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# A quantum chemical study on the reaction of 1-aryl-1,2-dihydrophosphinine oxides with dimethyl acetylenedicarboxylate

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**Abstract**

A β-oxophosphorane/ylide (**2a**) and an oxaphosphete (**3a**), the product and the possible intermediate of an inverse Wittig type reaction of 1-(2,4,6-triisopropylphenyl-)1,2-dihydrophosphinine oxide with dimethyl acetylenedicarboxylate were studied by quantum chemical calculations. The reaction of the title reagents following either a traditional [4 + 2] cycloaddition protocol to afford phosphabicyclo[2.2.2]octadiene **5** or a novel route yielding eventually β-oxophosphorane/ylide **2** was evaluated by energy calculations. The mechanism for the formation of intermediate $\mathbf{3a_2}$ was refined by HF/6-31G* transition state calculations. Analysis of the HOMO–LUMO orbitals of the reagents justified the reactivity experienced.


*Keywords:* P-heterocycles; Phosphoranes/ylides; Oxaphosphetes; Transition states; HOMO–LUMO orbitals

## 1. Introduction

The dynamically developing discipline of P-heterocyclic chemistry has attracted much attention recently [1].

Organophosphorus compounds with a sterically demanding substituent on the phosphorus atom are of special importance, as a bulky group affects the properties, stability and hence the reactivity of the parent molecule due to, mainly, steric effects [2].

Leading by different considerations, we aimed at the synthesis of P-heterocycles having a bulky substituent, such as a 2,4,6-trialkylphenyl group on the heteroatom. On one hand, arylphospholes with a flattened P-pyramid were prepared that exhibited aromatic character [3]. On the other hand, model compounds with sterically congested P-substituent were utilised during the evaluation of the mechanism for the fragmentation-related phosphorylations by phosphabicyclo derivatives [4].

The presence of the trialkylphenyl group on the phosphorus atom may bring about a novel reactivity of the P=O moiety. It was found that the interaction of cyclic phosphine oxides, such as 2,3-dihydro- and 2,3,4,5-tetrahydro-1H-phosphole oxides, as well as with 1,2-dihydrophosphinine oxides bearing a 2,4,6-trialkylphenyl substituent on the phosphorus atom (**1**) and dialkyl acetylenedicarboxylate (DAAD) gave, surprisingly, β-oxophosphoranes (**2**) that can be regarded to be stabilised phosphonium ylides (Scheme 1) [5,6].

The only criterion of the novel reaction affording β-oxophosphoranes/ylides is the presence of an electron-donating trialkylphenyl substituent on the phosphorus atom of the phosphine oxide. As a result of this, the P=O group is capable of reacting with DAAD.

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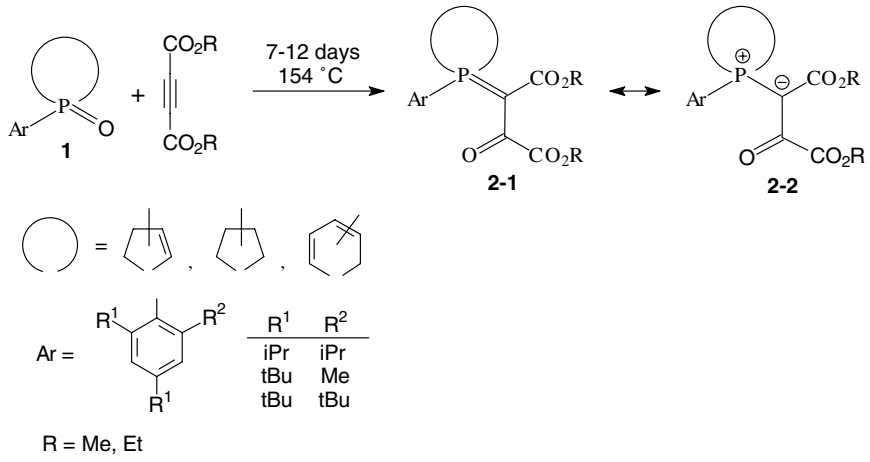



Scheme 1.

