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Synthesis of 1*H*-1,2 λ^5-Azaphosphinin-6-ones from *N*-Alkoxycarbonyl phosphazenes and DMAD

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Abstract: 1*H*-1,2 λ^5-Azaphosphinin-6-ones are prepared by reaction of DMAD with metallated *N*-alkoxycarbonyl alkyldiphenylphosphazenes. Copyright © 1996 Elsevier Science Ltd

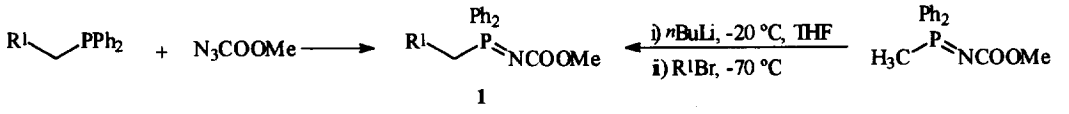
There have been recently a renewed interest in the synthesis of λ^5-azaphosphinines[1]. A few procedures are known for the preparation of derivatives of this compound-class with the heteroatoms occupying the 1,2-, 1,3-, and 1,4-positions of the ring[2]. A successful strategy leading to a variety of these phosphorus containing heterocycles is based on the ability of λ^5-phosphazenes to insert dimethylacetylene dicarboxylate (DMAD) into the P=N bond[3]. The resulting stabilized phosphorus ylides afford 1,4 λ^5-azaphosphinines by thermal cyclocondensation[4] and 1,4 λ^5-azaphosphininones when the cyclization is promoted by potassium hydride[5]. Additionally, the intramolecular condensation of *N*-*o*-(methoxycarbonyl)phenyl alkyldiphenylphosphazenes yields 1*H*-1,2 λ^5-benzazaphosphinin-4-ones[6].

In principle, the reactivity of the alkyldiphenylphosphazenes towards electrophiles can be tuned to the P=N bond or to the α-position of the aliphatic substituent depending of the reaction conditions. Under neutral conditions the addition to the P=N is exclusively observed, while by metalation of the phosphazene with LDA or ^{n}BuLi the reaction takes place regioselectively through the carbon adjacent to the P=N moiety[7]. Here we report the synthesis of 1*H*-1,2 λ^5-azaphosphinin-6-ones from *N*-methoxycarbonyl alkyldiphenylphosphazenes **1** and DMAD.

Phosphazenes **1** are easily obtained through the Staudinger reaction between the corresponding phosphine and ethyl azidoformate[8]. For R^1= allyl and benzyl we have found that the addition of the respective bromide to the lithio methyldiphenylphosphazene is a better route because of the comparatively low yields obtained in the preparation of the phosphines necessary for the Staudinger reaction (scheme 1).

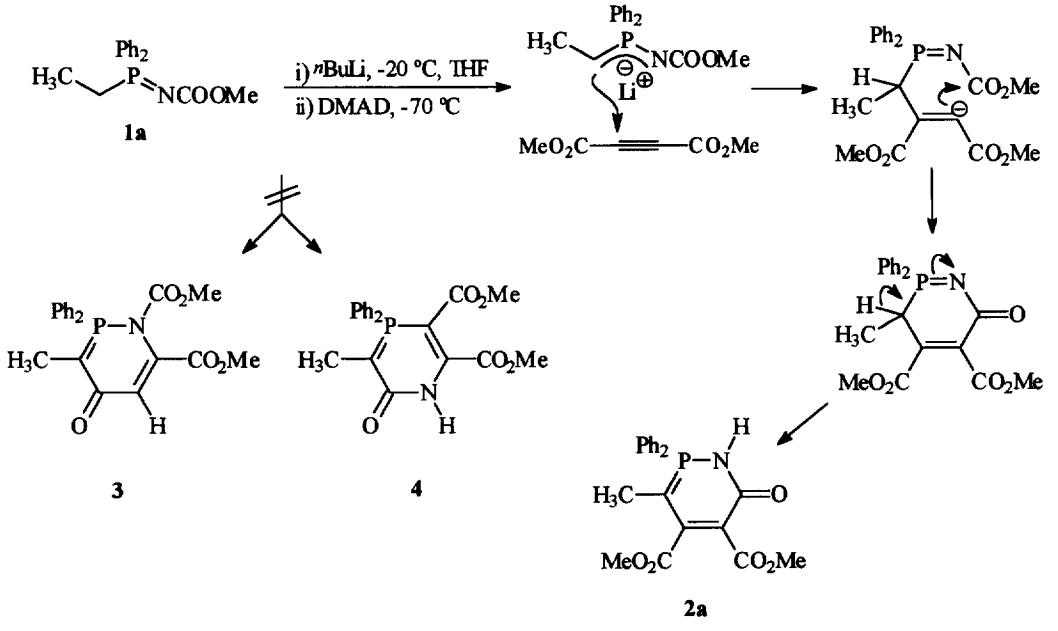
The metalation of **1a** with ^{n}BuLi in THF at -20 °C for 30 min. followed by addition of DMAD at -70 °C and aqueous work-up once room temperature is reached afford 50% of 1*H*-1,2 λ^5-azaphosphinin-6-one **2a**

(scheme 2). Under these reaction conditions 50% of the starting phosphazene is recovered. The heterocycle **2a** was purified by column chromatography using ethyl ether as eluent and then recrystallyzed from hexane-chloroform. The structure assignment is based on its spectroscopic data[9].



