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Systemic fungicidal and insecticidal activities of 1- and 2-[bis (dimethylamido)phosphoryl]-3-alkyl-5-anilino-1,2,4-triazoles

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Abstract

The compounds referred to in the title have been investigated for fungicidal, insecticidal and acaricidal activities in laboratory and greenhouse tests. Several representatives of this class of compounds were active against powdery mildew on apple, cucumber, and barley, and against aphids and spider mites, both when applied to the leaves and when added to the nutrient solutions of test plants. Treatment of leaf halves resulted in protection of the entire leaves. A striking difference in pesticidal activity was observed between two series of isomers. Representatives of the series with the phosphoryl group in the 1-position showed much greater pesticidal activities than their corresponding isomers with the phosphoryl group in the 2-position. The optimum activity within the two homologous series (R–H, CH_3 ... C_6H_{13}) was determined: generally the lower homologues (R–H, CH_3, C_2H_5 and i–C_3H_7) showed the greatest pesticidal activity in the systemic tests. After leaf-application the influence of the length of R was less pronounced or even reversed.

Introduction

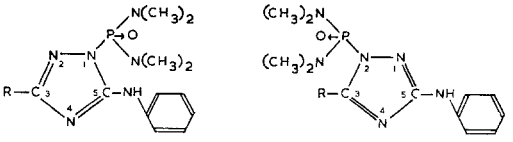
Since van den Bos et al. (1960) and Meltzer (1961) recognized the systemic fungicidal, insecticidal and acaricidal properties of the reaction products of bis(dimethylamido)-phosphoryl chloride and substituted triazoles, a great number of analogues have been synthesized and screened (van den Bos et al., 1961).
The present paper describes the fungicidal, aphicidal and acaricidal properties of two homologous series of compounds, both when applied to the leaves and when added to the nutrient solutions of test plants. These compounds were synthesized and their structures determined by van den Bos et al. (1966).
The members of these two series were identified as having the bis(dimethylamido)-phosphoryl group in the 1- and 2-position respectively and will be designated further on as the N_1- and N_2-series respectively (Fig. 1).

Methods

Acaricidal activities were determined by dipping potted seedlings of French beans

Fig. 1. N_1- and N_2-series

Fig. 1. N_1- en N_2-reeks



(*Phaseolus vulgaris*) in aqueous emulsions of the compounds. After the leaves had dried they were provided with plastic cages 1 inch in diameter and 10 females of *Tetranychus cinnabarinus* were placed in these cages. The plants were kept in climatically conditioned cabinets at R.H. 65% and 24 °C and illuminated 16 h per day by fluorescent light tubes. Final death counts took place after 5 days. The aphicidal activity was tested by dipping potted seedlings of broad beans (*Vicia faba*) in aqueous emulsions of the compounds. Each plant was placed in a perspex cylinder and subsequently infected with 20 *Aphis fabae* adults. After that the cylinders were covered with lens paper. Incubation took place under the same conditions as specified for the acaricidal test. Systemic acaricidal and aphicidal activities were determined by adding the compounds to the nutrient solutions in which the test plants were grown.

Fungicidal activity against *Sphaerotheca fuliginea* was evaluated on cucumber seedlings, cultivar 'Lange gele tros', which were grown in pots in the greenhouse until the cotyledons were well developed. These cotyledons were sprayed with aqueous suspensions of the chemicals, which were finely divided in glass mortars. They were then dusted with spores of the fungus by shaking over them cucumber plants heavily infected with powdery mildew. After an incubation period of 10–14 days in the greenhouse the results were assessed and recorded as percentages of the mildew on the cotyledons of unsprayed control plants.

An analogous method was followed for the evaluation of activity against *Podosphaera leucotricha* on apple seedlings. In this case the infection of the third and fourth leaves of the seedlings was assessed.