The reactivity of the stabilised phosphonium ylides (**2**) was in accord with their chemical structure [7].

In this paper, the results of quantum chemical calculations are discussed in the context of the mechanism of the novel reaction of cyclic phosphine oxides and dialkyl acetylanedicarboxylate.

## 2. Results and discussion

### 2.1. Calculations on the geometry of a dihydrophosphinine-based β-oxophosphorane/ylide

The simplified version (**2a***) of a representative product (**2a**) has now been evaluated by HF/6-31G* calculations. The perspective view of the most stable conformers together with the geometrical data selected is shown in Fig. 1. In the lack of single crystal analysis, all information is valuable on the geometry of the new products. On the other hand, phosphorane/ylide **2a*** is a distinguished compound from the point of view the content of this paper (see later).

### 2.2. Oxaphosphetes as possible intermediates in the reaction of cyclic phosphine oxides and DMAD

The reaction of cyclic phosphine oxides bearing a 2,4,6-trialkylphenyl substituent on the phosphorus atom (**1**) with DMAD affording phosphorane/ylide **2** was assumed to involve an intermediate of oxaphosphete type (**3**) formed by the reaction of the P═O group and the acetylenic moiety. Ring opening of the strained oxaphosphete (**3**), that may adopt different conformations (in $\mathbf{3_1}$ the oxygen atom occupies an axial position, while in $\mathbf{3_2}$ the oxygen is equatorial (Fig. 2)) gives the phosphorane/ylide (**2**) [8]. This kind of reaction has never been

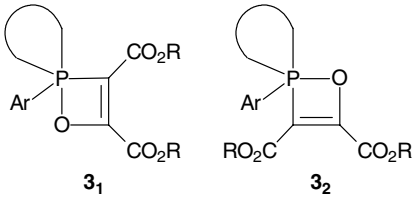



Fig. 2. Possible intermediates in the reaction of cyclic phosphine oxides and dialkyl acetylenedicarboxylate.

