COMPOUNDS CONTAINING CARBON–PHOSPHORUS BONDS

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Phosphorus-containing organic compounds present a variety of features of chemical interest. Many complex esters and amides of phosphoric and condensed phosphoric acids play important parts in metabolic processes, but compounds whose molecules contain carbon atoms linked directly to phosphorus do not occur naturally. They are discussed, together with other organic compounds of phosphorus, in Kosolapoff's book [1] which summarises the literature up to the beginning of 1950 and is a mine of information for all workers in this field. It is usefully supplemented by a recent review [2] dealing with the preparation and properties of phosphonic acids, the most important class of compounds containing C–P bonds.

Although phosphorus follows nitrogen in Group V of the Periodic Table there is very little resemblance between the organic chemistry of these two elements. Phosphorus analogues of important classes of organic nitrogen compounds such as nitro-compounds, aromatic nitrogen-heterocycles and azo-compounds are mostly unknown and where formal similarities do exist, as between primary phosphines and primary amines or between phosphine oxides and amine oxides, there are considerable differences in reactions. These dissimilarities arise because of the lower electronegativity of phosphorus which leads to its forming stronger bonds with oxygen and with halogens, and because of the greater reactivity of the unshared electrons on tervalent phosphorus which results in a strong tendency to quinquevalency.

Nomenclature of Organic Compounds of Phosphorus.—The problem of providing suitable, unambiguous names for organic phosphorus compounds is one which has caused considerable difficulty. The majority of organic phosphorus compounds can be considered as derived from various acids of phosphorus; the existence of two valency states and of both mono- and di-basic acids, together with the problem of whether negative substituents such as chlorine or amino-groups should be considered as replacing hydrogen or hydroxyl in the parent structure, led to several different systems of nomenclature. The resulting confusion was dispelled as far as British and American publications are concerned by the adoption in 1952 by the Chemical Society and the American Chemical Society of a new system of nomenclature for compounds containing one phosphorus atom.[3]

This system uses, as parent structures, a number of phosphorus hydrides and acids, some of which exist only hypothetically. In naming compounds, groups which are attached by C–P bonds are considered as replacing hydrogen

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[1] Kosolapoff, " Organophosphorus Compounds ", John Wiley and Sons, New York, 1950.

[2] Freedman and Doak, *Chem. Rev.*, 1957, **57**, 479.

[3] *J.*, 1952, 5122.

in the appropriate parent structure and are prefixed to its name, whereas negative groups are considered as replacing hydroxyl or oxygen (either doubly bonded to phosphorus or in a hydroxyl group) and are indicated either as a separate word (*e.g.*, chloride or amide) replacing the word acid or, if the compound is itself an acid or an ester, by a suitable affix (*e.g.*, -chlorid- or -amid-) immediately preceding the valency suffix (-ic acid, -ate, -ous acid, or -ite). Ester groups precede the name as a separate word or words, as in normal usage, and in cases of ambiguity (as in acids in which some, but not all, of the oxygen atoms of the parent structure have been replaced by sulphur atoms, or in substituted amides) the symbols *O*-, *S*-, *N*-, *P*-, etc., may be used. The parent structures most frequently met are H_3P phosphine, $P(OH)_3$ phosphorous acid, $H{\cdot}P(OH)_2$ phosphonous acid, $H_2P(OH)$ phosphinous acid, $H_3P(O)$ phosphine oxide, $P(O)(OH)_3$ phosphoric acid, $H{\cdot}P(O)(OH)_2$ phosphonic acid, and $H_2P(O)(OH)$ phosphinic acid.

Examples of this system of nomenclature are: Me_3P trimethylphosphine, $EtMePhP(O)$ ethylmethylphenylphosphine oxide, $P(OEt)_3$ triethyl phosphite, $MeP(OEt)_2$ diethyl methylphosphonite, $Me_2P(NEt_2)$ *NN*-diethyldimethylphosphinous amide, $MeP(O)Cl_2$ methylphosphonic dichloride, $MeP(O)(OEt)Cl$ ethyl methylphosphonochloridate, and $Me_2P(S)(OEt)$ *O*-ethyl dimethylphosphinothioate.

Starting Materials for the Synthesis of Compounds containing Carbon–Phosphorus Bonds.—Many reactions leading to the formation of C–P bonds start with inorganic phosphorus compounds such as phosphine, phosphorus trichloride, and phosphorus oxychloride, but for the preparation of compounds in which an aliphatic carbon atom is linked to quinquevalent phosphorus the dialkyl and trialkyl esters of phosphorous acid are of particular value.

Phosphorus trichloride reacts readily with primary and secondary alcohols in the presence of a tertiary base (preferably diethylaniline because its hydrochloride is non-hygroscopic and readily filtered off) to give trialkyl phosphites :

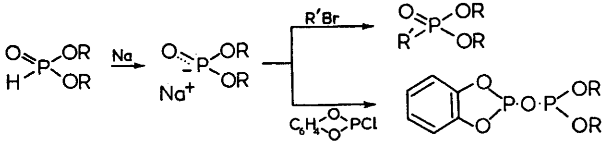
$$PCl_3 + 3ROH + 3B \longrightarrow P(OR)_3 + 3B,HCl$$

These esters are reactive because they contain a phosphorus atom, the unshared electrons of which make it strongly nucleophilic, together with readily displaced alkyl groups.

Partial dealkylation of trialkyl phosphites to the dialkyl esters occurs very rapidly under the influence of hydrogen chloride. Because of this, reaction of phosphorus trichloride with primary and secondary alcohols in the absence of a base results in the formation of dialkyl phosphites :

$$PCl_3 + 3ROH \longrightarrow P(OR)_2{\cdot}OH + 2HCl + RCl$$

Although they are almost always referred to as such, these compounds are not true phosphites but are phosphonates $H{\cdot}P(O)(OR)_2$, the quinquevalent phosphorus atom being the cause of their relative stability towards further dealkylation. They provide the best-known example of the instability of a hydroxyl group attached to a tervalent phosphorus atom; in practically all cases when a compound having this structural feature might be expected, the isomer in which the phosphorus atom is quinquevalent is obtained instead. It may be that a tautomeric equilibrium exists between the two forms with the equilibrium well over on the phosphonate side. This idea is supported by the fact that whereas dialkyl phosphites themselves possess little nucleophilic reactivity they react readily with sodium, evolving hydrogen and giving derivatives which are powerful nucleophilic reagents. The anions of these sodium derivatives appear to be mesomeric, with the charge divided between phosphorus and oxygen, since in different reactions, groups may become attached to either of these atoms. A similar reactivity



is shown by dialkyl phosphites on addition of sodium alkoxide solutions or of tertiary bases. Formation of a mesomeric anion which can be alkylated (and which can also add to activated double bonds) is reminiscent of compounds that exhibit keto–enol tautomerism and there is, in this respect, a general resemblance between dialkyl phosphites and diethyl malonate, resulting in several analogies with familiar organic reactions.

Types of Compound containing Carbon–Phosphorus Bonds.—*Compounds of Tervalent Phosphorus.*—These are considered, for nomenclature purposes, to be derived from one of the three parent structures, phosphine PH_3, phosphonous acid $HP(OH)_2$, or phosphinous acid $H_2P(OH)$, by replacement by organic radicals of some or all of the hydrogen atoms attached to phosphorus and by replacement of the hydroxyl groups by negative substituents. They include primary, secondary, and tertiary phosphines $R{\cdot}PH_2$, R_2PH, and R_3P, phosphonous dichlorides $R{\cdot}PCl_2$ and phosphinous chlorides R_2PCl. From previous remarks on the instability of hydroxyl groups attached to tervalent phosphorus atoms it will be evident that phosphonous and phosphinous acids are not stable compounds, although their esters $R{\cdot}P(OR')_2$ and $R_2P{\cdot}OR'$ are, like trialkyl phosphites, capable of existence.

All tervalent phosphorus compounds are susceptible to oxidation. This is particularly true of those in which the phosphorus atom has attached to it alkyl groups which, since they are electron-repelling, increase the already high electron density on the phosphorus atom. Compounds with bonds between aliphatic carbon and tervalent phosphorus atoms tend, therefore, to be rather troublesome to prepare and to work with. This, together with the nauseating smells, tendency to spontaneous inflammability, and toxicity of the lower members has led to their being relatively little investigated. In particular, few preparations of primary and secondary aliphatic phosphines have been reported since the pioneering work of Hofmann [4] who alkylated phosphine by heating phosphonium iodide with alkyl iodides and

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[4] Hofmann, *Ber.*, 1871, **4**, 430, 605; 1873, **6**, 292.

zinc oxide. This leads to mono-, di-, and tri-substitution; a variant achieving better control of the extent of alkylation is the reaction of alkyl halides with sodium or potassium phosphides in liquid ammonia.[5] Another route, which has been used more particularly for the preparation of primary and secondary arylphosphines, is hydrolysis of phosphonous and phosphinous chlorides, the monosubstituted phosphinic acids and disubstituted phosphine oxides, which are formed initially, undergoing oxidative disproportionation when heated:[6]

$$3R{\cdot}PCl_2 \rightarrow 3R{\cdot}PH(O){\cdot}OH \rightarrow R{\cdot}PH_2 + 2RP(O)(OH)_2$$
$$2R_2PCl \rightarrow 2R_2PH(O) \rightarrow R_2PH + R_2P(O){\cdot}OH$$

Phenylphosphine has been prepared by reduction, with lithium aluminium hydride, of phenylphosphonous dichloride,[7] phenylphosphonic dichloride,[8] and phenylphosphinic acid.[9] Similar reductions appear to provide relatively easy routes to other primary and secondary phosphines.

Tertiary phosphines containing three identical groups are readily prepared from phosphorus trichloride and Grignard reagents. By using less reactive organometallic compounds substitution may be limited to intermediate stages and phosphonous and phosphinous chlorides thus obtained. Esters of phosphonous and phosphinous acids are obtained by reaction of the chlorides with alcohols or phenols in presence of a tertiary base or, less satisfactorily, with sodium alkoxides.

Compounds of Quinquevalent Phosphorus.—This group includes more chemical types and far more known compounds than those which contain tervalent phosphorus. Almost all quinquevalent phosphorus compounds having C–P bonds contain four atoms covalently bound to phosphorus and the majority of these are related to one of the three parent structures phosphonic acid $H{\cdot}P(O)(OH)_2$, phosphinic acid $H_2P(O){\cdot}OH$, and phosphine oxide $H_3P(O)$. They thus contain three single bonds (one, two, or three of which may be C–P bonds) to phosphorus and one double (or semipolar) bond between phosphorus and oxygen, the place of which may be taken by other bivalent atoms or groups such as $=S$, $=NR$ or $=CR_2$. Other quinquevalent phosphorus compounds containing C–P bonds are quaternary phosphonium salts $R_4P^+X^-$ and the small but very interesting group of penta-arylphosphoranes Ar_5P which contain five covalent bonds to phosphorus. These compounds are often referred to as phosphorus penta-aryls; phosphorane is the systematic name for the hypothetical parent compound H_5P.

