A New Synthesis of 1,2-Dihydro-1,3,2-P^V-diazaphosphorine Derivatives by Reaction of 4-Amino-1-azabutadienes and Phosphorus Halides

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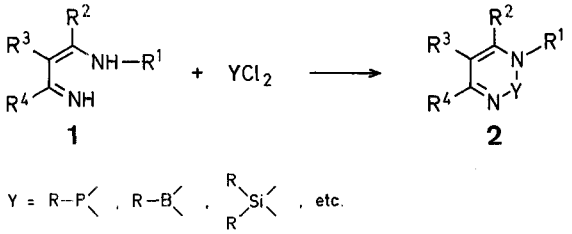
4-Amino-1-azabutadienes **1** are versatile starting materials in the synthesis of five- and six-membered heterocycles[1]. Two different reaction pathways operate depending on the structure of **1**[2]; the most facile for the synthesis of six-membered heterocycles consists of a double condensation process. For instance, 1,2,6-thiadiazines (**2**, Y = S) are obtained in a regioselective manner by reacting **1** with sulfur halides[1a]. This type of reaction represents a new strategy for the synthesis of six-membered heterocycles containing an N—Y—N grouping in which Y could be different heteroatoms (Scheme **A**).



Scheme **A**

On the other hand, organic phosphorus derivatives have attracted in the last few years a great deal of attention, specially due to their important role in many physiological processes[3]. In this context, it has been shown that heterocycles containing nitrogen and phosphorus[4] could be of interest because of their pharmacological properties[5].

In the present paper, we report our results on the reaction of 4-amino-1-azabutadienes **1** with different phosphorus halides. Heterocycles **5**, **6**, and **7** are obtained in high yields when compounds **1** are allowed to react with phosphoryl chloride **(3a)**, benzenephosphonic dichloride **(3b)**, or benzenephosphonothioic dichloride **(3c)** in benzene/triethylamine solution (Scheme **B**, Table 1). Intermediate compounds **4**, resulting from the intermolecular condensation of the imine NH and the phosphorus halide have never been isolated.

The 1,2-dihydro-1,3,2-P^V-diazaphosphorines **5**, **6**, and **7** are stable to dilute alkaline solutions and air. However, the products resulting from the reactions of phosphorus(III) halides and **1**[6] decompose rapidly and are sensitive to air and moisture.

Table 1. Diazaphosphorines **5**, **6**, and **7** from 4-Amino-1-azabutadienes **1**

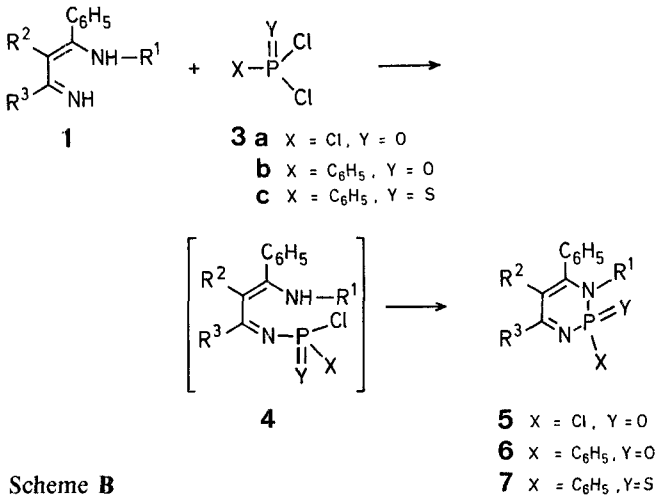
Compound	R^1	R^2	R^3	Y	X	Yield [%]	m.p. [°C] (ether)	Molecular formula[a]
5a	C_6H_5	H	4-H_3C—C_6H_4	O	Cl	90	222–224°	$C_{22}H_{16}ClN_2OP$ (392.8)
5b	4-H_3C—C_6H_4	CH_3	C_6H_5	O	Cl	84	198–200°	$C_{23}H_{20}ClN_2OP$ (406.9)
5c	*c*-C_6H_{11}	CH_3	C_6H_5	O	Cl	72	173–175°	$C_{22}H_{24}ClN_2OP$ (398.9)
5d	4-H_3C—C_6H_4	H	C_6H_5	O	Cl	94	265–266°	$C_{22}H_{18}ClN_2OP$ (392.8)
6a	C_6H_5	CH_3	4-H_3C—C_6H_4	O	C_6H_5	67	170–172°	$C_{29}H_{25}N_2OP$ (448.5)
6b	*c*-C_6H_{11}	CH_3	C_6H_5	O	C_6H_5	67	110–113°	$C_{28}H_{29}N_2OP$ (440.5)
6c	4-H_3C—C_6H_4	CH_3	C_6H_5	O	C_6H_5	89	135–139°	$C_{29}H_{25}N_2OP$ (448.5)
6d	C_6H_5	CH_3	C_6H_5	O	C_6H_5	62	212–214°	$C_{28}H_{23}N_2OP$ (434.5)
6e	4-H_3C—C_6H_4	CH_3	4-H_3C—C_6H_4	O	C_6H_5	69	305–308°	$C_{30}H_{27}N_2OP$ (462.6)
7a	C_6H_5	H	C_6H_5	S	C_6H_5	80	173–175°	$C_{27}H_{21}N_2PS$ (436.6)
7b	4-H_3C—C_6H_4	CH_3	C_6H_5	S	C_6H_5	69	207–209°	$C_{29}H_{25}N_2PS$ (464.6)
7c	4-H_3C—C_6H_4	H	*c*-C_6H_{11}	S	C_6H_5	89	169–171°	$C_{28}H_{29}N_2PS$ (456.6)
7d	*c*-C_6H_{11}	CH_3	C_6H_5	S	C_6H_5	58	115–117°	$C_{28}H_{29}N_2PS$ (456.6)

