Physical Chemistry

Conformational analysis and regioisomerism of mono- and diadducts of *O,O*-diisopropyl isoxazolinophosphonate with C_{60}

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Theoretically, cycloaddition of two molecules of phosphorylated nitrile oxide to C_{60} can give rise to 22 regioisomers. A simple convenient nomenclature was proposed for their classification based on the well-known Hirsh nomenclature. A combination of HPLC, semiempirical quantum-chemical PM3 calculations, and the dipole moment method demonstrated that the *equatorial*, *trans*-4(*tt*), and *trans*-3(*tt*) adducts are most probable.

Key words: [60]fullerene, mono- and diadducts, isoxazoline derivatives of [60]fullerene, phosphonates, conformational analysis, regioisomerism.

Previously,[1] we have reported that the reaction of di(isopropoxy)phosphorylformonitrile oxide with C_{60} afforded (according to HPLC data) three products, which were isolated by column chromatography. Based on the data from elemental analysis, ^1H, ^{13}C, and ^{31}P NMR spectroscopy, and UV spectroscopy, these compounds were characterized as diisopropyl isoxazolinophosphonate derivatives of fullerene at the closed 6,6-bond of the latter. We suggested that monoadduct **1** is the least polar product, whereas the other two products are mixtures of regioisomeric diadducts.[1] In the present study, we carried out semiempirical PM3 calculations and analyzed the polarities of the probable structures by the dipole moment (DM) method for the purpose of establishing the three-dimensional structures of the products obtained.

O,O-Diisopropyl isoxazolinophosphonate addends of mono- and diadducts with C_{60} have a large number of internal rotation axes and, consequently, a large number of probable conformers. Hence, the conformational composition of *O,O*-diisopropyl 5-phenylisoxazolin-3-ylphosphonate (**2**), which was chosen as a model of the phosphonate-containing fragment of the adducts under consideration, was analyzed by the PM3 and DM methods to simplify the theoretical analysis of the three-dimensional structures of the products, *i.e.*, to exclude sterically overcrowded and energetically equivalent structures from consideration. Phosphonate **2** was synthesized according to a known procedure.[2]

The applicability of the PM3 method to the conformational analysis of phosphonate **2** was tested with the

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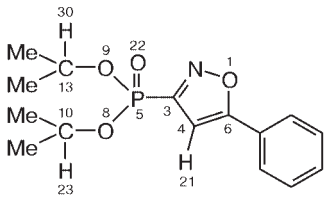

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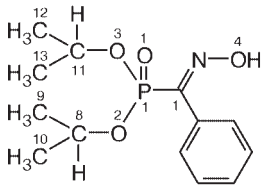

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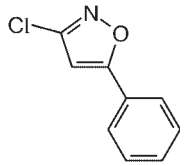

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use of *O,O*-diisopropyl *E*-α-hydroxyiminobenzylphosphonate (**3**), whose phosphonate oxime fragment simulates the isoxazolinophosphonate portion of molecule **2**, and 3-chloro-5-phenylisoxazole (**4**), which serves as a model of the isoxazolinophenyl fragment of phosphonate **2**. As can be seen from Table 1, the semiempirical quantum-chemical PM3 calculations with full geometry optimization adequately reproduced (except for the O(1)—P(1)—O(3)—C(11) torsion angle) the geometry of molecule **3** observed in the crystal.[3] The calculated dihedral angle between the heterocyclic and aromatic rings of compound **4** (5°) also agrees with the X-ray diffraction data[4] (13°).

Table 1. Geometric parameters of molecule **3** according to the results of X-ray diffraction analysis[5] and PM3 calculations

Parameter	X-ray diffraction analysis	PM3
Bond	*d*/Å	
P=O	1.46	1.46
P—O	1.55	1.60
C—O	1.47	1.43
Bond angle	ω/deg	
O=P—O	114—117	114—115
P—O—C	120—128	124—125
O—P—O	103	104
Torsion angle	φ/deg	
O(1)—P(1)—O(2)—C(8)	77.4	63.7
O(1)—P(1)—O(3)—C(11)	35.5	−10.38
P(1)—O(3)—C(11)—C(12)	−113.5	−105.8
P(1)—O(3)—C(11)—C(13)	128.6	133.88
O(1)—P(1)—C(1)—N(1)	−5.0	0.53
P(1)—O(2)—C(8)—C(9)	−70.7	−111.99
P(1)—O(2)—C(8)—C(10)	162.9	127.45
O(1)—P(1)—C(1)—C_{ar}	179.4	−178.84
P(1)—C(1)—N(1)—O(4)	−178.12	−179.63

Note. The atomic numbering scheme for compound **3** is given in the text.

