# Pyridyloxy Analogues of the Systemic Fungicide N-[2,2,2-Trichloro-1-(3-pyridylamino)ethyl] formamide

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The piperazine derivative triforine (I) has attracted considerable interest in recent years because of its systemic fungicidal properties against several plant pathogens particularly rusts and powdery mildews (1-3). It is readily taken up by plant roots and translocated in the plant system. We have been interested in the past few years in ascertaining the chemical features of the triforine molecule necessary for systemic activity. From these studies it appears that the formamide group (NHCHO) is necessary for systemic activity (4,5). Systemic activity is retained in molecules of type II, where R is O-alkyl, NH-alkyl and to some extent S-alkyl but is generally lost when R is O-aryl or S-aryl (4-6). The few compounds of type II where R is NH-aryl which have so far been examined, for example, the protectant mildew fungicide chloraniformethan (III), are also much less active systemically (4) although some compounds of this type have been claimed to be systemic fungicides in a patent (7). The chlorine atoms of compounds of type II can be replaced by bromine without substantial loss of systemic activity (8). Several bis-formamide derivatives related to triforine are also highly effective systemic fungicides (9.10). Recently we prepared N-[2,2,2-trichloro-1-(3-pyridylamino)ethyl]formamide (IV). This compound was found to be an outstanding systemic fungicide against wheat powdery mildew, Erysiphe graminis, when applied to the roots of sand-grown wheat seedlings (11). It was completely effective at 5 ppm. We now report on an extension of this investigation involving the preparation and evaluation as fungicides of four related pyridyloxy compounds.

The compounds (II; R = 2-pyridyloxy), (II; R = 3-pyridyloxy) and (II; R = 8-quinolyloxy) were prepared

by reacting 1-(2,2,2-trichloro-1-formamid oethyl)pyridinium chloride (V) (12) with the appropriate hydroxypyridine in acetone solution. The pyrimidylthio derivative (II; R = 2-pyrimidylthio) was obtained by reacting N-(1,2,2,2-tetrachloroethyl)formamide (II; R = Cl) (cf. ref. 2) with 2-mercaptopyrimidine. Physical constants and spectroscopic data on these compounds are given in Tables I and II.

The four compounds were tested as fungicides against several plant pathogenic fungi by methods described previously (4,5,13). In spore germination tests against Alternaria brassicicola, Botrytis cinerea, Septoria nodorum and Uromyces viciae-fabae none of the compounds (II; R = 2-pyridyloxy), (II; R = 3-pyridyloxy) and (II; R = 2-pyrimidylthio) completely inhibited germination below 500 ppm. Compound (II; R = 8-quinolyloxy), however, inhibited germination of A. brassicicola at 25 ppm, S. nodorum below 5 ppm and U. viciae-fabae at 50 ppm. It was not effective against B. cinerea at 500 ppm. The high fungitoxicity shown by this compound confirms a previous report (14).

As protectant foliage sprays for the control of wheat powdery mildew, Erysiphe graminis, compound (II; R = 3-pyridyloxy) gave 97% disease control at 100 ppm. The other three compounds were almost inactive (less than 10% disease control). Against wheat brown rust, Puccinia recondita, compound (II; R = 8-quinolyloxy) gave over 95% disease control at 100 ppm. The other compounds gave moderate control (10.45%).

In systemic fungicide tests by root application against *E. graminis* on sand-grown wheat seedlings, compound (II; R = 2-pyridyloxy) gave complete control at 100 ppm but was ineffective at 50 ppm. The other compounds gave good control too (70-85%) at 100 ppm but were somewhat phytotoxic. The highly active compound (IV) (11) was included in the tests for comparison. It was fully effective at 25 ppm, the lowest concentration tested.

### **EXPERIMENTAL**

Microanalyses were performed by the Australian Microanalytical Service, Melbourne. Nmr spectra (60 MHz) were determined for 10% w/v solutions using tetramethylsilane as the internal standard.

 $\label{eq:Table I} \mbox{$N$-(2,2,2-Trichloro-1-pyridyloxyethyl) formamides (II)}$ 

				Analysis					
				Calcd.			Found		
R	М. р.	Solvent	Formula	C	Н	N	С	Н	N
2-Pyridyloxy	206	chloroform	$C_8H_7Cl_3N_2O_2$	35.6	2.6	10.4	35.4	2.8	10.2
3-Pyridyloxy	101	petrol-benzene (a)	$C_8H_7Cl_3N_2O_2$	35.6	2.6	10.4	35.5	2.7	10.4
8-Quinolyloxy	167-168 (b) (c)	petrol-benzene (a)	$C_{12}H_9Cl_3N_2O_2$	45.1	2.8	8.8	45.1	2.9	8.7
2-Pyrimidylthio	152	petrol-benzene (a)	C7H6Cl3N3OS	29.3	2.1	14.6	29.6	2.1	14.4

(a) Petrol had b. p. 60-80°. (b) With decomposition. (c) Literature (14) m. p. 168° dec.

Table II

Ir and Nmr Spectra of N-(2,2,2-Trichloro-1-pyridyloxyethyl)formamides (II)

R	Ir (a) ν CO (cm <sup>-1</sup> )	Nmr δ (deuteriochloroform) ppm
2-Pyridyloxy	1710	(b)
3-Pyridyloxy	1700	CCl <sub>3</sub> CH, d, 6.36-6.52; NH and 4,5-aromatic protons, m, 7.14-7.71; CHO and 2,6-aromatic protons, m, 8.25-8.45.
8-Quinolyloxy	1700	CCl <sub>3</sub> CH, d, 6.70-6.88; NH and 3,5,6,7-aromatic protons, m, 7.25-7.65; CHO and 4-aromatic protons, m, 8.05-8.30; 2-aromatic proton, q, 8.85-8.96.
2-Pyrimidylthio	1680	CCl <sub>3</sub> CH, d, 6.23-6.40; NH and 5-aromatic proton, m, 6.98-7.55; CHO, s, 8.30; 4,6-aromatic protons, d, 8.53-8.61.

(a) Nujol mull. (b) Too insoluble in deuteriochloroform.

#### N-(2,2,2-Trichloro-1-pyridyloxyethyl)formamides.

 $1\cdot(2,2,2\cdot\text{Trichloro-1-formamidoethyl})$ pyridinium chloride (12) (0.01 mole) was suspended in acetone and then added to an excess of the appropriate hydroxypyridine (0.03 mole) dissolved in acetone. The mixture was refluxed for 2-6 hours. The acetone was partly removed under vacuum and the residue poured onto crushed ice. An oil formed which soon solidified. The solid was washed with water, dried and crystallised. Yields were 50-75%.  $N\cdot[2,2,2\cdot\text{Trichloro-1-(2-pyrimidylthio)ethyl]}$  formamide (II; R = 2-pyrimidylthio).

N-(1,2,2,2-tetrachloroethyl) formamide (2) (0.02 mole) and 2-mercaptopyrimidine (0.02 mole) were refluxed in acetone solution for 4 hours. The solid obtained on cooling was collected and crystallised. Yield 50%.

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