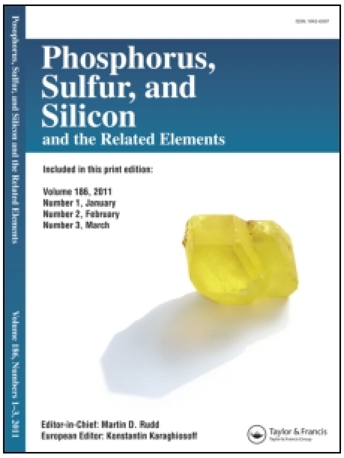

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS AND CYCLIZATION OF PHOSPHORYLATED β-ALLENIC AMINES

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To cite this Article Amedjkouh, Mohamed , Faure, Robert , Hatem, Jacques , Tordo, Paul and Grimaldi, Jacques(1997) 'SYNTHESIS AND CYCLIZATION OF PHOSPHORYLATED β-ALLENIC AMINES', Phosphorus, Sulfur, and Silicon and the Related Elements, 126: 1, 53 — 64

To link to this Article: DOI: 10.1080/10426509708043545

URL: http://dx.doi.org/10.1080/10426509708043545

Phosphorus, Sulfur, and Silicon, 1997, Vol. 126, pp. 53-64
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Printed in Malaysia

SYNTHESIS AND CYCLIZATION OF PHOSPHORYLATED β-ALLENIC AMINES

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(Received 18 December, 1996; in final form 13 January, 1997)

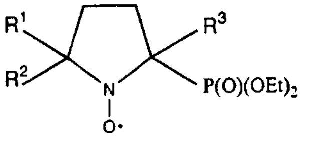
Phosphorylated β-allenic amines were obtained by aminophosphorylation of β-allenic aldehydes and ketones. When treated by silver tetrafluoroborate in methylene chloride, they generated phosphorylated nitrogen cycles such as 1-pyrrolines and 1.2,3,6-tetrahydropyridines, with dephosphorylation of the latter tetrahydropyridines producing 3,6-dihydropyridines.

Keywords: Aminophosphorylation; phosphorylated β-allenic amines; cyclic aminophosphonates; pyrrolines; aminophosphonates

INTRODUCTION

The greatest number of stable radicals can be found in the family of nitroxide radicals $(R)_2$-N-O·. These radicals have many different applications, such as in magnetometers designed to measure weak magnetic fields[1], or as spin labelling markers in the study of biomembranes and molecular dynamics[2].

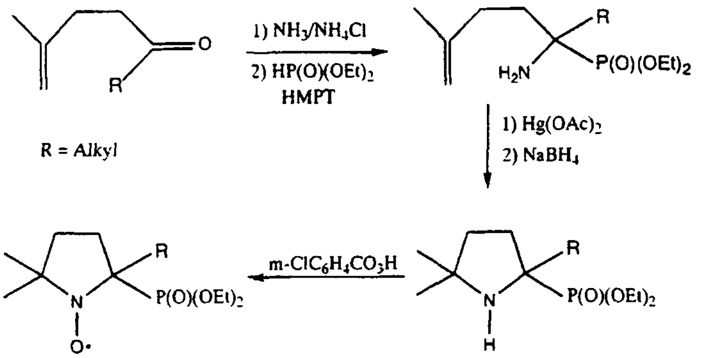
Several studies have shown that phosphorylated nitroxides of the type[3] (scheme 1):



R^1, R^2 and R^3 = alkyl

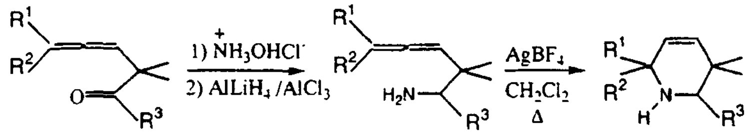
SCHEME 1

are particularly stable, and that the following synthetic route (scheme 2) is an interesting way of obtaining such compounds.



SCHEME 2

Aminophosphorylation of a γ-ethylenic ketone produced an aminophosphonate, which was then cyclized into the corresponding pyrrolidine. Oxidation of the latter produced the corresponding nitroxide. During recent experiments[4], β-allenic amines coming from β-allenic aldehydes **1** or β-allenic ketones **2** have been cyclized to 1,2,3,6-tetrahydropyridines (scheme 3).



1, $R^3 = H$; 2, $R^3 = CH^3$ R^1, R^2 = alkyl

SCHEME 3

As a result, it appears interesting to apply the synthetic route shown in scheme 2 to compounds **1** and **2**, which are likely to lead to new phosphorylated nitroxides.

In this article we will describe the synthesis of phosphorylated β-allenic amines **3** and **4** resulting from aldehydes **1** and ketones **2**, and then describe their cyclization and the nitrogen heterocycles that we isolated.

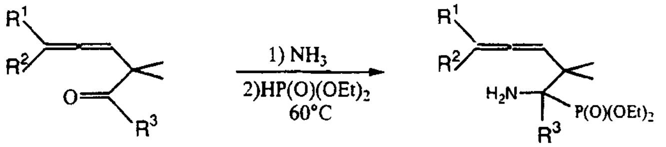
RESULTS AND DISCUSSION

Synthesis of Phosphorylated β-Allenic Amines 3 and 4.

The phosphorylated β-allenic amines **3** and **4** were obtained by aminophosphorylation[5] of β-allenic aldehydes and ketones **1** and **2**.

Synthesis of β-allenic aldehydes and ketones 1 and 2.

The β-allenic aldehydes **1** were easily prepared from isobutyraldehyde and a-acetylenic alcohol[6]. The β-allenic ketones **2** were obtained in the standard manner, first by the action of methyl magnesium iodide on β-allenic aldehydes and then by oxidation of the ensuing β-allenic alcohols[7]. Aminophosphorylation of **1**and **2** was achieved by bubbling ammonia gas through a solution of the carbonyl compound in diethylphosphite[5] (scheme 4).



