From the best variant of the signs, an E series was constructed in which 28 out of the 36 nonhydrogen atoms were found (R factor 0.37). For a more accurate localization of the atoms, several $\rho(xyz)$ syntheses were calculated, in one of which all the nonhdyrogen atoms of fexerol were revealed (R factor 0.36). Then the structure was refined by successive electron-density syntheses and the presence of the molecule of water of crystallization was revealed (R factor 0.23). The structure was refined further by the method of least squares (MLS) in the anisotropic approximation to R 0.105. The coordinates of the atoms of molecules 1A and 1B from the last stage of the MLS are given in Table 3. Attempts to determine the coordinates of the H atoms from a difference synthesis were unsuccessful.

SUMMARY

The spatial structure of fexerol has been determined unambiguously by x-ray structural analysis.

LITERATURE CITED

1. G. V. Sagitdinova, A. I. Saidkhodzhaev, and V. M. Malikov, Khim. Prir. Soedin., 721 (1983).
2. G. V. Sagitdinova and A. I. Saidkhodzhaev, Khim. Prir. Soedin., 790 (1977).
3. M. E. Cradwick, P. D. Cradwick, and G. A. Sim, J. Chem. Soc., 404 (1973).
4. Yu. V. Gatilov and Zh. V. Dubovenko, Zh. Strukt. Khim., 319 (1979).
5. International Tables for X-Ray Crystallography, Kynock Press, Birmingham, Vol. 3 (1962).
6. Tables of Interatomic Distances and Configuration in Molecules and Ions, Chemical Society (London) (1958).
7. G. Pimentel and O. MacClellan, The Hydrogen Bond, W. H. Freeman, San Francisco (1960).
8. V. I. Andrianov, Z. Sh. Sadina, and V. L. Tarnopol'skii, Zh. Strukt. Khim., 911 (1974).

THE STRUCTURE OF ARTELEIN — A DIMERIC LACTONE OF A NEW TYPE FROM Artemisia leucodes

A. Mallabaev, B. Tashkhodzhaev, I. M. Saitbaeva,
M. R. Yagudaev, and G. P. Sidyakin*

UDC 547.913+548.737

The structure of a dimeric lactone of a new type from Artemesia leucodes, artelein, has been established unambiguously on the basis of an analysis of the results of IR, high-resolution mass, PMR, and ^{13}C NMR spectroscopy of the substance itself and an x-ray structural investigation of its acetyl derivative.

We have continued the study of the chemical composition of the leaves and flower heads of Artemesia leucodes Shrenk collected in the flowering phase in the environs of Mount Alintau, Chimkent province, Kazakh SSR [1-3]. By chromatographing the lactone resin from an ethanolic extract of the plant we have isolated a new lactone with mp 465°C which we have called artelein (I).

In the mass spectrum of artelein the maximum peak is that of an ion with m/z 263 (100%) while the relative intensity of the peak of an ion with m/z 262 amounts to 48% and it corresponds to the formula $C_{15}H_{18}O_4$. The IR spectrum (Fig. 1) contains strong absorption bands of the carbonyl of a γ-lactone ring (1760 cm^{-1}), of a cyclopentanone (1735 cm^{-1}), and of a hydroxy group (3510 cm^{-1}). Artelein is readily acetylated under mild conditions. The IR spectrum of artelein acetate (II) lacks the band characteristic for the vibrations of a hydroxyl and shows the C=O band of an acetate (1728 cm^{-1}).

---

*Deceased.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 46-52, January-February, 1986. Original article submitted April 3, 1985.

