Translated from *Uspekhi Khimii*, 52 1993-2018 (1983) U.D.C. 541.6:546.1'118

Conformational Analysis of Phosphoryl Compounds with Phosphorus-Carbon Bonds

O.A.Raevskii and T.I.Ignat'eva

The literature data on the conformational analysis of phosphoryl compounds containing one or several phosphorus-carbon bonds are analysed. Attention is concentrated to the steric orientation of the phosphoryl group and the substituents at the α-carbon atom. Data concerning different phase states of the compounds are discussed. The necessity for a combined application of various physicochemical methods to the solution of conformational problems involving complex phosphoryl compounds in solution is emphasised.
The bibliography includes 121 references.

CONTENTS

I. Introduction 1156
II. Hindered internal rotation about a single P-C_{sp^3} bond 1156
III. Hindered internal rotation about a P-C_{sp^2} bond 1161
IV. The steric structures of compounds with two and three identical irregular fragments 1164
V. The steric structures of compounds with different irregular substituents at the phosphorus atom 1166

I. INTRODUCTION

Organic compounds containing the phosphoryl group have found extensive applications as complex-forming agents. In particular, such derivatives are used to synthesise new medicinal drugs effective in the elimination of toxic metal ions from the organism and in technological processes for the separation and concentration of the most valuable metals[1]. Phosphates and their derivatives play a key role in biochemical processes as structural elements in many biological components and as energy transferring agents, which is associated with their ability to form complexes with the so-called "metals of life"[2,3].

The importance of the class of compounds under consideration can be explained in the first place by the significant electron-donating capacity of the oxygen atom in the phosphoryl group—an effective centre for the formation of complexes with various metal ions. Data on the steric structures of the ligands, characterised by the bond length and the valence and dihedral angles, as well as information concerning the changes in the potential energy of the system occurring as a result of internal rotations are very important for the elucidation of the complex formation reaction mechanisms. These factors are in fact responsible for the growing interest in the stereochemical properties of phosphoryl compounds. We may note that the approaches to the theoretical analysis of the steric effects in complex formation and the results of the study of the complex-forming properties of polydentate ligands containing phosphoryl groups have been discussed in a number of communications[4-6].

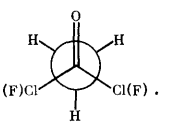
During the last decade vigorous studies have been made on the conformational analysis of phosphoryl compounds, but the complete analysis of the results obtained has not yet been carried out. The earlier reviews[7,8] include data obtained up to the end of the 1960s. In the monograph of Vilkov et al.,[9] the available data on the properties of phosphoryl compounds are described in an extremely concise form. The review of Bokii et al.[10] discusses only data obtained by X-ray diffraction while that of Arshinova[11] deals with data secured by the dipole moment and Kerr effect methods.

In the present review an attempt has been made to summarise the results of experimental and theoretical studies on the conformational properties of phosphoryl compounds with phosphorus–carbon bonds carried out in recent years. The review presents a logical analysis of the steric structures of compounds as a function of the character of the substituents at the phosphorus and carbon bonds.

II. HINDERED INTERNAL ROTATION ABOUT A SINGLE P–C_{sp^3} BOND

1. Alkylphosphonic Acid Dihalides

We shall discuss initially the conformational properties of compounds of the $\begin{matrix} R_1 \\ \diagdown \\ \\ \diagup \\ R_2 \end{matrix}$P(O)Alk series using as examples the dichloride $Cl_2P(O)CH_3$ (I) and difluoride $F_2P(O)CH_3$ (II) of methylphosphonic acid. Reliable structural data, obtained by electron diffraction, are available for compound (I) in the gas phase[12]. According to these results[12], the angles at the phosphorus atom deviate significantly from tetrahedral values: ∠O=P–C = 117.4° ± 1.0°, ∠O=P–Cl = 114.5° ± 0.5°, ∠CH_3–P–Cl = 103° ± 0.5°, and ∠Cl–P–Cl = 101.8° (calculated). Because all three atoms attached to the carbon atom are identical, the hindered internal rotation involves the formation of only one triply degenerate staggered conformation:



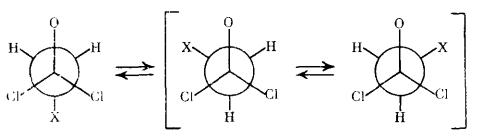
No information whatever has been published[12] concerning the character of the hindered internal rotation.

An effective method for conformational analysis is that of vibrational spectroscopy, which can yield information about the conformation mobility and the character of the changes in potential energy as a result of internal rotation. There have been a number of publications on the vibrational spectra of compounds (I) and (II) in different states of aggregation[13-22]. Thus, Durig and co-workers[18,19] analysed in detail the infrared and Raman spectra of compound (I) in gaseous, liquid, and solid states. The identification of the bands in the vibrational spectra was based on the available

literature assignments for related compounds. However, Durig et al.[18] were unable to isolate the torsional vibrations. Using improved infrared and Raman spectroscopic techniques, Durig and Casper[19] obtained clear-cut spectra of compounds (I) and (II) in the range 33–300 cm^{-1}. Having assigned specific lines and bands in this part of the spectra to torsional frequencies, the authors calculated the potential barriers to the rotation of the methyl groups in both compounds. Since this information is very important for the characterisation of intramolecular interactions, we shall consider in greater detail the interpretation of the experimental data obtained in the above study.

Eight bands were observed in the far infrared spectrum of a crystalline specimen of compound (I)[19]. Since five of these bands did not undergo any changes in frequency on raising the temperature from −190° to −80°C, the authors assigned them to intramolecular vibrations. Four of them, split into doublets (for specimens in the crystalline state), were assigned, by analogy with earlier studies[18,20], to different deformation vibrations. The "superfluous" fifth band at 264 cm^{-1} was assigned to a torsional vibration and the potential barrier was estimated from its frequency. Evidently, this approach is not rigorous without calculations for the vibrations. Furthermore, when torsional frequencies are employed, the correspondence between the mode of the observed vibration and that of the purely torsional vibration[21] and an exact estimate of the inertial parameters of the torsional vibration[22] are important. Finally, even for a correct estimate of the barrier, it is not clear to what type of interactions the characteristic obtained should be assigned. The neglect of the intermolecular interactions and of the crystal field effects can lead to a significant distortion of the true intramolecular component.

The replacement of even one hydrogen atom in the CH_3 group by some other substituent can lead to the appearance of different conformers and to equilibrium between them. Assuming that the presence of the barrier corresponds to conformations with eclipsed bonds, three stable staggered conformations can be put forward for compounds having the formula $Hal_2P(O)CH_2X$ (where X = alkyl):



The vibrational spectra of the compound $CH_3CH_2P(O)Cl_2$ (III, X = CH_3) have been discussed in a whole series of publications. Infrared absorption bands and Raman lines in the spectra of a liquid specimen of compound (III) were first interpreted by Gerding and Maarsen[13]. Analysis of the causes of the appearance of the $\nu_s(PCl_2)$ doublet led to the conclusion that a mixture of isomers is produced. The doublet in the range 1250–1300 cm^{-1} was assigned to the resonance of the Fermi stretching vibration of the phosphoryl linkage and the deformation vibration of the C–H bond. Although the above study[13] was in fact quoted in subsequent reports[23–25], the cause of the appearance of a doublet in the range 1250–1300 cm^{-1} was not discussed; the question of equilibrium between the conformers is interpreted in the same way as in the earlier investigation[13]. Steger and Kuntze[24] indicated a specific structure of the conformers (*gauche*- and *trans*-orientations of the P=O and C–C bonds). The available data concerning the assignment of the bands and lines to specific type of vibrations are extremely contradictory.

In later communications[26–28] there are no references to the earlier data[13,25]. It has been stated[26] that the study of the infrared spectra of compound (III) confirmed the conclusions reached by Steger and Kuntze[24]. Shagidullin et al.[27] estimated the thermodynamic parameters of the equilibrium involving the conformers of compound (III) in a non-polar medium (solvent–carbon tetrachloride, temperature 298 K). An estimate of ΔH for compound (III) has also been published by Fishman and Remizov[28], but it refers to a liquid specimen and the energy of the conformers includes in this instance intermolecular interactions. The above workers[28] estimated the height of the barrier to the internal rotation of compound (III) from the torsional frequency quoted by Steger and Kuntze[24]. $\Delta H_{trans\text{-}gauche}$ = 0.1 kcal mol^{-1} has been obtained for compound (III).[27]

The initial data concerning the structure of the compound $Cl_2P(O)CH(CH_3)_2$ (IV) were contradictory. Thus, in their study of the vibrational spectra of compound (IV), Gerding and Maarsen[13] did not observe signs of a conformational equilibrium. Christol and Christol[23] postulated equilibrium between two conformers on the basis of the doublet band assigned to the antisymmetric vibrations of the PCl_2 group.

Comparison of the infrared and Raman spectra of compound (IV) in various media and at different temperatures[29,30] permitted a more specific conclusion concerning its structure. It was found that equilibrium between two conformers is characteristic of this compound, as for the ethyl derivative. The thermodynamic parameters of the equilibrium were calculated from the temperature variation of the spectra of compound (IV) in solution (solvent–n-hexane, temperature 182–298 K): $\Delta H_{gauche,gauche/trans,trans}$ = −0.5 kcal mol^{-1}, ΔF = −0.2 kcal mol^{-1}, and ΔS = −1.0 kcal mol^{-1} K^{-1}.[30]

The substitution of all three hydrogen atoms at the α-carbon atom by CH_3 groups to give the compound $Cl_2P(O)C(CH_3)_3$ (V) also results in the stabilisation of the triply degenerate conformation by the hindered internal rotation. The barrier to the hindered internal rotation about the P–C bond in compound (V) is then greater than in compound (I) owing to the increased repulsion between the non-bonded atoms. The ^1H NMR spectra of compound (V) have been analysed[31,32]. Nixon and Schmutzler[32] did not observe any signs of hindered internal rotation about the P–C bond, but, on the basis of the broadening of the signals of the methyl protons on cooling the specimen, Bushweller and Brunelle[33] postulated the possibility of a barrier having a height of 7 ± 1 kcal mol^{-1}.

The dipole moment (DM) and Kerr effect methods and vibrational and ^1H NMR spectroscopic data were used in the identification of the steric structures of the conformers of compounds (III)–(V) formed[30] [the ^1H NMR spectra of the liquid compound (III), (IV), and (V) have also been published by Siddall and Prohaska[34]]. It was established on the basis of the Kerr constants that equilibrium between conformers with the *trans*- and *gauche*-dispositions of the P=O and C–CH_3 groups in proportions of 0.35:0.65 is characteristic of compound (III) in solution in CCl_4 at 298 K, while equilibrium with the *trans,gauche*- and *gauche,gauche* dispositions in proportions of 0.4:0.6 is characteristic of compound (IV). ^1H NMR spectroscopic data obtained under the same experimental conditions have led to the conclusion that there is equilibrium between the above conformers in proportions of 0.25:0.75 and 0.45:0.55. Thus the conclusions concerning the structure of the conformers and the quantitative estimates of the equilibrium positions for compounds (III) and (IV) obtained on the basis of infrared and ^1H NMR spectroscopic measurements agree, the latter to within 5%.

The NQR spectroscopic method has been resorted to in order to reach a conclusion about the conformations of compound (I), (II), and (IV) in the crystalline phase. It was established that symmetrical and asymmetric conformations are stabilised in the crystal cells of compounds (III) and (IV) respectively[35,36], which agrees with vibrational spectroscopic data for compound (III)[27] but conflicts with other results[30]. The NQR frequencies quoted[35,36] apparently do not allow in the given instance a reliable identification of the structure of the compound. In particular, a splitting of the signal by approximately 0.3 Hz has been observed for compound (I), which has a symmetrical structure, i.e. the splitting is of the same order of magnitude as that which has been attributed to the non-equivalent states of the two chlorine atoms owing to their different environments in other derivatives.

Spectroscopic data indicating a considerable structural similarity of phosphoryl, thiophosphoryl, and selenophosphoryl derivatives are also available for the analogous compounds with P=S and P=Se bonds. In particular, detailed studies have been made of the compounds $Cl_2P(S)C_2H_5$ (VI)[30,37,38] and $Cl_2P(S)C_3H_7$ (VII)[37], which led to the detection of conformational equilibria for these compounds in the liquid state.

