Original Article

Quantitative Structure-activity Relationships of Herbicidal *N*-(1-Methyl-1-phenylethyl)phenylacetamides*

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N-(1-Methyl-1-phenylethyl)phenylacetamides exhibited strong growth-inhibiting activity against bulrush, *Scirpus juncoides*, and barnyard grass, *Echinochloa crus-galli*, in the vial tests. The phenylacetyl group was essential for the high activity against *S. juncoides*. Structure-activity relationships of *N*-(1-methyl-1-phenylethyl)phenylacetamides having various benzene ring substituents in the acid and amine moieties were analyzed with substituent parameters and regression techniques. The variation in the activity of 83 compounds was related parabolically with the hydrophobicity of the substituents. The steric factor was also important for the activity: it increased with a decrease in length of the 4-substituents in the acid moiety. Electron-withdrawing effect of the substituents at the 3- or 4-position in the amine moiety increased the activity, too. A similar equation was obtained against *E. crus-galli*. The growth-inhibiting activity was highly correlated with the herbicidal activity in the pot tests.

INTRODUCTION

Our previous papers reported that *N*-benzylbutanamides like *N*-(1-methyl-1-phenylethyl)-2-bromo-3,3-dimethylbutanamide, bromobutide, exhibit potent herbicidal activity against a wide variety of weeds including perennial weeds.^{1,2)} The quantitative structure-activity relationships of these compounds were analyzed with substituent parameters and regression techniques.³⁻⁶⁾

This paper reports that *N*-benzylphenylacetamides such as *N*-[1-methyl-1-(3-chlorophenyl)ethyl]-2-fluorophenylacetamide possess high herbicidal activity. *N*-(1-Methyl-1-phenylethyl)phenylacetamides having various benzene ring substituents in the acid and amine moieties were synthesized and tested for their growth-inhibiting activity against *Scirpus juncoides* and *Echinochloa crus-galli* in the vial

tests. The effect of hydrophobicity of the molecule, the steric dimension of the substituents in the acid moiety and the electronic effect of the substituents in the amine moiety were examined by the Hansch-Fujita method.⁷⁾ Relationships between the growth-inhibiting activity and the herbicidal activity shown in the pot tests under paddy conditions are also discussed.

MATERIALS AND METHODS

1. Compounds

The structure of the compounds was confirmed by PMR and IR spectroscopy in addition to the elemental analyses for C, H, N, and halogens within $\pm 0.30\%$ of the theoretical values for C, H, and N and $\pm 0.45\%$ for halogens. All melting points are uncorrected. All *N*-(1-methyl-1-phenylethyl)phenylacetamides were prepared by the reaction of the appropriate phenylacetyl chloride with a 1-methyl-1-phenylethylamine in the presence of a base. The 1-methyl-1-phenylethylamines

* Herbicidal Activity of *N*-Benzylbutanamides (Part 8). For Part 7, see Ref. 6).

were obtained by the Hofmann reaction of corresponding carboxylic amides.^{8,9)} A typical procedure is shown below.

N-[1-Methyl-1-(3-chlorophenyl)ethyl]-2-fluorophenylacetamide (**78**): 2-Fluorophenylacetyl chloride (6.9 g, 0.04 mol) was added to a mixture containing 1-methyl-1-(3-chlorophenyl)ethylamine (6.8 g, 0.04 mol), triethylamine (5.1 g, 0.05 mol) and benzene (200 ml) under stirring at room temperature. After 4 hr, the reaction mixture was washed successively with water and dilute HCl. The organic layer, after drying with anhydrous sodium sulfate, was evaporated to dryness and the residue was recrystallized from ethanol to give 9.7 g (80%) of colorless crystals, mp 115–116°C.

2. Biological Tests

The growth-inhibiting activity in the vial tests and the herbicidal activity in the pot tests against bulrush, *S. juncoides* and barnyard grass, *E. crus-galli* were determined according to the method reported previously.¹⁾ The growth-inhibiting activity was expressed as the pI_{50} , negative logarithm of the molar concentration in the test solution required for the 50% inhibition of the shoot elongation after 12 days cultivation. The herbicidal activity was expressed as the pED_{50} , negative logarithm of the molar dosage per pot required for the 50% inhibition of the shoot elongation after 3 weeks cultivation.

