Original Article

Synthesis and Herbicidal Activity of *N*-Aryl-2-methyl-2-arylpropanamides and *N*-Aryl-2-methyl-2-arylbutanamides

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One hundred and twelve *N*-aryl-2-methyl-2-arylpropanamides and *N*-aryl-2-methyl-2-arylbutanamides were synthesized and their herbicidal activities were measured. Most of the compounds exhibited strong herbicidal activity against *Echinochloa oryzicola* VASING., *Scirpus juncoides* ROXB. subsp. *juncoides* ROXB. and *Cyperus serotinus* ROTTB. in pot tests. Introduction of substituents into the two benzene rings varied the activity to different extents. Both a meta alkyl substituent in the amine moiety and an ortho substituent in the acid moiety contributed to high activity, whereas introduction of strong electron-withdrawing substituents at the para position in the amine moiety or bulky substituents at the para position in the acid moiety was unfavorable to the activity. Among the compounds, *N*-(3-propylphenyl)-2-methyl-2-(2-methoxyphenyl)butanamide showed the strongest activity against the test plants, completely killing *Echinochloa oryzicola* VASING. at a dose of 0.625 g a.i./a in pot tests.

INTRODUCTION

It is known that arylacetic acids have a plant growth-regulating activity,¹⁾ and that their anilide derivatives show an herbicidal activity. The activity of arylacetanilides varies with substituents in the benzene rings and the α -carbon atom.

Shinohara *et al.*²⁾ reported on the herbicidal activity of arylacetanilides which have no substituent at the α -carbon atom. Borgna *et al.*³⁾ studied the herbicidal activity of *N*-aryl-2-phenylpropanamides, and found that *N*-(3,4-dichlorophenyl)-2-phenylpropanamide has the high activity, whereas *N*-(4-hexylthiophenyl)-2-phenylpropanamide shows the strongest inhibiting activity of the Hill reaction. Otsuki *et al.*⁴⁾ reported that *N*-aryl-2-methyl-2-aryl-

propanamides, which have a ureido group at the meta position in amine moiety, show herbicidal activity.

We synthesized one hundred and twelve *N*-aryl-2-methyl-2-arylpropanamides and *N*-aryl-2-methyl-2-arylbutanamides, and studied the effect of substituents on the herbicidal activity against *Echinochloa oryzicola* VASING., *Scirpus juncoides* ROXB. subsp. *juncoides* ROXB., *Cyperus serotinus* ROTTB. and annual broad-leaf weeds. The activity of these compounds varied with the substituents and their positions on two benzene rings.

MATERIALS AND METHODS

1. Synthesis of Compounds

N-Aryl-2-methyl-2-arylpropanamides and *N*-aryl-2-methyl-2-arylbutanamides were pre-

Scheme 1 Synthetic methods of 2-methyl-2-arylpropanoyl chlorides and 2-methyl-2-arylbutanoyl chlorides.

pared by the reaction of 2-methyl-2-arylpropanoyl chlorides and 2-methyl-2-arylbutanoyl chlorides with respective anilines in the presence of triethylamine. Acid chlorides were synthesized with method A or B in Scheme 1.⁵⁻⁷⁾ Arylacetonitriles, arylacetic acids and anilines were either obtained commercially or synthesized by general methods. 3-Propylaniline, 3-isopropylaniline, 3-butyylaniline, 3-*sec*-butylaniline and 3-*tert*-butylaniline were derived from respective 4-alkylaniline five steps.⁸⁻¹⁰⁾ 3-Ethyl,4-bromoaniline was synthesized from 3-ethylaniline.¹¹⁾ 3-Propyl,4-chloroaniline was derived from 3-propylaniline.¹²⁾ 3-Propyl,6-methoxyaniline and 3-ethyl,6-methoxyaniline were synthesized from 4-propylphenol and 4-ethylphenol respectively using conventional methods. The structures of the compounds were confirmed by IR and ¹H NMR spectroscopy. All refractive indexes, and melting and boiling points were uncorrected. IR spectra were recorded on a Hitachi 270-30 infrared spectrophotometer, and ¹H NMR spectra were measured on a JEOL PMX 60 spectrometer. Melting points were measured on a Meiho melting pointer, and refractive indexes were measured on an Atago refractometer. The followings are the examples of typical procedures.

