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Synthesis and Insecticidal Activity of Heterocyclic Carbothioamides against *Sogatodes orizicola*

Keywords: *Heterocyclic carbothioamides; insecticides; Sogatodes orizicola*

INTRODUCTION

Rice delphacids (or planthoppers) are major pests of agriculture that are found mostly in the Far East. A number of insecticides are currently available to control these pests in rice crops. Due to the development of resistant pests and toxicological issues associated with certain insecticides/miticides, there is a continuing need to discover novel chemical structures with potent activity (Dekeyser and Downer, 1994). Progress toward finding new classes of insecticides has been achieved with the introduction of novel chemical types, such as imidacloprid (Elbert et al., 1990).

Recently, a series of aryl carbothioamides of the formula RC(S)NHC(S)NHR′, in which R is an aryl group and R′ is an alkyl group, were reported to possess insecticidal and miticidal activities (Farooq, 1989). However, little attention has been given to the corresponding heterocyclic carbothioamides. Pyridinyl and pyrazinyl carbothioamides have been reported as antituberculotics (Mollin et al., 1988), quinolinyl carbothioamides have been reported as plant microbiocides (Kluge et al., 1986), and benzofuranyl, pyridinyl, and furanyl carbothioamides have been reported as antitumor agents (Brouwer and Van Hes, 1986).

To investigate the possibility of improving the insecticidal activity of the known carbothioamides, in the present work we synthesized a series of *N*-(alkylamino)thioxomethyl heterocyclic carbothioamides (Figure 1), in which the heterocyclic groups consist of furan, thiophene, pyridine, and pyrazine rings, and measured their insecticidal activity against the rice delphacid, *Sogatodes orizicola*.

Chemistry. Synthesis of the title compounds was achieved according to the method outlined in Scheme 1. The heterocyclic carbothioamides **2a**−**l** were prepared by the reaction of readily available carbothioamide starting materials **1a**−**l** with alkyl isothiocyanates. The physical properties of the synthesized compounds are found in Table 1. The structural determination of the synthesized compounds was based on ^{1}H NMR spectra (Table 2). Yields of heterocyclic carbothioamides **2a**−**l** were in the range 53−81%.

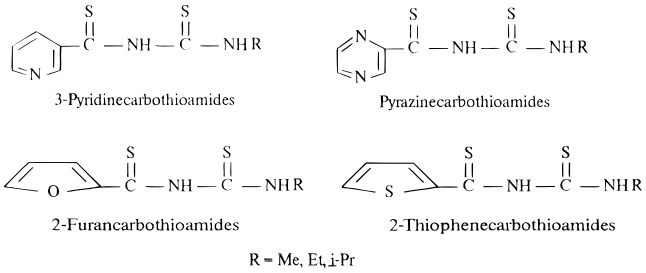
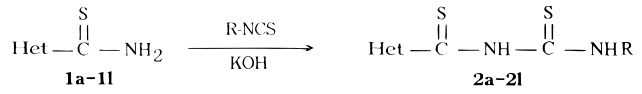


Figure 1. Structures of heterocyclic carbothioamides.

Scheme 1. Synthesis of *N*-(Alkylamino)thioxomethyl Heterocyclic Carbothioamides



	Het	R
1a, 2a	3-pyridinyl	methyl
1b, 2b	3-pyridinyl	ethyl
1c, 2c	3-pyridinyl	isopropyl
1d, 2d	pyrazinyl	methyl
1e, 2e	pyrazinyl	ethyl
1f, 2f	pyrazinyl	isopropyl
1g, 2g	2-furanyl	methyl
1h, 2h	2-furanyl	ethyl
1i, 2i	2-furanyl	isopropyl
1j, 2j	2-thienyl	methyl
1k, 2k	2-thienyl	ethyl
1l, 2l	2-thienyl	isopropyl

Biology. Data on the insecticidal activity of compounds **2a**−**l** are presented in Table 3. The activity of heterocyclic carbothioamides against rice delphacids was determined by spraying a pot containing about 20

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Table 1. Physical Properties of Heterocyclic Carbothioamides 2

compd	R	R′	mp (°C)	yield (%)
2a	3-pyridinyl	methyl	187−190	75
2b	3-pyridinyl	ethyl	155−157	81
2c	3-pyridinyl	isopropyl	148−151	72
2d	pyrazinyl	methyl	124−126	64
2e	pyrazinyl	ethyl	112−115	61
2f	pyrazinyl	isopropyl	65−67	65
2g	2-furanyl	methyl	83−86	70
2h	2-furanyl	ethyl	75−77	62
2i	2-furanyl	isopropyl	66−69	59
2j	2-thienyl	methyl	150−153	54
2k	2-thienyl	ethyl	86−89	53
2l	2-thienyl	isopropyl	117−120	54

Table 2. Spectral Data of Heterocyclic Carbothioamides 2

compd	R	R′	^{1}H NMR ($CDCl_3$) (ppm)
2a	3-pyridinyl	methyl	7.3−9.0 (m, 4H), 3.3 (d, 3H)
2b	3-pyridinyl	ethyl	7.3−9.0 (m, 4H), 3.9 (q, 2H), 1.5 (t, 3H)
2c	3-pyridinyl	isopropyl	7.3−9.0 (m, 4H), 4.4 (m, 1H), 1.2 (d, 6H)
2d	pyrazinyl	methyl	8.6−9.8 (m, 3H), 3.3 (d, 3H)
2e	pyrazinyl	ethyl	8.6−9.8 (m, 3H), 3.8 (q, 2H), 1.4 (t, 3H)
2f	pyrazinyl	isopropyl	8.6−9.8 (m, 3H), 4.5 (m, 1H), 1.4 (d, 6H)
2g	2-furanyl	methyl	6.6−7.6 (m, 3H), 3.3 (d, 3H)
2h	2-furanyl	ethyl	6.5−7.5 (m, 3H), 3.6 (q, 2H), 1.3 (t, 3H)
2i	2-furanyl	isopropyl	6.6−7.6 (m, 3H), 4.3 (m, 1H), 1.2 (d, 6H)
2j	2-thienyl	methyl	7.0−7.7 (m, 3H), 3.3 (d, 3H)
2k	2-thienyl	ethyl	7.0−7.7 (m, 3H), 3.7 (q, 2H), 1.3 (t, 3H)
2l	2-thienyl	isopropyl	7.0−7.8 (m, 3H), 4.3 (m, 1H), 1.2 (d, 6H)

