

# Reactivity of heterophospholes toward 1,3-dipolar cycloaddition of diazo compounds—an FMO analysis<sup>†</sup>

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**ABSTRACT:** The molecular geometries and the frontier orbital energies of three diazo compounds [diazodiphenylmethane (**2**), the  $\alpha$ -silyl- $\alpha$ -diazoketone **3** and the isomeric 2-siloxy-1-diazoalkene **4**], 10 heterophospholes with a P=C bond and two heterophospholes with a P=N bond were obtained from DFT calculations at the B3LYP/6-311+G\*\* level. The 1,3-dipolar cycloaddition reactivity of diazo compounds **2–4** toward the heterophospholes is discussed on the basis of FMO theory. It is concluded that in most cases, the dominant frontier orbital interaction is between the HOMO(diazo) and the LUMO(heterophosphole), and that the reactivity should decrease in the order **2** > **4** > **3**. The 1,2-thiaphosphole **9** and 1,3-azaphosphole **10** have HOMOs of high energy and, therefore, the HOMO(heterophosphole)–LUMO(diazo) interaction is also important. Among the different types of heterophospholes considered here, the 2-acyl-1,2,3-diazaphosphole **5**, 3*H*-1,2,3,4-triazaphosphole **8**, 1,2-thiaphosphole **9** and 1,3,4-thiazaphosphole **14** are predicted to have the highest dipolarophilic reactivities. These conclusions are in qualitative agreement with available experimental results. Copyright © 2003 John Wiley & Sons, Ltd.  
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**KEYWORDS:** 1,3-dipolar cycloaddition; diazo compounds; heterophospholes; frontier molecular orbital theory; DFT calculations

## INTRODUCTION

Heterophospholes are five-membered  $6\pi$  phosphorus heterocycles which contain one or more heteroatoms in addition to phosphorus. With a two-coordinate, three-valent ( $\sigma^2\lambda^3$ ) phosphorus atom, these heterocycles become fully conjugated. The prominent feature of this type of heterophospholes is the presence of a P=C (or P=N) double bond. In phosphalkenes  $R^1P=CR^2R^3$ , this hetero double bond is highly reactive, as evidenced by a variety of addition and cycloaddition reactions that occur much more readily than those of comparable C=C double bonds.<sup>1,2</sup> Incorporation of the P=C bond into the heterophosphole ring system leads to a thermodynamic stabilization due to the participation in cyclic  $6\pi$  conjugation. In fact, a number of spectroscopic and computational studies<sup>3–9</sup> have revealed the aromatic character of several different heterophosphole systems. Nevertheless, the enhanced reactivity of the P=C bond in such ring systems as compared with C=C bonds in the common five-membered heteroaromatic rings with one or

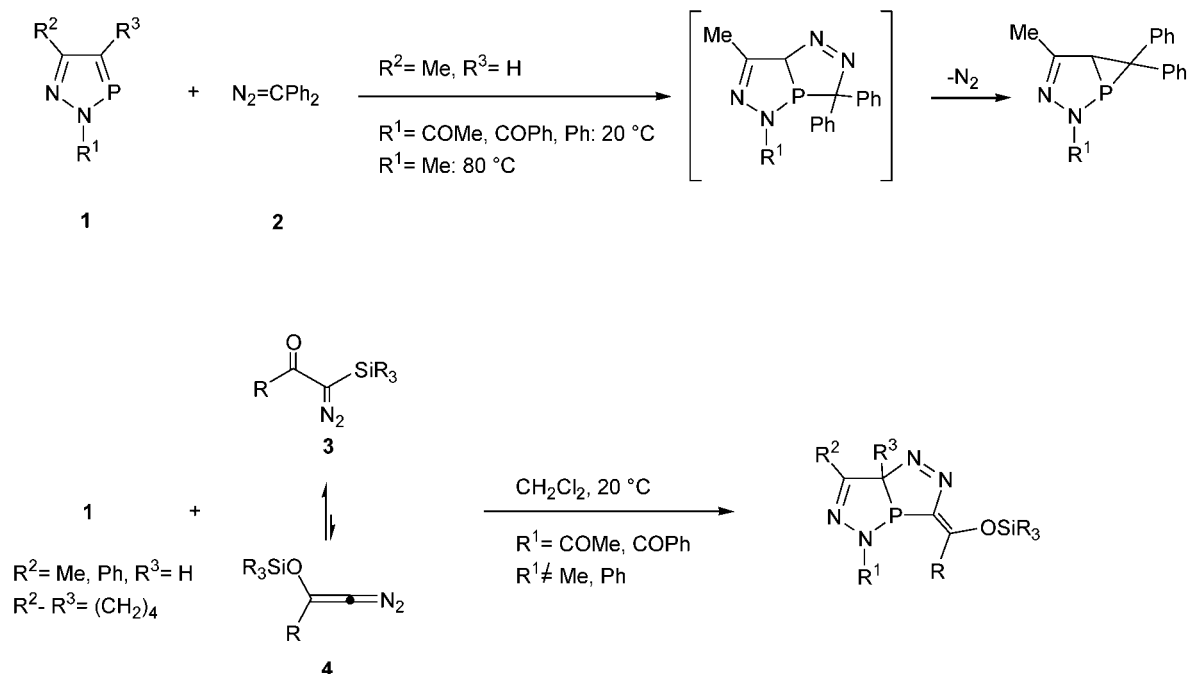
more heteroatoms is a fact that is documented by various types of 1,2-addition and, in particular, [3 + 2] and [4 + 2] cycloaddition reactions.<sup>2,10–12</sup>

