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A Solution and Solid State Conformation of 2-Diphenylphosphinoyl-1,3-dioxanes. The Nature of O-C-P Anomeric Interactions.

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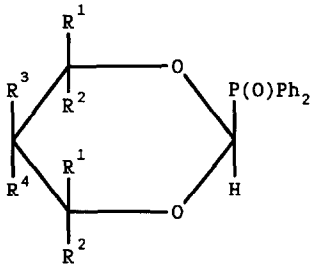
Abstract: Diastereoisomeric 2-diphenylphosphinoyl-1,3-dioxanes **1-4** were synthesized either *via* the Arbuzov reaction of isopropyl diphenylphosphinite with (1,3-dioxan-2-yl)trimethylammonium iodides or *via* the transacetalization reaction between 1,3-diols and diphenyl(diethoxymethyl)phosphine oxide. The latter reaction afforded less thermodynamically stable isomers of **3** and **4** in a good yield (44 and 56%, respectively). The magnitude of the anomeric effect in this system determined according to the Franck's equation was found to be 19.7 kJ/mol. Both the NMR and X-ray structural data concerning *cis*-4,6-dimethyl-1,3-dioxane derivatives **4** suggest that the anomeric effect could stem from several interactions, including the $n_O-\sigma^*_{C-P}$ negative hyperconjugation and intramolecular hydrogen bond formation.

INTRODUCTION

The anomeric effect involving second-row elements has been the subject of extensive investigations[1-5] during the past decade. While the importance of negative hyperconjugation as an origin of the anomeric effect in the case of first-row elements is well accepted now[3a], it is a matter of controversy for second- and especially third-row atoms[1,3b,4,5]. Thus, geometrical parameters in the crystal of 2-diphenylphosphinoyl-1,3-dithiane[1a,e] and 2-dimethoxyphosphoryl-1,3,5-trithiane[5a] did not come up to expectations based on the $n_S-\sigma^*_{C-P}$ negative hyperconjugation. The absence of a deuterium isotope effect on the conformational equilibrium in 2-deuterio-1,3-dithiane led Anet and

Kopelevich[6] to a similar conclusion concerning the $n_S-\sigma^*_{C-D(H)}$ negative hyperconjugation. However, the latter effect was observed[6] for the appropriate deuterated 1,3-dioxane and implied that negative hyperconjugation could govern the conformational equilibrium in other 1,3-dioxane derivatives.

In 1988 we briefly reported[5e] the overwhelming equatorial preference of the diphenylphosphinoyl group, $Ph_2P=O$, connected with the anomeric carbon atom of the 1,3-dioxane ring. However, in spite of the lack of manifestation of the anomeric effect in this system, its value estimated recently by Juaristi *et.al.*[1b] was found to be quite substantial and close to 12 kJ/mol. Unfortunately, these authors were not able to prepare the conformationally fixed derivatives containing phosphoryl group in the axial position, which could have been studied in order to gain better insight into the origin of the anomeric effect. Hence, the nature of the anomeric effect in O-C-P system remained obscure.



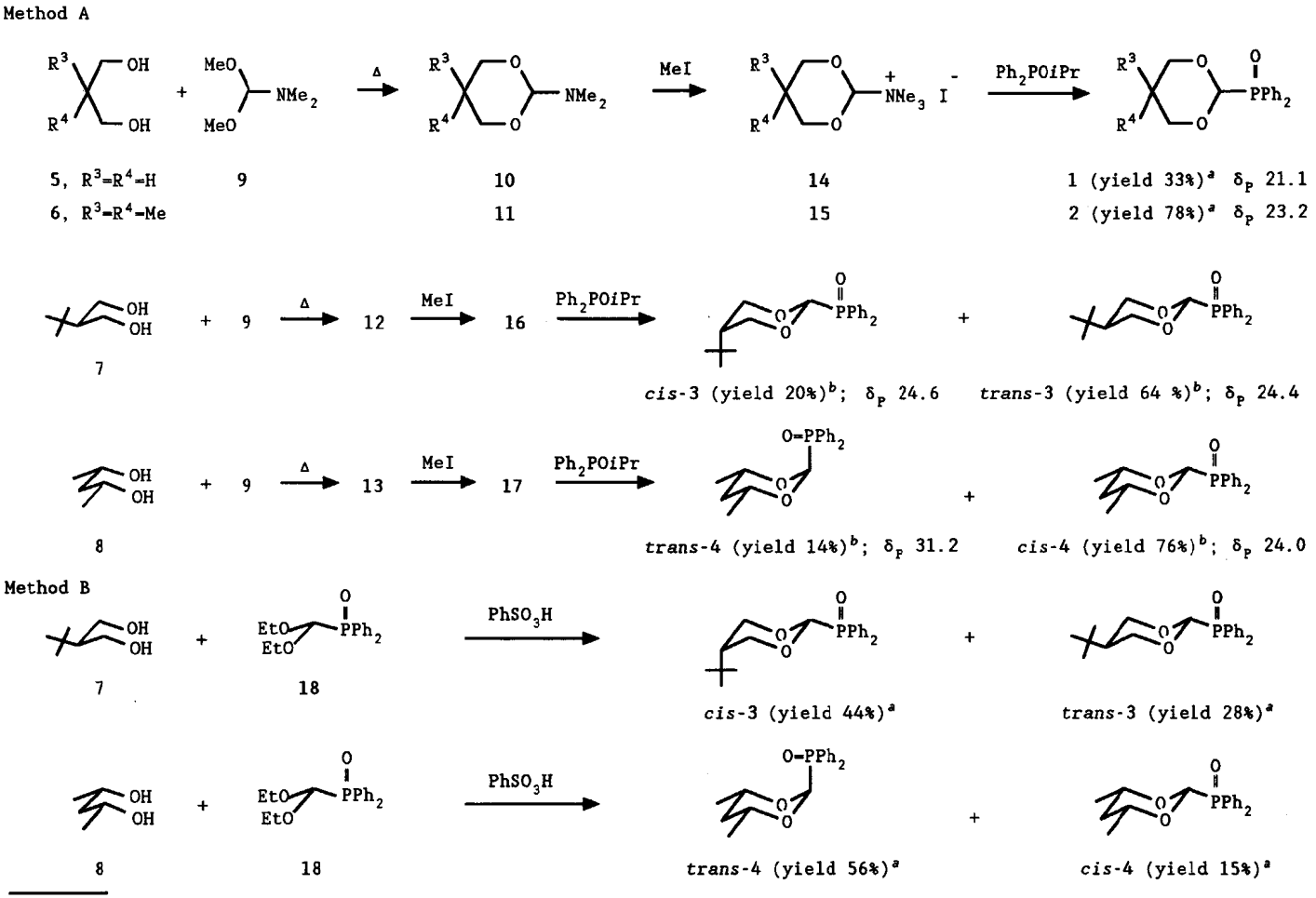
R^1	R^2	R^3	R^4	Compound
H	H	H	H	1
H	H	Me	Me	2
H	H	*t*Bu	H	*cis*-3
H	H	H	*t*Bu	*trans*-3
H	Me	H	H	*trans*-4
Me	H	H	H	*cis*-4

In this paper we would like to report full results of our studies on the conformation of 2-diphenylphosphinoyl-1,3-dioxanes **1-4** including two pairs of the diastereoisomeric compounds (*cis*- and *trans*-**3** and **4**) and to discuss the nature of the O-C-P anomeric interactions, based on the data from solution and solid state structural studies.

RESULTS AND DISCUSSION

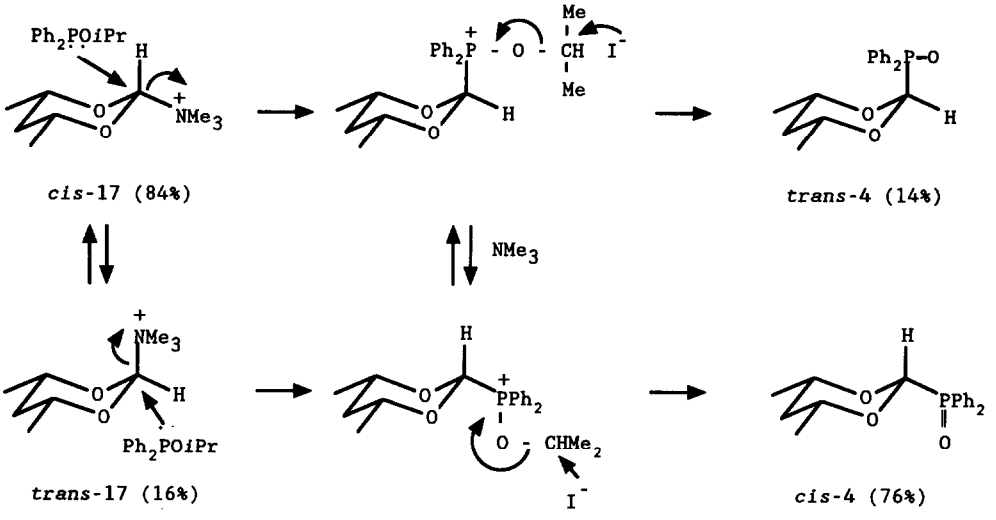
Synthesis of 2-Diphenylphosphinoyl-1,3-dioxanes

The preparation of 2-diphenylphosphinoyl-1,3-dioxanes **1-4** was accomplished following the procedure described by Costisella and Gross[7], which involves the Arbuzov reaction of isopropyl diphenylphosphinite with the appropriate ammonium iodides **14-17** as shown in Scheme 1.(Method A). Ammonium iodides **14-17** are easily available from the relevant 2-(N,N-dimethylamino)-1,3-dioxanes **10-13**. It is interesting that the overall yield of the reaction largely depends on alkyl substituents at a ring. While the 5-*t*-butyl derivative **16** reacted almost quantitatively (*cis*-**3**+*trans*-**3**, 84%), the phosphinoxide **1** was prepared in 33% yield only. As far as the diastereoisomeric pairs **3** and **4** are concerned, it should be stressed that the formation of *all*-equatorial *trans*-**3** and *cis*-**4** is preferred. Such behavior can be attributed, perhaps, to the epimerization of ammonium[8] or alkoxyphosphonium salts in the presence of a tertiary amine (see Scheme 2 for *cis*- and



[a]isolated, except otherwise stated; [b]estimated on the basis of ^{31}PNMR spectrum of the crude reaction mixture.

