Plant Growth Regulating Activity of Some IPC Analogs

CARBAMATE HERBICIDES

Relative Herbicidal and Growth Modifying Activity Of Several Esters of *N*-Phenylcarbamic Acid

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Increasing interest in recent years in the use of derivatives of carbamic acid as herbicides and plant-growth modifiers has prompted thorough investigations of many types of carbamates. A series of such carbamates analogous to the commercial herbicide, isopropyl *N*-phenylcarbamate (IPC), in which various substitutions have been made in or for the alcohol portion, is described. Chemical and physical properties, as well as preliminary screening evaluation results of their herbicidal and plant-growth-modifying activities, are reported. It is concluded that alterations of the structure of this portion of the molecule can exert profound effects upon the biological activity of such compounds.

THE PHYSIOLOGICAL EFFECTS of esters of carbamic acid and *N*-substituted carbamic acids, such as ethyl carbamate (urethan) and ethyl *N*-phenylcarbamate (phenylurethan), on both animal and plant life were first reported nearly 25 years ago (*2, 9*). Descriptions of additional experiments to determine the effects of this class of compounds on plants have appeared sporadically during the second decade of this period and with increasing frequency in recent years. The initial studies of the effects of a carbamate, ethyl *N*-phenylcarbamate, on the germination and growth of oat and wheat seedlings (*9*) was followed by reports of the regulatory effects of other carbamates on growth of various plants (*10, 13, 18*). However, it was not until 1941, in the British patent literature, that the first practical applications of these observations were suggested (*19*). This patent suggested the use of various esters of *N*-phenylcarbamic acid, and especially the ethyl and isopropyl esters, for the destruction of weeds and implied that, to be effective, the chemical should be applied to the germinating seeds or to the growing plants. Later reports (*15, 20*) first described the selective activity of these chemicals on monocotyledonous, as opposed to dicotyledonous, plants. The latter paper reported tests of a number of carbamates and stated that isopropyl *N*-phenylcarbamate (IPC) was the most active compound studied.

This report, published at about the time that the herbicidal properties of 2,4-dichlorophenoxyacetic acid were discovered, stimulated great interest, and many workers attempted to use isopropyl *N*-phenylcarbamate as a weed killer, applying it in the manner found so satisfactory for the 2,4-D type compounds—i.e., as a spray applied to the aerial plant parts. As reports of the almost uniformly unsuccessful results of such applications were circulated, much of the initial interest in carbamate plant-growth regulators subsided. However, the original British observations were confirmed and expanded by a few investigators, in particular those who observed what now appears to be the major prerequisite condition—i.e., application of the chemical to the soil so that it may be absorbed through plant roots. For example, it has been shown that isopropyl *N*-phenylcarbamate can prevent the establishment of cereal crops such as oats, wheat, corn, barley, and rice at a rate of application which does not affect broad-leaved plants such as soybeans, kidney beans, sunflowers, radishes, turnips, sugar beets, and tomatoes (*1*). In other experiments grassy weeds were controlled without crop damage in plantings of beets, spinach, beans, onions, carrots, and lettuce (*11, 12*).

Continued work has shown that rather specific conditions of temperature and moisture must exist in order to achieve maximum effectiveness with this chemical. The climatic conditions of the northwestern United States approach the conditions required for the best results. It is not surprising, therefore, that some of the most effective uses of this chemical have been observed in this area and that many of its outstanding proponents have appeared from this region. Freed and coworkers have reported a large amount of work with isopropyl *N*-phenylcarbamate (*3–8*), and the most recent paper of this group (*8*) discusses very completely most of the factors influencing its herbicidal efficacy.

These demonstrations prompted a reinvestigation of many related compounds which included, in addition to some compounds previously described, an extensive research survey of other representative members of the whole family of carbamates. The present paper is the first in a series which will describe briefly the preparation, physical properties, and plant-growth regulatory activity of a large number of carbamates and structurally related compounds and will attempt to summarize correlations of chemical structure with biological activity which have been observed in the course of the work. This series has been divided arbitrarily so that each paper describes compounds having close structural relationships. This paper describes 27 compounds which can be considered to be closely related structurally to isopropyl *N*-phenylcarbamate, in that all are alkyl or substituted alkyl esters of *N*-phenylcarbamic acid.

Preparation, Chemical and Physical Properties

Although some of these compounds have not previously been described in the chemical literature, they have, in the authors' work, all been made by well-known and commonly employed methods of synthesis for derivatives of carbamic acid. The identities of all compounds were confirmed by suitable analytical procedures, usually elemental microdetermination of carbon and hydrogen or nitrogen, supplemented normally, in the case of liquids, by molar refraction determinations. Therefore, inasmuch as the chemical information of major importance in the new compounds is data on physical properties of the new compounds, these properties, and for comparison the corresponding properties of some previously reported compounds, along with identifications of the methods of preparation and analytical data are tabulated in Table I.

Starting materials for the preparations reported were of the best quality readily available, and, although primary emphasis was placed on the isolation of pure products and no attempt was made to achieve maximum yields, the yields normally attained were satisfactory. Previous experience with this class of compounds has shown that by selection of appropriate conditions excellent yields of desired products may be secured.

With the exception of the sodium salt of α-carboxyethyl *N*-phenylcarbamate, which is very soluble in water, slightly soluble in the lower aliphatic alcohols, and insoluble in other common organic solvents, these compounds are very soluble in aromatic hydrocarbons, lower aliphatic alcohols, ketones, ethers, and chlorinated hydrocarbons, only slightly soluble in aliphatic hydrocarbons, and insoluble in water. The crystalline compounds can readily be purified by recrystallization from aqueous alcohol, aqueous acetone, or benzene–petroleum ether solvent mixtures. The majority of the liquid compounds can readily be purified by high vacuum distillation; in such distillations it has been found desirable, however, to complete the distillation as rapidly as possible at the lowest practical temperature and pressure obtainable, in order to minimize thermal decomposition.