Scheme 1

The structure of **2a** indicates that the lithio phosphazene **1a** is added regioselectively through the α-carbon of the P=N bond to the carbon-carbon triple bond of the DMAD. The vinyl carbanion thus obtained is cyclocondensed with the methoxycarbonyl group of the phosphazene yielding a 3*H*-1,2 λ^5-azaphosphinin-6-one which finally tautomerizes to the 1*H*-1,2 λ^5-azaphosphinin-6-one **2a** isomer exhibiting an extended conjugation of the double bonds in the heterocycle. Phosphazene-amineylide tautomerization processes are precedented in the literature[10].



Scheme 2

The formation of azaphosphinines **3** and **4** arising, respectively from the addition of the DMAD through the nitrogen of the lithio phosphazene **1a** and the insertion of the acetylenic ester into the P=N linkage can be excluded based on the ^{13}C NMR spectrum. For **3** one would expect a carbon signal close to 200 ppm for the carbonyl carbon of the ring, plus a $C(sp^2)$-H, while compound **4** should present two quaternary carbon atoms directly bonded to phosphorus showing a large $^1J_{PC}$ coupling constant ($\approx$ 100 Hz)[11]. Instead, only a quaternary carbon atom at 86.49 ppm is found directly bonded to phosphorus[9] ($^1J_{PC}$ = 105.6 Hz), and the ^1H NMR spectrum measured in $CDCl_3$ shows a broad singlet at 14.30 ppm corresponding to the N-H of **2a**. Moreover, when the ^1H NMR spectrum is acquired in DMSO-d_6 this signal is shifted to 14.03 ppm and the exchange processes involving the NH are slowed down so that a coupling $^2J_{PH}$ = 5.6 Hz can be observed.

The existence in **2a** of an acid proton could be the reason for the low yield of the reaction because as soon as it is formed it would quench the corresponding amount of lithio phosphazene **1a**. In order to optimize the procedure we varied the stoichiometry of the base and electrophile, and the best results are found for a 1:2:2 relation of phosphazene:^{n}BuLi:DMAD (table 1).

Table 1. Selected physical data for 1*H*-1,2 λ^5-azaphosphinin-6-ones **2**.

Compound	R^1	M.p. (°C)	$\delta^{31}P$ (ppm)[a]	Yield (%)[b]
2a	Me	172-173	26.22	90
2b	Et	130-131	25.67	91
2c	^{n}Pr	160-161	25.98	90
2d	^{i}Pr	147-148	23.71	92
2e	$CH_2CH{=}CH_2$	180-181	26.61	75
2f	$CH_2C_6H_5$	150-151	26.77	75

[a] Spectra recorded on a Bruker AC300 in $CDCl_3$ using 85% H_3PO_4 as external standard. [b] Isolated yield based on phosphazene **1**.

Surprisingly, no reaction is observed neither for the simplest phosphazene **1**, R^1= H, nor for the R^1= $CH{=}CH_2$ and C_6H_5. The stabilization of the carbanion in the allyl and benzyl derivatives would decrease its reactivity towards the DMAD. At present we have no explanation for the lack of reactivity when R^1= H. In fact, the corresponding lithio phosphazene smoothly reacts with methyl iodide, allyl bromide and benzyl bromide affording the respective alkylation product with good yields.

In summary a new synthesis of 1*H*-1,2 λ^5-azaphosphinin-6-ones **2** is reported based on the *C*-regioselective addition of DMAD to readily available *N*-methoxycarbonyl alkyldiphenylphosphazenes mediated by *n*-butyllithium.

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9. Selected spectral data for **2a**, $C_{21}H_{20}NO_5P$, IR (KBr pellets): 1624, 1737 cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$), δ (ppm), $^nJ_{PH}$ (Hz): 1.71 (d, ^3J = 12.1, 3H); 3.53 (s, 3H); 3.90 (s, 3H); 7.51-7.70 (m, $10H_{Arom}$). ^{13}C NMR (75.5 MHz, $CDCl_3$), δ (ppm), $^nJ_{PC}$ (Hz): 14.03 (d, ^2J = 8.7); 51.68; 52.04; 81.14; 86.49 (d, ^1J = 105.6); 127.0 (d, ^1J = 109.7); 128.82 (d, ^2J = 7.1); 132.18 (d, ^3J = 10.9); 132.80 (d, ^4J = 3.1); 149.46 (d, ^2J = 20.7); 168.49 (d, ^3J = 8.7 Hz); 170.41; 171.39 (d, ^2J = 6.0). MS (m/e): 397 (M^+, 100%); 350 (29%); 337 (33%).
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