1074. *The Abnormal Hydrolysis of Certain β-(Diarylphosphino)-propionic Esters. Part I.*

By Roy C. Hinton, Frederick G. Mann, and David Todd.

β-(Diphenylphosphino)propionitrile, $Ph_2P{\cdot}[CH_2]_2{\cdot}CN$, on alkaline hydrolysis gives the stable crystalline acid, $Ph_2P{\cdot}[CH_2]_2{\cdot}CO_2H$, but β-(*m*-methoxyphenylphenylphosphino)propionitrile, m-$MeO{\cdot}C_6H_4{\cdot}PPh{\cdot}[CH_2]_2{\cdot}CN$, gives *m*-methoxyphenylmethylphenylphosphine, m-$MeO{\cdot}C_6H_4{\cdot}PPhMe$. This phosphine is also produced when the corresponding methyl and ethyl propionate are subjected to alkaline or acid hydrolysis.

This " abnormal hydrolysis " is not shown when the ethyl ester is first oxidised to the phosphine oxide, which undergoes alkaline hydrolysis to the stable phosphine oxide carboxylic acid. Replacement of the *m*-methoxyl by the *m*-ethoxyl group in the above phosphine esters also causes hydrolysis to be normal.

Methyl β-(*p*-methoxyphenylphenylphosphino)propionate also undergoes " abnormal hydrolysis," to form *p*-methoxyphenylmethylphenylphosphine, but the replacement of the *p*-methoxyphenyl group by the *p*-ethoxyphenyl group ensures normal hydrolysis.

Production of these tertiary methylphosphines is not caused solely by alkaline or acidic hydrolysis, for the interaction of *m*-methoxyphenylphenylphosphine, m-$MeO{\cdot}C_6H_4{\cdot}PPhH$, and methyl acrylate gives the methylphosphine and methyl phosphinopropionate; similarly *p*-methoxyphenylphenylphosphine and ethyl acrylate give the corresponding methylphosphine and the ethyl ester.

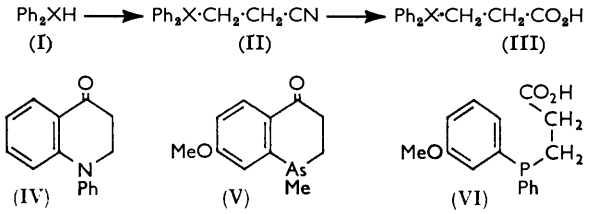
Ethyl γ-(*m*-methoxyphenylphenylphosphino)butyrate undergoes normal alkaline hydrolysis

Various aspects of these reactions are discussed.

Crystalline acids of type $Ph_2X{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ can be prepared by alkaline hydrolysis of the nitriles, obtained by the interaction of vinyl cyanide and diphenylamine,[1] diphenylphosphine,[2] and diphenylarsine[3] (I; X = N, P, or As). Whereas, however

[1] R. C. Cookson and Mann, *J.*, 1949, 67.
[2] Mann and Millar, *J.*, 1952, 4453.
[3] R. C. Cookson and Mann, *J.*, 1947, 618.

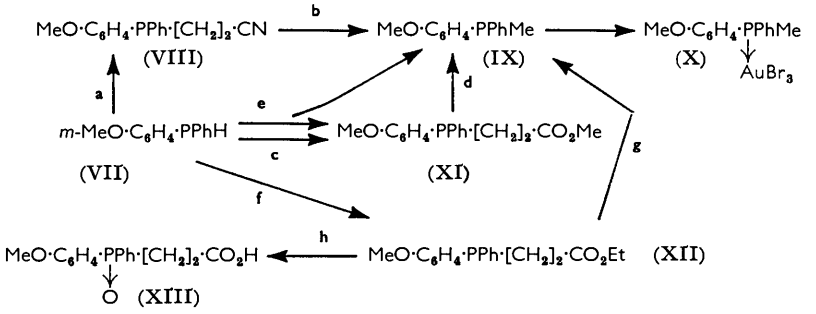
β-diphenylaminopropionic acid (III; X = N) is cyclised by phosphorus pentoxide in boiling xylene to 1,2,3,4-tetrahydro-4-oxo-1-phenylquinoline [1] (IV), no similar cyclisation of the phosphorus acid [2] (III; X = P) or the arsenic acid (III; X = As) could be achieved, although a wide variety of conditions and reagents was employed.



In the arsenic series, these difficulties were overcome by the use of the *m*-methoxyphenyl acid, *m*-MeO·C_6H_4·AsMe·$[CH_2]_2$·CO_2H, cyclisation of which afforded 1,2,3,4-tetrahydro-7-methoxy-1-methyl-4-oxoarsinoline [4] (V).

Since this successful cyclisation was clearly based on the activation of the phenyl group by the methoxyl group (a result also obtained in the indole series),[5] we have attempted to prepare β-(*m*-methoxyphenylphenylphosphino)propionic acid (VI), in order to study its cyclisation, for cyclic oxo-phosphines were unknown when this investigation was started. All our attempts to synthesise the acid (VI) have at present failed, owing to the intervention of an unexpected fission. This paper is primarily a record of our experimental results: a detailed discussion of reaction mechanisms will be deferred until adequate data are available.

m-Methoxyphenylphenylphosphine (VII) reacted normally with vinyl cyanide, to give the 2-cyanoethylphosphine (VIII), which, however, when boiled in aqueous-ethanolic sodium hydroxide furnished none of the required acid (VI) but instead afforded *m*-methoxyphenylmethylphenylphosphine (IX). This viscous phosphine was conclusively identified by (i) analysis and molecular-weight determinations; (ii) an independent synthesis in which a solution of the secondary phosphine (VII) in liquid ammonia was treated in turn with one equivalent of sodium and of methyl iodide; (iii) treatment in ethanol with tetrabromoauric acid which gave, by reduction and co-ordination, a colourless aurous bromide



a, CH_2:CH·CN. b, EtOH–aq. NaOH. c, Na, Br·$[CH_2]_2$·CO_2Me. d, MeOH–aq. NaOH, or dil. HCl. e, CH_2:CH·CO_2Me. f, Na, Br$[CH_2]_2$·CO_2Et or CH_2:CH·CO_2Et. g, EtOH–aq. NaOH, or dil. HCl. h, H_2O_2–aq. NaOH.

derivative and thence with one mol. of bromine the highly crystalline orange co-ordinated tribromo-gold derivative (X). The last compound was characterised by analysis and molecular-weight determinations and by its nuclear magnetic resonance spectrum, which showed the presence of MeO· and :PMe groups. Further, the phosphine (IX) showed no

[4] Mann and Wilkinson, *J.*, 1957, 3336.
[5] Mann and Tetlow, *J.*, 1957, 3352.

phenolic properties: there is therefore no indication that it was the isomeric ethyl-*m*-hydroxyphenylphenylphosphine, which could conceivably have arisen by demethylation and decarboxylation of the required acid (VI). The tribromo-gold compound (X), being readily prepared and purified by recrystallisation, and having a characteristic melting point, was used throughout this investigation as an additional check on the identity of samples of the phosphine (IX). Ethyl-*m*-methoxyphenylphenylphosphine, *m*-MeO·C_6H_4·PPhEt, similarly prepared by the action of sodium and ethyl iodide on the phosphine (VII), did not give a well-defined tribromo-gold derivative, but on treatment with a solution of silver iodide in aqueous sodium iodide readily gave a colourless stable compound $(C_{15}H_{17}OP)_2AgI$. The methylphosphine (IX) when similarly treated with silver iodide gave only a gum; with potassium palladobromide it gave a product $[(C_{14}H_{15}OP)_2PdBr_2]$ which after repeated recrystallisation had an indefinite melting point, owing possibly to the presence of racemic and *meso*-forms.

Since the striking difference between the hydrolyses of the unsubstituted nitrile (II; X = P) and its *m*-methoxy-derivative (VIII) might have been caused by the rather vigorous conditions of the hydrolysis, methyl β-(*m*-methoxyphenylphenylphosphino)-propionate (XI) was prepared, to enable milder hydrolysis to be employed. This liquid methyl ester was readily obtained by treating the phosphine (VII) in liquid ammonia with sodium and with methyl β-bromopropionate in turn. When hydrolysed by hot aqueous-ethanolic sodium hydroxide for a brief period, or (more slowly) by boiling 15% hydrochloric acid, it also furnished the phosphine (IX), and the required acid could not be detected.

The methyl ester (XI) was also obtained by heating the phosphine (VII) with pure methyl acrylate under nitrogen, but the crude product, when fractionally distilled, afforded both the ester (XI) and the phosphine (IX). The latter did not apparently arise by thermal decomposition of the former, for this ester was unaffected by being heated under nitrogen in a sealed tube at 100° for 5 hours. The formation of the phosphine (IX) therefore does not necessarily arise solely from a base- or acid-catalysed hydrolytic process.

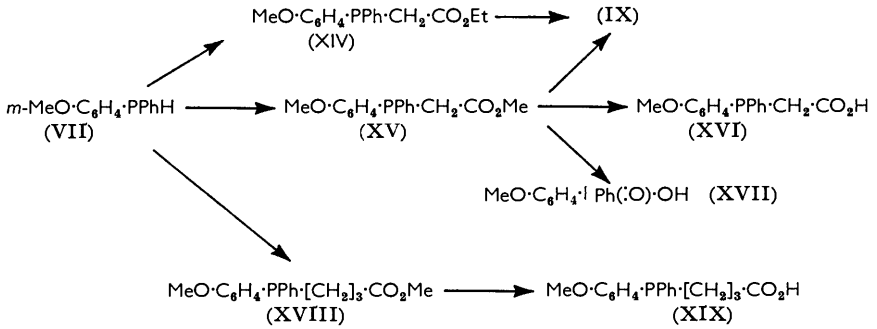
The corresponding ethyl ester (XII) was similarly prepared from the phosphine (VII) both by the reaction of sodium and ethyl β-bromopropionate and by the direct action of pure ethyl acrylate: in neither preparation, however, was the tertiary phosphine (IX) formed as a by-product. However, the ethyl ester (XII), when subjected to the previous alkaline or acidic hydrolysis, also gave the phosphine (IX) as the only volatile product detected. It is significant that when this ester (XII) was oxidised in acetone with hydrogen peroxide, and the resulting phosphine oxide then subjected to alkaline hydrolysis, the stable crystalline phosphine oxide acid (XIII) was obtained. It appears, therefore, that the tervalent phosphorus atom in the nitrile (VIII) and the esters (XI) and (XII) is intimately associated with the " abnormal hydrolysis " to the methylphosphine (IX).

