

beet, and Mung bean analyses also indicated that EPTC-S<sup>35</sup> was taken up readily from soil and translocated throughout the entire plant, with most of the sulfur-35 accumulating in the tops in all plants. The radioautographs of these

vegetables are shown in Figure 1, *F* to *I*.

#### Literature Cited

- (1) Fang, S. C., Theisen, Patricia, J. *AGR. FOOD CHEM.* 7, 770 (1959).
- (2) Mitchell, J. W., Linder, P. J., *Bot. Gaz.* 112, 126-9 (1950).

Received for review September 22, 1959  
Accepted March 8, 1960. Approved for publication as Technical Paper No. 1268 by the Director of the Oregon Agricultural Experiment Station. Work supported by grants from Stauffer Chemical Co. and the Atomic Energy Commission.

## HERBICIDAL ACTIVITY

### Molecular Size *vs.* Herbicidal Activity of Anilides

C. W. HUFFMAN<sup>1</sup> and S. E. ALLEN<sup>2</sup>  
Lion Oil Co., A Division of Monsanto Chemical Co., El Dorado, Ark., and Midwest Research Institute, Kansas City, Mo.

The search for better herbicides would be facilitated by some guiding principle. Molecular size was found to be very helpful. A number of the most effective herbicides were shown to have two common dimensions. Anilides were powerful foliage toxicants and the most active anilides possessed the two desired dimensions. Substitution of the phenyl ring also had a very marked effect on phytotoxicity. Maximum toxicity of anilides was associated with 3,4-chlorination of the phenyl ring. A chlorine atom in the 2 position greatly inhibited activity. Thioanilides were as active as anilides.

PREVIOUS INVESTIGATORS have made a number of attempts to correlate molecular size with physiological activity. Success has been limited to a few which relate activity to a single dimension. Maximum hormonal activity of diethylstilbestrol and related compounds was associated with a specific long dimension (7, 10, 16). On a similar basis it has been postulated (14) that the high insecticidal activity of the gamma isomer of hexachlorocyclohexane is due to its being the only isomer small enough to enter an insect cell membrane interspace of 8.5 A.

A number of the most active herbicides known at the present time were found to have two common dimensions. This may be the first time that biological activity has been correlated with two dimensions of a number of molecules.

An excellent tabulation of structure *vs.* herbicidal activity was given by Shaw and Swanson (17). We measured the dimensions of Fisher-Hirschfelder-Taylor models of the compounds listed. Two dimensions were necessary for most carbamates to have high herbicidal activity: 13 and 10 A. A third dimension could not be found which could be correlated with herbicidal activity.

Measurement of models of several of the most active herbicides being marketed showed them to have about the same 13-

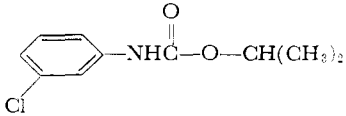
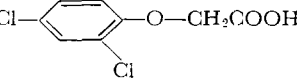
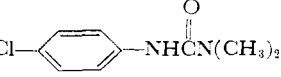
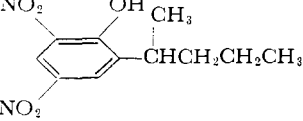
A. extended dimension as the highly active carbamates. The collapsed dimension was 10 A. for carbamates and phenoxyacetic acids (19) and 11 A. for ureas and phenols. Table I records the structures and dimensions of models of these four herbicides. Each represents a different type of molecule, but all contain a phenyl group. It was assumed that esters of 2,4-D hydrolyze to the free acid; thus measurement of models of the various esters was not warranted.

Therefore the desired dimensions are: Extended 13 A. Collapsed 10 or 11 A.

Some active herbicides do not have the dimensions described. Several smaller compounds (about 10-A. maximum length) have high herbicidal activity. These include the  $\alpha$ -chloroacetamides (8), 3-amino-1,2,4-triazole (7), and pentachlorophenol. Possibly different mechanisms of herbicidal action are operative with molecules which do not have the same dimensions.

