Pergamon

Tetrahedron 55 (1999) 3091–3104

TETRAHEDRON

A New and Efficient Strategy for the Preparation of 1,5,2-Diazaphosphorines from Primary β-Enaminophosphonates

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Received 11 November 1998; revised 24 December 1998; accepted 14 January 1999

Abstract- A new and efficient synthesis of 1,5,2-diazaphosphorines is described. The key step is a base-induced heterocyclization of functionalized urea compounds. These compounds are formed by addition of primary β-enaminophosphonates to isocyanates. © 1999 Elsevier Science Ltd. All rights reserved.

Pyrimidone ring systems represent an important class of compounds,[1] within which 2,4-dioxo-pyrimidines constitute a part of the backbone of the antibiotic Sparsomycin,[2a] and have been used for molecular recognition and self-replication.[2b] Likewise, thymine **Ia** is an important naturally occurring pyrimidine base, which is a constituent of nucleic acids.[3] Thymidine nucleosides derived from arabinofuranosyl-thymine have been used for the preparation of deuterated nucleosides for structural NMR analysis[4a] as well as of anti hepatitis B virus (HBV) agents with a favorable therapeutic index,[4b] and have shown anti-viral activity especially in the case of zidovudine **Ib** (3'-azido-3'-doeoxythymidine, AZT)[4c,d] or modified AZT derivatives,[4e-i] which are the most widely used anti-AIDS prodrugs.[4c-i] With this in mind, we are interested in the design of new pyrimidone analogues containing a phosphorus atom in the heterocyclic system, such as 1,5,2-diazaphosphorinones **II**.[5] These compounds **II** (Scheme 1) can be considered as thymine derivatives **I** by replacement of the carbonyl group with a phosphonyl group. The presence of the phosphorus atom in the heterocycle could regulate important biological functions and could increase the biological activity of these types of compounds, in a similar way to that reported for enzymatic inhibitors[6a,b] and for other pharmaceuticals.[6c,d] Classical approaches[7] to 1,3,2-diaza-phosphorines have been reported. However, to the best of our knowledge, the synthesis of only the 1,5,2-diazaphosphorine[8a], the 6-oxo[8b] and the 2, 6-dioxo-2-amino[8c] derivatives has been reported and the lack of general methods of synthesis of these heterocycles[7a] has probably limited the use of these compounds.

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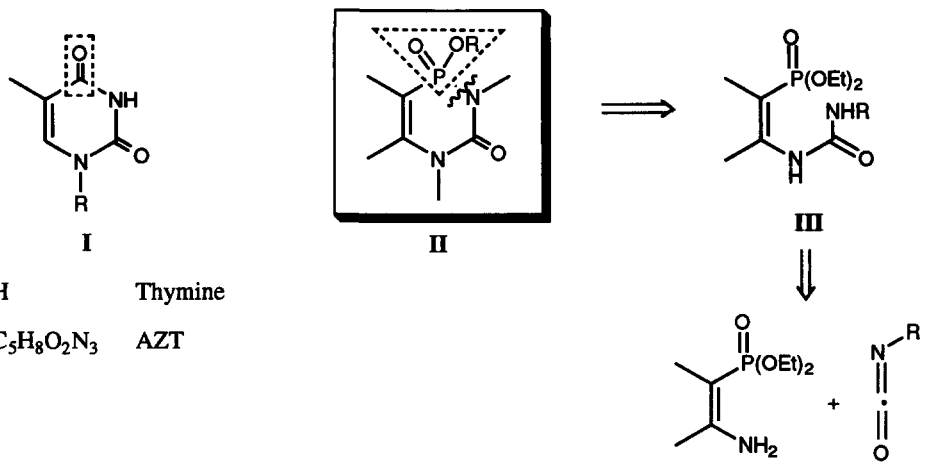
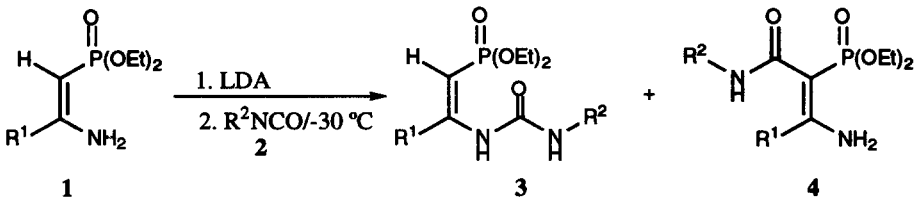
PII: S0040-4020(99)00068-X



Scheme 1

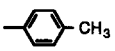
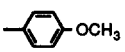
In connection with our interest in the synthesis of phosphorylated nitrogen heterocycles[9,10] and phosphorus containing heterocycles.[8b,11] we have used β-functionalized enamines derived from phosphazenes, phosphonium salts, phosphine oxides and phosphonates as synthetic intermediates in their synthesis. Furthermore, in previous papers we have reported a preparation of primary β-enamines derived from phosphazenes[12] and from phosphonates[10d] and have used them in the synthesis of cyclic[9b,10b,d,11,13] and acyclic[12,14] compounds. Continuing with our interest in the synthesis of new phosphorus heterocycles and with the reactivity of functionalized enamines, we report here an easy and high yielding synthesis of 1,5,2-diazaphosphininone derivatives from primary β-enaminophosphonates and isocyanates. Retrosynthetically, we envisaged obtaining these compounds by heterocyclization processes involving nitrogen-phosphorus bond formation of functionalized phosphonates **III** (Scheme 1) and preparing these key intermediates **III** by simple addition of isocyanates to primary β-enamino-phosphonates.

Preparation of the substituted urea derived from phosphonate **3** was initially attempted by means of the metallation of primary β-enamino-phosphonates **1**. However, when primary β-enamino-phosphonates **1** (R^1 =Ph) was allowed to react with lithium diisopropylamide (LDA) followed by addition of phenyl isocyanate **2** at low temperature (-30 °C), a mixture of not only the *N*-substituted compound **3a** ($R^1 = R^2$ = Ph) but also of the *C*-substituted enamine **4a** ($R^1 = R^2$ = Ph), in approximately 1:1 ratio, was obtained (see Scheme 2). Both compounds **3a** and **4a** were separated and isolated by crystallization and were characterized by their spectroscopic data. Mass spectrometry of **3a** showed the molecular ion peak (m/z, 374, 11%) and in the ^{1}H-NMR spectrum of **3a**, the vinylic proton resonates at δ_H = 4.70 ppm as a well resolved doublet with coupling constant of $^2J_{PH}$ = 12.2 Hz, while the vicinal coupling constant observed in the *ipso* aromatic carbon ($^2J_{PC}$ = 19.1 Hz) supports the *Z*-configuration[9b,16,17] of the *N*-substituted compound **3a**. Conversely, **4a** showed clearly different absorptions, with absence of absorption for the vinylic proton. The formation of both compounds **3a** and **4a** can be explained due to the marked ambident nucleophilicity which metallated enamines exhibit.[15]



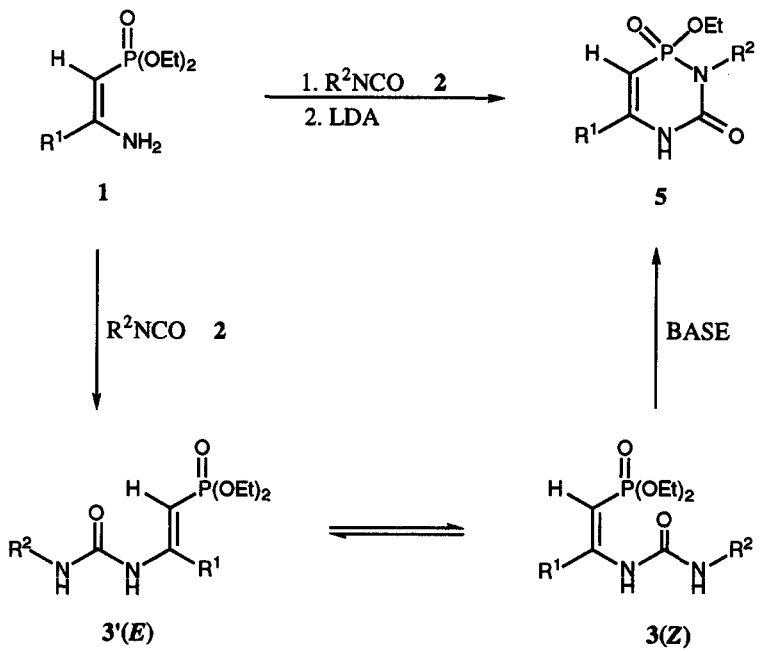
Scheme 2

Table 1. Functionalized enamines **3/3'** and **7/7'**.

