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# Biological Activities of 1,3,4-Thiadiazolo[3,2-a]pyrimidines and *s*-Triazolo[1,5-a]pyrimidines

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In 1,3,4-thiadiazolo[3,2-a]pyrimidine series, 5-methyl-7*H*-1,3,4-thiadiazolo[3,2-a]pyrimidin-7-one exhibited the larvicidal activity to housefly larvae, while the isomer, 7-methyl-5*H*-1,3,4-thiadiazolo [3,2-a] pyrimidin-5-one was very weak. 4-Methyl-2-thiocyanato-6(1*H*)pyrimidine, which is a common product of the two isomers by mild hydrolysis, was inactive on the development of the larvae. *s*-Triazolo[1,5-a]pyrimidine also disrupted morphogenesis to induce larva-pupa intermediates which were incapable of survival.

The protective activity of 7-methyl-6-nitro-5*H*-1,3,4-thiadiazolo[ 3,2-a] pyrimidin-5-one against bacterial leaf blight disease of rice plant was greater than that of nickel dimethyldithiocarbamate. 5,7-Dimethyl-1,3,4-thiadiazolo[3,2-a]pyrimidin-4-ium perchlorate showed a good protectivity to *Helminthosporium* leaf spot and rice blast.

The selective herbicidal activity for barnyard grass was found in 2,7-dimethyl-5*H*-1,3,4-thiadiazolo[3,2-a]pyrimidin-5-one and 2-benzylthio-7-methyl-5*H*-1,3,4-thiadiazolo [3,2-a]pyrimidin-5-one.

It is a conventional hypothesis that structural analogues of a natural product can exhibit some biological activities as metabolite-antagonist and might be potential chemotherapeutic agents.

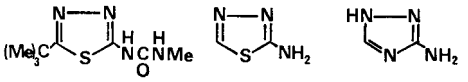
2,6-Diaminopurine and 8-azaguanine which had showed an antipurine effect on microbes were found to be inhibitors of tumors (Burchenal *et al., 1949).*

6-Mercaptopurine was also proved to be one of the most useful chemotherapeutic agents to acute leukemia (Gellhorn *et al.,* 1955). These findings prompted a great deal of synthetic study of purine and pyrimidine analogues to possess potent biological activities on a wide variety of organisms. Many hundreds of potential antagonists have been prepared by now and some of them were proved to be useful clinically. Besides purine and pyrimidine derivatives, certain heterocyclic compounds having closely related ring systems to the bases, such as 4-aminopyrazolopyrimidine (Sugiura *et al.,* 1950), inidazolopyridine (Röchling et *al.,* 1971), and *s*-triazolo[1,5-a]pyrimidine (Kano *et al., 1958,* 1959; Okabayashi *et al.,* 1960), are also shown as antagonists and potential chemotherapeutic agents.

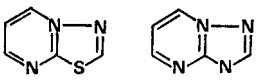
On the other hand, since the discovery of sulfa drug and of 2-acetoamino-1,3,4-thiadiazolo-3-sulfonamide as a carbonic anhydrase inhibitor, 2-amino-1,3,4-thiadiazoles have been pharmaceutically interesting compound (Sandström, 1965). Many compounds with various biological activities, such as anticancer, cytostatic, bactericidal and fungicidal activity, have been found in the derivatives of 2-

amino-1,3,4-thiadiazole.

With respect to pesticide, Kubo(1970) has found recently the herbicidal activity of 1-methyl-3-(5-*tert*-butyl-1,3,4-thiadiazol-2-yl) urea (I). 2-Amino-1,3,4-thiadiazole (II) was found to be effective on bacterial leaf blight of rice plant at a low concentration (Yakushiji et al., 1970). 3-Amino-1,2,4-triazole(III) is an effective herbicide to a great variety of weeds (Krdller, 1966).



