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Reaction of C-Silylated α-Diazophosphines as Nucleophiles toward Carbonyl Compounds: A Mechanistic Study and Application to the Synthesis of Alkynes and α-Hydroxyphosphonamides§

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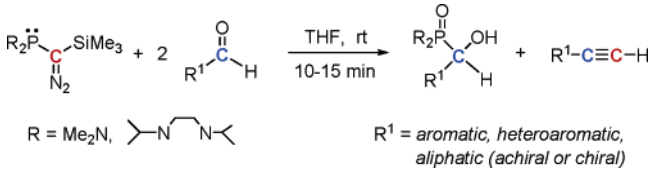

Diversely substituted α-hydroxyphosphonamides and alkynes have been efficiently synthesized through the reaction of C-silylated α-diazophosphines with different types of aldehydes (2 equiv) in a neutral medium under very mild conditions. The reaction with some chiral aldehydes is highly diastereoselective leading to phosphonamides as single diastereomers. The novel reaction is influenced by electronic and steric effects being precluded for aromatic aldehydes containing electron-releasing substituents on the phenyl ring and for bulky aliphatic aldehydes. The mechanistic studies of these processes, which are highly exothermic, provide evidence for a nucleophilic attack of the diazophosphine to the aldehyde leading to a betaine that rapidly rearranges to a diazomethylenephosphorane, which has been detected or captured in some instances. The diazomethylenephosphorane reacts with a second molecule of aldehyde according to a Wittig-type condensation, and the rate-determining step of the whole process is believed to be the decomposition of the resultant oxaphosphetane to afford the hydroxyphosphonamide and a diazocumulene. Finally, this intermediate loses molecular nitrogen giving a transient carbene that rapidly evolves toward the alkyne.

Introduction

The transformation of a carbonyl into an ethynyl moiety is a valuable tool in organic synthesis and was first developed by Corey in 1972 according to a two-step procedure that involves the formation of an intermediate 1,1-dibromoalkene.[1] Later, homologation of aldehydes and ketones into alkynes with one more carbon has been accomplished by treatment of the anion of trimethylsilyldiazomethane[2] or dimethylphosphonodiazomethane[3] via a Peterson and Horner−Wadsworth−Emmons-type reaction, respectively. This affords a transient diazocumulene **C**,[4] which upon loss of nitrogen rearranges into the corresponding alkyne (Scheme 1). Despite recent improvements of the original methodology,[5] all the reported procedures require the use of a base.

In this regard, the need for a nonionic Wittig equivalent of reagents **A** and **B** appears evident. Although tertiary phosphines do not usually react with carbonyl compounds,[6] Morton and Neilson reported, in 1982, the reactions of (silylamino)phos-

§ Dedicated to Professor Marcial Moreno-Mañas in memoriam.
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(1) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

(2) (a) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Chem. Commun.* **1973**, 151. (b) Ohira, S.; Okai, K.; Moritani, T. *J. Chem. Soc., Chem. Commun.* **1992**, 721. (c) Miwa, K.; Aoyama, T.; Shiori, T. *Synlett* **1994**, 107.

(3) (a) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Perkin Trans. 1* **1977**, 869. (b) Gilbert, J. C.; Weerasoriya, U. *J. Org. Chem.* **1979**, *44*, 4997. (c) Gilbert, J. C.; Weerasoriya, U. *J. Org. Chem.* **1982**, *47*, 1837. (d) Ohira, S. *Synth. Commun.* **1989**, *19*, 561.

(4) So far, the only spectroscopically characterized compound of type **C**, namely, difluorodiazoethene, appeared to be stable only up to 11 K. Brahms, J. C.; Dailey, W. P. *J. Am. Chem. Soc.* **1990**, *112*, 4046.

(5) (a) Muller, S.; Liepold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521. (b) Roth, G. J.; Liepold, B.; Muller, S. G.; Bestmann, H. J. *Synthesis* **2004**, 59.

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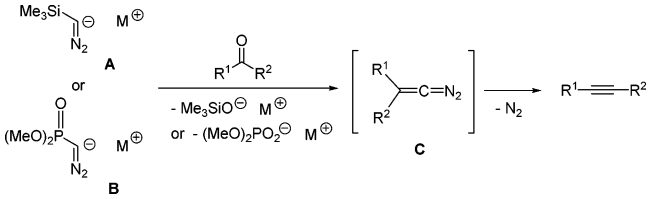
SCHEME 1



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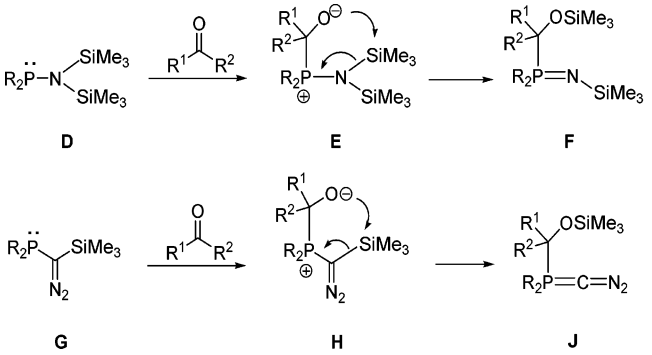
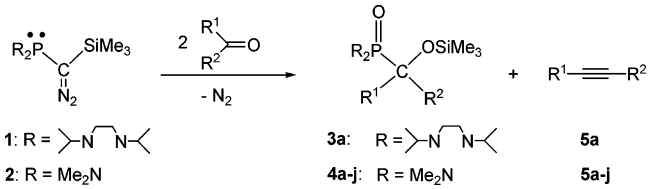


phines **D** with ketones and aldehydes to yield phosphinimines **F**.[7] Despite the lack of mechanistic evidence, the authors explained the formation of phosphinimines **F** through the phosphorus nucleophilic attack to the carbonyl carbon followed by migration of the trimethylsilyl group from nitrogen to oxygen in the betaine **E** and concomitant formation of the N=P double bond (Scheme 2).

Diazoalkanes react rarely with carbonyl compounds, and only a few examples on methylenation[8] or 1,3-dipolar cycloaddition[9] have been reported. Therefore, in the case of phosphino(silyl)diazoalkanes **G**, one would expect that the nucleophilic attack of phosphorus to the carbonyl could compete advantageously with the dipole behavior. Thus, this could constitute an original synthetic approach to halogen-free diazomethylenephosphoranes **J**.[10]

Usually, α-diazophosphines do not react with aldehydes or ketones. For instance, bis(diisopropylamino)phosphinodiazomethane reacts, only as a dipole, with electron-deficient olefins.[11,12] The absence of reactivity of the phosphine center is probably due to the steric protection of the phosphorus lone pair provided by the bulky diisopropylamino substituents.