Scheme 1. Synthesis of 2-Diphenylphosphinoyl-1,3-dioxanes 1-4

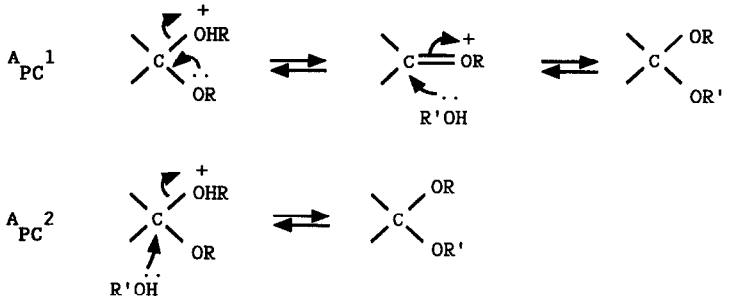


Scheme 2.

trans-4), as was observed by us[5g,i] for 2-phosphonio-1,3-dithianes. It is worthy to note that a similar preference (*cis*-3:*trans*-3=2:8) was described by Juaristi *et al.*[1b] for the reaction between 5-*t*-butyl-2-methoxy-1,3-dioxane and chlorodiphenylphosphine (procedure of Dietsche[9]).

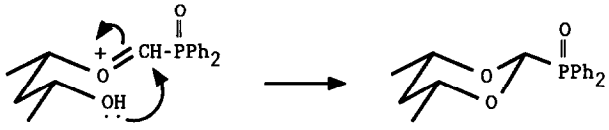
We found that *cis*-4 crystallized well enough to be isolated in 66% yield from the crude reaction mixture without chromatographic separation. This compound was also prepared by Juaristi *et al.*[1c], who used Dietsche's method[7], but they were not able to synthesize and characterize *trans*-4, since even traces of the latter were not observed.

In principle, method A could have been applied to obtain diastereoisomeric *cis*-3 and *trans*-4 *via* chromatographic separation, but the content of them in the crude mixture seemed to be too low. Therefore, we tried to synthesize the *cis*-3 and *trans*-4-enriched



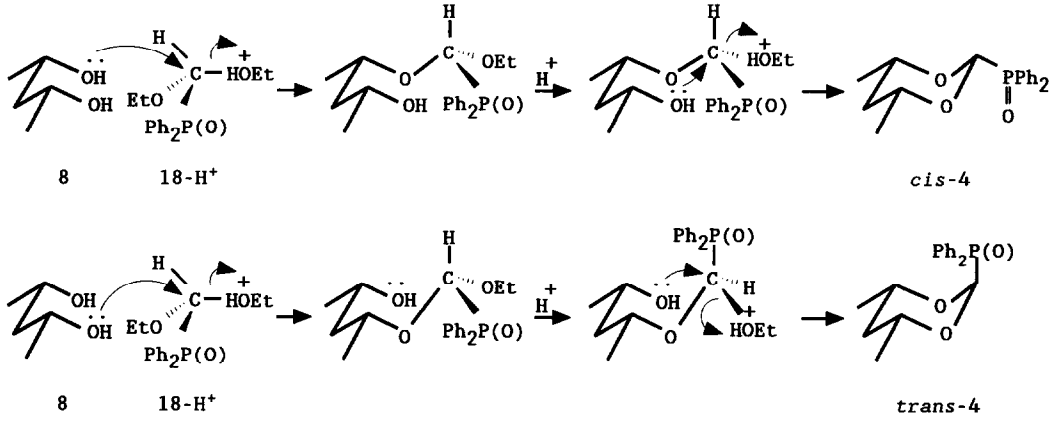
Scheme 3.

mixtures through the transacetalization between an appropriate 1,3-diol and diphenyl-(diethoxymethyl)phosphine oxide (**18**) in the presence of a catalytic amount of benzenesulfonic acid (Scheme 1.; Method B). It is clearly seen that the formation of the less thermodynamically stable isomers of 2-diphenylphosphinoyl-1,3-dioxanes, namely *cis*-**3** and *trans*-**4**, is preferred. This observation implies that the reaction does not occur *via* the oxocarbonium ion, which is the most common intermediate in the formation of acetals[10] (Scheme 3., mechanism $A_{PC}1$). If it had been involved in the reaction between 1,3-diols and **18** the position of the phosphoryl group in 1,3-dioxane ring would have been fixed at the last step of transacetalization (Scheme 4.), when steric factors (1,3-diaxial repulsions) force the P=O group into the equatorial position. The appropriate oxocarbonium ion is, perhaps, too unstable owing to strong electronwithdrawing properties of the $Ph_2P{=}O$ group connected with the procarbonyl carbon atom.



Scheme 4.

The observed stereoselectivity of transacetalization can be well accounted for in terms of the operation of S_N2-type mechanism, namely $A_{PC}2$ (Scheme 3). In this case, the configuration of phosphoryl group is set at the first step, when a protonated molecule of **18** makes a choice between two enantiotopic oxygen atoms of a diol (e.g. **8** during the formation of *cis*-**4** and *trans*-**4**; see Scheme 5). The axial position of the phosphoryl group in *trans*-**4** is due to the necessity of the linear arrangement of O-C-O$^+$HEt system, when the second C-O bond in *trans*-**4** is being formed.



Scheme 5.

It must be noted, that while method A leads only to the desired isomeric pairs of **3** and **4**, the transacetalization (method B) is accompanied by the formation of unidentified by-products of δ_{31P} 21.1; 30.5 and δ_{31P} 21.9 ppm, respectively.

The chromatographic separation of individual isomers of **3** was difficult due to very close R_F values, but it was achieved by medium-pressure column chromatography with careful gradient control. However, compound *trans*-**4** was not stable enough under these conditions, and it was necessary to separate it by means of flash-chromatography.

NMR Conformational Studies of 2-Diphenylphosphinoyl-1,3-dioxanes 1-4

In the ^{13}C NMR spectra of the 1,3-dioxane derivatives *trans*-**4** and *cis*-**4** one can observe the signals of carbons C(4,6) as doublets with coupling constant $^3J_{C-P}$ equal to 2.4 and 10.4 Hz, respectively. γ-Effect values also differ substantially (-3.60 and +1.86 ppm, respectively) and these data, if an analogy to other 2-phosphoryl-1,3-diheteroanes[5b,c] is assumed, suggest the axial and equatorial arrangement of the $Ph_2P{=}O$ group in *trans*-**4** and *cis*-**4**, respectively. It should be added that the carbon atom of the methylene group in *trans*-**4** appears as a doublet with the coupling constant with phosphorus $^4J_{C-P}$=2.1 Hz. Such a long range coupling, which is characteristic for the axial position of the phosphoryl group in 1,3-dithianes[5j] and 1,3-oxathianes[1c], may serve as additional evidence.

The ^1H NMR spectra of *trans*-**4** and *cis*-**4** firmly support the above configurational assignments. Axial attachment of phosphorus is responsible for the well known, considerable deshielding of the axial $H(4,6)_{ax}$ protons in *trans*-**4**, which resonate at δ about 5.0 ppm ($\delta_{H(4,6)}$ 3.70 ppm in the parent *cis*-4,6-dimethyl-1,3-dioxane). Long range coupling $^4J_{H-P}$= 0.7 Hz between $H(4,6)_{ax}$ and P additionally confirms the axial position of phosphorus in *trans*-**4**.

However, for the two isomeric 5-*t*-butyl-2-diphenylphosphinoyl-1,3-dioxanes **3** the γ-effect (-0.55 and +1.61 ppm) and $^3J_{C-P}$ (8.9 and 10.8 Hz) values are close and suggest an equatorial position of the phosphoryl group in both isomers. This problem was solved *via* ^1H NMR spectroscopy in such a way that the first value in parentheses corresponds to the isomer *cis*-**3** while the second to *trans*-**3**. The only difference between these two compounds is the position of the *t*-butyl group which is unexpectedly axial in *cis*-**3** and equatorial in *trans*-**3**; thus $^3J_{C-P}$ and γ-effect values should be close.

The main difference in the ^1H NMR spectra of *cis*-**3** and *trans*-**3** consists in the coupling pattern of H(5) proton. While in the spectrum of the major product of the Arbuzov reaction one can find two different coupling constants, which may be ascribed to *anti* and *gauche* coupling (11.4 and 4.3 Hz, respectively), in the spectrum of the second, minor isomer both constants are small (3.7 and 2.1 Hz) and typical for a *gauche*-type arrangement of nuclei. Therefore, the first product should contain the *t*-butyl group situated equatorially (*trans*-**3**) and the second one axially (*cis*-**3**). Equatorial protons $H(4,6)_{eq}$ in *cis*-**3** and *trans*-**3** are coupled with phosphorus with constants 1.8 and 1.4 Hz, respectively, in agreement with equatorial position of the phosphoryl group (*w*-type coupling). These conclusions were confirmed by NOE enhancement determination. The results are collected in Table 1. Following the usual practice[11], from the two possible irradiation modes we chose the one which was expected to afford a better possibility of relaxation of irradiated nucleus, and consequently to give a larger NOE enhancement coefficient. In particular, H(2) was not irradiated. In order to compare the results, both *cis*-**3** and *trans*-**3** were irradiated in the same way. As is seen, the enhancement due to the H(5) - $H(4,6)_{eq}$ interaction is the same in both isomers and confirms the

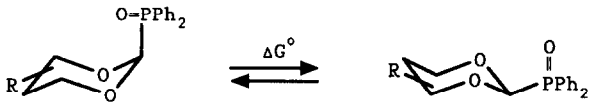
Table 1. NOE Enhancement Coefficients in the ^1H NMR Spectra of *cis*-3 and *trans*-3.