The spectra of compound (I), (III)–(V), and $Cl_2P(O)Bu$-iso (VIII) in the range 400–700 cm^{-1}, in which infrared absorption bands and Raman lines assigned to the stretching vibrations of the P–Cl bond are observed, have been compared[29,30]. Only two bands or lines (symmetrical and antisymmetric vibrations of the PCl_2 group) are observed for compounds (I), (V), and (VIII) in the above range under the experimental conditions (solutions of different polarity, temperature 180–300 K), which indicates the absence of a dynamic equilibrium between two conformers of compound (VIII) and the existence of a conformer with the *gauche*-disposition of the bulky substituent at the α-carbon atom relative to the P=O bond. The authors[29,30] explained this by the increase of the energy of the *trans*-orientation of the P=O and isobutyl groups owing to steric interactions. The conclusion reached has also been confirmed by the agreement between the frequencies ν_s and ν_{as} of the vibrations of the PCl_2 group in the spectrum of compound (VIII), on the one hand, and the components of the ν_s and ν_{as} doublets of the PCl_2 group in the thoroughly investigated compound (III), on the other. The character of the infrared and Raman spectra of compounds (I) and (V) is consistent with the existing view concerning their structure; the infrared spectra of compound (V) have also been published by Holmes and Fild[39].

In order to elucidate the character of the intramolecular effects, Raevskii et al.[30] carried out calculations for non-valence interactions within the framework of the atom–atom approximation. The calculations yielded somewhat high interaction energies. Thus the height of the barrier to internal rotation in compound (V) proved to be twice as high as in the study of Bushweller and Brunelle[33]. However, the character of the change in energy in the course of internal rotation was determined correctly[30]: the potential energy minima correspond to the *gauche*- and *trans*-dispositions of the $C-CH_3$ and P=O groups; a deeper minimum corresponds to the *gauche*-conformer of compound (III) and the *gauche*, *gauche*-conformer of compound (IV). It is noteworthy that, from the standpoint of steric non-valence interaction, the preference for the *gauche*-position compared with the *trans*-position in the case of the hindered internal rotation about the P–C bond is partly due to the deviations of the valence angles involving the phosphorus atom from the tetrahedral value[7]. On passing from compound (III) to compound (IV), there is an increase in the energy difference between the *conformers*, which has also been observed experimentally. A slight increase of energy compared with the skewed structure results from the CH_3 group being eclipsed by the oxygen atom of the phosphoryl group. The barrier corresponding to the conformation with eclipsed P–Cl and $C-CH_3$ bonds is found to be fairly high.

Thus the steric interactions of the non-bonded atoms determine the character of the changes in the potential energy curves in the course of internal rotation about the $P-C_{sp^3}$ bond in compounds (I)–(VI).

2. Phosphoryl and Thiophosphoryl Compounds with a Single Halogen or Cyanoalkyl Group

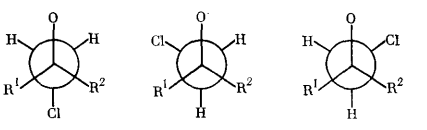
The phosphoryl compounds with a single halogen or cyanoalkyl group attached to the phosphorus atom can be regarded as more complex than compounds (I)–(VIII). Apart from the steric interactions, additional intramolecular effects may be manifested in derivatives of this series.

Fairly detailed spectroscopic studies have been made for the compounds $Cl_2P(O)CH_2Cl$ (IX)[40,41], $Cl_2P(S)CH_2Cl$ (X)[40,42], $F_2P(O)CH_2Cl$ (XI), $F_2P(S)CH_2Cl$ (XII), and $Cl_2P(O)CH_2CH_2Cl$ (XIII)[24].

The number of observed absorption bands in the infrared spectra and lines in the Raman spectra of compound (IX) in the liquid state is greater than 18, which is inconsistent with the concept of a conformationally rigid eight-atom non-linear molecule. Comparison of the spectra of liquid and solid specimens of compound (IX) revealed a tendency towards a simplification of certain parts of the spectrum on crystallisation, which also indicates the existence of a mixture of conformers in the liquid phase. An analogous picture has been observed also for compounds (X)–(XIII). It has been established by the dipole moment and Kerr effect methods that, in a non-polar medium, there is equilibrium between the *trans*-conformer (80%) and the *gauche*-conformer of compound (XI)[43]. Certain considerations concerning the structures of the conformers produced in a given series of compounds have been put forward[24,40]. Special conformational studies on compounds of the type $R_1R_2P(O)CH_2Cl$ undertaken to discover the influence of the nature of the substituents R_1 and R_2 on the hindered internal rotation about the $P-C_{sp^3}$ bond have been made by infrared spectroscopic and dipole moment methods[44], Raman spectroscopy, differential thermal analysis[45], and ^1H NMR.[46] Compounds with $R^1 = R^2 = Cl$ (IX), $R^1 = R^2 = CH_3$ (XIV), $R^1 = Cl$ and $R^2 = CH_3$ (XV), $R^1 = R^2 = C_6H_5$ (XVI), $R^1 = C_6H_5$ and $R^2 = Cl$ (XVII), and $R^1 = C_6H_5$ and $R^2 = CH_3$ (XVIII) were investigated.

The joint examination of Raman spectroscopic and differential thermal analysis data yielded additional evidence for the conformational inhomogeneity of compounds (XV) and (XVII) in different phase states. The joint analysis of the vibrational and ^1H NMR spectra made it possible to explain the changes in the geminal constants for the interaction of the phosphorus and proton nuclei in media of different polarity and to estimate the parameters for individual conformers. The results of an electron diffraction study of compound (IX)[47] are comparable with those obtained elsewhere[44–46].

The possibility of the existence of three conformers or their equilibria was examined for compounds (IX) and (XIV)–(XVIII):



The equilibrium between several conformers has been observed in a non-polar medium for all the compounds (Table 1)[44].

Table 1. The percentages of conformers in solutions of compounds (IX) and (XIV)–(XVIII) in CCl_4 at 298 K[44].

No.	Compound	*trans*-Conformer	*gauche*-1-Conformer	*gauche*-2-Conformer
(IX)	$Cl_2P(O)CH_2Cl$	60	20	20
(XIV)	$(CH_3)_2P(O)CH_2Cl$	90	5	5
(XV)	$Cl(CH_3)P(O)CH_2Cl$	60	10	30
(XVI)	$(C_6H_5)_2P(O)CH_2Cl$	10	45	45
(XVII)	$Cl(C_6H_5)P(O)CH_2Cl$	30	10	60
(XVIII)	$C_6H_5(CH_3)P(O)CH_2Cl$	30	35	35

The influence of the nature of the substituents at the phosphorus atom on the relative stabilisation of the conformers involved in the equilibria has been elucidated on the basis of conformational analysis: when the chlorine atoms in compound (IX) are replaced by methyl groups as in compound (XIV), the equilibrium shifts significantly towards the *trans*-form. Calculation of the energies of the steric and electrostatic interactions of the non-bonded atoms showed[44] that steric factors do not play a significant role in the displacement of the equilibrium for compound (IX) and that the greater stability of the *trans*-form is due to the mutual repulsion of the C–Cl dipole and the most polar P=O group. The role of steric interactions in compound (XIV) increases (there is some stabilisation of the *gauche*-form), but the interaction of the dipoles remains the decisive factor.

Analogously allowance for the steric and dipole–dipole interactions in compound (XV) permitted an explanation of the existing conformational equilibrium with satisfactory accuracy. As in compounds (IX) and (XIV), the electrostatic interaction plays the main role in compound (XV). Even for the two *gauche*-conformers, where the orientations of the C–Cl bond and of the P=O bond, which is the most polar of the bonds involving the phosphorus atom, are the same, the energy difference is wholly determined by the polar interactions involving the P–C and P–Cl dipoles which are weaker but their orientations are opposed.

When the methyl groups are replaced by phenyl groups [compounds (XVI)–(XVIII)]. the relative stabilities of the conformers change and the *gauche*-conformer predominates. This can be explained by the steric hindrance due to the aromatic rings. The *trans*-orientation of the chlorine atom is unfavourable even in the presence of only one phenyl group. There is an approximately 30% content of the *trans*-conformer of compound (III), while the proportion of the corresponding conformer of the methyl analogue (XV) is 60%.

An analogous investigation of thiophosphoryl derivatives has been carried out[48]. The infrared spectroscopic and dipole moment data and conformational calculations on compounds having the general formula $R^1R^2P(S)CH_2Cl$, where $R^1 = R^2 = Cl$ (X), $R^1 = Cl$ and $R^2 = C_2H_5$ (XIX), $R^1 = Cl$ and $R^2 = C_6H_5$ (XX), and $R^1 = Cl$ and $R^2 = p\text{-}ClC_6H_4$ (XXI), indicate the existence of conformational equilibrium. The content of the less polar *trans*-form is 80% for compound (XIX) and 40% for compounds (XX) and (XXI). As for the phosphoryl derivatives the *gauche*-conformers are not identical. Comparison of the experimental dipole moments of compounds (XIX)–(XXI) and the corresponding dipole moments calculated within the framework of Exner's method[49] permitted the conclusion that the *gauche*-1 form is involved in the equilibrium, i.e., of the two possible *gauche*-forms, that in which the C–Cl bond is in the *trans*-position relative to the most bulky substituent at the phosphorus atom is actually produced.

Thus the replacement of the phosphoryl oxygen by a sulphur atom hardly leads to any serious changes in the intramolecular interactions.

The energy of rotation about the $P-C_{sp^3}$ bond can change when the substituents are varied not only at the phosphorus atom but also at the carbon atom, as already noted for alkylphosphonic acid dichlorides examined in the previous section.

A series of recent publications describe a detailed conformational analysis of dichloromethylphosphonic acid dichloride $Cl_2P(O)CHCl_2$ (XXII)[50], dichloromethylphosphonothioic acid dichloride $Cl_2P(S)CHCl_2$ (XXIII)[51], the dichloride of α-chloroethylphosphonic acid $Cl_2P(O)CH(CH_3)Cl$ (XXIV)[52], and the dichloride of α-chloroethylphosphonothioic acid $Cl_2P(S).CH(CH_3)Cl$ (XXV)[53] by means of a combined application of infrared, Raman, and NMR spectroscopic, dipole moment, and Kerr effect methods as well as theoretical conformational calculations.

The effectiveness of the vibrational spectroscopic method in the estimation of the conformational inhomogeneity of the specimens has been clearly demonstrated[51] in relation to the vibrational spectra of compound (XXIII) in the liquid and crystalline states: conformational pair equilibrium is manifested by the doublet structures of seven pairs of bands and lines due to the stretching and deformation vibrations of the P–Cl, P=S, C–Cl, P–C, and C–H bonds (Table 2).

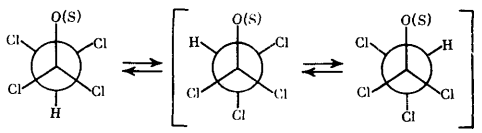
Table 2. Vibrational spectra of the compound $Cl_2P(S)CHCl_2$ (XXIII) (ν, cm^{-1})[51].

Raman spectra		I.r. spectra (liquid)	Assignment	Symmetry of isomer
liquid	crystal			
135 *dp*	135	—	—	—
190 *dp*	195	—	—	—
227 *dp*	227	—	—	—
270 *dp*	275	—	—	—
285 *dp*	285	—	—	—
365 *p*	365	—	—	—
475 *p*	473	463 m.	$\nu_s(PCl_2)$	C_1
485 *p*	—	483 m.	$\nu_s(PCl_2)$	C_s
540 *dp*	—	540 s.	$\nu_{as}(PCl_2)$	C_s
555	555	555 sh.	$\nu_{as}(PCl_2)$	C_1
625 *p*	—	624 m.	ν (P=S)	C_s
655 *p*	655	649 m.	ν (P=S)	C_1
730	727	725 sh.	ν_s (C–Cl)	C_1
740 *dp*	—	737 s.	ν_s (C–Cl)	C_s
775 *dp*	775	772 s.	ν_{as} (C–Cl)	—
810 *dp*	807	805 sh.	ν (P–C)	C_1
825	—	820 w.	ν (P–C)	C_s
1185	—	1185 v.w.	ρ (C–H)	—
1195	—	1195 v.w.	ρ (C–H)	—
2945	—	2945 w.	ν (C–H)	—
2955	—	2955 w.	ν (C–H)	—

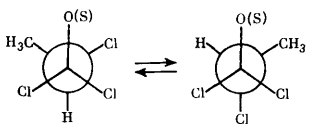
Note: *dp* = depolarised lines; *p* = polarised lines; band intensities: s. = intense (strong); m. = moderate; w. = weak; v.w. = very weak; sh. = shoulder.

It must also be emphasised that the "combined application of methods" is understood as the joint processing of information obtained independently by different physical methods using either analytical or graphical procedures. This principle was first proposed by Exner and Jehlicka[49] and Altona

et al.[54] and was subsequently developed by Vereshchagin and co-workers[55,56]. Thus graphical analysis of the squares of the dipole moments and Kerr constants (Fig. 1*a*), the squares of the dipole moments and the spin–spin coupling constants (Fig. 1*b*), and the Kerr and spin–spin coupling constants (Fig. 1*c*), and finally the joint analysis of all the three physicochemical characteristics indicated (Fig. 1*d*) led to an unambiguous identification of the conformational state of compound (XXIV)[56]. The following conformational pair equilibria have been observed for compounds (XXII)–(XXV) in a non-polar medium (dilute solutions in CCl_4):



(XXII) and (XXIII)



(XXIV) and (XXV).