1.1 2-Methyl-2-phenylpropanoyl chloride (method A)

n-Butyllithium (15% in hexane, 1260 ml, 2.04 moles) was added to a solution of diisopropylamine (207 g, 2.04 moles) in THF (1000 ml) below 4°C and stirred for 15 min. To the mixture, phenylacetonitrile (100 g, 0.85 mol) was added at -30 to -20°C and stirring continued for 30 min. Then, methyl iodide (291 g, 2.04 mol) was added below 0°C. The reaction mixture was stirred for 2 hr at room temperature,

then poured into water (500 ml) and extracted with ethyl acetate (500 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated to dryness *in vacuo* to afford a crude product. The crude product was purified by distillation to give 2-methyl-2-phenylpropanonitrile; yield: 101 g (82.1%), bp 130–132°C (37 mmHg), ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.74 (6 H, s, CH₃-C-CH₃), 7.28–7.72 (5 H, m, Ar-H), IR $\nu_{\text{max}}^{\text{Neat}}$ cm⁻¹: 3016(NH), 2280(CN).

A solution of potassium hydroxide (137 g, 85%) in 600 ml of ethyleneglycol was added to 2-methyl-2-phenylpropanonitrile (96 g, 0.66 mol) and refluxed for 7 hr. The reaction mixture was cooled, diluted with water (300 ml) and shaken with benzene (500 ml). The benzene extract was washed with water (200 ml). The combined aqueous phases were acidified with concentrated hydrochloric acid and shaken with ethyl acetate (700 ml). The ethyl acetate extract was washed with water, dried over anhydrous sodium sulfate and evaporated to dryness to afford a crude product. The crude product was purified by crystallization from *n*-hexane to produce 2-methyl-2-phenylpropanoic acid; yield: 97 g (89.4%), mp 75–76°C, ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.59 (6 H, s, CH₃-C-CH₃), 7.1–7.44 (5 H, m, Ar-H), 10.31(1 H, bs, OH), IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1693(CO).

A mixture of 2-methyl-2-phenylpropanoic acid (81.5 g, 0.596 mol) and thionyl chloride (71 g, 0.596 mol) in benzene (300 ml) was refluxed for 3 hr. The reaction mixture was cooled, and benzene and excess thionyl chloride were evaporated under reduced pressure to give a crude product. The crude product was purified by distillation to produce 2-methyl-2-phenylpropanoyl chloride; yield: 86.2 g (95.0%), bp 94–96°C (7 mmHg), ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.65 (6 H, s, CH₃-C-CH₃), 7.33 (5 H,

s,Ar-H), IR $\nu_{\text{max}}^{\text{Neat}}$ cm^{-1} : 1780(CO).

1.2 2-Methyl-2-(2-methoxyphenyl)butanoyl chloride (method B)

n-Butyllithium (15% in hexane, 178 ml, 0.288 mol) was added to a solution of 2-methoxyphenylacetic acid (23.9 g, 0.144 mol) in THF (600 ml) at -30 to -20°C . After stirring for 30 min, methyl iodide (20 g, 0.144 mol) was added below 0°C . The reaction mixture was stirred for 2 hr at room temperature, then poured into water (300 ml) and extracted with benzene (200 ml). The benzene extract was washed with water (100 ml). The combined aqueous phases were acidified with concentrated hydrochloric acid and extracted with ethyl acetate (500 ml). The ethyl acetate layer was washed with water, dried over anhydrous sodium sulfate and evaporated to dryness to afford a crude product. The crude product was purified by crystallization from *n*-hexane to produce 2-(2-methoxyphenyl)propanoic acid; yield: 21.5 g (83.0%), mp $97-99^\circ\text{C}$, ^1H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.46 (3 H,d, $J=7$ Hz, $-\text{CH}-\text{CH}_3$), 3.75 (3 H,s, $\text{O}-\text{CH}_3$), 4.05 (1 H,q, $J=7$ Hz, $-\text{CH}-\text{CH}_3$), 6.71–7.58 (4 H,m,Ar-H), 11.32 (1 H,bs,OH), IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1698(CO).

α -Ethylation of 2-(2-methoxyphenyl)propanoic acid was performed in the same manner as described above; yield: 14.5 g (63.6%), mp $106-107^\circ\text{C}$, ^1H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 0.75 (3 H,t, $J=7$ Hz, $-\text{CH}_2-\text{CH}_3$), 1.48 (3 H,s,C- CH_3), 2.02 (2 H,q, $J=7$ Hz, $-\text{CH}_2-\text{CH}_3$), 3.73 (3 H,s, $\text{O}-\text{CH}_3$), 6.75–7.41 (4 H,m,Ar-H), 11.75 (1 H,bs,OH), IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1700(CO).