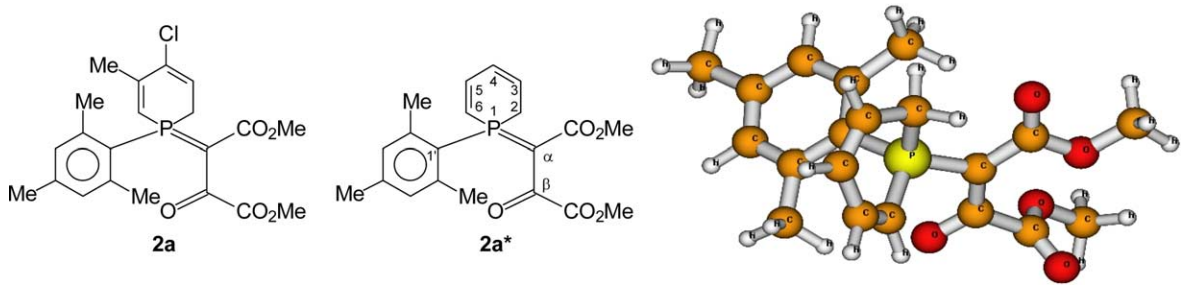



Fig. 1. Geometry of **2a*** obtained by HF/6-31G* calculations. Selected bond distances (Å): $P_1$–$C_2$, 1.833; $C_2$–$C_3$, 1.510; $C_3$–$C_4$, 1.323; $C_4$–$C_5$, 1.472; $C_5$–$C_6$, 1.326; $C_6$–$P_1$, 1.809; $P_1$–$C_\alpha$, 1.768; $C_\alpha$–$C_\beta$, 1.421; $P_1$–$C_{1'}$, 1.844; $P_1$–O: 2.806. Bond angles (°): $P_1$–$C_2$–$C_3$, 112.2; $C_2$–$C_3$–$C_4$, 123.5; $C_3$–$C_4$–$C_5$, 122.3; $C_4$–$C_5$–$C_6$, 124.5; $C_5$–$C_6$–$P_1$, 121.1; $C_2$–$P_1$–$C_{1'}$, 108.0; $P_1$–$C_\alpha$–$C_\beta$, 111.9; $P_1$–$C_2$–$C_3$–$C_4$, 36.7; $C_2$–$C_3$–$C_4$–$C_5$, −2.9; $C_3$–$C_4$–$C_5$–$P_1$, 4.2; $C_2$–$P_1$–$C_{1'}$–$C_{2'}$, 57.3; $C_2$–$P_1$–$C_\alpha$–$C_\beta$, 168.5; $C_3$–$C_2$–$P_1$–$C_{1'}$, 76.2; $P_1$–$C_\alpha$–$C_\beta$–O, 1.4.

observed before. On the basis of analogies [9,10], first we thought to have the spirocyclic oxaphosphetes (**3**) in hand [11]. The chemical properties of the products and the results of quantum chemical calculations suggested, however, that phosphoranes/ylides **2** were formed [5,6].

Oxaphosphete $\mathbf{3a}_2^*$ that is somewhat more stable than the other species ($\mathbf{3}_1$) was evaluated by HF/6-31G* ab initio calculations. The perspective view together with a selection of the bond angles is shown in Fig. 3. The sum of the deviations from the ideal angles (90°, 120° and 180°) in the TBP is 61.1, indicating a significant distortion around the central phosphorus atom. On the other hand, the oxaphosphete ring itself is also remarkably strained.

### *2.3. Dual reactivity of 1-aryl-1,2-dihydrophosphinine oxides towards DMAD; mechanism for the formation of the β-oxophosphoranes via oxaphosphetes*

The model reaction of 1-(2,4,6-triisopropylphenyl)-1,2-dihydrophosphinine oxide (**4a**) with DMAD was studied in detail. It is known that instead of giving a Diels–Alder cycloadduct (**5a**), the reaction of **4a** with DMAD yields a phosphorane/ylide (**2a**), presumably via oxaphosphete $\mathbf{3a_2}$ as an intermediate (Scheme 2/I).

HF/3-21G* calculations showed that the activation enthalpy ($\mathbf{TS_3}$) was lower for the formation of the oxaphosphete ($\mathbf{3a_2}$) (12.8 kcal/mol), than that ($\mathbf{TS_1}$) for the [4 + 2] cycloadduct (**5a**) (31.6 kcal/mol). At the same time, the reaction enthalpy for the formation of **5a** is −60.9 kcal/mol, while that for the oxaphosphete ($\mathbf{3a_2}$) is only 9.1 kcal/mol. This species ($\mathbf{3a_2}$) can be stabilised easily ($\Delta H^{\#} = 0.05$ kcal/mol obtained by PM3) to provide phosphorane/ylide **2a** with a reaction enthalpy of −7.1 kcal/mol (Fig. 4).

As a comparison, the energy profile of the two kinds of reaction of 1-phenyl-1,2-dihydrophosphinine oxide **4b** with DMAD was also calculated. In contrast to the reaction of the triisopropylphenyl starting material (**4a**), the cycloaddition of the phenyl derivative (**4b**) is

