STRUCTURE OF XANTHALIN

A. I. Sokolova and G. K. Nikonov

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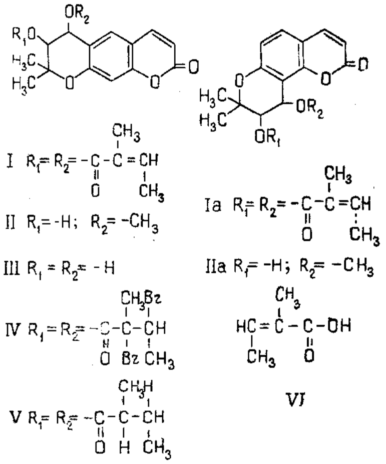
We previously reported the isolation of a new pyranocoumarin—xanthalin—from the roots of Xanthogalum purpurascens Lall. which grows in Transcaucasia (Beshumi region) [1]. The structure of 2',2'-dimethyl-3',4'-trans-α, β-dimethylacrylyloxy-3',4'-dihydropyrano-5',6':6,7-coumarin was assigned to xanthalin on the basis of its UV-, IR-, and NMR spectra.

In this paper the proposed structure is verified by the preparation of a number of xanthalin derivatives.

As seen from formula (I), xanthalin is a linear analog of nomalin (Ia) [2]. One should therefore have expected that two epimeric compounds of the cis and trans methylkhellactone type (IIa) would be obtained during the alkaline methanolysis of xanthalin. In fact, the product of composition $C_{15}H_{16}O_5$ and mp 135–136° C obtained under these conditions contained methoxy and hydroxy groups. Two spots with R_f 0.3 and 0.05 (system 1) were obtained by paper chromatography of this substance. The previously unknown hydroxy-lactone, which we have called isomethylkhellactone, was evidently a mixture of the cis and trans forms of 3'-hydroxy-4'methoxy-3',4'-dihydroxanthyletin (II). Chromatography of the mixture of the cis and trans isomers on silica gel led to the isolation of (±)-trans-3'-hydroxy-4'-methoxy-3',4'-dihydropyrano-5',6':6,7-coumarin with mp 136.5–138° C, R_f 0.3 (system I), and $[\alpha]_D^{20}$ −47.7° (c 0.7, ethanol).

Mild alkaline hydrolysis of xanthalin with 5% aqueous alkali in dioxane gave an optically inactive substance of composition $C_{14}H_{14}O_5$ with mp 213–215° C and R_f 0.00 which was a racemic mixture—(±)-3',4',dihydroxy-3',4'-dihydropyrano-5',6':6,7-coumarin (III)—a previously undescribed substance which we have called isokhellactone. Absorption bands of the coumarin nucleus appear in the IR spectrum of this compound (figure): 1710 cm^{-1} (lactone C=O), 1632, 1568, and 1496 cm^{-1} (aromatic ring). The disappearance of the bands in the 1323 and 1105 cm^{-1} regions, which are observed in the IR spectrum of xanthalin, indicates the splitting off of α, β-unsaturated acid residues with the liberation of two alcoholic hydroxy groups which give a broad absorption band at 3460–3300 cm^{-1}. The presence of two hydroxy groups was proved by elementary analysis.



I $R_1 = R_2 = -\underset{\underset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{C}=\underset{\underset{CH_3}{|}}{CH}$

II $R_1 = -H;\ R_2 = -CH_3$

III $R_1 = R_2 = -H$

IV $R_1 = R_2 = -\underset{\underset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{\underset{\underset{Bz}{|}}{C}}-\overset{\overset{Bz}{|}}{\underset{\underset{CH_3}{|}}{CH}}$

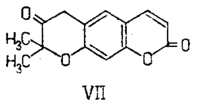
V $R_1 = R_2 = -\underset{\underset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{\underset{\underset{H}{|}}{C}}-\overset{\overset{H}{|}}{\underset{\underset{CH_3}{|}}{CH}}$

Ia $R_1 = R_2 = -\underset{\underset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{C}=\underset{\underset{CH_3}{\vdots}}{CH}$

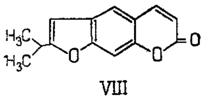
IIa $R_1 = -H;\ R_2 = -CH_3$

$\underset{\underset{CH_3}{|}}{HC}=\overset{\overset{CH_3}{|}}{C}-\underset{\underset{O}{\|}}{C}-OH$

VI



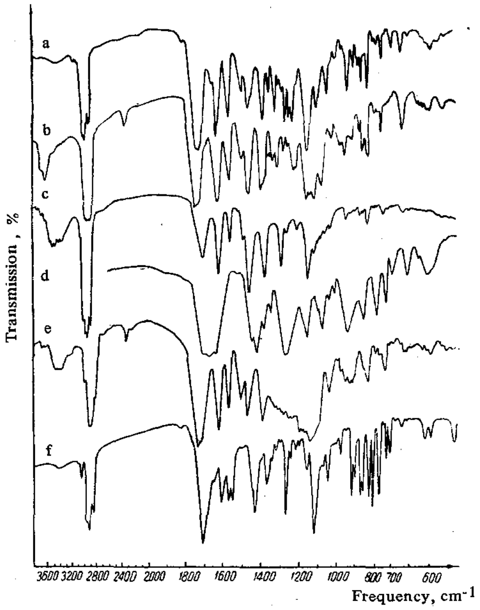
VII



VIII

In addition to compounds (II) and (III), the alkaline hydrolysis yielded an acid of composition $C_5H_8O_2$ which was identified as angelic acid (VI) from its melting point, mixed melting point with an authentic sample, R_f value, and