The most numerous class of compounds containing C–P bonds are the alkyl- and aryl-phosphonic acids and their simple derivatives. Phosphonic acids, or their chlorides or esters from which the acids themselves are easily obtained, may be prepared by most of the general methods for forming

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[5] Watt and Thompson, *J. Amer. Chem. Soc.*, 1948, **70,** 2295; Wagner and Burg, *ibid.*, 1953, **75,** 3869.

[6] Michaelis, *Annalen*, 1896, **293,** 193; **294,** 1; 1901, **315,** 43; Michaelis and Gleichmann, *Ber.*, 1882, **15,** 801.

[7] Horvat and Furst, *J. Amer. Chem. Soc.*, 1952, **74,** 562.

[8] Freedman and Doak, *ibid.*, p. 3414.

[9] Weil, Prijs, and Erlenmeyer, *Helv. Chim. Acta*, 1953, **36,** 142.

C–P bonds which are discussed in the next section. The acids are generally crystalline, the lower members being extremely soluble in water. Reactions and interconversions of these acids and their derivatives are dealt with later.

Fewer phosphinic acids $R_2P(O)\cdot OH$ are known, but the reactions by which they and their derivatives are prepared and which they undergo are similar to those of phosphonic acids.

Trialkyl- and triaryl-phosphine oxides, $R_3P(O)$, may be obtained by oxidation of the corresponding tertiary phosphines, either directly with air or oxygen, or by wet methods, or by conversion into phosphine dihalides R_3PHal_2 (which resemble phosphorus pentahalides and probably have similar structures) and hydrolysis of these. Tertiary phosphine oxides may also, more conveniently, be prepared by reaction of phosphorus oxychloride or of phosphonic or phosphinic chlorides with Grignard reagents.

Quaternary phosphonium salts which contain at least one alkyl radical may be prepared by reaction of an alkyl halide, preferably the iodide, with the appropriate tertiary phosphine. Tetra-arylphosphonium salts cannot be prepared in this way but may be by reaction of triarylphosphines with arylmagnesium halides and oxygen,[10] with aryl halides and aluminium chloride at high temperatures,[11] with aryldiazonium acetates,[12] or with an aryl halide together with a Grignard reagent and cobalt chloride.[13] The group which is introduced in the last reaction comes from the aryl halide rather than from the Grignard reagent.

That the bond between phosphorus and oxygen (or other elements) which is formally written as double does, in fact, have a considerable amount of double-bond character is shown by the fact that its dipole moment is much lower than that of co-ordinate links involving phosphorus (as in complexes of tervalent phosphorus compounds with metallic salts),[14] by its short length, and by its resemblance to the carbonyl group in producing α-methylenic reactivity. If this double-bond character were complete it would require an outer shell of ten electrons and these bonds are therefore probably best represented as hybrids of $P{=}O$ and $P^+{-}O^-$.

Compounds with five covalent bonds to phosphorus also require a ten-electron outer shell and only a few such compounds are known. Treatment of tetraphenylphosphonium iodide with phenyl-lithium gives pentaphenylphosphorane, the covalent character of which is shown by its insolubility in water, solubility in organic solvents, and comparatively low melting point (124°).[15] The equivalence of the five C–P bonds in phosphoranes is shown by the identity of tetraphenyl-*p*-tolylphosphorane prepared by reaction of *p*-tolyl-lithium and tetraphenylphosphonium iodide with that prepared from phenyl-lithium and triphenyl-*p*-tolylphosphonium iodide.[16]

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[10] Dodonow and Medox, *Ber.*, 1928, **61**, 907; Willard, Perkins, and Blicke, *J. Amer. Chem. Soc.*, 1948, **70**, 737.

[11] Lyon and Mann, *J.*, 1942, 666.

[12] Horner and Hoffmann, *Chem. Ber.*, 1958, **91**, 45.

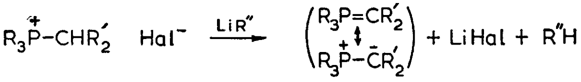
[13] *Idem, ibid.*, p. 50.

[14] Phillips, Hunter, and Sutton, *J.*, 1945, 146.

[15] Wittig and Rieber, *Annalen*, 1949, **562**, 187.

[16] Wittig and Geissler, *ibid.*, 1953, **580**, 44.

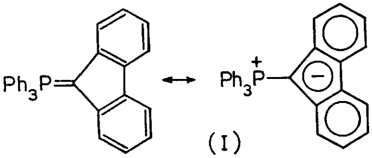
The preparation of tetraphenyl(triphenylmethyl)phosphorane from triphenyl(triphenylmethyl)phosphonium iodide and phenyl-lithium (but not from tetraphenylphosphonium iodide and triphenylmethylsodium) shows that it is not essential that all the C–P bonds in phosphoranes should involve aromatic carbon atoms.[16] Attempts to prepare phosphoranes of the form $R_4P{\cdot}CHR'_2$ have however been unsuccessful and have instead given compounds which may be written with a formal double bond between carbon and phosphorus.[17, 18] In fact, this bond appears to resemble the P=O double



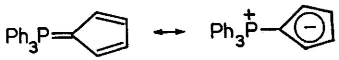
$$R_3\overset{+}{P}\text{–}CHR'_2\ \ Hal^- \xrightarrow{LiR''} \left(\begin{matrix} R_3P{=}CR'_2 \\ \updownarrow \\ R_3\overset{+}{P}\text{–}\overset{-}{C}R'_2 \end{matrix}\right) + LiHal + R''H$$

bond in having a considerable amount of dipolar character so that these compounds are best represented as resonance hybrids, as shown above. They are often referred to as phosphinemethylenes; although not mentioned in the new nomenclature scheme, they would appear to be more systematically called methylenephosphoranes.

Methylenephosphoranes are usually very reactive, being rapidly decomposed by air or moisture. This high reactivity is associated with the carbanionic centre in the dipolar structure and is decreased when the charge is dispersed by the attachment of phenyl or other electron-attracting groups to the methylenic carbon atom. Very stable methylenephosphoranes are known in which the methylenic carbon atom forms part of a *cyclo*pentadiene ring as in 9-fluorenylidenetriphenylphosphorane [19] (I) and triphenyl*cyclo*pentadienylidenephosphorane [20] (II). In these the instability normally associated with a carbanion is more than offset by the stabilisation arising from the extra aromatic ring.



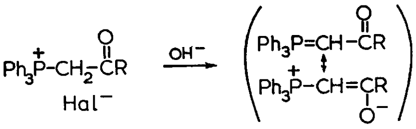
(I)



(II)

The dipole moment (7·0 D) of compound (II) indicates roughly equal contributions from the double-bonded and the dipolar structure.[20]

Stabilisation of methylenephosphoranes may also occur by mesomeric displacement of the negative charge to an oxygen atom, as in the compounds



(III)

$$Ph_3\overset{+}{P}\text{–}CH_2\text{–}\overset{\overset{\displaystyle O}{\|}}{C}R\ \ Hal^- \xrightarrow{OH^-} \left(\begin{matrix} Ph_3P{=}CH\text{–}\overset{\overset{\displaystyle O}{\|}}{C}R \\ \updownarrow \\ Ph_3\overset{+}{P}\text{–}CH{=}\underset{\underset{\displaystyle O^-}{|}}{C}R \end{matrix}\right)$$

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[17] Coffman and Marvel, *J. Amer. Chem. Soc.*, 1929, **51**, 3496.

[18] Wittig and Schollkopf, *Chem. Ber.*, 1954, **87**, 1318.

[19] Pinck and Hilbert, *J. Amer. Chem. Soc.*, 1947, **69**, 723.

[20] Ramirez and Levy, *ibid.*, 1957, **79**, 67.

(III) obtained by treatment with alkali of phenacyltriphenylphosphonium bromide and acetonyltriphenylphosphonium chloride.[18, 21] These compounds may be regarded as vinylogues of phosphine oxides.

Methylenephosphoranes which are not stabilised in any of the above ways react with carbonyl groups with the formation of carbon–carbon double bonds.[18] This, often referred to as the Wittig reaction, has been found synthetically useful both on a laboratory and an industrial scale, and has been reviewed.[22]

$$R_2CO + R''_3P{=}CR'_2 \longrightarrow R_2C{=}CR'_2 + R''_3PO$$

General Reactions for the Formation of Carbon–Phosphorus Bonds.—In this section some reactions, which are of particularly wide application or which have been more thoroughly investigated than those already mentioned, are discussed with regard to their general scope and to the reaction mechanisms involved. All of these general methods can be used, either directly or indirectly, for the preparation of phosphonic acids and their derivatives; that so many examples are of the synthesis of these compounds is an illustration of the pre-eminent position which they occupy amongst compounds containing carbon–phosphorus bonds.

(a) *Reactions in which the Phosphorus Atom acts as a Nucleophilic Centre.*—In these a phosphorus atom which is tervalent, or potentially so because of tautomerism (as in dialkyl phosphites), becomes quinquevalent with the establishment of a C–P bond. Since phosphorus cannot readily be reduced from the quinquevalent to the tervalent state these reactions cannot, in general, be used for forming several C–P bonds in one molecule. Compounds whose molecules contain more than one C–P bond (*e.g.*, phosphinic acids and their derivatives) may, however, be prepared by reactions of this type by starting with tervalent phosphorus compounds which already contain one or two C–P bonds.

(i) *The Arbusov reaction.* This reaction is the most completely investigated and one of the most widely used methods of forming C–P bonds.[23–26] Its simplest form is the reaction of an alkyl halide with a trialkyl phosphite to give a dialkyl alkylphosphonate, *e.g.*, the reaction of *n*-butyl bromide with triethyl phosphite to give diethyl *n*-butylphosphonate:

$$BuBr + P(OEt)_3 \longrightarrow Bu{\cdot}P(O)(OEt)_2 + EtBr$$

In general, the alkyl group of the halide becomes attached to the phosphorus atom and one of the alkyl groups from the trialkyl phosphite appears as alkyl halide. This by-product alkyl halide may compete with that used as starting material so that in the above example some diethyl ethylphos-

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[21] Michaelis and Kohler, *Ber.*, 1899, **32**, 1566; Ramirez and Dershowitz, *J. Org. Chem.*, 1957, **22**, 41.