2-Methyl-2-(2-methoxyphenyl)butanoic acid was converted into acid chloride in the same manner as described above; yield: 12.2 g (80%), bp $104-111^\circ\text{C}$ (5 mmHg), ^1H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 0.8 (3 H,t, $J=7$ Hz, $-\text{CH}_2-\text{CH}_3$), 1.58 (3 H,s,C- CH_3), 1.9–2.13 (2 H,m, $-\text{CH}_2-\text{CH}_3$), 3.90 (3 H,s, $\text{O}-\text{CH}_3$), 6.71–7.58 (4 H,m,Ar-H), IR $\nu_{\text{max}}^{\text{Neat}}$ cm^{-1} : 1800(CO).

1.3 *N*-(3-Propylphenyl)-2-methyl-2-phenylpropanamide (12)

2-Methyl-2-phenylpropanoyl chloride (9.3 g, 0.05 mol) was added to a mixture of 3-propylaniline (7 g, 0.05 mol) and triethylamine (5 g, 0.05 mol) in benzene (100 ml). After stirring for 3 hr at room temperature, the reaction mixture was poured into water (100 ml) and extracted with benzene (150 ml). The benzene

layer was washed with water (150 ml, 100 ml) twice, dried over anhydrous sodium sulfate and then evaporated to dryness to afford a crude product. The crude product was purified by crystallization from *n*-hexane to produce *N*-(3-propylphenyl)-2-methyl-2-phenylpropanamide; yield: 11.5 g (80.4%), mp $52.5-53.5^\circ\text{C}$, ^1H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 0.88 (3 H,t, $J=7$ Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_3$), 1.23–1.93 (2 H,m, $-\text{CH}_2-\text{CH}_2-\text{CH}_3$), 1.65 (6 H,s, $\text{CH}_3-\text{C}-\text{CH}_3$), 2.53 (2 H,t, $J=7$ Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_3$), 6.78–7.63 (10 H,m,Ar-H,NH), IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3300(NH), 1660(CO).

Other compounds were synthesized in the same manner as described above. When the compounds didn't crystallize, however, they were purified by silica gel column chromatography.

2. Herbicidal Activity

Ceramic pots (11 cm in diameter) packed with sandy loam soil were water-flooded at a depth of 3 cm to produce paddy conditions. In the pots, seeds of *Echinochloa oryzicola* VASING. and *Scirpus juncoides* ROXB. subsp. *juncoides* ROXB. were sown, and tubers of *Cyperus serotinus* ROTTB. were planted. Seeds of annual broad-leaf weeds, including *Rotala indica* (WILLD.) KOEHNE., *Elatine triandra* SCHK. and *Lindernia pyxidaria* L., were indigenously present in the soil. After three days, a homogenous suspension of 20% wettable powder of a test compound was added dropwise to the surface of the irrigating water. A dose of the compound was 30 g or 10 g a.i./a. After the treated pots were kept in a greenhouse for three weeks, the growth-inhibiting activity was observed and evaluated using a 0 to 5 grading scale (0: no effect, 5: complete killing). The treatment was duplicated.

RESULTS AND DISCUSSION

1. Synthesis of Compounds

Synthetic methods, yields and boiling points of 2-methyl-2-arylpropanoyl chlorides and 2-methyl-2-arylbutanoyl chlorides are shown in Table 1.

2-Methyl-2-arylpropanoyl chlorides were synthesized from arylacetonitriles according to method A in Scheme 1. Though arylacetonitriles are generally methylated with

Table 1 Structures and physical properties of 2-methyl-2-arylpropanoyl chlorides and 2-methyl-2-arylbutanoyl chlorides.

