Reaction of 4-Amino-1-azabutadiene Derivatives with Phosphorus(III) Halides: Synthesis of 1,2-Dihydro-1,3,2-P^{III}-diazaphosphorine Derivatives

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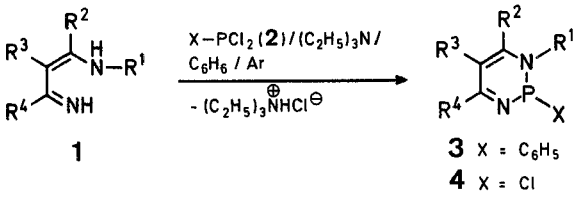
4-Amino-1-azabutadienes (**1**) are excellent building blocks in the preparation of heterocycles[1]. Recently, we have described a new method of synthesis of 1,2-dihydro-1,3,2-P^{V}-diazaphosphorines by reacting **1** with phosphorus (V) halides[2].

The role of organic phosphorus derivatives in biological processes has initiated the development of several synthetic methods for this class of compounds[3]. Phosphorus heterocycles[4], especially those containing the P-N group, are very important due to their pharmacological properties[5]. It should be pointed out that 1,2-dihydro-1,3,2-P^{V}-diazaphosphorines are rarely mentioned in the literature[2,6] while the corresponding P^{III} derivatives have not yet been described[7].

The reaction of 4-amino-1-azabutadiene derivatives (**1**) with phenylphosphonous dichloride (**2**; X = C_6H_5) or phosphorus trichloride (**2**; X = Cl) in benzene/triethylamine gives high yields of the heterocycles **3** and **4**, respectively (Table). Treatment of **3** and **4** with dilute alkaline or acid solutions at room temperature regenerates the starting 1-azabutadienes (**1**).



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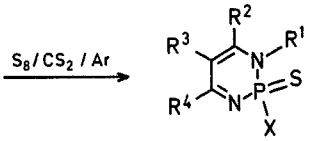
3 X = C_6H_5
4 X = Cl

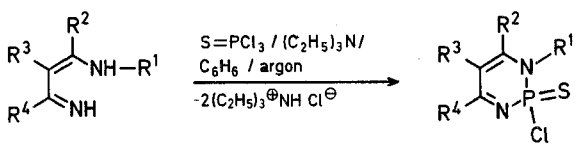


5 X = C_6H_5
6 X = Cl

1,3-6	R^1	R^2	R^3	R^4
a	C_6H_5	C_6H_5	CH_3	4-$H_3C-C_6H_4$
b	4-$H_3C-C_6H_4$	C_6H_5	CH_3	C_6H_5
c	4-$H_3C-C_6H_4$	C_6H_5	H	c-C_6H_{11}
d	C_6H_5	C_6H_5	H	C_6H_5
e	4-$H_3C-C_6H_4$	C_6H_5	H	4-$H_3C-C_6H_4$
f	C_6H_5	C_6H_5	CH_3	C_6H_5
g	4-$H_3C-C_6H_4$	C_6H_5	H	C_6H_5
h	c-C_6H_{11}	H	H	4-$H_3C-C_6H_4$

The structures of the new compounds **3** and **4** are confirmed by their spectral data (Table). The ^{13}C-N.M.R. spectra show characteristic coupling of the ring carbon atoms with the phosphorus heteroatom.

Treatment of **3** and **4** with elemental sulfur in carbon disulfide yields 1,3,2-diazaphosphorines **5** and **6**, respectively (Method A). Alternatively, the heterocycles **6** can be obtained by reaction of **1** with thiophosphoryl chloride, (Method B).



1 **6**

In conclusion, the described method gives access to new 1,2-dihydro-1,3,2-P^{III}-diazaphosphorines (**3, 4**). The high yields combined with the ready availability of the starting materials qualifies this synthesis as a convenient route to compounds **3** and **4**.

