ARTICLE

OBC
www.rsc.org/obc

Reaction of acetylenic esters and *N*-functionalized phosphazenes. 1,2- *versus* 1,4-addition of *N*-vinylic phosphazenes

Francisco Palacios,* Concepción Alonso, Jaione Pagalday, Ana María Ochoa de Retana and Gloria Rubiales

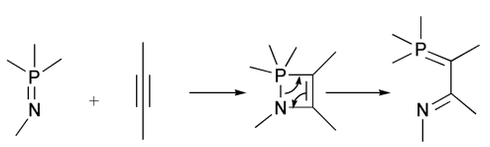
Departamento de Química Orgánica I, Facultad de Farmacia, Universidad del País Vasco, Apartado 450, 01080, Spain. E-mail: qoppagaf@vf.ehu.es; Fax: (+34)-945-013049.

Received 2nd January 2003, Accepted 29th January 2003
First published as an Advance Article on the web 28th February 2003

Reaction of phosphazenes derived from aminophosphonates with acetylenic esters leads to conjugated phosphorus ylides. The formation of these stabilized ylides is explained through a [2+2] cycloaddition reaction of the P=N linkage of the phosphazene (1,2-addition) and the triple bond of the acetylenic ester followed by ring opening of the azaphosphete intermediate. However, in the case of *N*-vinylic phosphazenes, the phosphazenes derived from triphenyl- and trimethyl-phosphine react as enamines (1,4-addition) with diacetylenic esters, whereas in phosphazenes derived from trimethylphosphine a 1,2-addition of ethyl propiolate to the P=N linkage of the phosphazene is produced.

Introduction

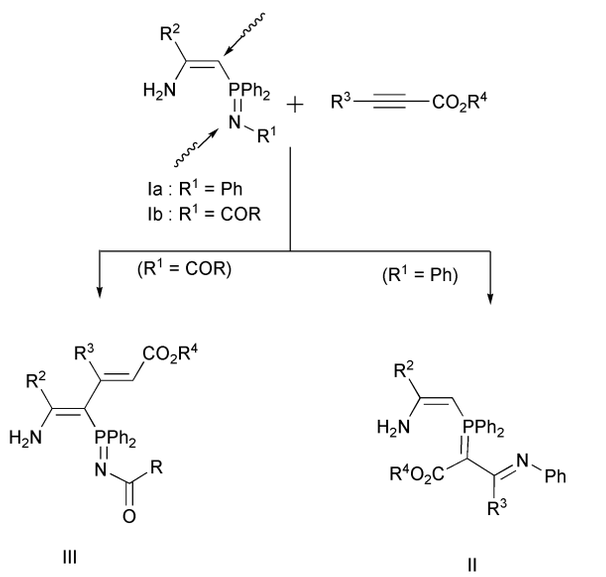
Phosphazenes[1,2] represent an important class of compounds and have attracted a great deal of attention in recent years because of their broad range of uses in the construction of acyclic compounds[3] and in the preparation of heterocycles.[4] Likewise, it is well known that these substrates are a useful tool for the construction of carbon–nitrogen double bonds (Aza–Wittig reaction)[1,5] but it is less known that phosphazenes react with acetylenic derivatives such as propargylic phosphonium salts[6] or acetylenedicarboxylic acid esters[7] with formation of conjugated phosphorus ylides through a formal insertion of the triple bond into the phosphazene linkage (Scheme 1).



Scheme 1 General reaction of phosphazenes with acetylenic derivatives.

In this context, we have previously studied the [2 + 2] cycloaddition reaction of simple *N*-aryl-[8a,b] and *N*-ethoxycarbonyl-phosphazenes[8c] derived from alkyldiphenylphosphines (1,2-addition through the phosphazene linkage) with acetylenic esters (diethyl acetylenedicarboxylate esters and ethyl propiolate). However, when *P*-functionalized phosphazenes such as β-enamino phosphazenes **I** (Scheme 2) were used, the presence of a new functional group offers new reactive centres towards the acetylenic triple bond and the reaction may have taken place either through the phosphazene linkage or through the enamine moiety, depending on the reactivity of the phosphazene. *N*-Aryl β-enamino phosphazenes **Ia** (R^1 = Ph) reacted with acetylenic esters through the phosphazene group to give conjugated phosphorus ylides **II**.[9a] However, when the reactivity of the phosphazene group decreased by the introduction of electron-withdrawing substituent in the nitrogen atom such as *N*-benzoyl-[9b] **Ib** (R^1 = COPh) or *N*-ethoxycarbonyl β-enamino phosphazenes[9c] **Ib** (R^1 = COOR) the reaction with acetylenic esters took place through the enamine moiety to give functionalized enamines **III** (Scheme 2), without altering the phosphazene group.

Following on from our previous studies on the reactivity and the synthetic utility of phosphazenes, here we aim to explore



Scheme 2 General reaction of β-enamino phosphazenes with acetylenic esters.

the reaction of phosphazenes derived from aminophosphonates with acetylenic esters. α-Aminophosphonates are very interesting compounds as they can be considered as surrogates for α-amino acids,[10a] and have been used as haptens in the generation of catalytic antibodies[10b] and as enzyme inhibitors.[10c,d] Moreover, the reaction of *N*-vinylic phosphazenes with acetylenic esters is studied in order to test whether the introduction at the nitrogen atom of a new functional group (a double bond) conjugated with the phosphazene group could drive the process either through the phosphazene linkage (1,2-addition) or through the vinyl carbon atom (1,4-addition).

Results and discussion

Reaction of *N*-phosphorylalkyl phosphazenes 1 and 7 with acetylenic esters 2

Phosphazenes **1**, derived from aminoalkylphosphonate, are very unstable compounds.[1e,11] For this reason, the phosphazene was generated *in situ* by Staudinger reaction of diethyl azidomethylphosphonate[12] with triphenylphosphine, and the crude reaction mixture, without purification, was treated with

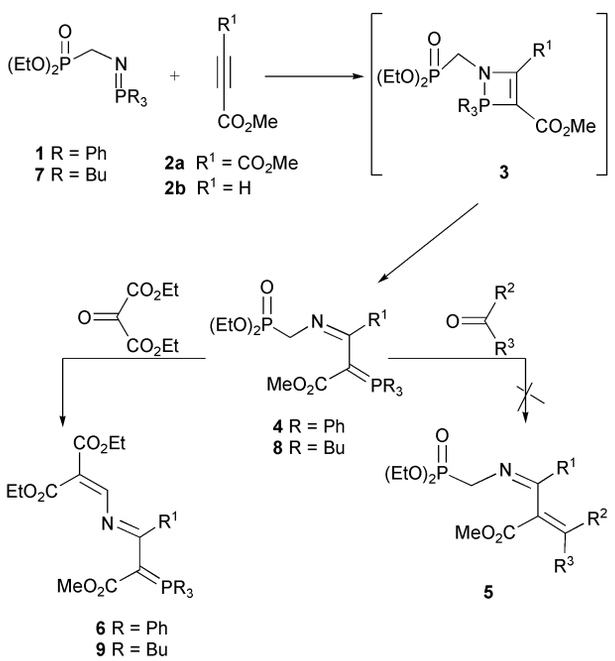
DOI: 10.1039/b212693a

Table 1 Conjugated phosphorus ylides obtained **4**, **6** and **9**

Entry	Compound	R	R^1	Yield (%)
1	**4a**	Phenyl	COOMe	88[a]
2	**4b**	Phenyl	H	76[b]
3	**6**	Phenyl	COOMe	65[b]
4	**9**	Butyl	COOMe	72[c]

[a] Yield after purification by recrystallization with hexane–dichloromethane. [b] Yield after purification by recrystallization with diethyl ether. [c] Yield after purification by recrystallization with hexane.

