# THE STRUCTURE OF SMYRNIORIDIN

A. A. Savina, M. E. Perel'son, and G. K. Nikonov

Khimiya Prirodnykh Soedinenii, Vol. 6, No. 2, pp. 185–190, 1970

UDC 577.15/17.582.89

From the roots of Smyrniopsis aucheri Boiss, collected by D. A. Pakalen in the region of Selimskii pereval (Armenia) in the fruit-bearing phase we have isolated a new coumarin with the composition $C_{21}H_{22}O_7$, mp 126–128° C (from methanol) $[\alpha]_D^{20}$ −229° (c 1.26; chloroform), mol wt 386 (mass spectrometry), and we have called it smyrnioridin. The nature of the UV spectrum [$\lambda_{max}$ 222 mμ, 300 mμ (inflection), 326 mμ (log ε 4.27, 3.88, 4.21)] shows that this substance is either a dihydrofuro-or a dihydropyranocoumarin [1]: its IR spectrum (Fig. 1) has the absorption bands appropriate to a coumarin skeleton, $cm^{-1}$: 1738, 1725 (C=O of an α-pyrone and an ester), 1632, 1577 (—C=C bond of an aromatic system).

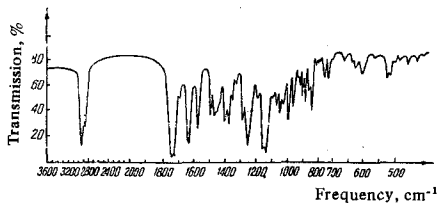
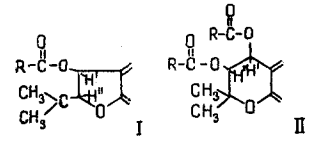



Fig. 1. IR spectrum of smyrnioridin.

The saponification of smyrnioridin in methanol under mild conditions led to the formation of a mixture of coumarin derivatives and two acids, of which the first, with the composition $C_5H_8O_2$, mp 41.5–43° C was shown by its IR and NMR spectra and a mixed melting point test to be identical with angelic acid, and the second was identified by paper chromatography as acetic acid.

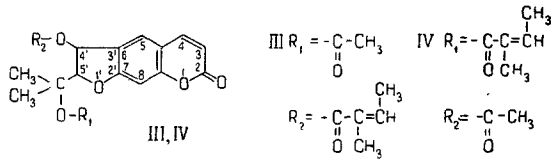
The presence in the NMR spectrum of smyrnioridin (Fig. 2a) of doublets at 6.10 and 7.52 ppm (J = 9.6 Hz) and of of singlets at 6.71 and 7.45 ppm (the latter superposed on one of the components of a doublet at 7.52 ppm) shows that the substance is a 6,7-disubstituted coumarin [2]. The doublets at 6.40 and 5.15 ppm (J = 6.6 Hz) are due to the protons of a dihydrofuran or dihydropyran ring in a structure of type I or II.



I II

The first of the signals mentioned is due to H' and the second to H" [3]. The choice between possibilities I and II in favor of I can be made on the basis of the positions of the signals of the protons of the gem-dimethyl grouping at 1.68 and 1.60 ppm [4, 5].

One of the acyl groups in smyrnioridin is acetyl (three-proton singlet at 1.95 ppm) and the other is angeloyl, giving the signals of methyl groups at 1.88 and 1.95 ppm (the latter fusing with the acetyl singlet) and a multiplet of an olefinic proton at 6.00 ppm [3, 5]. Consequently smyrnioridin must have structure III or IV.



