[^{14}C]mephosfolan in rats (Kapoor et al., 1976) and thiocyanate was identified as a major urinary and tissue metabolite.

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Phenylpyrazole Amide Herbicides

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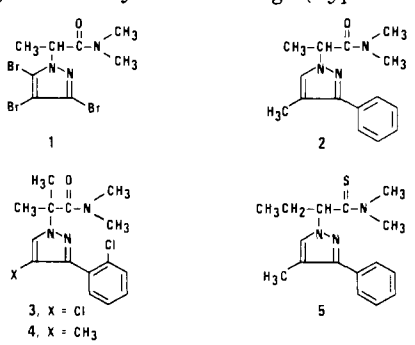
N,N,α,4-Tetramethyl-3-phenylpyrazole-1-acetamide (**2**) and a series of related phenylpyrazole amides have been found active as preemergence herbicides. The compounds showed activity at low rates on many broadleaf and grassy weeds and were exceptionally phytotoxic to yellow nutsedge. In greenhouse tests incorporated applications of the more active compounds controlled nutsedge at rates near 0.01 lb/acre. The effects of chemical placement, simulated rainfall, and application method on activity of the compounds are described. Information on soil mobility of representative compounds is presented. Results of field tests are presented showing weed control for several of the compounds at rates less than 1 lb/acre.

A report from our laboratories has described the herbicidal activity of 1 and other bromopyrazoles (Chambers et al., 1972). In related work we have found *N,N,α*,4-tetramethyl-3-phenylpyrazole-1-acetamide (**2**) to be active as a preemergence herbicide. The compound controlled many annual broadleaf and grassy weeds and was exceptionally active on yellow nutsedge (*Cyperus esculentus*



L.) and purple nutsedge (*Cyperus rotundus* L.). Many analogues of **2** have been prepared (Moon and Kornis, 1976) and compounds more active (e.g., **3** and **4**) and more selective (e.g., **5**) than **2** have been found. Activities of this

The Upjohn Company, Kalamazoo, Michigan 49004.

Scheme I. Synthesis of *N,N,α*,4-Tetramethyl-3-phenylpyrazole-1-acetamide

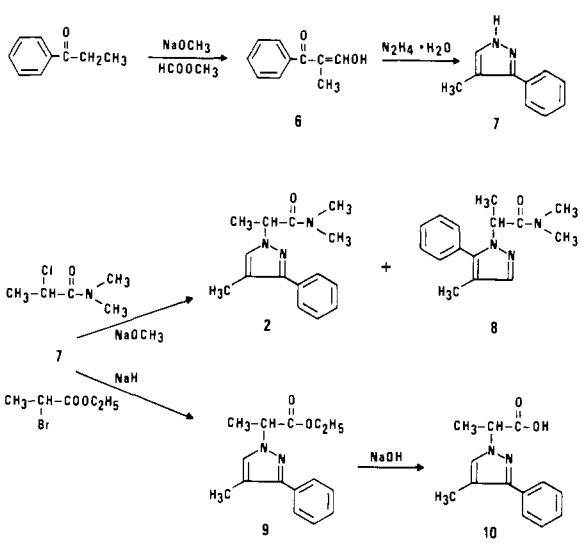
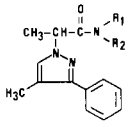


Table I. Chemical Data and Herbicidal Activities for Substituted α,4-Dimethyl-3-phenylpyrazole-1-acetamides



Compd no.	R_1	R_2	Mp, °C	Average preemergence herbicidal activity 10 lb/acre	6 lb/acre	3 lb/acre	1 lb/acre	ED_{50} (lb/acre) *C. esculentus*
15	H	H	99-101	3.6				>0.5
16	H	CH_3	111-112	6.6	7.0	5.2	4.0	0.4
17	H	C_2H_5	78-79	7.3	7.3	7.0	6.3	0.4
18	H	C_4H_9	82-84	5.9	7.3	6.8	7.0	>0.5
19	H	C_6H_5	79-82	4.1	6.0	5.5	4.0	>2.0
2	CH_3	CH_3	74-76[a]	8.1	9.5	7.8	5.8	0.10
20	CH_3	C_2H_5	59-61	8.6	10.0	10.0	8.0	0.06
21	CH_3	C_6H_5	111-114	5.7	6.3	6.0	4.0	>2.0
22	C_2H_5	C_2H_5	55-57	9.9	10.0	7.3	4.0	0.15
23	C_3H_7	C_3H_7	176 (0.6 mm)	6.7	9.3	7.8	6.5	>0.5
24	$-CH_2CH_2CH_2CH_2-$		77-79	8.0	7.8	7.3	5.0	0.5
25	$-CH_2CH_2-O-CH_2CH_2-$		83-96	8.0	8.8	7.3	3.5	0.20

[a] A polymorphic form of this compound, mp 87-89 °C, has been obtained from aqueous methanol or ethyl acetate.

series of compounds in greenhouse tests and field trials are described in this report. Factors that may affect performance of these herbicides, such as soil mobility, soil moisture level, soil type, seeding depth, and application method are also discussed.

MATERIALS AND METHODS

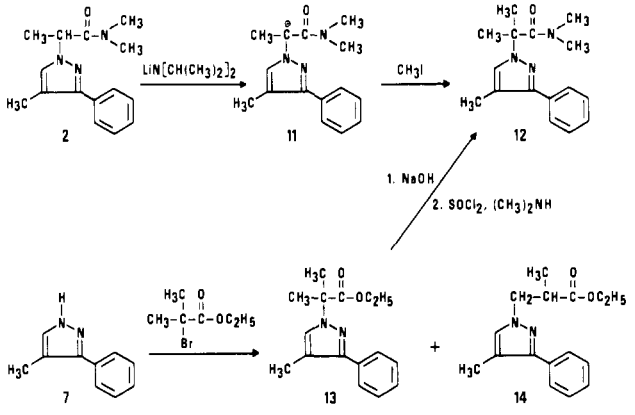
Chemical Methods. Propiophenone was condensed with methyl formate and hydrazine hydrate to give 4-methyl-3-phenylpyrazole (**7**, Buchi et al., 1955); the intermediate 3-hydroxy-2-methylacrylophenone (**6**, Claisen and Meyerowitz, 1889) could be isolated as a crystalline solid if desired, but its isolation was unnecessary. Alkylation of **7** (Scheme I) with *N,N*-dimethyl-2-chloropropionamide in THF using sodium hydride or sodium methoxide as a base gave a mixture of **2** (86%) and **8** (14%), which was readily separated by silica gel chromatography. That the major, less polar component was the 3-phenyl isomer was evident from the work of von Auwers and Breyhan (1935) and Jones et al. (1954); this isomer showed a characteristic NMR downfield shift for the ortho hydrogens in the benzene ring which was not found for the 5-phenyl isomer **8** (Tensmeyer and Ainsworth, 1966; Elguero et al., 1966).

Alkylation of **7** with ethyl 2-bromopropionate gave **9** as the major product. The alkylation reaction went to completion using sodium hydride in THF, but was incomplete in methanol using sodium methoxide as base. Alkaline hydrolysis of **9** gave **10**, which was converted via the acid chloride to amides **15–25** (Table I). The same reaction sequence was used to prepare amides **52–55** (Table IV) from the appropriate ester.

Alkylation of the appropriate phenylpyrazole, prepared by literature methods (see references cited in Table II), using *N,N*-dimethyl-2-chloropropionamide gave compounds **26–29**, **31–33**, **35**, **36**, and **38–46** (Table II); the 5-phenyl isomers were isolated as the minor alkylation products in several of these reactions (Table III). Compound **29** reacted with cuprous cyanide in dimethylformamide to give **30**. Bromination of **32** with bromine in acetic acid gave **34**, and chlorination of **36** with *tert*-butylhypochlorite in carbon tetrachloride gave **37**.

The α,α-dimethylamides of Table V were prepared in two ways as illustrated in Scheme II for the synthesis of **12**.

