THE STRUCTURE OF FERUTINOL

A. I. Saidkhodzhaev and G. K. Nikonov

UDC 547.913.5.668:547.587.52

Previously, on the basis of some chemical transformations and spectral characteristics a most probable structure was put forward for ferutinol – an alcohol obtained in the hydrolysis of a number of esters of Ferula: ferutin, ferutinin, and feringin [1-3].

On studying the mass spectra of sesquiterpene compounds of similar type – angrendiol [4, 5] and britanin [6] – it was established that the peak of the molecular ion in them is absent or has an extremely low intensity. This formed the grounds for a revision of the structure of ferutinol.

Rerecordings of its mass spectrum showed that it contained a peak with m/e 238 (4%). Thus, the intense peak with m/e 195 (68%), previously taken as the ion $(M-1)^+$ actually corresponds to the fragment $(M-43)^+$. This conclusion is confirmed by the presence in the spectrum (Fig. 1) of peaks of ions with m/e 220 $(M-H_2O)^+$, 195 (M−43), 177 $(M-43-H_2O)^+$, and 159 $(M-43-2H_2O)^+$, with relative intensities of 48, 68, 90, and 100%, respectively. Consequently, the molecular weight of ferutinol determined previously is erroneous, and its composition is $C_{15}H_{26}O_2$. With such a composition and with one double bond, the substance must have a bicyclic structure.

The IR spectrum of ferutinol (Fig. 2) shows absorption bands characteristic for a hydroxy group (3300-3500 cm^{-1}), an isopropyl group (1170, 1380 cm^{-1}), and a secondary-tertiary double bond (1660, 840 cm^{-1}) [7]. As shown previously, the NMR spectrum of this compound (Fig. 3) contains signals due to a methyl group on a double bond in the 1.76 ppm region, to a tertiary methyl group at 0.94 ppm (s, 3H each), and to two secondary methyls at 0.83 and 0.91 ppm, J = 4 Hz (d, 3H each). The equal spin–spin coupling constants of the protons of the secondary methyl groups, and also the peaks of the ions in the mass spectrum corresponding to the fragments $(M-43)^+$, $(M-43-H_2O)^+$, and $(M-43-2H_2O)^+$ give grounds for assuming that the two secondary methyl groups form part of an isopropyl grouping.

The dehydrogenation of ferutinol with selenium (250-300°C) gave a blue oil consisting of a mixture of two azulenes with R_f 0.62 and 0.72, which were separated on a column of alumina into the two components.

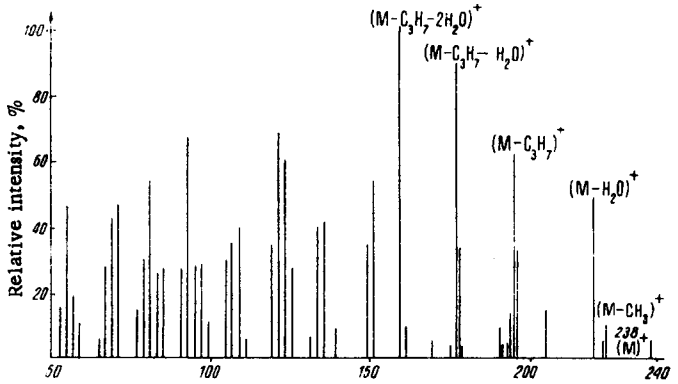


Fig. 1. Mass spectrum of ferutinol.

Order of the Red Banner of Labor Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 166-171, March-April, 1974. Original article submitted February 8, 1973.

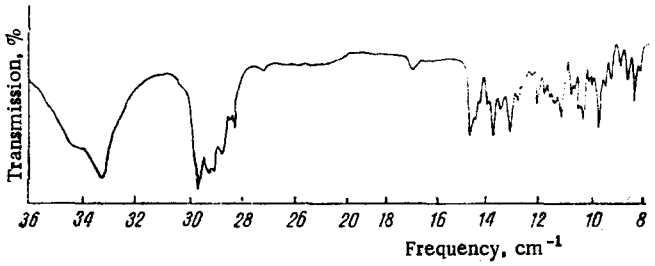
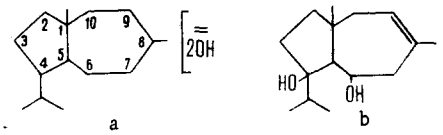


Fig. 2. IR spectrum of ferutinol.

In the visible region, the spectrum of the azulene with R_f 0.62 had absorption bands at 552, 574, 602, 638, 662 and 686 nm, corresponding to the values found for 4,8-dimethylazulene, and the azulene with R_f 0.72-554 had bands at 576, 602, 632, and 660 nm, corresponding to 2,4,8-trimethylazulene. In addition, by means of their UV spectra [8], the substances obtained were shown to be identical with azulenes from daucol and from carotol [9].

