925. *Synthesis of the* 1-*Substituted* 1,2,3,4-*Tetrahydro*-4-*oxophosphinoline System.*

By M. J. Gallagher, E. C. Kirby, and Frederick G. Mann.

The 1-phenyl member of the system named in the title, of interest as being intermediate between the corresponding known quinoline and arsinoline systems, has been prepared by cyclisation of 2-cyanoethyl-*o*-cyanophenylphenylphosphine to 4-amino-3-cyano-1,2-dihydro-1-phenylphosphinoline, followed by acid hydrolysis. The structure and certain reactions of the 1-phenyl derivative are discussed.

An alternative synthesis involving direct cyclisation of a β-(diphenylphosphino)propionic acid in which one phenyl group for activation carried a *m*-methoxyl or a *m*-methyl group or 3,5-dimethyl groups, succeeded only with the last compound, and in impracticably small yield. These diarylphosphinopropionic acids are in this respect in marked contrast to their nitrogen and arsenic analogues.

Earlier attempts to synthesise 1-substituted 1,2,3,4-tetrahydro-4-oxophosphinolines (as IX) by the cyclisation of β-(diphenylphosphino)-propionitrile or -propionic acid, $Ph_2P\cdot[CH_2]_2\cdot R$ (where $R = CN$ or CO_2H),[1] or β-(*m*-ethoxyphenylphenylphosphino)-propionic acid[2] gave either a very meagre or no yield of the cyclic phosphine. In case this failure was due to the two aryl groups linked to the phosphorus atom, 2-cyanoethylmethylphenylphosphine was prepared by the action of sodium methoxide on a boiling methanolic solution of di-(2-cyanoethyl)methylphenylphosphonium iodide,[3] but this nitrile and the corresponding acid could not be cyclised to the tetrahydro-1-methyl-4-oxophosphinoline (as IX) under a variety of conditions.

We have therefore synthesised *o*-chlorophenyl-2-cyanoethylphenylphosphine and the *o*-bromophenyl analogue (VI; R = Cl, Br) in order to investigate the possible cyclising action of lithium: the halogen groups were selected as being almost the only groups which would remain unchanged throughout the synthesis. *o*-Chloroaniline was converted into the diazonium fluoroborate (I; R = Cl) which when treated in ethyl acetate with phenylphosphonous chloride and cuprous bromide (the Doak–Freedman reaction[4]) yielded *o*-chlorophenylphenylphosphinic acid (II; R = Cl). Although phosphinic acids and their esters when reduced with an excess of lithium aluminium hydride in tetrahydrofuran normally

---

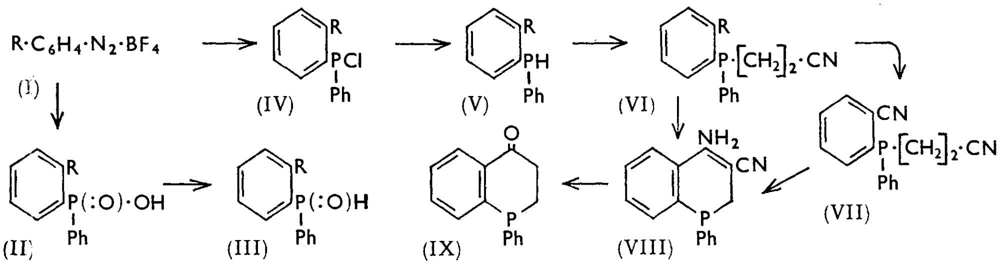
[1] Mann and Millar, *J.*, 1952, 4453.

[2] Hinton, Mann, and Todd, *J.*, 1961, 5454.

[3] Grayson, Keough, and Johnson, *J. Amer. Chem. Soc.*, 1959, **81**, 4803.

[4] Freedman and Doak, *J. Amer. Chem. Soc.*, 1952, **74**, 2884; see also Doak and Freedman, *ibid.*, 1951, **73**, 5658.

give secondary phosphines,[2,5] the ethyl ester of the acid (II; R = Cl) gave almost solely the secondary phosphine oxide (III; R = Cl); the acid (II; R = Cl) also gave the oxide as the main product, with a small proportion of diphenylphosphine and *o*-chlorophenylphenylphosphine (V; R = Cl). The phosphine oxide (III; R = Cl) is an unexpectedly stable compound, and was mainly unchanged when treated afresh with lithium aluminium hydride.



o-Chlorophenylphenylphosphinous chloride (IV; R = Cl) was therefore prepared by Quin and Humphrey's method,[6] the solution obtained by the interaction of the fluoroborate (I; R = Cl) in ethyl acetate with phenylphosphonous chloride being treated directly with magnesium: working up gave the chloride (IV; R = Cl) and di-(*o*-chlorophenyl)phenylphosphine in 31% and *ca.* 2% yield, respectively. The chloride (IV; R = Cl) was reduced to the phosphine (V; R = Cl), which with vinyl cyanide gave *o*-chlorophenyl-2-cyanoethylphenylphosphine (VI; R = Cl) and with ethyl acrylate gave the corresponding ethyl ester. The phosphine (V; R = Cl) was rapidly oxidised by air to the phosphine oxide (III; R = Cl).

The nitrile (VI; R = Cl), when treated in tetrahydrofuran at —35° with lithium, gave chiefly a mixture of diphenylphosphine and *o*-chlorophenylphenylphosphine (V; R = Cl). Similar treatment of the ethyl ester gave an unsatisfactory mixture. The nitrile, after being heated in dimethyl sulphoxide with cuprous cyanide at 120° for 7 hours, was recovered in 80% yield, and the dinitrile (VII) could not be obtained in this way.

To obtain greater reactivity in the aromatic ring, *o*-bromophenyldiazonium fluoroborate (I; R = Br) was similarly converted into the phosphinous chloride (IV; R = Br) with a small yield of di-(*o*-bromophenyl)phenylphosphine. The chloride was reduced with lithium aluminium hydride to the phosphine (V; R = Br), which in turn with vinyl cyanide afforded the nitrile (VI; R = Br). It is noteworthy that the chloride (IV; R = Br) was unaffected by lithium hydride, the product on hydrolysis giving solely the very stable phosphine oxide (III; R = Br), into which the phosphine (VI; R = Br) was rapidly converted by atmospheric oxidation; hydrogen peroxide converted the phosphine oxide (III; R = Br) into the phosphinic acid (II; R = Br).

