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SHORT COMMUNICATIONS

First Ligand of Phosphite Nature Based on 5,10,15,20-Tetrakis(4-hydroxyphenyl)porphin

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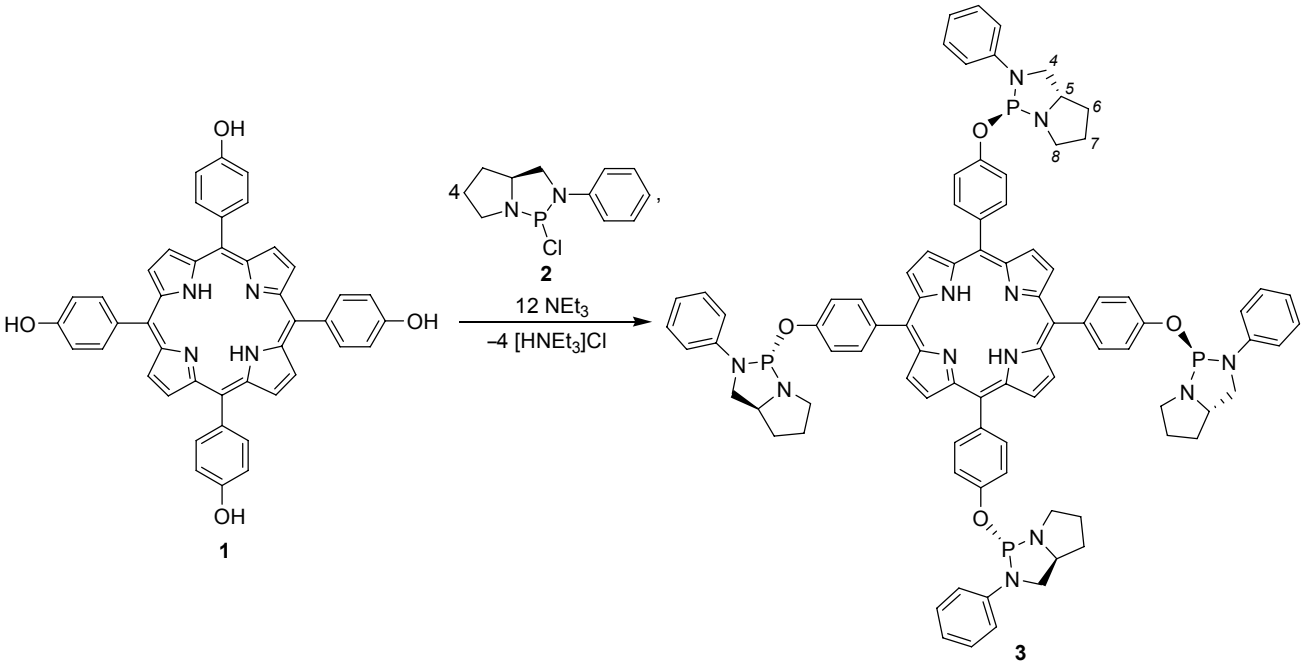
In modern asymmetric catalysis an important role belongs to ligands of phosphite nature characterized by stability against oxidation, pronounced π-acidity, easy preparation through a simple condensation, and low price [1–6]. A promising group of chiral inducers of phosphite type are compounds possessing stereogenic donor phosphorus atoms [7, 8].

