53. *Synthetic Plant Hormones. Part IV.* Aryloxymethylphosphinic Acids.*

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Several aryloxymethylphosphinic acids (I; X = H, Y = OH) have been prepared by the reduction of aryloxymethylphosphonic dichlorides (I; X = Y = Cl) with lithium aluminium hydride and aerial oxidation of the products. A new synthesis of aryloxymethyl chlorides from aryloxymethylphosphonic acids and phosphorus pentachloride is described; 2 : 4-dichlorophenoxymethyl chloride has been shown to undergo an Arbuzov reaction with triethyl phosphite.

The substitution of a carboxyl group, in a series of chloroaryloxyacetic acids, by the phosphonic acid group was described in Part III.* An extension of this approach to potential plant hormones has included the synthesis of some analogous phosphinic acids (I; X = H, Y = OH).

As phosphinic acids are monobasic (infrared studies of some alkyl- and aryl-phosphinic acids and their derivatives have shown them to exist in the " keto "-form containing

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* Part III, *J.*, 1955, 1756.

quinquevalent phosphorus[1,2]) it is expected that there would be a closer structural similarity between the carboxyl group and the phosphinic acid group than with the phosphonic acid group. This is to some extent confirmed by the greater sulphanilamide-like activity of *p*-aminobenzenephosphinic acid than of the corresponding phosphonic acid.[3,4] Thus it seemed possible that the phosphinic acids (I; X = H, Y = OH) might prove more interesting as plant hormones than the phosphonic acids (I; X = Y = OH), or that they might exhibit activity as aryloxyacetic acid antagonists.

(I) $ArO{\cdot}CH_2{\cdot}PO(X)(Y)$

The few known aliphatic or arylaliphatic phosphinic acids have generally been obtained by aerial oxidation[5] of a primary alkylphosphine $R{\cdot}PH_2$, or by hydrolysis[6] of a dihalogenophosphine $R{\cdot}PX_2$, and, with very few exceptions, have been isolated only as crude syrups.

Aliphatic dihalogenophosphines have been prepared by the reaction of phosphorus trichloride with mercury[7] or lead alkyls[8] and by halogenation of primary alkylphosphines;[7] these methods did not appear to be useful for the preparation of the required phosphinic acids. Alkylphosphines have been synthesised recently by the reaction of sodium,[9] potassium,[10] or lithium dihydrogen phosphide[11] with an alkyl halide. We have investigated a potentially more attractive method, the reduction of aryloxymethylphosphonic acids.

Attempts to obtain a half ester chloride (I; X = OEt, Y = Cl), which might be converted into a phosphinic ester, by the reaction of thionyl chloride with sodium ethyl 2 : 4-dichlorophenoxymethylphosphonate, were unsuccessful. A neutral salt was obtained, possibly a pyrophosphonate, since with water it gave the acidic sodium hydrogen 2 : 4-dichlorophenoxymethylphosphonate (I; X = OH, Y = ONa) and with *p*-toluidine the phosphonamidic acid (I; X = OH, Y = $NH{\cdot}C_7H_7$-*p*, Ar = 2 : 4-$C_6H_3Cl_2$); amidic acids of this type have been prepared previously.[12]

Attention was next turned to phosphonic dichlorides (I; X = Y = Cl). Phenylphosphonic dichloride has been reduced by lithium aluminium hydride and the product, possibly the phosphine, subsequently oxidised to phenylphosphinic acid.[13] 2- and 4-Chloro-, 2 : 4-dichloro-, and 2 : 4 : 5-trichloro-phenoxymethylphosphinic acid with phosphorus pentachloride in a 1 : 2 molar ratio afforded the aryloxymethylphosphonic dichlorides (I; X = Y = Cl) in 52—80% yields, together with 11—14% of the aryloxymethyl chlorides. Use of 3 mols. of phosphorus pentachloride and 1 mol. of 2 : 4-dichlorophenoxymethylphosphonic acid gave an 83·5% yield of 2 : 4-dichlorophenoxymethyl chloride, and phosphorus trichloride was also isolated. Hence the reaction may be written:

$$ArO{\cdot}CH_2{\cdot}POCl_2 + PCl_5 \longrightarrow ArO{\cdot}CH_2Cl + PCl_3 + POCl_3$$

Rupture of the C–S bond in sodium aryloxymethanesulphonates $ArO{\cdot}CH_2{\cdot}SO_3Na$ by phosphorus oxychloride or phosphorus pentachloride at room temperature has been found by Barber *et al.*[14] to give excellent yields of aryloxymethyl chlorides; the intermediate aryloxymethanesulphonyl chlorides could not, however, be isolated.

