Substituted Phenyl *N*-Methylcarbamates as Temporary Immobilizing Agents for Birds

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The temporary immobilization activity and acute oral toxicity of 22 substituted phenyl *N*-methylcarbamates were determined on red-winged blackbirds (*Agelaius phoeniceus*) and starlings (*Sturnus vulgaris*). Twelve compounds immobilized redwings and eight immobilized starlings at doses below 10 mg. per kg. Three were exceptionally effective: *o*-(2-propynyloxy)phenyl *N*-methylcarbamate on redwings, 6-chloro-3,4-xylyl *N*-methylcarbamate on starlings, and 4-(methylthio)-3,5-xylyl *N*-methylcarbamate on both redwings and starlings. Structure-activity correlations indicate that the presence of branched, low molecular weight alkyl or ether groupings at the two- or three-positions, or methyl groups at the three- or five-positions of the phenyl ring, or both, together with a substituted sulfur- or nitrogen-containing group at the four-position of the phenyl ring, enhance the temporary immobilizing action.

Anesthesia-producing chemicals, long used in medicine for temporary immobilization of man and domestic animals, are now finding a limited but expanding utility as damage control and banding agents for various avian species. In 1961, Ridpath *et al.* (*13*) presented an excellent review of the development and use of such anesthetics for control of depredating birds. Of the chemicals discussed, α-chloralose, which has been used in Europe for approximately 20 years with varied success, and 2,2,2-tribromoethanol (Avertin) were the most effective. More recently, Murton (*10*, *11*), Murton, Isaacson, and Westwood (*12*), and Thearle (*14*) reported capturing wood pigeons (*Columba palumbus*), house sparrows (*Passer domesticus*), and other avians with α-chloralose-treated baits. The mortality of affected birds was approximately 20%. Mosby and Cantner (*9*) experienced similar losses using 2,2,2-tribromoethanol to capture wild turkeys (*Meleagris gallopavo*), while Williams (*16*) reported a 10% mortality on this species using α-chloralose.

Birds that can create problems are more likely to do so when they become unusually abundant. Therefore, use of immobilizing agents in preventing damage will require widespread application of compounds that are effective at low levels, preferably below 10 mg. per kg. Unfortunately, dosages greater than 20 mg. per kg. of α-chloralose or 2,2,2-tribromoethanol are required to immobilize birds.

Since 1961, the authors have tested 94 chemicals as bird-immobilizing agents. The substituted phenyl *N*-methylcarbamates were the most active chemicals tested, whereas the phenyl *N*-ethyl-, *N*-benzyl-, and *N*-phenyl-derivatives were inactive. The purpose of this paper is to report the activity of the substituted phenyl *N*-methylcarbamates.

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Procedure

Starlings and red-winged blackbirds were chosen as the principal test birds because they are responsible for much of the agricultural damage in the United States. All birds were captured in the wild and held in captivity for 1 to 6 months before being tested. Adult male and female starlings and adult male redwings were used.

Individual birds were stomach tubed with approximately 175 μl. of an aqueous or propylene glycol solution of the appropriate carbamate, the exact volumes depending on the weight of the bird. Concentrations varied according to dosage. After the dosage had been administered, the birds were individually caged and periodically observed for 7 days or until death. Food and water were offered *ad libitum*. Data recorded included affectation time, induction and duration of immobilization, mortality, regurgitation, weight gain or loss, and any unique physiological effects exhibited by the birds.

In the initial screening, doses were adminstered to two birds at $^1/_4$ log intervals (three to 10 levels were usually necessary). Acute oral TI_{50} (temporary immobilization of 50% of birds tested) and LD_{50} values were approximated by assuming a logarithmic relationship between dose and effect. Values for the more active carbamates were obtained by Weil's method (*15*), using six birds at each interval.

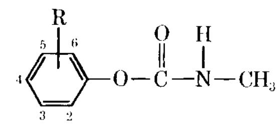
Materials

Chemicals coded DRC (Denver Research Center) were prepared in the authors' laboratory using the methods described by Kolbezen, Metcalf, and Fukuto (*2*). They were purified by repeated recrystallization from hexane, and melting points were used to verify their identity. All other carbamates were obtained from the chemical companies footnoted in Table I.