[22] Levisalles, *Bull. Soc. chim. France*, 1958, 1021.

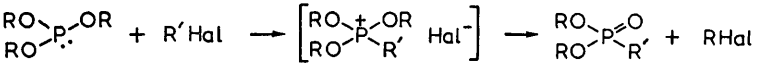
[23] A. E. Arbusov, *J. Russ. Phys. Chem. Soc.*, 1906, **38**, 687.

[24] Kosolapoff, *J. Amer. Chem. Soc.*, 1945, **67**, 1180.

[25] Ford-Moore and Williams, *J.*, 1947, 1465.

[26] Ford-Moore and Perry, *Org. Synth.*, 1951, **31**, 33.

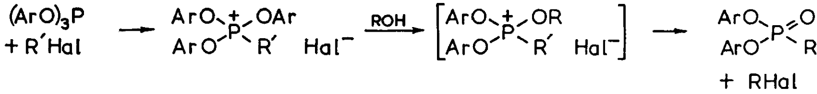
phonate would also be formed and would contaminate the product. Separation is usually easily effected by distillation and, unless the original alkyl halide is particular unreactive, the amount of contaminant is not unduly large. There is abundant evidence that the reaction, which is carried out by heating the reactants together at 120—160° for several hours, occurs in two stages: [27–29] the formation of an ionic intermediate and its subsequent decomposition, *viz.*,



The intermediate formation of these quasi-phosphonium compounds has been observed by changes in the refractive index and density of reaction mixtures [28] and by their isolation, in favourable cases, in crystalline form.[29, 30]

The Arbusov reaction may be written more generally as:

A and B may be primary alkoxy, secondary alkoxy, aryloxy, alkyl, aryl, or dialkylamino-groups. Since the reaction involves nucleophilic attack on RX by the unshared electrons of the phosphorus atom it is assisted if A and B are electron-repelling and hindered if they are electron-attracting groups, ease of reaction thus increasing in the order A, B = aryloxy < alkoxy < aryl < alkyl. For the reaction to proceed normally R should be aliphatic; if it is an aryl group the second stage, which involves nucleophilic attack by the ion X^- on the O–R bond, requires very strong heating, resulting in widespread decomposition. The quasi-phosphonium compounds obtained by reaction of alkyl halides with triaryl phosphites [30] may however be broken down by treatment with an alcohol. This causes rapid replacement of an aryloxy-group by an alkoxy-group which is then attacked by halide ion in the normal way:



This sequence of reactions provides a method for the preparation of some alkyl halides (*e.g.*, *neo*pentyl iodide) which are not otherwise readily accessible.[31]

Arbusov reactions on dialkyl aryl- and alkyl-phosphonites yield alkyl

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[27] Kosolapoff, *J. Amer. Chem. Soc.*, 1944, **66,** 109; Gerrard and Green, *J.*, 1951, 2550; Pudovik, *Doklady Akad. Nauk S.S.S.R.*, 1952, **84,** 519; B. A. Arbusov and Fuzhenkova, *ibid.*, 1957, **114,** 89.

[28] Abramov and Bol'shakova, *Zhur. obshchei Khim.*, 1957, **27,** 441.

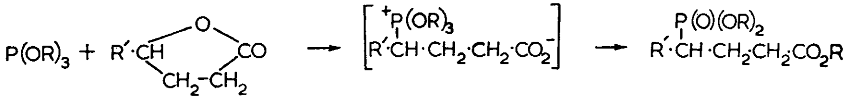
[29] Razumov and Bankovskaya, *Doklady Akad. Nauk S.S.S.R.*, 1957, **116,** 241.

[30] Michaelis and Kaehne, *Ber.*, 1898, **31,** 1048.

[31] Landauer and Rydon, *J.*, 1953, 2224.

alkylarylphosphinates $RArP(O){\cdot}OR'$ [32] and alkyl dialkylphosphinates $RR'P(O){\cdot}OR''$ [33] which have two different groups attached to the phosphorus atom and cannot therefore be obtained by reactions in which both C–P bonds are formed at the same time. Similarly, Arbusov reactions on alkyl dialkylphosphinites provide routes to tertiary phosphine oxides in which the organic radicals linked to the phosphorus atom are not all identical.[29, 34] Although reactions of these types proceed readily they have been little used because of the difficult accessibility of the starting materials.

Variations in the structure of $R''X$ are, from a preparative point of view, of much greater importance than those in the tervalent phosphorus compound, which is usually triethyl phosphite. The reaction is by no means confined to halides since dialkyl sulphates,[31] alkyl toluene-*p*-sulphonates,[35] and alkyl fluoroborates react similarly, whilst the reaction of trialkyl phosphites with lactones [36] is probably closely related:



In practice, however, the majority of Arbusov reactions involve halogen compounds and here it appears that virtually any halide which is capable of reacting with nucleophilic reagents by an S_N2 mechanism and does not contain potentially interfering groups (such as carbonyl or nitro) is suitable. Amongst alkyl halides the reaction only proceeds satisfactorily if R′ is a primary alkyl group but, contrary to an earlier report, long-chain primary alkyl halides react as well as those of lower molecular weight.[37] Aryl and vinyl halides are, of course, insufficiently reactive but allyl halides react normally [38] although isomerisation may cause difficulties in some cases.[39] Benzyl, diphenylmethyl, and triphenylmethyl halides all give the expected phosphonates,[40] as do halogenomethyl derivatives of condensed aromatic hydrocarbons [41] and of heterocyclic compounds.[42]

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[32] A. E. Arbusov and Razumov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1945, 167; Kamai, *Doklady Akad. Nauk S.S.S.R.*, 1947, **55**, 219; 1949, **66**, 389.

[33] B. A. Arbusov and Rizpolozhenskii, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1952, 854.

[34] A. E. Arbusov and Nikoronov, *Zhur. obshchei Khim.*, 1948, **18**, 2008.

[35] Myers, Preis, and Jensen, *J. Amer. Chem. Soc.*, 1954, **76**, 4172.

[36] McConnell and Coover, *ibid.*, 1956, **78**, 4453; Kreutzkamp, *Naturwiss.*, 1956, **43**, 81.

[37] Kosolapoff, *J. Amer. Chem. Soc.*, 1954, **76**, 615.

[38] A. E. Arbusov and Razumov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1951, 714.

[39] Pudovik and B. A. Arbusov, *ibid.*, 1949, 522.

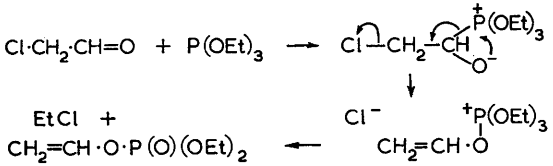
[40] A. E. Arbusov and B. A. Arbusov, *J. Russ. Phys. Chem. Soc.*, 1929, **61**, 217; Lugovkin and B. A. Arbusov, *Doklady Akad. Nauk S.S.S.R.*, 1948, **59**, 1301.

[41] B. A. Arbusov and Lugovkin, *Zhur. obshchei Khim.*, 1950, **20**, 1249.

[42] *Idem*, *ibid.*, 1951, **21**, 1869; 1952, **22**, 1193; B. A. Arbusov and Zoroastrova, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1954, 806.

Arbusov reactions of halogeno-ethers proceed normally, as do those of esters of 2-bromoethanol with aliphatic carboxylic acids.[43] The free phosphonic acids could not be obtained in the latter case because hydrolysis occurred more readily at the carboxylic ester linkage than at the phosphonic ester group. Acyl halides [44] and acid anhydrides [45] react readily with trialkyl phosphites, to give dialkyl acylphosphonates. Because of the weakness of the C–P bond in acylphosphonic acids they cannot be obtained from these esters by ordinary methods of hydrolysis although they may be prepared by dealkylation with dry hydrogen halides.[46] Esters of α-monochloro- and α-monobromo-monocarboxylic acids undergo normal Arbusov reactions with trialkyl phosphites, giving esters which can be hydrolysed to the free α-carboxyalkylphosphonic acids,[47] but halogeno-esters such as ethyl trichloroacetate and diethyl bromo- and dibromo-malonate, which have more than one halogen atom and one carboxyl group linked to the same carbon atom undergo anomalous reactions [48] like those of α-halogeno-aldehydes and -ketones, described below.

Trialkyl phosphites react readily with α-halogeno-aldehydes (exothermally without heating with chloral and bromal). The products do not contain C–P bonds but are unsaturated esters of phosphoric acid.[48, 49] The reaction appears to involve nucleophilic attack of the trialkyl phosphite on the carbonyl group, elimination of chloride ion, and dealkylation analogous to the second stage of the Arbusov reaction. Thus triethyl phosphite and chloroacetaldehyde give diethyl vinyl phosphate:



Formation of a solid intermediate was observed in the reaction of ethyl ethylene phosphite with chloral.[48]

α-Halogeno-ketones with trialkyl phosphites give both products of normal Arbusov reactions and anomalous products similar to those from α-halogeno-aldehydes. Unsaturated phosphates are the principal products from α-chloro-ketones whilst α-iodo-ketones give mainly phosphonates.[50, 51] The formation of phosphonates is also favoured by carrying out the reaction at high temperatures so that, whereas bromoacetone and triethyl phosphite

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[43] Ackerman, Jordan, and Swern, *J. Amer. Chem. Soc.*, 1956, **78**, 6025.

[44] Kabachnik and Rossiskaya, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1945, 364; Ackerman, Jordan, Eddy, and Swern, *J. Amer. Chem. Soc.*, 1956, **78**, 4444.

[45] Kamai and Kukhtin, *Zhur. obshchei Khim.*, 1957, **27**, 949.

[46] Cooke, Gerrard, and Green, *Chem. and Ind.*, 1953, 351.

[47] Ackerman, Chladek, and Swern, *J. Amer. Chem. Soc.*, 1957, **79**, 6524.

[48] Allen and Johnson, *ibid.*, 1955, **77**, 2871.

[49] Perkow, Krokow, and Knoevenagel, *Chem. Ber.*, 1955, **88**, 662.

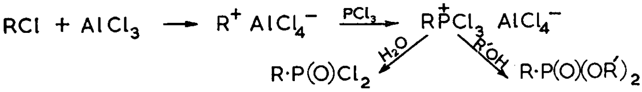
[50] Pudovik, *Doklady Akad. Nauk S.S.S.R.*, 1955, **105**, 735.

