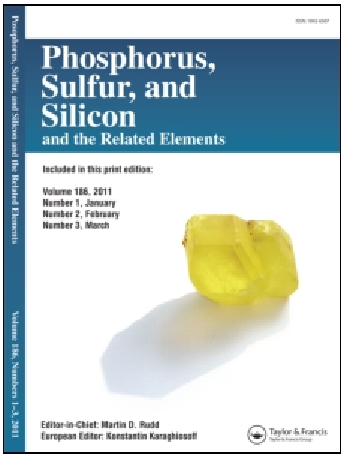

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SYNTHESIS OF NOVEL TYPES OF 2-SUBSTITUTED-MERCAPTO-7,8-DIMETHYLPYRANO[2,3-e]BENZOXAZOL-6(H)-ONES

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SYNTHESIS OF NOVEL TYPES OF 2-SUBSTITUTED-MERCAPTO-7,8-DIMETHYLPYRANO[2,3-e]BENZOXAZOL-6(H)-ONES

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7-Hydroxy-2,3-dimethylchromone (Ia) on nitration followed by reduction of the resultant 8-nitro-7-hydroxy-2,3-dimethylchromone (Ib) affords 8-amino-7-hydroxy-2,3-dimethylchromone (Ic). Reaction of (Ic) with CS_2 in alkaline medium furnishes 2-mercapto-7,8-dimethylpyrano-[2,3-e]benzoxazole-6(H)-one (IIa) which on treatment with alkylhalides and acid halides gives the corresponding thioethers II(b–f) and thioesters II(g–i), respectively, which have been confirmed on the basis of elemental analysis, IR, PMR and mass spectral data.

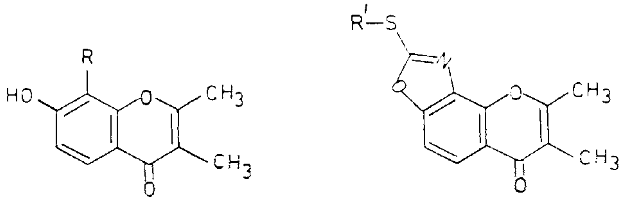
INTRODUCTION

Heterocyclic oxazoles have wide application in different industrial and biological fields.[1] Building up of an oxazoline nucleus on the antibiotic Gentamycin C_2 enhances its antibacterial properties.[2] Mercaptocoumarinoxazoles were found to exhibit appreciable antibacterial activity.[3] In an endeavour to design new compounds of therapeutic interest, another biologically important chromone has been introduced in this system and herein we report the synthesis of some thioethers (IIb–f) and thioesters (IIg–i) of 2-mercapto-7,8-dimethylpyrano[2,3-e]benzoxazol-6(H)-one to evaluate them for biological activity.

RESULTS AND DISCUSSION

7-Hydroxy-2,3-dimethylchromone (Ia) has been prepared under Kostanecki and Robinson reaction conditions.[4] Nitration of (Ia) afforded 8-nitro-7-hydroxy-2,3-dimethylchromone (Ib), which has been reduced to 8-amino-7-hydroxy-2,3-dimethylchromone (Ic) using sodium dithionite in the presence of 15% ammonia.[5] The reaction of (Ic) with carbondisulphide in the presence of ethanolic potassium hydroxide gives 2-mercapto-7,8-dimethylpyrano[2,3-e]benzoxazol-6(H)-one (IIa).

All these compounds have been confirmed by elemental and spectral analysis. IR spectrum of (IIa) is showing absorption bands at 1640 cm^{-1} ($>C{=}O$), 1610 cm^{-1} ($-N{=}C{=}S$), 1060 cm^{-1} ($>C{=}S$) and the stretching bands at 1590 cm^{-1}, 1360 cm^{-1} and 1170 cm^{-1} are assignable to the vibrations arising from the heterocyclic oxazole system.[6]



I a=R=H
b=R=NO$_2$
c=R=NH$_2$

II a=R'=H
b–f=R'=Alkyl
g–i=R'=Acyl

CHART 1

Reaction of IIa with alkylhalides and acid halides in presence of ethanolic potassium hydroxide gave the corresponding thioethers (IIb–f) and thioesters (IIg–i) respectively (Table I).

PMR spectrum of IIf in $CDCl_3$ (chemical shift values are expressed in δ-ppm down field from TMS internal reference) showed two singlets at 2.1 and 2.5 are assigned to methyl groups present at C_7 and C_8, respectively. Another singlet at 4.6 is assigned to —S—CH_2— group. Due to carbonyl cone effect, C_5 proton is deshielded to 8.1 as a doublet. The C_4 proton along with five aromatic protons appeared in complex multiplet pattern at 7.2 to 7.5.