Consideration of the mechanism of the formation of the phosphine (IX) required answers to the following questions: (A) Is the " abnormal hydrolysis " peculiar to β-propionic acid derivatives, or is it shown by homologues having a smaller or larger number of methylene groups? (B) Is it peculiar to the nature and position of the *m*-methoxy-substituent, *i.e.*, would it be shown (i) by the *m*-ethoxy- or (ii) by the *p*-methoxy-analogue?

To obtain evidence regarding factor (A), the *m*-methoxyphenylphenylphosphine (VII) was converted in ammonia by sodium and ethyl chloroacetate into ethyl *m*-methoxyphenylphenylphosphinoacetate (XIV). This ester proved very resistant to alkaline and acidic hydrolysis, but prolonged boiling with aqueous-ethanolic potassium hydroxide again furnished the methylphosphine (IX). The methyl ester (XV), similarly prepared, readily underwent alkaline hydrolysis to furnish the methylphosphine (IX), the carboxylic acid (XVI) (an oil giving a crystalline benzylthiouronium salt), and *m*-methoxyphenylphenylphosphinic acid (XVII). Since the phosphinic acid crystallised only when the initial oil was exposed to air, it is probable that its precursor as the true product of the

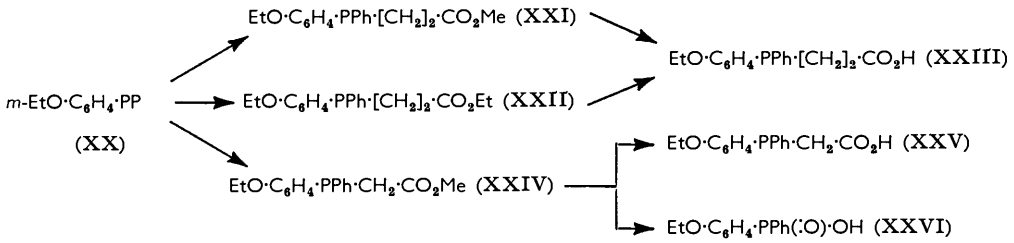
reaction was the corresponding phosphinous acid, $MeO{\cdot}C_6H_4{\cdot}PPh{\cdot}OH$ or the isomeric secondary phosphine oxide, $MeO{\cdot}C_6H_4{\cdot}P(:O)HPh$.

The phosphine (VII), when treated in the usual way with sodium and methyl γ-bromobutyrate, gave the methyl ester (XVIII), which underwent smooth alkaline hydrolysis to



the carboxylic acid (XIX), an oil giving a crystalline benzylthiouronium salt. It appears, therefore, that the " abnormal hydrolysis " does not extend to esters of acids beyond the propionic member.

Question B(i) was clarified by the reactions of *m*-ethoxyphenylphenylphosphine (XX). With methyl acrylate this gave solely the methyl ester (XXI), and with sodium and ethyl β-bromopropionate gave the ethyl ester (XXII). Both products underwent normal alkaline hydrolysis to the acid (XXIII), and there was no evidence of the formation of a neutral tertiary ethoxy-phosphine. The " abnormal hydrolysis," therefore, appears to require specifically the methoxyl group.

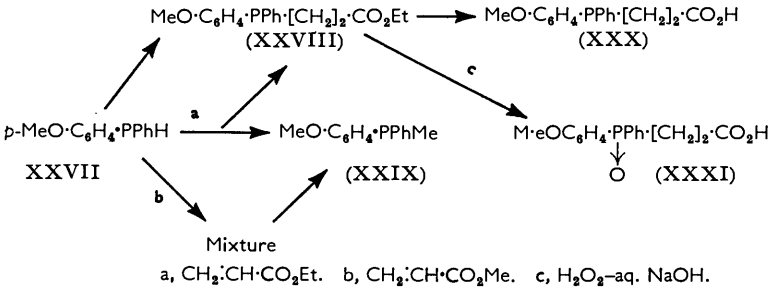


It is noteworthy that the methyl *m*-ethoxyphenylphenylphosphinoacetate (XXIV) on alkaline hydrolysis gave the carboxylic acid (XXV) and the phosphinic acid (XXVI). It is probable that the acid (XXV) was the first product, for longer treatment with the hot aqueous-ethanolic sodium hydroxide decreased the yield of the acid (XXV) and increased that of the acid (XXVI).

To answer the third question, B(ii), analogous reactions were carried out with *p*-methoxyphenylphenylphosphine (XXVII). This phosphine, when treated in liquid ammonia with sodium and ethyl β-bromopropionate, furnished solely ethyl β-(*p*-methoxyphenylphenylphosphino)propionate (XXVIII). When, however, a mixture of the phosphine (XXVII) and pure ethyl acrylate was heated under nitrogen, a mixture of the ethyl ester (XXVIII) and *p*-methoxyphenylmethylphenylphosphine (XXIX) was obtained. The phosphine (XXIX) was identified by its analysis and those of its methiodide and methotoluene-*p*-sulphonate, and by an independent synthesis in which the phosphine (XXVII) in ammonia was treated in turn with sodium and methyl iodide.

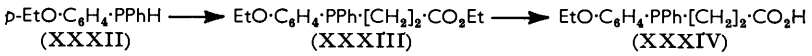
The ethyl ester (XXVIII) when subjected to either mild or vigorous alkaline hydrolysis gave only the corresponding acid (XXX). The stability of this acid under these conditions shows that, in the above interaction of the phosphine (XXVII) and ethyl acrylate, the

methylphosphine (XXIX) must almost certainly have been produced before hydrolysis of the reaction mixture. When the ethyl ester (XXVIII) was oxidised by hydrogen peroxide to the tertiary phosphine oxide, alkaline hydrolysis then afforded the stable phosphine oxide acid (XXXI).



a, $CH_2{:}CH{\cdot}CO_2Et$. b, $CH_2{:}CH{\cdot}CO_2Me$. c, H_2O_2–aq. NaOH.

Nevertheless, attempts to prepare the methyl ester (as XXVIII) from the phosphine (XXVII) and (*a*) methyl acrylate or (*b*) sodium and methyl β-bromopropionate gave mixtures. Separation of the components (available in only small amount) was difficult, but in each case the methylphosphine (XXIX) was isolated after alkaline hydrolysis of the mixture. Thus " abnormal hydrolysis " occurs also when the methoxyl group is in the *para*-position, but far less readily than when it is in the *meta*-position.



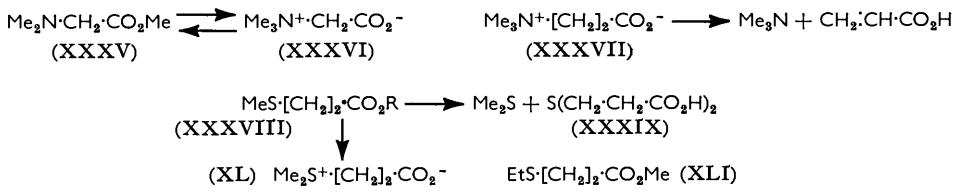
Finally, the *p*-ethoxyphenylphenylphosphine (XXII) with ethyl acrylate gave the ethyl ester (XXXIII), which on hydrolysis furnished the carboxylic acid (XXXIV), an oil which gave a crystalline benzylthiouronium salt. No evidence of the formation of a neutral tertiary phosphine analogous to the *p*-methoxy-phosphine (XXIX) could be obtained.

In considering the possible mechanism by which the *m*-methoxyphenylmethylphenylphosphine (IX) is formed, it should be noted that the hydrolysis of methyl (XV) and ethyl *m*-methoxyphenylphenylphosphinoacetate (XIV) may constitute a special case, because the methylphosphine (IX) may arise by simple decarboxylation of the acid (XVI), a mechanism which could not apply in hydrolysis of the analogous propionates. If therefore the special case of these acetates is excluded, the mechanism for the formation of the methylphosphine (IX) must explain the following facts: (1) The side chain of the hydrolysed compound must be a β-substituted propionic ester or nitrile. (2) The β-phosphorus atom must be present as a tertiary phosphine and not as a tertiary phosphine oxide. (3) The only known substituent required in the phenyl group is a methoxyl group: this group when in the *meta*- or *para*-position promotes " abnormal hydrolysis," but the stronger (or more rapid) effect comes from the *meta*-position. (4) Replacement of the methoxyl group in either position by ethoxyl suppresses " abnormal hydrolysis." (5) The formation of the methylphosphine (IX) occurs in basic aqueous ethanol or in dilute hydrochloric acid, but also occurs when the secondary phosphine (VII) is heated with methyl acrylate in the absence of a solvent or any other reagent: the presence of H^+ or OH^- ions is therefore not essential.

Two series of reactions, in the nitrogen and sulphur series respectively, appeared initially to be analogous to our results in the phosphorus series. Willstätter showed that methyl dimethylaminoacetate (XXXV) and trimethylacetobetaine (XXXVI) undergo interconversion, and that heating the propiobetaine (XXXVII) gives mainly trimethylamine and acrylic acid.[6]

[6] Willstätter, *Ber.*, 1902, **35**, 584; Willstätter and Kahn, *Ber.*, 1904, **37**, 401, 1853.