Y _m	R	Method	Yield (%)			bp (°C/mmHg)
			(I)	(II)	(III)	
H	Me	A	82.1	89.4	95.0	94–96/7
2-Cl	Me	A	76.3	53.1	43.6	85–87/3
3-Cl	Me	A	80.3	74.0	54.0	120–125/14
4-Cl	Me	A	83.8	89.1	81.7	86–87.5/2
4-F	Me	A	75.6	92.0	72.7	83–87/2
4-Br	Me	A	89.2	85.1	82.2	143–150/6
3-CF ₃	Me	A	82.0	95.2	73.2	65–68/2
2-Me	Me	A	95.1	76.9	71.1	94–96/3
3-Me	Me	A	88.0	75.1	75.9	85–90/6
4-Me	Me	A	92.0	83.0	93.1	103–104/6
2-OMe	Me	A	78.2	69.7	80.6	100–107/5
3-OMe	Me	A	82.7	64.8	85.5	96–99/5
4-OMe	Me	A	86.0	97.1	82.3	90–93/2
4-OEt	Me	A	91.0	77.3	92.3	105–110/5
H	Et	B		93.0	86.5	104–105/6
2-F	Et	B	89.1	89.6	78.9	85–89/3
2-Cl	Et	B	89.0	47.1	65.4	96–98/2
4-Cl	Et	B	95.2	88.0	85.1	96–97/2
3-CF ₃	Et	B	93.6	80.0	78.0	73–74/2
2-Me	Et	B	84.3	73.5	63.1	92–94/6
4-Me	Et	B	86.0	71.0	81.3	100–103/6
4-Isopr	Et	B	93.2	88.6	77.0	111–115/3
2-OMe	Et	B	83.0	63.6	80.0	104–111/5
4-OMe	Et	B	79.2	68.1	77.3	118–120/4
2-OEt	Et	B	74.9	67.1	66.1	108–110/9
2-Me, 4-Me	Et	B	74.3	63.2	70.1	94–96/3

halogenated methane and a strong base,^{13,14)} we used lithiumdiisopropylamide as a base. Yields of reactions (I), (II) and (III) were good, except for the reaction (II) and (III) of 2-methyl-2-(2-chlorophenyl)propanonitrile. The chlorine atom at the ortho position seemed to interfere the hydrolysis and the conversion of acid into acid chloride.

2-Methyl-2-arylbutanoyl chlorides were produced from arylacetic acids according to method B in Scheme 1. 2-Methyl-2-arylbutanoic acids were also produced by the hydrolysis of 2-methyl-2-arylbutanonitriles prepared with method A. However, 2-methyl-2-arylpropanonitriles derived as by-products were difficult to separate each other. Yields of

reactions (I), (II) and (III) were good, but the α -ethylation of 2-(2-chlorophenyl)propanoic acid and the conversion of acid into acid chloride was not so good. Bulky and electronic effects of the chlorine atom at the ortho position influenced the yields.

N-Aryl-2-methyl-2-arylpropanamides and *N*-aryl-2-methyl-2-arylbutanamides were synthesized with 2-methyl-2-arylpropanoyl chlorides or 2-methyl-2-arylbutanoyl chlorides and respective anilines in the presence of triethylamine. Every yield through reaction was good as shown in Tables 2 and 3.

2. Herbicidal Activity

As shown in Tables 2, 3 and 4, *N*-aryl-2-

Table 2 Structures, physical properties and pre-emergence herbicidal activities of *N*-aryl-2-methyl-2-arylpropanamides and *N*-aryl-2-methyl-2-arylbutanamides.