Complete mapping of the potential energy surface of model phosphonate **2** whose molecule possesses 10 internal rotation axes is a laborious problem, which was beyond the scope of the present study. Hence, we restricted ourselves to the examination of discrete points on the potential energy surface of compound **2**. The calculations were carried out with full geometry optimization. All six possible structures shown in Fig. 1, *c* with the classical torsion angles (60° and 180° for the *gauche* and *trans* orientations, respectively) were taken as the starting models. For each starting structure, the syncli-

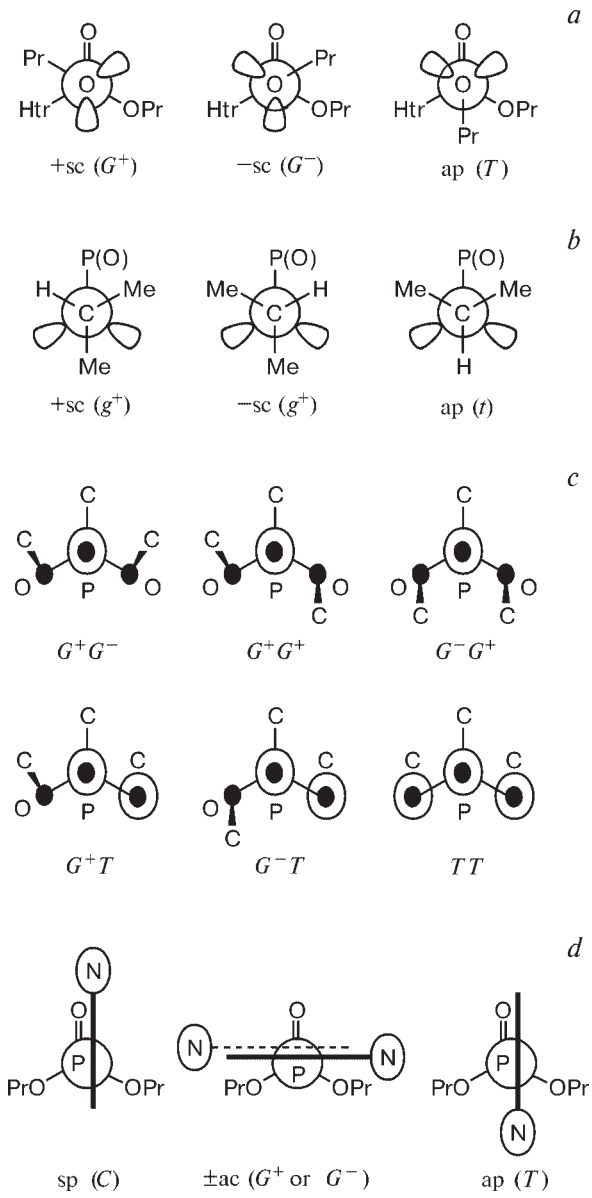


Fig. 1 Newman projections of the probable conformers of *O,O*-diisopropyl isoxazolylphenylphosphonate **2** along the O—P (*a*), C—O (*b*), O=P (*c*) (dotted circles represent the oxygen atoms), and P—C_{sp^2} (*d*) bonds.

nal and antiperiplanar conformations with respect to two O—C bonds (Fig. 1, *b*) were examined. In addition, one synperiplanar (*cis*, C), two anticlinal (*gauche*, G^+ and G^-), and one antiperiplanar (*trans*, T) conformations of the O=P—C=N fragment, which characterize the rotation of the isoxazolylphenyl fragment with respect to the P=O bond (Fig. 1, *d*), were assigned to each starting structure. In all cases, the eclipsed orientation of the planes of the isoxazoline and benzene rings was accepted. According to the results of our calculations, this orientation occurs in 3-chloro-5-phenylisoxazole (**4**) used as the model compound.

The calculated principal parameters of the probable conformers of phosphonate **2** are given in Table 2. Rotamers **2a,b** differ in the O=P—C—N torsion angles and belong to the G^-G^+ structural type. Rotamers **2c,d** belong to the G^-T structural type and also differ in the O=P—C—N torsion angles. It should be noted that the *trans* orientation of the isoxazolylphenyl fragment with respect to the P=O bond is impossible in the case of the G^+G^+, G^+G^-, and G^+T structures. The TT conformation (see Fig. 1, *c*) is not realized because of its steric overcrowding. As can be seen from Table 2, the relative enthalpies of formation (ΔH_f) of the rotamers of phosphonate **2** under consideration vary in the range of 0—1 kcal mol^{-1}, *i.e.*, all these structures are equally probable. A more detailed analysis of the potential energy surface in the vicinity of the resulting conformers revealed the following facts. For the rotamers of the G^-G^+ structural type, a change in the torsion angles of both O=P—O—C fragments in the range of 30—40° is accompanied by a change in the enthalpy of formation by no more than 0.5 kcal mol^{-1}. The variations in the torsion angles of the conformers of the G^-C and G^+C structural types (40—60° for the *gauche* orientation and 0±10° for the *cis* orientation) correspond to the same enthalpy range. Hence, it can be concluded that the synperiplanar (*cis*) orientation of the P=O and O—C bonds is not forbidden and the rotation about the P—O bonds is virtually free.

