

domly labeled materials, and as it is usually accompanied by material degradation, the possibility existed that the tritium-labeled materials were degradation or decomposition products.

Small quantities of the tritium-labeled materials were then reacted with an excess of diazomethane- C^{14} , and the resulting double-labeled products were subjected to various methods of purification:

Addition of trace amounts of the double-labeled material to a large excess of unlabeled ester and repeated crystallization.

Paper chromatography of the double-labeled material, extraction of the spots, addition of unlabeled ester in large excess, followed by repeated crystallization.

After each operation, the carbon-14-to-tritium ratio was determined. This value remained constant within the limits of error. The entire procedure was then repeated by reacting mixtures of the tritium-labeled material and of unlabeled material in various ratios with diazomethane- C^{14} . Again, subsequent fractionation of the carrier diluted specimens did not alter the expected ratios of the samples.

Finally, the tritium-labeled materials

were applied to plants and were biochemically nondistinguishable from the unlabeled materials as judged by concentration time and translocation data (7). Therefore, the slight difference in R_{GA} values is assumed to be caused by an isotope effect based upon a hyperconjugation phenomenon (Figure 3). Substitution of the alpha-hydrogens with tritium reduces the contribution of B , thereby enhancing the activity of the hydroxyl hydrogen. As a result, the tritium-labeled materials should exhibit a somewhat more hydrophilic behavior than the unlabeled compounds. Consequently, the R_{GA} values of the tritium-labeled compounds should be in between the R_{GA} values of the unlabeled compounds and the R_{GA} value of gibberellin A_2 (tetrahydrogibberellic acid, structure C). This is observed and shown in Figure 4.

On the practical side, this isotope effect could be used for the preparation of small quantities of tritium-labeled esters of very high specific activities.

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HERBICIDAL ACTIVITY AND STRUCTURE

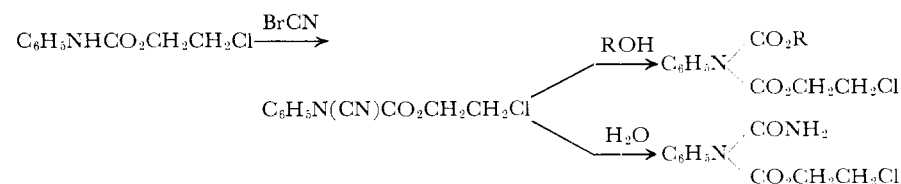
Comparative Herbicidal Activities of Carbamates and *N*-Substituted Derivatives

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Comparative tests between isopropyl carbamates and their *N*-substituted derivatives on oat plants indicate that a hydrogen atom is not necessary on the nitrogen to produce strong phytotoxic effects. Substitution with other groups alters, but does not destroy the toxicity. Relatively greater carbamate activity occurs if the phenyl ring contains a halogen substituent in the meta position. Phytotoxicity data on a series of these compounds are presented.

THE EXPLORATORY WORK of Templeman and Sexton (8) on the herbicidal activity of isopropyl carbamates (IPC) dwelt briefly with the replacement of the amide hydrogen by other functional groups. Thus, the growth-regulating properties of ethyl phenylimidodicarboxylate, which may be regarded as an *N*-substituted carbamate, were mentioned, but no conclusions were drawn as to its activity relative to other carbamates. As an extension of this work the synthesis of a homologous series of halogenated isopropyl phenylimidodicarboxylates was recently described (7). The amide hydrogen of the carbamate had been replaced by cyano and carbamyl groups during an unsuccessful

attempt to synthesize alkyl phenylimidodicarboxylates by the following reactions:



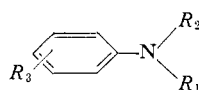
The investigations reported herein were carried out to obtain phytotoxicity data on this series of carbamates and their corresponding isopropyl phenylimidodicarboxylates, which they closely resemble structurally. It was further

the purpose of this study to correlate chemical structure with the effectiveness of the two types of compounds.

Methods and Materials

Ennis (2) described the effect of isopropyl carbamate on oats, barley, and other grasses. He demonstrated greater activity when the compound

