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Original Article

Photosynthetic Electron Transport Inhibitory and Herbicidal Activities of 2-(Fluorinated methyl)-4-benzylamino-6-methyl-1,3,5-triazines

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To investigate the substitution effect of the fluorine atom on methyl group, a methyl group of 2-benzylamino-4,6-dimethyl-1,3,5-triazines was replaced with fluoromethyl, difluoromethyl and trifluoromethyl groups and photosynthetic electron transport (PET) inhibitory and herbicidal activities of these (fluorinated methyl)-1,3,5-triazine compounds were evaluated. With increasing the number of fluorine atom of fluorinated methyl group, PET inhibitory activity became higher. Furthermore by introduction of a halogen atom to the 4-position of the benzyl group, PET inhibitory activity was much improved compared to the triazines having an un-substituted benzylamino group. The (fluorinated methyl)-1,3,5-triazine derivatives with higher PET inhibitory activity showed also stronger herbicidal activity in soil and foliar application tests.

Key words: photosynthetic electron transport (PET), PET inhibitory activity, herbicidal activity, 2-(fluorinated methyl)-4-(4-halogenobenzylamino)-6-methyl-1,3,5-triazines.

INTRODUCTION

Photosynthetic electron transport (PET) inhibitory activity and herbicidal activity of 2-benzylamino-4-methyl-6-trifluoromethyl-1,3,5-triazines have already been reported by Kuboyama *et al.*[1,2] in our group. Some of these compounds showed relatively strong activities and especially 2-(4-chloro or 4-bromobenzylamino)-4-methyl-6-trifluoromethyl-1,3,5-triazines exhibited much stronger herbicidal activity and more potent PET inhibition than simazine. The trifluoromethyl group on the 1,3,5-triazine ring was considered to be important to the both activities. However, the effects of the fluoromethyl and difluoromethyl groups replaced in the place of trifluoromethyl group on the activities have not been discussed yet. In this study, we synthesized 2-(fluorinated methyl)-4-(4-halogenobenzylamino)-6-methyl-1,3,5-triazines and investigated the contribution of the fluorinated methyl group to PET inhibitory and herbicidal activities.

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MATERIALS AND METHODS

1. Instrumental Analysis

Elementary analysis was performed with a Perkin-Elmer 240D elemental analyzer. IR and mass spectra were recorded on a JASCO FT/IR-420 spectrophotometer and a JEOL JMS-AX505W mass spectrometer, respectively. ^{1}H NMR spectra were measured on a JEOL JNM-GX400 spectrometer at 400 MHz using tetramethylsilane (TMS) as internal standard. Melting points were measured with a Yanagimoto Seisakusyo melting point apparatus. Refractive index was measured with an ATAGO Abbe refractometer.

2. Chemicals

Fine chemicals for assays were purchased from Kanto Chemical Co., Inc., Tokyo, Tokyo Kasei Kogyo Co., LTD., Tokyo or Sigma Chem. Co., München, Germany.

All the test compounds were synthesized by the nucleophilic substitution reaction of the corresponding trichloromethyl-1,3,5-triazine derivatives with the 4-halogenobenzylamines. Two starting trichloromethyl-1,3,5-triazines, 2,4-dimethyl-6-trichloromethyl-1,3,5-

triazine (mp 76–77°C, IR ν_{max}^{KBr} cm^{-1}: 1528) and 2-methyl-4-trichloromethyl-6-trifluoromethyl-1,3,5-triazine (bp 73–74°C/7 mmHg, $n_D^{24}=1.4671$. IR ν_{max}^{KBr} cm^{-1}: 1555), were prepared by condensation reaction of *N*-(acetimidoyl)-trichloroacetamidine with $(CH_3CO)_2O$ and $(CF_3CO)_2O$ in the yields of 91% and 70% respectively.[1,3] 2-Fluoromethyl-4-methyl-6-trichloromethyl-1,3,5-triazine and 2-difluoromethyl-4-methyl-6-trichloromethyl-1,3,5-triazine were obtained by the similar process (see, *2.1* and *2.2*).