[51] Jacobson, Griffin, Preis, and Jensen, *J. Amer. Chem. Soc.*, 1957, **79**, 2608.

give largely diethyl *iso*propenyl phosphate in ether at a low temperature, at 150—160° diethyl acetonylphosphonate is the main product.[50]

Methylene and other dihalides react normally but less readily than alkyl halides in the Arbusov reaction, one or both halogen atoms being replaced according to the ratio of the reactants.[25] Chloroform does not react with triethyl phosphite even under drastic conditions,[52] but carbon tetrachloride does so at lower temperatures than are required for Arbusov reactions of alkyl halides and gives excellent yields of diethyl trichloromethylphosphonate.[53] This surprisingly ready reaction has been shown to proceed by a free-radical chain mechanism, being inhibited by quinol and accelerated by dibenzoyl peroxide at 80° and occurring at room temperature on exposure to ultraviolet radiation.[54]

(ii) *Formation of alkylphosphonic dichlorides from alkyl chlorides, phosphorus trichloride, and aluminium trichloride.* The nucleophilic character of the phosphorus atom in phosphorus trichloride, being decreased by the influence on the unshared electrons of the inductive effect of the chlorine atoms, is insufficient to enable it to attack alkyl chlorides and form alkylphosphonic tetrachlorides, $R{\cdot}PCl_4$, by a bimolecular mechanism (as occurs in the formation of the quasi-phosphonium intermediates in the Arbusov reaction). If, however, alkyl chlorides are added, with cooling and stirring, to mixtures of phosphorus trichloride and aluminium trichloride, crystalline complexes, which are probably alkyltrichlorophosphonium tetrachloroaluminates, are rapidly formed. On careful hydrolysis these complexes yield alkylphosphonic dichlorides[55, 56] whilst treatment with alcohols gives dialkyl alkylphosphonates:[57]



Evidence that carbonium ions are involved in these reactions is provided by the isomerisation and degradation which has been observed with some alkyl groups. Thus *n*-propyl, *n*-butyl, and *iso*butyl chloride gave *iso*propyl-, *sec.*-butyl-, and *tert.*-butyl-phosphonic dichloride[56] whereas *tert.*-amyl chloride yielded a mixture of *tert.*-butyl- and *tert.*-amyl-phosphonic dichlorides.[58] With these limitations this reaction provides a good route to many phosphonic dichlorides derived from alkyl, *cyclo*alkyl, and aralkyl chlorides and polychloroalkanes. The polychloroalkanes always yield chlorides of monophosphonic acids, which is to be expected since reaction of two chlorine atoms would require the formation of doubly charged carbonium ions.

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[52] Crofts and Kosolapoff, *J. Amer. Chem. Soc.*, 1953, **75**, 5738.

[53] Kamai and Egorova, *Zhur. obshchei Khim.*, 1946, **16**, 1521; Kosolapoff, *J. Amer. Chem. Soc.*, 1947, **69**, 1002.

[54] Griffin, *Chem. and Ind.*, 1958, 415.

[55] Clay, *J. Org. Chem.*, 1951, **16**, 892.

[56] Kinnear and Perren, *J.*, 1952, 3437.

[57] Hoffmann, Simmons, and Glunz, *J. Amer. Chem. Soc.*, 1957, **79**, 3570.

[58] Crofts and Kosolapoff, *ibid.*, 1953, **75**, 3379.

Alkylphenylphosphinic acids RPhP(O)·OH have been prepared by reaction of alkyl chlorides with phenylphosphonous dichloride, Ph·PCl_2, and aluminium trichloride followed by hydrolysis.[59]

(iii) *Reaction of diazonium salts with halides of tervalent phosphorus.* Reaction of aryldiazonium fluoroborates with phosphorus trichloride in a dry solvent (ethyl acetate or dioxan), in presence of cuprous chloride or bromide, followed by addition of water and steam-distillation to hydrolyse the products and remove the solvent, has proved a valuable general method for the synthesis of arylphosphonic acids.[60] Aryldiazonium fluorosilicates may be advantageously used instead of fluoroborates in some cases.[61]

Although yields are variable (10—70%) the reaction is useful because of its generality (few failures having been reported), the ready availability of a large number of aromatic amines and the known orientation of the products. The reaction mechanism does not appear to have been investigated, but presumably involves formation of an aryltrichlorophosphonium

$$Ar{\cdot}N_2^+\,BF_4^- + PCl_3 \longrightarrow N_2 + Ar{\cdot}PCl_3^+\,BF_4^- \xrightarrow{H_2O} Ar{\cdot}P(O)(OH)_2$$

fluoroborate. This may occur by nucleophilic attack of phosphorus trichloride on aryl cations formed by decomposition of the diazonium salt. Alternatively, the occurrence of an induction period followed by a rapid reaction suggests a chain-reaction involving aryl radicals:

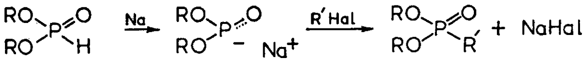
$$Ar{\cdot} + PCl_3 + Ar{\cdot}N_2^+ \longrightarrow Ar{\cdot}PCl_3^+ + N_2 + Ar{\cdot}$$

In many cases the diarylphosphinic acid is also formed, sometimes in quite considerable amounts. This presumably arises by an exchange reaction, resulting in the formation of arylphosphonous dichloride and reaction of this with more diazonium fluoroborate:

$$\begin{tikzcd}
Ar{\cdot}PCl_3^+\,BF_4^- + PCl_3 \arrow[r] & Ar{\cdot}PCl_2 + PCl_4^+\,BF_4^- \arrow[d, "Ar{\cdot}N_2^+\,BF_4^-"] \\
Ar_2P(O){\cdot}OH & Ar_2PCl_2^+\,BF_4^- + N_2 \arrow[l, "H_2O"']
\end{tikzcd}$$

By using alkyl- or aryl-phosphonous dichlorides instead of phosphorus trichloride, arylalkylphosphinic acids may be prepared.[62]

(iv) *The Michaelis reaction.* Alkali-metal derivatives of dialkyl phosphites react with alkyl halides to give dialkyl alkylphosphonates:[63]



Reactions of this type may be carried out with diethyl phosphite, dry ether being used as solvent, but nowadays dibutyl phosphite is more usually

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[59] Biddle, Kennedy, and Willans, *Chem. and Ind.*, 1957, 1481.

[60] Doak and Freedman, *J. Amer. Chem. Soc.*, 1951, **73**, 5658; 1952, **74**, 753; Ashby and Kosolapoff, *ibid.*, 1953, **75**, 4903; Freedman and Doak, *ibid.*, 1955, **77**, 173.

[61] *Idem, ibid.*, 1953, **75**, 4905.

[62] *Idem, ibid.*, 1952, **74**, 2884; *J. Org. Chem.*, 1958, **23**, 769.

[63] Michaelis and Becker, *Ber.*, 1897, **30**, 1003.

employed because of the high solubility of its sodium derivative in light petroleum and aromatic hydrocarbons which are more satisfactory as reaction media.[24] After completion of the reaction, under reflux for several hours, the sodium halide is removed by filtration or by washing with water, and the solution is distilled to give the phosphonate. Complete removal of sodium halide is important as otherwise undistillable sodium salts are formed on heating.

The Michaelis reaction has been used almost as widely as the Arbusov reaction for the preparation of esters of phosphonic acids. Its mechanism has not been investigated to the same extent but clearly involves a bimolecular nucleophilic attack on the alkyl halide by the mesomeric anion and resembles alkylation of diethyl malonate and ethyl acetoacetate.

Examples of the Michaelis reaction, are not confined to those involving dialkyl phosphites, but also include reactions of the sodium derivatives of monoalkyl aryl- and alkyl-phosphinates with alkyl halides to give alkyl alkylarylphosphinates $RArP(O)\cdot OR'$ [64] and alkyl dialkylphosphinates $RR'P(O)\cdot OR''$ [65] respectively. These routes to unsymmetrical phosphinic acids are, like analogous Arbusov reactions, hampered by the difficulties of preparing the phosphonites required as starting materials.

As with the Arbusov reaction, alkyl toluene-*p*-sulphonates [35] and dialkyl sulphates will react as well as halides, although in practice the latter are almost invariably used. The structural requirements for these are similar to, but generally somewhat more rigorous than, those in the Arbusov reaction because of the intervention of other reactions of the strongly basic and nucleophilic anion. Primary alkyl halides [24] and benzyl halides [66] (but not diphenylmethyl or triphenylmethyl halides) give good yields of phosphonates. Reactions of sodium dialkyl phosphites with allyl halides are complicated by the formation of diphosphonates by addition of dialkyl phosphite to the double bond,[39, 67] but by carrying out the reaction in a large volume of benzene or with free dialkyl phosphite present dialkyl allylphosphonates may be obtained as the sole products.[68]

Michaelis reactions have been used for the preparation of ω-aminoalkylphosphonic acids by reaction of sodium dibutyl phosphite with *N*-ω-bromoalkylphthalimides and hydrolysis of the undistilled products and also (preferably because it yields esters which may be purified by distillation) by reaction of ω-bromoalkylamine hydrobromides with two mols. of sodium dibutyl phosphite.[69]

Reactions of sodium dialkyl phosphites with α-halogeno-ketones do not give dialkyl 2-oxoalkylphosphonates, which would be expected from normal Michaelis reactions and are one of the products of interaction of trialkyl

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[64] Kosolapoff, *J. Amer. Chem. Soc.*, 1950, **72**, 4292.

[65] B. A. Arbusov and Rizpolozhenskiĭ, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1955, 253.

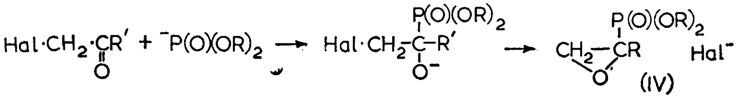
[66] Kosolapoff, *J. Amer. Chem. Soc.*, 1945, **67**, 2259.

[67] Rueggeberg. Chernak, and Rose, *ibid.*, 1950, **72**, 5336; Schwarzenbach, Ruckstuhl, and Zurc, *Helv. Chim. Acta*, 1951, **34**, 455.

[68] Pudovik and Frolova, *Zhur. obshchei Khim.*, 1952, **22**, 2052.

