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Reaction of *N*-Vinylic Phosphazenes with α,β-Unsaturated Aldehydes. Azatriene-Mediated Synthesis of Dihydropyridines and Pyridines Derived from β-Amino Acids

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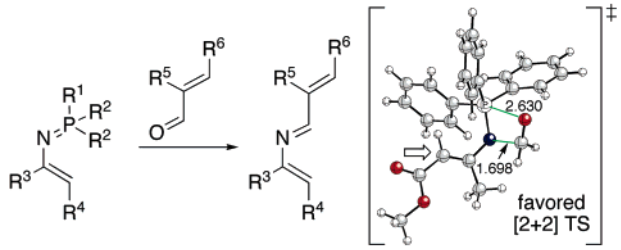

Aza-Wittig reaction of *N*-vinylic phosphazenes (1,2 addition), derived from diphenylmethylphosphine or derived from trimethylphosphine with α,β-unsaturated aldehydes, leads to the formation of 3-azatrienes through a [2 + 2]-cycloaddition−cycloreversion sequence. The presence of an alkyl substituent in position 3 of *N*-vinylic phosphazenes increases the steric interactions, and [4 + 2] periselectivity (1,4 addition) is observed. Reaction of azatrienes with α,β-unsaturated aldehydes yields pyridines.

Introduction

N-Vinylic phosphazenes[1] have proved to be useful building blocks not only for the synthesis of functionalized imine compounds such as electronically neutral,[2] or 3-fluoroalkyl-2-azadienes,[3] as well as electron-poor 2-azadienes derived from aminophosphorus derivatives,[4] α-[5] or β-amino acids,[6] but also as key intermediates in the preparation of glycosides[7] and cyclic compounds[2−6,8−11] as well as in the construction of the framework of pharmacologically active alkaloids.[12] Moreover, *N*-vinylic phosphazenes[13] are ambident nucleophilic reagents,

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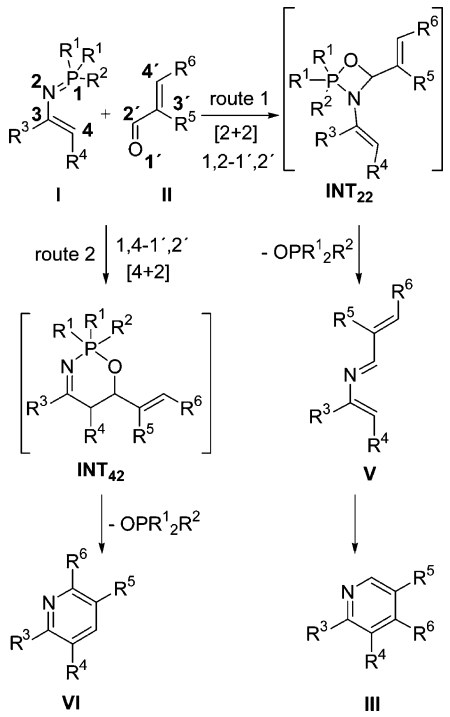
SCHEME 1. [4 + 2] and [2 + 2] Pathways for the Reaction of *N*-Vinylic Phosphazenes I and α,β-Unsaturated Aldehydes II



since the presence of an adjacent double bond in conjugation with the phosphazene moiety introduces a new site of reactivity toward electrophiles: either reaction at the nitrogen (1,2 addition) of the phosphazene[14] or reactions at the γ-carbon atom (1,4 addition).[1,9a,15,16]

In addition, α,β-unsaturated aldehydes[13] **II** have two reactive electrophilic centers: the carbonyl group (for 1′,2′ addition) or the β-carbon atom (for 1′,4′ addition), and therefore, the reaction of conjugated phosphazenes **I** with these substrates can be explained through different reaction pathways, as shown in Scheme 1 and Figure 1. Formation of pyridines **III** by an enamine alkylation of phosphazene **I** onto the β-carbon of the aldehyde **II** (conjugative 1,4−1′,4′ addition) by means of intermediate **IV** (Figure 1) has been reported previously.[1,17−19] Formation of these pyridines **III** can be also described (route 1, Scheme 1) by initial [2 + 2]-cycloaddition−cycloreversion aza-Wittig reaction[20] of *N*-vinylic phosphazenes **I** (1,2 addition) with the carbonyl group of α,β-unsaturated aldehydes **II** (1′,2′ addition) to give the nonisolable azatriene intermediates **V**,

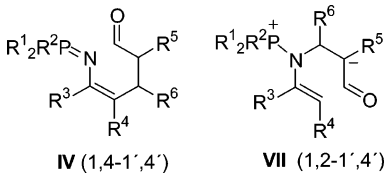


FIGURE 1. Potential intermediates for the reaction of *N*-vinylic phosphazenes **I** and α,β-unsaturated aldehydes **II**.

which after electrocyclization and aromatization afford pyridines **III**.[21] On the other hand, isomeric pyridines **VI** have been reported when similar *N*-vinylic phosphazenes **I** reacted with α,β-unsaturated aldehydes **II**.[21c,22] The reaction mechanism has been described as a formal [4 + 2] cyclization involving an initial nucleophilic attack of the γ-carbon atom (1,4 addition) of the phosphazene (route 2, Scheme 1) onto the carbonyl group of the aldehyde (1′,2′ addition) and subsequent loss of phosphine oxide and electrocyclization. An alternative pathway involving (1,2−1′,4′ addition) through intermediate **VII** (Figure 1) could also explain the formation of pyridines **VI**.

Within this context, the influence of phosphorus atom substituents in *N*-vinylic phosphazenes **I** can play an important role in the reactivity pattern observed with carbonyl compounds. In phosphazenes, the electron-donating alkyl groups should increase the nucleophilicity of imino nitrogen, and therefore, aza-Wittig reaction[14a] predominates over Michael reaction.[22] Reactivity also depends on the nature of substituents on the vinylic chain of phosphazenes. The ambident behavior observed for *N*-vinylic phosphazenes against α,β-unsaturated aldehydes prompted us to establish which one of the possible mechanisms (Scheme 1, routes 1 or 2) is involved in each process and whether the reaction of these phosphazenes **I** derived from diphenylmethylphosphine or trimethylphosphine gives the regioselective aza-Wittig reaction ([2 + 2] cycloaddition−cycloreversion) and allows the isolation of the corresponding 3-azatriene derivative **V** (route 1, Scheme 1). Therefore, we report here the combined theoretical and experimental study of the reaction of *N*-vinylic phosphazenes **I** derived from β-amino acids (R^3 = H, R^4 = CO_2Et) with α,β-unsaturated aldehydes, as well as whether theoretical calculations of charge distribution in conjugated phosphazenes **I** could support a [2 + 2] cycloaddition−cycloreversion sequence involving a charge (frontier orbital)-controlled attack (1,2 addition) to the carbonyl group of unsaturated aldehydes (1′,2′ addition). Moreover, we report that 3-azatrienes can be used as key intermediates in the synthesis of pyridine compounds derived from β-amino acids.

Results and Discussion

Aza-Wittig Reaction of Phosphazenes 6 Derived from Diphenylmethylphosphine or Trimethylphosphine with α,β-Unsaturated Aldehydes 2 ([2 + 2] Cyclization−Cycloreversion versus [4 + 2] Cyclization Processes). A previous report described the reaction of *N*-vinylic phosphazene **1** (Scheme 2) derived from triphenylphosphine with acrolein **2a** (R^6 = H) or cinnamaldehyde **2b** (R^6 = Ar), in *o*-xylene at 160 °C, in the presence of palladium on charcoal and in a sealed tube, giving

(13) Reactive centers of phosphazenes **I** (see Scheme 1) are numbered 1, 2, 3, and 4, and reactive centers of aldehydes **II** are numbered 1′, 2′, 3′, and 4′.