The results of PM3 calculations agree with the data published in the literature[5—15] according to which there is the conformational equilibrium between two or more rotational isomers of compounds of the $Alk_2P(O)R$ type (R = H, Me, Et, Ar, CCl_3, or Cl), the non-eclipsed *gauche* (G) and *trans* conformers (T) being preferable. For example, studies by the DM method and the Kerr effect measurements revealed the presence of the G^+G^- and G^+G^+ conformers for dimethyl arylphosphonates.[6] The calculations by the CNDO/2 method confirmed that dimethyl methylphosphonate adopts staggered conformations (see Fig. 1, *c*). However, the G^+G^- and G^+G^+ structures are higher in energy (2.5—4 kcal mol^{-1}) by the G^+T rotamer.[7] This inconsistency is attributable to an increase in steric overcrowding of the above-mentioned *gauche,gauche* structures upon the replacement of the aromatic ring at the phosphorus atom by the methyl group (see Fig. 1, *c*). According to the data from vibrational spectroscopy,[8—11] a wide range of dialkyl phosphites $(AlkO)_2P(O)H$, which contain rather bulky groups (Alk = Me, Et, Pr^n, Pr^i, or Bu^n) as alkyl substituents, adopt the G^+G^+, G^-G^+, or G^-T conformations in both the liquid state and solutions (see Fig. 1, *c*). The O=P—O—C torsion angle is so small that no difference between the "pure" *gauche* (60°) and "pure" *cis* (0°) mutual orientations of the P=O and O—C bonds was noted in the studies.[8,9] This is an agreement with the concept of a "diffuse minimum" between the *cis* and *gauche* conformations with respect to the P—O bond. Within the framework of this concept, it was suggested that the structures, which are formally in the regions of synperiplanar and synclinal conformations,[12,13] be called "cisoid".[14] Analysis of the vibrational spectra indicated that in the crystalline state dialkyl phosphites exist exclusively as the G^+G^+ conformer.[10] These results agree well with the X-ray diffraction data for *O,O*-diisopropyl phosphonates of the general formula $(Pr^iO)_2P(O)—C(R)=N—X$ (R = H, Cl, Ph), which are also indicative of the G^+G^+ structure.[5] Interestingly, according to the dipole moment method and the Kerr effect measurements,[6] the

Table 2. Principal parameters of the probable conformers of phosphonate **2** according to the PM3 calculations

Rotamer	Conformation	Torsion angle/deg			ΔH_f[a] /kcal mol^{-1}	μ[b] /D
		O(22)P(5)O(9)C(13)	O(22)P(5)O(8)C(10)	O(22)P(5)CN		
2a	G^-G^+	−37	32	48	0	5.74
2b	G^-G^+	−38	38	180	0.4	1.43
2c	G^-T	−29	177	−15	0.3	4.57
2d	G^-T	−30	171	180	0.5	1.76
2e	G^+G^+	36	43	66	0.9	3.81
2f	G^+G^-	30	−31	69	1.3	3.60
2g	G^+T	32	180	66	1.0	5.67

[a] The relative enthalpies of formation.
[b] The dipole moments calculated according to the vector-additive scheme.

O=P—O—C torsion angle in the G conformers deviates by 20—30° toward the synperiplanar (*cis*, C) conformation. In the crystalline state, this angle can be decreased even by 30—40° compared to the classical value (60°).[5] Thus, this angle in *N,N´*-bis[(diethoxyphosphinoyl)methyl]-1,4-diaminobenzene[16] is 22.5°. It should be noted that the O=P—O—C torsion angles calculated for phosphonate **2** (29—43°) are also substantially smaller than the "classical" values (see Table 2). Hence, the PM3 method adequately reproduces the data from the experimental methods (vibrational spectroscopy,[8—11] the dipole moment method, the Kerr effect,[6,15] and X-ray diffraction analysis[5,16]) for phosphonates, which provided evidence for the virtually free rotation about the P—O bonds and a decrease in the O=P—O—C torsion angles in the synclinal conformers to 30—40°.

To establish the conformational composition of model phosphonate **2**, we also employed the vector-additive scheme,[18] which has worked well in the conformational analysis of organophosphorus compounds.[15,17] We used the following values of the bond and group dipole moments: P=O, 2.95 D; O—P, 0.51 D; Pr^i—O, 0.29 D; C—P, 0.7 D;[19] and Ph—C, 0.37 D.[18] For the isoxazole ring, we used the group dipole moment of 2.82 D whose vector is directed toward the nitrogen atom at an angle of 72° with respect to the O—N bond.[20] The resulting dipole moment vector of the phenylisoxazoline fragment is located in the plane of the heterocycle and forms an angle of 85.2° with the C_{sp^3}—P bond. Table 2 gives the dipole moments of conformers **2a—g** of phosphonate **2**, which were calculated according to the vector-additive scheme using their structural parameters obtained by the PM3 method. Taking into account also the data from vibrational spectroscopy on the occurrence of different polarity structures of diisopropyl phosphite,[12] the experimental dipole moment of phosphonate **2** (3.7 D) would be more correctly described by the conformational equilibrium between the less polar (**2b**, **2d**) and more polar (**2a**, **2c**, **2e—g**) rotamers (see Table 2).

