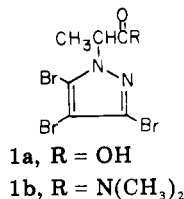


## Herbicide Activity of Alkylpyrazole Amides

Gabriel Kornis,\* Steven F. Rehrauer, and Henry J. Vostral

Alkylated pyrazole amides have been synthesized and evaluated as preemergence herbicides. 3,4-Dihalo-*N,N*, $\alpha$ ,5-tetramethylpyrazole-1-acetamides (9 and 40) were the most active compounds in greenhouse and field testing. Decrease in activity occurred when the halogen atoms were substituted for hydrogen and alkyl or when the methyl groups were homologated.

The herbicidal activity of tribromopyrazole alkanolic acids and amides has been disclosed previously by us (Chambers et al., 1972). The acid 1a was most effective



when applied postemergence on broadleaves, while the amide 1b showed preemergence activity both on broadleaves and on grasses. As a follow up to this work we now have found (Kornis, 1976) that while replacement of a halogen atom with an alkyl group in the pyrazole ring completely destroys the herbicidal activity of the acid 8, in the case of the amide 9, enhanced activity was observed. In the present publication the synthesis and herbicidal activity of ring alkylated pyrazoles is described.

## MATERIALS AND METHODS

**Chemical Methods.** Propionyl chloride was reacted with excess acetylene in the presence of aluminum chloride to give 1-chloro-1-penten-3-one which was further reacted with hydrazine hydrate to give 3-ethylpyrazole (2). This procedure (Alberti and Zerbi, 1961) was used for the synthesis of all the pyrazole intermediates required for Table I, with the exception of 11 (Scheme II; intermediate for compound 20). A different procedure for the synthesis of the pyrazole intermediates utilized in Table IV was also described by Alberti and Zerbi (1961) with the exception of 5-chloro-3-methylpyrazole (intermediate for 47; Veibel et al., 1954; Michaelis, 1910).

Bromination of 2 in acetic acid gave 3 which was reacted with *N,N*-dimethyl-2-chloropropionamide (Lehureau and Bernard, 1966) in toluene in the presence of sodium hydride to yield a mixture of 4 and 5. Separation was achieved by fractional crystallization/or chromatography.

This synthetic procedure (Scheme I) was used for the preparation of all the compounds shown in Table I, compounds 40 and 46 in Table III, and compounds 47 to 55 in Table IV.

An alternate procedure (Scheme II) which furnishes mainly one isomer consists in the alkylation of 6 with ethyl 2-bromopropionate, using potassium carbonate as the base, to yield 7. Hydrolysis to the acid 8 and treatment with thionyl chloride followed by dimethylamine gave the amide 9. This procedure was used to synthesize all the compounds in Table II and compounds 41 to 45 in Table III.

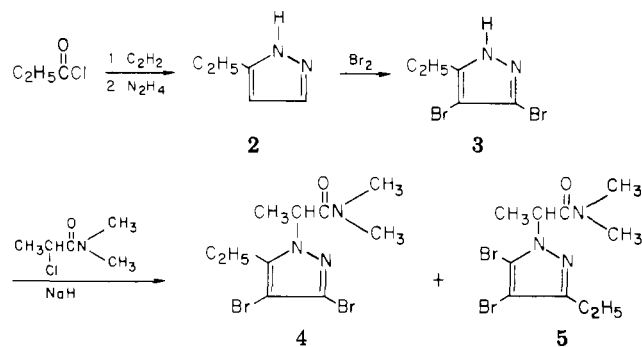
The dichloro analogue of 6 could not be prepared by direct chlorination of 3-methylpyrazole as described (Huttel et al., 1956). However, chlorination of 5-chloro-3-methylpyrazole (Veibel et al., 1954; Michaelis and

Table I. Substituted 4-Bromo-*N,N*, $\alpha$ -trimethylpyrazole-1-acetamide Properties and Test Results

