94. T.C.Wu, Iowa State Coll.J.Sci., 27, 282 (1953).
95. C.A.Kraus and H.Eatough, J.Amer.Chem.Soc., 55, 5008 (1933).

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STEREOCHEMISTRY OF ORGANIC COMPOUNDS OF PHOSPHORUS AND ARSENIC

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I. INTRODUCTION

Acquaintance with the world's chemical literature must lead to the conclusion that interest has grown appreciably during recent years in problems of the stereochemistry not only of carbon compounds but also of those of other elements — nitrogen, phosphorus, sulphur, arsenic, antimony, etc. — in the Periodic System. The reason for the increasing number of stereochemical investigations is undoubtedly that this field, which until not long ago was regarded as one of the most abstract, is beginning to acquire ever increasing practical importance. Stereochemical features of structure have a great influence on the biochemical properties of organic compounds. Knowledge of the configurational relationships among various types of optically active compounds is of practical and theoretical importance. It is required in many fields of biochemistry for the study of metabolism and the action of drugs, in working out theoretical problems of biogenesis, etc. The use of optically active reactants often considerably facilitates study of the mechanism of chemical reactions. A systematic study of the stereochemistry of reactions will inevitably lead in the future to a more profound understanding of the chemical changes occurring in living Nature.

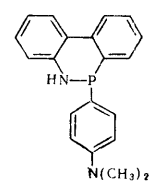
Interest has grown considerably during recent years in the stereochemistry of organic compounds of phosphorus and arsenic, especially the former. The first attempts to obtain optically active compounds containing asymmetric phosphorus and arsenic atoms were made at the beginning of the present century. In 1911 Meisenheimer[1,2] showed for the first time, with ethylmethylphenylphosphine oxide as example, that phosphorus can act as an asymmetric centre in a molecule. The first optically active organic compound of arsenic — the dextrorotatory benzylmethyl-1-naphthylphenylarsonium iodide — was obtained in 1921 by Burrows and Turner[3].

A. Michaelis, J. Meisenheimer, A. E. Arbuzov, B. A. Arbuzov, G. Kh. Kamai, D. M. Coyne, H. S. Aaron, L. Horner, J. Michalski, and many others have devoted their researches to the difficult but interesting field of the stereochemistry of organophosphorus and organoarsenic compounds, and definite progress has now been achieved.

II. STEREOCHEMISTRY OF ORGANIC COMPOUNDS OF TERVALENT PHOSPHORUS AND ARSENIC

The phosphorus atom has the electronic configuration $(1s^2)(2s^2)(2p^6)(3s^2)(3p^3)$, so that it can have covalencies of 3–6 in its compounds. Organic derivatives of tervalent phosphorus can be regarded as derivatives of phosphine PH_3 in which one, two, or three hydrogen atoms have been replaced by organic radicals. Phosphines have the configuration of a trigonal pyramid. This is evident from the fact that in the tervalent state phosphorus utilises only $3p$-electrons, as is confirmed by the valency angle of 94° in phosphine and 101 ± 3° in trimethylphosphine. Thus a tertiary phosphine $PR^1R^2R^3$ should exist in the form of two optical isomers, related to one another as an object to its mirror image. Until recently derivatives of tervalent phosphorus remained almost uninvestigated from the point of view of optical isomerism. The calculated frequency of oscillation of the phosphorus atom[4] is 5×10^6 s^{-1}. Calculations by Weston[5] showed on the basis of the oscillation frequency that the half-life (or rate of racemisation) for trimethylphosphine is 2 h at 7°. It appeared that optical isomers of asymmetric tertiary phosphines would be stable only at low temperatures. Until recently investigators adhered to this view, and in fact no-one attempted to resolve tertiary phosphines of the type $PR^1R^2R^3$ into optical isomers.

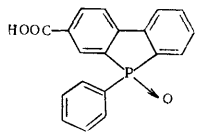
It was suggested that the stability of optical isomers of tervalent phosphorus compounds should be increased if the phosphorus atom formed part of a ring system, since oscillation of the phosphorus atom would then be impeded. Campbell and Way[6] have resolved the cyclic phosphine 10-*p*-dimethylaminophenyl-9,10-dihydro-9-aza-10-phosphaphenanthrene



into optical isomers by reducing the optically active isomeric oxides of this phosphine with lithium tetrahydroaluminate. The isolated isomers of the phosphine proved to have far greater optical stability than could have been expected from Weston's calculations[5]. The dextrorotatory isomer, which has an initial rotation of $[\alpha]_D^{21} = 141°$, acquires a rotation of 114° after 5 h; the corresponding specific rotation of the laevorotatory isomer changed from -128° to -97° in 4 h. It was discovered that the decrease in the angle of rotation was due not to racemisation

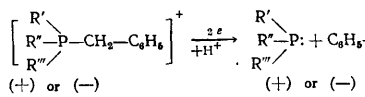
but to oxidation of the phosphine to the phosphine oxide. Molecular asymmetry is entirely probable in the phosphine owing to the presence of a ring containing nitrogen and phosphorus. In the opinion of Campbell and Way, the above azaphosphaphenanthrene proved an unfortunate example for elucidating the possibility of obtaining asymmetric compounds of tervalent phosphorus in an optically active form because of (1) the presence of a ring containing nitrogen and phosphorus, which may itself be a source of molecular asymmetry, and (2) the comparatively ready oxidisability of the phosphine to the phosphine oxide.

In order to avoid these drawbacks, Campbell and Way[7] synthesised a series of substituted phosphafluorenes and their oxides. They were able to resolve 9-phenyl-9-phosphafluorene-2-carboxylic acid



into optical isomers. However, reduction was accompanied by complete racemisation with both optically active oxides: the resulting phosphines were optically inactive. Racemisation of the phosphafluorene was not unexpected, in view of Weston's calculations[5], but it was inconsistent with the result obtained by Campbell and Way for reduction of the azaphosphaphenanthrene oxide[6]. These workers postulate that the participation of the nitrogen atom in the reduction confers on it a stereospecific character in the case of the azaphosphaphenanthrene. Thus Campbell and Way's investigations gave no positive answer to the possible existence of tervalent phosphorus compounds in an optically active form, since molecular asymmetry is possible, besides the asymmetric phosphorus atom, in azaphosphaphenanthrene derivatives, while phosphafluorene derivatives were not obtained in an optically active form.

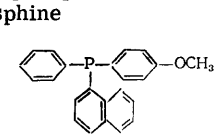
It was only in 1961 that Horner and his coworkers[8] showed for the first time that asymmetric tertiary phosphines can be resolved into optical antipodes. They reduced the corresponding optically active benzylphosphonium salts at a mercury cathode:



(+) or (−) (+) or (−)

and obtained[8] dextrorotatory methylphenyl-n-propylphosphine $(CH_3)(C_6H_5)(n\text{-}C_3H_7)$ having $[\alpha]_D = +16.8°$ (concentration 5.170 g/100 cm³ toluene), laevorotatory allylmethylphenylphosphine $(CH_2:CH.CH_2)(CH_3)(C_6H_5)P$ having -10.0° (4.5 in toluene), and dextrorotatory ethylmethylphenylphosphine $(C_2H_5)(CH_3)(C_6H_5)P$ having +15 ± 0.5° (6 ± 2 in toluene).

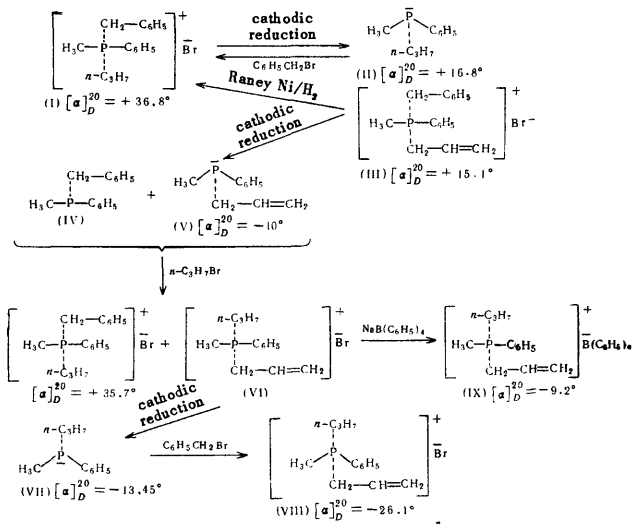
Using the same method, Horner et al.[9] were the first to obtain in an optically active form the asymmetric non-heterocyclic triarylphosphine — *p*-methoxyphenyl-1-naphthylphenylphosphine



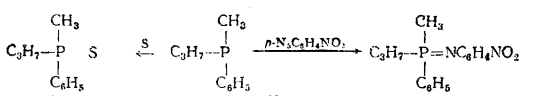
McEwen et al.[10] isolated dextrorotatory and laevorotatory isomers of benzyl-n-butylmethylphosphine having specific rotations $[\alpha]_D^{27}$ of +24 ± 2° and -28.2° (2.9 in benzene), by reducing with sodium methoxide[11] the optically active D(-)- and L(+)-benzyl-n-butyl-2-cyanoethylmethylphosphonium hydrogen dibenzoyltartrates.

Optically active tertiary phosphines proved to be optically far more stable than would have been expected from Weston's calculations[5]. Dextrorotatory methylphenyl-n-propylphosphine was very slowly racemised in boiling toluene[8]. Horner and Winkler[12] found that this compound was racemised according to a first-order equation in high-boiling solvents such as methylnaphthalene, decahydronaphthalene, and n-decane, whereas in diethylaniline and cyclohexanone the kinetics of racemisation was more complicated[12].