(I) (II) (III)



(IV) (V)

5-Chloro-, 5-mercapto- and 5-thiocyanato-7-methyl-*s*-triazolo[1,5-a]pyrimidine inhibited the growth of ***Lactobacillus casei*** and ***Streptomyces faecalis*** (Kubo ***et al.,*** 1953, 1959 ; Okabayashi ***et al.,*** 1960)

The derivatives of 1,3,4-thiadiazolo[3,2-a]pyrimidine (IV) and *s*-triazolo[1, 5-a]pyrimidine (V) are considered to be interesting compounds to investigate their biological activities, since these are not only the analogues of purine but also the derivatives of 2-amino-1,3,4-thiadiazole and 3-aminotriazole.

In the present paper, the biological activities of the pseudopurines derived from 2-amino-1,3,4-thiadiazole and 3-amino-1,2,4-triazole. As to chemistry it was already published (Okabe ***et al.,*** 1972, 1973).

## EXPERIMENTAL

### Inhibition of the development of housefly

The houseflies, ***Musca domestica vicina*** Macquart, were reared at 26°C with a diet comprising from a mixture of dry yeast and bran (1:1) with an appropriate amount of water. About 100 larvae on the third day after hatching were reared in a 100 ml beaker containing a mixture of the diet (25 g), a compound to be tested (25 mg) and water (25 ml). The number of pupae was counted every day for a week. The pupae were placed in a 100 ml beaker covered with a layer of gauze and kept at 26°C, and the number of adults emerged was counted for a week. A blank test was run in each experiment. The percentages of pupation and emergence to the blank lots were calculated respectively. Each of pupal and imaginal moult occurred in an average of 90 % in the blank tests. Twenty-one derivatives of the thiadiazolopyrimidine, 18 of the s-triazolopyrimidine and 7 of the skeletal analogues were supplied to the assay.

### Protective activity against plant diseases

The following pathogens were used to the assay : 1) ***Xanthomonas oryzae*** (bacterial leaf blight), 2) ***Ophiobolus miyabeanus (Helminthosporium*** leaf spot, 3) ***Piricularia oryzae*** (rice blast), 4) ***Sphaerotheca fuliginea*** (powdery mildew), 5)

***Xanthomonas citri*** (canker), 6) ***Alternaria solani*** (early blight), 7) ***Pseudomonas solanacearum*** (bacterial wilt), 8) ***Phytophthora parasitica,*** **9) *Rhizoctonia solani*** (damping-off), 10) ***Fusarium oxysporum*** (Fusarium wilt), 11) ***Alternaria citri,*** 12) ***Cladosporium fluvum***, 13) ***Corynespora melongenae.***

***Cup test***

One tenth ml of the acetone solution containing a chemical to be tested at a conentration of 0.1, 1, ***10*** and 100 ppm respectively, was spotted on a filter paper of 6 mm in diameter. After spontaneous evaporation of the solvent at room temperature, it was placed on the surface of an agar plate in a Petri dish. In each dish 5 samples and 1 control were placed and on the plate were added bacteria or spores of a fungus suspended in sterilized water. After incubation at 28°C for 24 hours, the diameters of the inhibition-zones were measured. As positive controls, blasticidin S, Bordeaux mixture, captan and captafol were supplied to the assays.

***Pot and bat test***

Forty ml of a test solution was sprayed on a plant, i.e., rice, orange and cucumber, and next day the suspension (x 200,15 per sight) of bacteria or spores of a fungus was sprayed. After 1 or ***2*** weeks (a month in the case of Ni-bis (dimethyldithiocarbamate)), the number of illed leaves and spots on the infected leaves were counted. As positive controls, maneb, ediphenphos, 4,5,6,7-tetra-chlorophthalide, nickel bis(dimethyldithiocarbamate), streptomycin and oxythioquinox were used.

All of the compounds to be tested were formulated in a ***20*** % wettable powder before the assay in pot or bat test,

***Protectivity against Phytophthora parasitica***

On a layer of a sterilized soil (50 ml) in a pot ($\phi$=7 cm), 50 ml of a mixture of the sterilized soil and a crushed cucumber infected by the pathogen was disposed and then covered with a small amount of the soil. After 4 days, 6 ml of a test solution was poured onto the soil and 4 seedlings of cucumber were planted out. After 26 days, the length of stalks and roots and the dry weight were measured.