Entry	Compound	R^1	R^2	Z/E[a]	Yield (%)[f]
1	**3/3'a**			0/100	98
2	**3/3'b**			0/100	97
3	**3/3'c**			0/100	97
4	**3/3'd**			60/40[b]	95
5	**3/3'e**			35/65[c]	96
6	**3/3'f**			0/100	97
7	**3/3'g**			0/100	98
8	**3/3'h**			25/75[c]	90
9	**3/3'i**		TMS	0/100[d]	53
10	**7/7'a**			85/15[e]	94
11	**7/7'b**			100/0[e]	96
12	**7/7'c**			100/0[e]	89
13	**7/7'd**			100/0[e]	95

[a] *Z*-**3**/*E*-**3'** Ratio determined by ^{31}P-NMR spectroscopy, method A (15h). [b] *Z*-**3d**/*E*-**3'd** Ratio determined by ^{31}P-NMR spectroscopy, method B. [c] *Z*-**3h**/*E*-**3'h** Ratio determined by ^{31}P-NMR spectroscopy, method A (1h). [d] *Z*-**3i**/*E*-**3'i** Ratio determined by ^{31}P-NMR spectroscopy, method A (15d). Desilylated product was obtained. [e] *Z*-**7**/*E*-**7'** Ratio determined by ^{31}P-NMR spectroscopy. [f] Yield of isolated products **3/3'** and **7/7'**, based on **1** and **6**.

In order to enhance the synthetic use of this process and to avoid mixtures of the *N*-substituted compound **3** and the *C*-substituted enamine **4** obtained from metallated enamines, the reaction of primary β-enaminophosphonates **1** and isocyanates without the presence of base was explored, with the aim of reducing the ambident character of the enamine. Thus, the addition of isocyanates **2** to β-enamino-phosphonates **1** led to the regioselective formation of the *N*-substituted compounds **3/3'** (Scheme 3), isolated as a mixture of the *Z*- and *E*-isomers (see Table 1, entries 4,5,8,10) separated by crystallization, although in some cases, when the process developed in the absence of solvent, only the **3'** *E*-isomers were obtained (see Table 1, entries 1-3, 6, 7, 9). The structure of the 1:1 adducts **3/3'** is supported by the spectroscopic data. In the ^{1}H-NMR spectrum of **3a**, the vinylic proton resonates at δ_H = 4.70 ppm for the *Z*-isomer, while a low-field chemical shift at δ_H = 6.45 ppm corresponds to the *E*-isomer **3'a**. On the other hand, in the ^{13}C-NMR spectrum of compound **3'a**, the coupling constant observed in the *ipso* aromatic carbon ($^3J_{PC}$ = 6.1 Hz) can be taken as an indication for the inversion of the *Z*-configuration[9b,16,17] around the enaminic moiety (C2-C3) of functionalized phosphonates **3'** related to the starting enamine. In this context, it is noteworthy that for our subsequent purposes the separation of both **3** (*Z*-) and **3'** (*E*- isomers) is not necessary, given that not only the treatment of compounds **3'**, but also of the mixture of isomers **3/3'** with LDA afforded 1,5,2-diazaphosphorines **5** (see Table 2, entries 1-9).

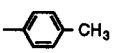
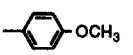


Scheme 3

Functionalized phosphonates **3/3'** underwent cyclocondensation to heterocyclic compounds **5** (see Table 2, entries 1-9) by expulsion of a molecule of ethanol when adducts **3/3'** were treated at low temperature (-78 °C) with LDA in tetrahydrofuran (Scheme 3), and were alternatively prepared in a "one pot" synthesis from β-enamine **1**, when crude 1:1 adducts **3/3'** were directly treated, without their isolation, with LDA in THF

(Table 2, entry 4). In some cases, the cyclocondensation of the *N*-substituted compounds **3/3'** took place at room temperature by using methyllithium as base (see Table 2, entries 6, 7, 9). Mass spectrometry of heterocyclic compounds **5a** showed the molecular ion peak (m/z, 328, 100%) and the cyclocondensation seems to involve the urea moiety and the ethoxy group bonded to the phosphorus atoms, while the ^{13}C-NMR spectrum of this compound **5a** showed absorption at δ_C = 153.1 ppm with a $^2J_{PC}$ = 6.5 Hz assignable to the urea carbonyl group, as well as doublets at δ_C = 86.7 ppm with a $^1J_{PC}$ = 171.2 Hz and δ_C = 150.5 ppm with a $^2J_{PC}$ = 3.5 Hz for the heterocyclic carbon atoms.

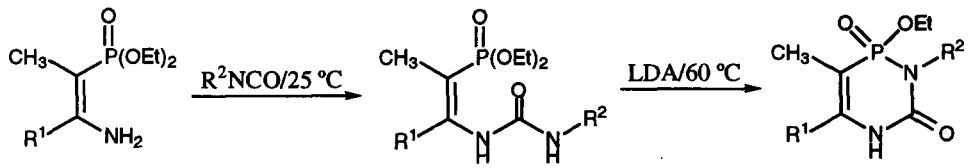
Table 2. 2,6-dioxo-1,5,2-P^V-diazaphosphorines **5** and **8**.

Entry	Compound	R^1	R^2	Reaction Conditions	Yield (%)[a]
1	**5a**			LDA/-78 °C	98
2	**5b**			LDA/-78 °C	85
3	**5c**			LDA/-78 °C	91
4	**5d**			LDA/-78 °C	87 (85)[b]
5	**5e**			LDA/-78 °C	96
6	**5f**			MeLi/r.t.	98
7	**5g**			MeLi/r.t.	99
8	**5h**			LDA/-78 °C	95
9	**5i**		H	MeLi/r.t.	61
10	**8a**			BuLi/Δ	99
11	**8b**			BuLi/Δ	98
12	**8c**			BuLi/Δ	80 (94)[b]
13	**8d**			BuLi/Δ	87

[a] Yield of isolated products **5** and **8** based on **3/3'** and **7/7'**. [b] Yield of isolated products **5** and **8** based on **1** and **6** in a "one pot" reaction.

These results prompted us to extend the scope of this reaction, and to explore the synthesis of 1,5,2-diazaphosphorines **8** substituted with a methyl group. The reaction of primary β-enamino-phosphonates **6** with LDA, or in absence of base, followed by addition of isocyanates at room temperature gave exclusively the *N*-substituted compound **7** in a regioselective fashion, principally as *Z*-isomers (see Table 1, entries 11-13). Spectral data are in agreement with structure **7** keeping the Z-configuration around the enamidic moiety

of functionalized β-ureidophosphonates **7** related to the starting enamine **6**. Heating these compounds **7** for 2-4 days at 60 °C in the presence of LDA afforded 3-methyl-6-oxo-1,5,2-diazaphosphorines **8** in excellent yields (see Table 2, entries 10-13). These heterocycles **8** can also be prepared in a "one pot" synthesis from β-enamines **6**, without isolation of compounds **7**, when the enamines **6** are directly treated with LDA and isocyanates in THF and the reaction is preformed at 60 °C (see Table 2, entry 12).



6 **7** **8**

Scheme 4

In conclusion, we describe a new and efficient method of synthesis of 1,5,2-diazaphosphorinones **5**, **8** making use of readily available starting materials. These phosphorus heterocycles **5**, **8** may be useful compounds in medicinal chemistry since they could display a broad range of biological activities and could be widely used as enzymatic inhibitors[6] and as pharmaceuticals.[3,4]

ACKNOWLEDGEMENTS

The present work has been supported by the Dirección General de Investigación Científica y Técnica (Madrid. DGICYT, PB96-0252) and by the Departamento de Educación, Universidades e Investigación del Gobierno Vasco (Vitoria, PI96-36).

