Synthetic Plant Hormones. Part II. Some Glucosides and Aldehydes.*

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[Reprint Order No. 5450.]

Several chlorophenyl and chlorophenoxyethyl glucosides and chlorophenoxyacetaldehydes have been prepared in an attempt to obtain readily translocatable plant-growth inhibitors.

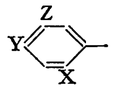
An extension of the ideas described in Part I* for the preparation of readily translocatable plant-growth inhibitors has led us to prepare a series of chlorophenyl (I) and chlorophenoxyethyl β-D-glucosides (II) and chlorophenoxyacetaldehydes (III). Chlorophenoxyethyl tetra-*O*-acetyl-β-D-glucosides were prepared by the Koenigs–Knorr reaction (Helferich and Klein, *Annalen*, 1926, **450**, 219 : Reynolds and Evans, *J. Amer. Chem. Soc.*, 1938, **60**, 2559) from tetra-*O*-acetyl-α-D-glucopyranosyl bromide with the appropriate chlorophenoxyethanol and silver oxide in dry chloroform. Chlorophenyl tetra-*O*-acetyl-β-D-glucosides were prepared by Helferich and Smitz-Hillebrecht's method (*Ber.*, 1933, **66**, 378) from the chlorophenol, penta-*O*-acetyl-β-D-glucose, and toluene-*p*-sulphonic acid. Catalytic deacetylation with sodium or barium methoxide (" Polarimetry, Saccharimetry and the Sugars," Circular C 440, Nat. Bur. Stand., U.S.A., 1942, p. 493) of the tetra-*O*-acetyl derivatives gave the required glucosides.

Several routes to the aldehydes (III) were investigated. Phenoxyacetaldehyde (III; R = Ph) has been prepared in small yield by the oxidation of 2-phenoxyethanol with chromic acid (Halasz, *Bull. Soc. chim.*, 1941, **8**, 170); oxidation of (III; X = Y = Cl, Z = H) with this reagent gave no aldehyde but a moderate amount of the ester (IV; X = Y = Cl). A newer oxidant, *tert.*-butyl chromate (Oppenhauer and Oberrausch, *Anal. Asoc. Quim. Argentina*, 1949, **37**, 246) is claimed to oxidise primary alcohols to aldehydes exclusively, but with 2-*p*-chlorophenoxyethanol gave much tar and a small yield of the acid. Phenoxyacetaldehyde has also been synthesised, in unstated yield, by hydrolysis of its acetal obtained from chloroacetal and sodium phenoxide (Autenrieth, *Ber.*, 1891, **24**, 162); an attempt to duplicate this reaction but with sodium 2 : 4-dichlorophenoxide was unsuccessful. Hatch and Nesbitt (*J. Amer. Chem. Soc.*, 1945, **67**, 39) prepared phenoxyacetaldehyde in 45% yield by the oxidation of glycerol α-phenyl ether with lead tetra-acetate. This method was adopted by us and with minor modifications gave generally better yields than

$RO{\cdot}G$ (I)

$RO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}G$ (II)

R =



$RO{\cdot}CH_2{\cdot}CHO$ (III)

$RO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CH_2{\cdot}OR$ (IV)

G = β-D-glucopyranosyl

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* Part I, *J.*, 1953, 1479.

those claimed for the phenyl compound. The aldehydes readily polymerised at room temperature but formed water-soluble adducts with sodium hydrogen sulphite, and biological tests were carried out on these adducts. The aldehyde (III; X = Y = Cl, Z = H) formed a remarkably stable adduct with water which could be distilled *in vacuo* without dehydration.