**Herbicidal activity**

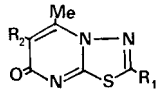
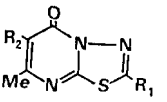
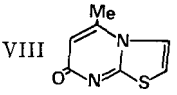
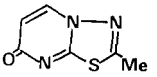
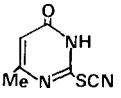
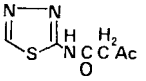
Ten seeds were placed on a filter paper in a Petri dish ($\phi$=9 cm) containing 5 ml of a test solution at a concentration of 100 ppm and allow to stand at room temperature for 9 days. Distilled water was sometimes supplied to the dish to avoid drying during the assay. Positive controls were run by using molinate and simetryn at a concentration of 50 ppm. The lengths of roots and leaves or stalks were measured. The herbicidal activity was shown in a ratio of the averaged lengths to those of control run in distilled water. Rice, barnyard grass and radish were used for the assay.

## RESULTS AND DISCUSSION

**Inhibition of the development of housefly**

As summarized in Table 1, in the 5-methyl-7*H*-1,3,4-thiadiazolo[3,2-a]pyrimi-

Table 1. Inhibition of the development of housefly.

| Compound | $R_1$ | $R_2$ | Rate of moult (%) Pupal | Imaginal |
|---|---|---|---|---|
| VI  | H | H | 30 | 0 |
| | H | H | 90** | 0** |
| | H | H | 100* | 100* |
| | Me | H | | 24 |
| | Et | H | 100 | 100 |
| | iso-Pro | H | 100 | 86 |
| | SMe | H | 100 | 100 |
| | Cl | H | | 17 |
| | $NHNH_2$ | H | 100 | 65 |
| | H | Cl | 100 | 66 |
| VII  | H | H | 98 | 54 |
| | Me | H | 97 | 62 |
| | $NHC_3H_7$ | H | 100 | 69 |
| | Cl | H | 100 | 67 |
| | $NH_2$ | H | 100 | 46 |
| | SMe | H | 97 | 64 |
| | H | Cl | 100 | 78 |
| | Me | Cl | 96 | 94 |
| | Et | Cl | 100 | 88 |
| | SMe | Cl | 100 | 70 |
| | SMe | Cl | 93 | 72 |
| | Me | Br | 98 | 64 |
| VIII  | | | 100 | 40 |
| IX  | | | 100 | a5 |
| X  | | | 77 | 86 |
| XI  | | | 100 | 73 |

Concn. is 1,000 ppm, otherwise indicated. * 500 ppm, ** 100 ppm

din-7-one series, the nonsubstituted compound (VI: R,, $R_2$ =H) showed a considerable inhibition on pupal and imaginal moult of housefly. At a level of 1,000 ppm the larvae could not survive to emerge, although 30% of them moulted to pupea. At a concentration of 500 ppm, 90% of the larvae appeared to moult normally, but the pupae again could not emerge to die. The compound, however, did not exhibited lethal effect on the larvae and pupae at a concentration of 100 ppm. Introduction of substituents in the methylthiadiazolopyrimidine ring resulted in a great decrease of potency; even at 1,000 ppm the derivatives did not affect the pupation. As for the imaginal moult, 2,5-dimethylthiadiazolopyrimidin-7-one was far active than the corresponding 2-ethyl or 2-isopropyl

derivative, while leaving the methyl group at 5-position made the compound to diminish the activity. 2-Chloro derivative was still inhibitory on the imaginal moult, but the 6-chloro isomer lost the activity. 5-Methyl-7*H*-1,3,4-thiadiazolo [3,2-a]pyrimidin-5-one (VIII), which is a ring analogue of VI, did not inhibit the pupation, but a half of the resulting pupae could not emerge to adults.

In the 7-methyl-5*H*-1,3,4-thiadiazolo[3,2-a]pyrimidin-5-one series (VII), all of the derivatives tested showed almost no effect on the pupation and were far weaker than the corresponding 5-methyl-7-ones in the imaginal moult.