Compd no.	R <sub>3</sub>	R <sub>5</sub>	Mp, °C	Average preemergence herbicide activity			
				10 lb/acre	6 lb/acre	3 lb/acre	1 lb/acre
9	Br	CH <sub>3</sub>	69-71	8.2	7.8	6.9	5.9
4	Br	C <sub>2</sub> H <sub>5</sub>	94-95.5	7.6	6.2	4.4	2.1
13	Br	C <sub>3</sub> H <sub>7</sub>	100-101	5.0	5.8	2.9	0.5
14	Br	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	117.5-118	1.7			
15	Br	C <sub>4</sub> H <sub>9</sub>	84.5-85	4.4			
16	CH <sub>3</sub>	Br	109-110	6.7	6.4	5.6	5.0
5	C <sub>2</sub> H <sub>5</sub>	Br	61-63	6.1			
17	C <sub>3</sub> H <sub>7</sub>	Br	39-41	0			
18	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	Br	Oil	3.4			
19 <sup>a</sup>	C <sub>4</sub> H <sub>9</sub>	Br	40-44	3.3			
20 <sup>b</sup>	Br	Br		8.1	6.2	5.0	4.1

<sup>a</sup> Contains 20% of 15. <sup>b</sup> 3,5-Dibromo-4-methyl isomer.

## Scheme I



Lachwitz, 1910) with chlorine-potassium carbonate in carbon tetrachloride or bromination as for 3 gave the required intermediates for Table III. The synthesis of dibromopyrazoles with a methyl group in the 4 position (compound 20, Table I; 56, Table IV) was best achieved by treating tribromopyrazole (10, Kornis and Nidy, 1973) with butyllithium, followed by methyl iodide to yield 11 which was then alkylated in the usual manner. Thioamide 12 and compounds 56 to 58 (Table IV) were obtained by treating the corresponding amides with phosphorous pentasulfide in pyridine solution.

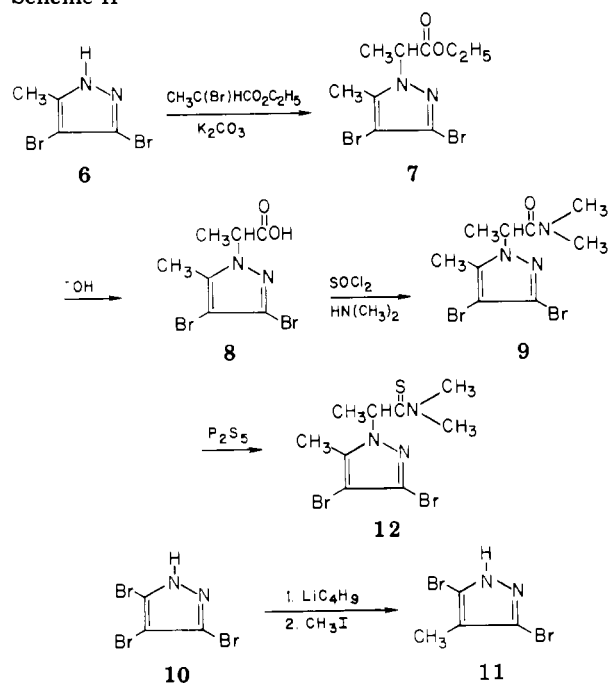
The structure assignment of the pyrazole amides rests on nuclear magnetic resonance (NMR) evidence. It has been shown (Janssen and Habraken, 1971; Brugel, 1967) that the 5 hydrogen in 1-substituted pyrazoles is more deshielded and has a larger coupling constant than the

The Upjohn Company, Kalamazoo, Michigan 49001.

Table II. Substituted 3,4-Dibromo-5-methylpyrazole-1-acetamide Properties and Test Results