1,2-Dihydro-1,3,2-P^{III}-diazaphosphorines (3, 4); General Procedure: The phosphorus (III) halide (**2**; 5 mmol) in dry benzene (10 ml) is added dropwise at 5–10°C to a stirred solution of the 1-aza-

Table 1. 1,2-Dihydro-1,3,2-P^{III}-diazaphosphorines (**3, 4**) and 1,2-Dihydro-1,3,2-*p*-diazaphosphorine 2-Sulfides (**5,6**) prepared

Product	Yield [%]	m.p. (dec.) [°C]	Molecular formula[a] or Lit. m.p. [°C]	I.R. (Nujol) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]	^{13}C-N.M.R. ($CDCl_3$) δ [ppm] ($J_{^{13}C^{31}P}$ [Hz])			
						C-4	C-5	C-6	others
3a	93	105–107°	$C_{29}H_{25}N_2P$ (432.5)	1610, 1630	1.77 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 6.82–7.96 (m, 19H$_{arom}$)	174.3 (8.6)	119.1 (12.4)	147.5 (3.1)	18.2; 20.5; 123.5–138.6, 140.3, 144.1, 145.3 (C_{arom})
3b	96	88–90°	$C_{29}H_{25}N_2P$ (432.5)	1600, 1620	1.75 (s, 3H, CH_3); 2.12 (s, 3H, CH_3); 6.5–8.02 (m, 19H$_{arom}$)	173.8 (8.7)	118.2 (12.2)	149.3 (3.5)	18.2; 20.4; 124.7–135.5, 139.7, 139.8, 142.3 (C_{arom})
3c	90	55–57°	$C_{28}H_{29}N_2P$ (424.5)	1610, 1640	0.94–2.64 (m, 11H$_{Cyclohexyl}$); 1.97 (s, 3H, CH_3); 6.07 (s, 1H); 6.66–7.96 (m, 14H$_{arom}$)	178.1 (9.2)	111.5 (14.9)	150.8 (3.4)	20.1; 25.7; 25.9; 30.9; 48.5; 124.5 – 137.3; 140.5, 142.0, 143.1 (C_{arom})
3d	95	58–60°	$C_{27}H_{21}N_2P$ (404.5)	1580, 1610	6.74 (s, 1H); 6.86–8.28 (m, 20H$_{arom}$)	167.6 (9.1)	109.7 (13.0)	151.9 (3.1)	123.8–139.2, 139.4, 141.0, 145.3 (C_{arom})
3e	88	123–125°	$C_{29}H_{25}N_2P$ (432.5)	1590, 1610	2.05 (s, 3H, CH_3); 2.32 (s, 3H, CH_3); 6.78 (s, 1H); 6.90–8.12 (m, 18H$_{arom}$)	167.5 (9.1)	109.9 (13.4)	151.8 (3.2)	20.4; 21.0; 124.6–139.9, 140.6, 141.5, 142.1 (C_{arom})
4b	93	151–153°	$C_{23}H_{20}ClN_2P$ (390.8)	1610, 1630	1.81 (s, 3H, CH_3); 2.01 (s, 3H, CH_3); 6.70–7.68 (m, 14H$_{arom}$)	172.3 (8.7)	114.6 (15.4)	155.1 (3.0)	18.5; 20.6; 126.6–134.5, 135.5, 138.4, 140.3 (C_{arom})
4c	86	158–160°	$C_{22}H_{24}ClN_2P$ (382.9)	1590, 1620	0.98–2.00 (m, 10H$_{Cyclohexyl}$); 2.01 (s, 3H, CH_3); 2.24–2.68 (m, 1H$_{Cyclohexyl}$); 6.19 (s, 1H); 6.70–7.45 (m, 9H$_{arom}$)	178.7 (9.5)	107.9 (15.7)	156.6 (6.4)	20.3; 25.3; 25.4; 30.4; 47.5; 125.9–129.1, 135.9; 138.0 (C_{arom})
4f	88	161–163°	$C_{22}H_{18}ClN_2P$ (376.8)	1590, 1610	1.89 (s, 3H, CH_3); 6.90–7.88 (m, 15H$_{arom}$)	171.4 (8.7)	114.6 (13.7)	154.1 (3.0)	18.5; 126.1–138.2, 138.7, 140.5, 141.5 (C_{arom})
4g	96	124–126°	$C_{22}H_{18}ClN_2P$ (376.8)	1600, 1610	2.21 (s, 3H, CH_3); 6.86 (s, 1H); 6.96–8.28 (m, 14H$_{arom}$)	166.6 (8.0)	106.5 (14.2)	157.8 (3.0)	20.3; 125.5–134.9, 137.0, 138.2 (C_{arom})
4h	87	68–70°	$C_{16}H_{20}ClN_2P$ (306.8)	1590, 1610	0.86–2.12 (m, 10H$_{Cyclohexyl}$); 2.25 (s, 3H, CH_3); 3.23–3.78 (m, 1H$_{Cyclohexyl}$); 6.66 (d, J = 8 Hz, 1H); 7.01–7.96 (m, 4H$_{arom}$); 8.17 (d, J = 8 Hz, 1H)	165.2 (14.7)	102.5 (16.5)	149.6 (7.3)	20.6; 24.0; 24.7; 33.3; 63.4; 127.4, 128.7, 132.3, 142.4 (C_{arom})
5a	70(A)	181–183°	$C_{29}H_{25}N_2PS$ (464.6)	1590, 1610	1.82 (s, 3H, CH_3); 2.44 (s, 3H, CH_3); 6.68–8.12 (m, 19H$_{arom}$)	175.1 (10.3)	111.2 (22.4)	151.9	18.8; 21.3; 126.0–135.1, 136.5, 137.7, 139.6, 140.1 (C_{arom})
5b	75(A) 69(B)	207–209°	207–209°[2]	–[2]	–[2]	174.1 (10.0)	110.7 (22.8)	152.7	18.6; 20.6; 126.8–135.0, 135.2, 135.8, 136.9, 139.6 (C_{arom})
5c	73(A) 89(B)	169–171°	169–171°[2]	–[2]	–[2]	181.3 (12.8)	104.0 (24.0)	155.7 (2.1)	20.6; 25.9; 30.4; 30.8; 48.7; 124.7–131.4, 132.2, 132.8, 136.2, 136.4 (C_{arom})
5d	77(A) 80(B)	173–175°	173–175°[2]	–[2]	–[2]	168.3 (10.1)	102.3 (23.7)	154.6	126.0–135.6, 136.3, 136.7 (C_{arom})
6c	76(A) 72(B)	143–145°	$C_{22}H_{24}ClN_2PS$ (414.9)	1590, 1600	0.98–2.44 (m, 11H$_{Cyclohexyl}$); 2.16 (s, 3H, CH_3); 5.99 (s, 1H); 6.78–7.64 (m, 9H$_{arom}$)	174.5 (4.6)	100.7 (8.6)	165.1 (1.1)	20.8; 25.3; 25.6; 30.5; 44.8; 124.1–130.2, 135.0, 135.3, 137.7, 137.8 (C_{arom})
6e	68(B)	154–156°	$C_{23}H_{20}ClN_2PS$ (428.9)	1600, 1620	2.09 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 6.58 (s, 1H); 6.66–7.53 (m, 13H$_{arom}$)	172.1	104.7 (23.0)	160.6	19.8; 20.6; 126.0–129.6, 133.4, 136.4, 142.7 (C_{arom})
6g	75(A) 79(B)	170–172°	$C_{22}H_{18}ClN_2PS$ (408.9)	1600, 1610	2.12 (s, 3H, CH_3); 6.58 (s, 1H); 6.70–8.20 (m, 14H$_{arom}$)	173.6	100.3	161.1	20.8; 122.2–128.7, 134.3, 135.6 (C_{arom})