In inhibition of germination tests, the glucosides and aldehyde-bisulphite compounds 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., Canberra. The order of activity was 2 : 4-D or (III; X = Y = Cl, Z = H)>(II; X = Y = Cl, Z = H; or X = Z = H, Y = Cl) or (III; X = Z = H, Y = Cl; or X = Y = Z = Cl)>(II; X = Y = Z = Cl)>(I; X = Y = Z = Cl)>(inactive) (II; Y = Z = H, X = Cl) or (III; Y = Z = H, X = Cl) or (I; X = Y = Cl, Z = H; or X = Z = H, Y = Cl; or Y = Z = H, X = Cl). The results are similar to those obtained with aryl and aryloxyethyl phosphates (Part I, *loc. cit.*) and substantiate the suggestion that a *p*-chloro-group and a precursor of a phenoxyacetic acid are prerequisites for activity. Preliminary tests on mature skeleton weed (*Chondrilla juncea*) showed that, whereas all the more active compounds affected the aerial parts of the plant, only (III; X = Y = Cl, Z = H) had any significant effect on the root; the action of this compound is slow and its full effects have not, as yet, been assessed.

EXPERIMENTAL

[α] are for *c* = 2 in MeOH unless otherwise stated.

Aryloxyethyl Glucosides (II).—A solution of tetra-*O*-acetyl-β-D-glucopyranosyl bromide (Jeremias, Lucas, and MacKenzie, *J. Amer. Chem. Soc.*, 1948, **70**, 2598) (9 g.) in dry chloroform (60 ml.) was added with vigorous stirring during 45 min. to *p*-chlorophenoxyethanol (3·8 g.), iodine (0·3 g.), silver oxide (5·2 g.), " Drierite " (12 g.), and chloroform (250 ml.), and the mixture stirred for 9 hr., then filtered. The filtrate was evaporated, giving a viscous red residue (11·9 g.); this when crystallised from ethanol gave 2-p-*chlorophenoxyethyl tetra*-O-*acetyl*-β-D-*glucopyranoside* (3·1 g.) as colourless needles, m. p. 78°, $[\alpha]_D^{28}$ −20·5° (in $CHCl_3$) (Found: C, 52·45; H, 5·25. $C_{22}H_{27}O_{11}Cl$ requires C, 52·5; H, 5·45%). A solution of the acetate (3·05 g.) in anhydrous methanol (100 ml.) containing a small amount of sodium methoxide was kept overnight at 0°, then neutralised with methanolic acetic acid (phenolphthalein) and evaporated to a clear viscous gum; this was dissolved in boiling ethyl acetate, sodium acetate was filtered off, and the filtrate was evaporated. The residue crystallised when rubbed with dioxan and it recrystallised from dioxan–ether, to give 2-p-*chlorophenoxyethyl* β-D-*glucopyranoside hemihydrate* (dried *in vacuo*) (1·53 g.) as deliquescent needles, m. p. 52—53°, $[\alpha]_D^{17}$ −15·5° (*c*, 3·346) (Found : C, 49·0; H, 6·05. $C_{14}H_{19}O_7Cl,\frac{1}{2}H_2O$ requires C, 48·9; H, 5·85%).

