LITERATURE CITED

1. S. M. Adekenov and A. D. Kagarlitskii, The Chemistry of the Sesquiterpene Lactones [in Russian], Bylym, Alma-Ata (1990).
2. J. M. Cassady, M. F. Bean, J. L. McLaughlin, and Y. Aynehchi, Experientia, 40, 930-931 (1984).
3. M. N. Mukhametzhanov, V. I. Sheichenko, K. S. Rybalko, and D. A. Pakaln, Khim. Prir. Soedin., No. 2, 125 (1969).
4. F. C. Seaman, Bot. Rev., 48, No. 2, 121-551 (1982).
5. F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, J. Chem. Soc. Perkin Trans. II, S1 (1987).
6. Z. Samek and J. Harmatha, Collect. Czech. Chem. Commun., 43, 2779 (1978).
7. M. J. Bovill, P. J. Cox, P. D. Cradwick, M. H. Guy, G. A. Sim, and D. N. J. White, Acta Crystallogr., B32, 3203 (1976).
8. G. Appendino, G. H. Nano, M. Calleri, and G. Chiari, Gazz. Chim. Ital., 116, 57 (1986).
9. W. H. Watson and V. Zabel, Acta Crystallogr., B38, 834 (1982).
10. W. Herz, J. S. Prasad, and J. F. Blount, J. Org. Chem., 47, 3991 (1982).
11. R. G. Gerr, A. I. Yanovskii, and Yu. T. Struchkov, Kristallografiya, 28, 1029 (1983).

STRUCTURE OF A NEW PHENOL ALDEHYDE FROM THE LEAVES OF *Eucalyptus viminalis*

A. A. Savina, V. F. Zakharov, and N. S. Tsybul'ko

UDC 547.56+583.883

A new terpenoid phenol aldehyde has been isolated from an alcoholic extract of the leaves of the ribbon eucalyptus by column chromatography on silica gel, and on the basis of the results of ^1H and ^{13}C NMR spectroscopy and mass spectrometry the structure of 4-[1-(3,5-diformyl-2,4,6-trihydroxyphenyl)-3-methylbutyl]-1edol is proposed for it. The relative configurations of the substituents in the terpenoid moiety of the molecule have been determined.

Continuing a chemical study of the leaves of the ribbon eucalyptus [1, 2], we have isolated a new compound, euvimal-1, with the composition $C_{28}H_{40}O_6$, mp 198-199°C, which, on the basis of its spectral characteristics, has been assigned to the euglobals – terpenoid phenol aldehydes of the phloroglucinol series. These compounds, which have the chromophoric fragment of diformylphloroglucinol, have been isolated previously from the Tasmanian blue eucalyptus [3]. The nature of the UV spectrum of euvimal-1 (λ_{max}^{EtOH,H^+} 278, 344 nm, ε 61562, 7646) is typical for the euglobals. The IR spectrum (ν 1630 cm^{-1}), the PMR spectrum (10.12, 10.20 ppm), and the ^{13}C NMR spectrum (191.61 and 192.82 ppm) confirmed the presence of two aldehyde groups in the molecule. Singlets at 13.4 and 13.7 ppm and a broad signal at 6.4 ppm (PMR, $CDCl_3$) were due to two chelated and one free phenolic hydroxyls.

The positions of the signals of the carbon atoms of the aromatic ring [107.80, 106.88, 106.93 (C-1, C-3, and C-5) and 171.51, 171.83, and 172.68 (C-2, C-4, and C-6)] also agreed with the type of substitution and the nature of the substituents characteristic of the euglobals [4, 5] and the robustadiols isolated from *Eucalyptus robusta* [6]. The peak of the molecular ion (M^+ 472) showed that the terpenoid moiety of the molecule consisted of four isoprene units.

A peak with m/z 251 (21.1%) is characteristic for the euglobals [4, 5]. It is due to ion A, which consists of the aromatic ring with one isopentyl residue. The further dissociative fragmentation of the ion took place with the elimination of an isobutyl fragment

All-Union Scientific-Research Institute of Medicinal Plants and Production Association, Moscow. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 789-795, November-December, 1991. Original article submitted February 11, 1991; revision submitted June 26, 1991.

