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Reaction of *N*-Vinylic Phosphazenes with Carbonyl Compounds. Reactivity of the Vinyl Side Chain *Versus* Aza-Wittig Reaction.

Francisco Palacios*, Domitila Aparicio, Jesús M. de los Santos

Departamento de Química Orgánica. Facultad de Farmacia. Universidad del País Vasco.
Apartado 450. 01080 Vitoria. SPAIN.

Abstract: *N*-Vinylic phosphazenes **2** are obtained by Staudinger reaction of conjugated azides **1** and phosphines. Reactions of phosphazenes **2a,b** derived from triphenylphosphine with carbonyl compounds **3** involve the γ-carbon atom of the vinyl side chain as nucleophilic center to give monoadducts **4**, while phosphazene derived from diphenylmethylphosphine **2c** undergoes Aza-Wittig reaction with ethyl glyoxalate and leads to the formation of substituted 2-azadiene **10**.

The chemistry of phosphazenes[1] has attracted a great deal of attention in recent years because of their broad range of applications. They have been used as polymeric materials with high ionic conductivity in the solid state,[2] as "proton sponges"[3] and, in organic synthesis[1] for the preparation not only of acyclic compounds such as amino-containing phosphines,[4a] peptides,[4b] imines,[4c] 1-azadienes[4d] but also in the preparation of cyclic compounds such as azasugars,[5a] carbodiimides,[5b] bicyclic guanidines,[5c] macrolactames,[5d] poliazamacrocycles,[5e] zwitterionic heteropolycyclic pyrazoles,[5f] pyridines,[5g] isoxazolo-quinolines,[5h] pteridinones,[5i] steroidal pyrazines[5j] and isoquinoline alkaloids,[5k] showing that phosphazenes lead to a very efficient and mild condition method for the construction of carbon-nitrogen double bonds.[6]

Furthermore, *N*-vinylic phosphazenes[7] have recently gained importance as a result of their usefulness in the synthesis of functionalized imine compounds such as 2-azadienes,[8] and as key intermediates in the preparation of heterocycles such as pyridine derivatives,[9] polycyclic pyrroles,[10] polycyclic azulenes,[7,11] benzodiazepines[12] as well as in elegant routes to the preparation of biologically active natural products such as the antibacterial alkaloids Eudistomin U[13a] and Fascaplysin,[13b] the antitumor antibiotic Lavendamycin,[13c] and for the construction of the framework of pharmacologically active azafluoranthene,[13d] azacarboline[13e] and aplysinopsine-type[13e,13f] alkaloids. *N*-Vinylic phosphazenes were limited to aryl-,[7,14] heterocyclic-[8b] derivatives and the corresponding compounds derived from α-[1,8d,13] and β-aminoacids:[8a] However, to the best

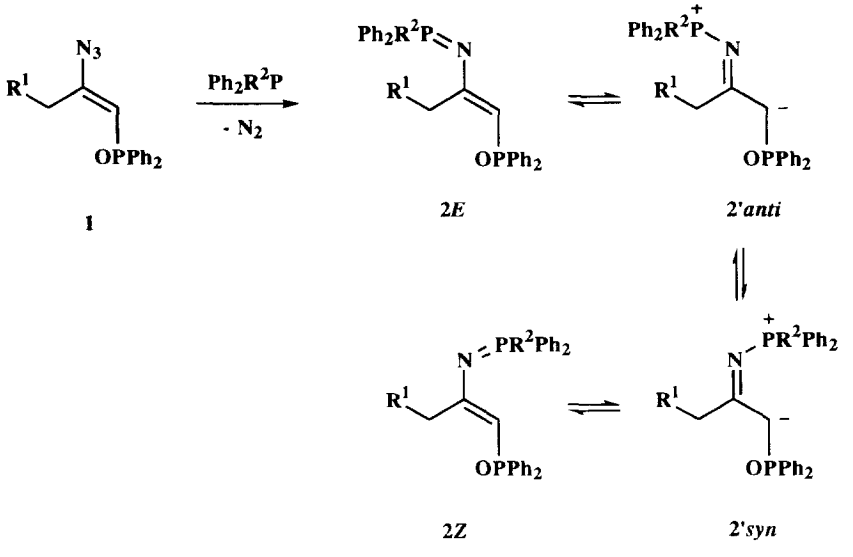
of our knowledge, no information has been reported on the synthesis and reactivity of phosphazenes substituted with a phosphorus containing group.

In recent years, we have been involved in the study of simple and functionalized phosphazenes[1] as well as in their usefulness in the preparation of acyclic[8,15,16] and heterocyclic compounds.[17] It is noteworthy that while in some cases the reaction involves the nitrogen-phosphorus double bond[8,15,17] in other examples the phosphazene group remains unaffected.[16] Moreover, an adjacent double bond in conjugation with the phosphazene moiety introduces the interesting problem of site selectivity; i.e., reaction at the nitrogen (1,2-addition) of the phosphazene group in a similar way to previously reported aza-Wittig reactions[6,8] *versus* reactions at the γ-C-atom (1,4-addition), such as protected enamines.[7] In this context, it is noteworthy that we have used phosphorus functionalized enamines as intermediates in the preparation of allylamines,[18] aminodienes,[19] unsaturated hydrazones[20] and phosphorylated pyridines.[21] In connection with our interest in the application of *N*-vinylic phosphazenes as intermediates in organic synthesis we report here the synthesis of the first example of conjugated phosphazenes substituted with a phosphorus containing group as well as their reactions with carbonyl compounds and their use in the preparation of functionalized phosphazenes, enamines and 2-azadienes.

RESULTS AND DISCUSSION

Preparation of *N*-vinylic phosphazenes **2**.