Scheme II. Synthesis of *N,N,α,α,4*-Pentamethyl-3-phenylpyrazole-1-acetamide

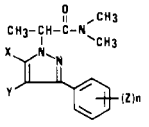


Addition of 1 equiv of lithium diisopropylamide to a solution of **2** in tetrahydrofuran generated anion **11** which reacted with methyl iodide to give **12**. This rapid reaction was conveniently run on a small scale (5–100 g) and was used to prepare compounds **56–71** (Tables IV and V) from the appropriate pyrazole amide intermediates (Table II). A procedure more suitable for the synthesis of large quantities of **12** involved reacting 4-methyl-3-phenylpyrazole (**7**), with ethyl 2-bromo-2-methylpropionate. This reaction gave a mixture of pyrazole esters **13** (78%) and **14** (15%), together with smaller amounts of the 5-phenyl isomers of **13** and **14** (7%); compound **14** resulted from elimination of hydrogen bromide from the bromo ester, followed by Michael addition of **7** to the resulting ethyl methacrylate. Ester **13** was purified by chromatography on silica gel and was hydrolyzed to the acid and converted to dimethylamide **12** via the acid chloride. The crude ester mixture was also directly converted to **12** which was readily freed from isomeric amides by crystallization.

Thioamide **5** was readily prepared by heating **53** with phosphorus pentasulfide at 130 °C. Compounds **72–74** (Table VI) were prepared by refluxing the corresponding amides (**2**, **12**, and **4**) in pyridine with phosphorus pentasulfide.

Structures and purities of the new chemicals were determined by NMR, GC, IR, and TLC analyses; satisfactory chemical analyses (±0.3%) were obtained for all com-

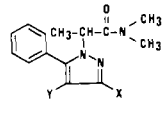
Table II. Chemical Data and Herbicidal Activities for Substituted N,N,α-Trimethyl-3-phenylpyrazole-1-acetamides[a]



Compd no.	X	Y	(Z)n	Mp, °C[b]	Average preemergence herbicidal activity 10 lb/acre	6 lb/acre	3 lb/acre	1 lb/acre	ED_{50} (lb/acre) *C. esculentus*
26	H	H		79-80	8.4	9.0	4.3	2.5	>0.50
2	H	CH_3		74-76	8.1	9.5	7.8	5.8	0.10
27	H	C_2H_5		73-75	7.6	9.3	4.0	2.9	0.06
28	H	Cl		73-75	7.6	9.5	8.5	7.5	0.17
29	H	Br		90-91	6.3	4.0	3.3	2.0	0.13
30	H	CN		144-146	6.4	5.5	1.8	1.8	>0.50
31	H	C_6H_5		151-153	4.1				>2.00
32	CH_3	H		98-99	6.9	8.8	5.8	0.3	>1.00
33	CH_3	CH_3		76-79	8.3	9.5	8.8	4.8	0.50
34	CH_3	Br		88-89	8.1	7.5	6.3	1.8	0.50
35	C_6H_5	H		133-135	3.4				>2.00
36	H	H	2-Cl	176 (0.1 mm)	9.1	10.0	10.0	9.3	0.11
37	H	Cl	2-Cl	108-111	8.6	8.8	7.5	5.5	0.08
38	H	CH_3	2-Cl	98-100	8.4	9.3	9.3	7.8	0.03
39	H	CH_3	3-Cl	73-75	4.5	7.0	5.8	0.5	2.0
40	H	CH_3	4-Cl	99-101	4.5	3.3	2.5	0.8	>2.0
41	H	CH_3	2,4-Cl_2	190 (0.3 mm)	3.5				0.5
42	H	CH_3	2,5-Cl_2	190 (0.3 mm)	6.3				>1.0
43	H	CH_3	2,6-Cl_2	76-79	7.0	9.5	7.5	6.0	0.15
44	H	CH_3	3,4-Cl_2	109-111	1.1				>2.0
45	H	CH_3	2-CH_3	178 (0.7 mm)	6.7	9.0	8.8	6.5	0.07
46	H	CH_3	2-OCH_3	180 (0.6 mm)	6.4	7.3	7.5	4.3	0.10

[a] The phenylpyrazole intermediates were prepared by the procedure described in Scheme I for the synthesis of **7** or by related literature procedures. The compounds had the following melting points (compound number for amide product, mp of phenylpyrazole intermediated): **26**, 76-78 °C (Knorr and Boettinger, 1894); **27**, 73-75 °C, **28**, 101-104 °C (von Auwers and Breyhan, 1935); **29**, 112-114 °C (Knorr, 1895); **31**, 149-152 °C (Wislicenus and Ruthing, 1911); **32**, 115-125 °C (Sjollema, 1894); **33**, 105-107 °C (Jacquier et al., 1966); **35**, 202-207 °C (Knorr and Duden, 1893); **36**, 90-92 °C (Kochetkov et al., 1957); **38**, 92-95 °C; **39**, 93-96 °C; **40**, 127-130 °C; **41**, 111-113 °C; **42**, 115-116 °C; **44**, 131-132 °C; **45**, 75-78 °C; **46**, 109-112 °C. [b] Boiling points at reduced pressure are provided for liquids.

Table III. Chemical Data and Herbicidal Activities for Substituted N,N,α-Trimethyl-5-phenylpyrazole-1-acetamides



Compd no.	X	Y	Mp, °C	Average preemergence herbicidal activity, 10 lb/acre
47	H	H		2.7
8	H	CH_3	88-90	4.6
48	H	Cl	100-102	3.6
49	H	Br	117-119	5.0
50	H	C_6H_5	151-153	3.4
51	CH_3	H	91-93	2.3

pounds. The general synthetic procedures used are illustrated below for the synthesis of representative compounds.

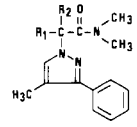
4-Methyl-3-phenylpyrazole (7). A solution of sodium methoxide in methanol (22%, 1.7 mol base) was added over a period of 20 min to a stirred solution of propiophenone (268 g, 2.0 mol) in methyl formate (500 mL). After stirring for an additional 15 min, excess methyl formate was evaporated under reduced pressure. The residual oil was diluted with methanol (250 mL) and water (250 mL), acidified with acetic acid (150 mL), and cooled to 10 °C. Addition of hydrazine hydrate (100 g, 2 mol) raised the temperature of the solution to 60 °C. After cooling and addition of Skellysolve B (300 mL), the solution was filtered to give 180.7 g (57%) of **7**, mp 113–116 °C.

Reaction of 7 with *N,N*-Dimethyl-2-chloropropionamide. To a stirred solution of the sodium salt of **7**, prepared by addition of sodium hydride (3.0 g, 57% in oil, 0.071 mol) to 4-methyl-3-phenylpyrazole (10.5 g, 0.066 mol) in THF (100 mL), was added 10.0 g (0.075 mol) of *N,N*-dimethyl-2-chloropropionamide. After 18 h, the solution was evaporated and the residue was partitioned between chloroform and water. The residue obtained on evaporation of the chloroform phase was chromatographed on silica gel using benzene–ethyl acetate as eluent to give, as the first product eluted from the column, N,N,α,4-tetramethyl-3-phenylpyrazole-1-acetamide (**2**, 17.7 g). Two recrystallizations from cyclohexane gave the analytical sample, mp 74.5–76.5 °C: NMR ($CDCl_3$) δ 1.63 (d, 3, CH_3-CH), 2.20 (s, 3, $ArCH_3$), 2.92 (s, 3, N-CH_3), 3.02 (s, 3, N-CH_3), 5.43 (q, 1, CH_3CH), 7.30–7.50 (m, 4, ArH), and 7.56–7.80 (m, 2, ArH).

Anal. Calcd for $C_{15}H_{19}N_3O$: C, 70.00; H, 7.44; N, 16.33. Found: C, 70.18; H, 7.46; N, 16.62.

