SYNTHESIS OF SOME CHROMONO (7, 8) OXAZOLES AND THEIR ANTIBACTERIAL ACTIVITY

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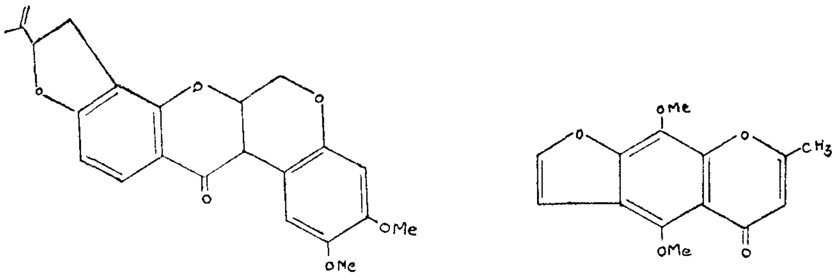
ABSTRACT

The synthesis of a few 2-substituted aryl-8-methyl-chromono (7, 8) oxazoles is described. A study of the antibacterial activities of these compounds has revealed that 2-(*p*-nitrophenyl) 8-methyl-chromono (7, 8) oxazole is active in 1 in 10,000 parts concentration.

INTRODUCTION

CHROMONES and a number of their heterocyclic condensed ring systems have been reported to exhibit a wide variety of physiological activity. The best known example is the well-known fish poison and insecticide Rotenone (I), which possesses a furano-chromano-chromone skeleton.[1,2] The furano-chromone-khellin (II) has been found to be a coronary vaso-dilator[3] and is extensively used for the treatment of bronchial asthma.[4]



I

II

FIG, 1

Schönberg and Co-workers[5] postulated that the presence of a furan ring on chromone ring system enhanced the activity of the parent chromone. A number of Coumarino (6, 7), (7, 8,)[6] and (3, 4)[7] oxazoles as well as a few flavono (7, 8)[8] oxazoles have earlier been prepared for the purpose of evaluating their antibacterial and antifungal activity. In analogy with the furanochromones, it has been considered worthwhile to synthesise a few chromono (7, 8) oxazoles, with a view to elucidating their antibacterial properties.

The starting material for the synthesis of these chromono oxazoles is 7-hydroxy-2-methyl chromone, which is obtained from resacetophenone by refluxing with acetic anhydride and fused sodium acetate under the Kostanecki and Robinson[9] reaction conditions. Nitration[10] afforded the 8-nitro derivative, which is reduced to the corresponding 8-amino compound by treatment with sodium dithionite. This reduction of the nitro derivative to the amino compound was reported[11] earlier with iron and ferrous sulphate in neutral medium, but in relatively low yields. In the present work, the reduction with dithionite has been found to proceed very smoothly with good yields and the experimental conditions are much simpler.

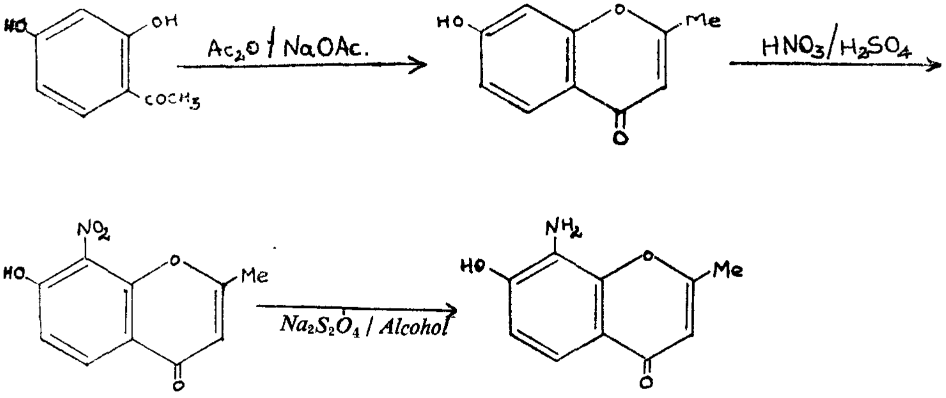


FIG. 2

These amino hydroxy chromones are cyclised to the corresponding chromono oxazoles by reflexing them with various aromatic aldehydes in nitrobenzene medium. The chromono oxazoles prepared are included in Table I.