No.	R	R ₁	X _n	Yield (%)	mp(°C) or <i>n</i> _D ²⁵	Herbicidal activity ^{a)}			
						E.c. ^{b)}	S.j. ^{c)}	C.s. ^{d)}	A.B. ^{e)}
1	Me	H	H	92.3	100–101	4	2	3	1
2	Me	H	2-Cl	74.5	38–39	3	3	1	4
3	Me	H	2-Me	70.1	94–96	3	0	1	0
4	Me	H	2-Et	63.2	103–105	0	2	2	0
5	Me	H	2-OMe	65.7	1.5690	4	2	2	3
6	Me	H	2-OEt	70.6	1.5660	0	0	0	0
7	Me	H	3-F	80.8	99.5–101.5	5	2	4	2
8	Me	H	3-Cl	81.5	113.5–115.5	4	2	3	0
9	Me	H	3-Br	78.3	129–130	3	0	0	0
10	Me	H	3-Me	81.0	101–102	4	2	3	2
11	Me	H	3-Et	78.1	78–79	5	4	5	2
12	Me	H	3-Pr	80.4	52.5–53.5	5	5	5	2
13	Me	H	3-Isopr	79.2	69–70	5	2	2	3
14	Me	H	3-Bu	81.6	65–66	4	4	2	3
15	Me	H	3- <i>sec</i> -Bu	74.2	51–52	5	4	3	3
16	Me	H	3- <i>tert</i> -Bu	72.9	89–90	2	0	0	0
17	Me	H	3-OMe	80.3	134–135	5	0	3	0
18	Me	H	3-OEt	82.0	124–125	4	0	2	0
19	Me	H	3-O-Pr	88.0	106–107	3	1	1	0
20	Me	H	3-O-Isopr	85.7	103.5–104.5	4	1	2	0
21	Me	H	4-Cl	94.1	136–138	0	0	0	0
22	Me	H	4-Me	90.5	89–91	0	1	2	1
23	Me	H	4-Et	89.0	92–93	5	4	5	4
24	Me	H	4-Pr	78.0	71–72	5	1	4	2
25	Me	H	4-Isopr	86.5	108–109	4	4	2	3
26	Me	H	4-Bu	73.2	88–89	2	1	4	2
27	Me	H	4- <i>sec</i> -Bu	76.0	69–70	4	2	2	3
28	Me	H	4- <i>tert</i> -Bu	81.7	120–121	1	2	1	1
29	Me	H	4-OMe	87.3	137–138	4	2	5	0
30	Me	H	4-NO ₂	79.0	160–163	0	0	0	0
31	Me	H	2-Cl, 3-Cl	69.1	58–59	3	2	1	2
32	Me	H	2-Cl, 4-Cl	72.1	39–41	0	0	0	0
33	Me	H	3-Cl, 4-Cl	81.5	112–113	0	0	0	0
34	Me	H	3-Cl, 5-Cl	80.3	140–142	0	0	0	0
35	Me	H	2-Me, 3-Me	78.0	97–99	2	3	4	0
36	Me	H	2-Me, 4-Me	77.1	62.5–63.5	1	3	4	2
37	Me	H	2-Me, 5-Me	70.7	69.5–70.5	5	4	1	4
38	Me	H	3-Me, 4-Me	83.2	105–106	4	3	4	2
39	Me	H	3-Me, 5-Me	80.5	137–140	3	2	2	0
40	Me	H	2-Me, 6-Me	62.0	162–163	1	1	2	0
41	Me	H	3-Et, 4-Br	79.5	99–100	1	2	1	2
42	Me	H	3-Et, 6-OMe	77.0	69.5–70.5	5	4	1	4
43	Me	H	3-Pr, 6-OMe	71.7	1.5562	5	4	2	4
44	Me	H	3-Pr, 4-Cl	61.4	1.5648	1	0	0	0
45	Me	Me	H	70.6	1.5448	2	0	0	0
46	Me	Me	3-Cl	78.0	1.5726	3	1	2	0

Table 2 (continued)

No.	R	R ₁	X _n	Yield (%)	mp(°C) or n_D^{25}	Herbicidal activity ^{a)}			
						E.c. ^{b)}	S.j. ^{c)}	C.s. ^{d)}	A.B. ^{e)}
47	Me	Me	3-Me	77.0	43-44	2	2	3	2
48	Me	Me	3-Et	69.2	1.5483	4	2	3	0
49	Me	Et	H	66.6	1.5546	0	0	0	0
50	Me	Et	2-Me	65.3	1.5524	0	2	0	0
51	Me	Et	3-Me	68.2	1.5423	2	0	2	0
52	Me	Et	4-Me	70.9	62-63	2	2	1	0
53	Et	H	H	82.0	79-80	4	3	4	1
54	Et	H	2-F	79.5	46-48	0	0	0	0
55	Et	H	2-Cl	66.8	39-40	1	0	0	0
56	Et	H	2-Br	65.3	1.5848	2	0	2	1
57	Et	H	2-I	70.4	65-66	3	0	0	0
58	Et	H	2-Me	71.0	111-112	1	0	2	2
59	Et	H	2-Et	68.3	102-104	0	0	0	0
60	Et	H	2-OEt	62.8	1.6164	1	1	1	0
61	Et	H	2-SEt	60.3	1.5846	2	1	1	0
62	Et	H	3-Cl	75.0	106-107	4	3	4	1
63	Et	H	3-Me	74.2	84-85	4	3	4	2
64	Et	H	3-Et	82.1	52-53	5	4	5	3
65	Et	H	3-Pr	83.0	53-54	5	5	5	3
66	Et	H	3-OMe	85.4	74.5-75.5	4	3	4	1
67	Et	H	3-OEt	80.2	79-80	4	4	4	3
68	Et	H	4-Cl	92.7	107.5-108.5	0	0	0	0
69	Et	H	4-Me	85.6	90-91	0	1	1	0
70	Et	H	4-Et	70.2	71-72	4	2	4	3
71	Et	H	4-Pr	74.3	1.5629	4	1	2	1
72	Et	H	4-Bu	67.6	56-57	3	0	1	0
73	Et	H	4-sec-Bu	71.3	61-62	3	0	0	0
74	Et	H	4-tert-Bu	76.6	95-96	0	0	0	0
75	Et	H	4-OEt	71.0	105-106	4	1	4	1
76	Et	H	4-SEt	63.4	1.5942	0	0	0	0
77	Et	H	2-Cl, 3-Cl	66.4	86-88	0	0	0	0
78	Et	H	2-Me, 3-Me	69.4	96-97	0	0	0	0
79	Et	H	2-Me, 4-Me	73.5	71-72	0	2	0	0
80	Et	H	3-Me, 4-Me	77.0	102-103	2	1	2	1
81	Et	H	3-Me, 5-Me	72.6	116-118	1	0	0	0
82	Et	H	2-Et, 6-Et	64.8	154-156	0	0	0	0
83	Et	H	2-OMe, 5-OMe	71.2	1.5699	3	0	0	0