These facts permit the conclusion that ferutinol has the carbon skeleton of daucane (a).



a b

In order to establish the structure of ferutinol it was necessary to determine the positions of the double bond and of the two hydroxy groups. It has been shown previously that the hydroxy groups are secondary and tertiary and that ferutinol is esterified at the secondary hydroxyl in ferutin, ferutinin, and feringin. From the comparative constancy of the chemical shifts of the signals of the methyl groups in the NMR spectra of ferutin, ferutinin, ferutinol, and ferutinol acetate, it may be concluded that the secondary hydroxy group is remote from these groups.

The double bond in the ferutinol molecule possesses a secondary-tertiary nature. This follows from the presence in the NMR spectrum of signals of one olefinic proton (5.32 ppm) and of a methyl on a double bond at 1.76 ppm, and also from an absorption band in the IR spectrum at 840 cm^{-1} which is characteristic of a secondary-tertiary double bond. Hence, the double bond may be in one of two possible positions at C_7-C_8 or C_8-C_9.

The hydrogenation of ferutinol gave dihydroferutinol, the IR spectrum of which lacked the absorption of a double bond while in its NMR spectrum the signal of the olefinic proton had disappeared and the signal of the methyl on a double bond had shifted upfield (0.88 ppm) and was split into a doublet ($J = 5.5$ Hz). The oxidation of dihydroferutinol with chromium trioxide in acetic acid led to dihydroferutinone, the IR spectrum of which had an absorption band at 1690 cm^{-1}, which is characteristic for the carbonyl group of a cycloheptanone [6, 7]. This shows that the secondary hydroxy group is located in a seven-membered ring.

The position of the hydroxyl follows from a consideration of the UV and NMR spectra of ferutinol and its derivatives.

The signals of the hemihydroxyl (ferutinol, dihydroferutinol) and geminal (ferutin, ferutinin, feringin, ferutinol acetate) protons appear in the NMR spectra in the form of a triplet with secondary splitting, i.e. they form a four-spin system. Consequently, the geminal proton interacts with three neighboring protons, which is possible only if the secondary hydroxyl is located at C_6 and the double bond at C_8-C_9.

The IR spectrum of ferutinone has a maximum at 240 nm showing the presence of a conjugated keto group in the molecule. This can be explained by the migration of the double bond from the C_8-C_9 to the C_7-C_8 position, since in the IR spectrum of ferutinol monoacetate the absorption band of the carbonyl group is in the 1735 cm^{-1} region, which shows the absence of its conjugation with a double bond.

All that remain for the tertiary hydroxy group are the C_4 and C_5 positions, but the latter is excluded because of the stability of ferutinol to oxidation with periodic acid, i.e. the hydroxy groups in ferutinol do not form a glycol system. Consequently, the tertiary hydroxy group can be located only on C_4.

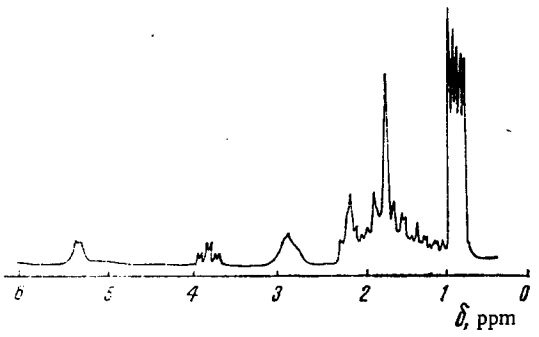
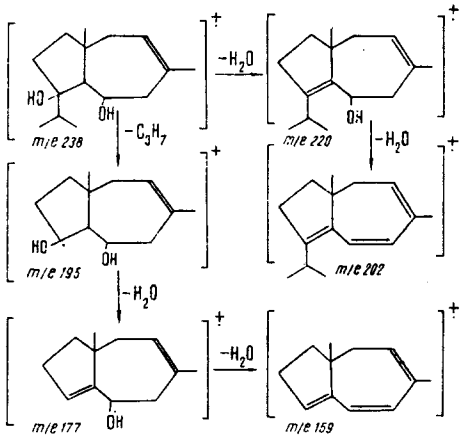


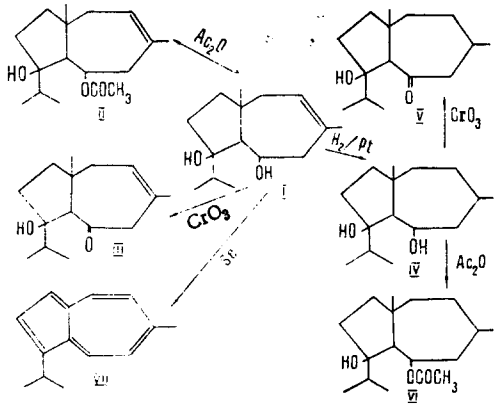
Fig. 3. NMR spectrum of ferutinol.

On the basis of what has been said above, we propose for ferutinol the most probable structure of 4,6-dihydroxydauc-8-ene (b).