Hence, the results of our investigation on the conformational composition of model phosphonate **2** and analysis of the published data[5—15] led us to a conclusion that the internal rotation about the P—O bonds is virtually free. Consequently, only one of the forms given in Table 2 can be taken as the starting conformation of the phosphonate addend to simplify the calculations in the theoretical study of the structures of phosphorylated adducts of isoxazoline with fullerene obtained by us previously.[1]

Let us consider the mono- and diadducts of diisopropyl isoxazolinophosphonate with fullerene C_{60}. As mentioned above, cycloaddition of the first molecule of phosphorylformonitrile oxide to C_{60} afforded monoadduct **1** with the closure of the isoxazoline ring at the bond between two six-membered rings (6,6-closed monoadduct). The 6,6-closed monoadducts each have 29 C=C bonds, which can be subjected to the secondary attack of the nucleophilic reagent. If the monoadduct has no symmetry elements, all 29 C=C bonds are nonequivalent. If the monoadduct has the symmetry C_{2v}, the number of the nonequivalent C=C bonds is decreased to nine. The latter case has been considered by Hirsh.[21] According to Hirsh's nomenclature, the addition of the second addend molecule to the monoadduct of C_{60} with the symmetry C_{2v} can lead to three *cis* isomers, four *trans* isomers, and two equatorial (*eq*) isomers. The yields of the regioisomers of different diadducts of fullerene were determined by HPLC.[22] The results can be divided with certainty into two groups. In one group involving $C_{62}(CO_2Et)_4$, $C_{62}(anisyl)_4$, and $C_{62}(anisyl)_2(CO_2Et)_2$, the yields of the isomers (*Y*) of diadducts decrease in the series $Y_{eq} \approx Y_{trans} \gg Y_{cis}$, the yields of the *trans* isomers being changed in the series $Y_{trans\text{-}3} > Y_{trans\text{-}2} > Y_{trans\text{-}4} \gg Y_{trans\text{-}1}$. In another group including the aziridine-substituted diadducts $C_{60}(NCO_2Et)_2$ and $C_{61}(CO_2Et)_2(NCO_2Et)$, the yield of the *cis*-1 isomer is comparable with the yield of the equatorial isomer. It should be noted that the semiempirical and *ab initio* calculations predicted that the equatorial regioisomers of all addends and the *cis*-1 regioisomers of sterically non-overcrowded addends must be more stable.[22]

If the monoadduct has the local symmetry C_s, the number of the nonequivalent C=C bonds decreases to 15. This type of symmetry is observed in monoadduct **1**. However, we have previously demonstrated[23] that the theoretically possible number of regioisomers of the diadducts that formed upon the addition of phosphorylated nitrile oxide to monoadduct **1** increases to 30 of which only 22 regioisomers are nonequivalent. The number of the regioisomers is increased because the oxygen atom of di(isopropoxy)phosphorylformonitrile oxide can attack different carbon atoms of the C=C bond of fullerene C_{60}. The addition at the *trans*-1 bond affords two regioisomers with the symmetry C_{2v} and C_{2h} (Fig. 2). Due to the lowering of the symmetry of the monoadduct, the equatorial diadduct with the mutual orthogonal orientation of the heterocycles in which the phosphorus-containing substituent (R) of one addend is directed toward the plane of the heterocycle of another addend (regioisomer *e´*) differs from the equatorial product in which the phosphorus-containing substituent of one addend is directed away from the plane of the heterocycle of another addend (regioisomer *e″*) (see Fig. 2).

The attack of a nucleophile at the *cis*-1, *cis*-2, and *cis*-3 positions and the *trans*-2, *trans*-3, and *trans*-4 positions gives rise to three orientational regioisomers instead of one regioisomeric diadduct (according to Hirsh's classification[21,22]). These regioisomers differ in the mutual orientation of the oxygen atoms and the substituents R at the carbon atoms of the isoxazoline rings of two addends relative to one another (Fig. 3).