0009-3130/86/2201-0042$12.50

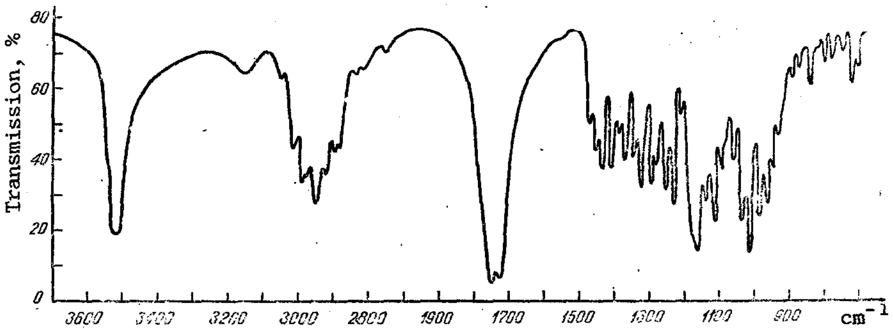


Fig. 1

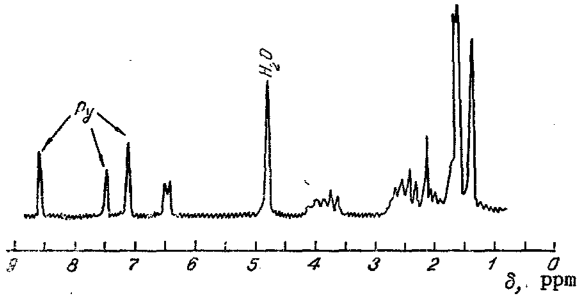


Fig. 2

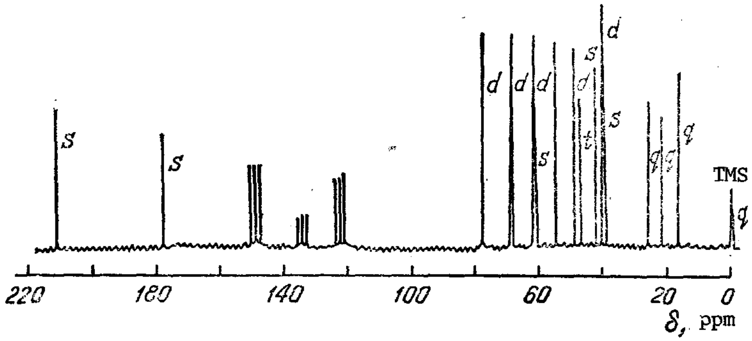


Fig. 3

The PMR spectrum of artelein (Fig. 2) shows singlets of tertiary methyl groups at 1.35 and 1.61 ppm (3 H) and the doublet of a secondary methyl group at 1.61 ppm, J = 7 Hz (3 H), a one-proton singlet at 2.10 ppm obviously relating to the signal of the proton present in the α position relative to the carbonyl group, a triplet of the H-6 lactone proton at 3.67 ppm, $^3J_1$ = $^3J_2$ = 10 Hz, the multiplet of a hemihydroxylic proton with its center at 3.92 ppm, and the doublet of an OH proton at 6.46 ppm, J ≅ 5 Hz. The five remaining protons resonate in the 2.2-2.7 ppm region. In the PMR spectrum of artelein acetate the signal of the methyl of the acetoxy group appears in the form of a singlet at 1.95 ppm, and the signal of the hemiacyl proton at 5.03 ppm in the form of a triplet with $^3J_1$ = $^3J_2$ = 10 Hz, with broadened components. The values of the SSCCs of the lactone proton H-6 with H-7 and H-5 show their mutual transoid arrangement and, accordingly, the trans linkage of the lactone ring and the seven-membered ring.

In the ^{13}C NMR spectrum (Fig. 3) of artelein there are the signals of 15 carbon atoms in the 212.3-16.4 ppm region, these being in the form of five singlets, six doublets, three quartets, and only one triplet (48.12 ppm). The singlet signals with δ 212.30 and 178.74 ppm belong to the carbon atoms of the C=O groups of a cyclopentanone and of a γ-lactone ring, respectively [4], and the three remaining signals relate to quaternary carbon atoms. Doublets with CSs of 78.35 and 69.39 ppm correspond to the carbon atoms linked to the oxygen atoms of the γ-lactone and the OH group, i.e., to C-6 and C-8. Consequently, the other three singlets (61.47, 43.45, and 40.62 cm) and four doublets (62.19, 56.00, 49.94, and 41.20 ppm)