EXPERIMENTAL SECTION

Melting points were determined with a Buchi SPM-20 apparatus and are uncorrected. Analytical *TLC* was performed on 0.25mm silica gel plates (Merck). Visualization was accomplished by *UV* light and iodine. Solvent used in reactions was freshly distilled from appropriate drying agent before use: THF (sodium benzophenone ketyl). All other reagents were recrystallized or distilled as necessary. Mass spectra were obtained on a Hewlett Packard 5890 spectrometer. Infrared spectra were taken on a Nicolet IRFT Magna 550 spectrometer. ^{1}H-NMR spectra were recorded on a Varian 300 MHz spectrometer using tetramethylsilane (0.00 ppm) or chloroform (7.26 ppm) as an internal reference in $CDCl_3$ solutions. ^{13}C-NMR spectra were recorded at 75 MHz with chloroform (77.0 ppm) as an internal reference in $CDCl_3$ solutions. ^{31}P-NMR spectra were recorded at 120 MHz with 85% phosphoric acid as an external reference. Elemental analyses were performed in a Leco CHNS-932 instrument. Chemical shifts are given in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), dd (double doublet), t (triplet), q (quadruplet) or m (multiplet). Coupling constants, *J*, are reported in Hertz. Infrared spectra (IR) were obtained as solids in KBr. Peaks are reported in cm^{-1}. Mass spectra (EI) were obtained with an ionization voltage of 70 eV. Data are reported in the form m/z (intensity relative to base = 100). All reactions were performed in oven (125 °C) or flame-dried glassware under an inert atmosphere of dry N_2.

General Procedure for Preparation of functionalizated β-enaminophosphonates 3/3' and 7/7'

Method A. A dry flask, 100-mL, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 5 mmol of β-enaminophosphonate **1/6** and 5 mmol of isocyanate. The mixture was stirred and heated below the boiling point of isocyanate, until *TLC* indicated the disappearance of the β-enaminophosphonate **1** (1 hour - 15 days). The crude product was purified by recrystallization (Et_2O).

Method B. A dry flask, 100-mL, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 5 mmol of β-enaminophosphonate **1**, and 25 mL of THF. A solution of 5 mmol of isocyanate and 10 mL of THF was added over 10 min. The mixture was stirred and refluxed until *TLC* indicated the disappearance of the β-enaminophosphonate **1** (15 hours). The crude product was purified by recrystallization (Et_2O).

Method C. A dry flask, 100-mL, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 5 mmol of β-enaminophosphonate **6**, and 25 mL of THF. The temperature was allowed to descend to 0 °C and a solution of butyllithium (1.6 M in n-hexane) (5 mmol) in THF was then added. The mixture was allowed to stir for 1 hour. A solution of 5 mmol of isocyanate in 10 mL of THF was added at this temperature. The mixture was stirred and refluxed until *TLC* indicated the disappearance of the β-enaminophosphonate **1** (15 hours). The mixture was washed with water and extracted with CH_2Cl_2. The organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by recrystallization (Et_2O).

Method D. A dry flask, 100-mL, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 5 mmol of lithium diisopropylamide (LDA), and 25 mL of THF. The temperature was allowed to descend to -30 °C and a solution of β-enaminophosphonate **1** (5 mmol) in THF was then added. The mixture was allowed to stir for 1 hour. A solution of 5 mmol of isocyanate in 10 mL of THF was added at this temperature. The mixture was stirred at -30 °C during 7 hours, and then the mixture was washed with water and extracted with CH_2Cl_2. The organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by recrystallization (Et_2O).

3 and **3'** were separated from each other by fractionated crystallization (Et_2O).

***Z*-N-Phenyl-N'-(1-phenyl-2-diethoxyphosphoryl ethenyl) urea (3a)**. 1440 mg (77%) of **3a** following the method B, and 860 mg (46%) of **3a** following the method D as a white solid. Data for **3a**: mp 149-150 °C; *^{1}H-NMR* (300 MHz): 1.29 (m, 6H, CH_3), 4.07 (m, 4H, OCH_2), 4.70 (d, 1H, $^2J_{PH}$= 12.2 Hz, CH), 7.18-7.42 (m, 10H, arom), 8.66 (s, 1H, NH), 9.53 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 16.2 (CH_3), 62.1 (OCH_2), 92.2 (d,$^1J_{PC}$= 184.3 Hz, CH), 118.9-129.7 (CH-arom), 137.9 (d,$^3J_{PC}$= 19.1 Hz, C-*ipso,arom.*), 138.7 (C-*ipso,arom.*), 151.7 (CN), 158.5 (d,$^4J_{PC}$= 4.0 Hz, C=O). *^{31}P-NMR* (120 MHz). 20.3; *IR* (*KBr*) 3297, 3213, 1722, 1231 cm^{-1}; *MS* (EI) 374 (M^+, 11). Anal. Calcd for $C_{19}H_{23}N_2O_4P$: C, 60.96; H, 6.15; N, 7.49. Found: C, 60.78; H, 6.32; N, 7.23.

***E*-N-Phenyl-N'-(1-phenyl-2-diethoxyphosphoryl ethenyl) urea (3'a)**. 1830 mg (98%) of **3'a** following the method A as a white solid. Data for **3'a**: mp 188-189 °C; *^{1}H-NMR* (300 MHz): 0.96 (m, 6H, CH_3), 3.47 (m, 4H, OCH_2), 6.45 (d, 1H, $^2J_{PH}$= 12.8 Hz, CH), 7.21-7.53 (m, 10H, arom), 8.34 (s, 1H, NH), 8.63 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 16.0 (CH_3), 61.4 (OCH_2), 90.0 (d,$^1J_{PC}$= 205.0 Hz, CH), 118.9-129.8 (CH-arom), 136.5 (d,$^3J_{PC}$= 6.1 Hz, C-*ipso,arom.*), 139.0 (C-*ipso,arom.*), 152.7 (CN), 154.4 (d,$^4J_{PC}$= 17.6 Hz, C=O). *^{31}P-NMR* (120 MHz). 22.4; *IR* (*KBr*) 3301, 3225, 1716, 1221 cm^{-1}; *MS* (EI) 374 (M^+, 14). Anal. Calcd for $C_{19}H_{23}N_2O_4P$: C, 60.96; H, 6.15; N, 7.49. Found: C, 60.69; H, 6.46; N, 7.34.

***E*-2-Amino-2-phenyl-1-phenylcarboxamide ethenyl diethyl phosphonate (4a).** 900 mg (48%) of **4a** following the method D as a white solid. Data for **4a**: mp 170-171 °C; *^{1}H-NMR* (300 MHz): 1.04 (m, 6H, CH_3), 3.76 (m, 4H, OCH_2), 5.29 (s, 1H, NH), 7.19-7.34 (m, 10H, arom), 10.99 (s, 1H, NH), 11.24 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 15.7 (CH_3), 61.3 (OCH_2), 83.8 (d,$^1J_{PC}$= 191.5 Hz, C=), 118.5-128.9 (CH-arom), 137.9 (C-*ipso,arom.*), 139.1 (C-*ipso,arom.*), 168.3 (d,$^2J_{PC}$= 18.2 Hz, CN), 170.6 (d,$^2J_{PC}$= 15.1 Hz, C=O). *^{31}P-NMR* (120 MHz). 24.7; *IR* (*KBr*) 3210, 3121, 3088, 1667, 1203 cm^{-1}; *MS* (EI) 374 (M^+, 9). Anal. Calcd for $C_{19}H_{23}N_2O_4P$: C, 60.96; H, 6.15; N, 7.49. Found: C, 61.13; H, 5.89; N, 7.40.

***E*-N-Phenyl-N'-(1-(2-thiophenyl)-2-diethoxyphosphoryl ethenyl) urea (3'b).** 1840 mg (97%) of **3'b** following the method A as a white solid. Data for **3b**: mp 165-167 °C; *^{1}H-NMR* (300 MHz): 1.08 (m, 6H, CH_3), 3.64 (m, 4H, OCH_2), 6.30 (d, 1H, $^2J_{PH}$= 12.4 Hz, CH), 6.68-7.33 (m, 8H, arom), 8.48 (s, 1H, NH), 8.60 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 16.0 (CH_3), 61.5 (OCH_2), 92.3 (d,$^1J_{PC}$= 203.9 Hz, CH), 119.1-132.8 (CH-arom), 137.1 (d,$^3J_{PC}$= 7.5 Hz, C-*ipso,arom.*), 138.9 (C-*ipso,arom.*), 146.9 (d,$^4J_{PC}$= 16.6 Hz, C=O), 152.5 (CN). *^{31}P-NMR* (120 MHz). 21.9; *IR* (*KBr*) 3286, 3214, 1735, 1246 cm^{-1}; *MS* (EI) 380 (M^+, 8). Anal. Calcd for $C_{17}H_{21}N_2O_4PS$: C, 53.68; H, 5.52; N, 7.36; S, 8.42. Found: C, 53.89; H, 5.43; N, 7.30; S, 8.51.

