An Efficient and General Strategy for the Synthesis of 1,4-Dihydro-λ^3- and -λ^5-azaphosphinines from 2-Aza-1,3-dienes

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The first example of the use of 2-aza-1,3-dienes in the preparation of six-membered heterocycles containing phosphorus and nitrogen is described; 1,4-dihydro-1,4-λ^3- and -λ^5-azaphosphinines (**3**) have been prepared by reaction of 2-aza-1,3-diene (**1**) with halogenophosphines.

Synthesis and reactions of λ^3- and λ^5-phosphinines, phosphorus analogues of pyridine, have attracted a great deal of interest in recent years.[1] However, very little is known about the corresponding heterocycles containing both phosphorus and nitrogen, probably owing to the lack of general methods of synthesis of these types of compounds. Thus, while 1,2-dihydro-1,2-λ^3- and -λ^5-azaphosphinines have recently been reported,[2] only a few examples of 2,6-disubstituted 1,4-dihydro-1,4-λ^3- and -λ^5-azaphosphinines have been described.[3—5]

The strategy developed for the synthesis of the 1,4-dihydro derivatives[3—5] was always the formation of C–N–C bonds by reaction of bis-(β-ketoalkyl)-phosphine oxides, obtained from 1-alkynes[3,4] or buta-1,3-dienes[5] in a multi-step process, and ammonium acetate. However, the processes described do not seem to satisfy the requirements of simplicity and generality. Thus, the λ^3-derivatives is always produced from the corresponding λ^5-derivative by deoxygenation with silanes, the method apparently being limited to the synthesis of 3,5-unsubstituted-1,4-dihydro derivatives.[3,4]

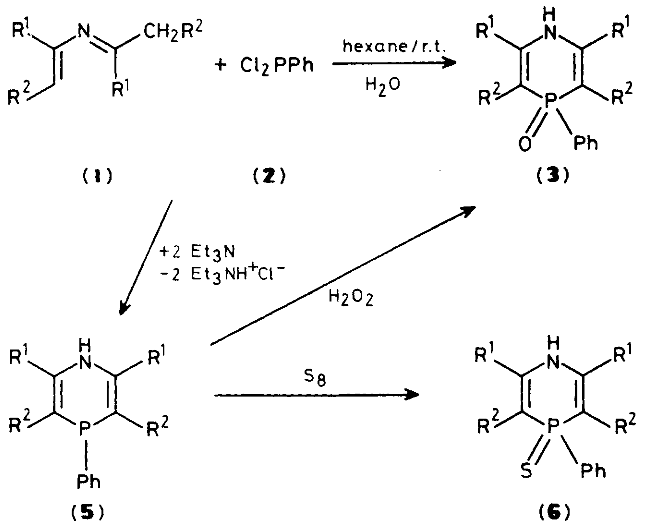
In addition, it is well known that 2-aza-1,3-dienes are versatile reagents in the synthesis of different types of 6-membered heterocyclic rings, mostly *via* [4 + 2] cycloaddition.[6] Other types of reactivity are scarce.[7]

Our own interest in the preparation of phosphorus and nitrogen containing heterocycles,[8] and also in the study of the reactivity of unactivated 2-aza-1,3-dienes of type (**1**),[9] prompted us to explore the behaviour of (**1**) with halogenophosphines. We report a new, simple, and one-pot synthesis of

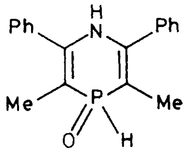
Table 1. 1,4-Dihydro-1,4-λ^5-azaphosphinines (**3**) from 2-aza-1,3-dienes (**1**) and (**2**).

Compound[a]	R^1	R^2	Yield/%	M.p./°C
(**3a**)	Ph	Me	80	310—312
(**3b**)	Ph	Et	76	230—232
(**3c**)	Ph	Pr^n	77	214—216
(**3d**)	p-MeC_6H_4	Me	82	303—305
(**3e**)	Pr^n	Et	75	201—203
(**3f**)	c-C_6H_{11}	Me	85	257—259

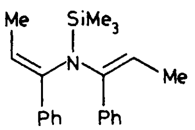
[a] All new compounds reported here gave satisfactory elemental analyses.



Scheme 1



(4)



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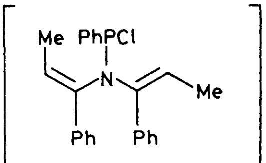

(8)

1,4-dihydro-1,4-λ^3- (5) and -λ^5-azaphosphinines (3) from 2-aza-1,3-dienes (1) and dichlorophenylphosphine (2).