2.1 Synthesis of 2-fluoromethyl-4-methyl-6-trichloromethyl-1,3,5-triazine

Fluoroacetic pivalic anhydride (bp 79°C/17 mmHg) was prepared from $CH_2FCOONa$ and $(CH_3)_3CCOCl$. To a solution of *N*-(acetimidoyl)-trichloroacetamidine (7.9 g, 39 mmol) in 20 ml of diethyl ether, fluoroacetic pivalic anhydride (9.1 g, 56 mmol) in 15 ml of diethyl ether was added at 0–5°C. After stirring at room temperature for 20 hr, the reaction mixture was concentrated under reduced pressure. The residue was diluted with saturated brine and extracted with CH_2Cl_2. After drying over anhydrous sodium sulfate, the organic layer was evaporated and the residue was purified by column chromatography over silica gel using benzene: hexane = 1 : 1 to give 2-fluoromethyl-4-methyl-6-trichloromethyl-1,3,5-triazine as pale yellow liquid ($n_D^{25}=1.5132$). Yield: 4.33 g (45%).

Anal. Found: C, 29.58; H, 2.08; N, 17.24. Calcd. for $C_6H_5Cl_3FN_3$: C, 29.47; H, 2.06; N, 17.19%. IR ν_{max}^{KBr} cm^{-1}: 1537, 1557 (1,3,5-triazine ring). ^1H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.87 (3H, s, CH_3), 5.57 (2H, d, $J=46.4$ Hz, CH_2F). MS m/z: 243 (M^+), 208 (M^+-Cl) and 108 (CCl_2CN).

2.2 Synthesis of 2-difluoromethyl-4-methyl-6-trichlorometyl-1,3,5-triazine

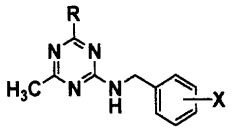
2-Difluoromethyl-4-methyl-6-trichlorometyl-1,3,5-triazine was prepared by the condensation reaction of *N*-(acetimidoyl)trichloroacetamidine with $(CHF_2CO)_2O$ according to the same procedure mentioned in section *2.1*. Yield: 28.1 g (54%).

Bp: 66–68°C/3 mmHg ($n_D^{24}=1.4926$). Anal. Found: C, 27.50; H, 1.60; N, 16.02. Calcd. for $C_6H_4Cl_3F_2N_3$: C, 27.45; H, 1.54; N, 16.01%. IR ν_{max}^{KBr} cm^{-1}: 1543, 1557 (1,3,5-triazine ring). ^1H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.93 (3H, s, CH_3), 6.63 (1H, t, $J=53.7$ Hz, CHF_2). MS m/z: 261 (M^+), 242 (M^+-F), 226 (M^+-Cl) and 108 (CCl_2CN).

*2.3 Synthesis of 2-(4-chlorobenzylamino)-4-fluoromethyl-6-methyl-1,3,5-triazine (**2-3**)*

To a solution of 2-fluoromethyl-4-methyl-6-trichloromethyl-1,3,5-triazine (1.0 g, 4.1 mmol) in 5 ml of THF, 4-chlorobenzylamine (0.64 g, 4.5 mmol) was added. After stirring over night at room temperature, the reaction mixture was concentrated under reduced

Table 1 2-(Fluorinated methyl)-4-(un)substituted benzylamino-6-methyl-1,3,5-triazines synthesized.