III, IV

The positions of the acid residues were determined by studying the NMR spectra of the product of partial saponification of smyrnioridin. A compound $C_{17}H_{18}O_6$ was obtained, in NMR spectrum whose (Fig. 2b) signals of the protons of the angeloyl group had disappeared while the singlet of the acetyl group was still present (1.92 ppm). Simultaneously, there was a shift in the signals from $H_{(4')}$ and $H_{(5')}$ in the strong-field direction, as a result of which two doublets with a coupling constant of 2.4 Hz appeared at 4.78 and 4.98 ppm. In structures of the type discussed, further spin-spin coupling exists between $H_{(4')}$ and $H_{(8)}$, causing some broadening of the components of the doublet from $H_{(4')}$ [6]. Such broadening was observed in the spectra of smyrnioridin (doublet at 6.40 ppm) and in the product of its partial saponification (doublet at 4.98 ppm). Accordingly, the signal at 4.98 ppm was assigned to $H_{(4')}$ and the signal at 4.78 ppm to $H_{(5')}$. The signal of the proton at $C_{(4')}$ thus undergoes a greater diamagnetic shift ($\Delta\delta$ 1.42 ppm) than the signal from $H_{(5')}$ ($\Delta\delta$ 0.37 ppm), which shows the splitting off of the acid residue from $C_{(4')}$. The positions of the signals of the methyl groups (1.48 and 1.60 ppm) are also in harmony with this conclusion. In the IR spectrum of the saponification product there is no absorption band of a hydroxyl group and in the NMR spectrum there is a three-proton singlet of an aliphatic methoxyl group at 3.41 ppm. The appearance in this group of the molecule of the product of partial hydrolysis is due to the replacement of the angeloyl residue split out by a residue from the methanol in which the hydrolysis was performed. A similar phenomenon has been reported frequently for esters of khellactone [7–9].

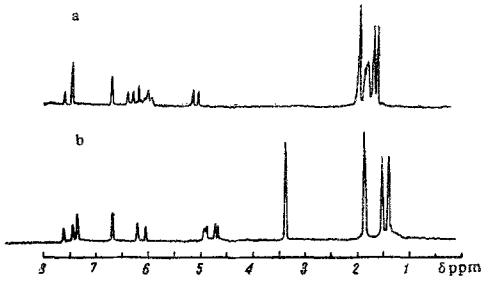
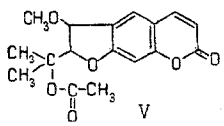
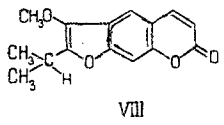



Fig. 2. NMR spectrum of smyrnioridin (a) and the product of its incomplete saponification (b).

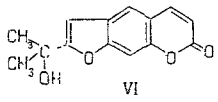
Thus, the structure of the hydrolysis product mentioned is 5'-(1-acetoxy-1-methylethyl)-4'-methoxy-4', 5'-dihydro-2', 3' : 7, 6-coumarin (V), and smyrnioridin is 5'-(1-acetoxy-1-methyl)-4'-angeloyloxy-4', 5'-dihydro-2', 3' : 7, 6-coumarin (III).

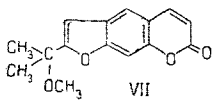
In addition to V, the alkaline methanolysis of smyrnioridin gave substances with the composition $C_{14}H_{12}O_4$, mp 146–148° C (VI) and $C_{15}H_{14}O_4$, mp 165.5–168° C (VII). An absorption band at 3400 $cm^{-1}$ in the IR spectrum of VI shows the presence of a hydroxyl group, the tertiary nature of which is confirmed by the capacity of the compound for being reduced with concentrated hydriodic acid in the cold with the formation of anhydromarmesin. The formation of the latter is a convincing proof of the furo-2', 3' : 7, 6-coumarin nature of VI. According to its elementary analysis, compound VII contains a methoxy group. The similarity of the NMR spectra of VI and VII with the exception of the signals due to the protons of the hydroxyl and methoxyl groups, accordingly showed the identity of the structures of the coumarin parts of their molecules (table). The position of the methoxyl in VII can only be on the tertiary carbon atom of the isopropyl grouping. This is confirmed by the NMR spectrum of VII and the fact that VII is not identical with peucedanin (VIII) but must be an isomer of it.


