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***NOTE***

# Synthesis of Some New 2-Aryloxymethyl-1,3,4-thiadiazolo[2,3-b]quinazol-4-ones as Antifungal Agents

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Some quinazolones derivatives of 2-aryloxymethyl-1,3,4-thiadiazolo-[3,2-b]quinazol-4-one have been synthesized and assayed for their possible antifungal activity against *Alternaria porri* and *Helminthosporium oryzae* and were compared with standard drug carbendazim. Some of the compounds show notable activity. The structures of these compounds have been elucidated by IR, NMR and elemental analysis.

**Key Words: Quinazolones and Antifungal activity.**

Quinazolines[1] are nitrogen containing compounds having broad spectrum of agricultural and medicinal value such as antifungal[2] antiviral[3,4], antibacterial[5,6], antitubercular[7] and antiinflammatory[8] *etc*. Thiadiazoles have been reported to possess pesticidal[9,10], hypoglycemic[11] and antitubercular[12] activity. Thus combining these two versatile rings *i.e*., 1,3,4- thiadiazole and quinazol-4-one would enhanced the fungicidal activity. Thus increasing its usefulness as agricultural fungicides.

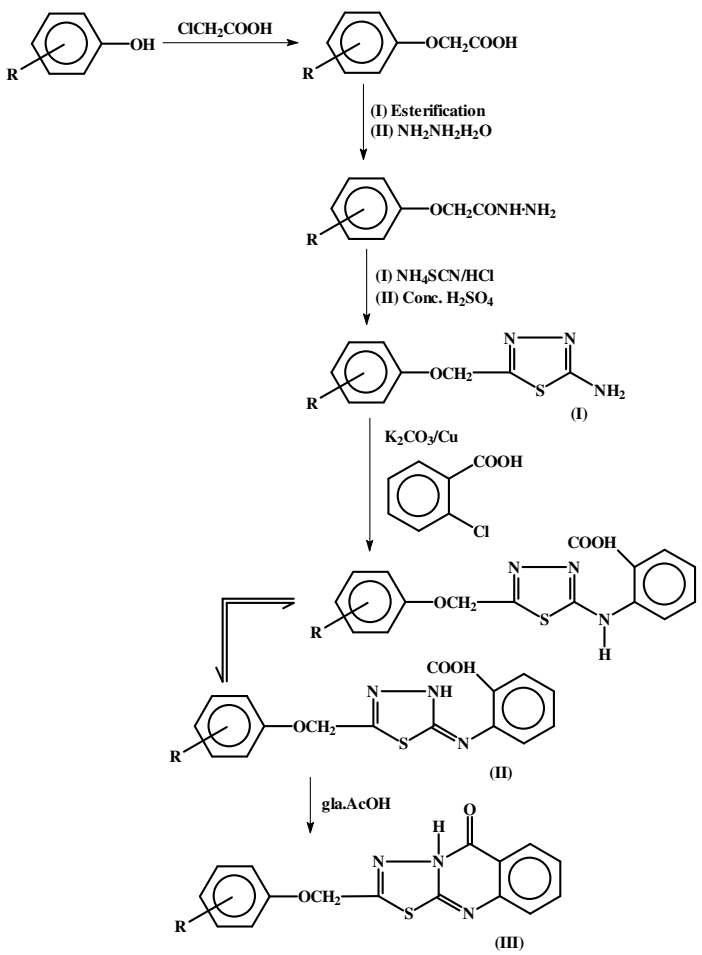
2-Amino-5-aryloxymethyl-1,3,4-thiadiazole (**I**) was synthesized by the method of Maffii *et al*.[13]. The reaction of 2-amino-5-aryloxymethyl-1,3,4-thiadiazole (**I**) with chloro/benzoic acid in the presence of potassium carbonate and copper powder in methanol gave the compound (**II**), which on heating with glacial acetic acid gives the final compound (**III**).

All melting points were uncorrected. IR-spectra were recorded on Perkin-Elmer spectrophotometer in KBr and PMR-spectra in $CDCl_3$ on Brucker 300-FT instrument.