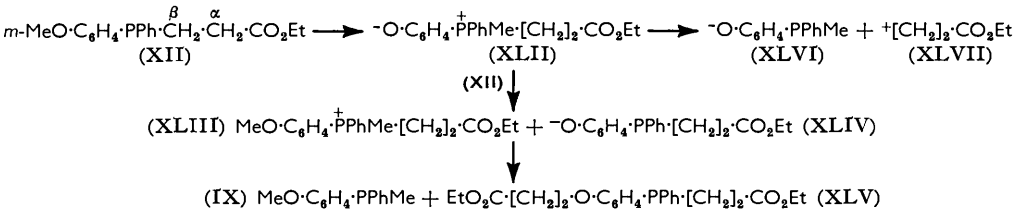
Barger and Coyne [7] showed that ethyl β-(methylthio)propionate (XXXVIII; R = Et) undergoes normal hydrolysis by boiling N-hydrochloric acid to the acid (XXXVIII; R = H), but Challenger and Hollingworth [8] showed that the methyl ester (XXXVIII; R = Me) when boiled with 6N-hydrochloric acid gives dimethyl sulphide and bis-2-carboxyethyl sulphide (XXXIX). The plausible explanation that this " abnormal



hydrolysis " occurs through the intermediate formation of the thetine (XL) or its hydrochloride was refuted * by Challenger *et al.*,[8] who showed that the ethyl ester (XXXVIII; R = Et) when similarly treated also gives dimethyl sulphide, whilst methyl β-(ethylthio)-propionate (XLI) gives diethyl sulphide: neither ester furnishes ethyl methyl sulphide.

Neither the more detailed and complex mechanism suggested by Challenger *et al.*[8] for the abnormal hydrolysis of their sulphur compounds, nor Willstätter's simple mechanism for the nitrogen compounds can apply to our phosphorus compounds, for the methylphosphine (IX) was produced from the nitrile (VIII) and the methyl and ethyl esters (XI, XII), and the hydrolysis of the first and the last of these derivatives was conducted in the absence of any methyl group except that in the *m*-methoxyphenyl unit.

Our results initially appeared to indicate that during the hydrolysis of our nitrile and esters, *e.g.*, the ethyl ester (XII), the propionic acid chain underwent fission between the α- and the β-carbon atom, with formation of the methylphosphine (IX). This mechanism was discarded because (i) the mother liquor from the acidic hydrolysis of the ester (XII) was carefully but fruitlessly examined for aliphatic acids, such as glycollic acid, which might be formed from the α-portion by this process, (ii) if this fission, in spite of its intrinsic improbability, did occur under the influence of the methoxyl group, it should also occur with the corresponding ethoxy-compounds.



We therefore very tentatively suggest that the first stage may be migration of the methyl group in the ester (XII) to the phosphorus atom, to give the phosphonium zwitter-ion (XLII). If this zwitter-ion is an essential intermediate, it would explain (*a*) the stability of the oxidised acid (XIII) which cannot form this type of ion, and (*b*) the fact that abnormal hydrolysis is limited to the methoxy-compounds, for the methyl portion of a methoxyl group has much greater activity than the ethyl portion of an ethoxyl group. The zwitter-ion (XLII) may then react with a second molecule of the ester (XII) to give the *m*-methoxy-cation (XLIII) and the anion (XLIV). The side-arm in the cation (XLIII) will be under strain, however, owing to the opposing electron attractions of the

* In a preliminary note (Hinton, Mann, and Todd, *Proc. Chem. Soc.*, 1959, 365) it was erroneously stated that Challenger *et al.* suggested this mechanism.

[7] Barger and Coyne, *Biochem. J.*, 1928, **22**, 1417.

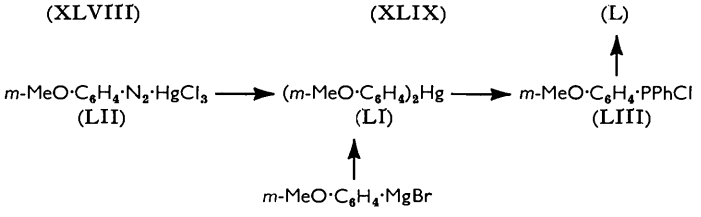
[8] Challenger and Hollingworth, *Chem. and Ind.*, 1954, 463; *J.*, 1959, 61.

positive pole and the carbonyl unit: fission may therefore occur between the phosphorus atom and the β-carbon atom, generating the methylphosphine (IX) and the cation (XLVII), which will unite with the anion (XLIV) to give the ether-ester (XLV). Alternatively this overall process might occur by the direct fission of the zwitter-ion (XLII) into the anion (XLVI) and the cation (XLVII): the anion (XLVI) then reacts with the ester (XII) to give the methylphosphine (IX) and the anion (XLIV), which in turn unites with the cation (XLVII) to give the ether-ester (XLV).

If the formation of the zwitter-ion (XLII) is also significantly influenced by the inductive effect of the carboxylic unit, the absence of the " abnormal hydrolysis " when the side-chain extends beyond the propionic member becomes explicable. Moreover, the above reactions may well precede the true hydrolysis, which would apply only to the final ether-ester (XLV). Thus could be formed the methylphosphines (IX and XXIX) by direct action of methyl acrylate on the phosphine (VII), and of ethyl acrylate on the phosphine (XXVII), respectively. Further, a free-radical mechanism parallel to the above ionic mechanism may be involved in these reactions.

Although this mechanism thus provides a tentative explanation of the points (1)—(5) (above), its verification must rest on the isolation of the hydrolysed ether-ester (XLV). In all our distillations of the ether-extracted methylphosphines, a considerable residue of dark, intractable material was obtained. This must now be examined for evidence of the presence of the dicarboxylic acid (as XLV) or any of its likely decomposition products.

Preparation of Methoxy(and Ethoxy)phenylphenylphosphinic Acids, $R{\cdot}C_6H_4{\cdot}PPh(:O){\cdot}OH$, *and the Secondary Phosphines,* $R{\cdot}C_6H_4{\cdot}PPhH$.—The preparation of the above *m*- and *p*-methoxy (and ethoxy)phenylphenylphosphinic acids was based on the work of Freedmann and Doak;[9] *m*-methoxyaniline, for example, was converted into the solid diazonium fluoroborate (XLVIII; R = *m*-MeO), which was treated in ethyl acetate suspension with phenylphosphonous chloride and cuprous chloride, subsequent hydrolysis affording the phosphinic acid (XLIX; R = *m*-MeO). The reaction (XLVIII) ⟶ (XLIX) (R = *m*-MeO or *m*-EtO) required very careful control (see Experimental) to ensure a sufficiently vigorous yet not uncontrollably violent reaction: the corresponding reactions of the flouroborates derived from *p*-anisidine and *p*-ethoxyaniline were much less vigorous, and quite mild, respectively. Reduction of the phosphinic acids (XLIX) by lithium aluminium hydride in tetrahydrofuran, instead of ether as recorded[10] for diphenylphosphinic acid, gave the secondary phosphines (L) in very moderate yield: the rather higher yield obtained by converting the acid into its methyl ester before reduction did not, however, justify the extra stage.



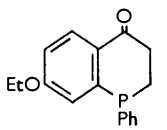
The second method, which was investigated only in *m*-methoxy-series, involved the preparation of di-(*m*-methoxyphenyl)mercury (LI) by treating the diazonium mercury trichloride (LII) in acetone with copper powder,[11] or by treating mercuric chloride with *m*-methoxyphenylmagnesium bromide. Reaction of di-(*m*-methoxyphenyl)mercury (LI)

[9] Doak and Freedman, *J. Amer. Chem. Soc.*, 1951, **73**, 5658; Freedman and Doak, *ibid.*, 1953, **75**, 4905; *J. Org. Chem.*, 1958, **23**, 769.
[10] Hein, Isslieb, and Rabold, *Z. anorg. Chem.*, 1956, **287**, 208.
[11] Nesmejanow and Kohn, *Org. Synth.*, Coll. Vol. II, p. 381; Nesmjeanow, *ibid.*, p. 432.

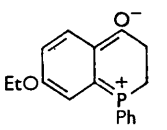
with phenylphosphonous chloride gave only a low yield of rather impure chlorophosphine (LIII), and the reduction of this to the secondary phosphine was also unsatisfactory.

It might appear that all the above difficulties encountered in the synthesis of the acid (VI) might have been evaded by utilising the direct union of the secondary phosphine (VII) and β-propiolactone. However, experiments with diphenylphosphine and the lactone gave none of the corresponding acid, apparently because the secondary phosphine catalyses polymerisation of the lactone too effectively.

Cyclisation of *m*-methoxyphenylphenylphosphino-acetic (XVI) and -butyric acid (XIX), and of *m*-ethoxyphenylpropionic acid (XXIII) has been very briefly investigated. The acids (XVI) and (XIX) when boiled in xylene with phosphorus pentoxide gave only intractable dark gums which did not give 2,4-dinitrophenylhydrazones. The acid (XXIII) gave analogous results when similarly treated in boiling benzene and in xylene, and when



(LIV)



(LIVA)

heated with polyphosphoric acid at 100° for 3 hours was recovered unchanged. A solution of this acid in toluene containing phosphoric anhydride, when boiled for 30 minutes, gave a brown gum which on microdistillation gave a fraction having the composition of the cyclic ketone (LIV): its infrared spectrum had a reasonably strong band at 1720 cm.$^{-1}$, corresponding to a :CO group. The small yield and the difficulty of preparing satisfactory crystalline derivatives caused these attempts to be abandoned: meanwhile the identification of the fraction as the oxo-phosphine (LIV) must be treated with reserve.

It is possible that these failures under conditions of cyclisation that are excellent for the analogous nitrogen acid (III; X = N), may arise largely because the more basic tertiary phosphines form salts with the phosphoric acid: the positive charge on the phosphorus atom would then oppose the activating effect of the *m*-ethoxyl group. The basic properties, moreover, might cause the oxo-phosphine (LIV) to exist mainly as the ionic form (LIVA) and thus increase the difficulty of preparing crystalline derivatives such as hydrazones.

The phosphine oxide propionic acid (XIII) also failed, as expected, to undergo cyclisation under the above conditions or when treated in benzene with phosphorus pentachloride and aluminium chloride in turn: in this acid the phosphorus atom undoubtedly has some positive character.

Experimental

To ensure consistent m. p.s, certain compounds were heated in evacuated tubes (indicated as E.T.). All compounds were colourless unless otherwise described.

All experiments involving the preparation or subsequent manipulation of secondary or tertiary phosphines were conducted under nitrogen: this is therefore stated later only when particularly necessary.