dimethyl acetylenedicarboxylate **2a** (R^1=CO_2Me) in THF at room temperature to give conjugated ylide **4a**, derived from aminophosphonates, in good yield (Scheme 3, Table 1, entry 1). The presence of phosphazene **1** in the crude reaction mixture and the evolution of the process was monitored by ^{31}P-NMR spectroscopy.[13] Compound **4a** was characterized on the basis of its spectroscopic data. Thus, the ^{31}P NMR spectrum of compound **4a** showed absorptions at δ_P = 23.9 and 16.6 ppm for the phosphonate and the phosphorus ylide group, while the ^{1}H NMR showed a doublet for the methylene group (δ_H = 3.27 ppm; $^2J_{PH}$ = 16.1 Hz). ^{13}C NMR displayed doublets for the methylene group at δ_C = 47.9 ppm ($^1J_{PC}$ = 163.2 Hz) and for the carbon bonded to the phosphorus atom at δ_C = 57.5 ppm with a coupling constant $^1J_{PC}$= 119.4 Hz, and a double doublet for the imine carbon at δ_C = 164.1 ppm ($^2J_{PC}$ = 6.8 Hz, $^3J_{PC}$ = 20.4 Hz,). The formation of conjugated phosphorus ylide **4a**, derived from aminophosphonates, in a similar manner to simple phosphazenes,[8] could be explained through [2 + 2] cycloaddition of the phosphazene linkage of **1a** to the carbon–carbon triple bond of the acetylenic ester **2a** followed by an electrocyclic ring opening of the unstable four-membered phosphor heterocycle **3**. The reaction was not limited to acetylenic diester given that *N*-phosphorylalkyl phosphazene **1a** also reacted with monoester methyl propiolate **2b** (R^1 = H) to afford functionalized aldimine **4b** (R^1 = H) (Scheme 3, Table 1, entry 2).

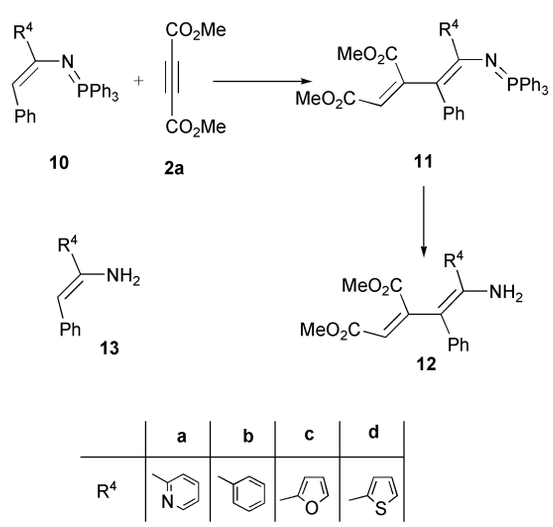


Scheme 3 Reaction of *N*-phosphorylalkyl phosphazenes **1** and **7** with acetylenic esters **2**.

These polyfunctionalized ylides **4** present two potential reactive centres capable of producing olefination reactions such as the phosphorus ylide group (Wittig reactions)[14] and the phosphonate group (Wadsworth–Emmons reaction).[15] Due possibly to the stabilized character of the phosphorus ylide moiety, they reacted neither with benzaldehyde nor with diethyl ketomalonate, even when heating the reagents to 70 °C, in order to obtain 1-azadiene **5** and the starting materials were recovered. However, a selective olefination reaction was performed with formation of conjugated ylide derived from triphenylphosphine (R = Ph) **6**, when compound **4a** was treated with diethyl ketomalonate in refluxing THF in the presence of a base such as sodium hydride (Scheme 3, Table 1, entry 3). Spectroscopic data were in agreement with the assigned structure **6**. Mass spectrometry of the compound showed the molecular ion peak (*m*/*z* 589, 4%), while in the ^{31}P NMR spectrum the phosphorus ylide group resonated at δ_P = 16.5 ppm and the ^{13}C-NMR spectrum of **6** showed very characteristic doublets at δ_C = 69.1 ppm ($^1J_{PC}$ = 111.3 Hz) and at δ_C = 165.8 ppm ($^2J_{PC}$ = 14.1 Hz) for the carbon directly bonded to the phosphorus atom and for the imine carbon. In order to explore the selective olefination reaction with ethyl ketomalonate through the stabilized phosphorus ylide, we thought that the substitution of triphenylphosphine for an aliphatic phosphine (tributylphosphine) could increase the reactivity of the stabilized phosphorus ylide **4**. Therefore, following the synthetic strategy used before, we needed the *N*-phosphorylmethyl phosphazene **7**, derived from tributylphosphine (R = Bu). Phosphazene **7** was generated *in situ* by Staudinger reaction of diethyl azidomethylphosphonate[12] with tributylphosphine, and the crude reaction mixture without purification was treated with dimethyl acetylenedicarboxylate **2a** (R^1 = CO_2CH_3) in THF at room temperature and with ethyl ketomalonate. However, 1-azadiene **5** (R^1 = R^2 = $CO_2C_2H_5$) was not obtained and conjugated phosphorus ylide **9** derived from tributylphosphine was obtained. (Scheme 3, Table 1, entry 4).

Reaction of *N*-vinylic phosphazenes 10, 16 with acetylenic esters 2

Continuing with our interest in the reactivity of phosphazenes with acetylenic esters, we explored the behaviour of *N*-vinylic phosphazenes, since an adjacent double bond in conjugation with the phosphazene moiety introduces the interesting problem of selectivity: *i.e.*, reaction at the nitrogen (1,2-addition) or at the γ-C-atom (1,4-addition). *N*-vinylic phosphazenes **10** were easily obtained by reaction of phosphorus ylides and nitriles,[5c] and the treatment of phosphazene **10a**, derived from triphenylphosphine (R^4 = 2-pyridyl), with dimethyl acetylenedicarboxylate **2a** in $HCCl_3$ at room temperature gave conjugated phosphazene **11a**, in good yield (Scheme 4, Table 2, entry 1). Compound **11a** was characterized on the basis of spectroscopic data. A ^{31}P NMR spectrum of compound **11a** showed



Scheme 4 Reaction of *N*-vinylic phosphazenes **10** with acetylenic esters.

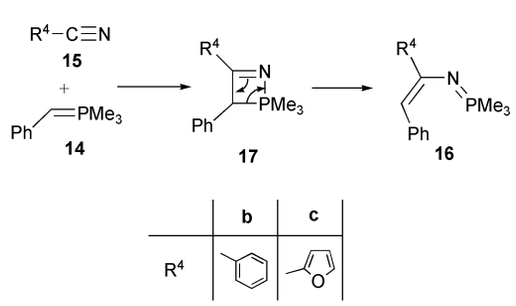
Table 2 Compounds **11**, **12**, **21**, **22** obtained

Entry	Compound	R^4	Yield (%)[a]
1	**11a**	2-Pyridyl	60
2	**11b**	Phenyl	93[b]
3	**11c**	2-Furyl	80[c]
4	**12b**	Phenyl	93[b] : 88[d]
5	**12c**	2-Furyl	80[c] : 79[d]
6	**12d**	2-Thienyl	54
7	**21**	2-Furyl	85
8	**22**	2-Furyl	94

[a] Yield after purification by flash chromatography. [b] Proportion **11a** : **12a**: 67 : 33. [c] Proportion **11c** : **12c**: 90 : 10. [d] Obtained from phosphazenes **16**.

absorption at δ_P = 7.52 ppm, while the ^{13}C NMR displayed singlets at δ_C = 147.5 ppm for the enamine carbon bonded to the nitrogen atom and at δ_C = 168.2 and 170.5 ppm for carboxylate esters. The *cis* configuration of the ester groups on the C5–C6 double bond is supported by NOE experiments. However, when the reaction was performed with phosphazenes **10b** (R^4 = Ph) and **10c** (R^4 = 2-furyl), not only conjugated phosphazenes **11b**,**c** but also primary enamines **12b**,**c**, as minor components (Scheme 4, Table 2, entries 2–5) were isolated. Mass spectrometry of **12a** (R^2 = Ph) showed the molecular ion peak (*m*/*z* 337, 100%) is in agreement with the structure of compounds **12**. However, in the case of phosphazene **10d** (R^4 = 2-thienyl) only primary enamine **12d** (Scheme 4, Table 2, entry 6) was obtained. The reaction cannot be extended to ethyl propiolate **2c** since a very complex mixture of products was obtained under similar reaction conditions. The formation of conjugated phosphazenes **11** could be explained by Michael addition of the γ-C-atom (1,4-addition) of phosphazenes **10** to the carbon–carbon triple bond of the acetylenic ester **2a** in a similar way to that observed by the conjugative addition of the γ-C-atom (1,4-addition) of *N*-vinylic phosphazenes to simple[5b,d] and unsaturated carbonyl compounds.[16] Hydrolysis of the phosphazene linkage could give primary enamines **12b**,**c** (Scheme 4, Table 2, entries 4, 5). Therefore, from a synthetic point of view, *N*-vinylic phosphazenes **10** can be considered as protected primary enamines and therefore as synthetic equivalents of primary enamines **13** when they reacted with acetylenic esters. It is noteworthy that primary enamines are very unstable unless conjugated with an electron-withdrawing group at the β-carbon atom.[17] For this reason, it is interesting to develop new synthetic strategies for the preparation of protected primary enamines without stabilizing electron-withdrawing groups.

