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NOTE

Quinoline and Quinazoline Compounds as Antitubercular Agents

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Dimethyl quinolinyl and styryl-1,4-quinazolines as well as substitued such hydrazines have been prepared and tested for antitubercular activity.

2-methyl-4-(3H)-quinazolinone is prepared by the known method and possesses antibacterial activity.[1] It has been now observed to show antitubercular activity at 5 μg/mL against *Mycobacterium tuberculosis* $H_{37}Rv$.

In the present work 4,5-dimethyl-2-(1H)-quinazolinone and its chloro derivatives have been synthesized for the first time. It is tautomeric. 2,5-Dimethyl-2-(1H)-quinazolinone, 2,5-dimethyl-2-hydroxy quinazoline, 2,8-, 2,5-and 2,6-dimethyl-quinolinyl-4-quinazolinones and 2-styryl-, 2-chloro- and 4-methoxy-styryl-4-quinazolinones have been prepared. 2-Methyl-4-chloroquinoline was prepared by the known method.[3] Styryl-4-hydroxy quinazolines were prepared by refluxing the parent compound with respective aldehyde with acetic anhydride and quinolinyl, quinazolines or arylamine were obtained by refluxing 4-chloroquinolines with the parent compounds in acetic acid or butanol.

4,5-Dimethyl-2(1H) of 3-methyl phenyl urea (15 gm, 0.01 M) and acetic anhydride (30 mL) were heated in the presence of potassium iodide (1.0 g) till the solution was clear. Then sulphuric acid (15 mL) was added carefully to the hot solution. The reaction mixture was poured on ice and neutralised with ammonia. The product (8–9 g, yield 55%) was crystallised from ethanol, m.p. (dec) 243°C; m.w. = 176; N (calcd.) = 16.0%, (found) 15.9%. IR: CH—CH_3 stretching 3045 cm^{-1}; C=O stretching 1640 cm^{-1}; C—N stretching 1360 cm^{-1}.

^1H NMR: (δ)2.52 (—CH_3 group) 5.75 (proton (OH)); 6.65 (proton (—NH)); ketone 7.6–8.1 (Ar—H).

Similarly other dimethyl-quinazolinones were prepared from corresponding acetyl aryl ureas.

4,5-Dimetyl-2-chloroquinazoline

The mixture of 4,5-dimethyl-2-hydroxy quinazoline (1.74 g, 0.01 M) and phosphorus oxy-chloride (10 mL) was refluxed for 45 min. Solution was treated with ice and neutralised with sodium hydroxide; the precipitate (1.32 g, yield

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68%) was crystallized from chloroform, m.p. (dec) 197–200°C; m.w. 191.5; N = 14.62% (calcd), 14.35% (found); Cl = 18.53% (calcd), 18.40% (found). IR: CH—CH_3 stretching 3060 cm^{-1}, C—N stretching 1350 cm^{-1}, ring structure 1580 cm^{-1}.

^1H NMR: (δ)2.449 (—CH_3 group at 5 position); 4.2 (—CH_3 at 4 position); 7.1–8.2 (Ar—H).

The authenticity and purity of compounds were confirmed by elemental analysis, IR and NMR spectra, TLC and molecular weight determination by non-aqueous titration method.[4]

Products have been tested (*in vitro*) against $H_{37}Rv$ strain using Middlebrook 7H10 agar medium.

TABLE-1
ANTITUBERCULAR ACTIVITY OF THE COMPOUNDS

Sr. No.	Name of the compound	m.p. (°C)	Yield (%)	*M. tuberculosis* $H_{37}Rv$	
				5 μg/mL	10 μg/mL
1.	2,8-Dimethyl-quinolinyl-4-hydrazine	198	62	++	+
2.	2,5-Dimethyl-quinolinyl-4-hydrazine	115	58	+	–
3.	2,6-Dimethyl-quinolinyl-4-hydrazine	224	65	++	–
4.	2-Methyl-8-methoxy-quinolinyl-4-hydrazine	184	55	+++	++
5.	2-Methyl-6-methoxy-quinolinyl-4-hydrazine	210	56	++	+
6.	2-Methyl-6-ethoxy-quinolinyl-4-hydrazine	176	58	+	+
7.	2,5,8-Trimethyl-quinolinyl-4-hydrazine	176	51	+	–
8.	2-Methyl-8-chloro-quinolinyl-4-hydrazine	307	48	–	–
9.	2-Methyl-5-chloro-quinolinyl-4-hydrazine	305	45	–	–
10.	2- Methyl-6-chloro-quinolinyl-4-hydrazine	310	59	+	–
11.	2-styryl-4(3H)-quinazolinone	249	51	++	++
12.	2-(4′-Methoxystyryl)-4-(3H)-quinazolinone	274	61	++	+
13.	2-(2′-Chlorostyryl)-4(3H)-quinazolinone	251	55	–	–
14.	4,8-Dimethyl-quinozin-2-yl-iminobenzene	234	73	+	–
15.	4,8-Dimethyl-quinozin-2-yl-(2′-methyl-imino benzene)	226	79	–	–
16.	2-Methyl -4(3H)-quinazolinone	239	90	–	–
17.	(2′,8′-Dimethyl-quinolinyl-4′)-2-methyl-4-quinazolinone	206	77	–	–
18.	(2′,5′-Dimethyl-quinolinyl-4′)-2-methyl-4-quinazolinone	212	79	+	–
19.	(2′,6′-Dimethyl-quinolinyl-4′)-2-methyl-4-quinazolinone	216	44	+	–

Symbols "+" = Growth; "–" = No growth

Out of nine substituted hydrazines, chloro substitution indicates efficiency at 5 μg/mL, while others are active at 10 μg/mL against $H_{37}Rv$, Among styryl

derivatives one chlorosubstitution product is effective at 5 μg/mL. Among nineteen products six inhibited $H_{37}Rv$ growth at 5 μg/mL, while others at 10 μg/mL. When old anti-TB drugs are losing efficiency against resistant TB strains, such products should be tested clinically.

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