The treatment of (1) (10 mmol) with dichlorophenylphosphine (2) (10 mmol) in dry hexane (20 ml) at room temperature for several hours produced 1,4-dihydro-1,4-λ^5-azaphosphinines (3) in high yields after aqueous work-up (Scheme 1 and Table 1).

Compounds (3) were characterized on the basis of their spectroscopic data and mass spectrometry.† For instance, the methyl groups of (3a) give a ^{1}H resonance at δ 1.7 ($^3J_{PH}$ 13.6 Hz) and a ^{13}C resonance at δ 12.9 ($^2J_{PC}$ 6.7 Hz) as doublets; the olefinic carbon β to nitrogen gives a ^{13}C n.m.r. doublet at δ 98.0 ($^1J_{PC}$ 98.4 Hz). The δ values and J values for compounds (3) are consistent with the proposed structure.

In a similar way, the reaction of (1) (R^1 = Ph, R^2 = Me) with phosphorus trichloride at room temperature and aqueous work-up gave rise to the secondary phosphine oxide, (4)† (70% yield).

The formation of (3) can be easily understood through a cyclocondensation reaction with loss of two HCl-equivalents, following a mechanism similar to that proposed[10] when 5,10-dihydrophenophosphazine derivatives were obtained from diarylamines and PCl_3.

The above mentioned products (3) were obtained when *N*-trimethylsilyldivinylamines (7)[11] were used under the same conditions instead of 2-aza-1,3-dienes (1). Taking into account the stereochemistry of (7), this result suggests that the process is initiated by the nitrogen atom, giving rise to the intermediate (8) (Figure 2), which has not been isolated, which subsequently undergoes rearrangement and further condensation to yield (3a).

Finally, 1,4-dihydro-1,4-λ^3-azaphosphinine (5) (R^1 = Ph, R^2 = Me) was formed (δ_P −12.6 p.p.m.) when the HCl was removed from the reaction by means of triethylamine. Treatment of (5) with H_2O_2 afforded the above-prepared λ^5-azaphosphinine oxide (3a); compound (5) was also converted into the crystalline sulphide (6) (R^1 = Ph, R^2 = Me)† (73% yield) by reaction with sulphur (Scheme 1).

We have thus described a general, simple, and new (formation of C–P–C bonds) strategy for the synthesis of substituted 1,4-dihydro-1,4-λ^3- and -λ^5-azaphosphinines from easily available starting materials. Moreover, the versatility and potential of 2-aza-1,3-dienes (1) in heterocyclic chemistry is shown, not only in [4 + 2] cycloaddition reactions,[9] but also in other types of processes *e.g.* cyclocondensation reactions.

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† *For example*: (3a) ^{1}H n.m.r. (300 MHz, $CDCl_3$) δ 1.7 (d, 6H, $^3J_{PH}$ 13.6 Hz), 6.5 (br., 1H, exchangeable with D_2O), 7.3—8.0 (m, 15 H); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 145.1, 136.1—127.8, 98.0 (d, $^1J_{PC}$ 98.4 Hz), 12.9 (d, $^2J_{PC}$ 6.7 Hz); ^{31}P n.m.r. δ +16.2; *m/z* 371 (M^+), 247. (4), m.p. 204—206 °C; ^{1}H n.m.r. (300 MHz, $CDCl_3$) δ 1.9 (d, 6H, $^3J_{PH}$ 12.5 Hz), 6.8 (br, 1H, exch. with D_2O), 7.2—7.4 (m, 10H), 8.0 (d, 1H, $^1J_{PH}$ 492 Hz); ^{13}C ($CDCl_3$, 75 MHz) δ 145.5 (d, $^2J_{PC}$ 6.4 Hz), 135.5 (d, $^3J_{PC}$ 12.9 Hz), 129.3, 128.7, 128.2, 98.8 (d, $^1J_{PC}$ 125.7 Hz), 14.5 (d, $^2J_{PC}$ 10.6 Hz); ^{31}P n.m.r. δ +6.4; *m/z*, 295 (M^+), 247. (6), m.p. 198—200 °C; ^{1}H n.m.r. (300 MHz, $CDCl_3$) δ 1.7 (d, 6H, $^3J_{PH}$ 13.6 Hz), 6.3 (br. 1H, exch. with D_2O), 7.3—8.1 (m, 15H); ^{13}C n.m.r. (75 MHz, $CDCl_3$) δ 143.4, 136.2, 132.4, 132.3, 130.6—127.8, 94.8 (d, $^1J_{PC}$ 79.7 Hz), 13.2 (d, $^3J_{PC}$ 9.1 Hz); ^{31}P n.m.r. δ +27.8; *m/z* 387 (M^+).