Chiral 1,3,2-dioxaphospholane amidophosphite in the palladium-catalyzed enantioselective allylation

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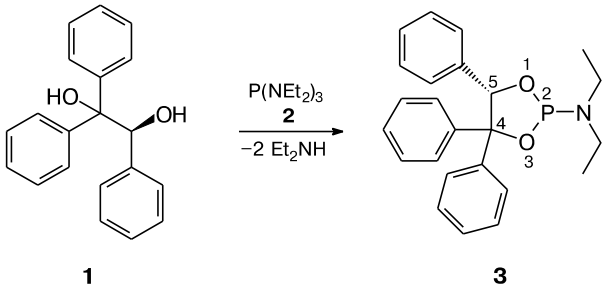
Phosphorylation of (*S*)-1,1,2-triphenylethane-1,2-diol furnishes cyclic *P**-chiral amidophosphite, whose application as a ligand in the Pd-catalyzed allyl substitution in 1,3-diphenylallyl acetate provides the products *ee* up to 70%.

Key words: amidophosphites, allylation, 1,3,2-dioxaphospholanes.

Development of simple and efficient methods for the preparation of inexpensive ligands based on available enantiopure synthons belongs to the key trends in the development of asymmetric metal complex catalysis.[1—3] Ligands of the phosphite nature are of considerable interest, since they are favorably distinguished by synthetic availability, stability to oxidation, pronounced π-acidity, and low cost.[3—5] Amidophosphites of the 1,3,2-dioxaphospholane series are attractive among them, which, being efficient π-acceptors, possess sufficient σ-donor ability, whereas the presence of a phosphorus atom in the five-membered ring increases stability of the ligands to oxidation and hydrolysis.[6] If in this case the donor phosphorus atom is asymmetric, this significantly assists in the transfer of chirality in the key step of the catalytic cycle.[7,8]

The *P**-monodentate amidophosphite of the 1,3,2-dioxaphospholane series **3** described in the present work completely meets all the aforementioned characteristics. It was synthesized by a one-step phosphorylation of (*S*)-1,1,2-triphenylethane-1,2-diol (**1**) with the agent **2** in toluene (Scheme 1).

Scheme 1



1 **3**

Conditions: 110 °C, 2 h, PhMe.

Note that the starting diol **1** is a well known chiral inductor[9,10] and can be obtained by the reaction of available methyl (*S*)-mandelate and PhMgBr (see Ref. 11). Ligand **3** is stereoindividual, since its ^{31}P NMR spectrum (in $CDCl_3$) exhibits the only sharp singlet signal at δ 142.9. It should be noted that the related to it (2*R*,5*S*)-2-chloro-4,4,5-triphenyl-1,3,2-dioxaphospholane is also stereoindividual and according to the X-ray crystallographic data has the (*R*)-configuration of the *P**-stereocenter.[12] The closeness of the spin-spin coupling constant values $^2J_{C(4),P}$ and $^2J_{C(5),P}$ in the ^{13}C NMR spectra of this compound (7.1 and 7.0 Hz, respectively) and amidophosphite **3** (9.0 and 8.9 Hz, respectively) allowed us to suggest[13] that compound **3** has also the (*R*)-configuration of the asymmetric phosphorus atom. Compound **3** is well soluble in most organic solvents and is stable on prolonged storage under dry atmosphere.

For the preliminary evaluation of stereodifferentiating ability of the ligand **3**, we used a standard Pd-catalyzed asymmetric allylation of dimethyl malonate and pyrrolidine with (*E*)-1,3-diphenylallyl acetate (**4**) (Scheme 2) (*cf.* Refs 14—17).

The complex $[Pd(allyl)Cl]_2$ was the source of palladium, the reaction was carried out in CH_2Cl_2. The results are summarized in Table 1. Allylic alkylation of **4** with dimethyl malonate showed good enantioselectivity (to 70% *ee*), whereas its amination with pyrrolidine is somewhat less enantioselective (to 63% *ee)*. A decrease in the molar ratio L/Pd from 2 to 1 leads to the increase in the asymmetric induction, especially in the allylic alkylation (see Table 1, entries *1*, *2* and *3*, *4*). It can be suggested that this

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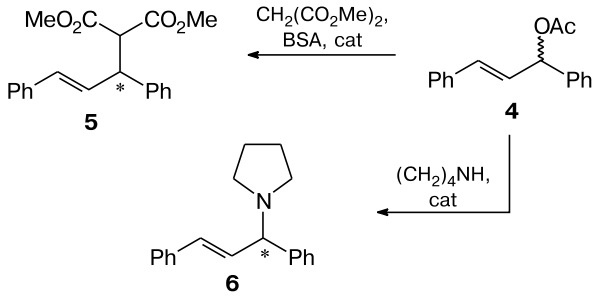
Scheme 2



BSA is the bis(trimethylsilylacetamide)

Table 1. The data on the Pd-catalyzed allylation of dimethyl malonate and pyrrolidine with compound **4** involving ligand **3**[a]

Entry	Nucleophile	L/Pd	Conversion	*ee*[b,c]
			(%)	
1	$CH_2(CO_2Me)_2$	1	100	70 (*S*)
2	$CH_2(CO_2Me)_2$	2	100	37 (*S*)
3	$(CH_2)_4NH$	1	100	63 (*R*)
4	$(CH_2)_4NH$	2	99	57 (*R*)

[a] All the reactions were carried out in CH_2Cl_2 at 20 °C, 48 h, 2 mol.% of $[Pd(allyl)Cl]_2$.