[a] Satisfactory microanalysis obtained: C ±0.47, H ±0.28, N ±0.29.

butadiene (**1**; 5 mmol) and triethylamine (10 mmol) in dry benzene (60 ml) under an argon atmosphere. The mixture is stirred at room temperature for 4 h. After filtering off the precipitated triethylamine hydrochloride, the filtrate is evaporated to give a yellow-brownish solid. The crude product is washed with dry hexane and filtered (Table).

1,2-Dihydro-1,3,2-P^V-diazaphosphorine-2-sulfides (5, 6); General Procedure for Method A:

Under an argon atmosphere compound **3** or **4** (5 mmol) in carbon disulfide (40 ml) and elemental sulfur (6.4 g, 20 mmol) are stirred until the ^{1}H-N.M.R. spectra indicate the disappearance of the starting compounds (~ 4 days). The carbon disulfide is evaporated leaving behind a solid which is dissolved in benzene to eliminate the excess of sulfur. The product obtained after the evaporation of the benzene is purified by column chromatography on silica gel with diethyl ether as eluent (Table).

2-Chloro-1,2-dihydro-1,3,2-P^V-diazaphosphorine-2-sulfides (6); General Procedure for Method B:

Compound **1** (5 mmol) and triethylamine (10 mmol) are dissolved in benzene (60 ml) under argon. The solution is cooled to 5°C and thiophosphoryl chloride (0.85 g, 5 mmol) 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 presure to give a yellow solid residue which is purified by column chromatography on silica gel using diethyl ether as eluent (Table).

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