No.	R	X	Yield (%)*	mp (°C)	Characteristic absorption of 1,3,5-triazine (IR spectrum, cm^{-1})
1-1	CH_3	H	52	113–114 (Lit.[1] 113–114)	1532, 1559
1-2	CH_3	4-Br	23	141.5–142	1532, 1566
1-3	CH_3	4-Cl	80	133–134	1531, 1566
2-1	CH_2F	H	53	83–84 (Lit.[4] 83–84)	1542, 1572
2-2	CH_2F	4-Br	46	116–118	1550, 1574
2-3	CH_2F	4-Cl	31	110–112	1542, 1570
3-1	CHF_2	H	72	62–63 (Lit.[4] 61–63)	1543, 1577
3-2	CHF_2	4-Br	32	61–64	1539, 1577
3-3	CHF_2	4-Cl	71	90–91	1549, 1577
3-4	CHF_2	3-Cl	31	oil	1521, 1581
3-5	CHF_2	4-CH_3	92	66–68	1520, 1578
3-6	CHF_2	4-NO_2	57	99–101	1547, 1578
4-1	CF_3	H	83	57–59 (Lit.[1] 45–47)	1547, 1583
4-2	CF_3	4-Br	49	99–100 (Lit.[1] 88–90)	1545, 1581
4-3	CF_3	4-Cl	89	74–76 (Lit.[1] 74–76)	1548, 1581
4-4	CF_3	3-Cl	85[1]	58–61[1]	1549, 1573[1]
4-5	CF_3	4-CH_3	91[1]	70–73[1]	1546, 1578[1]
4-6	CF_3	4-NO_2	79[1]	54–58[1]	1550, 1578[1]

*The figure indicates the yield of amination step of trichloromethyl-1,3,5-triazines.

pressure and the residue was purified by column chromatography over silica gel using ethyl acetate: hexane=1 : 1 to give 2-(4-chlorobenzylamino)-4-fluoromethyl-6-methyl-1,3,5-triazine (**2-3**). Yield: 0.34 g (31%).

Anal. Found: C, 54.14; H, 4.60; N, 21.03. Calcd. for $C_{12}H_{12}ClFN_4$: C, 54.04; H, 4.54; N, 21.01%. ^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm : 2.44 and 2.47 (total 3H, each s, CH_3), 4.64 and 4.66 (total 2H, each d, J=6.3 Hz and J=6.4 Hz, CH_2), 5.21 and 5.23 (total 2H, each d, J=46.9 Hz and J=46.6 Hz, CH_2F), 6.05 (1H, br, NH), 7.29 (4H, m, phenyl-H). MS m/z: 266 (M^+) and 247 (M^+-F).

The other 2-(fluorinated methyl)-4-(substituted benzylamino)-6-methyl-1,3,5-triazine derivatives (**1-1**, **1-2**, **1-3**; **2-1**, **2-2**; **3-1**, **3-2**, **3-3**, **3-4**, **3-5**, **3-6**; **4-1**, **4-2**, **4-3**) were prepared by the nucleophilic substitution reaction of the corresponding trichloromethyl-1,3,5-triazine derivatives with the substituted benzylamines according to the methods of Kuboyama *et al.*[1,4] ^{1}H NMR spectral data are shown below. The other data are shown in Table 1.

2.4 2-(4-Bromobenzylamino)-4,6-dimethyl-1,3,5-triazine (1-2)

^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.39 and 2.43 (total 6H, each s, CH_3), 4.68 (2H, d, J=6.3 Hz, CH_2), 5.70 (1H, br, NH), 7.19 (4H, m, phenyl-H).

2.5 2-(4-Chlorobenzylamino)-4,6-dimethyl-1,3,5-triazine (1-3)

^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.39 and 2.43 (total 6H, each s, CH_3), 4.64 (2H, d, J=6.1 Hz, CH_2), 5.62 (1H, br, NH), 7.29 (4H, m, phenyl-H).

2.6 2-Benzylamino-4-fluoromethyl-6-methyl-1,3,5-triazine (2-1)

^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.44 and 2.48 (total 3H, each s, CH_3), 4.68 (2H, m, CH_2), 5.20 and 5.24 (total 2H, each d, J=46.9 Hz and 46.9 Hz, CH_2F), 5.94 (1H, br, NH), 7.32 (5H, m, phenyl-H).