4-Methyl-2-thiocyanato-6(1*H*)-pyrimidone (X), which is the common intermediate of hydrolysis of VI ($R_1$, $R_2$=H) and VII ($R_1$, $R_2$=H), only weakly inhibited the development of housefly. Therefore, the remarkable difference of the toxicity between the isomers, 5-methyl-7-one and 7-methyl-5-one of the thiadiazolopyrimidine, might not depend on a different level of the compound X in the insect.

2-Acetoacetylamino-1,3,4-thiadiazole (XI), a ring-opened derivative of the 5-methylthiadiazolopyrimidin-7-one, exhibited only weak inhibition on the moulting.

From the above results, the high toxicity of 5-methyl-1,3,4-thiadiazolo[3,2-a]pyrimidin-7-one is assumed to be related to the methyl group at 5-position; the adjacent 6-position should not be substituted, but the thiadiazole moiety is allowable of some modification unless opening the ring.

The loss of toxicity in the 7-methyl-thiadiazolopyrimidin-5-one might be explained by weak or no interaction with an important component in biochemical process of the larva. The comparison of i. r. and n.m.r. data for VI and VII suggested that the carbonyl bond is more polarized in the 7-one than the 5-one and the proton at 6-position is more shielded.

As shown in Table 2, the unsubstituted *s*-triazolo[1,5-a]pyrimidine (XII ; $R_1$, $R_2$, $R_3$=H) showed the most inhibitory effect on the development of housefly in the s-triazolopyrimidines tested. The compound, at a concentration of 1,000 ppm, induced abnormal pupae, i.e. larva-pupa intermediates, which were incapable of survival. At a concentration of 250 ppm, 50 % of the larvae moulted normally to all appearence did not emerge to death. Except the 5-chloro derivative, introduction of substituents on the s-triazolopyrimidine ring resulted in a great decrease of inhibition on pupal and imaginal moult. Some of the ring-analogues such as benzimidazole (XIII), purine (XIV) and 7-hydroxy-*s*-triazolo[4,3-a] pyrimidine (XV) were almost non-toxic to housefly. At a concentration of 1,000 ppm tetrazolo[1,5-a]pyrimidine (XVI) inhibited the pupal moult in a degree of **80** % and the resulted small pupae were incapable of surviving.

These pseudopurines may affect nucleic acid metabolism to block the pupal and imaginal moult of housefly.

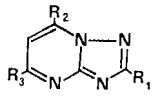
### Fungicidal and bactericidal activity

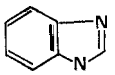
Among 15 of 1,3,4-thiadiazolopyrimidines tested, 5,7-dimethyl-1,3,4-thiadiazolo [3,2-a]pyrimidin-4-ium perchlorate (XVII) showed considerable inhibition on the growth of ***Ophiobolus miyabeanus*** and ***Cladosporium fulvum*** (Table 3).

As shown in Table 4, the perchlorate fairly protected rice plant from the invasion of ***Ophiobolus miyabeanus in*** pot tests. The number of leaf spots per an infected leaf was 9.8 at a concentration of 250 ppm and was comparable to the

**Table 2.** Inhibition of the development of housefly.

| | Compound | | | Rate of moult (%) | |
|---|---|---|---|---|---|
| | $R_1$ | $R_2$ | R3 | Pupal | Imaginal |
| | H | H | H | 96 | 0 |
| | H | H | H | 91** | 46** |
| | H | H | H | 100* | 84* |
| | H | Cl | H | 100 | 25 |
| | SMe | H | H | 100 | 85 |
| | H | H | Me | 90 | 0 |
| | H | Me | Me | 97 | 91 |
| | H | OH | Me | 98 | 68 |
| XII | H | SCN | Me | 97 | 87 |
| | H | $C_6H_5$ | Me | 96 | 48 |
| | SH | H | Me | 100 | 85 |
| | SH | Me | Me | 99 | 85 |
| | SH | $C_6H_5$ | Me | 99 | 81 |
| | SMe | H | Me | 93 | 58 |
| | SMe | Me | Me | 99 | 46 |
| | H | SCN | H | 96 | 45 |
| | H | OH | H | 98 | 85 |
| | H | OH | OH | 97 | 53 |
| XIII | | | | 100 | 89 |
| XIV | | | | 95 | 80 |
| x v | | | | 100 | 73 |
| XVI | | | | 20 | 0 |
| XVII | | | | 90*** | 74*** |
| — | | | | 100* | 100* |