 0009-3130/91/2706-0696$12.50

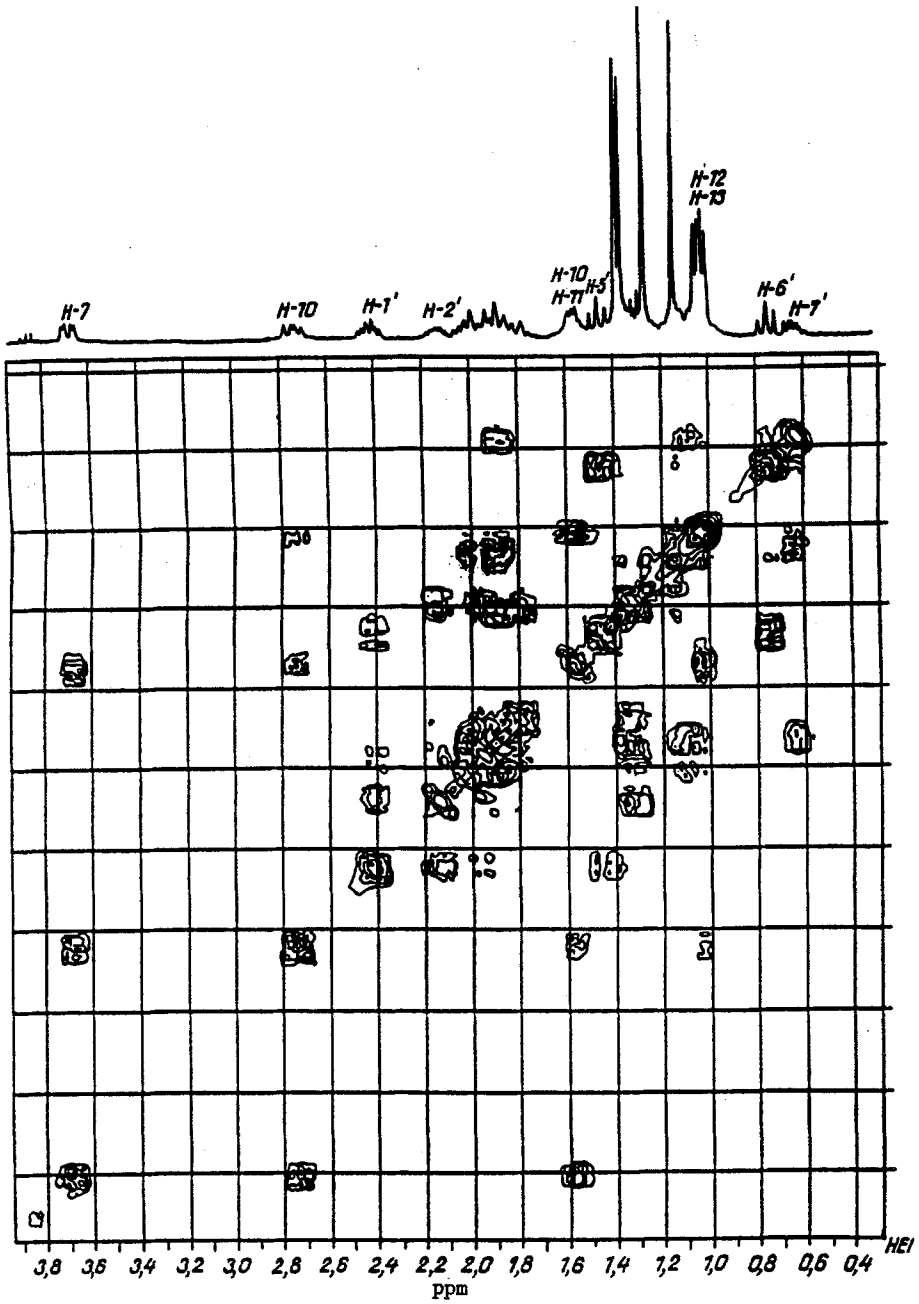
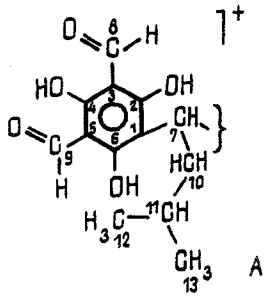


Fig. 1. Two-dimensional COSY H, H spectrum of euvimal-1 (300 MHz, C_5D_5N).

and the formation of an ion with m/z 195 (43.4%) which was confirmed by the peak of a metastable ion with m/z 152*. The PMR spectrum (C_5D_5N) also confirmed the structure of the isopentyl fragment: 3.70 ppm, 1H, dd, J_1 = 12.5 Hz, J_2 = 4.4 Hz, (H-7); 2.76 ppm., 1H, dd, J_1 = 12.5 Hz, J_2 = 9.7 Hz (H-10); 1.58 ppm, (dd, J_1 = 9.7 Hz, J_2 = 4.4 Hz) + 1.60 ppm, m 2H (h-10, H-11); 1.04, 1.12 each 3H, d, 6.0 Hz (H-12, H-13). The parameters of the signals of the protons at C-7, C-12, and C-13 agreed with those given in the literature [2, 4]. The assignment of the signals of the protons at C-10 and C-11 followed from the COSY H, H spectrum (Fig. 1). (See scheme on following page.)

