

Synthesis and Herbicidal Activity of *N*-{2,4-dichloro-5-(3-pyrazolyl)phenyl} imides

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Abstract : A series of *N*-{2,4-dichloro-5-(pyrazolyl)phenyl}imides **7** and **8** was prepared and evaluated their herbicidal activities. Those compounds in which either carboxylate or carboxamide moiety is on pyrazole moiety **7c-7l** showed no herbicidal activity whereas, the compounds in which trifluoromethyl group is substituted in pyrazolyl moiety showed moderate herbicidal activities against barnyardgrass, monochria and flat-sedge under paddy conditions with good rice tolerance at rate 63-250 g/ha. (Received July 10, 2000; accepted Sep. 15, 2000)

Key words : *N*-Phenyl imides, Protox inhibitor, pyrazole, herbicide, rice, barnyardgrass

N-Phenyl imides are peroxidizing herbicides that act by interrupting chlorophyll biosynthesis *via* inhibiting the activity of the protoporphyrinogen oxidase (Protox) (Dayan and Duke 1997). Also, 3-aryl-5-substituted pyrazole compounds have been known as peroxidizing herbicide, pyraflufen-ethyl and fluazolate which contain 5-difluoromethoxy and 5-trifluoromethyl substituent on pyrazole moiety being the typical examples in this category (Kobayashi, 1989; Woodard *et al.*, 1994). Recently, 1,3-dialkylpyrazole-5-carboxylic esters and 1,5-diphenyl pyrazole-3-carboxylic acids have been developed as agrochemicals (Okada *et al.*, 1990; Moser *et al.*, 1988).

In the course of our program to develop new herbicides, we were interested in the syntheses and herbicidal activities of compounds **7** and **8**, which have *N*-phenyl imide as well as pyrazole group in the molecule. Also, we were interested in investigating the effect of substituent in the pyrazole moiety such as carboxylate or carboxamide in place of the trifluoromethyl or difluoromethoxy group.

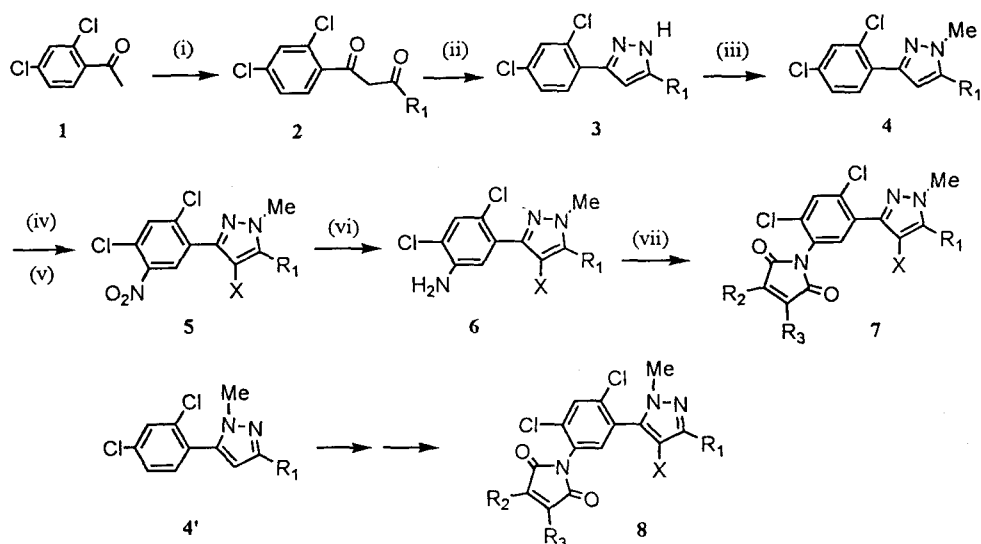
The compounds **7** and **8** were prepared in seven steps as shown by **Scheme 1**. The base-catalyzed condensation of 2,4-dichloroacetophenone with ethyl trifluoroacetate or diethyl oxalate gave the corresponding 1,3-diketones **2** (where R_1 is CF_3 or CO_2CH_3), which were reacted with hydrazine monohydrate in acetic acid to afford pyrazoles **3**. *N*-Methylation of the pyrazoles **3** by dimethyl sulfate in basic conditions (aqueous $NaHCO_3$ or $NaOH$) gave a mixture of 5-aryl pyrazoles **4** and 3-aryl pyrazoles **4'** in variable ratios, which could be separated using silica gel column chromatography; the characteristic 1H NMR singlet

