[(1*S*)-*endo*]-(−)-Borneol-tethered oxazoline phosphite as a *P*,*N*-bidentate ligand in palladium-catalyzed enantioselective allylic amination

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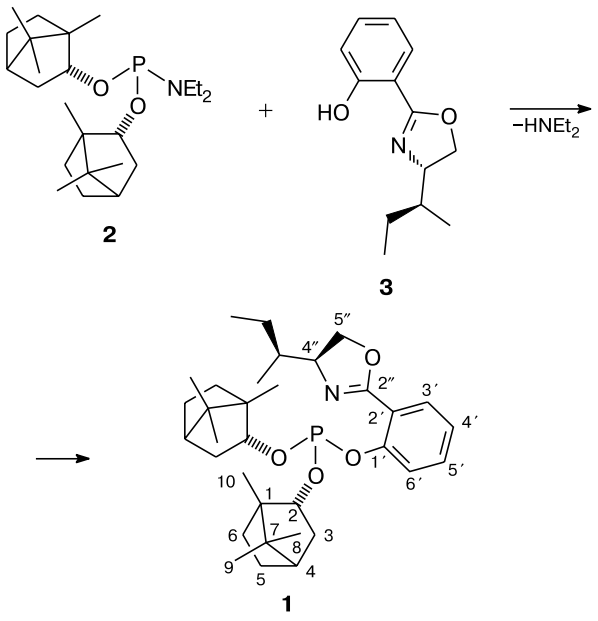
P,*N*-Bidentate oxazoline phosphite containing an acyclic phosphorus center with [(1*S*)-*endo*]-(−)-borneol fragments and its palladium chelate complex $[Pd(\eta\text{-}C_3H_5)(\eta^2\text{-}P,N)]BF_4$ were synthesized for the first time. The use of this new ligand in Pd-catalyzed asymmetric amination of 1,3-diphenylpropenyl acetate with pyrrolidine afforded the product with 86% *ee*.

Key words: chiral phosphites, ligands, palladium complexes, asymmetric amination, metal complex catalysis, asymmetric synthesis.

Oxazoline phosphites are highly-efficient ligands for asymmetric catalysis by transition metal complexes.[1,2] Their potentials as stereoselectors are largely determined by the structure of the phosphorus center. In recent years, considerable progress has been achieved in its rational design allowing various phosphocyclane systems[3—6] and acyclic pyrrolyl and aryl phosphites.[7—9] Oxazoline ligands with an acyclic phosphorus center are of interest because they have particular stereochemical and electronic characteristics and make it possible to avoid the formation of strained metal chelates with phosphorus as spiro atoms.[7,10] However, such compounds containing chiral substituents at the P atom have not been documented. Here we describe the first oxazoline phosphite with an acyclic phosphorus atom linked with chiral hydrocarbon fragments, as well as its successful use in Pd-catalyzed enantioselective amination.

Scheme 1



Results and Discussion

Previously unknown oxazoline phosphite **1** was obtained as shown in Scheme 1. This method is convenient and simple because dihydrooxazolylphenol **3** is directly phosphitilated with reagent **2** in the absence of any solvent. In turn, phosphitilating reagent **2** is easily accessible *via* alcoholysis of $P(NEt_2)_3$ with [(1*S*)-*endo*]-(−)-borneol in the absence of any solvent with subsequent purification by vacuum distillation.[11] Product **1** was isolated in high yield from the reaction mixture by single extraction with hexane. The compound obtained is stable in prolonged storage in a dry atmosphere and is well soluble in organic solvents. It should be emphasized that acyclic phosphites and phosphoramidites are prone to disproportionation on heating or even on standing; however, compounds **1** and **2** are stable.

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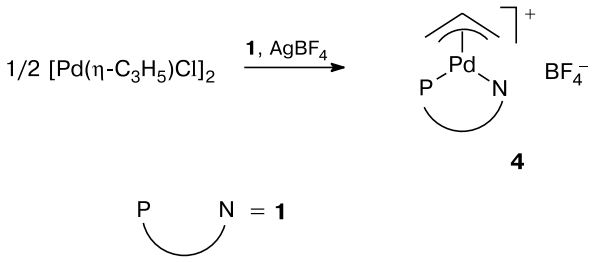
A reaction of phosphite **1** with $[Pd(\eta\text{-}C_3H_5)Cl]_2$ in the presence of $AgBF_4$ gave cationic metal chelate **4** with the *cis*-orientation of the P and N atoms (Scheme 2).

