Preparation of "Double Phenoxy" Compounds and Preliminary Evaluation of Their Herbicidal Activity on Mesquite Seedlings

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Chlorine-substituted phenoxyalkyl alcohol esters of substituted phenoxyalkylcarboxylic acids ("double phenoxy" compounds) have been prepared and evaluated as herbicides. Fourteen compounds tested on greenhouse-grown mesquite seedlings varied in herbicidal activity depending upon the phenoxyalkyl alcohol and the phenoxyalkyl acid used to prepare them. Some of the double phenoxy compounds showed considerable activity and compared favorably with 2,4,5-trichlorophenoxyacetic acid and 2-(2,4,5-trichlorophenoxy)propionic acid standards. Initial mesquite response to one compound applied by aerial spray under field conditions is described as marked. Final observations are to be made in the fall of 1959. From the general herbicidal activity of these compounds, as reported here, and the activity and persistence reported elsewhere, lasting effects are anticipated.

THE preparation of the first six members of a series of chlorine-substituted phenoxyalkyl alcohol esters of substituted phenoxyalkylcarboxylic acids, designated as "double phenoxy" compounds, was completed in 1954. The purpose in making these compounds was to secure a wide variety of phenoxy combinations to observe their behavior as intact molecules having plant growth-regulating effects, different from their parent compounds Esters of this type might also hydrolyze slowly and thus have a prolonged herbicidal action especially on pre-emergence application; they could be expected to possess the desirable property of low volatility.

The double phenoxy series was extended to 16 compounds following preliminary tests on greenhouse-grown mesquite plants which indicated that the herbicidal response to the double phenoxy compounds was considerable.
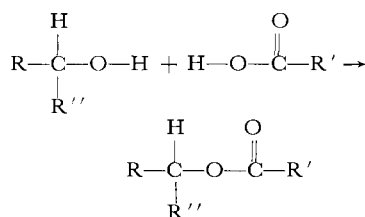
That the general herbicidal activity and persistence of several of these double phenoxy compounds (prepared by the authors) exceeds, and the selectivity is about equal to, that of the parent compounds has been reported by Gentner and Shaw (1). The 2-(2,4-dichlorophenoxy)ethanol ester of 2,4,5-trichlorophenoxyacetic acid (the only double phenoxy compound supplied) warrants further testing in preplanting and pre-emergence treatments for tomatoes, particularly where the crop is direct seeded (4).

Experimental

The double phenoxy compounds were

prepared by azeotropic dehydration using either anhydrous hydrogen chloride or concentrated sulfuric acid as a catalyst, according to the general reaction:

$$
\begin{array}{c}
\text{H} \qquad\qquad\qquad \text{O} \\
| \qquad\qquad\qquad\quad\ \| \\
\text{R}\!-\!\text{C}\!-\!\text{O}\!-\!\text{H} + \text{H}\!-\!\text{O}\!-\!\text{C}\!-\!\text{R}' \rightarrow \\
| \\
\text{R}'' \\
\ \\
\text{H} \qquad\ \text{O} \\
| \qquad\quad\ \| \\
\text{R}\!-\!\text{C}\!-\!\text{O}\!-\!\text{C}\!-\!\text{R}' \\
| \\
\text{R}''
\end{array}
$$

where R and R' represent chlorine-substituted phenoxyalkyl groups and R'' represents a hydrogen atom or an alkyl group. Various solvents were used for the removal of water at reflux temperatures, but petroleum ether was the preferred solvent.

The phenoxy acids used were of technical grade; the chlorinated phenoxy alcohols were supplied through the courtesy of the Dow Chemical Co. and Amchem Products, Inc. Any compound with a chlorine content deviating by more than 3% from the calculated value was purified by recrystallization before use.

Table I lists the double phenoxy compounds prepared.