Enhancement[a] [%]				
Between[b]	H(2)	$H(4,6)_{ax}$	$H(4,6)_{eq}$	H(5)
H(2)	-	5.4	0.0	0.0
$H(4,6)_{ax}$	*17.7*	-	24.0	4.4
$H(4,6)_{eq}$	*0.0*	*15.9*	-	2.6
H(5)	*0.2*	*0.9*	*2.7*	-

[a]for *cis*-3 in emboldened roman; for *trans*-3 in *italics* [b])irradiated nuclei: for *cis*-3 listed in horizontal line, for *trans*-3 given in column.

equatorial position of H(4,6) protons resonating at δ 4.39 and 4.31 in *cis*-3 and *trans*-3, respectively. On the other hand, H(5) - $H(4,6)_{ax}$ NOE coefficients are different (4 and 1%) and suggest a close contact between the interacting nuclei in *cis*-3, what is only possible if conformation with the axial *t*-butyl group is assumed. This conclusion is additionally supported by smaller H(2) - $H(4,6)_{ax}$ coefficient in *cis*-3 (5%) than in *trans*-3 (18%). Axial *t*-butyl group should flatten C(4)-C(5)-C(6) region of the 1,3-dioxane chair, and the distance between H(2) and axial H(4,6) would be larger in *cis*-3 than in *trans*-3, thus leading to a decrease of NOE enhancement coefficient. Obviously, a certain contribution from other conformers of 3 must also be taken into account, but the general conclusions seem to be qualitatively correct.

In the case of the conformationally labile 1,3-dioxanes **1-2** one should consider the equilibrium shown in Scheme 6. Low-temperature ^{31}P NMR spectrum of **2** (CD_2Cl_2, temp.180 K)



1,2-ax 1,2-eq

Scheme 6.

consists of one signal only. Although fortuitous identity of chemical shifts of ^{31}P nuclei in both conformers cannot be excluded this result indicates that practically one conformer is present in a solution. Since the shift in equilibrium toward more stable conformer should be expected with the decrease of temperature, the conformational equilibrium at room temperature need not be so one-sided. Conformational equilibrium constant K and the relevant free energy difference ΔG° can be estimated *via* the weighted

average method[12], assuming that the NMR data for the conformationally fixed ("anancomeric") models *trans*-**4** and *cis*-**4** correspond to the data for individual conformers of **1** and **2**. In the room-temperature ^{13}C NMR spectra of **1** and **2** the resonances of C(4,6) appear as doublets with rather large $^{3}J_{C-P}$ coupling constant equal to 10.4 Hz (Table 2.)

Table 2. Selected ^{1}H, ^{13}C and ^{31}P NMR[a] Data for Dioxanes 1-4.

Compound	^{1}H NMR					^{13}C NMR		^{31}P NMR
	$\delta_{H(4,6)ax}$ [ppm]	$\delta_{H(4,6)eq}$ [ppm]	$\Delta\delta$ [ppm]	$\delta_{H(2)}$ [ppm]	$^{2}J_{H-P}$ [Hz]	γ-Effect [ppm]	$^{3}J_{C-P}$ [Hz]	δ [ppm]
1	[b]	[b]	[b]	5.38	5.4	-0.35[c]	10.4	21.1[d]
2	3.48	3.74	0.26	5.27	5.9	-0.72[c]	10.4	23.2[d]
cis-3	3.91	4.39	0.48	5.44	9.3	-0.55	8.9	24.6
trans-3	3.62	4.31	0.69	5.22	5.7	1.61	10.8	24.4
trans-4	4.97	-	-	5.66	20.1	-3.60	2.4	31.2
cis-4	3.78	-	-	5.36	4.9	1.86	10.4	24.0

[a] ^{1}H, ^{13}C and ^{31}P NMR spectra were measured in $CDCl_3$ at 300.13, 75.45, and 121.49 MHz, respectively, unless otherwise stated [b] not determined [c] data for unsubstituted 1,3-dioxanes are taken from Ref.13 [d] at 24.3 MHz in $CHCl_3$.

and equal to the appropriate constant in the diastereoisomer *cis*-**4**. This observation strongly implies the equatorial position of phosphorus in both compounds **1** and **2**. Also the values of $^{2}J_{H-P}$ in the ^{1}H NMR spectra of **1** and **2** (5.4 and 5.9 Hz, respectively) are much close to the relevant value for *cis*-**4** (4.9 Hz) than for *trans*-**4** (20.1 Hz). The latter coupling constant applied as a conformational probe affords conformational equilibrium constants K=29.4 for **1** and K=14.2 for **2**, which correspond to ΔG°_{296}= -8.3 and -6.5 kJ/mol for **1** and **2**, respectively. Perhaps these values are slightly underestimated since a more accurate, counterpoise approach to this problem by Juaristi *et al.*[1b] gave ΔG°_{307}= -13.5 kJ/mol. The equatorial position of phosphorus in **2** is also supported by a small $\Delta\delta$ value, close to the observed for *cis*-**3** and *trans*-**3** ($\Delta\delta$=0.67 and 0.47 ppm, respectively). In the axially substituted *trans*-**4** axial protons are deshielded by more than 1.2 ppm with respect to the parent 1,3-dioxane, thus $\Delta\delta$ in the axial conformer of **2** should be large. Finally, it must be noted that **2** also exists in the solid state in a chair conformation with phosphorus in the equatorial position[5e].

All attempts to equilibrate isomeric **3** and **4** under basic conditions (sodium methanolate in benzene:methanol=6:4, v/v) failed, thus suggesting that the abstraction of H(2) does not occur. If the basic catalyst was replaced by perchloric acid in a methanol-d_4 solution of *trans*-**4**, the final ^{31}P NMR spectrum of the mixture consisted of four signals, different from that of substrate and of comparable integration. The reaction carried out in chloroform-*d* in the presence of a catalytic amount of boron

trifluoride etherate led to five products. Therefore, we had to abandon this method.

The application of Franck's methodology[14] to the estimation of the magnitude of the anomeric effect of the $Ph_2P=O$ group in **2**, assuming the magnitude[15] of Franck's factor F=2.29 and a free energy difference of the $Ph_2P=O$ group in a cyclohexane ring equal[18] to ΔG°_C=-11.46±0.38 kJ/mol, affords ΔG°_{AE}=-6.5-2.29x(-11.46)=19.7 kJ/mol. This value is larger than that found by Juaristi *et al.*[1b] for $Ph_2P=O$ in 1,3-dioxane (11.7 kJ/mol), but the diversity is connected with different methods of determination of ΔG°.

As it was pointed out by Juaristi *et al.*[1e] the magnitude of this effect is the largest yet recorded. In our opinion, it is due to the one-directionality of the interactions involved. It must be noted, however, that Tschierske *et al.*[2a] suggested that the magnitude of the anomeric effect in 1,3-dioxane (and 1,3-dithiane) derivatives should be divided by two owing to the presence of two heteroatoms in the ring. It seems to us that this point of view would be correct if *both* endocyclic oxygens equally participated in the interactions responsible for the anomeric effect, what seems to be not true (see below). Juaristi *et al.*[1e] noted that the results in tetrahydropyran-1,3-dioxane show a "saturation" of the effect and hence the dividing by two could be unjustified.

Crystal and Molecular Structure of trans- and cis-4,6-Dimethyl-2-diphenylphosphinoyl-1,3-dioxanes **4**.

Since the isomeric relationship between the *cis*-4,6-dimethyl-1,3-dioxane derivatives **4**, that were obtained by the Method B, could not be established *via* epimerization, the X-ray structure determination provided unquestionable proof of their constitution. Appropriate views of their solid state structures with a numbering system* are shown in Fig.1. and 2. The selected bond lengths and angles as well as some nonbonding distances are given in Table 3. The packing of both molecules in the unit cell is shown in Fig.3 and 4.

As it is seen from Fig.1 and Fig.2 the main product of the transacetalization reaction, being a 2:1 solvate with benzene (see Fig.3), contains the diphenylphosphinoyl group in the axial position i.e. it is *trans*-**4**. Consequently, in the main product of the Arbuzov reaction (Method A) the phosphoryl group occupies the equatorial position.

Analysis of the crystallographic data for *trans*- isomer of **4** revealed also that its crystal structure exhibits two slightly different molecules per crystallographic unit denoted in the text as *trans*-**4** and *trans*-**4'**. The Newman projections around the C1-P bond (see Fig.5a and 5b) for *trans*-**4** and *trans*-**4'**illustrate also these small differences in structural parameters. However, it should be noted that in both cases the phosphoryl oxygen atom O1 and the hydrogen atom H11 are antiperiplanar. On the other hand, the Newman projection of *cis*-**4** (Fig.5c) clearly shows that O1 and H11 are in the *gauche* arrangement

As expected, the six-membered 1,3-dioxane ring in both *trans*-**4** and *cis*-**4** adopts a chair-like conformation with the asymmetry parameters listed in Table 4. Interestingly, the flattening of the ring at the carbon atom C1 is greater for *trans*-**4** than for *cis*-**4** (see data in Table 4).

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*The numbering system shown in Fig.1 and 2 and used in crystallographic analysis is different from that based on chemical nomenclature. In the former numbering system the number of an atom is given without parentheses; in the latter the number is in parentheses. For example C1 is equivalent to C(2).