SCHEME 3



Therefore, to exalt the P-nucleophilicity, we decided to investigate the reactivity of α-diazophosphines, bearing smaller substituents at the phosphorus center, with several carbonyl compounds to document generality. We report herein the one-pot reaction of two C-silylated α-diazophosphines with carbonyl derivatives to afford alkynes with chain extension, as well as α-hydroxyphosphonamides, in high yields. Both types of products have been prepared by using nonionic reagents in a neutral medium and are useful synthetic intermediates. For instance, hydroxyphosphonamides have been used in the preparation of biologically active compounds,[13] and the synthetic potential of acetylene derivatives is well-known. The mechanism of the whole process has been investigated, and theoretical calculations have been performed to rationalize some insights of the multistep reaction.

Results and Discussion

1. Reactions of C-Silylated α-Diazophosphines with Carbonyl Compounds. When 2 equiv of carbonyl compound was added to a pentane or THF solution of α-diazophosphines **1**[14] or **2**,[10b] at room temperature, spontaneous and sometimes very exothermic reactions with loss of nitrogen gas were observed. The reactions were monitored by ^{31}P NMR spectroscopy following the concomitant disappearance of a peak at 100 ppm and the appearance of a new signal at 30−35 ppm and were complete in 10−15 min. In all cases, a mixture of phosphonamides (**3** and **4**) and the corresponding alkynes **5a**−**j** were produced in good yields. Although the high volatility and low polarity of some alkynes rendered their isolation difficult, products could be isolated and purified by distillation and/or by column chromatography and were fully characterized (Scheme 3, Table 1). The scope of this reaction is very broad because a variety of alkyl-, aryl-, and heteroaryl-substituted aldehydes are efficiently transformed into the corresponding phosphonamides and homologous alkynes. Steric and electronic factors play an important role in the reaction progress. Thus, sterically hindered pivalaldehyde was converted only in 50% after 30 h, and less electrophilic *p*-dimethylaminobenzaldehyde did not react at all. Activated ketones, such as 1,1,1-trifluoroacetone, also reacted affording products in satisfactory yields. The asymmetric version was achieved by the reactions of diazophosphine **2** with D-glyceraldehyde acetonide and two aldehydes derived from (−)-verbenone and (−)-pinene, respectively,[15] affording acetylene derivatives **5h**−**j** with a stereogenic

(6) Although several examples are reported in the literature on the reactivity of the trivalent phosphorous as a nucleophile, only a few instances are described on the nucleophilic reaction of a phosphine with a carbonyl compound. See, for instance: (a) Mark, M. *J. Am. Chem. Soc*. **1963**, *85*, 1884. (b) Emsley, J.; Hall, D. *The Chemistry of Phosphorous*; Halsted Press: New York, 1976; Chapter 4.

(7) Morton, D. W.; Neilson, R. H. *Organometallics* **1982**, *1*, 289.

(8) (a) Hagen, S.; Kilaas, L.; Lwande, W.; Anthonsen, T. *Carbohydr. Res*. **1981**, *89*, 163. (b) Díaz, M.; Branchadell, V.; Oliva, A.; Ortuño, R. M. *Tetrahedron* **1995**, *51*, 11841. (c) Kovtonyuk, V. N.; Kobrina, L. S.; Bagryanskaya, I. Y.; Gatilov, Y. V. *Russ. J. Org. Chem*. **1999**, *35*, 67.

(9) (a) Saladino, R.; Satassi, L.; Crestini, C.; Nicoletti, R.; Botta, M. *Tetrahedron* **1997**, *53*, 7045. (b) Boukamcha, N.; Gharbi, R.; Martin, M. T.; Chiaroni, A.; Mighri, Z.; Khemiss, A. *Tetrahedron* **1999**, *55*, 449.

(10) For works on diazomethylene(halogeno)phosphoranes, see: (a) Sotiropoulos, J. M.; Baceiredo, A.; Bertrand, G. *J. Am. Chem. Soc*. **1987**, *109*, 4711. (b) Sotiropoulos, J. M.; Baceiredo, A.; Bertrand, G. *Bull. Soc. Chim. France* **1992**, *129*, 367. (c) Baceiredo, A.; Nieger, M.; Niecke, E.; Bertrand, G. *Bull. Soc. Chim. France* **1993**, *130*, 757. (d) Dubau-Assibat, N.; Baceiredo, A.; Dahan, F.; Bertrand, G. *Bull. Soc. Chim. France* **1995**, *132*, 1139. (e) Bourissou, D.; Bertrand, G. *C. R. Acad. Sci. Paris* **1996**, *322*, 489.

(11) Kato, T.; Gornitzka, H.; Baceiredo, A.; Savin, A.; Bertrand, G. *J. Am. Chem. Soc*. **2000**, *122*, 998.

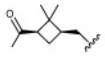
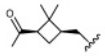
(12) Illa, O.; Muray, E.; Amsallem, D.; Moglioni, A. G.; Gornitzka, H.; Branchadell, V.; Baceiredo, A.; Ortuño, R. M. *Tetrahedron: Asymmetry* **2002**, *13*, 2593.

(13) (a) Blazis, V. J.; Koeller, K. J.; Spilling, C. D. *J. Org. Chem*. **1995**, *60*, 931. (b) Cermak, D. M.; Du, Y.; Wiemer, D. F. *J. Org. Chem*. **1999**, *64*, 388.

(14) Krysiak, J.; Lyon, C.; Baceiredo, A.; Gornitzka, H.; Mikolajczyk, M.; Bertrand, G. *Chem.−Eur. J*. **2004**, *10*, 1982.

(15) Moglioni, A. G.; García-Expósito, E.; Aguado, G. P.; Parella, T.; Branchadell, V.; Moltrasio, G. Y.; Ortuño, R. M. *J. Org. Chem*. **2000**, *65*, 3934.