***E*-N-Phenyl-N'-(1-(2-furyl)-2-diethoxyphosphoryl ethenyl) urea (3'c).** 1760 mg (97%) of **3'c** following the method A as a white solid. Data for **3'c**: mp 157-158 °C; *^{1}H-NMR* (300 MHz): 1.17 (m, 6H, CH_3), 3.93 (m, 4H, OCH_2), 6.44-7.49 (m, 8H, arom), 6.56 (d, 1H, $^2J_{PH}$= 9.6 Hz, CH), 8.37 (s, 1H, NH), 8.83 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 15.5 (CH_3), 60.7 (OCH_2), 91.3 (d,$^1J_{PC}$= 202.5 Hz, CH), 111.1-142.5 (CH-arom), 138.1 (C-*ipso,arom.*), 140.2 (d,$^4J_{PC}$= 15.7 Hz, C=O), 146.9 (d,$^3J_{PC}$= 7.5 Hz, C-*ipso,arom.*), 151.9 (CN). *^{31}P-NMR* (120 MHz). 20.8; *IR* (*KBr*) 3276, 3187, 1723, 1219 cm^{-1}; *MS* (EI) 364 (M^+, 14). Anal. Calcd for $C_{17}H_{21}N_2O_5P$: C, 56.04; H, 5.77; N, 7.69. Found: C, 56.31; H, 5.63; N, 7.49.

***Z*-N-Phenyl-N'-(1-(2-pyridyl)-2-diethoxyphosphoryl ethenyl) urea (3d).** 1060 mg (60%) of **3d** following the method B as a white solid. Data for **3d**: mp 156-157 °C (dec); *^{1}H-NMR* (300 MHz): 1.20 (m, 6H, CH_3), 4.06 (m, 4H, OCH_2), 5.22 (d, 1H, $^2J_{PH}$= 12.5 Hz, CH), 6.90-8.53 (m, 9H, arom), 8.61 (s, 1H, NH), 9.56 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 16.1 (CH_3), 62.2 (OCH_2), 95.5 (d,$^1J_{PC}$= 184.8 Hz, CH), 119.2-148.7 (CH-arom and C-*ipso,arom.*), 154.8 (d, $^3J_{PC}$= 20.6 Hz, C-*ipso,arom.*), 155.9 (CN), 157.0 (C=O). *^{31}P-NMR* (120 MHz). 19.8; *IR* (*KBr*) 3215, 3146, 1707, 1248 cm^{-1}; *MS* (EI) 375 (M^+, 9). Anal. Calcd for $C_{18}H_{22}N_3O_4P$: C, 57.60; H, 5.77; N, 5.87. Found: C, 57.46; H, 5.50; N, 6.08.

***E*-N-Phenyl-N'-(1-(2-pyridyl)-2-diethoxyphosphoryl ethenyl) urea (3'd).** 780 mg (40%) of **3'd** following the method B as a white solid. Data for **3'd**: mp 163-164 °C (dec); *^{1}H-NMR* (300 MHz): 1.05 (m, 6H, CH_3), 3.73 (m, 4H, OCH_2), 6.55 (d, 1H, $^2J_{PH}$= 10.8 Hz, CH), 6.97-8.53 (m, 9H, arom), 8.39 (s, 1H, NH), 8.55 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 16.0 (CH_3), 61.6 (OCH_2), 92.0 (d,$^1J_{PC}$= 203.5 Hz, CH), 119.3-148.7 (CH-arom and C-*ipso,arom.*), 148.4 (C-*ipso,arom.*), 152.6 (CN), 153.1 (C=O). *^{31}P-NMR* (120 MHz). 21.7; *IR* (*KBr*) 3254, 3119, 1698, 1239 cm^{-1}; *MS* (EI) 375 (M^+, 11). Anal. Calcd for $C_{18}H_{22}N_3O_4P$: C, 57.60; H, 5.77; N, 5.87. Found: C, 57.34; H, 5.91; N, 6.12.

***E*-N-Phenyl-N'-(1-*p*-tolyl-2-diethoxyphosphoryl ethenyl) urea (3'e).** 1211 mg (65%) of **3'e** following the method B as a white solid. Data for **3'e**: mp 173-174 °C; *^{1}H-NMR* (300 MHz): 1.09 (m, 6H, CH_3), 1.97 (s, 3H, CH_3), 3.43 (m, 4H, OCH_2), 6.30 (d, 1H, $^2J_{PH}$= 12.7 Hz, CH), 6.99-7.43 (m, 9H, arom), 8.29 (s, 1H, NH), 8.59 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 16.1 (CH_3), 20.7 (CH_3), 61.1 (OCH_2), 89.4 (d,$^1J_{PC}$= 203.9 Hz, CH), 119.2-129.3 (CH-arom), 133.7 (d, $^3J_{PC}$= 6.0 Hz, C-*ipso,arom.*), 139.4 (C-*ipso,arom.*), 140.8 (C-*ipso,arom.*), 152.6 (CN), 155.1 (d, $^4J_{PC}$= 17.6 Hz, C=O). *^{31}P-NMR* (120 MHz). 22.8; *IR* (*KBr*) 3211, 3104, 1723, 1214 cm^{-1}; *MS* (EI) 388 (M^+, 16). Anal. Calcd for $C_{20}H_{25}N_2O_4P$: C, 61.86; H, 6.44; N, 7.21. Found: C, 61.72; H, 6.28; N, 7.41.

***Z*-N-(1-Phenyl-2-diethoxyphosphoryl ethenyl)-N'-propyl urea (3f).** 1270 mg (75%) of **3f**, trough treatment of *E*-N-(1-Phenyl-2-diethoxyphosphoryl ethenyl)-N'-propyl urea **(3'f)** with MeLi at room temperature after 15 minutes gave compound 3f as a white solid. Data for **3f**: mp 135-136 °C; *^{1}H-NMR* (300 MHz): 0.79 (m, 3H, CH_3), 1.27 (m, 6H, CH_3), 1.40 (m, 2H, CH_2), 3.01 (m, 2H, NCH_2), 3.98 (m, 4H,

OCH_2), 4.53 (d, 1H, $^2J_{PH}$= 12.0 Hz, CH), 5.05 (s, 1H, NH), 7.19-7.39 (m, 5H, arom), 9.42 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 11.2 (CH_3), 16.2 (CH_3), 23.0 (CH_2), 42.0 (NCH_2), 61.8 (OCH_2), 91.0 (d,$^1J_{PC}$= 183.8 Hz, CH), 126.3-129.4 (CH-arom), 138.0 (d, $^3J_{PC}$= 18.6 Hz, C-*ipso,arom.*), 153.9 (CN), 158.8 (C=O). *^{31}P-NMR* (120 MHz). 20.8; *IR* (*KBr*) 3253, 3199, 1706, 1230 cm^{-1}; *MS* (EI) 340 (M^+, 19). Anal. Calcd for $C_{16}H_{25}N_2O_4P$: C, 56.47; H, 7.35; N, 8.23. Found: C, 56.22; H, 7.49; N, 8.01.