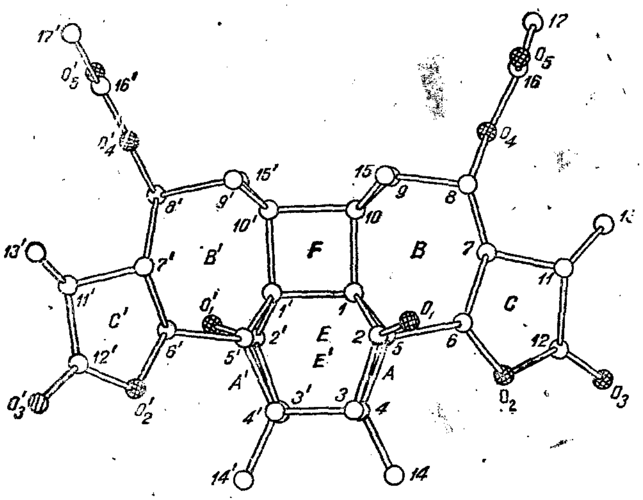


Fig. 4

TABLE 1. Main Planar Fragments of the Molecule of (I) and the Deviations of the Atoms from These Planes (δ, Å)

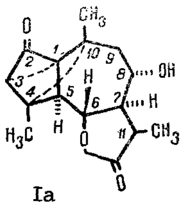
Plane	Atom	δ	δ'
Five-membered rings A and A'	C1*	0,811	0,826
	C2	0,003	—0,003
	C3	—0,005	0,004
	C4	0,005	—0,004
	C5	—0,003	0,003
Seven membered rings B and B'	C1*	—1,079	1,118
	C5	0,011	—0,016
	C6	—0,013	0,019
	C7	0,672	—0,768
	C8	0,012	—0,019
	C9	—0,010	0,016
	C10*	—1,168	1,196
Lactone rings C and C'	C6	—0,013	0,025
	O2	0,011	—0,028
	C12	0,016	—0,010
	O3	—0,016	0,021
	C11	0,002	—0,009
	C7	0,639	—0,596

Plane	Atom	δ	δ'
Four membered rings D and F	C3	0,012	
	C4	—0,012	
	C4'	0,012	
	C3'	—0,012	
	C1	0,021	
	C10	—0,020	
	C10'	0,020	
	C1'	—0,021	
Six membered rings E and E'	C1	0,022	—0,028
	C2*	—0,823	0,799
	C3	—0,022	0,028
	C4'	0,023	—0,027
	C5'*	—0,866	0,803
	C1'	—0,022	0,028
Ester groups	C8	0,000	—0,004
	O4	0,009	0,001
	C16	—0,032	0,012
	C17	0,009	0,006
	O5	0,014	—0,003

---

*Atoms not included in the calculation of the equations of the planes.

belong to carbon atoms not linked by oxygen atoms. Three quartet signals at 25.76, 22.33, and 16.42 ppm belong to the carbon atoms of the C-14, C-15, and C-13 methyl groups, respectively. The combination of the spectral characteristics and the elementary composition permit the hypothetical structure (Ia) to be assigned to artelein.



Ia

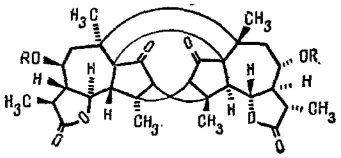
A consideration of the molecular model shows that no such skeleton of the (Ia) molecule can be assembled. Consequently, in order to establish the structure of artelein unambiguously we performed an x-ray structural investigation of its acetyl derivative (II).