a) Herbicidal activity was evaluated at a dose of 30 g a.i./a.

b) E.c. : *Echinochloa oryzicola* VASING.

c) S.j. : *Scirpus juncoides* ROXB. subsp. *juncoides* ROXB.

d) C.s. : *Cyperus serotinus* ROTTB.

e) A.B. : Annual broad-leaf weeds.

methyl-2-arylpropanamides and *N*-aryl-2-methyl-2-arylbutanamides exhibited strong herbicidal activity against *E. oryzicola* VASING., *S. juncoides* ROXB. subsp. *juncoides* ROXB., *C. serotinus* ROTTB. and annual broad-leaf weeds. Their activity against the weeds varied with

the kind and the position of substituents X_n, Y_m on the two benzene rings and *N*-substituents R₁.

2.1 X_n and herbicidal activity

The introduction of substituents X_n produced a significant effect on the activity of *N*-aryl-2-

methyl-2-arylpropanamides and *N*-aryl-2-methyl-2-arylbutanamides. The activity of all ortho-substituted derivatives was weak, while that of meta alkyl-substituted derivatives, ethyl (**11**, **64**) and propyl (**12**, **65**) in particular, was strong. Para ethyl (**23**, **70**) and propyl

(**24**, **71**) compounds showed high activity, while para chloro (**21**, **68**) and nitro (**30**) compounds were inactive even at 30 g a.i./a. The introduction of two substituents didn't improve the activity. Propanamides showed a little stronger activity than butanamides when they had

Table 3 Structures, physical properties and pre-emergence herbicidal activities of *N*-(3-alkylphenyl)-2-methyl-2-arylpropanamides and *N*-(3-alkylphenyl)-2-methyl-2-arylbutanamides.

