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Received for review January 28, 1977. Accepted April 25, 1977. Study supported in part by the National Institutes of Health (Grant 5 PO1 ES00049) and grants from: Agricultural Chemical Division, FMC Corp., Middleport, N.Y.; ICI United States Inc., Goldsboro, N.C.; Sumitomo Chemical Co., Osaka, Japan; Roussel-Uclaf-Procida, Paris, France; Mitchell Cotts & Co., Ltd., London, England; Wellcome Foundation Ltd., London, England; National Research Development Corp., London, England.

1-Phenylcarbamoyl-2-pyrazolines: a New Class of Insecticides. 1. Synthesis and Insecticidal Properties of 3-Phenyl-1-phenylcarbamoyl-2-pyrazolines

Kobus Wellinga, Arnold C. Grosscurt, and Roelof van Hes*

Upon the discovery of the powerful insecticidal properties of 3-(4-chlorophenyl)-1-(4-chlorophenylcarbamoyl)-2-pyrazoline (PH 60-41), a large number of analogues was prepared. The structures of these compounds were confirmed by NMR. Their insecticidal properties were evaluated with larval stages of *Aëdes aegypti* L., *Pieris brassicae* L., and *Leptinotarsa decemlineata* Say. Many of these compounds proved to be excellent insecticides, bringing about the same symptoms as PH 60-41. From the point of view of biological activity and of economic aspects, PH 60-41 appeared to be the most promising compound for several fields of application.

In a recent report from our laboratories (Mulder et al., (1975), the new insecticidal compound 3-(4-chlorophenyl)-1-(4-chlorophenylcarbamoyl)-2-pyrazoline (PH 60-41) was introduced. This compound originated from a research program with derivatives of 3-aryl-2-pyrazolines. On larvae and adults of several insect species this compound proved to be a powerful stomach toxicant with some contact activity. Within 24 h after application, susceptible insects showed convulsions. They lost their grip on the leaves, fell off the plants, and finally died.

In the present paper we report the synthesis of a series of 3-phenyl-1-phenylcarbamoyl-2-pyrazolines and their evaluation as potential insecticides. Parts 2 and 3 of this series of papers (van Hes et al., 1977; Grosscurt et al., 1978) will show that substitution in the 2-pyrazoline nucleus of two phenyl rings at the 3,5 and 3,4 positions, respectively, instead of one at the 3 position gives rise to products with insecticidal properties of the same order or even better.

CHEMICAL METHODS

Microanalyses were carried out in the Analytical Department of the Institute for Organic Chemistry TNO, Utrecht, Netherlands, under the supervision of W. J. Buis. The carbon-13 spectra were measured with a Bruker WH 270 spectrometer, operating at 67.89 MHz. Nuclear magnetic resonance spectra were recorded on a Varian HA 100 spectrometer. Chemical shifts were measured with tetramethylsilane as the internal reference and with deuteriodimethyl sulfoxide as a solvent. The melting points are uncorrected.

One general method was used for the preparation of the various compounds mentioned in Tables I and II. They were prepared according to Scheme I.

4′-Chloro-3-dimethylaminopropiophenone Hydrochloride. A suspension of 30.9 g of 4-chloroacetophenone (0.2 mol), 21.2 g of dimethylamine hydrochloride (0.26 mol), and 7.8 g of paraformaldehyde (0.26 mol) in a mixture of 32 mL of ethanol and 0.4 mL of concentrated hydrochloric acid was refluxed for 2 h. After cooling, 160 mL of acetone was added. The crystals formed were collected, washed with acetone, and dried. Yield 35.8 g (72%), mp 173–175 °C [literature (Nobles, 1958), 176 °C].

3-(4-Chlorophenyl)-2-pyrazoline. A warm solution of 24.8 g of 4′-chloro-3-dimethylaminopropiophenone hydrochloride (0.1 mol) in 70 mL of methanol was added in 10 min to a mixture of 14 mL of hydrazine hydrate, 7.2 mL of 50% sodium hydroxide, and 18 mL of methanol.

