



## Carbon–phosphorus bond formation and transformation in the reaction of 1,2-diaza-1,3-butadienes with alkyl phenylphosphonites

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### ABSTRACT

The reaction of 1,2-diaza-1,3-butadienes with dialkyl phenylphosphonites under solvent-free conditions proceeds via zwitterionic intermediate and gives, by precipitation, the stable ylidic  $\alpha$ -phosphanylidene-hydrazones that, in turn, can be transformed into the corresponding 3-phenyl-2*H*-1,2,3 $\lambda^5$ -diazaphospholes. The latter compounds are converted by hydrolytic cleavage in methanol–water (95:5) into *E*-hydrazonephosphonates that are useful for the preparation of the corresponding  $\beta$ -ketophosphonates and 4-[alkoxy(phenyl)phosphoryl]-1,2-diaza-1,3-butadienes. These peculiar 1,2-diaza-1,3-butadienes, bearing an alkoxy(phenyl)phosphoryl group on the carbon atom in position 4 are also able to add different nucleophiles, such as methanol or thiourea, giving 2-[alkoxy(phenyl)phosphoryl]-2-methoxyhydrazones and 5-phosphinate-substituted thiazol-4-ones, respectively.

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### 1. Introduction

Since the 1960s, investigations regarding 1,2-diaza-1,3-butadienes have drastically increased, showing the usefulness of these compounds in organic chemistry.<sup>1,2</sup> Our group has a 30-year experience in this field. In particular, we have studied the reactivity of these substrates, both in solution and solid phase,<sup>3</sup> toward a large variety of nucleophiles.<sup>1</sup> The 1,4-conjugate addition (Michael-type) of the latter on the terminal carbon atom of the heterodiene system and the subsequent internal ring closure of the 1,4-adduct hydrazone intermediates form polyfunctionalized five- or six-membered heterocycles, such as pyrroles,<sup>3a,4</sup> thiazoles,<sup>5</sup> thiazolinones,<sup>3a,c</sup> pyrazoles,<sup>3a,6</sup> thiadiazoles,<sup>7</sup> selenadiazoles,<sup>7</sup> indoles,<sup>8,4b,c</sup> imidazoles,<sup>9</sup> 1,2,4-triazines,<sup>1c</sup> pyrazines,<sup>10</sup> and pyridazines.<sup>11</sup>

On the other hand, the phospha-Michael (P-Michael) addition, i.e., the addition of a phosphorus nucleophile to an appropriate acceptor, is probably one of the most versatile tools for the formation of the P–C bond.<sup>12</sup> This occurrence is important because it offers an entry to many diversely functionalised derivatives. In addition, natural products containing a P–C bond exhibit important biological activity.<sup>13</sup>

In the past years, all these considerations suggested us to examine the reaction between 1,2-diaza-1,3-butadienes and triphenyl-<sup>14a</sup> or trialkyl-phosphines<sup>14b</sup> to obtain pyrazoles or 4-phosphoranylidene-4,5-dihydropyrazol-5-ones. More recently, we have investigated the reaction of the same 1,2-diaza-1,3-butadienes with trialkyl phosphites that represented a facile access to new 1,2,3-diazaphospholes, if the reaction was carried out under a nitrogen atmosphere, or to *E*-hydrazonephosphonates, in the presence of atmospheric moisture.<sup>15</sup>

With the aim to study the behavior of other trivalent phosphorus nucleophiles towards 1,2-diaza-1,3-butadiene systems and considering the different electron-donating effects of the phenyl group with respect to the alkoxy one, in this paper we consider the reaction of these compounds with dimethyl or diethyl phenylphosphonites. It turned out to be very interesting because, in some cases, the 1,4-addition products directly precipitate from the reaction medium, permitting us to define the mechanistic aspects of the reaction.