Although aryl bromides usually react readily with lithium in ether,[7] and the cleavage of phosphines by lithium which occurs readily in tetrahydrofuran does not occur in ether,[8] attempts to cyclise the nitrile (VI; R = Br) by the action of lithium in various ethers failed: where any reaction could be induced, phosphine cleavage was again observed.

The nitrile (VI; R = Br), when heated with cuprous cyanide in dimethyl sulphoxide at 170° for 5 hours, gave a mixture of the unchanged substance and 2-cyanoethyl-*o*-cyanophenylphenylphosphine (VII). Separation of these compounds was difficult, but the crude dinitrile (VI), when treated in xylene with sodium t-butoxide, gave 4-amino-3-cyano-1,2-dihydro-1-phenylphosphinoline (VIII). The use of more concentrated solutions in

[5] Mann, Tong, and Wystrach, *J.*, 1963, 1155.
[6] Quin and Humphrey, *J. Amer. Chem. Soc.*, 1961, **83**, 4124; *J. Org. Chem.*, 1962, **27**, 4120.
[7] Gilman, Zoellner, and Selby, *J. Amer. Chem. Soc.*, 1933, **55**, 1252.
[8] Wittenberg and Gilman, *J. Org. Chem.*, 1958, **23**, 1063.

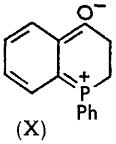
the cuprous cyanide treatment, however, gave the phosphinoline (VIII) in one stage in 28% yield, which could probably be increased. The two-stage process gave this product in 38% overall yield, but this hardly justified the extra manipulation.

The structure of the amino-cyano-phosphinoline (VIII) is confirmed by the close similarity of its infrared spectrum (wavelengths in cm.$^{-1}$) with those of (A) 4-amino-3-cyano-1-phenyl-1-phosphacyclohex-3-ene and (B) 4-amino-3-cyano-1,2,5,6-tetrahydro-1-phenylpyridine, whose structures have recently been determined: [9]

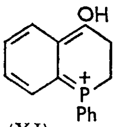
	NH_2 Bands	CN Band	NH_2 Deformation and C:C bands
(VIII)	3490, 3350, 3250	2170	1640
(A)	3400, 3330, 3240	2180	1640
(B)	3450, 3360, 3250	2190	1625, 1645

The successful hydrolysis of the amino-cyano-phosphinoline (VIII) required strict adherence to specific conditions, under which hot hydrochloric acid gave the crystalline 1,2,3,4-tetrahydro-4-oxo-1-phenylphosphinoline (IX) in 55% yield: it was characterised as its methopicrate, oxide, and 4-phenylsemicarbazone. It is a weak base and will not give a stable picrate but gives a crystalline perchlorate.

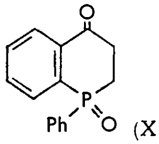
There is strong evidence that the oxo-phosphine has the structure (IX) and that the polar form (X) makes no detectable contribution to its structure, and furthermore that its salts with acids are formed by proton addition to the phosphorus atom, and not to the oxygen atom as in the cation (XI),. Both the oxo-phosphine and its perchlorate are colourless, whereas the structures (X) and (XI) would undoubtedly produce coloured products. The infrared spectrum of the oxo-phosphine (IX) shows marked carbonyl absorption at 1680 cm.$^{-1}$ (normal for aryl-conjugated ketones), whereas that of the oxide (XII) shows this absorption at 1700 cm.$^{-1}$, the change presumably being caused by the P=O group, which gives strong absorption at 1190 cm.$^{-1}$. The spectrum of the perchlorate shows carbonyl absorption at 1687 cm.$^{-1}$ but no hydroxyl absorption. The ultraviolet absorption spectra of the oxo-phosphine and its oxide (XII) in ethanol (annexed Figure) were unaffected by the addition of concentrated hydrochloric acid: the formation of the cation (XI) would have considerably changed the spectrum of the oxo-phosphine (IX). This spectrum of the oxo-phosphine bears no resemblance to that of the pale yellow 1,2,3,4-tetrahydro-1-methyl-4-oxoquinoline, but has a general resemblance to that of 1,2,3,4-tetrahydro-7-methoxy-1-methyl-4-oxoarsinoline.[10]



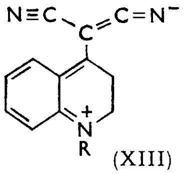
(X)



(XI)



(XII)



(XIII)

It is noteworthy that although 1-alkyl- and 1-aryl-1,2,3,4-tetrahydro-4-oxoquinolines condense readily with malononitrile to give deep red products, the colour and stability of which indicate that the polar form (XIII) must make a substantial contribution,[11] the oxo-phosphine (IX) and 1,2,3,4-tetrahydro-7-methoxy-1-methyl-4-oxoarsinoline [10] do not condense with malononitrile under similar conditions. This illustrates the great reluctance of phosphorus or arsenic in a six-membered ring to accept an " internal " positive charge, as in (XIII).

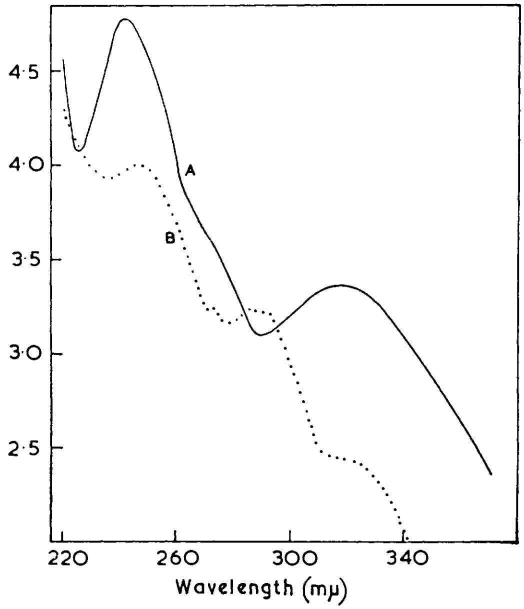
The oxo-phosphine (IX) and its oxide (XII) give 2,4-dinitrophenylhydrazones: that of the oxo-phosphine is dimorphic and its structure remains uncertain (p. 4853).