V


VIII

Thus, the products of the hydrolysis of VI and VII must correspond to the structures:


VI


VII

Substances VI and VII are linear analogs of oroselol and its methyl ether, obtained by the saponification of diesters of dihydrofurocoumarins of the angular series [10, 11]. In the compounds mentioned the furan ring is formed by the splitting out of a labile hydroxyl in position 4' of the dihydrofuran ring of intermediate hydrolysis products. The

phenomenon of spontaneous dehydration of such compounds has been mentioned repeatedly in the literature [7, 10, 11]. The formation of products V and VII methylated in different positions can be explained by the equal probability of the splitting off of either of the two acyl groups in the first stage of hydrolysis, with their simultaneous replacement by methoxyl groups. This equality of the rates of hydrolysis is possible if the angeloyl group is present in the more labile position 4' and the acetyl on the tertiary position of the hydroxyisopropyl grouping, which is in complete harmony with literature data [7] and does not contradict the structure proposed for smyrnioridin.

Features of the NMR Spectra of the Products of the Saponification of Smyrnioridin VI and VII

| Compound | δ, ppm | Multiplicity, J, Hz | Identity | Assignment |
|---|---|---|---|---|
| VI | 1.66 | Singlet | 6H | $CH_3$ $CH_3$ >C= |
| | 2.22 | " | | HO–C= \| |
| | 6.29 | Doublet, 9.6 | 1H | $H_3$ |
| | 6.60 | Singlet | | $H_{4'}$ |
| | 7.32 | " | | $H_8$ |
| | 7.53 | " | | $H_5$ |
| | 7.69 | Doublet, 9.6 | | $H_4$ |
| VII | 1.62 | Singlet | 6H | $CH_3$ $CH_3$ >C= |
| | 3.15 | " | 3H | $CH_3O$– |
| | 6.32 | Doublet, 9.6 | 1H | $H_3$ |
| | 6.65 | Singlet | | $H_{4'}$ |
| | 7.38 | " | | $H_8$ |
| | 7.58 | " | | $H_5$ |
| | 7.77 | Doublet, 9.6 | | $H_4$ |

## EXPERIMENTAL

The UV spectrum was taken in ethanol on an SF-4A spectrophotometer, the IR spectrum on a UR-10 spectrophotometer (mulls in paraffin oil) and the NMR spectra on an S-60-L (60 MHz) instrument with deuterochloroform as the solvent.

The mass-spectrometric determination of the molecular weight was carried out by P. I. Zakharov, and the microanalyses by E. A. Nikonova. Chromatography was performed on paper of Leningrad type (B). The coumarins were separated in the cyclohexane–benzene–methanol (5 : 4 : 1) system. The paper was impregnated with a 10% solution of formamide in methanol. The revealing agent was diazotized sulfanilamide. The acids were separated in the concentrated ammonia–butan-1-ol (5 : 95) system. The revealing agent in this case was a 0.2% solution of Bromophenol Blue in ethanol. The analytical data for the cleavage products of smyrnioridin corresponded to the calculated figures.

**Isolation of smyrnioridin.** One kilogram of the dried and comminuted roots was extracted with methanol (3 × 4.5 *l*). The combined extracts were evaporated in vacuum to a volume of 800 ml. The crystalline precipitate that deposited on standing (8.0 g) was separated off and recrystallized from methanol. This gave colorless acicular crystals with mp 126–128° C, $[\alpha]_D^{20}$ −229° (c 1.26; chloroform), $R_f$ 0.95.

Found, %: C 65.44, 65.66; H 5.99, 6.02. Mol wt 386 (mass spectrometry). Calculated for $C_{21}H_{22}O_7$, %: C 65.27; H 5.74. Mol wt 386.39.

