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Reaction of Phospholes with Aldimines: A One-Step Synthesis of Chelating, Alpha-C_2-Bridged Biphospholes

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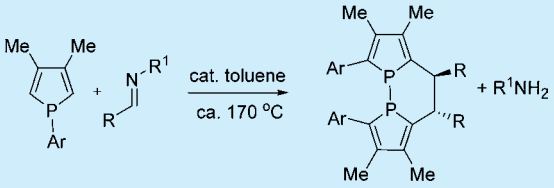
Supporting Information

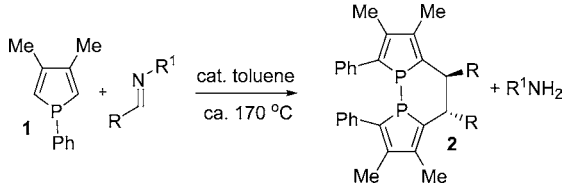
ABSTRACT: Phospholes react with aldimines at 170 °C in the presence of mild Lewis acids to give C_2-bridged biphospholes in good yields. The mechanism includes a series of [1,5] shifts of the P-substituents around the phosphole ring, a P−H + aldimine condensation, and the formation of a transient three-membered ring that dimerizes.



From a practical standpoint, the easy interconversion between 1*H*- and 2*H*-phospholes[1] offers a straightforward access to bicyclic phosphines by Diels−Alder cycloaddition between the 1-phosphadienic system of 2*H*-phospholes and a variety of unsaturated systems. The resulting bicyclic phosphines are characterized by a chiral nonracemizable bridgehead phosphorus atom of special interest for applications in asymmetric catalysis. A certain number of bicyclic phosphines have already been prepared with these ideas in mind.[2] In this context, the synthesis of α-C_2-bridged biphospholes is obviously interesting because it can offer an access to chelating biphosphines with two nonracemizable chiral phosphorus centers. Unfortunately, until now, only one such biphosphole has been described[3] and its lengthy multistep synthesis precludes its use for further developments. In this report, we wish to describe an extremely simple, one step synthesis of such species by reaction of phospholes with aldimines.

We had previously described the cycloaddition between 2*H*-phospholes and aldehydes.[4] Therefore, it was logical to investigate the reaction with aldimines. Since the Diels−Alder reactions of imines are known to be catalyzed by mild Lewis acids,[5] we decided to investigate the reaction of the prototypical 1-phenyl-3,4-dimethylphosphole **1**[6] with a variety of aldimines in the presence of Lewis acids. The results were completely unexpected. The end-products were the α-bridged biphospholes **2** (Scheme 1). In one case, the primary amine that is formed as a stoichiometric byproduct has been isolated and characterized for R^1 = Ph. It must be also noted that ketimines do not react with

Scheme 1. Reaction of Phosphole 1 with Aldimines



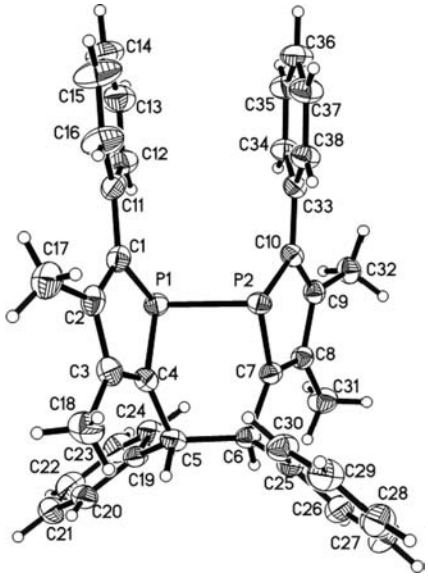


Figure 1. X-ray crystal structure of (**2a**) (R = Ph). The level set for thermal ellipsoids of all atoms is 30%. Main distances (Å) and angles (deg): P1−P2 2.1957(8), P1−C4 1.8019(19), C4−C5 1.511(2), C5−C6 1.579(2), C6−C7 1.513(2), C7−P2 1.8024(17), P1−C1 1.8097(18), C1−C2 1.361(3), C2−C3 1.463(3), C3−C4 1.362(3), P2−C10 1.8055(18), C10−C9 1.357(2), C9−C8 1.470(3), C8−C7 1.361(2), C1−P1−P2 101.24(6), C4−P1−P2 89.04(6), C1−P1−C4 90.96(9), C7−P2−P10 91.15(8), C7−P2−P1 90.10(6), C10−P2−P1 102.99(6), C1−P1−P2−C10 112.59(9), C4−P1−P2−C7 65.42(8).

