

1-[1-(置換フェニル)ビニル]イミダゾール類と1-[2-(置換フェニル)アリル]イミダゾール類の温室内での防除効果とin vitroの抗菌活性との相関関係

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# Relationship between Antifungal Activities in Greenhouse and *in Vitro* of 1-[1-(Substituted phenyl)vinyl]imidazoles and 1-[2-(Substituted phenyl)allyl]imidazoles

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Protective and curative antifungal activities of 16 1-[1-(2-substituted hydroxy-5-substituted phenyl)vinyl]imidazoles and 9 1-[2-(2-substituted hydroxy-5-substituted phenyl)allyl]imidazoles were measured against *Botrytis cinerea*, a phytopathogenic fungus, under greenhouse conditions. A relationship between their antifungal activity in greenhouse conditions and that *in vitro* was examined quantitatively based on the regression analysis with the aid of physicochemical and structural parameters. The higher the *in vitro* activity, the higher the protective activity in greenhouse conditions. The protective activity was more persistent in the vinylimidazoles than in the corresponding allylimidazoles. The curative activity in greenhouse conditions increased as the activity *in vitro* increased. Substitution of the 2,6-dichlorobenzoyloxy group at the 2-position on the benzene ring was favorable to the curative activity. The curative activity does not seem to depend on the hydrophobicity of the molecule, because the positive effect of the log *P* term on the *in vitro* activity and the negative effect on the mobility within the leaf cancel each other.

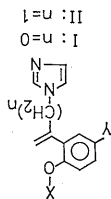
## INTRODUCTION

Recently we have synthesized series of 1-[1-(2-substituted hydroxy-5-substituted phenyl)vinyl]imidazoles (I)<sup>1-3</sup> and 1-[2-(2-substituted hydroxy-5-substituted phenyl)allyl]imidazoles (II)<sup>4,5</sup> which have antifungal activity against *B. cinerea in vitro*. Quantitative structure-activity relationships showed that molecular hydrophobicity as well as certain submolecular steric and structural factors is important in determining variations in the antifungal potency.<sup>4,5</sup> More recently, we have measured their protective and curative antifungal activities against *B. cinerea* under greenhouse conditions. This paper reports the relationships between the antifungal activities of vinylimidazoles I and allylimidazoles II in

## MATERIALS AND METHODS

### 1. Compounds

Vinylimidazoles I and allylimidazoles II used in the present test are listed in Table I. Compound 3 was newly synthesized using the same method as described in our previous paper.<sup>5</sup>



greenhouse and *in vitro* conditions with the aid of physicochemical and structural parameters and regression analysis.<sup>6</sup>

Table I Antifungal activity *in vitro* against *B. cinerea* and physicochemical parameters of vinylimidazoles I and allylimidazoles II used in the regression analyses.

