THE STRUCTURES OF FEROCIN AND FEROCININ

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The isolation from the roots of *Ferula ceratophylla* Rgl. et Schmalh. of ferocin, $C_{22}H_{28}O_3$ (I), and ferocinin, $C_{23}H_{30}O_4$ (II) — new esters of the sesquiterpene alcohol fecerol, $C_{15}H_{24}O$ (III), with p-hydroxybenzoic and vanillic acids, respectively — has been reported previously [1]. We now give proofs of the structures of (I-III).

The UV spectrum of (III) has a maximum at 244 nm (log ε 4.44), which is characteristic for conjugated dienes, and the IR spectrum has absorption bands at 3200-3500 cm^{-1} (OH), 3080, 1648, 910 cm^{-1} $>C=CH_2$), 1600, 970 cm^{-1} ($-\underset{H}{C}=C-$), and 895 cm^{-1} ($-CH=\underset{H}{C}-$) [2, 3].

In the PMR spectrum of fecerol (Table 1), the following signals appear in the region of olefinic protons: doublets at 5.32 and 5.74 ppm (1 H each, J = 16 Hz), relating to the protons of a trans-disubstituted double bond, doublets at 4.72 and 4.78 ppm (1 H each, J = 2 Hz), due to the protons on an exocyclic double bond, and a triplet at 5.17 ppm (1 H, $J_1 = J_2 = 7.5$ Hz) due to an olefinic proton on a trisubstituted double bond. In addition, in the strong-field region the signal of a vinyl methyl group is observed — a singlet at 1.45 ppm (3 H).

The hydrogenation of fecerol in the presence of a platinum catalyst in acetic acid led to the absorption of three moles of hydrogen and gave the hexahydro derivative $C_{15}H_{30}O$, M^+ 226, (V), which agrees with the spectral indications of the presence of three double bonds.

In the PMR spectrum of ferocin, signals from the protons of methyl groups are observed at 1.00 and 1.07 ppm (s, 3 H each), and in the spectrum of ferocinin at 0.90 and 1.07 ppm (s, 3 H each). The change in the difference between the chemical shifts (CS's) of the signals of these methyl groups shows that they are tertiary. This is confirmed by the PMR spectrum of the ketone derivative of fecerol in which the two methyls appear in the form of a six-proton singlet at 1.08 (6 H), i.e., they do not undergo vicinal spin—spin splitting.

With the composition $C_{15}H_{24}O$ and the presence of three double bonds, when the nature of the methyl groups is taken into account fecerol most probably has the skeleton of humulane (IV). Biogenetic considerations permit the conclusion that the double bonds in (III) can occupy one of two possible positions — (IVa) and (IVb), the latter of which corresponds to their arrangement in γ-humulene [2]. A comparison of the PMR spectra of fecerol and γ-humulene (see Table 1) permits an unambiguous choice in favor of (IVb). Thus, the double bonds in fecerol are present at C_2—C_3, C_7—C_8, and C_4—C_{14}.

Five positions remain possible for the hydroxy group: C_5, C_6, C_9, C_{10}, and C_{11}. The position at C_6 is excluded because of the multiplicity of the signal of the olefinic proton at C_7. The oxidation of fecerol with chromium trioxide in pyridine [4] formed the ketone (VI), M^+ 218, the UV spectrum of which lacked the absorption characteristic for an α,β-unsaturated ketone. The PMR spectrum of (VI) likewise showed no appreciable shift of the signals of the olefinic protons. Consequently, the hydroxy group cannot be at C_5 or C_9.

The hemihydroxylic proton appears in the PMR spectrum of fecerol in the form of a multiplet at 3.48 ppm ($1/2\Sigma = 18$ Hz), i.e., this proton forms a multispin system with the neighboring protons. This is possible only if the hydroxyl is present at C_{10}. This position is also confirmed by the fact that in the PMR spectrum of the ketone (VI) the methylene protons at C_9 give a signal in the form of a narrow singlet at 2.79 ppm (2 H). Furthermore, in the mass spectrum of the D analog of the ketone of the hexahydro derivative of fecerol (VII), M^+ 224, a displacement of the peak of the molecular ion by four units is observed.