Test Methods

Eight factors were considered to be of prime importance in the selection of an evaluation procedure, and the method described below is believed to be the best compromise possible among these requirements.

That the method give satisfactory reproducibility.

That it be convenient and simple and require minimum manipulation of test materials and plants.

That it be applicable to a wide variety of plant species.

That it eliminate, in so far as possible, from any one test, interferences from other chemicals being tested.

That it be free from soil effects—i.e., variable pH, organic content, microorganism population and type, etc.

That it allow chemical treatment at various stages of seed germination and plant growth.

That it be readily adaptable to year-round greenhouse use.

That it be designed to show selectivity of action—e.g., against narrow- as opposed to broad-leaved plants, as well as individual species selectivity.

The test method which was evolved in an attempt to meet these requirements has been described in detail (*16*). Briefly, it consists of applying various chemicals at known rates as pre- or postemergence treatments to different planted seeds or growing plants, and at various intervals thereafter examining these plants for differences in growth and development as well as for any evidences of abnormal behavior compared to untreated controls.

Two factors were considered most important in the selection of the test plants used in this screening evaluation. An attempt was made to use both crop and weed species of particular economic importance, and the selection was made to provide an approximately equivalent number of narrow- and broad-leaved species. It would have been possible, by the appropriate selection of plants, to show very high general activity for nearly all of the compounds tested; however, it was considered to be as important to show species tolerance as to show species susceptibility. The plants chosen for any test, usually eight in number, were selected from the group corn, cotton, soybeans, wheat, peas, perennial rye grass, crabgrass, pigweed green beans, barley, and fescue, and in most cases were the first eight of this group. Seeds were planted in clean sand in individual pots (2 $^1/_2$ inch Bird Neponset flower pots) in sufficient number to supply three pots of each plant species for each chemical tested. Sand was used as the supporting medium for planting, both to eliminate soil effects and to ensure conditions of maximum effectiveness for the chemicals being tested.

The chemicals were applied by spraying solutions of them on the surface of the sand in which the seeds had been planted. Ethyl alcohol was used as a solvent in nearly all cases; the exceptions were compounds insoluble in ethyl alcohol but soluble in water, in which case water was used. The spraying was done in a spray tower 34 inches tall and 8$^1/_2$ inches in diameter, which was large enough to accommodate the pots of the eight species being treated at a given rate. The spray was produced by a De Vilbiss atomizing spray gun operated at 10 pounds per square inch air pressure. The amount of chemical deposited was predetermined by weighing the deposit on a metal plate of known area resulting from spraying a known volume of test solution. The solvent evaporated very rapidly from thin film deposits under these conditions, as was determined by following the loss in weight of a freshly sprayed plate. The loss of carbamate by volatilization during this time was negligible. The rates of application used in these tests were usually 10 and 20 pounds per acre. These high rates were chosen because recognition of even minor activity aided the synthesis program in the selection of related or analogous compounds of potentially greater activity. Chemicals which showed sufficient activity at these rates were invariably tested further at lower rates in secondary screening tests which will be reported later.

Chemical treatments were applied to different pots of the same plant species on the day of planting, 3 days after planting, and 7 to 8 days after planting. The last application, which was least correlated with a specific stage of plant growth, was actually a postemergence treatment, as plants at this time were usually 0.5 to 2 inches in height. Before and after spraying the plants were kept in the greenhouse at 70° to 80° F., watered from overhead as required, and shielded when necessary from very intense sunlight with muslin curtains.

Symptoms resulting from treatment

were noted throughout a 2-week test period and the final reading was made at the end of this time. This length of test period was chosen because the plants could maintain normal growth for this time without additional nutrition, and it seemed desirable not to complicate the plant environment by nutrient feeding.

The chemical effect, in comparison to untreated control plants, was evaluated numerically on a scale of 0 to 10, representing no effect to complete inhibition of growth or failure to emerge, corresponding approximately to the following:

0, no effect.

1 to 3, slight effect (0 to 35% reduction in height).

4 to 6, moderate effect (35 to 65% reduction in height).

7 to 9, severe effect (65 to 95% reduction in height).

10, very severe effect (failure to emerge or failure to grow).

These evaluations had to be modified in some cases,—e.g., where height reduction was not particularly pronounced but malformation, chlorosis, or other abnormality was apparent. In such cases evaluations were based more on these effects than on height reduction.