IR spectrum. The presence of (VI) in the xanthalin molecule enabled us to explain its ability to decolorize a bromine solution to form a tetrabromo derivative of composition $C_{24}H_{26}O_7Br_4$ (IV). The presence of double bonds in the side chain is also confirmed by the catalytic hydrogenation of xanthalin over platinum oxide (Adams catalyst). Absorption bands which are characteristic for the coumarin skeleton (1749, 1635, 1572, 1500, and 1570 cm^{-1}) are present in the IR spectrum of the hydrogenation product, but the bands due to the presence of α, β-unsaturated acid groups (1323 and 1105 cm^{-1}) are absent. Consequently, hydrogenation occurred only in the side chain and did not affect the double bonds of the coumarin ring.



IR spectra of xanthalin (a) and its derivatives: isomethylkhellactone (b), isokhellactone (c), angelic acid (d), dihydroxanthalin (e), and anhydromarmesin (f).

The amount of hydrogen (2 moles) consumed in the reaction and the formation of a tetrahydro derivative of composition $C_{24}H_{30}O_7$ (V) showed the presence of two angelic acid residues in the xanthalin molecule.

Severe acidic hydrolysis in 10 N alcoholic H_2SO_4 led to the formation of a mixture of products from which we obtained 3'-oxo-3',4'-dihydroxanthyletin (VII) with mp 162–163.5° C (literature mp 164–165.5° C [3]) and R_f 0.95, and anhydromarmesin (VIII) with mp 136–137° C and R_f 0.9 by chromatographic separation on silica gel.

Absorption bands at 1730, 1638, 1599, and 1580 cm^{-1} which are associated with the coumarin ring were noted in IR spectrum of anhydromarmesin. The disappearance of the band at 905 cm^{-1} $\left(\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}\!\!>C{-}O\right)$ and the preservation of the bands at 1399 and 1370 cm^{-1} $\left(\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}\!\!>C\!\!<\right)$ showed the structural changes occurring in the 2',2'-dimethylchroman ring which were accompanied by the contraction of the six-membered ring to a five-membered ring. In fact, the absorption bands appearing at 3060 and 748 cm^{-1} in the IR spectrum of the product confirmed the formation of a furan ring.

Reactions of a similar type with dehydration of chromano-α-pyrones leading to the rearrangement of the carbon atoms of the 2',2'-dimethylchroman ring with the formation of a five-membered ring have repeatedly been described for khellactone derivatives [4, 5]. This is the first time that dehydration of a diester of 3',4'-dihydroxy-3',4'-dihydroxanthyletin (III) has been carried out. Obtaining such well-known compounds as 3'-oxo-3',4'-dihydroxanthyletin (VII) and anhydromarmesin (VIII) is evidence in favor of a linear structure for xanthalin.

The above-listed derivatives confirm the correctness of the previous conclusion that xanthalin is 2',2'-dimethyl-3',4'-diangeloyloxy-3',4'-dihydropyrano-5',6':6,7-coumarin.

EXPERIMENTAL

The IR spectra of the compounds were obtained with a UR-10 spectrograph (mulls in paraffin oil). Chromatographic separation was carried out on grade B Leningrad paper (descending method). System 1 (for coumarins): the stationary phase was a 10% solution of formamide in methanol, the mobile system was n-hexane–benzene–methanol (5 : 4 : 1), and the spots were revealed with diazotized sulfanilamide. System 2 (for acids): the stationary phase was butan-1-ol saturated with 1.5 N ammonium hydroxide, and the revealing agent was a 0.2% alcoholic solution of Bromophenol Blue.

Tetrabromoxanthalin. Xanthalin (0.25 g) was dissolved in 10 ml of chloroform and a 1% solution of bromine in chloroform was added dropwise until a faint pink coloration appeared. The solution was distilled and the residue was recrystallized from methanol to give small colorless plates with mp 50–52° C. Found %: C 38.64, 38.78; H 3.61, 3.85; Br 42.70, 42.69. Calculated for $C_{24}H_{26}O_7Br_4$, %: C 38.63; H 3.51; Br 42.84.