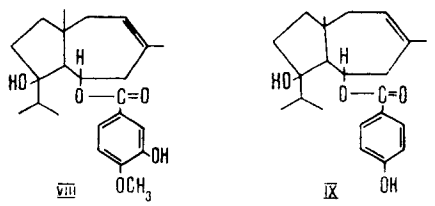
A similar structure has been given for jaeschkeandiol [10], obtained by Indian workers in a study of Ferula jaeschkeana. However, the absence of a detailed publication does not permit us to answer the question of whether these substances are identical or are isomers. It is not excluded that the chimgandiol described in the literature [11] also has a similar structure. The proposed structure agrees completely with the features of the mass spectra of ferutinol and of its acyl derivatives (ferutinol acetate, ferutin, ferutinin).



The transformations described may be represented in the following way:



Then ferutin (VIII) and ferutinin (IX) have the following structures:



EXPERIMENTAL

The conditions under which the spectra were taken have been reported previously [1].

Hydrogenation of Ferutinol. Ferutinol (0.15 g) was hydrogenated in the presence of 0.05 g of Adams platinum oxide in acetic acid. It absorbed 15.2 ml of hydrogen (1 mole).

Dihydroferutinol (IV) was isolated from the reaction mixture by the usual method. Vitreous substance with R_f 0.6.

Acetylation of Dihydroferutinol. The substance (0.1 g) was acetylated with acetic anhydride in pyridine. After the removal of the reactant, the acetyl derivative was extracted with ether. The ether was distilled off, and the residue consisted of (VI) in the form of a colorless powder with R_f 0.77. NMR spectrum: three-proton singlet at 1.8 ppm (CH_3-COO).

Oxidation of Dihydroferutinol. A solution of 0.1 g of the substance in 4 ml of 80% acetic acid was treated with 0.1 g of chromium trioxide in 6 ml of acetic acid. The mixture was heated in the water bath for 1 h.

Dihydroferutinone (V) was obtained in the usual way, R_f 0.51. IR spectrum: 1690 cm^{-1} (cycloheptanone).

Oxidation of Ferutinol. As described above, 0.2 g of ferutinol was oxidized with 0.2 g of chromium trioxide in 80% acetic acid. The reaction product (III) was isolated in the usual way. Oily substance with R_f 0.71.

Acetylation of Ferutinol. The substance (0.15 g) was acetylated with acetic anhydride in pyridine. The reaction product (II) was obtained in the usual way. Mp 75-76°C. IR spectrum: 1735 cm^{-1}. NMR spectrum: 1.9 ppm (CH_3COO).

Dehydrogenation of Ferutinol. Ferutinol (0.5 g) was dehydrogenated with 1.0 g of selenium at 250-300°C for 2 h. The reaction product was dissolved in petroleum ether and the solution was filtered. After concentration, the azulenes were passed through a column (h = 10 cm, d = 1.5 cm) containing alumina (activity grade II) and were eluted with petroleum ether. On TLC (silica gel; petroleum ether system) the eluent showed two spots, with R_f 0.62 and 0.72. The solvent was driven off and the residue was treated with 30 ml of concentrated hydrochloric acid, diluted with water, and extracted with ether. The ethereal extract was washed with water, dried over Na_2SO_4, and distilled. The residue was rechromatographed on a column (h = 50, d = 1.5 cm) of alumina (activity grade II) and washed with petroleum ether. The substances with R_f 0.72 and 0.62 were separated.

CONCLUSIONS

On the basis of chemical transformations and spectral characteristics, the structure of ferutinol has been corrected; it is 4,6-dihydroxydauc-8-ene.

LITERATURE CITED

1. A. I. Saidkhodzhaev and G. K. Nikonov, Khim. Prirodn. Soedin., 559 (1972).
2. A. I. Saidkhodzhaev and G. K. Nikonov, Khim. Prirodn. Soedin., 28 (1973).
3. Kh. M. Kamilov and G. K. Nikonov, Khim. Prirodn. Soedin., 718 (1972).
4. T. Kh. Khasanov, A. I. Saidkhodzhaev, and G. K. Nikonov, Khim. Prirodn. Soedin., 807 (1972).
5. A. Sh. Kadyrov, T. Kh. Khasanov, A. I. Saidkhodzhaev, and G. K. Nikonov, Khim. Prirodn. Soedin., 808 (1972).
6. P. V. Chugunov, V. I. Sheichenko, A. I. Ban'kovskii, and K. S. Rybalko, Khim. Prirodn. Soedin., 276 (1972).
7. L. Bellamy, Infrared Spectra of Complex Molecules, 2nd ed., Butterworth, London (1958).
8. P. A. Plattner, Helv. Chim. Acta, 24, B2, 283E (1941).
9. V. Sykora, L. Novotny, M. Holub, V. Herout, and F. Šorm, Collection Czech. Chem. Commun., 26, No. 3, 788 (1961).
10. M. S. Sriraman, B. A. Nagasampagi, R. S. Pandey, and Such Dev, 8th International Symposium on the Chemistry of Natural Compounds, Delhi (1972), p. 254.
11. N. P. Kir'yalov, Tr. BIN SSSR, Ser. 5, No. 15, 129 (1968).