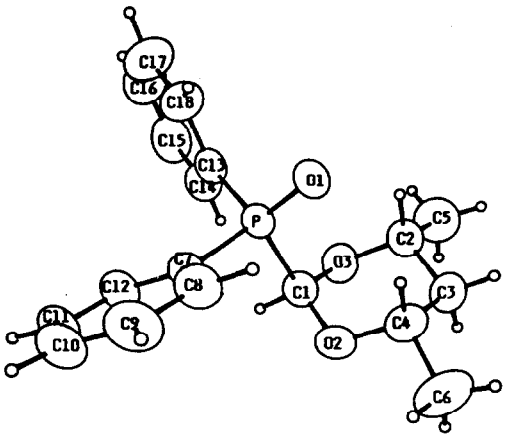

Fig.1. A Three Dimensional View of the Structure of *trans*-4 in the Crystal.

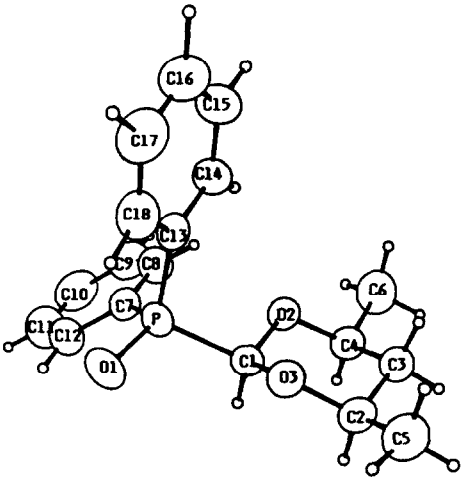

Fig.2. A Three Dimensional View of the Structure of *cis*-4 in the Crystal.

Comments on the Origin of the O-C-P Anomeric Interactions

With regard to the origin of the anomeric effect in the system under discussion, it should be pointed out that the significant elongation of the axial C-P bond (by 0.025 Å), which can be expected on the basis of the negative hyperconjugation, is in fact observed for *trans*-**4** *vs cis*-**4**. It must be noted that while in *cis*-**4** both C(2)-O bond lengths are equal, they differ by 0.008 Å in *trans*-**4**. Interestingly, the contacts between phosphoryl oxygen O1 and axial hydrogens at C(4) and C(6) equal to 2.40 and 2.53 Å for *trans*-**4** and 2.48 and 2.60 Å for *trans*-**4'** are rather short and therefore, it is reasonable[19], to take into account the possibility of intramolecular hydrogen bond formation (parameter *d* calculated for the shortest O1···H-C distance in each molecule is 0.3 Å for *trans*-**4** and 0.22 Å for *trans*-**4'**). Negative hyperconjugation should increase electron density at phosphorus and phosphoryl oxygen and decrease it at endocyclic oxygen atom. These changes are expected to increase the stabilizing energy due to hydrogen bond formation. Both effects i.e. negative hyperconjugation and hydrogen bond formation in the *trans*- isomer of **4** act in the same direction and are responsible for the differences between C(2)-O(1) and C(2)-O(3) distances. One may ask, however, why the shortest C(2)-O bond in *trans*-**4** is almost of the same length as the relevant bonds in *cis*-**4**, which cannot participate in n_O-σ^*_{C-P} interaction. It can be explained on the basis of large 1,3-syn diaxial repulsions which are responsible for the deformation of the 1,3-dioxane chair in *trans*-**4** and which are expected[20] to lengthen both C(2)-O bonds. It should be noted, that the large magnitude of the anomeric effect in 1,3-dioxane **2** can be attributed to the lack of a lone electron pair on phosphorus, since it implies the one-directionality[21] of the hyperconjugative interactions.

Table 3. Selected important distances and angles in the solid state structures of *cis*-4, *trans*-4, and *trans*-4'.

		cis-4	*trans*-4	*trans*-4'
bond distances [Å]:	P -C1	1.841(2)	1.866(3)	1.864(2)
	P -C7	1.807(3)	1.804(3)	1.810(2)
	P -C13	1.799(2)	1.804(2)	1.809(2)
	P -O1	1.483(2)	1.487(1)	1.486(1)
	C1-O2	1.399(3)	1.409(2)	1.405(3)
	C1-O3	1.400(3)	1.401(3)	1.411(2)
	O2-C4	1.446(3)	1.454(2)	1.454(2)
	O3-C2	1.452(3)	1.453(2)	1.450(3)
	C2-C3	1.520(3)	1.518(3)	1.508(4)
	C4-C3	1.512(4)	1.514(3)	1.511(3)
aver. bond distance in phenyl group [Å]		1.387(4)	1.382(3)	1.382(4)
aver. bond angle in phenyl group [°]		120.0(3)	120.0(3)	120.0(3)
dihedral angles between planes [°]:				
C1-O2-O3/C2-O3-O2-C4		57.3(2)	49.0(2)	48.6(1)
C3-C2-C4/C2-O3-O2-C4		49.1(2)	48.6(2)	50.0(2)
C7-C12/C13-C18		56.2(2)	88.7(1)	64.4(1)
selected distances [Å]:	O2 -O3	2.326(4)	2.344(3)	2.344(3)
	P -O2	2.628(4)	2.713(3)	2.727(3)
	P -O3	2.644(4)	2.750(3)	2.727(3)
	P -H41	4.22(1)	2.88(1)	2.91(1)
	P -H21	4.24(1)	2.90(1)	2.91(1)
	O1 -O2	3.911(4)	3.303(3)	3.295(3)
	O1 -O3	3.138(4)	3.410(3)	3.433(3)
	O1 -H21	4.60(1)	2.53(1)	2.60(1)
	O1 -H41	5.22(1)	2.40(1)	2.48(1)
	H11-H21	2.3(1)	3.6(1)	3.6(1)
	H11-H41	2.4(1)	3.6(1)	3.5(1)

The negative hyperconjugation usually[22-24] results in a decrease of the one-bond coupling constant through the acceptor bond in the NMR spectra of molecules exhibiting the anomeric effect. Indeed, in 1,3-dioxanes *trans*-4 and *cis*-4 $^{1}J_{C-P}$ coupling constants are equal to 94.3 and 118.8 Hz in agreement with the intuitive anticipation based on the $n_O-\sigma^*_{C-P}$ interaction.

The chemical shifts for aromatic carbons are a sensitive probe in studies of the polar and resonance effects of substituents[25] and were applied by Juaristi *et al.*[1e] to prove that some form of electron transfer occurs to the axial diphenylphosphinoyl group attached to the 1,3-dithiane ring. We found that the chemical shift of ortho carbons is indeed smaller for axial Ph_2P=O in 1,3-dioxane *trans*-4 *vs cis*-4 (δ 131.48 and 132.49 ppm, respectively). The chemical shift of para ones is almost the same in both isomers.

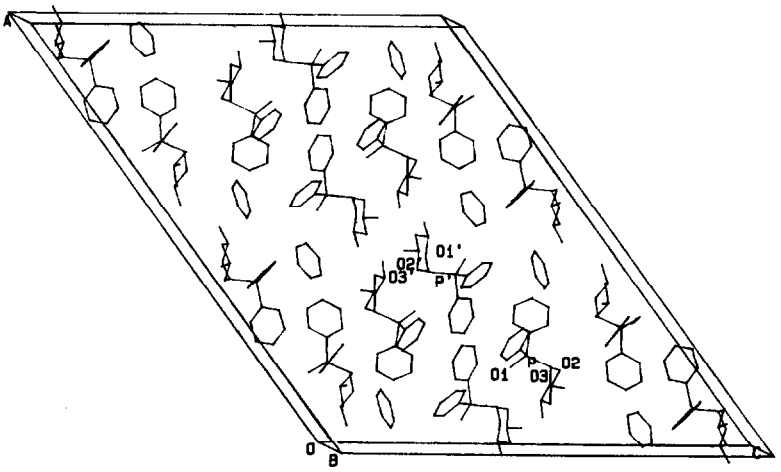

Fig.3. Packing of *trans*-4 in Unit Cell

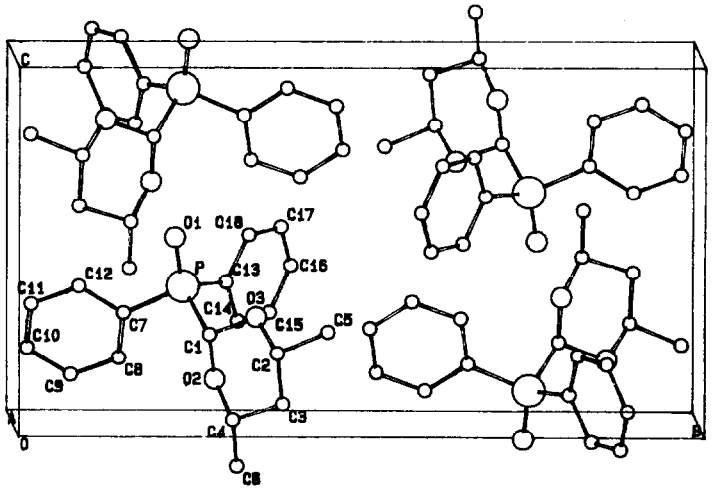

Fig.4. Packing of *cis*-4 in Unit Cell

The infrared spectra in the solid state (KBr) of *trans*-4 and *cis*-4 are very interesting with regard to the P=O stretching frequency. The corresponding $\nu_{P=O}$ values for *trans*-4 and *cis*-4 are equal to 1188 and 1196 cm^{-1}. The smaller force constant for axial P=O than for the equatorial one is consistent with the formation of a weak hydrogen bond with axial H(6) (the more so because the steric congestion in *trans*-4 should act on $\nu_{P=O}$ in opposite direction).

