SYNTHESIS OF SOME CHROMONO (6, 7) OXAZOLES AND THEIR PHYSIOLOGICAL ACTIVITY

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Abstract

The synthesis of a few chromono (6, 7) oxazoles has been carried out by condensing 6-amino-8-bromo-7-hydroxy-2-methyl chromone with various aromatic aldehydes in nitrobenzene medium. The ultraviolet and infrared spectral characteristics of these compounds have been described. A study of antibacterial and antifungal activities of these compounds has revealed that 2-*m*-hydroxyphenyl-7-methyl-9-bromo-chromono (6, 7) oxazole and 2-p-Anisyl-7-methyl-9-bromo-chromono (6, 7) oxazole possess antifungal activity.

Introduction

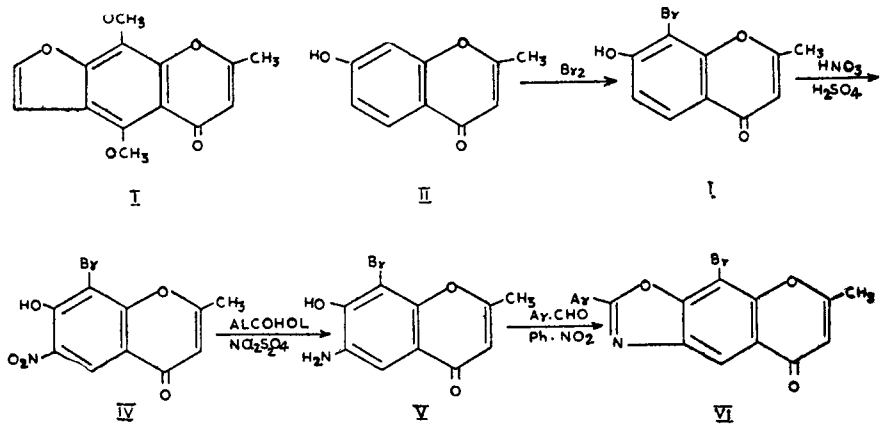
Chromone derivatives containing a furan or a pyran system fused to the benzene ring have been reported to possess pharmacological properties.[1] In a previous communication from these laboratories,[2] the synthesis of a few chromono (7, 8) oxazoles has been carried out with the purpose of elucidating their antibacterial activity. As an extension of this work, the preparation of a few chromono (6, 7) oxazoles has been undertaken in the current investigation with the hope that these may possess physiological activity. These compounds possess linear heterocyclic ring as in the case of furano (6, 7) chromones like Khellin (I). Moreover a bromine atom has been introduced in these compounds as the presence of halogen has been found to enhance the activity of the parent nucleus.[3]

For the purpose of synthesising the title compounds, 7-hydroxy-2-methyl chromone[4] (II) has been subjected to bromination under conditions reported earlier[5] to yield the corresponding 8-bromo-derivative (III). Nitration of the bromo compound with nitric acid (1·42) in concentrated sulphuric acid[5] afforded 7-hydroxy-8-bromo-2-methyl-6-nitro-chromone (IV). Reduction of 6-nitro-2-alkyl chromone was earlier carried out with iron in the

presence of sodium bicarbonate, but the yields reported were very low.[6] The use of dithionite was found by us earlier[2] to give good yields of the amino compound and therefore has been used in this reaction to convert (IV) to the corresponding compound (V).

The amino hydroxy chromone (V) is converted to the desired oxazoles (VI) by refluxing with various aromatic aldehydes in the presence of nitrobenzene. Recently, the synthesis of 2-carboethoxy-2-aryl oxazolo (6, 7) chromones was reported[7] by the cyclisation of the Schiff's bases, obtained by treating 2-carboethoxy-7-hydroxy-6-amino chromone with aromatic aldehydes, using lead tetra acetate.

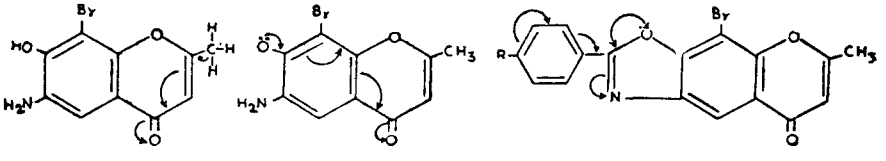
The chromono (6, 7) oxazoles synthesised have been included in Table I, along with their physical and analytical data.