Alkaline Hydrolysis.—For this hydrolysis of the phosphine esters, the following general conditions were observed, unless otherwise stated. A mixture of the ester (*ca.* 5 g.) and 20% aqueous sodium hydroxide (20—25 c.c.) was gently boiled under reflux, and sufficient ethanol (5—8 c.c.) added to give a homogeneous solution, which was boiled for the stated time.

m-*Methoxyphenylphenylphosphinic Acid* (XLIX; R = *m*-MeO).—Concentrated hydrochloric acid (200 c.c.) and *m*-anisidine (120 g.) were added in that order to a stirred solution of sodium fluoroborate (140 g.) in water (400 ml.), which was then cooled whilst a solution of sodium nitrite (68 g., 1·1 mol.) in water (140 c.c.) was added dropwise, so that the temperature remained below 10°. The stirred suspension was then chilled to 0° and the diazonium fluoroborate collected, and washed in turn with aqueous sodium fluoroborate (50 c.c.), methanol (50 c.c.), and with ether (*ca.* 1 l.) until the washings were colourless. The pale brown crystals were spread on drying paper for 1 hr.

A 5-l. round-bottomed flask was fitted with a 3-necked adaptor, the central neck carrying a stirrer, one side-neck being stoppered, and the other carrying a capacious reflux water-condenser, fitted at the top with a wide-bore, inverted U-tube, the open end of which dipped into a large conical overflow flask.

To purify cuprous chloride, it was dissolved in concentrated hydrochloric acid, reprecipitated by the addition of cold boiled water, and then collected, rapidly washed with water and methanol, and dried.

The diazonium fluoroborate was covered with dry ethyl acetate (750 c.c.) in the flask, and then stirred whilst phenylphosphonous chloride (174 g., 1 mol.) was added dropwise, with the intermittent addition of the cuprous chloride (6 g.); the colour of the suspension changed initially from red to brown and became red again when all the phosphine had been added. The flask was then gently warmed by a current of hot water flowing over the shoulders of the flask. After (usually) about 2 hr., a violent reaction started, nitrogen was copiously evolved, and the ethyl acetate began to boil vigorously. Ice-water was then poured copiously over the flask, and the reaction normally subsided at once; occasionally part of the mixture foamed over into the overflow flask, and was later returned to the main reaction mixture. The latter was heated on a boiling-water bath for *ca.* 15 min. and was then cooled, and water (*ca.* 100 c.c.) was cautiously added until hydrolysis was complete.

The ethyl acetate was removed by steam-distillation, and the black oily residual phosphinic acid solidified when cooled. It was purified by digestion with sufficient boiling acetone to dissolve the coloured impurities and most of the phosphinic acid, the latter separating again when the mixture was cooled (yield, 110 g., 46% calc. on the amine used). Recrystallisation from aqueous ethanol gave m-*methoxyphenylphenylphosphinic acid* (XLIX; R = *m*-MeO), m. p. 142—144° (Found: C, 62·7; H, 5·5. $C_{13}H_{13}O_3P$ requires C, 62·9; H, 5·3%). The acid gave a benzylthiouronium salt, m. p. 181—183° after one recrystallisation from water, identical with that prepared from the acid obtained by the hydrolysis of the ester (XV) (see below).

The following points should be noted: (i) to avoid premature decomposition of the fluoroborate, it must be thoroughly washed as described above; (ii) if the phosphonous chloride is added too rapidly, even to a cooled suspension, the fluoroborate may rapidly and vigorously decompose, without forming any phosphinic acid; (iii) the violent reaction described above must be allowed to proceed until the ethyl acetate is boiling vigorously before being cooled: if the reaction is checked prematurely by cooling, the yield of the phosphinic acid may be negligible.

The yield of the phosphinic acid might be increased if the proportion of diazonium fluoroborate were considerably increased:[12] this was not investigated, for the supply of the *m*-anisidine was the determining factor.

m-*Ethoxyphenylphenylphosphinic Acid* (XLIX; R = *m*-EtO).—Unless the conditions given above are carefully followed, the yield of this acid may decrease, even to zero. Although the preparation was carried out on a smaller scale, with pure *m*-phenetidine (80 g.), sodium fluoroborate (90 g.), sodium nitrite (41 g.), phenylphosphonous chloride (121 g., 1 mol.), and cuprous chloride (4 g.), the reaction usually became so violent (after *ca.* 30 minutes' warming) that some of the reaction mixture was blown into the overflow flask. The united mixture was worked up as before, yielding after the first acetone treatment the crystalline *phosphinic acid* (XLIX; R = *m*-EtO) (70 g., 46% calc. on the *m*-phenetidine). The acid usually required 2—3 more treatments with acetone to remove impurities; a sample, recrystallised in turn from acetone, water, and acetone and dried at 100°/0·1 mm., had m. p. 131—134° (E.T.) (Found: C, 64·55; H, 6·1. $C_{14}H_{15}O_3P$ requires C, 64·1; H, 5·8%). It gave a crystalline *benzylthiouronium salt*, m. p. 176°, from water (Found: C, 61·5; H, 6·2. $C_{22}H_{25}N_2O_3PS$ requires C, 61·7; H, 5·9%).

p-*Methoxyphenylphenylphosphinic Acid* (XLIX; R = *p*-MeO).—This was prepared as the *m*-methoxy-analogue, *p*-anisidine (80 g.) and concentrated hydrochloric acid (150 c.c.) being added to sodium fluoroborate (90 g.) in water (300 c.c.), followed by sodium nitrite (44 g.) in water (90 c.c.). The diazonium fluoroborate suspended in ethyl acetate (300 c.c.) was treated with phenylphosphonous chloride (121 g., 1 mol.) and cuprous chloride (0·5 g.). The moderate reaction started after *ca.* 30 min., and external cooling was not always required. The acetone treatment of the final residue gave the *phosphinic acid* (XLIX; R = *p*-MeO) (99 g., 62%);

[12] Denham and Ingram, *J. Org. Chem.*, 1958, **23**, 1298.

a sample recrystallised from water and then from ethanol formed needles, m. p. 184° (E.T.) (Found: C, 63·0; H, 5·1. $C_{13}H_{13}O_3P$ requires C, 62·9; H, 5·3%). The yield was fairly consistent, unlike that of the two *meta*-substituted acids. In this and the following preparation, a very small amount of the copper catalyst is required (in one preparation of the *p*-methoxyphenyl acid, a piece of copper wire wound around the stirrer proved excellent): for the two *meta*-substituted acids, the stated quantities of cuprous chloride are required.

p-*Ethoxyphenylphenylphosphinic Acid* (XLIX; R = *p*-EtO).—This was prepared by converting *p*-phenetidine (120 g.) as before into the diazonium fluoroborate, which was thoroughly washed, dried, and treated in ethyl acetate (400 ml.) with phenylphosphonous chloride (174 g., 1·1 mol.) and cuprous chloride (0·5 g.). The vigorous reaction started after *ca.* 15 min. and did not require controlling. The black residue solidified on cooling, and direct recrystallisation from acetone gave the *phosphinic acid* (XLIX; R = *p*-EtO) (50 g., 22% calc. on the phenetidine): a sample, recrystallised twice from water and then from acetone, had m. p. 148—149° (E.T.) (Found: C, 64·1; H, 5·8%).

m-*Methoxyphenylphenylphosphine* (VII).—All these reductions were carried out under nitrogen. A suspension of the phosphinic acid (XLIX; R = *m*-MeO) (90 g.) in dry tetrahydrofuran (300 c.c.) was cautiously treated with lithium aluminium hydride (10 g.): the mixture sometimes became deep black at this stage owing to contamination with copper but the final yield was unaffected. When the initial reaction had subsided, the mixture was heated under reflux for 4 hr., then concentrated by distillation, and the cold residue hydrolysed with undried ether (*ca.* 500 c.c.), followed by 20% aqueous potassium sodium tartrate (*ca.* 300 c.c.). After the solvent had been removed from the dried ethereal layer, distillation gave the *phosphine* (VII) (13 g., 17%), b. p. 135—140°/0·5 mm. (Found: C, 72·5; H, 6·4. $C_{13}H_{13}OP$ requires C, 72·2; H, 6·1%).

m-*Ethoxyphenylphenylphosphine* (XX).—This was prepared from the phosphinic acid (XLIX; R = *m*-EtO) (90 g.) in the same way as the *m*-methoxy-analogue, but with heating under reflux for 6 hr. The *phosphine* (18 g., 23%) had b. p. 135—136°/0·5 mm. (Found: C, 71·8; H, 6·4. $C_{14}H_{15}OP$ requires C, 73·0; H, 6·6%).

p-*Methoxyphenylphenylphosphine* (XXVII), similarly obtained (12·8 g., 15%) from the phosphinic acid (XLIX; R = *p*-MeO) (98 g.), had b. p. 122—130°/0·5 mm., m. p. 15—16° (Found: C, 71·95; H, 6·2%).

p-*Ethoxyphenylphenylphosphine* (XXXII), similarly prepared from the phosphinic acid (XLIX; R = *p*-EtO) (50 g.), was isolated as a liquid (5·7 g., 13%), b. p. 140—150°/0·8 mm. (Found: C, 72·7; H, 6·7%).

Di-(m-*methoxyphenyl*)*mercury* (LI).—(*A*) *m*-Anisidine (54·4 g.) was dissolved in a warm stirred mixture of concentrated hydrochloric acid (250 c.c.) and water (250 c.c.), which on cooling deposited fine crystals of the amine hydrochloride. The mixture was vigorously stirred and cooled in ice–salt whilst powdered sodium nitrite (30 g.) was added during 45 min., ice being added when necessary to keep the temperature at 5—6°. A solution of mercuric chloride (119 g.) in concentrated hydrochloric acid (140 c.c.), mixed with ice (140 g.), was slowly added to the diazonium solution, the temperature being kept at 0°. Vigorous stirring was required as the heavy diazonium mercury trichloride (LII) was deposited. The complete mixture was stirred for 30 min., then filtered at the pump, the trichloride being washed with ice-water (2 × 100 c.c.) and ice-cold acetone (2 × 125 c.c.). The product, dried in a vacuum for 1 hr., afforded orange-brown crystals (68·5 g.). This material, as soon as it was dry, was suspended in acetone (300 c.c.), which was cooled in ice-water and vigorously stirred whilst fine copper powder (59 g.) was added during 30 min. The mixture was stirred for 3 hr., then treated with aqueous ammonia (*d* 0·880; 500 c.c.) and set aside overnight. The product was collected, washed in turn with water and ethanol, and extracted with boiling chloroform. The hot extract was filtered, concentrated, diluted with an equal volume of ethanol, and cooled. *Di*-(m-*methoxyphenyl*)*mercury* (20 g., 22% yield from the *m*-anisidine) which had separated had m. p. 165—167°, raised to 167—168° by recrystallisation from chloroform (Found: C, 40·2; H, 3·7. $C_{14}H_{14}HgO_2$ requires C, 40·5; H, 3·4%).