No.	X <sub>1</sub> <sup>a)</sup>	Y	n	mp (°C)	Molecular formula	pI <sub>50</sub> <sup>b)</sup> log P <sup>b)</sup> I <sub>A11</sub> <sup>c)</sup> I <sub>D01</sub> <sup>c)</sup>
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1	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub>	CH <sub>3</sub>	0	d)	C <sub>15</sub> H <sub>18</sub> N <sub>2</sub> O·(CO <sub>2</sub> H) <sub>2</sub>	4.76
2	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub>	H	0	d)	C <sub>15</sub> H <sub>18</sub> N <sub>2</sub> O	3.82
3	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>	Cl	0	129.5-130	C <sub>16</sub> H <sub>18</sub> CIN <sub>2</sub> O·(CO <sub>2</sub> H) <sub>2</sub>	5.20
4	Bz	Cl	0	e)	C <sub>18</sub> H <sub>15</sub> CIN <sub>2</sub> O·HCl·1/10H <sub>2</sub> O	4.85
5	2-Cl-Bz	H	0	d)	C <sub>18</sub> H <sub>15</sub> CIN <sub>2</sub> O	4.71
6	3-Cl-Bz	H	0	f)	C <sub>18</sub> H <sub>15</sub> CIN <sub>2</sub> O·HCl	4.71
7	4-Cl-Bz	H	0	d)	C <sub>18</sub> H <sub>15</sub> N <sub>2</sub> O·HCl	5.45
8	2,4-Cl <sub>2</sub> -Bz	H	0	d)	C <sub>18</sub> H <sub>14</sub> Cl <sub>2</sub> N <sub>2</sub> O	6.58
9	2,4-Cl <sub>2</sub> -Bz	CH <sub>3</sub>	0	d)	C <sub>19</sub> H <sub>16</sub> Cl <sub>2</sub> N <sub>2</sub> O	6.02
10	2,4-Cl <sub>2</sub> -Bz	F	0	d)	C <sub>18</sub> H <sub>15</sub> Cl <sub>2</sub> FN <sub>2</sub> O	5.71
11	2,4-Cl <sub>2</sub> -Bz	Cl	0	d)	C <sub>18</sub> H <sub>15</sub> Cl <sub>3</sub> N <sub>2</sub> O	6.32
12	2,6-Cl <sub>2</sub> -Bz	H	0	d)	C <sub>18</sub> H <sub>14</sub> Cl <sub>2</sub> N <sub>2</sub> O	6.39
13	2,6-Cl <sub>2</sub> -Bz	CH <sub>3</sub>	0	d)	C <sub>19</sub> H <sub>16</sub> Cl <sub>2</sub> N <sub>2</sub> O	6.07
14	2,6-Cl <sub>2</sub> -Bz	F	0	d)	C <sub>18</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>2</sub> O	6.79
15	3,4-Cl <sub>2</sub> -Bz	H	0	e)	C <sub>18</sub> H <sub>14</sub> Cl <sub>2</sub> N <sub>2</sub> O·HCl	5.74
16	2-Cl-Thi	H	0	e)	C <sub>16</sub> H <sub>18</sub> CIN <sub>2</sub> OS·HCl	5.76
17	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub>	H	1	e)	C <sub>16</sub> H <sub>20</sub> N <sub>2</sub> O	3.84
18	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>7</sub>	H	1	e)	C <sub>20</sub> H <sub>28</sub> N <sub>2</sub> O·(CO <sub>2</sub> H) <sub>2</sub>	5.95
19	4-C <sub>6</sub> H <sub>5</sub> -Bz	H	1	e)	C <sub>25</sub> H <sub>28</sub> N <sub>2</sub> O	5.90
20	2,4-Cl <sub>2</sub> -Bz	H	1	e)	C <sub>18</sub> H <sub>16</sub> Cl <sub>2</sub> N <sub>2</sub> O	5.44
21	2,4-Cl <sub>2</sub> -Bz	CH <sub>3</sub>	1	e)	C <sub>20</sub> H <sub>18</sub> Cl <sub>2</sub> N <sub>2</sub> O·(CO <sub>2</sub> H) <sub>2</sub>	6.09
22	2,4-Cl <sub>2</sub> -Bz	F	1	e)	C <sub>19</sub> H <sub>17</sub> Cl <sub>2</sub> FN <sub>2</sub> O·(CO <sub>2</sub> H) <sub>2</sub>	7.19
23	2,6-Cl <sub>2</sub> -Bz	F	1	e)	C <sub>18</sub> H <sub>15</sub> Cl <sub>2</sub> FN <sub>2</sub> O·(CO <sub>2</sub> H) <sub>2</sub>	5.73
24	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub>	H	1	e)	C <sub>20</sub> H <sub>20</sub> N <sub>2</sub> O·(CO <sub>2</sub> H) <sub>2</sub>	4.85
25	C <sub>6</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>2</sub>	H	1	e)	C <sub>20</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub> ·(CO <sub>2</sub> H) <sub>2</sub>	3.93

a) Symbols Bz and Thi indicate benzyl and thiophen-3-yl groups, respectively.  
 b) Compounds 1, 2 and 4-16 are reported in Ref. 5) and compounds 17-25 in Ref. 4).  
 c) Indicator variables; see text.  
 d) Reported in Ref. 5).  
 e) Reported in Ref. 2).  
 f) Reported in Ref. 1).  
 g) Reported in Ref. 4).