1, R^3 = H ; 2, R^3 = CH_3 3, R^3 = H ; 4, R^3 = CH_3

1a and 2a : $R^1 = R^2 = CH_3$: 3a and 4a
1b and 2b : $R^1 = CH_3$; R2 = C_2H_5 : 3b and 4b
1c and 2c : R^1-R^2 = -$(CH_2)_5$- : 3c and 4c

SCHEME 4

The yields (**3a**: 42%, **3b**: 37%, **3c**: 18%, **4a**: 56%, **4b**: 54%, **4c**: 38%) are better in the case of amines **4** obtained by the aminophosphorylation of ketones **2**.

Another method of aminophosphorylation was tested, using ammonium acetate instead of ammonia gas[8]. However, while this approach was more practical, it produced lower yields.

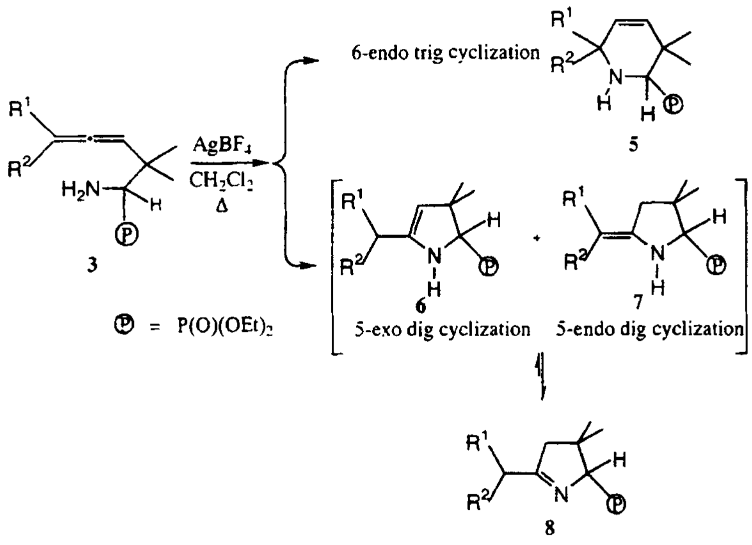
Cyclization of Phosphorylated β-Allenic Amines 3 and 4.

The intramolecular nucleophilic additions to an allenic moiety constitutes a particularly effective means of obtaining heterocycles. These reactions are carried out in the presence of catalysts like mercury[9] or silver[10] salts which activate the allenic moiety.

The literature mentions several examples of cyclizations conducted on β-allenic compounds[11] which, among the different cyclizations possible, often form 6-membered heterocycles (by 6 endo-trig cyclization)[12], as was seen in the case of β-allenic amines[4].

When the phosphorylated β-allenic amines **3** and **4** were treated in refluxing methylene chloride in the presence of $AgBF_4$ as catalyst, they cyclized easily with a yield of roughly 90%. Both amines **3** and **4** produced a mixture of 5- and 6-membered nitrogen heterocycles.

As shown in scheme 5, for example, the compounds produced from phosphorylated β-allenic amines $3(R^P = H)$ are 1,2,3,6-tetrahydropyridines and 1-pyrrolines.



SCHEME 5

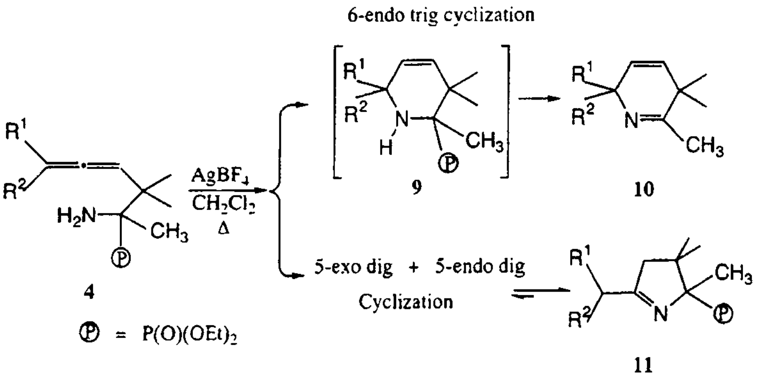
The following compounds have been obtained in these proportions:

5a/8a = 73/27	**5b/8b** = 70/30	**5c/8c** = 66/34
$R^1 = R^2 = CH_3$	$R^1 = CH_3$; $R^2 = C_2H_5$	$R^1\text{-}R^2 = \text{-}(CH_2)_5\text{-}$

The nucleophilic attack of the nitrogen lone pair on the distal trigonal carbon of the allenic moiety led to compounds **5** as expected. A similar attack on the digonal carbon led to 1-pyrrolines **8**. This probably resulted from a tautomeric equilibrium occuring after the formation of **6** and **7** which were never themselves characterized.

The relative proportions of compounds **5** and **8** show that the formation of compounds **5** is impeded by an increase in the steric crowding.

Similarly (as shown in scheme 6), phosphorylated β-allenic amines **4** ($R^3 = CH_3$) led to the corresponding 1-pyrrolines **11**, and to a small amount of 3,6-dihydropyridines **10**, which resulted from the rapid dephosphorylation of the 1,2,3,6-tetrahydropyridines **9** that were not isolated.