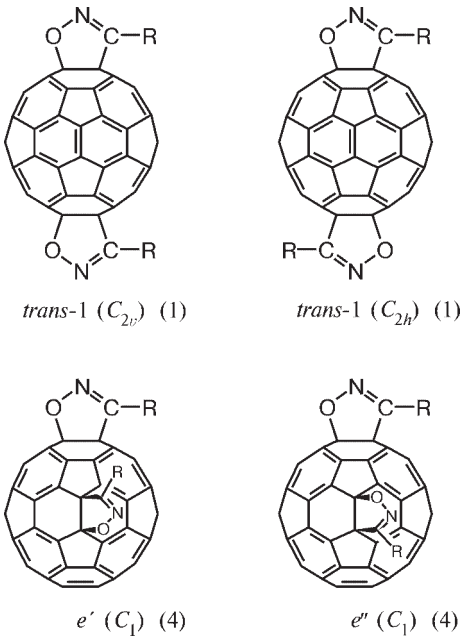
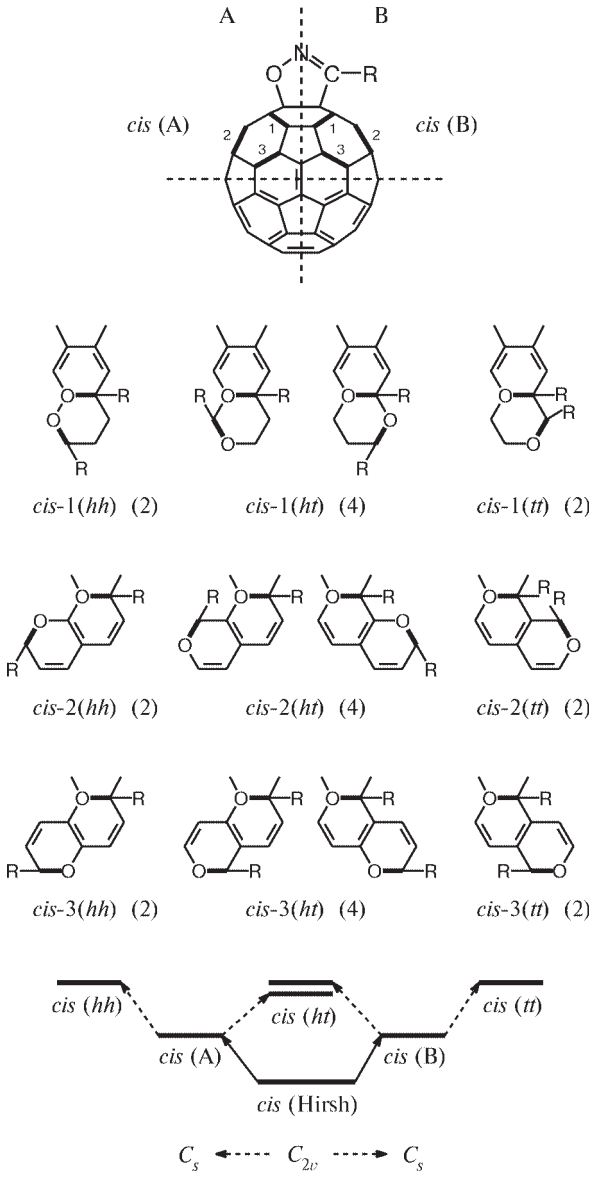


Fig. 2. Theoretical models of the regioisomers of the products of the secondary addition to monoadduct **1** at the *trans*-1 and equatorial bonds. The statistical weights of the regioisomers are given in parentheses.

The simple nomenclature proposed by Hirsh is unsuitable for the designation of all these orientational isomers. In our opinion, in this case it is appropriate to use the following nomenclature. The additional indices *hh* (*head-to-head*) and *tt* (*tail-to-tail*)) can be assigned to the orientational regioisomers in which the oxygen atoms of the five-membered rings are directed toward or away from each other, respectively (Figs. 3 and 4).

For the structures in which the oxygen atom is directed toward the substituent R, it is advisable to use the notation *ht* (*head-to-tail*), the statistical weight of this orientational regioisomer being equal to 2. Hence, if the symmetry of the C_{60} monoadduct is lowered from C_{2v} to C_s, two regioisomers appear instead of two diadducts (one equatorial and one *trans*-1), and three orientational regioisomers appear for the *cis*-1, *cis*-2, *cis*-3, *trans*-2, *trans*-3, and *trans*-4 adducts (see Fig. 2—4). Hence, taking into account the orientational regioisomerism, the number of possible secondary addition products in the case under consideration is equal to 22. Consequently, we denote the orientational regioisomers within one bond as *hh*, *tt*, and *ht*.

It should be noted that attempts to develop a nomenclature for orientational regioisomers have been made earlier.[24] However, in our opinion, the classification of the possible orientational regioisomers of the [60]fullerene diadducts proposed in the present study is much simpler. Our classification includes a smaller number of notations and is closer to Hirsh's nomenclature.[21,22] Since