Thus, fecerol has the structure of 1,1,8-trimethylcycloundeca-2,4(14),7-trien-10-ol, and

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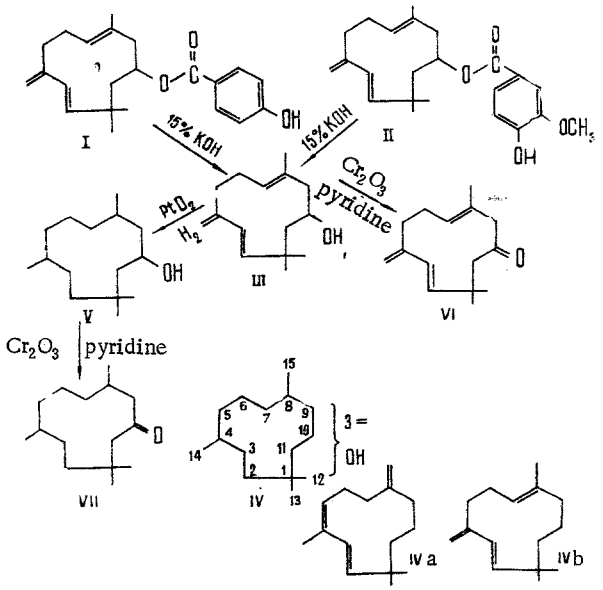
TABLE 1. Chemical Shifts (ppm) and Spin–Spin Coupling Constants (Hz) of the Signals of Compounds (I-IV and VI)

Substance	C_2–H	C_3–H	C_1=CH_2	C_7–H	C_{10}H	C_8–CH_3	C_1–2CH_3
Ferocin (I)*	5,81d J=16	5,34d J=16	4,80 d 4,86 d J=2	5,34t $J_1=J_2=7,5$	4,80 m	1,55s 3H	1,00; 1,07s 3H each
Ferocinin* (II)	5,94 d J=16	5,40 d J=16	4,82 br.s	5,28t $J_1=J_2=7,5$	5,1 m	1,53s 3H	0,90; 1,04s 3H each
Fecerol (III)	5,74d J=16	5,32d J=16	4,72d 4,82d J=2	5,17t $J_1=J_2=7,5$	3,48m $\frac{1}{2}\sum=18$	1,45s 3H	0,97:1,07 s 3H each
γ-Humulene (IVb)	5,79d J=16	5,46 d J=16	4,73d 4,81d J=2	5,21t $J_1=J_2=7,5$	—	1,41s 3H	0,86; s 6H
Ketone from fecerol	5,80d J=16	5,44 d J=16	4,74 d 4,83d J=2	5,18 t $J_1=J_2=7,5$	—	1,38s 3H	1,08s 6H

*The spectra of compounds (I) and (II) also contain the signals from the protons of p-hydroxybenzoic and vanillic acid residues, respectively; s) singlet; d) doublet; t) triplet; m) multiplet.

ferocin is p-hydroxybenzoylfecerol and ferocinin is vanilloylfecerol. The transformations described above can be represented by the following scheme:



EXPERIMENTAL

The UV spectra were taken on a Hitachi spectrophotometer (in ethanol), the IR spectra on a UR-20 instrument (tablets with KBr, and films), the mass spectra on an MKh-1303 mass spectrometer, and the PMR spectra on a JNM-4H 100/100 MHz instrument ($CDCl_3$ and CCl_4). The chemical shifts are given in the δ scale from the signal of HMDS taken as zero.

The purity of the substances was checked and the course of the reactions was monitored by TLC on Silufol (chloroform solution), the chromogenic agents being a 1% solution of vanillin in concentrated sulfuric acid and a 3% solution of potassium permanganate.