TABLE 2. Interatomic Distances (R and R', Å) and Valence Angles (ω and ω', deg) in the Molecule of (I)

Distance	*R*	*R'*	Angle	ω	ω'	Angle	ω	ω'
C1—C1'	1,555(11)		C1—C1—C10	92,5	90,3	C6—C7—C8	115,3	112,2
C10—C10'	1,634(11)		C1—C1—C2	107,4	107,9	C6 C7—C11	101,2	102,2
C3—C4'	1,530(12)		C1—C1—C5	113,8	114,2	C8—C7—C11	117,9	117,0
C4—C3'	1,567(12)		C2—C1—C5	97,9	99,3	C7—C8—C9	114,2	111,4
C1—C2	1,552(11)	1,549(13)	C2—C1—C10	122,6	122,1	C7—C8—O4	101,2	103,6
C2—C3	1,548(15)	1,455(12)	C5—C1—C10	124,5	122,9	C9 C8—O4	104,5	107,5
C2—O1	1,219(13)	1,221(9)	C1—C2—C3	103,6	103,0	C8 C9 C10	116,2	114,7
C3—C4	1,591(14)	1,560(11)	C1—C2—C10	130,0	127,9	C9—C10—C1	112,8	113,6
C4—C5	1,607(16)	1,568(11)	C3—C2—C10	126,4	128,9	C1—C10 C10	89,3	87,6
C4—C14	1,479(11)	1,560(14)	C2—C3 C4	110,0	111,9	C1—C10—C15	116,2	115,8
C5—C6	1,458(12)	1,515(11)	C2—C3—C4	103,0	104,5	C9—C10 C10	114,4	113,1
C5—C1	1,540(11)	1,547(12)	C4—C3—C4	90,6	90,3	C9—C10—C15	107,9	110,0
C6—C7	1,557(14)	1,530(12)	C3—C4—C3	88,2	90,8	C10—C10—C15	115,6	115,4
C6—O2	1,441(9)	1,463(14)	C3—C4—C5	104,1	105,0	C7—C11—C12	99,0	98,2
C7—C8	1,514(12)	1,566(14)	C3—C4—C14	115,2	115,3	C7—C11—C13	119,9	118,0
C7—C11	1,521(9)	1,534(12)	C3—C4—C5	109,6	109,2	C12—C11—C13	111,2	112,8
C8—C9	1,504(9)	1,534(12)	C3—C4—C14	116,7	112,5	C11—C12—O2	108,9	112,2
C8—O4	1,486(13)	1,459(9)	C5—C4—C14	118,5	119,3	C11—C12—O3	126,6	125,4
C9—C10	1,538(13)	1,505(12)	C4—C5—C1	100,5	97,9	O2—C12—O3	124,5	122,3
C10—C1	1,546(12)	1,599(12)	C4—C5—C6	120,2	119,3	C6—O2—C12	111,5	109,7
C10—C15	1,537(14)	1,532(12)	C1—C5 C6	112,2	109,4	C8—O4—C16	116,8	120,2
C11—C12	1,518(13)	1,524(14)	C5—C6—C7	116,2	113,6	O4—C16 O5	119,7	122,0
C11—C13	1,513(14)	1,482(14)	C5—C6—O2	115,5	111,7	O4—C16—C17	108,4	117,3
C12—O2	1,344(12)	1,312(10)	C7—C6—O2	101,2	101,4	O5—C16—C17	131,7	120,7
C12—O3	1,176(9)	1,214(15)						
C16—O4	1,416(13)	1,272(10)						
C16—C17	1,504(14)	1,490(13)						
C16—O5	1,170(12)	1,264(12)						

At a preliminary stage of the x-ray structural analysis it was observed that in the independent part of the elementary cell there were two molecules of artelelin acetate or, as was subsequently established, artelein has a dimeric structure (I). The spatial structure of the molecule of artelein diacetate found by x-ray structural analysis is shown in Fig. 4 in a projection on the plane of the a and b axes. As can be seen from Fig. 4, the dimeric lactone is formed from two identical monolactones linked by four covalent bonds – C3–C4', C4–C3', C1–C1', and C10–C10' – which is unusual, in our view, since there is no information in the literature on similar dimeric lactones. The molecule of (II) has a well-pronounced intrinsic symmetry. A pseudo-twofold axis passing through the points x = 0.25 and z = 31 and parallel to the b axis separates the molecule into two identical monolactones: left and right (the left part is denoted by primes). This symmetry obviously explains the coincidence of the CSs of all the carbons in the ^{13}C spectra of artelein. However, it must be mentioned that, in the crystal structure, as the atoms become more remote from this axis of symmetry some disturbances of the symmetrical nature and arrangement of the atoms appear. This becomes appreciable in the terminal atoms of the ester groups, C17 and O5 and in the substituents of ring C remote from the center of the molecule, C13 and O3. Such a disturbance of symmetry, which is not observed in the liquid phase, can be explained by the packing factor of the crystal lattice.