Lowering of the symmetry of the monoadduct

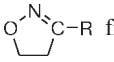
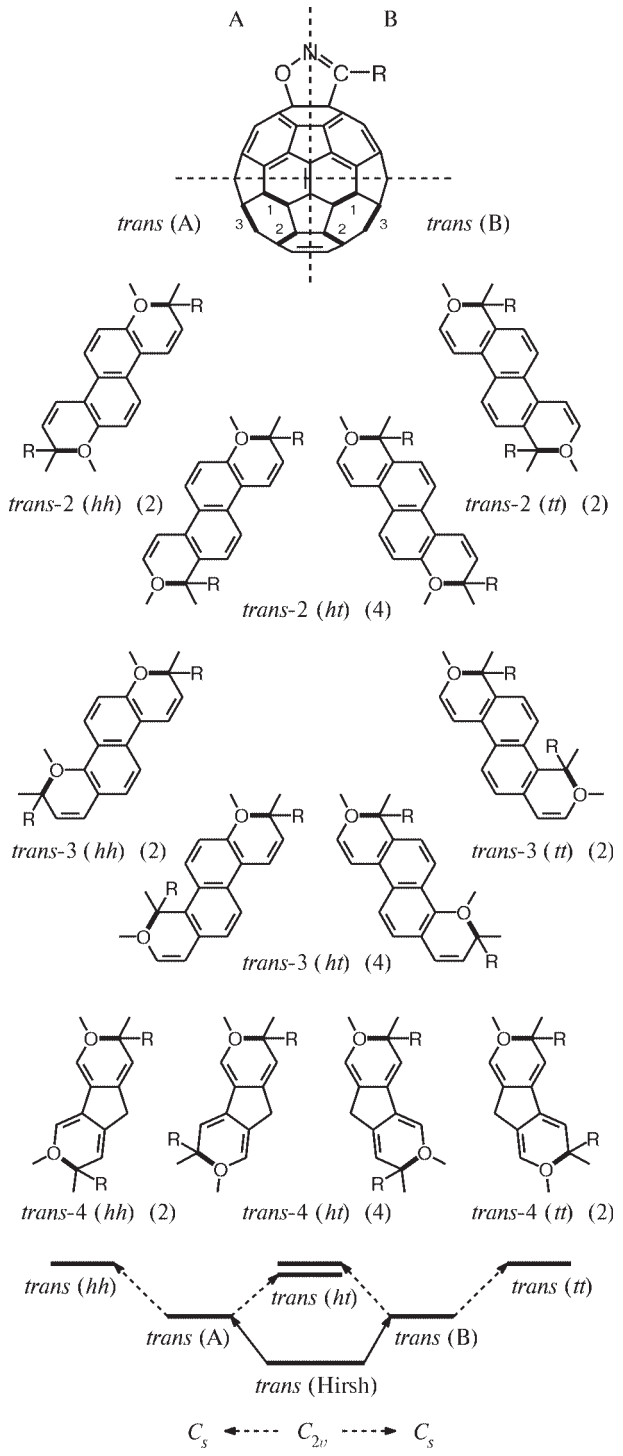
Note. The  fragment is shown as  .

Fig. 3. Six nonequivalent (upon the formation of diadducts) bonds in the upper hemisphere of monoadduct **1** at which the secondary attack can occur and the schematic representation of the orientational regioisomers of diadduct **5**. The statistical weights of the regioisomers are given in parentheses.

the monoadduct containing an unsymmetrical addend has the symmetry C_s, we carried out the classification of 22 regioisomers with the use of one hemisphere, while Irngartinger and coworkers[24] modeled 40 structures, grouped them into 22 types, and used both hemispheres and a much larger number of additional indices in the analysis.



Lowering of the symmetry of the monoadduct

Note. The  fragment is shown as  .

Fig. 4. Six nonequivalent (upon the formation of diadducts) bonds in the lower hemisphere of monoadduct **1** at which the secondary attack can occur and the schematic representation of the orientational regioisomers of diadduct **5**. The statistical weights of the regioisomers are given in parentheses.

To perform theoretical analysis of the regioisomerism of *O,O*-diisopropyl isoxazolinophosphonate diadducts of C_{60} **5**, we calculated the relative stabilities of the orientational regioisomers and their geometric parameters by the PM3 method. As mentioned above, the conformation of the phosphonate addend can be described by one of the forms given in Table 2 for the purpose of simplifying quantum-chemical calculations. We chose the G^-G^+ structure, both the mutual *cis* and *trans* orientations of the phosphoryl group (R) and the C=N bond of the isoxazoline ring being taken into account. In the theoretical conformational analysis, we examined all possible orientational (*trans*, *cis*, and *equatorial*) regioisomeric diadducts **5**.

The calculated enthalpies of formation of regioisomeric diadducts **5** differ substantially (Table 4), unlike those calculated previously by the AM1 method[22] for a wide range of compounds including $C_{62}(CO_2Et)_4$, $C_{62}(anisyl)_4$, $C_{62}(anisyl)_2(CO_2Et)_2$, $C_{60}(NCO_2Et)_2$, and $C_{61}(CO_2Et)_2(NCO_2Et)_2$, where virtually equal enthalpies have been obtained. The reason is that both the monoadduct and the addend have lower symmetry compared to that of the compounds considered previously.[22]

Table 3. Theoretical estimations of the relative stabilities (ΔH/kcal mol^{-1}) of the possible regioisomers of diisopropyl isoxazolylphosphonate diadducts **5** by the PM3 method

Regioisomer	$Orn_{P=O,C=N}$*	ΔH
e´	*cis,cis*	0
e″	*cis,cis*	2.4
trans-1(C_{2v})	*cis,cis*	9.1
trans-1(C_{2h})	*cis,cis*	9.9
trans-2(*hh*)	*cis,cis*	3.0
trans-2(*tt*)	*cis,cis*	3.3
trans-2(*ht*)	*cis,cis*	3.1
trans-3(*hh*)	*cis,cis*	2.7
trans-3(*tt*)	*cis,cis*	2.2
trans-3(*ht*)	*cis,cis*	2.7
trans-4(*hh*)	*trans,trans*	3.2
trans-4(*tt*)	*trans,trans*	1.5
trans-4(*ht*)	*cis,cis*	3.2
cis-1(*hh*)	*cis,cis*	5.1
cis-1(*tt*)	—	—
cis-1(*ht*)	*trans,trans*	12.8
cis-2(*hh*)	*cis,cis*	5.8
cis-2(*tt*)	—	—
cis-2(*ht*)	*trans,trans*	11.2
cis-3(*hh*)	*cis,cis*	4.8
cis-3(*tt*)	*trans,trans*	4.0
cis-3(*ht*)	*trans,trans*	4.0

* The orientation of the phosphoryl group and the C=N bond of the isoxazoline ring in each addend.