(*B*) A Grignard reagent was prepared by the interaction of activated magnesium (4·48 g.) in ether (100 c.c.) and *m*-bromoanisole (37·7 g., 1 mol.) in ether (50 c.c.), the complete mixture being boiled under reflux for 3 hr. Powdered dry mercuric chloride (22·5 g.) was added in small portions during 1 hr. to the stirred mixture, giving a vigorous reaction: the mixture was then boiled for 3 hr. The cold stirred mixture was treated with N-hydrochloric acid (10 c.c.)

and filtered, the grey solid residue being washed with fresh ether. This material (24 g.) contained *m*-methoxyphenylmercuric chloride. A sample (2·1 g.) was therefore purified by boiling it in 95% ethanol (100 c.c.) containing sodium iodide (7·5 g.) for 1 hr.;[13] the solution, on cooling, deposited di-(*m*-methoxyphenyl)mercury (1·3 g.), m. p. and mixed m. p. 164—167°. The total yield was 9 g.; some material had been expended investigating methods of working up.

Chloro-m-*methoxyphenylphenylphosphine* (LIII).—Di-(*m*-methoxyphenyl)mercury (LI) (50·6 g.) and phenylphosphonous chloride (34·2 g.) were thoroughly mixed and heated under nitrogen at 215—220° for 1 hr. Dry sand (20 g.) was stirred into the viscous reaction mixture, which was extracted thoroughly with cold benzene (3 × 100 c.c.). The combined filtered extracts, after removal of the solvent, gave on distillation a main fraction (14·3 g.), b. p. 164°/1·5 mm.; further distillation caused contamination with a dark flocculent material. The fraction was taken up in light petroleum (b. p. 80—100°; 100 c.c.), which was rapidly filtered; the solvent was removed and the residue redistilled. The main fraction, of unchanged b. p., was the impure chlorophosphine (LIII) (Found: C, 59·7, 59·3; H, 5·6, 5·95. Calc. for $C_{13}H_{12}ClOP$: C, 62·3; H, 4·3%).

Reduction of this compound by lithium aluminium hydride gave the crude phosphine (VII) in low yield, and this route was not further investigated.

m-*Methoxyphenylmethylpherylphosphine*[14] (IX).—*m*-Methoxyphenylphosphine (VII) (6·4 g.) was added to liquid ammonia (*ca.* 125 c.c.) contained in a well-lagged three-necked flask (250 c.c.) fitted with a stirrer. Sodium pellets (0·7 g., 1 equiv.) were added slowly to the stirred solution which finally (20 min.) became bluish-black. Methyl iodide (4·2 g., 0·86 mol.) in ether (15 c.c.) was added dropwise, the solution becoming pale yellow or almost colourless. Evaporation of the ammonia was then hastened by warming. The residue was treated with cold, freshly boiled water (*ca.* 100 c.c.), and the mixture extracted with ether (50 c.c.). The dried ethereal layer on distillation under nitrogen gave a fraction (4·8 g.), b. p. 130—140°/0·5 mm., which on refractionation gave the *methylphosphine* (IX), b. p. 133°/0·5 mm. (Found: C, 72·7; H, 6·4%; *M*, in freezing benzene, 243. $C_{14}H_{15}OP$ requires C, 73·0; H, 6·6%; *M*, 230).

Tetrabromoauric acid was prepared by adding an excess of aqueous-ethanolic sodium bromide to a similar solution of tetrachloroauric acid. This brown solution was then added dropwise with shaking to a cold ethanolic solution of the phosphine (IX) until the solution just attained a permanent red colour. Bromine in fine drops was carefully added until precipitation of the highly crystalline red *tribromo*-m-*methoxyphenylmethylphenylphosphinegold* (X) was complete: the latter, when collected and recrystallised from methanol, had m. p. 151—152° [Found: C, 25·1; H, 2·6%; *M*, in methylene dichloride solution at 30° (thermister method), 686. $C_{14}H_{15}AuBr_3OP$ requires C, 25·2; H, 2·4%; *M*, 667; on evaporation the methylene dichloride solution deposited the unchanged solute, m. p. 148—148·5°].

Nuclear magnetic resonance spectra of hydrogen nuclei were obtained at 40 Mc. by using a Varian Associates 4300B spectrometer and 12″ electromagnet, with flux stabilisation and sample spinning. Positions of the resonances are quoted as chemical shifts on the tetramethylsilane scale. For a chloroform solution of the compound (X), the solvent band precluded observation of resonance of the aromatic C–H bonds, but the methoxyl groups showed up clearly as a sharp peak at the expected value of $\tau = 5{\cdot}3$, and the PMe groups as a doublet at $\tau = 6{\cdot}5$, with a spacing of 12 c./sec. caused by interaction with the magnetic phosphorus atom of spin $\frac{1}{2}$.

When aqueous-ethanolic tetrachloroauric acid was similarly added to an ethanolic solution of the phosphine (IX) and the orange solution then treated with bromine, the crystalline pale orange *dibromochlorophosphinegold* (as X) was deposited, having m. p. 139° (E.T.) after crystallisation from ethanol (Found: C, 26·7; H, 2·2. $C_{14}H_{15}AuBr_2ClOP$ requires C, 27·0; H, 2·4%).

Aqueous-ethanolic potassium palladobromide, when added to slight excess of the ethanolic phosphine (IX), deposited the *dibromodiphosphinepalladium* initially as a brown gum which after three recrystallisations from ethanol still melted indefinitely below 100° (Found: C, 45·8; H, 3·5. $C_{28}H_{30}Br_2O_2P_2Pd$ requires C, 46·3; H, 4·2%).

Only syrups or gums were obtained by the interaction of the phosphine (IX) with methyl iodide, methyl toluene-*p*-sulphonate, rhombic sulphur in benzene solution, hydrogen peroxide in aqueous acetone, ethanolic chloramine-T, or solutions of cuprous iodide and of silver iodide in aqueous potassium iodide.

[13] Whitmore and Sobatski, *J. Amer. Chem. Soc.*, 1933, **55**, 1128.
[14] Cf. Hitchcock and Mann, *J.*, 1958, 2081.

Ethyl-m-*methoxyphenylphenylphosphine*.—This phosphine was prepared as was the methyl analogue (IX), the phosphine (VII) (6·85 g.) in liquid ammonia being treated with sodium (0·7 g.) and ethyl bromide (3·5 g., 0·87 mol.). The residue gave a fraction (5·0 g.), b. p. 133—140°/0·5 mm., which on refractionation gave the pure *ethylphosphine*, b. p. 140°/0·5 mm. (Found: C, 74·0; H, 6·9. $C_{15}H_{17}OP$ requires C, 73·8; H, 7·0%).

No solid co-ordinated derivatives of this phosphine with gold tribromide or palladium dibromide could be isolated. When, however, a mixture of the phosphine and a saturated solution of silver iodide in concentrated aqueous sodium iodide was vigorously shaken, a white gum separated that solidified when kneaded with water, and when then recrystallised from ethanol afforded the *iododiphosphinesilver*, m. p. 114° (E.T.) (Found: C, 49·4; H, 4·7%; *M*, in methylene dichloride solution at 30°, 729, 742. $C_{30}H_{34}AgIO_2P_2$ requires C, 49·8; H, 4·7%; *M*, 723). Cuprous iodide similarly gave a white gum but this did not crystallise.

A solution of the ethylphosphine in aqueous-ethanolic sodium hydroxide was boiled under reflux for 2 hr. The phosphine when recovered gave no crystalline tribromogold derivative and therefore was not contaminated with the methylphosphine (IX): the remote possibility that the ethylphosphine is the immediate precursor of the methylphosphine during alkaline hydrolyses of the propionic esters is thus discounted.

Reactions of m-*Methoxyphenylphenylphosphine* (VII).—(A) *Vinyl cyanide*. Freshly distilled vinyl cyanide (2·7 g., 1 mol.) was added dropwise to the phosphine (VII) (11·1 g.) in acetic acid (8 c.c.) under nitrogen. The mixture, which had become hot, was boiled under reflux for 10 min., treated with more vinyl cyanide (2·7 g.), and again boiled for 1 hr. The excess of vinyl cyanide and the acetic acid were then boiled off, and the residue was distilled at 0·35 mm.; a small forerun was followed by the main fraction (7·1 g.), b. p. 158—190°, leaving a considerable undistilled black residue. The distillate on refractionation gave 2-*cyanoethyl*-m-*methoxyphenylphenylphosphine* (VIII), b. p. 192—193°/0·35 mm. (Found: C, 71·0; H, 6·3. $C_{16}H_{16}NOP$ requires C, 71·4; H, 6·0%). This phosphine did not give a crystalline gold tribromide derivative.

A solution of the cyano-phosphine in 20% aqueous-ethanolic sodium hydroxide under nitrogen was boiled under reflux until no more ammonia was evolved (*ca.* 7 hr). After the ethanol had been removed, the clear solution when cooled and made faintly acid with 10% hydrochloric acid deposited an oil, which was extracted with ether. The dried extract, after removal of the ether, gave on distillation the methylphosphine (IX), b. p. 125—130°/0·5 mm. (Found: C, 72·5; H, 7·0%). This phosphine, both before and after the distillation, gave the tribromogold derivative (X), m. p. and mixed m. p. 151—152° (E.T.) (Found: C, 25·0; H. 2·0%).