Results

The numerical designations assigned to indicate the effects of the chemicals

Table I. Preparation and Properties of Esters of *N*-Phenylcarbamic Acid

Compound[a]	Preparative[b] Method	M.P., ° C.[c]	B.P., ° C.[c]	n_D^{25}	d_{25}	Analysis[d] Theory	Found
Methyl	B	48 – 49	.....	....	...	N, 9.27	N, 9.30
Ethyl	A_1	49 – 50	.....	....	...	C, 65.43 H, 6.71	C, 65.53 H, 6.94
n-Propyl	A_2	49 – 51	.....	....	...	C, 67.02 H, 7.31	C, 66.97 H, 7.51
Isopropyl	A_1	87 – 88	.....	....	...	C, 67.02 H, 7.31	C, 66.80 H, 7.48
n-Butyl	A_1	63 – 64	.....	....	...	C, 68.37 H, 7.82	C, 68.14 H, 7.99
sec-Butyl	A_1	66 – 67	.....	....	...	C, 68.37 H, 7.82	C, 68.57 H, 8.13
Isobutyl	B	82 – 83	.....	....	...	N, 7.25	N, 7.42
tert-Butyl	C	134 –135	.....	....	...	C, 68.37 H, 7.82	C, 68.29 H, 7.86
Amyl	B	45 – 46.5	.....	....	...	N, 6.76	N, 6.87
Hexyl	A_1	43.5– 44.5	146–8/0.5 mm.	....	...	N, 6.33	N, 6.29
2-Ethylhexyl	A_2	.....	173–4/3 mm.	1.5088	1.003	C, 72.25 H, 9.30	C, 72.29 H, 9.39
Lauryl	A_3	74 – 75	.....	....	...	C, 74.46 H, 10.53	C, 74.35 H, 10.39
Allyl	B	67.5– 69	.....	....	...	C, 67.78 H, 6.26	C, 67.90 H, 6.45
3-Butenyl	B	.....	124–5/0.1 mm.	1.5370	1.082	MR, 55.37[e]	MR, 55.10
2-Chloroethyl	A_1	48.5– 49.5	.....	....	...	N, 7.02	N, 7.08
3-Chloropropyl	B	38 – 40	138–9.5/0.1 mm.	....	...	C, 56.21 H, 5.66	C, 56.32 H, 5.91
2-(1-Chloropropyl)	A_1	.....	148–50/1 mm.	1.5415	1.203	C, 56.21 H, 5.66	C, 56.32 H, 5.99
2-(1,3-Dichloropropyl)	B	72 – 74	.....	....	...	C, 48.41 H, 4.47	C, 48.50 H, 4.69
Cyclohexyl	B	83 – 84	.....	....	...	N, 6.39	N, 6.34
Benzyl	D	74.5– 75	.....	....	...	C, 73.99 H, 5.76	C, 74.12 H, 5.70
2-Cyanoethyl	B	55 – 56	.....	....	...	C, 63.14 H, 5.30	C, 62.86 H, 5.57
2-Nitro-2-methylpropyl	B	125 –127	.....	....	...	C, 55.45 H, 5.93	C, 55.22 H, 6.37
2-Diethylaminoethyl	B	.....	[f]	1.5228	1.049	MR, 68.88	MR, 68.72
Ethylene glycol bis	B	155 – 57	.....	....	...	N, 9.33	N, 9.40
Diethylene glycol bis	A_1	115 – 16.5	.....	....	...	C, 62.78 H, 5.85	C, 62.62 H, 6.15
α-Carboxyethyl	A_3	143 –145	.....	....	...	N, 6.70	N, 6.68
α-Carboxyethyl, sodium salt	E	213 (dec.)	.....	....	...	N, 6.06	N, 6.13

[a] Ester of *N*-phenylcarbamic acid.

[b] A. Reaction of aniline with corresponding alkyl chloroformate in presence of (1) aqueous sodium hydroxide, (2) pyridine, or (3) excess aniline.
B. Reaction of phenyl isocyanate with corresponding alcohol in benzene solution.
C. Reaction of *N*-phenylcarbamyl chloride with corresponding sodium alkoxide.
D. Transesterification of ethyl *N*-phenylcarbamate with benzyl alcohol in presence of sodium benzoxide.
E. Prepared by careful neutralization of corresponding acid in aqueous acetone with appropriate amount of sodium hydroxide followed by crystallization from aqueous acetone and thorough washing with acetone.

[c] Uncorrected.

[d] Results of elemental microdetermination of carbon, hydrogen, or nitrogen or of molar refraction.

[e] Molar refraction.

[f] This compound showed evidences of decomposition during distillation. The sample for which properties are given, and which was used in the herbicidal evaluation, was a residual product obtained as follows: The reaction solvent, benzene, was removed by distillation, and the resultant residue was diluted with hexane to precipitate a small amount of diphenyl urea as a side reaction product. The latter was removed by filtration, and the filtrate was concentrated at reduced pressure to yield the desired compound as a residue.