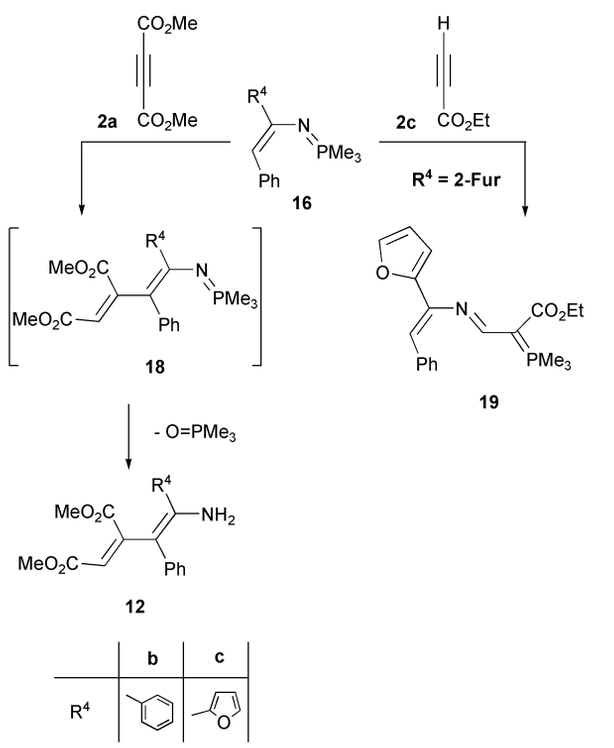
The influence of substituents on the phosphorus in phosphazenes can play an important role in their reactivity.[5b,5d,18] For this reason, we tried to prepare new *N*-vinylic phosphazenes derived from aliphatic phosphines, since a higher reactivity through the phosphazene linkage is expected. Reaction of the phosphorus ylide derived from trimethylphosphine **14** and nitrile **15b** (R^4 = Ph) and **15c** (R^4 = 2-furyl) led to *N*-vinylic phosphazenes **16b**,**c** (Scheme 5), whose formation can be explained by construction and ring opening of azaphosphete **17**, in a similar way to that reported for *N*-vinylic phosphazenes



Scheme 5 Preparation of *N*-vinylic phosphazenes **16b**,**c**.

10, derived from triphenylphosphine.[5c] Spectroscopic data were in agreement with the assigned structure **16**. The phosphorus ylide group for **16c** resonated in the ^{31}P NMR spectrum at δ_P = 9.56 ppm, while ^{1}H-NMR and the ^{13}C-NMR spectrum of **16c** showed very characteristic data for CH= at 6.10 ppm as a singlet and at 111.4 ppm respectively. These unstable phosphazenes **16b**,**c** were used without isolation for the following purposes.

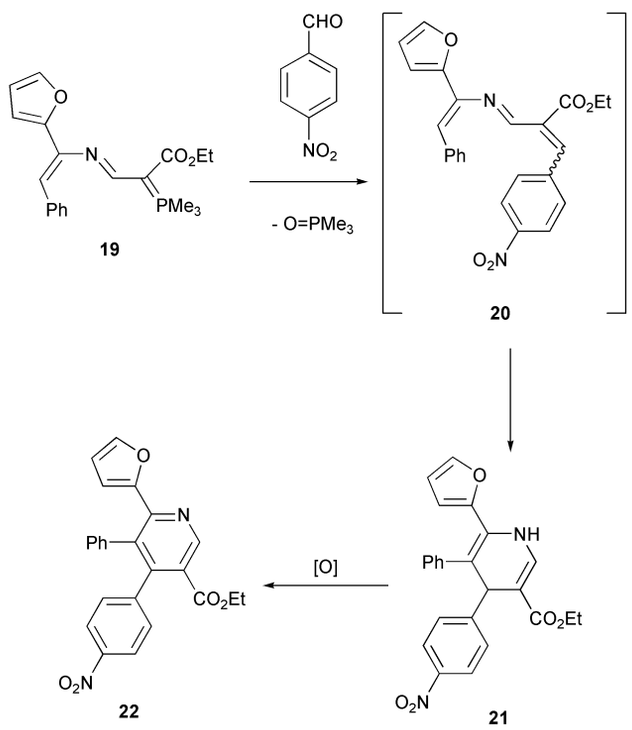
Reaction of these *N*-vinylic phosphazenes derived from trimethylphosphine **16b**,**c** with dimethyl acetylenedicarboxylate **2a** in $HCCl_3$at room temperature and even at low temperature (−78 °C) gave conjugated enamines **12b**,**c** (Scheme 6, Table 2, entries 4, 5). As before, the formation of conjugated enamines **12** could be explained by Michael addition of the γ-C-atom (1,4-addition) of phosphazenes **16** to the carbon–carbon triple bond of the acetylenic ester **2a** followed by hydrolysis of the unstable phosphazenes derived from trimethylphosphine **18**. However, selective reaction through the phosphazene linkage can be achieved when phosphazene **16c**, derived from trimethylphosphine, is reacted with monoacetylenic ester. Treatment of *N*-vinylic phosphazene **16c** with ethyl propiolate **2c** gave conjugate phosphorus ylide **19** in good yield (Scheme 6). This functionalized phosphorus ylide **19**, derived from trimethylphosphine, proved to be unstable during distillation or chromatography and therefore was not isolated in a pure form. However, this unstable phosphorus ylide **19** was characterized by its spectroscopic data. The phosphorus ylide group resonated in the ^{31}P NMR spectrum at δ_P = 9.29 ppm, while the ^{1}H-NMR spectrum of **19** showed a very characteristic doublet at 8.51 ppm with a coupling constant of 26.2 Hz corresponding to the iminic compound. The formation of conjugated phosphorus ylide **19** could be explained through [2 + 2] cycloaddition of the phosphazene linkage of **19** (1,2-addition) (Scheme 6).



Scheme 6 Reaction of *N*-vinylic phosphazenes **16** with acetylenic esters.

Finally, we tried to study whether the stabilized phosphorus ylide group **19**, derived from trimethylphosphine, could be used as an intermediate in the preparation of azatrienes **20**. Selective olefination reaction of compound **19** (Wittig reaction) was explored. However, treatment of conjugated phosphorus ylide

19 with *p*-nitrobenzaldehyde in refluxing toluene did not give azatriene **20**, but 1,4-dihydropyridine **21** was obtained instead (Scheme 7, Table 2, entry 7). The formation of this compound can be explained by electrocyclic ring closure of azatriene **20**. An oxidation reaction of 1,4-dihydropyridine **21** with *p*-benzoquinone led to the formation of pyridine **22** (Scheme 7, Table 2, entry 8). It is worth noting that 1,4-dihydropyridines are compounds with interesting therapeutic[19] and bioorganic[20] applications due to the fact that they can exhibit selective inhibitory activities against type-N calcium channels and are used as remedies for various diseases related to them.[21] Pyridine compounds derived from β-aminoacids are also useful heterocycles not only for their biological activity[22] but also because the pyridine nucleus is a structural unit appearing in many natural products.[23]



Scheme 7 Wittig reaction of ylide **19** with *p*-nitrobenzaldehyde.