The others were the same samples as used in the previous tests.<sup>1,2,4,5)</sup>

## 2. Biological Tests

### 2.1 Antifungal activity *in vitro*

An I<sub>50</sub> value (molar concentration for 50% inhibition of mycelial growth) of a compound against *B. cinerea* was determined by the agar medium dilution method after 2 days of incubation at 20°C. The activity of the present test compounds, except 3, was previously reported.<sup>4,5)</sup>

### 2.2 Protective and curative activities

*Cucumber plant and application of com-*

*found:* Water-soaked seeds of cucumber (cv. Tsukuba shirubo) were grown in plastic pots (350 ml in volume) filled with sandy loam soil containing some fertilizers. The pots were kept in a greenhouse. Seedlings in the second-leaf stage were used for the assessment of biological activity. A 50 mg/ml dimethylformamide solution of each compound was diluted with distilled water containing a 20 ppm surfactant to give a concentration of 500 μg/ml. The solution was subsequently diluted (four fold) with distilled water to reach the final concentrations of 500-0.5 μg/ml. Then the water suspension of each compound was

sprayed on the cucumber seedlings, 24 hr before inoculation for the evaluation of protective activity and 24 hr after inoculation for the evaluation of curative activity.

*Inoculation of fungus: B. cinerea* was grown on a potato-sucrose-agar (PSA) medium for 2 days at 20°C to form colonies. Agar disks 4 mm in diameter, including hyphal tips, were cut off at the peripheral regions of fresh colonies. Four disks were inoculated face-down on the leaf surface of a cucumber seedling. The seedlings were incubated for 3 days after the inoculation at 20°C in a humid chamber and the diameters of diseased areas around the four disks were measured and the values were averaged. Potency to inhibit the growth relative to an untreated seedling was expressed by

$$A = \left( 1 - \frac{\text{The averaged diameter in a treated plot}}{\text{The averaged diameter in a control plot}} \right) \times 100$$

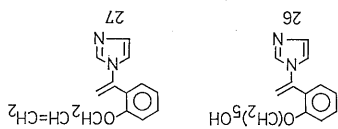
From relationships between the percentage (*A*) value and concentration in the protective and curative tests, molar  $EC_{90}$  (90% protection) and molar  $EC_{50}$  (50% cure) concentrations of each test compound were determined, respectively. The results are listed in Table 2, expressed as  $\log 1/EC_{90}$  and  $\log 1/EC_{50}$ . The ranges of the experimental errors:  $EC_{90}$ : 1-16%, average 7%;  $EC_{50}$ : 4-23%, average 11%.  
 2.3 Duration of protective activity  
 Protective activity was evaluated in the

Table 2 Antifungal activities of vinylimidazoles I and allylimidazoles II against *B. cinerea* in greenhouse conditions.

Compound No.	Obsd.	Protective activity: $\log 1/EC_{90}$		Obsd.	Curative activity: $\log 1/EC_{50}$	
		Eq. (3) Cald. by	Eq. (4) Cald. by		Eq. (5) Cald. by	Eq. (6) Cald. by
1	2.18	2.14	2.28	3.42	3.24	3.33
2	2.50	2.43	2.96	3.78	3.92	3.85
3	3.08	2.98	2.96	3.54	3.62	3.60
4	2.59	2.64	2.69	3.41	3.32	3.37
5	2.85	2.79	2.80	3.85	3.75	3.70
6	2.18	2.52	2.60	3.13	3.23	3.31
7	2.72	2.60	2.65	3.56	3.37	3.42
8	3.22	3.29	3.20	4.08	4.00	3.89
9	3.18	3.06	3.07	3.83	2.93	3.06
10	3.37	3.29	3.21	3.72	3.72	3.67
11	3.19	3.24	3.21	3.21	3.09	3.17
12	3.31	3.20	3.14	4.34	4.30	4.30
13	3.18	3.18	3.16	3.66	3.73	3.86
14	3.27	3.44	3.32	4.60	4.57	4.50
15	2.83	2.83	2.87	2.92	3.13	3.22
16	2.72	2.74	2.74	3.68	3.90	3.82
17a)	2.53	2.40	2.28	3.10	3.84	3.79
18a)	2.99	3.36	3.10	3.71	3.62	3.59
19a)	3.04	3.71	3.35	3.86	4.34	4.14
20a)	3.18	3.60	3.24	4.14	4.57	4.32
21a)	3.13	3.51	3.22	3.96	3.78	3.71
22a)	3.35	3.66	3.30	4.19	4.40	4.19
23a)	3.38	3.40	3.12	4.50	4.48	4.44
24a)	2.77	2.66	2.50	3.83	3.83	3.78
25a)	2.15	2.56	2.40	3.84	4.06	3.96