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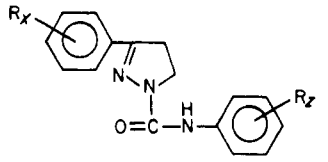
Table I.[a] Insecticidal Activities of



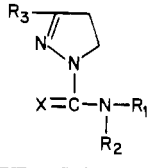
Compd no.	R_x	R_z	Lowest test concentration with ≥90% mortality: *Leptinotarsa decemlineata* Say	*Pieris brassicae* L.	*Aëdes aegypti* L.	Mp, °C
		a. R_x = H, alkyl				
1	H	H	100	>300	>1	160
2	H	4-n-C_3H_7	10	300	1	120
3	H	4-t-C_4H_9	10	300	>1	145
4	H	4-F	30	>300	>1	137
5	H	4-Cl	3	>300	1	148
6	H	3,4-Cl_2	10	>300	>1	168
7	4-CH_3	4-CH_3	30	>300	1	159
8	4-CH_3	4-Cl	30	>300	0.3	139
9	4-C_2H_5	4-Cl	30	100	>1	116
10	4-C_2H_5	4-$SO_2C_2H_5$	30	300	>1	172
11	4-n-C_3H_7	4-Cl	100	>300	>1	153
12	4-i-C_3H_7	4-Cl	10	100	>1	131
13	4-i-C_3H_7	4-$SO_2C_2H_5$	300	>300	>1	195
14	4-n-C_4H_9	4-C_2H_5	300	100	1	147
15	4-t-C_4H_9	4-Cl	30	300	>1	150
		b. R_x = halogen; R_z = H, alkyl				
16	2-Cl	4-n-C_3H_7	100	>300	>1	87
17	4-Cl	H	30	>300	>1	160
18[b]	4-Cl	2-CH_3	>300	>300	>1	162
19	4-Cl	4-CH_3	30	>300	>1	182
20	4-Cl	4-C_2H_5	10	>300	>1	140
21	4-Cl	4-n-C_3H_7	3	10	0.3	151
22	4-Cl	4-i-C_3H_7	1	10	>1	143
23	4-Cl	4-n-C_4H_9	30	30	>1	134
24	4-Cl	4-i-C_4H_9	30	10	>1	153
25	4-Cl	4-t-C_4H_9	3	30	>1	162
26	4-Cl	4-n-C_8H_{17}	100	>300	>1	107
27[b]	4-Cl	4-n-$C_{12}H_{25}$	>300	>300	>1	87
28[b]	2,4-Cl_2	4-CH_3	>300	>300	>1	123
29	4-Br	H	100	>300	>1	155
30	4-Br	4-n-C_3H_7	10	100	0.3	167
		c. R_x = R_z = halogen				
31	4-F	4-Cl	3	>300	1	150
32	4-F	3,4-Cl_2	30	>300	>1	162
33	2-Cl	4-Cl	100	>300	>1	123
34	2-Cl	3,4-Cl_2	100	>300	>1	144
35	3-Cl	4-Cl	30	>300	1	161
36	3-Cl	3,4-Cl_2	100	>300	>1	180
37	4-Cl	4-F	10	>300	>1	173
38[b]	4-Cl	2-Cl	>300	>300	>1	175
39	4-Cl	3-Cl	100	>300	>1	147
40	4-Cl	4-Cl	3	100	0.3	178
41	4-Cl	2,4-Cl_2	100	>300	>1	168
42[b]	4-Cl	2,5-Cl_2	>300	>300	>1	240
43	4-Cl	3,4-Cl_2	10	300	>1	187
44[b]	4-Cl	3,5-Cl_2	>300	>300	>1	202
45	4-Cl	2,4,5-Cl_3	>300	>300	>1	227
46	4-Cl	3,4,5-Cl_3	>300	>300	>1	200
47	4-Cl	4-Br	10	100	0.3	181
48	4-Cl	4-I	1	30	0.3	162
49	3,4-Cl_2	4-Cl	10	>300	1	180
50	3,5-Cl_2	4-Cl	300	>300	>1	200
51	4-Br	4-Cl	3	100	0.3	144
52	4-Br	3,4-Cl_2	10	300	>1	192
53	4-Br	4-Br	3	30	>1	147
54	4-I	4-Cl	10	300	0.3	165
		d. R_x = halogen; R_z = electron-donating groups				
55	2-Cl	4-O-i-C_3H_7	100	>300	>1	93
56	4-Cl	4-CH_3, 3-Cl	30	>300	>1	189
57	4-Cl	4-$N(CH_3)_2$	100	>300	>1	163
58	4-Cl	4-OCH_3	3	>300	>1	135
59	4-Cl	4-OC_2H_5	10	300	1	139
60	4-Cl	4-O-i-C_3H_7	3	10	0.3	130
61	4-Cl	4-SCH_3	30	300	1	141