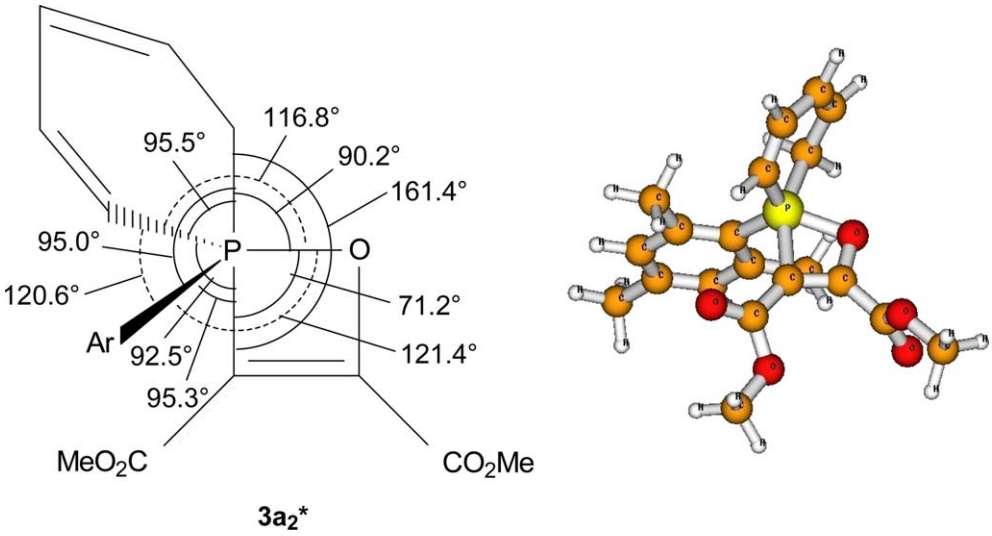
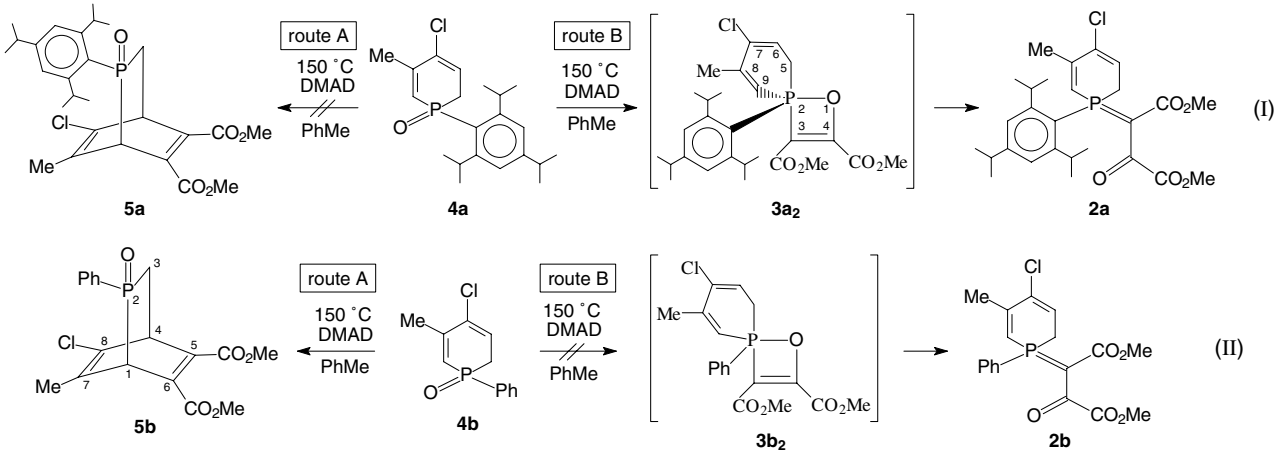



Fig. 3. Bond angles in the trigonal bipyramid of $\mathbf{3a}_2^*$ calculated by HF/6-31G* calculations.




Scheme 2.