To prepare sufficient 2-(2,4-dichlorophenoxy)ethanol ester of 2,4,5-trichlorophenoxyacetic acid for aerial spraying on mesquite foliage under field conditions, 2-, 4-, 8-, and 12-mole quantities of materials were utilized batchwise. One of these 12-mole batch esterifications was made as follows:

2-(2,4-Dichlorophenoxy)ethanol Ester of 2,4,5-Trichlorophenoxyacetic Acid. To 2-(2,4-dichlorophenoxy)ethanol (2484 grams) and to 2,4,5-trichlorophenoxyacetic acid (3066 grams) placed

in a 12-liter two-necked flask were added 2 liters of benzene and 8 ml. of concentrated sulfuric acid. The mixture was mechanically stirred and heated at reflux temperature for 5 hours. The theoretical amount of water (216 ml.) was collected in a moisture tube (improvised by using a large Soxhlet extractor with the syphon side-arm tube sealed off and an outlet tube with attached stopcock sealed in at a low point in the bottom of the extractor's reservoir). At the end of the reaction period 600 ml. of benzene were withdrawn through the moisture tube and the hot residual solution was separated from the sulfuric acid, by decantation through an asbestos filter pad (Republic-Seitz, S-3) with the aid of suction. To the chilled filtrate were added 4 liters of petroleum ether (boiling range 63° to 70° C.). The product which separated after refrigeration was filtered off, slurried in a mixture of 0.5 liter of benzene and 3 liters of petroleum ether, filtered again and washed with 3 liters of petroleum ether, then dried to a constant weight of 3810 grams; yield 71.5%, melting point 97° to 99° C. (chlorine: calculated 39.88%; found 39.54%). Additional product was not recovered from the mother liquor.

The technique was simplified for the preparation of the 2-(2,4-dichlorophenoxy)ethanol ester of 4-(2,4-dichlorophenoxy)butyric acid. Petroleum ether was substituted for benzene, or other azeotropic solvents, alkaline washings were eliminated, and no recrystallization was necessary to give a product of good quality. Only 1 liter of petroleum ether and 2 ml. of concentrated sulfuric acid were used in the removal of water from 0.5M quantities of reactants.

By this procedure two liquid layers formed when stirring was discontinued. The supernatant phase was decanted through an asbestos filter pad. The hot residual liquid was extracted repeatedly with boiling portions of petroleum ether until only several milliliters of charred residual sulfuric acid remained. The colored impurities remained with the sulfuric acid only when petroleum ether was used for azeotropic removal of water. The petroleum ether extracts were also filtered hot and added to the original supernatant layer material.

Evaluation of Double Phenoxy Compounds of Mesquite Seedlings. The herbicidal activity of a number of double phenoxy compounds was determined in tests on seedlings of mesquite (*Prosopis juliflora* var. *glandulosa*). Greenhouse-grown mesquite seedlings were treated by dipping the plants in 50% acetone-water solutions of the various compounds. An alkylarylsulfonate (trade name Vel) was added at 1 to 1000 ratio to ensure uniform wetting of the mesquite foliage. Seedlings varied in age from 6 weeks to 6 months depending on the availability at the time of treatment. The herbicidal activity was determined by measuring the length of stem tissue killed and converting it to per cent of stem tissue killed. Stem kill measurements were made from 17 to 30 days after treatment, depending on

the rapidity of response in a particular test. Estimates of leaf kill and counts on the number of plants killed were made. Because the same relative herbicidal activity was indicated by the stem kill percentage, data on leaf and plant kill were not included.

In a preliminary evaluation, mesquite plants were dipped in solutions containing 100 mg. per liter of acid equivalent of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) (*3*), and the 2-(2,4-dichlorophenoxy)ethanol ester of 2,4,5-trichlorophenoxyacetic acid. Stem kill measurements made 40 days after treatment disclosed that both compounds had killed 88% of the mesquite stem tissue. This indicated that the 2-(2,4-dichlorophenoxy)ethanol ester of 2,4,5-trichlorophenoxyacetic acid was a very active compound.

Because of the activity shown by this ester, a group of double phenoxy compounds was evaluated for herbicidal activity on mesquite seedlings (Table II, column 1). Thirty seedlings were used for treatment with each compound in this experiment. A considerable range of activity was evident. When 50 mg. per liter concentrations were used the most active combinations utilized either 2,4,5-trichlorophenoxyacetic acid or DL-2-(2,4,5-trichlorophenoxy)propionic acid (Silvex) (*3*) as the parent acid.

Seven of the more active double phenoxy compounds from the previous test were evaluated on mesquite seedlings along with 2,4,5-T and Silvex which were included as standards. Twenty-six seedlings were used for each compound tested. The activity of all but one of the double phenoxy compounds compared favorably with that of the standards when concentrations of 12.5, 25, and 50 mg. per liter of each compound were used (Table II, columns 2, 3, and 4).