(B) *Methyl acrylate*. The phosphine (VII) (8 g.) was treated under nitrogen dropwise with redistilled methyl acrylate (3·2 g., 1 mol.), with considerable heat evolution. The mixture was heated under reflux for 10 min., treated with more methyl acrylate (4 g.), and then heated for 1 hr. The excess of acrylate was removed and the residue, when fractionally distilled, gave the fractions, (i) b. p. 50—130°/0·06 mm. (2 c.c.), and (ii) b. p. 130—170°/0·06 mm. (10 c.c.). Fraction (i) was chiefly dimerised methyl acrylate. Fraction (ii) on refractionation gave fractions (iia) b. p. 110—158°/0·2 mm. (2 c.c.), and (iib) b. p. 158—172°/0·2 mm. (7 c.c.). Fraction (iia) was mainly the methylphosphine (IX), for it gave in high yield the gold tribromide derivative (X) (Found: C, 25·2; H, 2·1%), m. p. and mixed m. p. 149—150° (E.T.) after recrystallisation from methanol. Fraction (iib) on refractionation gave *methyl* β-(m-*methoxyphenylphenylphosphino*)*propionate* (XI), b. p. 168—170°/0·2 mm. (Found: C, 67·4; H, 6·1. $C_{17}H_{19}O_3P$ requires C, 67·6; H, 6·3%).

This is a typical experiment, but it must be emphasised that in repetitions of this experiment carried out under apparently identical conditions the ratio of phosphine (IX) to the ester (XI) varied considerably, and the precise factor determining this ratio is still unknown.

(C) *Methyl* β-*bromopropionate*. A solution of the phosphine (VII) (4·8 g.) in liquid ammonia was treated with sodium pellets (0·5 g., 1 equiv.) and with the propionate (3·8 g.). The mixture was worked up as for the phosphine (IX). The residue on distillation gave a fraction, b. p. 133—172°/0·2 mm., which on refractionation furnished the methyl ester (XI) (2·0 g.), b. p. 156—165°/0·1 mm. (Found: C, 67·7; H, 6·0%). The methyl ester (XI), treated with tetrabromoauric acid and with bromine, as for (X), gave the *phosphinopropionate tribromogold* (as X), red crystals, m. p. 94—95° (E.T.), from ethanol (Found: C, 27·4; H, 2·7. $C_{17}H_{19}AuBr_3O_3P$ requires C, 27·6; H, 2·6%); the crystals decomposed at room temperature within 24 hr.

The methyl ester was heated under nitrogen in a sealed tube at 100° for 5 hr. It was

recovered unchanged, but now gave a second form of the tribromogold derivative as stable yellowish-orange crystals, m. p. 113° (E.T.) (from methanol) (Found: C, 27·4; H, 2·6%).

The methyl ester (XI) in 20% aqueous-methanolic sodium hydroxide solution was shaken at room temperature for 2 hr. The methanol was boiled off, and the cold aqueous solution made just acid with 10% hydrochloric acid and extracted with ether. Distillation of the dried extract furnished the pure methylphosphine (IX), b. p. 130—140°/0·2 mm. (Found: C, 72·6; H, 6·4%), which gave the tribromogold derivative (X), m. p. and mixed m. p. 149—150° (E.T.) (from methanol) (Found: C, 25·45; H, 2·35%). A considerable dark residue remained undistilled.

A mixture of the ester (XI) and 10% hydrochloric acid was heated in nitrogen under reflux until a clear solution was formed (*ca.* 2 hr.). The cold solution deposited an oil, which was extracted with benzene. The dried extract contained the phosphine (IX), for it readily furnished the tribromogold derivative, m. p. and mixed m. p. 149—150° (E.T.). To identify the other products of hydrolysis, the extracted solution was reduced to small bulk in a vacuum desiccator and then neutralised (phenolphthalein) with aqueous sodium carbonate. This solution, when treated with boiling ethanolic benzylthiouronium chloride, deposited however the *benzylthiouronium salt* of the phosphine oxide propionic acid (XIII), a portion of the acid having undergone oxidation during the working up. The first time this salt was prepared, it had m. p. 125—126° after crystallisation from water: all subsequent preparations gave a salt of m. p. 84° from water (Found, for the high-melting form: C, 60·8; H, 5·6. $C_{24}H_{27}N_2O_4PS$ requires C, 61·25; H, 5·8%). Other components of the extracted solution could not be identified.

(D) *Ethyl acrylate.* Addition of this ester was carried out as that of the methyl ester, but with the phosphine (VII) (10·8 g.) and two additions each of ethyl acrylate (5 g.). The residue on distillation at 0·05 mm. gave fractions, (i) b. p. 65—125° (2 c.c.), and (ii) b. p. 125—190° (13 c.c.). Fraction (i) was mainly polymerised ethyl acrylate. Fraction (ii) on refractionation gave *ethyl* β-(m-*methoxyphenylphenylphosphino*)*propionate* (XII), b. p. 155—158°/0·1 mm. (Found: C, 68·7; H, 6·7. $C_{18}H_{21}O_3P$ requires C, 68·3; H, 6·7%). No methylphosphine (IX) could be detected. The ester (XII) gave a crystalline tribromogold derivative melting below 0°.

(E) *Ethyl* β-*bromopropionate.* This reaction was performed as for the methyl ester, with the phosphine (VII) (12·7 g.), sodium (1·35 g., 1 equiv.), and ethyl β-bromopropionate (10·7 g., 1 mol.). The residue on distillation gave a fraction, b. p. 95—130°/0·015 mm., and an undistilled dark material (3·0 g.). The distillate on refractionation at 0·015 mm. gave the fractions, (i) b. p. 110—115° (2·1 g.), and (ii) b. p. 117—122° (3 g.), and a very small residue. Fraction (ii) was the pure ethyl ester (XII) (Found: C, 68·6; H, 6·8%).

A mixture of the ester and 20% aqueous-ethanolic sodium hydroxide under nitrogen was boiled under reflux for 5 hr. and worked up as before. Distillation of the residue from the ethereal extract gave the methylphosphine (IX), b. p. 115—130°/0·05 mm., identified as the tribromogold derivative (X), m. p. and mixed m. p. 151—152° (E.T.) (Found: C, 25·4; H, 2·5%). The methylphosphine (IX) was also isolated when the cold alkaline solution, after removal of the ethanol, was extracted with benzene.

A mixture of the ester (XII) and 10% hydrochloric acid was boiled under reflux for 4 hr. and worked up as before. The oil, which was extracted with benzene, gave the tribromogold derivative (X), m. p. and mixed m. p. 150—151° (E.T.) (Found: C, 25·3; H, 2·2%).

The ester (0·5 g.) was treated with a solution of hydrogen peroxide (100-vol.; 2 c.c.) in acetone (6 c.c.). When the vigorous reaction had subsided, aqueous sodium hydroxide was added, the acetone distilled off, and then ethanol added to the boiling mixture to give a clear solution, which was boiled under reflux for 6 hr. The ethanol was removed, and the cold solution made almost neutral and extracted with ether to ensure absence of unhydrolysed ester. Acidification of the aqueous solution deposited a white gum, which solidified when rubbed with acetone; recrystallisation from water then gave the 2-*carboxyethyl*-(m-*methoxyphenyl*)*phenylphosphine oxide* (XIII), m. p. 153—155° (Found: C, 63·2; H, 5·95%; equiv., 307·5. $C_{16}H_{17}O_4P$ requires C, 63·2; H, 5·6%; equiv., 304).

This acid was also prepared by converting the phosphine (VII) by atmospheric oxidation into the phosphine oxide, which was then mixed with vinyl cyanide (4 mols.) and heated under reflux for 1½ hr. The excess of vinyl cyanide was removed and the gummy residue hydrolysed with aqueous-ethanolic sodium hydroxide. The solution was concentrated, cooled, acidified, and extracted with ether, which when then evaporated left the crystalline acid (XIII), m. p. 153—155·5° after recrystallisation from aqueous methanol (Found: C, 63·0; H, 5·9%).

(F) *Ethyl bromoacetate.* The phosphine (VII) (2·8 g.) was treated in liquid ammonia with sodium (0·3 g.) and ethyl bromoacetate (2·2 g.). The residue when distilled at 0·1 mm. gave a small fore-run and a main fraction (3 g.), b. p. 160—200°: some decomposition appeared to occur during the distillation, leaving much black material. The main fraction when refractionated gave the *ethyl* (m-*methoxyphenylphenylphosphino*)*acetate* (XIV), b. p. 170°/0·1 mm. (Found: C, 67·4; H, 6·5. $C_{17}H_{19}O_3P$ requires C, 67·6; H, 6·3%). This ester did not give crystalline tribromogold or dibromopalladium derivatives. The forerun did not contain the methylphosphine (IX).

A mixture of the phosphine (XIV) and 10% hydrochloric acid, when boiled as before for 12 hr., gave a neutral oily gum, possibly containing unchanged ester. The gum was therefore boiled with aqueous-ethanolic sodium hydroxide for 4 hr. No acidic component could be detected, but the neutral component gave the tribromogold derivative (X), m. p. and mixed m. p. 148·5° (E.T.).

(G) *Methyl bromoacetate.* The phosphine (VII) (10·3 g.) was similarly treated with sodium (1·1 g.) and methyl bromoacetate (7·3 g.). The residue on distillation also gave a small forerun and a main fraction, b. p. 175—220°/0·7 mm. (4·8 g.), which on refractionation gave the pure *methyl ester* (XV), b. p. 176—178°/0·5 mm. (Found: C, 66·95; H, 6·2. $C_{16}H_{17}O_3P$ requires C, 66·65; H, 5·9%). The ester (XV) gave a red *tribromogold derivative*, m. p. 143° (E.T.) (from ethanol) (Found: C, 26·5; H, 2·6. $C_{16}H_{17}AuBr_3O_3P$ requires C, 26·5; H, 2·4%). No unchanged phosphine (VII) could be detected in the small forerun.