I. R = H
II. R = Ac



The conformations of the rings of the (II) molecule can be judged unambiguously from Table 1, which gives the main planar fragments of the molecule and the deviations of the atoms from them. The cyclobutane rings D and F formed by the linkage of the monolactones have a planar structure (the deviation from coplanarity is not worse than 0.021 Å). The five-membered cyclopentanone rings A and A' and lactone rings C and C' have the envelope conformation. The seven-membered rings C and C' have the chair conformation and the cyclohexane rings E and E' the boat conformation. The linkage of rings A/B is trans and of rings B/C trans. The bonds from the rings to the substituents have the following orientations: C10–C15, β-axial; C8–C4, α-equatorial; C11–C13, α; and C4–C14, β.

The lengths of the bonds and the sizes of the valence angles are given in Table 2. The molecule contains five types of valence bonds. Their mean values (C_{sp^3}–C_{sp^3} 1.540 Å, C_{sp^3}–C_{sp^2} 1.512 Å, C_{sp^3}–O 1.462 Å, C_{sp^2}–O 1.336 Å, and C=O 1.211 Å) agree well with the standard values [5]. However, individual bond lengths are anomalous. Thus, for example, some bonds of the C_{sp^3}–C_{sp^3} type show distances of 1.458 and 1.634 Å. Such anomalies in the lengths of the valence bonds can be explained by an inadequate set of experimental reflections (for each nonhydrogen atom there were 40 reflections). The sizes of the valence angles (Table 2) were determined with an error of not more than 0.9°. On the whole, the lengths of the valence bonds and the angles (II) coincide, within the 3σ limits, with those in other lactones containing similar molecular fragments (see, for example, [6, 7]).

An analysis of intermolecular contacts in the packing of the crystal lattice showed the absence of anomalously short distances.

After establishing the structure of artelein acetate by x-ray structural analysis, we repeated the recording of its high-resolution mass spectrum and detected the peak of the molecular ion with M^+ 608 having an intensity of 0.03% in relation to the peak of the ion with m/z 245 (100%), which corresponds to the elementary composition $C_{34}H_{40}O_{10}$.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrophotometer (KBr); PMR spectra on a JNH-4H-100/100 MHz instrument in Py-d_5, 0 – HMDS; ^{13}C NMR spectra on a Varian CFT-20 spectrometer at a frequency of 20 MHz in Py-d_5, 0 – TMS in the pulsed regime under conditions of complete and incomplete decoupling of C–H interactions; and mass spectra on a MKh 1310 instrument. Melting points were determined in a metal block.

TABLE 3. Coordinates (× 10^4) of the Basis Atoms of the Molecule of (I)

