SYNTHESIS OF PYRANOBENZOXAZINES AND 2-CHLOROMETHYLPYRANOBENZOXAZOLES

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SEVERAL derivatives of pyranobenzoxazine and pyranobenzoxazole have been reported in literature [1-4] to possess interesting pharmacological properties. It was therefore thought of interest to synthesise some new pyranobenzoxazines and pyranobenzoxazoles employing aminohydroxycoumarins and aminohydroxychromones as starting materials[5-8].

The reaction of aminohydroxycoumarins and aminohydroxychromones with chloroacetyl chloride (1:1 mole) in dry benzene at reflux temperature for 4 hr afforded the corresponding N-chloroacetyl derivatives as crystalline solids (table 1). The latter were cyclised in boiling alcohol in the presence of anhydrous potassium acetate to yield the corresponding pyranobenzoxazines as crystalline solids in about 60–70% yields (table 2).

It is interesting to note that when the cyclisation of the N-chloroacetyl derivatives was carried out by heating them in presence of PPA and phosphorus oxychloride at 120–25° for 4 hr, the corresponding 2-chloromethylpyranobenzoxazole derivatives were isolated as crystalline solids in 60–70% yields (table 3).

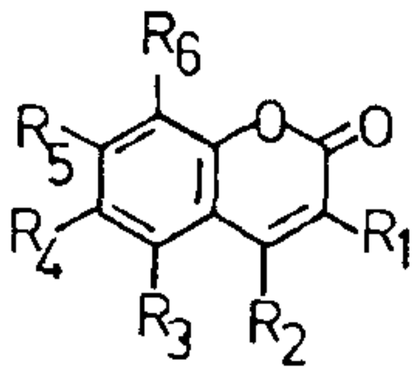
The 2-chloromethylpyranobenzoxazole derivatives were reacted with equimolar amounts of piperidine, pyrrolidine, morpholine and piperazine in absolute alcohol to afford the corresponding N-heterocycles as crystalline solids in 50–60% yields (table 4).

The IR spectra of pyranobenzoxazines in general showed bands at 3200 (-NH), 1680, 1620 (> CO of lactone, > CO of lactam), 1570, 1470, 1380 (aromatic) cm^{-1}.

The IR spectra of 2-chloromethylpyranobenzoxazoles gave bands at 1760 (> C=O), 1635, 1600, 1575 (heteroaromatic system) cm^{-1}.

All the above compounds were tested for antibacterial activity using *Staphylococcus aureus*, *E coli* and *Pseudomonas aeruginosa* as representative species employing the tube dilution method. However, none of the compounds exhibited any appreciable antibacterial activity.

Table 1 *Physical constants of N-chloroacetyl derivatives.*



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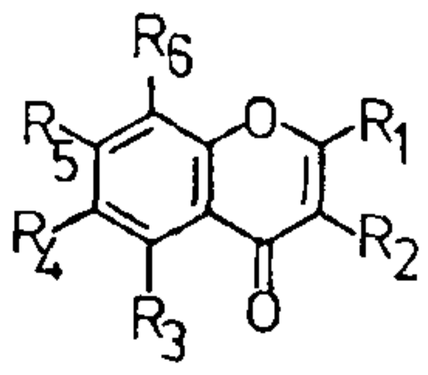
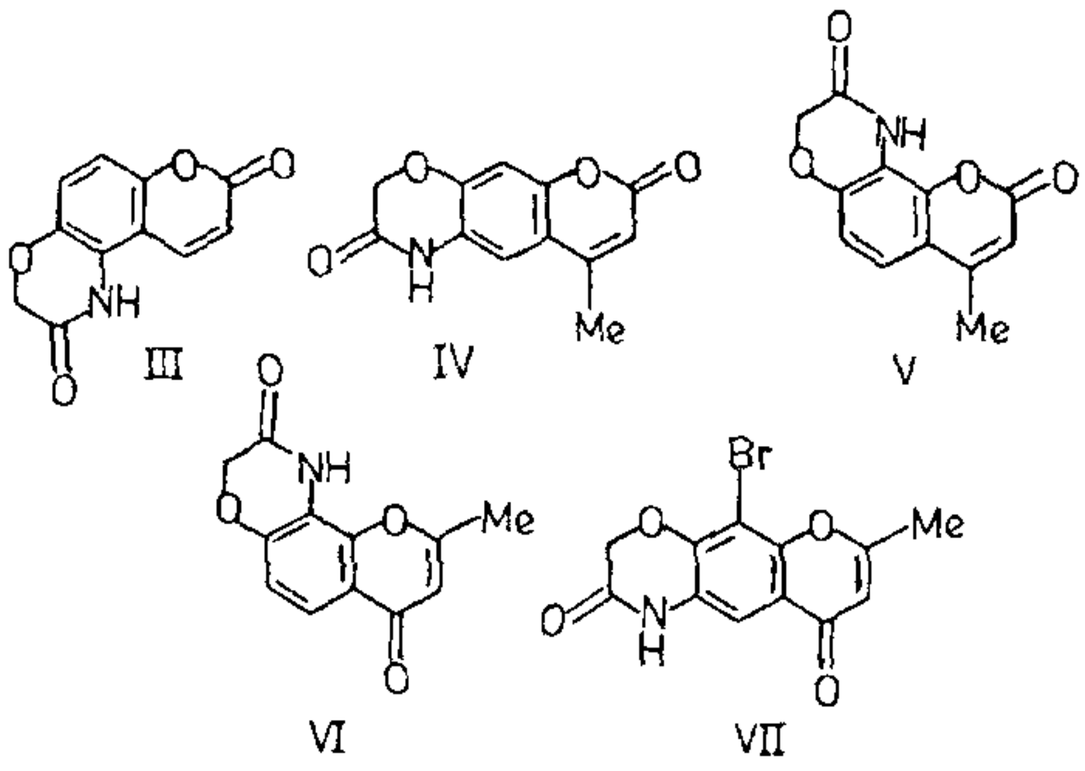