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[1] Bennett, Emeléus, and Haszeldine, *J.*, 1954, 3598.
[2] Daasch and Smith, *Analyt. Chem.*, 1951, **23**, 865.
[3] Klotz and Morrison, *J. Amer. Chem. Soc.*, 1947, **69**, 473.
[4] Kosolapoff, "Organophosphorus Compounds," Wiley, New York, 1950, p. 145.
[5] Hoffman, *Ber.*, 1871, **4**, 605.
[6] Guichard, *Ber.*, 1899, **32**, 1572.
[7] Ref. 4, p. 42.
[8] Kharasch, Jensen, and Weinhouse, *J. Org. Chem.*, 1949, **14**, 429; Beeby and Mann, *J.*, 1951, 411.
[9] Albers and Schuler, *Ber.*, 1943, **76**, 23.
[10] Watt and Thompson, *J. Amer. Chem. Soc.*, 1948, **70**, 2295.
[11] Kreutzkamp, *Chem. Ber.*, 1954, **87**, 919.
[12] Ref. 4, p. 297.
[13] Freedman and Doak, *J. Amer. Chem. Soc.*, 1952, **74**, 3414.
[14] Barber, Fuller, Green, and Zwartouw, *J. Appl. Chem.*, 1953, **3**, 266.

Reduction of 2- and 4-chloro-, 2 : 4-dichloro-, and 2 : 4 : 5-trichloro-phenoxymethylphosphonic dichloride with lithium aluminium hydride gave malodorous oils, possibly aryloxymethylphosphines, which on aerial oxidation gave the phosphinic acids (I; $X = H$, $Y = OH$) albeit in rather low yield. In addition the chlorophenols and, in one case (2 : 4 : 5-trichlorophenoxymethylphosphonic dichloride), the chloroanisole were isolated.

An alternative route to aryloxymethylphosphonic acids (cf. Part III), namely, reaction of an aryloxymethyl chloride with triethyl phosphite, has now been realised. 2 : 4-Dichlorophenoxymethyl chloride gave a 75% yield of diethyl 2 : 4-dichlorophenoxymethylphosphonate, which was hydrolysed by concentrated hydrochloric acid to the phosphonic acid.

Preliminary biological tests on the phosphinic acids have been carried out by Mr. C. G. Greenham of the Division of Plant Industry, C.S.I.R.O., Canberra. 2-Chlorophenoxymethylphosphinic acid had weak auxin activity but the 2 : 4-dichloro-derivative was inert. In contrast 4-chloro- and 2 : 4 : 5-trichloro-phenoxymethylphosphinic acids were anti-auxins.

EXPERIMENTAL

Thionyl chloride was purified by distillation from dry quinoline and fractionation of the distillate.

Reaction of Sodium Ethyl 2 : 4-Dichlorophenoxymethylphosphonate with Thionyl Chloride.—A solution of ethyl hydrogen 2 : 4-dichlorophenoxymethylphosphonate (10·0 g.) in aqueous ethanol was neutralised (phenolphthalein) with aqueous sodium hydroxide, and the solution so obtained evaporated on a water-bath, to a crystalline residue. *Sodium ethyl 2 : 4-dichlorophenoxymethylphosphonate trihydrate* (9·5 g.) separated from ethyl acetate–light petroleum as plates, m. p. 62—63° (Found : C, 29·75; H, 4·35. $C_9H_{10}O_4Cl_2NaP,3H_2O$ requires C, 29·95; H, 4·45%). Dehydration of the salt at 100° *in vacuo* for 4 hr. gave the *hemihydrate* (Found : C, 34·0; H, 3·25. $C_9H_{10}O_4Cl_2NaP,\frac{1}{2}H_2O$ requires C, 34·2; H, 3·5%). Thionyl chloride (3·5 g.) was added to the dried salt (7·1 g.); a vigorous reaction occurred immediately. The mixture was heated for 15 min. on a water-bath, then evaporated *in vacuo* to a viscous oil which when cooled set to a glass. This was stirred with 4% sodium hydroxide solution, crystals (3·67 g.) separating which were neutral but when crystallised from water gave *sodium hydrogen 2 : 4-dichlorophenoxymethylphosphonate hydrate* as plates (Found : C, 28·8; H, 2·8; Cl, 24·0. $C_7H_6O_4Cl_2NaP,H_2O$ requires C, 28·3; H, 2·7; Cl, 23·85%). A solution of the neutral salt in water was acidified with hydrochloric acid to precipitate a crystalline acid of indefinite m. p. (104—230°). The acid (20 mg.) was mixed with a few drops of *p*-toluidine and the mixture warmed for 30 min., cooled, treated with dilute hydrochloric acid, and adjusted to pH 3 with aqueous ammonia; crystals separated; P-2 : *4-dichlorophenoxymethyl*-N-p-*tolylphosphonamidic acid hydrate* recrystallised from water as needles, m. p. 192—193° (decomp.) (Found : C, 46·05; H, 4·2; N, 4·0. $C_{14}H_{14}O_3Cl_2NP,H_2O$ requires C, 46·15; H, 4·4; N, 3·9%).