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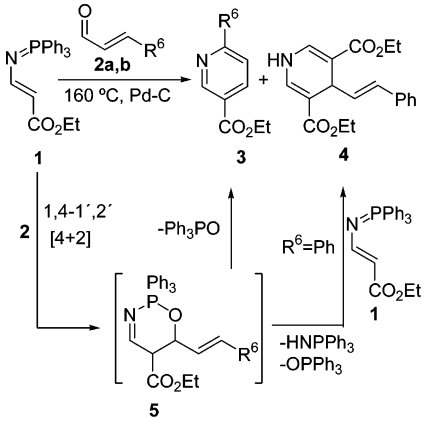
SCHEME 2. Reaction of *N*-Vinylic Phosphazene 1 Derived from Triphenylphosphine with Acrolein 2a and Cinnamaldehyde 2b



pyridine **3** (R^6 = H) in the first case and a mixture of pyridine **3** (R^6 = Ar) and 4-(2-arylethenyl)-3,5-diethoxycarbonyldihydropyridine **4** in moderate yields when cinnamaldehyde **2b** (R^6 = Ar) was used (Scheme 2).[22]

The authors suggested that the formation of these heterocycles **3**, **4** could be explained by a formal [4 + 2]-cyclization process involving an initial addition of the β-carbon atom of the *N*-vinylic phosphazene **1** (1,4 addition) to the carbonyl carbon atom of the α,β-unsaturated aldehydes **2** (1′,2′ addition) to give 1,2,5-oxaazaphosphorane cycloadduct **5**.[23] Intramolecular cyclization of this intermediate with concomitant elimination of triphenylphosphine oxide and aromatization gave pyridines **3**, while regioselective attack of a second molecule of the phosphazene **1** to 1,2,5-oxaazaphosphorane **5** afforded dihydropyridine **4** (Scheme 2).

However, these findings are in contrast with our results reported here (vide infra). We found that the reaction of *N*-vinylic phosphazene **6a** (R^1 = Ph, R^3 = H, R = Et) derived from diphenylmethylphosphine with acrolein **2a** (R^5 = R^6 = H), cinnamaldehyde **2b** (R^5 = H, R^6 = Ph), methacrolein **2c** (R^5 = Me, R^6 = H), or crotonaldehyde **2d** (R^5 = H, R^6 = Me) in chloroform at 60 °C gave pyridines **7a**−**d** (Scheme 3, Table 1). Isomeric pyridines **8** were not obtained. Pyridine **8** (R^3 = Ph, R^5 = H, R^6 = Me) was prepared by reaction of ethyl 2-amino-2-phenylprop-2-enoate **9** with crotonaldehyde **2d** (R^5 = H, R^6 = Me) in toluene at 110 °C in a manner similar to that reported for enaminophosphonates[24] or enaminonitriles.[25] The values of the coupling constant (ca. 8.5 Hz) of the vicinal H-3 and H-4 hydrogens in these compounds **7** (R^5 = H) are higher than expected (ca. 5 Hz) for the H-2 and H-3 hydrogens in isomeric pyridines **8** (R^5 = H) and are consistent with the literature.[22]

Formation of pyridines **7a**−**d** could be explained, either by a [4 + 2] cyclization−cycloreversion process involving a 1,4 addition of the phosphazene to the carbonyl group (1′,2′ addition) of the unsaturated aldehyde (1,4−1′,2′ addition, Scheme 1, route 2) and formation of oxaazaphosphoranes **INT**$_{42}$,

SCHEME 3. Synthesis of Azatrienes 11 and Pyridines 7 from *N*-Vinylic Phosphazenes 6 Derived of Diphenylmethyl- and Trimethylphosphine

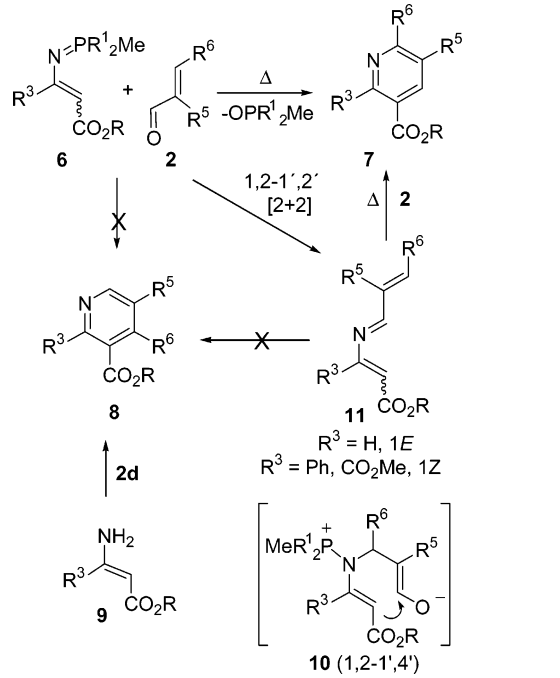


TABLE 1. Pyridines 7 Obtained by Reaction of Phosphazene 6a with Unsaturated Aldehydes

							reaction conditions		
entry	starting aldehyde	products	R^3	R	R^5	R^6	*T* (°C)	time (h)	yield[a] (%)
1	**2a**	**7a**	H	Et	H	H	60	38	28[b]
2	**2b**	**7b**	H	Et	H	Ph	60	39	32[b]
3	**2c**	**7c**	H	Et	Me	H	60	40	30[b]
4	**2d**	**7d**	H	Et	H	Me	60	40	31[b]

[a] Purified by chromatography. [b] A very high proportion of phosphazene **6a** gave hydrolysis products (40−45%).

similar to the one reported in the reaction of phosphazene **1** with cinnamaldehyde,[22] (Scheme 2) or through a Michael addition involving a 1,2 addition of the phosphazene to the β-carbon atom (1′,4′ addition) of the unsaturated aldehyde followed by intramolecular cyclization of intermediate **10** (1,2−1′,4′ addition, Scheme 3), or in concordance with our previous results,[2,5,6] by a [2 + 2] process (aza-Wittig reaction) involving a 1,2 addition of the phosphazene to the carbonyl group (1′,2′ addition) of the unsaturated aldehyde and formation of azatrienes **11** (1,2−1′,2′ addition, Scheme 3) followed by their reaction with a second molecule of aldehyde **2**.

Therefore, we tried to test if azatrienes **11** were intermediates in the reaction, and to confirm the mechanism, if they could be isolated by the reaction of conjugated phosphazenes with unsaturated carbonyl compounds, in a similar way to that observed in the case of simple aldehydes,[2,5,6] as well as to explore if the reaction of these azatrienes with aldehydes led to the formation of pyridines **7**. The reaction of *N*-vinylic phosphazenes **6a** (R^1 = Ph) derived from ethyl β-azidoacrylate (R^3 = H, R = Et) with unsaturated aldehydes **2a**−**d** at room temperature, gave the [2 + 2] aza-Wittig products (1,2−1′,2′ addition) **11a**−**d** in good yields (Scheme 3, Table 2, entries 1−4). However, these azatrienes **11a**−**d** were unstable during distillation and/or chromatography and were used without

(23) This intermediate is also designed as [4 + 2]-intermediate or **INT**$_{42}$ (vide infra, computational studies).

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TABLE 2. Azatrienes 11 Obtained

entry	starting phosphazene	aldehyde	products	R^3	R	R^5	R^6	reaction conditions		
								T (°C)	time (h)	yield[a] (%)
1	**6a/6b**	**2a**	**11a**	H	Et	H	H	rt	1/0.5	70/95
2	**6a/6b**	**2b**	**11b**	H	Et	H	Ph	rt	7/1	75/98
3	**6a/6b**	**2c**	**11c**	H	Et	Me	H	rt	30/4	60/92
4	**6a/6b**	**2d**	**11d**	H	Et	H	Me	rt	24/5	65/90
5	**6c**	**2d**	**11e**	Ph	Et	H	Me	60	60	75
6	**6c/6d**	**2b**	**11f**	Ph	Et	H	Ph	60/rt	16/24	80/90
7	**6c**	**2c**	**11g**	Ph	Et	Me	H	60	56	80
8	**6c**	**2a**	**11h**	Ph	Et	H	H	rt	8	65
9	**6e**	**2d**	**11i**	CO_2Me	Me	H	Me	70	98	70

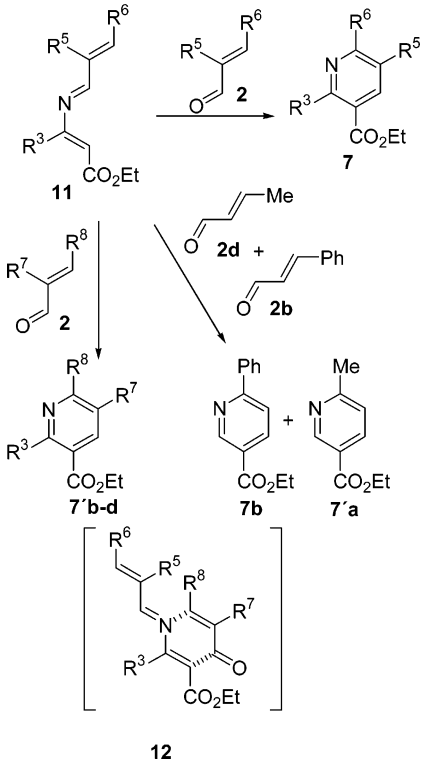
[a] Yield calculated by ^1H NMR.