Table I (*Continued*)

Compd no.	R_x	R_z	Lowest test concentration with ≥90% mortality: *Leptinotarsa decemlineata* Say	*Pieris brassicae* L.	*Aëdes aegypti* L.	Mp, °C
62	4-Cl	4-OCH_3, 3-Cl	300	>300	>1	208
		e. R_x = halogen; R_z = electron-attracting groups				
63	4-Cl	3-CF_3	10	>300	>1	138
64	4-Cl	4-CF_3	1	10	0.1	120
65	4-Cl	3-NO_2	100	>300	>1	210
66	4-Cl	4-NO_2	10	>300	>1	225
67	4-Cl	4-$COCH_3$	300	>300	>1	174
68	4-Cl	4-CN	3	>300	>1	210
69	4-Cl	4-SO_2CH_3	30	>300	>1	225
70	4-Cl	4-$SO_2C_2H_5$	10	100	>1	187
71	4-Cl	4-SO_2-*n*-C_4H_9	30	100	>1	146
72	4-Br	4-CN	10	>300	>1	227
		f. R_x = electron donating groups				
73	4-$N(CH_3)_2$	4-Cl	3	>300	1	189
74	4-$N(CH_3)_2$	4-$N(CH_3)_2$	300	>300	>1	209
75	3-OCH_3	4-Cl	30	>300	>1	129
76	3-OCH_3	3,4-Cl_2	100	>300	>1	136
77	4-OCH_3	4-Cl	10	>300	1	132
78	4-OCH_3	3,4-Cl_2	30	>300	>1	170
79	4-O-*i*-C_3H_7	4-Cl	10	30	0.3	141
80	4-SCH_3	4-Cl	30	>300	1	154
		g. R_x = electron attracting groups				
81	4-C_6H_5	4-Cl	30	>300	>1	290
82	3-NO_2	4-Cl	30	>300	>1	214
83	3-NO_2	3,4-Cl_2	300	>300	>1	210
84	4-SO_2CH_3	4-Cl	300	>300	>1	246

[a] Applied concentrations, in parts per million: *Aëdes aegypti* L., 1, 0.3, 0.1, 0.03, etc.; *Pieris brassicae* L., 300, 100, 30, 10, etc.; *Leptinotarsa decemlineata* Say, 300, 100, 30, 10, etc. [b] These compounds are slightly active on *Leptinotarsa decemlineata* Say and/or on *Pieris brassicae* L. at a concentration higher than 300 ppm.

Table II.[a] Insecticidal Activities of



Compd no.	R_1	X	R_2	R_3	Lowest test concentration with ≥90% mort.: *Leptinotarsa decemlineata* Say	*Pieris brassicae* L.	*Aëdes aegypti* L.	Mp, °C
1	4-ClC_6H_4	O	CH_3	4-ClC_6H_4	10	300	>1	146
2	4-ClC_6H_4	O	C_2H_5	4-ClC_6H_4	10	300	>1	133
3	4-ClC_6H_4	O	*n*-C_3H_7	4-ClC_6H_4	100	300	>1	132
4	CH_3	O	H	4-ClC_6H_4	>300	>300	>1	138
5	*n*-C_4H_9	O	H	4-ClC_6H_4	>300	>300	>1	123
6	*c*-C_6H_{11}	O	H	4-ClC_6H_4	100	>300	>1	156
7	*n*-$C_{11}H_{23}$	O	H	4-ClC_6H_4	>300	>300	>1	71
8	4-ClC_6H_4	O	H	*n*-C_3H_7	>300	>300	>1	90
9	4-ClC_6H_4	S	H	4-ClC_6H_4	30	>300	>1	198