TABLE 1. Isolated Yield (%), Enantiomeric Excess, (ee, %), and Diastereomeric Excess (de, %) for Products 3a, 4a−j, and 5a−j

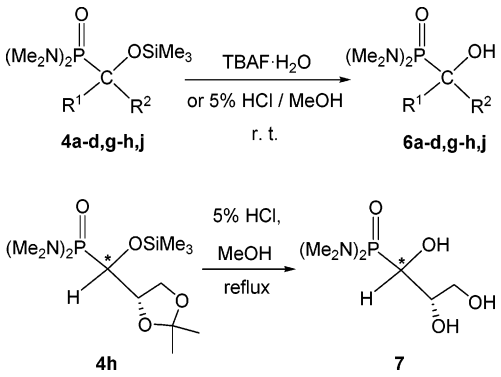
R^1	R^2	Compound	Yield	ee[a]	de[b]
H	Ph	**3a**	90		
H	Ph	**4a**	97		
H	Ph	**5a**	45		
H	*p*-NO_2-C_6H_4	**4b**	70		
H	*p*-NO_2-C_6H_4	**5b**	44		
H	furan-3-yl	**4c**	93		
H	furan-3-yl	**5c**	40		
H	pyridin-3-yl	**4d**	91		
H	pyridin-3-yl	**5d**	46		
H	Me	**4e**	91		
H	Me	**5e**	<10[c]		
H	^{t}Bu	**4f**	30		
H	^{t}Bu	**5f**	14[c]		
CF_3	Ph	**4g**	87		
CF_3	Ph	**5g**	50		
H		**4h**	91	>99.5	>99.5
H		**5h**	62	>99.5	
H		**4i**	92	95	>99.5
H		**5i**	67	95	
H		**4j**	80	97	<5
H		**5j**	47	97	

[a] The enantiomeric excess for products was limited by 95% ee and 97% ee for commercial precursors (−)-verbenone and (−)-pinene, respectively. [b] Determined by ^{1}H and ^{13}C NMR. [c] Extremely volatile compound that is difficult to isolate.

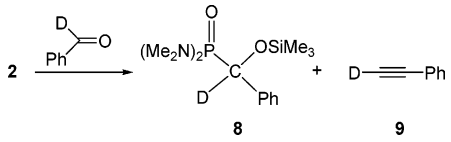
center at the propargyllic position. Diastereoselectivity in the production of phosphonamides **4h**,**i** was total, and consequently, these products were obtained as single diastereomers. Nevertheless, phosphonamide **4j** was obtained as a 1:1 mixture of diastereomers due to a larger distance from the carbonyl to the stereogenic centers in the reactant aldehyde.[16]

The silyl ether group was often totally or partially removed during the purification process of the phosphonamides. The corresponding alcohols **6** could be easily obtained by treatment of the silyl ethers **4** with TBAF hydrate or, alternatively, with 5% HCl in methanol. Compound **4h** was also transformed into triol **7** under HCl-catalyzed methanolysis (Scheme 4). Unfortunately, alcohols **6h** and **7**, as well as compounds **4h**−**j**, did not afford crystals suitable for X-ray diffraction analysis precluding the unambiguous configuration assignment to the new stereogenic center in these products.

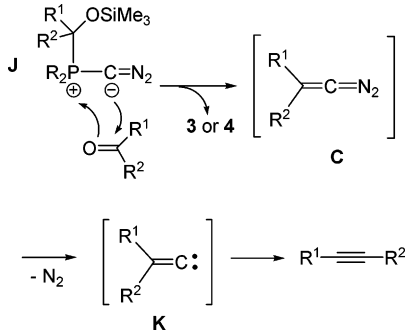
SCHEME 4



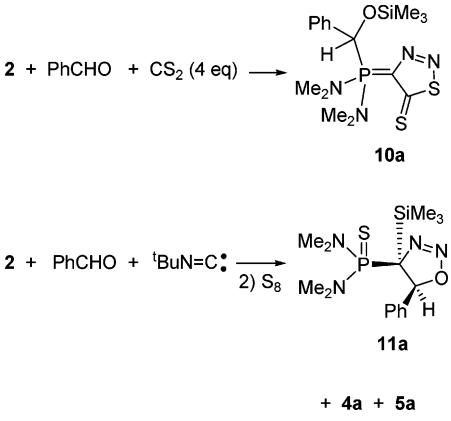
SCHEME 5



SCHEME 6



SCHEME 7



2. Mechanistic Studies. The concomitant formation of phosphonamides and acetylene derivatives is in good agreement with the proposed mechanistic pathway shown in Scheme 2. Moreover, when the reaction of **2** with deuterated benzaldehyde was carried out, phosphonamide **8** and deuterated phenylacetylene **9** were obtained thus showing the origin of the alkyne hydrogen atom (Scheme 5).

(16) For stereochemical induction in similar substrates, see: (a) Moglioni, A. G.; García-Expósito, E.; Álvarez-Larena, Á.; Branchadell, V.; Moltrasio, G. Y.; Ortuño, R. M. *Tetrahedron: Asymmetry*, **2000**, *11*, 4903. (b) Aguado, G. P.; Moglioni, A. G.; García-Expósito, E.; Branchadell, V.; Ortuño, R. M. *J. Org. Chem.* **2004**, *69*, 7971.

