A Theoretical Study on the Conformation of 3-Phosphinoxido- and 3-Phosphono-1,2,3,4,5,6-hexahydrophosphinine 1-Oxides

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ABSTRACT: *The title compounds (**2** and **4**) obtained by the diastereoselective hydrogenation of the corresponding 1,2,3,6-tetrahydrophosphinine oxides (**1** and **3**) were subjected to a detailed quantum chemical study. The possible chair conformers were calculated at the HF/6-31G* level of theory, according to which, the 1-phenyl-3-P(O)Y$_2$-substituted products (**2**) exist in the trans$_1$ form, in which all substituents are equatorial. At the same time, the 1-ethoxy-3-dialkylphosphono compounds (**4**) adopt the cis conformations, in which the 1-ethoxy group is axial and the 3-P(O)(OR)$_2$ moiety is equatorial. The major diastereomer (**4–1**) is cis$_3$, in which the 5-methyl group is axial, while the minor one is cis$_1$ with an equatorial methyl substituent. It is noteworthy that the rotational position of the exocyclic P(O)Z$_2$ function affected the energy content of the chair conformer to a high extent. The possibility of the involvement of the twist conformers was also considered.* © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16:520–524, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20148

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INTRODUCTION

The 1,2,3,4,5,6-hexahydrophosphinine oxides form a relatively well-studied group of P-heterocycles [1–3]. Simple 1,2,3,4,5,6-hexahydrophosphinine oxides were synthesized by the catalytic hydrogenation of 1,2-dihydrophosphinine oxides [4], or even by the reduction of 3-phosphabicyclo[3.1.0]hexane 3-oxides [5,6]. Recently, 1,2,3,6-tetrahydrophosphinine oxides with an exocyclic P-moiety in position 3 were introduced [7,8] that were suitable starting materials for the title compounds [9]. In this paper, the results of a quantum chemical study on the possible conformations of 3-P(O)Y$_2$ substituted 1,2,3,4,5,6-hexahydrophosphinine oxides are summarized.

RESULTS AND DISCUSSION

Catalytic hydrogenation of 1-phenyl-3-diphenylphosphinoxido- and 3-dialkylphosphono-1,2,3,6-tetrahydrophosphinine oxides **1a–c** gave the corresponding 1,2,3,4,5,6-hexahydrophosphinine oxides **2a–c** as single diastereomers (Scheme 1) [9].

Hydrogenation of the 1-ethoxy-3-dialkylphosphono starting materials (**3a,b**) led to the products (**4a,b**) as a mixture of a major (**4–1**) and a minor (**4–2**) diastereomer (Scheme 2) [9]. Stereostructures of the products (**2** and **4**) were identified by
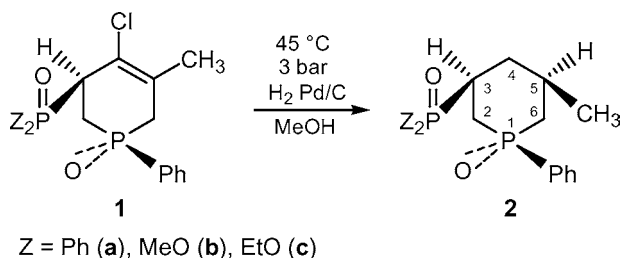
SCHEME 1

stereospecific $^3J(P,C)$ and $^3J(P,H)$ NMR couplings [9].

Conformational situation of 3-substituted hexahydrophosphinine oxides (**2** and **4**) was elucidated by HF/6-31G* calculations. The possible chair conformers of **2** and **4** are shown in Fig. 1. One can see that $trans_1/trans_2$, $trans_3/trans_4$, cis_1/cis_2, and cis_3/cis_4 equilibria can be imagined. It is noted that the relative position of the 3-P(O)Y$_2$ and the 1-oxygen atom is distinguished in the *trans* and *cis* forms. Further conformers are allowed by the different rotational positions of the exocyclic 3-P(O)Y$_2$ moiety around the P—C bond. From among these, three rotamers (**A**, **B**, and **C**) were found to have energy minima in each case. In rotamer **A**, the P=O group of the 3-P(O)Y$_2$ moiety is in *anti* position with the hydrogen of the C(3)—H unit. In rotamers **B** and **C**, the P=O group of the 3-P(O)Y$_2$ moiety is in *gauche* relationship with the C(4) and C(2) atoms, respectively. The relative zero point vibrational energy (ZPVE) corrected energies for the possible chair-conformers of the hexahydrophosphinine oxides (**2** and **4**) are listed in Table 1.