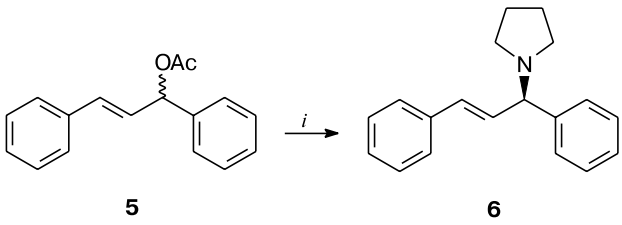
Scheme 2



The presence of a slightly broadened singlet at δ_P 135.7 in the ^{31}P NMR spectrum of complex **4** in $CDCl_3$ indicates relatively slow interconversions of its *exo*- and *endo*-isomers.[7,9]

Oxazoline phosphite **1** and its complex **4** were tested in a model Pd-catalyzed enantioselective amination of 1,3-diphenylpropenyl acetate with pyrrolidine (Scheme 3).

Scheme 3



i. Pyrrolidine, catalyst **4**.

The results obtained are summarized in Table 1. The catalytic systems $[Pd(\eta\text{-}C_3H_5)Cl]_2$/2L and $[Pd(\eta\text{-}C_3H_5)Cl]_2$/4L in THF ensured virtually equal conversions of substrate **5** and *ee* values of product **6** (see Table 1, entries *1*, *2*). The reaction in CH_2Cl_2 was more enantioselective for the molar ratio L/Pd = 2 (see Table 1, entries *3* and *4*). Preliminarily prepared complex **4** proved to be an optimum stereoselector: the conversions and asymmetric inductions were comparable in both solvents (see Table 1, entries *5*, *6*), the highest optical yield (86% *ee*) being reached in CH_2Cl_2.

Table 1. Data on the palladium-catalyzed allylic amination of compound **5** with pyrrolidine in the presence of different palladium complexes with ligand **1**

Entry	Catalyst	Solvent	*C** for **5**	*ee* of **6**
			%	
1	$[Pd(\eta\text{-}C_3H_5)Cl]_2$/2L	THF	43	63 (*R*)
2	$[Pd(\eta\text{-}C_3H_5)Cl]_2$/4L	THF	46	67 (*R*)
3	$[Pd(\eta\text{-}C_3H_5)Cl]_2$/2L	CH_2Cl_2	73	47 (*R*)
4	$[Pd(\eta\text{-}C_3H_5)Cl]_2$/4L	CH_2Cl_2	67	65 (*R*)
5	**4**	THF	86	80 (*R*)
6	**4**	CH_2Cl_2	71	86 (*R*)

* Conversion.

To conclude, we accomplished for the first time the synthesis of chiral *P*,*N*-bidentate oxazoline phosphite with an acyclic phosphorus center on the basis of accessible [(1*S*)-*endo*]-(−)-borneol. Its Pd complex is highly active in Pd-catalyzed allylic amination and ensures its good enantioselectivity.

Experimental

^{31}P and ^{13}C NMR spectra were recorded on a Bruker AMX-400 instrument (161.98 (^{31}P) and 100.61 MHz (^{13}C)) with reference to 85% H_3PO_4 in D_2O and $CDCl_3$ (δ_C 76.91), respectively. The DEPT technique and data from Ref. 11 were used to assign the signals in the ^{13}C NMR spectra. Mass spectra (EI, 70 eV) were recorded on a Varian MAT-311 instrument. Mass spectra (ESI) were recorded on a Finnigan LCQ Advantage instrument. The conversion of substrate **5** and the *ee* values of product **6** were determined by HPLC on a Daicel Chiralcel OD-H chiral column as recommended earlier.[12] The optical rotation was measured on an SM-3 polarimeter. The rotation is given in deg mL g^{-1} dm^{-1}; the concentration of the solution is given in g (100 mL)$^{-1}$. Elemental analysis was performed at the Laboratory of organic microanalysis (A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences).