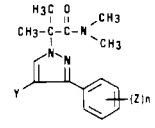
Continued elution of the column gave N,N,α,4-tetramethyl-5-phenylpyrazole-1-acetamide (**8**, 2.4 g). Recrystallization from benzene–Skellysolve B followed by ethyl acetate gave the analytical sample, mp 88–90 °C; NMR ($CDCl_3$) δ 1.67 (d, 3, CH_3CH), 1.97 (s, 3, $ArCH_3$), 2.57 (s, 3, N-CH_3), 2.83 (s, 3, N-CH_3), 5.02 (q, 1, CH_3CH), and 7.15–7.55 (m. 6, ArH).

Table IV. Chemical Data and Herbicidal Activities for Substituted *N,N*,4-Trimethyl-3-phenylpyrazole-1-acetamides



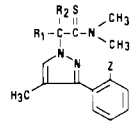
Compd no.	R_1	R_2	Mp, °C	Average preemergence herbicidal activity				ED_{50} (lb/acre) *C. esculentus*
				10 lb/acre	6 lb/acre	3 lb/acre	1 lb/acre	
52	H	H	80-82	7.6	7.5	4.8	2.0	0.50
2	H	CH_3	74-76	8.1	9.5	7.8	5.8	0.10
53	H	C_2H_5	86-88	7.3	10.0	10.0	7.3	0.06
54	H	C_3H_7	84-86	6.9	8.5	7.5	7.3	0.06
55	H	C_6H_5	135-138	3.9				>2.00
12	CH_3	CH_3	107-109	8.6	9.8	9.3	9.3	0.04
56	CH_3	C_2H_5	102-104	9.3	10.0	10.0	9.8	0.04
57	CH_3	C_3H_7	90-92	8.0	10.0	10.0	8.8	0.05
58	CH_3	C_6H_5	107-109	7.7	9.5	9.0	8.0	0.15
59	C_2H_5	C_2H_5	135-136	7.6	7.5	8.3	6.8	0.20

Table V. Chemical Data and Herbicidal Activities for Substituted *N,N*,α,α-Tetramethyl-3-phenylpyrazole-1-acetamides



Compd no.	Y	(Z)*n*	Mp, °C	Average preemergence herbicidal activity				ED_{50} (lb/acre) *C. esculentus*
				10 lb/acre	6 lb/acre	3 lb/acre	1 lb/acre	
60	H		99-102	7.0	7.8	7.8	6.5	0.20
61	Cl		117-119	8.2	10.0	10.0	8.3	0.09
12	CH_3		107-109	8.6	9.8	9.3	9.3	0.04
62	H	2-Cl	79-81	9.3	9.8	9.8	9.5	0.06
3	Cl	2-Cl	161-163	8.6	10.0	9.2	8.0	0.01
4	CH_3	2-Cl	175-176	8.3	10.0	10.0	9.3	0.01
63	CH_3	3-Cl	144-147	5.5	5.3	4.5	2.5	>1.0
64	CH_3	4-Cl	121-123	5.0	5.3	3.8	1.8	>1.0
65	CH_3	2,4-Cl_2	110-111	6.0	7.3	8.8	5.5	0.5
66	CH_3	2,5-Cl_2	129-131	3.5				>0.5
67	CH_3	2,6-Cl_2	76-79	7.3	9.5	9.8	9.0	0.07
68	CH_3	2-F	112-114	7.7	10.0	10.0	9.8	<0.01
69	CH_3	2-Br	191-194	6.9	9.5	9.8	9.8	0.02
70	CH_3	2-CH_3	145-147	8.8	9.3	9.3	8.0	0.02
71	CH_3	2-OCH_3	146-148	7.6	9.8	9.8	8.3	0.04

Table VI. Chemical Data and Herbicidal Activities of Substituted *N,N*,4-Trimethyl-3-phenylpyrazole-1-thioacetamides



Compd no.	R_1	R_2	Z	Mp, °C	10 lb/acre	6 lb/acre	3 lb/acre	1 lb/acre	ED_{50} (lb/acre) *C. esculentus*
72	CH_3	H		87-89	6.8	9.0	8.0	5.0	
5	CH_3CH_2	H		107-110	6.3	6.3	5.3	5.3	0.13
73	CH_3	CH_3		115-117	6.9	8.3	8.0	5.8	0.10
74	CH_3	CH_3	Cl	146-148	6.7	9.8	9.8	9.8	0.04

Anal. Calcd for $C_{15}H_{19}N_3O$: C, 70.00; H, 7.44; N, 16.33. Found: C, 70.13; H, 7.51; N, 16.49.

α,4-Dimethyl-3-phenylpyrazole-1-acetic acid (10). Sodium hydride (50.0 g, 57% in oil, 1.2 mol) was added over 20 min to a stirred solution of 4-methyl-3-phenylpyrazole (158 g, 1.0 mol) in THF (1.0 L) maintained at 10–20 °C. Ethyl 2-bromopropionate (235 g, 1.3 mol) was added and the solution stirred for 18 h, after which time ethanol was added and the solvent was removed by evaporation at reduced pressure. The residue was treated at 90 °C with sodium hydroxide (100 g, 2.5 mol) in 800 mL of 60% aqueous methanol for 30 min. After cooling, the solution was extracted with ether (3 × 200 mL), and the aqueous phase was acidified with concentrated hydrochloric acid to give 148 g of crude α,4-dimethyl-3-phenylpyrazole-1-acetic acid (**10**), mp 151–162 °C. Recrystallization from aqueous methanol gave 111 g of **10**, mp 168–172 °C. The analytical sample was recrystallized from ethyl acetate, mp 170–172 °C.

Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 68.32; H, 6.14; N, 12.06.

***N*-Ethyl-α,4-dimethyl-3-phenylpyrazole-1-acetamide (17).** A mixture of α,4-dimethyl-3-phenylpyrazole-1-acetic acid (**10**, 11.5 g, 0.05 mol), thionyl chloride

(7.5 g, 0.06 mol), and benzene (300 mL) was heated under reflux for 1 h and then cooled. Ethylamine (30 mL of 25% aqueous solution) was added with stirring to one-half of the above solution. The benzene layer was separated, washed with water, and the benzene evaporated. The residual oil (8.3 g) was recrystallized twice from benzene–Skellysolve B to give 4.2 g of **17**, mp 78–80 °C.

Anal. Calcd for $C_{15}H_{19}N_3O$: C, 70.00; H, 7.44; N, 16.33. Found: C, 70.14; H, 7.30; N, 16.49.

4-Cyano-*N*,*N*,α-trimethyl-3-phenylpyrazole-1-acetamide (30). A mixture of 4-bromo-*N*,*N*,α-trimethyl-3-phenylpyrazole-1-acetamide (**29**, 8.0 g, 0.025 mol), cuprous cyanide (25.0 g, 0.28 mol), and dimethylformamide (200 mL) was heated under reflux for 18 h. Water was added and the solution was repeatedly extracted with chloroform. Evaporation of the chloroform gave a residue (7.5 g), which was recrystallized from benzene–Skellysolve B to give 6.5 g of **30**, mp 143–146 °C. Two recrystallizations from ethyl acetate gave the analytical sample, mp 144–146 °C.

Anal. Calcd for $C_{15}H_{16}N_4O$: C, 67.14; H, 6.01; N, 20.88. Found: C, 67.12; H, 6.12; N, 21.18.

4-Bromo-*N*,*N*,α,5-tetramethyl-3-phenylpyrazole-1-acetamide (34). Bromine (3.68 g, 0.023 mol) was added to a solution of *N*,*N*,α,5-tetramethyl-3-phenylpyrazole-1-acetamide (**32**, 5.0 g, 0.019 mol) in acetic acid (25 mL). After 1 h, the solution was diluted with water to give 6.3 g of **34**, mp 88–89.5 °C. Recrystallization from benzene–Skellysolve B and finally ether gave the analytical sample, mp 88–89.5 °C.

Anal. Calcd for $C_{15}H_{18}BrN_3O$: C, 53.58; H, 5.40; Br, 23.77; N, 12.50. Found: C, 53.69; H, 5.54; Br, 23.69; N, 12.30.