---

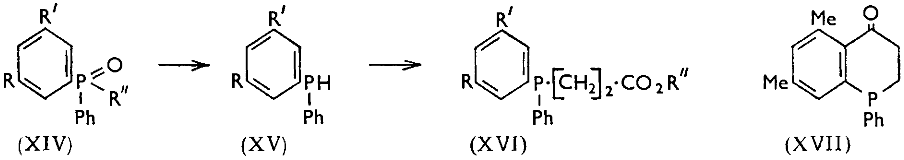
[9] Gallagher and Mann, *J.*, 1962, 5110.
[10] Mann and Wilkinson, *J.*, 1957, 3336.
[11] Ittyerah and Mann, *J.*, 1956, 3179.

Whilst the direct synthesis of the oxo-phosphine (IX) was in progress, we have investigated the direct cyclisation of three β-(diphenylphosphino)propionic acids, in which one phenyl group for activation carried a *m*-methoxyl, or a *m*-methyl, or 3,5-dimethyl substituents.

β-(*m*-Methoxyphenylphenylphosphino)propionic acid in boiling toluene or xylene with phosphoric anhydride gave no evidence of cyclisation (unlike its *m*-methoxyphenylmethylarsino-analogue[10]), but the small amount of the acid available from earlier work[5] precluded detailed investigation. *m*-Toluenediazonium fluoroborate, when subjected to the Doak–Freedman reaction with phenylphosphonous chloride, gave the phenyl-*m*-tolylphosphinic acid (XIV; R = Me, R′ = H, R″ = OH), which was converted into the ethyl ester. Reduction of the acid and of the ester gave the phosphine (XV; R = Me, R′ = H), which could not be purified but which, after reaction with methyl and ethyl acrylate, gave the pure methyl and ethyl β-phosphino-propionates (XVI; R = Me, R′ = H, R″ = Me or Et). Hydrolysis of these esters gave the crystalline β-(phenyl-*m*-tolylphosphino)propionic acid (XVI; R = Me, R′ = R″ = H), but attempted cyclisation gave indefinite products.



Ultraviolet spectra of (A) the oxo-phosphine (IX) (2·270 mg. in 100 ml. of ethanol) and (B) the oxo-phosphine oxide (XII) (2·250 mg. in 100 ml. of ethanol).



(XIV) (XV) (XVI) (XVII)

3,5-Dimethylaniline, prepared by Hull's method,[12] was similarly converted into 3,5-dimethylphenylphenylphosphinic acid (XIV; R = R′ = Me, R″ = OH) and then into its ethyl ester.

This ester on reduction gave the phosphine (XV; R = R′ = Me), which also could not be fully purified by distillation. A second product of higher boiling point has since

---

[12] Hull, *J.*, 1951, 1136.

been identified by Mr. K. B. Mallion as 3,5-dimethylphenyl-4'-hydroxybutylphenylphosphine, $Me_2C_6H_3{\cdot}PPh{\cdot}[CH_2]_4{\cdot}OH$. The infrared spectra of this phosphine and its methiodide showed the presence of the hydroxyl group. The nuclear magnetic resonance spectrum of the phosphine in chloroform, obtained at 40 Mc./sec., showed the sharp peaks: τ(O–H), 5·91; τ($CH_2{\cdot}OH$), 6·47; τ(Me–aryl), 7·83; and a broad peak centred at 8·37, probably a group of overlapping peaks based on $P{\cdot}[CH_2]_3$ {chemical shifts on the τ scale [$\tau(SiMe_4) = 10{\cdot}00$] measured against tetramethylsilane as an internal reference}. The infrared spectrum of the phosphine is almost identical with that of 4-hydroxybutyldiphenylphosphine, which is formed during the prolonged action of lithium aluminium hydride on diphenylphosphinic acid in tetrahydrofuran, rather more rapidly by that of the Ph_2P^- ion on this solvent,[13] and very rapidly by the action of magnesium or aluminium on a tetrahydrofuran solution of diphenylphosphinous chloride.[14]

The phosphine (XV; R = R' = Me) was converted into the β-phosphinopropionic acid (XVI; R = R' = Me, R'' = H) which in boiling xylene with phosphoric anhydride gave only unidentified syrups. The acid when heated, however, with polyphosphoric acid gave a crude viscous oil which furnished a deliquescent methiodide: this in turn afforded a crystalline methopicrate, which on analytical evidence was the salt of 1,2,3,4-tetrahydro-5,7-dimethyl-4-oxo-1-phenylphosphinoline (XVII). The very small yield made the method of very little synthetic value.

EXPERIMENTAL

Unless otherwise stated, all compounds were colourless, all molecular weights were determined by the modified Thermistor method in benzene solutions, and the petroleum used was light petroleum of b. p. 60—80°. All operations involving phosphines were performed under nitrogen.

2-*Cyanoethylmethylphenylphosphine*.—A solution of di-(2-cyanoethyl)methylphenylphosphonium iodide [1] (14·2 g.) in boiling absolute methanol (30 ml.) was treated dropwise with a solution obtained from sodium (1 g., 1 equiv.) and methanol (25 ml.). The mixture was boiled for 3·5 hr., and the methanol removed by distillation. The black semi-solid residue was shaken with water (20 ml.) and benzene (20 ml.), and the benzene layer, when dried and distilled, gave the pure *phosphine* (4·1 g., 58%), b. p. 100—101°/0·3 mm., n_D^{20} 1·569 (Found: C, 68·1; H, 7·0; N, 8·2. $C_{10}H_{12}NP$ requires C, 67·8; H, 6·8; N, 7·9%). It gave a *methiodide*, m. p 172—173° (from ethanol) (Found: C, 41·3; H, 4·6; N, 4·0. $C_{11}H_{15}INP$ requires C, 41·4; H, 4·7; N, 4·3%), and a yellow *methopicrate*, m. p. 123—125° (from water) (Found: C, 48·9; H, 4·0; N, 13·5. $C_{17}H_{17}N_4O_7P$ requires C, 48·6; H, 4·05; N, 13·3%).