[a] Applied concentrations, in parts per million: *Aëdes aegypti* L., 1, 0.3, 0.1, 0.03, etc.; *Pieris brassicae* L., 300, 100, 30, 10, etc.; *Leptinotarsa decemlineata* Say, 300, 100, 30, 10, etc.

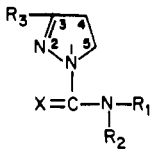
After refluxing for 45 min, the methanol was distilled off at reduced pressure. The residue was dissolved in dichloromethane and washed with water. Evaporation of the solvent gave the crude 2-pyrazoline (16.0 g), which could be used without further purification. The 2-pyrazolines of this type were not very stable and had to be stored under nitrogen in the refrigerator.

3-(4-Chlorophenyl)-1-(4-chlorophenylcarbamoyl)-2-pyrazoline [Table I, Compound 40 (I,40); PH 60-41]. To a suspension of 5.4 g of 3-(4-chlorophenyl)-2-pyrazoline (0.03 mol) in 100 mL of dry ether, three drops of triethylamine and 4.6 g of 4-chlorophenylisocyanate (0.03 mol) were added. The solution became clear and a precipitate of the reaction product appeared. After stirring for 1.5 h, the precipitate was collected and dried, yielding 7.5 g (75%) of compound 40, mp 176–178 °C.

Anal. Calcd for $C_{16}H_{13}Cl_2N_3O$ (mol wt, 334.20): C, 57.50; H, 3.92; Cl, 21.22; N, 12.57. Found: C, 57.2; H, 3.9; Cl, 21.4; N, 12.6.

3-(4-Chlorophenyl)-1-[*N*-(4-chlorophenyl)-*N*-methyl]carbamoyl-2-pyrazoline (II,1). To a stirred suspension of 3.3 g of 3-(4-chlorophenyl)-1-(4-chlorophenylcarbamoyl)-2-pyrazoline (= I,40; 0.01 mol) and 1 g of potassium carbonate in 20 mL of DMF,