RESULTS AND DISCUSSION

1. Growth-inhibiting Activity

As shown in Table 1, the phenylacetyl derivative (**2**) exhibits high growth-inhibiting activity against *S. juncoides* in the vial test but benzoyl (**1**), 3-phenylpropionyl (**8**) and 4-phenylbutanoyl (**11**) derivatives show low activity. Alkyl substitutions at the α -position of the phenylacetyl group (compounds **3–7**) also decreased the activity. Dimethyl substitutions at the α - or β -position of the 3-phenylpropionyl group (compounds **9** and **10**) were slightly effective to increase the activity of the unsubstituted compound but their activity was weaker than that of the phenylacetyl derivative. These results may strongly indicate that the phenylacetyl group has the optimum structure as the acid moiety.

Table 1 *N*-(1-Methyl-1-phenylethyl)phenyl substituted-acetamides and their growth-inhibiting activity against *Scirpus juncoides*.

No.	R	mp (°C)	pI_{50}
1	Ph	163–164	2.70
2	PhCH ₂	132–133.5 ^{a,b)}	5.70
3	Ph(Me)CH	114.5–116	5.43
4	Ph(Et)CH	109.5–111	5.22
5	Ph(<i>i</i> -Pr)CH	154–155	<3.7
6	Ph(Me) ₂ C	113–115	5.22
7	Ph(Et) ₂ C	111–112.5	4.91
8	PhCH ₂ CH ₂	96–98	4.52
9	Ph(Me) ₂ CCH ₂	94–95	5.32
10	PhCH ₂ (Me) ₂ C	101–102.5	5.02
11	PhCH ₂ CH ₂ CH ₂	60.5–62	4.55

^{a)} Lit. value: 132–132.7°C (T. Takematsu *et al.*: Jpn. Pat. Kokai Sho-55-104240).

^{b)} Lit. value: 132–133°C (H. Takahashi & T. Suzuki: Jpn. Pat. Kokai Sho-57-139052).

2. Structure-activity Correlation

As shown in Table 2, the growth-inhibiting activity of *N*-(1-methyl-1-phenylethyl)phenylacetamides against *S. juncoides* and *E. crus-galli* varies considerably with the variation of the benzene ring substituents. The results were quantitatively analyzed by the Hansch-Fujita method⁷⁾ using substituent parameters listed in Table 3.

Changes in steric dimensions of the 4-substituents of the benzene ring in the acid moiety cause considerable variation in activity. The activity of *N*-(1-methyl-1-phenylethyl)-mono-substituted-phenylacetamides (compounds **2** and **12–30**) against *S. juncoides* was roughly represented by Eq. (1) in Table 4 with only the STERIMOL length parameter¹⁰⁾ for the 4-substituents, L_{4X} . No significant correlation was derived from other steric parameters such as Taft's steric parameter, E_s ,¹¹⁾ van der Waals volume, V_w ,¹²⁾ or molar refractivity, MR.¹³⁾ Adding hydrophobic π^2 and π terms to Eq. (1) to yield Eq. (2) significantly improved the correlation ($F_{2,16}=7.62$; $F_{2,16,0.005}=7.51$). The π values from the benzene system¹⁴⁾ were used in Eq. (2) because they were slightly superior to those from the phenylacetic acid system and

Table 2 *N*-(1-Methyl-1-phenylethyl)phenylacetamides and their growth-inhibiting and herbicidal activities against *Scirpus juncoides* and *Echinochloa crus-galli*.