SCHEME 6

The following compounds have been obtained in these proportions:

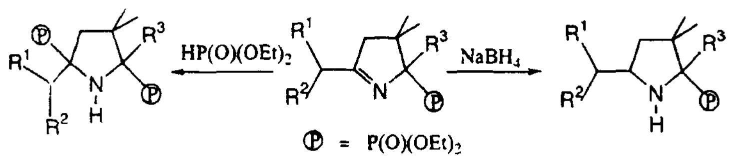
10a/11a = 19/81	**10b/11b** = 6/94	**10c/11c** = 12/88
$R^1 = R^2 = CH_3$	$R^1 = CH_3$; $R^2 = C_2H_5$	R^1-R^2 = -$(CH_2)_5$-

Compounds **5**, which are stable, differ from **9** only in possessing an hydrogen atom in place of the methyl group. Thus, the dephosphorylation of **9** can be attributed to an increase in the steric constraint caused by the methyl group.

CONCLUSION

We have described a method of synthesizing a new series of 5- and 6-membered phosphorylated nitrogen heterocycles. These compounds were obtained from phosphorylated β-allenic amines **3** and **4** through the nucleophilic attack of the nitrogen lone pair on either the central or the distal carbon of the allenic moiety.

Different compounds obtained could be of interest in the synthesis of phosphorylated nitroxides. Compounds such as **5** can be oxidized directly. Others such as **8** can first be transformed into pyrrolidines **12** or **13**, either by reduction or by addition of diethylphosphite[13], and then oxidized (scheme 7). Work on this second phase is in progress, and results will be published in the near future.



13 **8 et 11** **12**

SCHEME 7

EXPERIMENTAL

^{1}H- and ^{13}C- NMR spectra were performed in $CDCl_3$with tetramethylsilane as internal reference, and recorded on Bruker AC 100, AC 200 and AM 400 X spectrometers. Merck Silica gel 60 (230-400 Mesh) was used for column chromatography.

Typical procedure for the preparation of β*-allenic aminophosphonates* **3** *and* **4**. Ammonia was bubbled into a mixture of β-allenic carbonyl compound (20 mmoles) and diethylphosphite (22 mmoles) at 60°C, for about 15 hours. Then the mixture was acidified with diluted (5%) hydrochloric acid and washed several times with ether, to remove non reacted starting materials. The aqueous layer was poured over potassium carbonate and extracted with ether. The organic layer was dried over magnesium sulfate. Filtration and removal of the solvent gave the β-allenic aminophosphonate which was pure enough for further uses.

3a Diethyl (1-amino-2,2,5-trimethylhexa-3,4-dien-1-yl)phosphonate. Yellow oil. Yield: 42 %. ^{1}H NMR: (200 MHz) δ (ppm): 1.19 (s,6H); 1.34 (t, 6H; J = 6.9 Hz); 1.71 (d, 6H; J = 2.9 Hz); 2.84 (d, 1H; J = 14.6 Hz); 4.17 and 4.19 (2quin, 4H; J = 7.1 Hz); 5.05 (sept, 1H; J = 2.9 Hz). ^{13}C NMR: (50.32 M Hz) δ (ppm): 16.39 and 16.50 (2C, $O\text{-}CH_2\text{-}\underline{C}H_3$); 20.67 (2C, $(\underline{C}H_3)_2C=$); 24.51 and 26.48 (2d, 2C, J = 6.0 Hz and J = 4.0 Hz, $C\text{-}(\underline{C}H_3)_2$); 38.81 (1C, $\underline{C}\text{-}(CH_3)_2$); 57.30 (d, 1C, J = 147,4 Hz: C-P); 61.68 and 62.00 (2d, 2C, J = 7.3 Hz, $O\text{-}\underline{C}H_2\text{-}CH_3$); 97.10 (d, 1C, J = 11.4 Hz; $C=\underline{C}\text{-}H$); 97.29 (1C, $(CH_3)_2\underline{C}=$); 200.72 (1C, =C=). ^{31}P NMR:(40.53 MHz) δ (ppm): 26.79. Anal. Calcd. for $C_{13}H_{26}NO_3P$: C, 56.69; H, 9.52; N, 5.09. Found: C, 56.61; H, 9.58; N, 5.02.

3b Diethyl(1-amino-2,2,5-trimethylhepta-3,4-dien-1-yl) phosphonate. Yellow oil. Yield: 37 %. For compounds **b**, the splittings of some figures are caused by the existence of two diastereoisomers. ^{1}H NMR: (200 MHz) δ (ppm): 1.00 and 1.01 (2t, 3H, J = 7.4 Hz); 1.17-1.19 (2 perturbed s 6H); 1.34 (t, 6H, J = 7.0 Hz);

1.71 (d, 3H, J = 2.8 Hz); 1.96 (q.d, 2H, J = 7.2 Hz and J = 2.8 Hz); 2.82 and 2.84 (2d, 1H, J = 14.6 Hz); 4.15 and 4.17 (2quin., 4H, J = 7.2 Hz); 5.16 (sext, 1H, J = 2.8 Hz).^{13}C NMR: (50,32 MHz) δ (ppm): 12.27 (1C, $\underline{C}H_3$-CH_2-C=); 16.34 and 16.45 (2C, O-CH_2-$\underline{C}H_3$); 19.23 (1C, $\underline{C}H_3$-C=); 24.79 and 26.59 (2d, 2C, J = 8.7 Hz, C-($\underline{C}H_3)_2$); 26.94 (1C, CH_3-$\underline{C}H_2$-); 38.78 (1C, $\underline{C}(CH_3)_2$); 57.76 (d, J = 147.1 Hz, 1C, C-P); 61.63 and 61.95 (2d, J = 7.2 Hz, 2C, O-$\underline{C}H_2CH_3$); 98.90, (d, J = 11.2 Hz, 1C, =C-H); 103.55 (1C, CH_3-$\underline{C}$=); 199.66 (1C, =C=),^{31}P NMR: (40.53 MHz) δ (ppm): 21.75.