signal of $N-CH_3$ protons of *N*-methyl-3-(2,4-dichlorophenyl)-5-methoxycarbonylpyrazole (**4**) appeared at δ 4.24, while that of *N*-methyl-5-(2,4-dichlorophenyl)-3-methoxycarbonylpyrazole (**4'**) appeared at δ 3.81 (Tensmeyer and Ainsworth, 1966). When the reaction was carried out with an excess amount of dimethyl sulfate without using base in refluxing acetonitrile, 5-aryl pyrazole **4** was obtained as a sole product in 98 % yield. Halogenation of the resulting pyrazoles **4** and **4'** was respectively carried out with *N*-chlorosuccinimide (NCS) or *N*-bromosuccinimide (NBS) in DMF solution at 80 °C. Nitration of the aryl group followed by reduction of nitro group gave the compound **6**, which was then reacted with 3,4-dimethylmaleic anhydride or 3,4,5,6-tetrahydrophthalic anhydride afforded the corresponding 3-aryl pyrazoles **7**. Similarly, 5-aryl pyrazoles **8** were prepared by the same procedures starting from *N*-methyl pyrazole isomer **4'**.

For the herbicidal evaluation, seeds of pre-germinated *Oryza sativa* L. and dry seeds of various plants to be tested were sown in white plastic pots having surface area of 350 cm² filled with sandy loam with 1.2 % of organic matter and pH 6.0 in the green house. After the plants reached a desirable growth stages, treatments were made at various growth stages. A solution containing the target herbicide was prepared by dissolving the compound in 50 % of aqueous acetone containing 0.2 % of Tween-20 and applied in a spray volume of 4,000 L/ha at 8-12 days after seeding. Herbicidal activities were determined fourteen days after treatment and recorded as percent control on a scale 0 to 100, where 0 indicated no visible effect and 100 indicated complete killing of plants. The results of the herbicidal activities were summarized in **Table 1**.

Interestingly, the results of the herbicidal evaluation of

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Compds.	R1	R2	R3	X	Yield(%)	Compds.	R1	R2	R3	X	Yield(%)
7a	CF ₃	CH ₃	CH ₃	Cl	71	7b	CO ₂ H	-(CH ₂) ₄	-	Cl	44
7b	CF ₃	-(CH ₂) ₄	-	Cl	59	7i	CO ₂ NH ₂	CH ₃	CH ₃	Cl	33
7c	CO ₂ Me	CH ₃	CH ₃	Cl	53	7j	CO ₂ NH ₂	-(CH ₂) ₄	-	Cl	64
7d	CO ₂ Me	-(CH ₂) ₄	-	Cl	59	7k	CO ₂ NEt ₂	CH ₃	CH ₃	Br	41
7e	CO ₂ Me	CH ₃	CH ₃	Br	63	7l	CO ₂ NEt ₂	-(CH ₂) ₄	-	Br	67
7f	CO ₂ Me	-(CH ₂) ₄	-	Br	73	8a	CF ₃	CH ₃	CH ₃	Cl	69
7g	CO ₂ H	CH ₃	CH ₃	Cl	36	8b	CF ₃	-(CH ₂) ₄	-	Cl	54

Conditions : (i) Na/MeOH and then CF₃CO₂Et or diethyl oxalate, reflux 16h, 78~85% (ii) NH₂NH₂/AcOH, reflux 1h, 78~91% (iii) dimethylsulfate(4 equiv.), CH₃CN, reflux, 2h, 83~98% (iv) NCS or NBS, DMF, 80°C, 18h, 67~86% (v) HNO₃, H₂SO₄, rt, 18h, 74~81% (vi) Fe/ACOH, reflux, 8h, 72~83% (vii) 3,4-dimethylmaleicanhydride or 3,4,5,6-tetrahydrophthalic anhydride, ACOH, reflux, 18h, 33~73%.

