estimated titrimetrically using standard ferrous sulphate or iodometrically using starch as the indicator, after diluting the solution. Alternatively, the manganese(III) complex is found to obey Beer-Lambert law at 510 mμ when increased amount of nitrate is employed. It has been found that nearly two equivalents of Mn(III) are produced per mole of nitrate. This supports the fact that nitrite or nitrogen(III) oxides are the reaction product.

The role of urea is to remove the lower oxides of nitrogen as well as nitrite formed as mentioned above. When urea is replaced by sulphamic acid, NH_2SO_3H, the results are found to be the same. However, longer time of heating or bringing the solution to boiling is necessary in the latter case. For the same reason, the results are found to be not quantitative with sulphamic acid. A reverse estimation, *i.e.*, by taking excess nitrate and smaller amount of manganous compound, is found to be not quantitative. This can be expected due to the incomplete removal of nitrite.

The chemical nature of nitrate or nitric acid in strong acids is connected with the formation of nitronium ion, NO_2^+[6]. The origin of NO_2^+ is explained to be due to the ionisation of the type :

$$HNO_3 + H_2PO_4 = NO_2^+ + H_2PO_4^- + H_2O \quad (1)$$

NO_2^+ thus formed can be involved in an electron transfer reaction as :

$$Mn\ (II) + NO_2^+ = Mn\ (III) + NO_2 \quad (2)$$

or

$$2\ Mn\ (II) + NO_2^+ = 2\ Mn\ (III) + NO_2^-. \quad (3)$$

This may result in the formation of the coloured manganese(III) complex in phosphoric acid.

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SYNTHESIS AND BACTERIOSTATIC ACTIVITY OF LINEAR (7, 6) AND ANGULAR (7, 8)-α-PYRONOCHROMONES

Investigations carried out by several groups of workers in oxygen heterocycles have revealed that both benzo α-pyrone and benzo γ-pyrone moieties are inherently physiologically active, and suitable substituents enhanced their activity. It is this consideration that has prompted us to build condensed ring systems containing α-pyrone as well as γ-pyrone rings with a view to examine their physiological activity. In continuation of our earlier work on α-pyronoisoflavones[1] we now report the synthesis and bacteriostatic activity of a number of 7, 6- and 7, 8-α-pyronochromones.

In the present work linear (7, 6)-α-pyronochromones have been synthesized by building a γ-pyrone over an α-pyrone moiety whereas angular (7, 8)-α-pyronochromones have been synthesised by building either a γ-pyrone over a coumarin or by building an α-pyrone over a chromone.

4-Methyl-6-propionyl-7-hydroxy coumarin and 4-methyl-6-phenylacetyl-7-hydroxy coumarin[1] when subjected to Kostanecki reaction with sodium acetate, acetic anhydride and sodium propionate and propionic anhydride yielded the 2-methyl and 2-ethyl α-pyronochromones respectively. These 0-hydroxy acyl coumarins when condensed with various aryl chlorides like benzoyl veratroyl piperminoyl, trimethyl galloyl and *p*-nitrobenzoyl chlorides in the presence of potassium carbonate in refluxing acetone yielded the corresponding 2-aryl-α-pyronochromones, in a single step, in very good yields. The compounds prepared along with their analytical data are presented in Table I.

Similarly 5-hydroxy-6-propionyl-4-methyl coumarin and 4-methyl-6-phenylacetyl-5-hydroxy coumarin[3] when subjected to Kostanecki reaction and Baker-Venkataraman reaction with same acid chlorides yielded the corresponding 2-alkyl and 2-aryl-7, 8-α-pyronochromones in excellent yields. The compounds prepared along with their analytical data are listed in Table II.