The mass spectrum of IIf showed peaks at *m/z* 337 (M^+), 304 (M^+-SH), 247, 246, 235, 220, 219, 218, 164, 136, 128, 121, 120, 108, 92, 91, 90, 89 and 77. The ratio of intensity of the isotopic peaks $(M + 1)^{+\cdot}$ and $(M + 2)^{+\cdot}$ with the molecular ion peak indicated the presence of one sulphur atom. The base peak at *m/z* 91 is attributable to the tropylium cation.

The investigation of biological studies on these compounds is under progress. The results will be communicated in due course.

TABLE I

Physical data of 2-substituted mercapto-7,8-dimethylpyrano[2,3-e]benzoxazol-6(H)-ones (II)

Compound[a]	R	Yield %	m.p. (°C)[c]	Mol. Formula	N%[b] Found	N%[b] Calc.	S% Found	S% Calc.
IIa	—H	65	225	$C_{12}H_9NO_3S$	5.8	5.7	12.8	12.9
IIb	—CH_3	60	134	$C_{13}H_{11}NO_3S$	5.3	5.4	12.2	12.3
IIc	—CH_2—CH_3	60	160	$C_{14}H_{13}NO_3S$	5.2	5.1	11.4	11.6
IId	—CH_2—CH_2—CH_3	63	116	$C_{15}H_{15}NO_3S$	4.9	4.8	11.2	11.1
IIe	—CH_2—CH=CH_2	62	140	$C_{15}H_{13}NO_3S$	4.7	4.9	11.0	11.1
IIf	—CH_2—C_6H_5	70	120	$C_{19}H_{15}NO_3S$	4.2	4.1	9.6	9.5
IIg	—CO—CH_3	65	265	$C_{14}H_{11}NO_4S$	4.7	4.8	11.2	11.1
IIh	—CO—C_6H_5	65	270	$C_{19}H_{13}NO_4S$	3.8	3.9	8.9	9.1
IIi	—CO—CH=CH—C_6H_5	68	273	$C_{21}H_{15}NO_4S$	3.8	3.7	8.4	8.5

[a] Compounds were obtained in 60–70% yield.

[b] Satisfactory elemental analyses for C and H were also obtained.

[c] Compounds IId, f and i were recrystallised from water–dioxane; the rest were recrystallised from ethyl alcohol.

The melting points are uncorrected. IR spectra (ν_{max} in cm^{-1}) were recorded in KBr disc and nujol on a Perkin-Elmer 283 instrument. PMR spectrum on EM-360, 60 MHz spectrometer using TMS as the internal reference and mass spectrum on a Varian MAT CH-7 instrument.

EXPERIMENTAL

7-Hydroxy-8-nitro-2,3-dimenthylchromone (Ib). 7-Hydroxy-2,3-dimethylchromone (Ia, 5 gr) was added slowly at 0°C to a mixture of conc. nitric acid (25 ml) and conc. sulphuric acid (25 ml). The reaction mixture was kept at 0°C for 4 hours, and poured into the crushed ice. The separated solid was filtered and recrystallized from alcohol (80% yield), m.p. 246°C (Found: C, 55.94; H, 3.74; N, 5.82; $C_{11}H_9NO_5$ requires C, 56.16; H, 3.83; N, 5.96%). IR (KBr) 3450 (—OH), 1640 ($>$C=O), 700, 660 (aromatic) in cm^{-1}.

8-Amino-7-hydroxy-2,3-dimethylchromone (Ic). A mixture of Ib (2.05 g), sodium dithionite (8 g), ethyl alcohol (15 ml), water (30 ml) and liquor ammonia (30 ml) were refluxed for 3 hours, cooled, neutralised with dil. HCl. The separated product was filtered and recrystallised from ethanol (50–60% yield). m.p. 215°C. (Found: C, 63.85; H, 5.61; N, 6.75; $C_{11}H_{11}NO_3$ requires C, 64.39; H, 5.36; N, 6.83%). I.R. in cm^{-1}-3430 (—OH), 2950 (—NH_2), 1610 ($>$C=O), 690, 650 (aromatic).

2-Mercapto-7,8-dimethylpyrano[2,3-*e*]*benzoxazol-*6(*H*)*-one* (IIa). A mixture of Ic (0.01 mol), carbondisulphide (10 ml), KOH (0.02 mol), methyl alcohol (40 ml) and water (10 ml) was refluxed for 24 hours and cooled. The reaction mixture was acidified. The separated solid was recrystallised from ethyl alcohol, (70% yield), m.p. 225°C (Table I).

Reaction of IIa *with alkyl halides and acid halides.* Compound IIa (0.005 mol) was dissolved in ethanol (20 ml) in the presence of potassium hydroxide (0.005 mol) and the appropriate alkylhalide (0.005 mol) or acid halide (0.005 mol) was added and refluxed for 3 hours on water bath, cooled, filtered and recrystallised from suitable solvent to give corresponding thioethers (IIb–f) or thioesters (IIg–i) (Table I).

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