2.7 2-(4-Bromobenzylamino)-4-fluoromethyl-6-methyl-1,3,5-triazine (2-2)

^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.45 and 2.47 (total 3H, each s, CH_3), 4.63 (2H, t, J=27.8 Hz, CH_2), 5.17 and 5.28 (total 4H, each d, J=46.9 Hz and J=46.6 Hz, CH_2F), 5.99 (1H, br, NH), 7.26 (4H, m, phenyl-H).

2.8 2-Benzylamino-4-difluoromethyl-6-methyl-1,3,5-triazine (3-1)

^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.49 and 2.54 (total 3H, each s, CH_3), 4.70 and 4.70 (total 2H, each d, J=5.9 Hz and J=5.9 Hz, CH_2), 5.95 (1H, br, NH), 6.26 and 6.31 (total 1H, each t, J=54.3 Hz and J=54.3 Hz, CF_2H), 7.34 (5H, m, phenyl-H).

2.9 2-(4-Bromobenzylamino)-4-difluoromethyl-6-methyl-1,3,5-triazine (3-2)

^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.49 and 2.53 (total 3H, each s, CH_3), 4.65 and 4.66 (total 2H, each d, J=5.9 Hz and 5.9 Hz, CH_2), 6.13 and 6.16 (total 1H, each br, NH), 6.27 and 6.30 (total 1H, each t, J=54.4 Hz and 54.4 Hz, CHF_2), 7.20 and 7.21 (total 2H, each d, J=8.3 Hz and J=8.3 Hz, H-2 and H-6 of benzene ring), 7.48 (2H, d, J=8.3 Hz, H-3 and H-5 of benzene ring).

2.10 2-(4-Chlorobenzylamino)-4-difluoromethyl-6-methyl-1,3,5-triazine (3-3)

^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.48 and 2.53 (total 3H, each s, CH_3), 4.66 and 4.67 (total 2H, each d, J=4.0 Hz and 4.0 Hz, CH_2), 5.90 and 5.97 (total 1H, each br, NH), 6.27 and 6.30 (total 1H, each t, J=54.4 Hz and J=54.4 Hz, CHF_2), 7.258 and 7.263 (total 2H, each d, J=8.6 Hz and 8.6 Hz, H-2 and H-6 of benzene ring), 7.32 (2H, d, J=8.3 Hz, H-3 and H-5 of benzene ring).

2.11 2-(3-Chlorobenzylamino)-4-difluoromethyl-6-methyl-1,3,5-triazin (3-4)

^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.49 and 2.54 (total 3H, each s, CH_3), 4.68 and 4.69 (total 2H, each d, J=4.2 Hz and 4.2 Hz, CH_2), 6.03 (total 1H, each br, NH), 6.27 and 6.31 (total 1H, each t, J=59.3 Hz and J=59.3 Hz, CHF_2), 7.26 (4H, m, phenyl-H)

2.12 2-Difloromethyl-4-methyl-6-(4-nitorobenzylamino)-1,3,5-triazine (3-5)

^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.51 and 2.52 (total 3H, each s, CH_3), 4.82 (total 2H, each d, J=4.1 Hz, CH_2), 6.09 (total 1H, br, NH), 6.28 and 6.29 (total 1H, each t, J=59.3 Hz and J=59.3 Hz, CHF_2), 7.26 (4H, m, phenyl-H)

2.13 2-Difluoromethyl-4-methyl-6-(4-methylbenzylamino)-1,3,5-triazine (3-6)

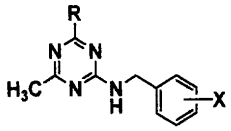
^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.35 and 2.47 (total 6H, each s, CH_3), 4.15 and 4.20 (total 2H, each d, J=4.0 Hz CH_2), 5.89 (total 1H, br, NH), 6.26 and 6.31 (total 1H, each t, J=54.3 Hz and J=54.3 Hz, CF_2H), 7.20 (4H, m, phenyl-H).