purification.[26] The use of conjugated phosphazenes **6b** derived from trimethylphosphine (R^1 = Me, R^3 = H, R = Et) was more favorable because the formation of azatrienes **11a**−**d** took place in shorter periods of time and the elimination of trimethylphosphine oxide from the reaction mixture was easier (Table 2, entries 1−4). The scope of this aza-Wittig reaction was not limited to the phosphazenes derived from ethyl *β*-azidoacrylate. *N*-Vinylic phosphazenes substituted with electron-withdrawing groups on the 3 position such as 3-phenyl- **6c** (R^1 = Ph, R^3 = Ph) and **6d** (R^1 = Me, R^3 = Ph) and 3-methoxycarbonyl-substituted phosphazenes **6e** (R^1 = Ph, R^3 = CO_2Me) also reacted with aldehydes leading to the formation of azatrienes **11e**−**i** (Table 2, entries 5−9, Scheme 3). Then, the synthetic utility of azatrienes **11** was studied.

Heating of azatriene **11b**, generated "in situ" by reaction of *N*-vinylic phosphazenes **6a** derived from diphenylmethylphosphine or **6b** derived from trimethylphosphine with excess of cinnamaldehyde **2b**, in chloroform at 60 °C yielded 60% of pyridine **7b** (Scheme 3), while isomeric pyridine **8** (R^5 = H, R^6 = Ph, Scheme 3), whose formation could be expected by electrocyclization of 3-azatriene **11b**, was not observed, even when this azatriene was heated at 120 °C. These results seem to infer that the electrocyclization of 3-azatrienes[27] is more difficult than in the case of the isomeric 2-azatrienes.[8b,28]

Formation of pyridines **7** (Scheme 3) seems to indicate that a second molecule of aldehyde is involved in the process. For this reason, we explored if the reaction of azatrienes **11** with unsaturated aldehydes **2** would lead to the formation of pyridines **7**. Thus, azatrienes **11a**−**g** generated "in situ" from the corresponding *N*-vinylic phosphazenes **6** and acrolein **2a**, cinnamaldehyde **2b**, methacrolein **2c**, or crotonaldehyde **2d** reacted with a second molecule of the same aldehyde **2** in chloroform at 60 °C or toluene at 90 °C to give pyridines **7a**−**g** (Scheme 4, Table 3, entries 1−7). However, when azatriene **11b** (R^3 = R^5 = H, R^6 = Ph), generated "in situ" with cinnamaldehyde **2b**, was treated subsequently with two different aldehydes, namely a second molecule of the same aldehyde **2b** used in its formation and crotonaldehyde **2d**, a mixture of two pyridines **7b** and **7′a** was obtained (Table 3, entry 8). The presence of the new pyridine **7′** in the process seems to show that aldehyde **2b** (the same as for the preparation of the precursor) is involved in the formation of pyridine **7b**, while the new aldehyde **2d** participates in the formation of pyridine

SCHEME 4. Synthesis of Pyridines 7 and 7′ from Azatrienes 11



7′a (Scheme 4). For this reason, we attempted to prepare pyridines **7′** only. Azatrienes **11c**,**d**,**f** were prepared from phosphazenes **6b** and **6d** and unsaturated aldehydes **2c**,**d**,**b**, respectively. After elimination of the excess of aldehyde under reduced pressure from the reaction mixture, a different aldehyde **2** was added (**2d**, **2b**, and **2a**, respectively) to give pyridines **7′b-d** respectively (Scheme 4, Table 3, entries 9−11). From these results, a formal aza-[3 + 3] cycloaddition reaction (see **12**, Scheme 4) involving the azatriene and the unsaturated aldehydes could explain the formation of pyridines **7′**, in a manner similar to that observed by enamines and unsaturated carbonyl compounds.[29]

On the other hand, the presence of an electron-releasing group in the phosphazene **6** (R^3 = Me) seems to change the reactivity of these ambident nucleophiles toward unsaturated aldehydes. The reaction of *N*-vinylic phosphazene **6k** (R = R^1 = R^2 = R^3 = Me) with cinnamaldehyde **2b** (Scheme 5) was attempted at

(26) The reaction was monitored by ^{31}P and ^1H NMR showing the disappearance of phosphazene **6** and the formation of azatrienes **11**.

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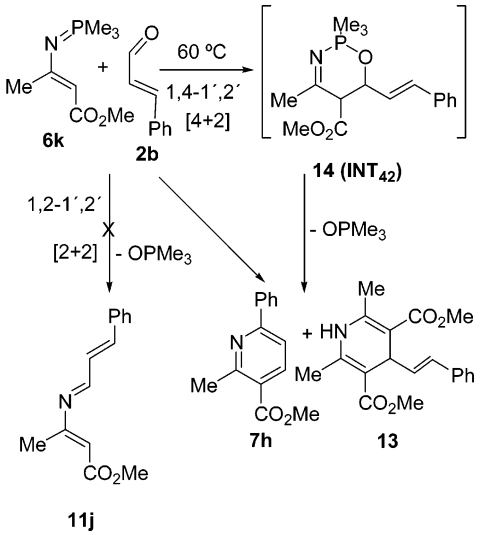
TABLE 3. Pyridines 7, 7′ Obtained

entry	starting azatriene	aldehyde	products	R^3	R^5	R^6	R^7	R^8	reaction conditions T (°C)	time (h)	yield[a] (%)
1	**11a**	**2a**	**7a**	H	H	H			60	34	53
2	**11b**	**2b**	**7b**	H	H	Ph			60	35	60
3	**11c**	**2c**	**7c**	H	Me	H			60	36	58
4	**11d**	**2d**	**7d**	H	H	Me			60	37	60
5	**11e**	**2d**	**7e**	Ph	H	Me			90	62	55
6	**11f**	**2b**	**7f**	Ph	H	Ph			90	60	51
7	**11g**	**2c**	**7g**	Ph	Me	H			90	48	50
8	**11b**	**2b** + **2d**	**7b** + **7′a**[b]	H	H	Ph	H	Me	60	50	10/30
9	**11c**	**2d**	**7′b**[b]	H			H	Me	60	46	38
10	**11d**	**2b**	**7′c**[c]	H			H	Ph	60	48	35
11	**11f**	**2a**	**7′d**	Ph			H	H	90	36	81

[a] Purified by chromatography. [b] Structures of pyridines **7′a** and **7′b** are the same as that of pyridine **7d**. [c] Structure of pyridine **7′c** is the same as that of pyridine **7b**.

SCHEME 5. Synthesis of Pyridines 7h and 13 from Phosphazene 6k



room temperature using chloroform as solvent, but no reaction took place. However, when the reaction was performed in chloroform at 60 °C, the expected azatriene **11j** was not obtained and a mixture of pyridine **7h** (30%) and 4-(2-arylethenyl)-3,5-dimethoxycarbonyl-2,6-dimethyl-1,4-dihydropyridines **13** (25%) was obtained (Scheme 5). Formation of these heterocycles **7h** and **13** could be explained through a [4 + 2] cycloaddition−cycloreversion process with an initial 1,4 addition of the phosphazene **6k** to the carbonyl carbon atom of cinnamaldehyde **2b** (1,4−1′,2′ addition, Scheme 5) involving the 1,2,5-oxaazaphosphorane intermediate **14** (**INT_{42}**).

This behavior ([4 + 2] cyclization) of the reaction of *N*-vinylic phosphazene **6k** with cinnamaldehyde **2b** toward the observed results ([2 + 2] cycloaddition−cycloreversion) by the reaction of other *N*-vinylic phosphazenes **6f**−**q** with unsaturated aldehydes leads us to study by computational methods both alternatives of this reaction, in other words, the [2 + 2] cycloaddition−cycloreversion sequence versus the [4 + 2] cyclization process, to explain the observed experimental results.