***E*-N-(1-Phenyl-2-diethoxyphosphoryl ethenyl)-N'-propyl urea (3'f).** 1650 mg (97%) of **3'f** following the method A as a white solid. Data for **3'f**: mp 167-168 °C; *^{1}H-NMR* (300 MHz): 0.84 (m, 3H, CH_3), 0.93 (m, 6H, CH_3), 1.39 (m, 2H, CH_2), 3.00 (m, 2H, NCH_2), 3.44 (m, 4H, OCH_2), 6.26 (d, 1H, $^2J_{PH}$= 13.3 Hz, CH), 6.42 (s, 1H, NH), 7.18-7.28 (m, 5H, arom), 8.05 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 11.5 (CH_3), 15.9 (CH_3), 23.0 (CH_2), 41.3 (NCH_2), 61.1 (OCH_2), 89.6 (d,$^1J_{PC}$= 205.5 Hz, CH), 127.9-129.4 (CH-arom), 137.0 (d, $^3J_{PC}$= 6.1 Hz, C-*ipso,arom.*), 154.1 (d,$^4J_{PC}$= 17.6 Hz, C=O), 155.5 (CN). *^{31}P-NMR* (120 MHz). 22.7; *IR* (*KBr*) 3231, 3128, 1690, 1214 cm^{-1}; *MS* (EI) 340 (M^+, 20). Anal. Calcd for $C_{16}H_{25}N_2O_4P$: C, 56.47; H, 7.35; N, 8.23. Found: C, 56.36; H, 7.29; N, 8.07.

***E*-N-Propyl-N'-(1-(2-thiophenyl)-2-diethoxyphosphoryl ethenyl) urea (3'g).** 1690 mg (98%) of **3'g** following the method A as a white solid. Data for **3'g**: mp 150-151 °C; *^{1}H-NMR* (300 MHz): 0.86 (m, 3H, CH_3), 1.03 (m, 6H, CH_3), 1.42 (m, 2H, CH_2), 3.03 (m, 2H, NCH_2), 3.63 (m, 4H, OCH_2), 6.20 (d, 1H, $^2J_{PH}$= 12.8 Hz, CH), 6.50 (s, 1H, NH), 6.84-7.27 (m, 3H, arom), 8.21 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 11.4 (CH_3), 16.0 (CH_3), 23.1 (CH_2), 41.4 (NCH_2), 61.4 (OCH_2), 91.5 (d,$^1J_{PC}$= 204.5 Hz, CH), 126.6-129.5 (CH-arom), 137.6 (d, $^3J_{PC}$= 7.0 Hz, C-*ipso,arom.*), 146.7 (d,$^4J_{PC}$= 16.1 Hz, C=O), 155.3 (CN). *^{31}P-NMR* (120 MHz). 22.3; *IR* (*KBr*) 3277, 3189, 1735, 1251 cm^{-1}; *MS* (EI) 346 (M^+, 12). Anal. Calcd for $C_{14}H_{23}N_2O_4PS$: C, 48.55; H, 6.65; N, 8.09; S, 9.25. Found: C, 48.67; H, 6.81; N, 7.88; S, 9.34.

***E*-N-(1-Phenyl-2-diethoxyphosphoryl ethenyl)-N'-*p*-methoxyphenyl urea (3'h).** 1360 mg (75%) of **3'h** following the method A as a white solid. Data for **3'h**: mp 176-177 °C; *^{1}H-NMR* (300 MHz): 1.02 (m, 6H, CH_3), 3.54 (m, 4H, OCH_2), 3.79 (s, 3H, OCH_3), 6.48 (d, 1H, $^2J_{PH}$= 13.0 Hz, CH), 6.82-7.35 (m, 9H, arom), 8.31 (s, 1H, NH), 8.58 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 15.9 (CH_3), 55.4 (OCH_3), 61.2 (OCH_2), 89.8 (d,$^1J_{PC}$= 204.0 Hz, CH), 113.9-129.7 (CH-arom), 132.1 (C-*ipso,arom.*), 136.6 (d,$^3J_{PC}$= 6.0 Hz, C-*ipso,arom.*), 152.9 (C-*ipso,arom.*), 154.4 (d,$^4J_{PC}$= 18.1 Hz, C=O), 155.2 (CN). *^{31}P-NMR* (120 MHz). 22.6; *IR* (*KBr*) 3204, 3098, 1742, 1210 cm^{-1}; *MS* (EI) 404 (M^+, 9). Anal. Calcd for $C_{20}H_{25}N_2O_5P$: C, 59.40; H, 6.19; N, 6.93. Found: C, 59.23; H, 6.34; N, 6.77.

***E*-N-(1-Phenyl-2-diethoxyphosphoryl ethenyl) urea (3'i).** 790 mg (53%) of **3'i** following the method A as a white solid. Data for **3'i**: mp 159-160 °C; *^{1}H-NMR* (300 MHz): 1.00 (m, 6H, CH_3), 3.67 (m, 4H, OCH_2), 6.21 (s, 1H, NH), 6.45 (d, 1H, $^2J_{PH}$= 12.6 Hz, CH), 6.79 (s, 1H, NH), 7.33-7.41 (m, 5H, arom), 8.36 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 15.8 (CH_3), 60.2 (OCH_2), 91.2 (d,$^1J_{PC}$= 203.5 Hz, CH), 127.1-129.2 (CH-arom), 136.8 (d,$^3J_{PC}$= 6.0 Hz, C-*ipso,arom.*), 152.0 (C-*ipso,arom.*), 152.6 (d,$^2J_{PC}$= 17.1 Hz, CN), 155.4 (d,$^4J_{PC}$= 13.6 Hz, C=O). *^{31}P-NMR* (120 MHz). 21.8; *IR* (*KBr*) 3461, 3210, 3176, 1719, 1213 cm^{-1}; *MS* (EI) 298 (M^+, 6). Anal. Calcd for $C_{13}H_{19}N_2O_4P$: C, 52.34; H, 6.37; N, 9.40. Found: C, 52.01; H, 6.56; N, 9.64.

***Z*-N-Phenyl-N'-(1-phenyl-2-diethoxyphosphoryl-1-propenyl) urea (7a).** 1550 mg (85%) of **7a** following the method A and 1760 mg (91%) of **7a** following the method C as a white solid. Data for **7a**: mp 179-180 °C; *^{1}H-NMR* (300 MHz): 1.31 (m, 6H, CH_3), 1.59 (d, 3H, $^3J_{PH}$= 13.9 Hz, CH_3), 4.07 (m, 4H, OCH_2), 6.84-7.36 (m, 10H, arom), 7.63 (s, 1H, NH), 9.99 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 14.5 (d,$^2J_{PC}$= 7.0 Hz, CH_3), 16.2 (CH_3), 61.9 (OCH_2), 98.5 (d, $^1J_{PC}$= 174.2 Hz, C=), 119.2-129.6 (CH-arom), 136.2 (d,$^3J_{PC}$= 17.6 Hz, C-*ipso,arom.*), 138.6 (C-*ipso,arom.*), 151.7 (CN), 152.5 (d,$^4J_{PC}$= 8.0 Hz, C=O). *^{31}P-NMR* (120 MHz). 24.2; *IR* (*KBr*) 3278, 3087, 1718, 1214 cm^{-1}; *MS* (EI) 388 (M^+, 21). Anal. Calcd for $C_{20}H_{25}N_2O_4P$: C, 61.85; H, 6.44; N, 7.22. Found: C, 62.21; H, 6.18; N, 7.35.

***Z*-N-Phenyl-N'-(1-(2-pyridyl)-2-diethoxyphosphoryl-1-propenyl) urea (7b).** 1870 mg (96%) of **7b** following the method A and 1850 mg (95%) of **7b** following the method C as a white solid. Data for **7b**: mp

170-171 °C; *^{1}H-NMR* (300 MHz): 1.27 (m, 6H, CH_3), 1.55 (d, 3H, $^3J_{PH}$= 13.9 Hz, CH_3), 4.06 (m, 4H, OCH_2), 6.84-8.63 (m, 9H, arom), 7.52 (s, 1H, NH), 10.15 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 13.7 (d, $^2J_{PC}$= 7.0 Hz, CH_3), 16.2 (CH_3), 62.0 (OCH_2), 99.3 (d, $^1J_{PC}$= 173.2 Hz, C=), 119.1-151.5 (CH-arom, CN and C=O), 154.8 (d,$^3J_{PC}$= 20.6 Hz, C-*ipso,arom.*). *^{31}P-NMR* (120 MHz). 23.8; *IR* (*KBr*) 3278, 3087, 1718, 1214 cm^{-1}; *MS* (EI) 389 (M^+, 23). Anal. Calcd for $C_{19}H_{24}N_3O_4P$: C, 58.61; H, 6.17; N, 10.80. Found: C, 58.98; H, 5.83; N, 10.66.