The desired size concept was of value in the selection of the compounds to be synthesized. A preliminary seed-germination test had shown that most of the compounds with the desired dimensions

Table I. Molecular Dimensions of Active Herbicides

Designation	Structure	Extended A.	Collapsed A.
CIPC		13.2	9.8
2,4-D		12.9	10.2
CMU		13.1	10.8
DNAP		13.5	11.0

<sup>1</sup> Present address, Central Research Laboratories, International Minerals and Chemical Corp., Skokie, Ill.

<sup>2</sup> Research Center, U. S. Rubber Co., Wayne, N. J.

**Table II. Effect of Substituents in Anilides with the Desired Dimensions**

Compound No.	Structure	Size, A.		Activity (8 Lb./Acre)	
		Extended	Collapsed	Pre-emergence	Post-emergence
1		13.1	10.5	1	4
2		13.1	10.3	1	4
3		13.1	10.8	1	3
4		13.0	10.2	0	3
5		13.3	10.4	0	3
6		13.2	10.2	0	3
7		13.4	11.0	1	2
8		12.8	10.0	0	2
9		13.4	11.0	1	2
10		13.2	10.5	0	1
11		13.1	10.3	0	1
12		12.9	10.4	0	1
13		13.1	10.5	0	0
14		13.0	10.5	0	0
15		13.0	9.8	0	0
16		13.2	10.5	0	0
17		13.3	10.4	0	0
18		13.2	10.5	0	...
19		12.8	9.8	0	0
20 <sup>a</sup>		13.0	9.7	0	0

<sup>a</sup> Both isomers tested.

were active. This test was too sensitive. Further greenhouse tests showed that several types of compounds were active. An illustration of the desired size concept is given in this article, using some of the data obtained from a study of anilides. Little is available (8, 17) on the herbicidal activity of anilides. It should be obvious that the desired size concept would reduce the number of compounds to be tested. Nevertheless, many anilides with dimensions outside the desired range were tested to confirm the desired size concept.

### Measurement of Atomic Models

Prior to synthesis, a model of each compound was constructed with Fisher-Hirschfelder-Taylor atomic models (scale: 1 cm. = 1 A.). The longest possible extended dimension of the model was measured with 30-cm. calipers (No. 122M, Starrett Co., Athol, Mass.), then the model was compressed to its smallest size and the maximum collapsed dimension was measured. The first step in the application of the desired size concept was the preparation of anilides with the desired dimensions.

### Greenhouse Experiments

**Formulation.** Compounds were prepared for testing, by solution in an appropriate solvent (dimethylformamide or methyl isobutyl ketone), followed by dispersion in water with aid of an emulsifier (Agrimul GM or C). By preparing the emulsions in suitable volume and concentration, all treatments could be applied at a rate of 8 pounds per 100 gallons per acre. Testing of blank formulations showed no toxicity in any treatment.

### Seeds Used

Corn, *Zea mays*, variety U-S-13  
 Cotton, *Gossypium sp.*  
 Beans, *Phaseolus vulgaris*, variety top crop  
 Rye grass, *Lolium perenne*  
 Bindweed, *Convolvulus arvensis*  
 Morning glory, *Ipomea purpurea*  
 Mustard, *Brassica kaber*  
 Pigweed, *Amaranthus retroflexus*

**Pre-emergence Test.** The seeds were planted in soil in 1 × 2 foot flats. Within 48 hours after planting, the soil surface was sprayed with the test compounds. All treatments were duplicated. Results were evaluated by observation, emergence counts, photography, and estimates of stand and yield at termination of the tests (usually 6 to 8 weeks after planting). Based on these results, a toxicity rating was assigned.