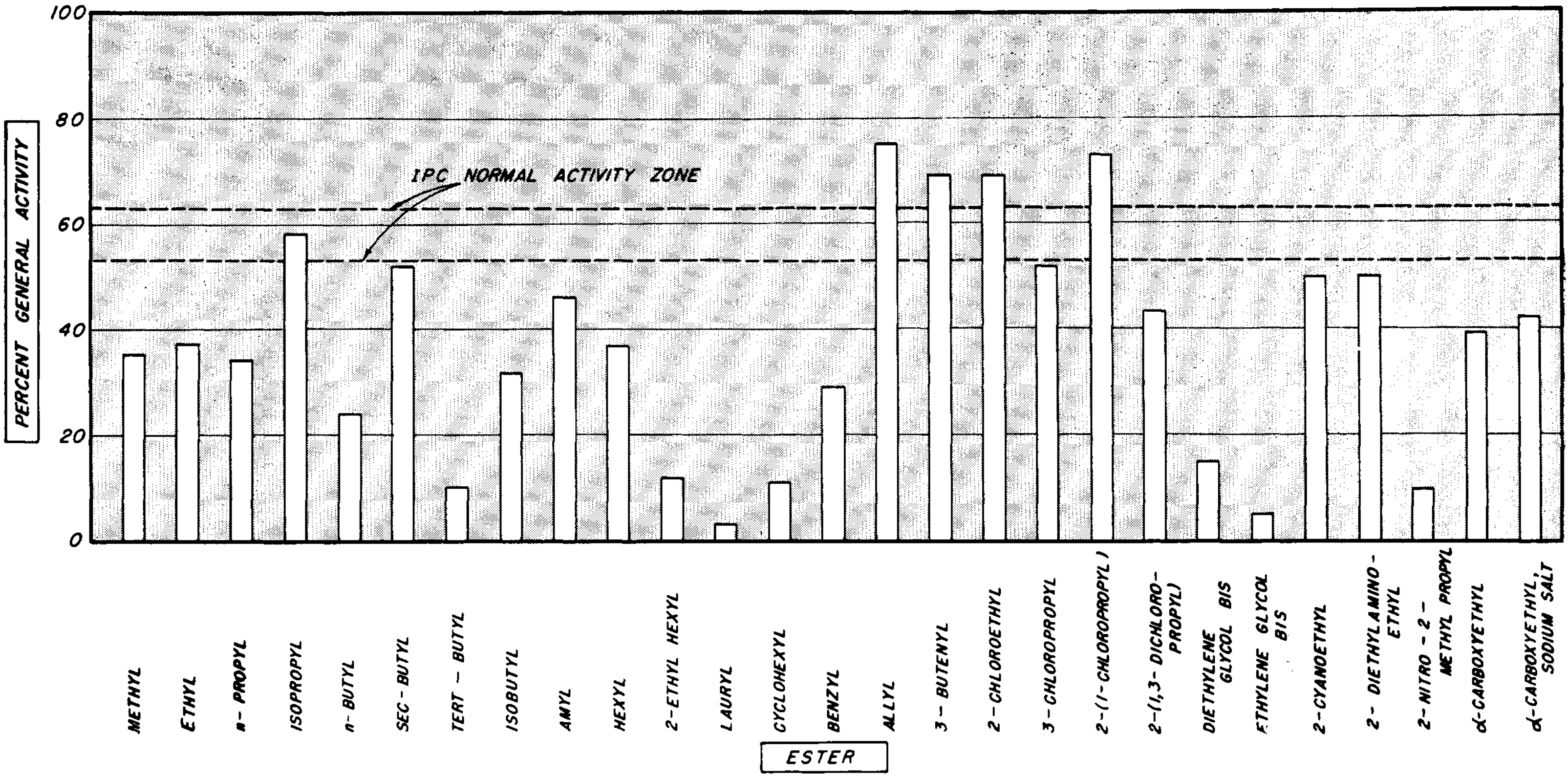


Figure 1. General activity of esters of *N*-phenylcarbamic acid

tabulated in Table II are broken down to show the effect of each of two rates of application at three separate stages of growth for each species. The effects of these chemicals vary significantly in only two particulars, general order of activity and order of selectivity. Significant variations of activity in relation to the time of application of the chemical might also have been expected, since these compounds must in general be classified as pre-emergence or preplanting herbicides and, especially, since it has been shown (*14*) that for many germinating seeds there is a very specific stage of development at which maximum susceptibility to carbamates occurs. Indications of such differences were obtained, although with the most active compounds they were not appreciable. At lower rates of application than were employed in these studies such effects might be much more readily apparent.

A numerical index which is useful for a comparison of these compounds is the per cent general activity. This may be calculated readily, as each individual treatment which is totally effective herbicidally is given a score of 10. If all treatments using a given chemical at all rates of application and on all dates of application were 100% effective, a test of eight species, three dates of application, and two rates would have a maximum score of 480 points. The percentage actually obtained of the total possible score for any given chemical is referred to as its per cent general activity. Corrections must be made, of course, in determining the total possible score, for failures of seeds to germinate or of plants to grow, which can be attributed to effects other than those of the chemical treatment.

An index of selectivity can be obtained in a somewhat similar manner. In a given test there is always a total possible effect against monocotyledons as well as a total possible effect against dicotyledons. Using these figures, it is possible to calculate a per cent monocotyledonous activity and a per cent dicotyledonous activity. For convenience the quotient per cent monocotyledonous activity–per cent dicotyledonous activity has been designated as the "selectivity quotient." On the most active compounds, at least, this quotient affords an indication of the chemical's selectivity.

The per cent general activities of the herbicides tested are compared graphically in Figure 1, and the selectivities of compounds which have greater than 20% general activity are compared in Figure 2 for applications at 10 pounds per acre. (Calculation of selectivities for compounds of minimal activity is believed to be of questionable validity.) On each of these graphs the IPC value given is an average calculated from a large number of individual tests over several years and in each case a zone has been indicated which defines reasonably accurately the limits of variability observed on apparently normal tests. The reproducibility of IPC results was generally poor, a fact noted by others (*17*). Isopropyl *N*-phenylcarbamate is apparently extremely susceptible to differences in moisture and temperature. The coincidence of high temperature and/or low moisture with low IPC activity has frequently been observed.