[69] Chavane, *Compt. rend.*, 1947, **224**, 406.

phosphites and α-halogeno-ketones. Sodium diethyl phosphite and chloroacetone have been reported [70] to yield diethyl *iso*propenyl phosphate (the abnormal product from the reaction of triethyl phosphite and chloroacetone), but B. A. Arbusov and his co-workers [71] have found that the products of these and similar reactions are dialkyl 1 : 2-epoxyalkylphosphonates (IV) which they suggest are formed by attack of the dialkyl phosphite anion on the carbonyl group followed by formation of the epoxide ring with expulsion of chloride ion:



The first stage is similar to that proposed (see p. 350) for the formation of anomalous products in reactions of trialkyl phosphites with α-halogeno-aldehydes and -ketones. That the negatively charged oxygen atom forms a bond to phosphorus in the anomalous Arbusov reaction and to the α-carbon atom in the anomalous Michaelis reaction is presumably due to the positive charge which is present on the phosphorus atom in the former but not in the latter case.

(v) *Reactions of aldehydes and ketones with chlorides of tervalent phosphorus.* When aldehydes (1 mol.) are heated with phosphorus trichloride (1—1·5 mols.) at about 200° for several hours, α-chloro-phosphonic dichlorides are formed.[72, 73] The reaction proceeds well with most aromatic aldehydes and with formaldehyde, but gives poor results with other aliphatic aldehydes because of ready elimination of hydrogen chloride from the products. Similar reactions occur with other tervalent phosphorus chlorides, including diaryl phosphorochloridites, alkyl- and aryl-phosphonous dichlorides, and diarylphosphinous chlorides.[72, 74]

In addition to these high-temperature reactions, α-hydroxyalkylphosphonic acids may be prepared (at room temperature or slightly above) from phosphorus trichloride by reaction either with three mols. of an aldehyde followed by water,[75] or with one mol. of an aldehyde or ketone followed by addition of glacial acetic acid and subsequent hydrolysis:[76]

(vi) *Addition of compounds containing* P–H *bonds to carbonyl and imino-groups.* Aldehydes react with phosphine in presence of hydrogen chloride to give tetra-(α-hydroxyalkyl)-phosphonium chlorides:[77]

$$\mathrm{PH_3 + 4R{\cdot}CHO + HCl \longrightarrow [R{\cdot}CH(OH)]_4P^+Cl^-}$$

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[70] Krentzkamp and Kayser, *Chem. Ber.*, 1956, **89**, 1614.

[71] B. A. Arbusov, Vinogradova, and Polezhayeva, *Doklady Akad. Nauk S.S.S.R.*, 1956, **111**, 107; B. A. Arbusov, *Chem. Soc. Special Publ. No.* 8, 1957, p. 47.

[72] Kabachnik and Shepeleva, *Doklady Akad. Nauk S.S.S.R.*, 1950, **75**, 219.

[73] *Idem, Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1950, 39; 1951, 185.

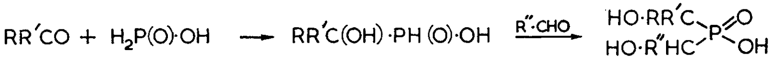
[74] *Idem, ibid.*, 1953, 862.

[75] Fossek, *Monatsh.*, 1884, **5**, 121; 1886, **7**, 20; Page, *J.*, 1912, **101**, 423.

[76] Conant, MacDonald, and Kinney, *J. Amer. Chem. Soc.*, 1921, **43**, 1928.

[77] de Girard, *Ann. Chim. Phys.*, 1884, **2**, 1; Reeves, Flynn, and Guthrie, *J. Amer. Chem. Soc.*, 1955, **77**, 3923.

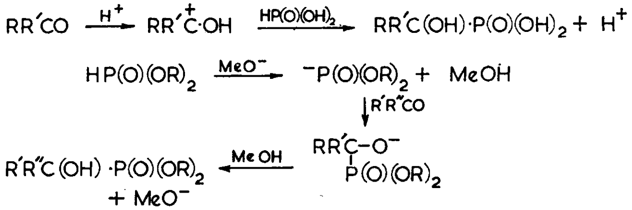
Similarly, reaction of aldehydes and ketones occurs with phosphorous acid, giving α-hydroxyalkylphosphonic acids, and more readily with hypophosphorous acid, giving α-hydroxylalkyl- and di-(α-hydroxyalkyl)-phosphinic acids.[78] In reactions with hypophosphorous acid it is possible to isolate the product of the first addition and, by reaction with a different aldehyde or ketone, to prepare an unsymmetrical di-(α-hydroxyalkyl)-phosphinic acid:



$$RR'CO + H_2P(O)\cdot OH \longrightarrow RR'C(OH)\cdot PH(O)\cdot OH \xrightarrow{R''\cdot CHO} \begin{matrix} HO\cdot RR'C \\ HO\cdot R''HC \end{matrix} P \begin{matrix} {}^{\nearrow}O \\ {}_{\searrow}OH \end{matrix}$$

All these reactions require several days for completion and involve rather tedious separations of the water-soluble acids. In contrast to these slow reactions, dialkyl phosphites react rapidly and exothermally with aldehydes and ketones, on addition of a few drops of sodium methoxide in methanol, to give dialkyl α-hydroxyalkylphosphonates.[79]

The reactions of phosphorous (and hypophosphorous) acid, and of dialkyl phosphites, with carbonyl groups are similar to acid-catalysed and base-catalysed aldol reactions and, like these and other additions to carbonyl groups, are reversible. The acids are more stable than the esters, being unaffected by alkali, and reasonably stable towards acids, so that they may be obtained by acid-hydrolysis of the esters; they are, however, hydrolysed to the carbonyl compound and phosphorous acid by prolonged boiling with strong acids. The esters, on the other hand, are readily decomposed by dilute sodium hydroxide [80] or sometimes (with bulky carbonyl compounds) on attempted distillation.[81]



$$RR'CO \xrightarrow{H^+} RR'\overset{+}{C}\cdot OH \xrightarrow{HP(O)(OH)_2} RR'C(OH)\cdot P(O)(OH)_2 + H^+$$

$$HP(O)(OR)_2 \xrightarrow{MeO^-} {}^-P(O)(OR)_2 + MeOH \;\; \xrightarrow{R'R''CO} \;\; \begin{matrix} RR'C{-}O^- \\ | \\ P(O)(OR)_2 \end{matrix} \xrightarrow{MeOH} \begin{matrix} R'R''C(OH)\cdot P(O)(OR)_2 \\ + MeO^- \end{matrix}$$

Addition reactions of compounds with P–H bonds, similar to both the above acid-catalysed and base-catalysed types, take place with carbon–nitrogen double bonds in anils. Thus hypophosphorous acid reacts with anils (or with primary amines together with an aldehyde or ketone), to give substituted α-aminoalkylphosphinic acids:[82]

$$R'R''C{=}NR + H_2P(O)\cdot OH \longrightarrow R'R''C(NHR)\cdot PH(O)\cdot OH$$

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[78] Ville, *Ann. Chim. Phys.*, 1891, **23**, 289; Marie, *ibid.*, 1904, **3**, 35.

[79] Abramov, *Zhur. obshchei Khim.*, 1952, **22**, 647, and numerous other papers by Abramov *et al.*

[80] Abramov, Semenova, and Semenova, *Doklady Akad. Nauk S.S.S.R.*, 1952, **84**, 281.

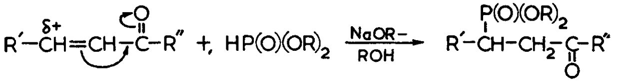
[81] Abramov and Semenova, *Sbornik Statey po obshchei Khim.*, 1953, **1**, 393.

[82] Schmidt, *Chem. Ber.*, 1948, **81**, 477.

whilst base-catalysed additions of dialkyl phosphites to anils yield *N*-monosubstituted dialkyl α-aminoalkylphosphonates.[83, 84] These, and *NN*-disubstituted or unsubstituted esters, may also be prepared [83, 85] by reaction of a dialkyl phosphite with an aldehyde or ketone and a primary or secondary amine or ammonia in Mannich-type reactions [86] which are unusual in that the carbonyl compound need not be formaldehyde.

Examples, using less common starting materials, of the reactions considered in this section are those of dialkylphosphine oxides with aldehydes and ketones, giving dialkyl-α-hydroxyalkylphosphine oxides,[87] and those of alkyl alkyl- and aryl-phosphinates with anils [88] and with ammonia and aldehydes or ketones.[89]

(vii) *Nucleophilic addition of compounds containing* P–H *bonds to activated double bonds.* These reactions are 3 : 4-additions corresponding to some of the 1 : 2-additions described in the previous section. The discovery that dialkyl phosphites are able to add to carbon–carbon double bonds activated by electron-withdrawing groups was made as a result of attempted Michaelis reactions of allyl halides, which yielded esters of diphosphonic acids instead of dialkyl allylphosphonates.[39, 67] These additions are complicated by allylic shifts resulting in the formation of both 1 : 2- and 1 : 3-diphosphonates;[68] more straightforward and synthetically more useful reactions are the additions of dialkyl phosphites to αβ-unsaturated ketones, esters, and nitriles. These have been extensively investigated by Pudovik and his co-workers [90, 91] and are analogous to Michael reactions. They are carried out by addition to the reactants of a few drops of an alcoholic sodium alkoxide solution (having the same alkyl group as in the dialkyl phosphite in order to avoid interchange) followed by distillation. Yields vary, but are often around 70%. The phosphonic acid group enters the β-position [92] as would be expected of attack by a dialkyl phosphite anion:



$$R'{-}\overset{\delta+}{C}H{=}CH{-}\overset{O}{\overset{\|}{C}}{-}R'' + HP(O)(OR)_2 \xrightarrow[ROH]{NaOR} R'{-}\overset{P(O)(OR)_2}{\overset{|}{C}H}{-}CH_2{-}\underset{O}{\underset{\|}{C}}{-}R''$$

Substituents, particularly if attached to the β-carbon atom, make reaction more difficult [93] and may lead to addition at the carbonyl group rather than at the olefinic double bond.[91] This also occurs with αβ-unsaturated aldehydes which yield αβ-unsaturated α-hydroxyalkylphosphonates instead of β-oxoalkylphosphonates.[91, 94]

[83] Fields, *J. Amer. Chem. Soc.*, 1952, **74,** 1528.

[84] Pudovik, *Doklady Akad. Nauk S.S.S.R.*, 1952, **83,** 865.

[85] Chalmers and Kosolapoff, *J. Amer. Chem. Soc.*, 1953, **75,** 5278.

[86] Blicke, *Organic Reactions*, 1942, **1,** 303.

[87] Miller, Miller, Rogers, and Hamilton, *J. Amer. Chem. Soc.*, 1957, **79,** 424.

[88] Pudovik, *Doklady Akad. Nauk S.S.S.R.*, 1953, **92,** 773.

[89] Kabachnik and Medved, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk,* 1954, 1024.

[90] Pudovik and B. A. Arbusov, *Doklady Akad. Nauk S.S.S.R.*, 1950, **73,** 327.