[a] Satisfactory microanalysis obtained: C, ±0.30; H, ±0.23; N, ±0.17; Cl, ±0.25; P, ±0.28; S, ±0.30.

Table 2. Spectral data for compounds **5**, **6**, and **7**

Compound	I.R. (Nujol) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]	M.S. *m/e* (M^+)
5a	700, 730, 760, 820, 1300	2.3 (s, 3H, CH_3); 6.6 (s, 1H, 4-H); 6.9–8.1 (m, 14 H_{arom})	
5b	680, 700, 730, 760, 800, 830, 870, 1280	1.8 (s, 3H, CH_3); 2.2 (s, 3H, CH_3); 6.7–8.1 (m, 14 H_{arom})	406
5c	720, 750, 790, 840, 1300	0.55–2.6 (m, 10H); 1.6 (s, 3H, CH_3); 2.8–3.5 (m, 1H); 7.1–7.7 (m, 10 H_{arom})	
5d	680, 700, 750, 760, 1290	2.1 (s, 3H, CH_3); 6.5 (s, 1H, 4-H); 6.7–8.2 (m, 14 H_{arom})	
6a	680, 700, 715, 730, 740, 1280	1.8 (s, 3H, CH_3); 2.4 (s, 3H, CH_3); 6.6–7.8 (m, 9 H_{arom})	448
6b	700, 730, 750, 760, 1300	0.6–2.5 (m, 10H); 1.5 (s, 3H, CH_3); 2.8–3.7 (m, 1H); 6.4–7.7 (m, 5 H_{arom})	
6c	720, 750, 780, 840, 1300	1.8 (s, 3H, CH_3); 2.0 (s, 3H, CH_3); 6.6–7.9 (m, 9 H_{arom})	
6d	690, 700, 720, 750, 760, 770, 1290	1.7 (s, 3H, CH_3); 6.5–7.5 (m, 20 H_{arom})	
6e	680, 700, 710, 730, 1270	1.7 (s, 3H, CH_3); 2.0 (s, 3H, CH_3); 2.3 (s, 3H, CH_3); 6.4–7.6 (m, 8 H_{arom})	
7a	700, 750, 770, 1120	6.5 (s, 1H, 4-H); 6.6–8.2 (m, 20 H_{arom})	436
7b	630, 680, 700, 730, 750, 770, 870, 1000	1.8 (s, 3H, CH_3); 2.0 (s, 3H, CH_3); 6.4–7.9 (m, 9 H_{arom})	
7c	680, 720, 730, 740, 760, 800, 1100	0.7–2.8 (m, 11H); 1.9 (s, 3H, CH_3); 5.9 (s, 1H, 4-H); 6.8–8.0 (m, 14 H_{arom})	
7d	700, 740, 780, 980	0.5–2.5 (m, 10H); 1.4 (s, 3H, CH_3); 2.7–3.3 (m, 1H); 6.9–8.3 (m, 5 H_{arom})	

The structures of the new compounds **5**, **6**, and **7** were confirmed by microanalytical and spectral data. The I.R. spectra show a characteristic absorption band at 1300 cm^{-1} assigned to P=Y bond stretching in the ring (Table 2).



Scheme **B**

The present method is advantageous for the preparation of 1,2-dihydro-1,3,2-P^V-diazaphosphorines on account of its simplicity and the ready availability of the reactants used.

1,2-Dihydro-1,3,2-P^V-diazaphosphorine Derivatives 5, 6, and 7; General Procedure:

Compound **1** (5 mmol) and triethylamine (10 mmol) are dissolved in benzene (60 ml) under an inert atmosphere. The solution is cooled to 0 °C and the phosphorus halide **3** (5 mmol) dissolved in dry benzene (10 ml) is added with stirring. The resultant solution is allowed to warm to room temperature and then stirred for 4 h. Triethylamine hydrochloride is filtered off, and the filtrate is evaporated under reduced pressure to give a yellow-orange solid residue which is purified by column chromatography on silica gel eluting with diethyl ether.

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