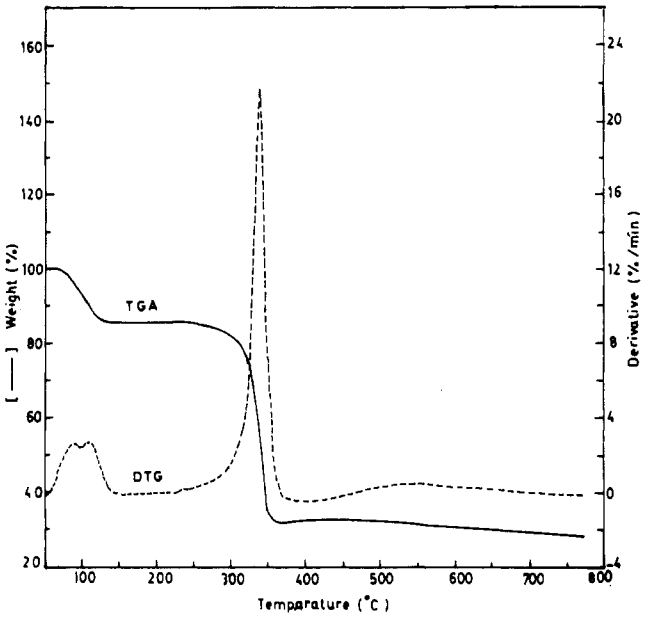


**Figure 2.** Thermogram of the ligand.

diffraction patterns were recorded by a Philips PW 1140/90 X-ray diffractometer using nickel filtered CuK$\alpha$ radiation and setting the goniometer speed at 1°/min. A Du Pont 1090 thermal analyzer having a 951 TGA module was used to study the thermal decomposition pattern of the ligand at a heating rate of 10 °C/min in the nitrogen atmosphere (Figure 2). The results are tabulated in Tables I-VI.


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**Registry No.** $VO(HMICdt)_2$, 15005-23-9; $Cr(HMICdt)_3$, 60351-87-3; $Ni(HMICdt)_2$, 14434-67-4; $Cu(HMICdt)_2$, 14353-95-8; $Zn(HMICdt)_2$, 35215-07-7; $Cd(HMICdt)_2$, 15308-66-4; $Hg(HMICdt)_2$, 94491-00-6.


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# Synthesis of Some New 3-(2′-Benzothiazolyl)-4(3*H*)-quinazolinones as Antifungal Agents


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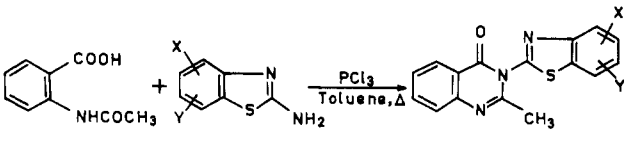
**Five new 2-methyl-3-[(substituted)benzothiazol-2′-yl]-4(3*H*)-quinazolinones have been synthesized. Three of them were tested for their antifungal activity against agricultural fungi by the food poison technique and the activity was compared with that of Dithan M-45.**


Certain remarkable pharmacological and antimicrobial activities are known to be associated with the 4(3*H*)-quinazolinone ring system. Typically, quinazolinone derivatives are potent hypertensive (*1*), amoebicidal (*2*), antifungal (*3*), herbicidal (*4*), pesticidal (*5*), and bactericidal agents (*6*).

Several 4(3*H*)-quinazolinones have also been synthesized by incorporating other heterocyclic nuclei into the ring system with encouraging results. Kumar et al. (*7*) have synthesized a number of thiadiazolylquinazolinones and correlated their structure with in vitro antitubercular activity against *Mycobacterium smegmatis* and *Mycobacterium tuberculosis* $H_{37}Rv$ strain. Furthermore, 6,8-disubstituted 2-methyl- and 2-styryl-3-[(substituted)benzothiazol-2-yl]-4(3*H*)-quinazolinones prepared by Chaurasia and co-workers (*8*) are found to exhibit both central nervous system (CNS) stimulating and depressive activities on mice.

