

New Fungicidally Active Pyrazolyl-Substituted 1,3,4-Thiadiazole Compounds and Their Preparation

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Abstract: The potassium dithiocarbazate **2** was obtained through condensation of 5-pyrazole hydrazide **1** with carbon disulfide in ethanolic potassium hydroxide, and its cyclization gave 5-pyrazolyl-1,3,4-thiadiazole-2-thione **3** in concentrated sulfuric acid. Alkylation of **3** yielded 2-alkylthio-5-pyrazolyl-1,3,4-thiadiazole **4**. The preliminary bioassay tests indicated that compounds **3** and **4** have fungicidal activity.

Keywords: Pyrazole, 1,3,4-thiadiazole, biheterocyclic compound, fungicide.

It is well known that the study of heterocycles containing nitrogen atom is one of the highlights of pesticide chemistry at present. Among them some biheterocyclic compounds have excellent biological activities. For example, imazethapyr ((RS)-5-ethyl-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl) nicotinic acid) is effective in controlling a wide variety of broadleaf and grass weed species¹. Thiabendazole (2-(thiazol-4-yl)benzimidazole) is a broad spectrum systemic fungicide². Busoxinone

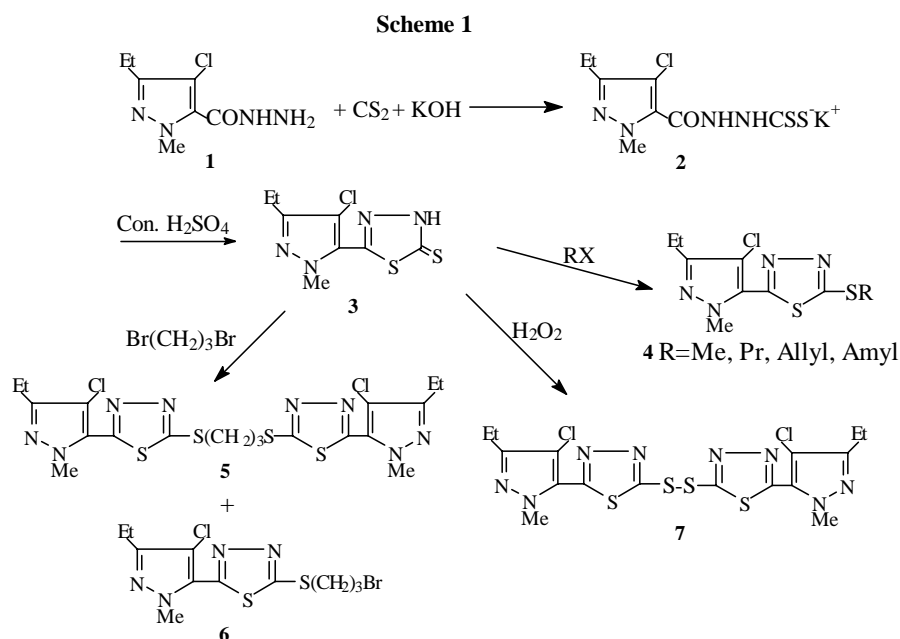
(3-(5-(1,1-dimethylethyl)-3-isoxazoly)-4-hydroxy-1-methyl-2-imidazolylidone) is a selective herbicide which is used in weed control in drilled vegetable crops³.

Pyrazole and 1,3,4-thiadiazole derivatives were both reported to have a variety of biological activities, such as fungicidal^{4,5}, insecticidal^{6,7}, herbicidal^{8,9}. However, pyrazolyl-substituted 1,3,4-thiadiazole compounds have up to now not been reported, let alone their bioactivity. As part of our research program aimed at developing a new class of agrochemicals, we synthesized the title compounds.

In our previous paper, we reported the synthesis of 5-pyrazole hydrazide **1**¹⁰, and the synthesis of 2-alkylthio-5-(4'-chloro-3'-ethyl-1'-methyl-1H-pyrazole-5'-yl)-1,3,4-thiadiazole **4** was outlined in **Scheme 1**. 5-Pyrazole hydrazide **1** reacted with carbon disulfide in ethanolic potassium hydroxide at room temperature to yield the potassium 3-(4'-chloro-3'-ethyl-1'-methyl-1H-pyrazole-5'-carbonyl)dithiocarbazate **2** which was cyclized in concentrated sulfuric acid to afford 5-(4'-chloro-3'-ethyl-1'-methyl-1H-pyrazole-5'-yl)-1,3,4-thiadiazole-2-thione **3**, followed

by alkylation with alkyl halides to give compounds **4**.

In our experiments, when **3** reacted with 1,3-dibromopropane using the phase transfer catalyst tetrabutylammonium bromide, the mixture of bis(5-pyrazolyl-1,3,4-thiadiazole-2-thio)propane **5** and 2-bromopropylthio-5-pyrazolyl-1,3,4-thiadiazole **6** were obtained. When **3** was oxidized by hydrogen peroxide in ethanol, the corresponding disulfide **7** was produced quantitatively.



The structures of all new compounds were characterized by ^1H NMR spectra and elemental analysis.

Biological activities of all new compounds are being investigated. The preliminary test showed that compounds **3** and **4** possess fungicidal activity against *Rhizoctonia solani* (Sheath blight on rice).

References

- 1 M. R. Van Ellis and D.L. Shaner, *Pestic. Sci.*, **1988**, 23(1), 25.
- 2 V.J. Grenda, R. E. Jones, G. Gal *et al.*, *J. Org. Chem.*, **1965**, 30, 259.
- 3 W. Bond, *Tests Agrochem. Cultiv.*, **1987**, 8, 106.
- 4 K. S. Norman, US 2,510,724, **1950**.
- 5 G. Funatsukuri and M. Ueda, JP 20944, **1966**.
- 6 F. Colliot, K. A. Kukorowski, D.W. Hawkins *et al.*, *Brighton Crop Prot. Conf.-Pest Dis*, **1992**, 1, 29.
- 7 J. Granett, B. Bisabri Ershadi and M.J. Hejazi, *J. Econ. Entomol.*, **1983**, 76(3), 399.
- 8 Y. Miura, M. Ohnishi, T. Mabuchi *et al.*, *Brighton Crop Prot. Conf.-Weeds*, **1993**, 1, 35.
- 9 R. Deege, H. Foester, R.R. Schmidt *et al.*, *Brighton Crop Prot. Conf.-Weeds*, **1995**, 1, 43.
- 10 Z.M. LI, H.S. CHEN, W.G. ZHAO *et al.*, *Chem. J. Chin. Universities*, **1997**, 18(11), 1794.

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