α-Ethyl-*N*,*N*,α,4-tetramethyl-3-phenylpyrazole-1-acetamide (56). Lithium diisopropylamide (0.055 mol) was prepared by adding butyllithium (36 mL of 1.6 M solution in hexane) to a stirred solution of diisopropylamine (5.6 g) in THF (100 mL) at −40 °C. A solution of *N*,*N*,α,4-tetramethyl-3-phenylpyrazole-1-acetamide (**2**, 12.8 g, 0.05 mol) in THF was added and after 15 min ethyl iodide (30 g) was added. The reaction was stirred for a further 30 min and the solvent was then evaporated under reduced pressure. The residual oil was partitioned between chloroform and water. Evaporation of the chloroform gave an oil which was crystallized from ethyl acetate to give 10.1 g of **56**, mp 102–104 °C.

Anal. Calcd for $C_{17}H_{23}N_3O$: C, 71.54; H, 8.12; N, 14.73. Found: C, 71.59; H, 7.75; N, 14.91.

***N*,*N*,α,α,4-Pentamethyl-3-phenylpyrazole-1-acetamide (12).** Sodium hydride (25.0 g of 57% dispersion in oil, 0.6 mol) was added to a stirred solution of 4-methyl-3-phenylpyrazole (79.0 g, 0.5 mol) in tetrahydrofuran. Ethyl-2-bromoisobutyrate (136.0 g, 0.7 mol) was added and the solution was refluxed for 4 h. The solvent was removed by evaporation and the residual ester mixture was hydrolyzed by refluxing with methanolic sodium hydroxide solution (40 g of sodium hydroxide in 600 mL of 30% methanol–water). After cooling, the alkaline reaction solution was extracted with ether and the aqueous phase was acidified with concentrated hydrochloric acid. The solution was extracted with chloroform, and the chloroform layer was evaporated to give a crude acid mixture in which α,α,4-trimethyl-3-phenylpyrazole-1-acetic acid was the major isomer.

The crude acid was dissolved in benzene (1.0 L), thionyl chloride (59.5 g, 0.5 mol) was added, and the solution was refluxed for 3 h. After cooling, the solution was added slowly to a stirred solution of 25% aqueous dimethylamine (300 mL) containing ice (500 g). After 10 min, the benzene layer was separated, washed with water, and evaporated to afford 100 g of mixed dimethylamides.

Chromatography on silica gel afforded 66 g of *N*,*N*,-α,α,4-pentamethyl-3-phenylpyrazole-1-acetamide (**12**), which was recrystallized from ethyl acetate; mp 107–109 °C.

Anal. Calcd for $C_{16}H_{21}N_3O$: C, 70.82; H, 7.80; N, 15.49. Found: C, 70.98; H, 7.90; N, 15.73.

Further elution of the column afforded 3.7 g of *N*,*N*,-α,α,4-pentamethyl-5-phenylpyrazole-1-acetamide, which was recrystallized twice from ethyl acetate for analysis; mp 136–139 °C.

Anal. Calcd for $C_{16}H_{21}N_3O$: C, 70.82; H, 7.80; N, 15.49. Found: C, 71.03; H, 7.98; N, 15.74.

Further elution of the column afforded 6.2 g of *N*,*N*,-α,4-tetramethyl-3-phenylpyrazole-1-propionamide, which was recrystallized twice from ethyl acetate for analysis; mp 51–54 °C.

Anal. Calcd for $C_{16}H_{21}N_3O$: C, 70.82; H, 7.80; N, 15.49. Found: C, 71.08; H, 7.79; N, 15.42.

α-Ethyl-*N*,*N*,4-trimethyl-3-phenylpyrazole-1-thioacetamide (5). A mixture of phosphorus pentasulfide (5.5 g, 0.025 mol) and α-ethyl-*N*,*N*,4-trimethyl-3-phenylpyrazole-1-acetamide (**53**, 27.1 g, 0.1 mol) was heated with stirring at 130 °C for 45 min. The dark-red solution was cooled to 70 °C and was dissolved in methanol (200 mL). After cooling to −10 °C, the precipitate of compound **5** (24.6 g, 86%) was filtered off; mp 103–107 °C.

Anal. Calcd for $C_{16}H_{21}N_3S$: C, 66.85; H, 7.37; N, 14.62; S, 11.15. Found: C, 66.76; H, 7.56; N, 14.70; S, 11.02.

Biological Methods. Activity of the chemicals under greenhouse conditions was determined using a soil mixture composed of equal parts by volume of soil (Fox sandy clay loam), peat moss, and No. 2 sand. Initial testing involved a single treatment on seven weed species sown in rows across 5.5 × 7.5 × 2.5 in. trays. Each chemical was ball-milled in water containing Polyfon F (0.01%), Nekal BA-75 (0.01%), LF-330 (0.01%), and Polyglycol P-4000 (0.005%). For the initial tests, chemicals were applied preemergence at 10 lb/acre to field bindweed (*Convolvulus arvenis* 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). 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 (Tables I–VI).

Active chemicals were then applied preemergence at 6, 3, and 1 lb/acre rates to barnyardgrass (*Echinochloa crus-galli* (L.) Beauv.), bermudagrass (*Cynodon dactylon* (L.) Pers.), blackgrass (*Alopecurus myosuroides* L.), and johnsongrass. The test involved two replicates with the four species planted in the corners of 5.5 × 5.25 × 2.7 in. trays; treatments were visually rated and the ratings were averaged as in the initial test (Tables I–VI).

The chemicals were further evaluated in triplicate in 5.5 × 5.25 × 2.75 in. trays (700 g of air dry soil) on yellow nutsedge (*Cyperus esculentus* L., 9–12 tubers/tray). For these tests, the appropriate amount of chemical from a stock solution (0.50 mg/mL in acetone) was diluted with water and uniformly incorporated throughout the soil. Initial testing was carried out at 2.0, 1.0, and 0.5 lb/acre. Compounds showing good control at the lowest rate were further evaluated at six rates (0.5, 0.4, 0.3, 0.2, 0.1, and 0.05 lb/acre). Control percentages were calculated based on

Table VII. Rates of Compounds Required to Give 85% Growth Reduction of Various Species

Species	Rate, lb/acre			
	2	12	3	4
Grasses/Grasslike weeds				
Barnyardgrass (*Echinochloa crus-gali* L.)	1.0	0.4	0.4	0.2
Downeybromegrass (*Bromus tectorum* L.)	0.3	0.3	0.2	<0.1
Fall panicum (*Panicum dicholomiflorum* Michx.)	1.7	0.8	0.4	0.2
Giant foxtail (*Setaria faberi* Herrm)			0.2	0.4
Green foxtail (*Setaria virdis* (L.) Beauv.)	1.2	0.6	0.2	0.1
Johnsongrass (*Sorghum halepense* L.)	5.1	1.2	0.8	0.8
Purple nutsedge (*Cyperus rotundus* L.)	0.18			0.12
Wild oat (*Avera fatua* L.)	5.1	3.1	2.0	
Yellow foxtail (*Setaria lutescens* (Weigel) Hubb.)	1.0	0.5	0.2	0.1
Broadleaf weeds				
Pale smartweed (*Polygonum lapathifolium* L.)	0.4	0.2	0.2	0.2
Velvetleaf (*Abutilon theopasti* Medic.)	1.6	1.6	0.8	0.8
Wild mustard (*Brassica kaber* D.C.)	0.3	0.1	0.1	

Table VIII. Effect of Soil Type on Yellow Nutsedge Control

Soil	Organic matter, %	ED_{50} (lb/acre) *C. esculentus*		
		2	3	4
Sandy clay loam[a]	2.7	0.020	0.011	0.008
Sandy loam[b]	5.3	0.039	0.011	0.018
Clay loam[c]	11.7	0.067	0.033	0.020

[a] 58.0% sand, 18.7% silt, 23.3% clay, 2.7% organic matter; pH 7.2. [b] 79.0% sand, 8.4% silt, 12.6% clay, 5.3% organic matter; pH 7.0. [c] 33.5% sand, 34.4% silt, 32.2% clay, 11.7% organic matter; pH 5.5.

comparison between treated and untreated average per plant weights. The rate required to cause 50% reduction of growth (ED_{50}) was then determined. The most active chemicals were again tested at six rates below 0.2 lb/acre to allow accurate determination of the ED_{50} values on nutsedge (Tables I–VI).