In view of the diverse biological activities of 4(3*H*)-quinazolinones and the benzothiazole ring (*9*, *10*), it was considered worthwhile to synthesize some 4(3*H*)-quinazolinones incorporating the substituted benzothiazolyl moiety. 2-Methyl-3-[(substituted)benzothiazol-2′-yl]-4(3*H*)-quinazolinones (III)




(I) (II) (III)

were prepared by heating the corresponding 2-aminobenzo-

**Table I. 2-Methyl-3-[(mono- or disubstituted)benzothiazol-2′-yl]-4(3*H*)-quinazolinones[a] (III)**

| no. | substituents X | substituents Y | yield, % | mp, °C |
|---|---|---|---|---|
| 1 | 5-$NO_2$ | H | 70 | 185 |
| 2 | 6-$NO_2$ | H | 72 | 200 |
| 3 | 4-$CH_3O$ | 7-Cl | 65 | 195[b] |
| 4 | 4-$NO_2$ | 6-Cl | 68 | 245 |
| 5 | 4-Cl | 6-$NO_2$ | 66 | 188 |

[a] All these compounds gave elemental analyses (C, H, N, S) within ±0.4% of the theoretical values. [b] NMR ($Me_2SO$-$d_6$) $\delta$ 2.06 (s, 3 H, $CH_3$), 2.15 (s, 3 H, $OCH_3$), 7.06-8.53 (m, 6 H, Ar-*H*).

Table II. Antifungal Activity of 2-Methyl-3-[(mono- or disubstituted)benzothiazol-2′-yl]-4(3*H*)-quinazolinones (III)

| | substituents | | % inhibition of fungi at given dilutions | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *Sclerotium rolfsii* | | *Rhizoctonia solani* | | *Trichoderma harzianum* | |
| no. | X | Y | 1:500 | 1:5000 | 1:500 | 1:5000 | 1:500 | 1:5000 |
| 1 | 5-$NO_2$ | H | 62 | 54 | 43 | 15 | 78 | 0 |
| 2 | 6-$NO_2$ | H | 100 | 80 | 79 | 48 | 100 | 83 |
| 5 | 4-Cl | 6-$NO_2$ | 100 | 62 | 100 | 14 | 33 | 11 |
| | | | 66 | 52 | 57 | 36 | 60 | 39 |
| Dithan M-45[a] | | | (88) | (70) | (76) | (48) | (80) | (52) |

[a] Values in parentheses denote the extrapolated percentage inhibition of the standard fungicide for 100% active ingredient.

thiazoles (II) with *N*-acetylanthranilic acid (I) in the presence of phosphorus trichloride in toluene (*8*). The structures of the compounds were established by elemental analyses and IR and NMR spectra.

## Experimental Section

Melting points were determined in an open capillary with a Gallenkamp apparatus and are uncorrected. Elemental analyses were carried out on a Coleman analyser. The IR spectra were recorded on a Perkin-Elmer 720 grating spectrophotometer and NMR spectra on a Jeol FX90Q spectrometer at the probe temperature of 27 °C in $Me_2SO$-$d_6$ solutions with $Me_4Si$ as an internal reference.

***N*-Acetylanthranilic acid (*I*)** was obtained by a known method (*11*).

***2*-Amino-6-chloro-4-nitrobenzothiazole (*II*).** This compound was prepared by the oxidative cyclization of 1-(4-chloro-2-nitro)phenylthiourea (11.5 g) in dry chloroform (100 mL) with liquid bromine (5.5 mL) as described earlier (*12*). The product was crystallized from ethanol to form yellow needles, yield 60%, mp 262 °C. It gave satisfactory elemental analyses (C, H, N, S) and they were submitted for review. The structure of the compound was confirmed by its IR spectrum: IR(Nujol) 3400, m; 3100, m ($NH_2$ stretchings); 1650, s (C=N); 1580, m; 1540, m $cm^{-1}$.