In conclusion, the reaction of *N*-functionalized phosphazenes **1** and **7**, derived from aminophosphonates, with acetylenic esters takes place through the phosphazene linkage to give *N*-phosphorylmethyl imines **4**. However, in the case of *N*-vinylic phosphazenes, the presence of an olefinic group in conjugation with the phosphazene group opens new synthetic pathways depending on the substituents at the phosphorus atom. *N*-vinylic phosphazenes derived from triphenyl **10** or trimethyl phosphine **16** reacted like enamines (1,4-addition) with diacetylenic esters such as dimethyl acetylendicarboxylic ester to afford conjugated phosphazenes **11** and **18**. However, *N*-vinylic phosphazenes derived from trimethyl phosphine reacted through the phosphazene linkage (1,2-addition) with monoacetylenic esters such as ethyl propiolate giving the conjugated phosphorus ylide **19**. The selective olefination reactions of *N*-phosphorylalkylimines derived from triphenyl **4** or tributylphosphoranes **8** are produced through the phosphonate group (Wadsworth–Emmons reaction) with the formation of heterodienes containing the phosphorus ylide group **6**,**9**. Nevertheless, the selective olefination reaction of conjugated phosphorane derived from trimethylphosphines (Wittig reaction) led to the formation of heterocyclic compounds through azatrienes. Heterodienes,[24,25] 1,4-dihydropyridines,[19–21] pyridines[22,23] and functionalized phosphorus ylides[14] are important synthons in organic synthesis and in the preparation of biologically active compounds.

Experimental

General

Chemicals were purchased from Aldrich Chemical Company. Solvents for extraction and chromatography were technical grade. All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen. Analytical TLC was performed with Merck silica gel 60 F_{254} plates. Visualization was accomplished by UV light. Flash chromatography was carried out using Merck silica gel 60 (230–400 mesh ASTM). Melting points were determined with a Electrothermal IA9100 Digital Melting Point Apparatus and are uncorrected. ^{1}H (300 MHz), ^{13}C (75 MHz) and ^{31}P NMR (120 MHz) spectra were recorded on a Varian VXR 300 MHz spectrometer using $CDCl_3$ or CD_3OD solutions with TMS as an internal reference for ^{1}H and ^{13}C NMR spectra and phosphoric acid (85%) for ^{31}P NMR spectra. Chemical shifts (δ) are reported in ppm. Coupling constants (J) are reported in Hertz. Low-resolution mass spectra (MS) were obtained at 50–70 eV by electron impact (EIMS) on a Hewlett Packard 5971 or 5973 spectrometer and by chemical ionization (CI) on a Hewlett Packard 1100MSD. Data are reported in the form *m*/*z* (intensity relative to base = 100). Infrared spectra (IR) were taken on a Nicolet IRFT Magna 550 spectrometer, and were obtained as solids in KBr or as neat oils. Peaks are reported in cm^{-1}. Elemental analyses were performed in a LECO CHNS-932 apparatus. Diethyl azidomethylphosphonate was synthesized according to literature procedures.[12]

General procedure for the synthesis of conjugated phosphorus ylides 4

To a solution of triphenylphosphine (1.18 g, 4.5 mmol) in THF (10 ml) was added dropwise with stirring and with an ice-bath a solution of diethyl azidomethylphosphonate. Phosphazene **1** was generated *in situ* and the presence of **1** in the crude reaction mixture was monitored by ^{31}P NMR spectroscopy.[13] To the crude reaction was added dimethyl acetylenedicarboxylate **2a** (4.5 mmol) or methyl propiolate **2b** (4. 5 mmol) and the mixture was stirred at room temperature for 10 h. The crude product was concentrated under vacuum and the residual product was crystallized with diethyl ether to afford the ylides **4**

1,1,1-Triphenyl-2,3-dimethoxycarbonyl-4-diethoxyphosphoryl-methyl-1,4-phosphazabutadiene 4a

The general procedure was followed using dimethyl acetylenedicarboxylate **2a** (0.64 g, 4.5 mmol) Recrystallization with hexane–dichloromethane (10 : 1) gave **4a** (2.25 g, 88%) as a yellow solid; mp 152–153 °C (Found: C, 61.30; H, 5.87; N, 2.49. $C_{29}H_{33}NO_7P_2$ requires C, 61.16; H, 5.84; N, 2.46%); ν_{max}(KBr)/cm^{-1} 1727 (C=O), 1238 (P=O); δ_H(250 MHz; $CDCl_3$; Me_4Si) 1.01 (6 H, m, CH_3), 3.18 (3 H, s, OCH_3), 3.27 (2 H, d, $^2J_{PH}$ = 16.1, NCH_2), 3.65 (4 H, m, OCH_2), 3.88 (3 H, s, OCH_3), 7.43–7.78 (15 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) 16.1, 16.2, 47.9 (d, $^1J_{PC}$ = 163.2), 51.6, 57.5 (d, $^1J_{PC}$ = 119.4), 61.4, 61.5, 125.9 (d, $^1J_{PC}$ = 94.2), 128.2–133.9 (m), 164.1 (dd, $^3J_{PC}$ = 20.4, $^2J_{PC}$ = 6.8), 166.5 (d, $^3J_{PC}$ = 13.1), 168.3 (d, $^2J_{PC}$ = 14.6); δ_P(120 MHz; $CDCl_3$) 16.6 (PPh_3), 23.9 (P=O); *m*/*z* (EI) 570 (M^+ + 1, 48%).

1,1,1-Triphenyl-2-methoxycarbonyl-4-diethoxyphosphoryl-methyl-1,4-phosphazabutadiene 4b

The general procedure was followed using methyl propiolate **2b** (0.38 g, 4.5 mmol). Recrystallization with hexane–dichloromethane (10 : 1) gave **4b** (1.75 g, 76%) as a yellow solid; mp 97–98 °C (Found: C, 63.39; H, 6.10; N, 2.72. $C_{27}H_{31}NO_5P_2$ requires C, 63.40; H, 6.11; N, 2.74%), ν_{max}(KBr)/cm^{-1} 1690(C=O); δ_H(250 MHz; $CDCl_3$; Me_4Si) 1.05 (6 H, m, CH_3), 3.37 (3 H, s, OCH_3), 3.27 (2 H, d, $^2J_{PH}$ = 15.1, NCH_2), 3.72 (4 H, m, OCH_2),

7.41–7.70 (15 H, m, CH_{arom}), 8.45(1H, dd, $^3J_{PH}$ = 25.1, $^4J_{PH}$ = 3.2, CH=); δ_C(75 MHz; $CDCl_3$) 16.2, 16.3, 49.8, 55.4 (d, $^1J_{PC}$ = 117.9), 56.5 (d, $^1J_{PC}$ = 154.5), 61.4, 61.5, 125.1–133.9, 165.5 (d, $^2J_{PC}$ = 18.2), 169.3 (d, $^2J_{PC}$ = 15.4); δ_P(120 MHz; $CDCl_3$) 18.2 (PPh_3), 23.7 (P=O); *m/z* (EI) 512 (M^+ + 1, 35%).

