301. *Synthetic Plant Hormones. Part I. Some Esters of Phosphoric Acid.*

By (Miss) M. H. Maguire and G. Shaw.

Several chloroaryloxyethyl and chloroaryl hydrogen phosphates have been prepared in an attempt to elaborate a growth-controlling substance with selective activity against perennials with long tap-roots notably the skeleton weed (*Chondrilla juncea*).

This paper is concerned primarily with the synthesis of substances which may be effective in controlling the growth of plants with characteristically long tap roots, especially the skeleton weed (*Chondrilla juncea*), which cause heavy loss of wheat in New South Wales. From measurements of the hydrogen-ion concentration of skeleton-weed tissue to a depth of 33 inches and field work involving the mechanical destruction of the root at various levels, Greenham, Currie, and Allan (Austral. Counc. Sci. Ind. Res., Report No. 99, 1940) concluded that, to ensure effective control, a translocated poison is required which should penetrate the root to a depth of at least 4 feet and be soluble at pH 4·4—5·9 and toxic at pH 5·2—5·9.

Of the many chemicals investigated, the most effective—arsenic oxide, arsenious oxide, and sodium chlorate [Greenham *et al.*, *loc. cit.*; Cashmore and Carn, *J. Counc. Sci. Ind. Res.* (*Austral.*), 1940, **13**, 74; Greenham and Wilkinson, *ibid.*, 1942, **15**, 154; 1946, **19**, 341]—had an adverse effect on the wheat owing to partial sterilisation of the soil. Chloroaryloxyacetic acids (*idem*, *ibid.*, 1946, 341; Greenham, *Austral. J. Agr. Res.*, 1950, **1**, 148) gave no promise, probably because, having too great an initial toxicity, their movement in the plant was limited, the aerial parts alone being destroyed. We therefore attempted to elaborate molecules which would be (1) readily translocated by the plant (and consequently water-soluble) and (2) precursors of active plant-growth regulators, in particular, chloroaryloxyethyl and chlorophenyl hydrogen phosphates. Phosphates are known to move very readily in deep-rooted plants (Greenham, personal communication) and it was hoped that the chloroaryloxy-residues would provide a source of hormonal activity.

Plimmer and Burch (*J.*, 1929, 279) prepared alkyl hydrogen phosphates from an alcohol and excess of phosphorus oxychloride in chloroform, but the resultant mixture of mono- and di-esters obtained from 2 : 4-dichlorophenoxyethanol evinced little tendency to hydrolyse in chloroform and thus could not be separated by means of water, and fractional distillation of the mixed acid chlorides led to extensive decomposition.

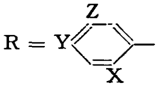
The required esters (I and II; X = Cl, Y = Z = H; Y = Cl, X = Z = H; X = Y = Cl, Z = H; and X = Y = Z = Cl) were obtained in excellent yield by boiling equimolecular amounts of the corresponding alcohol and phosphorus oxychloride in chloroform for 3 hours and hydrolysing the resultant mixed acid chlorides with a small amount of water. The dihydrogen phosphates (I) were then separated by dissolution in ice-cold ethanol. Under these conditions little or no neutral material (triesters, aryloxyethyl halides, etc.) could be detected.

$RO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}PO(OH)_2$ (I)

$(RO{\cdot}CH_2{\cdot}CH_2{\cdot}O)_2PO{\cdot}OH$ (II)

$RO{\cdot}PO(OH)_2$ (III)

$(RO)_2{\cdot}PO{\cdot}OH$ (IV)



Numerous aryl hydrogen phosphates have been prepared (cf. Kosolapoff, " Organophosphorus Compounds," Wiley, New York; Jacobsen, *Ber.*, 1875, **8**, 1521; Rapp, *Annalen*, 1884, **224**, 156; Zetsche and Nachmann, *Helv. Chim. Acta*, 1926, **9**, 420; Rosenmund and Vogt, *Arch. Pharm.*, 1943, **281**, 317; Kekulé, *Ber.*, 1872, **5**, 876; 1873, **6**, 944), but usually in poor yield and of doubtful purity. However, good yields of the esters (III and IV; X = Cl, Y = Z = H; Y = Cl, X = Z = H; X = Y = Cl, Z = H; and X = Y = Z = Cl) were obtained by a modification of Rosenmund and Vogt's method (see Experimental section), which usually gave also some of the triester.