Discussion

It is difficult to recognize relationships between changes in chemical structure and herbicidal activity from the results of the tests reported, and this task is even more difficult because the test species were occasionally changed. As a result, all the compounds were not tested against exactly the same species of plants. These changes were justified because they represented efforts to arrive eventually at a species selection which showed as many degrees of susceptibility as possible—i.e., from susceptible to resistant. Where especially susceptible plants were used, the compounds tested showed relatively higher activities than might have been expected. This point may be illustrated by the amyl and hexyl esters, each of which showed a somewhat higher activity than would have been expected in view of the results obtained for the other lower *n*-alkyl esters. In the case of each of these compounds high activity against a single spe-

Table II. Herbicide Screening Evaluations of Esters of *N*-Phenylcarbamic Acid

(Application figures in pounds per acre)

Ester	*Day of Applic.*[a]	*Peas*		*Cotton*		*Soy-beans*		*Corn*		*Rye Grass*		*Crab-grass*		*Barley*		*Wheat*		*Green Beans*		*Pig-weed*		*Fescue 31*		*% General Activity*				*Selectivity Quotient*[b]	
																								Monocot.		*Dicot.*			
		10	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*	*10*	*20*
Methyl	1	..	1	0	0	..	0	0	0	6	9	0	0	..	..	0	9	..	..	0	0	..	..						
	3	6	8	0	0	4	..	0	4	7	10	0	2	..	..	8	8	..	..	1	3	..	..						
	7	3	1	1	8	0	..	7	7	1	6	0	6	..	..	1	9	..	..	7	10	..	..	25	58	22	31	1.1	1.9
Ethyl	1	0	0	0	0	0	0	0	1	3	8	0	0	0	9	0	9	..	..	..	..	..	..						
	3	3	6	0	3	4	3	0	3	7	8	1	7	6	5	4	5	..	..	..	..	..	..						
	7	1	8	7	10	7	9	0	7	0	1	7	10	0	6	0	9	..	..	..	..	..	..	19	59	24	43	0.8	1.4
n-Propyl	1	0	0	3	5	0	1	0	1	10	8	0	2	6	8	..	..	..	..	..	..	0	7						
	3	0	0	3	5	0	4	0	0	6	10	0	8	6	10	..	..	..	..	..	..	3	9						
	7	0	0	0	0	0	4	3	3	3	8	3	9	0	8	..	..	..	..	..	..	3	3	31	63	7	21	4.4	3.0
Isopropyl	1	0	7	0	3	0	0	9	10	10	10	0	0	9	9	9	9	..	..	..	..	..	..						
	3	8	8	3	3	6	7	9	8	10	10	7	9	7	8	7	9	..	..	..	..	..	..						
	7	7	7	5	7	7	8	5	7	5	7	10	8	3	3	0	1	..	..	..	..	..	..	62	80	29	50	2.1	1.6
n-Butyl	1	0	0	0	3	0	0	0	1	3	4	4	10	3	2	..	..	..	..	..	..	0	0						
	3	0	0	0	0	0	3	0	2	2	2	3	6	0	2	..	..	..	..	..	..	0	10						
	7	0	6	0	3	0	4	3	8	0	3	10	10	4	2	..	..	..	..	..	..	0	0	21	41	0	21	>21	1.9
sec-Butyl	1	0	3	4	3	0	1	5	8	10	10	0	2	10	10	..	..	..	..	..	..	10	10						
	3	5	7	0	3	3	6	0	9	9	10	4	6	8	9	..	..	..	..	..	..	10	10						
	7	6	4	2	3	0	0	6	9	0	3	10	10	0	3	..	..	..	..	..	..	2	7	56	77	22	33	2.5	2.3
tert-Butyl	1	0	0	..	..	0	0	0	4	0	6	0	0	0	5	..	..	0	1	..	..	0	0						
	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..						
	7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Isobutyl	1	0	0	0	0	0	0	2	3	10	8	9	10	10	9	0	0	..	..	..	..	..	..						
	3	5	5	0	0	2	3	0	5	6	10	9	5	7	7	0	0	..	..	..	..	..	..						
	7	1	2	1	1	0	3	4	5	0	0	..	..	0	0	0	4	..	..	..	..	..	..	38	44	10	16	3.8	2.7
Amyl	1	1	1	0	0	7	8	3	3	..	..	4	4	..	..	7	4	..	..	1	10	..	..						
	3	0	4	0	0	7	7	3	1	..	..	6	9	..	..	5	3	..	..	10	10	..	..						
	7	0	1	7	10	4	5	1	5	..	..	7	8	..	..	0	7	..	..	10	10	..	..	40	49	39	55	1.0	0.9
Hexyl	1	0	3	0	0	0	7	0	0	7	8	7	5	..	..	7	5	..	..	10	10	..	..						
	3	0	0	0	0	6	5	0	3	4	7	0	5	..	..	0	0	..	..	10	10	..	..						
	7	0	0	0	1	0	0	3	3	0	1	7	10	..	..	0	8	..	..	10	10	..	..	29	42	32	42	0.9	1.0
2-Ethylhexyl	1	2	3	0	0	0	0	0	4	0	1	0	2	0	1	..	..	..	..	..	..	0	0						
	3	..	0	0	0	0	0	3	0	0	3	0	0	0	0	..	..	..	..	..	..	0	0						
	7	0	0	0	0	0	0	9	8	0	3	0	2	6	8	..	..	..	..	..	..	0	0	12	21	2	3	..	..
Lauryl	1	0	5	..	..	..	0	1	0	0	0	0	0	0	1	..	..	0	0	..	..	0	0						
	3	0	0	..	..	0	0	0	0	0	0	0	0	0	0	..	..	0	0	..	..	0	0						
	7	0	0	..	..	0	0	0	5	0	0	0	0	0	0	..	..	..	0	..	..	0	0	1	4	0	6	..	..
Cyclohexyl	1	0	0	0	0	0	0	0	0	0	8	5	8	0	0	0	0	..	..	..	..	..	..						
	3	0	0	0	0	0	1	0	6	0	6	10	8	0	0	0	0	..	..	..	..	..	..						
	7	0	0	0	0	0	0	0	0	0	0	0	..	0	0	0	0	..	..	..	..	..	..	10	24	0	1	..	..
Benzyl	1	0	0	..	..	0	0	0	6	4	5	10	10	2	2	..	..	0	0	..	..	1	6						
	3	4	4	..	..	0	0	2	1	1	1	4	4	2	2	..	..	0	0	..	..	0	2						
	7	4	8	..	..	3	4	4	4	3	3	10	10	2	4	..	..	3	1	..	..	5	3	31	42	16	19	1.9	2.2