As in the systems examined previously, the steric structures formed are influenced by two intramolecular effects: the steric and electrostatic interactions of the substituents at the phosphorus–carbon bond. However, allowance for only these effects in compounds (XXII) and (XXIV) is insufficient to account for the observed picture. Comparison of quantitative data on the thermodynamic parameters of the conformational equilibria of compounds (III), (IV), and (XXII) (Table 3) can be of definite assistance in this instance. In the absence of specific intramolecular interactions, the difference between the entropies of the conformers usually corresponds to their statistical weighting factors within the limits of the error of the measurements (~ 0.5 cal mol^{-1} K^{-1}), which has in fact been observed for compounds (III) and (IV), in the molecules of which there are no electronegative substituents at the α-carbon atom. The replacement of the hydrogen atoms of the alkyl fragment by chlorine atoms leads to a significant deviation from this relation. This is also accompanied by the stabilisation of the conformers with the C_1 symmetry. These changes can be explained by the formation of a weak intramolecular hydrogen bond. Its existence in one of the conformers of compound (XXII) has been demonstrated by an estimate[50] of the ratio of the absolute integral ν_{CH} band intensities due to different conformers. Thus, in the presence of protons, which have appreciable electron-accepting properties, at the α-carbon atom, the intramolecular hydrogen bond can influence the hindered internal rotation about the phosphorus–carbon bond.

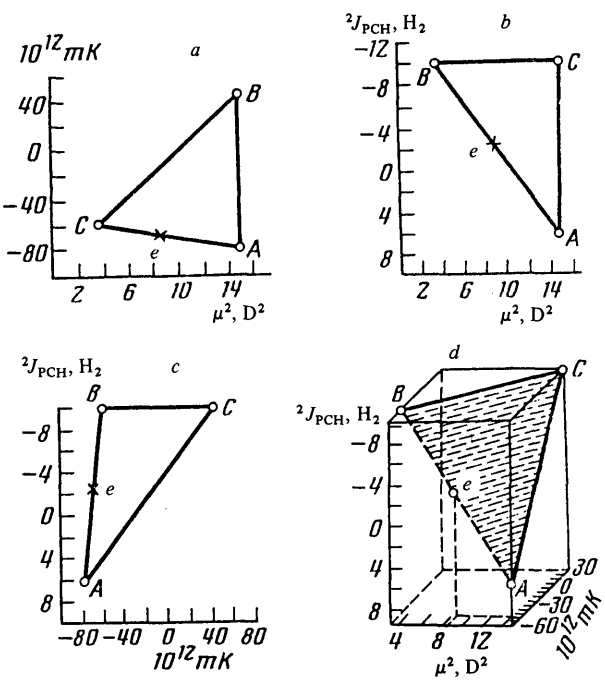


Figure 1. Graphical comparison of the squares of the dipole moments μ^2, the spin–spin coupling constants $^2J_{PCH}$, and the Kerr constants *mK* for the possible conformations of the compound $Cl_2P(O)CH(CH_3)Cl$ (XXIV): *a*) graphical comparison of μ^2 and *mK*; *b*) graphical comparison of μ^2 and $^2J_{PCH}$; *c*) graphical comparison of *mK* and $^2J_{PCH}$; *d*) graphical comparison of μ^2, *mK*, and $^2J_{PCH}$; *e*) experimental points[52].

Table 3. Thermodynamic parameters of the conformational equilibria in solutions of a number of compounds in CCl_4 at 298 K[57].

No.	Compound	$\Delta H_{C_1-C_S}$, kcal mol^{-1}	$\Delta S^{exp}_{C_1-C_S}$, cal mol^{-1} K^{-1}	$\Delta S^{theor}_{C_1-C_S}$, cal mol^{-1} K^{-1}	$\Delta\Delta S$, cal mol^{-1} K^{-1}
(III)	$Cl_2P(O)CH_2CH_3$	0.00	1.65	1.40	−0.25
(IV)	$Cl_2P(O)CH(CH_3)_2$	0.50	1.00	1.40	0.40
(XXII)	$Cl_2P(O)CHCl_2$	−1.32	−2.30	1.40	3.70
(XXIII)	$Cl_2P(O)CH(CH_3)Cl$	−1.00	−2.50	0.00	2.50
(XXV)	$Cl_2P(S)CH(CH_3)Cl$	0.10	1.30	1.40	0.10

Note: $\Delta H_{C_1-C_S}$ and $\Delta S_{C_1-C_S}$ are the differences between the enthalpies and entropies respectively; $\Delta\Delta S$ are the differences between the experimental entropies and the entropies calculated from the statistical weights of the conformers.

The hindered internal rotation in a compound with a single bromomethyl group at the phosphorus atom has been investigated in relation to the dibromide of bromomethylphosphonic acid $Br_2P(O)CH_2Br$ (XXVI)[41]. The authors[41] suggested that the bands in the infrared spectra of these compounds, whose intensity increases with decrease of temperature, are associated with the conformer having a plane of symmetry (i.e. a *trans*-disposition of the P=O and C–Br bonds). However, this initial hypothesis cannot be regarded as correct. Comparison of the spectra of compounds (IX) and (XXVI)[57] showed that the replacement of substituents [in the given case of chlorine atoms at the phosphorus atom and in the chloromethyl group of compound (IX) by bromine atoms, as in compound (XXVI)] can entail a redistribution of the contributions of different intramolecular interactions. Therefore, in some cases the *trans*-conformation can be stable, while in others the *gauche*-conformation is stable.

The incorrect hypothesis put forward by Nyquist[41] led to his assignment of the high-frequency component of the doublet ν(P=O) band in the spectrum of compound (IX) to the conformer with the C_1(*gauche*) symmetry and of the corresponding component in the spectrum of compound (XXVI) to the conformer with the C_s(*trans*) symmetry. Spectroscopic studies of a large series of phosphoryl compounds have shown[44] that the high-frequency component of the ν(P=O) vibration corresponds to the more polar conformer in the given series. It is therefore more logical to assume that the high-frequency component of the ν(P=O) band in the spectrum of compound (XXVI) corresponds to the *gauche*-isomer. Comparison of the spectra of compounds (IX) and (XXVI), obtained under identical conditions, reveals a redistribution of the intensities of the ν(P=O) and $\nu_{as}(PX_2)$ bands on passing from the chloromethyl to the bromomethyl derivative. This is apparently due to the displacement of the conformational equilibrium and not to a change in the ratio of the absolute integral intensities, since a parallel behaviour of absorption bands of different types has been observed. Temperature measurements have shown that, with decrease of temperature, the intensities of the low-frequency component of the ν(P=O) band in the spectrum of compound (IX) and of the high-frequency component in the spectrum of compound (XXVI) increase.

Thus a greater stability of the *trans*-conformer is characteristic of the dichloride of chloromethylphosphonic acid in a non-polar medium, while the *gauche*-conformer of the dibromide of bromomethylphosphonic acid is the more stable, which can also be explained primarily by the intensification of the influence of steric interactions on the energetic stabilities of the conformers. The significant increase in the bulk of the substituents at the phosphorus atom and in the halogenomethyl group led to an increase of the energy of the molecule in the *trans*-conformation (the bromine atom of the bromomethyl group is located in the projection between the two bulky bromine atoms) compared with the *gauche*-conformation (the bromine atom of the bromomethyl group is located between the bromine atom and the small oxygen atom).

The conformations of bromomethyldimethylphosphine oxide $(CH_3)_2P(O)CH_2Br$ (XXVII) and iodomethyldimethylphosphine oxide $(CH_3)_2P(O)CH_2I$ (XXVIII) have been investigated[58,59] by infrared and ^1H NMR spectroscopy and the dipole moment and Kerr effect methods. The agreement between the estimates of the conformational composition obtained by each of the above physical methods is to within 5%. It has been established that the *trans*-conformation predominates in compounds (XXVII) and (XXVIII) in a non-polar medium. This emphasises the decisive role of the electrostatic interaction of the polar group (namely P—O and C—Hal).

The steric structures of phosphoryl compounds with cyanomethyl groups, namely cyanomethyldiethylphosphine oxide $(C_2H_5)_2P(O)CH_2CN$ (XXIX) and cyanomethyldiphenylphosphine oxide $(C_6H_5)_2P(O)CH_2CN$ (XXX), have been investigated by the dipole moment and infrared spectroscopic methods[60,61]. The ratio of the *trans*- and *gauche*-conformers (0.8:0.2) of compound (XXIX) proved similar to the experimental ratio determined under the same conditions for compound (IX). The estimation of the contributions of the intramolecular effect showed that the repulsion of the dipoles leads to a relative energy gain for the *trans*-conformer by 1.3 kcal mol^{-1}. The equilibrium position for compound (XXX) is also somewhat displaced towards the *trans*-form. Comparison of the proportions of the conformers of compounds (XIV) and (XVI) (Table 1), on the one hand, and compounds (XXIX) and (XXX), on the other, has shown that for the latter pair of compounds the bulk of the substituents at the phosphorus atom no longer plays a significant role. The dipole–dipole interactions (the differences between the interaction energies of the dipoles of the *gauche*- and *trans*-conformers calculated theoretically virtually agree with the experimental values) have a greater influence in this case. Even a small decrease in the bulk of the substituents at the α-carbon atom probably weakens appreciably the steric interactions with the substituents at the phosphorus atom. The experimental difference between the free energies for compound (XXIX) is greater by 0.2 kcal mol^{-1} than for compound (XXX). The electrostatic interaction energies for these compounds differ similarly.

Thus the electrostatic factor can explain not only the observed ratio of the conformers but also the influence of the nature of the substituents at the phosphorus atom on the position of the conformational equilibrium.

Summarising the data discussed above concerning the hindered internal rotation about a single P—C_{sp^3} bond, the following observations may be made. Despite the availability of only a small amount of direct reliable quantitative data for the magnitudes of the potential barriers, detailed conformational studies of the series of compounds (I)–(XXX) which we selected suggest that the hindered internal rotation about the given bond obeys all the rules known for non-conjugated compounds and can be described satisfactorily with the aid of simple models[62,63]. This conclusion is confirmed by the results of calculations on steric and electrostatic interactions mentioned above. A distinctive feature of the group of compounds considered is the presence of the polar P=O bond, which can exert a significant influence on the orientation of the polar substituents at the α-carbon atom.

III. HINDERED INTERNAL ROTATION ABOUT A P—C_{sp^2} BOND

1. Derivatives of Vinylphosphonic Acid

The dichloride $Cl_2P(O)CH=CH_2$ (XXXI) can be regarded as the simplest derivative of vinylphosphonic acid. Its vibrational spectra in the gaseous, liquid, and crystalline states and in solutions of different polarity have been discussed[64]. The infrared spectra of the liquid compound (XXXI) and of its solutions show a doublet ν(C=C) band. The ratio of the intensities of the components of this doublet varies with the polarity of the medium and temperature. The spectrum simplifies on crystallisation: only the high-frequency component of the ν(C=C) band remains and the band at 485 cm^{-1}, which has not been assigned to a specific type of vibrations, disappears. All these factors enabled the authors[64] to postulate that the existence of two conformers is characteristic of the liquid state and solutions of compound (XXXI): the *S-cis*- and *S-trans*-conformers, analogously to the esters of acetyl- and benzoyl-phosphonic acids, vinylphosphonates, and vinylphosphine oxides whose conformations had been investigated previously by the dipole moment method[65,66]. Remizov et al.[64] also present data for the difference between the internal energies (0.6 kcal mol^{-1}) and the potential barrier (4.0–5.0 kcal mol^{-1}), which can be regarded as approximate in view of the narrow experimental temperature range and the uncertainty of the approximations used in the calculation of the heights of the barriers, which was already mentioned above.

Another paper[67] presents data obtained in an electron diffraction study of compound (XXXI). Comparison of the geometrical parameters of the molecules of compounds (XXXI) and (I) reveals insignificant differences between the corresponding bond lengths and in the valence angles. The bond lengths in compounds (I) and (XXXI) are respectively as

follows (Å): l_{P-C} = 1.800 ± 0.025 and 1.817 ± 0.033, l_{P-Cl} = 2.032 ± 0.009 and 2.016 ± 0.004, and $l_{P=O}$ = 1.448 ± 0.005 and 1.455 ± 0.011, while the valence angles in compound (XXXI) are ∠O=P—Cl = 116.8° ± 1.5°, ∠O=P—C = 119.5° ± 3.3°, and ∠Cl—P—Cl = 101.6° ± 1.2°. Electron diffraction studies[67] established that the *cis*-conformer predominates in the gas phase. Taking into account the data of Remizov et al.,[64] Naumov and Shaidullin[67] refined the geometrical parameters of the molecule for 10, 20, and 30% of the *trans*-conformer (assuming that the bond lengths and valence angles are the same in both conformations). The best agreement with experiment was achieved for the equilibrium with a 20% content of the *trans*-conformer. The revised bond lengths and valence angles thus obtained differ only slightly from those indicated above. The characteristic feature discovered in this system is that the O=P and C=C bonds in the dominant *cis*-conformation are not located in a single plane; the dihedral angle between them is 12°.