For the triphenyl product (**2a**), the **A** form of the $trans_1$ conformer with an equatorial position of all substituents was found to be the most preferable. Rotation of the 3-P(O)Ph$_2$ moiety around the P—C bond led to species (**B** and **C**) with higher energy content. It is noteworthy that rotation of the 3-P
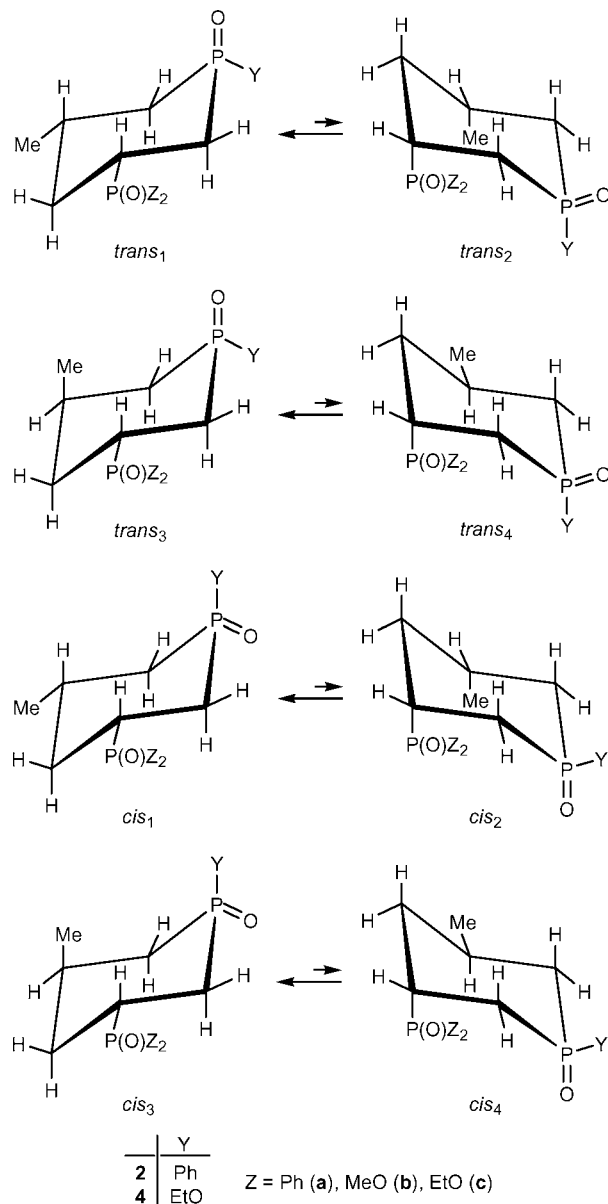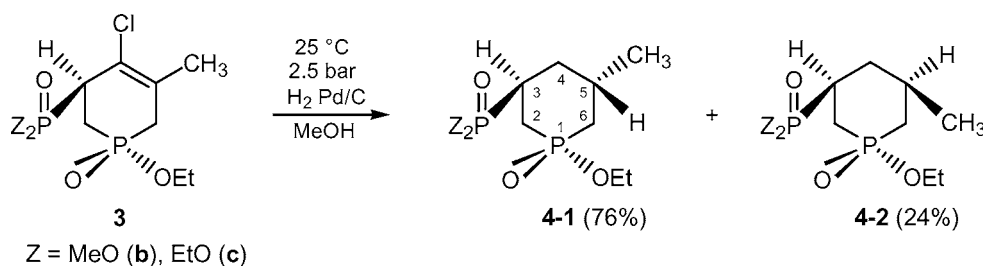

FIGURE 1 Possible chair conformers of 3-substituted 1,2,3,4,5,6-hexahydrophosphinine oxides **2** and **4**.

SCHEME 2

TABLE 1 Relative Energies (kcal/mol) for the **A**, **B**, and **C** Rotamers of the *Chair* Conformers of the Diastereomers of 3-Substituted Hexahydrophosphinine Oxides **2** and **4** Calculated at the HF/6-31G* Level of Theory

Conformer		2a	2c	4-1/c
*trans*₁	**A**	0	0	0.5
	B	3.7	0.3	0.2
	C	4.6	0.4	0.5
*trans*₂	**A**	16.0	16.2	9.1
	B		18.2	
	C		17.1	
*trans*₃	**A**	2.4	2.4	2.5
	B	6.2	2.2	8.5
	C	7.0	3.9	2.5
*trans*₄	**A**	8.7	7.2	4.6
	B		11.0	
	C		9.1	
*cis*₁	**A**	5.2	3.9	0
	B	8.1	4.3	0
	C	7.8	4.2	0.4
*cis*₂	**A**	14.5	10.1	10.1
	B		10.1	
	C		9.2	
*cis*₃	**A**	8.9	7.7	2.9
	B	11.5	7.7	2.6
	C	11.2	7.5	3.0
*cis*₄	**A**	8.2	2.8	4.8
	B		4.2	
	C		5.8	