The synthesis of the conjugated phosphazenes **2** was accomplished very easily through the classic Staudinger reaction[1] of azides[22] **1** and phosphines (see Scheme 1). Crystalline compounds **2** were characterized on the basis of their spectroscopic data, which indicate that they are isolated as a mixture of the *E*-**2** and *Z*-conjugated phosphazenes **2**, although for our purposes the separation of both isomers is not necessary for subsequent reactions. Thus, the *^{31}P-NMR* spectrum for **2*E*a** showed two different absorptions at δ_P 7.1 and 21.4 ppm, while the absorptions of the *Z*-isomer **2*Z*a** appeared at δ_P 1.1 and 22.0 ppm in an approximate isomer ratio 43 : 57 indicated by the relative peak areas for both isomers. Furthermore, in the *^{1}H-NMR* spectrum of **2*E*a**, vinylic proton resonates at 4.77 ppm as a well resolved double doublet with coupling constants of $^2J_{PH}$ 22.6 and $^4J_{PH}$ 10.2 Hz, and the methyl group gives a singlet at δ_H 2.11 ppm, while the *^{13}C-NMR* spectrum shows absorptions at δ_C 94.6 ($^1J_{PC}$ 117.9 Hz, $^3J_{PC}$ = 24.7 Hz) and 28.0 ppm ($^3J_{PC}$ 8.6 and 15.1 Hz) as well resolved double doublets assignable to the carbon bonded to phosphorus and the methyl group of the *E*-isomer. Conversely, the *Z*-isomer **2*Z*a** showed clearly different absorptions, namely a doublet at δ_H 4.31 ppm ($^2J_{PH}$ 20.9 Hz) for the vinylic protons as well as a high field signal for the methyl group at δ_H 1.60 ppm, while in the *^{13}C-NMR* spectrum the absorption of methine carbon is shifted to higher field (δ_C 92.7 ppm) related to the *E*-isomer and the methyl group absorption appeared at δ_C 26.9 ppm. The steric compression shift of about 1 ppm observed in the methyl group of both *E*- and *Z*-isomers is lower to that previously reported in structures containing an iminic carbon-nitrogen double bond such as the *syn*- and *anti*-isomers of oximes.[24]

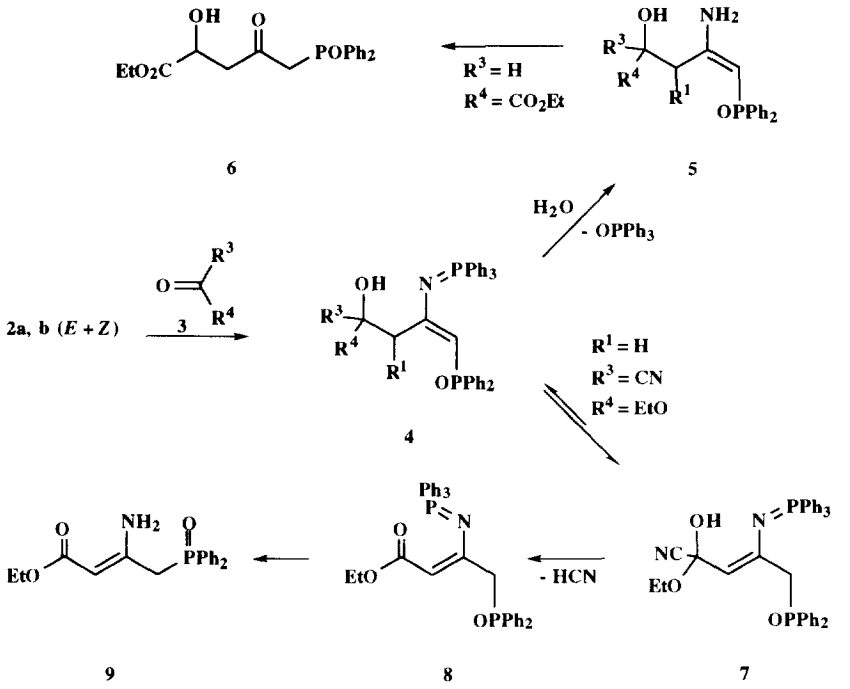


Scheme 1

The existence of two isomers **2*E*, *Z*** presupposes restricted rotation around the *N*-C_β bond[14] and the substituent on C_γ capable of delocalizing a negative charge, such as the phosphine oxide group, should increase the double bond character of the *N*-C_β bond **2'*syn*** and ***anti*** and consequently increases the barrier of rotation around that bond. Moreover, the upfield shifts observed in *NMR* for the γ-hydrogen and γ-carbon atoms of the vinyl moiety compared to those observed in simple alkenes[23] (or even with the starting azide **1** used in its preparation -the vinyl proton resonates at δ_H 5.59 ppm and the γ-carbon atom appears at δ_C 103.9 ppm-) suggest high electron density on the γ-carbon atom and enhanced nucleophilicity of the vinyl moiety[7] and the general canonical structures **2'*syn*** and ***anti*** become important in the resonance hybrid of the conjugated phosphazene **2**.

Reaction of *N*-vinylic phosphazenes derived from triphenylphosphine **2** with carbonyl compounds **3**.

It is known that phosphazenes, nitrogen analogues to the isoelectronic phosphorus ylides, react with carbonyl compounds and lead to a very efficient method for construction of carbon-nitrogen double bonds -Aza-Wittig reaction-.[1,6] This process has been extended to the reaction of simple aldehydes with *N*-vinylic triaryl-λ^5-phosphazenes containing an alkoxycarbonyl[8d] and a heterocyclic[8b] group in the 3-position, while the presence of an electron-withdrawing group in 4-position, such as an ester group, limited the reaction to very reactive carbonyl compounds.[8a] Here, the presence of an electron-withdrawing group in the phosphazene **2**, such as the phosphine oxide group, seems to play an important role in the reactivity of the conjugated phosphazene.



Scheme 2

Table 1. Compounds prepared.