The mass spectrum contained the peak of an ion with m/z 203 (100%, $C_{15}H_{23}$) which is characteristic for euglobals constructed from four isoprene units. This ion could be formed by two pathways. The first pathway is the elimination of water from the molecular ion M^+ 472, followed by the breakdown on the dehydrated product (m/z 454) into two fragments phenolic (m/z 251) and terpenoid (m/z 203).

By the second pathway, in the first stage of fragmentation the molecular ion M^+ 472 breaks down into phenolic (m/z 251) and terpenoid (m/z 221) fragments with the elimination



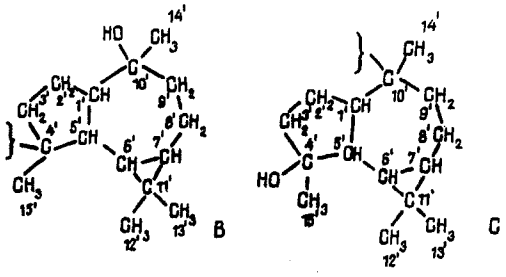
A

of water from the latter. The realization of the second fragmentation pathway and, consequently, of the position of the sixth oxygen function in the form of the hydroxyl in the terpenoid part of the molecule was confirmed by the presence in the mass spectrum of the metastable peak with m/z 186^+. According to its elementary composition ($C_{15}H_{25}O$) and the absence from the PMR spectrum of the substance of the signals of olefinic protons, this terpenoid part of the molecule was tricyclic. It contained four CH_3 groups (3-H singlets at 1.14, 1.27, 1.38, and 1.40 ppm in the PMR spectrum, C_5D_5N) bound to three quaternary carbon atoms (19.04, 49.51 and 74.45 ppm in the ^{13}C NMR spectrum).

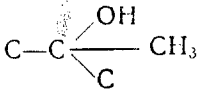
A singlet at 19.04 ppm was due to the carbon atoms of a cyclopropane ring linked with two CH_3 groups. The two methine protons of the cyclopropane ring were responsible for a triplet at 0.74 ppm ($J_1 = J_2 = 9.9$ Hz) and a triplet of doublets at 0.63 ppm ($J_1 = J_2 = 9.9$ Hz $J_3 = 6.0$ Hz; C_5D_5N, PMR spectrum). The multiplicities of the signals showed that one methine group of the cyclopropane ring was connected, in its turn, with a methine group and the other with a methylene group.

Spin-spin coupling between the protons of a methine group of the cyclopropane ring and a methine group in the α-position to it (triplet at 1.47 ppm, $J_1 = J_2 = 9.5$ Hz) was confirmed by double resonance and the COSY H, H PMR spectrum. It also followed from the latter (see Fig. 1) that the α-methine group was linked to a methine group in the β-position with respect to the cyclopropane ring (sextet at 2.40 ppm, $J_1 = J_2 = 9.9$ Hz, $J_3 = 6.0$ Hz.

In view of the presence in the cyclic terpenoid part of the molecule of another two quaternary carbons and two tertiary methyl groups, and also four out of the five methylene groups of the molecules (20.44, 24.61, 35.67, 39.97, and 44.76 ppm in the ^{13}C spectrum) it is possible to propose for it two variants of structures (B and C) with a guaiane skeleton and two variants at the position of the tertiary hydroxy group. The values of the SSCCs between H-1' and the methylene protons at C-2' (9.9 Hz and 6.0 Hz) showed that the methine and methylene protons belonged to a 5-membered ring. The equality of $J_{6',7''}$, $J_{5',6'}$, and $J_{5',1'}$ (9.9 Hz) indicated the cis-linkage of the 5-membered and 7-membered rings (corresponding dihedral angles amount to ~0, 180°, and 0°).