substituent may bring about even an energy difference of 4.6 kcal/mol. The **A**, **B**, and **C** forms of the *trans*₁ conformer of **2a** can be seen in Fig. 2. The other conformers (*trans*₂, *trans*₃, *trans*₄, *cis*₁, *cis*₂, *cis*₃, and *cis*₄) were found to be of higher energy content. A placement of the 3-P(O)Ph₂ and/or the 1-phenyl-

substituents into the axial position is rather unfavorable. An axial 3-P(O)Ph₂ deforms the ring significantly. The possible conformations of **2a** are characterized by a selection of dihedral angles shown in Table 2.

The same trends, i.e. a preference for the *trans*₁/**A** conformation and the highest energy content for the *trans*₂ and *cis*₂ conformations could be observed for the 1-phenyl-3-diethylphosphono product (**2c**). Conformation of the most advantageous arrangement is shown in Fig. 3. It is probable that product **2b** also has a preferred *trans*₁/**A** conformation.

In the case of conformers *trans*₁, *trans*₃, *cis*₂, and *cis*₄, the phenyl substituent on the ring P is parallel with the P=O group of the neighboring C(3)-P(O)Y₂ moiety. In the other cases, as a consequence of significant steric effects due to the ring H-atoms, the C(5)-Me or C(3)-P(O)Y₂ groups, the P-phenyl group was found to be perpendicular to the P=O group of the C(3)-P function.

As regards the conformation of the diastereomers of the triethoxy product (**4c**), no serious differences were found between the energy contents of the *trans*₁, *trans*₃, *cis*₁, and *cis*₃ conformations. Still, the *cis* forms seemed to be somewhat preferable. As a matter of fact, the stereospecific ^3J NMR couplings detected on the C(5)-Me group of **4c** promoted the assignment. The lack of an observable ^3J(P,C) coupling for C(5)—CH_3 together with a J(H,H) of 7.0 Hz for C(5)—CH_3 in the NMR spectra of the major component (**4-1/c**) of the triethoxy compound (**4c**) suggested the axial position of the methyl group and hence the involvement of the *cis*₃ conformer [9]. In this instance, the relative energies of rotamers **A**–**C** of the *cis*₃ conformation of **4-1/c** are quite close values.
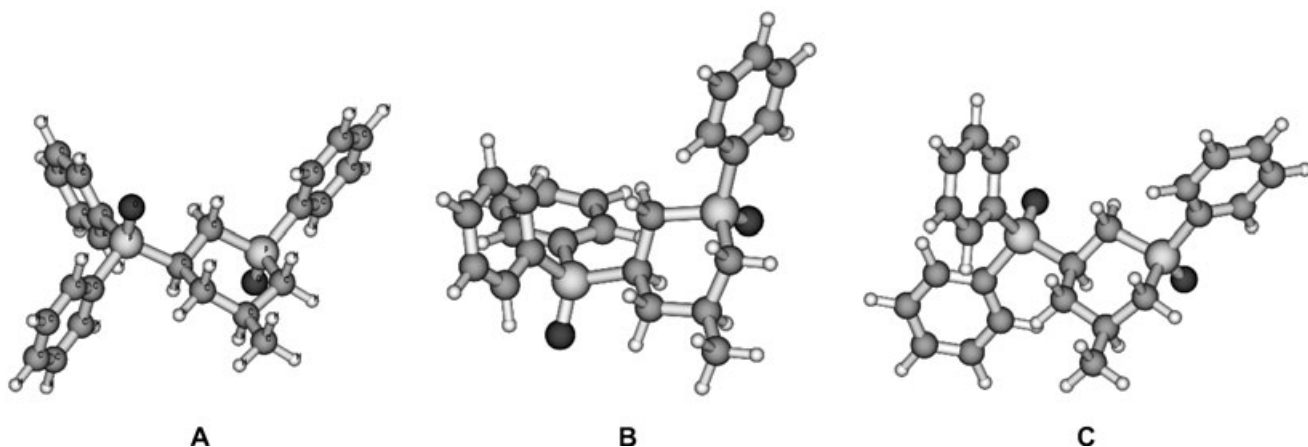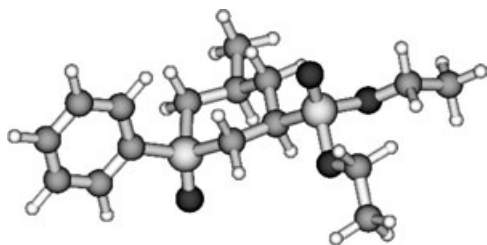