Isolation of Ferocinin (II). The dried and comminuted roots (1.2 kg) were extracted with ethanol (3 × 6 liters). The ethanol was distilled off and the residue was diluted with water to a volume of 1.5 liters and was treated with ether (3 × 500 ml). The ethereal ex-

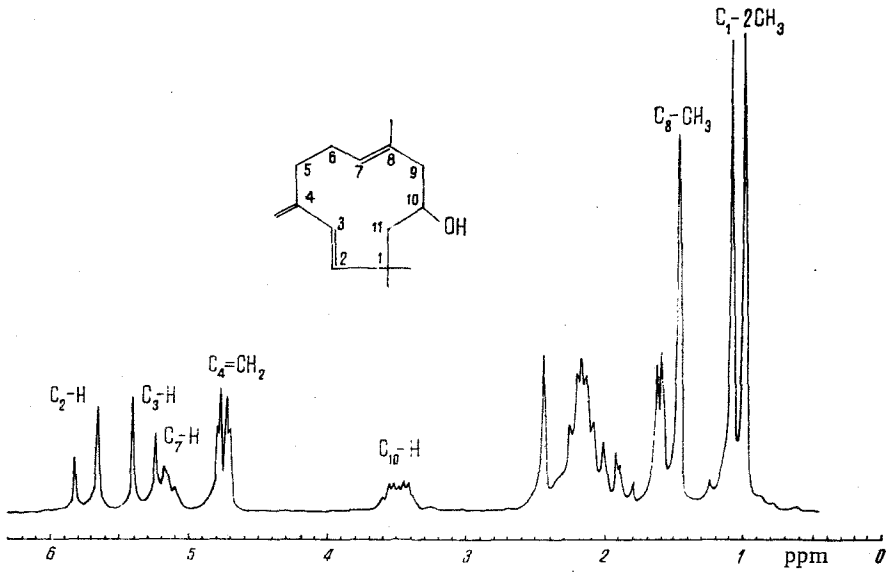


Fig. 1. PMR spectrum of fecerol.

tracts were combined and dried, and the ether was distilled off to give 150 g of a resinous residue, 75 g of which was dissolved in ether and was treated with 5% sodium carbonate solution (5 × 400 ml) and 5% caustic soda solution (6 × 400 ml). The caustic soda extract was brought to a weakly acid reaction and was treated with ether, and the ether was distilled off to give 34 g of a viscous amber-colored residue (phenolic fraction).

The phenolic fraction (24 g) was transferred to a column of silica gel (3.5 × 105 cm) and the substances were eluted with the hexane–benzene (2:1) system, 400-ml fractions being collected. Fractions 15-33 were combined, the solvent was distilled off to dryness, the residue was dissolved in hexane, and 2.4 g of colorless crystals, $C_{23}H_{30}O_4$, mp 107-108°C (hexane), M^+ 370, $[\alpha]_D^{20}$ — 197° (c 1.0; benzene), R_f 0.5, was obtained.

Isolation of Ferocin (I). When the column was then washed with the hexane–benzene (1:1) system, fractions 61-65 yielded 1.6 g of a colorless crystalline substance, $C_{22}H_{28}O_3$, with mp 127-128°C (hexane), $[\alpha]_D^{20}$ — 200° (c 1.0; benzene), R_f 0.35.

Alkaline Hydrolysis of Ferocinin. A solution of 1.5 g of the substance in 15 ml of 15% aqueous methanolic caustic soda was heated in the water bath for 7 h. After the end of the reaction, the hydrolyzate was diluted with water and extracted with ether (5 × 100 ml), and the ethereal solution was washed with water, dried, and evaporated. The oily residue (neutral fraction) (0.8 g) was passed through a column of silica gel (2 × 44 cm), the substance being eluted with benzene. This gave 0.65 g of colorless crystals of (III) with mp 82-83°C, R_f 0.4.

After the ether treatment, the hydrolyzate was acidified with 5% sulfuric acid and was again extracted with ether. The ethereal extract was washed with water and dried, and the ether was distilled off. The residue was recrystallized from aqueous ethanol, giving 0.55 g of a substance with mp 206-207°C. It was identified as vanillic acid by a mixed melting point and a comparison of IR spectra.

The alkaline hydrolysis of ferocin was performed similarly. From 1.2 g of ferocin was obtained 0.61 g of fecerol and 0.38 of an acid with mp 212-213°C identified as p-hydroxybenzoic.