(Application figures in pounds per acre)

Ester	Day of Applic.[a]	Peas		Cotton		Soybeans		Corn		Rye Grass		Crabgrass		Barley		Wheat		Green Beans		Pigweed		Fescue 31		% General Activity Monocot.		% General Activity Dicot.		Selectivity Quotient[b]	
		10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20
Allyl	1	1	7	3	4	4	5	8	10	10	10	0	10	9	10	9	10	..	..	..	..	..	..						
	3	7	9	3	5	5	7	9	10	9	10	3	10	9	9	8	8	..	..	..	..	..	..						
	7	7	8	9	10	6	9	7	8	6	9	10	10	7	10	3	9	..	..	..	..	..	..	71	95	50	71	1.4	1.3
3-Butenyl	1	4	9	0	5	1	6	7	7	8	10	10	10	7	8	8	9	..	..	..	..	..	..						
	3	5	7	1	1	5	7	5	5	7	9	10	10	6	7	7	7	..	..	..	..	..	..						
	7	5	9	6	9	7	8	6	9	4	10	10	10	6	10	6	10	..	..	..	..	..	..	71	87	38	73	1.9	1.2
2-Chloroethyl	1	3	9	1	3	3	8	7	8	10	10	7	9	..	..	4	6	..	..	10	10	..	..						
	3	5	5	6	7	6	8	5	5	10	10	10	10	..	..	5	6	..	..	10	10	..	..						
	7	4	8	6	7	6	8	3	3	4	7	10	10	..	..	1	9	..	..	10	10	..	..	63	77	58	77	1.1	1.0
3-Chloropropyl	1	0	0	3	1	3	5	5	5	10	10	9	10	6	7	5	9	..	..	..	..	..	..						
	3	0	0	0	1	3	4	0	0	6	10	9	10	0	3	0	5	..	..	..	..	..	..						
	7	0	7	1	7	8	8	6	9	4	10	10	10	10	10	3	6	..	..	..	..	..	..	55	76	20	37	2.7	2.1
2-(1-Chloropropyl)	1	4	8	7	6	1	5	3	9	10	10	10	10	10	10	10	10	..	..	..	..	..	..						
	3	9	9	0	1	2	8	8	9	9	10	8	10	7	7	5	6	..	..	..	..	..	..						
	7	8	8	6	6	6	7	8	10	8	10	10	10	0	6	9	8	..	..	..	..	..	..	77	90	48	65	1.6	1.4
2-(1,3-Dichloropropyl)	1	1	1	0	1	0	..	3	1	8	9	8	8	8	10	7	8	..	..	..	..	..	..						
	3	4	4	1	6	6	3	4	4	7	8	6	9	7	7	6	5	..	..	..	..	..	..						
	7	0	0	0	0	2	6	0	2	1	1	10	10	2	1	0	7	..	..	..	..	..	..	51	60	16	23	3.2	2.6
Diethylene glycol bis	1	0	0	0	0	0	0	0	0	4	4	0	0	2	3	..	..	0	0	..	..	..	..						
	3	4	5	0	0	0	0	1	2	10	10	0	0	4	4	..	..	0	0	..	..	..	..						
	7	..	..	0	0	0	0	3	3	2	1	0	4	0	0	..	..	..	0	..	..	..	..	17	21	4	5	..	..
Ethylene glycol bis	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	..	..	..	..	..	..						
	3	0	2	0	3	0	4	0	0	7	7	0	2	0	0	0	0	..	..	..	..	..	..						
	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	..	..	..	..	..	..	..	..	..	..	..	..
2-Cyanoethyl	1	..	5	0	4	0	7	0	0	3	7	6	9	8	9	7	9	..	..	..	..	..	..						
	3	0	8	1	5	4	7	0	0	5	7	7	7	0	6	2	4	..	..	..	..	..	..						
	7	6	9	7	9	7	9	0	9	3	4	4	10	3	7	3	6	..	..	..	..	..	..	33	63	28	70	1.2	0.9
2-Diethylaminoethyl	1	6	3	3	0	8	5	8	8	10	10	4	5	8	8	6	5	..	..	..	..	..	..						
	3	4	3	0	1	0	0	6	7	7	7	0	0	4	1	0	0	..	..	..	..	..	..						
	7	1	1	0	0	6	5	5	5	0	0	9	9	1	0	1	3	..	..	..	..	..	..	46	45	31	20	1.5	2.2
2-Nitro-2-methylpropyl	1	0	0	0	0	0	0	0	0	0	0	3	3	3	2	0	0	..	..	..	..	..	..						
	3	0	2	0	0	0	0	0	0	0	3	3	4	2	1	0	0	..	..	..	..	..	..						
	7	0	0	0	0	0	7	0	4	0	4	0	1	0	5	0	0	..	..	..	..	..	..	7	18	0	10	..	..
α-Carboxyethyl	1	0	3	6	7	4	6	6	9	9	9	0	7	..	..	9	10	..	..	1	5	..	..						
	3	0	0	3	3	1	5	7	7	7	7	0	7	..	..	5	6	..	..	1	7	..	..						
	7	0	3	3	4	0	3	3	4	0	0	1	1	..	..	0	1	..	..	2	6	..	..	39	56	17	43	2.3	1.3
α-Carboxyethyl, sodium salt	1	0	3	2	7	7	7	7	7	10	10	3	5	..	..	9	10	..	..	2	3	..	..						
	3	3	3	0	1	4	4	6	7	7	7	3	6	..	..	5	7	..	..	3	4	..	..						
	7	0	..	0	..	3	..	4	..	0	..	0	..	..	..	0	..	..	..	0	..	..	..	45	74	20	40	2.2	1.8

[a] Numbered consecutively from, and including, day of planting.