XII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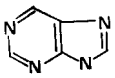
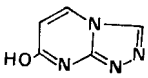
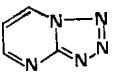
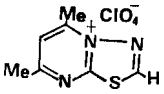

XIV


XV


XVI


XVII

Concn. is 1,000 ppm, otherwise indicated.
* 100 ppm, ** 250 ppm, *** 500 ppm.

**Table 3.** Fungicidal activity.*

| Compound | Concentration | Diameter of inhibition-zone (mm) | |
|---|---|---|---|
| | | ***Ophiobolus miyabeanus*** | ***Cladosporium fluvum*** |
| XVII | 1,000 | 19.0 | 35.3 |
| PMA | 500(Hg) | 35. 3 | 36.2 |

* Cup test on PDA-medium, at 28°C for 48 hours. PMA : Phenylmercuric acetate.

activity of maneb at 125 ppm, although all of the leaves were infected by the pathogen. This compound also exhibited inhibitory activity against ***Piricularia oryzae ;*** at a concentration 1,000 ppm the leaves were intact completely to the fungus, at 500 and 250 ppm the illed rates (the number of infected spots) were ***57 % (1.5)*** and 83 % ***(7.0)*** respectively. However, the compound was not

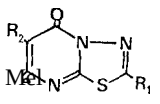
**Table 4.** Protectivity of 1,3,4-thiadiazolo[3,2-a]pyrimidines against pathogens.

| Pathogen | Compound | Concn. (ppm) | Infection rate (%) | No. of spots per leaf |
|---|---|---|---|---|
| *Xanthomonas oryzae* | XVII | 1,000 | 30 | |
| | ***XVIII*** | ***1,000*** | 10 | |
| | | | 24 | |
| | XVII | 1,000 | 25 | |
| | XIX | 500 | 59 | |
| | x x | 1,000 | 38 | |
| | Ni-bis(dimethyl-dithiocarbamate) | 1,300 | 26 | |
| | — | 0 | a4 | |
| *Ophiobolus* | | | 50 | 2.4 |
| | ***XVII*** | ***1,000*** | 61 | 4.6 |
| | XVII | 250 | 95 | 9.8 |
| | Maneb | 250 | 24 | 1. 3 |
| | Maneb | 125 | 95 | 13. a |
| | — | 0 | 97 | 77.0 |
| | | | 0 | |
| *Piricularia oryzae* | XVII | 1,000 | 57 | 0 |
| | XVII | 500 | | 1.5 |
| | XVII | 250 | 83 | 7.0 |
| | Ediphenphos | 300 | 0 | 0 |
| | 4,5,6,7-Tetra-chlorophthalide | 500 | 0 | 0 |
| | — | 0 | 9 | 24.4 |
| *Sphaerotheca fuliginea* | XVII | 500 | 100 | |
| | | | 5 | |
| | ***XVIII*** | ***500*** | 100 | |
| | ***x x*** | ***500*** | 100 | |
| | | | 5 | |
| | Oxythioquinox | 100 | 100 | |
| *Xanthomonus citri* | XVII | 1,000 | a3 | 20.7 |
| | | | | 6.6 |
| | Streptomycin | 200 | 21 | 19.6 |

effective on the diseases such as canker of citrus and powdery mildew of cucumber.