In a final evaluation test the 2-(2,4-dichlorophenoxy)ethanol ester of 2,4,5-trichlorophenoxyacetic acid and the 2-(2,4,5-trichlorophenoxy)ethanol ester of 2,4,5-trichlorophenoxyacetic acid were compared to equivalent mg. per liter concentrations of 2,4,5-T and a mixture of 2,4-dichlorophenoxyacetic acid (2,4-D) (*3*) and 2,4,5-T (Table II, columns 5 and 6). In this test 36 seedlings were used for each treatment. Again the herbicidal activity of the double phenoxy compounds compared favorably with that of 2,4,5-T and the mixture of 2,4-D and 2,4,5-T.

As a result of the greenhouse evaluations the 2-(2,4-dichlorophenoxy)ethanol ester of 2,4,5-trichlorophenoxyacetic acid was prepared in quantity and applied by aerial spraying to mesquite foliage under field conditions in the Spring of 1957. Observations indicated a marked

Table I. Physical and Analytical Data on Halogenated Phenoxyalkyl Alcohol Esters of Halogenated Phenoxyalkylcarboxylic Acids

Acid	M.P., ° C. (Corr.)[a]	Yield, % Crude	Yield, % Refined	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
2-(2,4-Dichlorophenoxy)ethanol Ester									
4-Chlorophenoxyacetic	84.5–85.5[c,d]	68.9	50.0	51.16	51.32	3.49	3.73	28.32	28.25
2,4-Dichlorophenoxyacetic	92.5–93.5[e]	92.7	70.2	46.86	46.94	2.95	3.14	34.59	34.75
2-Methyl-4-chlorophenoxyacetic	66.0–66.5	92.1	81.9	52.41	52.29	3.88	4.04	27.30	27.37
2,4,5-Trichlorophenoxyacetic	93.5–94.0[c,d]	66.7	55.5	43.23	43.51	2.74	2.69	39.88	39.55
DL-2-(2,4-Dichlorophenoxy)propionic	70.0–71.5[f]	42.3	40.6	48.14	48.32	3.57	3.47	33.44	33.45
DL-2-(2,4,5-Trichlorophenoxy)propionic[g]	99.0–100.0[e,f]	66.3	51.5	44.54	44.58	3.30	3.06	38.66	38.63
4-(2,4-Dichlorophenoxy)butyric[g]	53.0–55.0		81.2	49.34	49.35	3.68	3.55	32.37	32.00
2-(2,4,5-Trichlorophenoxy)ethanol Ester									
2,4-Dichlorophenoxyacetic	90.0–90.5[h]	91.0	78.7	43.20	43.11	2.49	2.64	39.88	39.61
2,4,5-Trichlorophenoxyacetic	90.5–91.0[d,h]	98.0	77.3	40.11	40.40	2.10	2.15	44.41	44.02
DL-2-(2,4,5-Trichlorophenoxy)propionic	93.0–94.0[h]	81.3	63.3	41.44	41.10	2.45	2.43	43.15	42.92
DL-1-(2,4,5-Trichlorophenoxy)-2-propanol Ester									
2,4-Dichlorophenoxyacetic	91.5–92.5[d]	73.1	73.1	44.52	44.83	2.86	2.86	38.66	38.24
2,4,5-Trichlorophenoxyacetic	95.5–96.5[d]	68.2	58.4	41.41	41.88	2.45	2.65	43.15	42.45
DL-2-(2,4,5-Trichlorophenoxy)propionic[i]	105.5–107.0[d]	44.2	34.2	42.63	42.92	2.78	3.34	41.96	41.41
DL-2-(2,4,5-Trichlorophenoxy)-1-propanol Ester									
2,4-Dichlorophenoxyacetic	64.0–66.0	54.0	54.0	44.52	44.49	2.86	3.03	38.66	38.45
2,4,5-Trichlorophenoxyacetic	77.0–79.0	79.3	79.3	41.41	41.58	2.45	2.73	43.15	42.37
DL-2-(2,4,5-Trichlorophenoxy)propionic	89.0–90.0[h]	50.4	50.4	42.63	43.11	2.78	3.25	41.96	41.93

[a] Xylene used for removal of water, first 6 compounds [anhydrous hydrogen chloride catalyst (*2*)]. Petroleum ether (b.p. 63° to 70° C.) in all others, unless otherwise indicated (sulfuric acid catalyst). Recrystallized once from petroleum ether.
[b] Analyses by J. S. Ard, R. B. Kelly, and K. Zbinden.
[c] Recrystallized from petroleum ether–xylene.
[d] Norit treated.
[e] Recrystallized from acetone-water.
[f] Benzene solution passed through alumina column.
[g] Not evaluated on mesquite.
[h] Recrystallized from petroleum ether–ethyl acetate.
[i] Toluene used for azeotropic removal of water.