2, 3-Dimethyl-7-hydroxy-8-formyl, 2-phenyl-3-methyl-7-hydroxy-8-formyl[5], 2(4'-nitro) phenyl-3-methyl-7-hydroxy-8-formyl and 2-methyl-3-phenyl-7-hydroxy-8-formyl chromones[6] when subjected to Perkin reaction with sodium acetate, acetic anhydride and sodium propionate, propionic anhydride yielded the corresponding α-unsubstituted and α-methyl substituted α-pyronochromones in good yields. Table III contains the M.P. and analytical data of angular (7, 8)-α-pyronochromones synthesised by this procedure.

TABLE I
7, 6 α-Pyronochromones

S. No.	α-Pyronecchromones	M.P. °C	Mol. Formula	Analysis			
				Calculated		Found	
				C%	H%	C%	H%
1	β, 2, 3 Trimethyl ..	276^{AA2}	..	..	..	..	..
2	2-Ethyl-β-3 dimethyl ..	254^{AA}	$C_{16}H_{14}O_4$	71·01	5·2	71·0	5·3
3	β, 3 Dimethyl 2 phenyl ..	230^{A}	$C_{20}H_{14}O_4$	75·5	4·4	75·6	4·4
4	2 (3′, 4′-Dimethoxy) phenyl-β, 3-dimethyl	259^{AA}	$C_{22}H_{18}O_6$	70·5	4·8	70·6	4·8
5	2 (3′, 4′-Methylenedioxy) phenyl β, 3-dimethyl	300^{AA}	$C_{21}H_{11}O_6$	69·6	3·9	69·8	3·8
6	2 (3′, 4′, 5′-Trimethoxy) phenyl β, 3-dimethyl	262^{AA}	$C_{23}H_{20}O_7$	67·6	4·9	67·7	5·0
7	2 (4′-Nitro) phenyl-β, 3-dimethyl ..	$>300^{AA}$	$C_{20}H_{13}NO_6$	6·1	63·7	66·3	3·4

AA = Acetic acid, A = Acetone.

TABLE II
7, 8 α-Pyronochromones

S. No.	α-Pyronochromones	M.P. °C	Mol. Formula	Analysis			
				Calculated		Found	
				C%	H%	C%	H%
1	β, 2, 3-Trimethyl ..	241^{E_3}	..	..	..	..	..
2	2-Ethyl-β, 3-dimethyl ..	229	$C_{16}H_{14}O_4$	71·01	5·2	71·3	5·2
3	β, 3 Dimethyl 2 phenyl ..	219^{M_4}	..	..	..	..	..
4	2 (3′, 4′-Dimethoxy) phenyl β 3-dimethyl	204^{AA}	$C_{22}H_{18}O_6$	70·5	4·8	70·4	4·7
5	3 (3′, 4′-Methylenedioxy) phenyl β, 3-dimethyl	$>300^{AA}$	$C_{21}H_{14}O_6$	69·6	3·9	69·8	3·8
6	2 (3′, 4′, 5′-Trimethoxy) phenyl β, 3-dimethyl	262^{AA}	$C_{23}H_{20}O_7$	67·6	4·9	67·4	4·9
7	2 (4′-Nitro) phenyl β, 3-dimethyl ..	295^{DMF}	$C_{20}H_{13}NO_6$	66·1	3·7	66·0	3·7
8	β-Methyl-3-phenyl ..	225^{A}	$C_{19}H_{12}O_4$	75·0	3·9	74·8	3·7
9	β, 2-Dimethyl-3 phenyl ..	235^{A_3}	..	..	..	..	..
10	β Methyl-2 ethyl-3-phenyl ..	248^{E}	$C_{21}H_{16}O_4$	75·9	4·8	75·9	4·9
11	β Methyl-2, 3-diphenyl ..	$>300^{DMF}$	$C_{25}H_{16}O_4$	78·9	4·2	79·1	4·3
12	β-Methyl-2 (3′, 4′-dimethoxy phenyl-3-phenyl	265^{AA}	$C_{27}H_{20}O_6$	73·6	4·5	73·8	4·6
13	β-Methyl-2 (3′, 4′ methylenedioxy) phenyl-3-phenyl	287^{DMF}	$C_{25}H_{16}O_4$	73·2	3·8	73·2	3·9
14	β-Methyl 2 (3′, 4′, 5′-trimethoxy) phenyl 3-phenyl	243^{AA}	$C_{28}H_{22}O_7$	71·5	4·7	71·6	4·8
15	β-Methyl-2-(4′-nitro) phenyl-3 phenyl ..	280^{AA}	$C_{25}H_{15}NO_6$	70·6	3·5	70·6	3·7