[91] Pudovik, *ibid.*, p. 499.

[92] Pudovik and B. A. Arbusov, *Zhur. obshchei Khim.*, 1951, **21,** 382.

[93] Pudovik, *ibid.*, 1952, **22,** 1371.

[94] Pudovik and Kitaev, *ibid.*, p. 467

Other compounds with P–H bonds take part in similar reactions. Thus alkyl alkyl- and aryl-phosphinates [95] and dialkylphosphine oxides [96] add to unsaturated ketones, esters, and nitriles. The only reported reactions of this type involving tervalent phosphorus compounds are those of phenylphosphine and diphenylphosphine with acrylonitrile when the reactants are heated, without a catalyst, at 130° for 6—7 hours: [97]

$$\mathrm{Ph{\cdot}PH_2 + 2CH_2{=}CH{\cdot}CN \rightarrow Ph{\cdot}P(CH_2{\cdot}CH_2{\cdot}CN)_2}$$

(b) *Reactions in which the Phosphorus Atom acts as an Electrophilic Centre.* These reactions, in which atoms and groups attached to phosphorus are replaced by organic groups by reactions with organometallic compounds, aromatic hydrocarbons, or olefins, mostly involve phosphorus halides. They provide methods for the formation of C–P bonds in many types of compounds and include the majority of reactions for the formation of bonds between carbon and tervalent phosphorus atoms.

(i) *Reactions involving organometallic compounds.* Interaction of phosphorus halides and of some other compounds with metal alkyls and aryls provides routes to many classes of compounds containing C–P bonds. Grignard reagents have been most frequently used. When they (or organolithium compounds) are present in excess their reactions with phosphorus trichloride and oxychloride result in replacement of all three chlorine atoms and the formation of trialkyl(or triaryl)-phosphines and -phosphine oxides. Unsymmetrical compounds of these types can be prepared by reactions of phosphorus chlorides which already contain C–P bonds with a Grignard reagent containing a different group.[98] The products are isolated after

$$\mathrm{R{\cdot}PCl_2 + 2R'{\cdot}MgCl \rightarrow RR'_2P + 2MgCl_2}$$

decomposition in the usual way, care being taken to avoid oxidation when working with phosphines. Yields are usually good if aryl or primary alkyl groups are being introduced, but reactions of secondary alkylmagnesium halides with phosphorus trichloride give only poor yields of tri-*sec.*-alkylphosphines.[99]

Reactions of organometallic compounds resulting in incomplete replacement of halogen atoms attached to phosphorus and the formation of compounds containing only one or two C–P bonds may be achieved in several ways. With bulky groups the extent of substitution appears to be limited by steric hindrance, and dialkylphosphinic acids have been prepared by reactions of *tert.*-butyl- and *iso*propyl-magnesium chloride with *tert.*-butylphosphonic chloride followed by hydrolysis.[58, 100] Attempts to limit the

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[95] Pudovik *et al.*, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1952, 902; 1954, 636; *Zhur. obshchei Khim.*, 1954, **24**, 1026; 1955, **25**, 778.

[96] Miller, Bradley, and Hamilton, *J. Amer. Chem. Soc.*, 1956, **78**, 5299.

[97] Mann and Millar, *J.*, 1952, 4453.

[98] Davies and Walters, *J.*, 1935, 1786; Davies and Mann, *J.*, 1944, 276; Morrison, *J. Amer. Chem. Soc.*, 1950, **72**, 4820.

[99] Davies, *J.*, 1933, 1043.

[100] Crofts and Fox, *J.*, 1958, 2995.

number of chlorine atoms replaced by employing "reversed addition" *i.e.*, by adding the Grignard reagent to the phosphorus halide, have given only poor yields of alkylphosphonic and dialkylphosphinic chlorides from phosphorus oxychloride and methyl- or ethyl-magnesium halides[101] but have been more successful in reactions involving aromatic Grignard reagents.[102,103]

For the preparation of phosphonous dichlorides, $R{\cdot}PCl_2$, the usual method has been to employ less reactive organometallic compounds. Organomercury compounds were the first to be used[104] but difficulties in obtaining completely mercury-free products have been reported and organic derivatives of other metals are now preferred. Excellent yields of ethyl phosphonous dichloride may be obtained by using tetraethyl-lead.[105] This and other phosphonous dichlorides can also be prepared in moderate yields by reaction of phosphorus trichloride with organo-cadmium[106] and -zinc compounds,[107] which are readily available from Grignard reagents and cadmium or zinc chloride.

$$PbEt_4 + 3PCl_3 \longrightarrow 3Et{\cdot}PCl_2 + PbCl_2 + EtCl$$

Diarylphosphinous chlorides, Ar_2PCl, have been prepared by the use of aryl-mercury[108] and -zinc compounds,[109] but most preparations of these and of dialkylphosphinous chlorides have been, not by this route, but by thermal decomposition of tertiary phosphine dichlorides (see p. 363).[110]

Limitation of the extent of substitution in reactions of organometallic compounds can also be achieved by the use of less reactive phosphorus halides. Phosphorus–fluorine bonds are less easily attacked by nucleophilic reagents than are phosphorus–chlorine bonds so that reaction of an alkylphosphonic difluoride with Grignard reagents may be used for the preparation of unsymmetrical dialkylphosphinic acids:[111]

$$R{\cdot}P(O)F_2 + R'MgHal \longrightarrow RR'P(O)F \longrightarrow RR'P(O){\cdot}OH$$

Reactions of thiophosphoryl chloride with alkylmagnesium halides result largely in disubstitution.[112] With methylmagnesium halides, tetramethyldiphosphine disulphide, a peculiar insoluble compound, is formed.[113] Oxida-

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[101] Jean *Bull. Soc. chim. France*, 1956, 569.

[102] Kosolapoff, *J. Amer. Chem. Soc.*, 1942, **64**, 2982.

[103] Burger and Dawson, *J. Org. Chem.*, 1951, **16**, 1250.

[104] Michaelis, *Ber.*, 1880, **13**, 2174; Guichard, *Ber.*, 1899, **32**, 1572.

[105] Kharasch, Jensen, and Weinhouse, *J. Org. Chem.*, 1949, **14**, 429.

[106] Fox, *J. Amer. Chem. Soc.*, 1950, **72**, 4147.

[107] Weil, Prijs, and Erlenmeyer, *Helv. Chim. Acta*, 1952, **35**, 1412.

[108] Michaelis, *Annalen*, 1901, **315**, 43.

[109] Weil, *Helv. Chim. Acta*, 1954, **37**, 654.

[110] Collie and Reynolds, *J.*, 1915, **107**, 367; Plets, Dissertation, Kazan, 1938, quoted in ref. 1, p. 57.

[111] Dawson and Kennard, *J. Org. Chem.*, 1957, **22**, 1671.

[112] Strecker and Grossman, *Ber.*, 1916, **49**, 63.

[113] Kabachnik and Shepeleva, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1949, 56.

tion of this, or of the products from similar reactions, yields dialkylphosphinic acids:[113, 114]

$$\mathrm{Me{\cdot}MgHal \xrightarrow{PSCl_3} Me_2P(S){\cdot}P(S)Me_2 \xrightarrow{[O]} 2Me_2P(O){\cdot}OH}$$

Another general route for the preparation of symmetrical dialkylphosphinic acids is reaction of dialkyl phosphites with Grignard reagents or organolithium compounds, and oxidation (with hydrogen peroxide or by reaction with phosphorus pentachloride followed by hydrolysis) of the resultant dialkyl- or diaryl-phosphine oxides.[115–117] Many of these intermediates have been isolated and characterised.[116]

$$\mathrm{HP(O)(OR)_2 + 2R'{\cdot}MgHal \longrightarrow R'_2HP(O) \longrightarrow R'_2P(O){\cdot}OH}$$

A general method for restricting the extent of substitution in reactions of Grignard reagents with phosphorus chlorides is the blocking of one or two of the positions by replacement of the chlorine atoms by unreactive groups which can subsequently be removed. Alkoxy- or aryloxy-groups are not generally satisfactory as they are replaced almost as readily as chlorine atoms,[117, 118] unless the Grignard reagent is sterically hindered,[103] but dialkylamino-groups are very effective for this purpose.[118, 119] Symmetrical phosphinic acids may be prepared by blocking one of the positions in phosphorus oxychloride:

$$\mathrm{POCl_3 \longrightarrow P(O)(NR'_2)Cl_2 \longrightarrow R_2P(O){\cdot}NR'_2 \longrightarrow R_2P(O){\cdot}OH}$$

and unsymmetrical dialkylphosphinic acids have been obtained by similar reactions starting with alkylphosphonic dichlorides.[100]

Blocking of one position in phosphorus trichloride has been used for the preparation of dimethylphosphinous chloride, [120] the dimethylamino-group being replaced in this case by reaction with dry hydrogen chloride at a low temperature:

$$\mathrm{PCl_3 \longrightarrow PCl_2{\cdot}NMe_2 \longrightarrow Me_2P{\cdot}NMe_2 \longrightarrow Me_2PCl}$$

(ii) *Aromatic substitution by phosphorus halides, oxides, and sulphides.* Phenylphosphonous dichloride can be conveniently prepared by heating the mixed vapours of benzene and phosphorus trichloride,[121] but similar reactions with other aromatic hydrocarbons do not give useful results. Friedel–Crafts reactions of aromatic compounds with phosphorus trichloride and

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[114] Kosolapoff and Watson, *J. Amer. Chem. Soc.*, 1951, **73**, 5466; Fox, Thesis, Manchester, 1957.

[115] Kosolapoff and Watson, *J. Amer. Chem. Soc.*, 1951, **73**, 4101.

[116] Williams and Hamilton, *ibid.*, 1952, **74**, 5418; 1955, **77**, 3411.

[117] Willans, *Chem. and Ind.*, 1957, 235.

[118] Michaelis and Wegner, *Ber.*, 1915, **48**, 316.

[119] Kosolapoff, *J. Amer. Chem. Soc.*, 1949, **71**, 369.

[120] Burg and Slota, *ibid.*, 1958, **80**, 1107.