Table I. Comparative Effectiveness of Carbamates and Phenylimidocarboxylates



Name	N-Substitutions		Phenyl Substitutions, R ₃	Inhibition		Visual Effect Rating	Visual Effects
	R ₁	R ₂		5 lb./A	8 lb./A		
Isopropyl phenylcarbamate	-COOCH(CH ₃) ₂	H	None	100	100	10	a
3-Fluoroisopropyl	-COOCH(CH ₃) ₂	H	3-Cl	100	100	10	a
3-Chloro-	-COOCH(CH ₃) ₂	H	3-Cl	100	100	10	a
3-Bromo-	-COOCH(CH ₃) ₂	H	3-Br	100	100	10	a
3-Iodo-	-COOCH(CH ₃) ₂	H	3-I	71	100	8	a
3-Methyl-	-COOCH(CH ₃) ₂	H	3-CH ₃	100	100	10	a
4-Fluoro-	-COOCH(CH ₃) ₂	H	4-F	83	100	8	a
4-Bromo-	-COOCH(CH ₃) ₂	H	4-Cl	-7	-6	1	b
4-Iodo-	-COOCH(CH ₃) ₂	H	4-Br	-1	42	2	b
	-COOCH(CH ₃) ₂	H	4-I	-6	18	2	b
Isopropyl phenylimidodicarboxylate	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	None	48	78	8	a
3-Fluoro-	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	3-F	66	87	10	a
3-Chloro-	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	3-Cl	100	100	10	a
3-Bromo-	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	3-Br	55	100	8	a
3-Iodo-	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	3-I	-6	59	5	b
3-Methyl-	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	3-CH ₃	48	59	3	a
4-Fluoro-	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	4-F	-2	-4	1	b
4-Chloro-	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	4-Cl	-4	-16	1	b
4-Bromo-	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	4-Br	-2	30	2	b
4-Iodo-	-COOCH(CH ₃) ₂	-COOCH(CH ₃) ₂	4-I	43	100	8	a
Diisopropenyl phenylimidodicarboxylate	-COOCH ₂ CH:CH ₂	-COOCH ₂ CH:CH ₂	None	-17	2	1	b
Bis(2,3-dibromopropyl)phenylimidodicarboxylate	-COOCH ₂ CHBrCH ₂ Br	-COOCH ₂ CHBrCH ₂ Br		33	100	7	a
2-Chloroethyl, N-cyanophenylcarbamate	-COOCH ₂ CH ₂ Cl	-CN	None	-18	12	1	b
2-Chloroethyl, N-carbamylphenylcarbamate	-COOCH ₂ CH ₂ Cl	-CONH ₂	None	-2	-7	1	b

^a Moderate to severe stunting, leaves become dark green in color, severe tip burn, leaf die back, no development beyond 3-leaf stage.
^b No visual effect.

was applied to the soil than when it was applied directly to the plant. It has been the author's experience also that soil applications are more effective than spray treatments. In some cases no activity at all was noticeable from foliar applications.

Fuelleman (3), Roland (5), and Blouch and Fults (7) have concluded that activity is influenced by the type of soil and its condition. To eliminate the possible influence of soil type, a single soil was used throughout these experiments.

Clinton oats were planted in a mixture of 3 parts of soil and 1 of part sand in 0.25-gallon glazed pots and allowed to grow under greenhouse conditions. When they were approximately 4 inches tall, they were thinned to eight uniform plants per pot. Fifty-milliliter aliquots of the test compounds dissolved in acetone (10%) were applied to the soil at rates of 5 to 8 pounds per acre when the plants had reached the two- to three-leaf stage. The treated plants were harvested after 14 days and the fresh weights were determined. Activity or effectiveness of the compounds was expressed as the per cent inhibition of plant growth. A numerical rating similar to that described by Moore, George, Martin, and Garman (4) and Shaw (6) was also used to describe visual effects where:

No effect	0
Slight	1-3
Moderate	4-6
Severe	7-10

The carbamates and imidodicarboxylates were prepared by the method of Stefanye, Howard, and Beidler (7).

2-Chloroethyl N-Cyanocarbamate. A solution of N-cyanoaniline in ether reacted under reflux, with an equivalent amount of sodium dispersed in toluene, with stirring for 4 hours, whereupon a white precipitate gradually formed. To this was added the requisite amount of 2-chloroethyl chloroformate in ether and the mixture was stirred for another 8 hours. The mixture was then filtered, the filtrate was washed with water and dried over anhydrous sodium sulfate, and the solvent was evaporated leaving an oil which solidified on standing. The crude 2-chloroethyl N-cyanocarbamate was recrystallized from ether-ligroin, giving waxy plates, melting point 51.5-53.5° C. (corr.).

Analysis. Calcd. for C₁₀H₉ClN₂O₂: C, 53.55; H, 4.02%.

Found. C, 53.53; H, 3.77.

O-Pseudourea Derivatives. An ether solution of the N-cyano compound was mixed with an equivalent amount of 2-chloroethanol. Dry hydrogen chloride gas was introduced, the reaction being cooled in an ice bath and moisture

excluded. A precipitate of 2-(2-chloroethyl) - 3 - phenyl - 3 - (2 - chloroethoxyformyl) pseudourea hydrochloride formed which was filtered, washed with ether, and dried in vacuo over phosphorus pentoxide. This compound melted at 118-21° C. with decomposition and was not stable in storage.

Analysis. Calcd. for C₁₂H₁₅Cl₃N₂O₃: ionic Cl = 10.38%.