The [3 + 2] cycloaddition reactions involving 1,3-dipoles and the P=C bond of heterophospholes give access to a multitude of novel phosphorus-containing heterocycles, but the full potential of this synthetic transformation has not yet been exploited, nor has the reactivity of different types of heterophospholes towards 1,3-dipoles been compared in a systematic manner. 2*H*-1,2,3-Diazaphospholes **1** represent by far the best investigated heterophospholes, and cycloadditions with most of the common dipoles, such as diazo compounds,<sup>2</sup> nitrile ylides,<sup>13</sup> nitrile imines,<sup>14</sup> nitrile oxides<sup>15</sup> and organic azides,<sup>16</sup> have been reported, although the initial cycloadduct was not isolated in some cases. The rate of the reaction of diazaphospholes **1** with diazodiphenylmethane (**2**) (Scheme 1) was found to depend on the substituent R<sup>1</sup>: when R<sup>1</sup> was an acceptor substituent, the reaction was markedly faster than with R<sup>1</sup> = Me.<sup>16,17</sup> In a similar manner, diazocumulenes **4**, co-existing as the minor component in equilibrium with (1-diazo-2-oxoalkyl)silanes **3**,<sup>18</sup> underwent [3 + 2] cycloaddition with **1** (R<sup>2</sup>, R<sup>3</sup> = alkyl, H) at 20 °C when R<sup>1</sup> = Ac or Bz, while in the case of R<sup>1</sup> = Me or Ph no reaction took place up to ca 60 °C, where thermal dediazonation of the diazo compound occurred.<sup>19</sup> Furthermore, we found that diazocumulenes **4** undergo 1,3-dipolar cycloaddition

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<sup>†</sup>Dedicated to the fathers of the KISPOC conference series, Profs. Yuho Tsuno and Hiroshi Taniguchi, and to the chief organizer, Shinjiro Kobayashi.

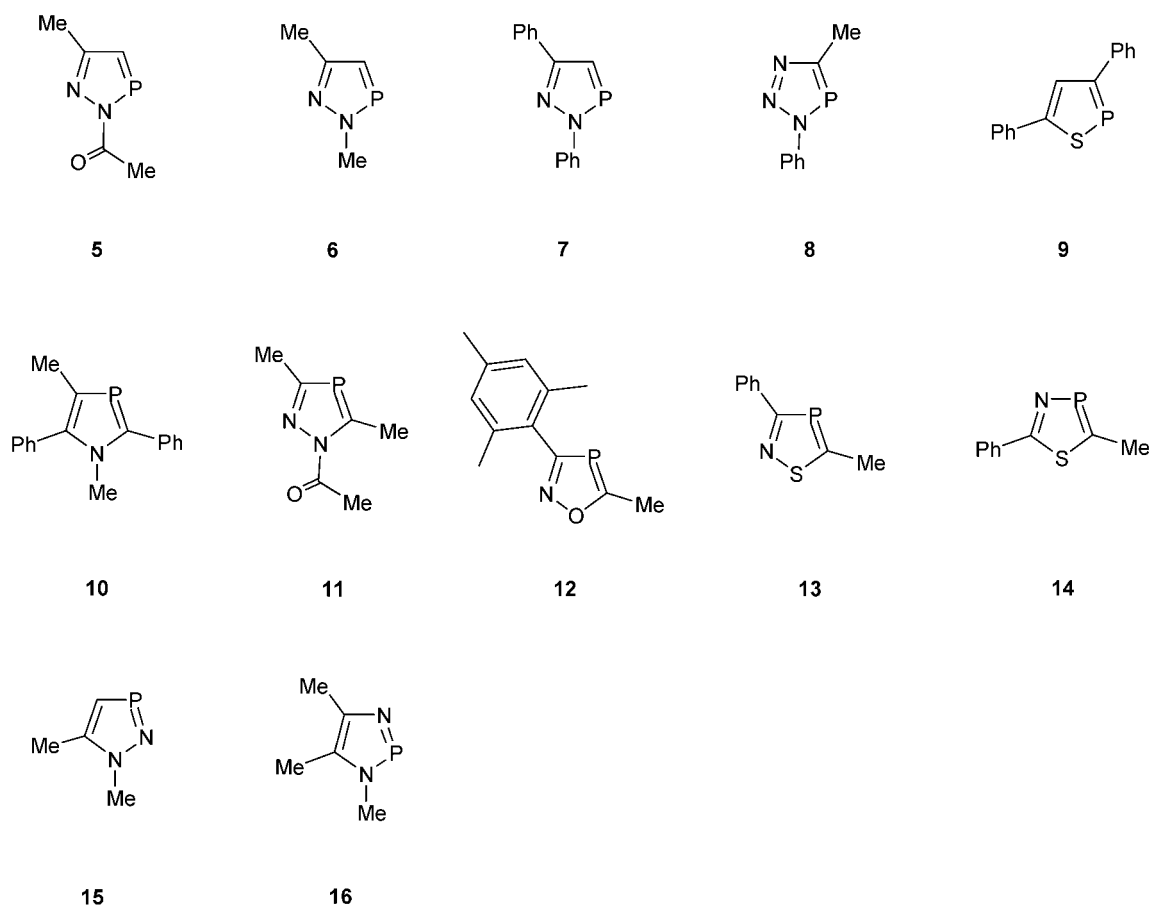
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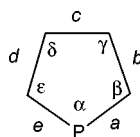


Scheme 1

across the P=C bond of 1,2,3,4-triazaphospholes<sup>20</sup> and 1,2-thiaphospholes,<sup>21</sup> while some other heterophosphole systems were not suited as dipolarophiles.