Scheme 1

the compounds 7 and 8 suggested that their herbicidal activities depended mainly on the substituent of the pyrazole moiety. The compounds 7c-7l which had either carboxylate or carboxamide group exhibited no herbicidal activity in the upland conditions at rate of 1kg/ha, even though *N*-3,4-dimethylmaleimide or *N*-3,4,5,6-tetrahydrophthalimide moiety was present in the molecule. The moderate herbicidal activity was observed in the compounds (7a, 7b, 8a and 8b) in which trifluoromethyl group is substituted on 3- or 5-positions of the pyrazole moiety. Under the paddy conditions, compounds 7 and 8 exhibited similar trend of herbicidal activity, as shown in Table 1. It is interesting to note that the compounds having 3-aryl-5-trifluoromethylpyrazolyl moiety (7a) showed strong tolerance on transplanted rice with a complete control of barnyardgrass at 250 g/ha along with excellent control of perennial weeds such as monochoria (MOOVA) and flat-sedge (CYPSE) at low rates. However, compounds 8a and 8b derived from pyrazol isomer 4'

showed less herbicidal activity than that of 7a and 7b derived from pyrazol isomer 4. Evaluation of herbicidal activity in a green house indicated that the compound 7a is useful as a potential post-emergent herbicide in rice field in 5-15 days after transplantation at rate of 250 g/ha.

In conclusion, most of compounds having the carboxylic group on the pyrazole moiety showed no herbicidal activity, and the compound having the trifluoromethyl substituent on pyrazole moiety showed moderate herbicidal activity under paddy conditions. Among them, compound 7a showed promising herbicidal activities against barnyardgrass with an excellent tolerance with 3-leaf rice at a rate of 250 g/ha.

Physical Data of compounds 7 and 8

7a: oil, ¹H NMR (200 MHz, CDCl₃) δ 2.07 (s, 6H, 2CH₃), 4.05 (s, 3H, NCH₃), 7.32 and 7.68 (2s, 2H, PhH).

7b: mp 75-78 °C, ¹H NMR (CDCl₃) δ 1.78-1.90 and

Table 1. Herbicidal Activities of compounds 7 and 8 under paddy condition.

Compound	Rate(g/ha)	ORYSA (3-leaf)	ORYSA (seed)	ECHOR	SCPJU	MOOVA	CYPSE	SAGPY
7a	1000	0	100	100	40	100	100	100
	250	0	100	100	30	100	100	0
	63	0	40	70	0	100	100	0
	16	0	40	20	0	90	70	0
7b	1000	0	100	100	40	100	100	100
7c	1000	0	0	80	0	100	×	0
7d	1000	0	50	70	0	0	0	0
7e	1000	0	0	0	0	0	0	0
7f	1000	0	0	60	0	100	×	0
7g	1000	0	0	30	0	100	×	0
7h	1000	0	0	0	0	0	0	0
7i	1000	0	0	0	0	0	0	0
7j	1000	0	0	0	0	100	×	0
7k	1000	0	0	50	100	70	0	0
7l	1000	0	30	85	0	100	0	30
8a	1000	0	50	70	20	100	100	0
	250	0	50	30	0	90	100	0
	63	0	0	20	0	70	100	0
	16	0	0	0	0	20	100	0
8b	1000	0	20	70	40	100	100	0
	250	0	0	20	30	100	100	0
	63	0	0	0	0	100	100	0
	16	0	0	0	0	90	70	0

ORYSA: *Oryza sativa* L. (rice), ECHOR: *Echinochloa crus-galli* (barnyardgrass), SCPJU: *Scirpus juncooides* ROXB. (bulrush), MOOVA: *Monochoria vaginalis* PRESL. (monochria), CYPSE: *Cyperus serotinus* ROTTB. (flat-sedge), SAGPY: *Sagittaria pygmaea* MIQ. (arrow head).

2.38-2.46 (m, 8H, $-(\text{CH}_2)_4-$), 4.03 (s, 3H, NCH_3), 7.30 and 7.67 (2s, 2H, PhH).

7c: mp 112-116 °C, ^1H NMR (CDCl_3) δ 1.98 (s, 6H, 2 CH_3), 3.77 (s, 3H, CO_2CH_3), 4.22 (s, 3H, NCH_3), 7.21 and 7.57 (2s, 2H, PhH).