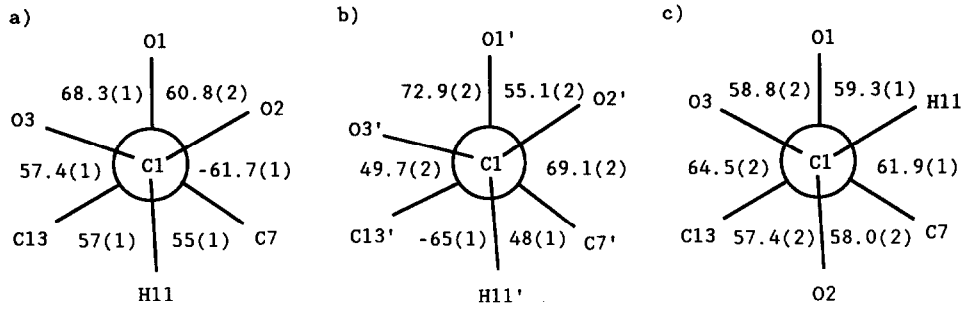

Fig.5. The Newman Projections Around C1-P Bond in a)*trans*-4 b)*trans*-4' c)*cis*-4

Table 4. Asymmetry Parameters of 1,3-Dioxane Rings in *cis*-4, *trans*-4 and *trans*-4'

Parameter	*cis*-4	*trans*-4	*trans*-4'	Parameter	*cis*-4	*trans*-4	*trans*-4'
ΔC_S^{O2}	7.6	2.3	2.5	ΔC_2^{O3-C1}	5.7	1.7	3.3
ΔC_S^{O3}	7.7	2.3	1.1	ΔC_2^{O2-C1}	5.3	1.6	4.3
ΔC_S^{C1}	0.3	0.1	3.4	conformation	deformed	almost ideal	almost
ΔC_2^{C2-O3}	10.3	3.3	1.0		chair	chair	chair

The second mechanism, which can contribute to the anomeric effect in 2-phosphoryl-1,3-dioxanes, consists of repulsive interactions[5f,26] between the lone electron pairs on endocyclic oxygens and the phosphoryl oxygen atom in the equatorial conformation. These interactions have, perhaps, decisive meaning as far as the conformation around the equatorial C(2)-P bond is concerned. In the rotamer *gauche*, with phosphoryl oxygen located *anti* to one of endocyclic oxygen atoms, two repulsive interactions between the lone electron pairs on P=O oxygen and ring oxygen atom are avoided. Such a *gauche* arrangement is actually observed in the solid state structures of **2** and *cis*-**4**. However, in the case of 1,3-dioxanes, the n_O-σ^*_{C-P} interaction, seems to be of larger importance, as far as the free energy difference ΔG° between axial and equatorial conformers is concerned.

EXPERIMENTAL

^1H NMR spectra of 0.5 ÷ 0.8% solutions in $CDCl_3$ containing 0.1% of tetramethylsilane were recorded at 200.13, 250.13 or 300.13 MHz on Bruker AC 200, Bruker WP 250, and Bruker MSL 300 spectrometers, respectively. The ^{13}C NMR spectra of about 4% solutions were measured at 50.32, 62.89 or 75.47 MHz on the Bruker instruments or at 25.16 MHz on Tesla spectrometer. The sign of coupling constants was not determined. The ^{31}P NMR spectra were measured on a Jeol JNM-FX 60, Bruker AC 200, and Bruker MSL 300 instruments at 24.3, 81.0, and 121.49 MHz, respectively, with 85% H_3PO_4 as an external reference. Solutions

were not degassed.

The following instrumental parameters for ^{1}H NMR spectra are typical: flip angle, 60÷75°; SW (sweep width), 2700 Hz; number of scans, 100÷400; TD (data size), 16K, AQ (acquisition time), 2.3÷3.1s.

The NOE procedure was as follows. The standard Bruker microprogram was used to perform steady-state NOE difference spectroscopy on MSL 300 instrument. Thirty two scans (proceeded by two dummy scans to establish equilibrium) were acquired for each irradiation frequency, and the entire process was automatically repeated to afford the requisite signal-to-noise ratio. The irradiation time was 3.0s, relaxation delay 7.5s. A 90° read pulse was employed in all cases. The decoupler power setting was chosen so as to minimize frequency spillover to neighboring multiplets. NOE enhancement values were calculated by comparing signal integrals in the difference spectra with the control irradiation spectrum. The error of determination of NOE enhancement coefficients is estimated to be less than 10%.

Typical parameters for ^{13}C NMR spectra: flip angle, 60÷75°; SW, 12000 Hz; number of scans, 100÷1000; TD, 16K, AQ, 0.67s. The assignment of signals, if not straightforward, was based on DEPT technique.

The following abbreviations are employed in description of NMR spectra: *s* (singlet); *d* (doublet); *t* (triplet); *q* (quartet); *dd* (doublet of doublets), *etc.*; *m* (multiplet)

All standard 16K FID's in the ^{1}H and ^{13}C NMR spectra were zero filled to 64K prior to the Fourier transformation.

Mass spectra were recorded with LKB 2091 spectrometer.

Infrared spectra were taken on a SPECORD 71IR or SPECORD M80.

Melting points were measured using Boëtius apparatus and are uncorrected.

Anhydrous hydrocarbons and diethyl ether were distilled from $LiALH_4$. Dichloromethane and chloroform were distilled from P_2O_5. Iodomethane was distilled prior to use. Dimethylformamide dimethyl acetal[29], isopropyl diphenylphosphinite[30], (diethoxymethyl)diphenylphosphine oxide (**18**)[9], (5,5-dimethyl-1,3-dioxan-2-yl)trimethylammonium iodide[7] (**15**), *meso*-pentanediol-2,4 (**8**)[31], diethyl *t*-butylmalonate[32], 5-*t*-butyl-1,3-dioxane[16], and *cis*-4,6-dimethyl-1,3-dioxane[16] were obtained according to known procedures. Other compounds, if not described below, were commercially available.

Chromatographic separation was achieved using Kieselgel 60, 230-400 mesh, purchased from Merck.

2-Diphenylphosphinoyl-1,3-dioxane (**1**).

Method A.

A mixture of freshly prepared **14** (3.758 g, 13.8 mmol) and isopropyl diphenylphosphinite (3.36 g, 13.8 mmol) in toluene (40 mL) was refluxed for 3 h. The reaction mixture was then cooled, filtered and concentrated to about 12 mL. *n*-Hexane (50 mL) was added and the mixture was left to stand overnight to give 1.294 g (32.6%) of **1** as colorless crystals: m.p.195-200°C. Recrystallization from dichloromethane-diethyl ether afforded analytically pure sample mp 207-210°C (lit.[1c] mp 213-215°C, lit.[9] mp 206-211°C). ^{1}H NMR (300.13 MHz, $CDCl_3$) δ 1.42 (*ddtt*, $^{2}J_{H-H}$=13.5 Hz, $^{5}J_{H-P}$=2.3 Hz, $^{3}J_{H-H}$=1.6 Hz, $^{3}J_{H-H}$=1.3 Hz, 1H, $H(5)_{eq}$), 2.21 (*dtt*, $^{2}J_{H-H}$=13.5 Hz, $^{3}J_{H-H}$=12.4 Hz, $^{3}J_{H-H}$=4.9 Hz, 1H, $H(5)_{ax}$), 3.82 (*ddd*, $^{3}J_{H-H}$=12.4 Hz, $^{2}J_{H-H}$=10.6 Hz, $^{3}J_{H-H}$=1.6 Hz, 2H, $H(4,6)_{ax}$), 4.24 (*dddd*, $^{2}J_{H-H}$=10.6 Hz, $^{3}J_{H-H}$=4.9 Hz, $^{4}J_{H-P}$=1.6 Hz, $^{3}J_{H-H}$=1.3 Hz, 2H, $H(4,6)_{eq}$), 5.38 (*d*, $^{2}J_{H-P}$=5.4 Hz, 1H, HCP), 7.4÷8.0 (*m*, 10H, Ph); ^{31}P NMR (24.3 MHz, $CHCl_3$) δ 21.1; ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 26.13 (*s*, C-CH_2-C), 68.35 (*d*, $^{3}J_{C-P}$=10.4 Hz, CH_2O), 101.78 (*d*, $^{1}J_{C-P}$=118.1 Hz, CHP), 128.28 (*d*, $^{3}J_{C-P}$=12.3, $C_{Ar(meta)}$), 129.58 (*d*, $^{1}J_{C-P}$=101.5 Hz, $C_{Ar(ipso)}$), 132.16 (*s*,

$C_{Ar(para)}$), 132.32 (*d*, $^2J_{C-P}$=9.1 Hz, $C_{Ar(ortho)}$); IR (KBr) 532(vs), 568(vs), 700(s), 724(s), 1008(s), 1090(vs), 1116(s), 1200(vs) cm^{-1}; MS(70 eV) m/e (relative intensity) 201(21), 88(7), 87(100), 77(30), 59(34). Anal. Calcd for $C_{16}H_{17}PO_3$: C,66.66; H,5.95. Found: C,66.49; H,6.05.

5,5-Dimethyl-2-diphenylphosphinoyl-1,3-dioxane (**2**). Following the procedure applied for **1**, iodide **15** (3.01 g, 10.0 mmol) was converted into **2** (2.82 g, 78%), white crystals, m.p. 140.8-141.8°C. Recrystallization from dichloromethane-diethyl ether gave an analytically pure sample of **2**: mp 142.0-143.0°C (lit.[7] mp 139-141°C). ^1H NMR (250 MHz, $CDCl_3$) δ 0.72 (*s*, 3H, CH_3), 1.03 (*s*, 3H, CH_3), 3.48 (*d*, $^2J_{H-H}$=11.0 Hz, 2H, $H(4,6)_{ax}$), 3.74 (*dd*, $^2J_{H-H}$=11.0 Hz, $^4J_{H-P}$=1.5 Hz, 2H, $H(4,6)_{eq}$), 5.27 (*d*, $^2J_{H-P}$=5.9 Hz, 1H, HCP), 7.4÷8.0 (*m*, 10H, Ph); ^{31}P NMR (24.3 MHz, $CHCl_3$) δ 23.2; ^{13}C NMR(62.89 MHz, $CDCl_3$) δ 21.92 (*s*, CH_3), 22.90 (*s*, CH_3), 30.97 (*s*, CMe_2), 78.38 (*d*, $^3J_{C-P}$=10.4 Hz, CH_2), 101.31 (*d*, $^1J_{C-P}$=118.1 Hz, CHP), 128.26 (*d*, $^3J_{C-P}$=12.0 Hz, $C_{Ar(meta)}$), 129.38 (*d*, $^1J_{C-P}$=100.9 Hz, $C_{Ar(ipso)}$), 132.22 (*s*, $C_{Ar(para)}$), 132.30 (*d*, $^2J_{C-P}$=9.6 Hz, $C_{Ar(ortho)}$); IR (KBr) 1087(vs), 1190(vs) cm^{-1}; MS(70 eV) m/e (relative intensity) 115(100), 69(67), 45(28), 41(20). Anal. Calcd for $C_{18}H_{21}PO_3$: C,68.34; H,6.69. Found: C,68.45; H,7.12.

