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

K. N. Gavrilov,[a] O. G. Bondarev,[b]★ V. N. Tsarev,[b] A. A. Shiryaev,[a] S. E. Lyubimov,[a] A. S. Kucherenko,[a] and V. A. Davankov[b]

[a]S. A. Esenin Ryazan State Pedagogic University, 46 ul. Svobody, 390000 Ryazan, Russian Federation. Fax: +7 (091 2) 44 4390. E-mail: chem@ttc.ryazan.ru

[b]A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. Fax: +7 (095) 135 6471. E-mail: bond@ineos.ac.ru

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 sulfonylation of 1,3-diphenylallyl acetate with sodium *p*-toluenesulfinate.

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

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.

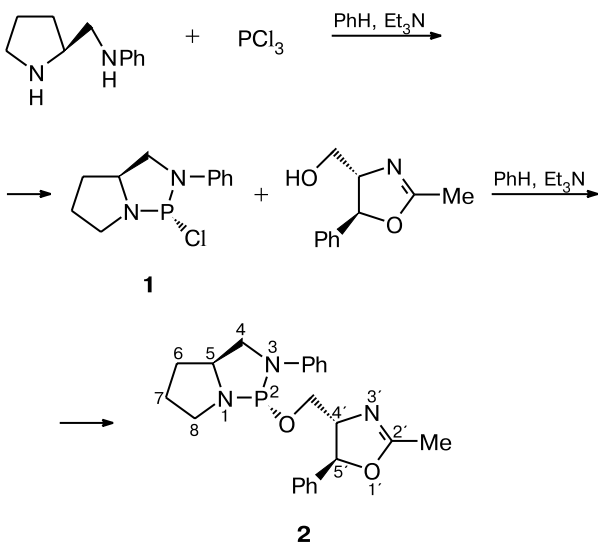
These systems have already made a considerable contribution to palladium-catalyzed amination and alkylation as well as to copper-catalyzed Diels—Alder reactions and the addition of diethylzinc to unsaturated ketones (see the study[4] and references cited therein).

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 sulfonylation.

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

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 1, pp. 116—118, January, 2003.

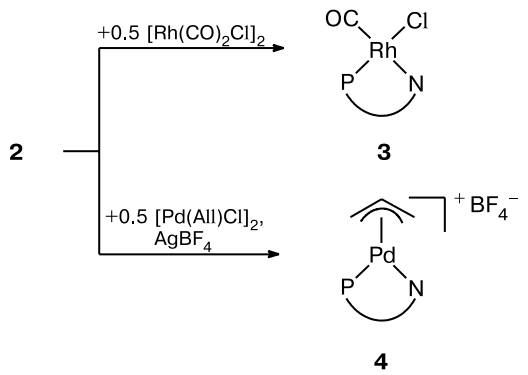
1066-5285/03/5201-122 $25.00

($P(NMe_2)_3$ or $P(NEt_2)_3$).[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 ($^2J_{C(8),P}$ = 38.2 Hz) in its ^{13}C NMR spectrum (see the Experimental section).

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

Scheme 2

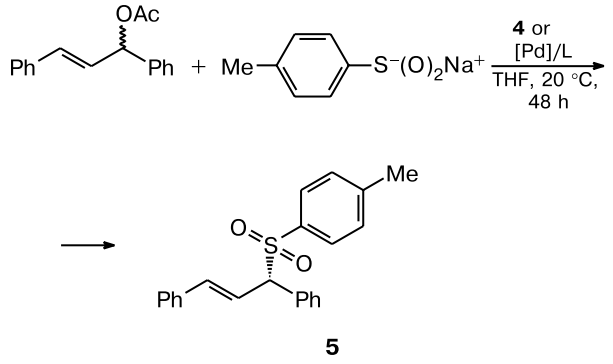


It should be noted that the reaction of ligand **2** with $[Rh(CO)_2Cl]_2$ proceeded nonselectively and afforded chelate compound **3** along with the *trans*-$[Rh(CO)Cl(\eta^1\text{-P}\frown\text{N})_2]$ complex,* as evidenced[4] by the presence of a doublet signal (δ_P 124.21, $^1J_{P,Rh}$ = 180.6 Hz) in the ^{31}P NMR spectrum of the reaction solution in $CHCl_3$. The parameters of the ^{31}P NMR and IR spectra of compound **3** (δ_P 119.68, $^1J_{P,Rh}$ = 242.9 Hz; ν(CO) = 2008 cm^{-1} ($CHCl_3$)) 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 ^{31}P NMR spectrum of its solution in $CDCl_3$ 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 ion peaks at *m/z* (I_{rel} (%)) 542 $[M - BF_4]^+$ (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).

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 $[Pd(All)(\eta^2\text{-P}\frown\text{N})]^+X^-$ ($X^- = BF_4^-$ or Cl^-) have similar structures. At the same time, the use of the Pd^0 complex $[Pd_2(dba)_3 \cdot CHCl_3]$ (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—$[Pd(PPh_3)_4]$ 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**	*ee*
		(%)	
1	Complex **4**	58	77 (*S*)
2	$[Pd(All)Cl]_2$/2L	66	82 (*S*)
3	$[Pd_2(dba)_3 \cdot CHCl_3]$/2L	33	92 (*S*)

* Hereinafter, the symbol «$\frown$» denotes the residue of ligand **2**, which does not contain P and N atoms.

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 λ = 254 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 physicochemical 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 $[Rh(CO)_2Cl]_2$ and $[Pd(All)Cl]_2$ 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, $Et_3N \cdot HCl$ 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. $C_{11}H_{14}ClN_2P$. 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 $[M]^+$ (56), 205 $[M - Cl]^+$ (100), 307 $[M - PCl]^+$ (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 $Et_3N \cdot HCl$ 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, $[\alpha]_D^{25}$ −204.7 (*c* 0.6, $CHCl_3$). Found (%): C, 67.12; H, 6.51; N, 10.77. $C_{22}H_{26}N_3O_2P$. 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), $^3J_{C,P}$ = 2.9 Hz); 31.99 (s, C(6)); 48.38 (d, C(8), $^2J_{C,P}$ = 38.2 Hz); 54.69 (d, C(4), $^2J_{C,P}$ = 7.3 Hz); 62.62 (d, CH_2O, $^2J_{C,P}$ = 5.0 Hz); 63.03 (d, C(5), $^2J_{C,P}$ = 8.9 Hz); 74.74 (d, C(4′), $^3J_{C,P}$ = 1.9 Hz); 83.30 (s, C(5′)); 112.07—147.51 (C_{Ph}); 165.10 (s, C(2′)). MS (EI), *m/z* (I_{rel} (%)): 395 $[M]^+$ (2), 237 (18), 70 $[N(CH_2)_4]^+$ (100). MS (PD), *m/z* (I_{rel} (%)): 395 $[M]^+$ (42), 205 (100), 70 $[N(CH_2)_4]^+$ (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 $[Pd(All)Cl]_2$ (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 (2×5 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. $C_{25}H_{31}BF_4N_3O_2PPd$. 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 $[Pd(All)Cl]_2$ (3.7 mg, 0.01 mmol) or $[Pd_2(dba)_3 \cdot CHCl_3]$ (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 (3×7 mL). The organic phase was washed with a saturated aqueous solution of NaCl (2×7 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.

We thank the Regis Technologies (USA) for a gift of an (R, R) WHELK-01 chiral column.

This study was financially supported by the Russian Foundation for Basic Research (Project Nos. 00-15-99341 and 00-15-97427) and Haldor Topsøe A/S.

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Received July 2, 2002;
in revised form October 2, 2002