The photoelectron spectrum of vinylphosphonic acid dichloride (XXXI) has been investigated and calculated by the CNDO/2 method[68,69]. According to the calculations, the dependence of the total energy of the molecule of compound (XXXI) on the dihedral O=P—C=C angle has an absolute minimum for the *cis*-orientation of the P=O and C=C bonds and a relative minimum for the *trans*-orientation. The total energy minimum in the case of the *cis*-conformation is due to the non-valence interactions, while the minimum in the case of the *trans*-conformation arises as a consequence of the electrostatic interactions of the polar group, which are related to the effective charges on the corresponding atoms. The infrared spectra quoted by Zverev et al.[69] (see also Remizov et al.[64]) showed signs of a conformational equilibrium for compounds in the liquid state and in solutions and the stabilisation of one of the structures in the gas phase. According to Zverev et al.,[69] the photoelectron spectra make it possible to interpret, to a first approximation, the experimental ionisation potentials as the ionisation energies of the orbitals of individual fragments. The high π(C=C) ionisation potential for compound (XXXI) can be explained by the inductive effect and not the specific manifestation of the π—π interaction.

The study of vinylphosphonic acid difluoride $F_2P(O)CH=CH_2$ (XXXII) by electrical methods showed[43] that equilibrium between the *cis*- and *trans*-conformers, with an appreciable predominance (70%) of the former, is characteristic of compound (XXXII) in a non-polar medium, i.e. the replacement of Cl atoms by F atoms has an insignificant influence on the conformational equilibrium.

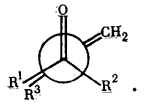
According to Remizov et al.,[64] the replacement of the hydrogen atom at the α-carbon atom in compound (XXXI) by a methyl group as in the compound $Cl_2P(O)C(CH_3)=CH_2$ (XXXIII) or of the phosphoryl oxygen atom by a sulphur atom to give the compound $Cl_2P(S)CH=CH_2$ (XXXIV) influences significantly the hindered internal rotation about the P—C_{sp^2} bond. No signs of conformational equilibrium were observed in the infrared spectra of these compounds. The stabilisation of a single structure of compound (XXXIV) can be explained, according to Remizov et al.,[64] by the fact that the replacement of the phosphoryl oxygen atom by a sulphur atom should entail a significant decrease of the P=X bond order as a result of the weaker π-bonding between the *p* orbital of the sulphur atom and the vacant 3*d* orbitals of the phosphorus atom. Consequently a higher electron density deficiency should be obtained at the phosphorus atom with increase of the P—C bond order. In order to explain the observed phenomenon, it is evidently also necessary to take into account the steric effects, since the steric factor should influence the conformational equilibrium following the replacement of the oxygen atom of the phosphoryl group by a sulphur atom or of the hydrogen at the α-carbon atom by a CH_3 group.

Substituted styrylphosphonates have been investigated by NMR using lanthanide shift reagents[70]: $Cl_2P(O)CH=CH(C_6H_5)$-*trans* (XXXV), $Cl_2P(O)CH=C(CH_3)C_6H_5$-*trans* (XXXVI), $Cl_2P(O)CH=CH(C_6H_5)$-*cis* (XXXVII), $Cl_2P(O)CH=C(Cl)C_6H_5$-*trans* (XXXVIII), and $(CH_3)_2P(O)CH=CH=CH(C_6H_5)$-*trans* (XXXIX). According to Berkova et al.,[70] in solutions of compounds (XXXV), (XXXVI), and (XXXIX) in carbon tetrachloride there is an equilibrium between the *S-cis*- and *S-trans*-conformers, while the stabilisation of the *S-trans*-conformer is characteristic of compounds (XXXVII) and (XXXVIII). On the other hand, under identical experimental conditions, it has been assumed that the *S-trans*- and *S-cis*-structures predominate for compounds (XXXV) and (XXXIX) respectively, which is due to the influence of the nature of the substituent at the phosphorus atom on the hindered internal rotation about the P—C_{sp^2} bond.

In order to solve the problem of the conformational equilibria in complex compounds such as (XXXV)—(XXXIX), it would be desirable to apply also the vibrational spectroscopic method. It is then essential to carry out a series of spectroscopic studies in order to assign reliably the set of bands in the infrared spectra or lines in the Raman spectra to rotational isomers, because the existence of a complex pattern in any one part of the spectrum does not alone constitute a confirmation of the existence of conformational equilibrium. Thus, in the study of the Raman spectra of the compounds $ROCH=\underset{\displaystyle Cl_2P(O)}{\overset{|}{C}}-CCl=CH_2$ (XL), Batuev et al.[71] noted a splitting of the ν(P=O) band into four components, and, without quoting any additional evidence, they assigned each component to a particular conformer; such interpretation of the spectra cannot be regarded as well founded.

Patanovskii et al.[43] investigated the compound $F_2P(O)CH=CH(C_6H_5)$ (XLI) by the dipole moment and Kerr effect methods. The experimental data obtained agree with the hypothesis of equilibrium between the *S-cis*-conformer (10%) and the *S-trans*-conformer (90%).

Data obtained as a result of the investigation of the steric structures of a small series of compounds (XXXI)—(XLI) provide only initial ideas concerning the character of the rotation about a single P—C_{sp^2} bond. In order to reach specific conclusions, it is necessary to obtain additional data for a large number of phosphoryl compounds with a single vinyl group and a wide variety of other substituents at the phosphorus atom. Nevertheless, within the framework of the concept of conformational energy as the sum of the contributions by the simplest intramolecular effects, it is already possible to postulate that the role of the steric non-valence interactions in the stabilisation of the conformers as the molecules of the compounds investigated is decisive. The absence of appreciably skewed forms in the series of derivatives with the vinyl bond, in contrast to the alkylphosphonic acids (I)—(XXX) for which these forms are energetically stable, can apparently be explained by the geometry of the bonds involving the α-carbon atom. The sp^2-hybridisation of the orbitals of the α-carbon atom in compounds (XXXI)—(XLI) is responsible for the disposition of all three bonds in a single plane. In the skewed conformation with the dihedral angle φ(O=P—C=C) = 60° the third bond associated with the α-carbon atom therefore eclipses one of the substituents at the phosphorus atom:



This apparently results in the loss of the energy of the steric interaction compared with the *S-cis*- and *S-trans*-conformations in which the CH_2 group or the substituent R^3 accepts the phosphoryl oxygen atom whose steric repulsion energy is minimal.

2. Derivatives With a Single Aryl Substituent at the Phosphorus Atom

The geometrical parameters of the molecule of phenylphosphonic acid dichloride $Cl_2P(O)C_6H_5$ (XLII) are fairly close to those of compound (XXXI)[72]. Only some shortening of the $P-C_{sp^2}$ bond in the phenol derivative (l = 1.76 Å) compared with the vinyl derivative (l = 1.82 Å) should be noted. The conformation in which the phosphoryl bond and the benzene ring are located in a single plane has been assigned to compound (XLII) in the gas phase. The steric interactions between the non-bonded atoms have been analysed[72] in terms of the scheme developed by Magnasco[73]; the analysis showed that this type of interaction together with conjugation can influence the stability of the structure presented above. The spectroscopic study of compounds (XLII) and $Cl_2P(S)C_6H_5$ (XLIII) demonstrated, according to Remizov and Kuramshi[74], the existence of only one isomer in the liquid phase.

Certain derivatives of arylphosphine oxides have been investigated by the dipole moment and Kerr effect methods. Data have been obtained for solutions in carbon tetrachloride of the oxides of dimethyl-*p*-tolylphosphine $(CH_3)_2P(O)(p\text{-}CH_3).C_6H_4$ (XLIV), di-t-butyl-*p*-tolylphosphine $(t\text{-}C_4H_9)_2P(O).(p\text{-}CH_3)C_6H_4$ (XLV), and *p*-cyanophenyldimethylphosphine $(CH_3)_2P(O)(p\text{-}CN)C_6H_4$ (XLVI)[75], as well as the oxides of dimethylphenylphosphine $(CH_3)_2P(O)C_6H_5$ (XLVII), *p*-chlorophenyldimethylphosphine $(CH_3)_2P(O)(p\text{-}Cl)C_6H_4$ (XLVIII), and *m*-chlorophenyldimethylphosphine $(CH_3)_2P(O)(m\text{-}Cl)C_6H_4$ (XLIX).[76] However, the conclusions of various investigators concerning the orientation of the benzene ring in compounds (XLIV)–(XLIX) do not entirely agree. Thus alternative structures have been proposed for compound (XLIV): the bisector structure[75] and the conformation in which the angle between the $C_{sp^2}-P=O$ plane and the plane of the benzene ring is 46°.[76] This discrepancy between the conclusions reached in the two investigations[75,76] cannot be explained solely by the discrepancy between the experimental molar Kerr constants. Evidently, the differences between the initial parameters used by the authors to calculate the anisotropy of the polarisability can also be a cause.

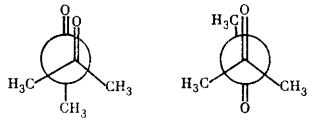
Since there are at present no rigorous criteria for the selection of the electro-optical parameters within the framework of an additive scheme, theoretical conformational calculations have been carried out in terms of the atom–atom approximation[77]. The energies of the non-valence interactions have been calculated for different conformations of the oxides of ethylphenylphosphine $C_2H_5(H)P(O)C_6H_5$ (L), diethylphenylphosphine $(C_2H_5)_2P(O)C_6H_5$ (LI), and di-t-butylphenylphosphine $(t\text{-}C_4H_9)_2P(O)C_6H_5$ (LII), in addition to compounds (XLII) and (XLVII). The results of the calculation showed that, in the presence of symmetrical substituents, the bisector orientation of the benzene ring is the most favourable from the standpoint of non-valence interactions. The barrier to internal rotation increases with the bulk of the substituents. It is noteworthy that the form of the calculated potential curves permits the possibility of torsional vibrations of the benzene ring relative to the P–C bond with an amplitude of ±15°.

When the methyl groups of one of the ethyl substituents in compounds (XL) and (LI) are in the *trans*-positions relative to the P=O bond, the benzene ring deviates from its bisector position towards one in which it eclipses the P–H bonds in the molecules of compound of (L) or one in which it eclipses the substituent with the *gauche*-conformation of the methyl group in compound (LI). Since there is no such possibility for compound (LII), it assumes a stable bisector conformation requiring considerable deformations of the valence angles at the phosphorus atom to the tetrahedral values. In the presence of identical substituents at the phosphorus atom, the benzene ring probably tends to assume the bisector position. Attention should also be drawn to the considerable similarity between the steric structures of phosphoryl compounds with vinyl and phenyl groups. The *S-cis*- and *S-trans*-conformations or their equilibrium mixture are characteristic of the first group. The bisector conformation of the benzene ring can be regarded as the *S-cis,trans*-form. Evidently, the non-valence steric interactions are decisive factors for the stabilisation of such orientation of the vinyl and phenyl groups. In agreement with Bochvar et al.,[78] no evidence has been found for the influence of conjugation of the $\pi-\pi$ or $p\pi-d\pi$ type on the stereochemistry of these molecules.

3. Derivatives with a Carbonyl Group at the Phosphorus Atom

Compounds containing the P(O)–C(O) fragment are convenient objects for investigation from the standpoint of vibrational spectroscopic and dipole moment methods in view of the presence of two polar bonds (phosphoryl and carbonyl). However, in the vast majority of cases the molecules investigated contain stereochemically irregular substituents at the phosphorus and carbon atoms and in a rigorous study must be treated as systems with several different axes of rotation. Only two compounds having fixed dispositions in space of the groups adjoining phosphorus and carbon have so far been investigated: the compounds $(CH_3)_2P(O)C(O)CH_3$ (LIII) and $[(CH_3)_3C]_2P(O)C(O)C(CH_3)_3$ (LIV).

