THE COUMARIN COMPOSITION OF *Seseli tortuosum*

A. Z. Abyshev and D. Z. Abyshev

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The results are given of the identification of the known pyranocoumarin campestrinol (I), and the structures of four new coumarin derivatives have been studied — tortuosin (II), tortuosinin (III), tortuosinol (IV), and tortuosidin (V). On the basis of their spectral characteristics and chemical transformations, the corresponding structures have been established for compounds (II)-(V).

In the flora of the Caucasus, the genus *Seseli* is represented by 16 species, of which four grow in Azerbaidzhan [1]: *S. grandivittatum*, *S. peucedanoides*, *S. campestre*, and *S. tortuosum*. We have studied the coumarin compositions of the first three species previously [2-5]. A number of coumarin derivatives have been obtained and characterized, the majority of them being pyranocoumarins possessing a pronounced antiarrhythmic activity [5-7].

In the present paper we give the results of a chemical investigation of the coumarin composition of *Seseli tortuosum* (L.)* collected in Kobustan (Azerbaidzhan SSR). This species contains 1% of coumarins as determined by the generally adopted method of Späth [8].

When a chloroform extract (40 g) from the roots (1.0 kg) of the plant under investigation was chromatographed on neutral alumina of activity grade II (3.5 × 80 cm, 500 g of Al_2O_3), we obtained a number of individual compounds (I-V), possessing the properties of coumarins:

Compound	*Elementary composition*	*mp, °C* $[\alpha]_D$	R_f *(fluorescence in UV light in the benzene–acetone (10:3) system on Silufol plates;*
I	$C_{24}H_{26}O_7$	116-118	0.54 (violet)
II	$C_{21}H_{22}O_6$	156-157	0.84 (yellow)
III	$C_{29}H_{20}O_5$	109	0.88 (bright violet)
IV	$C_{19}H_{20}O_6$	79-81	0.45 (bright violet)
V	$C_{24}H_{30}O_5$	−45 (c 2.8; ethanol)	0.75 (bright blue)

Substance (I), with the composition $C_{24}H_{26}O_7$, mp 116-118°C, belonged to the group of pyranocoumarins and, from its physicochemical constants and IR and PMR spectra, it corresponded to campestrinol [4].

Substances (II-V) were new, not having been described in the literature. We have called them tortuosin, tortuosinin, tortuosinol, and tortuosidin.

IR spectrum of (II) (cm^{-1}): 1727 (C=O of an α-pyrone), 1628, 1595, 1575, 1550 (–CH=CH– bond in an aromatic ring).

The PMR spectrum of (II) shows, in addition to the signals of the protons of a linear 3-monosubstituted furocoumarin ring (doublets at 6.20 and 8.11 ppm, J = 10 Hz, H-3 and H-4, and 6.87 and 7.53 ppm, J = 2.5 Hz, H-4' and H-5'; singlet at 7.11 ppm, H-8), the signals of the protons of three methyl groups at quaternary carbon atoms bearing a hydroxy group (singlets at 1.20, 1.29, and 1.36 ppm, 3 H each), of two methine protons (triplet 3.13 ppm, J = 6.5 Hz, 2 H), and of three methylene protons, one of them being attached to oxygen (multiplets at 4.42 ppm, $-O-CH_2-$ and 2.10-2.60 ppm, $-CH_2-CH_2-$).

On the basis of the facts given, the structure of 5-(3',7'-dimethyl-2',3':6',7'-diepoxyoctyloxy)furo-2',3':7.6-coumarin is proposed for (II), which agrees well with the results of

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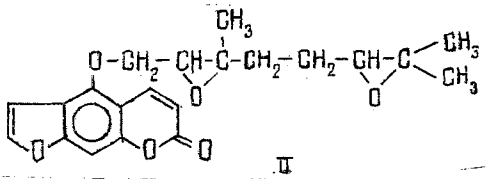
the acid hydrolysis of this compound, leading to the formation of the known furocoumarins. bergaptol (VI), $C_{11}H_6O_4$, mp 275-277°C and 5-geranyloxypsoralen (VII), $C_{21}H_{22}O_4$, mp 55-56°C, which were identified by comparing the characteristics that we obtained with those described in the literature for (VI) [9] and (VII) [10, 11].



