STRUCTURE OF FERULIDIN: A NEW SESQUITERPENE LACTONE

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Recently we reported [1–3] the isolation from the roots of Ferula oopoda (Boiss. et Buhse) Boiss. of two sesquiterpene lactones, badkhysin and ferulin, which have a guaiane carbon skeleton. A third guaianolide, isolated from this plant species, we have called "ferulidin."

The elementary formula of ferulidin, $C_{15}H_{18}O_4$, was calculated on the basis of its IR, UV, and NMR spectra; its mp is 170–172° C. The IR spectrum of the substance (Fig. 1) has bands at (cm^{-1}) 3400 (OH group), 1762 (γ-lactone), 1672 (conjugated ketone group of a five-membered ring), and 1630 and 1615 (double bonds); it does not contain an ester group. The solubility of the lactone on heating in alkaline solutions also shows the presence of a lactone ring. The UV spectrum confirms the presence of a conjugated system (λ_{max} 334 and 254 mμ, log ε 1.81 and 4.02).

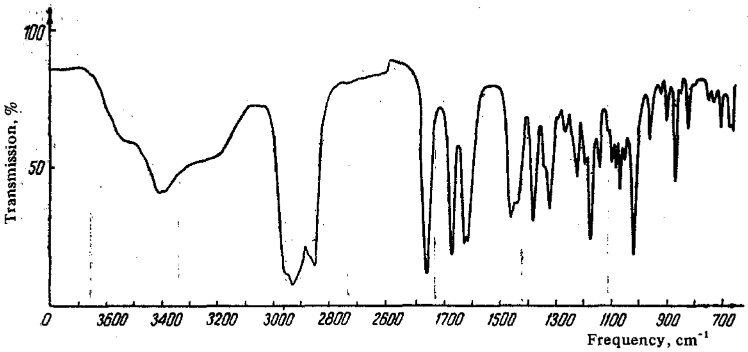

Fig. 1. IR spectrum of ferulidin.

Important information concerning the structure of ferulidin was obtained from its NMR spectrum (Fig. 2). The doublet with a center at 8.77 τ (J = 7 Hz, 3H) observed in the strongfield is due to a methyl group at C_{11}. The six-proton singlet at τ 7.70 shows the presence of two vinyl methyl groups in the investigated compound.

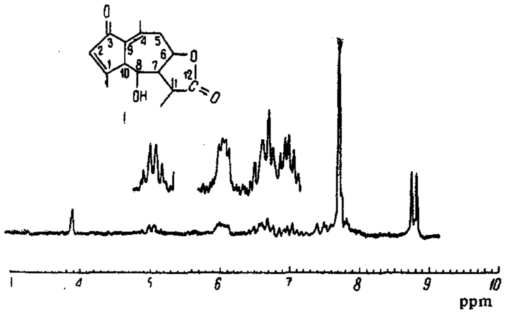

Fig. 2. NMR spectrum of ferulidin.

Thus, of the three methyl groups in the guaiane hydrocarbon skeleton two are located on double bonds. Since the spectrum has only one singlet characteristic for an olefinic proton (τ 3.88, —CH=), whose area is equal to one proton, the ketone group of the five-membered ring may confidently be ascribed to the C_3 position, and the conjugated double bonds to C_1—C_2 and C_4—C_9.

Comparing some information obtained from the interpretation of the IR, UV, and NMR spectra of ferulidin with the corresponding information for badkhysin [1] (table) we may conclude that ferulidin is formed from the badkysin during the treatment of the plant material. If this were correct, then, by analogy, the lactone ring in the molecule of ferulidin would be located at C_7—C_8 and the OH group at C_6.

Table

Compound	CO group, cm^{-1}		Double bonds, cm^{-1}	UV spectrum, λ, $m\mu$	NMR spectrum, τ	
	lactone	ketone			$CH_3-\overset{\vert}{C}=$ at C_1 and C_4	$-CH=$ at C_2
Badkhysin	1768	1678	1640 1610	334, log ϵ 1,74 254, log ϵ 4,12	s 7,7 (6H)	s 3,82
Ferulidin	1762	1672	1630 1615	334, log ϵ 1,81 254, log ϵ 4,02	s 7,7 (6H)	s 3,88

However, an analysis of the signals due to the protons adjacent to the lactone oxygen atom and to the hydroxyl group explain the hypothesis put forward in a different manner.