**Postemergence Test.** This test was conducted as above, but the plants were not treated until 3 to 4 weeks after emergence, at which time they were in

approximately the following stage:

Corn	8 to 12 inches tall, 4 to 5 leaves
Cotton	2 to 4 inches tall, 3 leaves
Beans	6 to 10 inches tall, 2 to 3 trifoliate leaves
Rye grass	4 to 6 inches tall
Bindweed	2 to 3 inches tall, 3 leaves
Pigweed	3 to 6 inches tall

**Toxicity Rating System.** To present the results with minimum confusion and facilitate a rapid comparison of compounds, the following rating system was established:

0. Inactive, no effect on any crop plant.
1. Low activity, injury to sensitive crops, with little or no effect on resistant plants.
2. Moderate activity, lethal to sensitive crops, with moderate injury or no effect on resistant plants.
3. High activity, lethal to sensitive crops, moderate to severe injury to resistant plants.
4. Maximum activity, lethal to all plants.

**Results.** The foliage effects produced by anilides usually begin to develop within 24 hours after treatment and gradually increase in severity for about 7 days. If plants are not killed within a week, slow recovery starts with a minimum of physiological effects, as indicated by the lack of appreciable malformation of newly formed tissue. As might be expected of poisons primarily contact in nature, meristematic regions are most sensitive. Plants treated with sublethal doses are characterized by rapid development of marginal leaf burning, followed within 48 hours by the appearance of chlorotic areas in less severely damaged tissues. Young corn plants sprayed from above often deteriorate near the ground level because of toxic material entering the opening whorl of leaves and touching the meristem below.

Table II lists anilides with the desired dimensions and in the order of their decreasing herbicidal activity.

Table II shows that maximum activity was obtained with 3,4-dichloroanilides (compounds 1 and 2). Replacement of the acyl oxygen by sulfur did not significantly alter the activity (No. 4 *vs.* No. 5). A sharp decrease in activity resulted from a 2-chloro (Nos. 11 and 12) substituent. Many compounds with 2-chloro atoms were inactive (Nos. 13, 14, and 20). A 2-methyl group also caused inactivation (Nos. 15, 16, and 17). A chlorine in the acyl group decreased postemergence activity (No. 7 *vs.* No. 2, No. 9 *vs.* No. 4, No. 10 *vs.* No. 6), but not pre-emergence activity.

Evidence that the desired size concept was valid for 3,4-dichloroanilides is given in Table III. These anilides are listed in accordance with their increasing extended size. It was gratifying to predict that the two 3,4-dichloroanilides with the desired dimensions (Nos. 1

**Table III. Molecular Size vs. Herbicidal Activity of 3,4-Dichloroanilides**

Structure, Clc1ccc(NC(=O)X)cc1Cl

Compound No.	X	Size, A.		Activity (8 Lb./Acre)	
		Extended	Collapsed	Pre-emergence	Post-emergence
21	—H (9)	11.0	10.4	0	3
22	—CH <sub>3</sub>	11.5	10.3	1	3
2	—C <sub>2</sub> H <sub>5</sub>	13.1	10.3	1	4
1	—CH(CH <sub>3</sub> ) <sub>2</sub>	13.1	10.5	1	4
7	—CHCH <sub>3</sub>	13.4	11.0	1	2
23	 —CH(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	14.0	10.4	0	1
24	—CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub>	14.1	10.3	0	3
25	—(CH <sub>2</sub> ) <sub>2</sub> CH <sub>3</sub>	14.5	10.2	1	3
26	—(CH <sub>2</sub> ) <sub>3</sub> CH <sub>3</sub>	15.2	10.3	0	3
27	—(CH <sub>2</sub> ) <sub>4</sub> CH <sub>3</sub>	18.0	10.3	0	1
28	—(CH <sub>2</sub> ) <sub>10</sub> CH <sub>3</sub>	22.4	14.5	0	0

and 2) would show the greatest herbicidal activity. Other variously substituted anilides (not shown) which did not have the desired dimensions had little or no activity.

Table IV records the foliage data obtained with specific plants and a dosage of 8 pounds per acre. These results were the basis for the herbicidal ratings given in Tables II and III. The selectivity of the various compounds as well as the degree of herbicidal activity is apparent from the data. The maximum figure, 1200, signified no activity. A low total shows high activity. Consequently, the value of 15 for compound 2 (3,4-dichloropropionanilide) represents a very high activity, or 4 on the toxicity rating system. CIPC is normally used as a pre-emergence herbicide. Its activity in postemergence treatments was not high.