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Table 1. Optimization of the Reaction Conditions

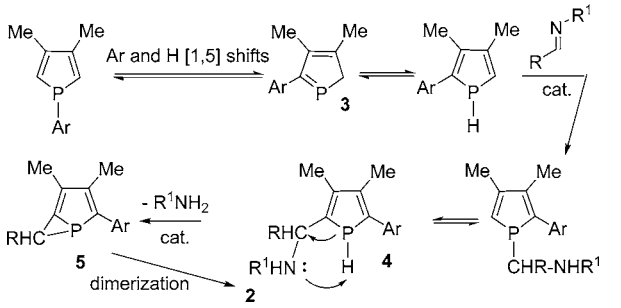
entry	cat. (20 mol %)	t = 170 °C time (h)	R = Ph R[1]	yield (%)
1	none	72	Ph	8
2	$ZnCl_2$[a]	72	Ph	10
3	$ZnCl_2$	72	Ph	49
4	$BF_3{\cdot}Et_2O$	24	Ph	trace
5	$AlCl_3$	24	Ph	14
6	$FeCl_2$	24	Ph	60
7	$FeCl_2$	16	Ph	58
8	$FeCl_2$	16	Cy	93

[a]With 5 mol % $ZnCl_2$

Table 2. Variation on the Substituents

product	P–Ar	R	R[1]	yield (%)
2b	Ph	2-thienyl	Ph	44
2b	Ph	2-thienyl	Cy	88
2c	Ph	*p*-MeO-C_6H_4	Cy	91
	Ph	*p*-NO_2-C_6H_4	Cy	NR
2d	Ph	*o*-Br-C_6H_4	Cy	62
2e	Ph	*p*-CN-C_6H_4	Cy	22
2f	Ph	*i*-Pr	Cy	86
2g	2-thienyl	Ph	Cy	75

Scheme 2. Mechanism of the Reaction



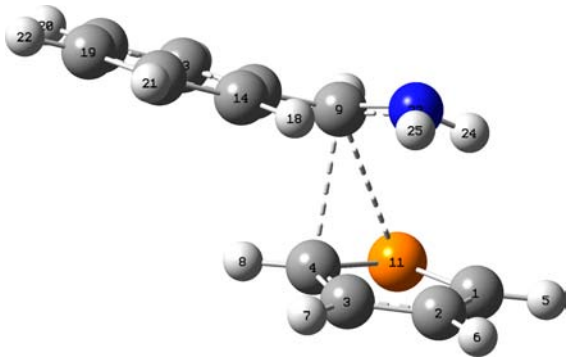
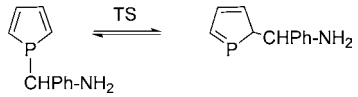


Figure 2. Computed transition state (one negative frequency) of the reaction:

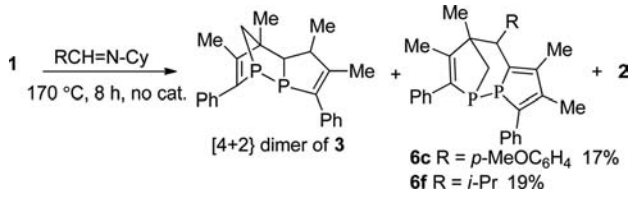


Main distances (Å) and angles (deg): C9–P 3.04, C9–C4 2.45, C9–N 1.34, C4–C9–P 36.5.

phosphole **1** under the same conditions. The X-ray crystal structure analysis of **2a** (R = Ph) is reported in Figure 1.