a) Not used in the derivation of Eq. (3) and Eq. (5).  
 b) Not determined.

Although compounds were used in free-base form or acid-addition-salt form, hydrophobicity of the free-base was regarded as that of the corresponding salt. The antifungal activity was not affected by adding acid, as described below.



4. Relationships between Activities in Greenhouse and in Vitro Conditions  
Relationships were analyzed on the basis of Eq. (2):<sup>6)</sup>

$$\log 1/BA = a \cdot I_{50} + b(\log P)^2 + d \log P + e I_{an} + f I_{D01} + c \quad (2)$$

In Eq. (2),  $BA$  is biological activity in greenhouse conditions,  $EC_{50}$  or  $EC_{90}$ ,  $a$ ,  $b$  ( $\leq 0$ ),  $d$ ,  $e$  and  $f$  are susceptibility constants, and  $c$  an intercept.  $I_{an}$  and  $I_{D01}$  are indicator variables. The  $I_{an}$  takes a value of 1 for allylimidazole **II** and the  $I_{D01}$  takes a value of 1 for derivatives having two chlorine atoms at the 2- and 6-positions on the benzene ring of the benzyl substituent at the X position. Relevant physicochemical parameters and indicator variables are listed in Table 1. The level of significance of each term was evaluated by  $F$  and the student's  $t$  tests.

## RESULTS AND DISCUSSION

### 1. Effect of Acid of Acid-addition Salts on Protective and Curative Activities

Our previous reports<sup>4,5)</sup> showed that antifungal activities *in vitro* were not influenced by a form of the molecule, a free-base or acid-

Table 4 Protective and curative activities of acid-addition salts of compound **8**<sup>\*)</sup> against *B. cinerea*.

Acid	$\log 1/EC_{90}$	$\log 1/EC_{50}$
$HNO_3$	3.34	3.66
$(CO_2H)_2$	3.38	3.76
HCl	3.41	3.58
<b>8</b> (free base)	3.53	3.36

<sup>\*)</sup> Compounds formulated as 50% wettable powder were used for biological tests.

Table 3 Duration of the protective activity of vinylimidazoles **8** and **10**, and allylimidazoles **20** and **22** against *B. cinerea* (spore).

Compound No.	Inoculation X day(s) after application	$\Delta^*) = (\log 1/EC_{90}, 8 \text{ days}) - (\log 1/EC_{90}, 1 \text{ day})$	
		X=8	X=1
<b>8</b>	4.02	4.84	-0.82
<b>10</b>	4.73	5.13	-0.40
<b>20</b>	3.90	5.72	-1.82
<b>22</b>	4.11	5.65	-1.54

same manner as described above using a spore as an inoculum. Cucumber seedlings were kept in the greenhouse for 1 or 8 days after the application of a compound suspension. The applied seedlings were inoculated with four droplets (10  $\mu$ l each) of conidia suspension ( $1 \times 10^6$  spores/ml) per leaf. Duration of protective activity was determined by comparing the  $EC_{90}$  value of a spore inoculated 8 days after the application with that of a spore inoculated 1 day after the application. The results are listed in Table 3.