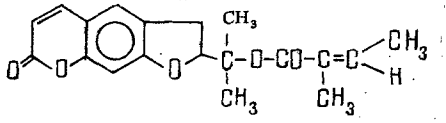
II

The IR and PMR spectra of tortuosinin (III) coincided with those of deltoin [12], but, unlike deltoin, (III) was optically inactive and it also had a different melting point.

IR spectrum of (III) (cm^{-1}): 1715 (C=O of an α-pyrone and of an ester grouping), 1630, 1565, 1515 (—CH=CH— bond in an aromatic ring).

PMR spectrum of (III) (ppm): 6.23, 7.50 (doublets, J = 10 Hz, H-3, and H-4); 6.64, 7.11 (singlets, H-6 and H-5); 5.93 (quartet, J_1 = 12 Hz, J_2 = 6 Hz, —CH=), 4.98 (triplet, J = 7.5 Hz, H-5'), 3.24 (doublet, J = 8.5 Hz, Ar—CH_2—). 1.52 (singlet, $-C(CH_3)_2$); 1.76, 1.84 (singlets, $-C(CH_3)=C(CH_3)_2$).

The alkaline hydrolysis of (III) with 5% KOH in methanol formed prangeferol (VIII), $C_{14}H_{14}O_4$, mp 175-176.5°C [13] and angelic acid (IX), $C_5H_8O_2$, mp 45-47°C, identified by means of PMR spectra. Hence, (III) is an ester of prangeferol (VIII) and angelic acid (IX)

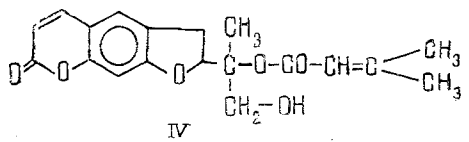


III

Tortuosinol (IV) also belongs to the group of 4',5'-dihydrofurocoumarins, as follows from its IR and PMR spectra.

IR spectrum of (IV) (cm^{-1}): 3430 (—OH), 1720-1735 (C=O of an α-pyrone and an ester grouping), 1625, 1585, 1560, 1510 (—CH=CH— bond in an aromatic ring).

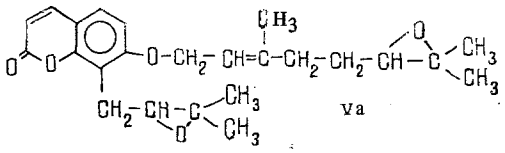
In the PMR spectrum of (IV) the same signals can be seen in weak field as in the spectrum of (III). Consequently, (IV) is also a 4',5'-dihydrofurocoumarin acylated in position 1", as is shown by the chemical shift of the signal of the H-5' proton observed in the spectrum of (IV) at 5.0 ppm (triplet, J = 7 Hz, 1 H). Together with this signal, at 5.15 ppm there is a signal characteristic for a —CH= grouping. The spectrum also shows the signals of the protons of the following groupings: —CH_2—O— (triplet, 4.03 ppm, J = 6 Hz, 2 H), Ar—CH_2— (doublet, 3.27 ppm, J = 8.5 Hz, 2 H), $-O-C(CH_3)-$ (singlet, 1.54 ppm, 3 H), $=C(CH_3)_2$ (singlets, 1.84, 2.04 ppm, 6 H). These facts are in complete agreement with the structure of 5'-(2"-hydroxy-1"-methyl-1"-senecioyloxy)-4',5'-dihydrofuro-2',3':7,6-coumarin, i.e., (IV) is an ester of prandiol [14] and senecioic acid. In actual fact, the alkaline hydrolysis of (IV) with 5% KOH in methanol gave prandiol (X), $C_{14}H_{14}O_5$, mp 130-131°C, and senecioic acid (XI), $C_5H_8O_2$, mp 70°C, identified from its PMR spectra.