FIGURE 2 Stereostructures of the rotamers (**A**, **B**, **C**) of the *trans*₁ *chair* conformer of hexahydrophosphinine oxide **2a** obtained at the HF/6-31G* level of theory [12]. Geometrical data are listed for **2a-A**: P(1)–C(2): 1.820 Å, C(2)–C(3): 1.544 Å, C(3)–C(4): 1.544 Å, C(4)–C(5): 1.539 Å, C(5)–C(6): 1.541 Å, C(6)–P(1): 1.819 Å, O–P(1)–C(2): 113.1°, O–P(1)–C(6): 113.7°, O–P(1)–C(1′): 112.5°, C(2)–P(1)–C(6): 101.6°.

TABLE 2 Dihedral Angles (°) Selected for the Chair Conformers of the Diastereomers of 3-Diphenylphosphinoxido-hexahydrophosphinine Oxide **2a** Obtained at the HF/6-31G* Level of Theory

	trans$_1$	trans$_2$	trans$_3$	trans$_4$	cis$_1$	cis$_2$	cis$_3$	cis$_4$
P(1)–C(2)–C(3)–P(2)	176.8	114.7	176.3	101.6	−176.5	83.7	−178.0	78.4
P(1)–C(2)–C(3)–C(4)	−61.2	−21.1	−62.2	−28.8	−55.0	−51.0	−56.7	−51.0
P(1)–C(6)–C(5)–CH$_3$	−177.8	−85.5	−73.9	174.7	172.1	−77.1	−80.2	−177.6
P(1)–C(6)–C(5)–C(4)	58.7	46.5	54.5	52.6	48.7	55.0	48.9	59.9
C(6)–C(5)–C(4)–C(3)	−60.9	−62.2	−58.5	−69.5	−61.4	−51.7	−59.9	−62.4
C(6)–P(1)–C(2)–C(3)	55.5	9.2	54.5	14.9	39.6	51.7	42.4	46.8

FIGURE 3 Stereostructure of rotamer A of the *trans$_1$ chair* conformer of hexahydrophosphinine oxide **2c** obtained at the HF/6-31G* level of theory [12]. P(1)–C(2): 1.821 Å, C(2)–C(3): 1.545 Å, C(3)–C(4): 1.543 Å, C(4)–C(5): 1.538 Å, C(5)–C(6): 1.541 Å, C(6)–P(1): 1.819 Å, O–P(1)–C(2): 113.0°, O–P(1)–C(6): 113.8°, O–P(1)–C(1′): 112.5°, C(2)–P(1)–C(6): 101.5°, P(1)–C(2)–C(3)–P(2): 175.7°, P(1)–C(2)–C(3)–C(4): −61.2°, P(1)–C(6)–C(5)–CH$_3$: −177.7°, P(1)–C(6)–C(5)–C(4): 58.8°, C(6)–C(5)–C(4)–C(3): −60.7°, C(6)–P(1)–C(2)–C(3): 55.1°.

For the minor component (**4-2/c**) of the triethoxy compound (**4c**) with a doublet of doublets (6.5 and 3.5 Hz) at δ_H 1.06 in the proton NMR spectrum, an equatorial skeletal methyl group was suggested that is realized in the *cis$_1$* conformer.

It is probable that hexahydrophosphinine oxides **4-1/b** and **4-2/b** have a similar conformational situation as compared with **4-1/a** and **4-2/a**, respectively.

Theoretically, compounds **2** and **4** may also exist in the twist conformation. These are, however, by 4–6 kcal/mol less favorable than the *trans$_1$* or *cis$_1$/cis$_3$* conformations.

It can be concluded that the 3-P(O)Y$_2$-5-methyl-1-substituted 1,2,3,4,5,6-hexahydrophosphinine oxides adopt the chair conformation with the exo-cyclic P-moiety in the equatorial position. The skeletal methyl group is mostly equatorial, but may also be axial. Regarding the P-substituent, the phenyl ring adopts the equatorial position, while the ethoxy group prefers the axial orientation.

EXPERIMENTAL

The 3-substituted-1,2,3,4,5,6-hexahydrophosphinine oxides **2** and **4** were prepared and characterized as described in the preliminary publication [9].

The geometry optimization of different conformers of molecules was performed by ab initio calculations by Gaussian 98 and Gaussian 03 [10,11]. HF/6-31G* basis was applied in the ab initio calculations. In the ab initio calculations, the force matrices of the fully optimized molecules had no negative eigenvalues. The factor of 0.8929 was used as scaling factor for the ZPVEs.

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