Results and Discussion

Twelve of the 22 phenyl *N*-methylcarbamates immobilized redwings at dosages below 10 mg. per kg. (Table I). Two compounds, *o*-(2-propynyloxy)phenyl

Table I. Biological Activities of Phenyl *N*-Methylcarbamates



No.	Company Designation	R 2	R 3	R 4	R 5	R 6	Redwing, Mg./Kg. TI_{50}	Redwing, Mg./Kg. LD_{50}	Starling, Mg./Kg. TI_{50}	Starling, Mg./Kg. LD_{50}	Housefly, μg./G. LC_{50} (Source)
I	RE 5305[a]	. . .	$(CH_3)CHCH_2$	. . .	. . .	. . .	1	4	3	5	100 (*1*)
II	H 5727[b]	. . .	$(CH_3)_2CH$	. . .	. . .	. . .	3	10	5	17	90 (*8*)
III	RE 5655[a]	. . .	$C_2H_5CHCH_3$	. . .	. . .	. . .	1	3	3	6	100 (*8*)
IV	RE 5454[a]	. . .	$CH_3CH_2C(CH_3)_2$	. . .	. . .	Cl	2	9	5	16	. . .
V	H 8717[b]	. . .	$CH{\equiv}CCH_2O$	. . .	. . .	. . .	9	15	84	150	7.5 (*7*)
VI	H 9699[b]	CH_2CCHO	. . .	. . .	. . .	. . .	5	45	45	80	6.5 (*7*)
VII	Bay 39007[c]	$(CH_3)_2CHO$	. . .	. . .	. . .	. . .	1.6[d]	3.8[d]	8	13	25.5 (*5*)
VIII	DRC 3345	. . .	. . .	. . .	. . .	. . .	>100	>100	>100	>100	500 (*8*) 70 (*2*)
IX	DRC 3341	. . .	CH_3	. . .	. . .	. . .	56	100	>100	>100	50 (*2*)
X	Bay 32651[e]	. . .	CH_3	CH_3S	. . .	. . .	50	90	9	40	11 (*7*)
XI	Bay 44646[c]	. . .	CH_3	$(CH_3)_2N$	. . .	. . .	16	50	37	210	. . .
XII	DRC 3344	. . .	CH_3	Cl	. . .	. . .	>100	>100	>100	>100	>500 (*4*)
XIII	DRC 3343	. . .	. . .	Cl	. . .	. . .	>100	>100	>100	>100	>500 (*2*)
XIV	DRC 3340	. . .	CH_3	. . .	CH_3	. . .	56	80	>100	>100	60 (*2*)
XV	HRS 1422[f]	. . .	$(CH_3)_2CH$	. . .	$(CH_3)_2CH$	. . .	6	10	75	>100	17.5 (*5*)
XVI	U-12,927[g]	. . .	CH_3	CH_3	. . .	Cl	2	6	2.1[h]	11.5[h]	<500 (*3*) >500 (*4*)
XVII	Bay 37344[c]	. . .	CH_3	CH_3S	CH_3	. . .	1.0[h]	8.4[h]	2	12	24 (*6*)
XVIII	Zectran[h]	. . .	CH_3	$(CH_3)_2N$	CH_3	. . .	4	11	16	24	60 (*6*)
XIX	Bay 50282[e]	. . .	CH_3	$[(CH_3)_2CH]_2N$	CH_3	. . .	10	13	18	18	. . .
XX	DRC 3342	. . .	CH_3	Cl	CH_3	. . .	>100	>100	>100	>100	>500 (*3*) <500 (*4*)
XXI	U-14,540[g]	Cl	CH_3	Cl	CH_3	. . .	>100	>100	>100	>100	<500 (*3*)
XXII	U-17,556[g]	Cl	CH_3	Cl	CH_3CH_2	. . .	8	13	>100	>100	<500 (*3*)

[a] Courtesy of Ortho Div., Chevron Chem. Co., Richmond, Calif.
[b] Courtesy of Hercules Powder Co., Wilmington, Del.
[c] Courtesy of Chemagro Corp., Kansas City, Mo.
[d] Determined by the method of Weil (*15*).
[e] Courtesy of Vero Beach Labs., Vero Beach, Fla.
[f] Courtesy of Hooker Chem. Co., Niagara Falls, N. Y.
[g] Courtesy of Upjohn Co., Kalamazoo, Mich.
[h] Courtesy of Dow Chemical Co., Midland, Mich.