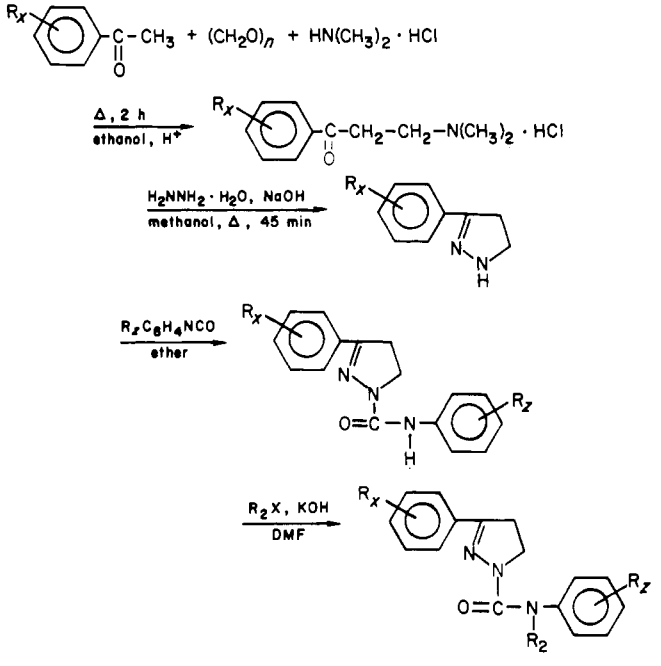
Table III. Proton NMR Data of



				Average chemical shifts in δ value[a]								
	Substituents			Pyrazoline		Phenyl R_1			Phenyl R_2	Phenyl R_3		
X	R_1	R_2	R_3	H_4	H_5	Ortho	Meta	Para		Ortho	Meta	Para
S	Phenyl	H	Phenyl	3.35	4.30	7.58	7.25		9.89	7.89	7.41	
O	Phenyl	H	Phenyl	3.28	3.97	7.61	7.21	6.89	8.86	7.81	7.38	7.32
O	Phenyl	H	Alkyl	2.58	3.78	7.58	7.14		8.55			
O	Alkyl	H	Phenyl	3.19	3.87				5.91[b]-6.84[c]	7.71	7.36	
O	Phenyl	Alkyl	Phenyl	3.04	3.92	{7.16 {7.26	{7.23 {7.13			{7.13 {7.28	{7.25 {7.10	

[a] The pyrazoline protons appear as broad triplets with J = 11 Hz. Actually it is an AA'XX' spin system with $J_{AX} + J_{AX'}$ = 22 Hz and $J_{AX} - J_{AX'} < 7$ Hz. The standard deviation from the average chemical shifts of the pyrazoline protons was 0.03. The chemical shifts of the phenyl and NH protons are calculated for the unsubstituted derivatives, with the help of the aromatic substituent shifts of Table IV. The standard deviation for the aromatic protons was 0.05 and for the NH protons 0.07. [b] Cyclohexyl. [c] *n*-alkyl.

Scheme I. Preparation of Substituted 3-Phenyl-1-phenylcarbamoyl-2-pyrazolines



0.7 g of powdered potassium hydroxide (0.0125 mol) was added at 0 °C. After 15 min 0.7 mL of methyl iodide was added. The mixture was stirred for 0.5 h at 0 °C, then for 1.5 h at room temperature, and finally poured into ice water. The precipitate was collected, dried, and washed with petroleum ether. Yield 2.8 g (80%), mp 144–146 °C.

Anal. Calcd for $C_{17}H_{15}Cl_2N_3O$ (mol wt, 348.25): C, 58.63; H, 4.34; Cl, 20.37; N, 12.07. Found: C, 58.4; H, 4.4; Cl, 20.4; N, 12.0.

The compounds **4–7** and **9** of Table II were prepared according to the procedure described for compound **I,40**.

1-(4-Chlorophenylcarbamoyl)-3-*n*-propyl-2-pyrazoline (II,8). 3-*n*-Propyl-2-pyrazoline was prepared according to procedures described in the literature (Kossanyi, 1965; Smith, 1952). The compound II,8 was prepared from 3-*n*-propyl-2-pyrazoline according to the procedure described for compound **I,40**; mp 88–90 °C.

Anal. Calcd for $C_{13}H_{16}ClN_3O$ (mol wt, 265.75): Cl, 13.34; N, 15.82. Found: Cl, 13.4; N, 15.7.

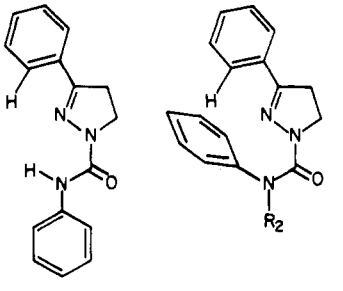
The following compound has been prepared for comparison with compound **I,40** (see Results and Discussion section).

3-(4-Chlorophenyl)-1-(4-chlorophenylcarbamoyl)-pyrazole. The synthesis of 3-(4-chlorophenyl)pyrazole is described in the literature (Kochetkov, 1958). To a solution of 1.96 g of 3-(4-chlorophenyl)pyrazole (0.011 mol) in 25 mL of acetone, 1.7 g of 4-chlorophenylisocyanate (0.011 mol) and three drops of triethylamine were added. After refluxing for 1 h, the reaction mixture was allowed to stand at room temperature for 24 h. The crystals were collected, washed with ether, and dried, yielding 2.3 g (63%): mp 149–150 °C; NMR (Me_2SO) δ 7.13 (1, d, J = 2.6 Hz, N-*CH*=CH), 8.49 (1, J = 2.6 Hz, NCH=*CH*), 8.11 (2, d, 1-phenyl), 7.56 (2, d, 1-phenyl), 7.85 (2, d, 3-phenyl), 7.45 (2, d, 3-phenyl), 10.43 (1, S, NH).