Computational Studies on the Periselectivity of the Reaction of *N*-Vinylic Phosphazenes 6 with α,β-Unsaturated Aldehydes 2. Methods. All of the calculations reported in this paper have been performed in the gas phase within density functional theory,[30] using the hybrid three-parameter functional customarily denoted as B3LYP.[31] The standard 6-31G* basis set[32] as implemented in the GAUSSIAN 98[33] suite of programs has been used in all cases. In a previous work,[20] we have found that this theoretical level is adequate for this particular reaction.

For several selected concerted transformations, synchronicities (Sy)[34] were quantified using a previously described approach.[35,36] According to this method, a value of Sy = 1 indicates a perfectly synchronous reaction, in which bonds are formed and cleaved at the same rate. Similarly, δB_{av} values denote the average degree of advancement of the corresponding transition structures. Thus, $\delta B_{av} < 0.5$ and $\delta B_{av} > 0.5$ indicate early and late transition structures, respectively (see the Supporting Information for additional details).

Donor−acceptor interactions were evaluated using the natural bond orbital (NBO) method.[37]

Nucleus-independent chemical shifts (NICS) as defined by Schleyer[38] were computed at the ring points of electron density[39] using the gauge invariant atomic orbital[40] (GIAO) approach at the GIAO−B3LYP/6-31G*//B3LYP/6-31G* level.

Energy densities at selected bond points of electron density$H(r_b)$[41] were computed to evaluate the nature of the chemical bonds under study. According to this method, if a given

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(33) Gaussian 98, Revision A.5: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1998.
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(35) (a) Moyano, A.; Pericás, M. A.; Valentí, E. *J. Org. Chem.* **1989**, *54*, 573.
(36) (a) Lecea, B.; Arrieta, A.; Roa, G.; Ugalde, J. M.; Cossío, F. P. *J. Am. Chem. Soc.* **1994**, *116*, 9613. (b) Lecea, B.; Arrieta, A.; Lopez, X.; Ugalde, J. M.; Cossío, F. P. *J. Am. Chem. Soc.* **1995**, *117*, 12314.
(37) (a) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899. (b) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735.
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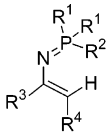
CHART 1



6f-q

	R^1	R^2	R^3	R^4
6f	H	H	H	H
6g	H	H	H	CHO
6h	CH_3	CH_3	H	H
6i	CH_3	CH_3	H	CHO
6j	CH_3	CH_3	H	CO_2CH_3
6k	CH_3	CH_3	CH_3	CO_2CH_3
6l	Ph	Ph	H	CO_2CH_3
6m	Ph	Ph	CH_3	CO_2CH_3
6n	CH_3	Ph	H	CO_2CH_3
6o	CH_3	Ph	CH_3	CO_2CH_3
6p	Ph	CH_3	H	CO_2CH_3
6q	Ph	CH_3	CH_3	CO_2CH_3

interatomic interaction has a negative value of $H(r_b)$, this interaction is covalent in nature, and a positive value of $H(r_b)$ at the corresponding bond critical point indicates an ionic bond (see the Supporting Information for additional details).

Activation energies (ΔE_a) and reaction energies (ΔE_{rxn}) were computed at the B3LYP/6-31G* level including zero-point vibrational energy (ZPVE) corrections, which were not scaled.

In a previous paper, we reported the tandem [2 + 2] cycloaddition−cycloreversion sequence of the aza-Wittig reaction of simple phosphazenes and aldehydes (1,2−1′,2′ addition) as well as the effects of substituents in both phosphazenes and aldehydes.[20] In this work, we extend our study to the reaction between conjugated phosphazenes **6f**−**q** (Chart 1), which present two potential reactivity patterns (1,2- and 1,4 addition) and aldehydes **2a**,**e** (Scheme 6) in order to determine the most favorable process (routes 1 or 2, Scheme 1, vide supra) to yield either 5,6-dihydro-1,3,2-λ^5-oxaazaphosphinines **INT$_{42}$a**−**p** (Chart 2) via [4 + 2] cycloadditions or imines **11k**−**p** (Chart 3) and phosphine oxides **15a**−**e** (Chart 4) via tandem [2 + 2] cycloadditions−cycloreversions, through 1,3,2-λ^5-oxaazaphosphetidine intermediates **INT$_{22}$a**−**p** (Scheme 6).

As model reaction for this study on the periselectivity of the aza-Wittig reaction, we chose the interaction between formaldehyde **2e** and phosphazene **6f** ($H_3P{=}N{-}CH{=}CH_2$). The main features of the transition structures and reaction intermediates located on the B3LYP/6-31G* potential energy surface are reported in Figures 2 and 3.

SCHEME 6. Possible [2 + 2] and [4 + 2] Mechanisms for the Reaction between Phosphazenes 6f−q and Aldehydes 2a,e to Yield either 5,6-Dihydro-1,3,2-λ^5-oxaaza-phosphinines INT$_{42}$a−p or Imines 11k−p and Phosphine Oxides 15a−e via 1,3,2-λ^5-Oxaazaphosphetidines INT$_{22}$a-p

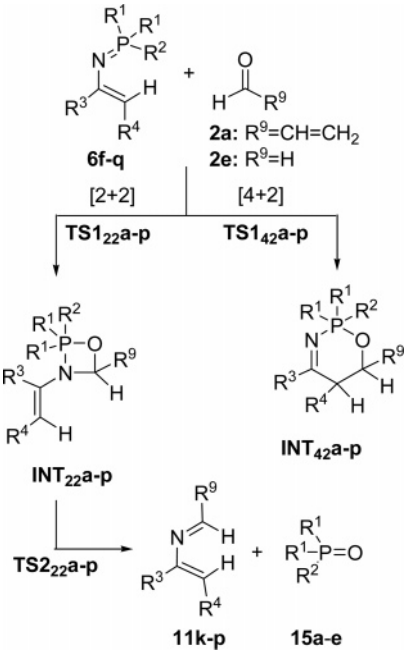
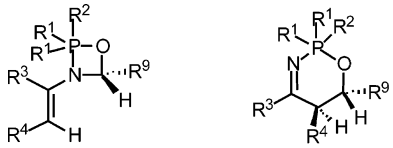


CHART 2



INT$_{22}$a-p **INT$_{42}$a-p**

	R^1	R^2	R^3	R^4	R^9
a	H	H	H	H	H
b	H	H	H	CHO	H
c	CH_3	CH_3	H	H	H
d	CH_3	CH_3	H	CHO	H
e	CH_3	CH_3	H	CHO	$CH{=}CH_2$
f	CH_3	CH_3	H	CO_2CH_3	H
g	CH_3	CH_3	H	CO_2CH_3	$CH{=}CH_2$
h	CH_3	CH_3	CH_3	CO_2CH_3	H
i	CH_3	CH_3	CH_3	CO_2CH_3	$CH{=}CH_2$
j	Ph	Ph	H	CO_2CH_3	H
k	Ph	Ph	CH_3	CO_2CH_3	H
l	CH_3	Ph	H	CO_2CH_3	H
m	CH_3	Ph	CH_3	CO_2CH_3	H
n	CH_3	Ph	CH_3	CO_2CH_3	$CH{=}CH_2$
o	Ph	CH_3	H	CO_2CH_3	H
p	Ph	CH_3	CH_3	CO_2CH_3	H

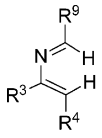
According to our results, the first step of the simplest (2 + 2) reaction between formaldehyde and $H_3P{=}N{-}CH{=}CH_2$ (Figure 3) was found to be quite synchronous (Table 4). In this

(39) (a) Morao, I.; Lecea, B.; Cossío, F. P. *J. Org. Chem.* **1997**, *62*, 7033. (b) Bader, R. F. W. *Atoms in Molecules*−*A Quantum Theory*; Clarendon Press: Oxford, 1990; pp 13−52. According to Bader, a critical point of the electron density is characterized by its (ω,σ) pair of values, ω and σ being the rank and the signature, respectively. The rank is the number of non-zero curvatures of the electron density at the critical point and the signature is the algebraic sum of the signs of these eigenvalues.

(40) Wolinski, K.; Hilton, J. F.; Pulay, P. *J. Am. Chem. Soc.* **1990**, *112*, 8251.