Synthesis of 1-triphenyl-2,3-dimethoxycarbonyl-6,6-diethoxycarbonyl-1,4-phosphaza-1,3,5-hexatriene 6

To a solution of HNa (0.14 g, 6 mmol) in THF (10 ml) to 0 °C was added dropwise with stirring a solution of ylide **4a** (1.71 g, 3 mmol) in THF (10 ml). The mixture was stirred to 0 °C for 1 hour, afterwards was added a solution of diethyl ketomalonate (0.52 g, 3 mmol) in THF (2.5 ml) and was stirred at reflux for 50 hours. The crude was concentrated under vacuum and the residual product was washed with water, extracted with dichloromethane and evaporated under vacuum. The residue was purified by recrystallization with diethyl ether to afford the ylide **6** as a yellow solid (1.27 g, 72%); mp 150–151 °C (Found: C, 65.25; H, 5.48; N, 2.40. $C_{32}H_{32}NO_8P$ requires C, 65.20; H, 5.47; N, 2.38%); ν_{max}(KBr)/cm^{-1} 1733 (C=O), 1728 (C=O), 1712 (C=O), 1680 (C=O); δ_H(250 MHz; $CDCl_3$; Me_4Si) 0.88 (3 H, t,$^3J_{HH}$ = 7.2, CH_3), 1.08 (3 H, t,$^3J_{HH}$ = 7.2, CH_3), 3.16 (3 H, s, OCH_3), 3.33 (2 H, q, $^3J_{HH}$ = 7.2, OCH_2), 3.87 (3 H, s, OCH_3), 3.97 (2H, q, $^3J_{HH}$ = 7.2, OCH_2), 7.38–7.62 (16 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) 13.4, 13.6, 50.0, 51.5, 59.2, 59.4, 69.1 (d, $^1J_{PC}$ = 111.3), 113.9, 124.0 (d, $^1J_{PC}$ = 94.2), 128.1–133.1, 148.7, 164.9, 165.0, 165.8 (d, $^2J_{PC}$ = 14.1), 166.6 (d, $^3J_{PC}$ = 13.6), 167.9 (d, $^2J_{PC}$ = 5.5); δ_P(120 MHz; $CDCl_3$) 16.5; *m/z* (EI) 589 (M^+, 4%).

Synthesis of 1-tributyl-2,3-dimethoxycarbonyl-6,6-diethoxycarbonyl-1,4-phosphaza-1,3,5-hexatriene 9

To a solution of tributylphosphine (0.91 g, 4.5 mmol) in toluene (10 ml) was added dropwise with stirring and with an ice-bath a solution of diethyl azidomethylphosphonate (0.97 g, 5 mmol). The mixture was stirred at room temperature for 1 hour. To the crude reaction was added dimethyl acetylenedicarboxylate **2a** (0.64 g, 4.5 mmol) and the mixture was stirred at room temperature for 14 h, afterwards was added diethyl ketomalonate (0.52 g, 3 mmol) and was stirred at reflux for 47 hours. The crude was concentrated under vacuum and the residual product was recrystallized with hexane to afford the ylide **9** as a yellow solid (1.55 g, 65%); mp 82–83 °C (Found: C, 58.92; H, 8.35; N, 2.67. $C_{26}H_{44}NO_8P$ requires C, 58.98; H, 8.32; N, 2.65%), ν_{max}(KBr)/cm^{-1} 1736 (C=O), 1710 (C=O), 1657 (C=O); δ_H(250 MHz; $CDCl_3$; Me_4Si) 0.92 (9 H, t,$^3J_{HH}$ = 6.7, CH_3), 1.24 (3 H, t,$^3J_{HH}$ = 7.1, CH_3), 1.29 (3 H, t,$^3J_{HH}$ = 7.1, CH_3), 1.42 (12H, m, CH_2), 2.27 (6H, m, PCH_2), 3.62 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 4.18 (4H, m, OCH_2), 7.69 (1 H, s, CH=); δ_C(75 MHz; $CDCl_3$) 13.6, 14.3, 21.0 (d, $^1J_{PC}$ = 53.1), 23.9 (d, $^3J_{PC}$ = 16.1), 24.2 (d, $^2J_{PC}$ = 4.1), 51.0, 51.8, 60.0, 60.3, 69.0 (d, $^1J_{PC}$ = 99.2), 112.5, 151.7, 165.9, 166.0 (d, $^2J_{PC}$ = 13.1), 167.1 (d, $^3J_{PC}$ = 13.6), 167.2, 169.2 (d, $^2J_{PC}$ = 5.0); δ_P(120 MHz; $CDCl_3$) 26.2; *m/z* (EI) 529 (M^+, 5%).

General procedure for the synthesis of phosphazenes 11 and enamines 12

To a solution of phosphazene **10** (5 mmol) in chloroform (20 mL) was added dimethyl acetylenedicarboxylate (0.67 mL, 5 mmol), and the mixture was stirred at room temperature in an atmosphere of nitrogen until TLC indicated the disappearance of phosphazene. Evaporation of solvent under reduced pressure afforded an oil that was separated on silica gel to give compounds **11** and **12**.

1,1,1,4-Tetraphenyl-5,6-bis(methoxycarbonyl)-3-(2-pyridyl)-2-aza-1,λ^5-phosphahexa-1,3,5-triene 11a

The general procedure was followed using 1,1,1,4-tetraphenyl-3-(2-pyridyl)-2-aza-1,λ^5-phosphabuta-1,3-diene **10a** (2.28 g). Chromatographic separation (1 : 1, hexane–ethyl acetate) gave **11a** (1.80 g, 60%) as a yellow solid; mp 171–172 °C (from hexane–dichloromethane, 10 : 1) (Found: C, 74.33; H, 5.28; N, 4.63. $C_{37}H_{31}N_2O_4P$ requires C, 74.24; H, 5.22; N, 4.68%); ν_{max}(KBr)/cm^{-1} 1694 (C=O), 1241 (P=N); δ_H(250 MHz; $CDCl_3$; Me_4Si) 3.74 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 6.45–6.97 (3 H, m, CH_{arom}), 7.18 (1 H, s, CH=), 7.20–7.60 (21 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) 50.7, 53.0, 122.0 (d, *J* 75, C=), 127.8–147.5 (m), 157.6, 162.3, 168.2, 170.5; *m/z* (EI) 599 (M^+, 50).

1,1,1,3,4-Pentaphenyl-5,6-bis(methoxycarbonyl)-2-aza-1,λ^5-phosphahexa-1,3,5-triene 11b and methyl 5-amino-4,5-diphenyl-3-methoxycarbonylpenta-2,4-dienoate 12b

The general procedure was followed using 1,1,1,3,4-pentaphenyl-2-aza-1,λ^5-phosphabuta-1,3-diene **10b** (2.28 g). Chromatographic separation (5 : 1, hexane–ethyl acetate) gave **11b** (1.67 g, 56%) as a yellow solid; mp 107–108 °C (from hexane–dichloromethane, 10 : 1) and **12b** (0.62 g, 37%) as a yellow solid; mp 107–108 °C (from hexane–dichloromethane, 10 : 1). For compound **11b** (Found: C, 76.33; H, 5.38; N, 2.33. $C_{38}H_{32}NO_4P$ requires C, 76.37; H, 5.40; N, 2.34%), ν_{max}(KBr)/cm^{-1} 1705 (C=O), 1407 (P=N); δ_H(250 MHz; $CDCl_3$; Me_4Si) 3.33 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 6.75–7.83 (26 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) 50.4, 52.0, 126.2–132.8 (m), 137.1, 138.4, 142.7, 168.1, 170.2; *m/z* (EI) 597 (M^+, 100). For **12b** (Found: C, 71.33; H, 5.70; N, 4.13. $C_{20}H_{19}NO_4$ requires C, 71.20; H, 5.68; N, 4.15%); ν_{max}(KBr)/cm^{-1} 3424 (NH_2), 1710(C=O), 1690 (C=O); δ_H(250 MHz; $CDCl_3$; Me_4Si) 3.65 (3 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 4.75 (2 H, s, NH_2), 6.86–7.26 (11 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) 50.9, 52.0, 91.4, 127.0–140.5 (m), 161.1, 169.9, 170.1; *m/z* (EI) 337 (M^+, 100).