Hydrolysis of this nitrile in boiling aqueous-ethanolic sodium hydroxide afforded β-(*methylphenylphosphino*)*propionic acid* (96%) as a clear yellow oil; its infrared spectrum showed no cyano-absorption, but a strong band at 1730 cm.$^{-1}$. It gave a *benzylthiouronium salt*, needles, m. p. 130—131° (from water) (Found: C, 59·2; H, 6·2; N, 7·7. $C_{18}H_{23}N_2O_2PS$ requires C, 59·7; H, 6·35; N, 7·7%), and a *methiodide*, m. p. 176—177° (from ethanol) (Found: C, 38·75; H, 4·6. $C_{11}H_{16}IO_2P$ requires C, 39·05; H, 4·7%).

No indication of the formation of the cyclic oxo-phosphine (as IX) was obtained when the cyanoethylphosphine was treated with a molten mixture of aluminium chloride, sodium chloride, and potassium chloride,[15] or when the acid in boiling xylene solution was treated with phosphoric anhydride under various conditions.[16,11]

o-*Chlorobenzenediazonium fluoroborate* (I; R = Cl).—This salt was prepared as described earlier,[5] from *o*-chloroaniline (63·5 g.), sodium fluoroborate (75 g., 1·36 mol.) in water (150 ml.), concentrated hydrochloric acid (100 ml.), and sodium nitrite (38·5 g., 1 mol.) in water (100 ml.), ether (100 ml.) being added to the stirred suspension before diazotisation to reduce frothing. The fluoroborate (90 g., 80%) was dried in a vacuum-desiccator in order to reduce the induction period and the violence of the reaction in the following preparation.

o-*Chlorophenylphenylphosphinic Acid* (II; R = Cl).—This was prepared by reaction with

---

[13] Mallion and Mann, *Chem. and Ind.*, 1963, 654.

[14] Garner and Tedeschi, *J. Amer. Chem. Soc.*, 1962, **84**, 4734.

[15] Allison, Braunholtz, and Mann, *J.*, 1954, 403; Braunholtz, Mallion, and Mann, *J.*, 1962, 4346.

[16] Cookson and Mann, *J.*, 1949, 67.

phenylphosphorous chloride, with the precautions noted earlier,[2,5] but with cuprous bromide instead of cuprous chloride. The *acid* (crude, 50%) had m. p. 186—187° (from ethanol) (Found: C, 56·7; H, 3·8. $C_{12}H_{10}ClO_2P$ requires C, 57·0; H, 4·05%): it gave a *benzylthiouronium salt*, m. p. 182—183° [from ethanol–petroleum (1 : 1 v/v)] (Found: C, 57·65; H, 5·0; N, 6·9. $C_{20}H_{20}ClN_2O_2PS$ requires C, 57·35; H, 4·8; N, 6·7%).

Ethyl o-*Chlorophenylphenylphosphinate*.—The acid was converted into the *phosphinic chloride* (87%), b. p. 170—171°/0·3 mm., m. p. 79·5—81° (from petroleum) (Found: C, 53·2; H, 3·6. $C_{12}H_9Cl_2OP$ requires C, 53·1; H, 3·3%), and then into the *ethyl ester* (89%), b. p. 158—161°/0·02 mm., m. p. 68—69° (from petroleum) (Found: C, 59·6; H, 5·2. $C_{14}H_{14}ClO_2P$ requires C, 59·9; H, 5·0%), by the methods previously recorded.[5] The ester was unaffected by 3 days' exposure to the air, but when mixed with water rapidly gave the acid.

Reduction. This was performed under nitrogen throughout. The redistilled ester (14 g.) in pure tetrahydrofuran (50 ml.) was added dropwise to a stirred suspension of lithium aluminium hydride (2 g., 1 mol.) in tetrahydrofuran (50 ml.). The mixture became orange and boiled gently: it was boiled for 1 hr. more, then concentrated, cooled, and treated with wet ether (100 ml.) and then 5% aqueous sodium hydroxide (*ca.* 25 ml.) until a sharp separation of aluminium salts occurred. The organic layer was collected, the aqueous layer twice extracted with ether, and the united dried ether solution distilled: it gave the fractions: (i) b. p. 100—154°/0·2 mm. (0·3 g.), oil and crystals; (ii) b. p. 154—156°/0·2 mm. (2·1 g.), rapidly crystallising. This o-*chlorophenylphenylphosphine oxide* (III; R = Cl), when recrystallised by adding ethanol dropwise to a boiling suspension in petroleum to give a clear solution, had m. p. 72·5—74·5° (Found: C, 60·8; H, 4·5%; *M*, in methylene dichloride, 226. $C_{12}H_{10}ClOP$ requires C, 60·9; H, 4·2%; *M*, 236): its infrared spectrum showed strong absorption at 1190 cm.$^{-1}$ (P=O) and weak absorption at 2300 cm.$^{-1}$ (P–H). The aqueous slurry from the ether extraction gave, on acidification, the acid (II; R = Cl) (2 g.): after allowance for this, the yield of the oxide is 19%.

When this reduction was repeated on the oxide (8·0 g.), distillation gave early runnings (0·7 g.) and the unchanged oxide (4·3 g.).

The acid (II; R = Cl) (38 g.) was similarly reduced with lithium aluminium hydride (6 g., 1·05 mol.) with 4½ hours' boiling. Distillation of the final product at 0·25 mm. gave the fractions: (i) b. p. 96—110° (1·0 g.); (ii) b. p. 110—125° (0·2 g.); (iii) b. p. 144—160°, m. p. 68—70° (4·4 g.), the oxide (III; R = Cl). After allowance for recovered acid (11 g.), the yield of the oxide was 17%. Fraction (i), which showed strong absorption at 2280 cm.$^{-1}$ (P–H), on redistillation gave the fractions: (*a*) b. p. <105°/0·25 mm. (0·2 g.); (*b*) 105—115°/0·25 mm. (0·7 g.). Fraction (*a*), crude diphenylphosphine, on oxidation with hydrogen peroxide, gave diphenylphosphinic acid, m. p. and mixed m. p. 188—190°. Fraction (*b*), crude phosphine (V; R = Cl), gave a methiodide, m. p. 205—207° (after repeated recrystallisation from ethanol), unchanged when mixed with authentic *o*-chlorophenyldimethylphenylphosphonium iodide.