(41) (a) Bader, R. F. W. *Atoms in Molecules*−*A Quantum Theory*; Clarendon Press: Oxford, 1990; pp 276−277. (b) Cremer, D.; Kraka, E. *Croat. Chim. Acta* **1984**, *57*, 1259.

CHART 3



11k-p

	R^3	R^4	R^9
11k	H	H	H
11l	H	CHO	H
11m	H	CHO	$CH=CH_2$
11n	H	CO_2CH_3	H
11o	CH_3	CO_2CH_3	H
11p	CH_3	CO_2CH_3	$CH=CH_2$

CHART 4

15a-e

	R^1	R^2
15a	H	H
15b	CH_3	CH_3
15c	Ph	Ph
15d	CH_3	Ph
15e	Ph	CH_3

case a (3,+1) ring critical point[39] of electron density was located for **TS1$_{22}$a** (Figure 3), thus indicating that, according to the Poincaré−Hopf relationship,[42] there is a (3,−1) bond critical point[39] between the O and P atoms, with a bond order of 0.156. In the corresponding 1,3,2-λ^5-oxaazaphosphetidine intermediate **INT$_{22}$a** this bond order is 0.495, and the negative value of the energy density at this bond point indicates that the P−O bond

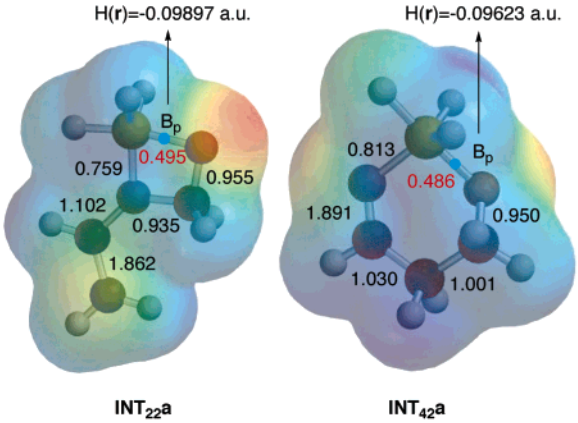


FIGURE 2. Electrostatic potentials of 1,3,2-λ^5-oxaazaphosphetidines **INT$_{22}$a** and 5,6-dihydro-1,3,2-λ^5-oxaazaphosphinine **INT$_{42}$a** projected on the respective electron density surfaces (isocontour value: 0.002 au). Energies range from −12.3 kcal/mol (red) to +12.3 kcal/mol (blue). The Wiberg bond indices are reported on the corresponding bonds. The P−O bond indices are highlighted in red. The P−O (3,−1) bond critical points (Bp) are represented in blue.

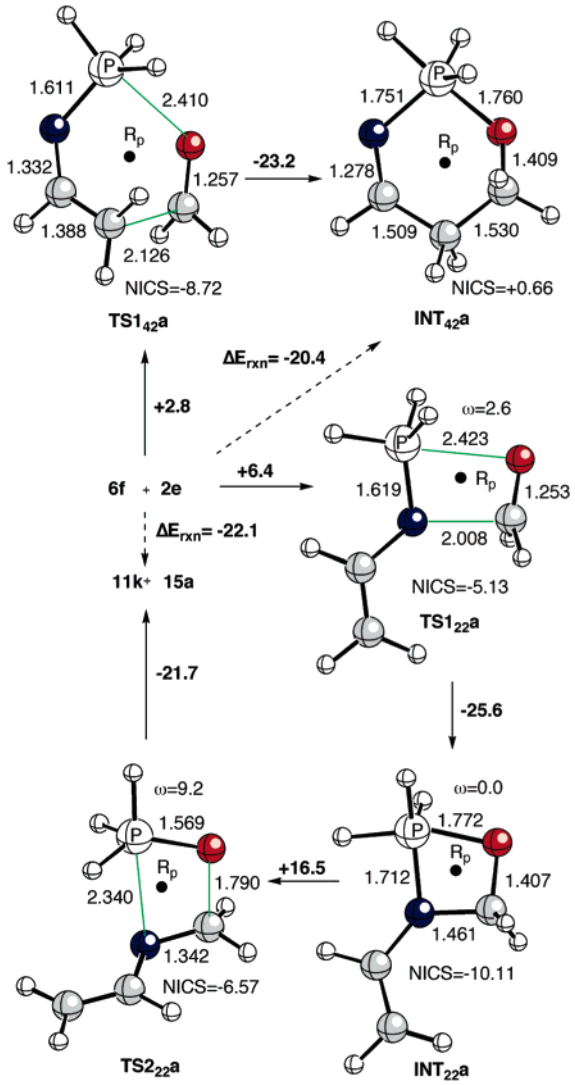


FIGURE 3. Transition structures and reaction intermediates for the reactions depicted in Scheme 6. Fully optimized transition structures and intermediate (B3LYP/6-31G* level of theory) and the reaction profile associated with the **6f** + **2e** → **11k** + **15a** reaction. Bond distances are given in Å. ω (in deg, absolute value) denotes the P−O−C−N dihedral angle. The relative energies (in kcal/mol) have been computed at the B3LYP/6-31G*+ΔZPVE level of theory. NICS (ppm/mol, B3LYP-GIAO/6-31G*//B3LYP/6-31G* level) have been calculated at the corresponding ring points of electron density, denoted as Rp. Nitrogen and oxygen atoms are represented in blue and red, respectively. In transition structures **TS1$_{22}$a**, **TS1$_{42}$a**, and **TS2$_{22}$a**, the green lines denote the bonds being formed.

TABLE 4. Average Bond Index Variation[a] (δB_{av}) and Synchronicities[a] (Sy) of Concerted Transformations Included in Scheme 6

transformation	δB_{av}	Sy
6f + **2e** → **INT$_{22}$a**	0.382	0.83
INT$_{22}$a → **11k** + **15a**	0.572	0.89
6f + **2e** → **INT$_{42}$a**	0.372	0.89

[a] See the Supporting Information for additional details.

is mainly covalent in nature (Figure 2). The next [2 + 2] cycloreversion step was found to be also pseudopericyclic in

(42) Collard, K.; Hall, G. C. *Int. J. Quantum Chem.* **1977**, *12*, 623.

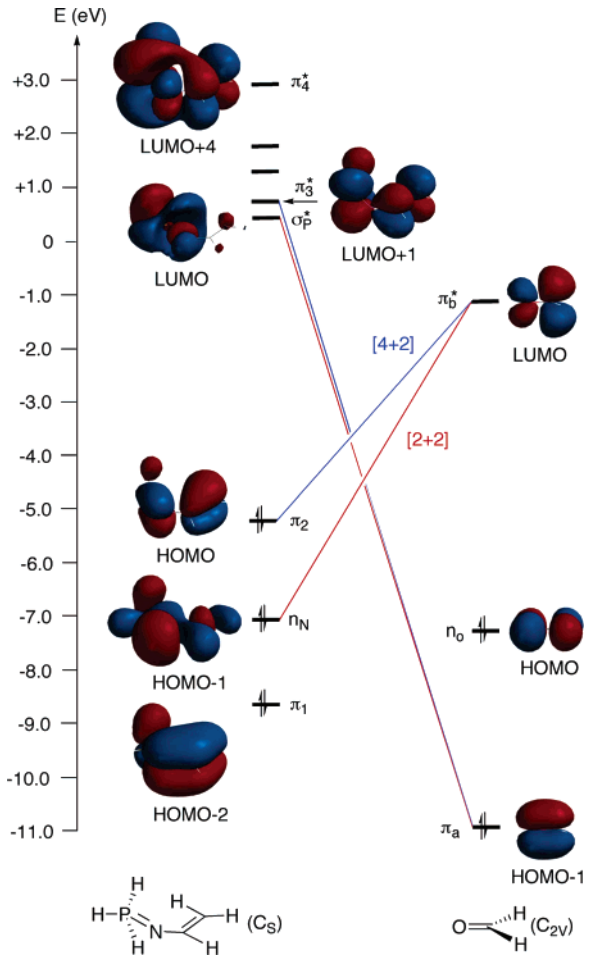


FIGURE 4. Main two-electron orbital interactions associated with the [2 + 2] (red) and [4 + 2] (blue) interactions between phosphazene **6f** and formaldehyde **2e**.

nature,[20] and its activation energy was calculated to be higher than that associated with the first [2 + 2] reaction (Figure 2).