SCHEME 1



The separation of racemic asymmetric tertiary phosphines into optical isomers was a remarkable development in the chemistry of phosphorus. The application of optically active tertiary phosphines made possible a very delicate study of the mechanism of the reactions. Horner and his coworkers[8,13], who investigated the interconversion of optically active tertiary phosphines and optically active phosphonium salts (Scheme 1), ascertained that the configuration of the asymmetric phosphorus atom is preserved during these changes. The use of optically active tertiary phosphines facilitated the elucidation of the structure of phosphine dihalides[14-16]. Dextrorotatory and laevoroatory benzyl-n-butylmethylphosphines were converted into the optically active benzyl-n-butylmethylphosphine sulphides by the action of cyclohexene sulphide, monatomic sulphur, and octa-atomic sulphur. The configuration of the asymmetric phosphorus atom was preserved in all these reactions[17]. The reactions of dextrorotatory methylphenyl-n-propylphosphine with sulphur and with *p*-nitrophenyl azide also take place with preservation of the configuration of the asymmetric phosphorus atom[18]:



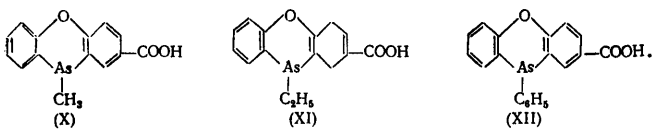
$[\alpha]_{546} = 21.5°$ (methanol) $[\alpha]_D = 18.4°$ (toluene) $[\alpha]_{546} = 18.92°$ (benzene).

Study of the oxidation of optically active methylphenyl-n-propylphosphine with t-alkyl hydroperoxides[19] confirmed the view expressed previously that the reactions of tertiary

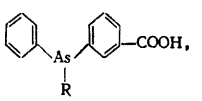
phosphines and phosphites with these hydroperoxides involve nucelophilic attack by hydroxyl oxygen.

The arsenic atom has the electronic configuration $(1s^2)(2s^2)(2p^6)(3s^2)(3p^6)(3d^{10})(4s^2)(4p^3)$, and, like the phosphorus atom, it may have covalencies of 3–6. Organic derivatives of tervalent arsenic are regarded as derivatives of arsine in which one, two, or three hydrogen atoms have been replaced by organic radicals. Arsines have the configuration of a trigonal pyramid, as is indicated by measurements of dipole moments and by the valency angles determined by different physicochemical methods[20-22]. The oscillation frequency of the arsenic atom in arsine is $16 \times \times 10^4$ s^{-1} [23] (in phosphine it is 5×10^6 s^{-1},[4] and in an amine 2.3×10^{10} s^{-1} [24]). Weston calculated[5] the energy barrier to racemisation of an arsine, the results being expressed as the temperature at which the half-life (or rate of racemisation) would be 2 h. For trimethylarsine this temperature is 107° according to his calculations[5]. Until 1962 no single case had been described of the resolution of an asymmetric tertiary arsine: As$\begin{smallmatrix}/\mathrm{R}'\\ -\mathrm{R}''\\ \backslash\mathrm{R}'''\end{smallmatrix}$ into optical isomers.

Tervalent compounds in which arsenic forms part of a cyclic system have been successfully resolved into optical isomers.

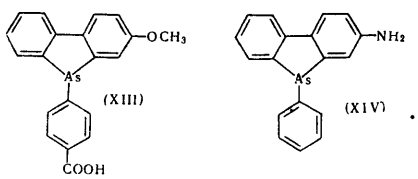


Lesslie and Turner[25] resolved 10-methylphenoxarsine-2-carboxylic acid (X), as well as the 10-ethyl (XI) and 10-phenyl (XII) homologues of this acid. These acids proved to be optically stable, racemising quite slowly even on being heated. Their optical activity is probably due mainly to molecular asymmetry, since the similar acids of tervalent arsenic synthesised by Kamai[26-30], differing from those of Lesslie and Turner in the absence of the oxygen atom linking the two phenyl radicals, and of general formula



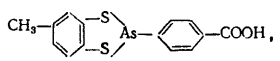
could not be resolved into optical antipodes.

Campbell and Poller[31] resolved the two cyclic compounds of tervalent arsenic — 2-methoxy-9-phenyl-9-arsafluorene-*p*-carboxylic acid (XIII) and 2-amino-9-phenyl-9-arsafluorene (XIV)



The isomers thus obtained were optically stable at room temperature.

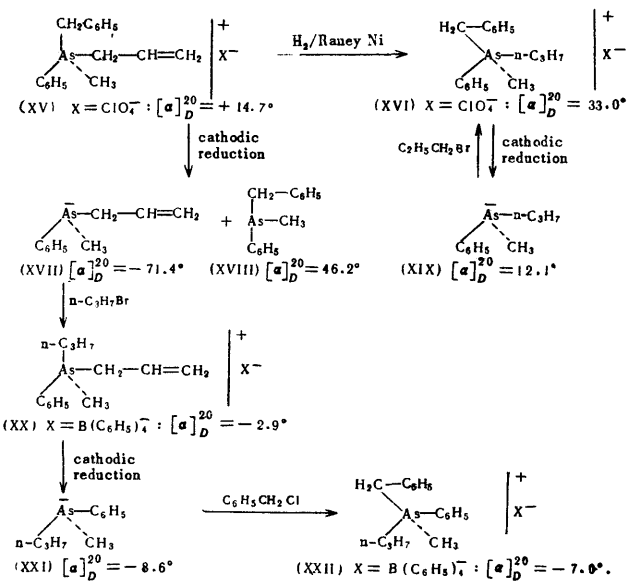
The compound 2-*p*-carboxyphenyl-5-methyl-1,3-dithia-2-arsindane



which was resolved by Campbell[32], was optically stable in chloroform and ethanol, but racemised in aqueous alkali, probably owing to cleavage of an arsenic–sulphur bond. The existence of arsindane enantiomers provides further evidence that arsenic is able to maintain a stable pyramidal configuration when present as a tervalent atom in a heterocyclic compound.

Horner and Fuchs[33] isolated optical isomers of ethylmethylphenylarsine and butylmethylphenylarsine by cathodic reduction of the optically active benzylethylmethylphenylarsonium and benzylbutylmethylphenylarsonium perchlorates by the technique used to reduce quaternary ammonium[34] and phosphonium[35] salts. Dextrorotatory ethylmethylphenylarsine $(C_2H_5)(CH_3)(C_6H_5)As$ boiled at 64–65° (3.3 mm) and had a specific rotation $[\alpha]_D^{20}$ of 1.9°, while the laevorotatory isomer of this arsine boiled at 69–71° (4 mm) and had a specific rotation of -1.15°. The corresponding optically active arsine sulphides were isolated by the addition of sulphur to the optically active arsines.

SCHEME 2



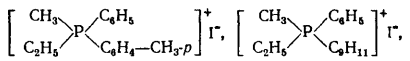
Horner and Fuchs[36] studied the interconversion of optically active tertiary arsines and quaternary arsonium salts (Scheme 2). The interconversions (XVI) → (XVII) and (XVII) → (XVI) indicate that the configuration of the arsenic atom is maintained during these changes. Compounds (XVIII) and (XIX) were separated by distillation. The difference in rotation between (XXI) and (XVII) (with the opposite sign of rotation) is explained by partial racemisation of (XX), since optically active quaternary arsonium halides (in contrast to the sulphates and perchlorates) are more or less rapidly racemised in organic solvents. The arsonium salts (XV) and (XVI) have the same configuration, since the asymmetric centre is unaffected by catalytic hydrogenation.

The preparation of stable optically active non-heterocyclic tertiary phosphines and arsines has been an important event in the stereochemistry of organophosphorus and organoarsenic compounds: it has opened up a path for the stereochemical study of reaction mechanisms involving asymmetric phosphorus and arsenic atoms, and it has

shown once again that certain concepts which have been regarded as "absolute" at some stage in the development of science prove to be "extremely relative" and yield place to new concepts, which are sometimes the direct opposite. This has occurred in connection with the oscillation of tervalent phosphorus and arsenic atoms in phosphines and arsines. Until recently the vast majority of investigators regarded the presence of this oscillation as indisputable. The researches of Horner and his collaborators [8-10,12,13,17,18,33,36] have now convincingly demonstrated that tervalent phosphorus and arsenic atoms do not undergo such oscillation.

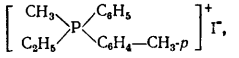
III. STEREOCHEMISTRY OF QUATERNARY PHOSPHONIUM AND ARSONIUM COMPOUNDS

The first attempts to resolve unsymmetrical phosphonium and arsonium compounds into optical antipodes were made at the beginning of the present century. Michaelis [37,38] synthesised and tried to resolve ethylmethylphenyl-*p*-tolylphosphonium iodide (I), ethylmethylphenyl-2,4,5-trimethylphenylphosphonium iodide (II)



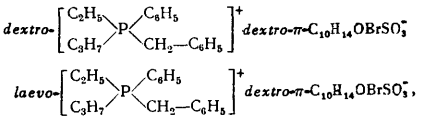
(I) (II)

and ethylmethylphenyl-*p*-tolylarsonium iodide (III)



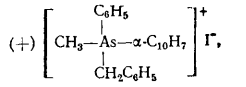
(III)

but no positive results were obtained. Wedekind [39] tried unsuccessfully to resolve ethylmethylphenyl-*p*-tolylphosphonium and benzylmethylphenyl-*p*-tolylphosphonium iodides. Winmill [40] was likewise unsuccessful in resolving a series of unsymmetrical arsonium salts into optical isomers. Nor did the endeavours of Radcliffe and Brindley [41], Meisenheimer [2], or Kamai [42] lead to a positive result. Meisenheimer considered that all the failures in resolving asymmetric phosphonium salts of the type [abcdP]Hal into optical antipodes were due merely to experimental difficulties, since the salts [Pabc(OH)]X (oxides with *dextro*-π-bromocamphorsulphonic acid) were obtained in an optically active form [1,2]. Kamai and Khismatullina [43] were able to isolate the crystalline *dextro*-π-bromocamphorsulphonate salt from allylbenzylbutylphenylphosphonium bromide. Two diastereoisomeric *dextro*-π-bromocamphorsulphonates

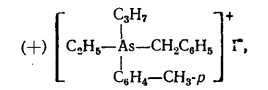


were obtained from allylbenzylethylphenylphosphonium bromide, but the individual isomers could not be isolated when these diastereoisomers were decomposed, this being explained by the great experimental difficulties. Kumli et al.[44] successfully resolved a non-heterocyclic phosphonium salt — benzylethylmethylphenylphosphonium iodide — into optical antipodes, as will be discussed in greater detail later.