3. Phytotoxic Assays

3.1 Determination of PET inhibitory activity

According to the methods reported,[5-7] thylakoids prepared from spinach (*Spinacia oleracea*) leaves were used for the assay for PET inhibitory activity of the 1,3,5-triazines synthesized. PET inhibition of the compounds was determined with the system $H_2O \rightarrow$ ferricyanide, uncoupled by NH_4Cl.[7,8] The freshly-prepared thylakoids suspension was added to the mixture containing 0.1 M of sucrose, 50 mM of Tricine (pH8.0), 5 mM of $MgCl_2$, 1 mM of NH_4Cl and 1 mM of potassium ferricyanide, to prepare chlorophyll content 15μg/ml. And the final concentration of the solvent (MeOH) in which each 1,3,5-triazine compound was dissolved was kept below 1% (v/v). The oxygen formed was measured with the oxygen electrode (Rank Brothers Bottisham, Cambridge, England). The molar concentration (I_{50}) required for 50% inhibition of PET was calculated for each compound by the probit method. The pI_{50} value is the logarithm of the reciprocal I_{50}. The results of PET inhibitory activity are shown in Table 2.

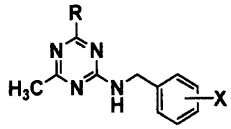
Table 2 PET inhibitory activity of 2-(fluorinated methyl)-4-(un)substituted benzylamino-6-methyl-1,3,5-triazines.



No.	R	X	pI_{50} (Spinach)*	No.	R	X	pI_{50} (Spinach)*
1-1	CH_3	H	4.20 (Lit.[2]4.19)	**3-4**	CHF_2	3-Cl	6.43
1-2	CH_3	4-Br	5.98	**3-5**	CHF_2	4-CH_3	6.45
1-3	CH_3	4-Cl	5.78	**3-6**	CHF_2	4-NO_2	6.49
2-1	CH_2F	H	4.98	**4-1**	CF_3	H	6.86 (Lit.[2]6.85)
2-2	CH_2F	4-Br	6.48	**4-2**	CF_3	4-Br	6.92 (Lit.[2]6.94)
2-3	CH_2F	4-Cl	6.15	**4-3**	CF_3	4-Cl	6.97 (Lit.[2]6.98)
3-1	CHF_2	H	5.63	**4-4**	CF_3	3-Cl	7.21
3-2	CHF_2	4-Br	6.94	**4-5**	CF_3	4-CH_3	6.74
3-3	CHF_2	4-Cl	6.62	**4-6**	CF_3	4-NO_2	7.16
	Simazine		6.28				

*$pI_{50} = -\log I_{50}$ (I_{50} : 50% inhibition concentration for PET)

Table 3 Herbicidal activity of 2-(fluorinated methyl)-4-(un)substituted benzylamino-6-methyl-1,3,5-triazines.



			Soil application test						Foliar application test					Paddy application test				
No.	R	X	Dose g a.i./10a	Ec	Dc	Ca	Pl	Al	Dose g a.i./10a	Ec	Dc	Ca	Pl	Dose g a.i./10a	Eo	Sj	Mv	Ri
1-1	CH_3	H	800	0	0	0	—	—	400	0	0	0	0	800	3	0	6	1
2-1	CH_2F	H	400	1	1	5	2	4	400	0	1	6	4	400	0	0	0	0
2-2	CH_2F	4-Br	400	4	4	5	5	5	400	4	5	6	6	400	5	5	5	6
2-3	CH_2F	4-Cl	400	3	3	5	4	4	400	4	4	6	6	400	5	4	5	6
3-1	CHF_2	H	400	5	4	6	6	4	400	3	4	6	6	400	4	5	6	5
3-2	CHF_2	4-Br	400	4	5	6	6	5	400	6	6	6	6	400	6	6	6	6
3-3	CHF_2	4-Cl	400	4	5	6	6	5	400	6	6	6	6	400	5	6	6	6
3-4	CHF_2	3-Cl	400	4	4	5	5	4	400	3	4	6	6	400	4	5	5	5
3-5	CHF_2	4-CH_3	400	3	4	5	5	4	400	4	4	6	6	400	4	5	5	5
3-6	CHF_2	4-NO_2	400	4	4	5	5	5	400	4	5	6	6	400	5	5	5	6
4-1	CF_3	H	400	2	3	6	—	4	400	3	4	6	—	400	3	0	6	4
4-2	CF_3	4-Br	400	5	5	5	—	5	400	4	6	6	6	400	4	6	5	5
4-3	CF_3	4-Cl	400	3	5	5	—	6	400	4	6	6	6	400	6	6	6	6
	Simazine		100	2	3	5	—	5	—	—	—	—	—	—	—	—	—	—