We have also located and characterized a transition structure **TS1$_{42}$a** associated with a [4 + 2] cycloaddition between $H_3P{=}N{-}CH{=}CH_2$ **6f** and formaldehyde **2e**. This saddle point corresponds to a quite synchronous reaction (Table 4) and was found to lie 3.6 kcal/mol below its [2 + 2] analogue. Despite its larger ring size, the calculated NICS at the (3,+1) ring point is larger than that found for **TS1$_{22}$a** (Figure 3), thus indicating a higher aromatic character for this six-electron transition structure. The corresponding 5,6-dihydro-1,3,2-λ^5-oxaazaphosphinine **INT$_{42}$a** was calculated to be nonaromatic. Analysis of the bond orders of this intermediate revealed that it is an authentic [4 + 2] cycloadduct, with a C−N bond order close to 2.0 (Figure 2).

According to our results, there is an intrinsic kinetic preference for the [4 + 2] mechanism with respect to the alternative [2 + 2] tandem cycloaddition−cycloreversion pathway, the thermodynamic preference in favor of the [4 + 2] 5,6-dihydro-1,3,2-λ^5-oxaazaphosphinine cycloadduct being less pronounced (see the corresponding ΔE_{rxn} values in Figure 3). This intrinsic periselectivity can be rationalized by analyzing the main orbital and electrostatic stabilizing interactions operating during the early stages of both cycloaddition pathways.

The preference for the [4 + 2] pathway emerges clearly from inspection of the orbital interactions reported in Figure 4. Thus, in both cycloadditions the main stabilizing interactions take place between occupied MOs of the phosphazene and unoccupied MOs of the carbonyl compound, which acts as an electrophile. The reverse interactions, namely those involving occupied MOs of the carbonyl compound and virtual MOs of the phosphazene, are of lower energy and similar for both the [4 + 2] and [2 + 2] cycloadditions. In the former mechanism, the main interaction requires the overlap between the HOMO of **6f** and the LUMO of **2e**, both MOs being of π-symmetry and close in energy to each other. In contrast, the [2 + 2] mode involves the nucheophilic attack of the nitrogen atom of the phosphazene on the carbon atom of the carbonyl compound. Since the energy gap between the HOMO (**6f**)−LUMO (**2e**) two-electron interaction is lower than that between the [HOMO-1] (**6f**)−LUMO (**2e**) interaction, the [4 + 2] mechanism will be the preferred one.[43]

If electrostatic interactions are considered, the only difference for the two pathways is that, in the case of the [2 + 2] channel, the most important nucleophilic attack takes place in part through the Coulombic interaction between the nitrogen atom of the phosphazene and the sp^2-hybrydized carbon atom of the carbonyl compound. In contrast, in the case of the [4 + 2] reaction, the specific electrostatic interaction takes place between the β-carbon of the phosphazene and the electrophilic *ipso*-carbon of the carbonyl compound. Our computed NBO charge for the nitrogen atom of **6f** is −1.02, whereas that computed for the CH_2 moiety of **6f** is only −0.14, the charge of the PH_3 group being +0.95. Therefore, the orbital preference for the [4 + 2] reaction is in part canceled by the more favorable electrostatic interactions involved in the [2 + 2] reaction. It was therefore expected that electron-withdrawing groups located at the β-position of the phosphazene would result in a different periselectivity in favor of the [2 + 2] pathway. To test this hypothesis, both [2 + 2] and [4 + 2] routes were explored for phosphazenes **6f**−**q** and aldehydes **2a**,**e** as specified in Charts 1−3. The corresponding activation energies are collected in Table 5.

Our results show that inclusion of an electron-withdrawing group such as formyl or methoxycarbonyl results in a significant reduction of the energy gap in favor of the [4 + 2] cycloadduct. For this reason, when phosphazenes **1** derived from triphenylphosphine (see Scheme 2, vide supra) are used, pyridine derivatives **3** and **4** are formed. However, electron-donating groups at the phosphine moiety as well as changing from triphenyl to trimethyl derivatives also reduce this energy difference. Therefore, inclusion of both effects (Table 5, entries 4−7) induces a reversion of the periselectivity in favor of the [2 + 2] cycloaddition, thus surpassing the intrinsic [4 + 2] preference for the unsubstituted case. This trend is maintained regardless the alkyl/aryl substitution pattern at the phosphine moiety (Table 5, entries 10, 12, and 15). These results are in nice agreement with our experimental results (see Scheme 3, vide supra).

Another variable that can be relevant in the periselectivity of the reaction is the substitution at the R3 position. When there is a substituent other than hydrogen at this position, the steric congestion between R3 and R1,2 substituents (Chart 3) is much more important in the case of transition structures associated

(43) For a more detailed quantitative treatment of the relevance of electrostatic (Coulombic) and orbital interactions within the second-order perturbation theory framework, see: Vivanco, S.; Lecea, B.; Arrieta, A.; Prieto, P.; Morao, I.; Linden, A.; Cossío, F. P. *J. Am. Chem. Soc.* **2000**, *122*, 6078.

TABLE 5. Activation Energies[a,b] (ΔE_a, kcal/mol) Associated with Reactions[a,b] Depicted in Scheme 6

							ΔE_a		ΔE_{arel}	
entry	INT	R^1	R^2	R^3	R^4	R^9	[2 + 2]	[4 + 2]	[2 + 2]	[4 + 2]
1	**a**	H	H	H	H	H	6.38	2.78	+3.6	0.00
2	**b**	H	H	H	CHO	H	7.35	6.83	+0.57	0.00
3	**c**	CH_3	CH_3	H	H	H	5.97	2.81	+3.16	0.00
4	**d**	CH_3	CH_3	H	CHO	H	8.83	12.15	0.00	+3.32
5	**e**	CH_3	CH_3	H	CHO	$HC{=}CH_2$	15.91	19.69	0.00	+3.78
6	**f**	CH_3	CH_3	H	CO_2CH_3	H	7.07	9.16	0.00	+2.09
7	**g**	CH_3	CH_3	H	CO_2CH_3	$HC{=}CH_2$	13.84	20.74	0.00	+6.90
8	**h**	CH_3	CH_3	CH_3	CO_2CH_3	H	11.73	7.77	+3.96	0.00
9	**i**	CH_3	CH_3	CH_3	CO_2CH_3	$HC{=}CH_2$	23.48	15.61	+7.87	0.00
10	**j**	Ph	Ph	H	CO_2CH_3	H	10.20	11.91	0.00	+1.71
11	**k**	Ph	Ph	CH_3	CO_2CH_3	H	13.83	8.52	+5.31	0.00
12	**l**	CH_3	Ph	H	CO_2CH_3	H	8.65	10.91	0.00	+2.27
13	**m**	CH_3	Ph	CH_3	CO_2CH_3	H	13.98	9.43	+4.55	0.00
14	**n**	CH_3	Ph	CH_3	CO_2CH_3	$HC{=}CH_2$	22.08	17.56	+4.52	0.00
15	**o**	Ph	CH_3	H	CO_2CH_3	H	9.15	11.46	0.00	+2.31
16	**p**	Ph	CH_3	CH_3	CO_2CH_3	H	12.77	6.46	+6.31	0.00

[a] All energies have been computed at the B3LYP/6-31G* + ΔZPVE level. [b] The [2+2] activation energies are associated with the reaction between phosphazenes **6f**−**q** with aldehydes **2a**,**e** to form intermediates **INT$_{22}$a**−**p**. See Charts 1−5 for the assignation of the R^1−R^4 and R^9 substituents.

