

Some New Methylcarbamate Pre-emergence Crabgrass Herbicides

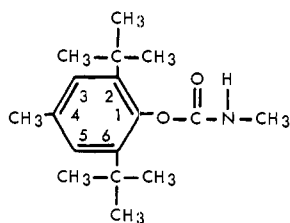
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The synthesis, physical properties, and pre-emergence crabgrass herbicidal activity of a number of 2,4,6-trisubstituted phenyl methyl carbamates are described. The properties and pre-emergence herbicidal activity of Azak (2,6-di-*tert*-butyl-*p*-tolyl methylcarbamate) are given in more detail. Pre-emergence crabgrass activity is specific to the type of substituents in the 2-, 4-, and 6-positions of the phenyl groups in the phenyl methylcarbamates, but some correlations of chemical structure with biological activity have been made.

MANY substituted-phenyl methylcarbamates are insecticides (5). Although a patent discloses some phenyl methylcarbamates as herbicides (2), most herbicides of this type are alkyl-substituted carbanilates (7). We have found a number of 2,4,6-trisubstituted phenyl methylcarbamates that are non-insecticidal but have marked pre-emergence herbicidal activity against crabgrass and certain other grasses.

One of the more active of these compounds is 2,6-di-*tert*-butyl-*p*-tolyl methylcarbamate (3), identified in earlier work as Hercules 9573 (registered by Hercules Powder Co. under the trade-name Azak).



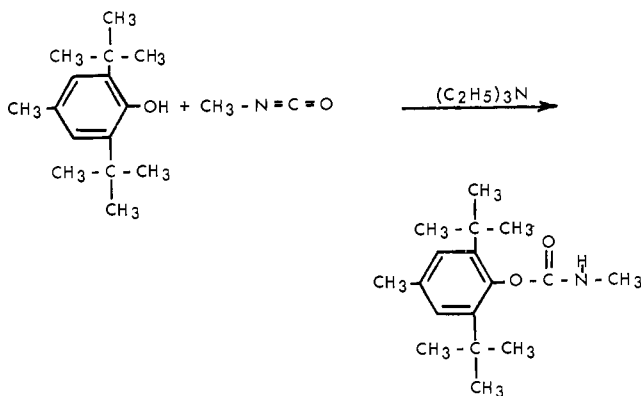
A number of related carbamates have been synthesized and their properties studied. As a result of these studies, some correlations have been made of the pre-emergence crabgrass herbicidal activity with change of substituents in the 2-, 4-, and 6-positions of the phenyl group in the phenyl methylcarbamates.

Synthesis

Preparation of 2,6-Di-*tert*-butyl-*p*-tolyl Methylcarbamate. To 220 grams (1 mole) of 2,6-di-*tert*-butyl-*p*-cresol in 330 grams of toluene containing 14 grams (0.145 mole) of triethylamine at 70° C. was added 57 grams (1.0 mole) of methyl isocyanate over 0.5 hour. The reaction mixture was held at 70° C. for 5 hours, cooled, and filtered. The white crystalline product, melting at 185–90° C., weighed 260 grams (95% yield). Recrystallization from ethanol gave pure white crystals (m.p. 200–01° C. uncorrected).

ANALYSIS. Calculated for $C_{17}H_{27}O_2N$: C, 73.61; H, 9.81; N, 5.05; molecular weight, 277.4. Found: C, 73.58; H, 9.91; N, 4.97; molecular weight (Mechrolab vapor pressure osmometer) 269.

The reaction is illustrated by the following equation:



Preparation of Other Substituted-Phenyl Methylcarbamates. The other carbamates were prepared in the same manner and are listed in Table I.

Testing Procedure

Experimental compounds were tested pre-emergence on crabgrass as one of the initial screening tests for candidate herbicides. A mixture of *Digitaria ischaemum* and *Digitaria sanguinalis* was planted in pint berry boxes and sprayed before emergence with test compounds at 2 and 10 pounds per acre.

Toxic effects were estimated 3 weeks after germination was initiated in the pre-emergence tests. Toxicity ratings were 0 to 10, with 10 indicating complete kill. Pre-emergence screening results for Azak and related compounds are given in Table I.

Selectivity was determined on compounds such as Azak by similar application to 19 plant species at rates of 2, 4, and 8 pounds per acre. In Table II, results of a pre-emergence selectivity test for Azak are given.