We screened a variety of Lewis acids as shown in Table 1. This led us to select $FeCl_2$ as the catalyst of choice while the

Scheme 3. Trapping Intermediates 5



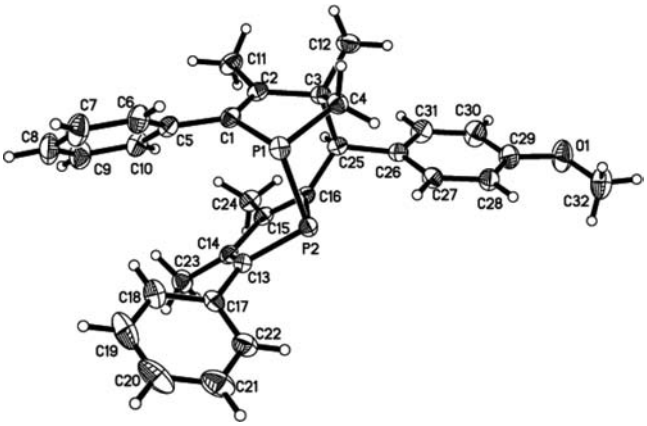
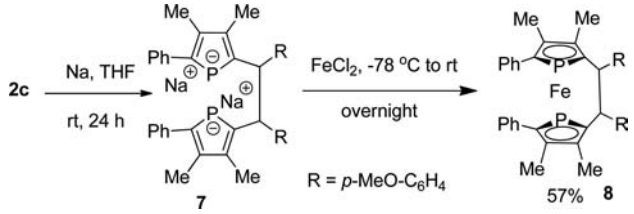


Figure 3. X-ray crystal structure of (**6c**). The level set for thermal ellipsoids of all atoms is 30%. Main distances (Å) and angles (deg): P1–P2 2.2393(7), P2–C1 61.8031(18), C16–C25 1.509(3), C25–C3 1.607(2), C3–C4 1.538(3), C4–P1 1.846(2), P1–C1 1.837(2), C1–C2 1.345(3), C2–C3 1.527(3), P2–C1 31.8048(19), C13–C14 1.356(3), C14–C15 1.468(3), C15–C16 1.359(3), C1–P1–C4 88.74(9), C13–P2–C16 91.10(9), C3–C4–P1 107.23(13).

Scheme 4. Synthesis a Diphosphaferrocenophane



temperature was set a 170 °C. We also noticed that a cyclohexyl substituent at nitrogen is more favorable than a phenyl.

We then investigated the range of aldimines that can be used with the optimized conditions (170 °C, 16 h, $FeCl_2$). The reaction appears to be quite general. The electron-withdrawing substituents disfavor the reaction (Table 2). It is also possible to replace the phenyl group at P by another aryl or heteroaryl substituent.

On the basis of what is known on the chemistry of 2*H*-phospholes,[1] we propose the following mechanism (Scheme 2). One critical point of this mechanism involves the [1,5] sigmatropic shift of the α-aminobenzyl substituent from P to Cα. It is known that sp^3 carbon substituents do not normally migrate,[1] and, thus, we needed to check this point. The DFT computations[7] were carried out at the B3LYP/6-311+G(d,p) level. The transition state is shown in Figure 2.

The computed barrier is very low at only 17.4 kcal mol^{-1} (zero-point energy included). It is quite clear that the amino substituent favors the ionization of the P–C bond and weakens it, thus favoring the migration of the sp^3 carbon group. The conversion of **4** into **5** implies a deprotonation of the phosphole

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ring at P by the nitrogen lone pair. This explains why a higher basicity of the amino group favors the reaction. While trying to characterize some intermediates in the reaction, we were able to separate polycyclic derivatives **6** of the bicyclic phosphiranes **5** (Scheme 3). The products result from the [4 + 3] cycloaddition of the 2*H*-phosphole **3** with **5**. The formula of **6c** was confirmed by X-ray crystal structure analysis (Figure 3). Its formation fully demonstrates the proposed mechanism.

The ready availability of biphospholes such as **2** offers a lot of synthetic possibilities using the chemistry of the P−P bond. The synthesis of a 1,1′-diphosphaferroceneophane is given as an example (Scheme 4).

Many more applications of these new products can be envisaged.

■ ASSOCIATED CONTENT

Supporting Information

Experimental section, NMR data for **2**−**7**, and X-ray data for **2a** and **6c** The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b01604.

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Notes

The authors declare no competing financial interest.

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