These few examples suggest that it is desirable to have an estimate of the dipolarophilic reactivity of various types of heterophospholes. Within the theoretical frame-



**Table 1.** Calculated (B3LYP/6-311+G\*\*) bond lengths (Å) and bond angles (degrees) for heterophospholes **5–16**<sup>a</sup>

Compound	<i>a</i>	<i>b</i>	<i>c</i>	<i>d</i>	<i>e</i>	$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$
<b>5</b>	1.707	1.423	1.319	1.356	1.743	86.94	111.85	115.02	109.49	116.69
<b>6</b>	1.719	1.410	1.332	1.338	1.715	87.87	110.57	114.94	109.92	116.69
<b>7</b>	1.712	1.415	1.332	1.339	1.734	87.75	111.10	114.69	110.32	116.13
<b>8</b>	1.730	1.359	1.292	1.345	1.730	85.70	113.07	114.32	111.89	115.01
<b>9</b>	1.737	1.417	1.377	1.743	2.119	92.83	117.05	119.07	114.36	96.67
<b>10</b>	1.743	1.374	1.392	1.378	1.778	89.64	112.39	113.55	113.10	111.32
<b>11</b>	1.731	1.377	1.366	1.307	1.796	87.06	111.23	116.06	110.51	115.13
<b>12</b>	1.720	1.340	1.398	1.301	1.809	85.29	114.73	114.22	109.94	115.82
<b>13</b>	1.720	1.723	1.656	1.313	1.817	92.43	113.99	99.88	114.84	118.86
<b>14</b>	1.721	1.731	1.784	1.291	1.695	96.94	113.89	94.35	116.57	118.25
<b>15</b>	1.667	1.336	1.369	1.380	1.758	92.10	110.68	117.12	110.68	109.42
<b>16</b>	1.633	1.353	1.396	1.370	1.733	92.27	112.46	114.26	110.31	110.70

<sup>a</sup> Bond *a* is the P=C or P=N bond.

**Table 2.** Calculated (B3LYP/6-311+G\*\*) and experimental ring geometries for heterophospholes **5**, **7**, **14** and **15**

Compound	Method	<i>a</i> (Å)	<i>b</i> (Å)	<i>c</i> (Å)	<i>d</i> (Å)	<i>e</i> (Å)	$\alpha$ (°)	$\epsilon$ (°)
	Exp., electron diffr. <sup>a,b</sup>	1.729(15)	1.439(13)	1.300(6)	1.413(8)	1.729(15)	88.8(5)	116.0(5)
	HF/6-31G	1.719	1.424	1.303	1.350	1.777	86.33	115.26
	HF/6-31G*	1.676	1.429	1.289	1.344	1.707	88.16	116.02
	B3LYP/6-31G*	1.712	1.424	1.323	1.355	1.746	86.78	116.94
	B3LYP/6-311+G**	1.707	1.423	1.319	1.356	1.743	86.94	116.69
	Exp., electron diffr. <sup>c</sup>	1.75	1.42	1.32	1.32	1.64	92.0	110.0
	B3LYP/6-311+G**	1.712	1.415	1.332	1.339	1.734	87.75	116.13
	Exp., x-ray diffr. <sup>d,e</sup>	1.669(10)	1.728(6)	1.728(6)	1.324(25)	1.684(15)	98.0(14)	94.3(4) ( $\gamma$ )
	B3LYP/6-311+G**	1.721	1.731	1.784	1.291	1.695	96.94	94.35 ( $\gamma$ )
	Exp., x-ray diffr. <sup>f</sup>	1.654(3)	1.330(4)	1.356(4)	1.381(5)	1.723(3)	92.9(2)	117.0(2) ( $\gamma$ )
	B3LYP/6-311+G**	1.667	1.336	1.369	1.380	1.758	92.1	117.12 ( $\gamma$ )

<sup>a</sup> Ref. 28.

<sup>b</sup> Values were obtained by refinement of a model that assumed equal P–N and P=C bond lengths; standard deviations in this case are given as  $3\sigma$  values.

<sup>c</sup> Data are for 5-methyl-2-phenyl-1,2,3-diazaphosphole.<sup>29</sup>

<sup>d</sup> Ref. 30.

<sup>e</sup> Experimental results are for the 2,5-diphenyl analogue. The heterophosphole ring is disordered so as to have crystallographic  $C_2$  symmetry; therefore, the given bond geometries are not very accurate.

<sup>f</sup> Ref. 31.

**Table 3.** Calculated (B3LYP/6-311+G\*\*) total energies ( $E_{\text{tot}}$ ), zero-point vibration corrected energies, bond lengths (Å) and bond angles (degrees) of diazo compounds **2-4**

Parameter	<b>2</b>	<i>s-cis-3</i>	<i>s-trans-3</i>	<b>4<sup>a</sup></b>
$E_{\text{tot}}$ (au)	-611.0113	-710.2350	-710.2393	-710.2267 (-710.2184)
$E_{\text{tot}} + \text{ZPE}$ (au)	-610.8165	-710.0628	-710.0672	-710.0545 (-710.0463)
<i>a</i> (Å)	1.139	1.126	1.133	1.136 (1.133)
<i>b</i> (Å)	1.308	1.317	1.308	1.297 (1.304)
<i>c</i> (Å)	1.477	1.481	1.471	1.360 (1.357)
<i>d</i> (Å)		1.220	1.223	1.336 (1.349)
<i>e</i> (Å)		1.518	1.519	1.502 (1.499)
Others (Å)		C—Si 1.902	1.909	O—Si 1.729 (1.705)
$\alpha$ (°)	180.00	178.76	178.46	170.53 (170.11)
$\beta$ (°)	116.73	112.31	118.17	120.96 (119.91)
$\gamma$ (°)		122.38	119.41	120.97 (121.57)
$\delta$ (°)		120.76	121.54	111.98 (117.59)
Others (°)		N—C—Si 116.23	119.89	C—O—Si 129.24 (139.20)
Torsion angles (°)	C <sub>Ph</sub> CNN 180.00	CCNN 0.81	180.00	CCNN 180.00
		NCCO 0.82	180.00	NCCO 0.01