3c Diethyl(1-amino-2,2-dimethyl-5-pentamethylenepenta-3,4-dien-1-yl)phosphonate. Yellow oil. Yield: 18 %. ^{1}H NMR: (100 MHz) δ (ppm): 1.19 (s, 6H); 1.33 (t, 6H, J = 7.1 Hz); 1.54 (M, 6H); 2.12 (M, 4H); 2.84 (d, 1H, J = 14.5 Hz) ; 4.14 and 4.16 (2 quin, 4H, J = 7.1 Hz); 5.05 (m, 1H). ^{13}C NMR: (25.18 MHz) δ (ppm): 15.67 and 15.94 (2C, O-CH_2-$\underline{C}H_3$); 23.96 and 25.79 (2d, J = 3.7 Hz and J = 6.2 Hz, 2C, C-($\underline{C}H_3)_2$); 25.64, 26.89 and 31.11 (5C, -$(CH_2)_5$-); 37.93 (d, 1C, J = 3.9 Hz, $\underline{C}$-$(CH_3)_2$); 57.52 (d, 1C, J = 147.1 Hz, C-P); 60.93 and 61.30 (2d, 2C, J = 7.2 Hz, O-$\underline{C}H_2$-CH_3); 96.30 (d, 1C, J = 10.3 Hz, =C-H); 103.70 (1C, $(CH_3)_2\underline{C}$=); 198.75 (1C, =C=). ^{31}P NMR: (40.53 MHz) δ (ppm): 26.63. Anal. calcd for $C_{16}H_{30}NO_3P$: C, 60.93; H, 9.59; N, 4.44.

4a Diethyl(2-amino-3,3,6-trimethylhepta-4,5-dien-2-yl)phosphonate. Yellow oil. Yield: 56 %. ^{1}H NMR: (200 MHz) δ (ppm): 1.15 and 1.19 (2s, 6H); 1.28 (d, 3H, J = 15.9 Hz); 1.32 (t, 6H, J = 7.1 Hz); 1.69 (d, 6H, J = 2.8 Hz); 4.14 and 4.16 (2 quin, 4H, J = 7.3 Hz); 5.28 (sept, 1H). ^{13}C NMR: (50.32 MHz) δ (ppm) : 16.21 and 16.34 (2C, O-CH_2-$\underline{C}H_3$); 20.10 (1C, H_2N-C-$\underline{C}H_3$); 20.36 (2C, =C-($\underline{C}H_3)_2$); 23.45 and 24.41 (2C, C-($\underline{C}H_3)_2$); 41.06 (d, 1C, J = 8.4 Hz, $\underline{C}$-$(CH_3)_2$); 57.84 (d, 1C, 145.2 Hz, C-P); 61.62 and 61.98 (2d, 2C, J = 8.1 Hz, O-$\underline{C}H_2$-CH_3); 96.12 (d, 1C, J = 7.5 Hz, =C-H); 96.27 (1C, $(CH_3)_2$-$\underline{C}$=); 200.82 (1C, =C=). ^{31}P NMR: (40.53 MHz) δ (ppm): 29.99. Anal. calcd for $C_{14}H_{28}NO_3P$: C, 58.1; H, 9.76; N, 4.84. Found: C, 58.0; H, 9.72; N, 4.80.

4b Diethyl(2-amino-3,3,6-trimethylocta-4,5-dien-2-yl)phosphonate. Yellow oil. Yield: 54 %. ^{1}H NMR: (200 MHz) δ (ppm): 1.01 and 1.08 (2t, 3H, J = 7.4 Hz); 1.15 , 1.17 , 1.20 and 1.22 (4s, 6H); 1.30 (d, 3H, J = 16.9 Hz); 1.34 (t, 6H, J = 7.1 Hz); 1.70 (d, 3H, J = 2.5 Hz); 1.97 (q.d, 2H, J = 7.2 Hz and J = 2.8 Hz); 4.14 and 4.16 (2quin, 4H, J = 7.3 Hz); 5.42 (sex, 1H, J = 7.4 Hz). ^{13}C NMR: (50.32 MHz) δ (ppm): 12.36 and 12.45 (1C, $\underline{C}H_3$-CH_2); 16.53 and 16.65 (2C, O-CH_2-$\underline{C}H_3$); 19.19 and 19.27 (2s, 1C, $\underline{C}H_3$-C-NH_2); 20.27 and 20.45 (1C, $\underline{C}H_3$-C=); 23.51 -23.94 and 24.60 - 24.98 (4d, 2C, C-($\underline{C}H_3)_2$); 27.03 and 27.15 (1C, C-$\underline{C}H_2$-CH_3); 41.38 (d, 1C, J = 7.2 Hz, $\underline{C}(CH_3)_2$); 58.13 (d, 1C, J = 144.8 Hz, C-P); 61.73 and 62.24 (2d, 2C, J = 8.0 Hz, O-$\underline{C}H_2CH_3$); 98.37 (d, 1C, J = 7.1, =C-H); 102.58 (1C, CH_3-$\underline{C}$=); 200.04 (1C, =C=). ^{31}P NMR: (40.53 MHz) δ (ppm): 30.01 and 30.15. Anal. calcd for $C_{15}H_{30}NO_3P$: C, 59.37; H, 9.97; N, 4.62. Found: C, 59.0; H, 9.93; N: 4.59.