7d: ^1H NMR (CDCl_3) δ 1.78-1.80 and 2.35-2.39 (m, 8H, $-(\text{CH}_2)_4-$), 3.78 (s, 3H, CO_2CH_3), 4.23 (s, 3H, NCH_3), 7.19 and 7.58 (2s, 2H, PhH).

7e: oil, ^1H NMR (CDCl_3) δ 2.01 (s, 6H, 2 CH_3), 3.79 (s, 3H, CO_2CH_3), 4.25 (s, 3H, NCH_3), 7.22 and 7.59 (2s, 2H, PhH).

7f: mp 75-79 °C, ^1H NMR (CDCl_3) δ 1.78-1.80 and 2.36-2.39 (m, 8H, $-(\text{CH}_2)_4-$), 3.91 (s, 3H, CO_2CH_3), 4.24 (s, 3H, NCH_3), 7.20 and 7.59 (2s, 2H, PhH).

7g: mp 54-57 °C, ^1H NMR (CDCl_3) δ 2.01 (s, 6H, 2 CH_3), 4.25 (s, 3H, NCH_3), 7.22 and 7.59 (2s, 2H, PhH), 10.2 (br s, 1H, CO_2H).

7h: mp 180-184 °C, ^1H NMR (CDCl_3) δ 1.78-1.82 and 2.38-2.44 (m, 8H, $-(\text{CH}_2)_4-$), 4.25 (s, 3H, NCH_3), 4.6 (br s, 1H, CO_2H), 7.21 and 7.61 (2s, 2H, PhH).

7i: mp 195-198 °C, ^1H NMR (CDCl_3) δ 2.01 (s, 6H, 2 CH_3),

4.25 (s, 3H, NCH_3), 6.2 (br s, 2H, CONH_2), 7.22 and 7.59 (2s, 2H, PhH).

7j: mp 162-165 °C, ^1H NMR (CDCl_3) δ 1.78-1.82 and 2.37-2.44 (m, 8H, $-(\text{CH}_2)_4-$), 4.25 (s, 3H, NCH_3), 6.3 (br s, 2H, CONH_2), 7.21 and 7.61 (2s, 2H, PhH).

7k: oil, ^1H NMR (CDCl_3) δ 1.32 (m, 6H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 1.97 (s, 6H, 2 CH_3), 3.28 and 3.51 (2q, 4H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 3.97 (s, 3H, NCH_3), 7.22 and 7.59 (2s, 2H, PhH).

7l: oil, ^1H NMR (CDCl_3) δ 1.15 (m, 6H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 1.77-1.82 (m, 4H), 2.33-2.41 (m, 4H), 3.32 and 3.54 (2q, 4H, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 3.95 (s, 3H, NCH_3), 7.27 and 7.58 (2s, 2H, PhH).

8a: oil, ^1H NMR (CDCl_3) δ 2.08 (s, 6H, 2 CH_3), 3.79 (s, 3H, NCH_3), 7.25 and 7.77 (s, 1H, Ph).

8b: oil, ^1H NMR (CDCl_3) δ 1.78-1.84 and 2.41-2.44 (m, 8H, $-(\text{CH}_2)_4-$), 3.80 (s, 3H, NCH_3), 7.25 and 7.77 (2s, 2H, PhH).

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N-[2,4-Dichloro-5-(3-pyrazolyl)phenyl]imide 유도체의 합성 및 제초활성

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요약 : 제초제 후보물질로서 N-[2,4-dichloro-5-(N-methylpyrazol-3-yl)phenyl] imide **7** 과 N-[2,4-dichloro-5-(N-methylpyrazol-5-yl)phenyl]imide **8**의 유도체들을 합성하여 제초활성을 온실조건에서 조사하였다. 처리량 1 kg/ha에서 pyrazole moiety에 carboxylate나 carboxamide 치환기가 있는 화합물들 (**7c-7l**)은 제초활성을 나타내지 않았으나, pyrazole moiety에 trifluoromethyl기가 있는 화합물들은 처리량 63-250 g/ha에서 논피, 물달개비, 너도방동산이등의 잡초들에 대해 제초활성을 보였고 벼에 대해서는 안전한 결과를 보였다.

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