The activity of selected compounds on additional species (Table VII) was determined at six rates with three replications using 3 in. diameter plastic pots (200 g of air dry soil/pot). The chemicals were uniformly incorporated in the soil and activity, based on average fresh weight per plant as compared to untreated controls, was determined 3 weeks after application.

The effect of chemical placement on activity was determined by planting 40 yellow nutsedge tubers on a slant at depths of 0.4 to 4.0 in. in 9.0 × 6.0 × 9.0 in. containers (Figure 4). Compounds **3**, **4**, **12**, and **53** at a 0.5 lb/acre rate were uniformly incorporated in the upper 2 in. of the soil. Two replications of each compound and untreated controls were included in a completely random design. Fresh top weight was obtained approximately 25 days after treatment. Weights were collected from ten equal increments across the length of each container's top in order to relate chemical effect and tuber depth. In all cases, percentage control values were calculated. Because growth was a function of tuber depth as well as chemical effect, treated growth per increment was equated to untreated control growth from tubers planted at a similar depth.

Activation of compounds by simulated rainfall was studied using corn planted 0.5 or 2.0 in. deep in 5.5 × 5.7 × 2.5 in. trays. Compounds were applied on the surface of the trays at appropriate rates (Table IX), and not incorporated or incorporated with 0.1 and 0.3 in. of simulated rain. Four replicates, each containing ten corn plants, were included in the test. Top fresh weights were collected 2 weeks after treatment and these were averaged and converted to percentages of control.

Injury to yellow nutsedge and corn with timed pre- and postemergence applications was determined using compound **12** at 0.5 lb/acre (Figure 5). The chemical was applied to soil in 5.5 × 5.7 × 2.5 in. trays into which were sown nine pregerminated yellow nutsedge tubers or eight corn seed. Application timing included: (a) preplant incorporation, (b) preemergence immediately after planting, (c) treatment 5 days after planting at corn emergence (nutsedge emerged 3 days after planting), (d) postemergence 7 and 12 days after corn emergence. An equivalent of 0.2 in. of rainfall was applied immediately after completion of the preemergence, emergence, and postemergence applications. A randomized complete block design was used, and four treated and untreated trays were included at each time. Treated and untreated plant fresh top weights were collected 14 days after each application. Average per plant weights were determined, then treated corn growth as a percentage of the untreated control or nutsedge growth as percent control were calculated.

Mobility of compounds on soil columns was determined using a Fox sandy clay loam soil (58% sand, 19% silt, 23% clay, 2.7% organic matter; soil pH 7.2). The soil (7% moisture content) was sieved through a 10-mesh screen and thoroughly mixed with an equal weight of silica sand. The base of a metal tube (12 in. × 3 in. i.d.) was covered with filter paper on an 18-mesh fiberglass screen. Silica sand (135 g) was introduced into the tube, and 1200 g of the soil mixture was packed, 50 g at a time, into the tube so as to

Table IX. Percentage of Control Values for Corn Planted at Two Depths and Treated with Surface Applications of Compounds 2, 12 and 53, or Alachlor followed by Simulated Rainfall for Activation

Compd	Rate, lb/acre	Seed depth, in.	Corn (% of control)			$LSD_{0.05}$	CV%
			No rain	0.1 in. rain	0.3 in. rain		
12	1.0	0.5	21	14	23	19	24
		2.0	38	30	19		
2	2.0	0.5	26	27	19	21	21
		2.0	34	38	21		
53	2.0	0.5	16	17	9	19	21
		2.0	44	34	18		
Alachlor	1.0	0.5	101	103	128	24	15
		2.0	74	90	86		

Table X. Rates of Various Compounds Tolerated by Crops (90% of Control Growth) and Required to Control Weeds (90% Inhibition of Growth Compared to the Control)

Species	Rate, lb of AI/acre						
	2	28	53	5	12	4	3
Crops							
Corn (*Zea mays* L.)	0.4	0.8	0.5	1.0	0.5	0.1	0.5
Cotton (*Gossipium hirsutum* L.)	0.2	0.4	1.0	2.0	0.3	0.1	0.5
Peanut (*Arachis hypogaea* L.)	1.5	1.5	1.5	2.4	2.4	2.4	0.8
Soybean (*Glycine max* L.)	1.0	2.0	0.5	1.0	0.3	<0.1	0.5
Tomato (*Lycopersicon esculentum* L.)	0.5	0.5	0.2	0.2	0.8	0.4	0.2
Average reading for crops	0.7	1.0	0.7	1.3	0.9	0.6	0.5
Broadleaf weeds							
Common ragweed (*Ambrosia artemisiifolia* L.)	2.0	4.0	1.0	1.6	0.8	0.1	0.3
Florida pusley (*Richardia scabra* L.)	1.5	1.0	0.5	0.8	0.8	0.2	0.4
Lambsquarters (*Chenopodium album* L.)	1.0	2.0	0.5	1.6	0.5	0.4	1.6
Redroot pigweed (*Amaranthus retroflexus* L.)	0.4	0.8	0.3	1.2	0.1	0.2	0.1
Tumbling pigweed (*Amaranthus albus* L.)	0.4	2.0	1.0	0.1	0.4	0.1	0.3
Velvetleaf (*Abutilon theophrasti* Medic.)			0.5	1.5	0.5	0.3	0.3
Average reading for broadleaf weeds	1.1	2.0	0.6	1.1	0.5	0.2	0.5
Grass/grasslike weeds							
Large crabgrass (*Digitaria sanguinalis* (L.) Scop.)	0.5	0.5	1.6	2.4	0.8	0.2	0.8
Stinkgrass (*Eragrostis cilianensis* (All.) Lutati.)	0.8	2.0	0.5	2.4	0.5	0.1	0.6
Yellow foxtail (*Setaria lutescens* (Weigel) Hubb.)	0.8	2.0	1.0	2.4	0.5	0.1	0.1
Yellow nutsedge (*Cyperus esculentus* L.)	2.0	>4.0	1.6	2.4	0.8	0.8	1.6
Average reading for grasslike weeds	1.0	2.1	1.2	2.4	0.7	0.3	0.8

give a 6 in. high soil column. Stock solutions (25 mL, 1 mg of compound/mL) of *N*,*N*-dimethyl-2,2-diphenylacetamide (diphenamid) and the pyrazole amides were prepared in acetone. One milliliter of the diphenamid solution and 1 mL of a pyrazole solution were added to 20 mL of water, and the resulting solution was applied to the top of the column. The column was covered with silica sand (180 g), and water (350 mL) was applied to the column. The water percolated through the column in 3–4 h, at which time the eluate (ca. 160 mL) was removed, concentrated ammonia solution (2 mL) added, and the solution was extracted with methylene chloride (3 × 50 mL). The combined methylene chloride extract was washed with water (25 mL) and evaporated. The residue was transferred to a small test tube using acetone (2 × 1.0 mL). Additional water (116 mL) was applied to the column, and the eluate was processed in the same manner. The process was repeated to give ten fractions over a period of about 36 h.

Solvent was removed from the test tubes and the residue was reconstituted in chloroform (0.50 mL). An aliquot (2 μL with a 2 μL solvent flush) was analyzed using a Microtek 220 gas chromatograph [a column of 3% OV-1 on 100–120 mesh Gas-Chrom Q (4 ft × 2 mm i.d.) at a temperature of 180–190 °C, nitrogen carrier gas (flow rate 40 mL/min), and a hydrogen flame ionization detector] to determine percentage of applied dose recovered in each fraction (Figure 6).

Mobility of the compounds was also determined by bioassay (Figure 7). In these experiments the column was washed with 3 in. (350 mL) of water and the soil column was then extruded from the tube and cut into 1-in. segments. These were placed in 150-mL containers (3 in. diameter) and planted with barnyardgrass; growth was compared to that for untreated controls after 14 days.