In preliminary tests for inhibition of germination the phosphate esters were compared with an equimolar amount of 2 : 4-dichlorophenoxyacetic acid (2 : 4-D) at a concentration equivalent to 5 lb. per acre, by Mr. C. G. Greenham of the Division of Plant Industry, C.S.I.R.O. The order of activity was 2 : 4-D > (I; X = Y = Cl, Z = H; or X = Z = H, Y = Cl) > (I or II; X = Y = Z = Cl) > (II; X = Y = Cl, Z = H) > (II; X = Z = H, Y = Cl) > (I or II; X = Cl, Y = Z = H), (III and IV; all variations). The final group of compounds was inactive whereas (I; X = Y = Cl, Z = H; and X = Z = H, Y = Cl) were only slightly less active than 2 : 4-D. The results suggest that possible precursors of a phenoxyacetic acid alone are active and that a 4-chloro-group is essential.

The esters were twice tested on mature skeleton weed with little or no effect; the plants used in these experiments, however, were unusually resistant to known poisons.

These results will be published in full elsewhere.

EXPERIMENTAL

The aryloxyethanols were prepared by Kirner's method (*J. Amer. Chem. Soc.*, 1926, **48**, 2748; cf. Powell, *J. Amer. Chem. Soc.*, 1923, **45**, 2709) from 2-chloroethanol (1 mole), the phenol (1·3 mole), and 2N-sodium hydroxide (1 l.) under reflux (30 min.). 2 : 4 : 5-*Trichlorophenoxyethanol* separated from light petroleum as needles, m. p. 65—66° (Found: C, 39·8; H, 2·75. $C_8H_7O_2Cl_3$ requires C, 39·8; H, 2·9%).

2 : 4-*Dichlorophenoxyethyl Hydrogen Phosphates* (I and II; X = Y = Cl, Z = H).—2 : 4-Dichlorophenoxyethanol (80 g.) in chloroform (300 ml.) was added gradually with stirring to phosphorus oxychloride (60 g.) in chloroform (200 ml.). The solution was boiled under reflux for 3 hours, then evaporated *in vacuo* to an oily residue which was heated on the steam-bath with water (20 ml.) for 3 hours with stirring. The crystalline mass which separated on cooling was stirred with ice-cold ethanol, and the solid filtered off; *di-*(2 : 4-*dichlorophenoxyethyl*) *hydrogen phosphate* crystallised from benzene as needles (35 g.), m. p. 141° (Found: C, 40·9; H, 3·5%; equiv., 476. $C_{16}H_{15}O_6Cl_4P$ requires C, 40·35; H, 3·2%; equiv., 476). Attempted hydrolysis of the diester with aqueous sodium hydroxide gave the *sodium* salt only, needles (from water), m. p. 300° (Found: C, 38·4; H, 2·85. $C_{16}H_{14}O_6Cl_4PNa$ requires C, 38·6; H, 2·85%). Evaporation of the above alcoholic extract *in vacuo* gave an oil which crystallised. 2 : 4-*Dichlorophenoxyethyl dihydrogen phosphate* (30 g.) separated from chloroform as needles, m. p. 111—112°, soluble in water and ethanol (Found: C, 33·45; H, 3·15%; equiv., 143. $C_8H_9O_5Cl_2P$ requires C, 33·45; H, 3·15%; equiv., 143·5). Distillation of the mixture of acid chlorides *in vacuo* resulted in extensive decomposition and formation of a purple gum.