No.	R	X	Y _m	Yield (%)	mp(°C) or n _D ²⁵	Herbicidal activity ^{a)}			
						E.c. ^{b)}	S.j. ^{c)}	C.s. ^{d)}	A.B. ^{e)}
11	Me	Et	H	78.1	78–79	4	3	4	1
84	Me	Et	2-Cl	67.7	104–105	5	3	4	1
85	Me	Et	2-Me	81.3	67–68	5	4	4	1
86	Me	Et	2-OMe	78.0	83–84	5	4	5	2
87	Me	Et	3-Cl	75.8	72–73	4	3	3	0
88	Me	Et	3-Me	78.5	1.5691	4	4	3	1
89	Me	Et	3-OMe	87.6	69–70	4	3	3	0
90	Me	Et	4-F	77.5	58–59	4	3	4	1
91	Me	Et	4-Cl	80.2	91–92	4	2	1	0
92	Me	Et	4-Br	77.3	103–104	3	0	0	0
93	Me	Et	4-Me	83.5	90–91	4	2	4	0
94	Me	Et	4-OMe	83.0	71–72	4	2	2	0
95	Me	Et	4-OEt	81.3	87–88	4	2	2	1
12	Me	Pr	H	80.4	52.5–53.5	4	4	4	1
96	Me	Pr	2-Me	76.0	1.5538	5	4	5	2
97	Me	Pr	2-OMe	82.6	60–61	5	4	5	3
64	Et	Et	H	82.1	52–53	4	4	4	1
98	Et	Et	2-F	77.8	57–58	5	4	4	1
99	Et	Et	2-OMe	80.7	51–52	5	4	5	3
100	Et	Et	4-Cl	86.4	1.5691	4	2	4	3
101	Et	Et	4-Isopr	90.6	124–125	1	0	0	0
65	Et	Pr	H	81.6	53–54	5	4	5	1
102	Et	Pr	2-F	65.4	72.5–73.5	5	5	5	2
103	Et	Pr	2-Cl	73.9	79–80	5	5	5	4
104	Et	Pr	2-Me	66.2	57.5–58.5	5	5	5	4
105	Et	Pr	2-OMe	71.2	67.5–68.5	5	5	5	5
106	Et	Pr	2-OEt	64.8	73–74	5	2	3	1
107	Et	Pr	3-CF ₃	76.2	1.5154	4	3	4	2
108	Et	Pr	4-Cl	70.8	1.5704	4	2	4	1
109	Et	Pr	4-Me	79.3	1.5619	4	3	3	2
110	Et	Pr	4-Isopr	80.6	100–101	0	0	0	0
111	Et	Pr	4-OMe	78.6	1.5508	4	2	2	1
112	Et	Pr	2-Me, 4-Me	68.3	1.5545	5	4	5	2

^{a)} Herbicidal activity was evaluated at a dose of 10 g a.i./a.

^{b)} E.c. : *Echinochloa oryzicola* VASING.

^{c)} S.j. : *Scirpus juncoides* ROXB. subsp. *juncoides* ROXB.

^{d)} C.s. : *Cyperus serotinus* ROTTB.

^{e)} A.B. : Annual broad-leaf weeds.

two substituents.

In the case of acylanilide herbicides, it is known that the introduction of chlorine or bromine or a methyl group at the meta and para positions on the benzene ring improves herbicidal activity, while the substitution of chlorine at the ortho position reduces the activity.^{15,16)} Borgna *et al.*⁸⁾ reported that the 3,4-dichloro derivative is the most active compound among *N*-aryl-2-phenylpropanamides in pot tests. However, *N*-aryl-2-methyl-2-arylpropanamides and *N*-aryl-2-methyl-2-arylbutanamides showed the strongest activity when an alkyl group was substituted at the meta position, whereas the 3,4-dichloro derivative (**33**) didn't show any activity at all.

The relative order of activity of meta alkyl-substituted derivatives was ethyl (**11**), propyl (**12**)>isopropyl (**13**), *sec*-butyl (**15**)>methyl (**10**), butyl (**14**)>*tert*-butyl (**16**). The length of an alkyl group may be an important factor to the activity.

2.2 *R*₁ and herbicidal activity

Substitution of methyl (**45-48**) or ethyl (**49-52**) for hydrogen on the imino group was unfavorable to the activity, as is the case with acylanilide herbicides,¹⁶⁾ indicating that the unsubstituted imino group of *N*-aryl-2-methyl-2-arylpropanamides or *N*-aryl-2-methyl-2-arylbutanamides is also important for high activity.^{17,18)}

2.3 *Y*_m and herbicidal activity

N-(3-Alkylphenyl)-2-methyl-2-arylpropanamides and *N*-(3-alkylphenyl)-2-methyl-2-arylbutanamides and their herbicidal activity are listed in Table 3. The effect of substituents *Y*_m on the activity was similar in propanamides and butanamides, although it was a little stronger in the later than in the former. Compounds substituted with fluorine (**102**), chlorine (**103**), methyl (**104**) and methoxy (**105**) at the ortho position exhibited remarkably high activity, whereas para-substituted compounds (**90-95**, **100**, **101**, **108-111**) showed low activity compared with others. Bulky substituents, such as bromine (**92**) and isopropyl (**101**, **110**), reduced the activity considerably. Meta-substituted compounds (**87-89**) showed the same level of activity as an unsubstituted compound (**11**). The activity of ortho-substituted compounds

Table 4 Pre-emergence herbicidal activity of *N*-(3-propylphenyl)-2-methyl-2-arylbutanamides against *Echinochloa oryzicola* VASING.