Compd no.	R <sub>0</sub>	R <sub>1</sub>	R <sub>2</sub>	Mp, °C	Average preemergence herbicide activity			
					10 lb/acre	6 lb/acre	3 lb/acre	1 lb/acre
9	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	69-71	8.2	7.8	6.9	5.9
21	CH <sub>3</sub>	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	55-56	8.1	8.0	6.4	7.1
22	CH <sub>3</sub>	CH <sub>3</sub>	CH(CH <sub>3</sub> ) <sub>2</sub>	95-96	6.8	4.4	1.1	0
23	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	49-50	7.7	8.0	7.4	5.5
24	CH <sub>3</sub>	C <sub>3</sub> H <sub>7</sub>	C <sub>3</sub> H <sub>7</sub>	92-94	7.6	3.3	3.3	1.8
25	CH <sub>3</sub>	CH <sub>2</sub> CH=CH <sub>2</sub>	CH <sub>2</sub> CH=CH <sub>2</sub>	81-82.5	7.3	6.9	4.8	2.5
26	CH <sub>3</sub>	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	58-59	3.3	4.1	3.8	2.4
27	CH <sub>3</sub>	-CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> -		94-95	0.8			
28	CH <sub>3</sub>	-CH <sub>2</sub> CH <sub>2</sub> -O-CH <sub>2</sub> CH <sub>2</sub> -		128-130	1.1			
29	CH <sub>3</sub>	CH <sub>3</sub>	H	195-197	7.0	5.4	4.2	2.0
30	CH <sub>3</sub>	CH <sub>2</sub> CH=CH <sub>2</sub>	H	168-169	1.0			
31	CH <sub>3</sub>	C <sub>6</sub> H <sub>11</sub>	H	208-209	1			
32	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	74-75	8.3	4.8	4.0	1.2
33	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	58.5-61	8.3	7.4	6.1	2.9
34	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	70-70.5	7.8	7.4	5.9	3.4
35	H	CH <sub>3</sub>	CH <sub>3</sub>	106.5-108	6.1	4.4	2.6	0
36	H	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	94-95	7.6	3.4	2.5	1.4
37	H	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	83-85	6.0	4.2	3.1	1.5
38	H	C <sub>3</sub> H <sub>7</sub>	C <sub>3</sub> H <sub>7</sub>	58-60	6.3	1.4	0.2	0
39	H	CH <sub>3</sub>	H	181-181.5	4.8	0.8	0	0

Scheme II



hydrogen in the 3 position. Similarly, the methyl or methylene group in the 5 position is more deshielded and shows a higher chemical shift ( $\delta$ ) than in the 3 position. Further evidence was obtained by the use of shift reagents. Sequential addition of tris(dipivalomethanato)europium [Eu(dpm)<sub>3</sub>] to a mixture of isomers 9 (Scheme II) and 16 (Table I) in deuterated acetone solution caused a paramagnetic shift of all protons in the spectrum. The two methyl groups could be clearly distinguished, and the more deshielded one in the spectrum moved the furthest on the addition of the reagent. This is explained by the closer proximity of the 5-methyl group than the 3-methyl group

Table III. Substituted 3-Chloro- $\alpha$ ,5-dimethylpyrazole-1-acetamide Properties and Test Results

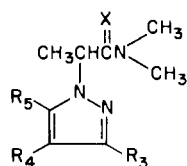
Compd no.	R <sub>1</sub>	R <sub>2</sub>	R <sub>4</sub>	Mp, °C	Average preemergence herbicide activity			
					10 lb/acre	6 lb/acre	3 lb/acre	1 lb/acre
40	CH <sub>3</sub>	CH <sub>3</sub>	Cl	54-57	7.4	5.8	5.8	5.1
41	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	Cl	39-40	7.3	6.5	6.0	3.6
42	CH <sub>3</sub>	H	Cl	180-181	6.6	6.8	5.8	4.8
43	C <sub>2</sub> H <sub>5</sub>	H	Cl	157-159	6.3	4.9	3.9	2.0
44	CH <sub>3</sub>	CH <sub>3</sub>	Br	80-82	7.8	6.8	6.4	5.9
45	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	Br	51-53	6.4	5.2	5.1	3.0
46 <sup>a</sup>	CH <sub>3</sub>	CH <sub>3</sub>	Cl	67-69	6.7	6.5	5.5	4.1

<sup>a</sup> 4,5-Dichloro-3-methyl analogue.

to the amide function, which in general is the major chelating center.

Structures and purities were ascertained by IR, NMR, GC, and TLC; satisfactory elemental analyses ( $\pm 0.3\%$ ) were obtained for all new compounds. Illustrative synthetic procedures are outlined below.