Similar experiments led to 2-o-*chlorophenoxyethyl tetra*-O-*acetyl*-β-D-*glucopyranoside* (2·7 g. from 6·34 g. of alcohol), needles (from ethanol–water, after extraction with light petroleum), m. p. 63—64°, $[\alpha]_D^{28}$ −16·5° (in $CHCl_3$) (Found : C, 52·6; H, 5·3%); 2-o-*chlorophenoxyethyl* β-D-*glucopyranoside* (1·4 g. from 2 g. of acetate) was obtained as a brittle gum, $[\alpha]_D^{17.5}$ −16·9° (*c*, 3·086), but analysis indicated it to be substantially pure (Found: C, 50·4; H, 5·95. $C_{14}H_{19}O_7Cl$ requires C, 50·23; H, 5·7%); 2-2′ : 4′-*dichlorophenoxyethyl tetra*-O-*acetyl*-β-D-*glucopyranoside* (6·26 g. from 7 g. of alcohol) separated from ethanol–water (after seeding with the *p*-chloro-analogue) as plates, m. p. 62—63°, $[\alpha]_D^{28}$ −14·5° (in $CHCl_3$) (Found : C, 49·25; H, 4·85. $C_{22}H_{26}O_{11}Cl_2$ requires C, 49·15; H, 4·9%), and 2-2′ : 4′-*dichlorophenoxyethyl* β-D-*glucopyranoside* (2 g. from 4 g. of acetate) as a brittle gum, $[\alpha]_D^{23}$ −16·6° (*c*, 2·77) (Found : C, 46·05; H, 5·1. $C_{14}H_{18}O_7Cl_2$ requires C, 45·5; H, 4·9); 2-2′ : 4′ : 5′-*trichlorophenoxyethyl tetra*-O-*acetyl*-β-D-*glucopyranoside* (48%) separated from ethanol–water as needles, m. p. 101—102°, $[\alpha]_D^{28}$ −15·0° (in $CHCl_3$) (Found : C, 45·9; H, 4·45. $C_{22}H_{25}O_{11}Cl_3$ requires C, 46·2; H, 4·4%), and 2-2′ : 4′ : 5′-trichlorophenoxyethyl β-D-glucopyranoside hydrate (as an *adduct* with dioxan) crystallised from dioxan–ether as needles, m. p. 57—60° (softening at 50°), $[\alpha]_D^{17.5}$ −12·5° (*c*, 3·291) (Found: C, 42·25; H, 5·05. $C_{14}H_{17}O_7Cl_3,C_4H_8O_2,H_2O$ requires C, 42·4; H, 5·3%). The *anhydrous trichloroglucoside* was obtained when the adduct (0·1435 g.) was heated at 100°/1 mm. for 24 hr. to give, eventually, needles (0·1135 g. Calc. for loss of dioxan and water in the above molar proportions, 0·1136 g.), m. p. 118—119° (Found : C, 41·85; H, 4·35. $C_{14}H_{17}O_7Cl_3$ requires

C, 41·65; H, 4·25%); the anhydrous compound readily reverted to the adduct when rubbed with moist dioxan.

Aryl Glucosides (I).—Penta-*O*-acetyl-β-D-glucopyranose (20 g.), 2 : 4-dichlorophenol (33·5 g.), and toluene-*p*-sulphonic acid (0·3 g.) were heated together on a water-bath for 1½ hr., then cooled and treated with benzene (60 ml.), and the resultant solution was washed with water and 2N-sodium hydroxide until free from phenol, then dried and evaporated to a syrup (20 g.).

2 : 4-*Dichlorophenyl tetra*-O-*acetyl*-β-D-*glucopyranoside* (21%) separated from methanol as needles, m. p. 184—185°, [α]$_D^{22}$ −40·5° (in $CHCl_3$) (Found : C, 48·95; H, 4·55. $C_{20}H_{22}O_{11}Cl_2$ requires C, 48·7; H, 4·5%). A solution of the acetate (4·36 g.) in methanol (300 ml.) containing a small amount of sodium methoxide was boiled under reflux for 15 min., then kept at room temperature for 24 hr. The solution was neutralised with methanolic acetic acid (phenolphthalein) and filtered, and the filtrate evaporated to give a crystalline residue; 2 : 4-*dichlorophenyl* β-D-*glucopyranoside* (4·3 g.) crystallised from propan-2-ol as needles, m. p. 173—174°, [α]$_D^{20}$ −66° (Found : C, 44·15; H, 4·35. $C_{12}H_{14}O_6Cl_2$ requires C, 44·3; H, 4·35%).