***Z*-N-(1-Phenyl-2-diethoxyphosphoryl-1-propenyl)-N'-propyl urea (7c).** 1570 mg (89%) of **7c** following the method A as a white solid. Data for **7c**: mp 164-165 °C; *^{1}H-NMR* (300 MHz): 0.75 (m, 3H, CH_3), 1.29 (m, 6H, CH_3), 1.31 (m, 2H, CH_2), 1.51 (d, 3H, $^3J_{PH}$= 13.7 Hz, CH_3), 2.93 (m, 2H, NCH_2), 4.05 (m, 4H, OCH_2), 5.37 (s, 1H, NH), 7.15-7.31 (m, 5H, arom), 9.65 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 10.9 (CH_3), 14.1 (d, $^2J_{PC}$= 7.5 Hz, CH_3), 16.0 (CH_3), 22.7 (CH_2), 41.6 (NCH_2), 61.5 (OCH_2), 96.4 (d, $^1J_{PC}$= 173.7 Hz, C=), 125.8-131.0 (CH-arom), 136.3 (d,$^3J_{PC}$= 17.6 Hz, C-*ipso,arom.*), 152.6 (d,$^2J_{PC}$= 8.5 Hz, CN), 154.1 (C=O). *^{31}P-NMR* (120 MHz). 24.3; *IR* (*KBr*) 3224, 3159, 1729, 1208 cm^{-1}; *MS* (EI) 354 (M^+, 29). Anal. Calcd for $C_{17}H_{27}N_2O_4P$: C, 57.63; H, 7.63; N, 7.91. Found: C, 57.49; H, 7.72; N, 7.83.

***Z*-N-(1-(2-Pyridyl)-2-diethoxyphosphoryl-1-propenyl)-N'-propyl urea (7d).** 1520 mg (90%) of **7d** following the method A as a white solid. Data for **7d**: mp 158-159 °C; *^{1}H-NMR* (300 MHz): 0.77 (m, 3H, CH_3), 0.91 (m, 2H, CH_2), 1.29 (m, 6H, CH_3), 1.48 (d, 3H, $^3J_{PH}$= 13.9 Hz, CH_3), 2.97 (m, 2H, NCH_2), 4.06 (m, 4H, OCH_2), 4.83 (s, 1H, NH), 7.21-8.56 (m, 4H, arom), 9.97 (s, 1H, NH). *^{13}C-NMR* (75 MHz): 11.0 (CH_3), 13.9 (d, $^2J_{PC}$= 7.3 Hz, CH_3), 16.0 (CH_3), 23.0 (CH_2), 41.4 (NCH_2), 62.0 (OCH_2), 98.6 (d, $^1J_{PC}$= 174.1 Hz, C=), 125.8-154.3 (CH-arom, C-*ipso,arom.*, CN and C=O). *^{31}P-NMR* (120 MHz). 24.5; *IR* (*KBr*) 3289, 3111, 1716, 1204 cm^{-1}; *MS* (EI) 355 (M^+, 7). Anal. Calcd for $C_{16}H_{26}N_3O_4P$: C, 54.08; H, 7.32; N, 11.83. Found: C, 54.51; H, 6.88; N, 11.39.

General Procedure for Preparation of 2,6-dioxo-1,5,2-P^V-diazaphosphorines 5 and 8

Method A. A dry flask, 100-mL, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 5 mmol of lithium diisopropylamide (LDA), and 25 mL of THF. The temperature was allowed to descend to -78 °C and a solution of the functionalizated β-enaminophosphonate **3/3'** (5 mmol) in THF was then added. The mixture was allowed to stir for 1 hour at this temperature. The temperature was allowed to ascend to room temperature. The mixture was stirred at room temperature during 5 hours, and then the mixture was washed with water and extracted with CH_2Cl_2. The organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by recrystallization (Et_2O).

Method B. A dry flask, 100-mL, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 5 mmol of the functionalizated β-enaminophosphonate **3/3'**, and 25 mL of THF. Then was added, at room temperature, a solution of methyllithium (1.6M in diethyl ether) (5 mmol) in THF. The mixture was stirred at this temperature during 18 hours. The mixture was washed with water and extracted with CH_2Cl_2. The organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by recrystallization (Et_2O).

Method C. A dry flask, 100-mL, 2-necked, fitted with a dropping funnel, gas inlet, and magnetic stirrer, was charged with 5 mmol of the functionalizated β-enaminophosphonate **3/3'**, and 25 mL of THF. Then, at room temperature, a solution of butyllithium (1.6 M in n-hexane) (5 mmol) in THF was added. The mixture was stirred at this temperature during 1 hour, and then was refluxed until *TLC* indicated the disappearance of the functionalizated β-enaminophosphonate **3/3'** (2-4 days). The mixture was washed with water and extracted with CH_2Cl_2. The organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by recrystallization (Et_2O).

1,4-Diphenyl-2,6-dioxo-2-ethoxy-1,2,5,6-tetrahydro-3,5-(H)-1,5,2-P^V-diazaphosphorine (5a). 1610 mg (98%) of **5a** following the method A as a white solid. Data for **5a**: mp 212-214°C; *^{1}H-NMR* (300 MHz) 1.04 (m, 3H, CH_3), 3.71 (m, 1H, OCH_2), 3.89 (m, 1H, OCH_2), 5.38 (d, 1H, $^2J_{PH}$= 8.9 Hz, CH), 7.18-7.46 (m, 10H, arom), 9.17 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 16.0 (CH_3), 63.7 (OCH_2), 86.7 (d,$^1J_{PC}$= 171.2 Hz, CH), 126.2-130.8 (CH-arom), 132.8 (C-*ipso,arom.*), 133.8 (d,$^3J_{PC}$= 18.6 Hz, C-*ipso,arom.*), 150.5 (d,$^2J_{PC}$= 3.5 Hz, CN), 153.1 (d,$^2J_{PC}$= 6.5 Hz, C=O). *^{31}P-NMR* (120 MHz) 14.0; *IR (KBr)* 3337, 1681, 1241 cm^{-1}; *MS* (EI) 328 (M^+, 100). Anal. Calcd for $C_{17}H_{17}N_2O_3P$: C, 62.19; H, 5.18; N, 8.54. Found: C, 62.01; H, 5.33; N, 8.42.

2,6-Dioxo-2-ethoxy-1-phenyl-4-(2-thiophenyl)-1,2,5,6-tetrahydro-3,5-(H)-1,5,2-P^V-diazaphosphorine (5b). 1420 mg (85%) of **5b** following the method A as a white solid. Data for **5b**: mp 206-208°C; *^{1}H-NMR* (300 MHz) 1.06 (m, 3H, CH_3), 3.75 (m, 1H, OCH_2), 3.95 (m, 1H, OCH_2), 5.45 (d, 1H, $^2J_{PH}$= 6.3 Hz, CH), 6.81-7.41 (m, 8H, arom), 9.12 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 16.2 (CH_3), 63.8 (OCH_2), 85.6 (d,$^1J_{PC}$= 173.7 Hz, CH), 120.2-132.9 (CH-arom), 136.2 (d,$^3J_{PC}$= 21.1 Hz, C-*ipso,arom.*), 137.5 (C-*ipso,arom.*), 143.5 (d,$^2J_{PC}$= 4.5 Hz, CN), 153.0 (d,$^2J_{PC}$= 6.5 Hz, C=O). *^{31}P-NMR* (120 MHz) 13.3; *IR (KBr)* 3327, 1675, 1213 cm^{-1}; *MS* (EI) 334 (M^+, 72). Anal. Calcd for $C_{15}H_{15}N_2O_3PS$: C, 53.89; H, 4.49; N, 8.38; S, 9.58. Found: C, 53.67; H, 4.78; N, 8.29; S, 9.46.