Compound	R^1	R^2	R^3	R^4	Yield (%)[a]	m.p. (°C)
2a[b]	H	C_6H_5			94	164-165
2b[b]	CH_3	C_6H_5			80	173-174
2c[b]	H	CH_3			98	139-140
4aa	H	C_6H_5	CO_2Et	CO_2Et	70	162-163
4ab	H	C_6H_5	CN	Me	72	153-154
4ba	CH_3	C_6H_5	CO_2Et	CO_2Et	75	163-164
5	H	C_6H_5	CO_2Et	CO_2Et	78	143-144
6	H	C_6H_5	CO_2Et	H	85	oil[c]
8	H	C_6H_5	CN	OEt	76	182-183
9	H	C_6H_5	CN	OEt	70	223-224

[a] Yield of isolated purified product. [b] *E* / *Z* ratio for **2a**, 43 : 57; for **2b**, 31 : 69 and for **2c**, 37 : 63.

[c] Purified by flash chromatography.

Reaction of compounds **2a,b** with diethyl ketomalonate and pyruvonitrile in $CHCl_3$ (TLC control) gave very high yields of functionalized phosphazenes **4** (see Scheme 2). Pure compounds were obtained after flash-

chromatography followed by crystallisation. Compounds **4** were characterized on the basis of their spectroscopic data. The *^{1}H-NMR* spectrum of **4aa** indicates a methylene group at δ_H 3.44 ppm as a doublet due to the long-range coupling constant of $^4J_{PH}$ 3.8 Hz and the vinylic proton resonates at 4.27 ppm as a well resolved doublet with coupling constant of $^2J_{PH}$ 19.6 Hz, while the *^{13}C-NMR* spectrum shows absorptions at δ_C 42.8 ppm for the methylene group as a doublet with a coupling constant of $^3J_{PC}$ 21.0 Hz which indicates the *E*-stereochemistry of methylene group with the triphenylphosphine group. Hydrolysis of compounds **4aa** gave the corresponding functionalized primary enamine **5**. However, when ethyl glyoxalate was used as carbonyl compound in the reaction with **2a** neither the phosphazene **4** nor the enamine **5** was obtained and β-ketophosphine oxide **6** was isolated instead. A mechanism that rationalizes the formation of compounds **4** can be explained taking into account the high electron density on the γ-carbon atom of **2** revealed by the *NMR* spectroscopic data of these compounds **2**, which suggest enhanced nucleophilicity of the vinyl moiety and therefore the reaction with carbonyl compounds could be assumed to proceed via nucleophilic attack of the γ-carbon atom of *N*-vinylic phosphazenes **2** on the carbonyl group with carbon-carbon simple bond construction leading to functionalized phosphazenes **4**. Previous examples of enamine-type reactions of *N*-vinylic phosphazenes with Michael acceptors[7] and carbodiimides[25] in a inter- and intramolecular fashion, respectively, have been reported.

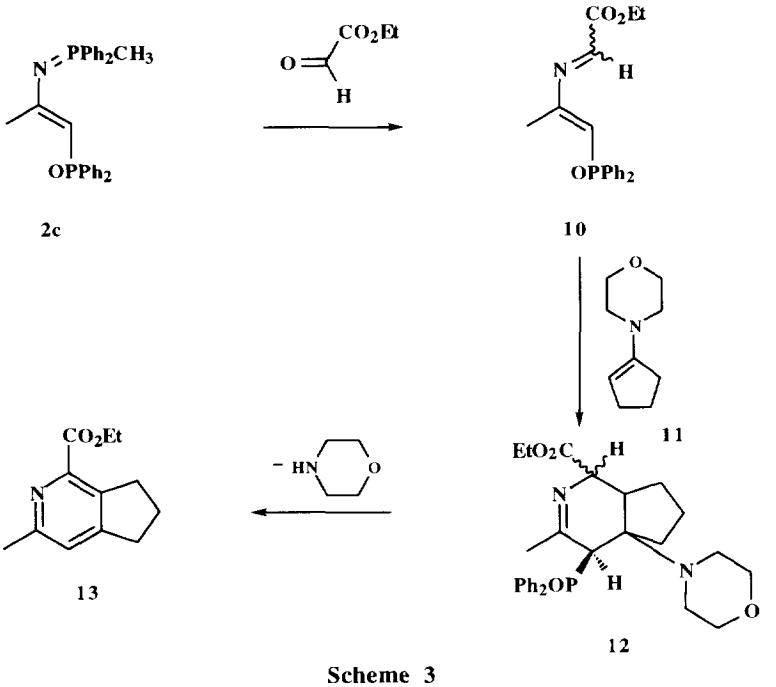
Ethyl cyanoformate also reacts with phosphazene **2a** in $CHCl_3$ (TLC control), however in this case the product **8** corresponding to the cyanogen acid elimination was isolated instead of the 1:1 adduct **4**. The structure of compound **8** was ascertained on the basis of its spectroscopic data and mass spectrometry, which shows a molecular ion at m/z 589 (19 %). Thus the *^{31}P-NMR* spectrum of **8** showed two different absorptions at δ_P 7.0 and 29.8 ppm. Furthermore, the *^{1}H-NMR* spectrum of **8** gives a singlet at 4.43 ppm for the vinylic protons and the methylene group resonates at 4.46 ppm as a double doublet with $^2J_{PH}$ 13.8 Hz and long-range coupling constant of $^4J_{PH}$ 4.1 Hz, while the *^{13}C-NMR* spectrum shows absorptions at δ_C 97.0 ppm ($^3J_{PC}$ 12.1 Hz) for the olefinic carbon which indicates that this group is in *trans*-position wich the triphenylphosphine group, and a double doublet at δ_C 39.5 ppm ($^1J_{PC}$ 67.9 and $^3J_{PC}$ 24.7 Hz) assignable to the methylene group. Hydrolisis of **8** gave phosphorylated β-enamino ester **9**. Formation of compound **8** could be explained through enamine-type carbon-carbon bond formation leading to the monoadduct **4**, followed by subsequent cyanogen acid elimination.