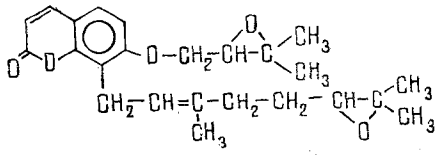
IV

Tortuosidin (V), unlike the compounds described above, belongs to the group of 7,8-disubstituted coumarins and forms a viscous mass readily soluble in organic solvents. IR spectrum of (V) (cm^{-1}): 1720 (C=O of an α-pyrone), 1625, 1580, 1505 (—CH=CH— bond in an aromatic ring).

In the PMR spectrum of (V), together with the signals of the protons of a 7,8-disubstituted coumarin nucleus (doublets at 6.09 and 7.49 ppm, J = 10 Hz; and 6.64 and 7.16 ppm, J = 9 Hz, H-3—H-6), the signals of the following fragments are observed: 2—C(CH$_3$)(O—)CH$_3$ (singlets at 1.18 ppm, 6 H, and 1.25 and 1.37 ppm, 3 H each), =C—CH$_3$ (singlet at 1.78 ppm, 3 H); 2 —CH—O— and Ar—O—CH$_2$— (multiplet at 4.40-4.65 ppm, 4 H), —CH$_2$—Ar (doublet at 3.30 ppm, J = 8.5 Hz, 2 H); —CH= (triplet at 5.30 ppm, J = 6.5 Hz, 1 H), and —CH$_2$—CH$_2$— (multiplet at 2.50-2.80 ppm, 4 H). On the basis of the facts given, two structures may be proposed for the compound under investigation: (Va) or (Vb)



Va



Vb

The choice between the structures (Va or Vb) was made on the basis of a study of the products of the acid hydrolysis of (V), which gave osthenol (XII), $C_{14}H_{14}O_3$, mp 124-126°C [15]. The latter, on methylation with methyl iodide in the presence of K_2CO_3, gave osthole (XIII), $C_{15}H_{16}O_3$, mp 83.5-84.5°C, identified from its PMR spectrum, which permitted the unambiguous selection of structure (Va). Hence, tortuosidin (Va) has the structure of 7-(7'-methoxy-3',7'-dimethyl-6',7'-epoxyoct-2'-enyloxy)-8-(3'-methyl-2',3-epoxybutyl)coumarin.

Thus, the coumarin composition of the roots of the plant under investigation is characterized by the presence of compounds of different structures — angular pyranocoumarins, linear furocoumarins, and 7,8-disubstituted coumarins — while the roots of *Seseli campestre* were distinguished by containing only angular pyranocoumarins [4].

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer in a paraffin oil, and PMR spectra on a HX-90 MHz spectrometer (in $CDCl_3$, 0 — TMS). Melting points were determined on a Kofler block. The purity of the compounds obtained was checked on Silufol plates in the benzene—acetone (10:3) system. The elementary analyses of the compounds investigated corresponded to the calculated figures.

Isolation of the Coumarins. The dry resin (40 g) obtained by the exhaustive extraction of the roots (1 kg) of *Seseli tortuosum* was chromatographed on a column (3.5 × 85 cm) of neutral alumina (300 g, activity grade II). Elution was performed with petroleum ether (fractions 1-8), petroleum ether—chloroform (2:1) (fractions 9-20) and (1:1) (fractions 21-32), and with chloroform (fractions 33-42). The volume of each fraction was 50 ml.

Fractions 3-8, after the solvent had been distilled off and they had been subjected to rechromatography yielded three individual substances: (II) (0.85 g), with the composition $C_{21}H_{22}O_6$, mp 156-157°C (from ethanol); (III) (0.35 g) with the composition $C_{19}H_{20}O_5$, mp 109°C (from ether); and (V) (1.05 g) with the composition $C_{24}H_{30}O_5$, $[\alpha]_D^{22}$ − 45° (c 2.8; ethanol).

Fractions 23-30 and 36-42 contained individual substances. After the solvent had been distilled off from these fractions, substances (I) (0.75 g) with the composition $C_{24}H_{26}O_7$, mp 116-118°C (from a mixture of chloroform and petroleum ether) and (IV) (0.55 g) with the composition $C_{19}H_{20}O_6$, mp 79-81°C (from benezene), respectively, were obtained.