N-methylcarbamate (VI) and 4-(methylthio)-3,4-xylyl *N*-methylcarbamate (XVII), possessed LD_{50}/TI_{50} ratios greater than 8.

Eight of the 22 carbamates immobilized starlings below 10 mg. per kg. Two compounds, 6-chloro-3,4-xylyl *N*-methylcarbamate (XVI) and 4-(methylthio)-3, 5-xylyl *N*-methylcarbamate (XVII), had LD_{50}/TI_{50} ratios greater than 5. Starlings regurgitate more readily when treated with XVII than XVI.

A correlation apparently exists between the contact toxicity of the various carbamates to houseflies (*Musca domestica*) and avian immobilization activity (column 4, Table I), Generally, those compounds which are topically lethal to flies below 100 μg. per gram also immobilize birds below 100 mg. per kg.

The mammalian toxicity of 18 of the 22 phenyl *N*-methylcarbamates tested lies between 50 and 150 mg. per kg.; chemicals I and II are more toxic, while III and IV are less toxic.

Structure Correlations

Although too few compounds have been examined to permit conclusions regarding chemical structure and bird immobilization activity, several correlations are indicated. The unsubstituted phenyl *N*-methylcarbamate molecule (VIII) is ineffective as an immobilizing agent for starlings or redwings, but immobilizing activity is observed when branched low molecular weight alkanes or ethers (C_{1-5}) are added at the two or three positions of the phenyl ring. The presence of methyl groups at the three position or the three and five positions appears to increase this activity; also, the addition of an organic group containing either sulfur or nitrogen at the para position of the phenyl ring, in conjunction with methyl groups at the three or five positions, or both, often results in more active immobilizing agents. Addition of chlorine at the para position, rather than sulfur- or nitrogen-containing groups, lessens avian activity.

Effectiveness on Other Avian Species

Data obtained on other birds with three of the more promising carbamates are presented in Table II. Of particular interest are the safety factors shown by: *o*-isopropoxyphenyl *N*-methylcarbamate (VII) on crows (*Corvus brachyrhynchos*);. 6-chloro-3,4-xylyl *N*-methylcarbamate (XVI) on house finches (*Carpodacus mexicanus*); and 4-(methylthio)-3,5-xylyl *N*-methylcarbamate (XVII) on house sparrows. The latter is also relatively nontoxic to pheasants (*Phasianus colchicus*).

To obtain an indication of the possible secondary hazard of carbamates to avian predators, a sparrow hawk (*Falco sparverius*) and a sharp-shinned hawk (*Accipiter striatus*) were fed red-winged blackbirds killed with 4-(methylthio)-3,5-xylyl *N*-methylcarbamate (XVII). Water was freely offered but no other food was available. During a period of 135 days the hawks consumed 92 and 150 redwings, respectively, with no observable adverse symptoms.

Table II. Immobilization Activity and Acute Oral Toxicity of Promising Carbamates to Other Avian Species

Chemical	Bird	TI_{50}, Mg./Kg.	LD_{50}, Mg./Kg.
VII	Crow (*Corvus brachyrhynchos*)	3	15
	House finch (*Carpodacus mexicanus*)	3	10
	Pigeon (*Columbia livia*)	6	8
	Ring-necked pheasant (*Phasianus colchicus*)	6	15
	House sparrow (*Passer domesticus*)	8	15
XVI	House finch	1	3
	House sparrow	2	4
	Pigeon	2	4
	Ring-necked pheasant	6	11
XVII	Lark bunting (*Calanospiza melanocorys*)	1	2
	Ring-billed gull (*Larus delawarensis*)	3	8
	Brown-headed cowbird (*Molothrus ater*)	3	8
	House finch	3	3
	Crow	4	8
	House sparrow	4	18
	Pigeon	6	18
	Ring-necked pheasant	...	225

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