No.	X	Y	mp (°C)	pI ₅₀				pED ₅₀	
				<i>S. juncoides</i>		<i>E. crus-galli</i>		<i>S. juncoides</i>	<i>E. crus-galli</i>
				Obsd.	Calcd. ^{a)}	Obsd.	Calcd. ^{b)}	Obsd.	Obsd.
2	H	H	132–133.5	5.70	5.39	4.95	4.81	5.6	5.3
12	2-Me	H	132–134 ^{c)}	5.43	5.72	5.15	5.16	5.4	5.2
13	2- <i>i</i> -Pr	H	78–81 ^{d)}	5.29	5.76	4.67	5.07	5.0	4.8
14	2-F	H	139–140	5.78	5.49	5.39	4.93	5.4	5.4
15	2-Cl	H	142–143 ^{e, n)}	5.76	5.77	5.28	5.20	5.4	5.3
16	2-OMe	H	127.5–129 ^{d)}	5.45	5.37	5.05	4.80	5.2	5.2
17	2-NO ₂	H	152–154 ^{e)}	5.15	5.13	4.28	4.54	5.0	4.5
18	3-Me	H	99.5–101.5	5.58	5.72	5.15	5.16	5.1	5.4
19	3-F	H	114–115	5.58	5.49	5.15	4.93	5.2	5.3
20	3-Cl	H	111–113 ^{h, o)}	5.58	5.77	5.16	5.20	5.1	5.1
21	3-CF ₃	H	86–88 ^{j)}	5.53	5.81	5.01	5.22	5.3	4.7
22	3-OMe	H	102–103.5	5.45	5.37	4.82	4.80	5.5	4.9
23	3-NO ₂	H	116–117.5	4.67	5.13	4.28	4.54	5.0	4.8
24	4-Me	H	133–134.5	5.43	5.26	5.03	4.80	5.3	4.9
25	4- <i>i</i> -Pr	H	104.5–106	4.71	4.75	4.17	4.29	4.7	4.7
26	4-F	H	125.5–127 ^{j)}	5.43	5.20	4.59	4.70	5.1	4.5
27	4-Cl	H	128–130 ^{k)}	5.46	5.06	4.76	4.64	5.3	4.7
28	4-Br	H	123.5–125.5	4.81	4.94	4.32	4.54	4.6	4.3
29	4-OMe	H	123–124 ^{l)}	4.27	4.43	4.05	4.06	4.7	4.4
30	4-OEt	H	111–113	4.27	4.24	4.17	3.98	4.4	4.0
31	2,5-Me ₂	H	151.5–152.5	5.09 ^{s)}	5.82	4.15 ^{s)}	5.22	5.1 ^{s)}	5.1 ^{s)}
32	2,4-Cl ₂	H	161.5–163	4.94 ^{s)}	5.07	4.28 ^{s)}	4.57	4.5 ^{s)}	4.5 ^{s)}
33	3,4-OMe ₂	H	106.5–107.5	3.50 ^{s)}	4.41	3.62 ^{s)}	4.04	4.1 ^{s)}	4.0 ^{s)}
34	H	2-Me	130–132	5.55	5.72	5.03	5.16	5.0	5.1
35	H	2-Cl	109.5–110.5	5.60	5.77	5.01	5.20	5.2	5.4
36	H	3-Me	120.5–122	5.74	5.71	5.13	5.15	5.4	5.1
37	H	3-F	141–143	6.52	6.42	5.45	5.47	5.4	5.0
38	H	3-Cl	114–115	6.66	6.58	5.74	5.67	5.5	5.3
39	H	3-Br	108–109	6.42	6.61	5.42	5.70	5.6	5.5
40	H	4-Me	132–133	6.03	5.71	5.43	5.15	5.4	5.0
41	H	4-Et	116–120	5.96	5.81	4.85	5.22	5.0	4.6
42	H	4- <i>i</i> -Pr	157–158.5	5.57	5.74	4.51	5.07	4.6	4.3
43	H	4-F	129.5–131	6.43	6.34	5.27	5.21	5.2	4.9
44	H	4-Cl	139–140	6.20	6.51	5.38	5.45	5.4	5.3
45	H	4-Br	162–163	6.24	6.54	5.14	5.47	5.3	5.0
46	H	4-OMe	110.5–112	5.65	5.84	4.65	4.96	5.2	5.2
47	H	2,5-Me ₂	166–168	5.20 ^{s)}	5.81	4.91 ^{s)}	5.21	4.8 ^{s)}	5.0 ^{s)}
48	H	2,4-Cl ₂	117.5–119	5.60 ^{s)}	6.52	5.00 ^{s)}	5.37	4.9 ^{s)}	5.2 ^{s)}
49	H	2,6-Cl ₂	151–152	4.11 ^{s)}	5.79	3.95 ^{s)}	5.13	4.3 ^{s)}	4.0 ^{s)}
50	H	3,4-Cl ₂	134–135	6.29 ^{s)}	7.33	5.60 ^{s)}	5.85	5.3 ^{s)}	5.0 ^{s)}
51	2-Me	2-Me	127–128.5	5.85	5.82	5.45	5.22	5.6	5.5
52	2-F	2-Me	125.5–127	5.68	5.77	5.22	5.20	5.6	5.1
53	2-Cl	2-Me	143–146	5.72	5.81	5.30	5.18	5.5	5.3
54	2-OMe	2-Me	112–113	6.07	5.71	5.17	5.15	5.6	5.2
55	3-Me	2-Me	110.5–111.5	5.89	5.82	5.30	5.22	5.6	5.5
56	3-Cl	2-Me	133–134	6.00	5.81	5.25	5.18	5.6	5.5
57	2-Me	2-Cl	124–125	5.58	5.81	5.07	5.18	5.5	5.7
58	2-F	2-Cl	119–120.5	5.44	5.81	5.53	5.22	5.4	5.3

