was concentrated *in vacuo* (40 Torr) to ~0.5 mL and precipitated with Et_2O . The precipitated that formed was separated by centrifugation, washed with Et_2O ($2 \times 5\text{ mL}$), and dried in air and *in vacuo* (1 Torr). The yield was 0.548 g (87%), a white powder, m.p. 160–162 °C (with decomp.). Found (%): C, 47.43; H, 5.32; N, 6.34. $\text{C}_{25}\text{H}_{31}\text{BF}_4\text{N}_3\text{O}_2\text{PPd}$. Calculated (%): C, 47.68; H, 4.96; N, 6.67.

Palladium-catalyzed allylic sulfonylation of 1,3-diphenylallyl acetate with sodium *p*-toluenesulfinate (general procedure). A solution of $[\text{Pd}(\text{All})\text{Cl}]_2$ (3.7 mg, 0.01 mmol) or $[\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3]$ (10.3 mg, 0.01 mmol) and ligand **2** (7.9 mg, 0.02 mmol) in THF (5 mL) was stirred for 40 min (or complex **4** (0.02 mmol), which has been prepared beforehand, was dissolved in THF (5 mL)). Then 1,3-diphenylallyl acetate (0.1 mL, 0.5 mmol) was added, the reaction mixture was stirred for 15 min, and sodium *p*-toluenesulfinate (178 mg, 1 mmol) was added. The reaction mixture was stirred for 48 h. Then a saturated aqueous solution of NaCl (10 mL) was added. The reaction mixture was stirred for 1 h and extracted with THF ($3 \times 7\text{ mL}$). The organic phase was washed with a saturated aqueous solution of NaCl ($2 \times 7\text{ mL}$) and dried with MgSO_4 after which MgSO_4 was filtered off. The filtrate was recrystallized from 95% EtOH and dried *in vacuo* (12 h, 10 Torr). Product **5** was obtained as a milk-white crystalline compound. The theoretical yield was 174 mg.

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