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Note

Synthesis and fungicidal activity of 3-aryl-2-(4'-aryl thiazol-2'-ylaminomethyl) quinazol-4 (3*H*)-ones

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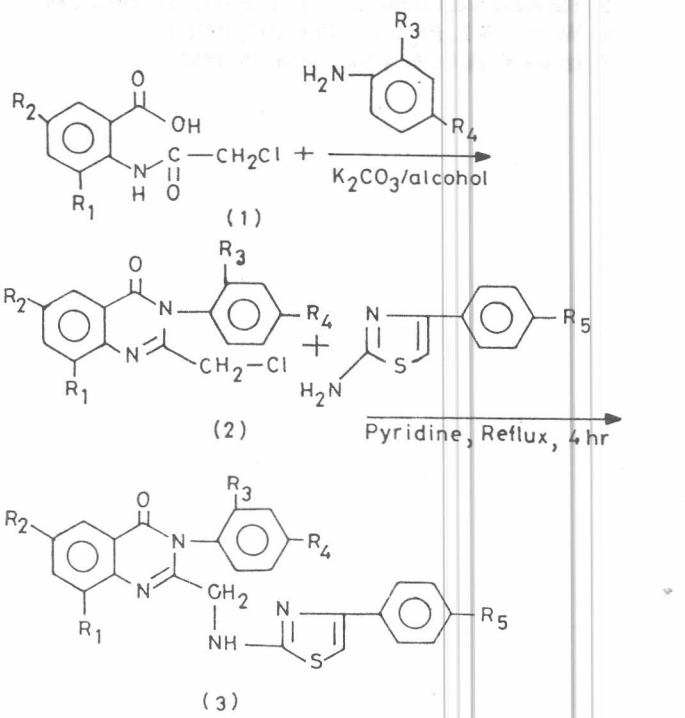
A series of 3-aryl-2-(4′-aryl thiazol-2′-ylaminomethyl) quinazol-4(3*H*)-ones **3a-p** have been prepared by condensing 3-aryl-2-chloromethylquinazol-4(3*H*)-ones with 2-amino-4-substituted phenylthiazoles. Another group of 3-aryl-6, 8-dibromo-2-(4′-arylthiazol-2′-ylaminomethyl) quinazol-4 (3*H*)-ones **3q-gg** have also been synthesized from 3-aryl-6, 8-dibromo-2-chloromethylquinazol-4(3*H*)-ones and 2-amino-4-substituted phenylthiazoles in the same manner. The prepared compounds have been characterised by spectral data. Their antifungal activity has also been determined.

Quinazolones possess antiinflammatory, analgesic and antitumor activities[1,2]. Some 2-alkyl- and 3-aryl quinazol-4(3*H*)-ones also show antibacterial as well as tuberculostatic activities [3-5]. Inspired by these observations some new quinazolone derivatives having halogen in the quinazolone moiety were prepared with a view to study their fungicidal activities.

Quinazolone derivatives **3** showed a strong band at ≈1668 cm^{-1} indicating the presence of an –N–C=O group. Bands at around 1532, 1488, 435 cm^{-1} were observed which were attributed to thiazole and phenyl ring vibration[6]. ^1H NMR spectra of compounds **3** in DMSO-d_6 exhibited a singlet at δ 2.5 integrating for 2 protons and was assigned to a methylene substituted in position-2 of the quinazolone nucleus. Other signals appeared in the aromatic region at δ 6.5-8.2 integrating for 10 to 14 protons depending on the substitution[7]. The reaction path is shown in **Scheme I**. Analytical data of quinazolones are given in **Table I**.



Scheme I

Experimental Section

General. The purity of the compounds was checked by TLC. Melting points were determined using a Melting Point apparatus and are uncorrected. IR spectra of the compounds were recorded on a Perkin-Elmer infrared-283 spectrophotometer in KBr discs.

Preparation of *N*-chloroacetyl-3, 5-dibromoanthranilic acid 1[8, 9]. 3,5-Dibromoanthranilic acid (0.01 mole) was treated with chloroacetyl chloride (0.015 mole) in benzene with 4 to 5 drops of pyridine. The mixture was refluxed for 6 hr and the solid thus obtained was recrystallised from acetone-ethyl alcohol mixture (1:1) and to give **1** which was used in subsequent steps, yield 59%, mp 198°C.

Following the same procedure N-chloroacetylanthranilic acid (**1**; R_1=R_2=H) as prepared, yield 72%, mp 169°C.