(to be continued)

Table 2 (Continued).

No.	X	Y	mp (°C)	pI ₅₀				pED ₅₀	
				<i>S. juncoides</i>		<i>E. crus-galli</i>		<i>S. juncoides</i>	<i>E. crus-galli</i>
				Obsd.	Calcd. ^{a)}	Obsd.	Calcd. ^{b)}	Obsd.	Obsd.
59	2-Cl	2-Cl	143-145	5.65	5.79	5.22	5.13	5.2	5.6
60	2-OMe	2-Cl	79.5-81.5	5.46	5.77	5.05	5.19	5.1	5.1
61	3-Me	2-Cl	98-99	5.57	5.81	5.08	5.18	5.2	5.4
62	3-Cl	2-Cl	125-127	5.65	5.79	5.15	5.13	5.3	5.6
63	3-OMe	2-Cl	96-97	5.42	5.77	5.12	5.19	5.1	5.1
64	4-Me	2-Cl	109-110	5.18	5.35	5.18	4.82	5.2	5.2
65	4-Cl	2-Cl	128-132	5.41	5.07	5.06	4.57	4.9	4.9
66	2-Me	3-Me	103-104	5.79	5.81	5.17	5.21	5.4	5.4
67	2-F	3-Me	112-113	5.92	5.75	5.41	5.19	5.8	5.5
68	2-Cl	3-Me	94-95	6.10	5.80	5.28	5.17	5.5	5.5
69	2-OMe	3-Me	73-74.5	5.79	5.70	5.03	5.14	5.5	5.5
70	3-Me	3-Me	95-98	5.82	5.81	5.19	5.21	5.5	5.4
71	3-Cl	3-Me	105-106	6.22	5.80	5.32	5.17	5.7	5.6
72	3-CF ₃	3-Me	79-82	5.73	5.76	5.08	5.11	5.5	5.5
73	4-Br	3-Me	109-112	4.64	4.90	4.50	4.44	4.5	4.5
74	4-OEt	3-Me	98-100	4.32	4.40	3.64	4.12	4.3	4.1
75	2-Me	3-F	150-151.5	6.47	6.69	5.56	5.74	5.9	5.7
76	2-Cl	3-F	147-148	6.57	6.73	5.80	5.77	5.9	6.0
77	2-Me	3-Cl	132-133.5	6.49	6.62	5.71	5.65	5.8	6.1
78	2-F	3-Cl	115-116	7.04	6.61	5.88	5.70	6.1	6.3
79	2-Cl	3-Cl	125-126.5	6.71	6.59	5.91	5.60	6.0	6.1
80	2-OMe	3-Cl	95-96.5 ^{p)}	6.53	6.57	5.60	5.67	5.8	6.0
81	3-Me	3-Cl	121-122.5	6.38	6.62	5.48	5.65	5.6	6.2
82	3-Cl	3-Cl	139-140	6.95	6.59	5.63	5.60	5.8	6.2
83	2-Cl	3-Br	130-131	6.47	6.54	5.60	5.53	5.9	5.8
84	2-Me	4-Me	155-156	5.82	5.81	5.13	5.22	5.4	5.2
85	2-F	4-Me	135-136.5	6.01	5.75	5.22	5.19	5.6	5.5
86	2-Cl	4-Me	134-136	6.22	5.80	5.12	5.17	5.0	5.5
87	2-OMe	4-Me	111-113	5.82	5.70	5.11	5.14	6.0	5.0
88	3-Me	4-Me	123-124	5.89	5.81	5.05	5.22	5.1	5.5
89	3-Cl	4-Me	135.5-136.5	5.92	5.80	5.40	5.17	5.2	5.4
90	2-Me	4-F	150-151	6.25	6.62	5.36	5.48	6.1	5.6
91	2-Cl	4-F	143.5-144.5	7.05	6.65	5.98	5.51	5.7	6.0
92	2-OMe	4-F	113-114	6.44	6.33	5.49	5.20	5.5	5.8
93	3-Me	4-F	96.5-99	6.50	6.62	5.22	5.48	5.9	5.5
94	3-Cl	4-F	116-117	6.39	6.65	5.39	5.51	5.6	5.7
95	2-Me	4-Cl	178-179.5 ^{d)}	6.68	6.55	5.38	5.43	5.8	5.9
96	2-F	4-Cl	155-156	6.63	6.54	5.34	5.47	5.8	5.6
97	2-Cl	4-Cl	167-168.5 ^{m,r)}	6.91	6.52	5.61	5.37	5.7	5.8
98	3-Me	4-Cl	114-115	6.84	6.55	5.38	5.43	5.7	5.5
99	2-F	4-Br	178-179	6.60	6.56	5.44	5.47	5.6	5.9
100	3-Cl	4-Br	160-161	6.49	6.48	5.51	5.30	5.5	5.5