### 3. Partition Coefficient

A  $\log P$  (1-octanol/ $H_2O$ ) value was used to represent molecular hydrophobicity.  $\log P$  values of the compounds except compound **3** were reported previously.<sup>4,5)</sup> They were estimated by using the CLOGP3 (Ver. 3.3)<sup>7-9)</sup> program on a Vax 11/780 computer.

The CLOGP3 program is to calculate a  $\log P$  value of a compound by summing up the component value ( $f$ ) assignable to each sub-structure.<sup>8)</sup> Since the  $f$  value of 1-N atom of the vinylimidazole ring is not available, an estimated  $\log P$  value does not represent that of the whole molecule. Since the 1-N atom is common in all vinylimidazoles **1**, the difference between the observed and estimated  $\log P$  values of compounds **26** and **27** were averaged and -0.52 was taken as the  $f$  value of the 1-N.<sup>5)</sup> The  $\log P$  value used in the regression analysis was corrected by the factor as shown in Eq. (1):

$$\log P = \log P^{\text{calcd}} - 0.52 \quad (1)$$

addition salts. We, therefore, prepared several acid-addition salts of compound **8** as a representative, and determined their protective and curative activities against *B. cinerea*. As shown in Table 4, the antifungal activities of the salts were almost identical with those of free-base **8**, suggesting that the protective and curative activities are not influenced by the counter anions which form the salts.

## 2. Relationships between Protective Activity in Greenhouse Conditions and Antifungal Activity in Vitro

First, we examined the protective activity data on vinylimidazoles **1-16** in Table 2. Equation (3) showed the best correlation.

$$\log I/EC_{50} = 0.660(\pm 0.130)P_{150} - 1.00 \quad (3)$$

$$n=16, s=0.134, r=0.941, F_{1,14}=108.7$$

In this and the following equations,  $n$  is the number of data used in the correlation,  $s$  is the standard deviation,  $r$  the multiple correlation coefficient, and  $F_{v_1, v_2}$  the  $F$  ratio of the correlation where  $v_1 = m$ , and  $v_2 = n - m - 1$ ;  $m$  is the number of independent variables used in the correlation. Figures in the parentheses are the 95% confidence intervals. In Eq. (3), all terms were justified above a 99.5% level. The correlation between the protective activity and the activity *in vitro* was excellent.

An addition of  $\log P$  or  $I_{D01}$  term to Eq. (3) did not afford any significant improvement. Equation (3) indicates that the higher the antifungal activity *in vitro*, the higher the protective activity in greenhouse conditions. We have suggested<sup>4</sup> that the mode of interaction of vinylimidazoles **I** with a target site is similar to that of allylimidazoles **II**, since the quantitative structure-activity relationship is similar between the vinylimidazoles and the allylimidazoles. We, therefore, estimated the  $\log I/EC_{50}$  value of the allylimidazoles by Eq. (3). The observed  $\log I/EC_{50}$  values of allylimidazoles **17-25** were generally lower than those estimated from Eq. (3) (Table 2). We assumed that this could be represented by the indicator variable,  $I_{A11}$ . What it means will be discussed later. Thus, Eq. (4) was derived for all vinyl- and allyl-imidazoles **1-25**, as shown in Table 2.

In Eq. (4), all terms were justified above a 99.5% level. The addition of  $\log P$  or  $I_{D01}$  term to Eq. (4) did not afford any significant improvement. Equation (4) shows that the antifungal activity *in vitro*, the higher the protective activity. The coefficient of the  $I_{A11}$  term in Eq. (4) is negative, indicating that the protective activity of compound **II** is lower than that of compound **I** although their  $P_{150}$  values are the same. The term  $I_{A11}$  was not a necessary factor to determine the curative activity of imidazoles **I** and **II**, however. For the evaluation of protective activity, a compound was applied to the seedlings 24 hr before inoculation, while for the evaluation of curative activity, the compound was applied 24 hr after inoculation. We, therefore, examined the persistency of their protective activity. Table 3 shows that the duration of the protective activity was longer in vinylimidazoles **I** than in allylimidazoles **II**. The  $I_{A11}$  term would suggest a difference in a rate of decomposition or metabolism on or within the leaf between **I** and **II**.