4c Diethyl(2-amino-3,3 -dimethyl -6-pentamethylenehexa-4,5-dien-2-yl)phosphonate. Yellow viscous oil. Yield: 38 %. ^1H NMR: (200 MHz) δ (ppm): 1.17 and 1.21 (2s,6H); 1.28 (d,3H, J = 15.9 Hz); 1.33 (t, 6H, J = 7.0 Hz); 1.56 (M, 6H); 2.12 (M, 4H); 4.14 and 4.16 (2 quin, 4H, J = 7.10 Hz); 5.29 (broad s, 1H). ^{13}C NMR: (50.32 MHz) δ (ppm): 15.79 and 15.90 (2C, O-$CH_2\underline{C}H_3$); 25.50; 26.83 and 31.02 (5C, -$(CH_2)_5$-); 19.72 (1C,H_2N-C-$\underline{C}H_3$); 23.12 - 24.05 (2C, C-$(\underline{C}H_3)_2$); 40.40 (d, 1C, J = 8.2 Hz, $\underline{C}(CH_3)_2$); 57.46 (d, 1C, 144.9 Hz, C-P); 61.07 and 61.43 (2d, 2C, J = 7.5 Hz, O-$\underline{C}H_2CH_3$); 95.68 (d, 1C, J = 7.5 Hz, =C-H); 103.05 (1C, $(CH_2)_5$-$\underline{C}$=); 197.03 (1C, =C=). ^{31}P NMR: (40.53 MHz) δ (ppm): 29.79. Anal. calcd for $C_{17}H_{32}NO_3P$: C, 61.97; H, 9.80; N, 4.25. Found : C, 61.81; H, 9.84; N: 4.17.

Typical procedure for the cyclization of β*-allenic aminophosphonates* **3** *and* **4**. $AgBF_4$ (0,1 mmole, 20 mg) was added to a well stirred solution of the β-allenic aminophosphonate (2mmoles) in dichloromethane (10 ml). The reaction mixture was heated under reflux for 24 hours. After cooling, an aqueous saturated solution of NaCl (10 ml) was added to precipitate AgCl. After filtration, the mixture was extracted with ether, the extracts were dried over anhydrous $MgSO_4$. Filtration and removal of solvent afforded the cyclized compounds which were separated by flash column chromatography (eluant: pentane-acetone 60:40 v/v) on Merck silica gel.

The following derivatives were obtained:

5a Diethyl(3,3,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-2-yl.)phosphonate. Yellow viscous oil. Yield: 54%. ^1H NMR: (200 MHz) δ (ppm): 1.10 and 1.12 (2s, 6H); 1.18 and 1.19 (2s, 6H); 1.35 and 1.36 (2t, 6H, J = 7.1 Hz); 3.10 (d, 1H, J = 21.7 Hz); 4.22 (m, 4H); 5.29 - 5.55 (AB d system, 2H, J = 10.2 Hz; J = 1.3 Hz (5.55), and J = 7.7 Hz (5.29)). ^{13}C NMR: (50.32 MHz) δ (ppm): 15.84 and 16.02 (2C, O-$CH_2\underline{C}H_3$); 22.85; 26.12; 27.38 and 29.84 (4C, C$(\underline{C}H_3)_2$); 31.89 (1C, N-$\underline{C}$-$(CH_3)_2$); 50.29 (d, 1C, J = 14.7 Hz, $\underline{C}(CH_3)_2$); 56.11 (d, 1C, J = 157.5 Hz, C-P); 61.16 and 62.18 (2d, 2C, J = 6.6 Hz, O-$\underline{C}H_2$-CH_3); 133.49 (1C, =C-H); 135.60 (d, 1C, J = 15.0 Hz, H-C=). ^{31}P NMR: (40.53 MHz) δ (ppm): 23.88. Anal. calcd. for $C_{13}H_{26}NO_3P$: C, 56.69; H, 9.52; N, 5.09. Found: C, 56.66; H, 9.43; N, 5.12.

5b Diethyl(6-ethyl -3,3,6-trimethyl-1,2,3,6-tetrahydropyridin-2-yl.)phosphonate. Colourless oil. Yield: 50%. ^1H NMR: (400 MHz)δ (ppm): 0.84 (t, 3H, J = 7.5 Hz); 1.02; 1.04; 1.07 and 1.08 (4s, 6H); 1.13 and 1.14 (2s, 3H); 1.29 and 1.31 (2t, 6H, J = 6.9 Hz); 1.44 (q, 2H, J = 7.5 Hz); 3.04 and 3.08 (2d, 1H, J = 21.8 Hz); 4.16 (M, 4H); 5.29 - 5.49 (AB d, system, J = 10.2 Hz, J = 1.2 Hz (5.49) and J = 7.8 Hz (5.29)); 5.29 - 5.49 and 5.32 - 5.40 (2 AB d systems, 2H, J = 10.2 Hz, J =

2.1 Hz (5.40) and J = 7.0 Hz (5.32)). A simple spectra was obtained by decoupling the proton from phosphorus nuclei using an irradiating r.f. Thus spectral interpretation is greatly simplified. ^{13}C NMR: (50.32 MHz) δ (ppm): 8.00 and 8.31 (1C, $\underline{C}H_3$-CH_2-); 16.25 and 16.37 (2C, -O-CH_2-$\underline{C}H_3$); 23.27 and 25.10 (2C, C($\underline{C}H_3$)$_2$); 26.48 and 27.69 (1C, $H_3\underline{C}$-C); 32.28 (1C, N-$\underline{C}$-CH_2-CH_3); 31.39 and 34.67 (1C, CH_3-$\underline{C}H_2$.); 52.73 and 53.45 (2d, 1C, J = 14.3 Hz, $\underline{C}$(CH_3)$_2$); 56.59 and 56.66 (2d, 1C, J = 151.5 Hz, C-P); 61.62 and 62.52 (2M, -O-$\underline{C}H_2$-CH_3); 132.11 and 133.43 (1C, =C-H); 136.08 and 137.04 (2d, 1C, J = 15.6 Hz, H-C=). ^{31}P NMR: (40.53 MHz) δ (ppm): 22.62 and 26.44.