Table 3. Insecticidal Screening Results of Heterocyclic Carbothioamides 2

	% mortality *in vivo* at 5 days against *S. orizicola*			
compd	1000 ppm	500 ppm	100 ppm	25 ppm
2a	100	100 (±0)[a]	49 (±5)	33 (±2)
2b	100	100 (±0)	84 (±5)	51 (±0)
2c	100	100 (±0)	95 (±1)	21 (±0)
2d	95	94 (±1)	29 (±4)	16 (±4)
2e	100	61 (±3)	42 (±0)	10 (±2)
2f	15	nd[b]	nd	nd
2g	90	44 (±3)	0 (±0)	0 (±0)
2h	100	83 (±5)	9 (±1)	9 (±1)
2i	50	nd	nd	nd
2j	100	100 (±0)	11 (±4)	0 (±0)
2k	100	94 (±1)	20 (±0)	0 (±0)
2l	99	90 (±2)	32 (±2)	21 (±1)
carbofuran	100	100 (±0)	100 (±0)	53 (±3)

[a] Mean and standard error of two experiments. [b] nd, not determined.

rice seedlings at the two-leaf stage to runoff with a solution of each compound dissolved in a minimum volume of acetone and diluted with water containing a wetting agent. One day after treatment, each pot was covered with a tubular cage and about 20 rice delphacids were transferred into each cage. Five days later, counts of the surviving delphacids in each cage were made, and percentage mortality was estimated with Abbott's formula (Abbott, 1925). One replicate of each compound was tested at a concentration of 1000 ppm. Compounds yielding at least 90% mortality were tested further at 500, 100, and 25 ppm. In these studies, 10 delphacids were transferred into each cage and two replicates were used at each concentration. A commercial insecticide, carbofuran, was tested for comparative purposes under the same conditions as the heterocyclic carbothioamides.

EXPERIMENTAL PROCEDURES

Melting points were determined in open glass capillaries and are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-360L (60 MHz) NMR spectrometer in $CDCl_3$ using TMS as internal reference; chemical shifts are expressed in parts per million. 3-Pyridinecarbothioamide, 2-furancarbothioamide, pyrazinecarbothioamide, and 2-thiophenecarbothioamide were all commercially available.

Heterocyclic Carbothioamides 2a−l. A solution of appropriate heterocyclic carbothioamide **1a−l** (0.1 mol) in actronitrile (50 mL) was treated with powdered potassium hydroxide (0.1 mol) at room temperature and stirred for 20 min. Next, a solution of appropriate isothiocyanate (0.1 mol) in acetonitrile (10 mL) was added dropwise. The mixture was stirred for 30 min at room temperature, diluted with water (100 mL), and neutralized with concentrated hydrochloric acid. The precipitated solid was filtered off and washed with water, leaving the desired product.

RESULTS AND DISCUSSION

Melting points and yields of heterocyclic carbothioamide derivatives **2a−l**, obtained from the reaction of heterocyclic carbothioamides **1a−l** with various isothiocyanates, are shown in Table 1. Twelve compounds, consisting of two types of five-membered and two types of six-membered heterocyclic moieties, were prepared in which the alkyl group varied from one to three carbon atoms. Nuclear magnetic resonance spectra of the title compounds showed the protons of the alkyl carbon atom attached to nitrogen (N*H*−C*H*) at increasing chemical shifts as the group varies from a methyl to an ethyl then to an isopropyl group.

The mortality data in Table 3 indicate that 10 heterocyclic carbothioamides showed excellent activity at 1000 ppm against rice delphacids, but the furan **2i** was marginally active and the pyrazine **2f** was almost devoid of insecticidal activity. In both of these cases, the alkyl group was isopropyl. The pyridines **2b** and **2c** were the only two compounds that maintained high insecticidal activity at levels down to 100 ppm. The most active compound (**2b**) possessed an ethyl group in the alkyl portion of the molecule as well as a 3-pyridinyl group in the heterocyclic portion, showing the highest level of activity at 25 ppm, the lowest concentration tested. This compound attained approximately the same level of insecticidal activity as the commercial insecticide carbofuran.

Results presented in this paper revealed high insecticidal activity of heterocyclic carbothioamides against *S. orizicola*. Carbothioamides in which the heterocyclic portion is a pyridine ring possess higher insecticidal activities than those that contain pyrazine, furan, or thiophene rings. High insecticidal activity was generally associated with a two-carbon chain in the alkyl portion of the molecule. Attempts to prepare the *N-tert*-butyl derivative were unsuccessful. The best compounds from this study showed greater insecticidal activity than those reported by Farooq (1989), which possess an aromatic carbocyclic ring in place of the heterocyclic ring of the present compounds.

The results of our study indicate that heterocyclic carbothioamides are an attractive new area of insecticide chemistry and warrant further synthesis.

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