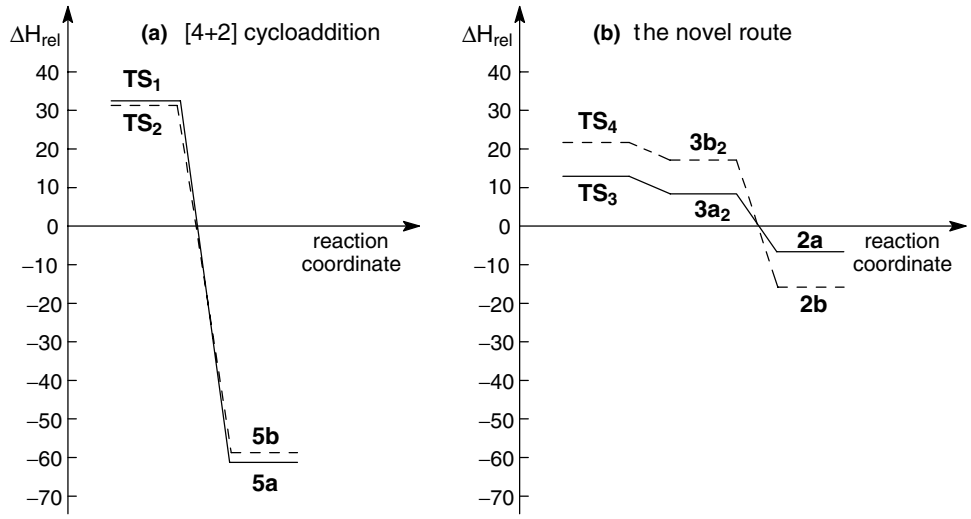


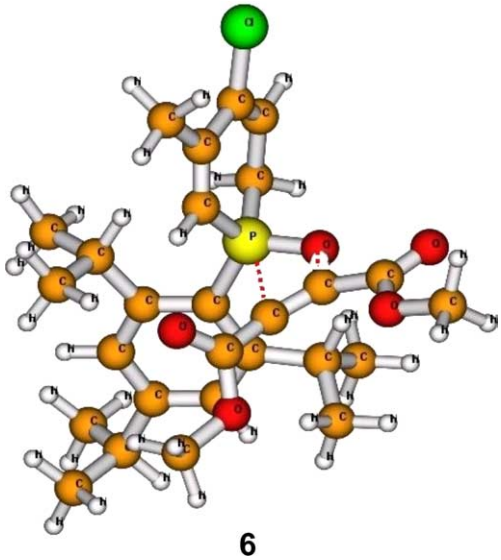

Fig. 4. Energy profile of the possible routes (A and B) for the reaction of 1,2-dihydrophosphinine oxides **4b** (dotted line) and **4a** (continuous line) with DMAD.

known to result in the formation of the Diels Alder cycloadduct (**5b**) (Scheme 2/II) [12].

The activation-($\mathbf{TS_2}$) and reaction enthalpies (31.5 and −59.0 kcal/mol, respectively) calculated for the Diels Alder reaction of **4b** with DMAD were almost the same, as those obtained for the similar reaction of **4a**. It is no wonder that the triisopropylphenyl to phenyl change does not affect significantly the 4 + 2 route, as the aryl group is not close to the reaction centers involved. The other route starting with **4b** and giving the corresponding P-phenyl oxaphosphete ($\mathbf{3b_2}$) was characterised by an activation enthalpy of 21.3 ($\mathbf{TS_4}$) and by a reaction enthalpy of 17.2 kcal/mol, while for the ring opening leading to the phenylphosphorane (**2b**), the reaction enthalpy is −16.5 kcal/mol (Fig. 4).

The activation enthalpy is by 9 kcal/mol smaller for the novel reaction of **4a** affording oxaphosphete ($\mathbf{3a_2}$), than that for the similar reaction of **4b**. In other words, the formation of the oxaphosphete and then that of the phosphorane is faster for the triisopropylphenyl- than for the phenyl substituted case. This must be due to the presence of the isopropyl groups on the phenyl ring. The trends in Fig. 4 look as if the pathway leading eventually to phosphorane (**2a** or **2b**) is determined by kinetic control, while the Diels Alder route giving adducts **5a** or **5b** is determined by thermodynamic control. It is an experimental fact that in case of a triisopropylphenyl substituent, the dihydrophosphinine oxide reacts fast with DMAD according to the novel protocol. At the same time, the interaction of phenyl-dihydrophosphinine oxide **4b** with DMAD gives rather a phospha[2.2.2]bicyclooctadiene (**5b**) than an oxaphosphete ($\mathbf{3b_2}$) (and subsequently phosphorane **2b**) can be explained by assuming the reversibility of the reaction step resulting in the formatin of $\mathbf{3d_2}$.