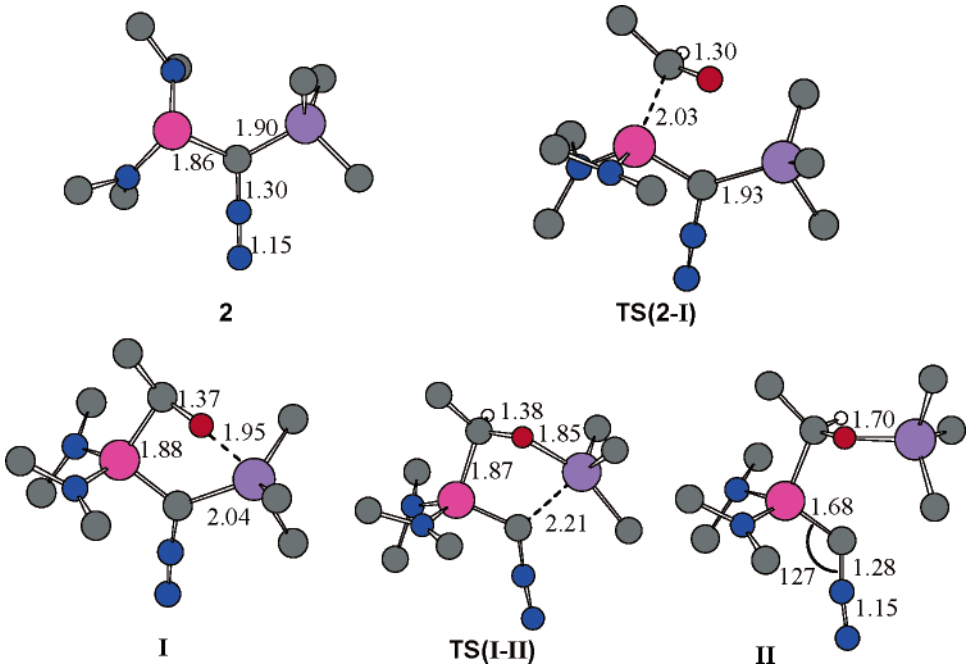


FIGURE 1. Structure of B3LYP/6-31G(d) stationary points corresponding to the reaction between **2** and acetaldehyde. Interatomic distances in Å and bond angles in degrees. Hydrogens of methyl groups have been omitted for clarity.

The transient formed diazomethylenephosphoranes of type **J** undergo a Wittig reaction with a second equivalent of carbonyl compound leading to phosphonamides and transient diazocumulenes **C**, which are known to be unstable with respect to nitrogen extrusion giving the corresponding alkynes (Scheme 6).[17] Moreover, reaction of **2** with only 1 equiv of benzaldehyde yielded **4a** and **5a** along with recovered starting materials. This result indicates that reaction of the aldehyde with diazomethylenephosphorane **J**, as a C-nucleophile, is much faster than reactions with the diazophosphine as a P-nucleophile.

This is the first example in which transient diazomethylenephosphoranes are able to transfer a "CN_2" fragment via a Wittig-type reaction.[18] However, when the reaction of **2** with benzaldehyde was performed in the presence of 4 equiv of carbon disulfide, diazomethylenephosphorane **J** (R^1 = H, R^2 = Ph) was quantitatively captured leading to the [2+3]-cycloadduct **10a**. In this case, the behavior of **J** as a 1,3-dipole prevailed over its C-nucleophilicity (Scheme 7).

One last point remained unclear. Extrusion of nitrogen from diazocumulene **C** to produce the alkyne could occur concomitant to the hydrogen 1,2-migration or could generate an unsaturated carbene **K** that, upon rearrangement, would lead to the alkyne. Diazoalkene **C** could not be converted into the corresponding enamine when the reaction of **2** with benzaldehyde was carried out in the presence of an excess of diisopropylamine. This result is in agreement with the work previously reported by Aoyama and Shioiri.[19] Moreover, trapping of the hypothetical carbene was attempted by reaction of **2** with benzaldehyde (2 equiv) in the presence of 2 equiv of *tert*-butylisonitrile. However, the expected adduct between carbene and *tert*-butylisonitrile was not observed. Instead, a mixture of **4a**, **5a**, and compound **11a** was obtained. Heterocycle **11a** was isolated, as a single isomer, in 35% yield and results from the 1,3-dipolar cycloaddition of **2** to the carbonyl of benzaldehyde (Scheme 7). A similar result was found by using a large excess of *tert*-butylisonitrile. Then, we could conclude that hydrogen migration from **K** (R^1 = H) must be very fast.

(17) (a) Stang, P. J. *Acc. Chem. Res*. **1982**, *15*, 348. (b) Gilbert, J. C.; Giamalva, D. H. *J. Org. Chem*. **1992**, *57*, 4185.

(18) Diazomethylene(halogeno)phosphoranes, in contrast, have been shown not to behave as Wittig-type reagents.[10]

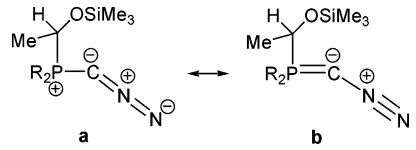
(19) Miwa, K.; Aoyama, T.; Shioiri, T. *Synlett* **1994**, 109. These authors describe the formation of enamines from diazoalkenes **C** with R^1, R^2 = alkyl, but the alkyne was the only identified product when R^1 or R^2 = H.

TABLE 2. Energies and Gibbs Energies[a] Corresponding to the Stationary Points[b] of the Reaction between 2 and Acetaldehyde

	ΔE	ΔG^c
TS(2-I)	17.7	33.4 (30.8)
I	15.6	32.1 (29.0)
TS(I-II)	16.3	33.4 (30.8)
II	−3.7	12.4 (10.4)

[a] Relative to reactants at the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) level. In kcal mol^{-1}. [b] See Figure 1. [c] Values in THF solution are in parentheses.

SCHEME 8



3. Theoretical Calculations. To rationalize the obtained results and to better understand the whole process, we have studied, by means of theoretical calculations, the reaction between **2** and acetaldehyde, which is the simplest aldehyde used in experiments. Figure 1 shows the stationary points corresponding to the nucleophilic attack of **2** to acetaldehyde, and relative energies and Gibbs energies are presented in Table 2.

The first step of the reaction leads to the formation of betaine **I**, which is stabilized through the donation from an O lone pair to an empty σ^*(Si−C) orbital. The computed bond index between O and Si is 0.316. **I** is very unstable and evolves to the diazomethylenephosphorane **II** with a very low energy barrier. This intermediate presents a bent P−C−N_2 arrangement.