Abbreviation (weeds); Ec: *Echinochloa crus-galli* (L) Beauv. var. *crus-galli*, Dc: *Digitaria ciliaris*, Ca: *Chenopodium album*, Pl: *Polygonum longisetum*, Al: Amaranthus lividus, Eo: *Echinochloa oryzicola*, Sj: *Scirpus juncoides* Roxb. var. *hotarui* Chwi, Mv: *Monochoria vaginalis*, Ri: *Rotala indica*. Evaluation; **6**: 100% weed control (complete kill), **5**: 91 to 99% weed control, **4**: 76 to 90% weed control, **3**: 51 to 75% weed control, **2**: 26 to 50% weed control, **1**: 1 to 25% weed control, **0**: 0% weed control (no effect).

3.2 Evaluation of herbicidal activity

Each compound was formulated as 10% wettable powder including the condensation product of naphthalensulfonic acid and formalin (1%), polyoxyethylene alkylphenol ether (0.5%), white carbon (0.5%) and diatomaceous earth (88%). Evaluation was carried out in soil (pre-emergence), foliar (post-emergence) and paddy (pre-emergence) application tests. Weeds used in soil and foliar applications were commonly *Echinochloa crus-galli* (L) Beauv. var. *crus-galli, Digitaria ciliaris, Chenopodium album, Polygonum longisetum*, but *Amaranthus lividus* was added only in soil application test.

While, weeds used in paddy application test were *Echinochloa oryzicola, Monochoria vaginalis, Scirpus juncoides* Roxb. var. *hotarui* Ohwi and *Rotala indica*. Suspension, which was prepared by dilution of the wettable powder of each test compound, was sprayed onto the soil, weed leaves and water surface modeled in paddy condition. Three weeks after the treatments, herbicidal activity was evaluated by visual observation of treated weeds in comparison with the untreated controls on the scale of 0–6, where 6 indicates the complete kill of test weeds and zero indicates no effect. The results are shown in Table 3.

RESULTS AND DISCUSSION

1. *PET Inhibitory Activity of the 2-(Fluorinated methyl)-4-(un)substituted benzylamino-6-methyl-1,3,5-triazines*

Table 2 shows PET inhibitory activity of the 1,3,5-triazine compounds. The order of PET inhibitory potency of the 2-benzylamino-1,3,5-triazines tested was CF_3->CHF_2->CH_2F->CH_3-1,3,5-triazines. 2-Benzylamino-4-methyl-6-trifluoromethyl-1,3,5-triazine (**4–1**) had about 460 times stronger activity than 2-benzylamino-4,6-dimethyl-1,3,5-triazine (**1–1**) and 17 times stronger activity than 2-benzylamino-4-difluoromethyl-6-methyl-1,3,5-triazine (**3–1**). On the other hand, 2-(4-halogenobenzylamino)-4-fluoromethyl-6-methyl-1,3,5-triazines (**2–2** and **2–3**) had only about 2–3 times stronger activity than 2-(4-halogenobenzylamino)-4,6-dimethyl-1,3,5-triazines (**1–2** and **1–3**) and 2-(4-halogenobenzylamino)-4-(fluorinated methyl)-6-methyl-1,3,5-triazines had not so much differences in pI_{50}-values (6.15–6.97) caused by introduction of the fluorine atom(s), compared to 2-benzylamino-4-(fluorinated methyl)-6-methyl-1,3,5-triazine derivatives. Therefore, introduction of the two or three fluorine atoms to a methyl group of 2-(4-halogeno)benzylamino-4,6-dimethyl-1,3,5-triazines revealed much to improve PET inhibitory activity. And the activity of 2-benzylamino-4,6-dimethyl-1,3,5-triazine which has unsubstituted benzylamino group was gradually improved with the increase of the number of fluorine atoms.