The transition states leading to oxaphosphete $\mathbf{3a_2}$ ($\mathbf{TS_3}$) and to cycloadduct **5b** ($\mathbf{TS_2}$) were also calculated by the HF/3-21G* method and are shown as **6** (Fig. 5) and **7** (Fig. 6), respectively, together the geometrical data selected. In transition state **6**, the $CH_2$ group is in the axial position. Another, but thermodynamically by 1.1 kcal/mol less stable species, having the CH = unit in the axial position, may also be formed. In this case,



**6**

Fig. 5. Geometry of the transition state in the reaction of the P=O moiety of 1-(2,4,6-triisopropylphenyl)-1,2-dihydrophosphinine oxide **4a** with DMAD calculated by the HF/3-21G* method. Selected distances (Å): $O_1$–$C_4$, 1.608; $P_2$–$C_3$, 2.865; $O_1$–$P_2$, 1.552; $C_3$–$C_4$, 1.256; $P_2$–$C_5$, 1.799; $C_5$–$C_6$, 1.514; $C_6$–$C_7$, 1.319; $C_7$–$C_8$, 1.488; $C_8$–$C_9$, 1.332; $P_2$–$C_{1'}$, 1.810; $P_2$–$C_9$, 1.774. Bond angles (°): $P_2$–$C_5$–$C_6$, 112.8; $C_5$–$C_6$–$C_7$, 124.3; $C_6$–$C_7$–$C_8$, 125.5; $C_7$–$C_8$–$C_9$, 122.1; $O_1$–$P_2$–$C_3$, 58.8; $P_2$–$C_3$–$C_4$, 67.7; $O_1$–$P_2$–$C_{1'}$, 115.3; $O_1$–$P_2$–$C_5$–$C_6$, −81.0; $P_2$–$O_1$–$C_4$–$C_3$ 17.4; $O_1$–$P_2$–$C_9$–$C_8$, 86.3; $O_1$–$P_2$–$C_{1'}$–$C_{2'}$, 165.5.

