

Derivatives of phosphorous acid as a new class of ligands for Pd-catalyzed allylation

S. K. Moiseev, R. V. Lebedev, A. I. Polosukhin, and V. N. Kalinin*

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
28 ul. Vavilova, 117813 Moscow, Russian Federation.

Fax: +7 (095) 135 6549. E-mail: vkalin@ineos.ac.ru

Amido- and aminophosphites and hydrospirophosphoranes can be used as ligands in the Pd-catalyzed allylation of ethyl malonate with ethyl (3-phenylprop-2-enyl) carbonate. Bidentate ligands $(\text{RO})_2\text{P}-\text{O}(\text{CH}_2)_n-\text{NR}'_2$ ($n = 2$ and 3) were found to be the most effective ligands.

Key words: allylation, palladium, *P,N*-ligands, aminophosphites.

Pd-catalyzed allylation of various organic compounds is an important method for constructing carbon–carbon and carbon–heteroatom bonds.¹ This reaction proceeds through the formation of cationic η^3 -allylpalladium(II) intermediates that are attacked by a nucleophile. The nature of palladium-coordinated ligands is essential in this process. Reactions of allylic esters (allyl carbonates, allyl acetates, *etc.*) with alkyl malonates are a standard test for the efficiency of one or another ligand in catalytic processes.²

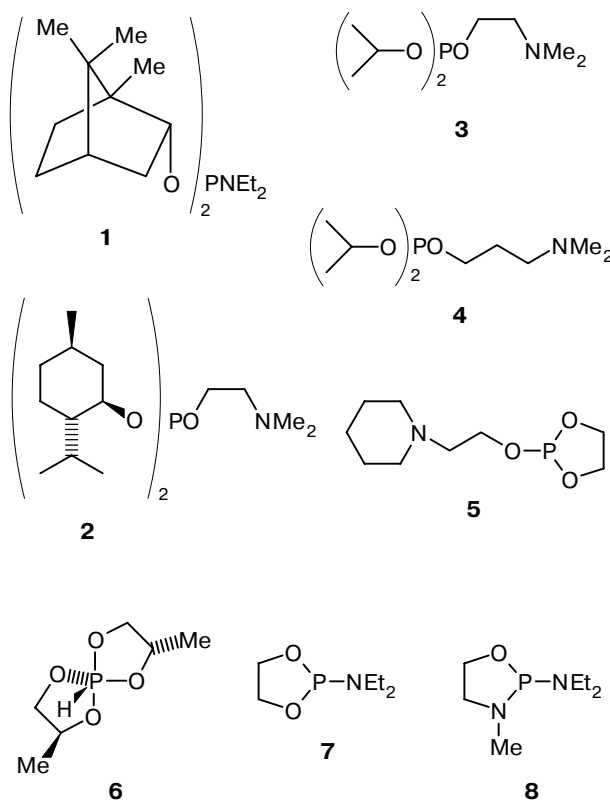
The number of current papers dealing with phosphorous acid derivatives in catalytic processes increases steadily. The reasons for this tendency are the following. These compounds are easily prepared, contain no P–C bond and are thus resistant to oxidation, and have pronounced π -acceptor character, making a transition metal atom more electrophilic.³

In this work, amido- and aminophosphites and hydrospirophosphoranes were used as ligands for the first time. The goal of this work is to study how the catalytic efficiency of these ligands depends on the character of P- and N-donor centers (*i.e.*, the type and bulkiness of substituents and the length of a chain between the donor atoms). This will enable one to synthesize ligands with the desired properties. The mono- and bidentate compounds **1–8** we studied^{4–8} are shown in Scheme 1.

The reaction of ethyl malonate with ethyl (3-phenylprop-2-enyl) carbonate (**9**) was chosen as a model (Scheme 2). It is known that allyl carbonates are of special interest for Pd-catalyzed allylation, because in many cases they can react in neutral media, *i.e.*, no base is needed.⁹ In addition, the reaction of ethyl malonate with compound **9** yields one isomer of product **10**, while the use of the corresponding acetate can also result in allylic rearrangement.¹⁰

The catalytic agent was generated *in situ* by ligand exchange reaction. The precursor of a catalyst was a palladium complex with dibenzylideneacetone (dba) $\text{Pd}_2(\text{dba})_3$, in which the bond between the olefin and the

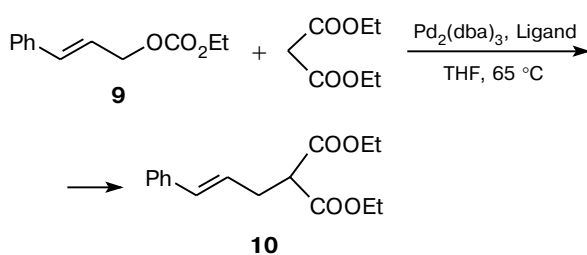
Scheme 1



complexing atom is very labile.¹¹ Ligands **1–8** were added to a dark red solution of $\text{Pd}_2(\text{dba})_3$. A light yellow color of the reaction mixture indicated the completion of the exchange reaction. The ligand exchange rate can be estimated from the time it takes for this change in color.