Found. Ionic Cl = 10.28%.

2-Chloroethyl N-Carbamylcarbamate. A solution of 3 grams of the N-cyano compound in 20 ml. of concentrated sulfuric acid was stirred in an ice bath until all the solid matter had dissolved. The solution was then poured over cracked ice, giving a colorless solid, the N-carbamyl derivative. Recrystallization from benzene gave crystals of melting point 185-5° C.

Analysis. Calcd. for C₁₀H₁₁N₂ClO₃: C = 48.52; H = 4.54.

Found. C = 49.45; H = 4.54.

Discussion and Conclusions

The results of the comparative tests are indicated in Table I.

In experiments where inhibition of growth is measured and a 100% response is observed, it is customary to dilute the phytotoxic agent to a suitable concentration when testing is per-

formed and a less severe effect is measured. On the other hand, when a series of compounds is compared, the less active members will not demonstrate any activity, because of this dilution. Thus, a concentration range of 5 and 8 pounds per acre was chosen which was felt to demonstrate optimally both the more and the less active members of the series.

The carbamates tested are more phytotoxic than the corresponding imidodicarboxylates. Thus, out of 10 comparisons, the carbamate was of equal or greater activity than the imidodicarboxylate in seven instances irrespective of the substituent on the benzene ring. A similar comparison between the two

types with respect to activity due to para or meta substitution shows that seven out of eight compounds were more toxic with substitution in the latter position, the sole exception being the 4-iodophenyl imidodicarboxylate.

This evidence also leads to the broader conclusion that an imino group is not requisite for activity in compounds of these types because substitution of the hydrogen by the isopropyl carboxylate group or by similar groups does not destroy, but only alters, the toxicity.

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HERBICIDE RESIDUES

Dalapon Residue in Bird's-foot Trefoil

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A detectable amount of dalapon due to a residue in a forage crop may appear in a food product. The effects of rate and time of application of dalapon to bird's-foot trefoil were determined. Residues were found in all samples, the amount depending upon initial rate, weather conditions, growing season, and stage of growth at the time of application. Spring applications up to 5.0 pounds per acre effectively controlled grass and produced residue levels below 25 p.p.m. when the time interval between treatment and harvest exceeded 100 days. Applications resulting in extremely low dalapon residues closely correspond to the present and proposed use of dalapon in bird's-foot trefoil seed fields and seedling establishments. These residues may be undetectable in animal products.

DALAPON, 2,2-dichloropropionic acid, an effective grass herbicide (5, 72-74), is readily absorbed by the foliage of plants (7, 2, 70) as well as by the roots of forage grasses and other plant species (2, 9, 77).

The presence of grass in legume seed fields, particularly in bird's-foot trefoil seed fields, has a marked effect on the potential seed yield (7)—generally, the more grass, the lower the yield of seed.

Extensive tests show that grass in bird's-foot trefoil stands can be controlled by the proper use of dalapon. If there is any seasonal application advantage, it is spring, primarily on the basis of less broad-leaved weed encroachment.

Dairy animals fed forages containing dalapon residue may produce milk containing measurable quantities of dalapon. Bird's-foot trefoil, even though grown for seed, may be used as a feed crop once the seed has been harvested.

Seed production may fail and the forage be directly cut for hay or left for pasture.

This paper summarizes 3 years' data, which are applicable to the use of dalapon in bird's-foot trefoil seed fields, in pasture renovation for grass suppression or elimination (9, 73), and in legume seedling establishment (5, 6, 8). All reference to dalapon is on the basis of acid equivalent.

Materials and Methods

Experiment 1, Location 1. A 12-year-old stand of Empire bird's-foot trefoil at Lodi, N. Y., a variety which constitutes a high percentage of the crop grown for seed and forage in New York, was treated with 5, 10, and 20 pounds of dalapon applied in 30 gallons of water per acre. Treatments were applied in replicated 6 × 50 foot plots using a tractor-mounted sprayer modified especially for plot spraying, cali-

brated to ensure uniform coverage. Applications were made April 23, 1955, when the bird's-foot trefoil plants were 1 to 2 inches tall. Forage samples for residue analyses were taken from the first cutting of hay on July 18, 1955. Random samples were taken from each treated plot and untreated strips, immediately oven-dried at 70° C. for 14 hours, packed in plastic bags, and sent to The Dow Chemical Co. for dalapon residue analyses. Because of the reduced forage in all experiments on the plots receiving the high rates of dalapon (15 and 20 pounds per acre), the forage from each replication for these rates was pooled for one analysis.

Experiment 1, Location 2. A 6-year-old stand of Empire bird's-foot trefoil located at Ithaca, N. Y., was treated with 10 pounds of dalapon applied in 30 gallons of water per acre. Replicated applications were made May 17, 1955, when the plants were 4 inches tall.