## 3. Relationships between Curative Activity in Greenhouse Conditions and Antifungal Activity in Vitro

First, we analyzed the curative activity data on vinylimidazoles, **1-8**, **10**, and **12-16** in Table 2. Equation (5) showed the best correlation.

$$\log I/EC_{50} = 1.04(\pm 0.309)P_{150}$$

$$- 0.764(\pm 0.277)\log P$$

$$+ 0.569(\pm 0.284)I_{D01} \quad (5)$$

$$+ 1.31$$

$$n=14, s=0.155, r=0.952, F_{3,10}=32.2$$

In Eq. (5), all terms were justified above a 99.5% level. The correlation of the curative activity with  $P_{150}$ ,  $\log P$ , and  $I_{D01}$  was excellent. An addition of  $(\log P)^2$  term to Eq. (5) did not afford any significant improvement. Equation (5) shows that the higher the antifungal activity *in vitro*, the higher the curative

Table 5 Development of Eq. (6)<sup>a)</sup>.

Eq. No.	$F$ of difference between Eqs. (7)	$I_{DCI}$	Intercept <sup>b)</sup>	$s^c$	$F_{v_1, v_2}^d$	$pI_{50}$	$\log P$	$I_{DCI}$	$\log P$	$pI_{50}$			
(7)			1.71	0.616	0.321	0.344	0.281	0.410 <sup>e)</sup>	2.03	0.724	0.288	$F_{2,20}=11.0$	$F_{1,21}=12.8$
(8)			2.03	0.724	0.288	0.281	0.714	0.410 <sup>e)</sup>	2.03	0.724	0.288	$F_{2,20}=6.09$ <sup>s)</sup>	$F_{1,20}=11.0$
(9)			1.53	0.739	0.281	0.714	0.407 <sup>e)</sup>	0.621	1.92	0.919	0.173	$F_{2,20}=12.0$	$F_{1,20}=7.38$ <sup>b)</sup>
(6)			0.621	0.919	0.173	0.791	0.597	0.621	1.92	0.919	0.173	$F_{2,20}=38.2$ , $r^2=35.6$ <sup>b)</sup>	$F_{1,19}=24.4$

<sup>a)</sup> Figures in the parentheses are the 95% confidence intervals. All terms are justified above a 99.5% level by the  $t$ -test unless noted otherwise.

<sup>b)</sup> Multiple correlation coefficient.

<sup>c)</sup> Standard deviation.

<sup>d)</sup>  $F$  value of the correlation.  $v_1 = m$ ,  $v_2 = n - m - 1$ ,  $n$  and  $m$  are the number of data and independent variables used in the correlation, respectively.

<sup>e)</sup> Justified at a level between 99.5 and 95%.

<sup>f)</sup>  $F_{1,20,0.025} = 5.87$ ,  $F_{1,19,0.005} = 10.1$ .

<sup>g)</sup> Eqs. (7) and (8).

<sup>h)</sup> Eqs. (7) and (9).

<sup>i)</sup> Eqs. (8) and (9).

<sup>j)</sup> Eqs. (9) and (6).

activity. The coefficient of term  $I_{DCI}$  was positive. Substitution of the 2,6-dichlorobenzoyloxy group at the 2-position on the benzene ring was favorable to the curative activity although the physicochemical meaning has not yet been clarified. The  $\log P$  term will be discussed in detail later.