^{a)} Calculated by Eq. (5).^{b)} Calculated by Eq. (6).^{c-m)} Lit. value, respectively: 132-134°C, 78-81°C, 140-141.5°C, 127.5-129°C, 152-154°C, 115.5-116.5°C, 86-88°C, 125.5-127°C, 128-130°C, 111-113°C, 164-165.5°C (H. Takahashi & T. Suzuki: Jpn. Pat. Kokai Sho-57-139051).^{n,o)} Lit. value, respectively: 140.5-141.5°C, 115.5-116.5°C (T. Takematsu *et al.*: Jpn. Pat. Kokai Sho-55-104240).^{p-r)} Lit. value, respectively: 83.8-84.5°C, 178-178.8°C, 164-164.8°C (T. Takematsu *et al.*: Jpn. Pat. Kokai Sho-56-110655).^{s)} Not included in the correlation.

Table 3 Substituent parameters used for correlations.

Substituent	π^a	L^b	σ_I^c	Substituent	π^a	L^b	σ_I^c
H	0.00	0.00	0.00	Br	0.86	1.77	0.47
Me	0.56	0.94	-0.01	CF ₃	0.88		
Et	1.02		-0.01	OMe	-0.02	1.92	0.30
<i>i</i> -Pr	1.53	2.05	0.01	OEt	0.38	2.86	
F	0.14	0.59	0.54	NO ₂	-0.28		
Cl	0.71	1.46	0.47				

^a) π values from the benzene system, taken from Ref. 13).

^b) STERIMOL parameters, taken from Ref. 10). The values of the reference is shifted to $L(H)=0$.

^c) Electronic effect constants, taken from Ref. 15).

Table 4 Correlation equations^{a)} for the growth-inhibiting activity of *N*-(1-methyl-1-phenylethyl)phenylacetamides against *Scirpus juncoides* and *Echinochloa crus-galli*.