**4,5-Dibromo-3-ethylpyrazole (3).** To a stirred suspension of sodium acetate (10.16 g, 0.124 mol) in acetic acid (30 mL) and water (5 mL), 3-ethylpyrazole 2 (4.8 g, 0.05 mol) was added, followed by dropwise addition of bromine (19.2 g, 0.12 mol), keeping the internal temperature below 35 °C. The mixture was kept at room temperature for 48 h, treated with water (150 mL) containing sodium bisulfite (2.5 g), and filtered. Recrystallization from hexane of the

Table IV. Substituted *N,N*, $\alpha$ -Trimethylpyrazole-1-acetamide and -1-thioacetamide Properties and Test Results

Compd no.	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	X	Mp, °C bp, °C (mmHg)	Average preemergence herbicide activity			
						10 lb/acre	6 lb/acre	3 lb/acre	1 lb/acre
47	Cl	H	CH <sub>3</sub>	O	88-89	6.7	5.6	5.0	3.6
48	CH <sub>3</sub>	Cl	H	O	54-55	4.8	3.6	0.9	0
49	CH <sub>3</sub>	Br	CH <sub>3</sub>	O	125 (0.07)	7.0			
50	H	Br	CH <sub>3</sub>	O	78-80	6.4			
51	CH <sub>3</sub>	CH <sub>3</sub>	H	O	77 (0.03)	5.1			
52	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	O	63-66	4.1			
53	CH <sub>3</sub>	H	CH <sub>3</sub>	O	100-104 (0.03)	2.7			
54	CH <sub>3</sub>	Br	H	O	85-87	6.1			
55 <sup>a</sup>	CH <sub>3</sub>	H	H	O	42-55	4.7			
12	Br	Br	CH <sub>3</sub>	S	159-161	7.4	5.2	4.5	2.1
56 <sup>b</sup>	Br	CH <sub>3</sub>	Br	S	189-191	4.8	1.9	1.1	0
57	C <sub>4</sub> H <sub>9</sub>	Br	H	S	37-39	1.1			
58	CH <sub>3</sub>	Br	CH <sub>3</sub>	S	119.5-121	6.8	2.9	1.4	0

<sup>a</sup> Contains 22% of the 5-methyl isomer. <sup>b</sup> *N,N*-Diethylamide.

precipitate gave **3** (9.9 g, 78%), mp 98-100 °C.

Anal. Calcd for C<sub>5</sub>H<sub>8</sub>Br<sub>2</sub>N<sub>2</sub>: C, 23.64; H, 2.38; N, 11.03; Br, 62.94. Found: C, 23.83; H, 2.44; N, 11.37; Br, 62.99.

**3,4-Dibromo-5-ethyl-*N,N*, $\alpha$ -trimethylpyrazole-1-acetamide (4) and 4,5-Dibromo-3-ethyl-*N,N*, $\alpha$ -trimethylpyrazole-1-acetamide (5).** To a suspension of sodium hydride (0.757 g, 0.018 mol, 57% oily dispersion) in toluene (30 mL), 4,5-dibromo-3-ethylpyrazole (**3**) (3.81 g, 0.015 mol) in toluene (75 mL) was added, followed by a solution of 2-chloro-*N,N*-dimethylpropionamide (2.43 g, 0.018 mol) in toluene (6 mL). The mixture was heated under reflux for 2 h, cooled, and treated with toluene (60 mL) and water (40 mL). The solid (95% yield) obtained after removal of the toluene layer consisted of a mixture of **4** and **5** in a ratio of 1 to 1.5, respectively. Crystallization from Skellysolve F yielded **4**: mp 94-99 °C; NMR [(CD<sub>3</sub>)<sub>2</sub>CO]  $\delta$  1.13 (t, 3, CH<sub>3</sub>CH<sub>2</sub>), 1.60 (d, 3, CH<sub>3</sub>CH), 1.92 (q, 2, CH<sub>3</sub>CH<sub>2</sub>), 2.96 [s, 6, N(CH<sub>3</sub>)<sub>2</sub>], 5.56 (q, 1, CH<sub>3</sub>CH).

Anal. Calcd for C<sub>10</sub>H<sub>15</sub>Br<sub>2</sub>N<sub>3</sub>O: C, 34.01; H, 4.29; N, 11.90; Br, 45.26. Found: C, 34.01; H, 4.27; N, 11.82; Br, 45.50.

Concentration of the mother liquors yielded **5**: mp 61-63 °C; NMR [(CD<sub>3</sub>)<sub>2</sub>CO],  $\delta$  1.16 (t, 3, CH<sub>3</sub>CH<sub>2</sub>), 1.58 (d, 3, CH<sub>3</sub>CH), 1.75 (q, 2, CH<sub>3</sub>CH<sub>2</sub>), 2.90 [s, 6, N(CH<sub>3</sub>)<sub>2</sub>], 5.41 (q, 1, CH<sub>3</sub>CH-).