Preparation of 2-chloromethyl-3-substituted-phenylquinazol-4 (3*H*) ones[10, 11] **2**. N-Chloroacetyl-3, 5-dibromoanthranilic acid **1** was refluxed for 6 hr with equimolecular amount of an aromatic amine in the presence of anhydrous K_2CO_3 and ethanol (20 mL). The reaction mixture

Table 1—Analytical and fungicidal data of 3-aryl-2-(4′-aryl thiazol-2′-ylamino methyl) quinazol-4 (3*H*) ones **3**

Compd	R_3	R_4	R_5	Mol. formula	mp* (°C)	N (%) Found	N (%) Calcd	S (%) Found	S (%) Calcd	% of fungal inhibition	Yield (%)
3a	H	H	CH_3	$C_{25}H_{20}ON_4S$	193	12.87	13.25	7.88	7.56	65.3	52.00
3b	H	H	Cl	$C_{24}H_{17}ON_4SCl$	172	12.99	12.67	6.98	7.21	68.8	55.00
3c	CH_3	H	CH_3	$C_{26}H_{22}ON_4S$	189	12.83	12.81	7.01	7.32	64.9	56.20
3d	CH_3	H	Cl	$C_{25}H_{19}ON_4SCl$	153	12.15	12.24	6.81	6.99	66.5	49.10
3e	OCH_3	H	OCH_3	$C_{26}H_{22}O_3N_4S$	208	11.52	11.94	6.52	6.82	71.2	51.70
3f	OCH3	H	Cl	$C_{25}H_{19}ON_4SCl$	154	11.32	11.82	6.48	6.75	73.6	60.00
3g	Cl	H	CH_3	$C_{25}H_{19}ON_4SCl$	188	12.01	12.24	6.53	6.99	71.8	55.50
3h	Cl	H	Cl	$C_{24}H_{16}ON_4SCl_2$	138	11.63	11.71	6.48	6.69	76.5	57.10
3I	H	CH_3	CH_3	$C_{26}H_{22}ON_4S$	158	12.65	12.81	7.06	7.32	65.5	58.00
3j	H	CH_3	OCH_3	$C_{26}H_{22}O_2N_4S$	152	12.29	12.36	6.90	7.06	66.9	52.00
3k	H	CH_3	Cl	$C_{25}H_{19}ON_4SCl$	137	12.05	12.24	6.80	6.99	67.2	48.00
3l	H	Cl	CH_3	$C_{25}H_{19}ON_4SCl$	163	11.97	12.24	6.72	6.99	66.2	53.00
3m	H	Cl	OCH_3	$C_{25}H_{19}O_2N_4SCl$	135	11.53	11.82	6.57	6.75	72.9	54.00
3n	H	Cl	Cl	$C_{24}H_{16}ON_4SCl_2$	142	11.29	11.71	6.32	6.69	76.4	52.00
3o	H	OCH_3	CH_3	$C_{26}H_{22}O_2N_4S$	181	12.12	12.36	6.81	7.06	67.1	51.00
3p	H	OCH_3	Cl	$C_{25}H_{19}O_2N_4SCl$	167	11.21	11.82	6.52	6.75	73.8	61.50
3q	H	H	CH_3	$C_{25}H_{18}N_4OSBr_2$	151	9.45	9.98	5.43	5.70	71.5	52.5
3r	H	H	Cl	$C_{24}H_{15}ON_4SBr_2Cl$	154	9.07	9.31	5.02	5.32	73.5	53.5
3s	CH_3	H	CH_3	$C_{26}H_{20}ON_4SBr_2$	178	9.20	9.41	5.08	5.37	75.9	54.5
3t	CH_3	H	OCH_3	$C_{26}H_{20}O_2N_4SBr_2$	172	8.88	9.09	4.95	5.19	75.8	53.9
3u	OCH_3	H	OCH_3	$C_{26}H_{20}O_3N_4SBr_2$	191	8.36	8.96	4.78	5.12	81.4	55.6
3v	OCH_3	H	Cl	$C_{25}H_{17}O_2N_4SBr_2Cl$	207	8.58	8.86	4.81	5.06	82.5	57.2
3x	Cl	H	OCH_3	$C_{25}H_{17}O_2N_4SBr_2Cl$	166	8.83	9.09	4.93	5.19	76.2	49.0
3y	Cl	H	Cl	$C_{24}H_{14}ON_4SBr_2Cl_2$	152	8.63	8.80	4.13	5.06	79.9	51.10
3z	H	CH_3	CH_3	$C_{26}H_{20}ON_4SBr_2$	151	9.26	9.41	5.02	5.37	72.9	59.0
3aa	H	CH_3	OCH_3	$C_{26}H_{20}O_2N_4SBr_2$	149	8.57	8.73	4.73	4.99	74.5	50.5
3bb	H	CH_3	Cl	$C_{25}H_{17}ON_4SBr_2Cl$	127	8.87	9.10	4.94	5.19	76.5	60.5
3cc	H	Cl	CH_3	$C_{25}H_{17}ON_4SBr_2Cl$	173	8.92	9.10	4.88	5.19	73.8	48.5
3dd	H	Cl	OCH_3	$C_{25}H_{17}O_2N_4SBr_2Cl$	148	8.32	8.87	4.78	5.66	82.3	56.5
3ee	H	Cl	Cl	$C_{24}H_{14}ON_4SBr_2Cl_2$	136	8.39	8.80	4.77	5.03	85.9	59.2
3ff	H	OCH_3	OCH_3	$C_{25}H_{20}O_3N_4SBr_2$	206	8.71	9.13	5.02	5.22	83.4	54.5
3gg	H	OCH_3	Cl	$C_{25}H_{17}O_2N_4SBr_2Cl$	162	8.68	8.86	4.85	5.06	82.4	52.5

