Note

New Synthesis and Fungicidal Efficacy of *S*, *N*-Diarylthiophosphoroamidates

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INTRODUCTION

In the previous paper,¹⁾ we have presented the insecticidal and fungicidal efficacy of *S*-arylthiophosphoroamidates against many kinds of crop insects and diseases. In our continuous screening to enhance the fungicidal potentialities of chemicals in similar groups, we found another class of fungicidal *S*, *N*-diarylthiophosphoroamidates and a new synthetic method relevant to the derivatives.

Because of the structural novelty, we investigated the structure-activity relationship of this type of chemicals to develop potential fungicides, and found that the *S*, *N*-diarylthiophosphoroamidates had high activity against rice blast (*Pyricularia oryzae*) and rice sheath blight (*Rhizoctonia solani*) without being phytotoxic to the host plant. The present paper reports the synthetic variation and fungicidal activity of these compounds.

MATERIALS AND METHODS

1. Synthesis of Compounds

Almost all *S*, *N*-diarylthiophosphoroamidates in Table 1 were synthesized by the standard reaction between *S*-phenylphosphorochloridothioates and anilines, which was described in the previous papers.^{2,3)} Since it was difficult to obtain *O*-methyl phenylthiophosphoroamidates due to demethylation, a new synthetic procedure

Fig. 1 Synthetic route of *O*-methyl phenylthiophosphoroamidates.

Table 1 Fungicidal activity of *S*, *N*-diarylthiophosphoroamidates against rice blast and rice sheath blight.

No.	R ₁	R ₂	X	Control value (%)	
				Rice blast	Rice sheath blight
				100 ppm	150 ppm
1	Me	Me	H	95	91
2	Me	<i>n</i> -Pr	H	100	98
3	Et	H	H	85	83
4	Et	Me	H	100	91
5	Et	Et	H	99	87
6	Et	<i>n</i> -Pr	H	100	82
7	Et	<i>i</i> -Pr	H	78	87
8	Et	<i>n</i> -Bu	H	100	80
9	Et	<i>n</i> -Hex	H	56	52
10	<i>n</i> -Pr	H	H	97	90
11	<i>n</i> -Pr	<i>n</i> -Pr	H	100	79
12	<i>i</i> -Pr	H	H	84	78
13	<i>i</i> -Pr	<i>n</i> -Pr	H	88	70
14	<i>n</i> -Bu	H	H	94	89
15	Et	H	2-Me	100	94
16	Et	H	3-Me	96	79
17	Et	H	4-Me	87	81
18	Et	H	2-Et	99	90
19	Et	H	4-Et	68	65
20	Et	H	4- <i>n</i> -Pr	47	37
21	Et	H	2-Cl	100	96
22	Et	H	3-Cl	98	67
23	Et	H	4-Cl	74	70
24	Et	H	4-CF ₃	78	78
25	Et	H	2-MeO	93	70
26	Et	H	4-MeO	98	75

Fungicidal test: In a greenhouse, preventive foliar spraying was done 1 day before inoculation, and the effect was observed 6 days after inoculation. The control value (%) was calculated as follows.

Control value (%) on rice blast

$$= \left(1 - \frac{\text{Number of lesions in a treated leaf}}{\text{Number of lesions in an untreated leaf}} \right) \times 100$$

Control value (%) on rice sheath blight

$$= \left(1 - \frac{\text{Length of lesions in a treated leaf}}{\text{Length of lesions in an untreated leaf}} \right) \times 100$$

Table 2 Fungicidal activity of **2**, **6** and **21** against rice blast and rice sheath blight at low concentration.

Compound	Control value (%)		
	Rice blast		Rice sheath blight
	25 ppm	12.5 ppm	62.5 ppm
2	99	88	93
6	81	72	29
21	96	91	78

Efficacy: same as Table 1.

shown in Fig. 1 was separately developed by the authors. A typical run is as below.

O-Methyl *S*-phenyl *N*-*n*-propyl *N*-phenylthiophosphoroamidate (**2**): Sodium methoxide (6.5 g) was added dropwise to a mixture of *S*-phenyl *N*-*n*-propyl *N*-phenylthiophosphoroamidechloridate (32.6 g) and tetrahydrofuran (100 ml) under ice cooling. After stirring at ambient temperature for 10 min, the reaction mixture was extracted with benzene. The extract was washed with water, dried over anhydrous sodium sulfate and condensed *in vacuo*. The residue was chromatographed on a silica gel column (eluent; toluene:acetone=5:1) to give colorless oil, *Y*=27.7 g (86%), *n*_D²⁵ 1.5746. Anal. Found: C, 60.25; H, 6.20; N, 4.33. Calcd. for C₁₆H₂₀NO₂PS: C, 60.16; H, 6.32; N, 4.39%. ¹H NMR (CDCl₃) δ ppm: 0.80 (3H, t, *J*=7 Hz, CH₂CH₂CH₃), 1.16–1.56 (2H, m, CH₂CH₂CH₃), 3.24–3.58 (2H, m, NCH₂), 3.80 (3H, d, *J*=13 Hz, OMe), 6.96–7.64 (10H, m, PhH).

S-Phenyl *N*-*n*-propyl *N*-phenylthiophosphoroamidechloridate (intermediate of **2**): A mixture of *N*-*n*-propylaniline (35.2 g) and benzene (30 ml) was added dropwise to a mixture of *S*-phenylthiophosphorodichloridate (22.7 g) and benzene (100 ml). After boiling for 1 hr and removing the salts, the solution was successively washed with an aqueous solution of 5% hydrochloride and 5% sodium carbonate. The benzene solution was dried over anhydrous sodium sulfate and condensed *in vacuo*. The residue was distilled at 170–177°C/0.04 mmHg to give pale yellow oil, *Y*=25.7 g (79%), *n*_D²⁵ 1.6009.

The other compounds in Table 1 were synthesized in similar manners, and their elemental analyses (C, H, N) and NMR spectra were in good agreement with the corresponding structures.

2. Fungicidal Activity

The test results are shown in Tables 1 and 2 along with the test method in note.

RESULTS AND DISCUSSION

The bioassay revealed that many *S,N*-diarylthiophosphoroamidates had high potency against both rice blast and rice sheath blight (Table 1). Although the number of derivatives was relatively limited for satisfactory elucidation of the structure-activity relationship, substituents such as Me and Et on the oxygen atom, H and Me on the nitrogen atom, and 2-Me, 2-Et, 2-Cl on the *N*-phenyl ring were advantageous to enhance the fungicidal activity.

Of all the compounds examined, **2**, **6** and **21** were chosen for further testing at lower concentrations and **2** was found most preventively active (Table 2). Compound **2**, which was synthesized by the new method reported in this paper, showed encouraging results even under field condition (data not presented), and it paved the way for development of a new series of fungicidally useful compounds. Studies on the mode of action of this series of compounds are in progress in comparison with that of EDDP (*O*-ethyl diphenyl phosphorodithioate).⁴⁾

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要 約

S,N-ジアリールチオホスホロアミデート誘導体の新規合成法と病害防除効果

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新規な基本骨格を有する有機燐系化合物の生理活性試験を続行する中で, 新たに *S,N*-ジアリールチオホスホロアミデート誘導体が稲いもち病および稲紋枯病に高い防除効果を有すること

を見出した。化学構造と病害防除効果の相関性を配慮し一連の化合物を合成し試験した結果、新規に開発した合成法により得られた *O*-メチル *S*-フェニル *N*-ノルマルプロピル *N*-フェニル

チオホスホロアミデートが代表として選ばれ高い防除効果を示すことが判明した。