Similar experiments led to: *bis*-o-*chlorophenoxyethyl hydrogen phosphate* (56·5 g. from 80 g. of the alcohol), needles (from toluene), m. p. 135—136° (Found: C, 47·1; H, 4·2%; equiv., 405. $C_{16}H_{17}O_6Cl_2P$ requires C, 47·2; H, 4·2%; equiv., 407), and o-*chlorophenoxyethyl dihydrogen phosphate* (30 g.), plates (from chloroform), m. p. 143—144° (Found: C, 37·75; H, 3·8%; equiv., 126. $C_8H_{10}O_5ClP$ requires C, 38·05; H, 4·0%; equiv., 126); *bis*-p-*chlorophenoxyethyl hydrogen phosphate* (30 g. from 80 g.), needles (from ethanol–water), m. p. 164° (Found: C, 46·95; H, 4·5%; equiv., 405), and p-*chlorophenoxyethyl dihydrogen phosphate* (25 g.), plates (from chloroform), m. p. 127° (Found: C, 37·8; H, 4·0%; equiv., 126); and *di*-(2 : 4 : 5-*trichlorophenoxyethyl*) *hydrogen phosphate* (21 g. from 83 g.), needles (from ethanol–water), m. p. 172° (Found: C, 35·2; H, 2·4%; equiv., 547. $C_{16}H_{13}O_6Cl_6P$ requires C, 35·25; H, 2·4%; equiv., 545), and 2 : 4 : 5-*trichlorophenoxyethyl dihydrogen phosphate* (27 g.), needles (from acetone–chloroform), m. p. 139—140° (Found: C, 30·05; H, 2·65%; equiv., 159·5. $C_8H_8O_5Cl_3P$ requires C, 30·0; H, 2·5%; equiv., 161).

2 : 4-*Dichlorophenyl Hydrogen Phosphates* (III and IV; X = Y = Cl, Z = H).—2 : 4-Dichlorophenol (65 g.), phosphorus oxychloride (69 g.), and magnesium turnings (0·1 g.) were kept at 130—140° for 3 hours, hydrogen chloride being steadily evolved. Distillation *in vacuo* (air-stream dried with P_2O_5) gave 2 : 4-*dichlorophenylphosphorodichloridate* (51 g.) as a dense, colourless, fuming liquid, b. p. 115°/1·5 mm. (Found: C, 25·9; H, 1·25. $C_6H_3O_2Cl_4P$ requires C, 25·75; H, 1·1%). This (42·8 g.) was slowly added to warm water (100 ml.) with stirring; when cooled, the solution deposited 2 : 4-*dichlorophenyl dihydrogen phosphate* (32 g.) which separated from toluene as needles, m. p. 65—66° (Found: C, 29·7; H, 2·25%; equiv., 121·5. $C_6H_5O_4Cl_2P$ requires C, 29·65; H, 2·05%; equiv., 121·5). A further 5 g. of the acid were extracted from the aqueous solution with ether. The residue (45 g.) from the distillation was largely di-(2 : 4-dichlorophenyl) phosphorochloridate and was hydrolysed on the water-bath with 2N-sodium hydroxide (500 ml.). When cooled, the solution deposited a small amount (1 g.) of *tri*-(2 : 4-*dichlorophenyl*) *phosphate* which crystallised from light petroleum as needles, m. p. 95° (Found: C, 40·7; H, 1·85. $C_{18}H_9Cl_6P$ requires C, 40·55; H, 1·7%). The alkaline filtrate was strongly acidified with hydrochloric acid and extracted with ether (3 × 100 ml.); evaporation of the extract left a crystalline solid (45 g.) which had a strong phenolic odour. The solid was triturated with 10% potassium carbonate solution and the salt which separated was washed with dry ether (it is soluble in moist ether) and ground with a slight excess of 5N-hydrochloric acid, giving *di*-(2 : 4-*dichlorophenyl*) *hydrogen phosphate* (20 g.) (from chloroform–light petroleum), m. p. 131° (Found: C, 37·0; H, 2·05%; equiv., 385. $C_{12}H_7O_4Cl_4P$ requires C, 37·15; H, 1·8%; equiv., 388).