[b] Equals per cent monocotyledonous activity-per cent dicotyledonous activity. No quotients calculated for compounds of very low activity.

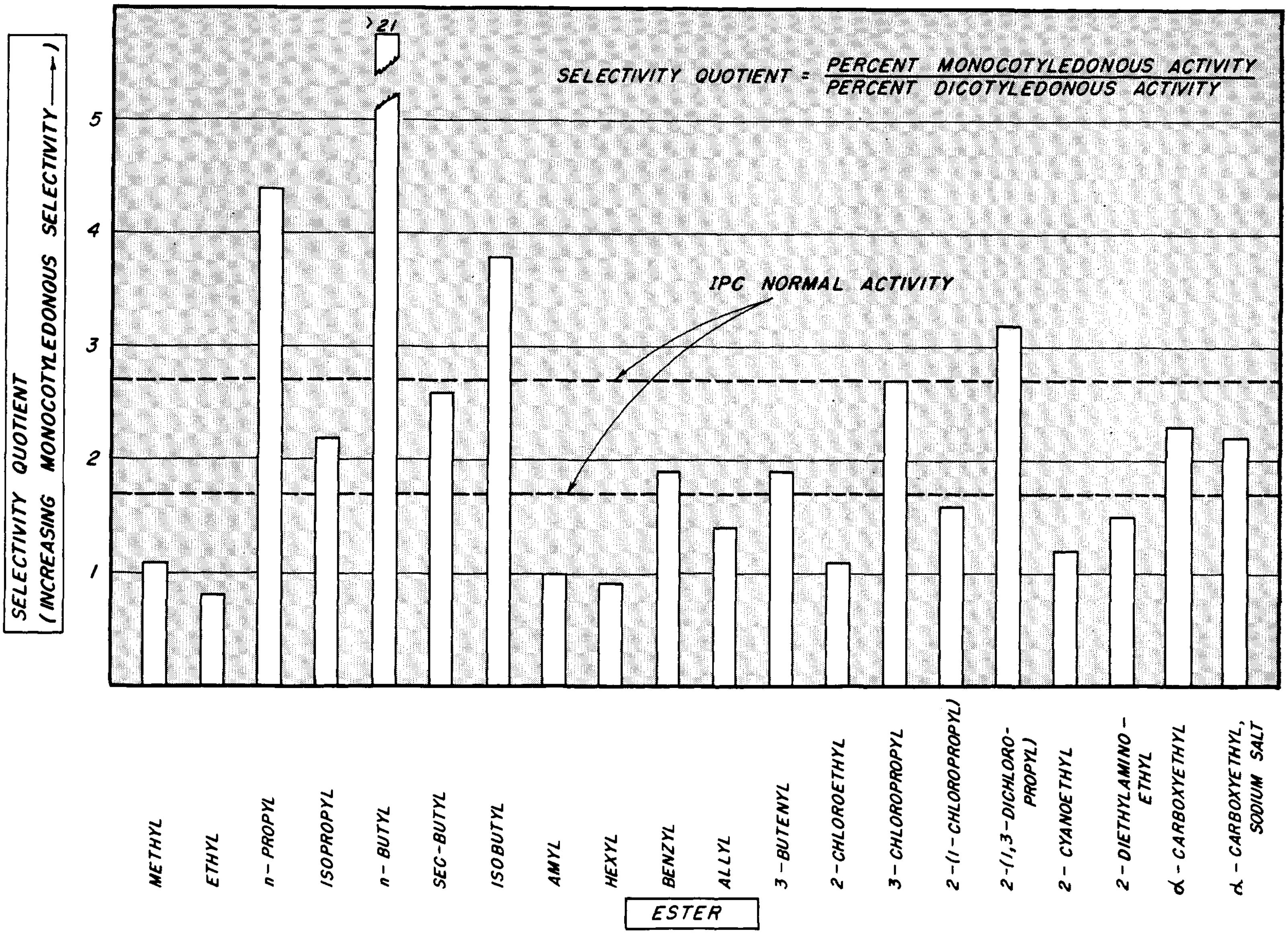
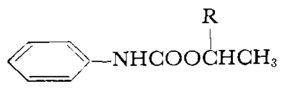


Figure 2. Selectivity of esters of N-phenylcarbamic acid applied at rate of 10 pounds per acre

cies, pigweed, contributed very significantly, and possibly disproportionately, to their per cent general activities. Actually, only four compounds, the allyl, 3-butenyl, 2-chloroethyl, and 2-(1-chloropropyl) esters, are considered to be more active than isopropyl *N*-phenylcarbamate, and four other compounds, the *sec*-butyl, 3-chloropropyl, 2-cyanoethyl, and 2-diethylaminoethyl esters, are considered to be approximately as active. These compounds have no common structural characteristics, and it is difficult to explain why any one should be more active than other compounds tested. It is possible, however, upon inspection of the group as a whole to find some indications of the structural requirements for activity.