o-*Chlorophenylphenylphosphinous Chloride* (IV; R = Cl).—A Doak–Freedman reaction was performed on the fluoroborate (I; R = Cl) (97 g.), and the dark brown ethyl acetate solution of the product was stirred whilst magnesium (10·3 g., 1 equiv.) was added portionwise, the temperature being kept below 50°. Most of the ethyl acetate was removed below 80°/15 mm., and the residual viscous brown syrup was thrice extracted with 1 : 1 benzene–cyclohexane (400, 200, 100 ml.). Removal of the solvent from the united extracts gave a residue which solidified, and on distillation gave the fractions: (i) b. p. 26°/0·7 mm. (30 g.); (ii) b. p. 140—146°/0·7 mm. (33·6 g., 31%). The bath-temperature had to be kept at 300—320° for 1½ hr. to complete the distillation of fraction (ii).

Fraction (i) was probably the boron trifluoride–ethyl acetate complex: it fumed in air, and its infrared spectrum showed strong ester C=O absorption. Fraction (ii) on redistillation gave the *chlorophosphine* (IV; R = Cl) (27 g.), b. p. 132—133°/0·2 mm., n_D^{21} 1·645 (Found: C, 56·55; H, 3·7. $C_{12}H_9Cl_2P$ requires C, 56·5; H, 3·5%): on exposure to air it slowly hydrolysed to the oxide (III; R = Cl). The residue from the redistillation, when recrystallised from ethanol, furnished di-(*o*-chlorophenyl)phenylphosphine (*ca.* 1 g.), m. p. and mixed m. p. 137—138°.

o-*Bromophenylphenylphosphinous Chloride* (IV; R = Br).—The diazonium fluoroborate (I; R = Br) (119 g.), prepared as for the analogue (I; R = Cl), when treated as above gave a product which on distillation gave the fractions (i) b. p. 34°/0·3 mm., n_D^{21} 1·559 (19 g.), the trifluoride–acetate complex, (ii) b. p. 110—140°/0·3 mm. (30 g., 21%), and (iii), by strong heating of the residue, a yellow oil (3 g.). Fractionation (ii) on refraction gave the *chloride* (IV; R = Br), b. p. 145—146°/0·5 mm., n_D^{22} 1·662 (24·4 g.) (Found: C, 47·9; H, 3·3. $C_{12}H_9BrClP$ requires C, 48·1; H, 3·0%). Fraction (iii), crystallised from ethanol, gave *di-*(o-*bromophenyl*)-*phenylphosphine*, m. p. 122—123° (Found: C, 51·7; H, 3·0; P, 7·5%; *M*, 429. $C_{18}H_{13}Br_2P$ requires C, 51·4; H, 3·1; P, 7·4%; *M*, 420).

Reduction of the Chlorides.—The chloride (IV; R = Cl) (30 g.) in ether (75 ml.) was added to lithium aluminium hydride (1·5 g.) in ether (75 ml.), and the mixture was boiled for 1 hr., cooled, treated with ethyl acetate (15 ml.) in ether (50 ml.), and then with water to coagulate aluminium derivatives. The ether layer and extracts on distillation gave o-*chlorophenylphenylphosphine* (V; R = Cl) (16·5 g.), b. p. 113—117°/0·4 mm., n_D^{20} 1·641 (Found: C, 65·3; H, 4·6. $C_{12}H_{10}ClP$ requires C, 65·3; H, 4·5%). The phosphine, (*a*) when exposed to the air rapidly gave the oxide (III; R = Cl), m. p. and mixed m. p. 70—72°, and (*b*) when heated with methyl iodide gave o-*chlorophenyldimethylphenylphosphonium iodide*, m. p. 208·5—210° (from ethanol) (Found: C, 44·5; H, 3·5. $C_{14}H_{15}ClIP$ requires C, 44·6; H, 4·0%).

The chloride (IV; R = Br) (51·6 g.), similarly reduced, gave o-*bromophenylphenylphosphine* (V; R = Br) (37·7 g., 82%), b. p. 128—130°/0·1 mm., n_D^{23} 1·656 (Found: C, 53·3; H, 3·7. $C_{12}H_{10}BrP$ requires C, 54·4; H, 3·8%). It also on exposure to air gave the oxide (III; R = Br), m. p. and mixed m. p. 79—82°, and with methyl iodide gave o-*bromophenyldimethylphenylphosphonium iodide*, m. p. 228—230° (from ethanol) (Found: C, 40·1; H, 3·4. $C_{14}H_{15}BrIP$ requires C, 39·9; H, 3·6%).

When the chloride (IV; R = Br) in ether was added to lithium hydride in ether, no reaction was detected. The mixture was boiled for 1·5 hr., cooled, and hydrolysed. The ether extracts furnished o-*bromophenylphenylphosphine oxide* (III; R = Br) (61%), b. p. 173°/0·25 mm., m. p. 83·5—85° (from petroleum) (Found: C, 51·5; H, 3·7%; *M*, in methylene dichloride, 272. $C_{12}H_{10}BrOP$ requires C, 51·25; H, 3·6%; *M*, 281). Its spectrum showed weak absorption at 2290 cm.$^{-1}$ (P–H) and strong absorption at 1190 cm.$^{-1}$ (P=O). Oxidation with hydrogen peroxide in acetone gave the acid (II; R = Br), m. p. 208—209° (lit.,[4] 206—209°).

A mixture of the phosphine (V; R = Cl) (14 g.) and ethyl acrylate (14 g., 2·2 mol.) was heated under reflux for $1\frac{1}{4}$ hr., and then fractionally distilled, giving the unchanged ester (7 g.) and finally pure *ethyl* β-(o-*chlorophenylphenylphosphino*)*propionate* (13·2 g.), b. p. 189—190°/0·45 mm., n_D^{23} 1·598 (Found: C, 63·7; H, 5·6. $C_{17}H_{18}ClO_2P$ requires C, 63·65; H, 5·6%). A portion of the ester was hydrolysed, and the phosphinopropionic acid characterised as its *benzylthiouronium salt*, m. p. 148—148·5° (from water) (Found: C, 60·1; H, 5·1. $C_{23}H_{24}ClN_2O_2PS$ requires C, 60·2; H, 5·2%). All attempts to cyclise the ester by using lithium in tetrahydrofuran proved unsatisfactory.