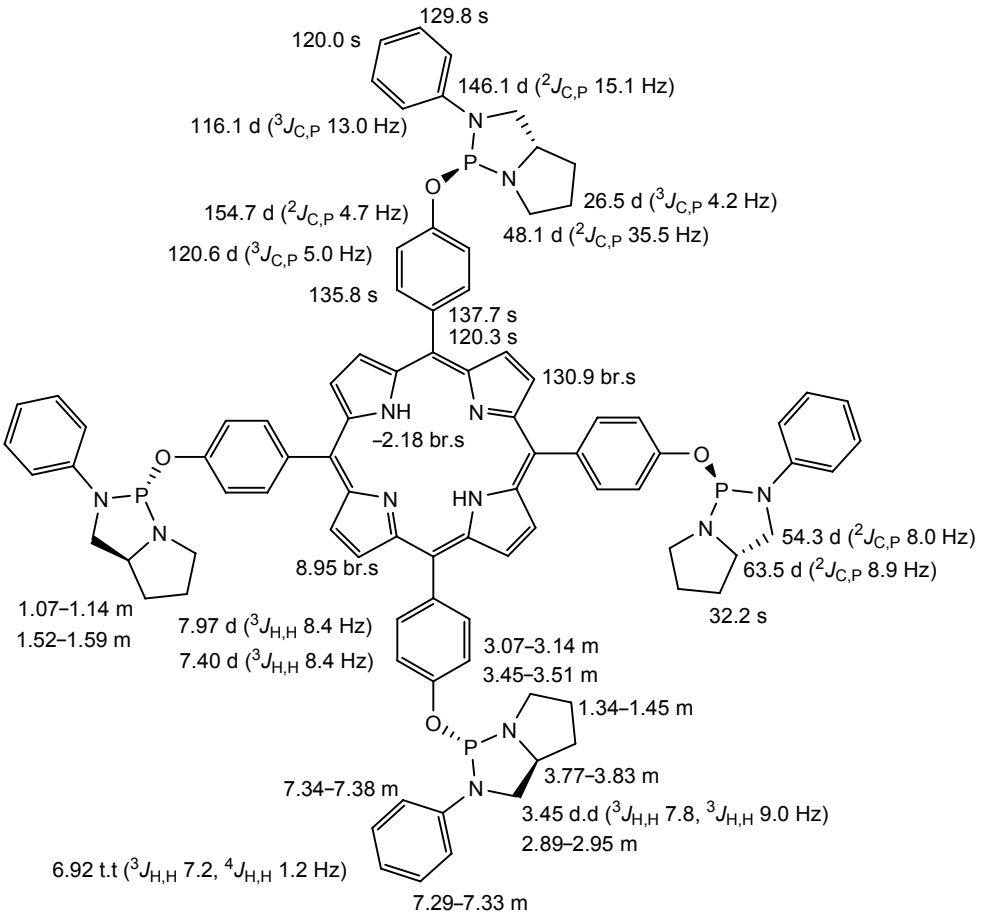
Supramolecular asymmetric catalytic systems are formed involving chiral phosphites and amidophosphites underlain by metalloporphyrins [9–15], yet only one chiral phosphite has been prepared with a porphyrin fragment without a metal ion [9]. No published information exists on diamidophosphite porphyrin derivatives, in particular, with asymmetric phosphorus atoms, and also on compounds containing in their composition more than one phosphorus site linked to the porphyrin scaffold.

By reaction of 5,10,15,20-tetrakis(4-hydroxyphenyl)porphin **1** with phosphorylating reagent **2** in THF we obtained diamidophosphite **3** (Scheme 1). It is

Scheme 1.



Scheme 2.

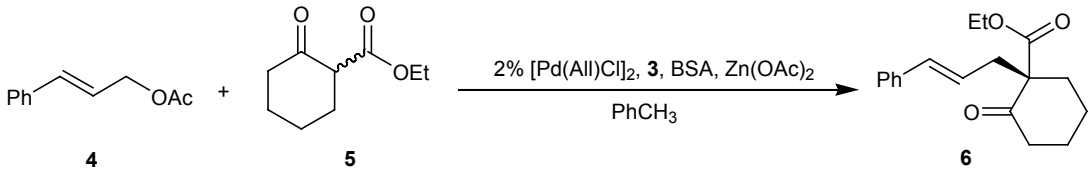


easily purified by flash-chromatography, is sufficiently stable in air, and is suitable for long storage in dry atmosphere.

The structure of compound **3** was proved by the combined data of ^{1}H, ^{13}C, ^{31}P NMR spectra, MALDI TOF mass spectra, and elemental analysis. It is an individual isomer and possesses the (*R*)-configuration of P*-stereocenters as indicated by the presence in the ^{31}P NMR spectrum taken in C_6D_6 of a singlet signal at δ 124.2 ppm, and in the ^{13}C NMR spectrum, of a coupling constant $^2J_{C^8,P}$ 35.5 Hz (Scheme 2). The large value of the constant indicates the *anti*-orientation of the pseudoequatorial exocyclic substituent at the phosphorus atom and the $(CH_2)_3$ fragment of the pyrrolidine ring of 1,3-diaza-2-phosphabicyclo[3.3.0]-octane scaffold and consequently the *syn*-orientation of the phosphorus lone electron pair and atom C^8 [16–18].

The detailed examination of compound **3** solution in C_6D_6 by the methods of 2D NMR spectroscopy ^{1}H-^{1}H COSY, ^{1}H-^{1}H NOESY, ^{1}H-^{13}C HSQC, and ^{1}H-^{13}C HMBC made it possible to assign completely all signals in the ^{1}H and ^{13}C NMR spectra (Scheme 2). The signal of quaternary carbon atoms of pyrrole rings was not detected apparently due to dynamic exchange processes of the rate comparable with the time scale of NMR method. Actually, the width at half maximum of

Scheme 3.