Similar experiments gave 2 : 4 : 5-*trichlorophenyl phosphorodichloridate* (45·6 g. from 79 g. of phenol), b. p. 115—119°/0·5 mm. (Found: C, 23·7; H, 0·7. $C_6H_2O_2Cl_5P$ requires C, 22·9; H, 0·9%; the poor analysis may be due to slight hydrolysis), 2 : 4 : 5-*trichlorophenyl dihydrogen phosphate* (26 g. from 38·6 g. of dichloride), needles (from chloroform–light petroleum), m. p. 179° (Found: C, 25·8; H, 1·6%; equiv., 138·5. $C_6H_4O_4Cl_3P$ requires C, 25·95; H, 1·45%; equiv., 138·8), *tri*-(2 : 4 : 5-*trichlorophenyl*) *phosphate* (3·1 g.), needles (from chloroform–light petroleum), m. p. 161—162° (Found: C, 34·0; H, 1·15. $C_{18}H_6O_4Cl_9P$ requires C, 34·0; H, 0·95%), and *di*-(2 : 4 : 5-*trichlorophenyl*) *hydrogen phosphate monohydrate* (20·5 g.), needles (from chloroform–light petroleum), m. p. 152—153° (Found: C, 30·6; H, 1·5%; equiv., 474. $C_{12}H_5O_4Cl_6P,H_2O$ requires C, 30·4; H, 1·5%; equiv., 475); *o*-chlorophenyl phosphorodichloridate (30·7 g. from 51·4 g. of phenol), b. p. 85°/0·6 mm. (Anschutz, *Annalen*, 1918, **415**, 64, gives b. p. 135—137°/12 mm.), n-*amylammonium* o-*chlorophenyl phosphate*, plates (from methanol–ether), m. p. 179—180° (Found: C, 50·25; H, 8·3; N, 7·15. $C_6H_6O_4ClP,2C_5H_{13}N$ requires C, 50·2; H, 8·35; N, 7·3%), di-*o*-chlorophenyl hydrogen phosphate (23 g.), plates (from chloroform–light petroleum), m. p. 120° (Found: C, 44·55; H, 2·9%; equiv., 316. Calc. for $C_{12}H_9O_4Cl_2P$: C, 45·15; H, 2·85%; equiv., 319) (Brusch and Kechin, *Rec. Fac. sci. Univ. Istanbul*, 1942, 7*a*, 182, give m. p. 121·5°); *p*-chlorophenyl phosphorodichloridate (64 g. from 51·4 g. of phenol), b. p. 91—94°/0·8 mm. (Rosenmund and Vogt, *loc. cit.*, record b. p. 95—115°/0·1 mm., and Zetsche and Nachmann, *loc. cit.*, b. p. 142°/11 mm.), p-*chlorophenyl dihydrogen phosphate hemihydrate* (40 g.), needles (from benzene–chloroform), m. p. 123—124° (Found: C, 33·3; H, 3·15%; equiv., 108·4. $C_6H_6O_4ClP,\frac{1}{2}H_2O$ requires C, 33·1; H, 3·25%; equiv., 108·8), and di-*p*-chlorophenyl hydrogen phosphate (17 g.), plates (from chloroform–light petroleum), m. p. 131—132° (Found: C, 44·95; H, 2·8%; equiv., 319·5) (Zetsche and Nachmann, *loc. cit.*, give m. p. 133—135°).

The approximate dissociation constants of the acids (I and III) at M/50-concentration and of (IV) at M/500, in water at 23—25°, were determined from the titration curves (Cambridge pH meter) and are tabulated below; the acids (II) were too insoluble in water for accurate measurement.

Compound	10^3K_{a1}	10^7K_{a2}
(I; X = Cl, Y = Z = H)	9·32	2·82
(I; Y = Cl, X = Z = H)	9·41	3·16
(I; X = Y = Cl, Z = H)	8·94	2·82
(I; X = Y = Z = Cl)	9·21	2·82
(III; Y = Cl, X = Z = H) ...	9·49	15·9
(III; X = Y = Cl, Z = H)......	9·32	23·5
(III; X = Y = Z = Cl)	9·32	50·1

Compound	10^3K_{a1}	10^7K_{a2}
(IV; X = Cl, Y = Z = H) ...	0·226	—
(IV; Y = Cl, X = Z = H) ...	0·130	—
(IV; X = Y = Cl, Z = H) ...	0·226	—
(IV; X = Y = Z = Cl)	0·256	—

The authors thank Mr. C. G. Greenham at whose request this work was undertaken, the Commonwealth Scientific and Industrial Research Organisation for a maintenance grant (to M. H. M.), Timbrol Ltd. for gifts of chemicals, and Dr. E. Challen for the semi-micro analyses.

THE UNIVERSITY OF TECHNOLOGY,
SYDNEY, N.S.W., AUSTRALIA.

[*Received, October 7th,* 1952.]