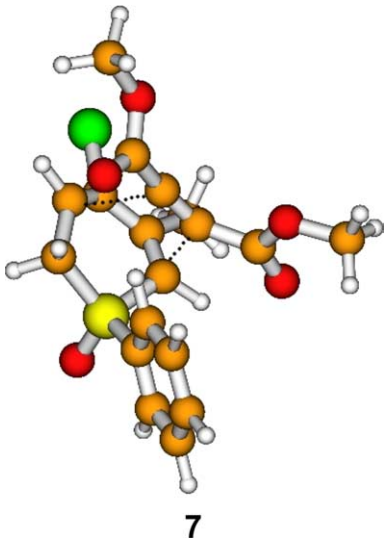


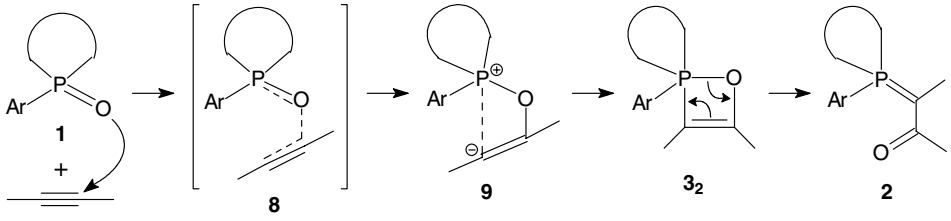

Fig. 6. Geometry of the transition state in the Diels–Alder reaction of 1-phenyl-1,2-dihydrophosphinine oxide **4b** with DMAD obtained by RHF/6-31G* calculations. Selected distances (Å): $C_4$–$C_5$, 2.489; $C_6$–$C_1$, 2.088; $C_5$–$C_6$, 1.230; $P_2$–$C_3$, 1.822; $P_2$–$C_1$, 1.812; $C_3$–$C_4$, 1.508; $C_4$–$C_8$, 1.361; $C_8$–$C_7$, 1.413; $C_7$–$C_1$, 1.387; $P_2$–$C_{1'}$, 1.817. Bond angles (°): $P_2$–$C_3$–$C_4$, 112.8; $C_3$–$C_4$–$C_8$, 125.9; $C_4$–$C_8$–$C_7$, 123.4; $C_8$–$C_7$–$C_1$, 117.8; $C_1$–$C_6$–$C_5$, 114.6; $C_4$–$C_5$–$C_6$, 105.5; O–$P_2$–$C_{1'}$, 110.81; $C_1$–$C_6$–$C_5$–$C_4$, −0.8; $P_2$–$C_3$–$C_4$–$C_8$, 17.2; $C_{2'}$–$C_{1'}$–$P_2$–$C_3$, −28.4; O–$P_2$–$C_3$–$C_4$, −101.9.

activation enthalpies of 17.8 and 21.3 kcal/mol were obtained for the formation of $\mathbf{3a_2}$ and $\mathbf{3b_2}$, respectively. At the same time, the reaction enthalpies were 16.3 and 18.3 kcal/mol, respectively, in the latter instance. In transition state **6**, the distance between the oxygen of the P=O group and the acetylenic carbon atom is 1.61 Å, while that between the phosphorus and the other acetylenic carbon is 2.87 Å.

Consequently, formation of the β-oxophosphoranes/ylides (**2**) is possible according to the following general mechanism (Scheme 3). The oxygen atom of the P=O group may attack one of the acetylenic carbon, to afford intermediate **9** via transition state **8** that can be exemplified by **6**. Ring closure of species **9** may lead to oxaphosphete $\mathbf{3_2}$ that is stabilised by the rupture of the P–O bond to give the final product **2**. This means that the formation of the oxaphosphete $\mathbf{3_2}$ is more probable via a stepwise sequence involving intermediate **9**, than by a direct [2 + 2] cycloaddition with a rather asymmetric transition state.

### 2.4. HOMO–LUMO calculations on the 1-aryl-1,2-dihydrophosphinine oxide and DMAD reactants

The HOMO and LUMO orbitals for the reactants **4a**, **4b** and DMAD were calculated by HF/3-21G* calculations and are shown in Figs. 7–9, respectively. An overlap is possible between the LUMO of 1-triiso-propylphenyl-1,2-dihydrophosphinine oxide (**4a**) and the HOMO of DMAD justifying the novel reaction between the P=O function of P-heterocycle **4a** and DMAD. In




Scheme 3.

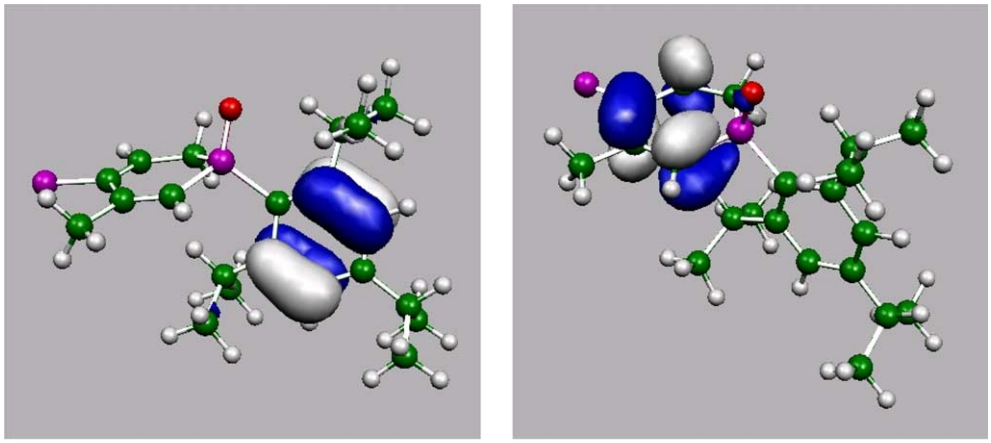



Fig. 7. HOMO–LUMO orbitals of 1-(2,4,6-triisopropylphenyl)-1,2-dihydrophosphinine oxide **4a**.