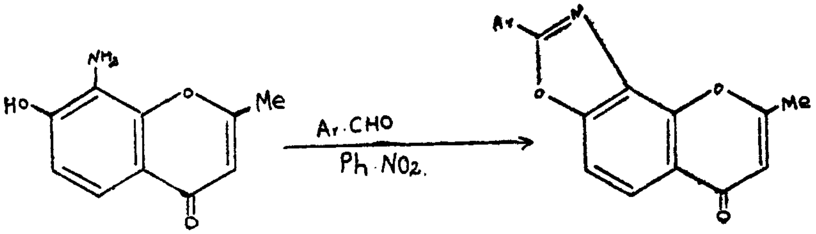


FIG. 3

TABLE I

Sl. No.	Chromone (7, 8) oxazole	M.P. (°C)	Yield %	Calculated			Found		
				C	H	N	C	H	N
1	2-Phenyl-8-methyl ..	220–21	61	73·6	4·0	5·1	73·9	4·0	5·2
2	2-*m*-Hydroxyphenyl-8-methyl	284-85	75	70·0	3·8	4·8	70·3	3·9	4·9
3	2-*p*-Anisyl-8-methyl ..	219–20	81	70·4	4·3	4·6	70·2	4·4	4·4
4	2-Vanillyl-8-methyl ..	327–28	86	66·9	4·0	4·3	67·0	4·1	4·1
5	2-Piperonyl-8-methyl ..	230–31	66	67·3	3·4	4·4	67·6	3·5	4·3
6	2-*p*-Chlorophenyl-8-methyl	222–23	91	65·6	3·2	4·5	65·8	3·4	4·4
7	2-2′-4′-Dichloro phenyl 8-methyl	245–46	51	58·9	2·6	4·0	59·2	2·6	4·2
8	2-*m*-Nitrophenyl-8-methyl	272–73	71	63·3	3·1	8·7	63·0	3·2	8·4
9	2-*p*-Nitrophenyl-8-methyl	236–37	55	63·3	3·1	8·7	63·1	3·2	8·4
10	2-*p*-Dimethyl amino phenyl-8-methyl	237–38	45	71·3	5·0	8·8	71·0	5·1	8·8

The yields in all these cases are fairly good.

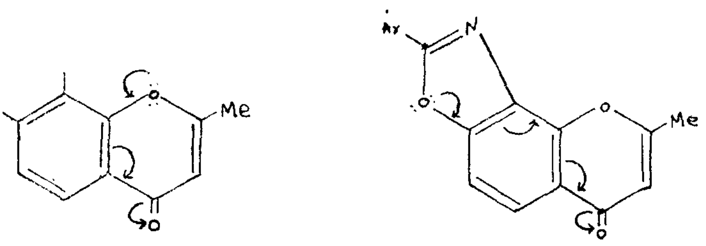
Physiological Activity

The bactereostatic acitivity of all the compounds prepared has been tested using *Staphyllococcus aureus*, *Bacillus subtilis* and *Bacillus coli* as representative species, employing the tube dilution method. Of all the compounds only 2-(*p*-nitrophenyl) 8-methyl chromono (7, 8) oxazole exhibited appreciable activity against all the three bacteria, the others being inactive. The incativity of the others may be attributed to their very poor solubility.

Spectra

All these chromono oxazoles have been found to exhibit two maxima in the ultraviolet, one around 275 ± 10 mμ and another at 310 ± 10 mμ. These values are in agreement with those reported earlier for oxazolo (7, 8) flavones.[8] The former may be due to the γ-pyrone transition (*a*) and the latter may be attributed to transition (*b*).

In the infrared, all these compounds exhibit a band around 1660–1620 cm^{-1}, characteristic of the chromone carbonyl group. In addition, peaks at 1560–1570 cm^{-1}, 1070 cm^{-1}, 1360 ± 10 cm^{-1} have also been found to be common, attributable to $>C=N$, $-C-O-C-$ and $\geqslant C-N=$ of the oxazole system. Absence of any bond in the hydroxyl region points to the fact, that these are not uncyclised Schiff's bases.



[a]

[b]

FIG. 4

EXPERIMENTAL

8-*Amino-7-hydroxy-2-methyl chromone*.—7-Hydroxy-8-nitro-2-methyl chromone (2·05),[10] sodium dithionite (8 g), alcohol (15 ml), water (30 ml), and liquor ammonia (30 ml) were refluxed for about half an hour or until a clear solution was obtained. Then it was neutralised with dilute hydrochloric acid until the neutralisation point was reached. The product was filtered and recrystallised from ethanol, m.p 253° C, yield 1·1 g (52%).

General Procedure

7-Hydroxy-8-amino-2-methyl chromone (2 g) an aromatic aldehyde (2·5 g) and nitrobenzene (30 ml) were refluxed for 4 to 5 hours. Nitrobenzene was removed by steam distillation. The residue that was left in the flask was filtered, washed with petroleum ether to remove traces of nitrobenzene. Recrystallisation was effected from benzene-petroleum ether mixture to yield yellow to orange crystals.

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