Variable substituent	Test plant	$a(\Sigma m)^2 + b\Sigma\pi + cL_{\alpha} + d\sigma_I^{\text{meta}} + e\sigma_I^{\text{para}} + \text{const}$				n^b	s^c	r^d	F_{ν_1, ν_2}^e	Eq. No.
X, Y=H	<i>S. juncoides</i>	-0.390 (0.163)				5.492 (0.173)	20	0.308	0.765	25.38 (1)
X, Y=H	<i>S. juncoides</i>	-0.599 (0.369)	0.917 (0.498)			5.384 (0.157)	20	0.234	0.887	19.76 (2)
Y, X=H	<i>S. juncoides</i>			1.634 (0.276)	1.000 (0.270)	5.723 (0.074)	14	0.200	0.883	19.44 (3)
(X, Y=H & Y, X=H)	<i>S. juncoides</i>	-0.562 (0.135)	0.897 (0.183)	-0.446 (0.052)	1.747 (0.273)	5.400 (0.064)	33	0.215	0.940	40.96 (4)
X, Y	<i>S. juncoides</i>	-0.369 (0.104)	0.805 (0.162)	-0.490 (0.042)	1.708 (0.156)	5.387 (0.064)	83	0.235	0.931	99.45 (5)
X, Y	<i>E. crus-galli</i>	-0.454 (0.096)	0.864 (0.149)	-0.383 (0.039)	1.011 (0.144)	4.815 (0.059)	83	0.217	0.874	49.67 (6)

^a) Figures in parentheses are the 95% confidence intervals. All the terms are justified above 99.5% level by the *t* test unless noted otherwise.

^b) The number of compounds used in the correlation.

^c) Standard deviation.

^d) Multiple correlation coefficient.

^e) *F* values of the correlation. $\nu_1=m$ and $\nu_2=n-m-1$; *m* is the number of independent variables used in the correlation.

Table 5 The squared correlation matrix for variables used in Eqs. (5) and (6).

	$(\Sigma\pi)^2$	$\Sigma\pi$	L_{4X}	σ_I^{meta}	σ_I^{para}
$(\Sigma\pi)^2$	1.000	0.884	0.001	0.009	0.001
π		1.000	0.000	0.012	0.000
L_{4X}			1.000	0.022	0.027
σ_I^{meta}				1.000	0.034
σ_I^{para}					1.000

applicable for the benzene ring substituents in the amine moiety. Adding $(L_{4X})^2$ and electronic $\sigma^{13)}$ terms singly or together to Eq. (2) did not significantly improve the correlation. In the case of *N*-(1-methyl-1-monosubstituted-phenylethyl)phenylacetamides (compounds **2** and **34-46**), the electronic property of the benzene ring substituents in the amine moiety was important for correlating the activity variation. The Eq. (3) with the electronic effect parameter $\sigma_I^{15)}$ for substituents at the 3- and 4-positions, σ_I^{meta} and σ_I^{para} , showed a good correlation. The electronic effect of the substituents at the 2-position was not significant. The use of electronic $\sigma^{13)}$, $\sigma^{o16)}$, $F^{17)}$, or $R^{17)}$ constant instead of σ_I did not afford any significant improvement. Thus, Eq. (4) was derived for the combined set of both monosubstituted phenyl series of *N*-(1-methyl-1-phenylethyl)phenylacetamides against *S. juncooides*.

The derivatives having two substituents in the same phenyl group (compounds **31-33** and **47-50**) showed considerably reduced activity. The activity of this type of disubstituted derivatives was not well represented by Eq. (4), the equation obtained from the monosubstituted derivatives. However, the activity of disubstituted derivatives having one substituent in the acid moiety and the other in the amine moiety (compounds **51-100**) was well predicted by the equation. Finally Eqs. (5) and (6) with $(\Sigma\pi)^2$, $\Sigma\pi$, L_{4X} , σ_I^{meta} , and σ_I^{para} were derived for 83 compounds including mono- and di-substituted derivatives against *S. juncooides* and *E. crus-galli*. $\Sigma\pi$ is the sum of π values of substituents X and Y. The squared correlation matrix of the variables used in Eqs. (5) and (6) is shown in Table 5.