Compound (LIII) has been studied by Kostyanovskii et al.,[79,80] by infrared and ^1H NMR spectroscopic methods. The infrared spectra of the liquid compound (LIII) have been found to contain two bands, assigned to $\nu(C=O)$ vibrations, with maxima at 1723 and 1760 cm^{-1}. Apart from the equilibrium between two conformers, the authors of these studies discussed also other possible causes of the appearance of doublet absorption bands in the range 1700–1800 cm^{-1}. In particular the hypothesis of the occurrence of the Fermi resonance of the vibrations in the given range was considered and ruled out, since both bands remained intense in different solutions. The ^1H NMR data also agree with the hypothesis of equilibrium between two conformers. Structures with the *cis*- and *trans*-disposition of the P=O and C=O bonds were proposed as the possible conformers.



Laskorin et al.[81] noted a unique and symmetrical character of the absorption in the spectrum of compound (LIII) at the $\nu(C=O)$ frequency and, although they do not discuss a specific structure of compound (LIII), comparison of the results of the above investigations[79–81] throws doubt on the initial conclusion concerning the conformational equilibrium.

A subsequent study by Laskorin et al.[82] was undertaken to solve the problem of the possible steric structure of ketophosphoryl derivatives. Only one $\nu(C=O)$ band was

observed in the infrared spectra of the compounds, including (LIV). Considering the possibility of the existence of compound (LIV) as the *cis*-, *trans*-, and *gauche*-isomers, the authors[82] assumed that the *trans*-conformation is the most probable having resorted to the Stuart–Briegleb model. The inadequate information about the structure of the group of compounds considered so far precludes a conclusion concerning the specific features of the steric orientation of the P=O and C=O bonds in the absence of internal rotation of other fragments.

IV. THE STERIC STRUCTURES OF COMPOUNDS WITH TWO AND THREE IDENTICAL IRREGULAR FRAGMENTS

1. Derivatives with Alkyl Groups

It is evident from the data described above (Section II) that a skewed position relative to the bonds adjoining the phosphorus atom is characteristic of alkyl fragments. There exist three such positions for each alkyl group. The number of possible different steric structures in the case of two and three alkyl fragments therefore increases as a result of internal rotation about the P–C_{sp^3} bonds, which leads to additional problems in the conformational analysis of such systems. X-Ray diffraction data for the compounds $(C_2H_5)_3$. .P(S) (LV) and $(C_2H_5)_3P(Se)$ (LVI) confirm that the skewed disposition of the alkyl fragment is preferred[83,84]. The vibrational spectra of such compounds in the crystalline state have been interpreted[84].

Solutions of trialkylphosphine oxides having the general formula $Alk_3P(O)$, where Alk are normal unbranched hydrocarbons in which the number of carbon atoms ranges from one as in the compound $(CH_3)_3P(O)$ (LVII) to 16 as in the compound $[(CH_3)(CH_2)_{15}]_3P(O)$ (LXXII), have been investigated[85–87].

The steric structures of the conformers of compounds (LVII)–(LXXII) have not been described accurately but the possibility of rotations about the P–C_{sp^3} and C_{sp^3}–C_{sp^3} bonds, which lead to a disposition of the alkyl fragment in the vicinity of the phosphoryl linkage, has not been ruled out.

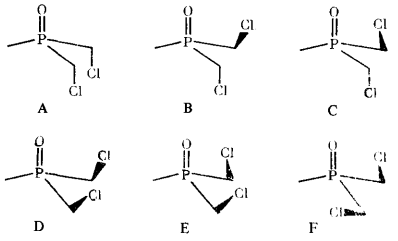
There exist definite data in the literature concerning the conformational equilibria of compounds with two alkyl groups at the phosphorus atom. Thus detailed analysis of the infrared spectra of compounds of the type $ClP(O)Alk_2$, where Alk = CH_3 [compound (LXXIII)], C_2H_5 [compound (LXXIV)], C_3H_7 [compound (LXXV)], iso-C_3H_7 [compound (LXXVI)], C_4H_9 [compound (LXXVII)], s-C_4H_9 [compound (LXXVIII)], or C_5H_{11} [compound (LXXIX)],[88] made it possible to isolate a single ν(P–Cl) band in the spectrum of compound (LXXIII) and a doublet in the spectra of compounds (LXXIV)–(LXXIX). The disappearance of one of the components of the doublet from the spectrum of the solid compound (LXXIV) and the redistribution of the band intensities in the spectra when the temperature of the liquid compounds (LXXIV)–(LXXVIII) is altered indicate the existence of a mixture of conformers; the differences between the internal energies should be of the order of magnitude of ~ 0.4 kcal mol^{-1}.

Electrical methods proved to be fairly effective in the determination of the structures of such complex systems. Thus the application of the dipole moment and Kerr constant methods to diethylpropynylphosphine oxide $(C_2H_5)_2P(O)C{\equiv}C(CH_3)$ (LXXX) showed that the C–CH_3 bonds in the ethyl groups are only in the *gauche*-positions relative to the P=O bond[89].

In view of the large number of possible conformational equilibria and the small amount of reliable data available, one cannot at present reach unambiguous conclusions concerning the conformational composition of the group of compounds considered.

2. Derivatives with Two and Three Halogenomethyl Groups

The structures of dichloromethyl(methyl)phosphine oxide $CH_3P(O)(CH_2Cl)_2$ (LXXXI) and the chloride of di(chloromethyl)phosphinothioic acid $ClP(S)(CH_2Cl)_2$ (LXXXII) have been discussed[90] on the basis of data obtained by the vibrational spectroscopic, dipole moment, and Kerr effect method. It was established that each of the C–Cl bonds in the molecules of these compounds can have the *trans*-orientation or one of the two possible *gauche*-orientations (g_1–in the direction of the methyl group, g_2–in the direction of the chloromethyl group), i.e. altogether there is a possibility of six sterically incompatible conformations:

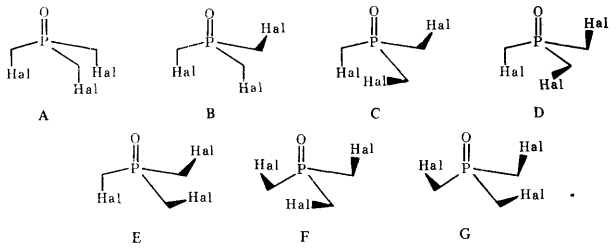


Equilibrium between two conformers, with the less polar conformer predominating (0.7:0.3), has been observed in a dilute solution of compound (LXXXI) in CCl_4. The measured dipole moments and Kerr constants led to the conclusion that the weakly polar form A and also one or several forms (B, C or D) having positive Kerr constants are involved in the equilibrium. This conclusion was confirmed by plotting the square of the dipole moment against the Kerr constant. The equilibria A ⇌ B and A ⇌ C agreed best with these spectroscopic data. The structure thus discovered proved comparable to the structure described previously for the analogue of this compound with a single chloromethyl group, i.e. the *trans*-orientation of the P=O and C–Cl bonds proved to be preferable.

Substitution of the phosphoryl oxygen atom by sulphur and of the CH_3 group by chlorine, as in compound (LXXXII), leads to a considerable stabilisation of one of the least polar forms (A or B); the fraction of the more polar structure (most probably the C structure) does not then exceed 10%.

In order to follow the variation of the steric structures of compounds when the halogen atom in the halogenomethyl group is replaced, a study was made of dibromomethyl(methyl)phosphine oxide $CH_3P(O)(CH_2Br)_2$ (LXXXIII) and di-iodomethyl(methyl)phosphine oxide $CH_3P(O)(CH_2I)_2$ (LXXXIV) by means of a combined study of the infrared, Raman, and ^1H NMR spectra, the dipole moments, and the Kerr effect[91]. It was established that substitution of chlorine atoms by bromine and iodine atoms in the halogenomethyl groups leads to a fairly appreciable alteration of the molecular structure. For compounds with two bromo- and iodo-methyl groups, the conformation with the *trans*-orientation of both C-Hal bonds is not involved in the equilibrium. The most stable proved to be the form with the *trans–gauche* disposition of the C–Hal bonds, where the halogen atoms are remote from one another, which rules out steric hindrance and, as a consequence of the electrostatic interaction, one C–Hal bond is in the *trans*-position relative to the P=O group.

Molecules in which three conformationally irregular groups are attached to the phosphorus atom are the most interesting and at the same time most complex. In the molecules of tri(halogenomethyl)phosphine oxides each C–Hal bond has either the *trans*-orientation or one of the *gauche*-orientations relative to the phosphoryl group, i.e. there is a possibility of seven conformations:



The conformational equilibrium of tri(chloromethyl)phosphine oxide $(CH_2Cl)_3P(O)$ (LXXXV) has been analysed[92]. The infrared spectra of this compound indicated equilibrium between two conformers in non-polar solutions (in proportions of 0.7:0.3), the less polar component predominating. Comparison of the experimental dipole moments and Kerr constants with the corresponding quantities evaluated by a graphical method established that all three C–Cl bonds in the dominant conformer are in the *trans*-positions relative to the P=O bond (structure A), while in the energetically less favourable conformer they are in the *gauche*-positions, all being rotated to one side (structure F). In principle, this result agrees with data obtained for phosphine oxide with one or two chloromethyl groups. It was of interest to note that the equilibrium found for tri(chloromethyl)phosphine oxide corresponds to a cooperative transition of all three chlorine atoms from the *trans,trans,trans*-positions to the *gauche,gauche,gauche*-positions.

The predominance of the B structure in the case of three bromomethyl groups was observed in an analogous study of tri(bromomethyl)phosphine oxide $(CH_2Br)_3P(O)$ (LXXXVI) and tri(iodomethyl)phosphine oxide $(CH_2I)_3P(O)$ (LXXXVII), which indicates an appreciable role of not only steric but also electrostatic interactions of the strong P=O and C–Br dipoles in the conformational equilibrium. The subsequent replacement of bromine atoms by iodine atoms led to the displacement of the conformer having the *trans,trans*-orientations of the P=O and C–Hal bonds from the equilibrium. The *gauche, gauche,gauche*-structure F was found to predominate in this case.

Thus the influence of two intramolecular effects (those of the steric and electrostatic interactions of the non-bonded atoms) on the structures of compounds with several halogenomethyl groups has been clearly followed. The equilibrium which obtains in the case of tri(chloromethyl)phosphine oxide indicates the approximately identical influence of two of the factors indicated above: the *trans,trans,trans*-structure is a result of the Coulombic repulsion of the dipoles of the P=O and C–Cl groups, while the *gauche,gauche,gauche*-structure is determined by steric interactions. Steric interactions predominate for compounds with iodomethyl groups, so that the *gauche,gauche,gauche*-disposition of the P=O and C–I bonds is observed in the preferred conformation.

3. Two and Three Vinyl or Phenyl Groups at the Phosphorus Atom

The structure of the compound $ClP(O)(CH{=}CH_2)_2$ (LXXXVIII) has been investigated by electron diffraction[67]. Complete agreement between the experimental and calculated data was not obtained in the above studies, but the authors concluded that the conformer in which the C=C and P=O groups have a disposition intermediate between *cis* and *gauche* (which corresponds to the model with C_S symmetry and dihedral angles close to 35°) predominates. The deviation from the rigorously eclipsed disposition of these groups may be associated with the interaction of the *p* orbitals of the vinyl groups. Evidently, the solution of the problem of the structure of compound (LXXXVIII) requires its more detailed investigation using other independent methods.

The data for the steric structures of compounds containing two and three benzene rings at the phosphorus atom can be divided into three groups: the results of X-ray diffraction analysis, the results of studies in solutions, and the results of theoretical conformational calculations.