The ester (XV) (4·8 g.) was added under nitrogen to 20% aqueous-ethanolic sodium hydroxide, which was boiled under reflux for 4 hr. The ethanol was boiled off, and the clear solution when chilled deposited a small amount of the methylphosphine (IX) as a neutral gum which was extracted with ether and identified as the tribromogold derivative, m. p. and mixed m. p. 148° (E.T.) (from ethanol). The residual aqueous layer when acidified deposited a white gum, which was also isolated by extraction with ether and evaporation of this extract. When the gum was stirred with acetone, the greater part dissolved, leaving crystalline *m*-methoxyphenylphenylphosphinic acid (XVII) (0·3 g.), which had m. p. 144—145° after crystallisation from acetone and then from water (Found: C, 63·3; H, 5·5%). This was confirmed by preparation of the *benzylthiouronium salt*, m. p. 182° (E.T.) (from water) (Found: C, 60·4; H, 5·6; N, 6·9. $C_{21}H_{23}N_2O_3PS$ requires C, 60·8; H, 5·6; N, 6·8%).

The acetone solution of the gum on evaporation gave the syrupy *m*-methoxyphenylphenylphosphinoacetic acid (XVI), identified as the *benzylthiouronium salt*, m. p. 129—130° (E.T.) after two recrystallisations from water (Found: C, 62·7; H, 5·8; N, 6·4. $C_{23}H_{25}N_2O_3PS$ requires C, 62·7; H, 5·7; N, 6·4%). This salt, when treated with hot dilute sulphuric acid, regenerated the acid (XVI) as a gum.

To determine whether the gummy acid (XVI) was readily decarboxylated, it was dissolved in aqueous sodium hydroxide, which was boiled for 1½ hr. The solution when worked up yielded the unchanged acid (XVI), a small quantity of the phosphinic acid (XVII), but none of the methylphosphine (IX). A mixture of the acid (XVI) and 10% hydrochloric acid was therefore boiled for 2 hr., but the mixture on working up gave solely the unchanged acid (XVI), identified as the benzylthiouronium salt, m. p. 125° (E.T.) after one recrystallisation from water.

(H) *Methyl γ-iodobutyrate.* The phosphine (VII) (10·7 g.) was treated in ammonia with sodium (1·14 g.) and with methyl γ-iodobutyrate (11·5 g.). The residue on distillation gave a fraction, b. p. 150—195°/0·15 mm. (8·2 g.), which on refractionation gave *methyl γ-*(m-*methoxyphenylphenylphosphino*)*butyrate* (XVIII), b. p. 172—180°/0·15 mm. (Found: C, 68·25; H, 6·8. $C_{18}H_{21}O_3P$ required C, 68·3; H, 6·7%). No crystalline co-ordinated metallic derivatives could be isolated.

This ester was hydrolysed as before, by 20% aqueous sodium hydroxide to which *ca.* 5% of ethanol had been added, a clear solution being obtained after 1 hour's boiling. On working up as usual, no neutral product could be isolated: acidification gave the acid (XIX) as an oil which gave a crystalline *benzylthiouronium salt*, m. p. 119—120° (E.T.) (from water) (Found: C, 63·7; H, 6·65; N, 6·3. $C_{25}H_{29}N_2O_3PS$ requires C, 64·1; H, 6·2; N, 6·0%). The salt was apparently stable to atmospheric oxidation, but the oily free acid, when treated with hydrogen peroxide in acetone, gave the phosphine oxide which did not apparently give a thiouronium salt.

Reactions of m-*Ethoxyphenylphenylphosphine* (XX).—(A) *Ethyl β-bromopropionate.* The

phosphine (XX) (8·9 g.) was treated as usual with sodium (0·9 g.) and ethyl β-bromopropionate (7·0), and the residue on distillation gave *ethyl* β-(m-*ethoxyphenylphenylphosphino*)*propionate* (XXII) (6·7 g.), b. p. >250°/0·5 mm. (Found: C, 69·3; H, 6·9. $C_{19}H_{23}O_3P$ requires C, 69·1; H, 7·0%). Undistilled residue was very small. The ester gave a tribromogold derivative which did not crystallise.

The ester (XXII) (6·7 g.) in aqueous-ethanolic sodium hydroxide was boiled for 1½ hr., the ethanol was removed, and the chilled, clear solution was extracted with ether. No neutral product was isolated from the extract. The aqueous solution when acidified deposited an oil which was extracted with ether: the dried extract when evaporated left the β-(m-*ethoxyphenylphenylphosphino*)*propionic acid* (XXIII) as a gum (5·3 g.) which quickly solidified. For purification, water was added dropwise to a hot ethanolic solution of the acid to produce a faint turbidity: the solution was filtered hot, and when cooled deposited the acid, m. p. 95—95·5° (E.T., shrinks from 90°) (Found: C, 67·2; H, 6·3%; equiv., 295, 298·5. $C_{17}H_{19}O_3P$ requires C, 67·0; H, 6·3%; equiv., 302·5). The acid showed no signs of atmospheric oxidation. It gave a crystalline *benzylthiouronium salt*, m. p. 130—131° (E.T.) (from water) (Found: C, 63·6; H, 6·0; N, 6·3. $C_{25}H_{29}N_2O_3PS$ requires C, 64·1; H, 6·2; N, 6·0%).

(B) *Methyl acrylate*. When the phosphine (XX) (12·8 g.) was added under nitrogen to freshly distilled methyl acrylate (4·8 g., 1 mol.), no heat was evolved. The mixture was boiled under reflux for 70 min., more acrylate (4·8 g.) being added after the first 10 min. Distillation removed the excess of acrylate and then gave only the *methyl ester* (14·4 g.) (XXI), b. p. 178—185°/0·2 mm. (Found: C, 68·3; H, 6·8. $C_{18}H_{21}O_3P$ requires C, 68·3; H, 6·7%).

The methyl ester (XXI) (14·4 g.), when hydrolysed as was the ethyl ester (XXII), required only 15 minutes' boiling, and when similarly worked up afforded the acid (XXIII) (11·8 g.).

(C) *Methyl bromoacetate*. The phosphine (XX) (10 g.) was treated in ammonia with sodium (1 g.) and methyl bromoacetate (6·7 g.). Distillation of the residue gave a fraction, b. p. 155—175°/0·5 mm. (4·4 g.), and much black residue. The fraction on redistillation gave *methyl* (m-*ethoxyphenylphenylphosphino*)*acetate* (XXIV), b. p. 175°/0·5 mm. (Found: C, 67·8; H, 6·7. $C_{17}H_{19}O_3P$ requires C, 67·5; H, 6·3%).

A mixture of the methyl ester (XXIV) (4·4 g.) and 20% aqueous sodium hydroxide containing 5% of ethanol was boiled under reflux in nitrogen for 2 hr. After removal of the ethanol, the cold solution was extracted with ether: this extract on evaporation left no residue. The aqueous solution was acidified, and the precipitated oily acid extracted with ether: this extract when dried and evaporated gave an oily mixture of the acids (XXV) and (XXVI). A portion of the mixture gave the crystalline *benzylthiouronium salt*, m. p. 134° (E.T.) (from water), of (*m*-ethoxyphenylphenylphosphino)acetic acid (XXV) (Found: C, 63·4; H, 6·0; N, 6·2. $C_{24}H_{27}N_2O_3PS$ requires C, 63·1; H, 6·2; N, 6·2%). The remainder of the mixture was stirred with acetone, and after a short period deposited crystalline *m*-ethoxyphenylphenylphosphinic acid (XXVI) (0·43 g.), m. p. 132—135° (E.T.) after two recrystallisations from acetone (Found: C, 64·1; H, 5·6%): the acid gave a *benzylthiouronium salt*, m. p. 176° (E.T.) (from water) (Found: C, 61·9; H, 6·0; N, 6·7. $C_{22}H_{25}N_2O_3PS$ requires C, 61·7; H, 5·9; N, 6·5%). The initial acetone extract on evaporation gave the oily phosphinoacetic acid (XXV) (2·6 g.).

The acid (XXV) (2·6 g.) in 20% aqueous-ethanolic sodium hydroxide was boiled under reflux in nitrogen for 2 hr.; the solution, worked up as before, gave the phosphinic acid (XXVI) (0·25 g.) and a residue of the unchanged acid (XXV) (1·2 g.).

Reactions of p-*Methoxyphenylphenylphosphine* (XXVII).—(A) *Methyl iodide*. This preparation was carried out as was that of the *m*-methoxyphenyl analogue (IX). The phosphine (XXVII) (10·8 g.) in liquid ammonia (125 c.c.) was treated in turn with sodium (1·2 g.) and methyl iodide (7·1 g.). After working up, the residue on distillation gave p-*methoxyphenylmethylphenylphosphine* (XXIX), b. p. 135—138°/0·5 mm. (7 g.), as the sole distillate (Found: C, 73·45; H, 6·45; *M*, in benzene by the thermister method, 222. $C_{14}H_{15}OP$ requires C, 73·0; H, 6·6%; *M*, 230).

It readily gave a gummy *methiodide* which solidified when washed with ether, and after recrystallisation from acetone–methyl iodide had m. p. 135° (E.T., shrinking from 130°) (Found: C, 48·8; H, 4·6. $C_{15}H_{18}IOP$ requires C, 48·4; H, 4·9%). It underwent partial dissociation when recrystallised from acetone alone. The phosphine also gave a *methotoluene*-p-*sulphonate*, m. p. 132° (E.T., shrinks at 127°) (from acetone) (Found: C, 63·5; H, 6·2. $C_{22}H_{25}O_4PS$ requires C, 63·4; H, 6·0%). The phosphine gave a silver iodide complex which readily

dissociated in solution: the tribromogold and the dibromopalladium derivative were too soluble in organic solvents for ready isolation.

(B) *Ethyl bromide.* This preparation was similarly performed with the phosphine (XXVII) (10 g.), sodium (1·1 g.), and ethyl bromide (5·1 g.) in ammonia. It afforded *ethyl*-p-*methoxyphenylphenylphosphine* (8·7 g.), b. p. 125—135°/0·3 mm. (Found: C, 74·1; H, 7·1. $C_{15}H_{17}OP$ requires C, 73·8; H, 7·0%). No crystalline derivatives could be isolated.

(C) *Ethyl β-bromopropionate.* The phosphine (XXVII) (10·9 g.) in ammonia was treated with sodium (1·2 g.) and ethyl β-bromopropionate (9·2 g., 1 mol.). The residue, distilled at 0·5 mm., gave a main fraction (3·3 g.), b. p. 184—200°, which on refractionation gave *ethyl* β-(p-*methoxyphenylphenylphosphino*)*propionate* (XXVIII), b. p. 190°/0·5 mm. (Found: C, 68·3; H, 6·4. $C_{18}H_{21}O_3P$ requires C, 68·3; H, 6·7%).