#### Preparation of Compounds

Melting points (uncorrected) were taken with Anschütz thermometers.

The compounds listed in Table V were prepared by the procedure described for the preparation of 2,3',4'-trichloropropionanilide. In a few cases the product was obtained from the reaction mixture by precipitation with petroleum ether; in others it was necessary to remove the solvent by distillation. Details are given for the preparation of *p*-chlorothiopropionanilide.

**2,3',4'-Trichloropropionanilide** (No. 7). Benzene (50 ml.) and triethylamine (15.2 grams, 0.15 mole) were heated to boiling in a flask equipped with a stirrer, to dissolve technical 3,4-dichloroaniline (24.3 grams, 0.15 mole). A condenser, dropping funnel, and drying tube were installed. The heating mantle was removed, and  $\alpha$ -chloropropionyl chloride (19.0 grams, 0.15 mole) was added dropwise to the black solution, with cooling, over a 15-minute

period. The mixture was refluxed 1 hour and then cooled to room temperature. Water (50 ml.) was added to dissolve the crystalline triethylamine hydrochloride. About 1 hour later, the light tan product was removed by filtration and washed with water (20 ml.). The dry crude material weighed 36.2 grams (yield 96%) and melted at 124–9° C. with sintering at 110° C. A sample was recrystallized from benzene (charcoal). The white crystals had a melting point of 132.6–3.8° C.

***p*-Chlorothiopropionanilide** (No. 5). Beilenson and Hamer's (2) procedure for thioanilides was employed. Xylene (125 ml.) and *p*-chloropropionanilide (18.4 grams, 0.1 mole, m.p. 141° C.) were stirred on a steam bath. Phosphorus pentasulfide (11 grams, 0.5 mole) was added to the colorless solution. A lump formed in the reddish suspension, which was crushed after the reaction had proceeded about 15 minutes. Stirring was resumed for 1 hour. A hot filtration removed orange solid, which was washed with 3 × 50 ml. of hot xylene. The combined filtrate and washes were stored overnight in the ice-box. Additional sticky yellow solid was removed by filtration. Petroleum ether (200 ml.) was added to the yellow xylene filtrate, and the mixture was allowed to cool overnight. The first crop of crude product was collected by filtration and weighed 6.1 grams (30% yield). Concentration of the filtrate under vacuum gave 10.4 grams (52%) of crude second crop material as a dark oil. The first crop material (6.1 grams) was heated with cyclohexane (300 ml.) and the cyclohexane solution was decanted from an insoluble orange oil and treated with Nuchar C. The filtrate was cooled, and the product (4.7 grams) was collected by filtration (m.p. 78–80° C.). A second recrystallization of a sample (1 gram) from cyclo-