Anal. Calcd for C<sub>10</sub>H<sub>15</sub>Br<sub>2</sub>N<sub>3</sub>O: C, 34.01; H, 4.29; N, 11.90; Br, 45.26. Found: C, 34.11; H, 4.19; N, 12.14; Br, 45.22.

**Ethyl 3,4-Dibromo- $\alpha$ ,5-dimethylpyrazole-1-acetate (7).** To a solution of 4,5-dibromo-3-methylpyrazole (**6**) (13.7 g, 0.057 mol) in acetone (200 mL), anhydrous potassium carbonate (15.7 g, 0.114 mol) was added, followed by ethyl 2-bromopropionate (10.4 g, 0.06 mol) drop by drop. The mixture was stirred and heated under reflux for 2.5 h, filtered, the solvent removed, and the residue crystallized from hexane to yield **7** (14.5 g, 75%), mp 61-62 °C.

Anal. Calcd for C<sub>9</sub>H<sub>12</sub>Br<sub>2</sub>N<sub>2</sub>O<sub>2</sub>: C, 31.79; H, 3.56; N, 8.24. Found: C, 31.86; H, 3.55; N, 8.48.

**3,4-Dibromo- $\alpha$ ,5-dimethylpyrazole-1-acetic acid (8).** The ester **7** (5.1 g, 0.015 mol) in a solution of sodium hydroxide (0.8 g, 0.02 mol) in water (100 mL) was heated under reflux for 3 h, cooled, and extracted with ether. The aqueous layer was acidified with N hydrochloric acid and

extracted with ether, and after removal of the solvent and crystallization from acetone-hexane, **8** was obtained (4.0 g, 85%), mp 138 °C.

Anal. Calcd for C<sub>7</sub>H<sub>8</sub>Br<sub>2</sub>N<sub>2</sub>O<sub>2</sub>: C, 26.95; H, 2.59; N, 8.98. Found: C, 27.07; H, 2.61; N, 9.10.

**3,4-Dibromo-*N,N*, $\alpha$ ,5-tetramethylpyrazole-1-acetamide (9).** A suspension of the acid **8** in thionyl chloride (10 mL) was heated under reflux for 2.5 h and then evaporated to dryness under reduced pressure. A solution of the residue in benzene (100 mL) was added dropwise to a solution of dimethylamine (2 mL) in benzene (25 mL) and heated under reflux for 1 h. The reaction mixture was washed with water, the benzene removed, and the resulting oil (85% yield, 9:1 mixture of **9** and **16**) chromatographed on a column of silica gel. Elution with ether-chloroform (4:1) gave **16** which after crystallization from Skellysolve F had a melting point of 109-110 °C: NMR [(CD<sub>3</sub>)<sub>2</sub>CO]  $\delta$  1.60 (d, 3, CH<sub>3</sub>CH), 2.21 (s, 3, ArCH<sub>3</sub>), 2.95 [s, 6, N(CH<sub>3</sub>)<sub>2</sub>], 5.50 (q, 1, CH<sub>3</sub>CH-).

Anal. Calcd for C<sub>9</sub>H<sub>13</sub>Br<sub>2</sub>N<sub>3</sub>O: C, 31.88; H, 3.86; N, 12.40; Br, 47.14. Found: C, 31.96; H, 3.88; N, 12.68; Br, 46.92.

Further elution with the same solvent yielded **9** which was crystallized from ether-Skellysolve F and had a melting point of 69-71 °C: NMR [(CD<sub>3</sub>)<sub>2</sub>CO]  $\delta$  1.60 (d, 3, CH<sub>3</sub>CH), 2.31 (s, 3, ArCH<sub>3</sub>), 2.96 [s, 6, N(CH<sub>3</sub>)<sub>2</sub>], 5.50 (q, 1, CH<sub>3</sub>CH).

Anal. Calcd for C<sub>9</sub>H<sub>13</sub>Br<sub>2</sub>N<sub>3</sub>O: C, 31.88; H, 3.86; N, 12.40; Br, 47.14. Found: C, 31.82; H, 3.79; N, 12.53; Br, 46.89.