According to Eq. (5), the growth-inhibiting activity against *S. juncooides* is related parabolically to the hydrophobicity of the substitu-

ents and reaches a maximum when π is 1.09. Equation (6) shows that the activity against *E. crus-galli* is also related parabolically to the hydrophobicity and reaches a maximum when π is 0.95. These parabolic relationships seem to indicate that the compound should traverse a number of lipoidal-aqueous interfaces to reach a critical site for the activity.¹⁴⁾ The negative sign of the L_{4X} term in Eqs. (5) and (6) means that the activity decreases with an increase in length of the 4-substituents in the acid moiety. This result may reflect that the steric bulkiness of the 4-substituents interferes with molecular fit at the site critical for the activity. The positive sign of the σ_I^{meta} and σ_I^{para} terms in Eqs. (5) and (6) indicates that the activity increases with an increase in electron-withdrawing effect of the substituents at the 3- and 4-positions of the benzene ring in the amine moiety. The activity variation is more sensitive to the substitution at the 3-position than at the 4-position in both plant species, especially in *E. crus-galli*. The electronic effect for the substituents at the 2-position is lacking. This result concerning the benzene ring substituents in the amine moiety does not agree with our previous report of *N*-benzylbutanamide type herbicides stating that unsubstitution is favorable for high activity.⁴⁾

The simple correlation coefficient between the activity against *S. juncooides* and that against *E. crus-galli* is 0.870 for 83 compounds. Moreover, Eqs. (5) and (6) have the same terms and the optimum π value is similar between both plant species. Therefore, the mode of action of *N*-(1-methyl-1-phenylethyl)phenylacetamides against *S. juncooides* may be similar to that against *E. crus-galli*.

3. Herbicidal Activity

As shown in Table 2, *N*-(1-methyl-1-phenyl-

ethyl)phenylacetamides possess the herbicidal activity against *S. juncooides* and *E. crus-galli* in the pot tests under paddy conditions. The herbicidal activity, pED_{50} , for 90 compounds was represented by Eqs. (7) and (8) using growth-inhibiting activity, pI_{50} , in the vial tests.

$$\begin{aligned} pED_{50}(S. juncooides) \\ = 0.517pI_{50}(S. juncooides) + 2.334 \quad (7) \\ (0.036) \quad (0.207) \\ n=90, s=0.231, r=0.840, F=211.45 \end{aligned}$$

$$\begin{aligned} pED_{50}(E. crus-galli) \\ = 0.905pI_{50}(E. crus-galli) + 0.627 \quad (8) \\ (0.059) \quad (0.301) \\ n=90, s=0.269, r=0.854, F=238.08 \end{aligned}$$

In Eq. (7), the coefficient of pI_{50} (*S. juncooides*), 0.517, is considerably smaller than 1. This indicates that the variation in the activity against *S. juncooides* is reduced in the pot tests compared with that in the vial tests. However, the herbicidal activity in the pot tests against *S. juncooides* is correlated with the growth-inhibiting activity in the vial tests. In Eq. (8), the coefficient of the pI_{50} (*E. crus-galli*) is almost 1 and the intercept is small. This means that the herbicidal activity against *E. crus-galli* in the pot tests is similar to the growth-inhibiting activity in the vial tests.

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要 約

除草活性を有する *N*-(1-methyl-1-phenylethyl)phenylacetamides の定量的構造活性相関*

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N-(1-Methyl-1-phenylethyl)phenylacetamide 誘導体は、イヌホタルイ (*Scirpus juncooides*) およびノビエ (*Echinochloa crus-galli*) に対し、バイアル試験で強い生育阻害活性を示した。高活性発現には、フェニルアセチル基が必要であることがわかった。酸部位およびアミン部位のベンゼン環に種々の置換基を有する *N*-(1-methyl-1-phenylethyl)phenylacetamides の定量的構造活性相関を、置換基定数を用いた重回帰分析により解析したところ、83 個のイヌホタルイに対する活性変化は、置換基の疎水性に対して放物線的な関係にあることが明らかとなった。また、酸部位のベンゼン環の 4 位置換基の長さが短いほど活性は高く、アミン部位のベンゼン環の 3 位あるいは 4 位置換基の電子吸引性が、活性を増大させることがわかった。ノビエに対しても同様な解析式が得られた。さらに、バイアル試験における生育阻害活性とポット試験における除草活性との間には、密接な関係のあることが示された。

* *N*-Benzylbutanamides の除草活性 (第 8 報)