Table IV. Postemergence Stand and Yield Results at 8 Pounds per Acre

Com- pound No.		Broadleaf <sup>a</sup>		Pigweed		Rye Grass		Snap Beans		Corn		Cotton		Total
		% S <sup>b</sup>	% Y <sup>b</sup>	% S	% Y	% S	% Y	% S	% Y	% S	% Y	% S	% Y	
EFFECT OF SUBSTITUENTS IN ANILIDES WITH DESIRED DIMENSIONS														
CIPC	G	50	15	0	0	100	35	20	5	100	75	75	25	500
1	B	0	0	0	0	0	0	0	0	25	5	0	0	30
2	B	0	0	0	0	10	5	0	0	0	0	0	0	15
3	G	0	0	0	0	100	50	0	0	100	50	0	0	300
4	B	50	25	0	0	100	100	0	0	100	75	20	5	475
5	B	0	0	0	0	100	75	0	0	65	25	0	0	265
6	B	0	0	0	0	100	85	0	0	50	10	50	25	310
	M	0	0											
7	B	100	75	0	0	100	100	100	20	100	50	100	100	845
	M	0	0											(670)
8	B	100	75	0	0	100	100	100	25	100	85	100	75	860
9	B	100	75	0	0	100	100	100	20	100	85	100	75	855
	M	0	0											(680)
10	B	100	100	10	5	100	100	100	100	100	100	100	100	1015
11	...	...	...	100	75	100	100	100	75	100	100	100	50	[900]
12	B	100	100	100	100	100	100	100	50	100	100	100	100	1150
13 through 20				Little or no effect										1200
MOLECULAR SIZE vs. HERBICIDAL ACTIVITY OF 3,4-DICHLOROANILIDES														
21	B	0	0	0	0	100	100	100	25	100	50	50	25	550
	M	0	0											
22	B	0	0	0	0	100	75	50	5	60	30	100	75	495
	M	0	0											
2	B	0	0	0	0	10	5	0	0	0	0	0	0	15
1	B	0	0	0	0	0	0	0	0	25	5	0	0	30
7	B	100	75	0	0	100	100	100	20	100	50	100	100	845
	M	0	0											(670)
23	B	100	100	30	10	100	100	100	100	100	100	100	100	1040
	M	75	35											(950)
24	B	0	0	0	0	100	100	50	5	75	35	100	75	540
	M	0	0											
25	B	25	10	0	0	100	75	20	5	75	35	100	75	520
	M	0	0											(485)
26	B	30	10	0	0	100	100	50	5	60	30	100	75	560
	M	0	0											(520)
27	B	100	100	0	0	100	100	100	85	70	50	100	100	905
	M	100	50											(855)
28		No effect												1200

<sup>a</sup> B. Bindweed. G. Wild morning glory. M. Mustard. <sup>b</sup> S. Stand. Y. Yield. ( ) Test with alternate broadleaf weed. [ ] Broadleaf weed omitted from test.