**3,4-Dibromo-*N,N*, $\alpha$ ,5-tetramethylthiopyrazole-1-acetamide (12).** To a solution of **9** (6.78 g, 0.02 mol) in pyridine (30 mL), phosphorous pentasulfide (6.66 g, 0.03 mol) was added, and the mixture was heated under reflux for 2 h with stirring. The cold solution was poured on ice and the solid obtained was filtered, dried, and recrystallized from ethyl acetate to give the thioamide **12**, mp 159-161 °C (40-65%).

Anal. Calcd for C<sub>9</sub>H<sub>13</sub>Br<sub>2</sub>N<sub>3</sub>S: C, 30.44; H, 3.69; N, 11.83; S, 9.03; Br, 45.00. Found: C, 30.51; H, 3.78; N, 11.89; S, 9.14; Br, 45.01.

**3,5-Dibromo-4-methylpyrazole (11).** To a stirred solution of tribromopyrazole (30.4 g, 0.1 mol) in ether (130 mL) at -30 °C under a nitrogen atmosphere, a 1.6 M

solution of butyllithium in hexane (260 mL, 0.4 mol) was added during 1 h. Stirring was continued for an additional 3 h, the temperature was lowered to  $-70^{\circ}\text{C}$ , and the reaction mixture treated with methyl iodide (56.8 g, 0.4 mol) and then allowed to come to room temperature. To the vigorously stirred mixture, water (100 mL) was added while keeping the temperature below  $+25^{\circ}\text{C}$ . The organic phase was discarded, the aqueous phase extracted with ether, and the organic layer again discarded. The aqueous layer was acidified with 3 N hydrochloric acid to yield a precipitate which was crystallized from hexane to yield 5.5 g of 11 (25%), mp  $156\text{--}158^{\circ}\text{C}$ .

Anal. Calcd for  $\text{C}_8\text{H}_8\text{Br}_2\text{N}_2$ : C, 20.02; H, 1.68; N, 11.68; Br, 66.62. Found: C, 19.87; H, 1.68; N, 11.90; Br, 66.68.

#### BIOLOGICAL METHODS

Initially, preemergence activity of each chemical was determined in the greenhouse on seven weed species: field bindweed (*Convolvulus arvensis* L.), buckhorn plantain (*Plantago lanceolata* L.), large crabgrass [*Digitaria sanguinalis* (L.) Scop], curly dock (*Rumex crispus* L.), johnsongrass [*Sorghum halepense* (L.) Pers.], wild oat (*Avena fatua* L.) and green foxtail [*Setaria viridis* (L.) Beauv]. One row of each species was sown in  $5.5 \times 7.5 \times 2.5$  in. oblong trays containing a synthetic soil composed of equal parts by volume of Fox sandy clay loam, peat moss, and no. 2 sand. Each chemical was ballmilled in water containing Polyfon F (0.01%), Nekal BA-75 (0.01%), LF-330 (0.01%), and Polyglycol P-4000 (0.005%) and then applied at a 10 lb/acre rate, followed by sufficient overhead sprinkler watering to incorporate the compounds into the soil profile. Treatments were rated visually 3 weeks after application using a 0 (no effect) to 10 (plants dead) scale relative to an untreated control; the data were averaged for the seven weed species.

Active chemicals were then applied preemergence at rates of 6, 3, and 1 lb/acre in a 100 gal/acre (gpa) spray volume to: corn (*Zea mays* L. var. RX 42), cotton (*Gossypium hirsutum* L. var. Delta Pine 16), rice (*Oryza sativa* L. var. Nato), soybean [*Glycine max* (L.) Merr. var. Amsoy 71], barnyardgrass [*Echinochloa crus-galli* (L.) Beauv.], bermudagrass [*Cynodon dactylon* (L.) Pers.], blackgrass (*Alopecurus myosuroides* L.), johnsongrass, tall morningglory [*Ipomoea purpurea* (L.) Roth], and velvetleaf (*Abutilon theophrasti* Medic.). The test involved two replicates with the crop species planted in the corners of  $5.5 \times 5.3 \times 2.8$  in. trays and the weeds in rows in the oblong trays. Visual ratings of injury were recorded 3 weeks after treatment; averages for each species are presented.