Atom	x/a	y/b	z/c	x'/a	y'/b	z'/c
C1	−3338(9)	8831(7)	3083(6)	−1706(9)	8159(9)	3100(6)
C2	−3800(9)	9913(10)	3836(7)	−1215(8)	8788(10)	2343(5)
C3	−3266(9)	11066(9)	3590(7)	−1731(9)	10328(9)	2556(5)
C4	−3375(10)	11106(10)	2589(7)	−1664(8)	10355(8)	3538(5)
C5	−4000(9)	9951(9)	2372(6)	−1094(9)	8723(9)	3828(5)
C6	−5513(8)	10428(8)	2312(6)	477(9)	7803(9)	3881(5)
C7	−6004(9)	9382(8)	1841(6)	888(9)	6431(8)	4422(5)
C8	−5618(9)	7919(9)	2262(6)	599(9)	5219(9)	3962(6)
C9	−4063(8)	7001(8)	2348(5)	−963(10)	5656(9)	3875(7)
C10	−3354(9)	7314(9)	3121(7)	−1639(9)	6553(8)	3086(6)
C11	−7555(9)	10371(8)	1710(5)	2419(8)	6062(9)	4646(6)
C12	−7444(8)	11811(8)	1505(6)	2277(9)	7616(11)	4735(6)
C13	−8370(10)	10006(10)	1037(7)	3024(12)	5163(13)	5407(8)
C14	−4058(10)	12582(9)	2215(7)	−1004(9)	11342(9)	3912(6)
C15	−4005(9)	6987(10)	3915(5)	−1009(10)	5666(10)	2307(6)
C16	−6724(9)	6275(9)	1909(7)	1675(10)	2689(10)	4258(7)
C17	−7081(12)	5587(11)	1161(8)	2253(10)	1428(10)	4884(7)
O1	−4406(8)	9886(8)	4485(5)	−486(7)	8124(8)	1748(5)
O2	−6271(7)	11772(7)	1860(5)	1182(8)	8565(8)	4327(5)
O3	−8266(7)	12813(8)	1129(5)	3077(9)	7972(10)	5120(6)
O4	−6076(7)	7155(8)	1614(5)	1162(7)	3989(7)	4540(5)
O5	−6796(9)	6109(8)	2634(5)	1736(10)	2419(8)	3477(6)

Isolation of the Lactone. The comminuted leaves and flower heads (15 kg) were extracted with ethanol. The concentrated extract was diluted with water to give a 60% ethanolic solution. The precipitate that had deposited was filtered off, and the total lactones were extracted from the filtrate with chloroform.

The chloroform extract (380 g) was chromatographed on a column (d = 10 cm) containing neutral alumina (1:7), elution being performed with benzene (fractions 1-51) and then with ether (fractions 52-70). The volume of each fraction was 500-600 ml. Artelein (0.5 g) was isolated from the ethereal eluate (fraction 67).

Artelein, with mp 465-466°C, dissolved in pyridine and, with heating, in ethyl acetate. R_f 0.21 (on Silufol in the chloroform—ethyl acetate (1:1) system with iodine vapor as the revealing agent).

Artelein Diacetate. Artelein (0.1 g) was acetylated with acetic anhydride (1 ml) in pyridine (5 ml) at room temperature for 24 h, mp 370°C (ethanol—acetone). R_f 0.67 [on Silufol in the chloroform—ethyl acetate (9:1) system with antimony trichloride solution as the revealing agent]. The diacetate was soluble in acetone, chloroform, ethyl acetate, and pyridine.

Single crystals of artelein diacetate for x-ray structural investigations were grown from a solution in ethanol with the addition of acetone. The space group and the parameters of the elementary cell were determined from precession photographs and were defined on a Syntex $P2_1$ diffractometer (Institute of Bioorganic Chemistry, Academy of Sciences of the Uzbek SSR) using CuK_α radiation: $a = 10.538(2)$, $b = 10.135(2)$, $c = 15.865(3)$ Å; $\gamma = 64.65(1)°$, $d_{calc} = 1.320$ g/cm^3, space group $P2_1$, $z = 2$. The full set of experimental results was obtained on the above-mentioned diffractometer. In the calculations 1787 independent nonzero reflections with intensities exceeding 2σ were used.

The search for a model of the structure was performed by the direct method using programs of the Rentgen-75 group [8]. Calculation was begun in the automatic regime, but the structure could not be interpreted, and after this search was continued in the manual regime. After the selection of 11 (3k + 8ai) reference reflections, from the preceding set of TPSRs with R = 0.96 and σ = 0.75 we calculated 1024 phase variants. This operation with different reference reflections and with the inclusion of Sigma-1 was repeated several times, but unsuccessfully.