Table V. Anilides Prepared

Com- pound No. <sup>a</sup>	Ref.	Sol- vent <sup>b</sup>	Crude, % Yield	Recrystallization Solvent <sup>b</sup>	Pure, M.P., ° C.	Formula	Analyses							
							% Calcd.				% Found			
							C	H	Cl	N	C	H	Cl	N
1		B	96	Dioxane-water	134.6-5.2	C <sub>10</sub> H <sub>11</sub> Cl <sub>2</sub> NO	51.8	4.74	30.6	6.03	52.0	4.60	30.3	5.94
2		B	79	Cyclohexane	90.6-1.6	C <sub>9</sub> H <sub>9</sub> Cl <sub>2</sub> NO	49.6	4.13	32.5	6.42	49.6	3.90	32.4	6.34
3	(20)	B	95	B	152.6-3.0	C <sub>10</sub> H <sub>12</sub> ClNO	60.8	6.08	17.9	7.09	61.0	6.26	18.1	7.03
4	(6)	C	98	C-pet. ether	141	C <sub>9</sub> H <sub>10</sub> ClNO								
5		B	82	Cyclohexane	87-8	C <sub>9</sub> H <sub>10</sub> ClNS	54.2	5.01			54.6	4.86		
6		B	65	Cyclohexane	95.5-6.2	C <sub>10</sub> H <sub>12</sub> ClNO	60.8	6.08			61.1	5.97		
7		B	88	B	132.6-3.8	C <sub>9</sub> H <sub>9</sub> Cl <sub>2</sub> NO	42.8	3.17			43.5	3.12		
9		B	88	Cyclohexane	113.8-14.6	C <sub>9</sub> H <sub>9</sub> Cl <sub>2</sub> NO	49.6	4.13			50.1	4.50		
10		B	88	Cyclohexane	116.2-16.4	C <sub>10</sub> H <sub>11</sub> Cl <sub>2</sub> NO	51.8	4.74	30.6		52.1	4.68	30.6	
11	(6)	B	79	B-pet. ether	121	C <sub>9</sub> H <sub>9</sub> Cl <sub>2</sub> NO								
12		B	75	Ethanol	150-1	C <sub>9</sub> H <sub>9</sub> Cl <sub>2</sub> NO	42.8	3.17			42.2	3.51		
13		B	87	Ethanol	123.5-4.5	C <sub>10</sub> H <sub>11</sub> Cl <sub>2</sub> NO	51.8	4.74			52.1	4.78		
14		B	80	B	148.0-8.4	C <sub>10</sub> H <sub>10</sub> Cl <sub>2</sub> NO	45.1	3.75	39.9		45.3	3.79	39.8	
15		B	99	Cyclohexane	142-3	C <sub>11</sub> H <sub>14</sub> ClNO	62.4	6.62	16.8		62.8	6.54	16.8	
16	(4)	B	100	2-Propanol	139.8-40.2	C <sub>11</sub> H <sub>14</sub> NO								
17		B	100	B	143.8-44.2	C <sub>11</sub> H <sub>14</sub> ClNO	62.4	6.62	16.8	6.62	62.9	6.54	16.6	6.69
19	(13)	B	98	Dioxane-water	127	C <sub>9</sub> H <sub>10</sub> ClNO								
20	(18)	B	Total	Methylcyclohexane	70-6	C <sub>10</sub> H <sub>9</sub> Cl <sub>2</sub> NO	52.2	3.91		6.09	51.0	3.94		6.20
		B	94	Cyclohexane	150-1						52.8	4.05		
22	(3)	B	67	B	120.5	C <sub>8</sub> H <sub>7</sub> Cl <sub>2</sub> NO								
23		B	98	Cyclohexane	124.2-25.8	C <sub>12</sub> H <sub>15</sub> Cl <sub>2</sub> NO	55.4	5.77			55.8	5.72		
24		B	60	2-Propanol	81.8-7.4	C <sub>11</sub> H <sub>13</sub> Cl <sub>2</sub> NO	53.9	5.31			54.4	5.47		
25		B	65	B	76.6-7.9	C <sub>10</sub> H <sub>11</sub> Cl <sub>2</sub> NO	51.8	4.74			51.7	4.98		
26		B	58	B	71.4-3.2	C <sub>11</sub> H <sub>13</sub> Cl <sub>2</sub> NO	53.9	5.31			53.7	5.34		
27		B	90	Cyclohexane	59.8-61.4	C <sub>13</sub> H <sub>17</sub> Cl <sub>2</sub> NO	57.0	6.20			57.0	6.31		
28		B	91	A	81.1-2.5	C <sub>13</sub> H <sub>17</sub> Cl <sub>2</sub> NO	62.8	7.85			62.5	7.84		

<sup>a</sup> Structures given in Tables II-III.

<sup>b</sup> A. Acetonitrile. B. Benzene. C. Chloroform.

hexane gave 0.8 grams of fine white needles (m.p. 87–8° C.).

P. J. Stoffel, Monsanto, St. Louis Laboratories, has suggested pyridine as a useful solvent for thiations (17).

### Discussion

Although anilides are structurally similar to carbamates and ureas, their mode of action and structural requirements for maximum herbicidal activity differ to a marked degree. For example, the anilides are primarily foliage toxicants, while carbamates and ureas are much more effective in pre-emergence applications. Carbamates (17) show the greatest activity with a 3-chlorophenyl group, while phenyl, 2,4-dichloro-, and 4-chloro- analogs are lower in activity. Ureas with these substituents are all toxic (5). In contrast, the 3,4-dichloro-anilides are by far the most active anilides; 4-chloro- and phenyl derivatives are less active.

The clear-cut inhibition of activity produced by a 2-chloro- substituent was unique, as it did not occur in ureas, carbamates, or phenoxyacetic acids (19). Maximum activity was obtained with 2,4-dichlorophenoxyacetic acid, while 3,4-chlorination imparted a decreased activity (12). This was reversed in the anilide series. The cinnamic acids (15) follow a structure *vs.* activity pattern very similar to phenoxyacetic acids.

How should the data on the desired size concept be interpreted? Perhaps two enzyme interspaces were involved—one required a molecule with a maximum length of 13 Å., the second a 10- or 11-Å. size. Apparently the second interspace was not satisfied by a molecule which could be compressed to a size less than 10 Å.