5c Diethyl(3,3-dimethyl-6-pentamethylene-1,2,3,6-tetrahydropyridin-2-yl.)phosphonate.Colourless oil. Yield: 48%. ^{1}H NMR: (200 MHz) δ (ppm): 1.12 - 1.16 (2s, 6H); 1.34 - 1.36 (2t, 6H, J = 7.1 Hz); 1.3- 1.8 (M, 10H); 3.09 (d, 1H, J = 21.71 Hz); 4.19 and 4.24 (2quin., 4H, J = 7.2 Hz); 5.31 - 5.59 (AB d system, 2H, J = 10.3 Hz, J = 7,8 Hz (5.31) and J ≈ 1 Hz (5.59)). ^{13}C NMR: (50.32 MHz) δ (ppm): 16.13 and 16.26 (2C, O-$CH_2\underline{C}H_3$); 21.26; 24.52 and 38.88 (5C, -(CH_2)$_5$); 23.40 and 27.66 (2C, C-(CH_3)$_2$); 32.80 (d, lC, J = 3.5 Hz, (CH_2)$_5$-C-) ; 51.92 (d, 1C, J = 13.8 Hz, $\underline{C}$(CH_3)$_2$); 56.09 (d, 1C, J = 157.4 Hz, C-P); 61.24 and 62.80 (2d, 2C, J = 7.2 Hz, -O-$\underline{C}H_2$-CH_3); 133.25 (1C, =C-H); 136.35 (d, 1C, J = 15.8 Hz, H-C=). ^{31}P NMR: (40.53 MHz) δ (ppm): 24.56. Anal. calcd for $C_{16}H_{30}NO_3P$: C, 60.93; H, 9.59; N, 4.44. Found: C, 60.90; H, 9.49; N, 4.42.

8a Diethyl(5-isopropyl-3,3-dimethylpyrrolin-2-yl.)phosphonate. Yellow oil. Yield: 20%. ^{1}H NMR: (200 MHz) δ (ppm): 1.15 (d, 6H, J = 7.0 Hz); 1.17 (s, 3H); 1.32 (M, 9H); 2.28 - 2.65 (AB d system, J = 16.64 Hz, J = 4.7 Hz (2.28) and J = 5.10 Hz (2.65)); 2.69 (m, 1H, J = 6.9 Hz and J = 2.6 Hz); 3.90 (d, 1H, J = 18.3 Hz); 4.15 (m, 4H). ^{13}C NMR: (50.32 MHz) δ (ppm): 16.26 and 16.45 (2C, O-$CH_2\underline{C}H_3$); 19.60 (2C, H-C($\underline{C}H_3$)$_2$); 23.98 (d, lC, J = 4.5 Hz, C($C\underline{H}_3$)$_2$); 29.38 (d, 1C, J = 9.9 Hz, C($\underline{C}H_3$)$_2$); 32.94 (1C, H-$\underline{C}$(CH_3)$_2$); 41.50 (d, 1C, J = 9.4 Hz, $\underline{C}$(CH_3)$_2$); 49.88 (1C. N=C-$CH_{?.}$): 61.53 and 62.44 (2d. 2C. J = 7.2 Hz. -O-$CH_{2.}CH_3$): 77.48 (d. 1C. J = 153.7 Hz, C-P); 186.69 (d, 1C, J = 14.4 Hz, C=N). ^{31}P NMR: (40.53 MHz) δ (ppm): 21.65. Anal. calcd. for $C_{13}H_{26}NO_3P$: C, 56.66; H, 9.49; N, 5.12. Found: C, 56.72; H, 9.44; N, 5.10.

8b Diethyl(5-(1-methylpropyl-3,3-dimethylpyrrolin-2-yl))phosphonate.Colourless oil. Yield: 22%. ^{1}H NMR: (400 MHz) δ (ppm): 0.86 and 0.88 (2t, 3H, J = 7.5 Hz); 1.05 and 1.06 (2d, 3H. J = 6.9 Hz); 1.10 and 1.27 (2s, 6H); 1.28 and 1.31 (2t, 6H, J = 7.0 Hz); 1.40 and 1.55 (2m, 2H); 2.20 - 2.51 and 2.24 - 2.55 (2 AB d systems, J = 15.6 Hz, J = 5.2 Hz (2.51 and 2.55) and J = 4.7 Hz (2.24 and 2.20); 2.47 (m, 1H); 3.85 and 3.87 (2d, H, J = 18.3 Hz); 4.13 (M, 4H).A simple spectra was obtained by decoupling the proton from phosphorus nuclei using an irradiating r.f..Thus spectral interpretation is greatly simplified. ^{13}C NMR: (50.32 MHz) δ (ppm): 11.69 and 11.78 (1C, $\underline{C}H_3$-CH_2C); 16.42 and 16.54 (2C, O-$CH_2\underline{C}H_3$);

19.62 and 19.69 (1C, CH-$\underline{C}H_3$); 24.14 (d, 1C, J = 5.6 Hz, C($\underline{C}H_3)_2$); 27.37 (2d, 1C, C-$\underline{C}H_2CH_3$); 29.65 and 29,72 (2d, 1C, J = 11,7 Hz, C($\underline{C}H_3)_2$); 40,10 and 40,23 (1C, CH_3-$\underline{C}$-H); 41,48 (d, 1C, J = 12,7 Hz, $\underline{C}(CH_3)_2$); 49.32 and 49.86 (1C, $\underline{C}H_2$-C=N); 61.82 and 62.56 (2M, 2C, O-$\underline{C}H_2CH_3$); 77.44 and 77.95 (2d, 1C, J = 155.2 Hz, C-P); 185.57 and 186.59 (2d, 1C, J = 4.4 Hz and J = 3.0 Hz, C=N). ^{31}P NMR: (40.53 MHz) δ (ppm): 22.29 and 22.61.