In bat tests 6-nitro-(XVIII), 6-chloro-(XIX) and 2-isopropyl-7-methyl-5*H*-1,3,4-thiadiazolo[3,2-a]pyrimidin-5-one (XX) were effective on bacterial leaf blight of rice plant. Especially, the nitro derivative was effective as three times as nickel dimethyldithiocarbamate. The perchlorate salt XVII was also found to be protective to the disease. Powdery mildew was suppressed by the 6-nitro derivative at a concentration of 500 ppm, where the compound showed phytotoxicity to the host plant.

2-Amino-1,3,4-thiadiazole (II) is remarkably effective on bacterial leaf blight but the carcinogenic property limited the practical usage. The thiadiazole moiety of 7-methyl-5*H*-1,3,4-thiadiazolo[3,2-a]pyrimidin-5-one is easily cleaved to produce 4-methyl-2-thiocyanato-6(1*H*)-pyrimidine and methylthiouracil which are not toxic to mammals, Therefore, the present result reveals the possibility that an effective pesticide against bacterial leaf blight might be found in 1,3,4-thiadiazolopyrimidines .



(XVIII) ; $R_1$ = H, $R_2$ = NO,
(XIX) ; $R_1$ = H, $R_2$ = Cl
(XX) ; $R_1$ = $-CH(CH_3)_2$, $R_2$ = H

It has been reported that 7-methyl-5-thiocyanato-*s*-triazolo[1,5-a]-pyrimidine exhibited protectivity against various microorganisms (Okabe *et al.*,1972). Here will be described the results anew obtained. As shown in Fig.1, 7-methyl-5-thiocyanato-*s*-triazolo[1,5-a] pyrimidine (XXI) also completely inhibited the growth of ***Piricularia oryzae*** at a concentration of 100 ppm. At a level of 1 and