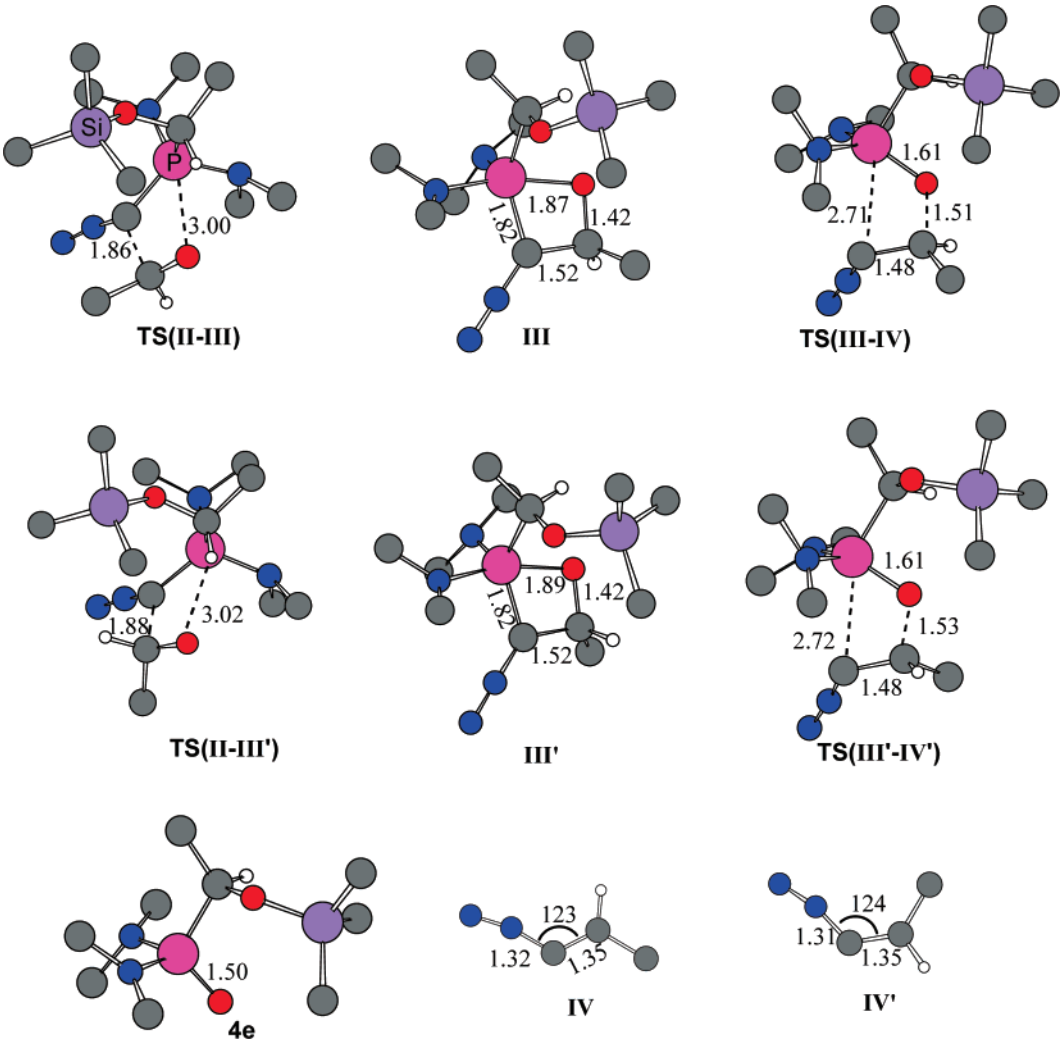


FIGURE 2. Structure of B3LYP/6-31G(d) stationary points corresponding to the reaction between **II** and acetaldehyde. Interatomic distances in Å and bond angles in degrees. Hydrogens of methyl groups have been omitted for clarity.

The computed bond indexes are 1.226 (P−C), 1.490 (C−N), and 2.232 (N−N) pointing to a major contribution of mesomer **a** (Scheme 8).

The diazomethylenephosphorane **II** reacts with a second acetaldehyde molecule in a Wittig-type reaction.[20] The structures of the stationary points associated to this process are shown in Figure 2, and the corresponding relative energies and Gibbs energies are presented in Table 3.

The first step of this process leads to the formation of an oxaphosphetane intermediate. Depending on the relative disposition of the methyl and CHMeOTMS groups, there are two possible isomers for this intermediate, cis and trans. The trans isomer (**III′**) is energetically more favorable than the cis one (**III**), but the situation is reversed when Gibbs energies are considered. This second step corresponds to the rate-determining transition state of this Wittig reaction. The reaction products are the phosphonamide **4e** and diazocumulene **IV** or **IV′**.

TABLE 3. Energies and Gibbs Energies[a] Corresponding to the Stationary Points[b] of the Reaction between II and Acetaldehyde

	ΔE	ΔG^c
TS(II-III)	8.9	24.5 (22.0)
III	0.3	17.1 (18.4)
TS(III-IV)	11.9	27.8 (23.1)
IV + 4e	−25.4	−24.2 (−23.4)
TS(II-III′)	8.3	23.9 (22.3)
III′	−0.2	17.2 (19.7)
TS(III′-IV′)	11.5	27.9 (23.9)
IV′ + 4e	−24.4	−23.1 (−22.4)

[a] Relative to reactants at the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) level. In kcal mol^{-1}. [b] See Figure 2. [c] Values in THF solution are in parentheses.

The P of oxaphosphetanes **III** and **III′** is in a trigonal bipyramidal environment, with the oxygen atom in an apical position. During the oxaphosphetane evolution to **4e**, there is a rearrangement around P, and in the corresponding transition states (**TS(III-IV)** and **TS(III′-IV′)**), the O is in an equatorial position. However, when the geometries of these transition states are allowed to relax, they evolve to the corresponding O-apical oxaphosphetanes **III** and **III′**.

The structures of diazocumulenes **IV** and **IV′** are similar to that of difluorodiazoethene computed at the MP2/4-31G level

(20) For theoretical studies of Wittig reactions, see: (a) Volatron, F.; Eisenstein, O. *J. Am. Chem. Soc.* **1987**, *109*, 1. (b) Naito, T.; Nagase, S.; Yamataka, H. *J. Am. Chem. Soc.* **1994**, *116*, 10080. (c) Vedejs, E.; Marth, C. F. *J. Am. Chem. Soc.* **1988**, *110*, 3948. (d) Yamataka, H.; Nagase, S. *J. Am. Chem. Soc.* **1998**, *120*, 7530. (e) Restrepo-Cossio, A. A.; Gonzalez, C. A.; Marí, F. *J. Phys. Chem. A* **1998**, *102*, 6993. (f) Seth, M.; Senn, H. M.; Ziegler, T. *J. Phys. Chem. A* **2005**, *109*, 5136.

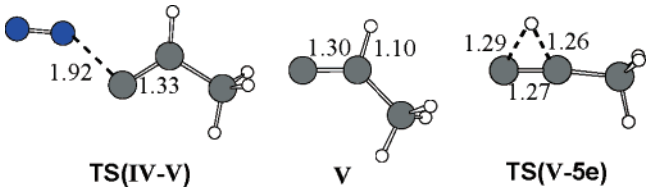


FIGURE 3. Structure of B3LYP/6-31G(d) stationary points corresponding to decomposition of **IV**. Interatomic distances in Å.