8c Diethyl(5-cyclohexyl-3,3-dimethylpyrrolin-2-yl))phosphonate. Yellow oil. Yield: 25%. ^{1}H NMR: (200 MHz) δ (ppm): 1.12 and 1.29 (2s, 6H); 1.31 (M, 6H); 1.2 - 1.4 and 1.5 - 2.0 (2M, 10H); 2.24 - 2.62 (AB d system , 2H, J = 16.7 Hz and J = 4.8 Hz); 2.36 (M, 1H); 3.89 (d, 1H, J = 18.3 Hz); 4.16 (M, 4H). ^{13}C NMR: (50.32 MHz) δ (ppm): 16.43 and 16.55 (2C, $OCH_2\underline{C}H_3$); 24.05 (perturbed s, 1C, C($\underline{C}H_3)_2$); 25.78; 25.99 and 30.06 (SC, -$(CH_2)_5$-); 29.53 (d,1C, J = 10.3 Hz, C($\underline{C}H_3)_2$); 41.36 (1C, $\underline{C}(CH_3)_2$); 42.90 (1C, $(CH_2)_5$-$\underline{C}$-H); 50.52 (1C, -$\underline{C}H_2$-C=N): 61.78 and 62.56 (2d, 2C. J = 7.2 Hz, -OCH_2-); 77.42 (d, 1C, J = 151.2 Hz, C-P); 186.20 (d, 1C, J = 14.7 Hz, C=N). ^{31}P NMR: (40.53 MHz) δ (ppm): 26.43. Anal. calcd for $C_{16}H_{30}NO_3P$: C, 60.93; H, 9.59; N, 4.44. Found : C, 60.90; H, 9.47; N, 4.40.

10a 2,3,3,6,6 -pentamethyl-3,6-dihydropyridine. Yellow oil. Yield:14%. Caracteristics of picrates salts, m. p.: 152°C. ^{1}H NMR: (200 MHz) δ (ppm): 1.45 (s, 6H); 1.54 (s, 6H); 2.54 (s, 3H); 5.56 - 5.76 (AB system, 2H, J = 10.5 Hz); 8.86 (s, 2H). ^{13}C NMR: (50.32 MHz) δ (ppm): 20.21 (1C, =C-$\underline{C}H_3$); 27.55 (2C, C-($\underline{C}H_3)_2$); 28.61 (2C, N-C-($\underline{C}H_3)_2$); 37.74 (1C, -$\underline{C}$-$(CH_3)_2$); 58.18 (1C, N-$\underline{C}$-$(CH_3)_2$); 127.60 and 128.24 (2C, C=C); 188.38 (1C, C=N); 126.25 , 128.24, 141.84 and 161.68 (6C, aromatic cycle). Anal. calcd. for $C_{16}H_{20}N_4O_7$: C, 50.51; H, 5.30; N, 14.73. Found: C, 50.83; H, 5.52; N: 14.93.

10b 6-ethyl-2,3,3,6 -tetramethyl-3,6-dihydropyridine. Colourless oil. Yield: 5%. ^{1}H NMR: (200 MHz) δ (ppm): 0.70 (t, 3H, J = 7.4 Hz); 1.16 (s, 6H); 1.23 (s, 3H); 1.47 - 1.67 (AB q system, 2H, J = 13.6 Hz - J = 7.4 Hz); 2.03 (s, 3H); 5.12 - 5.46 (AB system, 2H, J = 10 Hz). ^{13}C NMR: (50.32 MHz) δ (ppm): 9.09 (1C, CH_2-$\underline{C}H_3$); 21.83 (1C, N=C-$\underline{C}H_3$); 28.30 and 30.30 (2C, C($\underline{C}H_3)_2$); ≈ 35 (1C, $\underline{C}(CH_3)_2$); 35.26 (1C, $\underline{C}H_2$-CH_3); 58.80 (1C, N-C); 129.86 and 131.82 (2C, C=C); 186 (1C, C=N). These caracteristics were deduced from ^{13}C NMR spectrum of a mixture **10b** which was obtained with low yield and **11b** which was obtained pur.

10c 2,3,3-trimethyl-6-pentamethylene-3,6-dihydropyridine. Colourless oil. Yield: 8%. ^{1}H NMR: (200 MHz) δ (ppm): 1.15 (s, 6H); 1.3 - 1.80 (M, 10H); 2.01 (s, 3H); 5.43 - 5.99 (AB system, 2H, J = 10.2 Hz). ^{13}C NMR: (50.32 MHz) δ (ppm): 22.20 (1C, =C-$\underline{C}H_3$); 22.03; 25.84 and 39.70 (5C, -$(CH_2)_5$-); 28.29 (2C, -C-($\underline{C}H_3)_2$); 35.72 (1C, -$\underline{C}$-$(CH_3)_2$); 57.65 (1C, N-$\underline{C}$-$(CH_3)_2$); 129.49 and 131.14 (2C, C=C); 168.73 (1C, C=N).