[b] Conversion of the substrate **4** and enantiomeric excess of the product **5** were determined by HPLC (Daicel Chiralcel OD-H, $C_6H_{14}/Pr^iOH = 99 : 1$, 0.6 ml min^{-1}, 254 nm).

[c] Conversion of the substrate **4** and enantiomeric excess of the product **6** were determined by HPLC (Daicel Chiralcel OD-H, $C_6H_{14}/Pr^iOH/HNEt_2 = 200 : 1 : 0.1$, 0.9 ml min^{-1}, 254 nm).

is due to the reduction of the steric hindrance in the internal coordination sphere of the intermediate 1,3-diphenylallylpalladium complex[18] as the number of bulky ligands **3** in it decreases.

In conclusion, *P**-monodentate amidophosphite **3** is a promising stereoselector, whose application (as well as other ligands with the (5*S*)-4,4,5-triphenyl-1,3,2-dioxaphospholane framework) in asymmetric catalysis is under study in our laboratories.

Experimental

^{31}P, ^1H, and ^{13}C NMR spectra were recorded on an Avance 400 spectrometer (161.98, 400.13, and 100.61 MHz) relatively to 85% H_3PO_4 in D_2O and Me_4Si, respectively. The DEPT procedure was used to assign signals in the ^{13}C NMR spectra. Mass spectra with ionization by the electron impact (EI, 70 eV) were recorded on a Varian MAT-311 instrument, with ionization by the laser desorption (MALDI TOF/TOF), on a Bruker Daltonics Ultraflex instrument. Enantiomeric analysis of the products of catalytic reactions was performed by HPLC on an HP Agilent 1100 chromatograph. Elemental analysis was performed in the Laboratory of Organic Microanalysis INEOS RAS.

All the reactions were carried out under dry argon in anhydrous solvents. The starting complex $[Pd(allyl)Cl]_2$ and substrate, (*E*)-1,3-diphenylallyl acetate (**4**), were synthesized according to the known procedures.[19] Catalytic experiments on the asymmetric allylation of dimethyl malonate and pyrrolidine with the substrate **4**, determination of its conversion, and enantiomeric excesses of the products **5** and **6** were performed guided by the published procedures.[20,21]

(*S*)-Mandelic acid, dimethyl malonate, bis(trimethylsilylacetamide) (BSA), and pyrrolidine were commercially available from Fluka and Aldrich.

(5*S*)-2-Diethylamino-4,4,5-triphenyl-1,3,2-dioxaphospholane (3). A solution of (*S*)-1,1,2-triphenylethanediol (2.9 g, 10 mmol) and $P(NEt_2)_3$ (2.74 mL, 10 mmol) in toluene (30 mL) was refluxed with stirring for 2 h. After cooling to 20 °C, the reaction solution was filtered through a short column with alumina. The filtrate was concentrated *in vacuo* (40 Torr), the residue was purified by flash-chromatography on silica gel with CH_2Cl_2 as an eluent. The residue that obtained was thoroughly triturated in the hexane—ethyl acetate (25 : 1) mixture, a white precipitate that formed was separated by centrifugation and dried *in vacuo* (1 Torr) over 1 h. The yield was 2.54 g (65%), a white powder. Found (%): C, 73.87; H, 6.59; N, 3.46. $C_{24}H_{26}NO_2P$. Calculated (%): C, 73.64; H, 6.69; N, 3.58. ^{13}C NMR ($CDCl_3$), δ ($J_{C,P}$): 15.0 (d, CH_3, $^3J = 3.0$ Hz); 38.3 (d, CH_2, $^2J = 21.1$ Hz); 84.4 (d, C(5), $^2J = 8.9$ Hz); 90.6 (d, C(4), $^2J = 9.0$ Hz); 126.7 (s, CH_{Ph}); 126.9 (s, CH_{Ph}); 127.0 (s, CH_{Ph}); 127.4 (s, CH_{Ph}); 127.5 (s, CH_{Ph}); 127.7 (s, CH_{Ph}); 127.8 (s, CH_{Ph}); 128.1 (s, CH_{Ph}); 128.2 (s, CH_{Ph}); 137.5 (d, C_{Ph}, $^3J = 7.0$ Hz); 141.1 (d, C_{Ph}, $^3J = 3.1$ Hz); 143.6 (s, C_{Ph}). ^1H NMR ($CDCl_3$), δ: 1.04 (t, 6 H, $J = 7.5$ Hz); 3.04 (m, 4 H); 5.93 (s, 1 H); 6.92—7.14 (m, 10 H); 7.31 (d, 1 H, $J = 8.0$ Hz); 7.38 (t, 2 H, $J = 7.9$ Hz); 7.69 (d, 2 H, $J = 7.9$ Hz). MS (EI), m/z (I_{rel} (%)): 391 $[M]^+$ (1), 257 $[Ph_2CHCHPh]^+$ (100). MS (MALDI TOF/TOF), m/z (I_{rel} (%)): 430 $[M + K]^+$ (100), 273 $[Ph_2CHC(OH)Ph]^+$ (39), 257 $[Ph_2CHCHPh]^+$ (66).

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