Results and Discussion

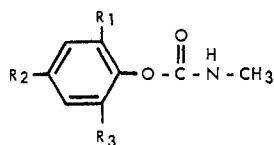
Technical Azak is a white, crystalline-solid, soluble in acetone and ethanol, slightly soluble (<5%) in toluene and benzene, and insoluble in hexane and kerosine. Water solubility is approximately 6 to 7 p.p.m. at 25° C. It is very

stable, in that it can be recovered unchanged after 5 hours at 130° C. in water. Mammalian toxicity is low. The acute oral LD_{50} for rats is greater than 34,600 mg. per kg. of body weight. The acute dermal LD_{50} is in excess of 10,250 mg. per kg. In acute inhalation studies no death or untoward behavioral reaction by rats, guinea pigs, or mice was observed at exposures of 2.8 mg. per liter. When applied directly into the eyes of rabbits, the technical material causes moderate irritation. If, however, the eyes are flushed with water a few minutes after introduction, no adverse effects are produced.

Entry into plants appears limited to roots, and highest toxicity is exhibited on germinating seeds or seedlings. At rates of 10 pounds per acre, foliar applications cause little or no injury to tomato, marigold, mustard, cotton, corn, and millet.

Toxicity is not confined to grass species, but many grasses are sensitive and the common smooth and hairy

Table I. Substituted Phenyl Methylcarbamate Properties and Test Results



Compound No.	R ₁	R ₂	R ₃	Melting Point, ° C. Uncorrected	Analysis Nitrogen, %		Crabgrass Soil Germination Test ^a	
					Calcd.	Found	10 lb./acre	2 lb./acre
I	<i>tert</i> -C ₄ H ₉ -	H-	<i>tert</i> -C ₄ H ₉ -	164	5.30	5.23	0	0
II	<i>tert</i> -C ₄ H ₉ -	CH ₃ -	<i>tert</i> -C ₄ H ₉ -	200-201	5.02	5.00	10	9
III	<i>tert</i> -C ₄ H ₉ -	C ₂ H ₅ -	<i>tert</i> -C ₄ H ₉ -	198-199	4.80	4.84	9	9
IV	<i>tert</i> -C ₄ H ₉ -	Iso-C ₃ H ₇ -	<i>tert</i> -C ₄ H ₉ -	197-199	4.62	4.59	0	0
V	<i>tert</i> -C ₄ H ₉ -	<i>sec</i> -C ₄ H ₉ -	<i>tert</i> -C ₄ H ₉ -	157-158	4.41	4.39	6	1
VI	<i>tert</i> -C ₄ H ₉ -	<i>tert</i> -C ₄ H ₉ -	<i>tert</i> -C ₄ H ₉ -	190-191	4.41	4.56	0	0
VII	<i>tert</i> -C ₄ H ₉ -	Br-	<i>tert</i> -C ₄ H ₉ -	215-216	4.08	4.20	10	7
VIII	<i>tert</i> -C ₄ H ₉ -	Cl-	<i>tert</i> -C ₄ H ₉ -	212-213	5.02	4.63	10	9
IX	<i>tert</i> -C ₄ H ₉ -	CH ₃ O-	<i>tert</i> -C ₄ H ₉ -	177-179	4.77	4.73	10	7
X	<i>tert</i> -C ₄ H ₉ -	C ₂ H ₅ O-	<i>tert</i> -C ₄ H ₉ -	153-156	4.56	4.55	3	2
XI	<i>tert</i> -C ₄ H ₉ -	<i>n</i> -C ₄ H ₉ O-	<i>tert</i> -C ₄ H ₉ -	152-153	4.47	4.15	1	0
XII	<i>tert</i> -C ₄ H ₉ -	CH ₃ OCH ₂ -	<i>tert</i> -C ₄ H ₉ -	125.5-126.5	4.56	4.53	4	0
XIII	<i>tert</i> -C ₄ H ₉ -	NO ₂ -	<i>tert</i> -C ₄ H ₉ -	164-168	9.15	8.76	0	0
XIV	<i>tert</i> -C ₄ H ₉ -	CH ₃ -	CH ₃ -	109-110	5.95	5.90	3	1
XV	<i>tert</i> -C ₄ H ₉ -	CH ₃ -	<i>n</i> -C ₃ H ₇ -	129-130	5.13	5.22	9	7
XVI	<i>tert</i> -C ₄ H ₉ -	CH ₃ -	Iso-C ₃ H ₇ -	168-170	5.13	5.30	10	9
XVII	<i>tert</i> -C ₄ H ₉ -	CH ₃ -	Iso-C ₄ H ₉ -	135-136	5.02	5.10	8	7
XVIII	<i>tert</i> -C ₄ H ₉ -	CH ₃ -	<i>tert</i> -C ₅ H ₁₁ -	183-185	4.81	4.83	9	8
XIX	<i>tert</i> -C ₄ H ₉ -	CH ₃ -	CH ₃ -	103-104	5.09	5.21	10	9
XX	<i>tert</i> -C ₄ H ₉ -	CH ₃ -		136-137	5.09	5.20	10	4
XXI	CH ₃ -	CH ₃ -	CH ₃ -	133-136	7.25	7.41	0	0
XXII	Iso-C ₃ H ₇ -	CH ₃ -	Iso-C ₃ H ₇ -	156-158	5.62	5.60	3	0
XXIII	<i>tert</i> -C ₅ H ₁₁ -	CH ₃ -	<i>tert</i> -C ₅ H ₁₁ -	160-165	4.59	4.71	4	0
XXIV	<i>tert</i> -C ₄ H ₉ -	Cl-	Iso-C ₃ H ₇ -	157.5-158	4.94	4.97	10	7
XXV	<i>tert</i> -C ₄ H ₉ -	CH ₃ O-	Iso-C ₃ H ₇ -	...	5.01	5.02	10	10
XXVI	<i>tert</i> -C ₄ H ₉ -	<i>tert</i> -C ₄ H ₉ -	CH ₃ -	183-185	5.02	5.04	0	0
XXVII	<i>tert</i> -C ₄ H ₉ ^b	CH ₃ -	<i>tert</i> -C ₄ H ₉ -	223-224	4.81	4.61	0	0
XXVIII	<i>tert</i> -C ₄ H ₉ ^c	CH ₃ -	<i>tert</i> -C ₄ H ₉ -	160-161	4.32	4.18	0	0