B C

As shown previously [7], in an acid medium terpenoid compounds with the fragment  undergo dehydration and prototropic rearrangement with the formation of an endocyclic double bond. Under these conditions the variant with the formation of the less substituted endocyclic double bond is formed. When euvimal-1 was treated with concentrated trifluoroacetic acid (TFA) we isolated a substance the PMR spectrum of which ($CDCl_3$) contained a broadened one-proton signal of an olefinic proton at 5.35 ppm the half-width ($W_{1/2}$) of

which amounted to 12.5 Hz. According to the literature [8], the $W_{1/2}$ value of the signal of an olefinic proton on a trisubstituted double bond in a five-membered ring of a guaiane system amounts to 5-7 Hz. This value agrees with the size of the dihedral angles between the H-3' and each of the H-2' atoms (60°).

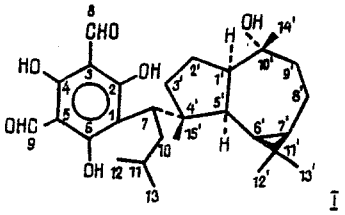
If the hydroxy group were attached to C-10' and the reaction had led to the formation of an endocyclic bond between C-10' and C-9', the dihedral angles between H-9' and each of the H-8' atoms would have amounted to ~40 and ~160°. In this case, the $W_{1/2}$ value of the olefinic proton should be about 12 Hz [9], as was observed for the product of the interaction of euvimal-1 with TFA. Consequently, structure B is more probable for the cyclic terpenoid moiety of the euvimal-1 molecule.

The considerable downfield shift of the signal of the methine proton at C-1' in C_5D_5N solution (2.40 ppm), due to the closeness of an oxygen atom, confirmed this variant of the structure. The methine group of euvimal-1 geminal to the hydroxyl experiences additional screening, since the signals of all the tertiary CH_3 groups lie in the 1.08-1.15 ppm region (PMR, $CDCl_3$). According to the literature [10], such methyl groups resonate at 1.3-1.6 ppm.

If the tertiary hydroxyls were located at C-10', such a screening factor for the CH_3 group would be the cyclopropane ring in the case of the trans position of the CH group in relation to the proton at C-1'. For a methyl group at C-4', the trans position with respect to the protons at C-1' and C-5', which causes less steric interaction between cyclopropane and arylisopentyl fragments, is most probable.

A convincing argument in favor of the structure under discussion for euvimal-1 is the presence of a response of the H-5' signal in the spectrum on irradiation of the H-7 signal in a NOE experiment. This effect is possible at a definite rotation around the C_4'-C_7 bond only in the case of the cis-arrangement of the H-5' proton and fragment A of the molecule (the distance between H-5' and H-7 being ~2 Å).

Euvimal-1 has the most probable structure (I)



I

A feature of the PMR spectrum of (I) in C_5D_5N is the considerable difference in the chemical shifts of the signals of the protons at C-10 (1.60 and 2.80 ppm) and the absence of spin-spin coupling between each of these protons and H-11 (COSY H, H PMR spectrum; Fig. 1). The first effect is due to descreening by the anisotropic influence of the oxygen of the chelated hydroxyl and the aromatic ring on one of the methylene protons with hindered rotation around the C-2—C-1 and also the C-7—C-10 bonds. The second effect is caused by the coincidence of the chemical shifts of one of the protons at C-10 and H-11 (1.58, 1.60 ppm) and, for the second signal, that position of the sterically hindered substituents at C-7 when the torsional angle between H-10 and H-11 is close to 90°.

Also unusual is the ratio of the absolute magnitudes of the vicinal and geminal constants ($J_{7,10}$ = 12.5 Hz; $J_{10,10}$ = 9.7 Hz). The assignment of the signals at 3.70 and 2.73 ppm to the vicinal protons (H-7 and H-10, respectively) and not to the geminal protons was confirmed by the absence of a response of either of these signals when the other was irradiated (PMR spectrum, NOE). Conversely, the very strong interaction of the 2.76 and 1.58 ppm signals showed the geminal character of the protons causing them. the value of the vicinal SSCC of 12.5 Hz and the absence of an Overhauser effect is connected with the maximum value of the dihedral angle between H-7 and H-10, i.e., a transoid conformation. The rigidity of the conformation of the isopentyl fragment of the (I) molecule because of the influence of the voluminous substituents can also explain the long-range spin-coupling through four bonds between one of the methylene protons at C-10 and one of the CH_3 groups (COSY H, H PMR spectrum; Fig. 1). A similar situation has been reported in [11] for a

1,2-dibromoisobutyrate and has been explained by the magnitude of the dihedral angle between the directions of the two C–H bonds.