The tests to determine systemic activity against cucumber and apple mildew were performed in a room maintained at an R.H. of about 70%, and a temperature of 21 °C during the 16 h of light (fluorescent light, 3.000–6.000 lux) and 18 °C during the 8 h of darkness. The test plants were grown in the greenhouse on nutrient solution; 48 h before infection they were moved to fresh solutions to which the chemicals had been added and placed under the conditions specified above; 7–8 days after the inoculation the solution which had been taken up was replaced; inoculation and assessment of the results 12–14 days later were performed in the same way as in the leaf tests.

In order to determine whether the fungicides were translocated after application to the leaves aqueous suspensions of the chemicals were brushed on one half of each fourth leaf of apple seedlings both on the upper and lower side of the leaf; inoculation and incubation were performed in the same way as in the leaf spray tests; the infection of both the treated and untreated leaf-halves was assessed.

Results

The results of the acaricidal tests of the two series of isomers are shown in Table 1 It appears that the position of the bis(dimethylamido)phosphoryl group is of grea.

Table 1. Acaricidal action of 1- and 2-[bis(dimethylamido)phosphory]-3-alkyl-5-anilino-1,2,4-triazoles. *Tetranychus cinnabarinus* on *Phaseolus vulgaris*. LC 95 in ppm.

*N_1-series**	*Dipping test*	*Systemic test*	*N_2-series*	*Dipping test*	*Systemic test*
H	10	50	H	> 1000	100
CH_3	30	15	CH_3	300	20
C_2H_5	10	20	C_2H_5	300	> 100
i-C_3H_7	10	50	i-C_3H_7	> 1000	> 100
C_3H_7	10	50	C_3H_7	> 1000	> 100
C_4H_9	10	100	C_4H_9	> 1000	> 100
C_5H_{11}	30	> 100			
C_6H_{13}	3		C_6H_{13}	> 1000	> 100
Triamiphos	10	5			

* See Fig. 1

Tabel 1. Acaricide werking van 1- en 2- [bis(dimethylamido)fosforyl] -3-alkyl-5-anilino-1,2,4-triazolen. Tetranychus cinnabarinus op stambonen. LC 95 in ppm.

importance; compounds of the N_1-series are much more active than their N_2-isomers, both in the dipping test and in the systemic test.
Within the N_1-series the 3-methyl compound is the most active one in the systemic test; lengthening of the alkyl group results in diminishing activity. However, within the same series the dipping test results show virtually no relationship to structures.
Most representatives of the N_2-series did not show any activity at screening concentrations, the 3-methyl compound being a remarkable exception in the systemic test.
Table 2, representing the aphicidal properties of the compounds, shows roughly the same pattern; in this case greater differences between higher and lower alkyl analogues are observed.
The activities against cucumber powdery mildew again follow almost the same pattern as shown in Table 3; of the N_1-isomers only those with R = H, CH_3 and C_2H_5 are

Table 2. Aphicidal action of 1- and 2-[bis(dimethylamido)phosphoryl]-3-alkyl-5-anilino-1,2,4-triazoles. *Aphis fabae* on *Vicia faba*. LC 95 in ppm.

*N_1-series**	*Dipping test*	*Systemic test*	*N_2-series*	*Dipping test*	*Systemic test*
H	20	100	H	> 1000	> 100
CH_3	20	20	CH_3	1000	20
C_2H_5	20	50	C_2H_5	> 1000	> 100
i-C_3H_7	10	100	i-C_3H_7	> 1000	> 100
C_3H_7	100	> 100	C_3H_7	> 1000	> 100
C_4H_9	100	> 100	C_4H_9	> 1000	> 100
C_5H_{11}	100	> 100			
C_6H_{13}	300	> 100	C_6H_{13}	> 1000	> 100
Triamiphos	70	15			

* See Fig. 1

Table 2. Aphicide werking van 1- en 2- [bis(dimethylamido)fosforyl] -3-alkyl-5-anilino-1,2,4-triazolen. Aphis fabae op tuinbonen. LC 95 in ppm.

