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Synthesis of Pyridazinonethiadiazoles as Possible Antifungal Agents

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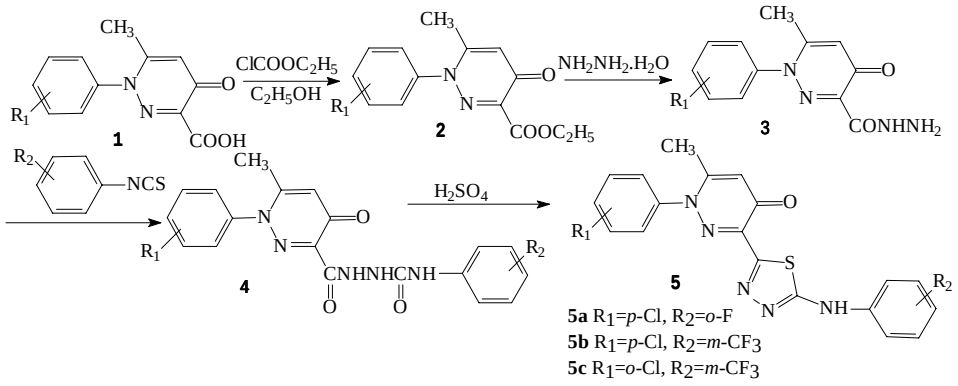
Abstract: Several 5-[1-aryl-1,4-dihydro-6-methylpyridazin-4-one-3-yl]-2-arylamino-1,3,4-thia diazoles were synthesized. The preliminary bio-active test shows that these compounds exhibit high antifungal activity.

Keywords: Pyridazinonethiadiazole, antifungal agent.

Pyridazine derivatives represent one of the most active classes of compounds possessing a wide spectrum of biological activity. They are widely used in pharmaceuticals and agrochemicals[1]. On the other hands, 1,3,4-thiadiazole derivatives exhibit a broad spectrum of biological activity[2-5]. In view of these facts and in continuation of our interest in the chemistry of pyridazines, it was attempted to synthesize novel tri-heterocyclic compounds containing both pyridazinone and 1,3,4-thiadiazole moieties in order to obtain compounds possessing better biological activity.

1-Aryl-1,4-dihydro-6-methylpyridazin-3-carboxy-4-one **1** was esterificated into ester **2**, which in turn was hydrazinolysised by hydrazine hydrate to give hydrazide **3**. Compound **3** reacted with various arylisothiocyanates resulting in the information of acylthiosemicarbazides **4**. Treatment of **4** with concentrated sulfuric acid yielded the corresponding 1,3,4-thiadiazoles **5**[6].



The preliminary biological tests showed that new compounds **5a~c** gave mortality levels of 100% against *Puccinia recondita* at 500 ppm. The further study of their bio-logical activity is underway.

Acknowledgment

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References and Notes

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6. Compound **5a** (yield 95%): mp>240°C, Anal. Calcd. For $C_{19}H_{13}ClFN_5OS$: C 55.10, H 3.16, N 16.98, Found: C 55.37, H 3.11, N 16.98; IR (KBr, cm^{-1}): 1619.1 (C=O), 3235.5 (N-H); ^{1}HNMR ($DMSOd_6$ δ ppm) 2.20 (s, 3H, CH_3), 6.64 (s, 1H, pyridazinone-H), 7.15~8.44(m, 8H, Ar-H).
   Compound **5b** (yield 95%): mp>240°C, Anal. Calcd. For $C_{20}H_{13}ClF_3N_5OS$: C 51.77, H 2.80, N 15.16; Found: C 51.55, H 2.81, N 15.25; IR(KBr, cm^{-1}): 1605.1(C=O), 3255.0(N-H); ^{1}HNMR($DMSOd_6$ δ ppm) 2.20(s, 3H, CH_3), 6.80(s, 1H, pyridazinone-H), 7.36~8.32(m, 8H, Ar-H), 10.96(bs).
   Compound **5c** (yield 90%): m. p>240°C, Anal. Calcd. For $C_{20}H_{13}ClF_3N_5OS$: C 51.77, H 2.80, N 15.16; Found: C 51.60, H 2.84, N 15.15; IR(KBr, cm^{-1}): 1604.7(C=O), 3261.0(N-H); ^{1}HNMR($DMSOd_6$ δ ppm) 2.20(s, 3H, CH_3), 6.80(s, 1H, pyridazinone-H), 7.36~8.40(m, 8H, Ar-H), 11.04(bs).

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