Euvimal-1, like other euglobals, is a fairly strong acid because of the electron-accepting influence of aldehyde groups in the ortho position with respect to phenolic hydroxyls. The high degree of dissociation is shown by a comparison of the UV spectra of the substance measured in 95% ethanol without acidification and with acidification. In order to suppress dissociation, the UV spectrum of the substance must be measured in acidified alcohol.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were obtained on a Bruker WM-300 instrument in $CDCl_3$ and C_5D_5N solutions, and mass spectra on a Varian MAT CH-8 instrument with electron (70 eV) ionization at an inlet temperature of 120°C. UV spectra were measured in acidified alcohol (1 ml of 1% HCL: 100 ml of 95% alcohol) on a Specord M-40 instrument.

The monitoring of the isolation of the phenolic components was performed by the TLC method in $HCOOH–CH_3OH–CHCl_3$ (1:1:25) system on Silufol plates with a 1% alcoholic solution of ferric chloride as the revealing agent.

Isolation of Euvimal-1. Ribbon eucalyptus leaves (1.0 kg) were extracted three times with 95% alcohol at a ratio of 1:7. The combined extracts were evaporated to dryness giving a total of 160.0 g of extractive substances. Of these, 20.0 g was dissolved in 100 g of alcohol and the solution was mixed with 100.0 g of silica gel 40/100 μ, and the mixture was dried and was deposited on a column with a diameter of 8 cm filled with 1.2 kg of silica gel 40/100 μ in chloroform. Elution was performed with chloroform, and fractions with volumes of 3.0 liters (1), 2.0 liters (2), and 1.0 liter (3-9) were collected.

Beginning from fraction 10, elution was carried out with chloroform–methanol (4:1) with the collection of 1.0-liter fractions. Fractions 10-15, containing the bulk of the phenolic components freed from resinous substances, were combined, and the solvent was evaporated. The residue was treated with chloroform–water (1:1) (3 × 100 ml). The chloroform extracts were treated with a 2% aqueous solution of sodium bicarbonate (3 × 50 ml). The bicarbonate extracts were acidified with 10% aqueous HCl to pH 1. The precipitate that deposited was washed with distilled weater and dried. The weight of the residue was 90 mg. A product prepared in a similar way (1.0 g) was rechromatographed on a column with a diameter of 1.8 cm filled with 110 mg of silica gel 40/100 μ in chloroform. the mixture of substances to be separated was deposited on the sorbent in the form of a 1:5 chloroform solution. Elution was carried out with acetic acid–chloroform–methanol (1:25:1), with the collection of 21 70-ml fractions. The residue from fractions 8-14 after the solvent had been driven off was crystallized from alcohol (1:20) and gave 60 mg of a crystalline substance with mp 194-197°C.

Recrystallization from 10 ml of acidified alcohol–water (5:1) (the acidified alcohol contained 0.25 ml of concentrated HCl in 100 ml of 95% alcohol) gave 38 mg of yellowish white crystals of euvimal-1 with mp 197-198°C, M^+ 472, UV (λ_{max}^{EtOH,H^+} 278, 344 nm; ε 61562, 7646, λ_{max}^{EtOH} 276, 290 infl., 392 nm; ε 40600, 34460, 12740). PMR spectrum of euvimal-1 – see Fig. 1. Mass spectrum (m/z, %): 472 (M^+, 0.8), 454 ($M^+–H_2O$, 3.9); 397 (10.5); 251(21.1); 221(8.6); 203(100); 195(43.4); 186*; 161(22.4); 152*; 147(27.6); 107*; 95(22.4).

Dehydration of Euvimal-1. A solution of 20 mg of euvimal-1 in 5 ml of trifluoroacetic acid was left for 2 h and was then poured in 50 ml of water. The precipitate that deposited was filtered off, washed with water, and dried. The product obtained was dissolved in chloroform and the solution was filtered through silica gel (5.0 g, column diameter 2 cm). The filtrate was evaporated, and the residue was dissolved in 2 ml of alcohol and, with stirring, this solution was poured into 200 ml of 0.1% HCl.

The precipitate that deposited was filtered off, washed, and dried in the air.