5-t-Butyl-2-diphenylphosphinoyl-1,3-dioxanes **3** (*cis, trans*-mixture).

This mixture was obtained following the procedure applied for **1** (Method A) using iodide **16** and isopropyl diphenylphosphinite. The ^{31}P NMR (121.49 MHz, $CDCl_3$) spectrum of the crude product consisted of five signals δ 21.8, 24.4, 24.6, 30.2, and 106.1 ppm of relative integration 3.9:63.8:20.1:2.9:9.3, respectively. In the ^1H NMR spectrum (300.13 MHz, $CDCl_3$) of the mixture the relative integration of doublets at δ 5.21 and 5.44 ppm was 78:22, respectively.

The mixture of *cis*- and *trans*-**3** was also obtained as follows.

Method B.

A mixture of **7** (5.55 g, 42.1 mmol), **18** (12.80 g, 42.1 mmol), and benzenesulfonic acid (0.5 g, 3.2 mmol) in benzene (60 mL) was heated under reflux with simultaneous removal of benzene-ethanol azetrope using 10 cm Vigreux column and appropriate distillation head. When temperature of vapors had reached 80°C (after about 2 h), additional 10 mL of distillate was collected, the mixture was cooled, washed with saturated aqueous sodium bicarbonate (20 mL), dried over anhydrous magnesium sulfate, and evaporated under reduced pressure. The ^{31}P NMR spectrum (24.3 MHz, C_6H_6) of the crude mixture consisted of three signals at δ 21.8, 24.6, and 29.1 ppm of relative integration as 8:66:26. In the ^1H NMR spectrum (300.13 MHz, $CDCl_3$) the relative intensity of singlets at δ 0.84 and 0.79 ppm was 2:3, respectively. The relative integration of doublets at δ 5.21 and 5.44 ppm was 38:62, respectively. This mixture was separated chromatographically on silicagel (500 g) with *n*-heptane-isopropanol mixture as an eluent (in gradient). Three chromatographically pure fractions were collected. Two of them were identified as:

cis-5-t-Butyl-2-diphenylphosphinoyl-1,3-dioxane (*cis*-**3**). 6.352 g (43.8%) of colorless oil, n^{22}_D=1.5352. ^1H NMR (300.13 MHz, $CDCl_3$) δ 0.78 (*s*, 9H, CH_3), 1.13 (*tt*, $^3J_{H-H}$=3.7 Hz, $^3J_{H-H}$=2.1 Hz, 1H, *t*BuC*H*), 3.91 (*dd*, $^2J_{H-H}$=12.4 Hz, $^3J_{H-H}$=3.7 Hz, 2H, $H(4,6)_{ax}$), 4.38 (*ddd*, $^2J_{H-H}$=12.4 Hz, $^3J_{H-H}$=2.1 Hz, $^4J_{H-P}$=1.4 Hz, 2H, $H(4,6)_{eq}$), 5.44 (*d*, $^2J_{H-P}$=9.3 Hz, 1H, HCP), 7.4÷8.0 (*m*, 10H, Ph); ^{31}P NMR (121.49 MHz, $CDCl_3$) δ 24.6; ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 28.74 (*s*, CH_3), 32.08 (*s*, CMe_3), 43.60 (*s*, *C*HtBu), 68.21 (*d*, $^3J_{C-P}$=8.9 Hz, CH_2), 100.53 (*d*, $^1J_{C-P}$=114.6 Hz, CHP), 128.27 (*d*, $^3J_{C-P}$=11.8 Hz, $C_{Ar(meta)}$), 129.60 (*d*, $^1J_{C-P}$=100.4 Hz, $C_{Ar(ipso)}$), 132.18 (*s*, $C_{Ar(para)}$), 132.35 (*d*, $^2J_{C-P}$=9.2 Hz, $C_{Ar(ortho)}$);

IR (film) 1080(s), 1136(vs), 1180(vs), 1440(s) cm^{-1}; MS(70 eV) m/e (relative intensity) 201(48), 143(88), 77(39), 57(100), 55(33), 41(91), 29(39). Anal. Calcd for $C_{20}H_{25}PO_3$: C,69.75; H,7.32. Found: C,69.45; H,7.27.

trans-5-t-Butyl-2-diphenylphosphinoyl-1,3-dioxane (*trans*-**3**). 4.112 g (28.4%) of colorless solid, mp 119-121°C. ^1H NMR (300.13 MHz, $CDCl_3$) δ 0.86 (*s*, 9H, CH_3), 1.89 (*tt*, $^3J_{H-H}$=11.4 Hz, $^3J_{H-H}$=4.3 Hz, 1H, *t*BuC*H*), 3.62 (*dd*, $^2J_{H-H}$=11.9 Hz, $^3J_{H-H}$=11.4 Hz, 2H, $H(4,6)_{ax}$), 4.31 (*ddd*, $^2J_{H-H}$=11.9 Hz, $^3J_{H-H}$=4.3 Hz, $^4J_{H-P}$=1.8 Hz, 2H, $H(4,6)_{eq}$), 5.22 (*d*, $^2J_{H-P}$=5.7 Hz, 1H, HCP), 7.4÷8.0 (*m*, 10H, Ph); ^{31}P NMR (121.49 MHz, $CDCl_3$) δ 24.4; ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 27.31 (*s*, CH_3), 30.63 (*s*, CMe_3), 43.81 (*s*, $CHtBu$), 70.39 (*d*, $^3J_{C-P}$=10.7 Hz, CH_2), 101.38 (*d*, $^1J_{C-P}$=117.8 Hz, CHP), 128.29 (*d*, $^3J_{C-P}$=12.0 Hz, $C_{Ar(meta)}$), 129.77 (*d*, $^1J_{C-P}$=100.2 Hz, $C_{Ar(ipso)}$), 132.16 (*s*, $C_{Ar(para)}$), 132.34 (*d*, $^2J_{C-P}$=9.1 Hz, $C_{Ar(ortho)}$); IR (KBr) 764(s), 1028(s), 1086(vs), 1122(s), 1194(s) cm^{-1}; MS(70 eV) m/e (relative intensity) 219(31), 201(31), 143(100), 77(43), 57(83). Anal. Calcd for $C_{20}H_{25}PO_3$: C,69.75; H,7.32. Found: C,69.98; H,7.38.

Besides the isomers of **3**, unidentified substance (1.368 g) was isolated. Its ^{31}P NMR(24.3 MHz, $CHCl_3$) spectrum showed the presence of two singlets at δ 21.1 and 30.5 ppm of the same intensity.

2-Diphenylphosphinoyl-cis-4,6-dimethyl-1,3-dioxane **4** (*cis, trans*-mixture).

This mixture was obtained following the procedure applied for **1** (Method A) using iodide **17** and isopropyl diphenylphosphinite. The ^{31}P NMR (24.3 MHz, $CHCl_3$) spectrum of the crude product consisted of three signals at δ 22.6, 28.8, and 104.3 of relative integration as 76:14:10, respectively. Crystallization of the crude product from toluene afforded *cis*-**4** (in 66.4% yield), mp 162-165°C, indistinguishable from the minor product obtained *via* Method B (see below).

Following the procedure B, diol **8** (6.24 g, 60.0 mmol) and **18** (18.23 g, 60.0 mmol) were converted into the mixture, which was separated by flash chromatography on silicagel with *n*-heptane:isopropanol=4:1 (v/v) as an eluent. Three chromatographically pure fractions were collected. Two of them were identified as:

r-2-Diphenylphosphinoyl-t-4,t-6-dimethyl-1,3-dioxane (*trans*-**4**). 10.6 g (55.8%) of colorless solid. Crystallization from *n*-heptane gave colorless crystals, mp 142-145°C. ^1H NMR(200.13 MHz, $CDCl_3$) δ 1.14 (*d*, $^3J_{H-H}$=6.2 Hz, 6H, CH_3), 1.38 (*dt*, $^2J_{H-H}$=13.2 Hz, $^3J_{H-H}$=11.1 Hz, 1H, $H(5)_{ax}$), 1.70 (*dtd*, $^2J_{H-H}$=13.2 Hz, $^3J_{H-H}$=2.5 Hz, $^5J_{H-H}$=0.7 Hz, 1H, $H(5)_{eq}$), 4.97 (*dqddd*, $^3J_{H-H}$=11.1 Hz, $^3J_{H-H}$=6.2 Hz, $^3J_{H-H}$=2.5 Hz, $^4J_{H-H}$=0.7 Hz, $^4J_{H-P}$=0.7 Hz, 2H, C*H*CH_3), 5.66 (*ddd*, $^2J_{H-P}$=20.1 Hz, $^4J_{H-H}$=0.7 Hz, $^5J_{H-H}$=0.7 Hz, 1H, HCP), 7.43÷7.80 (*m*, 10H, Ph); ^{31}P NMR (121.49 MHz, $CDCl_3$) δ 31.2; ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 21.89 (*s*, CH_3), 40.49 (*d*, $^4J_{C-P}$=2.1 Hz, CH_2), 69.10 (*d*, $^3J_{C-P}$=2.4 Hz, $CHCH_3$), 97.15 (*d*, $^1J_{C-P}$=94.3 Hz, CHP), 128.56 (*d*, $^3J_{C-P}$=11.2 Hz, $C_{Ar(meta)}$), 131.48 (*d*, $^2J_{C-P}$=8.8 Hz, $C_{Ar(ortho)}$), 131.70 (*d*, $^1J_{C-P}$=90.7 Hz, $C_{Ar(ipso)}$), 131.93 (*d*, $^4J_{C-P}$=2.6 Hz, $C_{Ar(para)}$); IR (KBr) 696(s), 722(s), 1040(s), 1118(s), 1188(vs) cm^{-1}; MS(70 eV) m/e (relative intensity) 202(14), 201(14), 115(100), 77(13), 69(78). Anal. Calcd for $C_{18}H_{21}PO_3$: C,68.34; H,6.69. Found: C,67.99; H,6.77. Crystallization of this product from benzene-*n*-hexane afforded colorless needles, mp 150-152°C, which on the basis of X-ray analysis were found to be 2:1 solvate with benzene. Anal. Calcd for $C_{18}H_{21}PO_3 \cdot 0.5C_6H_6$: C,70.97; H,6.81. Found: C,71.06; H,6.81.