Aza-Wittig reaction of *N*-vinylic phosphazenes **2** with ethyl glyoxalate.

N-vinylic phosphazenes may be considered to be an equivalent of enamine and to contain two nucleophilic centers at the γ-carbon atom and the nitrogen atom of the phosphazene group. Bearing in mind the enamine-type reactivity through the γ-carbon atom with the phosphazene group remainig unaffected, which was observed in the reaction of phosphazenes **2a** derived from triphenylphosphine with carbonyl compounds, we tried to increase the nucleophilic character of the nitrogen atom of *N*-vinylic phosphazenes by using a more reactive[1] phosphazene, such as compounds derived from diphenylmethylphosphine **2c** in order to explore the availability of the phosphazene group to undergo Aza-Wittig reactions with carbonyl compounds.

Reaction of conjugated phosphazenes **2c** with ethyl glyoxalate in $CHCl_3$ at room temperature gave very high yields of substituted 2-azadiene **10**. (Scheme 3). The isolation of diene **10** was cumbersome to carry out on a routine basis and compound **10** proved to be unstable during distillation or chromatography. However, the presence of the unstable azadiene **10** in the crude reaction mixture was detected by ^{1}H-NMR spectroscopy -the

vinylic proton gives resonance at δ_H 5.65 ppm ($^2J_{PH}$ = 20.1 Hz) and the methyl group resonates at δ_H 2.29 ppm as a singlet-. Moreover, the reactivity in [4 + 2] cycloaddition reaction of diene **10** was explored, and crude reaction mixture without purification was satisfactorily used for subsequent reaction with morpholinocyclopentene enamine **11**. Thus, azadiene **10** was allowed to react with enamine **11** in chloroform at 60 °C (TLC control) leading to bicyclic pyridine **13**. This compound **13** was characterized on the basis of its spectroscopic data and mass spectrometry. For instance, the pyridine proton gives ^1H resonances at δ_H 7.11 ppm, while mass spectrometry of this compound showed the molecular ion peak (m/z 205, 100 %). The formation of substituted pyridine **13** derived from α-aminoacids could be assumed *via* [4 + 2] cycloaddition of azadiene **10** and enamine **11** to give adduct **12** followed by β-elimination of amine and aromatization of corresponding nitrogen six membered heterocycle.



Scheme 3

In summary, the present study demostrates that *N*-vinylic phosphazenes **2** may be considered, from a synthetic point of view, to be equivalents of enamines, showing, like enamines, a nucleophilic ambident character. Reactions of phosphazenes derived from triphenylphosphine **2a,b** with carbonyl compounds occur at *C*-γ-atom with carbon-carbon simple bond formation, the phosphazene linkage **4** remaining unaffected, but reaction of phosphazene derived from diphenylmethylphosphine **2c** with ethyl glyoxalate takes place at nitrogen atom -Aza-Wittig reaction- leading to the formation of the nitrogen-carbon double bond **10**.

ACKNOWLEDGEMENTS

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EXPERIMENTAL SECTION

General. 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. Solvents for extraction and chromatography were technical grade and distilled from the indicated drying agents: CH_2Cl_2 (P_2O_5); Hexane and diethyl ether (sodium benzophenone ketyl); ethyl acetate (K_2CO_3). All solvents used in reactions were freshly distilled from appropriate drying agents before use: THF (sodium benzophenone ketyl); $CHCl_3$ (P_2O_5). All other reagents were recystallized or distilled as necessary. Column (flash) chromatography was carried out on silica gel (Merck, 70-230 mesh). 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 Unity Plus 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 150 MHz with 85% phosphoric acid as an external reference. Elemental analyses were performed in a Perkin Elmer Model 240 instrument. Chemical shifs are given in ppm (δ); multiplicities are indicated by s (singlet), d (doblet), dd (double-doublet), t (triplet) q (quadruplet) or m (multiplet). Coupling constants, *J*, are reported in hertz. Infrared spectra (IR) were obtained as neat liquids, or as solids in KBr. Peaks are reported in cm^{-1}. Mass spectra (EI) were obtained with a 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 the Preparation of the *N*-Vinylic λ^5-Phosphazenes 2. A solution of phosphine (5 mmol) in CH_2Cl_2 (10 mL) was added very slowly to a 0°C solution of of vinyl azide **1** (5 mmol) in anhydrous CH_2Cl_2 (15 mL) under N_2. The mixture was allowed to warm to room temperature and then stirred for 3h. at room temperature The crude product was purified by recrystallization (CH_2Cl_2 / hexane).

***Z*- and *E*-4-diphenylphosphoryl-3-methyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (2a).** Reaction of *E*-2-azido-1-propenyldiphenylphosphine oxide (5 mmol, 1.42 g) with 1.31 g (5 mmol) of triphenylphosphine (as described above) led to the isolation of 2.43 g (94 %) of compound **2a** as a white solid. Data for **2a**: mp 164-165 °C; *^{1}H-NMR* (300 MHz) 1.60 and 2.11 (s, 3H, *E*- and *Z*-CH_3), 4.31 (d, 1H, $^2J_{PH}$ = 20.9 Hz, *Z*-CH), 4.77 (dd, 1H, $^2J_{PH}$ = 22.6 Hz, $^4J_{PH}$ = 10.2 Hz, *E*-CH), 7.13-7.91 (m, 25H, arom); *^{13}C-NMR* (75 MHz) 26.9 (dd, $^3J_{PC}$ = 4.0 Hz, $^3J_{PC}$ = 23.1 Hz, *Z*-CH_3), 28.0 (dd, $^3J_{PC}$ = 8.6 Hz, $^3J_{PC}$ = 15.1 Hz, *E*-CH_3), 92.7 (dd, $^1J_{PC}$ = 118.9 Hz, $^3J_{PC}$ = 14.6 Hz, *Z*-CH), 94.6 (dd, $^1J_{PC}$ = 117.9 Hz, $^3J_{PC}$ = 24.7 Hz, *E*-CH), 127.9-138.5 (C-arom), 165.2 (C-N), 169.3 (d, $^2J_{PC}$ = 14.1 Hz, C-N); *^{31}P-NMR* (150 MHz) 1.1 and 22.0 (*Z*-isomer), 7.1 and 21.4 (*E*-isomer); *IR* (KBr) 3065, 1539, 1446, 1335, 1117; *MS* (EI) 517 (M^+, 16). Anal. Calcd for $C_{33}H_{29}NOP_2$: C, 76.57; H, 5.65; N, 2.71. Found: C, 76.38; H, 5.63; N, 2.72.