LITERATURE CITED

1. A. A. Savina, D. A. Fesenko, and T. A. Sokol'skaya, Khim. Prir. Soedin., 113 (1983).
2. A. A. Savina, T. A. Sokol'skaya, and V. F. Zakharov, Khim. Prir. Soedin., 295 (1988).

3. T. Amano, T. Komiya, M. Hori, M. Goto, M. Kozuka, and T. Sawada, J. Chromatogr., 208, 347 (1981).
4. M. Kozuka, T. Sawada, F. Kazahara, E. Mizuta, and T. Sawada, J. Chromatogr., 30, 1952 (1982).
5. M. Kozuka, T. Sawada, E. Mizuta, F. Kazahara, T. Amano, T. Komiya, and M. Goto, Chem. Pharm. Bull., 30, 1964 (1982).
6. Q. Cheng and J. K. Snyder, J. Org. Chem., 53, 4562 (1988).
7. V. Yu. Bagirov, V. I. Sheichenko, A. A. Savina, and N. V. Veselovskaya, Khim. Prir. Soedin., 722 (1979).
8. J. N. Marx and E. H. White, Tetrahedron, 25, 2117 (1969).
9. H. Günther, NMR Spectroscopy: An Introduction, Wiley, New York (1980).
10. K. S. Rybalko, Natural Sesequiterpene Lactones [in Russian], Meditsina, Moscow (1978), p. 57.
11. J. W. Emsley, J. Feeney, and L. H. Sutcliffe, High Resolution NMR Spectroscopy, Pergamon, Oxford (1965-1966).

STRUCTURE AND STEREOCHEMISTRY OF FERTIDIN

A. I. Saidkodzhaev, L. A. Golovina, V. M. Malikov

UDC 547.992:547.37

The new ester, fertidin, has been isolated from the phenolic fraction of Ferula tenuisecta, and on the basis of chemical transformations and spectral characteristics its structure and stereochemistry have been established as 10α-angeloyloxy-4β-hydroxy-6α-p-hydroxybenzoyloxycarot-(9)-ene.

Continuing a study of the terpenoid compounds of plants of the genus Ferula (family Apiaceae), from the phenolic fraction of the total extractive substances of Ferula tenuisecta Korov by chromatographic separation on a column of KSK silica gel we have isolated a new ester with the composition $C_{27}H_{35}O_6$, mp 163-164°C (decomp.), which we have called fertidin (I).

A maximum at 260 nm (log ε 4.17) in the UV spectrum of fertidin showed the presence of a p-hydroxybenzoic acid residue in its molecule, while a bathochromic shift of the maximum ($\Delta\lambda_{max}$ = 40 nm) in an alkaline medium showed the presence of phenolic hydroxy group.

The IR spectrum of (I) contained strong absorption bands of two conjugated ester carbonyl groups (1690, 1715 cm^{-1}), of a double bond (1650 cm^{-1}), of an aromatic ring (1615, 1590, 1520 cm^{-1}), and of hydroxy groups (3250, 3450 cm^{-1}).

In the PMR spectrum of fertidin ($CDCl_3$) the strong-field region contained the signals of two secondary methyl groups —doublets at 0.8 and 0.9 ppm (3 H each, J = 7 Hz), of an angular methyl group — singlet at 1.16 ppm (3 H), and of a methyl at a double bond — broadened singlet at 1.74 ppm (3 H). In addition, the spectrum showed the signals of two gem-acyl protons — a sextet at 5.36 ppm (1 H, J = 11, 6, and 3 Hz) and a doublet at 4.83 ppm (1 H, J = 8 Hz). A doublet at 5.69 ppm (1 H, J = 8 Hz) related to an olefinic proton, and its components were broadened because of allyl interaction with a vicinal methyl group.

Two-proton doublets at 6.78 and 7.81 ppm (2 H each, J = 9.5 Hz) were due to the protons of the p-hydroxybenzoic acid residue, while a multiplet with its center at 6.01 ppm and a group of signals in the 1.8-1.95 ppm region were characteristic for the protons of an angelic acid residue.

A comparison of the facts given above with literature information on known esters isolated from plants of the genus Ferula [1-3] gave grounds for assuming that fertidin was an ester of a carotane sesquiterpene alcohol with angelic and p-hydroxybenzoic acids. In

Institute of the Chemistry of Plant Substances, Uzbek., Academy of Sciences, Tashkent.
Translated from Khimiya Prirodnykh Soedinii, No. 6, pp. 795-797, November-December, 1991. Original article submitted February 18, 1991.

0009-3130/91/2706-0701$12.50