r-2-Diphenylphosphinoyl-c-4,c-6-dimethyl-1,3-dioxane (*cis*-**4**). 2.80 g (14.8%) of colorless solid. Crystallization from chloroform-diethyl ether gave colorless prisms, mp 162-165°C (lit.[1c] mp 150-153°C). ^{1}H NMR(300.13 MHz, $CDCl_3$) δ 1.23 (*d*, $^3J_{H-H}$=6.2 Hz, 6H, CH_3), 1.38 (*dt*, $^2J_{H-H}$=13.3 Hz, $^3J_{H-H}$=11.1 Hz, 1H, $H(5)_{ax}$), 1.58 (*dtd*, $^2J_{H-H}$=13.3 Hz, $^3J_{H-H}$=2.3 Hz, $^5J_{H-P}$=2.3 Hz, 1H, $H(5)_{eq}$), 4.97 (*dqd*, $^3J_{H-H}$=11.1 Hz, $^3J_{H-H}$=6.2 Hz, $^3J_{H-H}$=2.3 Hz, 2H, $CHCH_3$), 5.36 (*d*, $^2J_{H-P}$=4.9 Hz, 1H, HCP), 7.41÷7.97 (*m*, 10H, Ph); ^{31}P NMR (121.49 MHz, $CDCl_3$) δ 24.0; ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 21.55 (*s*, CH_3), 40.93 (*s*, CH_2), 74.55 (*d*, $^3J_{C-P}$=10.4 Hz, $CHCH_3$), 101.12 (*d*, $^1J_{C-P}$=118.8 Hz, CHP), 128.09 (*d*, $^3J_{C-P}$=11.9 Hz, $C_{Ar(meta)}$), 130.22 (*d*, $^1J_{C-P}$=100.1 Hz, $C_{Ar(ipso)}$), 131.91 (*d*, $^4J_{C-P}$=2.8 Hz, $C_{Ar(para)}$), 132.49 (*d*, $^2J_{C-P}$=9.0 Hz, $C_{Ar(ortho)}$); IR (KBr) 720(s), 1036(s), 1112(vs), 1196(vs) cm^{-1}; MS(70 eV) m/e (relative intensity) 202(11), 201(14), 115(100), 77(12), 69(81). Anal. Calcd for $C_{18}H_{21}PO_3$: C,68.34; H,6.69. Found: C,68.22; H,6.69.

Besides the isomers *trans*-**4** and *cis*-**4**, unidentified substance (3.8 g) was isolated. Its ^{31}P NMR(121.49 MHz, $CDCl_3$) spectrum showed the presence of two singlets at δ 21.9 and 24.1 ppm of relative integration 95:5, respectively.

2-t-Butyl-1,3-propanediol (**7**). The published[16] procedure was modified as follows. A solution of diethyl *t*-butylmalonate (168 g, 777 mmol) in diethyl ether (675 mL) was added dropwise and with stirring to a suspension of lithium aluminium hydride (43.0 g, 1.13 mol) in diethyl ether (730 mL) at such rate so as to maintain a gentle reflux. Addition took two hours, and the mixture was then boiled for an additional 2 h, and left to stand overnight. After careful addition of water (168 mL), 10% aqueous solution of sulfuric acid (250 mL) was dropped in. Ethereal phase was separated, and the remaining solid was dissolved in an additional portion of 10% aqueous solution of sulfuric acid (870 mL). The liquid was extracted with chloroform (3x150 mL). Combined organic solutions were washed with saturated aqueous sodium bicarbonate solution (100 mL), water (100 mL), and were dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, and the oily residue was crystallized from chloroform-*n*-pentane to afford **7** (87.1 g, 84.8%), colorless needles, mp 59-61°C (lit.[16] mp 57-58°C, lit.[33] mp 58-59°C).

2-N,N-Dimethylamino-1,3-dioxane (**10**). Following the general procedure of Arnold and Kornilov[29], 1,3-propanediol (**5**, 7.61 g, 100 mmol) and **9** (11.9 g, 100 mmol) gave **10** (11.1 g, 84.7%), colorless liquid, bp 55-56°C/9 mm Hg, n^{21}_D=1.4427. ^{1}H NMR (200.13 MHz, $CDCl_3$) δ 1.33 (*ddt*, $^2J_{H-H}$=13.4 Hz, $^3J_{H-H}$=2.6 Hz, $^3J_{H-H}$=1.8 Hz, 1H, $H(5)_{eq}$), 1.97 (*dtt*, $^2J_{H-H}$=13.4 Hz, $^3J_{H-H}$=12.0 Hz, $^3J_{H-H}$=4.9 Hz, 1H, $H(5)_{ax}$), 2.38 (*s*, 6H, CH_3-N), 3.81 (*dddd*, $^3J_{H-H}$=12.0 Hz, $^2J_{H-H}$=10.4 Hz, $^3J_{H-H}$=2.6 Hz, $^4J_{H-H}$=1.6 Hz, 2H, $H(4,6)_{ax}$), 4.14 (*dddd*, $^2J_{H-H}$=10.4 Hz, $^3J_{H-H}$=4.9 Hz, $^3J_{H-H}$=1.8 Hz, $^4J_{H-H}$=1.6 Hz, 2H, $H(4,6)_{eq}$), 4.76 (*s*, 1H, *H*CNMe$_2$); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 25.36 (*s*, C-CH_2-C), 37.78 (*s*, CH_3N), 66.05 (*s*, CH_2O), 108.80 (*s*, *C*HNMe$_2$).

5,5-Dimethyl-2-N,N-dimethylamino-1,3-dioxane (**11**). 2,2-Dimethyl-1,3-propanediol (**6**, 10.4 g, 100 mmol) and **9** (11.9 g, 100 mmol) were converted by the the general procedure of Arnold and Kornilov[29] into **11** (15.2 g, 95.4%), colorless liquid, bp 83°C/15 mm Hg, n^{21}_D=1.4440 (lit.[34] bp 68-70°C/7 mm Hg, n^{20}_D=1.4369). ^{1}H NMR (300.13 MHz, $CDCl_3$) δ 0.71 (*s*, 3H, CH_3), 1.15 (*s*, 3H, CH_3), 2.38 (*s*, 6H, CH_3-N), 3.46 (*dt*, $^2J_{H-H}$=11.1 Hz, $^4J_{H-N}$=0.7 Hz, 2H, $H(4,6)_{ax}$), 3.59 (*dt*, $^2J_{H-H}$=11.1 Hz, $^4J_{H-N}$=1.2 Hz, 2H, $H(4,6)_{eq}$), 4.69 (*d*, $^2J_{H-P}$=5.9 Hz, 1H, *H*CNMe$_2$); ^{13}C NMR(25.16 MHz, $CDCl_3$) δ 21.43 (*s*, CH_3), 22.77 (*s*, CH_3), 29.71 (*s*, *C*Me$_2$), 37.63 (*s*, CH_3N), 76.22 (*s*, CH_2O), 108.77 (*s*, CHNMe$_2$).

2-N,N-Dimethylamino-5-t-butyl-1,3-dioxane (**12**) - mixture of diastereoisomers. Following the general procedure of Arnold and Kornilov[29], **7** (22.0 g, 166 mmol) and **9** (19.8 g, 166 mmol) were converted into **12** (26.5 g, 85.0%), colorless liquid, bp 61°C/0.6 mm Hg, n^{21}_D=1.4505. Anal. Calcd for $C_{10}H_{21}NO_2$: C,64.13; H,11.30. Found: C,64.14; H,11.35.

The ^{1}H NMR spectrum of the mixture suggests that it consists of isomers *cis* and *trans* in the relative ratio of about 8:92, respectively (on the basis of integration of singlets δ 1.00 and 0.89 ppm, respectively). Some spectroscopic data for the isomers in the mixture are presented below.

cis-2-N,N-Dimethylamino-5-t-butyl-1,3-dioxane (*cis*-**12**). ^{1}H NMR (300.13 MHz, $CDCl_3$) δ 0.89 (*s*, 9H, CH_3), 1.74 (*tt*, $^3J_{H-H}$=11.4 Hz, $^3J_{H-H}$=4.3 Hz, 1H, *t*BuC*H*), 2.38 (*s*, 6H, CH_3-N), 3.64 (*ddt*, $^2J_{H-H}$=11.5 Hz, $^3J_{H-H}$=11.4 Hz, $^4J_{H-N}$=1.4 Hz, 2H, $H(4,6)_{ax}$), 4.16 (*ddt*, $^2J_{H-H}$=11.5 Hz, $^3J_{H-H}$=4.3 Hz, $^4J_{H-N}$=1.5 Hz, 2H, $H(4,6)_{eq}$), 4.71 (*s*, 1H, *H*CNMe$_2$); ^{13}C NMR (25.16 MHz, $CDCl_3$) δ 27.55 (*s*, CH_3), 30.31 (*s*, *C*Me$_3$), 37.70 (*s*, CH_3N), 43.08 (*s*, *C*H*t*Bu), 68.08 (*s*, CH_2), 108.70 (*s*, *C*HNMe$_2$).

trans-2-N,N-Dimethylamino-5-t-butyl-1,3-dioxane (*trans*-**12**). ^{1}H NMR (300.13 MHz, $CDCl_3$) δ 1.00 (*s*, 9H, CH_3), 2.30 (*s*, 6H, CH_3-N), 3.81 (*dd*, $^2J_{H-H}$=12.0 Hz, $^3J_{H-H}$=4.4 Hz, 2H, $H(4,6)_{eq}$), 4.67 (*s*, 1H, *H*CNMe$_2$); ^{13}C NMR (25.16 MHz, $CDCl_3$) δ 28.67 (*s*, CH_3), 38.37 (*s*, CH_3N), 64.35 (*s*, CH_2), 107.65 (*s*, *C*HNMe$_2$).