From its physicochemical constants and PMR spectrum, (I) was identified as campestrinol.

Acid Hydrolysis of Tortuosin (II). Compound (II) (0.4 g) was hydrolyzed with 10% sulfuric acid in ethanol at 80°C for 6 h. After cooling, the reaction mixture was diluted with water, and the reaction product was extracted with chloroform (3 × 50 ml). After drying and the elimination of the solvent by distillation, a mixture of substances (0.35 g) was obtained which was separated preparatively on Silufol plates in the benzene—acetone (10:3) system. This yielded (VI) (0.12 g), with the composition $C_{11}H_6O_4$, mp 275-277°C, and (VII) (0.08 g) with the composition $C_{21}H_{22}O_4$, mp 55-56°C, which were identified as bergaptol and 5-geranyloxypsoralen.

Alkaline Hydrolysis of Tortuosinin (III). Compound (III) (0.25 g) was hydrolyzed with 5% KOH (50 ml) in methanol at 70°C for 5 h. Then the reaction mixture was diluted with water and acidified with hydrochloric acid, and the reaction product was extracted with chloroform (2 × 40 ml). After the chloroform had been distilled off and the residue had been crystallized from benzene, 0.12 g of substance (VIII) was obtained with the composition $C_{14}H_{14}O_4$, mp 175-176.5°C, identified as prangeferol.

The mother solution was distilled with steam. The distillate was saturated with sodium chloride and extracted with chloroform. After the chloroform had been distilled off, a small amount of (IX) was obtained with mp 45-47°C, identified as angelic acid.

Alkaline Hydrolysis of Tortuosinol (IV). Compound (IV) (0.3 g) was hydrolyzed under the same conditions as (III). After the usual working up, 0.15 g of prandiol (X), $C_{14}H_{14}O_5$, mp 130-131°C, and 0.11 g of senecioic acid (XI), $C_5H_8O_2$, mp 70°C, were obtained.

Acid Hydrolysis of Tortuosidin (Va). Compound (Va) (0.5 g) was hydrolyzed under the same conditions as (II). After the usual working up, 0.32 g of osthenol (XII), $C_{14}H_{14}O_3$, mp 124-126°C, was obtained.

Methylation of Osthenol (XII). Compound (XII) (0.25 g) was methylated as described in [15]. This yielded 0.18 g of osthole (XIII), $C_{15}H_{16}O_3$, mp 83.5-84.5°C, identified from its PMR spectrum.

SUMMARY

From the roots of *Seseli tortuosum*, in addition to campestrinol, four new coumarins have been isolated — tortuosin, tortuosinin, tortuosinol, and tortuosidin.

Corresponding structures have been proposed for the new compounds on the basis of their IR and PMR spectra and chemical transformations.

LITERATURE CITED

1. A. A. Grossgeim, The Flora of the Caucasus [in Russian], Vol. 7 (1967), p. 88.
2. A. Z. Abyshev, P. P. Denisenko, D. Z. Abyshev, and Yu. B. Kerimov, Khim. Prir. Soedin., 640 (1977).
3. A. Z. Abyshev, P. P. Denisenko, D. Z. Abyshev, and Yu. B. Kerimov, Farmatsiya, No. 2, 42 (1977).
4. A. Z. Abyshev, I. P. Sidorova, D. Z. Abyshev, et al., Khim. Prir. Soedin., 434 (1982).
5. D. Z. Abyshev, Abstracts of Lectures at the IInd Intercollegiate Conference of Young Scientists and Specialists [in Russian], Perm' (1981), p. 4.
6. A. Z. Abyshev, D. Z. Abyshev, and G. I. D'yachuk, et al., Abstracts of Lectures at the 8th Urals Conference of Pharmacologists [in Russian], Perm' (1980), p. 5.
7. Yu. K. Mel'nik, A. Z. Abyshev, and G. I. D'yachuk, Abstracts of Lectures at a Conference on Current Questions of the Pharmacology of Neurotropic Agents [in Russian], Riga (1981), p. 69.
8. E. Späth, Chem. Ber., 70, 83 (1937).

