SEARCH FOR PHYSIOLOGICALLY ACTIVE COMPOUNDS

Part III. Synthesis of 7-nitro-2-methyl-3-aryl Quinazolones

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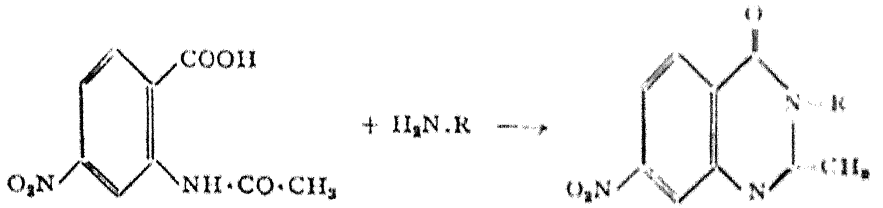
SEVERAL plant materials reported to have pharmacological action contain active principles possessing quinazolone structure.[1] The mature leaves of *Glycosmis arborea* Corr., which are extensively used in Ayurvedic medicine as febrifuge and anthelminitic, were found to contain the active principle 'arborin', which is a quinazolone derivative.[2] Further, one of the three alkaloids isolated from *Glycosmis pentaphylla* (Retz) DC. was proved to have a quinazolone skeleton.[3] Since a nitro group is known to enhance the physiological properties of compounds, attempts have been made to prepare 2:3-disubstituted quinazolones containing a nitro group para to the carbonyl in position 7.

For the synthesis of these substances, condensation of 4-nitro-N-acetyl anthranilic acid with a primary aryl amine was found to be the best method.[4]



The anthranilic acid required was prepared from *o*-toluidine by nitration followed by acetylation and oxidation with neutral potassium permanganate. By varying the aryl amine components, eight new 7-nitro-2-methyl-3-aryl quinazolones have been prepared.

The physiological activity of these compounds has been tested against two common types of bacteria, *B. coli* and *Staphylococcus aureus*. The quinazolone obtained by the condensation with *p*-bromo aniline possessed activity against *B. coli* at a concentration of one part per million, whereas most other compounds showed activity against both types of bacteria at a concentration of one part per ten thousand.

EXPERIMENTAL

4-Nitro-N-acetyl anthranilic acid was condensed with eight aromatic amines in toluene medium using phosphorous trichloride as the condensing agent following the procedure of Grimmel, Guenther and Morgan,[4] when

7-nitro-2-methyl-3-aryl quinazolones were obtained in good yields (above 80%). The analytical data and properties of the compounds so far not reported in literature are recorded in Table I.

TABLE I

*7-Nitro-2-methyl-3-aryl quinazolones**

No.	Amine condensed	Quinazolone obtained R	m.p. (in °C.)	Found %			Required %		
				C	H	N	C	H	N
1.	*o*-Anisidine	*o*-Anisyl	152	61·5	4·4	13·2	61·7	4·2	13·5
2.	*o*-Toluidine	*o*-Tolyl	184	64·8	4·9	14·0	65·1	4·4	14·2
3.	*p*-Toluidine	*p*-Tolyl	223	64·8	4·7	14·0	65·1	4·4	14·2
4.	*m*-Chloro aniline	*m*-Chloro phenyl	192	57·2	3·3	13·4	57·0	3·2	13·0
5.	*p*-Bromo aniline	*p*-Bromo phenyl	>300	49·7	3·2	11·7	50·0	2·8	11·7
6.	*o*-Nitro aniline	*o*-Nitro phenyl	170	55·0	2·9	17·0	55·2	3·1	17·1
7.	*m*-Nitro aniline	*m*-Nitro phenyl	192	55·2	3·4	17·2	55·2	3·1	17·1
8.	*p*-Nitro aniline	*p*-Nitro phenyl	298	54·8	3·1	16·9	55·2	3·1	17·1

* Thanks are due to Sri. C. V. Ratnam for the analysis of the compounds.

SUMMARY

7-Nitro-2-methyl-3-aryl quinazolones have been prepared by condensation of 4-nitro-N-acetyl anthranilic acid with aryl amines. These nitro quinazolones have been tested against bacteria. The 3-(*p*-bromo phenyl) derivative is found to have the maximum activity.

REFERENCES

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