Compounds 9 and 40 were evaluated for preplant incorporated and preemergence activity under field conditions on Fox sandy clay loam soil near Kalamazoo, Mich. Compound 9 was applied at 0.5, 1.0, 2.0, and 4.0 lb of active ingredient (AI)/acre to 20 ft<sup>2</sup> plots. The treatment solutions were prepared by suspending the appropriate amount of a 1 lb of AI/gal formulation in water and applying the equivalent of 40 gpa to the plots with a hand-held sprayer set to deliver spray solution at 40 psi. A power driven rototiller set to cut 2.5 in. deep was used for incorporations which were completed within 1 h after application. Two 20-ft rows spaced 6 in. apart each of corn, cotton, sorghum [*Sorghum bicolor* (L.) Moench var. Duet], soybean, sugarbeet [*Beta vulgaris* L. var. G.W. MonoHy A-1], and tomato (*Lycopersicon esculentum* Mill var. Rutgers) were sown with a drill immediately after incorporation was completed. One row of peanuts (*Arachis hypogaea* L. var. Starr) was also hand planted into the plots. Preemergence applications of the same rates of

compound 9 were made immediately after planting. Injury of crops and weeds was assessed visually 27 days after treatment. Compound 40 was applied at 0.2, 0.4, 0.8, 1.6, 2.4, and 3.2 lb AI/acre on 160 ft<sup>2</sup> plots. The treatment solutions were prepared by suspending the appropriate amount of a 25% wettable powder formulation in water and applying the equivalent of a 50 gpa spray solution. One 10-ft row with 36-in. spacing of the same crops, excluding peanuts, were sown immediately after incorporation was completed. Preemergence treatments of compound 40 were applied immediately after planting. Visual ratings were made 28 days after planting. All compound 9 and 40 treatments were replicated only once for each rate within each method. Untreated check plots were located in close proximity to all compound 9 and 40 treatments. All visual ratings were converted to percentages. Growth for each species within untreated plots was equated to 100%. Crop and weed percentage of control values were calculated and then fit to a semilog plot of rates for both compounds. The rates at which crop growth was 90% of control and weed control was 90% were then determined from a regression curve.

#### RESULTS AND DISCUSSION

The results in Tables I to IV suggest certain structure-activity relationships. The most active compounds are 9 and 40 (Tables I and III), both dihalopyrazoles with a methyl group in the 5 position and the *N,N*-dimethylpropionamide grouping linked to the ring nitrogen. Inspection of Table I shows that an increase in the length of the alkyl group leads to a decrease in herbicidal activity. This holds true whether the alkyl chain is in the 5 position of the pyrazole ring (compounds 9, 4, 13–15), or the 3 position (compounds 5, 16–19). It is also apparent that 9 (methyl in the 5 position) is more active than 16 or 20 (methyl in the 3 and 4 position, respectively).

In Table II it is shown that tertiary amides with short alkyl chains on the nitrogen have the best activity (compounds 21–25 vs. 26–28). This holds true for secondary amides also (29–31) which, however, are less active than tertiary amides. The size of the substituent on the carbon atom attached to the nitrogen of the pyrazole also has an effect on activity. Methyl (compounds 9, 21, and 23) imparts more activity than ethyl (32, 33, and 34) while hydrogen (35, 36, and 37) shows the least activity.

The results in Table III show that replacement of bromine with chlorine does not cause a marked change in activity. Again, the 5-methyl isomer (40) is more active than the 3-methyl isomer (46), and the tertiary amides (40, 41, and 44) are more active than the secondary amides (42 and 43). Replacement of one or both halogen atoms by hydrogen or alkyl generally decreases herbicidal activity. Out of the many compounds synthesized a selected number are shown in Table IV. Activity is decreased when chlorine is exchanged for hydrogen (40 vs. 47 and 46 vs. 48). Replacement of bromine with hydrogen or methyl in all three positions of the pyrazole ring also decreases activity (9 vs. 49 to 55).

Finally, tertiary amides are more active than tertiary thioamides, for example, 9 vs. 12, 20 vs. 56 and 49 vs. 58 (Tables I and IV).