Compounds active at low rates in greenhouse experiments were further evaluated under field conditions on a Fox sandy clay loam soil (Kalamazoo, Mich.), a loamy sand soil (Dothan, Ala.), or a Myakka sand soil (Delray Beach, Fla.). The compounds were applied to plots (160 to 200 sq ft) as preplant incorporated or preemergence surface treatments, usually in replicated tests. Incorporation was accomplished with tractor mounted power driven rototillers cutting 2 to 3 in. deep, or a double-disc cutting 4 in. deep. All compounds were formulated as 25% wettable powders or emulsifiable concentrates and suspended in water. They were applied at six rates ranging from 0.1 to 4.0 lb of active ingredient (AI)/acre (commonly rates were 0.2, 0.4, 0.8, 1.6, 2.4, and 3.2 lb AI/acre) with a hand-held CO_2 sprayer which delivered 40 to 50 gal/acre (gpa) spray volumes at 38 to 40 psi. Incorporation was completed immediately after treatment; preemergence applications were made the same day or one day after planting. The plots received 0.5 in. of sprinkler irrigation immediately after completion of all applications at the Michigan and Florida sites. Treated crops and indigenous weeds were visually rated (0–10 scale) for injury relative to untreated controls approximately 3 weeks after application (Table X).

The influence of seed planting depth and chemical incorporation depth was determined using corn as the test species. Two 36-in. corn rows were planted either 1.5 or 4.0 in. deep in 96 sq ft plots. The plots were treated with 0.8 lb/acre of compound **12** or 1.5 lb of AI/acre of compounds **2** or **53**. Each compound was incorporated shallow (1–2 in.) or deep (3–4 in.) with a power driven rototiller prior to planting; the compounds were also applied on the surface 1 day after planting. The 50% wettable powder formulations of each compound were suspended in water and applied at 40 gpa with a hand-held sprayer set at 40 psi. Atrazine [2-chloro-4-(ethylamino)-6-(isopropylamino)-*s*-triazine, 1.5 lb of AI/acre] plus alachlor [2-chloro-2′,6′-diethyl-*N*-(methoxymethyl)acetanilide, 2.0 lb of AI/acre] were included as a standard treatment together with handweeded and weedy control plots. A split-pot design was used with application methods as main plots and compounds as subplots. Seed depths were regarded as separate experiments. All treatments were replicated three times in each application method. Corn heights (flag leaf fully extended) were obtained from 19 plants/plot and averaged 62 days after treatment (Table XI). Corn ears were obtained from each plot in one destructive harvest 153 days after treatment. Yields reflect average plot values (Table XI).

RESULTS AND DISCUSSION

Compound **2** was active on broadleaf and grassy weeds at rates between 1 and 10 lb/acre (Table I). The compound was much more active on yellow nutsedge than on grasses (Figure 1). This finding was somewhat unex-

Table XI. Heights and Yields (in parentheses) of Corn Sown at Plots Treated with Preemergence, Shallow Incorporated, or Deep Incorporated Applications of Various Compounds

Treatment	Rate, lb/acre	Corn sown 1.5 in. deep			Corn sown 4.0 in. deep		
		Pre	PPI (1-2 in.)	PPI (3-4 in.)	Pre	PPI (1-2 in.)	PPI (3-4 in.)
Hand-weeded control[a]		70[b] (156)[c]	67 (128)	66 (150)	67 (152)	61 (126)	64 (140)
Weedy control		54 (50)	56 (66)	61 (72)	52 (50)	55 (60)	56 (50)
12	0.8	59 (160)	60 (152)	55 (146)	51 (112)	54 (130)	56 (144)
2	1.5	56 (146)	50 (120)	55 (116)	48 (118)	45 (116)	44 (136)
53	1.5	62 (158)	58 (144)	56 (154)	53 (152)	54 (126)	54 (136)
Atrazine + alachlor	1.5 + 2.0	69 (152)	70 (176)	69 (178)	63 (176)	63 (168)	61 (198)
$LSD_{5.05}$			5 (48)			6 (46)	
CV			14% (20%)			18% (20%)	

[a] These plots were hand-weeded for a period of 62 days. Late season weed competition in these plots reduced yields below those found for the atrazine plus alachlor plots. [b] Heights (inches) 62 days after application. [c] Bushel/acre yields collected 153 days after treatment.

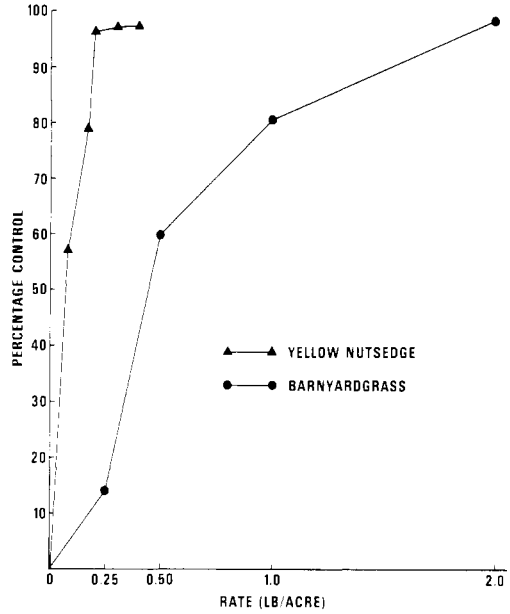


Figure 1. Yellow nutsedge and barnyardgrass control from incorporated applications of *N,N*,α,4-tetramethyl-3-phenylpyrazole-1-acetamide (**2**).

pected, as nutsedge is generally a difficult species to control. Many amides related to **2** have been prepared, and substituents at each position in the molecule have been modified in order to optimize activity. All of the compounds were active as herbicides and many were extremely active on nutsedge (Table I–VI). The compounds were most active as preemergence herbicides; postemergence activity was usually observed, but this was mainly a result of adsorption of the chemical from the soil by the plant roots rather than by foliar uptake.

The activity of amide analogues of **2** is shown in Table I. Secondary amides (**16–19**), tertiary amides (**20–23**), and cyclic amides (**24** and **25**) were all active at 1 lb/acre on grasses. The highest activity on nutsedge was found for **2** and its methylethylamide (**20**) and diethylamide (**22**) analogues.

Herbicidal activity was not limited to derivatives of 4-methyl-3-phenylpyrazole. Amides derived from other phenylpyrazoles were generally active as herbicides (compounds **26–46**, Table II). For compounds in which the phenyl group was unsubstituted (**26–35**) highest activity was found when the 4-substituent in the pyrazole ring was alkyl or halogen (**2**, **27–29**). Activity was reduced when the 4-substituent was large (**31**) or electron with-

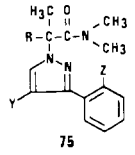


Figure 2. Structures of the most active phenylpyrazole amides.

drawing (**30**), or when a substituent was introduced at the 5 position (**32–35**). Compounds with an ortho substituent in the phenyl ring (**36–38** and **45**) were more active than the analogues (**26**, **28**, and **2**) lacking this substituent. The *m*- and *p*-chlorophenyl isomers (**39** and **40**) of **38** were much less active as herbicides. In the dichlorophenyl amides **41–44** it was similarly found that only the compound with both substituents in the ortho positions (**43**) had high activity.

Small amounts of the 5-phenyl isomers were formed in the synthesis of compounds **2** and **26–46** (see Scheme I). Several of these were isolated and tested as herbicides. The compounds were always less active than their 3-phenyl isomers (Table III).

Modification at the α position (R_1 and R_2, Table IV) significantly affected herbicide activity. The unsubstituted (**52**) and phenyl substituted amides (**55**) had the lowest activities. Monoalkyl derivatives (**2**, **53**, and **54**) were more active, while the most active compounds (**12**, **56–59**) had two alkyl substituents at the α position.

Activity of α,α-dimethylamides (Table V) followed a pattern similar to that found for the α-methylamides of Table II. Compounds with a 4-substituent (**12** and **61**; **3** and **4**) were more active than the analogues lacking this substituent (**60**, **62**). Most active were the compounds with an ortho substituent in the phenyl ring (**3**, **4**, and **68–70**); compounds **3** and **68** were the most active members of this series.