Similarly 2 : 4 : 5-*trichlorophenyl tetra*-O-*acetyl*-β-D-*glucopyranoside* (8·1 g. from 30 g. of penta-*O*-acetyl-β-D-glucose) separated from methanol as needles, m. p. 175°, [α]$_D^{24}$ −31° (in $CHCl_3$) (Found : C, 45·75; H, 4·0. $C_{20}H_{21}O_{10}Cl_3$ requires C, 45·5; H, 4·0%); 2 : 4 : 5-*trichlorophenyl* β-D-*glucopyranoside* (2·2 g. from 4·55 g. of acetate) separated from propan-2-ol as needles, m. p. 190—192°, [α]$_D^{24\cdot5}$ −69° (Found : C, 39·7; H, 3·55. $C_{12}H_{13}O_6Cl_3$ requires C, 40·1; H, 3·65%); *p*-chlorophenyl tetra-*O*-acetyl-β-D-glucopyranoside (40%) crystallised from ethanol as needles, m. p. 124°, [α]$_D^{24}$ −20° (in $CHCl_3$) (Found : C, 52·35; H, 5·05. Calc. for $C_{20}H_{23}O_{11}Cl$: C, 52·35; H, 4·95%) {(Dyfverman and Lindberg, *Acta Chem. Scand.*, 1950, **4**, 878, give m. p. 123—124°, [α]$_D^{20}$ −20°}; *p*-chlorophenyl β-D-glucopyranoside (2·2 g. from 4·5 g. of acetate) crystallised from propan-1-ol as needles, m. p. 174—175°, [α]$_D^{25}$ −65·5° (Found : C, 49·3; H, 5·35. Calc. for $C_{12}H_{15}O_6Cl$: C, 49·6; H, 5·2%) {(Dyfverman and Lindberg, *loc. cit.*, record m. p. 173—174°, [α]$_D^{25}$ −69·5° (*c*, 1 in H_2O)}; *o*-chlorophenyl tetra-*O*-acetyl-β-D-glucopyranoside (20%) formed needles (from ethanol), m. p. 141—143°, [α]$_D^{22}$ −46·5° (in $CHCl_3$) (Found : C, 52·55; H, 4·95%) {(Miller, *Contr. Boyce Thompson Inst.*, 1939, **11**, 25, records m. p. 150—151° (corr.), [α]$_D^{23}$ −44·6° (*c*, 3·7559 in $CHCl_3$)}; *o*-chlorophenyl β-D-glucopyranoside (1·1 g. from 3·64 g. of acetate) crystallised from ethyl acetate–light petroleum as needles, m. p. 163—164°, [α]$_D^{17\cdot5}$ −65·8° (*c*, 2·462) (Found : C, 49·9; H, 5·2%) {(Miller, *loc. cit.*, records m. p. 171—171·5° (corr.), [α]$_D^{26}$ −65·3° (*c*, 3·579 in EtOH)}.

Aryloxyacetaldehydes (III).—(a) *Chromic acid oxidation.* To a solution of 2-2′ : 4′-dichlorophenoxyethanol (4 g.) in acetic acid (200 ml.) was added chromium trioxide (1·3 g.) slowly and with vigorous stirring; the solution was warmed to 50°, stirred for a further 15 min., then poured on ice; an oil separated and was extracted with ether, and the extract washed with sodium hydrogen carbonate solution and water, then dried and evaporated to an orange oil which crystallised; 2-2′ : 4′-*dichlorophenoxyethyl* 2 : 4-*dichlorophenoxyacetate* (IV; X = Y = Cl, Z = H) (2·7 g.) separated from ethanol as plates, m. p. 88—89° (Found : C, 46·9; H, 3·1. $C_{16}H_{12}O_4Cl_4$ requires C, 46·85; H, 2·95%); oxidation of 2-*p*-chlorophenoxyethanol with chromic acid under Halasz's conditions (*loc. cit.*) for 2-phenoxyethanol gave starting material and tar.

(b) tert.-*Butyl chromate.* Chromic oxide (30·8 g.) was added gradually to *tert.*-butyl alcohol (61·7 g.), and the red solution obtained was diluted with benzene (250 ml.); the solution was dried by vigorous shaking with sodium sulphate. To the filtered solution was added 2-*p*-chlorophenoxyethanol (21·6 g.) in benzene (170 ml.), and the solution set aside for 2 days. The excess of oxidant was decomposed by shaking the solution with aqueous oxalic and sulphuric acid and at this stage much tar was formed; evaporation of the dried solution and distillation of the residue *in vacuo* gave 2-*p*-chlorophenoxyethanol (3·9 g.) and a residue which crystallised from water as needles, m. p. 148°, not depressed when mixed with 2-*p*-chlorophenoxyacetic acid, m. p. 150°.