Next, we analyzed the curative activity data in Table 2 including those on the allylimidazole, and obtained Eq. (6), which almost is equivalent to Eq. (5).

$$\log I/E_{C_{50}} = 0.791(\pm 0.203)pI_{50} - 0.597(\pm 0.215)\log P + 0.621(\pm 0.215)I_{DCI} + 1.92 \quad (6)$$

$$n = 23, s = 0.173, r = 0.919, F_{3,19} = 24.4$$

10.1 at a 99.5% level, as shown in Table 5. Edgington<sup>11)</sup> reported that one of chemical requisites for the mobility of the xenobiotics within plants is their  $\log P$  value. In the region where the  $\log P$  value is higher than 2, the mobility decreases as the  $\log P$  value increases. The  $\log P$  value for the present series of imidazoles I and II remains in the range of 3.82-6.09. In Eqs. (5) and (6), therefore, the  $\log P$  term may indicate an effect on the mobility of the molecule within the leaf. As the curative activity was assessed by the application of a compound to the leaf inoculated 24 hr before, the mobility of the molecule within the leaf may be important in determining the activity. As the protective activity was assessed by the application of the compound to the leaf 24 hr before the inoculation, however, the

In Eq. (6), all terms were justified above a 99.5% level. Tables 5 and 6 show the development of Eq. (6) and the internal correlation of independent variables, respectively. Although a squared correlation coefficient between variables  $pI_{50}$  and  $\log P$  was relatively high ( $r^2 = 0.724$ ), the addition of  $\log P$  term to Eq. (8) to give Eq. (6) was statistically significant since the  $F$  value<sup>10)</sup> of 38.2, a difference between Eqs. (8) and (6), was larger than the critical  $F$  value of

Table 6 Squared correlation matrix of the variables used in Eq. (6).

$pI_{50}$	$\log P$	$I_{DCI}$
$pI_{50}$	1.000	0.081
$\log P$	0.724	0.166
$I_{DCI}$	0.081	1.000

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要 約

I-[1-(置換7<sub>2</sub>=ニル)1-2]ニゾール類と I-[1-(置換7<sub>2</sub>=ニル)1-2-(置換7<sub>2</sub>=ニル)1-2]ニゾール類の温室内での防除効果と *in vitro* の抗菌活性との相関関係

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16個の1-[1-(2-置換7<sub>2</sub>=ニル)1-2]ニゾール類と9個の1-[2-(2-置換7<sub>2</sub>=ニル)1-2]ニゾール類と9個の1-[1-(2-置換7<sub>2</sub>=ニル)1-2]ニゾール類の予防効果と治療効果を測定した。ポット試験の効対試験条件下での灰色カビ病菌 (*Botrytis cinerea*) に対する予防効果と治療効果を測定した。ポット試験の結果を、果と先に報告した *in vitro* の殺菌活性との間の関係を、物理化学的および構造パラメータを用いて重回帰分析により定量的に解析した。その結果 *in vitro* の活性が高くなればなるほど予防効果は高くなることがわかった。ピニゾール類の予防効果は *in vitro* の活性が高くなるほど高くなることと、ベンゼン環の2位に2, 6-ジクロロベンジニオキシ基が存在すると、治療効果にともなう好ましいこととが明らかになった。さらに分子の疎水性の効果について、*in vitro* 活性に対する正の効果と葉内での浸透移行性に対する負の効果とが互いに相殺されることにより、治療効果は分子の疎水性には依存しないと考えられた。

mobility may be less important. In Eqs. (5) and (6), the  $p_{150}$  and the  $\log P$  terms statistically contributed to the curative activity. Since hydrophobicity ( $\log P$ ) is most important in determining the *in vitro* activity ( $p_{150}$ ) of I and II, <sup>4,5</sup> the curative activity does not seem to depend on the  $\log P$  term, because the positive effect of the  $\log P$  term on the  $p_{150}$  value and the negative effect on the mobility cancel each other in Eqs. (5) and (6); the coefficient of the  $\log P$  term in Eqs. (5) or (6) is  $-0.764$  and  $-0.597$ , respectively, and that of the  $p_{150}$  is  $0.55-0.67$ , <sup>4,5</sup> The relationship between the curative and *in vitro* activities of vinylimidazoles I and II were combined by Eq. (6). The combination shows that the difference in the rate of decomposition on or within the leaves between I and II might be relatively small, when imidazoles I and II were applied to the leaf inoculated 24 hr before.

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