<sup>a</sup> Values for the less stable isomer with Z configuration at the C=C bond are given in parentheses.

work of pericyclic reactions, reactivity differences in a series of dipoles/dipolarophiles can often be analyzed and predicted with the help of frontier molecular orbital (FMO) theory.<sup>22</sup> We decided, therefore, to apply this theory to the reactivity of selected heterophospholes in 1,3-dipolar cycloaddition reactions with aliphatic diazo compounds.

## RESULTS AND DISCUSSION

Heterophospholes **5-16** were chosen for the present study. They were selected because reactions with selected diazo compounds are known<sup>2,12,23</sup> or because they can be prepared conveniently in a few steps and in amounts that qualify them for future systematic studies of their cycloaddition chemistry. It should be noted that the majority of the parent ring systems are not yet known, and that available synthetic methods determine the substituent patterns.

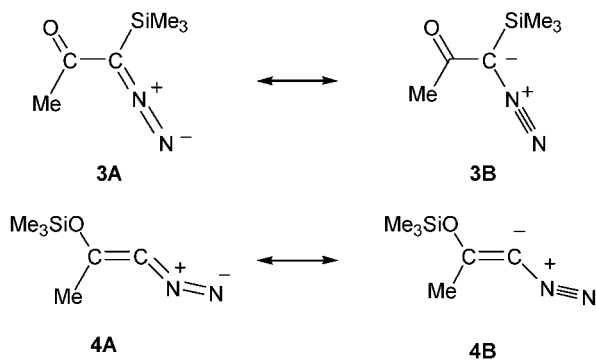
### Computational methods

Calculations for diazo compounds **2-4** and heterophospholes **5-16** were performed using conventional *ab initio* calculations of the Hartree-Fock type and density functional theory (DFT) methods using the hybrid B3LYP functional. In either case, Gaussian-type basis sets implemented in the Gaussian 98 program package<sup>24</sup> were applied. Geometries were first optimized at the HF/3-21G\* level and then refined using the B3LYP

method and the polarized 6-31G\* and 6-311+G\*\* basis sets. Standard convergence criteria as implemented in the modelling program (Gaussian 98) without any geometry constraints were applied. Frequency calculations were used to establish that the calculated structures were minima on the potential energy surface (no imaginary frequencies were found) and to obtain zero-point vibrational energies (ZPEs). For the discussion, we use B3LYP/6-311+G\*\* energies corrected for unscaled ZPE differences. The results were visualized using MOLDEN 3.6.<sup>25</sup> All calculations were performed on 900 MHz UltraSPARC-III + Solaris 9 computers at the Universitätsrechenzentrum Ulm.

### Structures

The calculated (B3LYP/6-311+G\*\*) ring geometries of heterophospholes **5-16** are given in Table 1. *Ab initio* structural calculations were carried out previously for the parent ring systems of **8**, **10**, **11** (all at HF/4-31G\*<sup>7,8</sup>) and **9** (MP2/6-31G\*<sup>9</sup>). Although some significant differences in numerical values exist between these and our studies, the data for **5-14** confirm the characteristic features, e.g. the P=C bond length is in the interval between the calculated values for a phosphorus-carbon single and double bond (H<sub>3</sub>C—PH<sub>2</sub>, 1.86 Å; H<sub>2</sub>C=PH<sub>2</sub>, 1.64 Å<sup>7</sup>), and the endocyclic angle at P increases when a sulfur atom is part of the ring. The PN bond length in **15** and **16** also has a value between those of 'typical' PN single and double bonds (see below). A comparison with experimentally obtained bond geometries is given in Table 2.



Scheme 2

Even with the largest basis set, some significant differences between the calculated and the experimental structures of 2*H*-1,2,3-diazaphospholes **5** and **7** and 1,3,4-thiazaphosphole **14** are found, but the limited accuracy of the experimental values in all three cases should be noted (see footnotes in Table 2). Furthermore, full agreement between calculated (gas-phase) and experimental (solid-state) structural data may not be expected.<sup>26</sup> In **14**, the calculated lengths of the P=C bond and one C—S bond are markedly larger than the solid-state values. On the other hand, very good agreement between experiment and theory was found for 1*H*-1,2,3-diazaphosphole **15**; remarkably, the P=N double bond length is about half way between the calculated values, using electron correlation (MP2/6–31G\*), of the simplest models containing PN double and single bonds, respectively (HP=NH, 1.594 Å; H<sub>2</sub>N—PH<sub>2</sub>, 1.720 Å<sup>27</sup>).

The effects of different basis sets on the ring geometry were studied for diazaphosphole **5** (Table 2). For the Hartree–Fock calculations, introduction of polarization functions for the non-hydrogen atoms leads to a strong decrease in the PC and PN bond lengths. With the 6–31G\* basis set, the DFT method gives better results than the HF method, although the PN single bond appears to be slightly too long. The changes in bond geometry are only marginal on going from 6–31G\* to 6–311+G\*\*.