Tetrahydroxanthalin. Xanthalin (0.6076 g) was dissolved in 30 ml of methanol, 0.0487 g of platinum oxide was added, and the mixture was hydrogenated for 2.5 hr. The hydrogenation required 71 ml of hydrogen. The alcoholic solution was filtered from the catalyst and evaporated to dryness. Found %: C 66.93, 66.76; H 7.08, 7.05. Calculated for $C_{24}H_{30}O_7$, %: C 67.27; H 7.05.

cis-trans-Isomethylkhellactone. Xanthalin (0.5049 g) was dissolved in 20 ml of a 10% methanolic solution of KOH and the solution was heated in a flask with a reflux condenser on a water bath for 5 hr. The mixture was then diluted with 40 ml of water, acidified with conc H_2SO_4, and extracted three times with 25-ml portions of ether. On removal of the solvent a yellow oil was obtained from which, after several recrystallizations from benzene, small colorless needles with mp 135–136° C were isolated which gave two spots with R_f 0.3 and 0.05 on a chromatogram (system 1). Found %: C 65.37, 65.46; H 5.94, 5.94; OCH_3 11.24, 10.61; H_{act} 0.339, 0.365. Calculated for $C_{15}H_{16}O_5$, %: C 65.20; H 5.84; OCH_3 11.23; H_{act} 0.36.

(−)-trans-Isomethylkhellactone. cis-trans-Isomethylkhellactone (0.05 g) was chromatographed on a column with 7 g of silica gel (diam. 1 cm, height 7.5 cm) by elution with benzene and then a benzene–methanol (95 : 5) mixture. Twelve 20-ml fractions were collected. Evaporation of the benzene from fractions 3–6 gave 0.01 g of crystals with mp 136.5–138° C (Kofler, from benzene), $[\alpha]_D^{20}$ −47.7° (c 0.7, ethanol), and R_f 0.3 (system 1).

Angelic acid. Xanthalin (0.5049 g) was saponified by the above-described method. The extract obtained after hydrolysis and treatment with ether was thrice treated with a saturated solution of sodium carbonate. The colored sodium carbonate solution was acidified with H_2SO_4 and extracted with ether. After removal of the solvent, a syrupy mass with a specific odor was obtained which gradually crystallized, mp 41–42.5° C. Found %: C 60.09, 60.12; H 8.11, 8.24; H_{act} 0.98, 1.03. Calculated for $C_5H_8O_2$, %: C 59.99; H 8.05; H_{act} 1.01.

(±)-Isokhellactone. Xanthalin (0.5 g) was dissolved in 6.25 ml of dioxane, 25 ml of 5% aqueous KOH was added, and the mixture was allowed to stand for 24 hr. The excess of xanthalin (0.34 g) which crystallized out was filtered off, and the above-described operation was repeated three times, i.e., until all the xanthalin taken had entered into the reaction. The colored reaction mixture was acidified with H_2SO_4 and treated with ether (3 × 20 ml). The combined ether extracts were washed with saturated $NaHCO_3$, dried over anhydrous Na_2SO_4, filtered, and evaporated to give 0.1 g of small colorless crystals with mp 213–215° C (from aqueous methanol), $[\alpha]_D^{20}$ 0° (c 0.13, ethanol), and R_f 0.00 (system 1). Found, %: C 64.14, 64.10; H 5.41, 5.35; H_{act} 0.75, 0.79. Calculated for $C_{14}H_{14}O_5$, %: C 64.11; H 5.38; H_{act} 0.77.

Dehydration of xanthalin. Xanthalin (0.2 g) was dissolved in 20 ml of ethanol, 20 ml of concentrated H_2SO_4 was added, and the mixture was heated in a flask with a reflux condenser on a water bath for 12 hr. The reaction mixture was then diluted with two volumes of water, and the precipitated black resin was extracted three times with ether (20-ml portions). The combined ether extracts were dried over anhydrous Na_2SO_4, filtered, and evaporated. The residue, which was a mixture of products, was chromatographed on a column with silica gel (diam. 3.5 cm, height 12 cm) being eluted with benzene and then a benzene–methanol (20 : 0.2) mixture. The percentage of methanol in the mixture was gradually increased until pure methanol was used. Thirty-four 100-ml fractions were collected.

3'-Oxo-3', 4'-dihydroxanthyletin. Concentration of the benzene eluate from fractions 3-4 yielded 3 mg of fine crystals with mp 162–163.5° C (from methanol) and R_f 0.95 (system 1) [literature mp 164–165.5° C (from CCl_4) [3]]. A more detailed identification of the substance was not carried out in view of the small amount of product obtained.

Anhydromarmesin. Concentration of the benzene eluate from fractions 5–6 yielded needles with mp 136–137° C (Kofler, from methanol) and R_f 0.9 (system 1). Found, %: C 74.06, 74.03; H 5.34, 5.28. Calculated for $C_{14}H_{12}O_3$, %: C 73.68; H 5.30.

CONCLUSIONS

1. Xanthalin has been shown to have the structure of 2',2'-dimethyl-3',4', -diangeloyloxy-3',4'-dihydropyrano-5',6':6,7-coumarin on the basis of the preparation of a number of derivatives and cleavage products.

2. The following products of the alkaline hydrolysis of xanthalin have been isolated and characterized for the first time: (±)-3',4'-dihydroxy-3',4'-dihydroxanthyletin (isokhellactone), $C_{14}H_{14}O_5$, with mp 213–215° C and (-)-trans-3'-hydroxy-4'-methoxy-3',4'-dihydroxanthyletin (isomethylkhellactone, $C_{15}H_{16}O_5$, with mp 136.5–138° C and $[\alpha]_D^{20}$ −47.7 (ethanol).

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