2-N,N-Dimethylamino-cis-4,6-dimethyl-1,3-dioxane (**13**) - mixture of diastereoisomers. Following the general procedure of Arnold and Kornilov[29], **8** (10.4 g, 100 mmol) and **9** (11.9 g, 100 mmol) were converted into **13** (14.0 g, 87.9%), colorless liquid, bp 27-28°C/1.0 mm Hg, n^{21}_D=1.4308. Anal. Calcd for $C_8H_{17}NO_2$: C,60.34; H,10.76. Found: C,60.61; H,10.94.

The ^{1}H NMR spectrum of the mixture suggests that it consists of isomers *trans* and all-*cis* in the relative ratio of about 6:94, respectively (on the basis of intensity of singlets δ 2.17 and 2.36 ppm, respectively). Some spectroscopic data for the isomers in the mixture are presented below.

r-N,N-Dimethylamino-c-4,c-6-dimethyl-1,3-dioxane (*cis*-**13**). ^{1}H NMR(300.13 MHz, $CDCl_3$) δ 1.13 (*dt*, $^2J_{H-H}$=13.0 Hz, $^3J_{H-H}$=11.2 Hz, 1H, $H(5)_{ax}$), 1.19 (*d*, $^3J_{H-H}$=6.2 Hz, 6H, CH_3), 1.44 (*dt*, $^2J_{H-H}$=13.0 Hz, $^3J_{H-H}$=2.4 Hz, 1H, $H(5)_{eq}$), 2.36 (*s*, 6H, CH_3N), 3.74 (*dqd*, $^3J_{H-H}$=11.2 Hz, $^3J_{H-H}$=6.2 Hz, $^3J_{H-H}$=2.4 Hz, 2H, C*H*CH$_3$), 4.77 (*s*, 1H, *H*CNMe$_2$); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 21.35 (*s*, *C*H$_3$C), 37.78 (*s*, CH_3N), 40.02 (*s*, CH_2), 71.42 (*s*, CHCH$_3$), 108.19 (*s*, *C*HNMe$_2$).

r-N,N-Dimethylamino-t-4,t-6-dimethyl-1,3-dioxane (*trans*-**13**). ^{1}H NMR(300.13 MHz, $CDCl_3$) δ 2.17 (*s*, 6H, CH_3N); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 21.57 (*s*, *C*H$_3$C), 63.64 (*s*, CHCH$_3$), 107.21 (*s*, *C*HNMe$_2$).

(1,3-Dioxan-2-yl)trimethylammonium iodide (**14**). The published[7] method for **15** was used to convert **10** (5.50 g, 42.0 mmol) and iodomethane (6.61 g, 46.6 mmol) in diethyl ether (40 mL) into **14** (8.35 g, 72.8%) as white powder, which after drying in vacuum was applied for the synthesis of **1**.

(5-t-Butyl-1,3-dioxan-2-yl)trimethylammonium iodide (**16**) - mixture of diastereoisomers. The published[7] method for **15** was used to convert **12** (3.33 g, 17.8 mmol) and iodomethane (2.90 g, 20.4 mmol) in diethyl ether (20 mL) into **16** (5.10 g, 87.3%) as white powder, which after drying in vacuum was applied for the synthesis of mixture of **3**.

(cis-4,6-Dimethyl-1,3-dioxan-2-yl)trimethylammonium iodide (**17**) - mixture of diastereoisomers. The published method for **15** was used to convert **13** (4.60 g, 28.9 mmol) and iodomethane (4.74 g, 33.4 mmol) in diethyl ether (40 mL) into **17** (7.80 g, 89.8%) as white powder, which after drying in vacuum was applied for the synthesis of mixture of **4**.

Attempts to perform acid-catalysed equilibration of trans- and *cis-***4**. The reactions were carried out a)in 5 mm o.d. NMR tubes and the progress of reaction was followed by ^{31}P NMR(81.02 MHz) spectra b)in 10 mm o.d. NMR tubes and followed by ^{31}P NMR(121.49 MHz) spectra.

a)With the use of perchloric acid.

To a solution of *trans-***4** (50 mg, 0.16 mmol) in methanol-d_4 (1.0 mL), 70% aqueous solution of perchloric acid (4 μL, 0.04 mmol) was added. The signal of *trans-***4** at δ 34.4 ppm began to disappear and after 2 h one could observe only signals at δ 24.9, 25.9, 26.5, and 26.8 ppm of the same integration. Under these conditions *cis-***4** (δ 28.4 ppm) remained unchanged.

b)With the use of boron trifluoride etherate.

To a solution of *trans-***4** (100 mg, 0.32 mmol) in chloroform-*d* (2.0 mL), boron trifluoride etherate (10 μL, 0.08 mmol) was added. After 15 min the spectrum consisted of six signals at δ 23.1, 27.0, 31.7, 35.3, 38.8, and 45.7 ppm of relative integration 25:3:34:21:7:10, respectively. After 1 h the ratio was 30:13:18:17:18:4, respectively.

Starting from *cis-***4**, after 20 min one could observe two singlets at δ 25.5 and 38.8 ppm of relative integration 61:39, which did not alter during additional 50 min.

*Crystallographic Measurements and Structure Analysis of cis- and trans-***4**. Suitable crystals of *cis-***4** and *trans-***4** were obtained from chloroform-diethyl ether and benzene-*n*-hexane, respectively. The crystal data and experimental details are presented in Table 5. Intensity data for compound *cis-***4** were collected using a CAD4 diffractometer with graphite monochromatized Mo-K_α radiation. Lattice constants were refined by least-squares fit of 25 reflections in the Θ range 9.92-14.17°. The structure was solved by direct methods (program MULTAN), then 3053 observed reflections [$I>3\sigma(I)$] were used to refine it by full matrix least-squares using F's; H atoms were found on the difference Fourier map and refined as isotropic. Anisotropic thermal parameters were applied for all other atoms. Refinement converged to R=0.047, R_w=0.046 with unit weight, for 283 refined parameters; largest shift over e.s.d. in the last cycle 0.02; largest residual peak in final difference Fourier map 0.21 e/Å^3. Absorption correction was not made. All calculations were carried out with the Enraf-Nonius SDP crystallographic computing package.

Intensity data for *trans-***4** were collected using a CAD4 diffractometer with graphite monochromatized Cu-k_α radiation. Lattice constants were refined by least-squares fit of 25 reflections in the Θ range 20.1-27.0°. The structure was solved by SHELXS-86 program, then 6018 observed reflections [$I>3\sigma(I)$] were used to refine it by full matrix least-squares using F's; H atoms were placed at idealized positions with fixed isotropic thermal parameters equal to 1.3 of isotropic thermal parameter of carbon atom and refined

Table 5. Experimental data for the crystallographic analyses*.

	cis-4	*trans*-4
Molecular formula	$C_{18}H_{21}O_3P$	$C_{18}H_{21}O_3P + 1/2C_6H_6$
Space group	$P2_1/n$	C2/c
a	9.519(2)Å	36.707(4)Å
b	17.918(2)Å	8.963(2)Å
b	9.948(2)Å	29.721(3)Å
β	95.72(1)°	126.56(1)°
Z	4	16
V	1688.3(3)Å^3	7854.5(9)Å^3
μ	1.7cm^{-1}	13.5cm^{-1}
D_x	1.245g/cm^3	1.202g/cm^3
Crystal dimension	0.5*0.5*0.4mm	0.15*0.15*0.5mm
Maximum 2Θ	54	150
Radiation	Mo-K_α-λ=0.71069Å	Cu-K_α-λ=1.54178Å
Scan mode	ω/2Θ	ω/2Θ
Scan width	0.77+0.35tanΘ	0.85+0.14tanΘ
hkl ranges	h=-12 12	h= 0 36
	k= 0 22	k= -8 0
	l= 0 12	l=-29 29
No. of refl. measured	4217 total	8252 total
	3805 unique	7900 unique
	3054 I>3σ(I)	6018 I>3σ(I)

*The tables containing full experimental data are deposited with the Cambridge Crystallographic Data Center (CCDC), UK.

as riding on carbon atoms. Anisotropic thermal parameters were applied for all other atoms. The independent unit contains two molecules of compound *trans*-4 and one molecule of benzene. The molecule of solution is disordered and exists in approximately coplanar two positions; the second position is twisted to the first one of about 25 deg. The soft occupation factor was refined for the both positions. Refinement converged to R=0.037, R_w=0.035 with unit weight, for 472 refined parameters; largest shift over e.s.d. in the last cycle 0.03; largest residual peak in final difference Fourier map 0.19 e/Å^3. Absorption correction was made by Difabs program. All calculations except solution by direct methods were carried out with the Enraf-Nonius SDP crystallographic computing package; scattering factors from International Tables for X-ray Crystallography (1974).

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