Experiments on the resolution of asymmetric arsonium salts have proved more successful. Burrows and Turner [3] isolated the dextrorotatory isomer of benzylmethyl-1-naphthylphenylarsonium iodide



having a maximum rotation of $[\alpha]_D = 0.1°$ and $[M]_D = 12°$ in alcoholic acetone; the rotation of the solution fell rapidly even at room temperature. Kamai [45] isolated the dextrorotatory isomer of benzylethylpropyl-*p*-tolylarsonium iodide



with a rotation of $[\alpha]_D = 9.86°$ and $[M]_D = 45°$. The salt lost its optical activity very rapidly. Kamai and Gatilov [46] resolved benzylethylpentylphenylarsonium bromide, but the optical isomers rapidly racemised when isolated. These workers [47] separated dextrorotatory and laevorotatory isomers of benzylethylpentylphenylarsonium iodide by adsorption on dextrorotatory and laevorotatory quartz, but the isomers rapidly lost their optical activity. Thus the optical isomers of arsonium halides are optically unstable and racemise rapidly, whereas, as recent investigations by Horner [36] have shown, arsonium perchlorates are optically stable.

Quaternary ammonium halides often racemise comparatively rapidly in such solvents as chloroform, whereas the sulphates and nitrates possess greater stability. Pope and Harvey [48] suggested that this racemisation is due to equilibrium dissociation of quaternary ammonium halides into a tertiary amine and an alkyl or aryl halide:

$$[abcdN]\,Hal \rightleftarrows abcN + dHal,$$

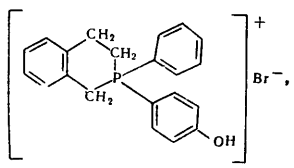
which in their view explained the optical stability of the nitrates and sulphates, these being incapable of undergoing such ready dissociation as the quaternary ammonium halides. Burrows and Turner [3] assumed that the instability of optically active non-heterocyclic arsonium salts was due to the occurrence of similar equilibrium dissociation in solution, and obtained some evidence for this assumption. They showed [3] that, if dimethylphenylarsine is treated with ethyl iodide, ethyldimethylphenylarsonium iodide is formed mixed with a considerable quantity of phenyltrimethylarsonium iodide:

$$(CH_3)_2(C_6H_5)As + C_2H_5I \rightleftarrows [(CH_3)_2(C_2H_5)(C_6H_5)As]\,I \rightleftarrows CH_3I + (CH_3)(C_2H_5)(C_6H_5)As,$$
$$(CH_3)_2(C_6H_5)As + CH_3I \rightleftarrows [(CH_3)_3(C_6H_5)As]\,I.$$

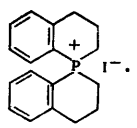
These results are readily explained by the equilibrium dissociation theory.

Mann [49] tried to explain by the presence of equilibrium dissociation the numerous unsuccessful attempts to resolve asymmetric phosphonium salts of the type [abcdP]Hal into optical antipodes, although Wedekind [39] had shown long before that ethylmethylphenyl-*p*-tolylphosphonium iodide does not dissociate into an alkyl or aryl halide and a tertiary phosphine in chloroform solution at room temperature or at the boiling point of chloroform. Holliman and Mann [49] attempted to resolve into optical antipodes two phosphonium salts — 1,2,3,4-tetrahydro-2-*p*-hydroxyphenyl-2-phenyl-phosphinolinium and -isophosphinolinium

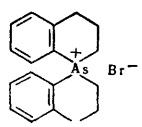
bromides — which were structurally incapable of dissociating into a tertiary phosphine and an alkyl halide. All attempts at the resolution of the former compound were unsuccessful, but a dextrorotatory form of the isophosphinolinium bromide



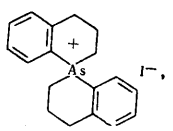
was isolated having a molecular rotation of $[M]_D = 32.9°$, although attempts to repeat its separation were unsuccessful. Hart and Mann[50] synthesised and successfully resolved into optical isomers a spirocyclic phosphonium salt possessing molecular asymmetry — *P*-spirobi-1,2,3,4-tetrahydrophosphinolinium iodide



The resolution of this salt was proof of the tetrahedral configuration of the phosphonium cation. Holliman and Mann's work[51,52] on the resolution of two spirocyclic arsonium salts — *As*-spirobi-1,2,3,4-tetrahydroarsinolinium bromide

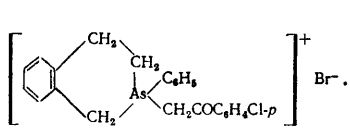


and the isomeric iodide



— confirmed the tetrahedral configuration of the tetrasubstituted arsonium cation. The isomers of the spirocyclic arsonium salts were optically stable.

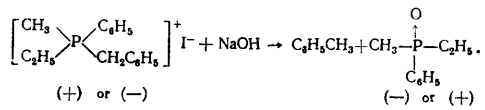
Holliman and Mann[53] resolved 1,2,3,4-tetrahydro-2-*p*-chlorophenacyl-2-phenylisoarsinolinium bromide



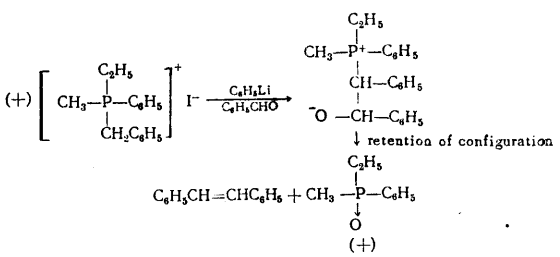
The isomers possessed relatively high optical stability, the rotation changing, in chloroform solution at room temperature, over the course of 5 days. The optical stability is assumed to be a consequence of the great chemical stability of this compound.

As already noted above, the first successful resolution of a non-heterocyclic asymmetric phosphonium salt — benzylethylmethylphenylphosphonium iodide — was accomplished by Kumli et al.[44] by means of the silver hydrogen salts of dextrorotatory and laevorotatory dibenzoyltartaric acid. The benzylethylmethylphenylphosphonium iodide isomers thus obtained were optically stable. The dextrorotatory benzylethylmethyl-*p*-tolyphosphonium chloride, bromide, and iodide prepared by Kamai and Usacheva[54] also exhibited high optical stability, which supports Wedekind's conclusion that equilibrium dissociation into a tertiary phosphine and an alkyl or aryl halide is absent in non-heterocyclic quaternary phosphonium salts containing at least one alkyl group attached to the phosphorus atom.

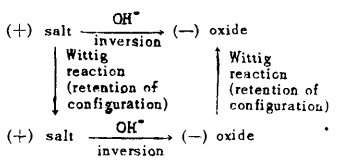
Kumli and his coworkers studied the conversion of dextrorotatory and laevorotatory benzylethylmethylphenylphosphonium iodide into the corresponding optically active ethylmethylphenylphosphine oxides:



This is a third-order reaction — of first order with respect to the concentration of phosphonium salt and of second order with respect to the concentration of sodium hydroxide[55] — involving inversion of the configuration of the asymmetric phosphorus atom[56]. The dextrorotatory benzylethylmethylphenylphosphonium iodide gave with inversion 100% of the laevorotatory ethylmethylphenylphosphine oxide, and the laevorotatory isomer of the phosphonium salt yielded dextrorotatory ethylmethylphenylphosphine oxide. In the Witting reaction with the optical isomers of benzylethylmethylphenylphosphonium iodide, the configuration of the phosphorus atom was maintained[56,57]:



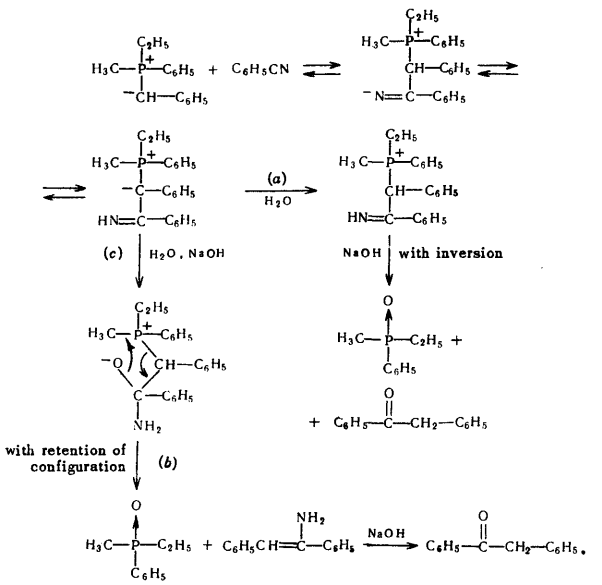
The two conversions of the optically active phosphonium isomers can be represented in the form of a cycle of processes:



Bladé-Font et al. studied the stereochemical course of the reaction of optically active ethylmethylphenylbenzylidenephosphorane[58], prepared by the interaction of laevorotatory

benzylethylmethylphenylphosphonium iodide with phenyl-lithium[44,56], with benzonitrile (see Scheme 3).