SCHEME 9

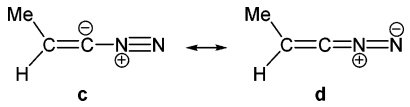


TABLE 4. Energies and Gibbs Energies[a] Corresponding to the Stationary Points[b] of the Nitrogen Elimination from IV and IV′

	ΔE	ΔG^c
TS(IV-V)	14.7	11.8 (11.9)
V + N_2	6.8	−7.4 (−5.3)
5e + N_2	−40.7	−52.5 (−48.2)

[a] Relative to **IV** at the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) level. In kcal mol^{-1}. [b] See Figure 3. [c] Values in THF solution are in parentheses.

of calculation.[4] The NBO analysis of **IV** leads to bond indexes of 1.764 (C−C), 1.364 (C−N), and 2.349 (N−N) showing a similar contribution of mesomers **c** and **d** (Scheme 9).

The last step of the reaction consists of the elimination of nitrogen from the diazocumulenes **IV** or **IV′** and the formation of the acetylene derivative **5e**. Figure 3 and Table 4 present the results obtained for the evolution of **IV**. The results obtained for **IV′** are very similar.

The process takes place in two steps: nitrogen elimination and carbene−alkyne rearrangement. Nitrogen elimination is the rate-determining step. For the second step, we have located the transition state shown in Figure 3. However, this structure is 0.1 kcal mol^{-1} lower in energy than **V** at the B3LYP/6-31G(d) level of calculation. In this transition state, the migrating H is nearly equidistant from both C atoms, so that the two electron pairs involved in the rearrangement are delocalized over three atomic centers. It has been shown that density functional methods may overestimate the stability of such structures.[21] When the energies of **V** and the transition state between **V** and **5** are recomputed at the CCSD(T)/6-31G(d) level of calculation, the transition state is 1.2 kcal mol^{-1} higher in energy than **V**. With the BHandHLYP functional, which includes 50% of exact exchange, the transition state is 2.2 kcal mol^{-1} higher than **V**. These results suggest that this last step is very fast, and it is consistent with the difficulty to trap carbene **V**.

Figure 4 shows the Gibbs energy diagram of the whole process. One can observe that the addition of the second aldehyde molecule ($\Delta G^{\ddagger} = 23.1$ kcal mol^{-1}) is faster than the addition of the first one ($\Delta G^{\ddagger} = 30.8$ kcal mol^{-1}), in excellent agreement with the experimental evidence. Moreover, the rate-determining transition state corresponds to the decomposition of the oxaphosphetane **III** in the Wittig-type reaction. The whole reaction is highly exergonic.

We have also studied the reaction between diazomethylenephosphorane **II** and CS_2. The structures of the stationary points

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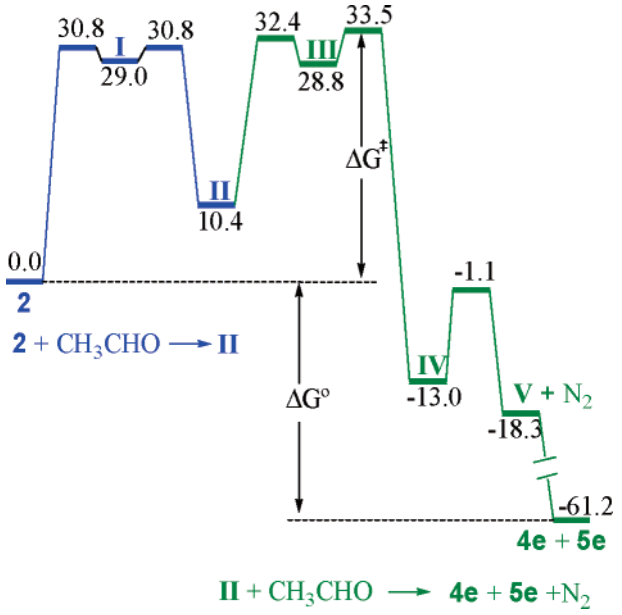

FIGURE 4. Gibbs energy diagram for reaction between **2** and acetaldehyde leading to the formation of phosphonamide **4e**, acetylene **5e**, and N_2. Gibbs energies in THF relative to reactants in kcal mol^{-1}. Blue and green colors are used for the addition of the first and second acetaldehyde molecules, respectively.

are presented in Figure 5, and the corresponding relative energies and Gibbs energies are shown in Table 5.

The process leads to the formation of **10e** in two steps, the first step being the rate-determining one. The computed Gibbs activation energies are 25.3 (gas phase) and 22.6 (THF) kcal mol^{-1}. These values are lower than those corresponding to the Wittig reaction between **IV** and acetaldehyde shown in Table 2, 27.8 (gas phase) and 23.1 (THF) kcal mol^{-1}. These results are consistent with the observed outcome of the reaction in the presence of an excess of carbon disulfide leading to heterocycle **10e**.

Concluding Remarks

C-Silylated α-diazophosphines **1** and **2** react as nucleophiles toward aldehydes leading to betaines that rearrange to diazomethylenephosphoranes. The intermediate, resulting from the addition to benzaldehyde, has been captured by reaction with carbon sulfide to afford a 1,3-adduct. The diazomethylenephosphoranes react with a second molecule of aldehyde according to a Wittig-type reaction, with the rate of this step being faster than the rate for the reaction of the initial diazophosphines with the first molecule of aldehyde. Decomposition of the corresponding oxaphosphetanes to afford phosphonamides and diazocumulenes is the rate-determining step of the whole process. In turn, diazocumulenes lose molecular nitrogen giving transitory carbenes that rapidly rearrange to alkynes. The lifetime of these carbenes is not long enough to be captured by reaction with *tert*-butyl isonitrile or with diisopropylamine. As a consequence of the novel behavior of these diazophosphines, reactions between **1** or **2** and aldehydes provide an easy and useful synthetic entry to diversely substituted phosphonamides and alkynes in a *neutral medium*. This synthetic method is excluded for aromatic aldehydes bearing electron-releasing substituents at the para position and sterically hindered alkyl aldehydes.