Table II. Per Cent Mesquite Seedling Stem Kill Using 50% Acetone Carrier in Dip Applications[a]

Compound	Mg./Liter					
	50	12.5	25	50	50	100
					17 Days after Treatment	
	30 Days after Treatment				Treatment	
2,4,5-Trichlorophenoxyacetic acid ester of						
DL-2-(2,4,5-Trichlorophenoxy)-1-propanol	71	15	29	51		
2-(2,4-Dichlorophenoxy)ethanol	70	16	30	56	46	61
2-(2,4,5-Trichlorophenoxy)ethanol	58	8	31	57	47	41
DL-1-(2,4,5-Trichlorophenoxy)-2-propanol	55			53		
DL-2-(2,4,5-Trichlorophenoxy)propionic acid ester o.						
2-(2,4,5-Trichlorophenoxy)ethanol	42	14	34	43		
DL-2-(2,4,5-Trichlorophenoxy)-1-propanol	37	10	25	47		
DL-1-(2,4,5-Trichlorophenoxy)-2-propanol	10			9		
2,4-Dichlorophenoxyacetic acid ester of						
2-(2,4,5-Trichlorophenoxy)ethanol	4					
DL-1-(2,4,5-Trichlorophenoxy)-2-propanol	3					
2-(2,4-Dichlorophenoxy)ethanol	3					
DL-2-(2,4,5-Trichlorophenoxy)-1-propanol	2					
2-(2,4-Dichlorophenoxy)ethanol ester of 2-methyl-4-chlorophenoxyacetic acid	4					
2-(2,4-Dichlorophenoxy)ethanol ester of DL-2-(2,4-dichlorophenoxy)propionic	2					
2-(2,4-Dichlorophenoxy)ethanol ester of 4-chlorophenoxyacetic acid	1					
DL-2-(2,4,5-Trichlorophenoxy)propionic acid		4	22	38		
2,4,5-Trichlorophenoxyacetic acid		6	8	29	49	53
2,4-Dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid (1 to 1 mixture)					43	48

[a] All concentrations on a phenoxyalkyl parent acid equivalent basis.

initial response to the application. Final evaluations of the field plots will not be possible until the fall of 1959.

The considerable herbicidal activity of this group of compounds on mesquite suggests that further evaluations should be made on a variety of weed and crop plants. They may have possible uses in foliage or soil applications for the control of unwanted vegetation; to some extent this has already been indicated by preliminary evaluations of other investigators (1, 4).

Literature Cited

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PESTICIDE RESIDUES

Quantitative Determination of Arsenic Residues in Plant Materials

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A total analytical method is presented for the microdetermination of arsenic in plant material as finally measured by means of the molybdenum blue reaction. The procedure is based on a wet-ashing process of the material to be analyzed, followed by distillation in special apparatus. From 1 to 60 γ of arsenic per sample can be determined by direct reading from a single standard curve. This method is especially valid for determination of arsenic residues in any crop after preharvest treatment with arsenical compounds. Some typical data are given from field experiments using the organic arsenic-containing Tuzet as a fungicide on apple trees.

MICROAMOUNTS OF ARSENIC such as are found in plant material after fungicidal or insecticidal treatment require especially sensitive analytical methods, as, for example, in investigations of mechanisms of action or of the ultimate disposition of the arsenic in plant tissues and systems. It is accordingly important to be able to demonstrate magnitudes of arsenic-containing residues in harvested commodities. The analytical method, of course, should respond to arsenic in any compound or oxidation state.

Extensive literature shows that the molybdenum blue reaction is generally used for the quantitative microdetermination of arsenic as well as phosphorus. However, the molybdate method cannot be used directly to determine trace amounts of arsenic in biological materials because of the influence of phosphorus upon arsenic determinations. All published procedures for the determination of arsenic therefore include an ashing process, with subsequent differential separation of the arsenic for quantitative measurement.

The usual molybdate reagent imposes certain definite restrictions—i.e., choice of reducing agent, the amount of acid used, and the concentrations of other reagents and foreign ions present. The influence of foreign ions is essentially eliminated in the present procedure, and the acid effect is discussed in detail