The amides were readily converted to thioamides; examples are shown in Table VI. In greenhouse tests these compounds were about half as active as the corresponding amides. Activity differences between amides and thioamides appear to be less under field conditions (see Table X).

Eighteen of the compounds in Tables I–V, compounds described by general structure **75** (Figure 2), have high activity on nutsedge (ED_{50} values <0.2 lb/acre). The compounds may be divided into three groups on the basis of structure and ED_{50} values. Least active are the compounds in which two of the groups R, Y, and Z are hydrogen (**2**, **27**, **28**, **36**, **53**, **54**, and **60**), which have nutsedge ED_{50} values between 0.06 and 0.2 lb/acre. More active (ED_{50} values between 0.04–0.09 lb/acre) are the com-

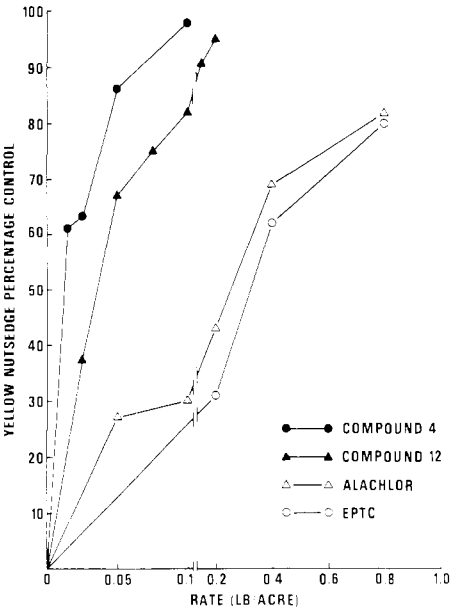


Figure 3. Yellow nutsedge control from incorporated application of various herbicides.

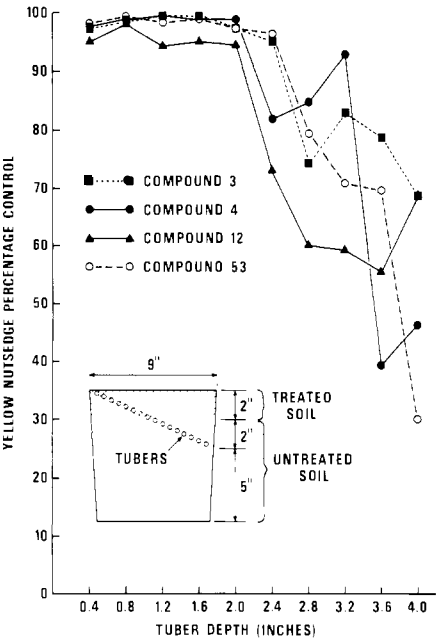


Figure 4. Yellow nutsedge control as influenced by tuber depth; the chemicals were incorporated 2 in. deep at 0.5 lb/acre.

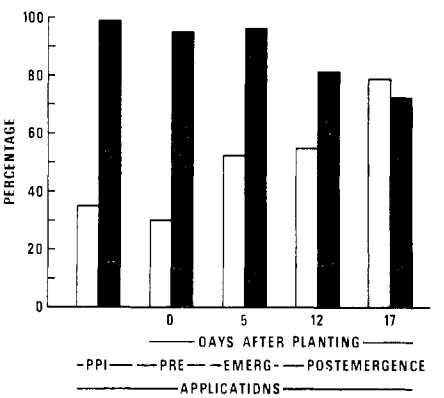


Figure 5. Corn percentage of control (▭) and Yellow Nutsedge control percentage (■) from compound **12** applied at 0.5 lb/acre preplant incorporated (PPI), preemergence (PRE), at corn emergence (EMERG), or postemergence (POSTEMERGENCE).

pounds where one of these substituent groups is hydrogen (**37**, **38**, **45**, **12**, **56**, **57**, **61**, and **62**). In the most active group (ED_{50} <0.02 lb/acre), all of the substituents R, Y, and Z are other than hydrogen (**3**, **4**, **68**, and **70**). The activity of representative members of each group on additional weeds and crops is shown in Table VII. The activity pattern parallels that found for nutsedge, with **2** being the least active compound and **3** and **4** showing the highest overall activity. The grass and broadleaf weed activities of compounds of structure **75** compare favorably with those of many commercial herbicides. All the compounds were more active on nutsedge than the herbicide alachlor and EPTC (*S*-ethyl-*N*,*N*-dipropylthiocarbamate (see, for example Figure 3).

Additional tests have been performed to provide more information about the activity characteristics of the phenylpyrazole amide herbicides. Yellow nutsedge was employed in most of these tests. At rates above 3 lb/acre the amides killed the nutsedge tubers, while at lower rates the compounds inhibited tuber growth. At rates permitting 0–20% top growth, buds (usually one or two) on the tuber sprouted and shoots emerged from the soil to a height of 1–2 in. The shoots became chlorotic and leaf tips showed necrosis which spread down the leaf blades. At these rates marked proliferation of number of shoots growing from the region of the basal bulb was observed; some six–ten shoots frequently developed rather than the customary two–three.

The herbicidal activity of the compounds varied across soil type (Table VIII). While several of the soil components vary in amount for the three soils, the results are most readily explained in terms of reduced activity with increasing organic matter content of the soil.

Nutsedge was best controlled when the tubers were planted in treated soil, as is illustrated in Figure 4 for compounds **3**, **4**, **12**, and **53**. These results indicated that for optimum activity on nutsedge the compounds should be incorporated into the soil profile and in close proximity to the germinating tubers.

Mechanical incorporation was very effective for placing compounds close to the tubers. Rainfall, depending on amount, also was effective. The critical chemical–tuber relationship had negative ramifications on crop tolerances. Crop injury occurred when the chemicals were close to the seed, but injury was reduced when the chemicals were some distance from the seed. Thus, deep sown corn exhibited less injury than shallow planted when surface applications of compounds **2**, **12**, and **53** were not followed by supplemental rainfall immediately after treatment (Table IX). The growth differences with seed at different depths were statistically different for compound **53**. However, supplemental rainfall of 0.1 or 0.3 in. of rainfall minimized the protection afforded by the deeper planting. The small amount of rainfall increased the injury for each compound. Corn injury from these phenylpyrazole amides was substantial compared to that from similar alachlor treatments.

The feasibility of utilizing application timing as a means of reducing crop injury without commensurate loss of nutsedge control was explored. Corn growth increased when the treatment times were delayed from preplant incorporation of compound **12** to postemergence 12 days after corn emergence (Figure 5). Unfortunately, nutsedge control diminished when the applications were delayed from preplant or preemergence or postemergence. The correlation coefficient between corn growth and yellow nutsedge control was –0.88. Thus, it seemed impractical to use delayed postemergence applications to minimized

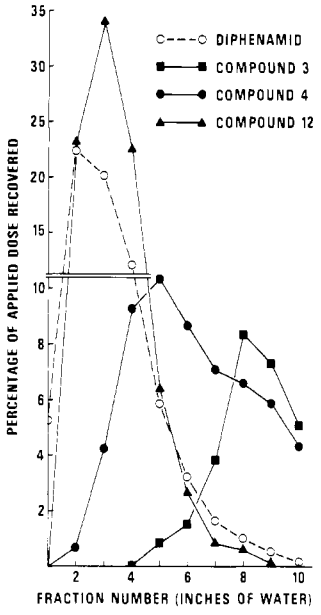


Figure 6. Elution curves for various herbicides from 6-in. soil columns; 12 in. of water were applied to the column giving ten 1-in. fractions at the base of the column.