1,1,1,4-Tetraphenyl-5,6-bis(methoxycarbonyl)-3-(2-furyl)-2-aza-1,λ^5-phosphahexa-1,3,5-triene 11c and methyl 5-amino-5-(2-furyl)-3-methoxycarbonyl-4-phenylpenta-2,4-dienoate 12c

The general procedure was followed using 1,1,1,4-tetraphenyl-3-(2-furyl)-2-aza-1,λ^5-phosphabuta-1,3-diene **10c** (2.22 g). Chromatographic separation (5 : 1, hexane–ethyl acetate) gave **11c** (2.05 g, 70%) as a yellow solid; mp 128–129 °C (from hexane–dichloromethane, 10 : 1) and **12c** (0.16 g, 10%) as a yellow solid; mp 143–144 °C (from hexane–dichloromethane, 10 : 1); For compound **11c** (Found: C, 73.53; H, 5.18; N, 2.33. $C_{36}H_{30}NO_5P$ requires C, 73.58; H, 5.15; N, 2.38%); ν_{max}(KBr)/cm^{-1} 1694 (C=O), 1406 (P=N); δ_H(250 MHz; $CDCl_3$; Me_4Si) 3.35 (3 H, s, OCH_3), 3.61 (3 H, s, OCH_3), 5.90 (2 H, s, H_{fur}), 6.82 (1 H, s, CH=), 7.22–7.74 (21 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) 50.7, 51.9, 109.3, 110.3, 128.0–140.4 (m), 152.4, 168.0, 170.0; *m/z* (EI) 587. For compound **12c** (Found: C, 66.10; H, 5.20; N, 4.20. $C_{18}H_{17}NO_5$ requires C, 66.05; H, 5.23; N, 4.28%); ν_{max}(KBr)/cm^{-1} 3509 (NH_2), 1705 (C=O), 1665 (C=O); δ_H(250 MHz; $CDCl_3$; Me_4Si) 3.54 (3 H, s, OCH_3), 3.72 (3 H, s, OCH_3), 6.33 (1 H, dd, *J* 1.7, 3,5, H_{fur}), 6.69 (1 H, d, *J* 3,5, H_{fur}), 7.25–7.77 (9 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) 50.7, 51.9, 109.3, 110.3, 128.0–148.1(m), 169.5, 169.8; *m/z* (EI) 327 (M^+, 100).

Methyl 5-amino-3-methoxycarbonyl-5-(2-thienyl)penta-2,4-dienoate 12d

The general procedure was followed using 1,1,1,4-tetraphenyl-3-(2-thienyl)-2-aza-1,λ^5-phosphabuta-1,3-diene **10d** (2.30 g). Chromatographic separation (5 : 1, hexane–ethyl acetate) gave **12d** (0.93 g, 54%) as a brown solid; mp 122–124 °C (from hexane–dichloromethane, 10 : 1) (Found: C, 63.02; H, 5.00; N, 4.10. $C_{18}H_{17}NO_4S$ requires C, 62.96; H, 4.99; N, 4.08%); ν_{max}(KBr)/cm^{-1} 3425 (NH_2), 1711 (C=O), 1680 (C=O); δ_H(250 MHz; $CDCl_3$; Me_4Si) 3.60 (3 H, s, OCH_3), 3.72 (3 H, s, OCH_3), 6.80–7.49 (11 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) 51.1, 52.2, 92.4, 126.8–141.7 (m), 153.4, 169.6, 169.8; *m/z* (EI) 343 (M^+, 100).

General procedure for the synthesis of *N*-vinylic phosphazenes 16

To a solution of benzyltrimethylphosphonium iodide (1.47 g, 5 mmol) in toluene (20 mL) cooled to 0 °C under N_2 was added dropwise a 0.5 M solution of potassium bis(trimethylsilyl)amide in toluene (2.5 mL, 5 mmol). The yellow solution was stirred at room temperature for 4 hours, afterwards was filtered under an inert atmosphere to remove the formed salts, and solvents and reagents were eliminated under vacuum. Toluene (20 mL) was added to the ylide and cooled to 0 °C and a solution of nitrile **15** (5 mmol) in toluene (10 mL) was added dropwise and stirred at room temperature for 24 hours. The mixture was evaporated under vacuum under an inert atmosphere, and the phosphazene **16** obtained was used without further purification.

1,1,1-Trimethyl-3,4-diphenyl-2-aza-1,λ^5-phosphabuta-1,3-diene 16b

The general procedure was followed using 0.500 mL (5 mmol) of benzonitrile. The reaction compound is unstable to distillation or chromatography and therefore was not isolated and used for the following reactions. δ_H(250 MHz; $CDCl_3$; Me_4Si) of crude reaction mixture 1.60 (9 H, d, *J* 12.3, CH_3), 5.84 (1 H, s, CH=), 6.67–7.75 (10 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) of crude reaction mixture 16.8 (d, *J* 67.6, CH_3), 124.5, 128.7, 129.0, 140.3.

1,1,1-Trimethyl-4-phenyl-3-(2-furyl)-2-aza-1,λ^5-phosphabuta-1,3-diene 16c

The general procedure was followed using 0.437 mL (5 mmol) of 2-furonitrile (2.22 g). The reaction compound is unstable to distillation or chromatography and therefore was not isolated and used for the following reactions. δ_H(250 MHz; $CDCl_3$; Me_4Si) of crude reaction mixture 1.51 (9 H, d, *J* 12.5, CH_3), 6.15 (1 H, s, CH=), 6.40 (1 H, m, CH_{fur}), 6.44 (1 H, d, *J* 3.2, CH_{fur}), 7.04–7.90 (6 H, m, CH_{arom}); δ_C(75 MHz; $CDCl_3$) of crude reaction mixture 17.0 (d, *J* 68.0, CH_3), 105.9, 111.4, 124.1, 127.7, 127.8, 140.3.

Ethyl 3-(1-furan-2-yl-2-phenylvinylimino)-2-(trimethyl-λ^5-phosphanylidene)propionate 19

To a solution of phosphazene **16c** (5 mmol) in toluene (20 mL) was added ethyl propiolate (0.51 mL, 5 mmol), and the mixture was stirred at room temperature under an inert atmosphere. The reaction was monitored by ^{31}P-NMR and after 2 hours the total disappearance of phosphazene was observed. Evaporation under reduced pressure afforded an oil, which is unstable to distillation or chromatography and therefore was not isolated and used for the following reaction. δ_H(250 MHz; $CDCl_3$; Me_4Si) of crude reaction mixture 1.23 (3 H, t, *J* 7.1, CH_3), 1.93 (9 H, d, *J* 13.8, CH_3), 4.10 (2 H, d, *J* 7.1, CH_2), 6.14 (1 H, s, CH=), 6.26 (1 H, d, *J* 3.2, CH_{fur}), 6.39 (1 H, dd, *J* 3.2, *J* 1.8, CH_{fur}), 6.93–7.53 (6 H, m, CH_{arom}), 8.54 (1 H, d, *J* 26.4, CH=N); δ_C(75 MHz; $CDCl_3$) of crude reaction mixture 12.4 (d, *J* 60.4, CH_3), 14.3 (CH_3), 57.8 (CH_2), 109.5, 110.4, 114.8, 124.7–151.4 (m), 160.1 (COO), 167.8 (d, *J* 16.6, CH=N).

3-Ethoxycarbonyl-6-(2-furyl)-4-(4-nitrophenyl)-5-phenyl-1,4-dihydropyridine 21

To a solution of ylide **19** (5 mmol) in toluene (20 mL) under an inert atmosphere was added *p*-nitrobenzaldehyde (0.75 g, 5 mmol), and the mixture was stirred at reflux until ^{31}P-NMR indicated the disappearance of the ylide. Evaporation of solvent under reduced pressure afforded an oil that was separated on silica gel to give compound **21**. Chromatographic separation (5 : 1, hexane–ethyl acetate) gave **21** (1.74 g, 84%) as a yellow solid; mp 168–169 °C (from hexane–dichloromethane, 10 : 1) (Found: C, 69.02; H, 4.30; N, 6.48. $C_{24}H_{20}N_2O_5$ requires C, 69.22; H, 4.84; N, 6.73%); ν_{max}(KBr)/cm^{-1} 3394 (NH), 1675 (C=O); δ_H(250 MHz; $CDCl_3$; Me_4Si) 1.18 (3 H, t, *J* 7.0, CH_3), 4.05–4.11 (2 H, m, CH_2), 4.77 (1 H, s, CH), 5.29 (1 H, d, *J* 3.5, CH_{fur}), 6.19 (1 H, dd, *J* 3.5, *J* 1.8, CH_{fur}), 6.83–7.62 (11 H, m, CH_{arom}), 8.09 (1 H, d, *J* 8.8, CH=); δ_C(75 MHz; $CDCl_3$) 14.3 (CH_3), 46.0 (CH), 59.8 (CH_2), 102.3, 109.8, 111.9, 114.6–153.5 (m), 167.0; *m*/*z* (EI) 416 (M^+, 9).