Anal. Calcd for $C_{16}H_{11}Cl_2N_3O$ (mol wt, 332.20): C, 57.85; H, 3.34; Cl, 21.35; N, 12.65. Found: C, 57.9; H, 3.3; Cl, 21.5; N, 12.6.

NMR SPECTRA

The proton NMR data of the 3-phenyl-1-phenylcarbamoyl-2-pyrazolines are presented in Tables III and IV. All the chemical shifts accord with expectations, except those of the aromatic protons of the N-alkyl (R_2 = alkyl) derivatives. Particularly the shifts of the ortho protons of the 3-phenyl ring are too low. However, the ^{13}C chemical shifts of these N-alkyl derivatives are normal, compared with those of the corresponding NH derivatives (Table V). The anomalous chemical shifts must therefore be due to steric effects rather than to effects through the bonds. It may be assumed that the main conformation of the NH derivatives is that of structure A. A great con-



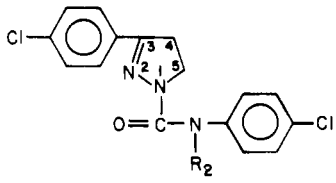
A B

Table IV. Aromatic Substituent Shifts, Solvent Me_2SO

	Proton					
	Aromatic protons			φ-NH proton[a]		
	Position of substituent					
Substituent	Ortho	Meta	Para	Ortho	Meta	Para
$-NO_2$	+0.94[a]	+0.27	+0.34[a]		+0.59	+0.61
$-COCH_3$	+0.67[a]	+0.26[a]				+0.34
$-SO_2R$	+0.59[a]	+0.29[a]				+0.46
-CN	+0.49	+0.24				+0.53
-F	−0.13[a]	+0.07[a]		−0.34		+0.11
-Cl	+0.10	+0.07	+0.03	−0.20	+0.25	+0.15
-Br	+0.24	+0.02				+0.17
-I	+0.38	−0.07[a]				+0.16
$-CF_3$	+0.39	+0.29	+0.36[a]		+0.42	+0.42
-C(=O)-	+0.03	−0.05				−0.08
-CH(=O)	−0.06	−0.02				−0.08
$-CH_2-$	−0.13	−0.07				−0.08
$-CH_3$	−0.17	−0.07		−0.48		−0.08
-OR	−0.41	−0.04				−0.10
$-SCH_3$	−0.05[a]	0[a]				+0.06
$-NR_2$	−0.67	−0.17				−0.25

[a] Data are calculated from 3-phenyl-1-phenylcarbamoyl-2-pyrazolines, 3,4-diphenyl-1-phenylcarbamoyl-2-pyrazolines (Grosscurt et al., 1978), 3,5-diphenyl-1-phenylcarbamoyl-2-pyrazolines (van Hes et al., 1977); other data were obtained from the literature (Gove, 1973).

Table V. ^{13}C NMR Chemical Shifts of



Carbon atoms		R_2 = H	R_2 = n-C_3H_7
Pyrazoline ring	C_3	151.7	151.4
	C_4	31.6	30.2
	C_5	44.8	46.6
1-Phenylcarbamoyl	C=O	152.7	154.7
	C_1	138.4	143.9
	C_2	120.8	127.5
	C_3	128.2	127.9
	C_4	126.0	129.2
3-Phenyl	C_1	130.3	130.6
	C_2	128.6	128.53
	C_3	128.3	128.45
	C_4	134.6	134.1
	α-CH_2		52.4
R_2 = n-C_3H_7	β-CH_2		21.0
	γ-CH_3		11.0

tribution of the conformation of structure B can for the N-alkyl derivatives bring about the strong deshielding of the ortho protons of the 3-phenyl ring. The stronger deshielding of the C_4 protons compared with the C_5 protons of the pyrazoline ring may also be due to this conformation.