The B3LYP-calculated bond geometries of diazo

**Table 4.** Frontier orbital energies (B3LYP/6–311+G\*\* for diazo compounds **2–4**)

Compound	Orbital	Energy (eV)
<b>2</b>	LUMO + 1 <sup>a</sup>	–1.11
	HOMO	–5.54
<b>3<sup>b</sup></b>	LUMO + 1 <sup>c</sup>	–1.44
	HOMO	–6.74
<b>4</b>	LUMO + 1 <sup>d</sup>	–0.85
	HOMO <sup>e</sup>	–6.50

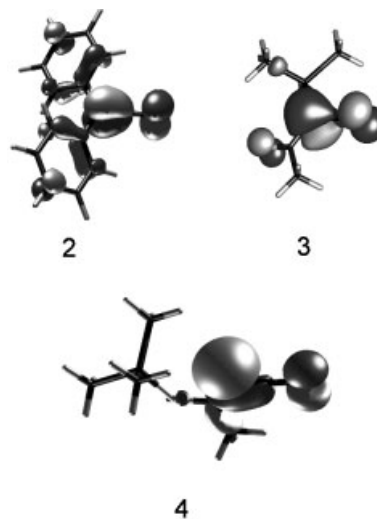
<sup>a</sup> The LUMO ( $E = -1.84$  eV) is of the  $\pi^*_{\text{NN}}$  type and located in the  $\sigma$  plane of the CNN unit.

<sup>b</sup> *s-trans* form.

<sup>c</sup> The LUMO ( $E = -1.96$  eV) has mainly  $\pi^*_{\text{NN}}$  character.

<sup>d</sup> The LUMO ( $E = -1.89$  eV) is of the  $\psi_3$  (1,2-diaza-1,3-butadiene) type.

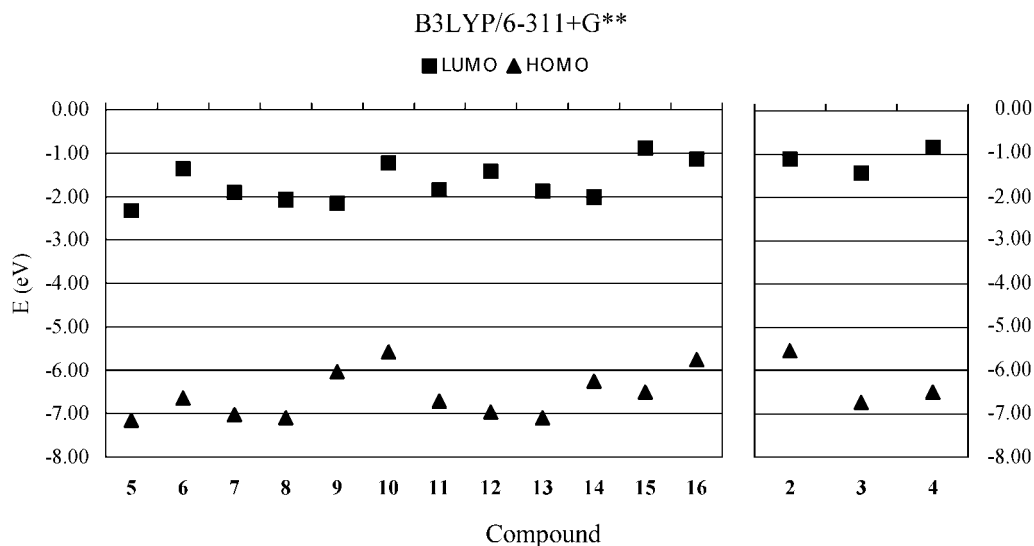
<sup>e</sup> In the  $\sigma$  plane of the CNN unit.



**Figure 1.** Shape of the highest occupied molecular orbitals of diazo compounds **2**, **3** and **4**

compounds **2–4** are given in Table 3. The bond lengths and angles of the CN<sub>2</sub> moiety of diazodiphenylmethane (**2**, C<sub>2v</sub> symmetry) and diazoketone **3** are in the ranges found in solid-state structures of related diazo compounds.<sup>32</sup> For **3**, the *s-trans* conformation at the C(O)—C(N<sub>2</sub>) bond is found to be more stable than the *s-cis* form by 2.77 kcal mol<sup>–1</sup> (1 kcal = 4.184 kJ) in terms of zero-point corrected energies, in line with the general observation that disubstituted  $\alpha$ -diazoketones exist in the *s-trans* conformation exclusively or preferentially.<sup>32</sup> The transition state of the *trans*–*cis* isomerization lies 13.21 kcal mol<sup>–1</sup> above *s-trans*-**3**.

For diazoalkene **4**, a non-linear C=C=N<sub>2</sub> unit is found with a bent CNN fragment (valence angle 170.5°) and a valence angle of 121.0° at the diazo carbon. The *E* configuration at the C=C bond is calculated to be more stable by 5.15 kcal mol<sup>–1</sup> than the *Z* configuration. The bent geometry of the diazoalkene resembles closely the calculated<sup>33</sup> (MP2/6–31G\*) structure of the elusive parent diazoethene, CH<sub>2</sub>=C=N<sub>2</sub> (CNN 165.4°, CCN 117.9°) which might be viewed<sup>33</sup> as a weakly bonded dinitrogen adduct of vinylidene. As with aliphatic diazo compounds in general, the dipolar resonance structures **A** and **B** are likely to be the major contributors to the bond state of the diazo function in **3** and **4** (Scheme 2). According to the calculations (Table 3), the C—N distance is shorter in **4** than **3**. Although the N—N bond length remains almost unchanged, this difference seems to suggest that resonance structure **4B** contributes less to the bonded state of the diazoalkene than **3B** does in the case of the diazoketone. While the ability of the trimethylsilyl group to stabilize an adjacent carbanion may be invoked to explain the relative importance of resonance structure **3B**, it is remarkable that the presumed low activation barrier of diazoalkene **4** towards loss of N<sub>2</sub> is not reflected in a substantial decrease of the C—N bond order. Such an expectation was supported by the comparison of the