Ethyl 6-furan-2-yl-4-(4-nitrophenyl)-5-phenylnicotinate 22

To a solution of 1,4-dihydropyridine **21** (1 mmol) in $CHCl_3$ (10 mL) under an inert atmosphere was added *p*-benzoquinone (0.10 g, 1 mmol), and the mixture was stirred at reflux temperature until TLC indicated the disappearance of starting material. Evaporation of solvent under reduced pressure afforded an oil that was separated on silica gel to give compound **22**. Chromatographic separation (5 : 1, hexane–ethyl acetate) gave **22** (0.39 g, 94%) as a yellow solid; mp 196–197 °C (from hexane–dichloromethane, 10 : 1) (Found: C, 69.92; H, 4.40; N, 6.78. $C_{24}H_{18}N_2O_5$ requires C, 69.56; H, 4.38; N, 6.76%); ν_{max}(KBr)/cm^{-1} 1713 (C=O); δ_H(250 MHz; $CDCl_3$; Me_4Si) 1.00 (3 H, t, *J*7.2, CH_3), 4.00–4.08 (2 H, m, CH_2), 5.47 (1 H, t, *J* 2.9, CH_{fur}), 6.14–6.18 (1 H, m, CH_{fur}), 6.61–7.96 (10 H, m, CH_{arom}), 9.19 (1 H, s, CH=); δ_C(75 MHz; $CDCl_3$) 13.7 (CH_3), 61.5 (CH_2), 111.8, 114.9, 116.1, 122.5–151.1 (m), 165.3; *m*/*z* (EI) 414 (M^+, 50).

Acknowledgements

The present work has been supported by the *Dirección General de Investigación del Ministerio de Ciencia y Tecnología* (MCYT, Madrid DGI, BQU2000–0217) and by the *Universidad del País Vasco* (UPV, G11/ 99). C. Alonso thanks the Consejería de Educación del Gobierno Vasco (Vitoria) for a postdoctoral fellowship.

References

1 For reviews see: (*a*) H. Wamhoff, G. Richardt and S. Stölben, *Adv. Heterocycl. Chem.*, 1995, **64**, 159–249; (*b*) P. Molina and M. J. Vilaplana, *Synthesis*, 1994, 1197–1218; (*c*) S. Eguchi, Y. Matsushita and K. Yamashita, *Org. Prep. Proced. Int.*, 1992, **24**, 209–243; (*d*) Y. G. Gololobov and L. F. Kaskhin, *Tetrahedron*, 1992, **48**, 1353–1406; (*e*) J. Barluenga and F. Palacios, *Org. Prep. Proced. Int.*, 1991, **23**, 1–59.

2 For recent contributions see: (*a*) S. A. Bell and T. Y. Meyer, Gelb, *J. Am. Chem. Soc.*, 2002, **124**, 10698–10705; (*b*) S. J. H. Steiner, S. Zacchini and P. I. Richards, *Coord. Chem. Rev.*, 2002, **227**, 193–216; (*c*) C. Andujar, I. Pérez and F. López, *Tetrahedron*, 2002, **58**, 2569–2575; (*d*) T. Rodima, I. Kaljurand, A. Pihl, V. Maeemets, I. L. Vahur and I. A. Koppel, *J. Org. Chem.*, 2002, **67**, 1873–1881.

3 (*a*) H. Kato, K. Ohmori and K. Suzuki, *Synlett*, 2001, 1003–1005; (*b*) J. J. García, F. Santoyo and A. Vargas, *Synlett*, 1997, 265–266; (*c*) I. Bosch, A. Gonzalez, F. Urpi and J. Vilarrasa, *J. Org. Chem.*, 1996, **61**, 5638–5643.

4 (*a*) J. Biao, C. G. Yang and J. Wang, *J. Org. Chem.*, 2002, **67**, 1396–1398; (*b*) P. Molina, P. M. Fresneda, S. Delgado and J. A. Bleda, *Tetrahedron Lett.*, 2002, **43**, 1005–1007; (*c*) S. Barthelemy, S. Schneider and W. Bannwarth, *Tetrahedron Lett.*, 2002, **43**, 807–810; (*d*) G. Turos, A. Csampai, M. Czugler, H. Wamhoff and P. Sohar, *J. Organomet. Chem.*, 2001, **634**, 122–130; (*e*) R. Alvarez, C. Peinador and J. M. Quintela, *Tetrahedron*, 2001, **57**, 5413–5420.

5 (*a*) F. Palacios, C. Alonso, P. Amezua and G. Rubiales, *J. Org. Chem.*, 2002, **67**, 1941–1946; (*b*) F. Palacios, E. Herrán and G. Rubiales, *J. Org. Chem.*, 1999, **64**, 6239–6246; (*c*) F. Palacios, C. Alonso and G. Rubiales, *J. Org. Chem.*, 1997, **62**, 1146–1152; (*d*) F. Palacios, D. Aparicio and J. M. de los Santos, *Tetrahedron*, 1996, **52**, 4857–4866; (*e*) F. Palacios, I. Pérez de Heredia and G. Rubiales, *J. Org. Chem.*, 1995, **60**, 2384–2390; (*f*) F. Palacios, C. Alonso and G. Rubiales, *Tetrahedron*, 1995, **51**, 3193–3190; (*g*) J. Barluenga, M. Ferrero and F. Palacios, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2193–2197; (*h*) J. Barluenga, M. Ferrero and F. Palacios, *Tetrahedron Lett.*, 1988, **29**, 4863–4864.

6 (*a*) J. Barluenga, I. Merino and F. Palacios, *J. Chem. Soc., Perkin Trans. 1*, 1991, 341–345; (*b*) J. Barluenga, I. Merino and F. Palacios, *Tetrahedron Lett.*, 1989, **30**, 5493–5496.