On the other hand, with the same reaction pathway, we can obtain 3-phenyl-2*H*-1,2,3 $\lambda^5$ -diazaphospholes, also in the presence of air. Furthermore, the procedure here described represents an easy alternative route to the synthesis of 1,2,3-diazaphospholes. In fact, the classical method for their preparation implicates the PCl<sub>3</sub> condensation of the alkylketone hydrazones<sup>16</sup> while 2,4,5-triphenyl-1,2,3-diazaphosphole is best prepared from the respective 1,2-diaza-1,3-butadiene and a fused benzothiadiphosphole as the phosphorus donating reagent.<sup>17</sup>

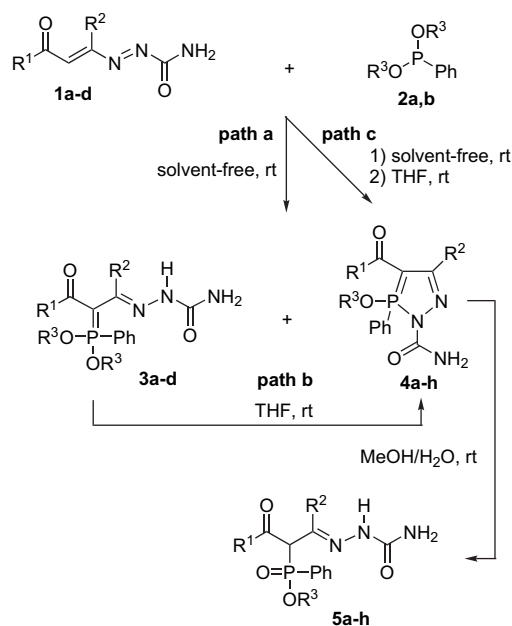
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Here, we also report the hydrolytic cleavage of 1,2,3-diazaphospholes to give the corresponding *E*-hydrazonophosphonates that can be conveniently used for the preparation of interesting  $\beta$ -ketophosphonates and 4-[alkoxy(phenyl)phosphoryl]-1,2-diaza-1,3-butadienes. Besides, we have tested the ability of these particular 1,2-diaza-1,3-butadienes to add some nucleophiles such as methanol and thiourea to give 2-[alkoxy(phenyl)phosphoryl]-2-methoxyhydrazones and 5-phosphinate-substituted thiazol-4-ones, respectively.

## 2. Results and discussion

1-Aminocarbonyl-1,2-diaza-1,3-butadiene-4-carboxylates **1a,b** easily reacted with dimethyl or diethyl phenylphosphonites **2a,b** in the presence of atmospheric moisture and in solvent-free conditions in 0.5 h to give a mixture of  $\alpha$ -phosphanylidene-hydrazones **3a–d** and 3-phenyl-2*H*-1,2,3 $\lambda^5$ -diazaphospholes **4a,b,e,f** (Scheme 1, path a, Table 1). Products **3** directly precipitated from the reaction medium, while the corresponding **4a,b,e,f** were obtained by chromatographic purification of the mother liquor. If the same reaction was carried out starting from **1c,d** with **2a,b**, the isolation of hydrazones **3** was not possible, either by precipitation or by chromatographic methods.



Scheme 1.

The ylidic nature of compounds **3a–d** is clearly supported by  $^{13}\text{C}$  chemical shifts of the P–C signals (55.3–56.6 ppm) and by their P–C coupling constants (167–168 Hz), which are in good agreement with the values found in the literature.<sup>15,18</sup>

The possibility to obtain in some cases intermediates **3** simply by precipitation and subsequent filtration can suggest that the presence of a phenyl group directly bound to the phosphorus atom enhances their stability.

The isolation and the characterization of the intermediates **3a–d** have represented the key to determine the exact mechanism for the formation of the 1,2,3-diazaphospholes **4**. The nucleophilic 1,4-addition of the phosphorus at the terminal carbon atom of the heterodiene system induces the formation of a zwitterionic intermediate (**I**) that exists in equilibrium with its ylidic form **3**, derived from the 1,4-shift of a proton. 1,2,3-Diazaphospholes **4** are obtained by means of an intramolecular attack of the NH hydrazonic nitrogen of **3** at the phosphorus atom, with loss of an alcohol molecule (Scheme 2).

Ylidic intermediates **3a–d** can be easily converted into the corresponding 1,2,3-diazaphospholes **4a,b,e,f** in tetrahydrofuran at room temperature (Scheme 1, path b, Table 1). This represents further support for the described mechanism.