Molecular size was an important factor in the herbicidal activity of varied compounds. Properly placed substituents were also necessary for maximum activity. Consequently, the de-

sired size concept enables the prediction of the most active compound in a series with similar substituents. Such a prediction was of value in reducing the number of compounds to be tested. Acceptance of the premise that the desired size concept would apply to anilides would have eliminated many compounds from the test program. A study is being made of lower rates of application of several of the active anilides. These studies, along with directed spraying, may enable their use as selective herbicides on various crops. Selectivity might also be achieved by choosing the less toxic compounds, or variants of these compounds.

Several years elapsed between the discovery of 2,4-D and the discovery of other active herbicides such as CMU and CIPC. This time would have been shortened considerably if the extended and collapsed dimensions of 2,4-D had been accepted as the desired dimensions. This reasonable conclusion establishes the validity of the desired size concept. Unfortunately, many compounds with these dimensions had little or no pre- or postemergence activity. Consequently, the desired size concept remains as only one facet of herbicidal activity.

Possibly the desired size concept will prove applicable to other biological problems. Molecular size measurements of models of fungicides, insecticides, nematocides, etc., may prove fruitful.

### Acknowledgment

The authors acknowledge the encouragement of R. C. Tallman, who suggested the herbicide project. Thanks are due to D. E. Swafford and Gary Greene for assistance in the preparation of the compounds and to the Monsanto Chemical Co. and Midwest Research Institute for permission to publish this article. Analyses were made by the Clark Microanalytical Laboratories, Urbana, Ill.

Measurement of atomic models and preparation of compounds were done at the Lion Oil Co. and greenhouse experiments at the Midwest Research Institute.

### Literature Cited

- (1) Allen, W. W. (to American Chemical Paint Co.), U.S. Patent **2,670,282** (Feb. 23, 1954).
- (2) Beilenson, B., Hamer, F. M., *J. Chem. Soc.* **139**, 1228 (1936).
- (3) Beilstein, F., Kurbatow, A., *Ann. Chem.* **196**, 217 (1879).
- (4) Bowen, C. V., Smith, L. E., *J. Am. Chem. Soc.* **62**, 3523 (1940).
- (5) Carlson, A. E., *Agr. Chem.* **9**, No. 6, 44–5 (1954).
- (6) Chattaway, F. D., *J. Chem. Soc.* **81**, 639 (1902).
- (7) Giacomello, G., Bianchi, E., *Gazz. chim. ital.* **71**, 667 (1941).
- (8) Hamm, P. C., Speziale, A. J., *J. Agr. Food Chem.* **4**, 518 (1956).
- (9) Huffman, C. W., *J. Org. Chem.* **23**, 727 (1958).
- (10) Keasling, H. H., Schueler, F. W., *J. Am. Pharm. Assoc., Sci. Ed.* **39**, 87–90 (1950).
- (11) Klingsberg, E., Papa, D., *J. Am. Chem. Soc.* **73**, 4988 (1951).
- (12) Leaper, J. M. F., Bishop, J. R., *Botan. Gaz.* **112**, 250–8 (1951).
- (13) Mayer, F., van Zütphen, L., Phillips, H., *Chem. Ber.* **60B**, 858–61 (1927).
- (14) Mullins, L. J., *Science* **122**, 118–19 (1955).
- (15) Plaisted, P. H., *Contribs. Boyce Thomp. Inst.* **18**, 231–42 (1955).
- (16) Schueler, F. W., *Science* **103**, 221 (1946).
- (17) Shaw, W. C., Swanson, C. R., *Weeds* **2**, 43–65 (1953).
- (18) Smith, A. E. W., Hofstetter, E., *Helv. Chim. Acta* **38**, 1092 (1955).
- (19) Weintraub, R. L., Brown, J. W., Throne, J. A., *J. Agr. Food Chem.* **2**, 996–9 (1954).
- (20) Williams, G., Hughes, S. P., *J. Chem. Soc.* **134**, 3130 (1931).

Received for review September 22, 1959.  
Accepted March 10, 1960.