By this procedure, the following 2-amino-(mono- or disubstituted)benzothiazoles were also prepared from the corresponding 1-aryl thioureas. Their yields and melting points are given as follows: 2-amino-5-nitrobenzothiazole, 62%, mp 308 °C (dec) [lit. (*13*) mp 308–09 °C (dec)]; 2-amino-6-nitrobenzothiazole, 60%, mp 248 °C (lit. (*14*) mp 245 °C); 2-amino-7-chloro-4-methoxybenzothiazole, 65%, mp 206 °C (lit. (*15*) mp 202–03 °C); 2-amino-4-chloro-6-nitrobenzothiazole, 55%, mp 250 °C (lit. (*16*) mp not given). It gave satisfactory microanalytical results.

The IR spectra of the 2-aminobenzothiazoles in Nujol show two variable-intensity bands in the 3480–3100-$cm^{-1}$ region ($NH_2$ stretchings), a strong absorption around 1650 $cm^{-1}$ (C=N), and 2–3 bands in the 1600–1500-$cm^{-1}$ region.

***2*-Methyl-3-(6′-nitrobenzothiazol-2′-yl)-4(3*H*)-quinazolinone (*III*).** A mixture of *N*-acetylanthranilic acid (1.2 g), 2-amino-6-nitrobenzothiazole (1.2 g), phosphorus trichloride (0.6 mL), and dry toluene (50 mL) was heated under reflux in an oil bath at 120–25 °C for 5 h. Excess toluene was removed by distillation. The residue was washed with 5% sodium hydrogen carbonate solution followed by water and dried. It was crystallized from ethanol, yield 72%, mp 200 °C. The structure of the compound was confirmed by the spectral data: IR(Nujol) 1680, s (C=O stretching); 1620, m; 1600, s; 1540, s $cm^{-1}$. NMR ($Me_2SO$-$d_6$) $\delta$ 2.06 (s, 3 H, $CH_3$), 7.00–8.50 (m, 7 H, Ar-*H*).

Similarly, four other 2-methyl-3-(substituted)benzothiazol-2′-yl-4(3*H*)-quinazolinones were prepared by reaction of different 2-amino-(substituted)benzothiazoles with *N*-acetylanthranilic acid. Their yields and melting points are reported in Table I. Their IR spectra (Nujol) exhibit strong C=O absorption bands in the 1760–1660-$cm^{-1}$ region.

***Antifungal Screening Results*.** Three synthetic compounds were tested for their antifungal activity against the agricultural fungi *Sclerotium rolfsii*, *Rhizoctonia solani*, and *Trichoderma harzianum* by the food poison technique. The activity was compared with that of a commercially used fungicide Dithan M-45. The results are recorded in Table II. From the results it is evident that the antifungal activity is considerably enhanced at low dilutions. The compound number 2 in Table II is relatively more active at the given dilutions against the fungi chosen in comparison to the commercial fungicide.

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**Registry No.** I, 89-52-1; II (X = 5-$NO_2$, y = H), 73458-39-6; II (X = 6-$NO_2$, y = H), 6285-57-0; II (X = 4-$CH_3O$, y = 7-Cl), 67618-12-6; II (X = 4-$NO_2$, y = 6-Cl), 26488-55-1; II (X = 4-Cl, y = 6-$NO_2$), 66188-30-5; III (X = 5-$NO_2$, y = H), 103852-52-4; III (X = 6-$NO_2$, y = H), 103852-53-5; III (X = 4-MeO, y = 7-Cl), 103852-54-6; III (X = 4-$NO_2$, y = 6-Cl), 103852-55-7; III (X = 4-Cl, y = 6-$NO_2$), 103852-56-8; 1-(4-chloro-2-nitro)phenyl thiourea, 39535-50-7; 1-(3-nitro)phenyl thiourea, 709-72-8; 1-(4-nitro)phenyl thiourea, 3696-22-8; 1-(2-methoxy-5-chloro)phenyl thiourea, 63980-69-8; 1-(2-chloro-4-nitro)phenyl thiourea, 103852-57-9.

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