[121] Michaelis, *Ber.*, 1873, **6**, 601; Bowles and James, *J. Amer. Chem. Soc.*, 1929, **51**, 1406.

aluminium trichloride provide, however, a method of preparing arylphosphonous dichlorides which is generally applicable to aromatic hydrocarbons, halides, ethers, and tertiary amines, but not to compounds which contain *meta*-directing groups.[122] The yields of products isolated were originally very low because of the formation of complexes with aluminium chloride, but have been increased to about 70% after the discovery that these complexes may be broken down, on completion of the reaction (2—8 hours under reflux with stirring), by the addition of phosphorus oxychloride which forms a stronger complex with aluminium chloride and thus liberates the arylphosphonous dichloride.[123] The main products from monosubstituted

$$\mathrm{ArH + PCl_3 \xrightarrow{AlCl_3} Ar{\cdot}PCl_2,AlCl_3 \xrightarrow{POCl_3} Ar{\cdot}PCl_2 + POCl_3,AlCl_3}$$

benzenes are the *para*-compounds although some *ortho*- and *meta*-substitution has also been reported.[124] An alternative to the above isolation procedure, useful when arylphosphonic acids or their esters are ultimately required, is chlorination followed by reaction with ethanol and distillation of the resulting diethyl arylphosphonate:[125]

$$\mathrm{Ar{\cdot}PCl_2\,AlCl_3 \xrightarrow{Cl_2} Ar{\cdot}PCl_4,AlCl_3 \xrightarrow{EtOH} Ar{\cdot}P(O)(OEt)_2}$$

Prolonged heating in Friedel-Crafts reactions of phosphorus trichloride leads to the formation of diarylphosphinous chlorides. These have not been isolated as such but have been converted into ethyl diarylphosphinites by the above procedure.[125]

Formation of C–P bonds also occurs on reaction of phosphorus pentasulphide and phosphorus pentoxide with aromatic compounds. Phosphorus pentasulphide and excess of benzene react, in presence of aluminium chloride, at the boiling point, to give an 80% yield of diphenylphosphinodithioic acid: [126]

$$\mathrm{8PhH + P_4S_{10} \longrightarrow 4Ph_2P(S){\cdot}SH + 2H_2S}$$

Benzene, *o*-xylene, anisole, phenetole, naphthalene, and 2-*iso*propylnaphthalene also react with phosphorus pentasulphide in the absence of aluminium trichloride,[127] although considerably higher temperatures (150—225°) are required and only one aryl group becomes attached to each phosphorus atom. It is suggested that the products, which have the empirical formula $\mathrm{Ar{\cdot}PS_2}$ and are found to be dimeric by cryoscopic measurements, have structures of the type (V). Reaction with chlorine yields first arylphosphonothioic dichlorides and then arylphosphonic tetrachlorides; prolonged hydrolysis gives arylphosphonic acids.

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[122] Michaelis, *Annalen*, 1896, **293,** 193; **294,** 1; 1901, **315,** 43.

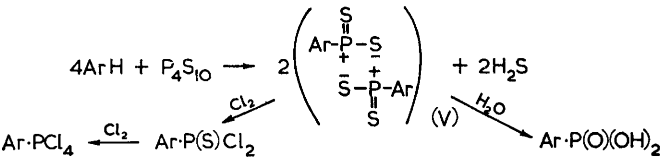
[123] Dye, *J. Amer. Chem. Soc.*, 1948, **70,** 2595; Buchner and Lockhart, *ibid.*, 1951, **73,** 755; *Org. Synth.*, 1951, **31,** 88.

[124] Kosolapoff, *J. Amer. Chem. Soc.*, 1952, **74,** 4119.

[125] Kosolapoff and Huber, *ibid.*, 1947, **69,** 2020.

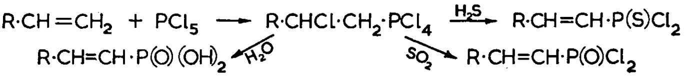
[126] Higgins, Vogel, and Craig, *ibid.*, 1955, **77,** 1864.

[127] Lecher, Greenwood, Whitehouse, and Chao, *ibid.*, 1956, **78,** 5018.



Reaction of aromatic compounds (benzene, *o*-xylene, chlorobenzene, and naphthalene) with phosphorus pentoxide at 250—325° yields pitch-like materials which give arylphosphonic acids on hydrolysis.[128] The reaction is of great interest but is not, at present, a useful preparative method.

(iii) *Addition of phosphorus pentachloride to olefins and acetylenes.* Phosphorus pentachloride adds to olefins which have a terminal methylene group, giving 2-chloroalkylphosphonic tetrachlorides. These readily lose hydrogen chloride and yield on hydrolysis $\alpha\beta$-unsaturated alkylphosphonic acids.[129] The reaction is usually carried out by adding an olefin to a cooled suspension of phosphorus pentachloride in benzene and keeping the mixture overnight. Hydrolysis of the adduct then yields an alkenylphosphonic acid; treatment with sulphur dioxide or with hydrogen sulphide gives an alkenylphosphonic dichloride [130] or an alkenylphosphonothioic dichloride [131] respectively.



Terminal acetylenic compounds with phosphorus pentachloride form similar adducts which are hydrolysed without elimination of hydrogen chloride:[132]

$$\mathrm{R{\cdot}C{\equiv}CH + PCl_5 \longrightarrow R{\cdot}CCl{=}CH{\cdot}PCl_4 \xrightarrow{H_2O} R{\cdot}CCl{=}CH{\cdot}P(O)(OH)_2}$$

(c) *Free-radical Reactions.*—Although many oxidation reactions of tervalent phosphorus compounds undoubtedly involve free radicals, reactions of this type are of relatively minor importance for the formation of C—P bonds. Some examples have already been noted, *e.g.*, some reactions for the formation of tetra-arylphosphonium salts, [10, 12, 13] Arbusov reactions involving carbon tetrachloride,[54] and possibly the formation of arylphosphonic acids *via* aryldiazonium fluoroborates (see p. 352); only two more reaction types, oxidative phosphonation and free-radical additions to unsaturated compounds, justify further discussion.

(i) *Reactions of organic compounds with oxygen and chlorides of tervalent phosphorus.* Alkylphosphonic dichlorides are formed by reactions which may be represented by the oversimplified equation:

$$\mathrm{RH + PCl_3 + \tfrac{1}{2}O_2 \longrightarrow R{\cdot}P(O)Cl_2 + HCl}$$

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[128] Lecher, Chao, Whitehouse, and Greenwood, *J. Amer. Chem. Soc*, 1954, **76**, 1045.

[129] Bergmann and Bondi, *Ber.*, 1931, **64**, 1455; Kosolapoff and Huber, *J. Amer. Chem. Soc.*, 1946, **68**, 2540.

[130] Anisimov and Nesmeyanov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1954, 610.

[131] Anisimov, Kolabova, and Nesmeyanov, *ibid.*, p. 796.

[132] Bergmann and Bondi, *Ber.*, 1933, **66**, 278.

when oxygen is passed through mixtures of phosphorus trichloride and saturated hydrocarbons.[133, 134] Because part of the phosphorus trichloride is simply oxidised to phosphorus oxychloride it is usual to employ an excess of this reactant but even so yields, calculated on the hydrocarbon, rarely exceed 30%. Usually oxygen is passed into the phosphorus trichloride–hydrocarbon mixture until the initial temperature rise subsides. Single products are only obtained from hydrocarbons such as ethane,[135] *neo*pentane,[136] *cyclo*hexane,[133] and *cyclo*pentane [137] in which all the hydrogen atoms are identically situated; in other cases a mixture of all possible isomeric products is obtained. As in other radical reactions tertiary carbon atoms are most easily attacked and primary carbon atoms are least reactive.[138] It has been suggested that the initial process is formation of a peroxide-like diradical which can then react in either of two ways:

$$\begin{aligned} Cl_3P{:} + O_2 &\longrightarrow Cl_3\dot{P}\text{-}O\text{-}O\cdot \\ Cl_3\dot{P}\text{-}O\text{-}O\cdot + PCl_3 &\longrightarrow 2POCl_3 \\ Cl_3\dot{P}\text{-}O\text{-}O\cdot + RH + PCl_3 &\longrightarrow POCl_3 + R{\cdot}P(O)Cl_2 + HCl \end{aligned}$$

the last equation representing several consecutive stages.[135, 138] Benzene does not react, but toluene and ethylbenzene are attacked in the side-chain.[136] Reaction occurs with alkyl chlorides (*n*-butyl chloride giving all four possible chlorobutylphosphonic dichlorides) and with ethers, although in the latter case cleavage at the oxygen atom also occurs.[138] By using methyl-, ethyl-, and phenyl-phosphonous dichloride instead of phosphorus trichloride, phosphinic chlorides RR′P(O)Cl have been prepared.[139]

Olefins and acetylenes also react when oxygen is passed through mixtures of these hydrocarbons with phosphorus trichloride, the overall reactions in these cases corresponding to addition of phosphorus oxychloride across the double or triple bond. Free-radical mechanisms may also be involved here, as is suggested by the formation of both 1 : 1- and 1 : 2-dichloroethylphosphonic dichloride from vinyl chloride; [140] with acetylenes, however, the phosphonic dichlorides obtained are single compounds identical with those obtained from reactions of the same acetylenes with phosphorus pentachloride.[141]

(ii) *Free-radical addition reactions of phosphorus compounds to olefinic bonds.* Addition of phosphorus compounds to carbon–carbon double bonds may occur by free-radical mechanisms as well as by those in which the phosphorus atom acts as a nucleophilic or electrophilic centre. Most of the

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[133] Clayton and Jensen, *J. Amer. Chem. Soc.*, 1948, **70**, 3880.

[134] Soborovskii, Zinov'ev, and Englin, *Doklady Akad. Nauk S.S.S.R.*, 1949, **67**, 293.

[135] Graf, *Chem. Ber.*, 1952, **85**, 9.

[136] Jensen and Noller, *J. Amer. Chem. Soc.*, 1949, **71**, 2384.

[137] Isbell and Wadsworth, *ibid.*, 1956, **78**, 6042.

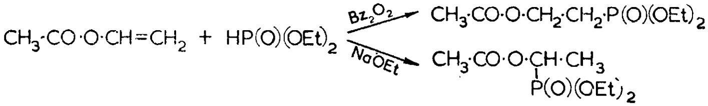
[138] Soborovskii, Zinov'ev, and Englin, *Doklady Akad. Nauk S.S.S.R.*, 1950, **73**, 333.

[139] Soborovskii and Zinov'ev, *Zhur. obshchei Khim.*, 1954, **24**, 516; Zinov'ev and Soborovskii, *ibid.*, 1956, **26**, 3030.

[140] Soborovskii, Zinov'ev, and Muler, *Doklady Akad. Nauk S.S.S.R.*, 1956, **109**, 98.