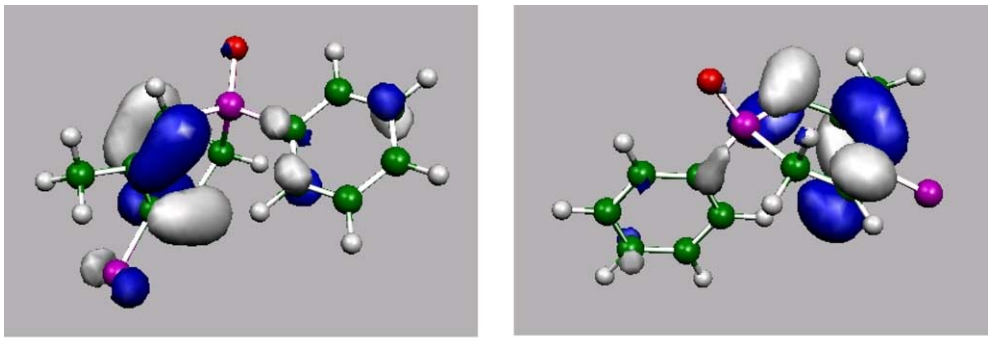



Fig. 8. HOMO–LUMO orbitals of 1-phenyl-1,2-dihydrophosphinine oxide **4b**.

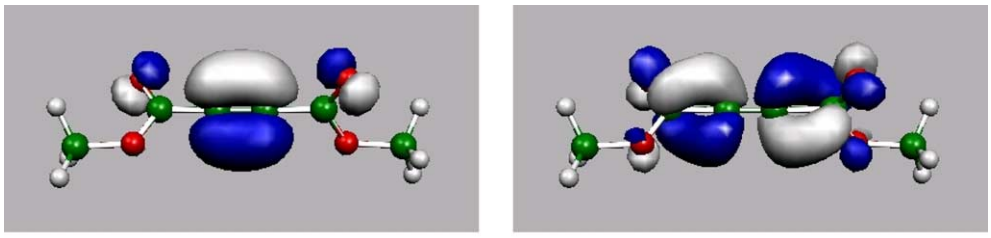



Fig. 9. HOMO–LUMO orbitals of dimethyl acetylenedicarboxylate.

this respect, the modest lobe around the P=O function is important. At the same time, for **4b**, the possibility of an overlap is negligible. Hence, the lobe theory seems to be in accord with the novel reactivity of the triisopropylphenyl substituted model compound **4a**. Moreover, it can be seen that the [4 + 2] cycloaddition is also allowed by the overlap between the LUMO of DMAD and the HOMO of both 1,2-dihydrophosphinine oxides (**4a** and **4b**), because the interactions between these frontier orbitals are stronger than between the HOMO of DMAD and the LUMO of **4a** and **4b**. (The differences between the LUMO of DMAD and the HOMO of **4a** and **4b** were found to be 0.432 eV and 0.447 eV, respectively. The same differences between the HOMO of DMAD and the LUMO of **4a** and **4b** were found to be 0.510 eV and 0.519 eV, respectively.)

## 3. Experimental

### *3.1. Quantum chemical calculations*

The structure of the stable molecules were calculated by full geometry optimization at the level of semiempirical quantum chemical method PM3 implemented in MOPAC 93 [13] and ab initio method using HF/3-21G*//HF/3-21G* and HF/6-31G*//HF/6-31G* basis in GAUSSIAN 98 [14]. The transition states were calculated by the method of eigenvalue following (PM3) and QST2 method (ab initio) [14]. Force matrices were found to be positive definit at the stable molecules and had one and only one negative eigenvalue (imaginary frequency) in the transition state. The structures were drawn by MOLDEN [15]. The molecular orbitals (HOMO and LUMO) were depicted by MOLEKEL [16].

## Acknowledgement

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