**2-(2-Carboxyphenyl amino)-5-(2-chlorophenoxymethyl)-1,3,4-thiadiazole (II):** A mixture of 2-amino-5-(2-chlorophenoxy methyl)-1,3,4-thiadiazoles (0.01 M), 2-chloro benzoic acid (0.01), potassium carbonate (0.021) and copper powder (0.5) was refluxed in methanol. Excess of solvent was removed. On acidification white precipitate was obtained. m.p. 111 °C, m.f. $C_{16}H_{12}N_3O_3SCl$, IR (KBr, $\nu_{max}$, $cm^{-1}$): 3400 (-OH), 3290 (-NH), 1665 (C=N), 2905 ($-OCH_2$), PMR 6.9-7.9 (m, 8H, aromatic protons), 4.5 (s, 2H, $-OCH_2$).

**2-(2-Chlorophenoxymethyl)-1,3,4-thiadiazolo[2,3-b]quinazol-4-one (III):** Cyclodehydration of above compound (**II**) (0.01) was carried out by refluxing in glacial acetic acid (25 mL). The reaction mixture was poured in water. Fine crystals

of desired compound (**III**) were obtained on recrystallization with methanol. m.p. 157 °C, $C_{16}H_{10}N_3O_2SCl$, IR (KBr, $\nu_{max}$, $cm^{-1}$): 1710 (>C=O), 1670 (C=N), 1030, 1230 (C-O-C), 2905 (-$OCH_2$), PMR 6.9-7.9 (m, 8H, aromatic protons), 4.5 (s, 2H, -$OCH_2$).




**Scheme-I**

**Antifungal activity:** All the compounds were screened for their antifungal activity against two fungi *A. porri* and *H. oryzae* at different concentration of 10, 100 and 1000 ppm. Concentrations by Horsfall and Rich procedure[14,15] with some modification. The compounds were dissolved in acetone and diluted further. Potato dextrose agar medium was allowed to set and fungi were inoculated on to this medium containing the chemical compound. The plates were incubated at 28 ± 1 °C in BOD incubator for 96 h. The reading for radical growth of fungus were taken after 96 h. The result were compared with those of commercial fungicides carbendazim tested under similar condition (Table-1).

TABLE-1

| Comp. No. | R | m.p. (ºC) | m.f. | Average % inhibition after 96 h | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | *A. Porri* | | | *H. oryzae* | | |
| | | | | 1000 | 100 | 10 | 1000 | 100 | 10 |
| **IIIa** | 2-$CH_3$ | 104 | $C_{17}H_{13}N_3O_2S$ | 56 | 44 | 40 | 61 | 48 | 43 |
| **IIIb** | 4-$CH_3$ | 160 | $C_{17}H_{13}N_3O_2S$ | 59 | 45 | 42 | 64 | 50 | 44 |
| **IIIc** | 2,4-di$CH_3$ | 170 | $C_{18}H_{15}N_3O_2S$ | 42 | 37 | 33 | 48 | 41 | 36 |
| **IIId** | 2-Cl | 157 | $C_{16}H_{10}N_3O_2ClS$ | 62 | 53 | 45 | 67 | 65 | 50 |
| **IIIe** | 4-Cl | 106 | $C_{16}H_{10}N_3O_2ClS$ | 64 | 55 | 46 | 68 | 69 | 52 |
| **IIIf** | 2,4-diCl | 178 | $C_{16}H_9N_3O_2Cl_2S$ | 69 | 57 | 48 | 70 | 69 | 54 |
| Carbendazim | | | | 98 | 84 | 78 | 98 | 85 | 78 |

All the compounds showed better antifungal activity at 1000 ppm but their activity decreased considerably upon dilution. The enhancement in activity is observed by the presence of chlorine atom rather than methyl group. Presence of two chlorine atoms in the either phenyl ring impart much fungitoxicity than one chlorine atom. The thiadiazol-quinazoles are active on both species of fungi but they are slightly more active against *H. oryzae* than *A. porri*. The most active compound was (**IIIf**) that of commertial fungicides carbendazim. On wider range of fungi as well as on more dilution is desirable.

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