We resolved gradually to decrease the number of normalized amplitudes taking part in the TPSRs, the numbers of $E_{hk\ell}$ values were 400, 350, 300, and 250. For each set of $E_{hk\ell}$ values the procedures described above were repeated. And, finally, for the $E_{hk\ell}$ set with the number 250 in the automatic regime a variant with the E_{II} R estimate of 0.914 and a R(E) factor of 0.239 was isolated. Analysis of the E synthesis showed the unusual nature of the structure — the fact that the compound was dimeric. Further electron-density (ED) syntheses constructed for the whole mass of reflections revealed the lacking basis atoms and confirmed the bislactone structure of the compound under investigation. The structure was refined first by successive approximations (R = 0.156) and subsequently in the anisotropic approximation (R = 0.100). At this stage, a difference ED synthesis was carried out and the positions of 30 of the H atoms out of 40 were found. The final value of the divergence factor after several MLS iterations taking the coordinates of the H atoms into account was 0.087. The coordinates of the basis atoms are given in Table 3.

SUMMARY

The structure of a dimeric lactone of a new type from Artemesia leucodes artelein, has been established unambiguously on the basis of an analysis of its IR, high-resolution mass, PMR, and ^{13}C NMR spectra and an x-ray structural investigation of its acetyl derivative.

LITERATURE CITED

1. A. Mallabaev, U. Rakhmankulov, and G. P. Sidikin, Khim. Prir. Soedin., 530 (1978).
2. I. M. Saitbaeva, A. Mallabaev, and G. P. Sidikin, Khim. Prir. Soedin., 247 (1981).
3. I. M. Saitbaeva, A. Mallabaev, and G. P. Sidikin, Khim. Prir. Soedin., 391 (1983).
4. G. Levy and G. Nelson, Carbon-13 in Nuclear Magnetic Resonance for Organic Chemists, Wiley-Interscience, New York (1972).
5. L. E. Sutton, Distances and Configuration in Molecules and Ions, Chemical Society Special Publication, No. 18, London (1965).
6. Z. Karimov, Sh. Z. Kasymov, M. R. Yugudaev, and G. P. Sidyakin, Khim. Prir. Soedin., 446 (1981).
7. Z. Karimov, Sh. Z. Kasymov, M. R. Yagudaev, and G. P. Sidyakin, Khim. Prir. Soedin., 729 (1980).
8. V. I. Andrianov, Z. Sh. Safina, and V. L. Tarnopol'skii, Zh. Strukt. Khim., 911 (1974).

STRUCTURE AND STEREOCHEMISTRY OF PALLININ

A. Yu. Kushmuradov, A. I. Saidkhodzhaev,
and V. M. Malikov

UDC 547.992:547.37

The roots of Ferula pallida Korov. have yielded pallinin, $C_{25}H_{38}O_5$, mp 79-80°C, $[\alpha]_D^{20}$ −148.5° (c 0.1; $CHCl_3$) — an ester of the new carotane alcohol pallinol and angelic acid. A structure and absolute configuration have been proposed for it on the basis of chemical transformations and spectral characteristics.

Continuing a study of the esters of Ferula pallida Korov. [1, 2], from the neutral fraction of the ethanolic extract of the roots collected in the Chimkent province, Kazakh SSR, we have isolated by column chromatography a new ester with the composition $C_{25}H_{38}O_5$ (M^+ 418), mp 79-80°C, $[\alpha]_D^{20}$ −148.5° (c 0.1; $CHCl_3$), which has been called pallinin (I).

The IR spectrum of pallinin was characteristic for esters of sesquiterpene alcohols and it showed the absorption bands of the carbonyl group of an ester of an unsaturated acid (1700 cm^{-1}), of a secondary-tertiary double bond (1650, 960 cm^{-1}), and of a hydroxy group (3400-3620 cm^{-1}).

The PMR spectrum of the substance contained the signals of the protons of an isopropyl group (d, 0.83, 0.90 ppm, J = 7.5 Hz, 6 H), of an angular methyl group (s, 1.15 ppm, 3 H), of a methyl group at a double bond (br.s, 1.76 ppm, 3 H), of two gem-acyl protons (d, 4.83

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 53-56, January-February, 1986. Original article submitted May 12, 1985.

0009-3130/86/2201-0048$12.50