II

Compd.	R_1	R_2	R_3	R_4	R_5	R_6	Nature of Crystals	M.P.°C.
Ia	H	H	X	OH	H	H	Colourless plates (e)	258–60
Ib	H	CH_3	H	X	OH	H	Pale pink powder (d)	250–51
Ic	H	CH_3	H	H	OH	X	Brown powder (a)	265–66
IIa	CH_3	H	H	H	OH	X	Colourless powder (b)	207–09
IIb	CH_3	H	H	X	OH	Br	Brownish powder (b)	260 (decomp.)

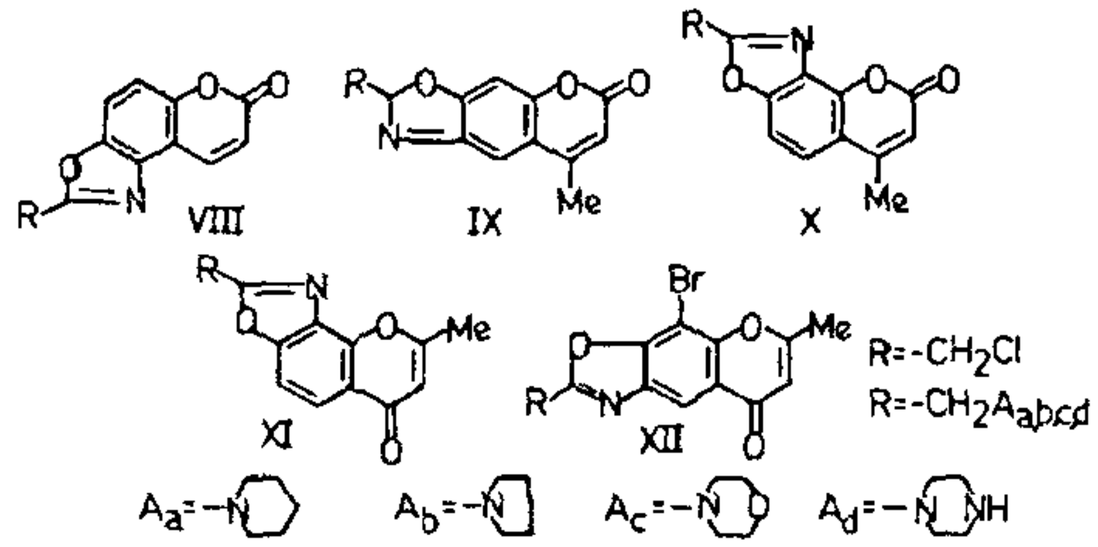
X = $NHCOCH_2Cl$

Table 2 *Physical constants of pyranobenzoxazines*



Compd.	Nature of crystals	M.P.°C
III	Pale yellow prims (c)	330
IV	Pale brown prisms (c)	325
V	Colourless needles(c)	244–45
VI	Pale brown powder (e)	335
VII	Brownish powder (e)	314

Table 3 *Physical constants of 2 chloromethyl pyranobenzoxazoles*



Compd.	Nature of Crystals	M.P.°C
VIII	Colourless prisms (a)	227–28
IX	Pale yellow prisms (a)	285–86
X	Colourless prisms (a)	215–16
XI	Colourless needles (b)	158–60
XII	Colourless needles (b)	210–12

All the melting points are uncorrected. All compounds (TLC single spot) gave satisfactory elemental analysis.

Table 4 *Physical constants of pyranopyrazoles*

Compd.	Nature of Crystals	M.P.°C
VIIIa	Pale brown plates (d)	305–07 (decomp.)
IXa	Colourless plates (e)	330
Xa	Yellow prisms (d)	252–54
XIa	Yellow powder (d)	337
VIIIb	Pale brown powder (d)	330
IXb	Colourless plates (e)	320
Xb	Yellowish powder (d)	244–45
XIb	Pale yellow plates(d)	335
XIIb	Colourless needles(d)	above 300
VIIIc	Colourless prisms (e)	320
IXc	Pale yellow plates(e)	340
Xc	Yellow needles (d)	245–46
XIc	Yellowish prisms (d)	325
XIIc	Grey cubes (d)	300
VIIId	Pale brown plates (e)	320
IXd	Pale yellow plates(e)	340
Xd	Yellow plates (d)	247–48
XId	Yellowish powder (d)	320
XIId	Colourless powder (d)	300

Solvents for crystallisation:
a: alcohol, b: ethyl acetate, c: acetic acid, d: dioxane e: DMF.

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