M = Methanol, AA = Acetic acid, E = Ethanol. A = Acetone DMF = Dimethyl formamide.

TABLE III
7, 8 α-pyronochromones

S. No.	α-Pyronochromones	M.P. °C	Mol. Formula	Analysis			
				Calculated		Found	
				C%	H%	C%	H%
1	2, 3-Dimethyl ..	285	$C_{14}H_{10}O_4$	69·4	4·1	69·6	4·1
2	α, 2, 3-Trimethyl ..	244^{AA}	$C_{15}H_{12}O_4$	70·3	4·7	70·5	4·9
3	2-Phenyl-3-methyl ..	231^{E}	$C_{19}H_{12}O_4$	74·9	3·9	75·2	4·1
4	2 Phenyl α, 3-dimethyl ..	256^{A}	$C_{20}H_{14}O_4$	75·5	4·4	75·6	4·4
5*	2 (4′-Nitro) phenyl-3-methyl	$>300^{A}$	$C_{19}H_{11}NO_6$	65·3	3·1	65·5	3·3
6*	2 (4′-Nitro) phenyl 3-dimethyl ..	$>300^{A}$	$C_{20}H_{13}NO_6$	66·1	3·6	65·0	3·7
7	2-Methyl-3-phenyl ..	203^{E_6}	..	..	..	..	..
8	α, 2-Dimethyl-3-phenyl ..	235^{AA}	$C_{20}H_{11}O_4$	75·6	4·4	75·6	4·4

* M.P. of 2-(4′-nitro) phenyl-3-methyl-7-hydroxy-8-formyl chromone is >300° C. Mol. formula $C_{17}H_{11}NO_6$ calculated: C% 62·8 and H% 3·4, found: C% 62·9 and H% 3·5.

All these thirty angular and linear α-pyronochromones and the other eight linear α-pyronoisoflavones previously described by us[1] were tested against three types of bacteria, *viz.*, *Staphylococus aureus, Bacillus subtilis* and *Escherichia coli* by the tube dilution method[7]. In general a methyl group either in α- or β-position of the α-pyrone ring has been found to decrease the activity. Among fifteen 7, 6-α-pyronochromones, 7, 6-α-pyrono-β, 3-dimethyl-2-(3', 4'-dimethoxy) phenyl, β, 3-dimethyl-2-(3', 4'-methylenedioxy) phenyl, β, 3-dimethyl-2-(4'-nitro) phenyl, β-methyl-3-phenyl, β-methyl-2-(3', 4'-methylenedioxy) phenyl-3-phenyl and β-methyl-2(4'-nitrophenyl)-3-phenyl chromones showed activity to *B. subtilis* at 100 ppm. The specific activity of these linear compounds to *B. subtilis* is noteworthy.

Of the twenty-three angular (7, 8)-α-pyronochromones screened, 7, 8-α-pyrono-2-phenyl-3-methyl chromone exhibited activity to all the three bacteria at 100 ppm and to *S. aureus* and *E. coli* at 20 ppm. The corresponding isomer, 7, 8-α-pyrono-2-methyl-3-phenyl chromone was effective to only *B. subtilis* at 100 ppm. The other compounds active are 7, 8-α-pyrono-α, 3-dimethyl-2-phenyl and 7, 8-α-pyrono-α, 3-dimethyl-2-(4'-nitro) phenyl chromones to *S. aureus* and *E. coli* at 100 ppm and inactive on further dilutions.