**Saponification of smyrnioridin.** A) Isolation of coumarin derivatives. A solution (1.3 g) of smyrnioridin in the minimum amount of chloroform was mixed with 100 ml of 0.4% KOH in methanol and the mixture was left at room temperature for 3 min. Then it was diluted with a double volume of water, acidified with 25% $H_2SO_4$, and treated with ether (5 × 25 ml). The ethereal extracts were washed with saturated sodium bicarbonate solution and then with water and were dried over sodium sulfate and evaporated in vacuum. According to paper chromatography, the residue

consisted of four substances with $R_f$ 0.85 (traces), 0.8, 0.7, and 0.12. Preparative separation in a thin layer of acidic alumina (Brockmann activity grade II) in the ether–petroleum ether (1 : 3) system gave the following substances: V, colorless vitreous mass, $R_f$ 0.7, mol wt 318 (mass spectrometry); VI, mp 146–148° C, $R_f$ 0.12; and VII, mp 165.5–168° C, $R_f$ 0.8.

**B) Isolation of the acids.** The combined extracts obtained by washing the ethereal extract of the total hydrolysis products with sodium bicarbonate solution were acidified with 25% $H_2SO_4$ and treated with ether (5 × 25 ml). The ethereal layer was dried over sodium sulfate, and the solvent was distilled off in vacuum. Paper chromatography in the presence of reference samples showed that the residue contained acetic acid ($R_f$ 0.1) and angelic acid ($R_f$ 0.47). 0.2 g of the acid fraction was sublimed in vacuum with heating in the water bath. Thin acicular crystals with mp 41.5–43° C deposited.

**C) Reduction of VI with hydriodic acid.** With ice-water cooling, 0.5 ml of conc HI was added to a solution of 0.1 g of VI in 3 ml of acetic anhydride, and the mixture was left at 0° C for 14 hr. Then it was diluted with a fivefold volume of water, a solution of sodium thiosulfate was added to reduce the iodine liberated, and it was treated with ether (5 × 10 ml). The ethereal extracts were washed with water and dried over sodium sulfate, and the solvent was distilled off in vacuum. The reaction product was purified by means of preparative chromatography in a thin layer of acidic alumina (Brockmann activity grade II) in the ether-petroleum ether (3 : 7) system. After recrystallizing from methanol, mp 135–137° C. IR spectroscopy and a mixed melting point showed that the compound obtained was anhydromarmesin.

## CONCLUSIONS

A new coumarin, which has been called "smyrnioridin," has been isolated from the roots of Smyrniopsis aucheri Boiss. The NMR spectrum and a study of the saponification products of smyrnioridin have shown that it is 5'-(1-acetoxy-1-methylethyl)-4'-angeloyloxy-4',5'-dihydrofuro-2',3' : 7,6-coumarin.

## REFERENCES


1. G. A. Kuznetsova, Natural Coumarins and Furocoumarins [in Russian], Leningrad, 30, 1967.
2. Yu. N. Sheinker, G. Yu. Pek, and M. E. Perel'son, DAN SSSR, 158, 1382, 1964.
3. M. E. Perel'son, Yu. N. Sheinker, G. P. Syrova, and A. P. Prokopenko, KhPS [Chemistry of Natural Compounds], 3, 344, 1967.
4. M. E. Perel'son, G. K. Nikonov, G. Yu. Pek, and Yu. N. Sheinker, DAN SSSR, 159, no. 1, 154, 1964.
5. A. I. Sokolova, G. K. Nikonov, M. E. Perel'son, Yu. N. Sheinker, and G. P. Syrova, KhPS [Chemistry of Natural Compounds], 4, 280, 1968.
6. E. V. Lassak and J. T. Pinhey, J. Chem. Soc., 2000, 1967.
7. E. Smith, N. Hosansky, W. G. Bywater, and E. von Tamelen, J. of Amer. Chem. Soc., 79, no. 13, 3534, 1957.
8. R. E. Willete and T. O. Soine, J. Pharm. Sci., 51, no. 2, 149, 1962.
9. A. Mustafa, N. A. Sterkowsky, and T. I. Selama, J. Org. Chem., 26, no. 3, 890, 1961.
10. A. P. Prokopenko, ZhOKh, 34, 4111, 1964.
11. A. P. Prokopenko, KhPS [Chemistry of Natural Compounds], 1, 215, 1965.


21 August 1969

All-Union Scientific-Research Institute of Medicinal Plants