In the NMR spectrum of ferulidin there is a multiplet at τ 5.05 with an area of one proton. The value of its chemical shift corresponds to the proton of a lactone ring. The nature of the splitting shows interaction with three neighboring protons and it is similar to the signal caused by the proton in the ester group of badkhysin [1]. Consequently, the C_6—C_7 position is proposed for the lactone ring. Thus, the OH group may be present at either C_5 or C_8. In the first case the proton in the OH group would show a doublet, and in the second case a quartet or at least a triplet. In actual fact, the spectrum shows a quartet at τ 6.05 (J_1 = 10 Hz, J_2 = 5 Hz, 1H). This shows that the OH group is located at C_8. If attention is directed to the spin-spin splitting constants of the quartet (H_8) it becomes clear that the proton of the hydroxyl group occupies the trans position (J = 10 Hz) with respect to one of the neighboring protons (H_7) or (H_{10}) and the cis position (J = 5 Hz) with respect to the other.

On the basis of the results obtained we may assume that ferulidin has the structure 8-hydroxy-3-oxoguia-1(2), 4(9)-dien-6, 12-olide (I).

The proposed structure (I) is also confirmed by the results obtained on acetylation. From the reaction mixture a substance with mp 175–176° C was isolated, and its IR and UV spectra agreed completely with the spectra of ferulin [2, 3]. A mixture of these compounds gave no depression of the melting point.

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrophotometer (paraffin oil), the UV spectra on an SF-4a instrument (96% ethanol), and the NMR spectrum on a JNM-4H-100 spectrometer (solution in deuterated chloroform). Tetramethylsilane was used as the internal standard.

Isolation of ferulidin. The roots of Ferula oopoda (0.5 kg) were boiled with an excess of 96% ethanol in a water bath (twice, 2 hr each time). The ethanol was filtered off. Then extraction was carried out with water under similar conditions and the filtered extracts were evaporated to dryness on a water bath. The residue was repeatedly extracted with chloroform. The chloroform extracts were combined, dried over Na_2SO_4, filtered, and distilled. The dark-brown viscous resin was dissolved in 5 ml of chloroform and chromatographed on alumina (column 10 cm high and 2 cm in diameter, activity grade II). Elution was carried out with chloroform (50 ml) and chloroform–ethanol (5 : 1). The fractions eluted with the chloroform–ethanol yielded 0.025 g of a substance with mp 170–172° C (from chloroform–petroleum ether).

Acetylation of ferulidin. A solution of 0.02 g of ferulidin in 2 ml of acetic anhydride was treated with 0.1 g of freshly fused sodium acetate. The mixture was boiled for 30 min, cooled, treated with 100 ml of water, and extracted with chloroform (2 × 50 ml). The combined chloroform extracts were washed with water, dried over Na_2SO_4, and evaporated. The residue was dissolved in chloroform and filtered through a 5-cm layer of alumina (diameter 1.5 cm, activity grade II). This gave a crystalline substance with mp 175–176° C (from aqueous ethanol). A mixture with ferulin gave no depression of the melting point.

CONCLUSIONS

1. From the roots of Ferula oopoda (Boiss. et Buhse) Boiss. a new sesquiterpene lactone $C_{15}H_{18}O_4$ with mp 170–172° C has been isolated; it has been called "ferulidin."

2. We have shown that ferulidin has the structure I.

REFERENCES

1. N. P. Kir'yalov and S. V. Serkerov, KhPS [Chemistry of Natural Compounds], **4**, 341, 1968.
2. S. V. Serkerov, KhPS [Chemistry of Natural Compounds], **6**, 134, 1970.
3. S. V. Serkerov, KhPS [Chemistry of Natural Compounds], **6**, 371, 1970.

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