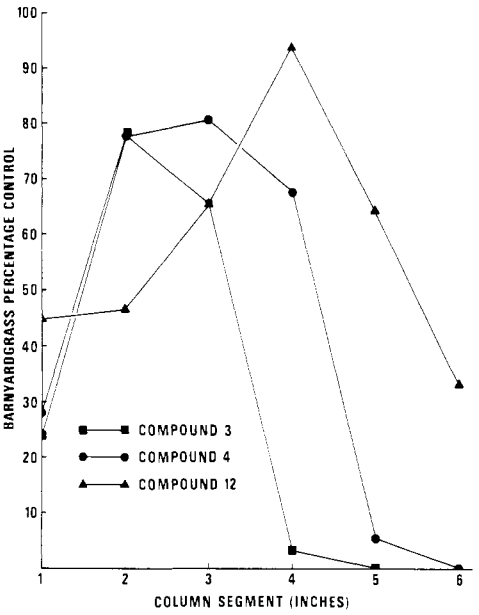


Figure 7. Barnyardgrass control in segments of soil columns treated with various chemicals at 0.2 lb/acre. Columns were eluted with 3 in. of water before the bioassay; segment 1 is the top of the column (0–1 in. depth).

crop injury because of the reduction of yellow nutsedge control. Feasibility of directed postemergence applications following cultivation was not explored.

Laboratory soil leaching studies provide a relative measure of how readily herbicides are moved in the soil by water. Studies with the phenylpyrazole amides indicate that **12** is more readily moved by applied water than **3** or **4** (Figures 6 and 7).

Several procedures are available for determining relative mobilities of herbicides in soil (Gerber and Guth, 1973; Helling and Turner, 1968; Harris, 1967; Lambert et al., 1965). Our studies used soil columns (6 in. × 3 in. i.d.) prepared from equal weights of Fox sandy clay loam and silica sand. Addition of the sand was necessary for adequate column flow rate (0.2–0.5 in. of water/h). In the initial experiment 2 lb/acre of the compound and 2 lb/acre of diphenamid were combined and applied to a column which was then eluted with 12 in. of water. The column effluent was analzyed for the chemicals and the elution patterns determined (Figure 6). The diphenamid elution curve was similar for all columns, indicating, at most, small variation from column to column; the average curve for this herbicide is plotted in Figure 6.

Diphenamid was the most mobile of the compounds studied with **12** having a slightly lower mobility. Chloramide **4** was less mobile, and the dichloroamide **3** was the least mobile compound studied. The same mobility order (**12** > **4** > **3**) was found when the compounds were applied separately at 0.2 lb/acre to soil columns which were then irrigated with 3 in. of water and bioassayed using barnyardgrass (Figure 7).

Several of the more active compounds have been evaluated further in field tests (Table X). As was found in the greenhouse tests, the α,α-dimethylamides **3**, **4**, **12**, and **68** were more active than the α-alkylamides **2**, **28**, and **53**. Indications of crop tolerance (<10% injury) at rates required to control weeds were obtained for several compounds (Table X). The tolerance of corn, cotton, peanuts, and soybeans to preplant applications of thioamide **5** was greater than from other phenylpyrazole amide field treatments. These crops tolerated 1.0 to 2.4 lb/acre of compound **5**. Peanuts also exhibited tolerance to compounds **2**, **4**, **12**, **28**, and **53** while soybeans exhibited tolerance to **2**, **28**, and **53**. Broadleaf weeds such as florida pusley, tumbling pigweed, and velvetleaf were sensitive to several of the compounds; likewise, annual grasses such as crabgrass, stinkgrass, and yellow foxtail were also controlled. In these tests, as under greenhouse conditions, the phenylpyrazole amides did not inhibit germination. Sensitive weeds often emerged, but the seedlings developed thickened stems with compressed internodes. Stunted broadleaf plants rarely developed beyond the cotyledonary leaf stage. Inhibition of primary roots was a very common injury symptom. Proliferation of short, thickened secondary roots also occurred. Plants exhibiting these symptoms usually died if short periods of environmental stresses such as drought or cool temperature occurred soon after emergence.

Yellow nutsedge control was also manifested under field conditions, but the level of activity was lower than predicted from greenhouse evaluations. Shallow tubers were controlled, but growth was often observed from tubers located well below the incorporation zone. Rainfall or sprinkler irrigation following treatment usually improved the weed control activity while reducing crop tolerance. Compounds **4**, **5**, and **12** selectively controlled yellow nutsedge in peanuts. Selectivity levels were marginal or unacceptable with the compounds on the other crops.

The interaction of application method, incorporation depth, and seed depth was assessed on corn under field conditions (Table XI). Phenylpyrazole amide treated plants, 62 days after application, were shorter than the atrazine plus alachlor treated plants and the hand-weeded control plants. The differences were significant at the 0.5 level of probability. Heights of corn treated with compounds **2**, **12**, and **53** were not statistically different. Surface applications of these compounds tended to be less phytotoxic than incorporated applications irrespective of planting depth, but the small differences were not significant. Eventually, corn treated with the experimental compounds outgrew the stunting. However, yields from these chemicals were significantly less than from the standard treatment. Thus application methods altered the level of corn injury, but did not reduce injury sufficiently to offer a practical, safe, and efficacious means for utilizing

the potentially high levels of nutsedge activity inherent in this series of compounds.

Greenhouse tests have indicated residual weed control for a period of several months with the phenylpyrazole amides; this was confirmed under field conditions. Fox silty clay loam soil treated with 0.8 lb/acre of compounds **3**, **4**, **5**, **12**, and **74** was collected 14, 77, and 155 days after application. Residual activity was determined by bioassaying with yellow nutsedge. The plots received 25 in. of rainfall during the experiment. Yellow nutsedge control exceeded 95% 14 or 77 days after treatment. Control percentages 155 days after treatment varied with compound and in order of increasing magnitude were: **5** (0%) < **12** (12%) < **3** (33%) < **74** (37%) < **4** (71%).

Field results similar to those presented for corn were also obtained for cotton, peanuts, and soybeans. In general, the compounds performed well on light to medium soils under conditions of adequate rainfall. While potential utility was demonstrated in several tests, performance of the compounds was inconsistent from site to site across a wide range of geographic locations.

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Clean-Up Techniques for the Determination of Parts per Trillion Residue Levels of 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD)

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Clean-up techniques are described for gas chromatography–mass spectrometric measurement of parts per trillion levels of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in nonfat and fat tissue, milk, cream, grain, feed, dry plant material, wet plant material, soil, and blood. A sensitivity of 10 parts per trillion TCDD was obtained for most types of samples. Animal tissue, milk, and cream are digested in an alkaline solution and a hexane extract is cleaned up using sulfuric acid and chromatography on silica gel and alumina. Grain and other plant material are extracted with hexane first and the oil obtained is digested with alkali. Recovery of 10 to 900 parts per trillion TCDD added to beef fat, soil, and rice averaged 76%. The types of interferences encountered are discussed.

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) is a trace contaminant in 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) herbicides. Because of its interesting biochemical properties, TCDD has been extensively studied (Blair, 1973; Environmental Health Perspectives, 1973). Early attempts to determine TCDD in biological samples using electron-capture gas chromatography had a detection limit of 50 ppb (Crummett and Stehl, 1973; Watts and Storherr, 1973; Woolson et al., 1973). This sensitivity was not low enough to detect TCDD in animal tissues from the feeding studies that were being carried out. In 1973, a method for TCDD was described which had a sensitivity approaching 1 part per trillion using direct probe introduction of a cleaned-up sample extract into a high-resolution mass spectrometer (Baughman and Meselson, 1973). In this method 1 ppb ^{37}Cl TCDD was added to the sample to provide a "carrier" and to provide recovery data. This implied that the use of ^{37}Cl TCDD was necessary to recover parts per trillion levels of TCDD but later data showed that recoveries were the same with and without the addition of ^{37}Cl TCDD (Baughman, 1974). Measurement of TCDD using gas chromatography–mass spectrometry (GC–MS) confirmed that parts per trillion levels of TCDD could be carried through a cleanup without using ^{37}Cl TCDD and most cleaned-up extracts could be analyzed using a gas chromatograph–low-resolution mass spectrometer. Use of ^{37}Cl TCDD as an internal standard is not necessary when using gas chromatographic introduction of the sample into the mass spectrometer because there is no variation in ion source pressure which would change the sensitivity for TCDD.

The objective of this study was to develop and validate procedures which could be used to analyze a wide variety of environmental samples and tissue samples for TCDD.

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