Table V shows results on individual species. Phytotoxicity to barnyardgrass, bermudagrass, blackgrass, and johnsongrass decreased when the methyl group was shifted from the 5 to the 4 or 3 positions (compound 9, 20, and 16, respectively). This reduction of activity was true for the dichloro compounds 40 and 46, as well as the dibromo compounds. Compound 9 was less phytotoxic to cotton and soybean than compound 40, but effects on weeds were

Table V. Response of Ten Plant Species to Preemergence Applications (Visual Ratings; 1 lb/acre) of Substituted *N,N*, $\alpha$ -Trimethylpyrazole-1-acetamides

Species	9	40	20	16	46
Corn	3	5	1	0	3
Cotton	1	7	2	1	3
Rice	10	9	10	0	9
Soybean	1	6	4	0	1
Barnyardgrass	10	10	7	2	5
Bermudagrass	10	10	10	4	10
Blackgrass	10	10	8	2	6
Johnsongrass	5	7	4	0	5
Tall morningglory	0	0	0	0	0
Velvetleaf	4	0	3	1	2
Averages					
Crops	3.8	6.8	4.3	0.3	4.0
Grassy weeds	8.8	9.3	7.3	2.0	6.5
Broadleaf weeds	2.0	0	1.5	0.5	1.0

Table VI. Compound 9 and 40 Rates (lb AI/acre) Tolerated by Crops (90% of Control Growth) and Required to Control Weeds (90% Inhibition of Growth) in Field Evaluations

Species	9		40	
	Pre	PPI	Pre	PPI
Corn	2.0	>4.0	<0.2	0.3
Cotton	2.0	>4.0	0.2	0.2
Peanut	>4.0	>4.0		
Sorghum	1.0	0.9	0.2	0.2
Soybean	2.0	>4.0	0.8	0.9
Sugarbeet	1.0	1.1	<0.2	0.2
Tomato	>4.0	>4.0	>4.0	>4.0
Common ragweed			1.7	1.9
Lambsquarters	3.2	1.7	0.5	0.7
Redroot pigweed	1.2	1.2	<0.2	<0.2
Stinkgrass			1.7	1.8
Yellow mustard	3.0	2.0		
Average				
Crops	2.3	3.1	0.9	1.0
Weeds	2.5	1.6	1.0	1.2

similar. Compound 16 was less phytotoxic to both crops and weeds than compound 46.

Activity of compounds 9 and 40 was further evaluated in preplant incorporated and preemergence field applications. Preemergence applications of compound 9 were more phytotoxic to soybean than the incorporated ap-

plications (Table VI). The incorporated treatments were more efficacious than the surface treatments. Corn, cotton, peanut, soybean, and tomato exhibited tolerance to compound 9 at rates (1.6 to 2.5 lb/acre) that selectively controlled some annual weeds. Compound 40 was more phytotoxic to both crops and weeds than compound 9, as expected from greenhouse results. Activity of compound 40 was not altered by application method. Only tomato exhibited tolerance to compound 40 at weed control rates (<2.0 lb/acre). Susceptible plants usually emerged from soil treated with these amides; but they remained stunted, often in the cotyledonary leaf stage. Roots of the injured plants were always bulbous and abnormally short. Secondary roots were usually highly proliferated. These injured plants usually did not die unless exposed to environmental stresses such as severe drying during hot weather.

These results suggest that compound 9 might selectively control annual weeds in a major food crop.

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## Herbicidal Activity and Redox Properties of 3-Aryl-6-(perfluoroalkyl)-1,2,4,5-tetrazines and 1,2-Dihydro Derivatives

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1,2-Dihydro-3-aryl-6-(perfluoroalkyl)-*s*-tetrazines (VI) and 3-aryl-6-(perfluoroalkyl)-*s*-tetrazines (VII) show postemergence activity against broadleaf weeds, with little activity on grasses. The responses to light and plant symptoms resulting from foliar applications of VI and VII are similar to those of redox herbicides such as paraquat. The chemical behavior supports this view, i.e., *s*-tetrazines are reversibly reduced to 1,2-dihydro-*s*-tetrazines. The *s*-tetrazines and their 1,2-dihydro derivatives are phytotoxic only when treated plants are in the light; they were relatively inactive in preemergence herbicide tests. In aqueous solution, especially at pH above 7, both VI and VII decompose to redox inactive products that are herbicidally inactive. In general, electron-withdrawing substituents tend to stabilize the tetrazine ring and increase herbicidal activity.

With the discovery of the phytotoxic properties of the dipyrindylum herbicides, paraquat and diquat, and by the

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knowledge that the one-electron transfer which is reversed by oxygen is intimately involved in their mode of biological action (Homer et al., 1960) interest in redox systems has increased. Investigations in our laboratories showed that 3-aryl-6-(perfluoroalkyl)-1,2,4,5-tetrazines and their 1,2-