Cyanoethylations.—Vinyl cyanide (5 g., 2·2 mol.) was added to the phosphine (V; R = Cl) (9·2 g.) in acetic acid (10 ml.). The mixture was heated at 140° for $1\frac{1}{2}$ hr., and on fractional distillation gave o-*chlorophenyl*-2-*cyanoethylphenylphosphine* (VI; R = Cl) (5·0 g.), b. p. 183—185°/0·005 mm., n_D^{19} 1·629 (Found: C, 65·4; H, 4·7; N, 5·5. $C_{15}H_{13}ClNP$ requires C, 65·8; H, 4·75; N, 5·1%). It gave an oily methiodide, which furnished a yellow *methopicrate*, m. p. 93—94° (from ethanol) (Found: C, 51·4; H, 3·2; N, 10·9. $C_{22}H_{18}ClN_4O_7P$ requires C, 51·1; H, 3·5; N, 10·8%).

The phosphine (V; R = Br) (37 g.), similarly treated with vinyl cyanide (22 g.) in acetic acid (30 ml.), with $2\frac{1}{2}$ hours' boiling, gave o-*bromophenyl*-2-*cyanoethylphosphine* (VI; R = Br) (38·8 g., 88%), b. p. 188—191°/0·03 mm., m. p. 61—62° (from cyclohexane) (Found: C, 56·45; H, 4·4; N, 4·5. $C_{15}H_{13}BrNP$ requires C, 56·6; H, 4·1; N, 4·4%). It gave a yellow *methopicrate*, m. p. 87·5—89° (from ethanol) (Found: C, 47·2; H, 3·4; N, 9·8. $C_{22}H_{18}BrN_4O_7P$ requires C, 47·1; H, 3·2; N, 10·0%), and, when heated in benzene with sulphur (1 equiv.), the *phosphine sulphide*, m. p. 96·5—97·5° (Found: C, 51·3; H, 3·7; N, 3·9. $C_{15}H_{13}BrNPS$ requires C, 51·4; H, 3·7; N, 4·0%).

Lithium (1 equiv.) reacted readily with a tetrahydrofuran solution of the nitrile (VI; R = Cl), or the corresponding ethyl ester, at −30° to −40°, but the product when hydrolysed and worked up gave a mixture of the secondary phosphines (V; R = Cl) and (V; R = H): 30% of the ester was recovered unchanged.

The nitrile (VI; R = Br) was unchanged when treated with lithium in boiling diethyl or di-n-butyl ether, but in cold tetrahydrofuran or hot ethylene glycol dimethyl ether gave a mixture of the phosphines (V; R = Br) and (V; R = H).

4-*Amino*-3-*cyano*-1,2-*dihydro*-1-*phenylphosphinoline* (VIII).—(*A*) A stirred mixture of the nitrile (VI; R = Br) (10 g.) and cuprous cyanide (10 g.) in dimethyl sulphoxide (100 ml.) was heated at 170° for 5 hr., cooled, and poured into dilute aqueous ammonia (500 ml.). The precipitated solid was washed with water and digested with 20% aqueous potassium cyanide (100 ml.) at 100° for 1 hr. The cold solution was extracted with benzene, which on distillation afforded a yellow, viscous oil (6·6 g.), b. p. 183—198°/0·35 mm., being a mixture of the nitrile (VI; R = Br) and the dinitrile (VII). The presence of the dinitrile was confirmed by the isolation of the yellow *2-cyanoethyl-*o*-cyanophenylphenylphosphine methopicrate*, m. p. 158—159° (after repeated crystallisation from ethanol) (Found: C, 53·9; H, 3·35; N, 13·7. $C_{23}H_{18}N_5O_7P$ requires C, 54·4; H, 3·55; N, 3·8%).

A solution of the crude nitrile (4·9 g.) in warm xylene (100 ml.) was treated with sodium t-butoxide [1 mol., from sodium (0·43 g.) and t-butyl alcohol (1·5 g.)], and then stirred at room temperature for 1 hr. at 120—140° for 30 min. The yellow sodium derivative was collected from the cold mixture, washed with benzene, and triturated with water, giving the *amino-nitrile* (VIII) (2·0 g.), having m. p. 180—181° after sublimation and recrystallisation from ethanol (Found: C, 72·9; H, 4·9; N, 10·6; P, 11·0%; *M*, 242. $C_{16}H_{13}N_2P$ requires C, 72·7; H, 4·9; N, 10·6; P, 11·7%; *M*, 264). The xylene filtrate, after treatment with water, gave a second crop (1 g.).

(*B*) A stirred mixture of the nitrile (VI; R = Br) (38 g.), cuprous cyanide (38 g.), and dimethyl sulphoxide (125 ml.) was treated as in (*A*). The black oil obtained by the cyanide digestion was separated, dissolved in chloroform, dried, and distilled, giving the amino-nitrile (VIII) (8·0 g., 28%), b. p. 205—206°/0·2 mm., m. p. 173—174° (from ethanol). It is probable that the distillation could be replaced by direct recrystallisation or sublimation.

Hydrolysis. Concentrated hydrochloric acid (250 ml.) was rapidly boiled and then added to the amino-nitrile (4·0 g.), and the solution was boiled under reflux for 10½ hr., cooled, and poured into freshly boiled water (1·5 l.) under nitrogen, and extracted with benzene (2 × 100 ml.) The dried extracts on distillation gave the 1,2,3,4-*tetrahydro*-4-*oxo*-1-*phenylphosphinoline* (IX) (2·0 g., 55%), b. p. 143—145°/0·05 mm., m. p. 46—47° (from aqueous ethanol) (Found: C, 74·6; H, 5·5. $C_{15}H_{13}OP$ requires C, 75·0; H, 5·4%). It gave a 4-*phenylsemicarbazone*, m. p. 225—226° (from benzene) (under nitrogen) (Found: C, 70·7; H, 5·25; N, 11·4. $C_{22}H_{20}N_3OP$ requires C, 70·8; H, 5·4; N, 11·3%), and an oily methiodide, which afforded a yellow *methopicrate*, m. p. 153—154° (from ethanol) (Found: C, 55·0; H, 3·6; N, 8·5. $C_{22}H_{18}N_3O_8P$ requires C, 54·7; H, 3·7; N, 8·7%). It gave an *oxide*, m. p. 124—126° (from benzene–cyclohexane) (Found: C, 70·0; H, 5·3%; *M*, 254. $C_{15}H_{13}O_2P$ requires C, 70·3; H, 5·1%; *M*, 256), when a film of the phosphine was warmed in the air.