No.	Y	Herbicidal activity				
		Dosage (g a.i./a)				
		10	5	2.5	1.25	0.625
102	F	5	5	5	4	3
103	Cl	5	5	5	5	4
104	Me	5	5	5	5	4
105	OMe	5	5	5	5	5
106	OEt	5	5	5	3	1

against *E. oryzicola* VASING. is in Table 4. The relative order of activity of ortho-substituted derivatives was methoxy (**105**)>methyl (**104**)≥chlorine (**103**)>fluorine (**102**)>ethoxy (**106**). Among these compounds, *N*-(3-propylphenyl)-2-methyl-2-(2-methoxyphenyl)butanamide (**105**) was the most active against *E. oryzicola* VASING., killing completely at a dose of 0.625 g a.i./a.

The above results show that not only the property of substituents, but also their position on the two benzene rings contribute to the herbicidal activity. In future investigations we would like to elucidate the mode of action and quantitatively analyze the relationship between substituents and the activity.

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REFERENCES

- 1) M. B. Pybus, R. L. Wain & F. Wightam: *Nature* **182**, 1094 (1958)
- 2) A. Shinohara, M. Hayakawa, C. Yazawa, T. Takematsu & M. Konnai (Ihara Chemical Kogyo K.K.): Jpn. Kokai Tokkyo Koho JP 55-162757 (1980)
- 3) P. Borgna, L. Vicarini & C. Gandini: *Farmaco Ed. Sci.* **31** (4), 284 (1976)
- 4) S. Otsuki, J. Takahashi, K. Takemoto, K. Kamoshita, R. Yoshida & T. Hashimoto (Sumitomo Chemical Co., Ltd.): Jpn. Kokai Tokkyo Koho

- JP 58-15949 (1983)
- 5) P. E. Pfeffer, L. S. Silbert & J. M. Chirinko, Jr.: *J. Org. Chem.* **37**, 451 (1972)
 - 6) F. S. Prout, R. J. Hartman & E. P.-Y. Huang: *Org. Synth.* **IV**, 93 (1963)
 - 7) B. Hlferich & W. Schaefer: *Org. Synth.* **I**, 147 (1941)
 - 8) P. E. Fanta & D. S. Tarbell: *Org. Synth.* **III**, 661 (1955)
 - 9) J. I. G. Cadogan & G. A. Molina: *J. Chem. Soc. Perkin Trans. 1* **1973**, 541
 - 10) T. Hirashima & O. Manabe: *Chem. Lett.* **3**, 259 (1975)
 - 11) R. H. Mitchell: *J. Org. Chem.* **44**, 4733 (1979)
 - 12) R. S. Neale, R. G. Schepers & M. R. Walsh: *J. Org. Chem.* **29**, 3390 (1964)
 - 13) M. Makosza & B. Serafin: *Rocz. Chem.* **39**, 1595 (1965)
 - 14) L. B. Taranko & R. H. Perry, Jr.: *J. Org. Chem.* **34**, 226 (1969)
 - 15) C. W. Huffman & S. E. Allen: *J. Agric. Food Chem.* **8**, 298 (1960)
 - 16) N. E. Good: *Plant Physiol.* **36**, 788 (1961)
 - 17) J. van Overdeak: *Weeds* **10**, 170 (1962)
 - 18) D. E. Moreland & K. L. Hill: *Weeds* **11**, 55 (1963)

要 約

***N*-Aryl-2-methyl-2-arylpropanamides および
N-aryl-2-methyl-2-arylbutanamides の合成と
除草活性**

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112種の *N*-aryl-2-methyl-2-arylpropanamides および *N*-aryl-2-methyl-2-arylbutanamides を合成し, これらの除草活性を測定した. その結果, 多くの化合物は, タイヌビエ, イヌホタルイ, ミズガヤツリに対しポット試験で強い除草活性を示した. 二つのベンゼン環へ置換基を導入することによって, 活性は大きく変化することがわかった. アミン部分のメタ位のアルキル基と酸部分のオルト位の置換基は高い活性を示すために重要であった. しかし, アミン部分でのパラ位への強い電子吸引性基の導入と酸部分でのパラ位への嵩高い置換基の導入は, 活性に対し好ましくなかった. 112種のなかで *N*-(3-propyl-phenyl)-2-methyl-2-(2-methoxyphenyl) butanamide は, 最も強い活性を示し, ポット試験において 0.625 g a.i./a の薬量でノビエを完全に枯殺した.