Hydrogenation of Fecerol. 0.5 g of (III) was hydrogenated in 8 ml of acetic acid in the presence of 100 mg of PtO_2 with shaking for 6 h. After the separation of the catalyst the solvent was distilled off in vacuum, giving 0.495 g of an almost colorless oily product with M^+ 226 (hexahydrofecerol (V)).

Oxidation of Hexahydrofecerol. A solution of 0.3 g of (V) in 5 ml of anhydrous pyridine

was treated with a solution of 0.3 g of chromium trioxide in 8 ml of pyridine, and the mixture was left at room temperature for a week. Then it was poured into 200 ml of cooled 15% sulfuric acid and was treated with hexane—ether (2:1; 3 × 70 ml). The residue obtained after washing and the distillation of the solvent was chromatographed on a column of silica gel (2 × 20 cm). The column was washed with the benzene—hexane (1:1) system. Fractions 4-6 were combined and evaporated in vacuum to give 0.05 g of the ketone (VI), R_f 0.73 (revealed with 2,4-dinitrophenylhydrazine).

Oxidation of Fecerol. Compound (III) (0.5 g) was oxidized with chromium trioxide (0.5 g) in 15 ml of pyridine with stirring for 6 h. The reaction mixture was treated in the manner described above. The residue after the distillation of the solvent was chromatographed on a column of silica gel treated with 5% $AgNO_3$ solution (2 × 15 cm). Elution was performed with benzene. Fractions 3-10 were combined and evaporated in vacuum, and the residue was crystallized from hexane giving 0.15 g of the ketone (VI) with mp 76-77°C, R_f 0.7.

SUMMARY

Ferocin and ferocinin — esters of the new sesquiterpene alcohol fecerol with p-hydroxybenzoic and vanillic acids, respectively — have been isolated from the roots of *Ferula ceratophylla*.

On the basis of spectral characteristics and chemical transformations, the structure of 1,1,8-trimethylcycloundeca-2,4(14),7-trien-10-ol is proposed for fecerol.

LITERATURE CITED

1. L. A. Golovina and G. K. Nikonov, Khim. Prirodn. Soedin., 707 (1977).
2. L. A. Smedman, E. Zavarin, and R. Teranishi, Phytochemistry, 8, 1457 (1969).
3. J. Jano and T. Nishijama, Photochemistry, 13, 1207 (1974).
4. G. J. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, J. Am. Chem. Soc., 75, 422 (1953).

A NEW LACTONE, ISORIDENTIN, FROM *Achillea biebersteinii*

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Sesquiterpene lactones (I), (II), and (III), isolated from *Achillea biebersteinii*, have been identified by spectral characteristics and chemical transformations as rupicolins A and B and artecalin, respectively [1, 2].

A fourth lactone with the composition $C_{15}H_{20}O_4$, mp 197-199°C, $[\alpha]_D^{22}$ + 181° (c 0.46; methanol) has proved to be new and has been called isoridentin (IV). It is soluble in ethyl acetate and ethanol.

The PMR spectrum of isoridentin taken in deuteropyridine showed the following characteristic signals: singlet at 1.83 ppm (H_3C-C=C-); triplet at 4.42 ppm (^3J 9.8 Hz each — lactone proton); singlets at 4.80 and 5.21 ppm (H_2C=C-); doublets at 5.29 and 6.12 ppm (exomethylene group conjugated with a lactone carbonyl); multiplets with broadened lines at 4.19 and 4.4 ppm (protons located geminally with respect to hydroxy groups); and doublets at 6.19 and 6.60 ppm (protons of hydroxy groups). Consequently, there are three double bonds in (IV). The elementary composition given and the results of a study of the PMR spectrum of the lactone show that it belongs to the sesquiterpene lactones of the germacrane series.

The presence in the isoridentin molecule of two secondary hydroxy groups was also shown by the preparation of a diacetyl derivative (V), the IR spectrum of which had the characteristic bands of the vibrations of an ester group at 1740 and 1240 cm^{-1}.

The hydrogenation of (IV) with $NaBH_4$ gave dihydroisoridentin (VI), $C_{15}H_{22}O_4$, mp 187-

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