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NOTE

Quinoline-4-yl-Hydrozino-Quinazolines as Antitubercular/ Antibacterial Agents. Part-II

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In the present note, the synthesis and antibacterial activity of quinazoline-4-yl-hydrozinoquinazolines are reported.

In continuation of our work on hydrazino-quinolines,[1] we communicate quinoline-4-yl-hydrazino-quinazolines as antitubercular/antibacterial agents in this paper.

Dimethyl-2-chloro-quinazolines have been condensed with dimethyl quinolinyl hydrazines in prsence of glacial acetic acid as solvent giving dimethyl-quinoline-4-yl hydrazino-dimethyl-quinazolines. Dimethyl-2-chloroquinazolines have been prepared from dimethyl-2-hydroxy-quinazolines by using phosphorus oxychloride by the known method, while 2-hydroxy-quinazolines $\rightleftharpoons$ 2(1H)-quinazolinones were prepared by cyclisation of acetyl-aryl ureas in presence of acetic anhydride and sulphuric acid with potassium iodide for the first time.[2]

These products were tested against *Mycobacterium tuberculosis* $H_{37}Rv$ using Middlebrook agar medium[3] and against *Staphylococcus aureus*, *Escherichia coli* and *Salmonella paratyphi-B* using Bryant's method.[4]

Synthesis of 4-8 dimethyl-2-(1H) quinazolinone: The mixture of 2-methyl phenyl urea (15 g, 0.1 M) and acetic anhydride (25 mL) was heated in presence of potassium iodide (1.0 g) till the solution was made clear. Then H_2SO_4 (15 mL) was carefully added to the hot solution; the heat of reaction was sufficient for cyclisation. The mixture was poured on ice and neutralized with ammonium hydroxide; the product obtained was crystallised from ethanol. mol. wt. 174, yield 62% and m.p. 254°C (dec).

Dimethyl-quinolin-4-yl hydrazines were prepared by refluxing hydrazines with 4-chlororoquinolines in butanol by the known method.

Synthesis of 2-(2',8'-dimethyl-quinoline-4'-yl-hydrazino)-4,8-dimethyl-quinazoline: The mixture of 4,8-dimethyl-2-chloro-quinazoline (0.01 M) and 2,8-dimethyl- quinolinyl hydrazine (0.01 M) was refluxed for 6 h using glacial acetic acid (20 mL). After treating the mixed solution with ice, it was neutralised and

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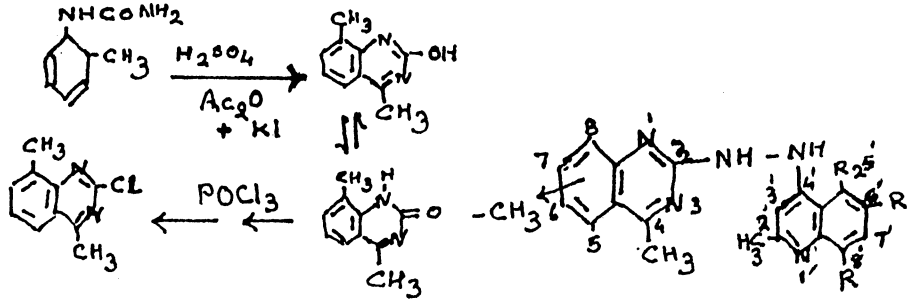

Structure I*

the product separated was crystallised from ethanol. Yield 48%, m.p. (dec) 257°C, m.w. 343, N% = (calcd) 20.39: (found) 20.36.

Similarly other quinolinyl hydrazino quinazolines were prepared (for details vide Table-1 and Structure II).

TABLE-1
ANTITUBERCULAR/ANTIBACTERIAL ACTIVITY OF THE COMPOUNDS

Sr. No.	Compound				Yield (%)	m.p. (°C) (dec)	Activity against (μg/mL)				
							$H_{37}Rv$		*S. aureus*	*E. coli*	*Sal. paratyphi*-B
	R	R_1	R_2	$-CH_3$			5	10	5	5	5
							(Zone size in mm)				
1.	CH_3	H	H	8	48	257	+	–	18	9.5	16
2.	H	H	CH_3	8	50	262	++	+	11	8	18
3.	H	CH_3	H	8	52	267	++	++	10.5	8	6
4.	OCH_3	H	H	8	50	246	+	+	10.5	8.5	6
5.	H	OCH_3	H	8	53	250	–	–	10.5	8	6
6.	CH_3	H	H	5	43	260	+	+	—	—	—
7.	H	H	CH_3	5	48	259	+++	+++	—	—	—
8.	H	CH_3	H	5	50	268	+++	++	—	—	—
9.	OCH_3	H	H	5	44	243	++	++	12	6	6
10.	H	OCH_3	H	5	48	248	++	–	11	10	9.5
11.	CH_3	H	H	6	54	259	+	–	—	—	—
12.	H	H	CH_3	6	58	270	++	–	—	—	—
13	H	CH_3	H	6	55	264	–	–	—	—	—
14.	OCH_3	H	H	6	54	248	–	–	20	10	12
15.	H	OCH_3	H	6	52	235	+	–	22	6	6

Symbols: " – " = No growth; " + " = Scanty growth; " ++ " = Moderate growth
" +++ " = Profuse growth

In the earlier work it was observed that substituents 6- or 8-methoxy and 6-ethoxy or 6-chloro in quinoline nucleus enhance the antibacterial activity in agreement with 6-methoxy substitution in quinoline antimalarial such as quinine, primaquine and pentaquinine imparting increased activity; however it was not possible to establish a correlation between antibacterial and antitubercular activity.

In quinolinyl-imino sulfa drugs also, 6- or 8-methoxy substitution enhances antibacterial activity.[5] In the present work also it is observed that —OCH_3 substitution in quinoline ring enhances increased antibacterial activity against *Staphylococcus aureus* and *Salmonella paratyphi*-B. Regarding antitubercular activity, three products inhibit growth of $H_{37}Rv$ at 5 μg/mL and five at 10 μg/mL, —OCH_3 substitution increasing the activity.

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