Among the 1,3,5-triazines having the same fluorinated methyl group, 4-halogenobenzylamino derivatives had much stronger activity than that of unsubstituted benzylamino derivatives. As Kuboyama *et al.* reported[2] that introduction of the halogen atom to the 4-position of the benzene ring of 2-benzylamino-4-methyl-6-trifluoromethyl-1,3,5-triazine was effective to enhance PET inhibitory activity, the similar effect was observed in the case of the fluoromethyl-1,3,5-triazine, difluoromethyl-1,3,5-triazine and 2,4-dimethyl-1,3,5-triazine derivatives. Especially 2-(4-bromobenzylamino)-4-fluoromethyl-6-methyl-1,3,5-triazine (**2–2**) and 2-difluoromethyl-4-(4-halogenobenzylamino)-6-methyl-1,3,5-triazine derivatives (**3–2** and **3–3**) showed higher PET inhibition than that of simazine as well as the trifluoromethyl derivatives (**4–2** and **4–3**). And also, 2-difluoromethyl-4-methyl-6-substituted benzylamino-1,3,5-triazine derivatives (**3–4**, **3–5** and **3–6**) showed a similar effect that of trifluoromethyl derivatives (**4–4**, **4–5** and **4–6**). However, difluoromethyl derivatives (**3–4**, **3–5** and **3–6**) were more effective to gave a high PET inhibitory activity for 2-benzylamino-4-difluoromethyl-6-methyl-1,3,5-triazine (**3–1**) than that of trifluoromethyl derivatives (**4–4**, **4–5** and **4–6**). For the strong PET inhibitory activity of 2-(4-halogeno)benzylamino-4-(fluorinated methyl)-6-methyl-1,3,5-triazines, the difluoromethyl group was considered to be the effective substitutent as well as the trifluoromethyl group.

2. *Herbicidal Activity of the 2-(Fluorinated methyl)-4-(4-halogeno)benzylamino-6-methyl-1,3,5-triazines*

Herbicidal activity of 2-(fluorinated methyl)-4-(4-halogeno)benzylamino-6-methyl-1,3,5-triazines are shown in Table 3. In the soil, foliar, and paddy application tests, the trifluoromethyl derivatives (**4–1**～**4–3**), which had the strongest PET inhibitory activity showed higher herbicidal activity. Furthermore 2-(4-chloro or 4-bromo benzylamino)-4-difluoromethyl-6-methyl-1,3,5-triazine (**3–2** and **3–3**), of which PET inhibitory activity was almost equal to that of 2-benzylamino-4-methyl-6-trifluoromethyl-1,3,5-triazine (**4–1**), showed 90 to 100% weed control at the dose of 400 g a.i./10 a in the three application tests. Herbicidal activity of 2-difluoromethyl-4-methyl-6-substituted benzylamino-1,3,5-triazine derivatives (**3–4**, **3–5** and **3–6**) were not so much as herbicidal activity of 2-(4-halogeno)benzylamino-4-difluoromethyl-6-methyl-1,3,5-triazine derivatives(**3–2** and **3–3**). Accordingly, introduction of halogen atom to the 4-position of the benzene ring of 2-benzylamino-4-difluoromethyl-6-methyl-1,3,5-triazine was more suitable than that of other substituents. Comparing between two compounds with lower PET inhibitory activity (pI_{50}< 5.00), *i.e.* 2-benzylamino-4,6-dimethyl-1,3,5-triazine (**1–1**) and 2-benzylamino-4-fluoromethyl-6-methyl-1,3,5-triazine (**2–1**), the fluoromethyl derivative (**2–1**) showed strong activity especially to the broad-leaf weeds at the dose of 400 g a.i./10 a, whereas the unfluorinated methyl derivative (**1–1**) had no herbicidal activity against all weeds tested even at the twice dose of 800 g a.i./10 a except strong control of *Monochoria vaginalis* in paddy application test. Consequently, it was considered that the fluorine atom(s) on the methyl group extremely contributed to enhancing the herbicidal activity. It was obvious that herbicidal activity of difluoromethyl-1,3,5-triazine (**3–3**) and trifluoromethyl-1,3,5-triazine (**4–3**) were found to be most active. The activity of the triazine (**3–3**) in soil and foliar application tests was superior to that in the paddy application test. It was also