X-Ray diffraction analysis was used to investigate diphenylphosphinic acid $(C_6H_5)_2P(O)OH$ (LXXXIX)[93,94], the diphenylphosphoryl alcohols $(C_6H_5)_2P(O)(CH_2)_3OH$ (XC)[95], $(C_6H_5)_2P(O)(CH_2)_2OH$ (XCI)[96], and $(C_6H_5)_2P(O)CH_2(o\text{-}OHC_6H_4)$ (XCII)[97], triphenylphosphine oxide $(C_6H_5)_3P(O)$ (XCIII)[98–100], *p*-chlorophenyldiphenylphosphine oxide $(p\text{-}ClC_6H_4)P(O)(C_6H_5)_2$ (XCIV)[101], tri(*o*-tolyl)phosphine oxide $(o\text{-}CH_3C_6H_4)_3P(O)$ (XCV), tri(*o*-tolyl)phosphine sulphide $(o\text{-}CH_3C_6H_4)_3P(S)$ (XCVI)[102,103], tri(*m*-tolyl)phosphine sulphide $(m\text{-}CH_3C_6H_4)_3P(S)$ (XCVII)[103], and tri(*o*-tolyl)phosphine selenide $(o\text{-}CH_3C_6H_4)_3P(Se)$ (XCVIII)[102,103]. A disposition of the planes of the benzene rings relative to the X=P–C plane (X = O, S, or Se) skewed to different extents has been established for all the derivatives listed above, but the cause of this has not been elucidated. The results of the X-ray diffraction analysis of the two crystalline modifications of compound (XCIII) show that the polymorphic transformation involves a fairly appreciable alteration of the conformation, i.e. the crystal packing has an effect. However, the extent to which the crystal field effects are responsible for the non-equivalence of the benzene rings is difficult to determine without reliable information about the molecular structure in the liquid phase and in solutions. In virtually all the studies which have yielded data for the structures of the above compounds in solutions, it was assumed that each of the three benzene rings attached to the phosphorus atom has been rotated by the same angle[104,105]. It has been found by the dipole moment and Kerr effect methods that their angle of rotation is 60°[104] or 55°[105] for compound (XCIII) and 62° for the compound $(C_6H_5)_3P(S)$ (XCIX)[104]. Analogous results have been obtained also for several substituted triarylphosphine oxides having the general formula $(XC_6H_4)_3P(O)$, where X = *p*-Cl [compound (CI)], *m*-Cl [compound (CI)], *p*-CH_3 [compound (CII)], or *m*-CH_3 [compound (CIII)][105]. However, a broadening of the signals due to the fluorine atoms in the *meta*-position has been observed in the NMR spectra of the fully fluorinated triphenylphosphine oxide[106], which disagrees with the results of Aroney et al.[104] and Bulgarevich et al.[105]

The same problems arise also in the study of compounds with two benzene rings at the phosphorus atom. According to the measurements of the dipole moments and Kerr constants for methyldiphenylphosphine oxide $(C_6H_5)_2P(O)CH_3$ (CIV)[76], the dihedral angle of the benzene rings and the P=O group is 58°. Somewhat different results have been obtained for analogous compounds in other investigations[89,107,108]. Ishmaeva et al.[107] examined two types of rotations for $(C_6H_5)_2P(O)CCl_3$ (CV), $(p\text{-}CH_3C_6H_4)_2P(O)CCl_3$ (CVI), and $(p\text{-}ClC_6H_4)_2P(O)CCl_3$ (CVII): the symmetrical rotation ($\phi_1 = -\phi_2$) and the antisymmetric rotation ($\phi_1 = \phi_2$). The dihedral angles obtained are 15°, in agreement with the symmetrical rotation. The dipole moment and Kerr constant data for the compound $(C_6H_5)_2P(O)CN$ (CVIII) indicated a

structure in which the planes of the benzene ring are almost parallel to the P=O bond[108]. Thus, according to the above workers[108], the addition of the strongly electron-accepting cyano-group to the phosphorus atom does not affect the conformational behaviour of the phenyl groups and is not manifested in the intramolecular electronic interactions involving the phosphorus atom. On the other hand, the experimental Kerr constants for the compound $(C_6H_5)_2P(O)C\equiv C-CH_3$ (CIX) agree with the conformation in which the planes of the phenyl groups are close to the arrangement in which the ethynyl group is eclipsed. In this case the authors[108] concluded that the interaction of the conjugated systems of the aromatic fragments with the triple bond is a stabilising factor.

An attempt has been made[109] to estimate the stereochemical properties of compound (CIV) and the compound $(C_6H_5)_2$.P(O)H (CX) with the aid of the relation found[110] between the ratio of the intensities of the symmetrical and asymmetric vibrations in the infrared spectra and the angle between the polarisation vectors of the out-of-plane vibrations. Relations of this kind may be useful in the study of the steric structures of complex compounds, but, so long as their universality has not been tested, they must be treated with caution.

Apart from the experimental studies on individual examples of the group of compounds considered, theoretical conformational calculations have been carried out. The calculation for compound (CIV) has been performed within the framework of the method of atom–atom potential functions and it was shown that the skewed state of the benzene rings attached to the phosphorus atom relative to the O=P–C–C plane is preferred[111].

The dependence of the conformational energy on the angles of internal rotation of the benzene rings relative to the $P-C_6H_5$ bonds has been investigated for the chloride of diphenylphosphinic acid $(C_6H_5)_2P(O)Cl$ (CXI) also within the framework of the atom–atom approach with simultaneous optimisation of the bond lengths and valence angles at the phosphorus atom[77]. The calculation showed that the two conformers for which the difference between the internal energies is 0.3 kcal mol^{-1} are the most stable in terms of the given approximation. The angles $\phi_1 = 10°$ and $\phi_2 = 76°$ were obtained for one conformer and $\phi_1 = 30°$ and $\phi_2 = 15°$ were found for the other conformer. It is noteworthy that the conformations with identical angles of rotation of the benzene rings ($\phi_1 = \phi_2$), in the range 10°–40°, have energies slightly different from those of the structures indicated above (~ 0.5 kcal mol^{-1}). The possibility therefore remains that a whole series of states obtains for the molecule of compound (CXI) with both identical and different angles of rotation of the planes of the benzene ring in the range from 10° to 40°.

On the basis of experimental data for compounds containing two or three phenyl groups at the phosphorus atom, one must conclude that it is difficult to obtain reliable results concerning the orientation of the plane of the benzene ring in such compounds when the latter are in solution. The employment of the vibrational spectroscopic method in this instance is complicated by the presence in the spectra of a large number of bands of the benzene ring. On the other hand, data obtained with the aid of electrical methods (in particular the Kerr effect methods) cannot be regarded as sufficiently accurate, despite their satisfactory sensitivity, owing to the limited amount of available information about the type of variation of the anisotropy of the polarisability of the benzene rings under the influence of electronic effects in the hindered internal rotation about the $P-C_{sp^2}$ bonds.

V. THE STERIC STRUCTURES OF COMPOUNDS WITH DIFFERENT IRREGULAR SUBSTITUENTS AT THE PHOSPHORUS ATOM

The conformational analysis of compounds with different irregular substituents at the phosphorus atom is undoubtedly even more complex than the study of compounds with identical groups. This is associated both with the removal of degeneracy, and hence the increase of the number of conformers having different properties, and with the possibility, in principle, of the stabilisation of those structures which might be disregarded in the case of derivatives with identical groups in view of their instability. The employment of any one physical method in the conformational analysis of compounds of the given series can therefore lead to erroneous conclusions.

For example, the ^{1}H NMR spectra of compounds (I) and (III)–(V), $CH_3(C_6H_5)P(O)Cl$ (CXII), $C_2H_5(C_6H_5)P(O)Cl$ (CXIII), and iso-$C_3H_7(C_6H_5)P(O)Cl$ (CXIV) have been discussed[34]. In contrast to compounds (CXII) and (CXIII), in the spectrum of compound (CXIV) a doublet is observed at the $\nu(CH_3)$ frequency. The authors[34] explained this finding by the conformational equilibrium, but the merging of the signals did not occur even following an appreciable increase of temperature. The observed spectroscopic pattern cannot apparently be explained by rotational isomerism and is in fact due to the manifestation of the magnetic non-equivalence, giving rise to spectra of type ABX and A_2X for the methyl groups of compound (CXIV), which the authors[34] failed to take into account. The same interpretation has been given[112] for the protons of the chloromethyl group in the compound $(CH_3)_2NP(O)Cl(CH_2Cl)$ (CXV).

In a stereochemical study of ketophosphonate compounds, the vibrational spectroscopic method was mainly used. It has been stated[113] that there is only a single $\nu(C=O)$ band in the spectra of compounds having the general formula $(C_2H_5O)_2P(O)C(O)(CH_2)_nCH_3$, where n = 10 [compound (CXVI)], 12 [compound (CXVII)], 14 [compound (CXVIII)] and 16 [compound (CXIX)]. Analogous conclusions were reached on the basis of the Raman spectra of the compound $(C_2H_5O)_2P(O)C(O)C_6H_5$ (CXX)[114] and the infrared spectra of the compound $(C_2H_5O)_2P(O)C(O)CH_3$ (CXXI)[115], as well as a whole group of compounds having the general formula $(R'O)_2P(O)C(O)R$, where R = CH_3 and R' = C_2H_5 [compound (CXXII)], R = C_2H_5 and R' = C_2H_5 [compound (CXXIII)], R = iso-C_3H_7 and R' = C_2H_5 [compound (CXXIV)], R = t-C_4H_9 and R' = C_2H_5 [compound (CXXV)], R = C_6H_5 and R' = C_2H_5 [compound (CXXVI)], R = C_5H_9 and R' = C_2H_5 [compound (CXXVII)], R = C_6H_{11} and R' = CH_3 [compound (CXXVIII)], R = C_6H_{11} and R' = C_2H_5 [compound (CXXIX)], and R = C_6H_{11} and R' = iso-C_3H_7 [compound (CXXX)][116]. However, two ranges of variation of $\nu(C=O)$ (1656–1666 and 1698–1700 cm^{-1}) have been indicated[117] for 33 different compounds having the general formula $R(R''O)$.P(O)C(O)R', where R = C_2H_5, C_6H_5, p-$CH_3C_6H_4$, or p-ClC_6H_4, R' = C_6H_5, CH_3, p-$CH_3C_6H_4$, or p-ClC_6H_4, and R'' = CH_3, C_2H_5, C_3H_7, or iso-C_4H_9.

Detailed infrared and ^{1}H NMR spectroscopic data for the compounds $(CH_3O)_2P(O)C(O)CH_3$ (CXXXI), $(C_2H_5O)_2P(O)$.C(O)CH_3 (CXXXII), and $(CH_3O)_2P(O)C(O)C_6H_5$ (CXXXIII) have been published[118]. The infrared spectra of compounds in different phase states, in solutions of different polarity, and at different temperatures have been obtained. The type of the band characterising the absorption by the carbonyl group has led to the conclusion that conformational pair equilibrium obtains for compounds (CXXI) and (CXXXII) and that one conformer of compound (CXXXIII) is stabilised. However, only a single $\nu(C=O)$ band has again been noted[81]

for compound (CXXXI). In a special investigation[82] it has been stated that the manifestation of the second ν(C=O) band with a maximum at 1710 cm^{-1} is apparently due to an admixture of decomposition products. In the infrared spectrum of a freshly prepared and purified specimen of compound (CXXXI), the splitting of the ν(C=O) band is not observed for a liquid film and for a solution in CCl_4, while the addition of traces of acetic acid to the specimen leads to the appearance of a second absorption band at 1710 cm^{-1}. Preference has been given[82] to the *trans*-orientation of the P=O and C=O bonds.

However, in a number of instances the high sensitivity of individual physical methods to hindered internal rotation makes it possible to obtain fairly definite results even when only one method is used to study the conformations of complex compounds. Thus the considerable polarity of the P=O and C≡N bonds makes it possible to identify their relative positions in space[61]. The dipole moment method has been used[119] to investigate the steric structures of compounds having the general formula $XC_6H_4CH{=}C(CN)P(O)OC_2H_5$, where X = H [compound (CXXXIV)], *p*-NO_2 [compound (CXXXV)], *p*-Cl [compound (CXXXVI)], *p*-OCH_3 [compound (CXXXVII)], *p*-$N(CH_3)_2$ [compound (CXXXVIII)], and *m*-NH_2 [compound (CXXXIX)]. The rigidity of the $XC_6H_4CH{=}C(CN)$ fragment made it possible to infer the orientations of the phosphoryl and vinyl bonds and hence their electronic interactions. A number of other examples of this approach to conformational studies have been described in a review[120].

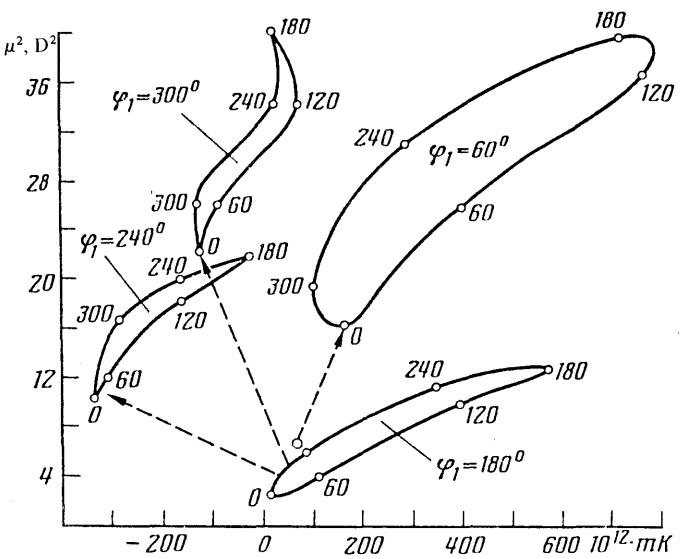
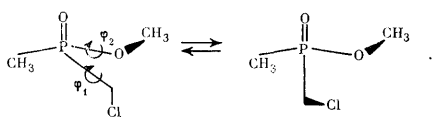


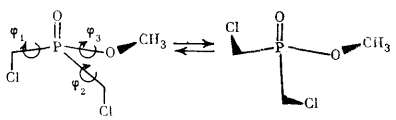
Figure 2. Graphical comparison of the dipole moments and Kerr constants for the compound $CH_3(CH_3O)P(O)CH_2Cl$ (CXL)[121].