This results, for example, in the substantial difference in the energy of the orientational regioisomers *e´* and *e″*. The structure *e´* (see Fig. 2) is most stable, whereas the energy of the structure *e″* with another orthogonal orientation of the addends is 2.4 kcal mol^{-1} higher. The energies of the *trans*-4(*tt*) and *trans*-3(*tt*) isomers differ from that of the *e´* isomer by 1.5 and 2.2 kcal mol^{-1}, respectively. However, according to our theoretical estimation, the former isomers are more stable than the *e″* isomer. The orientational isomers *trans*-3(*hh,ht*), *trans*-2(*hh,tt,ht*), and *trans*-4(*hh,ht*), which are energetically less stable than the *e″* isomer, belong to the next group. On the whole, the *cis* diadducts are less stable than the *e, trans*-2*, trans*-3, and *trans*-4 regioisomers. For steric reasons, the *cis*-1 and *cis*-2 isomers cannot assume the *tt* structures in which the phosphorus-containing substituents (R) of two addends are directed toward each other (see Fig. 3). Hence, according to the results of PM3 calculations, the orientational regioisomers of the diadducts of *O,O*-diisopropyl isoxazolinophosphonate with C_{60} are arranged in the following series according to their thermodynamic preference: *e´* > > *trans*-4(*tt*) > *trans*-3(*tt*) > *e″* > *trans*-3(*hh,ht*) > > *trans*-2(*hh,tt,ht*) ≈ *trans*-4(*hh,ht*) > *cis*-3(*tt,ht*) > > *cis*-1(*hh*) > *cis*-2(*hh*) > *trans*-1 (C_{2v}).

Analysis[23] of the available structural data[21,22] showed that the π-electronic structure of the bonds in [60]fullerene is transformed in much the same manner on going to its 6,6-closed monoadduct. The *cis*-1 bonds are substantially shortened and equalization of the single and double bonds is observed in the zone in which the *cis*-2 and *cis*-3 positions are located. In the second hemisphere of the molecule, the bonds are restored to their original lengths found in the starting fullerene C_{60}. The statistical analysis of the relative yields of the regioisomers of the diadducts synthesized by Hirsh and coworkers[22] adequately follows the above-mentioned variations in the π-electronic systems of the monoadducts. First, the addition at the *cis*-1 position in the reactions with sterically non-overcrowded addends exceeds the statistically expected yield by a factor of 1.5—2, whereas the sterically hindered approach of the second addend gives zero yield. In all six reactions considered in the study,[22] the addition of the second addend at the *cis*-2 and *cis*-3 positions affords products in yields, which are, on the average, half as high as the statistically expected values. The reactivity of the bond decreases as its order decreases and the length increases. Hence, even the above considerations provide conclusive evidence that in the case under examination, *viz.*, in the reaction of di(isopropoxy)phosphorylformonitrile oxide with C_{60}, the addition of the second nitrile oxide molecule at the hemisphere of monoadduct **1** containing already one open C=C bond is the least probable. Thus, the addition at the *cis*-1 position is highly improbable because the steric effect obviously dominates over the electronic effects, whereas the addition at the *cis*-2 and *cis*-3 positions is unlikely on account of the reduced reactivity due to the lower electron density on these double bonds. This assumption agrees well with the series of thermodynamical stabilities of diadducts **5** found by us.

As noted above, the difference between the enthalpies of formation (ΔH_f) of regioisomeric diadducts **5**, which we calculated by the PM3 method, is much larger than ΔH_f for diadducts of a broad range of compounds calculated by the AM1 method.[22] To find out whether this fact is associated with the parametrization of the semiempirical method, we employed also the AM1 method. The difference between the enthalpies of formation (15 kcal mol^{-1}) of the most stable equatorial (*e´*) isomer and the *trans*-1 (C_{2v}) regioisomers calculated by the AM1 method is also substantially distinct from those calculated previously by the AM1 method for a wide range of compounds.[22] Apparently, this indicates that the steric factor more essentially dominates over the electronic effects in the cycloaddition of phosphorylformonitrile oxide to C_{60}. Hence, the theoretical series of the preference of the secondary cycloaddition to monoadduct **1**, which was obtained based on the thermodynamical arguments (PM3 and AM1 calculations of the enthalpies of formation) agrees with the experimental data on the sterically crowded addends,[22] the results of analysis of the reactivity indices, and the consideration of the steric factors of this reaction. In the present study, we do not discuss the energies of the orientational regioisomers generated by the attack of the oxygen atom of the addend on different atoms of C_{60} belonging to the same bond. Note only that the theoretical estimates for some regioisomers, for example, for *cis*-1(*hh*) and *cis*-1(*ht*) as well as for *cis*-2(*hh*) and *cis*-2(*ht*), are indicative of a rather high selectivity of the attack (Table 3).