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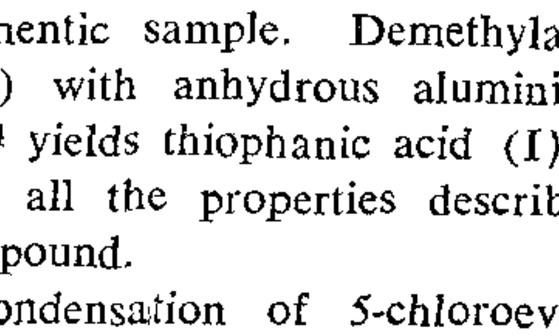
A NEW SYNTHESIS OF THIOPHANIC ACID

THIOPHANIC acid is an interesting naturally occurring chloro-xanthone derivative of lichen origin[1,2]. Its structure as 2, 4, 5, 7-tetrachloro-1, 3, 6-trihydroxy-8-methylxanthone (I) was recently proposed by Huneck[3] based largely on spectral properties. Jayalakshmi, Neelakantan and Seshadri[4] confirmed this structure by reporting its first synthesis. In this synthesis, 1, 3-dihydroxy-6-methoxy-8-methylxanthone[5] (II) was fully methylated and then chlorinated to yield compound (III) which was finally demethylated to thiophanic acid (I). More recently other reports[6,7] on the synthesis of this natural product have also appeared.

In the course of our studies on the synthesis of other naturally occurring xanthones, we have been able to prepare thiophanic acid (I) by following a route which is capable of giving partially dechlorinated thiophanic acid derivatives also. In this, 3, 5-dichloroeverninic acid (3, 5-dichloro-2-hydroxy-4-methoxy-6-methylbenzoic acid) and phloroglucinol are condensed together in the presence of phosphorus oxychloride and anhydrous zinc chloride. The resulting product, *viz.*, 5, 7-dichloro-1, 3-dihydroxy-6-methoxy-8-methylxanthone (IV) (m.p. 280–82°; reddish green ferric reaction) is fully methylated with dimethyl sulphate and potassium carbonate in acetone solution to the methyl ether (V) (m.p. 205–07°; negative ferric reaction) which undergoes dichlorination with chlorine (2·5 moles) in carbon tetrachloride solution yielding 2, 4, 5, 7-tetrachloro-1, 3, 6-trimethoxy-8-methylxanthone (thiophanic acid trimethyl ether) (III) (m.p. 215–16°), identical with an authentic sample. Demethylation of this product (III) with anhydrous aluminium chloride and benzene[4] yields thiophanic acid (I) (m.p. 240–41°) having all the properties described earlier[3,4] for this compound.

Similar condensation of 5-chloroeverninic acid with phloroglucinol gives 7-chloro-1, 3-dihydroxy-6-methoxy-8-methylxanthone (VI) (m.p. 299–301°; green ferric reaction) which is also converted into thiophanic acid (I) (m.p. and mixed m.p. 240–41°) by complete methylation to (VII) (m.p. 192–93°; negative ferric reaction), followed by chlorination with chlorine (3·5 moles) in carbon tetrachloride solution and final demethylation.



(I) $R = R_1 = H$; $R_2 = R_3 = R_4 = Cl$
(II) $R = CH_3$; $R_1 = R_2 = R_3 = R_4 = H$
(III) $R = R_1 = CH_3$; $R_2 = R_3 = R_4 = Cl$
(IV) $R = CH_3$; $R_1 = R_4 = H$; $R_2 = R_3 = Cl$
(V) $R = R_1 = CH_3$; $R_2 = R_3 = Cl$; $R_4 = H$
(VI) $R = CH_3$; $R_1 = R_3 = R_4 = H$; $R_2 = Cl$
(VII) $R = R_1 = CH_3$; $R_2 = Cl$; $R_3 = R_4 = H$
(VIII) $R = CH_3$; $R_1 = H$; $R_2 = R_3 = R_4 = Cl$