**Figure 2.** Calculated energies of highest occupied and lowest vacant molecular orbitals of appropriate symmetry for diazo compounds **2–4** and heterophospholes **5–16**

C—N distances of diazomethane and the thermally highly unstable diazoethene molecule.<sup>33</sup>

According to the B3LYP/6-311+G\*\* calculations, diazoalkene **4** is by 7.97 (5.21) kcal mol<sup>-1</sup> higher in energy than the *s-trans* (*s-cis*) form of isomeric diazoketone **3**.

### Frontier molecular orbitals and reactivity

The energies of the frontier orbitals of dipoles **2–4** and dipolarophiles **5–16** were taken from calculations using the DFT B3LYP method and the 6-311+G\*\* basis set. While it may be questionable from a rigorous theoretical point of view to use density functional theory, i.e., the

energies of the Kohn–Sham orbitals, in the context of an FMO treatment of chemical reactivity, there is growing support to accept these orbitals as tools in qualitative MO considerations.<sup>34,35</sup> Several recent studies have shown that a correspondence between Kohn–Sham and Hartree–Fock orbital energies can be achieved by an empirical scaling (separately for occupied and unoccupied orbitals) of the form  $ax + b$ .<sup>35–37</sup>

Energies of the frontier orbitals of diazo compounds **2–4** are given in Table 4. In the cases of diazoketone **3** and diazoalkene **4**, the LUMO is not suited for the FMO treatment of the 1,3-dipolar cycloaddition, and the LUMO + 1 must be considered instead. It should be mentioned that these two unoccupied orbitals were found reversed in energy in HF/3-21G\* calculations for **3**. The

**Table 5.** Energies and relative size of orbital coefficients of relevant frontier orbitals (calculated at the B3LYP/6-311+G\*\* level) of heterophospholes **5–16**

Compound	Orbital energy (eV)			Relative size of orbital coefficient $c$ in $p_z$ direction at P=C (or (P=N) bond)			
	HOMO-1	HOMO	LUMO	LUMO + 1	HOMO or HOMO-1	LUMO	LUMO + 1
<b>5</b>		-7.164	-2.307		$c_P > c_C$	$c_P > c_C$	
<b>6</b>	-7.092	<sup>a</sup>	-1.358		$c_P < c_C$	$c_P > c_C$	
<b>7</b>	-7.034	<sup>b</sup>	-1.912		$c_P \sim c_C$	$c_P > c_C$	
<b>8</b>	-7.097	<sup>c</sup>	-2.066		$c_P > c_C$	$c_P > c_C$	
<b>9</b>		-6.030	-2.163		$c_P > c_C$	$c_P > c_C$	
<b>10</b>		-5.591	-1.224		$c_P > c_C$	$c_P \sim c_C$	
<b>11</b>		-6.720	-1.855	-0.479	$c_P > c_C$	$c_P < c_C$	$c_P > c_C$
<b>12</b>		-6.980	-1.415		$c_P > c_C$	$c_P \sim c_C$	
<b>13</b>	-7.089	<sup>d</sup>	-1.883	-1.470	$c_P \sim c_C$	$c_P < c_C$	$c_P > c_C$
<b>14</b>		-6.253	-2.007	-1.213	$c_P > c_C$	$c_P < c_C$	$c_P < c_C$
<b>15</b>		-6.519	-0.894		$c_P > c_N$	$c_P > c_N$	
<b>16</b>		-5.760	-1.145		$c_P \gg c_N$	$c_P > c_N$	

<sup>a</sup> The HOMO ( $E = -6.646$  eV) is mainly a  $\pi_{\text{PNNC}}$  orbital.

<sup>b</sup> The HOMO ( $E = -6.172$  eV) is mainly a  $\pi_{\text{PNNC}}$  orbital.

<sup>c</sup> The HOMO ( $E = -6.993$  eV) is mainly a  $\pi_{\text{Ph}}$  orbital.

<sup>d</sup> The HOMO ( $E = -6.455$  eV) has a node at C<sub>a</sub>.

**Table 6.** B3LYP/6-311+G\*\* energy gaps (eV) for HOMO–LUMO interactions between diazo compounds **2–4** and heterophospholes **5–16**<sup>a</sup>

Heterophosphole	<b>2</b>		<b>3</b>		<b>4</b>	
	$\Delta E_1$	$\Delta E_2$	$\Delta E_1$	$\Delta E_2$	$\Delta E_1$	$\Delta E_2$
<b>5</b>	3.23	6.06	4.43	5.73	4.20	6.32
<b>6</b>	4.18	5.99	5.38	5.65	5.14	6.25
<b>7</b>	3.63	5.93	4.82	5.60	4.59	6.19
<b>8</b>	3.48	5.99	4.67	5.66	4.44	6.25
<b>9</b>	3.38	4.92	4.57	4.59	4.34	5.18
<b>10</b>	4.32	4.48	5.51	4.15	5.28	4.75
<b>11</b>	3.69	5.61	4.88	5.28	4.65	5.87
<b>12</b>	4.12	5.47	5.32	5.14	5.08	5.73
<b>13</b>	3.66	5.98	4.85	5.65	4.62	6.24
<b>14</b>	3.53	5.15	4.73	4.82	4.50	5.41
<b>15</b>	4.65	5.41	5.84	5.08	5.61	5.67
<b>16</b>	4.40	4.65	5.59	4.32	5.36	4.91

<sup>a</sup>  $\Delta E_1$  (eV) =  $|E_{\text{HOMO, diazo}} - E_{\text{LUMO, heterophosphole}}|$ ;  $\Delta E_2$  (eV) =  $|E_{\text{LUMO, diazo}} - E_{\text{HOMO, heterophosphole}}|$ .

shape of the highest occupied molecular orbitals is shown in Fig. 1.