Reaction of Aryloxymethylphosphonic Acids with Phosphorus Pentachloride.—(*a*) 2 : 4-Dichlorophenoxymethylphosphonic acid (18·7 g.) and powdered phosphorus pentachloride (30 g.) reacted vigorously; then the mixture was heated on a water-bath until no solid remained, and was distilled *in vacuo* to give 2 : 4-dichlorophenoxymethyl chloride (1·2 g.), b. p. 74—80°/0·2 mm. (Found : C, 39·85; H, 2·4. Calc. for $C_7H_5OCl_3$: C, 39·75; H, 2·4%), and 2 : *4-dichlorophenoxymethylphosphonic dichloride* (14 g., 65·5%), b. p. 138°/0·3 mm. (Found : C, 28·9; H, 1·8. $C_7H_5O_2Cl_4P$ requires C, 28·6; H, 1·7%).

(*b*) 2 : 4-Dichlorophenoxymethylphosphonic acid (14·92 g.) and powdered phosphorus pentachloride (36·32 g.) were mixed and then heated at 140° (bath) for 2 hr. The product was distilled at atmospheric pressure, to give a liquid (21·6 g.), b. p. 80—102°. The residue was distilled *in vacuo*, to give 2 : 4-dichlorophenoxymethyl chloride (10·26 g., 83·5%), b. p. 89°/0·6 mm., which crystallised. The material of b. p. 80—102° was fractionated, to give eventually phosphorus trichloride (3·8 g.), b. p. 75—78°, $n_D^{13.5}$ 1·518 (" International Critical Tables " give n_D^{14} 1·516 for phosphorus trichloride [15]).

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[15] Internat. Crit. Tables, Vol. I, pp. 109, 165.

Similar experiments lead to: (i) p-*chlorophenoxymethylphosphonic dichloride* (7·4 g. from 11·4 g. of acid), b. p. 132°/0·6 mm. (Found: C, 32·5; H, 2·45. $C_7H_6O_2Cl_3P$ requires C, 32·4; H, 2·35%), and *p*-chlorophenoxymethyl chloride (1·16 g.), b. p. 60°/0·4 mm. (Barber *et al.*[14] give b. p. 120—124°/18 mm.), which with thiourea gave a crystalline *thiuronium salt hydrate*, m. p. 119° (Found: C, 35·5; H, 4·4; N, 10·3. $C_8H_{10}OCl_2N_2S,H_2O$ requires C, 35·45; H, 4·45; N, 10·3%); (ii) *o*-chlorophenoxymethylphosphonic dichloride (4·4 g. from 7·2 g. of acid), b. p. 113°/0·5 mm. (ready hydrolysis of the compound resulted in an unsatisfactory analysis), and *o*-chlorophenoxymethyl chloride (0·8 g.), b. p. 45°/0·5 mm. (Barber *et al.*[14] record b. p. 100—105°/18 mm.), identified as a *thiuronium salt*, m. p. 145—147° (Found: C, 38·3; H, 3·8; N, 10·9. $C_8H_{10}OCl_2N_2S$ requires C, 37·95; H, 4·0; N, 11·05%); (iii) 2 : 4 : 5-*trichlorophenoxymethylphosphonic dichloride* (17·36 g. from 21·32 g. of acid), b. p. 150—151°/0·4 mm., m. p. 61—62° (Found: C, 25·7; H, 1·4. $C_7H_4O_2Cl_3P$ requires C, 25·6; H, 1·25;), and 2 : 4 : 5-trichlorophenoxymethyl chloride (2·01 g.), b. p. 110—115°/1·2 mm., m. p. (after sublimation) 87—87·5 (Found: C, 33·7; H, 1·6. Calc. for $C_7H_4OCl_4$: 34·2; H, 1·65%) (Barber *et al.*[14] record b. p. 103—105°/0·5 mm., and m. p. 83—84° respectively).