*All the compounds were recrystallised from ethanol.
3a-p: R_1=R_2=H
3q-3gg: R_1=R_2=Br

was filtered and ethanol evaporated. The residue was washed thoroughly with boiling water and recrystallised from acetone-ethanol mixture (1:1). Melting point of the synthesized compound was comparable with that reported[11] for **2,** yield 57.5%, mp 177°C.

In a similar manner other members of the series **2** were prepared. The yield varied from 53. 5 to 61.5%.

Preparation of 3-aryl-2-(4′-arylthiazol-2′-ylaminomethyl)quinazol-4(3*H*)-one-3. Compound **2** (0.01 mole) and 2-amino-4-substituted-phenylthiazole (0.01 mole) in pyridine were refluxed for 4 hr, and thereafter excess of pyridine was evaporated. The residue was mixed with crushed ice, filtered, washed and recrystallised from ethanol. Analytical and fungicidal activity data of the synthesized compounds are given in **Table I**.

Antifungal activity. For evaluating the antifungal activities of the synthesized compounds, poisoned food technique was adopted[12]. The quinazolone derivatives were tested for their toxicity towards *Helmonthsporium sativum* and the % of inhibition was calculated from the expression given below and the data are recorded in **Table I**.

% of inhibition = $(1-X/Y) \times 100$

where X = growth with drug, and

Y = growth in control.

The data indicate that quinazolones with bromo- and methoxy-substituents are more active than the corresponding unsubstituted ones.

References

1 Mikhalev A I, Konshin M E, Ovodunka L A & Zakas A S, *Khimfarm-zh,* 29, **1995,** 40.

2 Marhosym A I, Dilanyan S V, Kuroyan R A & Chachayan A A, *Khimfarm-zh,* 29, **1995,** 32.

3 Sabr S M, Sadeum E L & Alashmawim I, *J Pharmsic,* 29, **1988,** 243.

4 Hussain M I & Sukla S, *Indian J Chem,* 25, **1986**, 552.

5 Joshi V & Choudhuri R P, *Indian J Chem,* 26, **1987,** 602.

6 Dash B, Patra M & Prahraj S, *Indian J Chem,* 19, **1980,** 894.

7 Silverstein R M, Bassler C G & Morrill T C, in: *Spectroscopic identification of organic compounds*,. 5th Edn (John Wiley & Sons, Inc. New York), **1991,** p. 165.

8 Panda D, Ph.D Thesis, Utkal University, **1989,** p. 96.

9 Dash B, Mahapatra P K, Panda D & Pattanaik J M, *J Indian Chem Soc,* 61, **1994,** 1062.

10 Michiro I, Mosayukil, Takashi T & Shimamoto T, *Japan Kokai*, 7529, 575 C1 (CO7D) (March 1975), *Appl* 7378,906; (14 Jul 1973), *Chem Abstr*, 83, **1975,** 114464y.

11 Pentunin P A & Kozhrnikov Yu V, *Khim Geterotikl Soedin*, **1967**, Sb-1-415; *Chem Abstr*, , 70, **1969**, 87739q.

12 Nene Y L, in: *Fungicides in plant disease control* (Oxford and IBH Publishing Company, New Delhi) **1971.**