BIOLOGICAL METHODS

The insecticidal evaluations were performed with suspensions made by pouring out, with stirring, quantities of a 1% stock solution in acetone into water. Compounds insufficiently soluble in acetone were thoroughly milled with water in a laboratory glass mill. Various species were tested as follows.

a. *Aëdes aegypti* L. (yellow fever mosquito). Aliquots of 100 mL of tap water containing 1, 0.3, 0.1, 0.03, etc. ppm, respectively, of the substituted 3-phenyl-1-phenylcarbamoyl-2-pyrazolines were supplied with ten 1-day old larvae and kept at 25 °C. The larvae were fed with a mixture of brewer's yeast and wheaten bread in a 1:1 ratio. After 14 days, when the pupae of the untreated insects had hatched, the mortality percentages were assessed with a correction for the natural mortality according to Abbott (1925). There were three replicates per treatment.

b. *Pieris brassicae* L. (large white butterfly). Potted cabbage seedlings were sprayed with a suspension of the toxicant until runoff. The suspensions contained 300, 100, 30, 10, 3, etc. ppm of the compound, respectively. When dry, the plants were placed in plastic cylinders, provided with five third-instar caterpillars and kept under a day/night cycle of 18/6 h at a temperature and relative humidity of 24 °C, 60–70% and 19 °C, 80–90%, respectively. There were three replicates per treatment. After 5 days the mortality percentages were calculated according to Abbott's formulae.

c. *Leptinotarsa decemlineata* Say (Colorado potato beetle). Potato shoots, placed in flasks containing tap water, were sprayed with a suspension of the compound until runoff. The concentrations of the suspensions were 300, 100, 30, 10, 3, etc. ppm, respectively. When dry, the shoots were placed in plastic cylinders and provided with ten third-instar larvae. After this, the procedure and the environmental circumstances were identical with those described for the large white butterfly.

RESULTS AND DISCUSSION

The overwhelming number of substitution possibilities in these compounds induced us to a drastic limitation in the synthetic work. Nevertheless, for reasons of efficiency, we shall in this article report merely on some of the compounds prepared thus far.

In Table I, subdivided in sections a, b, c, etc., the insecticidal properties are presented of the different types of substituted 3-phenyl-1-phenylcarbamoyl-2-pyrazolines. Table II includes the compounds with certain modifications in the molecule with regard to the basic structures.

Table Ia shows the results of the compounds with an unsubstituted 3-phenyl ring, "ring 3", and with those substituted with an alkyl substituent at the para position. The phenyl ring in the carbamoyl group, "ring 1", carries

a somewhat miscellaneous substitution pattern. These compounds display a high level of activity on *Leptinotarsa*, particularly in the case of halogen and of (higher) alkyl substitution in the last mentioned ring (I: **5, 6, 12, 2**). The activity of *Pieris* and *Aëdes* varies from moderate to negligible. Compounds **2** and **14** were active on all three test objects.

From Tables Ib to Ie, recording the test results of all compounds with a halogen substituent in ring 3 and with various substituents in ring 1, the following may be concluded. Para substitution in ring 1 appears to be favorable, compared with ortho and meta substitution (I: **19** vs. **18**; **40** vs. **38** and **39**; **64** vs. **63**; **66** vs. **65**), while with an increasing number of halogen atoms the activity vanishes entirely (I: **42, 44, 45, 46**), the 3,4-dichloro compound **43**, however, being an exception. Compound **41** is but slightly active. The same holds true for ring 3 (I: **40** vs. **33** and **35**; **43** vs. **34** and **36**, **21** vs. **16**; **60** vs. **55**) and again introduction of additional halogen atoms brings about a decrease in activity (I: **28, 50**). Compound **49**, the other 3,4-dichloro derivative, remains about as active as compound **40** = PH 60–41, the first representative of this class of insecticides, which has been described elsewhere by Mulder et al. (1975).