Ligands **1**, **3**, and **4** change their color at room temperature within 5–10 min, while compound **5** dis-

Scheme 2



colors over a course of 30 min. It takes three hours for ligand **2** to coordinate at 45 °C. Ligands **7** and **8** are not coordinated by palladium under the chosen conditions.

The yields of product **10** and the reaction conditions are given in Table 1.

Ligands **3** and **4** were found to be most effective in the process under examination. They allow one to obtain compound **10** in high yields in neutral media. In the presence of **1**, allylation under neutral conditions is low-yielding. In the case of ligands **2**, **5**, and **6**, a base is required, and the product forms in moderate yields.

Amidophosphites **7** and **8** with the ring phosphorus atom proved to be unsuitable ligands for this catalytic process, as they cannot replace dba in the catalyst precursor under the given conditions.

Aminophosphite **1** containing the P atom in the side chain rather than in the cyclic fragment is capable of rapid ligand exchange with $\text{Pd}_2(\text{dba})_3$, but its catalytic power is low.

Ligands **2–5** differ in the length of a chain between the P and N atoms (three-atom chains in compounds **2**, **3**, and **5** and a four-atom chain in **4**). In addition, the P and N atoms in their molecules are included either in acyclic or in heterocyclic fragments. In the case of **3** and **4**, ligand exchange with $\text{Pd}_2(\text{dba})_3$ is rapid, despite different P...N chain lengths. The process occurs more slowly for ligand **5**, which contains heterocyclic P and N

Table 1. Pd-catalyzed allylation of ethyl malonate with ethyl (3-phenylprop-2-enyl) carbonate (**9**) in THF at 65 °C

Ligand	Base ^a	Time ^b /h	Yield ^c (%)
1	—	24	38
2	—	24	—
	BSA/KOAc	2	67
3	—	2	92
4	—	2	100
5	—	24	—
	BSA/KOAc	3	85
6	—	24	—
	BSA/KOAc	4	63

^a BSA = *N,O*-bis(trimethylsilyl)acetamide.

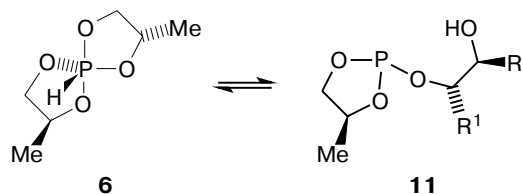
^b A point after which carbonate **9** is no longer detected by TLC.

^c Determined by HPLC on a Varian 5000 LIQUID chromatograph with ethylbenzene as the internal standard (Separon SGX, hexane/ Pr^iOH = 99.5/0.5).

atoms, and even more slowly for ligand **2** with a bulkier substituent at the oxygen atoms.

A special place among the ligands is occupied by hydrophosphorane **6**, whose structure appears unfit for coordination with metal (see Scheme 1). However, this compound was shown¹² to function as a P-monodentate phosphite ligand in complexation with Rh and Pd, coordinating in the form of P^{III} tautomer **11** with open chain (Scheme 3).

Scheme 3



$\text{R}^1 = \text{H}, \text{R}^2 = \text{Me}$ or $\text{R}^1 = \text{Me}, \text{R}^2 = \text{H}$

Thus, aminophosphites **3** and **4** ($(\text{RO})_2\text{P}-\text{O}(\text{CH}_2)_n-\text{NR}'_2$ ($n = 2$ and 3) with the P and N atoms in the acyclic fragments were found to be the most effective ligands among the compounds studied for Pd-catalyzed allylation.

Experimental

All reactions were carried out in an atmosphere of dry argon. Tetrahydrofuran was distilled over sodium benzophenone ketyl before use. $\text{Pd}_2(\text{dba})_3$ ¹³ and carbonate **9**¹⁴ were prepared according to the known procedures. Ethyl malonate was purified by vacuum distillation. The structure of product **10** was confirmed by comparing its boiling point and ^1H NMR and the mass spectra obtained in this work with the literature data.¹⁵

Palladium-catalyzed allylation (general procedure). *A. Neutral conditions.* A solution of $\text{Pd}_2(\text{dba})_3$ (10 mg, 0.01 mmol) and an equimolar amount of ligand (**1–8**) in 4 mL of THF was stirred at 20 °C until the solution turned light yellow. Then, ethyl malonate (240 mg, 1.5 mmol) in 2 mL of THF and ethyl (3-phenylprop-2-enyl) carbonate (206 mg, 1 mmol) (**9**) in 2 mL of THF were added. The reaction mixture was refluxed with stirring until compound **9** disappeared. The yield of product **10** was determined by HPLC with ethylbenzene as the internal standard.

B. Basic conditions. The reactions were carried out as described above, but in the presence of *N,O*-bis(trimethylsilyl)acetamide (BSA) (305 mg, 1.5 mmol) and anhydrous KOAc (5 mg, 0.05 mmol).

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