2,6-Dioxo-2-ethoxy-1-phenyl-4-(2-furyl)-1,2,5,6-tetrahydro-3,5-(H)-1,5,2-P^V-diazaphosphorine (5c). 1450 mg (91%) of **5c** following the method A as a white solid. Data for **5c**: mp 215-220°C (dec); *^{1}H-NMR* (300 MHz) 1.13 (m, 3H, CH_3), 3.81 (m, 1H, OCH_2), 3.98 (m, 1H, OCH_2), 5.64 (d, 1H, $^2J_{PH}$= 7.8 Hz, CH), 6.43-7.51 (m, 8H, arom), 8.82 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 16.1 (CH_3), 63.8 (OCH_2), 82.9 (d,$^1J_{PC}$= 175.7 Hz, CH), 111.3-145.6 (CH-arom, C-*ipso,arom.* and CN), 145.8 (d,$^3J_{PC}$= 20.4 Hz, C-*ipso,arom.*), 152.9 (C=O). *^{31}P-NMR* (120 MHz) 14.1; *IR (KBr)* 3229, 1709, 1207 cm^{-1}; *MS* (EI) 318 (M^+, 83). Anal. Calcd for $C_{15}H_{15}N_2O_4P$: C, 56.60; H, 4.72; N, 8.80. Found: C, 56.97; H, 4.88; N, 8.52.

2,6-Dioxo-2-ethoxy-1-phenyl-4-(2-pyridyl)-1,2,5,6-tetrahydro-3,5-(H)-1,5,2-P^V-diazaphosphorine (5d). 1430 mg (87%) of **5d** following the method A as a white solid. Data for **5d**: mp 196-197°C; *^{1}H-NMR* (300 MHz) 1.07 (m, 3H, CH_3), 3.76 (m, 1H, OCH_2), 3.94 (m, 1H, OCH_2), 5.86 (d, 1H, $^2J_{PH}$= 7.2 Hz, CH), 7.36-8.60 (m, 9H, arom), 9.46 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 16.1 (CH_3), 63.7 (OCH_2), 85.5 (d,$^1J_{PC}$= 172.7 Hz, CH), 120.1-148.6 (CH-arom), 137.5 (C-*ipso,arom.*), 145.2 (d,$^2J_{PC}$= 3.5 Hz, CN), 147.1 (d,$^3J_{PC}$= 22.2 Hz, C-*ipso,arom.*), 151.5 (d,$^2J_{PC}$= 6.0 Hz, C=O). *^{31}P-NMR* (120 MHz) 14.8; *IR (KBr)* 3284, 1695, 1254 cm^{-1}; *MS* (EI) 329 (M^+, 93). Anal. Calcd for $C_{16}H_{16}N_3O_3P$: C, 58.36; H, 4.86; N, 12.76. Found: C, 58.25; H, 4.99; N, 12.64.

2,6-Dioxo-2-ethoxy-1-phenyl-4-*p*-tolyl-1,2,5,6-tetrahydro-3,5-(H)-1,5,2-P^V-diazaphosphorine (5e). 1640 mg (96%) of **5e** following the method A as a white solid. Data for **5e**: mp 188-189°C; *^{1}H-NMR* (300 MHz) 1.05 (m, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.71 (m, 1H, OCH_2), 3.89 (m, 1H, OCH_2), 5.35 (d, 1H, $^2J_{PH}$= 9.0 Hz, CH), 7.07-7.44 (m, 9H, arom), 8.67 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 16.1 (CH_3), 21.3 (CH_3), 63.7 (OCH_2), 86.0 (d,$^1J_{PC}$= 171.2 Hz, CH), 126.0-131.0 (CH-arom), 131.2 (d,$^3J_{PC}$= 18.5 Hz, C-*ipso,arom.*), 132.9 (C-*ipso,arom.*), 141.5 (C-*ipso,arom.*), 150.2 (d,$^2J_{PC}$= 3.5 Hz, CN), 152.8 (d,$^2J_{PC}$= 6.5 Hz, C=O). *^{31}P-NMR* (120 MHz) 14.3; *IR (KBr)* 3317, 1711, 1208 cm^{-1}; *MS* (EI) 342 (M^+, 89). Anal. Calcd for $C_{18}H_{19}N_2O_3P$: C, 63.16; H, 5.55; N, 8.19. Found: C, 63.34; H, 5.19; N, 8.48.

2,6-Dioxo-2-ethoxy-4-phenyl-1-propyl-1,2,5,6-tetrahydro-3,5-(H)-1,5,2-P^V-diazaphosphorine (5f). 1440 mg (98%) of **5f** following the method B as a white solid. Data for **5f**: mp 135-136°C; *^{1}H-NMR* (300 MHz) 0.87 (m, 3H, CH_3), 1.27 (m, 3H, CH_3), 1.66 (m, 2H, CH_2), 3.39 (m, 1H, NCH_2), 3.51 (m, 1H, NCH_2), 3.96 (m, 2H, OCH_2), 5.23 (d, 1H, $^2J_{PH}$= 9.0 Hz, CH), 7.36-7.54 (m, 5H, arom), 9.32 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 11.3 (CH_3), 16.3 (CH_3), 22.4 (CH_2), 43.0 (NCH_2), 62.9 (OCH_2), 85.4 (d,$^1J_{PC}$= 166.7 Hz, CH), 126.4-130.9 (CH-arom), 134.1 (d,$^3J_{PC}$= 17.5 Hz, C-*ipso,arom.*), 150.9 (d,$^2J_{PC}$= 3.5 Hz, CN), 153.5 (d,$^2J_{PC}$= 5.5 Hz, C=O). *^{31}P-NMR* (120 MHz) 17.0; *IR (KBr)* 3227, 1696, 1246 cm^{-1}; *MS* (EI) 294 (M^+, 100). Anal. Calcd for $C_{14}H_{19}N_2O_3P$: C, 57.14; H, 6.46; N, 9.52. Found: C, 57.31; H, 6.28; N, 9.43.

2,6-Dioxo-2-ethoxy-1-propyl-4-(2-thiophenyl)-1,2,5,6-tetrahydro-3,5-(H)-1,5,2-P^V-diazaphosphorine (5g). 1480 mg (99%) of **5g** following the method B as a white solid. Data for **5g**: mp 141-143°C; *^{1}H-NMR* (300 MHz) 0.93 (m, 3H, CH_3), 1.29 (m, 3H, CH_3), 1.76 (m, 2H, CH_2), 3.47 (m, 1H, NCH_2), 3.60 (m, 1H, NCH_2), 3.98 (m, 2H, OCH_2), 5.33 (d, 1H, $^2J_{PH}$= 7.4 Hz, CH), 7.02-7.66 (m, 3H, arom), 9.63 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 11.4 (CH_3), 16.3 (CH_3), 22.5 (CH_2), 43.1 (NCH_2), 62.9 (OCH_2), 84.2 (d,$^1J_{PC}$= 169.7 Hz, CH), 127.2-128.7 (CH-arom), 136.4 (d,$^3J_{PC}$= 20.6 Hz, C-*ipso,arom.*), 144.1 (d,$^2J_{PC}$= 4.6 Hz, CN), 153.4 (d,$^2J_{PC}$= 6.0 Hz, C=O). *^{31}P-NMR* (120 MHz) 16.3; *IR (KBr)* 3341, 1669, 1236 cm^{-1}; *MS* (EI) 300 (M^+, 96). Anal. Calcd for $C_{12}H_{17}N_2O_3PS$: C, 48.00; H, 5.66; N, 9.33; S, 10.66. Found: C, 47.62; H, 5.78; N, 9.52; S, 10.69.

2,6-Dioxo-2-ethoxy-4-phenyl-1-*p*-methoxyphenyl-1,2,5,6-tetrahydro-3,5-(H)-1,5,2-P^V-diazaphosphorine (5h). 1700 mg (95%) of **5h** following the method A as a white solid. Data for **5h**: mp 192-194°C; *^{1}H-NMR* (300 MHz) 1.14 (m, 3H, CH_3), 3.79 (m, 1H, OCH_2), 3.84 (s, 3H, OCH_3), 3.97 (m, 1H, OCH_2), 5.40 (d, 1H, $^2J_{PH}$= 8.7 Hz, CH), 6.96-7.53 (m, 9H, arom), 8.44 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 16.2 (CH_3), 55.4 (OCH_3), 63.7 (OCH_2), 87.1 (d,$^1J_{PC}$= 170.2 Hz, CH), 114.5-131.1 (CH-arom), 134.2 (d,$^3J_{PC}$= 18.1 Hz, C-*ipso,arom.*), 150.1 (d,$^2J_{PC}$= 3.5 Hz, CN), 153.0 (d,$^2J_{PC}$= 7.0 Hz, C=O), 159.7 (C-*ipso,arom.*). *^{31}P-NMR* (120 MHz) 14.0; *IR (KBr)* 3306, 1696, 1246 cm^{-1}; *MS* (EI) 358 (M^+, 93). Anal. Calcd for $C_{18}H_{19}N_2O_4P$: C, 60.33; H, 5.31; N, 7.82. Found: C, 60.54; H, 5.07; N, 7.61.