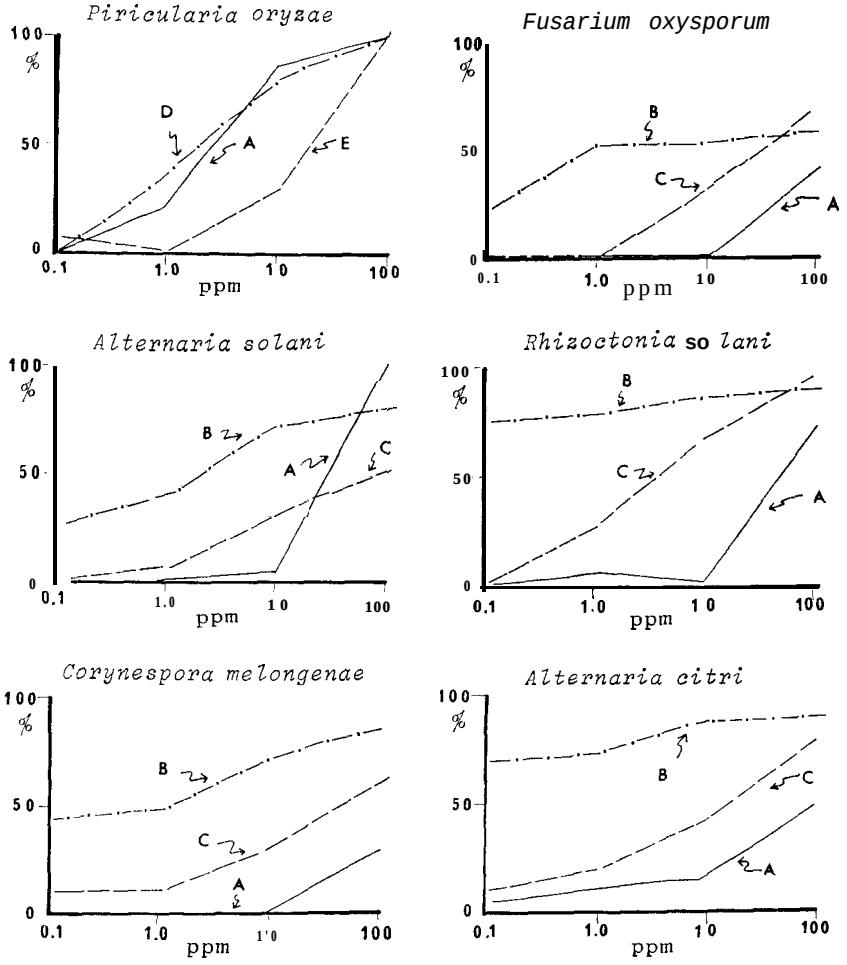



Fig. 1. Fungicidal activity of 7-methyl-5-thiocyanato-*s*-triazolo[1,5-a] pyrimidine. A: 7-Methyl-5-thiocyanato-*s*-triazolo[1,5-a]pyrimidine, B: Captafol, C: Captan, D : Blasticidin S. E: Bordeaux mixture.

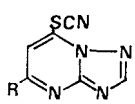
10 ppm, the inhibition was estimated as 21 and 86 % respectively; the activity was superior to that of Bordeaux mixture and nearly equal to that of blasticidin S. The growth of *Alternaria solani* was also inhibited by XXI; the protectivity of the compound was superior to those of captan and captafol at a level of 100 ppm, however, at lower concentrations inhibition of the growth was less. The other fungi tested, such as ***Rhizoctonia solani, Phytophthora capsici, Fusarium oxysporum, Alternaria citri*** and ***Corynespora melongenae*** were less affected by the triazolopyrimidine. In the pot test cucumber plants were apparently protected from the infestation by ***Phytophthora parasitica,*** however, the compound XXI caused wither and shrink of the leaves and stalks (Table 5). 5-Thiocyanato-*s*-triazolo-[1,5-a]pyrimidine (XXII) showed protectivity against ***Helminthosporium*** leaf spot and rice blast. However, the compound was also phytotoxic to cause brown spots on leaves, when applied to young rice plants by spraying a 500 ppm suspension prepared from a 20 % wettable powder (Table 6).

**Table 5.** Effect of 7-methyl-5-thiocyanato-*s*-triazolo[1,5-a]pyrimidine on ***Phytophthora parasitica.***

| Compound | Concn. (ppm) | Length (mm) | | Dry weight (mg) |
|---|---|---|---|---|
| | | Root | Stalk | |
| XXI | 1,000 | 53 | 69 | 78 |
| Captan | 1,000 | 88 | 81 | 124 |
| | 0 | 63 | 75 | 88 |

**Table 6.** Fungicidal activity of 5-thiocyanato-*s*-triazolo[1,5-a]pyrimidine.

| Fungus | Compound | Concn. (ppm) | Infection rate (%) | No. of spots per leaf |
|---|---|---|---|---|
| *Ophiobolus miyabeanus* | XXII | 1,000 | 85 | 4.5 |
| | XXII | 500 | | 3.1 |
| | XXII | 250 | 63 | 6.0 |
| | Maneb | 250 | 95 | I..3 |
| | Maneb | 125 | 97 | 14.0 |
| | —— | 0 | | 77.0 |
| *Pyricularia* | XXII | 1,000 | 0 | 0 |
| | Fthalide | 1,000 | 0 | 0 |
| | —— | 0 | 0 | 7.8 |



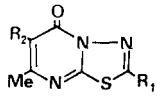
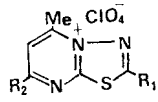

(XXI) R = CH,
(XXII) R = H

**Herbicidal activity**

As shown in Table 7, some 1,3,4-thiadiazolo[3,2-a]pyrimidines inhibited the growth of barnyard grass but not of rice plant. Especially, the selectivity was remarkable in 2,7-dimethyl-1,3,4-thiadiazolo[3,2-a]pyrimidin-5-one (VII; $R_1$ = Me, $R_2$=H) and 2-benzylthio-7-methyl-5*H*-1,3,4-thiadiazolo[3,2-a] pryimidin-5-one (VII ; $R_1$= S-Bz, $R_2$=H). The 2-benzylthio derivative did not affect rice plant, but inhibited the growth of root and leaf of barnyard grass at the extent

of 55 and 75 % respectively. The 2-methyl derivative strongly inhibited the growth of root of barnyard grass in a contrast to simetryn which affect on the leaf of the plant. It is interesting that 6-chloro-7-methyl-1,3,4-thiadiazolo[3,2-a]-pyrmidin-5-one (VII ; R,=Me, $R_2$=Cl) considerably prompted the growth of rice plant, while the compound slightly suppressed the growth of barnyard grass.