Aqueous perchloric acid was added to a warm saturated ethanolic solution of the oxo-phosphine, which on cooling deposited the crystalline *perchlorate*, that had m. p. 179·5—181° (decomp.) after it had been collected, washed with ethanol–ether, and dried at room temperature (Found: C, 53·1; H, 4·6. $C_{15}H_{13}OP,HClO_4$ requires C, 52·9; H, 4·1%).

An ethanolic solution of the oxo-phosphine (IX), when treated with a methanol–sulphuric acid solution of 2,4-dinitrophenylhydrazine, deposited an orange micro-crystalline *dinitrophenylhydrazone* (A), m. p. 156—157°: if the mixture was stirred or warmed, the deposit changed to a red highly crystalline form (B), m. p. 160—160·5° [Found, for (A) and (B), respectively, after drying at 100°/0·1 mm.: C, 58·1, 58·1; H, 4·0, 4·2; N, 13·0, 13·1. $C_{21}H_{17}N_4O_4P,H_2O$ requires C, 57·5; H, 4·3; N, 12·8%). A hot ethanolic solution of *form* (B), when diluted with ethyl acetate, deposited *form* (A): a mixture of (A) and (B) had m. p. 157—160°. The phosphine oxide (XII), similarly treated, gave an orange *dinitrophenylhydrazone* (C), m. p. 249—250°, depressed to 228—230° by admixture with (A) or (B) (Found: C, 57·1; H, 3·8; N, 13·1. $C_{21}H_{17}N_4O_5P$ requires C, 57·8; H, 3·9; N, 12·8%).

The ultraviolet spectra of the three compounds in ethanol show the principal maxima and minima (in mμ; log ε in parentheses): (A) $\lambda_{max.}$ 380 (4·452); $\lambda_{min.}$ 314 (3·687); $\lambda_{infl.}$ 240 (4·357), 290 (3·903). (B) $\lambda_{max.}$ 380 (4·443); $\lambda_{min.}$ 314 (3·683); $\lambda_{infl.}$ 240 (4·344), 290 (3·888). (C) $\lambda_{max.}$ 374 (4·470); $\lambda_{min.}$ 314 (3·658); $\lambda_{infl.}$ 245 (4·217), 290 (3·821).

The spectra of the oxo-phosphine (IX) and the phosphine oxide (XII) show peaks at 242 mμ (4·77) and 246 mμ (4·00), respectively.

The infrared spectra of the three forms were closely similar, but strong absorption in the 1100—1300 cm.$^{-1}$ region made detection of P=O absorption difficult: however, the spectrum of (C) showed weak bands at 1180 and 1200 cm.$^{-1}$ which were absent in those of (A) and (B). Although the spectra of the thoroughly dried compounds (A) and (B) showed no hydroxyl absorption, the balance of evidence indicates that (A) and (B) were hydrated derivatives of the phosphine (IX), and not isomers of the oxide derivative (C).

Phenyl-m-*tolylphenylphosphinic Acid* (XIV; R = Me, R′ = H, R″ = OH) *and its Reactions*.—This was prepared by interaction of the dry diazonium fluoroborate (69 g.) in ethyl acetate (600 ml.) with phenylphosphonous chloride (59 g.) and cuprous chloride (4 g.). The pure *acid* (32·1 g., 41%) formed needles, m. p. 140—141° (from aqueous ethanol) (Found: C, 67·5; H, 5·7. $C_{13}H_{13}O_2P$ requires C, 67·2; H, 5·6%).

The *phosphinic chloride* (91%), prepared as previously described, had b. p. 155—158°/0·2 mm. (Found: C, 62·1; H, 5·1. $C_{13}H_{12}ClOP$ requires C, 62·3; H, 4·8%): it gave the ethyl ester (79%), b. p. 149—155°/0·2 mm., which was not obtained pure (Found: C, 67·4; H, 6·9. Calc. for $C_{15}H_{17}O_2P$: C, 69·2; H, 6·6%).

The phosphinic acid, when reduced with lithium aluminium hydride in tetrahydrofuran, gave the phosphine (XV; R = Me, R′ = H), b. p. 102—103°/0·16 mm. (Found: C, 75·7; H, 6·9; P, 14·3. Calc. for $C_{13}H_{13}P$: C, 78·0; H, 6·5; P, 15·5%. Almost identical carbon and hydrogen values were obtained for the phosphine from the reduction of the ethyl ester.) The pure phosphine could not be isolated by distillation, although the whole operation had been conducted in nitrogen: it is possible that the impurity is 4-hydroxybutylphenyl-*m*-tolylphosphine, although there is no evidence for its presence. The infrared spectrum of the phosphine showed a marked peak at 2290 cm.$^{-1}$ (P–H) confirmed by peaks at τ 2·06 and 7·47 in the nuclear magnetic resonance spectrum.

A mixture of the phosphine and methyl acrylate (2·2 mol.), boiled under reflux for 70 min. and then fractionally distilled, gave *methyl* β-(*phenyl*-m-*tolylphosphino*)*propionate* (XVI; R = R″ = Me, R′ = H) (21%), b. p. 152—154°/0·15 mm. (Found: C, 71·3; H, 6·7. $C_{17}H_{19}O_2P$ requires C, 71·3; H, 6·9%). The *ethyl ester*, similarly prepared (54%), had b. p. 160—163°/0·2 mm. (Found: C, 71·5; H, 7·2. $C_{18}H_{21}O_2P$ requires C, 72·0; H, 7·05%): it became discoloured when set aside for a few days. Hydrolysis of each ester with hot aqueous-ethanolic sodium hydroxide gave the *acid* (XVI; R = Me, R′ = R″ = H), m. p. 89—90° [from ethanol–water (3 : 2 v/v)] (Found: C, 71·0; H, 6·7. $C_{16}H_{17}O_2P$ requires C, 70·6; H, 6·3%).