3-Phenyl-2*H*-1,2,3 $\lambda^5$ -diazaphospholes **4a–h** can also be obtained in a one-pot procedure. In fact, 1-aminocarbonyl-1,2-diaza-1,3-butadiene-4-carboxylates **1a,b,d** and 1-aminocarbonyl-1,2-diaza-1,3-butadiene-4-carboxamide **1c** easily reacted with dimethyl or diethyl phenylphosphonites **2a,b** in solvent-free conditions and in the presence of atmospheric moisture. After completion of the reaction, revealed by the disappearance of the red color of 1,2-diaza-1,3-butadiene, THF was directly added to the reaction medium giving 3-phenyl-2*H*-1,2,3 $\lambda^5$ -diazaphospholes **4a–h** in very good yields (Scheme 1, path c, Table 1). Probably, the presence of a phenyl moiety bound to the phosphorus atom confers a particular stability to compounds **4a–h**, which, if stored for one year at 4 °C, showed no decomposition nor any loss in purity.

The treatment of 1,2,3-diazaphospholes **4a–h** with THF–water (95:5) produced the corresponding *E*-hydrazonophosphonates **5a–h** in 6.0–10.0 h, in good yields (Scheme 1, Table 1). Their formation is due to the hydrolytic ring opening of diazaphosphole that occurs with the cleavage of the P–N bond of the intermediate **II** (Scheme 2). The *E*-configuration of the C=N was assigned by means of NOE experiments.<sup>15</sup>

These hydrazonic derivatives featured an interesting synthetic utility for a series of chemical transformations. In fact, when compounds **5a,b,d,f,g**, chosen as examples, were treated with 4 equiv of Amberlyst 15H in a mixture of acetone–water (9:1), they were converted into  $\beta$ -ketophosphonates **6a–e** in 3.0–5.0 h with good yields (59–72%) (Scheme 3, Table 2), by means of the hydrolytic cleavage of the C=N hydrazonic bond.<sup>19</sup>

Table 1

Yields and reaction times of  $\alpha$ -phosphanylidene-hydrazones **3a–d**, 3-phenyl-2*H*-1,2,3 $\lambda^5$ -diazaphospholes **4a–h**, and *E*-hydrazonophosphonates **5a–h**

1	R <sup>1</sup>	R <sup>2</sup>	2	R <sup>3</sup>	3	Yield <sup>a</sup> (%)	4	Yield <sup>a</sup> (%)	Yield <sup>b</sup> (%)	Yield <sup>c</sup> (%)	Time <sup>d</sup> (h)	5	Yield <sup>e</sup> (%)	Time <sup>f</sup> (h)
1a	OMe	Me	2a	Me	3a	45	4a	45	65	77	1.0	5a	79	9.0
1b	OEt	Me	2a	Me	3b	47	4b	47	68	78	2.0	5b	81	10.0
1c	NMe <sub>2</sub>	Me	2a	Me			4c			84	1.0	5c	74	8.0
1d	OMe	Et	2a	Me			4d			87	2.0	5d	62	6.0
1a	OMe	Me	2b	Et	3c	52	4e	22	63	78	2.0	5e	65	8.0
1b	OEt	Me	2b	Et	3d	51	4f	26	68	69	2.0	5f	63	10.0
1c	NMe <sub>2</sub>	Me	2b	Et			4g			88	1.0	5g	73	6.0
1d	OMe	Et	2b	Et			4h			93	2.0	5h	60	6.0

<sup>a</sup> Yield of pure isolated products, referred to the path a of Scheme 1, based on starting compounds **1a,b**.

<sup>b</sup> Yield of pure isolated products, referred to the path b of Scheme 1, based on starting compounds **3a–d**.

<sup>c</sup> Yield of pure isolated products referred to the path c of Scheme 1, based on starting compounds **1a–d**.

<sup>d</sup> Time for the formation of compounds **4a–h**.

<sup>e</sup> Yield of pure isolated products **5a–h**, based on starting compounds **4a–h**.

<sup>f</sup> Time of disappearance of the starting compounds **4a–h**.

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