7 (*a*) F. Palacios, A. M. Ochoa de Retana and J. Pagalday, *Tetrahedron*, 1999, **55**, 14451–14458; (*b*) J. Barluenga, F. López, F. Palacios and F. Sánchez-Ferrando, *J. Chem. Soc., Perkin Trans. 2*, 1988, 903–907.
8 (*a*) J. Barluenga, F. López, F. Palacios and F. Sánchez-Ferrando, *Tetrahedron Lett.*, 1988, **29**, 381–384; (*b*) J. Barluenga, F. López and F. Palacios, *J. Chem. Soc., Chem. Commun.*, 1986, 1574–1575; (*c*) J. Barluenga, F. López and F. Palacios, *J. Organomet. Chem.*, 1990, **382**, 61–67.
9 (*a*) J. Barluenga, F. López and F. Palacios, *Chem. Commun.*, 1985, 1681–1682; (*b*) F. López, E. Pelaez, F. Palacios, J. Barluenga, S. García, B. Tejerina and A. García, *J. Org. Chem.*, 1994, **59**, 1984–1992; (*c*) J. Barluenga, F. López and F. Palacios, *J. Chem. Soc., Perkin Trans. 1*, 1989, 2273–2277.
10 (*a*) A. B. Smith, K. M. Yager and C. M. Taylor, *J. Am. Chem. Soc.*, 1995, **117**, 10879–10888; (*b*) R. Hirschmann, A. B. Smith, C. M. Taylor, P. A. Benkovic, S. D. Taylor, K. M. Yager, P. A. Spengler and S. J. Benkovic, *Science*, 1994, **265**, 234–237; (*c*) D. Georgiadis, V. Dive and A. Yiotakis, *J. Org. Chem.*, 2001, **66**, 6604–6610; (*d*) J. H. Meyer and P. A. Bartlett, *J. Am. Chem. Soc.*, 1998, **120**, 4600–4609.
11 (*a*) F. Palacios, A. M. Ochoa de Retana and J. Pagalday, *Eur. J. Org. Chem.*, 2002, 913–919; (*b*) A. R. Katritzky, G. Zhang and J. Jiang, *J. Org. Chem.*, 1994, **59**, 4556–4560.
12 (*a*) F. Palacios, A. M. Ochoa de Retana and J. Pagalday, *Heterocycles*, 1995, **40**, 543–550; (*b*) T. Gadja and M. Matusiak, *Synthesis*, 1992, 367–368.
13 The reaction was monitored by ^{31}P-NMR showing the disappearance of triphenylphosphine (δ_P = −6.00 ppm. and the formation of phosphazene **1a** (δ_P = 40.6 and 22.5 ppm, $^3J_{PP}$ = 14.1Hz), which disappears after the addition of the acetylenic ester with the formation of the triphenylphosphine oxide (δ_P = 29.50 ppm).
14 O. I. Kolodiazhnyi, in *Phosphorus Ylides. Chemistry and Application in Organic Synthesis*, ed. O. I. Kolodiazhnyi, Wiley-VCH, Weinheim, 1999.
15 B. J. Walker, in *Organophosphorus Reagents in Organic Synthesis*, ed. J. I. Cadogan, Academic Press, New York, 1979, p. 155.
16 (*a*) T. Oikawa, N. Kanomata and M. J. Tada, *J. Org. Chem.*, 1993, **58**, 2046–2051; (*b*) M. Nitta, Y. Iino, T. Sugiyama and A. Akagi, *Tetrahedron Lett.*, 1993, **34**, 831–834; (*c*) N. Kanomata, H. Kawagi and N. Nitta, *J. Org. Chem.*, 1992, **57**, 618–625; (*d*) M. Nitta, M. Ohnuma and Y. Iino, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1115–1118.
17 (*a*) F. Palacios, S. Pascual, J. Oyarzabal and A. M. Ochoa de Retana, *Org. Lett.*, 2002, **4**, 769–772; (*b*) F. Palacios, A. M. Ochoa de Retana, S. Pascual and R. López de Munain, *Tetrahedron Lett.*, 2002, **43**, 5917–5919; (*c*) F. Palacios, A. M. Ochoa de Retana and J. Oyarzabal, *Tetrahedron. Lett.*, 1996, **37**, 4577–4580; (*d*) G. Erker, M. Riedel, S. Kch, T. Jödicke and E. H. Würthwein, *J. Org. Chem.*, 1995, **60**, 5284–5290.
18 (*a*) X. Ariza, F. Urpí and J. Vilarrasa, *Tetrahedron Lett.*, 1999, **40**, 7515–7517; (*b*) X. Ariza, F. Urpí, C. Viladomat and J. Vilarrasa, *Tetrahedron Lett.*, 1998, **39**, 9101–9102.
19 For reviews see: (*a*) G. Leonetti, B. Magnani, A. C. Pessina, A. Rappelli, B. Trimarco and A. Zanchetti, *Am. J. Hypertens.*, 2002, **15**, 932–940; (*b*) S. D. Pierdomenico, A. Bucci, D. Lapenna, F. Cuccurullo and A. Mezzetti, *J. Cardiovasc. Pharmacol.*, 2002, **40**, 288–295; (*c*) A. B. Miller, *Am. J. Cardiol.*, 2001, **88**, 21M–25M; (*d*) W. Gattis and C. M. O'Connor, *Drugs*, 2000, **59**, 17–24; (*e*) R. J. M. de Vries, D. J. van Veldhuisen and P. H. J. M. Dunselman, *Am. Heart J.*, 2000, **139**, 185–194; (*f*) F. H. Leenen, *Clin. Exp. Hypertens.*, 1999, **21**, 823–834; (*g*) D. J. Triggle, in *Comprehensive Medicinal Chemistry*, ed. C. Hansch, Pergamon, Oxford, 1990, vol. 3, p 1070.
20 (*a*) Y. Sambongi, H. Nitta, K. Ichihashi, M. Futai and I. M. L. Ueda, *J. Org. Chem.*, 2002, **67**, 3499–3501; (*b*) Bennasar, C. Juan and J. Bosch, *Tetrahedron Lett.*, 2001, **42**, 585–588; (*c*) H. Rudler, A. Parlier, T. Durand-Reville, B. Martin-Vaca, M. Audouin, E. Garrier, V. Certal and J. Vaissermann, *Tetrahedron*, 2000, **56**, 5001–5027; (*d*) O. Almarsson and T. C. Bruice, *J. Am. Chem. Soc.*, 1993, **115**, 2125–2138; (*e*) Y. D. Wu and K. N. Haunk, *J. Org. Chem.*, 1993, **58**, 2043.
21 (*a*) Z. Tomoskozi, O. Finance and P. Aranyi, *Eur. J. Pharm.*, 2002, **449**, 55–60; (*b*) B. Marciniec, E. Jaroszkiewicz and M. Ogrodowczyk, *Int. J. Pharm.*, 2002, **233**, 207–215; (*c*) K. Takara, M. Kakumoto, Y. Tanigawara, J. Funakoshi, T. Sakaeda and K. Okumura, *Life Sci.*, 2002, **70**, 1491–1500; (*d*) M. Katoh, M. Nakajima, H. Yamazaki and T. Yokoi, *Pharm. Res.*, 2000, **17**, 1189–1197; (*e*) M. Katoh, M. Nakajima, N. Shimada, H. Yamazaki and T. Yokoi, *Eur. J. Clin. Pharm.*, 2000, **55**, 843–852; (*f*) S. Oparil and S. E. Bakir, *Drugs*, 2000, **59**, 25–37; (*g*) G. Wennemuth, R. E. Westenbroek, T. Xu, B. Hille and D. F. Babcock, *J. Biol. Chem.*, 2000, **275**, 21210–21217; (*h*) A. Savanian, L. J. Shen and F. Ursini, *Pharm. Res.*, 2000, **17**, 999–1006; (*i*) J. T. Flynn and D. A. Pasko, *Pediatr. Nephr.*, 2000, **15**, 302–316; (*j*) H. Masumiya, T. Matsuda, Y. Takaka, H. Tanaka and K. Shinegobu, *Life Sci.*, 2000, **66**, PL239–PL244.
22 (*a*) D. Ma and H. Sun, *J. Org. Chem.*, 2000, **65**, 6009; (*b*) A. Renslo and R. L. Danheiser, *J. Org. Chem.*, 1998, **63**, 7840–7850; (*c*) M. J. Schneider, in *Alkaloids. Chemical and Biological Perspectives*, ed. S. W. Pelletier, Pergamon, Oxford, 1996, vol. 10. pp. 155–299.
23 S. Ohno, O. Komatsu, K. Mizukoshi, K. Ichihara, Y. Nakamura, T. Morishima and K. Sumita, *Chem. Pharm. Bull.*, 1986, **34**, 1589–1606.
24 (*a*) K. C. Nicolau, M. Nevalainen, B. S. Safina, M. Zak and S. Bulat, *Angew. Chem., Int. Ed.*, 2002, **41**, 1941–1945; (*b*) C. J. Moody, R. A. Hughes, S. P. Thompson and L. Alcaraz, *Chem. Commun.*, 2002, 1760–1761; (*c*) S. Jayakumar, M. P. S. Ishar and M. P. Mahajan, *Tetrahedron*, 2002, **58**, 379–471; (*d*) E. Jnoff and L. Ghosez, *J. Am. Chem. Soc.*, 1999, **121**, 2617; (*e*) L. F. Tietze and G. Kettschau, *Top. Curr. Chem.*, 1997, **189**, 1.
25 (*a*) F. Palacios, E. Herrán, G. Rubiales and J. M. Ezpeleta, *J. Org. Chem.*, 2002, **67**, 2131–2135; (*b*) F. Palacios, C. Alonso, G. Rubiales and J. M. Ezpeleta, *Eur. J. Org. Chem.*, 2001, 2115–2122; (*c*) F. Palacios, M. J. Gil, E. Martínez de Marigorta and M. Rodríguez, *Tetrahedron*, 2000, **56**, 6319–6330; (*d*) F. Palacios, M. J. Gil, E. Martínez de Marigorta and M. Rodríguez, *Tetrahedron Lett.*, 1999, **40**, 2411–2414.