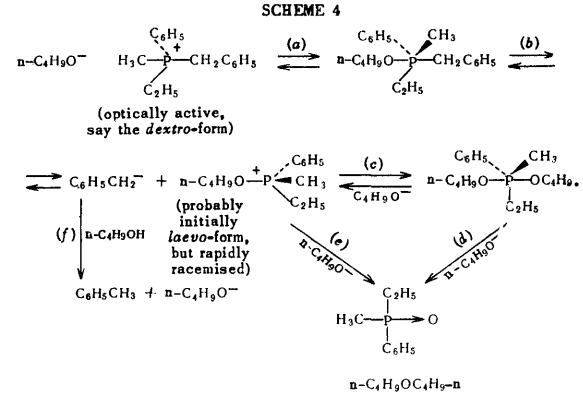
SCHEME 3



It was calculated that the reaction was accompanied by 68% inversion of configuration at the asymmetric phosphorus atom. They supposed that two competing reactions were taking place, one of which (*a*) gave ethylmethylphenylphosphine oxide with inversion of configuration, while the other reaction (*b*) gave the same oxide with maintenance of the configuration. Quite recently the reaction of optically active ethylmethylphenylbenzylidenephosphorane with styrene oxide has been studied[59], and shown to give ethylmethylphenylphosphine oxide with 50% inversion of configuration at the asymmetric phosphorus atom.

Grayson and Keough[60] showed that phosphonium alkoxides of the type $[R_3PCH_2C_6H_5]^+OR^-$ yield on decomposition toluene, a phosphine oxide, and an ether. Parisek et al.[61] investigated the stereochemistry of this reaction with optical isomers of benzylethylmethylphenylphosphonium n-butoxide, obtained from sodium n-butoxide and the optical isomers of the phosphonium iodide. Decomposition of the optically active phosphonium n-butoxide yielded ethylmethylphenylphosphine oxide with almost complete racemisation. This result can be explained by a reaction mechanism in which stage (*d*) or (*e*) is the slowest, whereas stage (*f*) is comparatively rapid (Scheme 4).

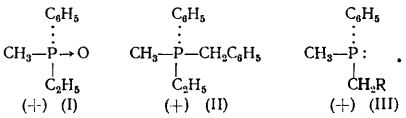
SCHEME 4



IV. STEREOCHEMISTRY OF OXIDES AND SULPHIDES OF PHOSPHORUS AND ARSENIC

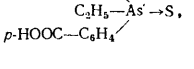
Meisenheimer and Lichtenstadt[1] were the first to show that phosphorus can give optically active compounds. Successful experimental resolutions of the oxides of tertiary amines into optical enantiomers[62,63] led Meisenheimer to study asymmetric phosphine oxides. By means of *dextro*-π-bromocamphorsulphonic acid he was able to isolate a dextrorotatory isomer of ethylmethylphenylphosphine oxide having a molecular rotation of $[M]_D = 50°$ and high optical stability. It is interesting that the value calculated by Sokolov and Reutov[64] for the molecular rotation of this phosphine oxide, using Brewster's rule of conformational asymmetry[65], is close to the value found experimentally[2] and by Meisenheimer[1,2]: a calculated value[64] of 40° compares with experimental values[2] of 47° in benzene and 40° in water or hydrochloric acid.

The laevorotatory isomer of ethylmethylphenylphosphine oxide was obtained by Meisenheimer only 14 years later[2]. The isolation of optically active isomers of this oxide, and later of benzylmethylphenylphosphine oxide[2], permitted Meisenheimer to conclude that phosphorus, like nitrogen, is able to give optically active compounds, for which it is sufficient to replace the five valencies of phosphorus by four different radicals. At the present time new paths for the synthesis of optically active oxides of tertiary phosphines have been opened as a result of the excellent work done by Horner et al.[8] and by Kumli and his coworkers[44,55,56] — (1) by the oxidation of optically active tertiary phosphines[8] and (2) by the action of sodium hydroxide on optically active phosphonium salts or by the Wittig reaction on the latter[55,56].



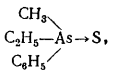
Sokolov and Reutov[64] assign the absolute configuration (I) to the dextrorotatory ethylmethylphenylphosphine oxide, on the basis of theoretical calculations of the molecular rotation of this isomer from Brewster's molecular asymmetry rule[65] and the indication by Limburg[66] that this rule correctly predicts the sign of rotation of compounds containing an asymmetric silicon atom. Since the configurational relationship among (I)–(III) has been established[67], (II) represents the absolute configuration of the optically active tetrasubstituted phosphonium cation, while (III) is the absolute configuration of the optically active tertiary phosphine.

Oxides of tertiary arsines have not yet been prepared in optically active form. The reason for this is still not understood. Sulphides of arsenic, on the other hand, have been successfully resolved into optical isomers. Mills and Raper[68] prepared optical isomers of *p*-carboxyphenylethylmethylarsine sulphide



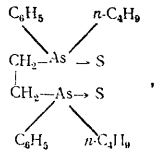
having rotations $[M]_{5780}$ of 51° and -52°. Both isomers possessed considerable optical stability: an aqueous solution of the sodium salt remained optically unchanged on

prolonged boiling. Horner and Fuchs[33] obtained dextrorotatory ethylmethylphenylarsine sulphide



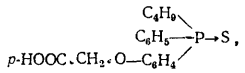
with a rotation of $[\alpha]_D^{20} = 24.5°$, by the addition of sulphur to the dextrorotatory arsine.

Chatt and Mann[69] isolated two forms of ethylene-1,2--bis-(n-butylphenylarsine sulphide)



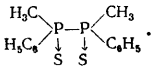
but were unable to determine which was racemic and which was the *meso*-form.

Davies and Mann[70] were the first to resolve butyl-*p*--carboxymethoxyphenylphenylphosphine sulphide

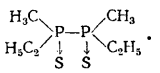


the resulting isomers having rotations $[M]_D$ of 9.6° and -9.7° with relatively high optical stability. The work of Horner[8] has opened up a new path for the synthesis of optically active phosphine sulphides, by the addition of sulphur to optically active tertiary phosphines.

Wheatley[71] isolated two forms (*meso* and racemic) of 1,2-dimethyl-1,2-diphenyldiphosphine disulphide

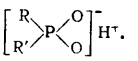


He established by means of X-rays that the modification having the higher melting point was centrosymmetric and represented the *meso*-form, while the other modification was the racemic form. Maier[72] tried to resolve the racemate by chromatographic adsorption on D(-)-mannitol, D(-)-lactose, and calcium D(-)-tartrate, but was unsuccessful. He isolated[72] two forms (racemic and *meso*) of 1,2-diethyl-1,2-dimethyldiphosphine disulphide

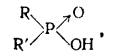


V. STEREOCHEMISTRY OF ORGANIC ACIDS OF PHOSPHORUS AND ARSENIC AND OF THEIR DERIVATIVES

Interest in the organic acids of four-coordinate phosphorus from the point of view of stereochemical research arose as long ago as the beginning of the twentieth century. Kipping and Luff[73,74] were the first to try to resolve the phenyl *p*-tolyl and phenyl 2-naphthyl esters of phosphoric acid, but without success. Nor was a positive result obtained from Pope and Gibson's experiments[75] on the separation of methylphenylphosphinic acid into optical isomers or from those of Turner[76] on the resolution of benzylphenylarsinic acid. The former workers[75] tried to explain their failure by the ease of transformation of the phosphinic acid into the ortho-form $(CH_3)(C_6H_5)P(OH)_3$, which entails loss of asymmetry at the phosphorus atom. The optical inactivity of compounds containing hydroxyl and double-bonded oxygen attached to the phosphorus atom can be explained on the basis of Werner's theory, as Meisenheimer[77] did mainly for ammonium, phosphonium, and similar compounds. The structure of phosphorus compounds of the type RR'P(O)OH can be represented

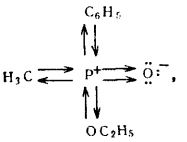


In this case the inner complex is not asymmetric. The replaceable hydrogen in the outer sphere does not affect the asymmetry of the molecule. It was deduced on the basis of these arguments that compounds of the type



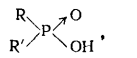
cannot be obtained in an optically active form.

Gibson and Johnson[78], starting from the electronic theory, reached the opposite conclusion. In their opinion the structure of ethyl methylphenylphosphinate can be written



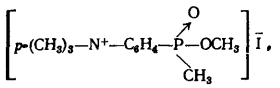
in which it can be seen that the outer octet of the phosphorus atom is complete without the oxygen atom. The octet of the oxygen atom can be complete only if the lone pair of electrons of the phosphorus atom are distributed between the two atoms, as is represented by the two arrows pointing in the same direction. The phosphorus atom thus becomes positive, while the oxygen becomes negative. The phosphorus–oxygen bond most probably becomes semipolar, as is confirmed by the change in parachor[79].