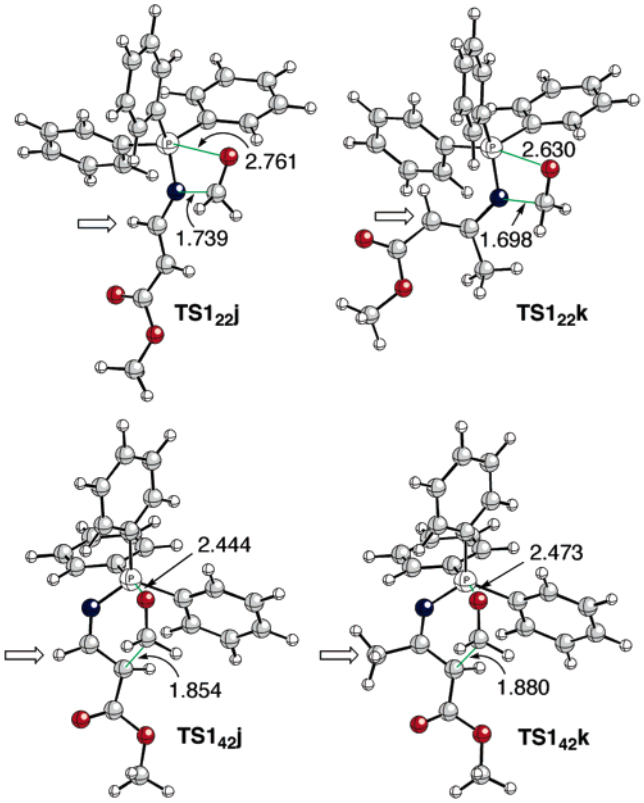


FIGURE 5. Ball and stick representation of transition structures involved in the reaction between phosphazenes **6l**,**m** and formaldehyde **2e**. See Figure 3 caption for additional details. The hollow arrows emphasize the steric effect of substitution at the α-carbon of the phosphazene and the phosphine moiety (see Chart 2).

with [2 + 2] cycloadditions than in the case of those corresponding to [4 + 2] cycloadditions, as can be seen by inspection of Figure 5. Therefore, this additional steric interaction is responsible for the [4 + 2] periselectivity reported in entries 8, 9, 11, 13, and 14 of Table 5. This result is again in agreement with the experimental results (see Scheme 5, vide supra).

Conclusions

We conclude that *N*-vinylic phosphazenes are ambident nucleophilic reagents. The nucleophilic character of the nitrogen atom of *N*-vinylic phosphazenes can be increased when they are derived from diphenylmethylphosphine **6a**,**c**,**e** or trimethylphosphine **6b**,**d,** and they undergo aza-Wittig reaction (1,2 addition) with the carbonyl group of unsaturated aldehydes (1,2 addition) through a [2 + 2] cycloaddition−cycloreversion sequence in a regioselective fashion. However, the presence of an alkyl group in position 3 of *N*-vinylic phosphazenes causes a change of periselectivity, and the process takes place by means of a [4 + 2] cyclization process. Computational studies are in agreement with these experimental findings. According to the computational model reported in this paper, there is an intrinsic preference for the [4 + 2] pathway because the HOMO of the phosphazene is π-symmetric, the HOMO-1 (associated with the [2 + 2] mechanism) being dominated by the lone pair of the nitrogen atom. The presence of electron-withdrawing groups at the β-position of the phosphazene results in a partial preference for the [2 + 2] pathway. Finally, the transition structures leading to the [2 + 2] intermediates are more sensitive to steric effects at the carbon atom contiguous to the nitrogen atom. The combination of these factors explains the different periselectivities observed experimentally for diverse substitution patterns. Azatrienes **11** are intermediates in the preparation of pyridines **7**, **7′** derived from β-amino acids. It is worth noting that pyridine compounds derived from β-amino acids are useful heterocycles not only for their biological activities[44] but also because the pyridine nucleus is a structural unit appearing in many natural products.[45]

Experimental Section

General Procedure for the Preparation of Pyridines 7a−d from Phosphazenes 6. Unsaturated aldehyde **2** (3 mmol) was added to a solution of phosphazene **6a** (0.939 g, 3 mmol) in $CHCl_3$ (6 mL) under N_2, and the mixture was stirred at 60 °C until TLC indicated the disappearance of phosphazene. Evaporation of solvent under reduced pressure afforded an oil which after chromatography purification on silica gel gave the compounds **7**.

(44) For reviews, see: (a) Plunkett, A. O. *Nat. Prod. Rep.* **1994**, *11*, 581. (b) Numata, A.; Ibuka, T. *The Alkaloids*; Brossi, A., Ed.; Academic Press: New York, 1987; Vol. 31. (c) Gould, S. J.; Weinreb, S. M. *Forsch. Chem. Org. Naturist*, **1982**, 4177. (d) Daly, J. L.; Spande, T. F. *Alkaloids. Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1986; Vol. 4, pp 1−274.

(45) For recent reviews, see: (a) Schneider, M. J. *Alkaloids. Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Pergamon: Oxford, 1996; Vol. 10, pp 155−299. (b) Shipman, M. *Contemp. Org. Synth.* **1995**, *2*, 1.

Ethyl 6-Methyl-3-pyridinecarboxylate (7d). The general procedure was followed using crotonaldehyde **2d** (0.246 mL, 3 mmol). The crude oil was chromatographed on silica gel (10:1 hexane/AcOEt) to give 0.153 g (31%) of **7d** as a yellow oil (R_f = 0.30, hexane/AcOEt 2:1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (t, $^3J_{(H,H)}$ = 7.1 Hz, 3H), 2.56 (s, 3H), 4.30 (q, $^3J_{(H,H)}$ = 7.1 Hz, 2H), 7.17 (d, $^3J_{(H,H)}$ = 8.1 Hz, 1H), 8.11 (d, $^3J_{(H,H)}$ = 8.1 Hz, 1H), 9.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 24.5, 61.0, 122.7, 123.4, 137.0, 150.2, 162.8, 165.2; IR (NaCl) 1730; MS (EI) *m*/*z* 165 (M^+, 93). Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.48; H, 6.69; N, 8.47.

General Procedure A for the Preparation of 3-Azatrienes 11. Unsaturated aldehyde **2** (4 mmol) was added to a 0−10 °C solution of phosphazene **6** (4 mmol) in $CHCl_3$ (10 mL) under N_2, and the mixture was stirred at room temperature or warmed at 60 °C until ^{1}H NMR indicated the disappearance of phosphazene. 3-Azatrienes **11** are unstable during distillation and/or chromatography and were used without purification for the following reactions.

General Procedure B for the Preparation of 3-Azatrienes 11. Unsaturated aldehyde **2** (4 mmol) was added to a 0−10 °C solution of phosphazene **6** (4 mmol), prepared "in situ" in $CHCl_3$ (10 mL) under N_2, and the mixture was stirred at room temperature until ^{1}H NMR indicated the disappearance of phosphazene. 3-Azatrienes **11** are unstable during distillation and/or chromatography and were used without purification for the following reactions.

1-Ethoxycarbonyl-3-azahepta-1,3,5-triene (11d). General procedure A was followed using phosphazene **6a** (1.252 g, 4 mmol) and crotonaldehyde **2d** (0.328 mL, 4 mmol) (room temperature/24 h): ^{1}H NMR (300 MHz, $CDCl_3$) of crude reaction mixture (**11d** + Ph_2MePO) δ 1.23 (t, $^3J_{(H,H)}$ = 7.2 Hz, 3H), 1.92 (dd, $^4J_{(H,H)}$ = 1.2 Hz, $^3J_{(H,H)}$ = 6.7 Hz, 3H), 1.96 (d, $^3J_{(H,H)}$ = 13.0 Hz, 3H), 4.15 (q, $^3J_{(H,H)}$ = 7.2 Hz, 2H), 6.00 (d, $^3J_{(H,H)}$ = 13.1 Hz, 1H), 6.33 (ddd, $^4J_{(H,H)}$ = 1.2 Hz, $^3J_{(H,H)}$ = 15.3 Hz, $^3J_{(H,H)}$ = 9.0 Hz, 1H), 6.48 (dq, $^3J_{(H,H)}$ = 6.7 Hz, $^3J_{(H,H)}$ = 15.3 Hz, 1H), 7.36−7.74 (m, 11H), 7.95 (d, $^3J_{(H,H)}$ = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) of crude reaction mixture (**11d** + Ph_2MePO) δ 14.0, 16.5 (d, $^1J_{(P,C)}$ = 74 Hz), 18.8, 60.0, 117.8, 128.3−134.5, 147.4, 153.7, 155.5, 166.8, 169.4. General procedure B was followed using phosphazene **6b** (4 mmol), prepared "in situ", and 0.328 mL (4 mmol) of crotonaldehyde **2d** (room temperature/5 h): ^{1}H NMR (300 MHz, $CDCl_3$) of crude reaction mixture (**11d** + Me_3PO) δ 1.23 (t, $^3J_{(H,H)}$ = 7.2 Hz, 3H), 1.47 (d, $^2J_{(P,H)}$ = 12.8 Hz, 9H), 1.92 (dd, $^4J_{(H,H)}$ = 1.2 Hz, $^3J_{(H,H)}$ = 6.7 Hz, 3H), 4.15 (q, $^3J_{(H,H)}$ = 7.2 Hz, 2H), 6.00 (d, $^3J_{(H,H)}$ = 13.1 Hz, 1H), 6.33 (ddd, $^4J_{(H,H)}$ = 1.2 Hz, $^3J_{(H,H)}$ = 15.3 Hz, $^3J_{(H,H)}$ = 9.0 Hz, 1H), 6.48 (dq, $^3J_{(H,H)}$ = 6.7 Hz, $^3J_{(H,H)}$ = 15.3 Hz, 1H), 7.68 (d, $^3J_{(H,H)}$ = 13.1 Hz), 7.95 (d, $^3J_{(H,H)}$ = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) of crude reaction mixture (**11d** + Me_3PO) δ 14.0, 17.8 (d, $^1J_{(P,C)}$ = 70 Hz), 18.8, 60.0, 117.8, 147.4, 153.7, 155.5, 166.8, 169.4.