Energies of the relevant frontier orbitals of heterophospholes **5–16** are listed in Table 5. A graphical representation of the frontier orbital energies is given in Fig. 2. Only those frontier orbitals were considered for which the  $p_z$  atom orbital coefficients at the P=C (P=N) bond are sufficiently large compared with the other ring atoms contributing to the MO (see graphic representations given in the supporting information). The data do not show a systematic difference in orbital energies between heterophospholes **5–9** (X–P=C type, where X = N, S) on one side and **10–14** (X–C=P type, X = N, O, S) on the other. However, 1,2-thiaphosphole **9** and 1,3-azaphosphole **10** are distinguished by their significantly higher HOMO energy from all the other P=C heterophospholes which contain an N=C (or N=N) bond in addition to the P=C bond. This reflects once more the fact that in its conjugative ability the P=C bond is closer to a C=C than to an N=C bond.<sup>3,5,7</sup> The two heterophospholes with a P=N bond, 1,2,3-1*H*-diazaphosphole **15** and 1,3,2-1*H*-diazaphosphole **16**, are characterized by high-lying frontier orbital levels which put them in the neighborhood of 1,3-azaphosphole **10**.

According to FMO theory, the energetic stabilization resulting from the interaction of dipole and dipolarophile is inversely proportional to the energy gaps between the highest occupied and lowest vacant molecular orbitals of the reactants. The energy differences  $\Delta E_1$  between the HOMO of dipoles **2–4** and the LUMO of dipolarophiles **5–16** and also the LUMO(dipole)—HOMO(heterophosphole) gaps ( $\Delta E_2$ ) are compiled in Table 6. According to these data, the 1,3-dipolar cycloadditions with diazodiphenylmethane (**2**) are strongly HOMO(dipole)—LUMO(dipolarophile) controlled, a typical situation for cycloaddition reactions with diazoalkanes.<sup>22</sup> Only in the case of **10** and **16**, the two heterophospholes with the highest HOMOs, does the opposite frontier orbital interaction makes a significant contribution also. Because

of the lower MO energies of diazoketone **3**, the  $\Delta E_1$  values increase by 1.2 eV and the  $\Delta E_2$  values decrease by 0.33 eV. As a consequence, the LUMO(dipole)—HOMO(dipolarophile) contribution becomes dominant in the cases of **10** and **16**, and gains importance for **9** and some other heterophospholes. This picture is reminiscent of methyl diazoacetate, which was found to be a typical type II dipole in the Sustmann classification, showing enhanced reactivity towards both electrophilic and nucleophilic dipolarophiles as compared with unactivated alkenes.<sup>22,38,39</sup> For diazoalkene **4**, both the  $\Delta E_1$  (0.97 eV) and the  $\Delta E_2$  values (0.26 eV) are higher than for diazoalkane **2**, resulting again in a strong dominance of the HOMO(dipole)—LUMO(dipolarophile) interaction, with the exception of **10** and **16**.

For the three diazo compounds, the energy differences of the HOMO(dipole)—LUMO(dipolarophile) controlled reactions increase in the order **2** < **4** < **3**, in qualitative agreement with the experimental results (see below). In addition to the FMO rationalization, it is expected that cycloadditions with **4** are favored over those of the isomer **3** because steric interactions in the transition state are smaller (owing to the removal of the SiMe<sub>3</sub> group from the diazo carbon) and the ground-state energy of the diazoalkene is considerably higher, as mentioned above.

Focusing on the dipolarophile, the HOMO–LUMO gaps predict that 2*H*-1,2,3-diazaphospholes bearing an electron-withdrawing substituent at N-2 (**5** and **7**), 3*H*-1,2,3,4-triazaphosphole **8**, 1,2-thiaphosphole **9**, 1-acyl-1,2,4-1*H*-diazaphosphole **11**, 1,2,4-thiazaphosphole **13**, and 1,3,4-thiazaphosphole **14** are the best candidates. A quantitative comparison of the P=C with the P=N heterophospholes would have to take into account the energetic differences in forming a C–C (or C–N, depending on regioselectivity) bond as compared with an N–C (N–N) bond. It appears, however, that this distinction can be neglected for P=N heterophospholes **15** and **16**. The former dipolarophile is not expected to

undergo cycloaddition with any diazo dipole (perhaps with the exception of the most nucleophilic ones, such as 2-diazopropane) because of the large frontier orbital gaps. The comparatively low  $\Delta E_2$  value for the **3** + **16** combination would suggest that the LUMO(dipole) controlled cycloaddition is feasible, e.g. with diazoacetates or even better diazomalونات. However, the atom orbital coefficient at the nitrogen atom of the P=N in the HOMO of **16** is very small so that significant stabilization from orbital overlap with the dipole cannot be expected.