It would appear that compounds of the type

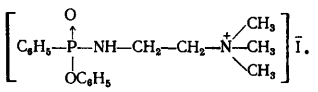


should exist in an optically active form. However, experiments by A. E. and B. A. Arbuzov[80] on the resolution of asymmetric phosphonecarboxylic acids, as well as those of A. E. Arbuzov and I. A. Arbuzova[81] on the resolution of isobutylphenylphosphinic and phenyltriphenylmethylphosphinic acids, did not yield a positive result. It was only in 1956 that Coyne[82], Marsi[83], and their collaborators obtained optically active forms of asymmetric derivatives

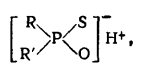
of phosphinic acids, as the quaternary ammonium salts — *p*-methoxy(methyl)phosphinylphenyltrimethylammonium iodide



and trimethyl-2-phenoxy(phenyl)phosphinylaminoethylammonium iodide

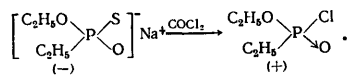


The first attempts to resolve asymmetric phosphinothioic acids, whose structure remains asymmetric



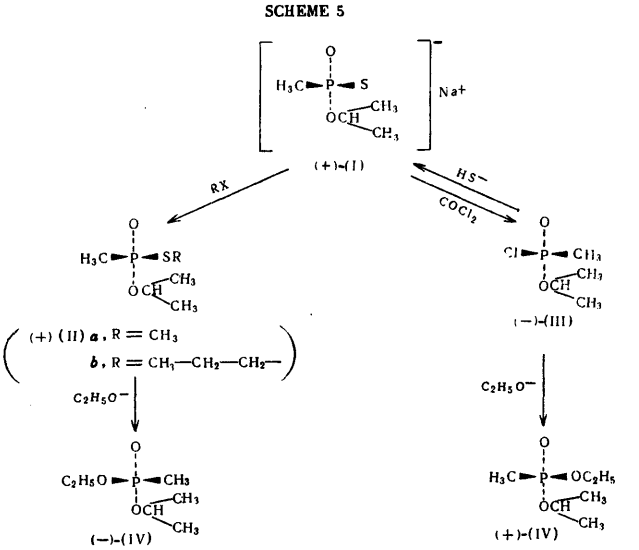
on Werner's coordination theory, were unsuccessful. Arbuzov and Kamai[84] prepared a series of these acids RR'PSOH, and hoped to separate them into optical isomers, since Mills and Raper[68] had successfully resolved the arsine sulphides RR'R"As → S, which were closely similar in type. Their experiments yielded no positive result. Aaron and Miller[85] were the first to resolve a derivative of phosphonothioic acid — ethyl hydrogen ethylphosphonothioate $C_2H_5PS(OC_2H_5)OH$ — by means of quinone. The isomers were isolated in the form of the dicyclohexylammonium salts, and were optically stable[86]. Subsequently[87] five more *O*-alkyl hydrogen alkylphosphonothioates — the ethyl, isopropyl, and methyl *P*-methyl esters, the ethyl *P*-isopropyl ester, and the methyl *P*-ethyl ester — were resolved via the brucine and quinine salts. The synthesis of racemic *O*-alkyl hydrogen alkylphosphonothioates has been described by Kabachnik et al.[88] and by Hoffmann et al.[89] Green and Hudson[90] resolved ethyl(phenyl)phosphinothiolic acid $C_2H_5(C_6H_5)POSH$, and Michalski et al.[91] have resolved *OO'*-dialkyl hydrogen phosphorothioates — the butyl ethyl and the ethyl isopropyl esters — through the cinchonine and cinchonidine salts. The successful separation of asymmetric derivatives of phosphinothioic acids has opened a new chapter in the investigation of optically active organophosphorus compounds, by permitting the study of (1) the stereochemistry of substitution reactions at an asymmetric phosphorus atom and (2) the biological activity of optical isomers of organophosphorus compounds.

By treating racemic *O*-ethyl hydrogen ethylphosphonothioate and its laevorotatory isomer with carbonyl chloride, Aaron[92] was able to isolate racemic ethyl ethylphosphonochloridate. By the action of carbonyl chloride on the sodium salt of laevorotatory *O*-ethyl hydrogen ethylphosphonothioate be obtained dextrorotatory *O*-ethyl ethylphosphonochloridate:



The racemisation half-life of the isolated optically active acid chloride was 6 h in dry acetone and 4 days in dry benzene at room temperature. The action of carbonyl chloride on dextrorotatory sodium *O*-isopropyl methylphosphonothioate gave laevorotatory *O*-isopropyl methylphosphonochloridate[92], irrespectively of whether the reaction took place in hexane, acetone, or dioxan.

SCHEME 5

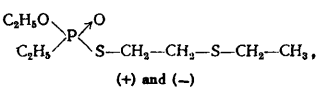


The optically active acid chloride thus obtained was subjected to various reactions as indicated in Scheme 5, the relative configurations of the compounds in which were deduced by the following reasoning. Dextrorotatory *O*-isopropyl *S*-methyl methylphosphonothiolate (+)-(II*a*) and laevorotatory *O*-isopropyl methylphosphonochloridate (-)-(III) were converted by the action of the ethoxide ion into the optical antipodes of ethyl isopropyl methylphosphonate:

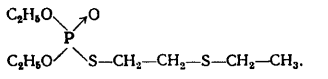
(+)-(II*a*) → (−)-(IV) and (−)-(III) → (+)-(IV).

The compounds (+)-(II*a*) and (-)-(III) probably had opposite configurations. The compounds (+)-(II*a*) and (+)-(II*b*) had the same sign of rotation and the same configuration. This was confirmed by the synthesis of both laevorotatory esters from laevorotatory sodium *O*-isopropyl methylphosphonothioate (I) under conditions such that the *S*-alkylated product was formed exclusively[93].

Aaron and Michel[94] used the optical isomers of *OO'*-diethyl hydrogen phosphorothioate to synthesise dextrorotatory and laevorotatory ethyl *S*-2-ethylthioethyl ethylphosphonothiolate

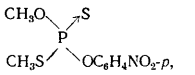


which were similar to the cholinesterase-inhibitor diethyl *S*-2-ethylthioethyl phosphorothiolate[95]

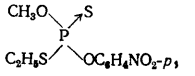


Study of the rate of suppression of cholinesterase by the two optical isomers of ethyl *S*-2-ethylthioethyl ethylphosphonothiolate showed that the laevorotatory isomer was a stronger inhibitor than the dextrorotatory isomer by a factor of 10–20.

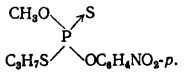
The difference in physiological activity between isomeric thionates and thiolates of phosphorus[95,96] and the biological activity of *cis* and *trans*-isomers of vinyl[97] and propenyl phosphates[98] led Hilgetag and Lehmann[99] to prepare the optically active thiophosphates — *OS*-dimethyl *O'*-*p*-nitrophenyl phosphorothiolothionate



S-ethyl *O*-methyl *O'*-*p*-nitrophenyl phosphorothiolothionate

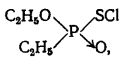


and *O*-methyl *O'*-*p*-nitrophenyl *S*-propyl phosphorothiolothionate



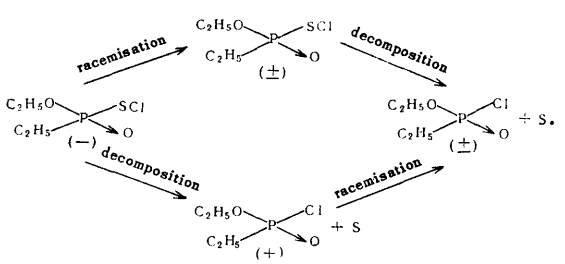
The optical isomers of *OS*-dimethyl *O'*-*p*-nitrophenyl phosphorothiolothionate were tested biologically on the fly *Drosophila funebris*. The enantiomers had the same effect on the fly, but exhibited different toxicities towards warm-blooded creatures: the values of LD_{50} were 135 and 25 mg kg^{-1} (mouse) for the dextrorotatory and laevorotatory isomers respectively.

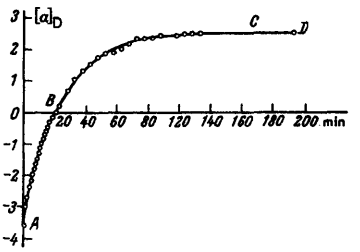
Very interesting investigations have recently been made by Michalski and Ratajczak with the optical isomers of *O*-ethyl hydrogen ethylphosphonothioate, which had been obtained by Aaron et al.[85] These were converted by means of sulphuryl chloride into the optically active sulphenyl chlorides[100,101]



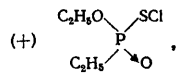
which lost their optical activity comparatively rapidly (racemisation half-life 6.8 min)[101]. A detailed study was made of the behaviour of laevorotatory ethyl chlorothio-(ethyl)phosphinate[101]. The rotation of this isomer changed from (-) to (+) only a few minutes after preparation, reached a maximum value in 3 h, and then gradually fell to zero. This variation in rotation of the laevorotatory sulphenyl chloride was explained[101] not only by racemisation but also by chemical changes, the sulphenyl chloride gradually decomposing into ethyl ethylphosphonochloridate and sulphur, with the former product also racemising comparatively rapidly.

The changes undergone by the laevorotatory ethyl chlorothio(ethyl)phosphinate were represented[101] by the cyclic scheme (see also diagram)

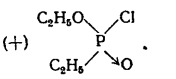




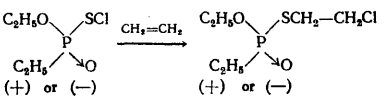
The diagram shows that the section *AB* of the curve predominates in racemisation of the dextrorotatory sulphenyl chloride itself



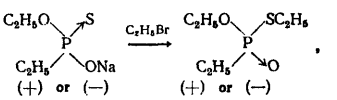
and corresponds to a first-order reaction. Section *CD* represents racemisation of dextrorotatory ethyl ethylphosphonochloridate



Addition of ethylene to the optically active ethyl chlorothio(ethyl)phosphinates gave dextrorotatory and laevorotatory *S*-alkyl esters[101,102]:



These were written A–S–R, where A = $C_2H_5OPO(C_2H_5)$– and R = $ClCH_2CH_2$–. Dextrorotatory and laevorotatory sodium *O*-ethyl ethylphosphonothioate gave with ethyl bromide the dextrorotatory and laevorotatory ethylthio-derivatives:



or A–S–C_2H_5. Michalski and Ratajczak[102] first studied the conversion of both dextrorotatory *S*-alkyl esters A–S–R