I II I

IV V VI

Spectral characteristics.—The parent amino hydroxy chromone (V) exhibited two maxima in the ultraviolet absorption around 231 nm. and 264 nm. The former may be attributed to the chromophore (*a*) and the latter to (*b*). In the case of chromono (6, 7) oxazoles, three maxima have been observed at 243 ± 2 nm., 275 ± 5 nm. and 315 ± 10 nm. The former two again are attributed to chromophores (*a*) and (*b*) respectively. The third is assignable to the 2-aryl chromono oxazole (*c*).



[a] [b] [c]

In the infrared, the aminohydroxy chromone exhibited peaks at 3500 $cm.^{-1}$, 3360 $cm.^{-1}$ and 1630 $cm.^{-1}$ for the hydroxyl, amino and chromone carbonyl groups respectively. The chromono (6, 7) oxazoles did not exhibit any band in the hydroxyl and amino regions, but contained bands at 1640 $\pm$ 20 $cm.^{-1}$ characteristic of the chromone carbonyl and bands around 1560 $cm.^{-1}$, 1370 $cm.^{-1}$ and 1070 $cm.^{-1}$ characteristic of oxazole ring system.

Physiological activity.—All the above compounds have been tested for antibacterial activity using *Staphyllococcus aureus* and *E. coli* and *Pseudomonas aerogenosa.* None of the compounds are found to be anti-bacterial. The same have been tested for antifungal activity using *Trichco phyton semii.* 2-*m*-hydroxyphenyl-7-methyl-9-bromo chromono (6, 7) oxazole and 2-*p*-anisyl-7-methyl-9-bromo-chromono (6, 7) oxazole exhibited potential antifungal activity in 1 in 10,000 parts concentration. 2-*m*-Nitrophenyl-

TABLE I

Sl. No.	Chromono (6, 7) Oxazole	M.P.° C.	Yield %	Calculated			Found			Solvent
				C	H	N	C	H	N	
1.	2-Phenyl-7-methyl-9-bromo	270–71	75	57·3	2·8	3·9	57·6	2·9	4·0	Benzene Petroleum Ether
2.	2-*m*-Hydroxyphenyl-7-methyl-9-bromo	307–08	82	54·8	2·7	3·8	54·9	2·8	3·9	Alcohol Petroleum Ether
3.	2-*p*-Anisyl-7-methyl-9-bromo	245–46	86	56	3·1	3·6	56·2	3·2	3·5	Benzene Petroleum Ether
4.	2-Vanillyl-7-methyl-9-bromo	322–23	90	53·7	3·0	3·5	53·7	3·2	3·6	Alcohol Petroleum Ether
5.	2-*m*-Nitrophenyl-7-methyl-9-bromo	239–40	86	50·9	2·3	7·0	50·7	2·3	6·8	Benzene Petroleum Ether
6.	2-p-Nitrophenyl-7-methyl-9-bromo	275–76	75	50·9	2·3	7·0	50·8	2·3	6·9	Xylene Petroleum Ether

7-methyl-9-bromo-chromono (6, 7) oxazole is moderately active in the same dilution, while 2-phenyl-7-methyl-9-bromo-chromono (6, 7) oxazole is slilghtly active.

EXPERIMENTAL

6-Amino-8-bromo-7-hydroxy-2-methyl chromone.—6-Nitro-8-bromo-7-hydroxy-2-methyl chromone (2·86 g.)[5], 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, decomposition 199–200° C, yield (1·4 g.).

Found: C = 44·2, H = 2·9, N = 5·1.

Calculated: C = 44·4, H = 3·0, N = 5·2.

General procedure.—6-Amino-8-bromo-7-hydroxy-2-methyl chromone (2 g.), an aromatic aldehyde (2·5 g.) and nitrobenzene (30 ml.) were refluxed for 5–6 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 using mixed solvents as shown in Table I.

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