The available experimental findings are in good qualitative agreement with most of the FMO arguments. Diazodiphenylmethane (**2**) reacts readily at 20 °C with **5** and **7**, but only at elevated temperature with **6** (Scheme 1). Although a bicyclic phosphirane rather than the [3 + 2] cycloaddition product was isolated in these cases, the initial formation of the latter can be assumed because the expected pyrazoline was obtained when 9-diazafluorene was used as the 1,3-dipole.<sup>2</sup> Bicyclic phosphiranes were also obtained from the reaction of **2** with **9** (T. Jikyo and G. Maas, unpublished results) and, in a fast but not clean reaction, with 5-ethoxycarbonyl-2-phenyl-1,3,4-thiazaphosphole,<sup>17</sup> which is expected to have an even lower LUMO energy than its analogue **14**. The reactivity of **2** towards the remaining heterophospholes has not yet been reported. As already mentioned in the Introduction, 1,3-dipolar cycloadditions to P=C bonds with the equilibrium system **3/4** originate only from the diazoalkene component **4** and occur at 20 °C with 2-acyl-2H-1,2,3-diazaphospholes such as **5**, but not with **6** or **7**, and furthermore with heterophospholes **8** and **9**. These dipolarophiles are in fact those with the lowest LUMO energies (Table 5, Fig. 1). An unspecific reaction was observed with **14** (Me and Ph substituents interchanged), whereas heterophospholes **10–13**, **15** and **16** were found to be unreactive towards **3/4** at room temperature. Since diazoketone **3** obviously cannot compete with **4** for the heterophosphole dipolarophiles, it would be interesting to know the reactivity of electronically similar diazocarbonyl compounds. A fitting case, reflecting the HOMO(dipole) control, is given by ethyl diazoacetate which was found to undergo smooth cycloaddition with **5** at 20 °C whereas the incomplete and inefficient reaction with **7** (5-Me instead of 5-Ph) occurred only at 100–120 °C.<sup>40</sup> The failure of diazoketone **3** to react with **10** in a LUMO(dipole) controlled reaction is notable, but may be due to steric hindrance because of the SiMe<sub>3</sub> substitution of the diazo carbon atom. This hypothesis could be tested by using monosubstituted  $\alpha$ -diazocarbonyl compounds (diazomethyl ketones and diazoacetic esters).

For the regioselectivity of 1,3-dipolar cycloaddition reactions, maximum orbital overlap between the bond-forming atoms can make an important contribution, although it may be overruled by other factors (see below and Conclusion section). Figure 2 shows that for the HOMOs of diazo compounds **2–4**, the orbital shape at the diazo carbon is clearly larger than at the terminal nitrogen

atom. For the HOMO(dipole) controlled reactions, it is therefore expected that the P—C bonded regioisomer is preferred for all heterophospholes that have a higher LUMO orbital coefficient at phosphorus than at carbon. The exclusive formation of the P—C bonded cycloaddition products from diazoalkene **4** and heterophospholes **5**, **8** and **9** (Scheme 1) is in agreement with these expectations. These findings should not be overemphasized, however, since Kohn–Shams orbitals are under consideration here and since orbital coefficients in general depend both on the method (i.e. HF vs DFT) and on the chosen density functional. Furthermore, the maximal orbital overlap approach to the regioselectivity of 1,3-dipolar cycloaddition may fail for other reasons. As an example that is chemically related to this study, the reaction of diazomethane with phosphacetylene (HC≡P) may be mentioned. Although the orbital coefficients at P and C in the HOMO and LUMO of the heteroalkyne are nearly equal, an expressed regioselectivity (for the P—C bonded cycloadduct) is found in the parent case and for most examples of substituted reaction partners.<sup>41</sup> High-level *ab initio* calculations<sup>42</sup> of the transition-state energies for the two regioisomeric approaches of the H<sub>2</sub>CN<sub>2</sub> + HCP cycloaddition confirm that the experimentally formed regioselectivity is kinetically favored. The authors of that study stated, however, that the small energy difference between the two transition structures is perhaps not a firm basis to rationalize the exclusive formation of one regioisomer with many substituted systems and that various other effects might have to be considered.

## CONCLUSION

A simple FMO analysis of 1,3-dipolar cycloaddition reactions of diazo compounds **2–4** with various classes of heterophospholes suggests in most cases HOMO(dipole)–LUMO(dipolarophile) control of the reactivity. Exceptions may be expected when heterophospholes of high HOMO energy, e.g. 1,3-azaphosphole **10** and 1,2-thiaphosphole **9**, are combined with more electrophilic diazo dipoles such as diazocarbonyl compounds. Of the 12 heterophospholes investigated computationally, successful cycloaddition reactions with diazo compounds have been reported in fact only for the five systems with the lowest LUMO energies.

The frontier molecular orbital energies given here for heterophospholes **5–16** may also be useful for estimating the dipolarophilic reactivity towards other 1,3-dipoles. However, owing to the approximations and assumptions of the method, not more than a qualitative prediction should be expected from this simple FMO treatment of dipolar cycloadditions. In contrast to its application to Diels–Alder reactions, the FMO theory is not always able to predict correctly the reactivity and regioselectivity of 1,3-dipolar cycloaddition reactions, in particular if one of



the reactants is strongly polarized so that charges and electrostatic interactions<sup>43</sup> cannot be neglected. Therefore, calculations of the interaction energy by orbital-independent methods based on density functional theory concepts have been used recently.<sup>44</sup> Furthermore, the transition structures and activation energies of selected 1,3-dipolar cycloadditions have recently been calculated using DFT methods. However, a computational treatment of the reaction pathway for a whole series of, e.g., dipole + heterophosphole reactions, does not yet appear as a practicable alternative because it still demands too much computer capacity and time.

## Supplementary material

MOLDEN representations of the frontier molecular orbitals of heterophospholes **5–16** are available as supplementary data at the epoc website at <http://www.wiley.com/epoc/>.

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