^a Toxicity rating 0 to 10, with 10 indicating complete kill.

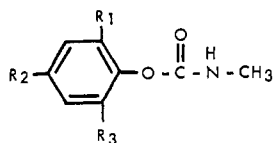
^b 2,6-Di-*tert*-butyl-*p*-tolyl ethylcarbamate.

^c 2,6-Di-*tert*-butyl-*p*-tolyl phenylcarbamate.

crabgrasses are the most sensitive weedy plants known. Toxicity to tomato and to mustards is indicated in Table II, while many species showed no response.

Azak is relatively resistant to leaching in soil. A 2-inch leaching did not reduce the toxicity of a 5-pound application. Azak remained active in moist soil in the greenhouse over a 2-month period. No weight loss was detected at 40° after 3 weeks; loss by volatility from soil is therefore very low.

From the large number of substituted-phenyl methylcarbamates studied, a few general rules have been postulated for correlation of chemical structure with crabgrass soil germination activity. If the general formula is:



the following rules apply (all compound numbers refer to Table I):

Table II. Response of 19 Plant Species to Pre-emergence Application of Azak in Greenhouse Tests

Species	Toxicity Rating ^a			Species	Toxicity Rating ^a		
	2 lb./acre	4 lb./acre	8 lb./acre		2 lb./acre	4 lb./acre	8 lb./acre
Millet	4	5	6	Alfalfa	0	1	2
Yellow foxtail	8	7	10	Onion	0	1	1
Crabgrass	9	10	10	Curled mustard	3	6	7
Wild oats	0	0	1	Wild mustard	2	3	4
Cotton	0	0	1	Flax	0	0	0
Peas	0	0	0	Pigweed	0	0	0
Buckwheat	0	0	1	Tomato	3	4	5
Sunflower	0	0	2	Carrot	0	1	2
Cucumber	0	0	0	Red kidney bean	0	0	0
Soybean	0	0	0				

^a Toxicity rating 0 to 10, with 10 indicating complete kill.

A methylcarbamate is apparently required. Neither 2,6-di-*tert*-butyl-*p*-tolyl ethyl- (XXVII) nor phenyl carbamate (XXVIII) was active.

When R₁ and R₃ are both *tert*-butyl, appreciable activity is obtained when R₂ = CH₃- (II), C₂H₅- (III), Br- (VII), Cl- (VIII), or CH₃O- (IX). As the alkoxy in the R₂ position increases in molecular weight, activity decreases

(IX, X, and XI). However, if R₁ and R₃ are both methyl (XXI), isopropyl (XXII), or *tert*-amyl (XXIII), there is little or no activity.

When R₁ is *tert*-butyl or *tert*-amyl and R₂ is CH₃-, Br-, Cl-, or CH₃O-, then R₃ may vary from C₃H₇- to C₅H₁₁- and still produce activity. Likewise, the hydrocarbon chain may be straight or branched (XV, XVI, XVII, XVIII,

XXIV, and XXV). R₃ may also be an unsaturated group such as methallyl (XIX) or methylpropenyl (XX).

Activity of methylcarbamate insecticides has been correlated with molecular weight (*f*). This relationship does not hold true for methylcarbamate crabgrass herbicides, because 2,4-di-*tert*-butyl-*o*-tolyl methylcarbamate (XXVI), an isomer of Azak, is inactive.