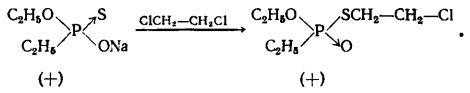
$$\begin{cases} A = (C_2H_5O)(C_2H_5)P(O)— \\ R = ClCH_2—CH_2—,\ C_2H_5 \end{cases}$$

into the optically active ethyl ethylphosphonochloridates by chlorolysis of the P–S bond:

$$A—S—R \longrightarrow A—Cl + R—S—Cl \quad \begin{cases} A = (C_2H_5O)(C_2H_5)P(O)— \\ R = ClCH_2—CH_2—,\ CH_3—CH_2. \end{cases}$$

Michalski and Ratajczak then carried out a similar reaction with the laevorotatory alkyl *S*-alkyl esters A–S–R.[103] They discovered that the direction of chlorolysis of the optically active alkyl alkylthio-derivatives A–S–R (where R = $ClCH_2CH_2$ and C_2H_5) to the acid chlorides A–Cl was

affected by the nature of the aliphatic radical attached to the sulphur: chlorolysis of the dextrorotatory *S*-alkyl ester (+)-$C_2H_5OPO(C_2H_5)SCH_2CH_2Cl$ gave the dextrorotatory ethyl ethylphosphonochloridate (+)-$C_2H_5OPO(C_2H_5)Cl$, whereas chlorolysis of the dextrorotatory *S*-alkyl ester (+)-$C_2H_5OPO(C_2H_5)SCH_2CH_3$ yielded the laevorotatory ethyl ethylphosphonochloridate (-)-$C_2H_5OPO(C_2H_5)Cl$. The two initial dextrorotatory *S*-alkyl esters A–S–R have the same configuration, since the dextrorotatory chloroethylthio-derivative was obtained also by reaction of dextrorotatory potassium or sodium *O*-ethyl ethylphosphonothioate with dichloroethane:



This reaction probably occurs without inversion of configuration at the asymmetric phosphorus atom, since the bonds around it are not involved.

Thus the dextrorotatory *S*-alkyl esters

$$(+)\,(C_2H_5O)\,(C_2H_5)\,P\,(O)\,SCH_2-CH_2-Cl \text{ and } (+)\,(C_2H_5O)\,(C_2H_5)\,P\,(O)\,S-CH_2-CH_3,$$

have the same configuration, whereas the ethyl ethylphosphonochloridates obtained from them by chlorolysis of the P–S bond have opposite configurations. Most probably chlorolysis of the two *S*-alkyl esters takes place by different mechanisms, the configuration being preserved with the chloroethylthio-derivative and inverted with the ethylthio-derivative. This mechanism for the latter derivative is supported also by the fact that laevorotatory ethyl ethylphosphonochloridate is converted into dextrorotatory diethyl ethylphosphonothiolate on treatment with sodium ethyl sulphide:

$$(-)\,(C_2H_5O)\,(C_2H_5)\,P\,(O)\,Cl \xrightarrow{C_2H_5SNa} (+)\,(C_2H_5O)\,(C_2H_5)\,P\,(O)\,S-CH_2-CH_3,$$

the reaction involving inversion of configuration at the asymmetric phosphorus atom [104].

In order to investigate the effect of chlorine in the side-chain on the stereochemical course of chlorolysis of *S*-alkyl esters A–S–R, the optically active compounds

$$(C_2H_5O)\,(C_2H_5)\,P\,(O)\,SCH_2-CH_2-CH_2-Cl,$$
$$(C_2H_5O)\,(C_2H_5)\,P\,(O)\,SCH_2-CH_2-CH_2-CH_2-Cl,$$

were examined. Chlorolysis of both these alkylthio--derivatives is accompanied by inversion of configuration at the asymmetric phosphorus atom. Table 1 lists results obtained for the chlorolysis to optically active ethyl ethylphosphonochloridates of all the optically active *S*-alkyl esters $C_2H_5OPO(C_2H_5)SR$ studied [103].

Ratajczak [105] studied the substitution of optically active ethyl ethylphosphonochloridates with various nucelophilic reagents such as RS^-, RO^-, R_2NH, and $C_2H_5OPS(C_2H_5)O^-$. Since kinetic data [104,106] indicate that the reactions of various organophosphorus acid chlorides with nucleophilic reagents have an S_N2 mechanism, while Ratajczak [107] and Green and Hudson [108,109] have shown that substitutions at the phosphorus atom under similar conditions involve inversion, Ratajczak [105] postulated that the reactions of optically active ethyl ethylphosphonochloridates with the

TABLE 1.

$(C_2H_5O)\,(C_2H_5)P(O)SR \rightarrow (C_2H_5O)\,(C_2H_5)P(O)Cl$

Rotation of S-alkyl ester	R	Rotation of acid chloride	Steric effect
(−)	C_2H_5	(+)	inversion
(+)	C_2H_5	(−)	inversion
(−)	CH_2-CH_2-Cl	(−)	retention
(+)	CH_2-CH_2-Cl	(+)	retention
(+)	$CH_2-CH_2-CH_2-Cl$	(−)	inversion
(−)	$CH_2-CH_2-CH_2-CH_2-Cl$	(+)	inversion

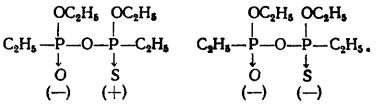
TABLE 2.

$(C_2H_5O)\,(C_2H_5)\,P\,(O)\,Cl\,(II) + :B \rightarrow (C_2H_5O)\,(C_2H_5)\,P\,(O)\,B + Cl^-$

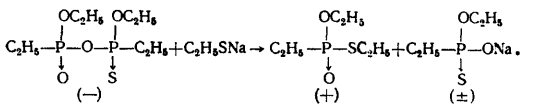
No. of reaction	$[\alpha]_D$, deg (II)	Nucleophile B	Substitution product	$[\alpha]_D$, deg product
(1)	−15	$C_2H_5S^-$	$(C_2H_5O)(C_2H_5)P(O)SC_2H_5$ (III)	+10.30
(2)	−13	$C_4H_9S^-$	$(C_2H_5O)(C_2H_5)P(O)SC_4H_9$ (IV)	+8.28
(3)	+15	$(C_4H_9)_2NH$	$(C_2H_5O)(C_2H_5)P(O)N(C_4H_9)_2$ (V)	−4.30
(4)	−37.10	CH_3O^-	$(C_2H_5O)(C_2H_5)P(O)OCH_3$ (VI)	−0.80
	−12.40	CH_3O^-	$(C_2H_5O)(C_2H_5)P(O)OCH_3$ (VI)	+0.40
(5)	40.05	$(\pm)(C_2H_5O)\,(C_2H_5)P(S)O^-$	$(C_2H_5O)(C_2H_5)P(O)-O-P(S)(OC_2H_5)C_2H_5$ (VII)	−10.90
	−10.50	$(\pm)(C_2H_5O)\,(C_2H_5)P(S)O^-$	$(C_2H_5O)(C_2H_5)P(O)-O-P(S)(OC_2H_5)C_2H_5$ (VII)	+1.85

above nucleophilic reagents entail inversion of configuration at the asymmetric phosphorus atom. The results obtained are indicated in Table 2.[105]

Of the compounds listed in Table 2, special interest attaches to (VII), obtained by reaction (5)[107]. It contains two asymmetric centres PO and PS, and can exist in four optically active and two racemic forms. Since thio-acids are acylated at the oxygen atom [101], the pyrophosphonothionate (VII) should exist as a mixture of diastereoisomers

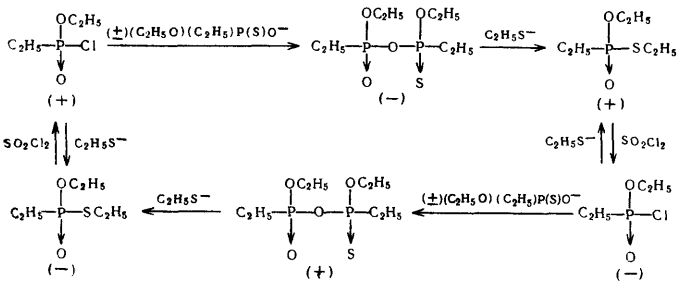


Studies had previously been made of the reactions of pyrophosphonothionates with the nucleophilic reagents sodium methoxide [110,111] and dimethylamine [112]. The latter were shown to attack the more electrophilic phosphorus (P→O) in the pyrophosphonothionate. Since organophosphorus anhydrides react with nucleophilic reagents by an S_N2 mechanism [113], it was supposed that reactions of the latter with pyrophosphonothionates should entail inversion [112]. The pyrophosphonothionate (-)-(VII) (Table 2) reacted with sodium ethyl sulphide to form racemic sodium *O*-ethyl ethylphosphonothioate and dextrorotatory diethyl ethylphosphonothiolate [107]:

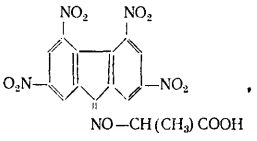


All the transformations of optically active acids of quadricovalent phosphorus derivatives studied Michalski and Ratajczak [103,105,107] can be summarised in the form of a

cycle similar to the Walden cycle in the chemistry of carbon, in which every change involves inversion[107]:

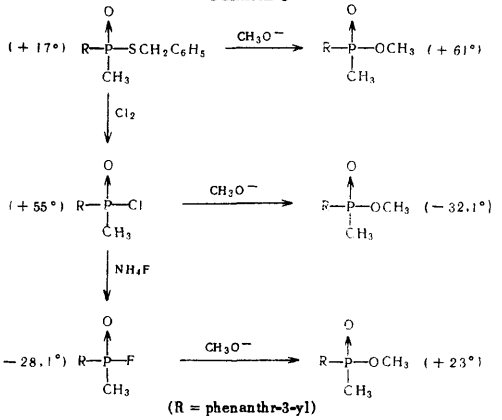


A very interesting method which has recently been discovered for resolving racemates into optical isomers is based on the spontaneous selective crystallisation of inclusion compounds formed by a complexing agent of open spiral structure with molecules of the compound to be separated which have penetrated into the cavities in its lattice[114]. Green and Hudson[115] isolated, via inclusion products with α-(2,4,5,7-tetranitrofluoren-9-ylideneamino-oxy)propionic acid



the dextrorotatory isomer of methyl 1-naphthyl methylphosphonate (+)-(1-$C_{10}H_7O$)CH_3POOCH_3 and both optical isomers of benzyl methyl(phenanthr-3-yl)phosphinothiolate. They used the dextrorotatory isomer of the ester to study[116] some of the substitutions shown in Scheme 6.