noted that all compounds with any fluorinated methyl groups showed high activity against *Chenopodium album* in foliar application test. In our laboratory, control of the atrazine-resistant *Chenopodium album* using compounds **3-3** and **4-3** has already been investigated.

As well as the PET inhibition activity, herbicidal activity of (4-chlorobenzylamino)-1,3,5-triazine derivatives was much stronger than that of unsubstituted benzylamino-1,3,5-triazines. And generally 2-(fluorinated methyl)-4-(4-halogenobenzylamino)-6-methyl-1,3,5-triazines synthesized had stronger herbicidal activity to broad-leaf weeds than grass weeds.

In both PET inhibitory and herbicidal activity tests, the introduction of the halogen atom at the 4-position of the benzyl group in 2-(fluorinated methyl)-4-benzylamino-6-methyl-1,3,5-triazines enhanced the activities, especially 2-difluoromethyl and trifluoromethyl-4-(4-halogenobenzylamino)-6-methyl-1,3,5-triazines were considered to be most effective. The activities of 2-fluoromethyl-4-(4-halogenobenzylamino)-6-methyl-1,3,5-triazines could never surpass those of 2-difluoromethyl and trifluoromethyl-4-(4-halogenobenzylamino)-6-methyl-1,3,5-triazines. Therefore, the difluoromethyl and trifluoromethyl group were considered to be important for the both activities.

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要　　約

2-フッ素置換メチル-4-ベンジルアミノ-6-メチル-1,3,5-トリアジン系化合物の光合成電子伝達(PET)阻害活性及び除草活性

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高いPET阻害活性を有する2-ベンジルアミノ-4-メチル-6-トリフルオロメチル-1,3,5-トリアジン系化合物において，フッ素原子の置換効果を調べるために，トリフルオロメチル基をジフルオロメチル基，フルオロメチル基，メチル基に変換した化合物を合成し，それら化合物のPET阻害活性を測定した．その結果，PET阻害活性は，フッ素原子数の増加とともに増大することが分かり，全体的には活性の強さは CF_3-≧CHF_2-＞CH_2F-＞CH_3- 誘導体の順であった．高いPET阻害活性を附与させるためにはトリアジン環の置換基の1つとして2個以上のフッ素原子で置換されたメチル基すなわち，トリフルオロメチル基またはジフルオロメチル基を導入する必要性が確認された．また，ベンジルアミノ基のベンゼン環4位にハロゲン原子を導入した化合物は無置換の化合物よりも高いPET阻害活性を示した．これらの化合物の除草活性を土壌，茎葉，湛水処理試験によって評価したところ，PET阻害活性の高い化合物が強い除草活性を示した．例えば，2-(4-ブロモベンジルアミノ)-4-ジフルオロメチル-6-メチル-1,3,5-トリアジンは，非常に強いPET阻害活性及び除草活性を示した．