2,6-Dioxo-2-ethoxy-4-phenyl-1,2,5,6-tetrahydro-1,3,5-(H)-1,5,2-P^V-diazaphosphorine (5i). 770 mg (61%) of **5i** following the method B as a white solid. Data for **5i**: mp 111-113°C; *^{1}H-NMR* (300 MHz) 1.18 (m, 3H, CH_3), 4.03 (m, 1H, OCH_2), 4.15 (m, 1H, OCH_2), 5.19 (d, 1H, $^2J_{PH}$= 8.7 Hz, CH), 7.41-7.65 (m, 5H, arom), 8.40 (s, 1H, NH), 10.15 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 16.1 (CH_3), 63.4 (OCH_2), 86.5 (d,$^1J_{PC}$= 171.5 Hz, CH), 113.7-158.2 (CH-arom, C-*ipso,arom.*, CN and C=O). *^{31}P-NMR* (120 MHz) 14.2; *IR (KBr)* 3395, 3372, 1685, 1249 cm^{-1}; *MS* (EI) 252 (M^+, 37). Anal. Calcd for $C_{11}H_{13}N_2O_3P$: C, 52.38; H, 5.16; N, 11.11. Found: C, 51.95; H, 5.37; N, 10.86.

1,4-Diphenyl-2,6-dioxo-2-ethoxy-3-methyl-1,2,5,6-tetrahydro-5-(H)-1,5,2-P^V-diazaphosphorine (8a). 1690 mg (99%) of **8a** following the method C as a white solid. Data for **8a**: mp 203-204°C; *^{1}H-NMR* (300 MHz) 1.03 (m, 3H, CH_3), 1.82 (d, 3H, $^3J_{PH}$= 14.4 Hz, CH_3), 3.72 (m, 1H, OCH_2), 3.89 (m, 1H, OCH_2), 7.26-7.42 (m, 10H, arom), 7.79 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 11.4 (d,$^2J_{PC}$= 7.0 Hz, CH_3), 16.1 (CH_3), 63.9 (OCH_2), 96.1 (d,$^1J_{PC}$= 161.6 Hz, C=), 128.0-130.0 (CH-arom), 133.0 (C-*ipso,arom.*), 133.5 (d,$^3J_{PC}$= 17.6 Hz, C-*ipso,arom.*), 144.8 (d,$^2J_{PC}$= 8.6 Hz, CN), 151.9 (d,$^2J_{PC}$= 6.0 Hz, C=O). *^{31}P-NMR* (120 MHz) 16.6; *IR (KBr)* 3314, 1723, 1236 cm^{-1}; *MS* (EI) 342 (M^+, 95). Anal. Calcd for $C_{18}H_{19}N_2O_3P$: C, 63.16; H, 5.55; N, 8.19. Found: C, 63.37; H, 5.28; N, 7.94.

2,6-Dioxo-2-ethoxy-1-phenyl-3-methyl-4-(2-pyridyl)-1,2,5,6-tetrahydro-5-(H)-1,5,2-P^V-diazaphosphorine (8b). 1680 mg (98%) of **8b** following the method C as a white solid. Data for **8b**: mp 171-173°C; *^{1}H-NMR* (300 MHz) 1.06 (m, 3H, CH_3), 2.16 (d, 3H, $^3J_{PH}$= 14.4 Hz, CH_3), 3.77 (m, 1H, OCH_2), 3.96 (m, 1H, OCH_2), 7.35-8.65 (m, 9H, arom), 8.46 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 12.1 (d,$^2J_{PC}$= 6.0 Hz, CH_3), 16.1 (CH_3), 63.9 (OCH_2), 97.7 (d,$^1J_{PC}$= 161.7 Hz, C=), 124.7-149.9 (CH-arom and C-*ipso,arom.*), 141.2 (d,$^2J_{PC}$= 8.0 Hz, CN), 151.5 (d,$^2J_{PC}$= 6.0 Hz, C=O). *^{31}P-NMR* (120 MHz) 17.0; *IR (KBr)* 3220, 1711, 1233 cm^{-1}; *MS* (EI) 343 (M^+, 100). Anal. Calcd for $C_{17}H_{18}N_3O_3P$: C, 59.47; H, 5.25; N, 12.24. Found: C, 59.36; H, 5.29; N, 12.31.

2,6-Dioxo-2-ethoxy-4-phenyl-3-methyl-1-propyl-1,2,5,6-tetrahydro-5-(H)-1,5,2-P^V-diazaphosphorine (8c). 1230 mg (80%) of **8c** following the method C as a white solid. Data for **8c**: mp 158-159°C; *^{1}H-NMR* (300 MHz) 0.90 (m, 3H, CH_3), 1.35 (m, 3H, CH_3), 1.68 (m, 2H, CH_2), 1.84 (d, 3H, $^3J_{PH}$= 13.8 Hz, CH_3), 3.37 (m, 1H, NCH_2), 3.54 (m, 1H, NCH_2), 4.06 (m, 2H, OCH_2), 7.31-7.45 (m, 5H, arom), 9.38 (s, 1H, NH); *^{13}C-NMR* (75 MHz) 11.2 (d,$^2J_{PC}$= 7.6 Hz, CH_3), 11.4 (CH_3), 16.3 (CH_3), 22.3 (CH_2), 43.1 (NCH_2), 62.8 (OCH_2), 94.5 (d,$^1J_{PC}$= 158.1 Hz, C=), 128.1-129.7 (CH-arom), 133.4 (d,$^3J_{PC}$= 16.6 Hz, C-*ipso,arom.*), 145.5 (d,$^2J_{PC}$= 8.1 Hz, CN), 152.4 (d,$^2J_{PC}$= 5.5 Hz, C=O). *^{31}P-NMR* (120 MHz) 19.6; *IR*

(KBr) 3361, 1688, 1256 cm^{-1}; *MS* (EI) 308 (M^+, 45). Anal. Calcd for $C_{15}H_{21}N_2O_3P$: C, 58.44; H, 6.82; N, 9.09. Found: C, 58.61; H, 6.67; N, 9.22.

2,6-Dioxo-2-ethoxy-3-methyl-4-(2-pyridyl)-1-propyl-1,2,5,6-tetrahydro-5-(H)-1,5,2-P^V-diazaphosphorine (8d). 1340 mg (87%) of **8d** following the method C as a white solid. Data for **8d**: mp 143-144°C; ^1H-*NMR* (300 MHz) 1.02 (t, 3H, $^3J_{HH}$= 7.5 Hz, CH_3), 1.41 (m, 3H, CH_3), 1.85 (m, 2H, CH_2), 2.21 (d, 3H, $^3J_{PH}$= 14.7 Hz, CH_3), 3.56 (m, 1H, NCH_2), 3.70 (m, 1H, NCH_2), 4.11 (m, 2H, OCH_2), 7.44-8.77 (m, 4H, arom), 8.70 (s, 1H, NH); ^{13}C-*NMR* (75 MHz) 11.2 (CH_3), 11.6 (d,$^2J_{PC}$= 6.6 Hz, CH_3), 16.1 (CH_3), 22.4 (CH_2), 43.0 (NCH_2), 62.8 (OCH_2), 96.0 (d,$^1J_{PC}$= 157.6 Hz, C=), 124.5-149.6 (CH-arom), 141.8 (d,$^2J_{PC}$= 7.5 Hz, CN), 149.8 (d,$^3J_{PC}$= 20.6 Hz, C-*ipso,arom.*), 151.8 (d,$^2J_{PC}$= 5.5 Hz, C=O). ^{31}P-*NMR* (120 MHz) 19.8; *IR (KBr)* 3316, 1712, 1208 cm^{-1}; *MS* (EI) 309 (M^+, 37). Anal. Calcd for $C_{14}H_{20}N_3O_3P$: C, 54.37; H, 6.47; N, 13.59. Found: C, 54.03; H, 6.72; N, 13.67.

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