SCHEME 6



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Research on the stereochemistry of organic compounds of phosphorus and arsenic, begun as long ago as the beginning of the century, entered a new phase around 1956–1959. Whereas before 1956 workers had devoted their efforts mainly to preparing individual representatives of various classes of organophosphorus and organoarsenic compounds in an optically active form, during recent years serious investigations have been started on the mechanism of various reactions involving optically active compounds of phosphorus and arsenic, and some interesting results have already been obtained. There is no doubt that the amount of work done on the stereochemistry of organic compounds of phosphorus and arsenic will increase every year, and will lead to still more interesting results.

After the present paper had been written, a series of communications appeared reporting interesting work on the stereochemistry of organophosphorus and organoarsenic compounds. Peerdeman et al.,[117] for the first time in the history of the stereochemistry of organoelementary compounds, have determined the absolute configuration of dextrorotatory benzylmethylphenyl-n-propylphosphonium bromide by X-ray examination, which has enabled absolute configurations to be determined for the optically active benzylmethylphenyl-n-propylarsonium and benzylmethylphenyl-n-propylammonium bromides[118].

Horner and Winkler[119] have determined by asymmetric synthesis the absolute configuration of dextrorotatory methylphenyl-n-propylphosphine. Horner and Balzer[120] have studied the stereochemical course of the reduction of optically active oxides of tertiary phosphines to the phosphines by means of trichlorosilane. Denney and Gershman[121] have taken the first step in studying the stereochemical course of the reaction of optically active methylphenylpropylphosphine with chloral. Horner and Hofer[122] have studied the dependence of the rate of racemisation of optically active quaternary arsonium salts on the chemical structure of the salts and the nature of the solvent, and have also put forward a new mechanism for this racemisation. Krawicki and Michalski[123] have resolved *O*-ethyl hydrogen ethylselenophosphonothioate by means of quinine.

1. J.Meisenheimer and L.Lichtenstadt, Ber., 44, 356 (1911).
2. J.Meisenheimer, Annalen, 449, 213 (1926).
3. G.J.Burrows and E.E.Turner, J.Chem.Soc., 426 (1921).
4. I.L.Finar, "Organic Chemistry", Vol. 2, "Stereochemistry of Natural Products", Longmans, London, 1960, p.192.
5. R.E.Weston, J.Amer.Chem.Soc., 76, 2645 (1954).
6. I.G.M.Campbell and I.K.Way, J.Chem.Soc., 5034 (1960).
7. I.G.M.Campbell and I.K.Way, J.Chem.Soc., 2133 (1961).
8. L.Horner, H.Winkler, A.Rapp, A.Mentrup, H.Hoffmann, and P.Beck, Tetrahedron Letters, 161 (1961).
9. L.Horner, F.Schedlbauer, and P.Beck, Tetrahedron Letters, 1421 (1964).
10. W.E.McEwen, C.A.Vanderwerf, A.Bladé-Font, C.B.Parisek, G.Keldsen, D.C.Velez, D.P.Young, K.Kumli, and G.Axelrad, "Abstracts of Papers Presented at the 140th National Meeting of the American Chemical Society, Chicago, 3rd–8th September 1961" p. 96Q.
11. M.Grayson, P.T.Keough, and G.A.Johnson, J.Amer.Chem. Soc., 81, 4803 (1959).
12. L.Horner and H.Winkler, Tetrahedron Letters, 461 (1964).
13. L.Horner, H.Fuchs, H.Winkler, and A.Rapp, Tetrahedron Letters, 965 (1963).
14. L.Horner and H.Winkler, Tetrahedron Letters, 455 (1964).
15. K.A.Jensen, Z.anorg.Chem., 250, 257 (1943).
16. K.Issleib and W.Seidel, Z.anorg.Chem., 288, 201 (1956).
17. D.P.Young, W.E.McEwen, D.C.Velez, J.W.Johnson, and C.A.Vanderwerf, Tetrahedron Letters, 359 (1964).
18. L.Horner and H.Winkler, Tetrahedron Letters, 175 (1964).
19. D.B.Denney and I.W.Hanifin, Tetrahedron Letters, 2177 (1963).
20. H.H.Nielsen, J.Chem.Phys., 20, 198 (1952).
21. C.C.Loomis and M.W.P.Stranberg, Phys.Rev., 81, 798 (1951).