For optimal activity on *Pieris*, parahalogen in ring 3 combined with a paraalkyl substituent $>C_2H_5$ in ring 1 turns out to be essential (I: **21, 22, 23, 24, 25**). A high activity level in this series is found with compounds **21**, **22**, and **25** on *Leptinotarsa*. Apart from the paraalkyl compounds, it appears from Table Id that derivatives with other electron-donating groups in ring 1 also yield good results with *Leptinotarsa* (I: **57, 58, 59, 60, 61**). Even more pronounced are these results in case of electron-attracting groups, including halogen, in ring 1 (I: **31, 40, 48, 51, 53, 64, 68**). The more outstanding compounds in both series are **21**, **60** and **40**, **48**, **51**, **64**, respectively, which are active on the three test organisms involved. Strong electron-donating groups, when present in ring 3, give rise to derivatives with fair results in the case of *Leptinotarsa* (I: **73, 77, 79**), while electron-attracting groups in this ring apart from halogen atoms, yield derivatives with rather moderate results, presented in Table Ig. Activity with *Pieris* and *Aëdes* in these series appears to be negligible, compound **79** being an exception.

With regard to Table Ic comprising compounds with halogen substituents in both rings, the following may be noted. *Leptinotarsa* responds rather similarly to the four possible 2-pyrazolines with a parachloro atom in ring 1 and with different parahalogens in ring 3 (I: **31, 40, 51, 54**). This is the case also if the rings 1 and 3 change places in the 2-pyrazoline nucleus (I: **37, 40, 47, 48**). In both cases the activity of the parafluoro derivatives is negligible on *Pieris* and *Aëdes* (I: **31, 37**).

Several alterations in the basic molecule are detrimental to insecticidal activity, as is exemplified in Table II. Replacement of ring 1 or of ring 3 by an alkyl group (II: **4, 5, 6, 7**, and **8**, respectively) or conversion of one of the outstanding compounds, PH 60-41 (I: **40**), to its sulfur analogue (II: **9**) reduces the activity considerably. PH 60-41 when converted to its 4,5-dehydro derivative, consequently the pyrazole analogue, appears to be practically inactive (not presented in the tables).

N-Alkylation in the carbamoyl group results also in a decrease in activity (II: **1, 2, 3**).

At present the toxicological data, with respect to vertebrates, of only five substituted 3-phenyl-1-phenylcarbamoyl-2-pyrazolines have been obtained. When administered orally the LD_{50} values of these compounds toward mice vary from 1780 mg/kg (I: **60**) to higher than 3160 mg/kg (I: **6, 21, 40, 48**), while intraperitoneally these values vary from 422 mg/kg (I: **60**), via 750 mg/kg (I: **21**) and >1000 mg/kg (I: **48**) to >3160 mg/kg (I: **6, 40**).

CONCLUSION

From the economic and practical aspects, 3-(4-chlorophenyl)-1-(4-chlorophenylcarbamoyl)-2-pyrazoline (I: **40**; PH 60-41), which is active not only against the test objects involved but also toward a great number of other arthropods (Mulder et al., 1975), appears to be one of the most promising compounds in this series.

ACKNOWLEDGMENT

The proton NMR spectra were measured and interpreted by Johan Brugman and Hans Schiereck. The carbon NMR spectra were measured and interpreted by Truus van der Chijs. The structural analyses were coordinated by Frits W. van Deursen of the Analytical Department of Philips-Duphar B.V. The authors wish to express their gratitude to Jacobus Tipker of the Biochemical Department for his suggestions regarding structure–activity relationships. A publication about this subject is in progress.

Supplementary Material Available: A listing of microanalyses (1 page). Ordering information is given on any current masthead page.

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Received for review May 7, 1976. Accepted February 14, 1977.