

Figure 2. Thermogram of the ligand.

diffraction patterns were recorded by a Philips PW 1140/90 X-ray diffractometer using nickel filtered $\text{CuK}\alpha$ radiation and setting the goniometer speed at $1^\circ/\text{min}$. 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 $10^\circ\text{C}/\text{min}$ in the nitrogen atmosphere (Figure 2). The

results are tabulated in Tables I-VI.

Acknowledgment

We thank Dr. K. C. Mittal, Director, USIC, Roorkee University, for help in recording X-ray powder patterns and magnetic measurements and greatly appreciate Dr. S. Chandra, Zakir Hussain College, Delhi, for useful discussion and suggestions.

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.

Literature Cited

- (1) Eisenberg, R. *Prog. Inorg. Chem.* **1970**, *12*, 295.
- (2) Coucouvanis, D. *Prog. Inorg. Chem.* **1970**, *11*, 234.
- (3) Fabretti, A. C.; Forghieri, F.; Giusti, A.; Preti, C.; Tosi, G. *Inorg. Chim. Acta* **1984**, *86*, 127 and reference therein.
- (4) Rawley, R. K.; Singh, A. K.; Puri, B. K., Indian Institute of Technology, Delhi, unpublished results, 1984.
- (5) Bonamico, M.; Dessy, G.; Mugnoli, A.; Vaclago, A.; Zambonelli, L. *Acta Crystallogr.* **1965**, *19*, 886.
- (6) Vanquickenborne, L. G.; McGlynn, S. P. *Theor. Chim. Acta* **1968**, *9*, 390.
- (7) Lever, A. B. P. *Inorganic Electronic Spectroscopy*; Elsevier: Amsterdam; 1968; p 204.
- (8) Jorgenson, C. K. *Helv. Chim. Acta* **1967**, 131.
- (9) Figgis, B. N. *Introduction to Ligand Fields*; Interscience: New York; 1966; p 134.
- (10) Bailhausen, C. J. *Introduction to Ligand Field Theory*; McGraw-Hill: New York, 1962; p 134.
- (11) Kivelson, D.; Neiman, R. J. *Chem. Phys.* **1961**, *35*, 149.

Received for review August 1, 1985. Revised manuscript received March 28, 1986. Accepted April 28, 1986.

Synthesis of Some New 3-(2'-Benzothiazoyl)-4(3H)-quinazolinones as Antifungal Agents

Ram Lakhan* and Babban J. Rai

Department of Chemistry, Banaras Hindu University, Varanasi 221 005, India

Five new

2-methyl-3-[(substituted)benzothiazol-2'-yl]-4(3H)-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(3H)-quinazolinone ring system. Typically, quinazolinone derivatives are potent hypertensive (1), amoebicidal (2), antifungal (3), herbicidal (4), pesticidal (5), and bactericidal agents (6).

Several 4(3H)-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* H₃₇Rv strain. Furthermore, 6,8-disubstituted 2-methyl- and 2-styryl-3-[(substituted)benzothiazol-2'-yl]-4(3H)-quinazolinones prepared by Chaurasia and co-workers (8) are found to exhibit both central nervous system (CNS) stimulating and depressive activities on mice.

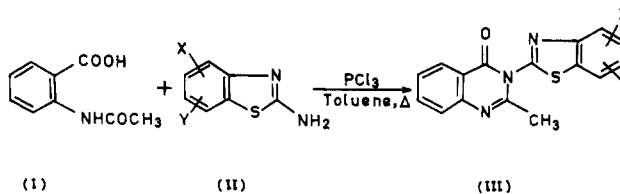
In view of the diverse biological activities of 4(3H)-quinazolinones and the benzothiazole ring (9, 10), it was con-

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

no.	substituents		yield, %	mp, °C
	X	Y		
1	5-NO ₂	H	70	185
2	6-NO ₂	H	72	200
3	4-CH ₃ O	7-Cl	65	195 ^b
4	4-NO ₂	6-Cl	68	245
5	4-Cl	6-NO ₂	66	188

^aAll these compounds gave elemental analyses (C, H, N, S) within $\pm 0.4\%$ of the theoretical values. ^bNMR ($\text{Me}_2\text{SO}-d_6$) δ 2.06 (s, 3 H, CH₃), 2.15 (s, 3 H, OCH₃), 7.06-8.53 (m, 6 H, Ar-H).