A solution of this acid in xylene was boiled for 1 hr. with phosphoric anhydride and " Hyflo-supercel " to prevent coagulation. The mixture was diluted with benzene, filtered, washed with 5% aqueous sodium hydroxide, and evaporated. The residual brown syrup showed strong carbonyl absorption at 1720 cm.$^{-1}$ which was unchanged by distillation of the syrup, which however gave no normal ketonic reactions. The use of toluene as a solvent with 40 minutes' boiling afforded only unchanged acid.

3,5-*Dimethylphenylphenylphosphinic Acid* (XIV; R = R′ = Me, R″ = OH) *and its Reactions*.—This acid, prepared from the fluoroborate (76·5 g.), phenylphosphonous chloride (80 ml.), and cuprous chloride (4 g.) in ethyl acetate (500 ml.), had m. p. 182—182·5° (from ethanol) (Found: C, 68·1; H, 6·1. $C_{14}H_{15}O_2P$ requires C, 68·3; H, 6·1%) (38·5 g., 45%). It gave the *phosphinic chloride* (80%), b. p. 153—155°/0·1 mm. (Found: C, 63·5; H, 5·9. $C_{14}H_{14}ClOP$ requires C, 63·5; H, 5·3%), which in turn gave *ethyl* 3,5-*dimethylphenylphenylphosphinate* (XIV; R = R′ = Me, R″ = OEt) (82%), m. p. 89·5—90·5° (Found: C, 70·0; H, 6·7. $C_{16}H_{19}O_2P$ requires C, 70·0; H, 7·0%).

Reduction of this ester (40 g.) with lithium aluminium hydride (7·3 g., 1·2 mol.) in tetrahydrofuran (100 ml.), with boiling for 3 hr. and the usual working up, gave an ether extract which on distillation at 0·3 mm. gave the fractions: (i) b. p. 100—109° (3·9 g.); (ii) b. p. 109—122° (14·6 g.); and (iii) b. p. 122—162°, mainly at 158—162° (5·9 g.). Fraction (ii) on refractionation gave the impure phosphine (XV; R = R″ = Me), b. p. 112—113°/0·25 mm. (Found: C, 76·2; H, 6·53. Calc. for $C_{14}H_{15}P$: C, 78·5; H, 7·1%).

Fraction (iii) was extracted with cold light petroleum (b. p. 40—60°) to remove secondary phosphine, and the insoluble layer on fractional distillation gave 3,5-*dimethylphenyl*-4′-*hydroxybutylphenylphosphine*, b. p. 170—172°/0·2 mm. (Found: C, 75·15; H, 8·1. $C_{18}H_{23}OP$ requires C, 75·5; H, 8·1%): this gave a *methiodide*, m. p. 146—147·5° (from ether–ethanol) (Found: C, 53·0; H, 5·7; P, 7·4. $C_{19}H_{26}IOP$ requires C, 53·3; H, 6·1; P, 7·2%). A mixture of this phosphine (0·5 g.), 4% aqueous sodium hydroxide (10 ml.), and hydrogen peroxide (5 ml.) (100-vol.) was heated at 100° for 30 min., cooled, and extracted with chloroform; the dried extract, on evaporation, gave the *phosphine oxide* (0·5 g.), m. p. 114·5—116° [from ethanol–light petroleum (b. p. 40—60°)] (Found: C, 71·7; H, 8·0. $C_{18}H_{23}O_2P$ requires C, 71·4; H, 7·7%).

The phosphine (XV; R = R′ = Me) with ethyl acrylate gave *ethyl* β-(3,5-*dimethylphenylphenylphosphino)propionate* (XVI; R = R′ = Me, R″ = Et) (59%), b. p. 149—150°/0·05 mm. (Found: C, 72·0; H, 7·7. $C_{19}H_{23}O_2P$ requires C, 72·6; H, 7·4%), whose *methiodide* had m. p. 103·5—105° (from ethanol–cyclohexane) (Found: C, 52·8; H, 5·7. $C_{20}H_{26}IO_2P$ requires C, 52·6; H, 5·7%). Alkaline hydrolysis of the ester as before gave the *acid* (XVI; R = R′ = Me, R″ = H), m. p. 119—119·5° (from aqueous ethanol) (Found: C, 71·2; H, 6·9. $C_{17}H_{19}O_2P$ requires C, 71·3; H, 6·7%). The acid distilled unchanged in a sublimation tube at 140—160°/0·08 mm.

Cyclisation. A stirred mixture of the acid (XVI; R = R′ = Me, R″ = H) (5·0 g.) and polyphosphoric acid (122 g.) was heated at 200—210° for 100 min., cooled, and diluted with water (400 ml.), and the pH was adjusted to 7. The solution was thrice extracted with ether, and the united extracts were thoroughly washed with 10% aqueous sodium hydroxide. The dried extract, on evaporation, gave a viscous brown syrup (2·24 g.), ν (CO) 1680 cm.$^{-1}$, which on distillation in a sublimation tube at 150—152°/0·2 mm. gave a colourless unstable viscous oil, also having ν(CO) 1680 cm.$^{-1}$, which did not apparently give a 2,4-dinitrophenylhydrazone or a 4-phenylsemicarbazone. In ethereal solution the latter oil gave a deliquescent crystalline methiodide, which in ethanol afforded a very small yield of 5,7-*dimethyl*-4-*oxo*-1-*phenylphosphinoline methopicrate*, forming yellow crystals, m. p. 170—171° (from ethanol) (Found: C, 56·1; H, 4·3; N, 8·4. $C_{24}H_{22}N_3O_8P$ requires C, 56·4; H, 4·3; N, 8·2%).

We are greatly indebted to Mr. K. B. Mallion for the assistance noted above, to the University of Queensland for a Research Scholarship (to M. J. G.), and to Albright and Wilson, Ltd., for a grant (to E. C. K.).

University Chemical Laboratory, Cambridge. [*Received, March 28th,* 1963.]