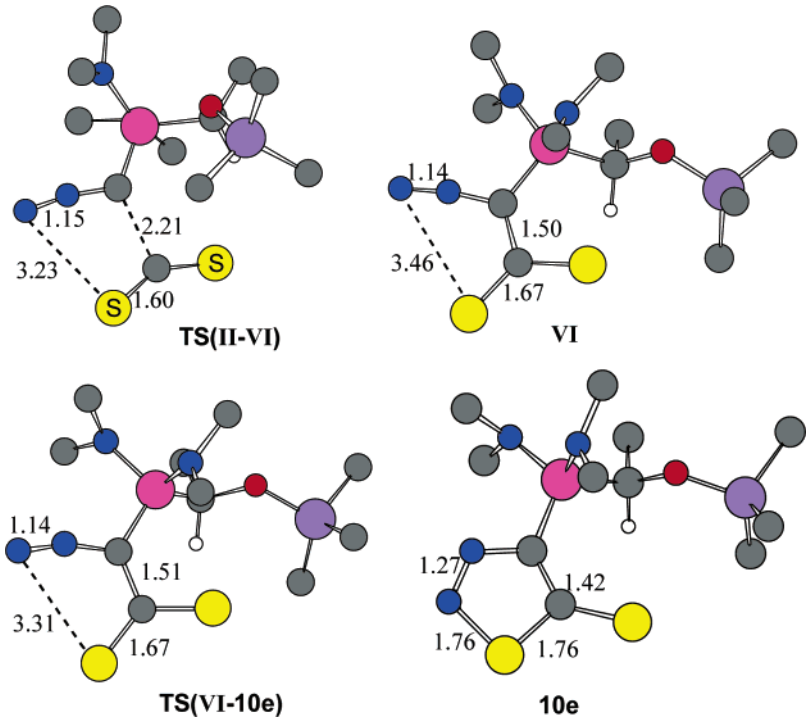

FIGURE 5. Structure of B3LYP/6-31G(d) stationary points corresponding to the reaction between **II** and carbon disulfide. Interatomic distances in Å. Hydrogens of methyl groups have been omitted for clarity.

TABLE 5. Energies and Gibbs Energies[a] Corresponding to the Stationary Points[b] of the Reaction between II and Carbon Disulfide

	ΔE	ΔG^c
TS(II-VI)	14.4	25.3 (22.6)
VI	2.9	15.9 (4.3)
TS(VI-10)	3.1	16.7 (5.7)
10e	−20.0	−5.5 (−12.2)

[a] Relative to reactants at the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) level. In kcal mol^{-1}. [b] See Figure 5. [c] Values in THF solution are in parentheses.

Experimental Section

Computational Details. All calculations have been done using the Gaussian 03 program.[22] Geometries have been fully optimized using the B3LYP[23] density functional method with the 6-31G(d) basis set.[24] The harmonic vibrational frequencies of all structures have been computed to characterize them as energy minima (all frequencies are real) or transition states (one, and only one, imaginary frequency). The energies of all structures have been recalculated using the 6-311+G(2d,p) basis set. The solvent effect has been included for the gas-phase optimized structures using the CPCM[25] method at the B3LYP/6-31G(d) level of calculation. The solvent considered is THF (ϵ =7.58). The reported Gibbs energies have been referred to 1 atm and 298.15 K for the gas-phase calculations and to 1 mol L^{-1} and 298.15 K for the THF solution.

For the carbene−alkyne rearrangement, energies have also been calculated using the CCSD(T)[26] method and the BHandHLYP[23b,27] density functional method.

Bonding in several structures has been analyzed through Wiberg[28] indexes evaluated using the natural bond orbital (NBO) method.[29]

Reactions of Diazophosphines 1 and 2 with Carbonyl Compounds. As a representative example, the reaction between **2** and benzaldehyde is described. Freshly distilled benzaldehyde (0.43 mL, 4.2 mmol) was added to a solution of diazophosphine **2** (500 mg, 2.1 mmol) in dry pentane (2 mL) under nitrogen atmosphere. Immediately, a gentle bubbling was observed showing nitrogen loss, which was finished in 10 min. Then, much pentane was evaporated and the concentrated solution was distilled under reduced pressure to afford phenyl acetylene, **5a**. Although the distillate was collected in a flask cooled in a liquid-nitrogen bath, **5a** was partially carried away. The residue was chromatographed on silica gel (EtOAc and MeOH were successively used as eluents) to afford silyl ether **4a** and alcohol **6a** in a 1:0.3 ratio (650 mg, 97% yield).

In other instances, when the alkyne was a solid or an oil, both reaction products were isolated by column chromatography.

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Alkynes **5a**, **5e**, and **5f** are commercial products. Compounds **5b**,[30] **5c**,[31] **5d**,[32] **5g**,[33] and **5h**[34] were previously described in the literature.

α-Trimethylsilyloxybenzyl-*N*,*N*′-ethylene-*N*,*N*′-diisopropylphosphonamide, 3a: 430 mg (90%); crystals, mp 74−75 °C (from ether); ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.03 (s, 9 H), 1.03 (t-like, J_{H-H} = 6.0 Hz, 6 H), 1.12 (d, J_{H-H} = 6.5 Hz, 3 H), 1.21 (d, J_{H-H} = 6.5 Hz, 3 H), 2.80−3.47 (m, 6 H), 5.0 (d, J_{P-H} = 11.1 Hz, 1 H), 7.24−7.48 (m, 5 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 0.4, 21.4, 21.8, 38.6 (d, $^2J_{P-C}$ = 8.3 Hz), 39.6 (d, $^2J_{P-C}$ = 8.3 Hz), 74.7 (d, $^1J_{P-C}$ = 142.4 Hz), 127.4, 127.5, 127.7, 139.3; ^{31}P NMR (101.2 MHz, $CDCl_3$) δ 31.0; MS 366.5 [M^+].

Desilylation of Ethers 4a−d,g: Preparation of Compounds 6a−d,g,h,j. (a) With TBAF. As a typical example, desilylation of **4a** is described. A mixture of silyl ether **4a** (190 mg, 0.6 mmol) and TBAF·H_2O (615 mg, 2.4 mmol) in 5 mL of THF was stirred at room temperature for 4 h. Then, THF was eliminated, and the residue was poured into CH_2Cl_2 and washed with water (3 × 10 mL). The organic phase was washed once with CH_2Cl_2 (10 mL), and the combined organic layers were dried ($MgSO_4$). Solvent was evaporated under reduced pressure to afford alcohol **6a** (107 mg, 67% yield), which was crystallized to render the analytical sample.

(b) With 5% HCl in MeOH. Desilylation of **4d** is described. A mixture of ether **4d** (0.95 g, 3.9 mmol) in 10 mL of methanol and some drops of aqueous 5% HCl was stirred at room temperature for 4 h. The solvent was evaporated, and the residue was chromatographed by using successively EtOAc and methanol as eluents to afford alcohol **6d** (0.63 mg, 66% yield).