***Z*- and *E*-4-diphenylphosphoryl-3-ethyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (2b).** Reaction of *Z*- and *E*-2-azido-2-butenyldiphenylphosphine oxide (5 mmol, 1.49 g) with 1.31 g (5 mmol) of triphenylphosphine (as described above) led to the isolation of 2.12 g (80 %) of compound **2b** as a white solid. Data for **2b**: mp 173-174 °C; *^{1}H-NMR* (300 MHz) 0.85 (t, 3H, $^3J_{HH}$ = 7.3 Hz, *E*-CH_3), 1.08 (t, 3H, $^3J_{HH}$ = 7.3 Hz, *Z*-CH_3), 1.87 (q, 2H, $^3J_{HH}$ = 7.3 Hz, *E*-CH_2), 2.52-2.56 (m, 2H, *Z*-CH_2), 4.25 (d, 1H, $^2J_{PH}$ = 20.9 Hz, *Z*-CH), 4.88 (dd, $^2J_{PH}$ = 22.1 Hz, $^4J_{PH}$ = 10.5 Hz, *E*-CH), 7.18-7.96 (m, 25H, arom); *^{13}C-NMR* (75 MHz) 7.4 and 12.8 (*E*- and *Z*-CH_3), 32.5 (dd, $^3J_{PC}$ = 4.5 Hz, $^3J_{PC}$ = 22.2 Hz, *Z*-CH_2), 33.5 (dd, $^3J_{PC}$ = 9.1 Hz, $^3J_{PC}$ = 13.6 Hz, *E*-CH_2), 91.1 (dd, $^1J_{PC}$ = 119.4 Hz, $^3J_{PC}$ = 24.7 Hz, *E*-CH), 91.5 (dd, $^1J_{PC}$ = 119.4 Hz, $^3J_{PC}$ = 13.4 Hz, *Z*-CH), 127.6-138.5 (C-arom), 170.4 and 174.2 (C-N); *^{31}P-NMR* (150 MHz) 1.2 and 22.4 (*Z*-isomer), 8.8 and 23.4 (*E*-isomer); *IR* (KBr) 3056, 1531, 1437, 1344, 1115; *MS* (CI) 532 (M^++1, 100). Anal. Calcd for $C_{34}H_{31}NOP_2$: C, 76.81; H, 5.88; N, 2.64. Found: C, 76.59; H, 5.86; N, 2.65.

***Z*- and *E*-1,3-dimethyl-1,1-diphenyl-4-diphenylphosphoryl-2-aza-1λ^5-phosphabuta-1,3-diene (2c).** Reaction of *E*-2-azido-1-propenyldiphenylphosphine oxide (5 mmol, 1.42 g) with 1.00 g (5 mmol) of methyldiphenylphosphine (as described above) led to the isolation of 2.23 g (98 %) of compound **2c** as a white solid. Data for **2c**: mp 139-140 °C; *^{1}H-NMR* (300 MHz) 1.73 (s, 3H, *E*-CH_3), 1.79 (d, 3H, $^2J_{PH}$ = 12.9 Hz, *E*-CH_3), 2.02 (d, 3H, $^2J_{PH}$ = 12.6 Hz, *Z*-CH_3), 2.04 (s, 3H, *Z*-CH_3), 4.18 (d, 1H, $^2J_{PH}$ = 20.1 Hz, *Z*-CH), 4.76 (dd, 1H, $^2J_{PH}$ = 23.1 Hz, $^4J_{PH}$ = 9.9 Hz, *E*-CH), 7.15-7.88 (m, 20H, arom); *^{13}C-NMR* (75 MHz) 14.3 (d, $^1J_{PC}$ = 76.5 Hz, *Z*-CH_3), 15.8 (d, $^1J_{PC}$ = 64.5 Hz, *E*-CH_3), 26.4 (dd, $^3J_{PC}$ = 4.0 Hz, $^3J_{PC}$ = 23.2 Hz, *Z*-CH_3), 27.4 (dd, $^3J_{PC}$ = 9.6 Hz, $^3J_{PC}$ = 15.1 Hz, *E*-CH_3), 91.7 (dd, $^1J_{PC}$ = 119.4 Hz, $^3J_{PC}$ = 16.6 Hz, *Z*-CH), 93.7 (dd, $^1J_{PC}$ = 117.8 Hz, $^3J_{PC}$ = 24.7 Hz, *E*-CH), 124.7-138.0 (C-arom), 165.2 and 169.3 (C-N); *^{31}P-NMR* (150 MHz) 1.0 and 21.5 (*E*-isomer), 9.5 and 21.6 (*Z*-isomer); *IR* (KBr) 3052, 1532, 1440, 1335, 1177, 1117; *MS* (EI) 455 (M^+, 14). Anal. Calcd for $C_{28}H_{27}NOP_2$: C, 73.82; H, 5.98; N, 3.08. Found: C, 73.61; H, 6.00; N, 3.06.