Table 3. The activity of 1- and 2- [bis(dimethylamido)phosphoryl] -3-alkyl-5-anilino-1,2,4-triazoles against *Sphaerotheca fuliginea* on cucumber seedlings. Infection in percentages.

*N_1-series**	*Leaf spray test 1000 ppm*	*Systemic test 100 ppm*	*N_2-series*	*Leaf spray test 1000 ppm*	*Systemic test 100 ppm*
H	30	0	H	100	100
CH_3	27	0	CH_3	65	8
C_2H_5	4	7	C_2H_5	100	39
i-C_3H_7	0	73	i-C_3H_7	94	40
C_3H_7	29	61	C_3H_7	94	100
C_4H_9	0	94	C_4H_9	100	100
C_5H_{11}	6	82			
C_6H_{13}	92	100	C_6H_{13}	100	100
Triamiphos	81	86	Control	100	100

* See Fig. 1

Tabel 3. De werking van 1- en 2-[bis(dimethylamido)fosforyl]-3-alkyl-5-anilino-1,2,4-triazolen tegen Sphaerotheca fuliginea op komkommerzaailingen. Aantasting in percentages.

active systemically whereas those with R = H, CH_3, ... C_5H_{11} show activity in the leaf spray test, with a tendency towards a decline in activity of the compounds with smaller alkyl substituents.

This tendency of the N_1-series is still stronger in the apple mildew test (Table 4).

In general the activity against apple mildew is greater than the activity against cucumber mildew.

Table 5 demonstrates the systemic activities of the N_1-isomers following leaf application. All compounds except the C_6H_{13}-analogue exhibit translocation of fungicidal action, those with R = C_2H_5, i–C_3H_7 and n–C_3H_7 showing the highest activities on the untreated leaf-halves.

Table 4. The activity of 1- and 2- [bis(dimethylamido)phosphoryl] -3-alkyl-5-anilino-1,2,4-triazoles against *Podosphaera leucotricha* on apple seedlings. Infection in percentages.

*N_1-series**	*Leaf spray test 300 ppm*	*Systemic test 30 ppm*	*N_2-series*	*Leaf spray test 300 ppm*	*Systemic test 30 ppm*
H	31	0	H	79	56
CH_3	18	13	CH_3	17	56
C_2H_5	19	30	C_2H_5	24	58
i-C_3H_7	15	20	i-C_3H_7	41	71
C_3H_7	8	53	C_3H_7	36	70
C_4H_9	3	86	C_4H_9	57	94
C_5H_{11}	0	69			
C_6H_{13}	7	58	C_6H_{13}	59	77
Triamiphos	14	11	Control	100	100

* See Fig. 1

Tabel 4. De werking van 1- en 2-[bis(dimethylamido)fosforyl]-3-alkyl-5-anilino-1,2,-4-triazolen tegen Podosphaera leucotricha op appelzaailingen. Aantasting in percentages.

Table 5. The leaf-systemic activity of 1- and 2-[bis(dimethylamido)phosphoryl]-3-alkyl-5-anilino-1, 2,4-triazoles against *Podosphaera leucotricha* on apple seedlings. Infection in percentages.

*N_1-series**	*Treated leaf-half 300 ppm*	*Untreated leaf-half*	*N_2-series*	*Treated leaf-half 300 ppm*	*Untreated leaf-half*
H	0	40	H	44	100
CH_3	0	24	CH_3	22	76
C_2H_5	0	16	C_2H_5	22	82
i-C_3H_7	0	16	i-C_3H_7		
C_3H_7	2	18	C_3H_7	46	80
C_4H_9	0	38	C_4H_9	38	80
C_5H_{11}	0	44			
C_6H_{13}	0	100	C_6H_{13}	52	96
Triamiphos			Control	100	100

* See Fig. 1

Tabel 5. De bladsystemische werking van 1- en 2-[bis(dimethylamido)fosforyl]-3-alkyl-5-anilino-1,2, 4-triazolen tegen Podosphaera leucotricha op appelzaailingen. Aantasting in percentages.