Acknowledgment

The authors thank T. K. Dickson for

conducting many of the tests on these compounds.

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Received for review March 27, 1965. Accepted June 25, 1965. Division of Agricultural and Food Chemistry, 149th Meeting, ACS, Detroit, Mich., April 1965.

METABOLISM BY PLANTS

Translocation and Metabolism of 2,6-Dichloro-4-nitroaniline by Lettuce and Tomato

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Lettuce plants were treated with soil and nutrient applications of C¹⁴-labeled 2,6-dichloro-4-nitroaniline (DCNA). After 50 days, labeled carbohydrates and unchanged DCNA were recovered from the plants grown in soil. The amino acid, chlorophyll, and uronic acid portions of the plants did not contain radioactivity, whereas a carbohydrate fraction was labeled. The possible transient metabolites, 2-chloro-4-nitroaniline, 2,6-dichloro-*p*-phenylenediamine, and *p*-nitroaniline, were not detected. DCNA was shown to be translocated by tomato seedlings.

THE FUNGICIDE, 2,6-dichloro-4-nitroaniline, has been used for the control of *Botrytis* and *Rhizopus* fungal diseases on plants and perishable fruits and vegetables under a temporary tolerance registration. The first commercial application of this material was in the United Kingdom, where it was used successfully to control *Botrytis* infections in greenhouse lettuce (*7*). A spectrophotometric method for the determination of DCNA was described by Roburn (*10*), who indicated that neither DCNA nor DPPD (2,6-dichloro-*p*-phenylenediamine), a possible metabolite, was absorbed by the roots or leaves of plants. In spite of this report, the possible uptake, translocation, and metabolism of DCNA by lettuce was investigated.

Materials and Methods

Preparation of DCNA-C¹⁴ and DPPD-C¹⁴. Uniformly labeled 2,6-dichloro-4-nitroaniline was prepared by the following sequence of reactions:

A yield of 30.7% (333.2 mg.) of uniformly labeled 2,6-dichloro-4-nitroaniline [m.p. 191–92° C. (0.97 mc./mmole)] was obtained from 5.1 mc. (0.147 gram) of uniformly labeled aniline sulfate. The radiochemical purity of the preparation was assessed by paper chromatography using a benzene-formamide system. The material to be separated was placed as a spot on Whatman No. 1 paper impregnated with formamide. The chromatogram was developed with benzene saturated with formamide as the solvent using the descending technique. The labeled DCNA gave only one radioactive peak at R_f 0.8. Good separations of 2-chloro-4-nitroaniline (R_f 0.4), *p*-nitroaniline (R_f 0.15), 2,6-dichloro-*p*-phenylenediamine (DPPD) (R_f 0.7), and DCNA were obtained with this system.

Uniformly C¹⁴-labeled 2,6-dichloro-*p*-phenylenediamine was prepared from uniformly C¹⁴-labeled DCNA by reduction with zinc and hydrochloric acid under reflux. Purification by transfer to water as the hydrochloride, neutralization, and extraction into ether gave, on removal of the solvent, DPPD-C¹⁴ (m.p.

119–120° C.) containing about 3% of labeled impurities when paper chromatographed using the benzene-formamide system. The DPPD-C¹⁴ was stored in benzene solution under N₂ in the dark at 5° C.

Radiocounting Equipment and Methods. All samples were counted using a Packard Tri-Carb liquid scintillation spectrometer, Model 314 EX-2, with a 200-sample counting chamber at 25° F. One channel was optimized for counting samples in toluene scintillator solution, 15 ml. per sample (18.75 grams of PPO (2,5-diphenyloxazole) plus 0.375 gram of POPOP [*p*-bis[2-(5-phenyloxazolyl)] benzene] in 3750 ml. of toluene). The second channel was optimized for counting Hyamine hydroxide Schöniger combustion (*7*) samples using Diotol (*5*) scintillator solution, 15 ml. per sample (73 grams of recrystallized naphthalene, 4.6 grams of PPO, and 0.88 gram of POPOP in a mixture of 350 ml. of toluene, 350 ml. of dioxane, and 210 ml. of methanol). Aqueous alkaline solutions (0.5-ml. aliquots) were counted in 15 ml. of Diotol plus 0.6 gram of Cab-O-Sil M5, a thixotropic dry silica-water absorbent and suspending agent. All samples were corrected for quenching by recounting following the addition of an aliquot of C¹⁴-labeled toluene. Paper chromatograms were counted using a Vanguard 880 chromatogram scanner or by cutting the paper strip into 1/2-inch × 5/8-inch sections and