General Procedure for the Addition of Carbonyl Compounds 3 to *N*-Vinylic λ^5-Phosphazenes derived from triphenylphosphine 2a and 2b. A solution of carbonyl compound **3** (5mmol) in anhydrous $CHCl_3$ (10 mL) was added dropwise to a solution of *N*-vinylic λ^5-phosphazene **2a** or **2b** (5 mmol) in anhydrous $CHCl_3$ (15 mL) under N_2, and the mixture

was stirred at room temperature until TLC indicated the disappearance of the phosphazene. The mixture was concentrated and the crude product was purified by recrystallization or by flash-chromatography.

3-[2,2-bis(ethoxycarbonyl)-2-hidroxyethyl]-4-diphenylphosphoryl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4aa). Reaction of 2.59 g (5 mmol) of phosphazene **2a** with 0.87 g (5 mmol) of ethyl ketomalonate (as described above in general procedure) for 0.5 h afford a solid which was recrystallized (hexane / CH_2Cl_2) to give 2.42 g (70 %) of compound **4aa** as a white solid. Data for **4aa**: mp 162-163 °C; *^{1}H-NMR* (300 MHz) 1.14 (t, 6H, $^3J_{HH}$ = 7.1 Hz, CH_3), 3.44 (d, 2H, $^4J_{PH}$ = 3.8 Hz, CH_2), 3.95-4.09 (m, 4H, CH_2), 4.27 (d, 1H, $^2J_{PH}$ = 19.6 Hz, CH), 7.20-7.76 (m, 25H, arom), 7.96 (s, 1H, OH); *^{13}C-NMR* (75 MHz) 14.0 (CH_3), 42.8 (d, $^3J_{PC}$ = 21.0 Hz, CH_2), 61.2 (CH_2), 78.8 (C), 94.1 (dd, $^1J_{PC}$ = 116.3 Hz, $^3J_{PC}$ = 13.5 Hz, CH), 126.8-137.3 (C-arom), 166.2 (d, $^2J_{PC}$ = 6.5 Hz, C-N), 170.4 (C=O); *^{31}P-NMR* (150 MHz) 12.7 (PPh_3), 24.9 ($POPh_2$); *IR* (KBr) 3448, 3053, 2975, 1741, 1540, 1439, 1353, 1117; *MS* (EI) 691 (M^+, 4). Anal. Calcd for $C_{40}H_{39}NO_6P_2$: C, 69.44; H, 5.69; N, 2.03. Found: C, 69.28; H, 5.71; N, 2.04.

3-[2-cyano-2-hidroxy-2-methylethyl]-4-diphenylphosphoryl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4ab). Reaction of 2.59 g (5 mmol) of phosphazene **2a** with 0.35 g (5 mmol) of pyruvonitrile (as described above in general procedure) for 3 h afford an oil which was purified by flash-chromatography on silica gel (hexane / diethyl ether, 1 / 2)) and recrystallized (hexane / CH_2Cl_2) to give 2.11 g (72 %) of compound **4ab** as a white solid. Data for **4ab**: mp 153-154 °C; *^{1}H-NMR* (300 MHz) 1.52 (s, 3H, CH_3), 2.74 (d, 1H, $^2J_{HH}$ = 15.2 Hz, CH_2), 3.52 (dd, 1H, $^2J_{HH}$ = 15.2 Hz, $^4J_{PH}$ = 6.6 Hz, CH_2), 4.34 (d, 1H, $^2J_{PH}$ = 18.5 Hz, CH), 7.19-7.76 (m, 25H, arom), 8.43 (s, 1H, OH); *^{13}C-NMR* (75 MHz) 28.4 (CH_3), 45.8 (d, $^3J_{PC}$ = 18.9 Hz, CH_2), 68.1 (C), 95.3 (dd, $^1J_{PC}$ = 115.2 Hz, $^3J_{PC}$ = 12.4 Hz, CH), 123.0 (CN), 126.1-135.5 (C- arom), 165.0 (d, $^2J_{PC}$ = 6.7 Hz, C-N); *^{31}P-NMR* (150 MHz) 15.7 (PPh_3), 23.5 ($POPh_2$); *IR* (KBr) 3425, 3059, 1547, 1440, 1336, 1240, 1179, 1121; *MS* (EI) 559 (M^+- HCN, 6). Anal. Calcd for $C_{36}H_{32}N_2O_2P_2$: C, 73.70; H, 5.50; N, 4.78. Found: C, 73.88; H, 5.51; N, 4.79.

3-[2,2-bis(ethoxycarbonyl)-2-hidroxy-1-methylethyl]-4-diphenylphosphoryl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4ba). Reaction of 2.66 g (5 mmol) of phosphazene **2b** with 0.87 g (5 mmol) of ethyl ketomalonate (as described above in general procedure) for 1 h afford an oil which was purified by flash-chromatography on silica gel (diethyl ether) to give 2.60 g (75 %) of compound **4ba** as a white solid. Data for **4ba**: mp 163-164 °C; *^{1}H-NMR* (300 MHz) 1.03 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3), 1.20 (t, 3H, $^3J_{HH}$ = 7.0 Hz, CH_3), 1.30 (d, 3H, $^3J_{HH}$ = 6.8 Hz, CH_3), 3.74-3.81 (m, 1H, CH), 4.05-4.29 (m, 5H, CH_2 and CH), 7.17-7.71 (m, 25H, arom), 7.91 (s, 1H, OH); *^{13}C-NMR* (75 MHz) 13.9 (CH_3), 13.9 (CH_3), 14.1 (CH_3), 42.4 (d, $^3J_{PC}$ = 20.2 Hz, CH), 61.2 (CH_2), 61.3 (CH_2), 82.4 (C), 93.4 (dd, $^1J_{PC}$ = 117.2 Hz, $^3J_{PC}$ = 13.9 Hz, CH), 126.5-138.1 (C-arom), 168.8 (d, $^2J_{PC}$ = 6.6 Hz, C-N), 170.7 (C=O); *^{31}P-NMR* (150 MHz) 15.1 (PPh_3), 21.1 ($POPh_2$); *IR* (KBr) 3437, 3055, 2987, 1733, 1548, 1441, 1230, 1117; *MS* (EI) 531 (M^+- $C_7H_{10}O_5$, 6). Anal. Calcd for $C_{41}H_{41}NO_6P_2$: C, 69.76; H, 5.86; N, 1.99. Found: C, 69.91; H, 5.88; N, 2.00.