22. P.W.Allen and L.E.Sutton, Acta Cryst., 3, 46 (1950).
23. I.L.Finar, see Ref. 4, p.196.
24. I.L.Finar, see Ref. 4, p.174.
25. M.S.Lesslie and E.E.Turner, J.Chem.Soc., 1170 (1934); 1051, 1268 (1935); 730 (1936).
26. G.Kh.Kamai, Zhur.Obshch.Khim., 5, 1402 (1935); Ber., 68, 960 (1935).
27. G.Kh.Kamai, Zhur.Obshch.Khim., 6, 176 (1936); Ber., 68, 1893 (1935).
28. G.Kh.Kamai, Zhur.Obshch.Khim., 10, 733 (1940).
29. G.Kh.Kamai, Zhur.Obshch.Khim., 12, 104 (1942).
30. G.Kh.Kamai, Zhur.Obshch.Khim., 17, 2149 (1947).
31. I.G.M.Campbell and R.C.Poller, J.Chem.Soc., 1195 (1956).
32. I.G.M.Campbell, J.Chem.Soc., 1976 (1956).
33. L.Horner and H.Fuchs, Tetrahedron Letters, 203 (1962).
34. L.Horner and A.Mentrup, Annalen, 646, 49 (1961).
35. L.Horner and A.Mentrup, Annalen, 646, 65 (1961).
36. L.Horner and H.Fuchs, Tetrahedron Letters, 1573 (1963).
37. A.Michaelis, Annalen, 315, 58 (1901).
38. A.Michaelis, Annalen, 321, 159 (1902).
39. E.Wedekind, Ber., 45, 2933 (1912).
40. T.F.Winmill, J.Chem.Soc., 720 (1912).
41. L.G.Radcliffe and W.H.Brindley, Chem.and Ind., 1159 (1923).
42. G.Kh.Kamai, Zhur.Obshch.Khim., 2, 524 (1932).
43. G.Kh.Kamai and L.A.Khismatullina, Dokl.Akad.Nauk SSSR, 92, 69 (1953); Zhur.Obshch.Khim., 26, 3426 (1956); Izv. Kazansk.Fil.Akad.Nauk SSSR, Ser.Khim.Nauk, No. 4, 79 (1957).
44. K.F.Kumli, W.E.McEwen, and C.A.Vanderwerf, J.Amer. Chem.Soc., 81, 248 (1959).
45. G.Kh.Kamai, Zhur.Obshch.Khim., 4, 184 (1934); Ber., 66, 1779 (1933).
46. G.Kh.Kamai and Yu.F.Gatilov, Dokl.Akad.Nauk SSSR, 137, 91 (1961).
47. G.Kh.Kamai, B.I.Klabunovski, Yu.F.Gatilov, and G.S.Khodakov, Dokl.Akad.Nauk SSSR, 139, 1112 (1961).
48. W.J.Pope and A.W.Harvey, J.Chem.Soc., 831 (1901).
49. F.G.Holliman and F.G.Mann, J.Chem.Soc., 1634 (1947).
50. F.G.Mann and F.A.Hart, J.Chem.Soc., 4107 (1955); Nature, 175, 952 (1955).
51. F.G.Holliman and F.G.Mann, J.Chem.Soc., 45 (1945).
52. F.G.Holliman, F.G.Mann, and D.A.Thornton, J.Chem.Soc., 9 (1960).
53. F.G.Holliman and F.G.Mann, J.Chem.Soc., 551 (1943).
54. G.Kh.Kamai and G.M.Usacheva, Zhur.Obshch.Khim., 34, 785 (1964).
55. M.Zanger, C.A.Vanderwerf, and W.E.McEwen, J.Amer. Chem.Soc., 81, 3806 (1959).
56. A.Bladé-Font, C.A.Vanderwerf, and W.E.McEwen, J.Amer. Chem.Soc., 82, 2396 (1960).
57. U.Schöllkopf, Angew.Chem., 71, 260 (1959).
58. A.Bladé-Font, W.E.McEwen, and C.A.Vanderwerf, J.Amer. Chem.Soc., 82, 2646 (1960).
59. W.E.McEwen, A.Bladé-Font, and C.A.Vanderwerf, J.Amer. Chem.Soc., 84, 677 (1962).
60. M.Grayson and P.T.Keough, J.Amer.Chem.Soc., 82, 3919 (1960).
61. C.B.Parisek, W.E.McEwen, and C.A.Vanderwerf, J.Amer. Chem.Soc., 82, 5503 (1960).
62. J.Meisenheimer, Ber., 41, 3966 (1908).
63. J.Meisenheimer, Annalen, 385, 17 (1911); 428, 252 (1922); 449, 191 (1926).
64. V.I.Sokolov and O.A.Reutov, Izv.Akad.Nauk SSSR, Otd. Khim.Nauk, 394 (1964).
65. I.H.Brewster, J.Amer.Chem.Soc., 81, 5475 (1959).
66. A.G.Brook and W.W.Limburg, J.Amer.Chem.Soc., 85, 832 (1963).
67. R.F.Hudson and M.Green, Angew.Chem., 75, 47 (1963).
68. W.H.Mills and R.Raper, J.Chem.Soc., 2479 (1925).
69. J.Chatt and F.G.Mann, J.Chem.Soc., 610 (1939).
70. W.C.Davies and F.G.Mann, J.Chem.Soc., 276 (1944).
71. P.J.Wheatley, J.Chem.Soc., 523 (1960).
72. L.Maier, Chem.Ber., 94, 3043 (1961).
73. B.D.Luff and F.S.Kipping, J.Chem.Soc., 1993 (1909).
74. F.S.Kipping and F.Challenger, J.Chem.Soc., 99 (1911).
75. W.J.Pope and C.S.Gibson, J.Chem.Soc., 740 (1912).
76. E.E.Turner, E.Roberts, and F.W.Bury, J.Chem.Soc., 1143 (1926).
77. J.Meisenheimer, Annalen, 397, 276 (1913).
78. C.S.Gibson and H.R.Johnson, J.Chem.Soc., 93 (1928).
79. S.Sugden, J.Chem.Soc., 1177 (1924); 1868, 2517 (1925); 1173 (1927).
80. A.E.Arbuzov and B.A.Arbuzov, Zhur.Russ.Fiz.-Khim. Obshch., 61, 1599 (1929).
81. A.E.Arbuzov and I.A.Arbuzova, Zhur.Russ.Fiz.-Khim. Obshch., 61, 1905 (1929).
82. D.M.Coyne, W.E.McEwen, and G.A.Vanderwerf, J.Amer. Chem.Soc., 78, 3061 (1956).
83. K.L.Marsi, C.A.Vanderwerf, and W.E.McEwen, J.Amer. Chem.Soc., 78, 3063 (1956).
84. A.E.Arbuzov and G.Kh.Kamai, Zhur.Russ.Fiz.-Khim. Obshch., 61, 2037 (1929).
85. H.S.Aaron and J.I.Miller, J.Amer.Chem.Soc., 78, 3538 (1956).
86. H.S.Aaron, T.M.Shryne, and J.I.Miller, J.Amer.Chem. Soc., 80, 107 (1958).
87. H.S.Aaron, J.Braun, T.M.Shryne, H.F.Frack, G.E.Smith, R.T.Uyeda, and J.I.Miller, J.Amer.Chem.Soc., 82, 597 (1960).
88. M.I.Kabachnik, N.I.Kurochkin, T.A.Mastryukova, S.T.Ioffe, E.M.Popov, and N.P.Rodionova, Dokl.Akad. Nauk SSSR, 104, 861 (1955).
89. W.Hoffmann, B.Kagan, and I.H.Canfield, J.Amer.Chem. Soc., 81, 148 (1959).
90. M.Green and R.F.Hudson, Proc.Chem.Soc., 145 (1961).
91. J.Michalski, A.Ratajczak, and Z.Tulimowski, Bull.Acad. polon.Sci., Ser.Sci.chim., 11, 237 (1963).
92. H.S.Aaron, R.T.Uyeda, H.F.Frack, and J.I.Miller, J. Amer.Chem.Soc., 84, 617 (1962).
93. M.I.Kabachnik, Zhur.Obshch.Khim., 26, 2228 (1956).
94. H.S.Aaron, H.O.Michel, B.Witten, and J.I.Miller, J. Amer.Chem.Soc., 80, 456 (1958).
95. T.R.Fukuto and R.L.Metcalf, J.Amer.Chem.Soc., 76, 5103 (1954).
96. R.L.Metcalf and R.B.March, J.Econ.Entomol., 46, 288 (1953).
97. I.E.Casida, Science, 122, 597 (1955).
98. I.E.Casida, P.E.Gatterdam, L.W.Getzin, and R.K.Chapman, J.Agric.Food Chem., 4, 236 (1956).
99. G.Hilgetag and G.Lehmann, Angew.Chem., 69, 506 (1957); J.prakt.Chem., 8, 224 (1959).
100. J.Michalski and A.Ratajczak, Chem.and Ind., 539 (1959).
101. J.Michalski and A.Ratajczak, Roczniki Chem., 36, 911 (1962).
102. J.Michalski and A.Ratajczak, Chem.and Ind., 1241 (1960).
103. J.Michalski and A.Ratajczak, Roczniki Chem., 37, 1185 (1963).
104. J.Dostrovsky and M.Halmann, J.Chem.Soc., 508 (1953).
105. A.Ratajczak, Bull.Acad.polon.Sci., Ser.Sci.chim., 12, 139 (1964).
106. R.F.Hudson and G.Moss, J.Chem.Soc., 3599 (1962).
107. A.Ratajczak, Bull.Acad.polon.Sci., Ser.Sci.chim., 12, 145 (1964).
108. M.Green and R.F.Hudson, Proc.Chem.Soc., 307 (1962).
109. M.Green and R.F.Hudson, J.Chem.Soc., 540 (1963).
110. J.Michalski, M.Mikolajczak, and A.Ratajczak, Chem.and

Ind., 810 (1962).
111. J.Michalski, M.Mikolajczak, and A.Ratajczak, Bull.Acad. polon.Sci., Ser.Sci.chim., 11, 11 (1963).
112. J.Michalski, M.Mikolajczak, and A.Skowronska, Chem. and Ind., 1053 (1962).
113. D.F.Heath, J.Chem.Soc., 3796, 3805 (1956).
114. F.Cramer, "Einschlussverbindungen" (Translated into Russian), Inostr.Lit., Moscow, 1958.
115. M.Green and R.F.Hudson, Proc.Chem.Soc., 323 (1957); J.Chem.Soc., 3129 (1958).
116. M.Green and R.F.Hudson, Proc.Chem.Soc., 227 (1959).
117. A.F.Peerdeman, J.P.C.Holst, L.Horner, and H.Winkler, Tetrahedron Letters, 811 (1965).
118. L.Horner, H.Winkler, and E.Meyer, Tetrahedron Letters, 789 (1965).
119. L.Horner and H.Winkler, Annalen, 685, 1 (1965).
120. L.Horner and W.D.Balzer, Tetrahedron Letters, 1157 (1965).
121. D.B.Denney and N.E.Gershman, Tetrahedron Letters, 3899 (1965).
122. L.Horner and W.Hofer, Tetrahedron Letters, 3281 (1965).
123. C.Krawicki, J.Michalski, and Z.Tulimowski, Chem.and Ind., 34 (1965).

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PROGRESS IN THE STUDY OF THE OXIDATION OF ORGANOMETALLIC COMPOUNDS

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1. INTRODUCTION

The chemistry of organometallic compounds has a history of more than one hundred years. Various organic compounds of zinc [1,2], boron [3,4], lead [5], and tin [6,7] were prepared as early as the middle of last century. A number of methods have now been developed, for the preparation of a variety of organic derivatives of a given metal, including those containing several atoms of different metals.

Considerable attention has been and is being paid to the study of the properties and reactions of organometallic compounds, since these compounds and their reactions are of considerable theoretical and practical interest. One of the most important reactions of organometallic compounds is their oxidation by oxygen and peroxides. It is well known that certain organometallic compounds, for example those of magnesium, zinc, and boron, are oxidised extremely readily by oxygen, but systematic studies in this direction were begun only in the last ten years.

Recent studies [8-15] have shown conclusively that the reaction of organometallic compounds with oxygen is accompanied by the formation of organometallic peroxides, which subsequently undergo various types of rapid conversion, including reaction with the original organometallic compounds. It has thus become necessary to study the reactions of organometallic compounds with various peroxides.

Systematic studies of the reactions of organometallic compounds with oxygen and peroxides are being carried out successfully in the USSR and abroad. The comprehensive, systematic, and detailed studies of Razuvaev are outstanding.

2. OXIDATION OF ORGANOMETALLIC COMPOUNDS WITH OXYGEN

Organometallic compounds differ extremely widely in their behaviour towards oxygen. Organic compounds of the alkali and alkaline-earth metals, zinc, cadmium, boron, aluminium, and titanium are often spontaneously flammable even at room temperature, whereas organic derivatives of germanium, tin, and lead have a high stability towards oxygen under ordinary conditions; organosilicon compounds are oxidised extremely slowly by oxygen even at elevated temperature.

The reactivity is undoubtedly influenced greatly by the energy of the metal–carbon and metal–oxygen bonds and by the electronic structure of the metal atoms in the organometallic compounds. In the reactions of these compounds with oxygen an important part may also be played by the formation of inorganic and organic peroxides and various complexes and associates, and also by temperature and the nature of the solvent.

It is not yet possible to put forward a fully substantiated single mechanism for the oxidation of all organometallic compounds by oxygen. This is due chiefly to the fact that there are no published data characterising quantitatively the influence of the above factors on the rate of the reaction of organometallic compounds with oxygen. For example, the energy of the metal–carbon bond is known only for a very small number of compounds [16]. Despite the difficulties, however, it is worth summarising the extensive information obtained by many workers on the oxidation of organometallic compounds by oxygen and trying to distinguish the characteristic features of the mechanism of these reactions. No one has yet undertaken this task, although the mechanism of the oxidation by oxygen of the organic compounds of certain metals, chiefly alkali metals, has been examined in a number of papers [17,18].

The oxidation of organometallic compounds by oxygen is a complex process involving several elementary chemical-conversion stages, the number of which depends on the specific conditions under which the reaction is carried out. Various intermediate or final stable products of the chemical transformation of organometallic compounds may be formed, depending on these conditions.

It is appropriate to consider first of all the oxidation by oxygen of those organometallic compounds which undergo this reaction very readily at room temperature or at even lower temperatures. The most characteristic feature of this group of compounds is that the formation of organometallic peroxides is much more rapid than their subsequent transformation. This relationship between the rates