Table 4. Dipole moments (μ/D) of monoadduct **1** and regioisomeric diadducts **5** estimated according to the vector-additive scheme and the relative energies (ΔH/kcal mol^{-1}) of the orientational regioisomers

Adduct	μ	ΔH	Adduct	μ	ΔH
Monoadduct	3.6	—	Diadduct*		
Diadduct*			*e″*	4.8	2.4
e´	5.4	0.0	*cis*-3(*ht*)	5.8	4.0
trans-4(*tt*)	4.7	1.5	*cis*-1(*hh*)	6.3	5.1
trans-3(*tt*)	4.2	2.2	*cis*-2(*hh*)	5.3	5.8

* The data are given for the regioisomers for which the theoretical dipole moments are larger than the dipole moment of monoadduct **1**. The mutual orientations of the oxygen and phosphorus atoms of two addends are given in parentheses (see comments in the text).

According to our theoretical estimations, the *trans*-4(*tt*), *trans*-3(*tt*), and *e´* regioisomers have close thermodynamical stabilities. It is difficult to give preference to a particular isomer based only on the results of calculations and analysis of the experimental data obtained in the previous studies because the resulting monoadduct **1** is sterically overcrowded only on one side due to molecular asymmetry. Of special interest is the theoretical analysis of the polarities of the mono- (**1**) and diadducts (**5**). Generally, since less polar compounds have larger retention times in reversed-phase chromatography as compared to those of more polar phases (it should be noted that according to the data from HPLC of the reaction mixture,[1] the starting fullerene C_{60}, being a nonpolar molecule, has the maximum retention time) the correlation of the dipole moments of the assumed products with the HPLC data shows considerable promise for studies of the regioselectivity of cycloaddition to fullerenes. For this purpose, we estimated the polarities of the structures of monoadduct **1** and all the above-considered regioisomeric diadducts **5** with the use of the vector-additive scheme.[18]

The molecule of fullerene C_{60} is nonpolar and can be described as a regular truncated icosahedron. The addition of substituents to this fullerene leads to a distortion of the fullerene core (see, for example, Ref. 25). One would expect that this will lead to asymmetry of the atomic charge distribution and, as a consequence, to the appearance of a dipole moment of the fullerene core. However, taking into account that the polarities of the *O,O*-diisopropyl isoxazolinophosphonate substituents under consideration are much higher (by 4—6 D, see Table 2) than that of the fullerene core, we assumed that the C_{60} fragment in molecules **1** and **5** is nonpolar and the bonds between the carbon atoms in this fragment have equal lengths. Hence, the polarities of monoadduct **1** and diadducts **5** depend only on the dipole moment of the phosphonate fragment, which was calculated according to the vector-additive scheme[18] with the use of the above-mentioned bond and group dipole moments and the geometric parameters obtained by the PM3 method. In the phosphorus-containing addend of monoadduct **1**, the rotation about the P—C_{sp^2} bond is virtually free, and the enthalpies of formation of the G^-G^+ conformers with the mutual *cis* and *trans* orientations of the phosphoryl group and the C=N bond of the isoxazole ring have equal values. On this basis, the dipole moments of the structures were averaged to simplify the analysis of the polarities of diadducts **5**. Of all the possible regioisomers of diadducts **5**, only the regioisomers whose dipole moments are higher than that of monoadduct **1** are included in Table 4 because the reaction under consideration afforded diadducts, which are more polar than monoadduct **1** (according to the HPLC data[1]).

As can be seen from Table 4, the equatorial diadducts e´ and *e″*, the diadducts *trans*-4(*tt*) and *trans*-3(*tt*), and the *cis* regioisomers are more polar than monoadduct **1**. Hence, from the viewpoint of polarity, the HPLC data (retention times) are consistent with the following order in which regioisomeric diadducts **5** are eluted from the column: *cis*-1, *cis*-3, *cis*-2 ≈ *e´*, *e″*, *trans*-4, and *trans*-3. However, taking into account the relative stabilities of the regioisomers of **5** estimated by the PM3 method (see Table 4) and the experimental data on the yields of the sterically crowded addends,[22] it can be concluded with a fair degree of assurance that the formation of the *cis* regioisomers is less probable than the formation of the *e´*, *e″*, and *trans* isomers. It should also be noted that the calculated enthalpies ΔH_f (and, consequently, the populations) adequately correlate with the integral intensities of the adducts determined by chromatography of the reaction mixture after storage for three hours.[1]

To summarize, the studies by the semiempirical (PM3 and AM1) quantum-chemical methods and the dipole moment method followed by the qualitative polarity—chromatographic retention time correlation demonstrated that monoadduct **1**, the equatorial diadducts *e´* and *e″*, and the *trans*-3 and *trans*-4 diadducts are the most probable reaction products of cycloaddition of di(isopropoxy)phsophorylformonitrile oxide to C_{60}.

Experimental

The dipole moment of *O,O*-diisopropyl isoxazolylphenylphosphonate **2** in C_6H_6 (3.7 D) was determined by the second Debye method[18] from the permittivities and refractive indices of solutions on an apparatus described previously.[26] The semiempirical calculations with full geometry optimization were carried out by the PM3 and AM1 methods using the AMPAC program.[27]

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