General procedure for the hydrolysis of compound **4aa**. Synthesis of **ethyl-4-amine-5-diphenylphosphoryl-2-ethoxycarbonyl-2-hidroxy-4-pentenoate (5).** A solution of compound **4aa** 1.38 g (2 mmol) in $CHCl_3$ was refluxed for 24 h with silica gel (SiO_2) and water. The mixture was filtered, washed with water and extracted with CH_2Cl_2. The conbined organic layers were dried over $MgSO_4$ and filtered. The mixture was concentrated and the crude product was purified by flash-chromatography on silica gel (diethyl ether) to give 0.67 g (78 %) of compound **5** as a white solid. Data for **5**: mp 143-144 °C; *^{1}H-NMR* (300 MHz) 1.18 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3), 1.35 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3), 2.05 (s, 1H, NH_2), 3.26 (d, 1H, $^2J_{HH}$ = 18.3 Hz, CH_2), 3.64 (d, 1H, $^2J_{HH}$ = 18.3 Hz, CH_2), 4.20 (q, 2H, $^3J_{HH}$ = 7.1 Hz, CH_2), 4.38 (q, 2H, $^3J_{HH}$ = 7.1 Hz, CH_2), 5.01 (s, 1H, NH_2), 6.04 (d, 1H, $^2J_{PH}$ = 21.1 Hz, CH), 7.26-7.77 (m, 10H, arom); *^{13}C-NMR* (75 MHz) 13.9 (CH_3), 14.0 (CH_3), 42.9 (CH_2), 62.5 (CH_2), 67.1 (CH_2), 80.8 (C), 102.9 (d, $^1J_{PC}$ = 113.1 Hz, CH), 128.4-133.4 (C-arom), 167.7 (d, $^2J_{PC}$ = 9.0 Hz, C-N), 170.9 (C=O), 179.2 (C=O); *^{31}P-NMR* (150 MHz) 23.3; *IR* (KBr) 3204, 3000, 1769, 1598, 1328, 1170; *MS* (EI) 413 (M^+-H_2O, 1). Anal. Calcd for $C_{22}H_{26}NO_6P$: C, 61.23; H, 6.08; N, 3.25. Found: C, 61.07; H, 6.09; N, 3.26.

Ethyl-5-diphenylphosphoryl-2-hidroxy-4-oxo pentanoate (6). Reaction of 2.59 g (5 mmol) of phosphazene **2a** with 0.51 g (5 mmol) of freshly distilled ethyl glyoxalate for 5 h afford an oil which was purified by flash-chromatography on silica gel (diethyl ether) to give 1.53 g (85 %) of compound **6** as a yelow oil. Data for **6**: R_f = 0.16 (ethyl acetate); *^{1}H-NMR* (300 MHz) 1.13 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3), 2.62 (s, 1H, OH), 3.10 (d, 2H, $^3J_{HH}$ = 5.5 Hz, CH_2), 3.64 (d, 2H, $^2J_{PH}$ = 14.7 Hz, CH_2), 4.08 (q, 2H, $^3J_{HH}$ = 7.1 Hz, CH_2), 4.40 (t, 1H, $^3J_{HH}$ = 5.5 Hz, CH), 7.26-7.73 (m, 10H, arom); *^{13}C-NMR* (75 MHz) 14.0 (CH_3), 47.0 (d, $^1J_{PC}$ = 57.4 Hz, CH_2), 48.9 (CH_2), 61.2 (CH_2), 67.0 (CH), 127.9-133.1 (C-arom), 173.3 (C=O), 200.4 (C=O); *^{31}P-NMR* (150 MHz) 27.5; *IR* (film) 3272, 3058, 2980, 1738, 1716, 1435, 1184, 1121. *MS* (EI) 360 (M^+, 3). Anal. Calcd for $C_{19}H_{21}O_5P$: C, 63.31; H, 5.88. Found: C, 63.18; H, 5.86.

3-(1-diphenylphosphorylmethyl)-4-ethoxycarbonyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (8). Reaction of 2.59 g (5 mmol) of phosphazene **2a** with 0.49 g (5 mmol) of ethyl cyanoformate for 6 h afford an oil which was purified by crystallization (ethyl acetate) to give 2.23 g (76 %) of compound **8** as a white solid. Data for **8**: mp 182-183 °C; *^{1}H-NMR* (300 MHz) 1.12 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3), 3.96 (q, 2H, $^3J_{HH}$ = 7.1 Hz, CH_2), 4.43 (s, 1H, CH), 4.46 (dd, 2H, $^2J_{PH}$ = 13.8 Hz, $^4J_{PH}$ = 4.1 Hz, CH_2), 7.26-7.94 (m, 25H, arom); *^{13}C-NMR* (75 MHz) 14.6 (CH_3), 39.5 (dd, $^1J_{PC}$ = 67.9 Hz, $^3J_{PC}$ = 24.7 Hz, CH_2), 58.3 (CH_2), 97.0 (d, $^3J_{PC}$ = 12.1 Hz, CH), 127.3-135.4 (C-arom), 162.8 (C-N), 168.9 (C=O); *^{31}P-NMR* (150 MHz) 7.0 (PPh_3), 29.8 ($POPh_2$); *IR* (KBr) 3049, 1663, 1545, 1143, 1115; *MS* (EI) 589 (M^+, 19). Anal. Calcd for $C_{36}H_{33}NO_3P_2$: C, 73.32; H, 5.65; N, 2.38. Found: C, 73.52; H, 5.63; N, 2.39.