General Procedure for the Preparation of Pyridines 7a−g from 3-Azatrienes 11. The same unsaturated aldehyde **2** (3 mmol), used for the preparation of 3-azatriene **11**, was added to a 0−10 °C solution of 3-azatriene **11**, prepared "in situ" in anhydrous $CHCl_3$ (10 mL) under N_2, and the mixture was stirred at 60 or 90 °C until ^{1}H NMR indicated the disappearance of 3-azatriene **11**. Evaporation of solvent under reduced pressure afforded an oil that was chromatographed on silica gel.

Ethyl 6-Methyl-2-phenyl-3-pyridinecarboxylate (7e). The general procedure was followed using 3-azatriene **11e** and crotonaldehyde **2d** (0.246 mL, 3 mmol). The mixture reaction was stirred at 90 °C during 62 h. The crude oil was chromatographed on silica gel (10:1 hexane/AcOEt) to give 0.398 g (55%) of **7e** as a brown oil (R_f = 0.49, hexane/AcOEt 2:1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, $^3J_{(H,H)}$ = 7.2 Hz, 3H), 2.56 (s, 3H), 4.03 (q, $^3J_{(H,H)}$ = 7.2 Hz, 2H), 7.10 (d, $^3J_{(H,H)}$ = 7.9 Hz, 1H), 7.19−7.85 (m, 5H), 7.93 (d, $^3J_{(H,H)}$ = 7.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5, 24.6, 61.1, 121.1, 124.3, 126.0, 128.2, 128.4, 138.1, 140.5, 158.6, 160.6, 168.0; IR (NaCl) 1726; M/S (EI) *m*/*z* 241 (M^+, 86). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81. Found: C, 74.75; H, 6.25; N, 5.80.

Preparation of a Mixture of Pyridines 7b and 7′a from 3-Azatriene 11b. Cinnamaldehyde **2b** (0.378 mL, 3 mmol) and crotonaldehyde **2d** (0.250 mL, 3 mmol) were added to a 0−10 °C solution of 3-azatriene **11b** (3 mmol) in $CHCl_3$ (10 mL) under N_2, and the mixture was stirred at 60 °C during 50 h until ^{1}H NMR indicated the disappearance of 3-azatriene. Evaporation of solvent under reduced pressure afforded an oil that was chromatographed on silica gel to give the compounds **7b** and **7′a** (10:1 hexane/AcOEt).

Ethyl 6-Phenyl-3-pyridinecarboxylate (7b). A 0.102 g (15%) portion of **7b** was obtained as a brown oil (see the spectroscopic data in the Supporting Information).

Ethyl 6-Methyl-3-pyridinecarboxylate (7′a). A 0.149 g (30%) portion of **7′a** were obtained as a yellow oil (see the spectroscopic data for the pyridine **7d**).

General Procedure the Preparation of Pyridines 7′. The excess of unsaturated aldehyde **2**, used for the preparation of the 3-azatriene **11** (3 mmol), was eliminated by reduced pressure from the mixture, and then 10 mL of $CHCl_3$ and 3 mmol of a different aldehyde **2** were added to a 0−10 °C solution of azatriene **11**. The mixture was stirred at 60 or 90 °C until ^{1}H NMR indicated the disappearance of 3-azatriene. Evaporation of solvent under reduced pressure afforded an oil that was chromatographed on silica gel to give the compounds **7′**.

Ethyl 2-Phenyl-3-pyridinecarboxylate (7′d). The general procedure was following using 3-azatriene **11f** and acrolein **2a** (0.201 mL, 3 mmol), and the mixture was stirred at 90 °C for 36 h. Evaporation of solvent under reduced pressure afforded an oil which was chromatographed on silica gel (20:1 hexane/AcOEt) to give 0.552 g (81%) of **7′d** as a yellow oil (R_f = 0.43, hexane/AcOEt 2:1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, $^3J_{(H,H)}$ = 7.2 Hz, 3H), 4.07 (q, $^3J_{(H,H)}$ = 7.2 Hz, 2H), 7.24 (dd, $^3J_{(H,H)}$ = 4.7 Hz, $^3J_{HH}$= 7.8 Hz, 1H), 7.32−7.50 (m, 5H), 8.02 (dd, $^3J_{(H,H)}$ = 7.8 Hz, $^4J_{(H,H)}$ = 1.7 Hz, 1H), 8.68 (dd, $^3J_{(H,H)}$ = 4.7 Hz, $^4J_{(H,H)}$ = 1.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5, 61.3, 121.4, 127.3, 127.7−128.4, 137.6, 140.1, 151.0, 158.7, 167.9; IR (NaCl) 1720; M/S (EI) *m*/*z* 227 (M^+, 10). Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.05; H, 5.76; N, 6.16.

Reaction of Phosphazene 6k and Cinnamaldehyde 2b. Cinnamaldehyde **2b** (0.378 mL, 3 mmol) was added to a 0−10 °C solution of phosphazene **6k**, prepared "in situ" (3 mmol), in $CHCl_3$ (10 mL). The mixture was stirred at 60 °C during 2 h. Evaporation of solvent under reduced pressure afforded an oil that was chromatographed (5:1 hexane/AcOEt) to give compounds **7h** and **13**.

Methyl 2-Methyl-6-phenyl-3-pyridinecarboxylate (7h). A 0.219 g (30%) portion of **7h** was obtained as a yellow oil (R_f = 0.55, hexane/AcOEt 2:1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.85 (s, 3H), 3.86 (s, 3H), 7.35−7.51 (m, 3H), 7.56 (d, $^3J_{(H,H)}$ = 8.3 Hz, 1H), 7.99 (d, $^3J_{(H,H)}$ = 7.3 Hz, 2H), 8.19 (dd, $^3J_{(H,H)}$ = 8.3 Hz, $^3J_{(H,H)}$ = 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.2, 52.1, 117.3, 123.3, 127.3, 128.8, 129.7, 138.5, 139.3, 159.2, 160.1, 167.0; IR (NaCl) 1723; M/S (EI) *m*/*z* 243 (M^+, 15). Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.02; H, 5.76; N, 6.15.

Dimethyl 2,6-Dimethyl-4-phenylethenyl-1,4-dihydro-3,5-pyridinedicarboxylate (13). A 0.245 g (25%) portion of **13** was obtained as a yellow solid: mp 169−170 °C (recrystallized from AcOEt/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.27 (s, 6H), 3.66 (s, 6H), 4.54 (m, 1H), 5.59 (s, 1H), 6.10−6.17 (m, 2H), 7.09−7.27 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 36.2, 51.1, 101.4, 126.3−131.7, 137.7, 145.1, 167.9; IR (KBr) 3334, 1698, 1649; M/S (EI) *m*/*z* 327 (M^+, 56). Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.68; H, 6.49; N, 4.27.

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Supporting Information Available: General methods, experimental details for phosphazenes **6b**,**d**,**f**, 3-azatrienes **11a**−**c**,**e**−**i**,pyridine **8**, pyridines **7a**−**c**,**f**,**g**, and pyridines **7′b**,**c**. Computational methods and tables including the total energies (hartrees), the zero-point vibrational energies (hartrees/particle), and the Cartesian coordinates (Å) of all of the stationary points discussed in the text. This material is available free of charge via the Internet at http://pubs.acs.org.

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