Results of Pd-catalyzed alkylation of cinnamyl acetate **4** with ethyl 2-oxocyclohexanecarboxylate **5** (20°C, toluene, 48 h, 2 mol % of $[Pd(All)Cl]_2$)[a]

L/Pd	Conversion of compound **4**, %	Enantiomeric excess of compound **6**, %
1 : 4	22	75 (*S*)
1 : 2	50	62 (*S*)
1 : 1	95	56 (*S*)
2 : 1	60	76 (*S*)

[a] The conversion of cinnamyl acetate **4** and enantiomeric excess in ethyl (1*S*)-2-oxo-1-[(2*E*)-3-phenylprop-2-en-1-yl]cyclohexanecarboxylate **6** was estimated by HPLC [Kromasil 5-CelluCoat, C_6H_{14}–*i*-PrOH, 95 : 5, 0.4 mL/min, 254 nm, t_r(*R*) 14.3 min, t_r(*S*) 16.4 min].

the signal at 130.9 ppm corresponding to the carbon atoms of pyrrole ring was ~150 Hz. Both effects are observed in a wide range of concentrations (5–20 mg mL^{-1}) of compound **3** solution in C_6D_6 and CD_2Cl_2. Mass spectra (MALDI TOF) confirmed the structure of compound **3**: the spectra contained both the molecular ion and characteristic products of its fragmentation resulting from the loss of one or several diazaphospholidine rings.

Compound **3** was used in asymmetric alkylation of cinnamyl acetate **4** with ethyl 2-oxocyclohexanecarboxylate **5** (Scheme 3), in which process a quaternary C*-stereocenter formed on a carbon atom belonging to the nucleophile.

This reaction is an example of enantioselective catalytic synthesis of compounds with a quaternary asymmetric atom, which is a fairly complex problem [16, 19–21]. The use in the reaction of compound **3** (L) as a chiral inducer resulted in enantioselectivity up to 76% (see the table). The highest values of the asymmetric induction were obtained at molar ratios L/Pd 1 : 4 and 2 : 1, the highest conversion, at the molar ratio L/Pd 1 : 1. In all cases (*S*)-enantiomer **6** prevailed.

The phosphorylating reagent **2** was prepared by procedure [16].

5,10,15,20-Tetrakis(4-{(2*R*,5*S*)-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octyloxy}phenyl)-porphin (3). To a solution of 0.481 g (2 mmol) of phosphorylating reagent **2** and 0.834 mL (6 mmol) of Et_3N in 10 mL of THF under vigorous stirring at 20°C was added in one portion 0.339 g (0.5 mmol) of compound **1**. The reaction mixture was heated to boiling, boiled for 20 min, cooled to 20°C, and filtered through a short column packed with alumina. The filtrate was concentrated in a vacuum (40 mmHg), the reaction product was purified by flash-chromatography on silica gel, eluent benzene. Yield 0.479 g (64%), violet powder, mp 160–161°C. Mass spectrum, *m/z* ($I_{rel.}$, %): 1497 (35) $[M + H]^+$, 1292 (32), 1088 (20), 884 (11), 680 (17), 205 (86). Found, %: C 70.98; H 5.25; N 11.03. $C_{88}H_{82}N_{12}O_4P_4$. Calculated, %: C 70.67; H 5.53; N 11.24. *M* 1495.57.

Asymmetric alkylation of cinnamyl acetate (4) with ethyl 2-oxocyclohexanecarboxylate (5) [20, 21]. A solution of 0.0037 g (0.01 mmol) of $[Pd(All)Cl]_2$ and 0.0075 g (0.005 mmol) [or 0.0015 g (0.01 mmol), or 0.0299 g (0.02 mmol), or 0.0598 g (0.04 mmol)] of ligand **3** in 5 mL of toluene was stirred for 40 min, 0.08 mL (0.5 mmol) of cinnamyl acetate was added, and the mixture was stirred for another 15 min, then 0.12 mL (0.75 mmol) of ethyl 2-oxocyclohexanecarboxylate, 0.5 mL (2 mmol) of bis(trimethylsilyl)acetamide (BSA), and 0.01 g of zinc acetate was added. The reaction mixture was stirred for 48 h, diluted with 5 mL of hexane, and filtered through Celite. The filtrate was concentrated in a vacuum (40 mmHg), the obtained residue was dried in a vacuum (10 mmHg). The conversion of substrate **4** and enantiomeric excess in ethyl (1*S*)-2-oxo-1-[(2*E*)-3-phenylprop-2-en-1-yl]-cyclohexanecarboxylate **6** was estimated by HPLC on a chiral stationary phase Kromasil 5-CelluCoat.

^{31}P, ^{13}C, and ^{1}H (242.9, 150.9, and 600.13 MHz respectively) NMR spectra were registered on a spectrometer Bruker Avance III 600. Mass spectra (MALDI TOF/TOF) were recorded on an instrument Bruker Daltonics Ultraflex. Enantiomeric analysis of products of the catalytic reaction was performed on a Sayer system HPLC. Elemental analysis was carried out on a CHN microanalyzer Carlo Erba EA1108 CHNS-O.

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