Aryloxymethylphosphinic Acids.—To a stirred, boiling solution of lithium aluminium hydride (2·2 g.) in ether (200 ml.) was added 2 : 4 : 5-trichlorophenoxymethylphosphonic dichloride (17 g.) in ether (80 ml.) dropwise during 2½ hr. The mixture was stirred and heated for a further hr., then kept overnight. A solid precipitate was filtered off and washed with ether, and the ethereal solution evaporated to 25 ml. and left open to the atmosphere for 2 days; a crystalline solid separated from the syrup. 2 : 4 : 5-*Trichlorophenoxymethylphosphinic acid* (1 g.) separated from benzene–*cyclo*hexane as prisms, m. p. 129—130° (Found: C, 30·35; H, 2·2%; equiv., 274. $C_7H_6O_3Cl_3P$ requires C, 30·5; H, 2·2%; equiv., 275·5). The remaining syrup was kept in the air for 2 weeks but it retained a garlic odour. It was treated with saturated sodium hydrogen carbonate solution, and the mixture extracted with ether. The aqueous solution was acidified and the precipitated oil extracted into ether. From this solution by evaporation a semicrystalline gum was obtained from which a further quantity of the phosphinic acid (0·8 g.) was recovered. The first-mentioned ether solution was extracted with 4% sodium hydroxide solution (3 × 5 ml.) and with water (5 ml.), then dried and evaporated to an oil which with sodium hydrogen carbonate solution gave a solid precipitate; 2 : 4 : 5-trichloroanisole (0·1 g.) recrystallised from ethanol–water as needles, m. p. and mixed m. p. 73—74°. The aqueous sodium hydroxide solution was acidified to precipitate an oil which crystallised; 2 : 4 : 5-trichlorophenol (2 g.) had m. p. and mixed m. p. 65—66°.

Similar experiments led to: (i) 2 : 4-*dichlorophenoxymethylphosphinic acid* (0·78 g.) from 14 g. of the acid chloride), needles (from benzene–*cyclo*hexane), m. p. 100—101° (Found: C, 34·75; H, 3·05%; equiv., 238. $C_7H_7O_3Cl_2P$ requires C, 34·9; H, 2·9%; equiv., 241) [p-*toluidine salt*, plates (from ethanol–ether), m. p. 145° (Found: C, 48·15; H, 4·75; N, 3·8. $C_{14}H_{16}O_3NCl_2P$ requires C, 48·3; H, 4·6; N, 4·0%)], and 2 : 4-dichlorophenol (1·2 g.); (ii) p-*chlorophenoxymethylphosphinic acid* (1·96 g. from 7·3 g. of acid chloride), plates (from benzene–light petroleum), m. p. 122—124° (Found: C, 40·55; H, 3·9%; equiv., 204. $C_7H_8O_3ClP$ requires C, 40·7; H, 3·9%; equiv., 206·5); (iii) *o*-chlorophenoxymethylphosphinic acid as a p-*toluidine salt hemihydrate* (0·58 g. from 4·4 g. of acid chloride), needles (from ethanol–ether), m. p. 124—127° (Found: C, 52·1; H, 5·5; N, 4·4. $C_7H_8O_3ClP,C_7H_9N,\frac{1}{2}H_2O$ requires C, 52·1; H, 5·6; N, 4·35%).

Reaction of 2 : 4-*Dichlorophenoxymethyl Chloride with Triethyl Phosphite.*—A mixture of triethyl phosphite (8·05 g.) and 2 : 4-dichlorophenoxymethyl chloride (10·26 g.) was heated at 140° (bath) for 30 min. during which a steady evolution of gas was observed. Heating was continued at 160° (bath) for 2 hr., and the solution was then distilled *in vacuo*, to give *diethyl* 2 : 4-*dichlorophenoxymethylphosphonate* (11·35 g.), b. p. 162°/0·7 mm. (Found: C, 42·25; H, 5·0; Cl, 22·1. $C_{11}H_{15}O_4Cl_2P$ requires C, 42·2; H, 4·85; Cl, 22·65%).

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