(2*R*)-1,2,3-Trihydroxypropyl-*N*,*N*,*N*′,*N*′-tetramethylphosphondiamide, 7. A mixture of **4h** (100 mg, 0.3 mmol) in 2 mL of MeOH and some drops of aqueous 5% HCl was heated to reflux for 8 h. Solvent was removed under reduced pressure, and the residue was poured into EtOAc to afford triol **7** as a solid (61 mg, 90% yield): crystals, mp 91−94 °C; $[\alpha]_D$ −9.6 (c = 1.25, CH_2Cl_2); ^{1}H NMR (250 MHz, acetone-d_6) δ 2.62 (s, 12 H), 3.55−3.80 (m, 4 H); ^{13}C NMR (62.5 MHz, acetone-d_6) δ 35.4, 65.1, 71.2, 72.9; ^{31}P NMR (101.2 MHz, acetone-d_6) δ 33.93.

α-*d*-α-Trimethylsilyloxybenzyl-*N*,*N*,*N*′,*N*′-tetramethylphosphondiamide, 8: yield 0.74 (94%); ^{1}H NMR (250 MHz, acetone-d_6) δ 0.02 (s, 9 H), 2.52 (d, $^3J_{P-H}$ = 8.7 Hz, 6 H), 2.56 (d, $^3J_{P-H}$ = 7.5 Hz, 6 H), 7.30 (m, 3 H), 7.56 (m, 2 H); ^{13}C NMR (62.5 MHz, acetone-d_6) δ 0.4, 36.3 (d, $^2J_{P-C}$ = 2.9 Hz), 37.0 (d, $^2J_{P-C}$ = 2.9 Hz), 79.5 (t, $^1J_{C-D}$ = 33.4 Hz), 127.5, 128.1, 128.7, 140.9; ^{31}P NMR (101.2 MHz, acetone-d_6) δ 32.7; MS (*m*/*e*) 316.1 [$M + H^+$], 338.1 [$M + Na^+$].

Phenyl-2-*d*-acetylene, 9. ^{1}H NMR (250 MHz, acetone-d_6) δ 7.29−7.34 (m, 3 H), 7.58−7.65 (m, 2 H); ^{13}C NMR (62.5 MHz, acetone-d_6) δ 7.1 (t, $^1J_{C-D}$ = 38.1 Hz), 83.6, 122.1, 128.3, 132.1, 134.4.

4-(1,1-Bis(dimethylamino)-1-α-trimethylsilyloxybenzyl-λ^5-phosphanyliden)-4,5-dihydro-1,2,3-thiadiazole-5-tione, 10a. Dry CS_2 (0.12 mL, 2.0 mmol) and freshly distilled benzaldehyde (0.05 mL, 0.5 mmol) were successively added to a solution of diazophosphine **2** (131 mg, 0.5 mmol) in 1 mL of anhydrous THF, under a nitrogen atmosphere. The mixture was stirred at room temperature for 15 min, and then solvent was removed. The residue was chromatographed (2:1 hexane/EtOAc as eluent) to provide compound **10** as an oil (178 mg, 86% yield): ^{1}H NMR (250 MHz, $CDCl_3$) δ −0.01 (s, 9 H), 2.51 (d, $^3J_{P-H}$ = 9.5 Hz, 6 H), 2.95 (d, $^3J_{P-H}$ = 9.5 Hz, 6 H), 7.09 (d, $^2J_{P-H}$ = 7.7 Hz, 1 H), 7.34 (m, 3 H), 7.54 (m, 2 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ −0.1, 38.4 (d, $^2J_{P-C}$ = 2.9 Hz), 38.7 (d, $^2J_{P-C}$ = 1.9 Hz), 73.0 (d, $^2J_{P-C}$ = 105.9 Hz), 127.8, 127.9, 128.7, 135.6, 138.5 (d, $^1J_{P-C}$ = 141.1 Hz), 192.2 (d, $^2J_{P-C}$ = 26.7 Hz); ^{31}P NMR (101.2 MHz, $CDCl_3$) δ 48.3; MS 387.1 [($M + H^+$) − N_2].

5-Phenyl-4-trimethylsilyl-4-(*N*,*N*,*N*′,*N*′-tetramethylaminothiophosphoryl)-4,5-dihydro-1,2,3-oxadiazole, 11a. *tert*-Butylisonitrile (0.11 mL, 1.0 mmol) and freshly distilled benzaldehyde (0.10 mL, 1.0 mmol) were successively added to a solution of diazophosphine **2** (131 mg, 0.5 mmol) in 1 mL of anhydrous THF, under a nitrogen atmosphere. After stirring the mixture at room temperature for 15 min, an excess of elemental sulfur was added and stirring was continued for 1 h. Then, solvent and phenyl acetylene was removed under reduced pressure and the residue was chromatographed (2:1 hexane/EtOAc and MeOH as eluents) to afford phosphondiamide **4a** (91 mg, 58% yield) and heterocycle **11** as an oil (63 mg, 35% yield). Spectral data for compound **11** follow: ^{1}H NMR (250 MHz, acetone-d_6) δ 0.14 (s, 9 H), 2.45 (d, $^3J_{P-H}$ = 13.1 Hz, 6 H), 2.66 (d, $^3J_{P-H}$ = 12.9 Hz, 6 H), 5.81 (d, $^3J_{P-H}$ = 7.9 Hz, 1 H), 7.38−7.40 (m, 5 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ −0.9, 35.5, 35.8, 51.6 (d, $^1J_{P-C}$ = 142.1 Hz), 71.42 (d, $^2J_{P-C}$ = 15.3 Hz), 124.9, 127.3, 128.1, 142.2; ^{31}P NMR (101.2 MHz, $CDCl_3$) δ 81.1; MS 393.1 [$M + Na^+$].

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Supporting Information Available: Analytical and spectroscopic data for products **4a**−**i**, **5b**, **5i**, **5j**, and **6a**−**j**. ^{1}H and ^{13}C NMR spectra for representative synthesized new compounds. Cartesian coordinates, total energies for all considered structures computed at the B3LYP/6-31G(d) level of calculation, and the value of the imaginary frequency at the transition states. This material is available free of charge via the Internet at http://pubs.acs.org.

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