sidered worthwhile to synthesize some 4(3H)-quinazolinones incorporating the substituted benzothiazoyl moiety. 2-Methyl-3-[(substituted)benzothiazol-2'-yl]-4(3H)-quinazolinones (III)



were prepared by heating the corresponding 2-aminobenzo-

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

no.	substituents		% inhibition of fungi at given dilutions					
	X	Y	<i>Sclerotium rolfisii</i>		<i>Rhizoctonia solani</i>		<i>Trichoderma harzianum</i>	
			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 Me₂SO-*d*₆ solutions with Me₄Si 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 (NH₂ 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 (NH₂ 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(3H)-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 (Me₂SO-*d*₆) δ 2.06 (s, 3 H, CH₃), 7.00–8.50 (m, 7 H, Ar-H).

Similarly, four other 2-methyl-3-(substituted)benzothiazol-2'-yl-4(3H)-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 rolfisii*, *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.

Acknowledgment

We are thankful to Professor S. M. Verma, Head of the Department of Chemistry, for providing the necessary facilities.

Registry No. I, 89-52-1; II (X = 5-NO₂, y = H), 73458-39-6; II (X = 6-NO₂, y = H), 6285-57-0; II (X = 4-CH₃O, y = 7-Cl), 67618-12-6; II (X = 4-NO₂, y = 6-Cl), 26488-55-1; II (X = 4-Cl, y = 6-NO₂), 66188-30-5; III (X = 5-NO₂, y = H), 103852-52-4; III (X = 6-NO₂, y = H), 103852-53-5; III (X = 4-MeO, y = 7-Cl), 103852-54-6; III (X = 4-NO₂, y = 6-Cl), 103852-55-7; III (X = 4-Cl, y = 6-NO₂), 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.

Literature Cited

- Hess, H. J.; Cronin, T. H.; Scriabine, A. *J. Med. Chem.* **1968**, *11*, 130.
- Sharma, M.; Shanker, K.; Bhargava, K. P.; Kishore, K. *Indian J. Pharm. Sci.* **1979**, *41*, 44.
- Das, N. B.; Mittra, A. S. *J. Indian Chem. Soc.* **1979**, *56*, 398.
- Chupp, J. P. U.S. Patent 3912492, 1975; *Chem. Abstr.* **1976**, *84*, 121883h.
- Bowie, R.; Cox, J. M.; Farrell, C. M.; Shepherd, M. C. *Ger. Offen.* 2539396, 1976; *Chem. Abstr.* **1976**, *85*, 5681n.
- Varma, R. S. *J. Indian Chem. Soc.* **1975**, *52*, 344.
- Kumar, P.; Dhawan, N. K.; Vrat, S.; Bhargava, K. P.; Kishore, K. *Arch. Pharm. (Weinheim, Ger.)* **1983**, *316*, 759.
- Chaurasia, M. R.; Sharma, S. K. *Arch. Pharm. (Weinheim, Ger.)* **1982**, *315*, 377.
- Edelson, E.; Haskin, A. H. *Arch. Dermatol. Syphilol.* **1952**, *66*, 244.
- Ravits, H. G. *J. Am. Med. Assoc.* **1952**, *148*, 1005.
- Erikson, J. *J. Chem. Educ.* **1972**, *49*, 688.
- Bhargava, P. N.; Baliga, B. T. *J. Indian Chem. Soc.* **1958**, *35*, 807.
- Vel'tman, R. P. *Zh. Obshch. Khim.* **1960**, *30*, 1363.
- Kaufmann, H. P.; Schulz, P. *Arch. Pharm. (Weinheim, Ger.)* **1935**, *273*, 31.
- Beckett, A. R.; Kerridge, K. A. *J. Pharm. Pharmacol.* **1956**, *8*, 661.
- Fishwick, B. R. *British Patent* 896232, 1962; *Chem. Abstr.* **1963**, *58*, 605h.

Received for review February 5, 1986. Revised manuscript received April 28, 1986. Accepted May 27, 1986. B.J.R. is thankful to the Vice-Chancellor, Banaras Hindu University, Varanasi, India, for the award of a research scholarship.