9. A. Z. Abyshev, P. P. Denisenko, N. P. Kostyuchenko, et al., Khim. Prir. Soedin., 45 (1972).
10. F. Bohlmann, M. Grenz, and C. Zdero, Chem. Ber., 108, 2955 (1975).
11. J. H. Totum and R. E. Berry, Phytochemistry, 18, 500 (1979).
12. G. K. Nikonov, Dokl. Akad. Nauk SSSR, 156, No. 5, 1210 (1964).
13. A. Z. Abyshev and P. P. Denisenko, Khim. Prir. Soedin., 114 (1972).
14. A. Z. Abyshev and I. V. Brodskii, Khim. Prir. Soedin., 574 (1974).
15. N. F. Gashimov, A. Z. Abyshev, A. A. Kagramanov, and L. I. Rozhkova, Khim. Prir. Soedin., 15 (1979).

STRUCTURE AND STEREOCHEMISTRY OF THE COUMARINS OF *Ferula lehmannii*

G. V. Sagitdinova, A. I. Saidkhodzhaev, and V. M. Malikov

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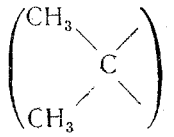
Two new 7-hydroxycoumarins have been isolated from the roots of *Ferula lehmannii* (Lehmann's giant fennel): lehmferidin (I), $C_{24}H_{28}O_4$, M^+ 380, mp 173-174°C, and lehmferin (II), $C_{24}H_{30}O_4$, M^+ 382, mp 118-119°C; and badrakemin (III) has also been identified. The structures and configurations of the asymmetric centers of the new coumarins have been established on the basis of spectral characteristics and conversion into known substances.

From the roots of *Ferula lehmannii* Boiss. (Lehmann's giant fennel) collected in the Taldy-Kurgan province of KazSSR, by column chromatography we have isolated three crystalline substances which were assigned on the basis of their UV spectra to derivatives of 7-hydroxycoumarin: $C_{24}H_{28}O_4$, M^+ 380 (I); $C_{24}H_{30}O_4$, M^+ 382 (II); and $C_{24}H_{30}O_4$, M^+ 382 (III). On acid hydrolysis, all three substances formed umbelliferone (IV). According to their constants and spectral characteristics, substances (I) and (II) differed from known compounds, and we have called them lehmferidin (I) and lehmferin (II).

Substance (III) was identified from its physicochemical constants and IR spectrum as badrakemin [1].

The IR spectrum of substance (I) shows the following absorption bands (cm^{-1}): 3600-3620 (OH), 1730 (C=O of an α-pyrone), 2840-2980,  , 1680 (=), and 1560, 1520, and 1480 (aromatic nucleus).

In the PMR spectrum of (I) there are signals of three methyl groups (figures in ppm): 0.8 (6 H, s) and 1.0 (3 H, s); of a hemihydroxylic proton at 3.41 ppm (1 H, br.s, 1/2 Σ = 8.0 Hz); of the methylene protons of a CH_2—O—Cou grouping at 4.15 ppm (2 H, m); of an exomethylene group at 4.80 and 4.90 ppm (two singlets of 1 H each); of olefinic protons at 5.61 (1 H, d, J = 12 Hz) and 6.12 (1 H, d, J = 12 Hz). In the weak field appear the signals of the protons of the coumarin moiety of the molecule (ppm): 7.51 and 6.14 (doublets, 1 H each, J = 9.5 Hz) — H_4 and H_3; 6.80 (q, 1 H, J_1 = 9.5 and J_2 = 2.5 Hz); 7.34 (d, 1 H, J = 9.5 Hz) and 7.29 (1 H, J = 2.5 Hz) — doublets of H_6, H_5, and H_8, respectively.

The fragmentation of the ions in the mass spectrum of lehmferidin is typical for 7-hydroxycoumarins with an iresane substituent: 380 (M^+), 219 (M — O—Cou), 201 (M — O—Cou — H_2O)$^+$, and 162 (CouOH) [2].

When lehmferidin was acetylated with acetic anhydride in pyridine, a monoacetate (V) was obtained with the formula $C_{26}H_{30}O_5$ in the IR spectrum of which there was no absorption

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