Nevertheless, a combined physicochemical investigation is required to a greater extent than in other cases for the identification of the steric structures of organophosphorus compounds with different substituents. Such a study has been carried out of the ester of chloromethyl(methyl)phosphinic acid $CH_3(CH_3O)P(O)CH_2Cl$ (CXL)[121]. Vibrational and ^1H NMR spectroscopic data have been used in studies by the dipole moment and Kerr effect methods have been carried out. When account is taken of the possible rotations of both groups in steps of 60°, one can imagine the occurrence of 36 structures. However, all the structures in which the P=O and C—Cl, P—C and C—Cl, and P—C and O—CH_3 pairs of bonds are eclipsed can be excluded from consideration according to the data presented above in the present review and the conclusions reached by Raevskii[63]. Vibrational spectra have shown that in dilute solutions in CCl_4 compound (CXL) exists as a mixture of two conformers in which the less polar form predominates appreciably (~ 90%).

Experimental dipole moment and Kerr effect data have been assessed under the same conditions[121]. Fig.2 compares the calculated squares of the dipole moments and Kerr constants with complete internal rotation relative to the P—O bond and four fixed positions of the P=O and C—Cl groups (the angles between the P=O and C—Cl bonds are 60°, 180°, 240°, and 300°). The experimental point is located in the vicinity of a closed curve corresponding to the set of conformations with the *trans*-orientation of the P=O and C—Cl bonds, which shows that the conformer with the *trans*-disposition of the C—Cl bond predominates in the equilibrium. The orientation of the O—CH_3 bond of this conformer can correspond to the *cis*- or *gauche*-disposition. The steric structure of the second conformer, the partner in the equilibrium in the given instance, cannot be determined with much reliability in view of its small amount. However, ^1H NMR data suggest the existence of equilibrium between the following conformers:



An analogous study has been carried out for a series of alkyl esters di(chloromethyl)phosphinic acid having the general formula $(CH_2Cl)_2P(O)OR$, where R = CH_3 [compound (CXLI)], C_2H_5 [compound (CXLII)], $CH_2CH{=}CH_2$ [compound (CXLIII)], iso-C_3H_7 [compound (CXLIV)], or C_4H_9 [compound (CXLV)].[121] The combined employment of various physical methods made it possible to identify the steric structures of these complex compounds for which the following equilibrium obtains in a non-polar medium:



Comparison of the steric structures of the series of compounds considered in this section with the simpler related compounds (IX)–(XXVIII) having the P—C_{sp^3} bonds shows that the *trans*-orientation of the P=O and C—Cl bond predominates in all the phosphoryl compounds investigated having the CH_2Cl group (groups) and small substituents at the phosphorus atom. The "cisoid" (60° ≥ φ ≥ 300°) orientation of the P=O and O—Alk bonds which has been established is common to phosphoric acid esters. Thus the steric structures of the compounds investigated having different substituents at the phosphorus atom correspond fully to the structures of related derivatives with a single irregular group and do not exhibit any new intramolecular effects.

Consequently, the features discovered previously for molecules with identical groups account fully for the structure of phosphoryl compounds with different substituents.

---o0o---

The data presented in this review lead to the conclusion that fairly extensive and quite definite information has now been accumulated on the hindered internal rotation about the phosphorus–carbon bond. Modern ideas concerning the nature of various intramolecular effects frequently permit an *a priori* determination of the preferential conformation of a compound which has not yet been studied. However, for subsequent successful conformational investigation of the given class of compounds, containing the P=O group, it is necessary to concentrate attention on the following problems: (1) the determination of quantitative data for the barriers to internal rotations; (2) the improvement and extensive employment of a scheme involving the combined application of the maximum possible number of independent physicochemical characteristics; (3) the estimation of the steric structures of compounds in aqueous media.

Quantitative information about the barriers to internal rotation can be obtained by employing microwave and NMR spectroscopy. However, experimental and theoretical difficulties significantly limit the application of these methods to the class of compounds under discussion. In this case the combination of vibrational spectroscopic and gas-phase electron diffraction methods, which make it possible to draw inferences about the nature of the change in the potential energy in the course of the hindered internal rotation from the torsional frequencies in the spectra and the geometrical parameters of the molecules determined, acquire special importance in this instance.

Analysis of data referring to the group of compounds with different irregular substituents shows that in the case of complex organic compounds the application of any one method cannot lead to a reliable solution of the conformational problem. The increase of the number of physicochemical parameters employed permits the analysis of the compatibility of the characteristics of the conformational equilibria with experimental data. When the number of equations relating the experimental and theoretical physicochemical characteristics corresponds to the number of the possible conformers, one can obtain a rigorous solution of the conformational problem[52]. The employment of the possibilities inherent in the NMR spectroscopic method involving different nuclei is evidently extremely promising for complex systems in this instance.

One should also note that the results presented in this review refer to gaseous, liquid (including solutions in non-polar and polar solvents), or crystalline states of the molecules. In order to assess the problem of the physiological activities of compounds, it is essential to have information about their steric structures in aqueous solutions. Such data are not available for the class of compounds discussed in this review. The present authors have recently obtained the infrared spectra of aqueous solutions of a phosphoryl compound with a halogenomethyl group using an IFS-113 Fourier spectrometer. It was found that in water the ratio of conformers with the *trans*- and *gauche*-orientations of the P=O and C–Hal bonds (0.4:0.6) differs significantly from the ratio in a non-polar medium (CCl_4, 0.9:0.1). The example presented indicates the necessity for a detailed study of the conformational state of compounds in an aqueous medium. At any rate, the neglect of the influence of the aqueous medium on the stereochemistry in the selection of structural elements responsible for the physiological activity of compounds of a given class can lead to erroneous constructions.

REFERENCES

1. M.I.Kabachnik, T.Ya.Medved', N.M.Dyatlova, and M.V.Rudomino, Uspekhi Khim., 1974, **43**, 1554 [Russ.Chem.Rev., 1974, **43**(9)].
2. D.R.Williams, "The Metals of Life: The Solution Chemistry of Metal Ions in Biological Systems" (Translated into Russian), Izd.Mir, Moscow, 1975.
3. G.L.Eichhorn (Editor), "Inorganic Biochemistry" (Translated into Russian), Izd.Mir, Moscow, 1978, Vol.1.
4. M.I.Kabachnik, V.G.Dashevskii, T.Ya.Medved', and A.P.Baranov, Teor.Eksper.Khim., 1977, **13**, 335.
5. V.G.Dashevskii, A.P.Baranov, T.Ya.Medved', and M.I.Kabachnik, Teor.Eksper.Khim., 1977, **13**, 340.
6. V.G.Dashevskii, A.P.Baranov, T.Ya.Medved', and M.I.Kabachnik, Teor.Eksper.Khim., 1978, **14**, 488.
7. L.S.Khaikin and L.V.Vilkov, Uspekhi Khim., 1971, **40**, 2174 [Russ.Chem.Rev., 1971, **40**(12)].
8. L.S.Khaikin and L.V.Vilkov, "Topics in Current Chemistry", Springer, Berlin, 1975, **53**, 25.
9. L.V.Vilkov, V.S.Mastryukov, and N.I.Sadova, "Opredelenie Geometricheskogo Stroeniya Svobodnykh Molekul" (Determination of the Geometrical Structures of Free Molecules), Izd.Khimiya, Leningrad, 1978, p.173.
10. N.G.Bokii, Yu.T.Struchkov, A.E.Kalinin, V.G.Andrianov, and T.N.Sal'nikova, in "Itogi Nauki i Tekhniki, Kristallokhimiya" (Advances in Science and Engineering. Crystal Chemistry), Izd. VINITI, Akad.Nauk SSSR, Moscow, 1977, p.56.
11. R.P.Arshinova, Uspekhi Khim., 1977, **46**, 1544 [Russ.Chem.Rev., 1977, **46**(9)].
12. V.A.Naumov and V.N.Semashko, Zhur.Strukt. Khim., 1971, **12**, 317.
13. H.Gerding and J.W.Maarsen, Rec.Trav.chim. Pays-Bas., 1957, **76**, 481.
14. J.Quinchon, M.Le Sech, and E.Gryszkiewick, Bull.Soc.chim.France, 1961, 735.
15. J.Quinchon, M.Le Sech, and C.Monard, Bull.Soc. chim.France, 1961, 1086.
16. L.C.Thomas and R.A.Chittenden, Spectrochim. Acta, 1965, **21**, 1905.
17. S.T.King and R.A.Nyquist, Spectrochim.Acta, 1970, **26A**, 1481.
18. J.R.Durig, F.Bloock, and J.W.Levin, Spectrochim. Acta, 1965, **21**, 1105.
19. J.R.Durig and J.M.Casper, J.Phys.Chem., 1971, **75**, 1956.
20. J.E.Griffiths, Spectrochim.Acta, 1965, **21**, 1135.
21. A.V.Cunliffe, in "Internal Rotation in Molecules" (Edited by W.J.Orville-Thomas) (Translated into Russian), Izd.Mir, Moscow, 1977, p.182.
22. J.Allen and S.Fuester, in "Internal Rotation in Molecules" (Edited by W.J.Orville-Thomas) (Translated into Russian), Izd.Mir, Moscow, 1977, p.211.
23. C.Christol and H.Christol, J.chim.phys.et phys.-chim.biol., 1965, **62**, 246.
24. E.Steger and M.Kuntze, Spectrochim.Acta, 1967, **23A**, 2189.
25. G.Geiseler, K.O.Bindernagel, and J.Fruwert, Ber.Bunsenges.Phys.Chem., 1967, **71**, 478.
26. A.N.Pudovik, I.Ya.Kuramshin, A.B.Remizov, A.A.Muratova, and R.A.Manapov, Zhur.Obshch. Khim., 1974, **44**, 44.