All reactions were carried out in anhydrous solvents under dry argon. Bis((1*S*,2*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl) *N*,*N*-diethylphosphoramidite (**2**), 2-((*S*)-4-*sec*-butyl-4,5-dihydrooxazol-2-yl)phenol (**3**), and the starting complex $[Pd(\eta\text{-}C_3H_5)Cl]_2$ were prepared according to known procedures.[11,13,14] Complex **4** (see Ref. 15) and 1,3-diphenylpropenyl acetate (**5**)[14] were synthesized as described earlier.

Catalytic allylic amination of compound **5** with pyrrolidine was carried out as described earlier.[16] Pyrrolidine (Acros Organics) was distilled over KOH and used freshly distilled over $LiAlH_4$.

2-((*S*)-4-*sec*-Butyl-4,5-dihydrooxazol-2-yl)phenyl bis((1*S*,2*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl) phosphite (1). Dihydrooxazolylphenol **3** (1.096 g, 5 mmol) was added to phosphitilating reagent **2** (2.048 g, 5 mmol). The mixture was heated with vigorous stirring to 130 °C, kept at this temperature for 1.5 h, and then evacuated (1 Torr) at 100 °C for 1 h. The resulting white suspension was shaken with hexane (5 mL) to extract the product and the extract was filtered and concentrated *in vacuo* (40 Torr). The residue was dried *in vacuo* (1 Torr) at 50 °C for 1 h. The yield was 2.278 g (82%), a colorless viscous oil, $[\alpha]^{20}_D$ −51.4 (*c* 1.0, CH_2Cl_2). Found (%): C, 71.04; H, 8.95; N, 2.59. $C_{33}H_{50}NO_4P$. Calculated (%): C, 71.32; H, 9.07; N, 2.52. ^{31}P NMR ($CDCl_3$), δ: 137.0. ^{13}C NMR ($CDCl_3$), δ: 10.8 (Me); 12.5 (C(10)); 13.9 (Me); 18.0 (C(8)); 19.1 (C(9)); 25.3 (CH_2); 25.8 (C(6)); 27.3 (C(5)); 37.1 (C(3)); 38.3 (CH); 44.2 (C(4)); 46.7 (C(7)); 48.8 (C(1)); 68.6 (C(5″)); 70.0 (C(4″)); 78.3 (d, C(2), $^2J_{C,P}$ = 8.1 Hz); 120.0 (C(2′)); 121.7 (C(6′));

127.1 (C(4′)); 130.5 (C(3′)); 132.3 (C(5′)); 150.9 (C(1′)); 159.1 (C(2′′)). MS (EI), m/z (I_{rel} (%)): 556 $[M]^{+\bullet}$ (3), 403 $[M - C_{10}H_{17}O]^+$ (5), 219 $[M - (C_{10}H_{17}O)_2P]^+$ (18), 137 $[C_{10}H_{17}]^+$ (100).

{[2-((*S*)-4-*sec*-Butyl-4,5-dihydrooxazol-2-yl)phenyl]bis((1*S*,2*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)phosphite-*P*,*N*}(π-allyl)palladium(2+) tetrafluoroborate (4). A solution of oxazoline phosphite **1** (0.556 g, 1 mmol) in $CHCl_3$ (15 mL) was added dropwise at 20 °C for 30 min to a vigorously stirred solution of $[Pd(\eta\text{-}C_3H_5)Cl]_2$ (0.183 g, 0.5 mmol) in $CHCl_3$ (15 mL). The reaction mixture was stirred at 20 °C for 1 h. After addition of a solution of $AgBF_4$ (0.195 g, 1 mmol) in THF (15 mL), stirring was continued for an additional 1 h. The precipitate of AgCl that formed was filtered off. The filtrate was concentrated *in vacuo* (40 Torr) to ~0.5 mL and the product was precipitated with Et_2O. The precipitate was separated by centrifugation, washed with Et_2O (2×5 mL), and dried in air and *in vacuo* (1 Torr). The yield was 93%, a yellow powder, m.p. 133—137 °C (decomp.). Found (%): C, 54.91; H, 7.13; N, 1.87. $C_{36}H_{55}BF_4NO_4PPd$. Calculated (%): C, 54.73; H, 7.02; N, 1.77. ^{31}P NMR ($CDCl_3$), δ: 135.7. MS (ESI), m/z (I_{rel} (%)): 703 $[M - BF_4]^+$ (100), 662 $[M - BF_4 - \eta\text{-}C_3H_5]^+$ (32), 556 $[L]^+$ (45).

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