Ethyl-3-amine-4-diphenylphosphoryl-2-butenoate (9). Reaction of 1.18 g (2 mmol) of compound **8** with silica gel and water (as described above in general procedure) for 24 h afford an oil wich was purified by flash-chromatography on silica gel (diethyl ether) to give 0.46 (70 %) of compound **9** as a white solid. Data for **9**: mp 223-224 °C; *^{1}H-NMR* (300 MHz) 1.21 (t, 3H,

$^3J_{HH}$ = 7.1 Hz, CH_3), 1.79 (s, 1H, NH), 3.12 (d, 2H, $^2J_{PH}$ = 13.1 Hz, CH_2), 4.05 (q, 2H, $^3J_{HH}$ = 7.1 Hz, CH_2), 4.39 (s, 1H, CH), 6.25 (s, 1H, NH), 7.49-7.75 (m, 10H, arom); *^{13}C-NMR* (75 MHz) 14.6 (CH_3), 37.2 (d, $^1J_{PC}$ = 64.5 Hz, CH_2), 58.7 (CH_2), 86.4 (CH), 128.7-132.4 (C-arom), 155.0 (C-N), 169.6 (C=O); *^{31}P-NMR* (150 MHz) 31.5; *IR* (KBr) 3396, 3298, 3211, 1666, 1621, 1585, 1161; *MS* (EI) 329 (M^+, 18). Anal. Calcd for $C_{18}H_{20}NO_3P$: C, 65.63; H, 6.12; N, 4.26. Found: C, 65.46; H, 6.10; N, 4.27.

Aza-Wittig reaction of *N*-vinylic phosphazenes **2c** with ethyl glyoxalate. Synthesis of **4-diphenylphosphoryl-1-ethoxycarbonyl-3-methyl-2-azabuta-1,3-diene (10).** A solution of 0.51 g (5 mmol) of freshly distilled ethyl glyoxalate in anhydrous $CHCl_3$ (10 mL) was added dropwise to a solution of 2.28 g (5 mmol) of *N*-vinylic λ^5-phosphazene **2c** in anhydrous $CHCl_3$ (15 mL) under N_2, and the mixture was stirred at room for 30 min. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used for the following reactions. Data for **10**: *^{1}H-NMR* (300 MHz) of crude reaction mixture (**10** + Ph_2MePO) 1.35 (t, 3H, $^3J_{HH}$ = 7.2 Hz, CH_3), 2.00 (d, 3H, $^2J_{PH}$ = 13.1 Hz, CH_3), 2.29 (s, 3H, CH_3), 4.35 (q, 2H, $^3J_{HH}$ = 7.2 Hz, CH_2), 5.65 (d, 1H, $^2J_{PH}$ = 20.1 Hz, CH), 7.29-7.77 (m, 21H, arom); *^{13}C-NMR* (75 MHz) of crude reaction mixture (**10** + Ph_2MePO) 13.7 (CH_3), 16.2 (d, $^1J_{PC}$ = 73.5 Hz, CH_3), 17.5 (CH_3), 62.0 (CH_2), 108.0 (d, $^1J_{PC}$ = 104.8 Hz, CH), 128.2-134.3 (C-arom), 149.9 (CH), 162.2 (C-N), 165.0 (C=O); *^{31}P-NMR* (150 MHz) of crude reaction mixture (**10** + Ph_2MePO) 19.8 (compound **10**), 28.7 (Ph_2MePO).

Synthesis of **Ethyl 6-methyl-3,4-trimethylene-2-pyridinecarboxylate (13).** A solution of 0.51 g (5 mmol) of freshly distilled ethyl glyoxalate in anhydrous $CHCl_3$ (10 mL) was added dropwise to a solution of 0.35 g (5 mmol) of phosphazene **2c** in anhydrous $CHCl_3$ (15 mL) under N_2, and the mixture was stirred for 30 min. A solution of 0.77 g (5 mmol) of freshly distilled morpholinocyclopentene enamine **11** in $CHCl_3$ (5 mL) was then added and the mixture was stirred and refluxed for 48h. The mixture was concentrated and the crude product was purified by flash chromatography (hexane /diethyl ether, 1 / 2) to give 0.81 g (79 %) of compound **12a** as a yelow oil. Data for **12a**: R_f = 0.14 (ethyl acetate);*^{1}H-NMR* (300 MHz) 1.34 (t, 3H, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.99 (dt, $^3J_{HH}$ = 7.3 Hz, $^3J_{HH}$ = 7.3 Hz, CH_2), 2.50 (s, 3H, CH_3), 2.82 (t, $^3J_{HH}$ = 7.3 Hz, CH_2), 3.16 (t, $^3J_{HH}$ = 7.3 Hz, CH_2), 4.34 (q, 2H, $^3J_{HH}$ = 7.3 Hz, CH_2), 7.11 (s, 1H, CH); *^{13}C-NMR* (75 MHz) 14.1 (CH_3), 24.0 (CH_3), 24.3 (CH_2), 32.1 (CH_2), 32.2 (CH_2), 61.1 (OCH_2), 122.6 (CH), 139.9 and 142.7 (C-arom), 155.6 (C=N), 156.0 (C-arom), 173.4 (C=O); *IR* (KBr) 2977, 1718, 1608, 1382, 1223, 1118; *MS* (EI) 205 (M^+, 100). Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.21; H, 7.37; N, 6.83. Found: C, 70.36; H, 7.39; N, 6.81.

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