As all these compounds function as pre-emergence herbicides—i.e., are applied to the soil and not to the seed or a plant part—some mechanism must be responsible for their getting into sufficiently intimate contact with the seed or the seedling to exert an effect. This contact might be achieved mechanically as the pre-emergent seedling grows through the treated zone of the soil, or might be the result of the diffusion of a solution of the compound in the soil moisture or of vapors of the compound among the soil particles. In only the first of these possibilities would the process be relatively independent of chemical structure; any alterations in structure might be anticipated to exert real effects upon both volatility and solubility. It is difficult to correlate either of these properties with activity. In comparison to isopropyl *N*-phenylcarbamate, the lauryl ester, which is both less soluble in water and less volatile, has practically no activity, while the 2-(1-chloropropyl) ester, which also is less volatile and less soluble in water, has even higher activity than isopropyl *N*-phenylcarbamate. Other pairs of compounds such as *n*-propyl and allyl, *n*-butyl and 3-butenyl, or 3-chloropropyl and 2-(1-chloropropyl), which have very similar solubilities and volatilities, actually have very different activities.

With very few exceptions these compounds can all be considered derivatives of ethyl *N*-phenylcarbamate, substituted either in the α- or β- position of the ethyl portion:



α- Substitution

β- Substitution

Monosubstitution at the α- position,

especially with an alkyl or a chloroalkyl group, increased activity over that of the unsubstituted ethyl compound. Substitution at this position with a carboxy or a sodium carboxy group produced relatively little change in activity; the mere fact that each of these compounds has about the same activity further indicates that water solubility and volatility per se are not determinants of activity. The single instance of disubstitution in the α- position produced a compound of very low activity, the *tert* butyl ester.

Alkyl monosubstitution in the β-position had relatively little effect upon activity, except to reduce it considerably for the higher members. However, substitution of chloromethyl, diethylamino, or cyano radicals in this position improved activity, and substitution of a chlorine atom or a vinyl group produced compounds which were among the most active tested. The allyl and benzyl esters might be considered examples of disubstitution in the β- position. The latter compound differed relatively little from the ethyl ester in activity, but the former was possibly the most active compound tested.

Two compounds can be considered to illustrate α, β- disubstitution, the cyclohexyl and the 2-(1,3-dichloropropyl) esters; the former was relatively inactive, but the latter had activity equivalent to or slightly greater than the ethyl compound. The 2-nitro-2-methylpropyl ester, the single instance of trisubstitution, had a very low activity.

One conclusion which can safely be drawn is that the nature of the alcohol portion of carbamate esters such as these can exert a real and a major influence on their modification of plant growth. Although a discussion of the relationships between chemical structure and biological activity is beyond the scope of this paper, it is interesting to consider the above data in light of current ideas about the structural requirements for a chemical to show activity in regulating plant growth. From a recent review of this subject by Thimann (*21*), the minimum structural requirements for primary activity might be summarized as: (1) a nuclear ring system, active interfacially, (2) an unsaturated linkage in this ring located adjacent to a side chain, (3) a side chain, (4) a carboxyl group, or carboxyl precursor, in the side chain at a position removed from the ring by at least one carbon atom, and (5) a precise geometric spatial relationship between the ring and the carboxyl group. The carbamates described in this paper conform to these requirements if it is assumed that separation of the carboxyl group from the ring by a nitrogen atom is approximately equivalent to separation by a carbon atom and that all compounds have sufficient free rotation to attain the required ring-carboxyl spatial arrangement. These requirements make no provision for many compounds, such as ethylene, acetylene, and carbon monoxide, which affect plant growth.

In the phenoxyacetic acid series, from which many of the ideas concerning structure and activity were developed, esters are generally active and hydrolyses to acid analogs are considered essential only for transport. No special study has been made in that series of the effect of the structure of the alcohol portion of the ester on primary activity; therefore, analogies to the carbamate series cannot be drawn. Suggestions have been made, however, that plant-growth regulators act by adsorption on enzyme prosthetic groups or plant substrates in some manner which requires multiple contact of certain molecular parts with particular receptor sites on the enzyme or the substrate. If such a mechanism does actually exist, the alkyl portion of the molecule may have to occupy a specific and limited position, in order that it, or an adjacent molecular part, can contact a receptor site. Under such conditions alkyl groups too large, or too bulky, to fit into the necessary position could greatly reduce, or even cancel, the potential activity of otherwise effective structures.

Supplementary to this possible mechanism has been a suggestion (*22*) that interfacial activity of the molecule is required in order that it may be presented in the proper orientation to the active centers. Obviously, interfacial orientation of these compounds must depend upon relative polarities of various portions of the molecule. Pronounced changes in the structure of the alkyl portion would undoubtedly cause changes in polarity and, consequently, in molecular orientation—e.g., lengthening the alkyl chain, or introducing an aralkyl group such as benzyl, would greatly increase the lipophilic properties of this portion of the molecule and result in its attraction to lipoid systems, causing a pronounced change in over-all molecular orientation.

Admittedly, these are only possible explanations for the observed differences in activities of the esters of *N*-phenylcarbamic acid. Detailed and quantitative studies of comparative activities would be essential in any attempt to support these theories with factual information. The suggestions, however, provide possible bases for explanations of the observations that changes in the chemical or the physical nature, or both, of the alkyl portion of compounds such as these carbamates can exert a profound effect upon activity.

Acknowledgment

The authors wish to express their indebtedness to many of the people working on weed control throughout the country, and especially to R. L. Lovvorn, W. C. Shaw, C. R. Swanson, and J. W. Mitchell, and their associates of the Bureau of Plant Industry, U. S. Department of Agriculture, who have in many discussions contributed freely of suggestions and advice concerning the methods of evaluation of the herbicides described.

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Received for review January 29, 1954. Accepted March 3, 1954.