27. R.R.Shagidullin, I.I.Vandyukova, and I.A.Nuretdinov, Izv.Akad.Nauk SSSR, Ser.Khim., 1976, 801.
28. A.I.Fishman and A.V.Remizov, Optika i Spektrosk., 1975, **38**, 858.
29. N.G.Mumzhieva, Candidate's Thesis in Chemical Sciences, Kazan State University, Kazan, 1977.
30. O.A.Raevskii, N.G.Mumzhieva, T.A.Zyablikova, A.N.Vereshchagin, E.I.Gritsaev, and M.M.Gilyazov, Izv.Akad.Nauk SSSR, Ser.Khim., 1978, 614.
31. R.Schmutzler and G.S.Reddy, Z.Naturforsch., 1965, **20b**, 832.
32. J.F.Nixon and R.Schmutzler, Spectrochim.Acta, 1966, **22**, 565.
33. C.H.Bushweller and J.A.Brunelle, J.Amer.Chem. Soc., 1973, **95**, 5949.
34. T.H.Siddall and C.A.Prohaska, J.Amer.Chem.Soc., 1962, **84**, 2502.
35. E.N.Tsvetkov, G.K.Semin, T.A.Babushkina, D.I.Lobanov, and M.I.Kabachnik, Izv.Akad.Nauk SSSR, Ser.Khim., 1967, 2375.
36. G.K.Semin and T.A.Babushkina, Teor.Eksper. Khim., 1968, **4**, 835.
37. E.M.Popov, T.A.Mastryukova, N.P.Rodionova, and M.I.Kabachnik, Zhur.Obshch.Khim., 1959, **29**, 1998.
38. F.N.Hooge and P.J.Christen, Rec.Trav.chim., 1958, **77**, 911.
39. R.R.Holmes and M.Fild, Spectrochim.Acta, 1971, **27A**, 1537.
40. E.Steger, J.Rehak, and H.Faltus, Z.phys.Chem., 1965, **229**, 110.
41. R.A.Nyquist, Appl.Spectrosc., 1968, **22**, 452.
42. L.S.Khaikin, L.V.Vilkov, A.F.Vasil'ev, N.N.Mel'nikov, T.F.Tulyakova, and M.G.Anashkin, Dokl.Akad. Nauk SSSR, 1972, **203**, 1090.
43. I.I.Patsanovskii, E.A.Ishmaeva, Ya.A.Levin, M.M.Gilyazov, and A.N.Pudovik, Zhur.Obshch. Khim., 1981, **51**, 985.
44. O.A.Raevskii, F.G.Khalitov, A.N.Vereshchagin, and I.M.Vetluzhskikh, Izv.Akad.Nauk SSSR, Ser. Khim., 1972, 2446.
45. O.A.Raevskii, N.G.Mumzhieva, P.P.Anoshina, and B.Ya.Teitel'baum, Izv.Akad.Nauk SSSR, Ser.Khim., 1980, 930.
46. O.A.Raevskii, N.G.Mumzhieva, N.A.Aleksandrova, and R.G.Gainullina, Izv.Akad.Nauk SSSR, Ser. Khim., 1977, 797.
47. E.Vaida, M.Kalonets, J.Hargittai, and S.Sroke, J.Molec.Struct., 1976, **35**, 235.
48. O.A.Raevskii, F.G.Khalitov, Yu.A.Donskaya, and I.M.Shermergorn, Izv.Akad.Nauk SSSR, Ser.Khim., 1973, 795.
49. O.Exner and V.Jehlicka, Coll.Chem.Comm., 1965, **30**, 639.
50. O.A.Raevskii, F.G.Khalitov, N.G.Mumzhieva, M.M.Gilyazov, D.U.Zakirov, I.A.Safin, and A.V.Aganov, Izv.Akad.Nauk SSSR, Ser.Khim., 1976, 2701.
51. N.G.Mumzhieva, N.A.Aleksandrova, A.N.Vereshchagin, and O.A.Raevskii, Izv.Akad.Nauk SSSR, Ser. Khim., 1977, 2355.
52. O.A.Raevsky, A.N.Vereshchagin, N.G.Mumzhieva, T.A.Ziablikova, and N.A.Alexandrova, J.Molec. Structure, 1977, **36**, 399.
53. O.A.Raevskii, N.G.Mumzhieva, T.A.Zyablikova, and N.A.Aleksandrova, Izv.Akad.Nauk SSSR, Ser. Khim., 1978, 838.
54. C.Altona, H.R.Buys, H.J.Hageman, and E.Havinga, Tetrahedron, 1967, **23**, 2265.
55. A.N.Vereshchagin, O.N.Nuretdinova, L.Z.Nikonova, and B.A.Arbuzov, Izv.Akad.Nauk SSSR, Ser.Khim., 1978, 758.
56. O.A.Raevskii and A.N.Vereshchagin, Voprosy Stereokhimii, 1972, **2**, 38.
57. O.A.Raevskii, Doctoral Thesis in Chemical Sciences, Rostov State University, Rostov-on-Don, 1977.
58. O.A.Raevskii, N.G.Mumzhieva, T.E.Kron, and E.N.Tsvetkov, Izv.Akad.Nauk SSSR, Ser.Khim., 1981, 1292.
59. O.A.Raevskii and N.G.Mumzhieva, Izv.Akad.Nauk SSSR, Ser.Khim., 1981, 1822.
60. E.A.Ishmaeva, A.N.Pudovik, and A.N.Vereshchagin, Izv.Akad.Nauk SSSR, Ser.Khim., 1970, 2790.
61. O.A.Raevskii, Yu.A.Donskaya, F.G.Khalitov, and L.A.Antokhina, Izv.Akad.Nauk SSSR, Ser.Khim., 1973, 1339.
62. B.A.Arbuzov, R.P.Arshinova, O.A.Raevskii, and A.N.Vereshchagin, Izv.Akad.Nauk SSSR, Ser.Khim., 1974, 5.
63. O.A.Raevskii, Voprosy Stereokhimii, 1976, **5**(1), 69.
64. A.B.Remizov, R.D.Gareev, and A.N.Pudovik, Zhur.Obshch.Khim., 1974, **44**, 1863.
65. E.A.Ishmaeva, M.G.Zimin, R.M.Galeeva, and A.N.Pudovik, Izv.Akad.Nauk SSSR, Ser.Khim., 1971, 538.
66. E.A.Ishmaeva, R.D.Gareev, G.E.Yastrebova, and A.N.Pudovik, Zhur.Obshch.Khim., 1972, **42**, 73.
67. V.A.Naumov and S.A.Shadullin, Zhur.Strukt.Khim., 1976, **17**, 304.
68. V.V.Zverev, Ya.Ya.Villem, L.V.Ermolaeva, and A.F.Lisina, Dokl.Akad.Nauk SSSR, 1979, **246**, 1368.
69. V.V.Zverev, Ya.Ya.Villem, R.G.Islamov, and Yu.P.Kitaev, Zhur.Obshch.Khim., 1979, **49**, 1737.
70. E.A.Berkova, V.I.Zakharov, B.I.Ionin, and A.A.Petrov, Zhur.Obshch.Khim., 1978, **48**, 66.
71. M.I.Batuev, L.I.Shmonina, A.D.Matveev, and M.F.Shostakovskii, Izv.Akad.Nauk SSSR, Ser.Khim., 1961, 513.
72. L.V.Vilkov, N.I.Sadova, and I.Yu.Zil'berg, Zhur. Strukt.Khim., 1967, **8**, 528.
73. V.Magnasco, Nuovo Cimento, 1962, **24**, 425.
74. A.B.Remizov and I.Ya.Kuramshi, Zhur.Prikl. Spektrosk., 1974, **20**, 324.
75. O.A.Raevskii, A.N.Vereshchagin, Yu.A.Donskaya, I.G.Malakhova, Yu.I.Sukhorukov, E.N.Tsvetkov, and M.I.Kabachnik, Izv.Akad.Nauk SSSR, Ser. Khim., 1976, 2243.
76. S.B.Bulgarevich, L.V.Goncharova, P.N.Kozachenko, A.A.Shvets, and O.A.Osipov, Zhur.Strukt.Khim., 1981, **22**, 157.
77. O.A.Raevskii, I.O.Umarova, and E.N.Tsvetkov, Teor.Eksper.Khim., 1983, **19**, 87.
78. D.A.Bochvar, N.P.Gambaryan, and L.M.Epshtein, Uspekhi.Khim., 1976, **45**, 1316 [Russ.Chem.Rev., 1976, **45**(7)].
79. R.G.Kostyanovskii, V.V.Yakshin, and S.L.Zimont, Izv.Akad.Nauk SSSR, Ser.Khim., 1967, 1398.
80. R.G.Kostyanovsky, V.V.Yakshin, and S.L.Zimont, Tetrahedron, 1968, **24**, 2295.
81. B.N.Laskorin, V.V.Yakshin, and L.I.Sokalskaya, Zhur.Obshch.Khim., 1972, **42**, 1261.
82. B.N.Laskorin, V.V.Yakshin, and L.I.Sokalskaya, Zhur.Obshch.Khim., 1974, **44**, 1716.
83. M.Van Meerssche and A.Leonard, Acta.Cryst., 1959, **12**, 1053.

84. J.R.Durig, J.S.Di Yorio, and D.W.Wertz, J. Molec.Spectr., 1968, **28**, 444.
85. Yu.Ya.Borovikov, E.V.Ryl'tsev, I.E.Boldeskul, N.G.Feshchenko, Yu.P.Makovskii, and Yu.P.Egorov, Zhur.Obshch.Khim., 1970, **40**, 1957.
86. E.V.Ryl'tsev, V.G.Koval', V.Ya.Semenii, and Yu.P.Egorov, Teor.Eksper.Khim., 1974, **10**, 637.
87. E.V.Ryl'tsev, V.G.Koval', V.Ya.Semenii, and Yu.P.Egorov, Teor.Eksper.Khim., 1974, **10**, 347.
88. G.Blasse, Rec.Trav.chim., 1965, **84**, 867.
89. E.A.Ishmaeva, A.N.Vereshchagin, N.G.Khusainova, Z.A.Bredikhina, and A.N.Pudovik, Izv.Akad.Nauk SSSR, Ser.Khim., 1978, 359.
90. O.A.Raevskii, A.N.Vereshchagin, F.G.Khalitov, and E.N.Tsvetkov, Izv.Akad.Nauk SSSR, Ser. Khim., 1973, 995.
91. O.A.Raevskii, A.N.Vereshchagin, Yu.A.Donskaya, F.G.Khalitov, and E.N.Tsvetkov, Izv.Akad.Nauk SSSR, Ser.Khim., 1974, 787.
92. O.A.Raevskii, A.N.Vereshchagin, S.G.Khalitov, and Yu.A.Donskaya, Izv.Akad.Nauk SSSR, Ser. Khim., 1972, 710.
93. Tung-Ts'ai Liang and Kuo-Chêng Ch'iao, Acta Chim. Sinica, 1965, **31**(2), 155; 1966, 423.
94. D.Fenske, R.Mattes, J.Lons, and K.-F.Tebbe, Chem.Berichte, 1973, **106**, 1139.
95. V.V.Tkachev, N.A.Bondarenko, E.I.Matrosov, E.N.Tsvetkov, L.O.Atovmyan, and M.I.Kabachnik, Izv.Akad.Nauk SSSR, Ser.Khim., 1979, 1159.
96. V.V.Tkachev, N.A.Bondarenko, E.I.Matrosov, E.N.Tsvetkov, L.O.Atovmyan, and M.I.Kabachnik, Izv.Akad.Nauk SSSR, Ser.Khim., 1981, 209.
97. V.V.Tkachev, N.A.Bondarenko, E.I.Matrosov, E.N.Tsvetkov, L.O.Atovmyan, and M.I.Kabachnik, Izv.Akad.Nauk SSSR, Ser.Khim., 1981, 211.
98. G.Bandoli, G.Bortolozzo, D.A.Glemente, U.Croatto, and C.Panattoni, J.Chem.Soc.(A), 1970, 2778.
99. A.I.Gusev, N.G.Bokii, N.N.Afonina, T.V.Timofeeva, A.E.Kalinin, and Yu.T.Struchkov, Zhur.Strukt. Khim., 1973, **14**, 116.
100. G.Ruban and V.Zabel, Cryst.Struct.Comm., 1976, **5**, 671.
101. W.Dreissing and K.Plieth, Acta Cryst., 1971, **B27**, 1146.
102. R.A.Shaw, M.Woods, T.S.Cameron, and B.Dahlen, Chem.Ind., 1971, 151.
103. T.S.Cameron, K.D.Howlett, R.A.Shaw, and M.Woods, Phosphorus, 1973, **3**, 71.
104. M.J.Aroney, R.J.W.Le Févre, and J.D.Saxby, J.Chem.Soc., 1964, 6180.
105. S.B.Bulgarevich, E.G.Amarskii, A.A.Shvets, and O.A.Osipov, Zhur.Obshch.Khim., 1976, **46**, 1708.
106. D.J.Nichols, J.Chem.Soc., 1969, A, 1471.
107. E.A.Ishmaeva, A.N.Vereshchagin, and S.M.Kharrasova, Zhur.Obshch.Khim., 1976, **46**, 281.
108. I.I.Patsanovskii, E.A.Ishmaeva, G.V.Romanov, V.N.Volkova, E.N.Strelkova, and A.N.Pudovik, Dokl.Akad.Nauk SSSR, 1980, **255**, 383.
109. E.G.Yarkova, Sh.M.Nazipov, O.B.Sobanova, A.A.Muratova, and A.N.Pudovik, Zhur.Obshch. Khim., 1978, **48**, 748.
110. S.Higuchi, H.Tsuyama, S.Tanaka, and T.Kamada, Spectrochim.Acta, 1974, **30A**, 463.
111. V.G.Dashevskii, A.P.Baranov, T.Ya.Medved', and M.I.Kabachnik, Teor.Eksper.Khim., 1979, **15**, 255.
112. D.G.Rowsell, J.Mol.Spectr., 1967, **23**, 32.
113. B.Ackerman, T.A.Jordan, C.R.Eddy, and D.Swern, J.Amer.Chem.Soc., 1956, **78**, 4444.
114. H.Bandler, Z.Elektrochem., 1955, **59**, 173.
115. B.A.Arbuzov, V.S.Vinogradova, N.A.Polezhaeva, and A.K.Shamsutdinova, Izv.Akad.Nauk SSSR, Ser.Khim., 1963, 675.
116. K.D.Berlin, D.M.Hellwege, and M.Nagabhushanam, J.Org.Chem., 1965, 1265.
117. A.I.Razumov and M.V.Gazizov, Zhur.Obshch.Khim., 1967, **37**, 2738.
118. A.B.Remizov, R.D.Gareev, and A.N.Pudovik, Zhur.Obshch.Khim., 1972, **42**, 1238.
119. E.A.Ishmaeva, A.N.Vereshchagin, N.A.Bondarenko, G.E.Yastrebova, and A.N.Pudovik, Izv.Akad.Nauk SSSR, Ser.Khim., 1970, 2695.
120. E.A.Ishmaeva, Uspekhi Khim., 1978, **47**, 1678 [Russ.Chem.Rev., 1978, **47**(9)].
121. O.A.Raevskii, N.G.Mumzhieva, M.M.Gilyazov, and A.A.Karelov, Izv.Akad.Nauk SSSR, Ser.Khim., 1979, 2251.

Institute of Physiologically Active Substances
USSR Academy of Sciences, Chernogolovka