Table 7. Herbicidal activity of 7-methyl-1,3,4-thiadiazolo[3,2-a]pyrimidin S-ones (VII), and 1,3,4-thiadiazolo[3,2-a]pyrimidin-4-ium perchlorates (XXIII).

| Compound | $R_1$ | $R_2$ | Rice (% of length) Leaves | Rice (% of length) Roots | Barnyard grass (% of length) Leaves | Barnyard grass (% of length) Roots |
|---|---|---|---|---|---|---|
|  VII | S-$CH_2\phi$ | H | 110 | 110 | 25 | 45 |
| | Me | H | 85 | 65 | 85 | 3 |
| | $C_6H_5$ | H | 100 | 70 | 85 | 60 |
| | Me | Cl | 140 | 130 | 75 | 80 |
|  XXIII | Me | Me | 50 | 65 | 55 | 50 |
| | H | Me | 100 | 120 | 55 | 80 |
| | Me | H | 70 | 150 | 50 | 75 |
| Molinate | | | 125 | 115 | 30 | 85 |
| Simetryne | | | 110 | 105 | 3.5 | 105 |
| Water | | | 100 | 100 | 100 | 100 |

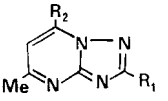
1,3,4-Thiadiazolo[3,2-a]pyrimidin-4-ium perchlorates such as 2-methyl and 7-methyl derivatives also exhibited the selective herbicidal activity between rice and barnyard grass.

In a preliminary test, 7-methyl-5*H*-1,3,4-thiadiazolo[3,2-a]pyrimidin-5-one, which showed no effect on the monocotyledonary plants, completely inhibited the germination of radish at a concentration of 50 ppm. Therefore, a high selective herbicidal activity between monocotyledonary and dicotyledonary plants may be expected.

The 7-methyl-*s*-triazolo[1,5-a]pyrimidines were less herbicidal than the thiadiazolopyrimidines. However, some of them such as 2-mercapto-5-phenyl- or 5-hydroxy-2-(*p*-nitrobenzylthio)- s-triazolopyrimidine remarkably prompted the growth of root of rice plant (Table 8).

The germination of radish was completely inhibited by *s*-triazolo[1,5-a]pyrimidine (XII: $R_1$,$R_2$,$R_3$= H) at a concentration of 50 ppm. Therefore, the selective phytotoxicity of s-triazolopyrimidines might be expected.

**Table 8.** Herbicidal activity of 7-methyl-*s*-triazolo[1,5-a]pyrimidines **(XXIV).**



| $R_1$ | $R_2$ | Rice Leaves | Rice Roots | Barnyard grass Leaves | Barnyard grass Roots |
|---|---|---|---|---|---|
| $SCH_2\phi Cl$ | Me | 130 | 90 | 70 | 85 |
| $S(CH_2)_2OH$ | Me | 110 | 120 | 95 | 150-90 |
| $S(CH_2)_2COOH$ | Me Me | 120 | 60 | 100 | 100 |
| $SCH_2\phi$ | | 85 | | | 75 |
| $SCH_2COOH$ | Me | 100 | 100 | 50 | 50 |
| $SCH_2\phi Cl$ | OH | 90 | 60 | 60 | 70 |
| $SCH_2\phi NO_2$ | OH | 130 | 145 | 75 | 100 |
| $SCH_2\phi Cl$ | $C_6H_5$ | 110 | 120 | 80 | 100 |
| $SCH_2CH_2OH$ | $C_6H_5$ | 110 | 90 | 95 | 60 |
| SH | $C_6H_5$ | 100 | 175 | 100 | 65 |
| Water | | 100 | 100 | | 100 |

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