In a separate test no translocation from treated leaves to untreated ones of the same plant could be demonstrated. The compounds did not cause phytotoxicity symptoms at normal screening concentrations in any of the described tests.

Discussion

The most striking phenomenon in the structure-activity relationships of the 1- and 2-[bis(dimethylamido)phosphoryl]-3-alkyl-5-anilino-1, 2, 4-triazoles is the difference observed between the activity of the 1- and 2-series of isomers. The assumption that this difference in pesticidal activity can be explained by different stereo situation by influencing either the strength of the N–P-bond or the interaction with the biological receptor (i.e. a hydrolytic enzyme) is being investigated.

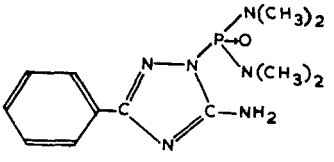
Within the active series, comprising the substances with the phosphoryl group in the 1-position, a remarkable difference is found between the results of the leaf application and the systemic tests. In the systemic tests the length of the alkyl group exerts a strong influence, the compounds with the shorter alkyl-substituents being the most active.

This influence is absent or even reversed (in the case of apple powdery mildew) in the leaf-application tests. Generally the activity of a compound is a function of its intrinsic activity and of its availability at the site of action. With triamiphos it has been demonstrated that it exerts its action on the germinating spore as well as on the haustoria within the epidermal host cells (Koopmans, 1960; Magendans and Dekker, 1966) (Fig. 2).

Long distance translocation does not play a part in the leaf spray tests for mildewicidal activity: the compounds are taken up directly by the spores or after penetration into the epidermis by the haustoria of the fungus. The positive influence of the length of the alkyl chain up to C_5H_{11} may be explained by a better uptake of the compounds

Fig. 2. Triamiphos, active ingredient of Wepsyn 155[R] (tradename N.V. Philips-Duphar)

Fig. 2. Triamiphos, actief bestanddeel van Wepsyn 155[R] (handelsmerk N.V. Philips-Duphar)



with longer alkyl chains by the spores or by a better penetration of these compounds into the epidermis.
In tests for root-systemic activity quite a different pattern develops. Here the lower homologues are superior, probably because they are transported more easily via the root system than their more lipophylic counterparts.
It is also possible that higher homologues are more subject to metabolic breakdown than their more hydrophylic analogues. The results of the leaf-systemic tests against *P. leucotricha* may be explained in such a way that because of the fact that translocation has to take place only over a shorter distance, the negative influence of the longer alkyl chains is less, resulting in an optimum activity somewhere in between (C_2H_5, i–C_3H_7).
At any rate the effect of such compounds on untreated parts of the leaves illustrates the importance of systemic properties even in case of application on the leaves.

Samenvatting

Systemisch fungicide en insekticide werking van 1- en 2-[bis(dimethylamido)fosforyl]-3-alkyl-5-anilino-1, 2, 4-triazolen

De in de titel genoemde stoffen zijn onderzocht op fungicide, insecticide en acaricide werking in laboratorium en kasproeven. Verscheidene vertegenwoordigers van dit type verbindingen waren werkzaam tegen echte meeldauw van appel, komkommer en gerst, en tegen bladluizen en spint, dit zowel na toepassing op de bladeren als na toevoeging aan de voedingsoplossingen van proefplanten. Behandeling van bladhelften resulteerde in bescherming van de gehele bladeren. Een opvallend verschil werd waargenomen tussen de werking van twee reeksen isomeren. Vertegenwoordigers van de reeks met de fosforylgroep op de 1-plaats waren veel werkzamer dan hun isomeren met de fosforylgroep op de 2-plaats. Het optimum binnen de twee homologe reeksen (R–H, CH_3 ... C_6H_{13}) werd bepaald: in het algemeen waren de lagere homologen (R–H, CH_3; C_2H_5 en i–C_3H_7) het werkzaamst in de systemische proeven. Na een preventieve bladbespuiting was de invloed van de lengte van R minder uitgesproken of zelfs omgekeerd.

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