11a Diethyl(5-isopropyl-2,3,3-trimethylpyrrolin-2-yl)-phosphonate. Colourless oil. Yield: 60%. ^{1}H NMR: (200 MHz) δ (ppm): 0.92 (s, 3H); 1.12 (d, 6H, J = 6.9 Hz); 1.30 and 1.32 (2t, 6H, J = 7.2 Hz); 1.32 (s, 3H); 1.39 (d, 3H, J = 16.2 Hz); 2.22 - 2.95 (AB d system, 2H, J = 16.4 Hz; J = 4.4 Hz (2.22) and J = 5.8 Hz (2.95)); 2.66 (sept d, 1H, J = 7.0 Hz , J = 2.6 Hz); 4.12 (quin, 4H, J = 7.2 Hz). ^{13}C NMR: (50.32 MHz) δ (ppm): 16.38 and 16.62 (2d, 2C, J = 6.5 Hz, O-CH$_2$-$\underline{C}$H$_3$); 17.25 (1C,$\underline{C}$H$_3$-C-P); 19.72 and 19.77 (2C, CH-($\underline{C}$H$_3$)$_2$); 23.99 (d, 1C, J = 3.6 Hz C($\underline{C}$H$_3$)$_2$); 25.51 (d, 1C, J = 10.0 Hz, -C-($\underline{C}$H$_3$)$_2$); 33.22 (1C, H-$\underline{C}$-(CH$_3$)$_2$); 44.18 (d, 1C, J = 5.6 Hz,-$\underline{C}$-(CH$_3$)$_2$); 50.22 (d, 1C, J = 6.0 Hz, =C-$\underline{C}$H$_2$-); 61.28 and 63.02 (2d, 2C, J = 8.5 Hz, O-$\underline{C}$H$_2$-CH$_3$); 78.33 (d, 1C, J = 148.9 Hz, C-P); 186.38 (d, 1C, C=N, J = 9.2 Hz). ^{31}P NMR: (40.53 MHz) δ (ppm): 26.19.

11b Diethyl(5-(1-methylpropyl)-2,3,3-trimethylpyrrolin-2-yl)-phosphonate.Colourless oil. Yield: 75%. ^{1}H NMR: (200 MHz) δ (ppm): 0.94 (s, 3H); 0.94 and 0.96 (2t, 3H, J = 7.2 Hz); 1,11 (d, 3H, J = 7.0 Hz); 1.32 and 1.34 (2t, 6H, J = 7.2 Hz); 1.34 (s, 3H); 1.42 (d, 3H, J = 16.4 Hz); 1.55 (m, 2H); 2.23 - 2.87 and 2.26 - 2.85 (2 AB d systems, 2H, J = 16.4 Hz; J = 5.8 Hz (2.85) and J = 4.3 Hz (2.26)) ; 2.47 (sex d , 1H, J = 7.2 Hz; J = 1.6 Hz); 4.12 (quin, 4H, J = 7.0 Hz). ^{13}C NMR: (50.32 MHz) δ (ppm): 11.57 and 11.75 (1C, C-CH$_2$-$\underline{C}$H$_3$); 16.33 (perturbed s, 2C, O-CH$_2$-$\underline{C}$H$_3$); 17.12 (1C, $\underline{C}$H$_3$-C-P); 17.30 and 17.62 (2d, 1C, J = 2.9 Hz, CH-$\underline{C}$H$_3$); 23.78 , 23.92 (2d, 1C, J = 4.4 Hz , C-($\underline{C}$H$_3$)$_2$), 25.40 and 25.51 (2d, 1C, J = 10.3 Hz, -C-($\underline{C}$H$_3$)$_2$); 27.03 - 27.39 (1C, C-$\underline{C}$H$_2$-CH$_3$); 40.19 and 40.46 (1C, H-$\underline{C}$-CH$_2$-CH$_3$); 40.09 and 43.89 (2d, 1C, J = 8.8 Hz, -$\underline{C}$-(CH$_3$)$_2$) ; 49.43 and 49.95 (1C, =C-$\underline{C}$H$_2$-); 61.11 and 62.64 (2M, 2C, O-$\underline{C}$H$_2$-CH$_3$); 78.11 and 79.44 (2d, 1C, J = 150.9 Hz, C-P); 185.59 - 186.74 (2d, 1C, C=N, J = 11.5 Hz). ^{31}P NMR: (40.53 MHz) δ (ppm): 26.31 and 26.58.

11c Diethyl(5-cyclohexyl-2,3,3-trimethylpyrrolin-2-yl)-phosphonate. Yellow oil. Yield: 60%. ^{1}H NMR: (200 MHz) δ (ppm): 0.90 (s, 3H); 1.30 (s, 3H); 1.30 and 1.32 (2t, 6H, J = 7.0 Hz); 1.3 - 1.7 (2M, 10H); 1.38 (d, 3H, J = 16.5 Hz); 2.26 - 2.86 (AB d system, 2H, J = 16.4 Hz , J = 4.4 Hz (2.26) and J = 5.9 Hz (2.86)); 2.35 (m, 1H); 4.12 (m, 4H). ^{13}C NMR: (50.32 MHz) δ (ppm): 16.37 and 16.63 (2C, O-CH$_2$-$\underline{C}$H$_3$); 17.29 (1C, $\underline{C}$H$_3$-C-P); 23.99 (d, 1C, J = 3.5 Hz, C($\underline{C}$H$_3$)$_2$) and 25.54 (d, C, J = 10.2 Hz, -C-($\underline{C}$H$_3$)$_2$); 26.02 , 26.21, 30.28 (5C, -(CH$_2$)$_5$-); 43.17 (d, 1C, J = 2.9 Hz, H-$\underline{C}$-(CH$_2$)$_5$); 44.36 (d, 1C, J = 6.0 Hz, -$\underline{C}$-(CH$_3$)$_2$); 51.34 (1C, =C-$\underline{C}$H$_2$-); 61.62 and 62.32 (2d, 2C, J = 7.6 Hz, O-$\underline{C}$H$_2$-CH$_3$); 78.95 (d, 1C, J = 137.8 Hz, C-P); 186.67 (d, 1C, C=N, J = 11.5 Hz). ^{31}P NMR: (40.53 MHz) δ (ppm): 26.14. Anal. calcd. for $C_{17}H_{32}NO_3P$: C, 61.97; H, 9.80; N, 4.25. Found: C, 61.36; H, 9.56; N, 4.20.

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