Oxidation of Glycerol Ethers with Lead Tetra-acetate.—The ethers were prepared by heating a mixture of the phenol, 3-chloropropane-1 : 2-diol and sodium hydroxide (Fairbourne and Stevens, *J.*, 1932, 1972). 3-2′ : 4′-*Dichlorophenoxypropane*-1 : 2-*diol* (74%) had b. p. 182—190°/3 mm. and crystallised from benzene–light petroleum as needles, m. p. 78—79° (Found : C, 45·8; H, 4·3. $C_9H_{10}O_3Cl_2$ requires C, 45·6; H, 4·25%). To a solution of 3-*p*-chlorophenoxypropane-1 : 2-diol (20·25 g.) in benzene (500 ml.) at 40—50° was added gradually and with vigorous stirring powdered lead tetra-acetate (44·32 g.); the mixture was kept at 50° for 1½ hr. and at 0° for 48 hr. The solution was filtered from lead acetate, washed with water, and again filtered to remove lead dioxide, then washed with sodium hydrogen carbonate solution (50 ml.; 5%) and water (2 × 50 ml.). Evaporation of the dried solvent gave a yellow viscous oil (15·5 g.); distillation of this gave p-*chlorophenoxyacetaldehyde* (12 g.) as a very pale yellow liquid,

b. p. 100—102°/2·5 mm. (Found: C, 56·35; H, 4·1. $C_8H_7O_2Cl$ requires C, 56·3; H, 4·15%); the *adduct* with sodium hydrogen sulphite separated from water as needles, m. p. 183° (Found: C, 35·1; H, 2·9. $C_8H_8O_5ClSNa$ requires C, 35·0; H, 2·95%), and the 2 : 4-*dinitrophenylhydrazone* from benzene–light petroleum as needles, m. p. 129—130° (Found: N, 16·05. $C_{14}H_{11}ON_4Cl$ requires N, 15·95%).

Similar experiments led to o-*chlorophenoxyacetaldehyde* (12·3 g. from 20·25 g. of ether), b. p. 104°/5 mm. (Found: C, 56·25; H, 4·2%), the sodium hydrogen sulphite *adduct hemihydrate*, needles (from water), m. p. 180° (Found: C, 33·85; H, 3·0. $C_8H_8O_5ClSNa,\frac{1}{2}H_2O$ requires C, 33·85; H, 3·2%), and the 2 : 4-*dinitrophenylhydrazone*, yellow needles (from ethanol), m. p. 153—154° (Found: N, 15·95%); 2 : 4-*dichlorophenoxyacetaldehyde hydrate* (13·3 g. from 23·7 g. of ether) had b. p. 120°/1·5 mm., m. p. 55—58° (Found: C, 43·36; H, 3·65. $C_8H_6O_2Cl_2,H_2O$ requires C, 43·05; H, 3·6%); the *adduct* with sodium hydrogen sulphite separated from water as needles, m. p. 175° (decomp.), and retained a small amount of water of crystallisation after drying *in vacuo* (Found: C, 30·5; H, 2·25. $C_8H_7O_5Cl_2SNa,\frac{1}{4}H_2O$ requires C, 30·65; H, 2·4%); the 2 : 4-*dinitrophenylhydrazone* separated from benzene–light petroleum as needles, m. p. 169° (Found: N, 14·6. $C_{14}H_{10}O_5N_4Cl_2$ requires N, 14·55%); 2 : 4 : 5-*trichlorophenoxyacetaldehyde* (17·6 g. from 27·15 g. of ether), b. p. 132—135°/1 mm., separated from light petroleum as needles, m. p. 109—110° (Found: C, 40·15; H, 2·2. $C_8H_5O_2Cl_3$ requires C, 40·1; H, 2·1%); the *adduct hydrate* with sodium hydrogen sulphite separated from water as plates, m. p. 183—184° (Found: C, 26·65; H, 2·2. $C_8H_6O_5Cl_3SNa,H_2O$ requires C, 26·55; H, 2·25%), and the 2 : 4-*dinitrophenylhydrazone* as needles, m. p. 167—168°, from benzene–light petroleum (Found: C, 40·15; H, 2·3; N, 13·1. $C_{14}H_9O_5N_4Cl_3$ requires C, 40·05; H, 2·15; N, 13·35%).

We thank Dr. E. Challen for the semimicro-analyses and the Commonwealth Scientific and Industrial Research Organisation for a maintenance grant (to M. H. M.).

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[*Received, June* 9*th*, 1954.]