(D) *Ethyl acrylate.* A mixture of the phosphine (XXVII) (17·6 g.) and freshly distilled ethyl acrylate (12 g., 1 mol.) under nitrogen was gently boiled under reflux for 30 min., more acrylate (6 g.) being added after 10 min. Distillation at 0·5 mm. gave the fractions, (i) b. p. 50—100° (2 c.c.), (ii) b. p. 115—145° (7·8 g.), and (iii) b. p. 150—175° (13·5 g.). Fraction (i) was polymerised ethyl acrylate. Fraction (ii) redistilled steadily over 115—130°/0·3 mm.; a sample of b. p. 125—128° was the pure methylphosphine (XXIX) (Found: C, 73·1; H, 6·8%), and gave the methotoluene-*p*-sulphonate, m. p. and mixed m. p. 133° (E.T., shrinks 130°) (from acetone) (Found: C, 63·6; H, 6·05%). Fraction (iii) on refractionation gave the ethyl ester (XXVIII), b. p. 185°/0·3 mm. (Found: C, 68·0; H, 6·8%). In a second apparently similar experiment, only fraction (iii) was obtained.

Hydrolysis of the Ethyl Ester (XXVIII). A mixture of the ester (6·2 g.) and aqueous-ethanolic sodium hydroxide was boiled under reflux for 3 hr. and, after removal of the ethanol, cooled and just acidified. [The precipitated β-(*p*-methoxyphenylphenylphosphino)propionic acid (XXX) separated initially as an emulsion which redissolved in an excess of hydrochloric acid; but when once the acid had collected in globules it dissolved far more slowly in the hydrochloric acid.] The oily acid was isolated by ether extraction but did not crystallise: it gave the crystalline *benzylthiouronium salt*, m. p. 143° (E.T.) (from water) (Found: C, 63·4; H, 6·4; N, 6·1. $C_{24}H_{27}N_2O_3PS$ requires C, 63·1; H, 6·2; N, 6·2%).

Oxidation of the Ester (XXVIII). An acetone solution of the ester (7·3 g.) was treated dropwise with an acetone solution of an excess of hydrogen peroxide (100-vol.), boiled under reflux for 30 min., and then cooled. The solution was basified with sodium hydroxide, the acetone removed, and the boiling continued for another 30 min.; then the clear, cold solution was extracted with ether. The aqueous solution when acidified deposited 2-*carboxyethyl*-(p-*methoxyphenyl*)*phenylphosphine oxide* (XXXI) (6·3 g.) as a white gum which readily solidified, and was purified by precipitation from an ethanolic solution by ether, followed by recrystallisation from ethanol containing 5% of water: the crystals had m. p. 181—182° (E.T.) (Found: C, 62·95; H, 5·9. $C_{16}H_{17}O_4P$ requires C, 63·2; H, 5·6%). The benzylthiouronium salt was too soluble for ready purification. Alternatively, the oily acid (XXX), obtained by hydrolysis of the ester (XXVIII), when similarly oxidised in acetone gave the acid (XXXI), m. p. 178—181° (E.T.) (from aqueous ethanol) (Found: C, 63·1; H, 6·0%).

(E) *Methyl acrylate.* A mixture of the phosphine (XXVII) (9 g.) and freshly distilled methyl acrylate (3·6 g., 1 mol.) was heated under reflux for 20 min. Distillation at 0·5 mm. gave a very small forerun, b. p. <100°, and a main fraction distilling steadily over a range 130—185° (9 g.). Refractionation gave the same fraction, and analysis of the final portion, b. p. 185°, indicated that it was a mixture of the methylphosphine (XXIX) and the methyl ester (as XXVIII) (Found: C, 70·6; H, 6·6%).

The same mixture was apparently formed when the phosphine (XXVII) (7 g.) in ammonia was treated with sodium (0·75 g.) and methyl β-bromopropionate (5·4 g., 1 mol.). The residue gave one main fraction, a sample, b. p. 175°/0·7 mm., being analysed (Found: C, 69·0; H, 6·6%).

The mixed phosphines (7 g.) in aqueous-ethanolic sodium hydroxide were boiled for 1½ hr., the ethanol removed, and the cold solution carefully neutralised: an oil, which was apparently soluble in acidic and basic solutions, separated and was extracted with ether. The ethereal extract after evaporation gave on distillation the methylphosphine (XXIX), b. p. 140—145°/0·5 mm., in very small yield (Found: C, 72·5; H, 6·55%), and a considerable undistilled residue which could not be identified and presumably arose from the amphoteric material. The phosphine (XXIX) was identified as its methotoluene-*p*-sulphonate, m. p. and mixed m. p. 130° (E.T., shrinks at 125°) (Found: C, 63·6; H, 6·3%).

Reactions of p-*Ethoxyphenylphenylphosphine* (XXXII).—A mixture of the phosphine (XXXII) (5·7 g.) and freshly distilled ethyl acrylate (2·2 g.) was heated under reflux for 30 min., and was then distilled, giving solely the *ethyl* β-(p-*ethoxyphenylphenylphosphino)propionate* (XXXIII) (7 g.), b. p. 170—175°/0·5 mm. (Found: C, 69·4; H, 7·3. $C_{19}H_{23}O_3P$ requires C, 69·1; H, 7·0%). No trace of a methylphosphine could be detected.

The ethyl ester (XXXIII) (7 g.) was heated as usual with the sodium hydroxide solution for 30 min., and the cold, clear solution acidified. The deposited oil, isolated by ether extraction, yielded the syrupy phosphinopropionic acid (XXXIV), which gave a *benzylthiouronium salt*, m. p. 151—152° (E.T.) (from water) (Found: C, 63·8; H, 6·2; N, 5·9. $C_{25}H_{29}N_2O_3PS$ requires C, 64·1; H, 6·2; N, 6·0%).

Methyl m-*Methoxyphenylphenylphosphinate*.—This ester was prepared to investigate its reduction to the phosphine (VII). A stirred mixture of the acid (XLIX; R = *m*-MeO) (30·8 g.) in benzene (50 c.c.) was treated with phosphorus trichloride (40 c.c.) and phosphorus pentachloride (26·0 g., 1 mol.) and set aside overnight. It was then boiled under reflux for 2 hr., and concentrated under reduced pressure: the residual dark oil on distillation gave the colourless acid chloride (27·8 g., 84%), b. p. 175—178°/0·6 mm. The residue yielded unchanged acid (4·0 g.).

The chloride was poured cautiously into a solution of methanol (20 c.c.) in benzene (50 c.c.) at 0°; the mixture was again set aside overnight, and then boiled under reflux for 30 min., and the solvent then removed. The residual oil, which partly crystallised, was dissolved in boiling benzene (*ca.* 75 c.c.), and light petroleum (b. p. 80—100°) (75 c.c.) added. The solution, when cooled in ice, deposited the acid (XLIX; R = *m*-MeO) (9·3 g.), m. p. 136—140°. The filtrate, after extraction with 5% aqueous sodium hydroxide, was dried and distilled, giving the *methyl ester* (15·0 g., 57%), b. p. 183—186°/103 mm., m. p. 45—49° (Found: C, 63·9; H, 5·8. $C_{14}H_{15}O_3P$ requires C, 64·1; H, 5·8%). The acid (9·3 g.) may have been formed by the competing reaction, $R_2P(:O)Cl + MeOH \longrightarrow R_2P(:O)\cdot OH + MeCl$.

Reduction of this ester by lithium aluminium hydride in tetrahydrofuran gave the crude phosphine (VII) in 40—45% yield.

Methyl β-(*Diphenylphosphino)propionate*.—In early pilot experiments diphenylphosphine and methyl acrylate were combined under nitrogen, initially at room temperature, then heated at 130—140°, to give the *methyl ester*, b. p. 151°/0·4 mm. (Found: C, 70·7; H, 6·5. $C_{16}H_{17}O_2P$ requires C, 70·5; H, 6·3%). It was characterised as the *dibromodi(phosphine ester)palladium*, golden plates, m. p. 193·5—194·5°, from methanol–benzene (Found: C, 47·1; H, 4·2. $C_{32}H_{34}Br_2O_4P_2Pd$ requires C, 47·4; H, 4·2%).

Attempted Cyclisation of the Acid (XXIII).—Some evidence of cyclisation was obtained only under the following conditions. The acid (XXIII) (10·8 g.) was added to a rapidly stirred suspension of phosphorus pentoxide (30 g.) and freshly heated Hyflo Supercel (15 g.) in dry toluene (100 c.c.), which was then boiled under reflux for 30 min. The chilled, pale brown mixture was cautiously hydrolysed with water, made alkaline, and extracted with ether. Evaporation of the dried extract gave a gum, the infrared spectrum of which showed a small peak at 1720 $cm.^{-1}$. The gum, when heated under nitrogen in a sublimation tube at 0·1 mm., afforded a distillate continuously from *ca.* 150—280°, and fractions were collected at *ca.* 50° intervals. The distillates removed at 180° and at 280° showed no peak in the 1720 $cm.^{-1}$ region, whereas that collected at 220° showed a marked peak at this value: a small sample of the distillate at 220—230° appeared to be 7-ethoxy-1,2,3,4-tetrahydro-4-oxo-1-phenylphosphinoline (LIV) (Found: C, 71·4; H, 6·8. Calc. for $C_{17}H_{17}O_2P$: C, 71·8; H, 6·3%). The compound, treated with a solution of silver iodide in saturated aqueous sodium iodide, gave a silver iodide complex, which, after crystallisation from ethanol containing some acetone, had m. p. 120° (E.T.) (Found: C, 38·95; H, 3·3. Calc. for $C_{17}H_{17}AgIO_2P$: C, 39·3; H, 3·3%). This agreement may have been fortuitous, however, for other samples, similarly prepared, had markedly discordant compositions.

University Chemical Laboratory, Cambridge.
[Present address (D. T.): Department of Chemical Engineering and Chemistry, Worcester Polytechnic Institute, Worcester, Mass., U.S.A.]

[*Received, July 5th*, 1961.]