[141] Zinov'ev, Muler, and Soborovskii, *Zhur. obshchei Khim.*, 1954, **24**, 380.

reactions initiated by peroxides or by ultraviolet irradiation have involved compounds with P–H bonds, but phosphorus trichloride has also been found to undergo peroxide-induced addition to olefins, the product from oct-1-ene being 2-chloro-octylphosphonous dichloride.[142] The same direction of addition, phosphorus becoming attached to the terminal carbon atom, has been found for additions of phosphine [143] and hypophosphorous acid [144] to olefins, and of diethyl phosphite to *iso*propenyl acetate [145] and to vinyl acetate.[146] In the last case addition occurs in the opposite direction to the base-catalysed reaction of the same compounds :



$$CH_3{\cdot}CO{\cdot}O{\cdot}CH{=}CH_2 + HP(O)(OEt)_2 \xrightarrow{Bz_2O_2} CH_3{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}P(O)(OEt)_2$$

$$CH_3{\cdot}CO{\cdot}O{\cdot}CH{=}CH_2 + HP(O)(OEt)_2 \xrightarrow{NaOEt} CH_3{\cdot}CO{\cdot}O{\cdot}\underset{P(O)(OEt)_2}{\underset{|}{C}H}{\cdot}CH_3$$

Reactions of Compounds containing Carbon–Phosphorus Bonds.—These reactions are of three types; those which result in the breaking of C–P bonds, those involving other atoms or groups directly attached to phosphorus, and those which occur at points remote from the phosphorus atom but are affected by it.

Cleavage of Carbon–Phosphorus Bonds.—Reactions of this type are relatively uncommon. Carbon–phosphorus bonds are comparable in strength to carbon–carbon bonds and are only broken under drastic conditions or when particularly weakened by their environment. Because of this, powerful reagents may generally be used for bringing about interconversions of compounds which contain C–P bonds without risk of these being broken. Thus, for example, prolonged heating under reflux with constant-boiling hydrochloric acid may be used for hydrolysis of esters of most phosphonic and phosphinic acids, and triarylphosphine oxides may be nitrated with mixtures of concentrated nitric and sulphuric acids.

Pyrolyses of phosphonium halides and of analogous compounds of the type $R_nPHal_{(5-n)}$ ($n = 1$—4) result in cleavage of one C–P bond and conversion of the phosphorus atom from the quinquevalent to the tervalent state, *e.g.*:

$$R_3PCl_2 \longrightarrow R_2PCl + RCl$$

In view of the apparent similarity between these thermal decompositions and those of quaternary ammonium hydroxides it is of particular interest that pyrolysis of quaternary phosphonium hydroxides does not proceed in this way but yields tertiary phosphine oxides:

$$R_4P^+ OH^- \longrightarrow R_3P(O) + RH$$

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[142] Kharasch, Jensen, and Urry, *J. Amer. Chem. Soc.*, 1945, **67**, 1864.
[143] Stiles, Rust, and Vaughan, *ibid.*, 1952, **74**, 3282.
[144] Williams and Hamilton, *ibid.*, 1955, **77**, 3411.
[145] Preis, Myers, and Jensen, *ibid.*, p. 6225.
[146] McConnell and Coover, *ibid.*, 1957, **79**, 1961.

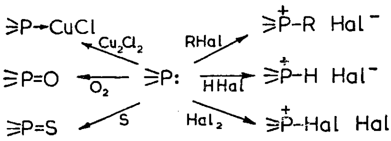
A similar reaction is the formation of phosphinic acids from phosphine oxides by fusion with alkali.[147]

The structural requirements for cleavage of C–P bonds in reactions occurring at lower temperatures differ according to whether an alkyl or an aryl group is being detached. In general, C–P bonds are stable towards hydrolysis but, when instability does occur, cleavage of C–alkyl bonds tends to take place under alkaline conditions and is assisted by electron-attracting substituents in the alkyl group. Thus trichloromethyl [148] and trifluoromethyl [149] groups attached to phosphorus are removed in alkaline solution, and dialkyl 2-chloro-1-hydroxyalkylphosphonates [150] and dialkyl 1-cyano-1-hydroxyalkylphosphonates [151] both undergo rearrangement, involving fission of the C–P bond, under alkaline conditions.

Cleavage of C–aryl bonds occurs in quite different circumstances, being brought about by hydrogen ions or other electrophilic reagents when the aryl group has electron-repelling groups in the *ortho-* or *para*-position. Examples of this are the hydrolysis of *p*-hydroxyphenylphosphonic acid by hot dilute hydrochloric acid, and the formation of tribromophenol by the action of bromine water on this phosphonic acid at room temperature.[152]

Other Reactions at the Phosphorus Atom.—Reactions involving the formation and breaking of other bonds to phosphorus are usually not greatly affected by the presence or absence of C–P bonds.

The predominant reactions of tervalent phosphorus compounds involve addition of reagents and cause the phosphorus atom to become quinquevalent. Thus all compounds of this type add oxygen, sulphur, or halogen more or less readily, whilst the more reactive ones (phosphines and phosphites) also combine with hydrogen halides, alkyl halides, and salts of transition metals.



Other reactions, such as elimination of alkyl halide, may follow, but these do not involve a reversion of the phosphorus atom to the tervalent state. Hydrolysis of chlorides of tervalent phosphorus, although a substitution, also cause the phosphorus atom to become quinquevalent:

$$>PCl + H_2O \text{ — } >P\begin{smallmatrix}\nearrow O \\ \searrow H\end{smallmatrix} + HCl$$

Most reactions of quinquevalent phosphorus compounds are substitutions and are quite readily brought about. Thus chlorine atoms in phosphonic

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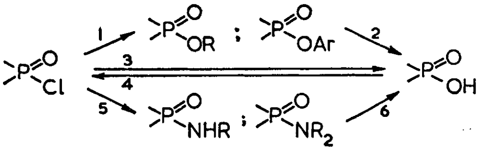
[147] Horner, Hoffmann, and Wippel, *Chem. Ber.*, 1958, **91,** 64.
[148] Bengelsdorf, *J. Amer. Chem. Soc.*, 1955, **77,** 6611.
[149] Emeléus, Haszeldine, and Paul, *J.*, 1955, 563.
[150] Barthel, Alexander, Giang, and Hall, *J. Amer. Chem. Soc.*, 1955, **77,** 2424.
[151] Hall, Stephens, and Drysdale, *ibid.*, 1957, **79,** 1768.

and phosphinic chlorides may be replaced by hydroxy-, alkoxy-, aryloxy-, or substituted amino-groups by reactions with water, alcohols (the liberated hydrogen chloride being removed by a base or reduced pressure), phenols, or amines respectively. Esters and amides of phosphonic and phosphinic acids are generally readily hydrolysed by heating them under reflux with constant-boiling hydrochloric acid, and the acids may be converted into the chlorides by phosphorus pentachloride or thionyl chloride.



1, ROH (+ base or *in vac.*) or ArOH. 2, HCl, reflux. 3, H_2O. 4, PCl_5 or $SOCl_2$. 5, Excess of $R{\cdot}NH_2$ or R_2NH. 6, HCl, reflux.

The effects of substituents on the dissociation constants of phosphonic and phosphinic acids are generally as would be expected, the dissociation constants being decreased by electron-repelling groups whilst electron-attracting groups strengthen the acids.[52, 58, 153] Alkylphosphonic and dialkylphosphinic acids are weaker than phosphoric acid and become more so with increase in the size and degree of branching of the alkyl groups.

Reactions not involving Bonds to Phosphorus.—Because of the ease with which tervalent phosphorus compounds undergo reactions at the phosphorus atom, most of the information on reactions occurring at other points refers to compounds in which the phosphorus atom is quinquevalent and particularly to those, such as phosphonic acids, phosphinic acids, and tertiary phosphine oxides, which contain a phosphoryl (P=O) group.

This group, being dipolar, is electron-attracting and many of its effects resemble those of carbonyl and nitro-groups. Thus, when attached to a benzene ring it is deactivating and *meta*-directing for electrophilic aromatic substitutions such as nitration,[154] but facilitates nucleophilic replacement of halogen atoms in the *ortho*- or *para*-position by amines and phenols.[155] In aliphatic compounds the phosphoryl group behaves like a carbonyl or ethoxycarbonyl group in activating hydrogen atoms attached to the adjacent carbon atom, so that triethyl phosphoacetate $(EtO)_2P(O){\cdot}CH_2{\cdot}CO_2Et$ and diethyl acetonylphosphonate, which contain a methylene group flanked by a $(EtO)_2P(O)$– group and an ethoxycarbonyl or carbonyl group respectively, form potassium derivatives which may be alkylated by alkyl halides.[156]

Tetraethyl methylenediphosphonate, in which the central carbon atom is flanked by two $(EtO)_2P(O)$– groups, undergoes similar reactions:[157]

[152] Bell and Kosolapoff, *ibid.*, 1953, **75**, 4901.

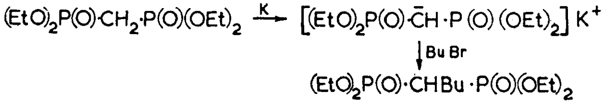
[153] Jaffé, Freedman, and Doak, *ibid.*, p. 2209; 1954, **76**, 1548.

[154] Kosolapoff, *ibid.*, 1949, **71**, 4021.

[155] Bauer, *ibid.*, 1941, **63**, 2137.

[156] Kosolapoff and Powell, *ibid.*, 1950, **72**, 4198.

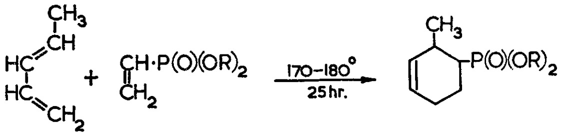
[157] Kosolapoff, *ibid.*, 1953, **75**, 1500.



$$(EtO)_2P(O){\cdot}CH_2{\cdot}P(O)(OEt)_2 \xrightarrow{K} [(EtO)_2P(O){\cdot}\bar{C}H{\cdot}P(O)(OEt)_2]K^+ \xrightarrow{BuBr} (EtO)_2P(O){\cdot}CHBu{\cdot}P(O)(OEt)_2$$

The phosphoryl group is also able to activate an adjacent double bond for addition of nucleophilic reagents. Thus amines, diethyl malonate, ethyl cyanoacetate, dialkyl phosphites, and conjugated dienes will add to esters of vinylphosphonic acid: [158]

$$CH_2{:}CH{\cdot}P(O)(OR)_2 + CH_2(CO_2Et)_2 \xrightarrow{NaOEt} (EtO_2C)_2CH{\cdot}CH_2{\cdot}CH_2{\cdot}P(O)(OEt)_2$$



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[158] Pudovik, *Doklady Akad. Nauk S.S.S.R.*, 1951, **80**, 65; Pudovik and Imaev, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1952, 916.