CHEMICAL COMPOSITION OF THE OLEORESIN OF THE GENUS Picea

IV. STRUCTURE AND ABSOLUTE CONFIGURATION OF AJANOL, A NEW SESQUITERPENE DIOL FROM Picea ajanensis

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Earlier [1] from the oleoresin of Picea ajanensis Fisch. (Yeddo spruce) we isolated the sesquiterpene compounds oplopanone, "X-cadinol," and bisabolol. In the present paper we report the isolation from the same oleoresin of a new sesquiterpene diol ajanol (I), $C_{15}H_{28}O_2$, mp 59-60°C, $[\alpha]_D^{20}$ −34.8°.

The NMR spectrum of ajanol (Fig. 1) exhibits the signals of an isopropyl group (two doublets at 0.78 and 0.82 ppm, J = 6.5 Hz), of an angular methyl group (1.05 ppm), and of a methyl group attached to a quaternary carbinol carbon atom (1.44 ppm). The signal of a proton attached to the same carbon atom as the hydroxy group appears in the form of a triplet at 3.74 ppm (J = 10 Hz). The magnitude of the spin−spin coupling constant and the shape of the signal shows that this proton interacts only with two neighboring axial hydrogen atoms [2].

When ajanol was subjected to catalytic hydrogenation conditions, no absorption of hydrogen took place, and when it was heated with selenium, eudalene was obtained. Consequently, ajanol has a 7-isopropyl-4,10-dimethyldecalin skeleton.

The acetylation of ajanol (I) gave a monoacetate (II) and the oxidation of (I) with chromium trioxide gave a hydroxy ketone (III) (1702 and 3540 cm^{-1}). The absence from the IR spectrum of the hydroxy ketone (III) of an absorption band for $-CH_2-CO-$ shows that the secondary hydroxyl group can be located only at C_6. According to the NMR spectrum, the tertiary hydroxy group is located at C_4. This position of the hydroxy groups in ajanol was confirmed by the formation of an α,β-unsaturated ketone (IV) in the dehydration of the hydroxy ketone (III) with $SOCl_2$ in pyridine.

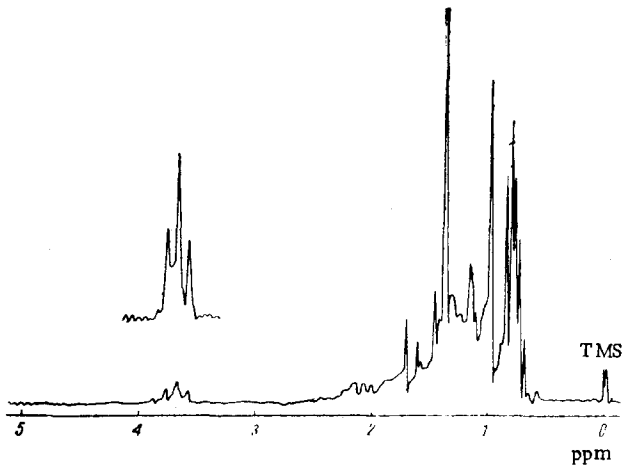

Fig. 1. NMR spectrum of ajanol (I) in benzene (100 MHz).

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TABLE 1. Chemical Shifts (δ) of the Methyl Groups and Protons at C_5 and C_6

	I	III	VII
Angular methyl			
CCl_4	0,98	0,99	1,26
C_6H_6	1,05	0,96	1,06
Δ^* (Hz)	+4,2	—	+12,0
CH_3 at C_4			
CCl_4	1,42	1,13	1,30
C_6H_6	1,44	1,16	1,43
Isopropyl			
CCl_4	0,91 0,85	0,90 0,87	0,98 0,93
C_6H_6	0,78 0,82	0,83 0,76	0,96 0,90
$H - C_6$			
CCl_4	3,66	—	4,30
C_6H_6	3,74	—	4,36
$H - C_5$			
CCl_4	—	2,10	—
C_6H_6	—	1,78	—
Δ (Hz)	—	+19,2	—

*Difference between the chemical shifts in CCl_4 and C_6H_6.

The equatorial nature of the two OH groups was found from the NMR spectra of ajanol taken in CCl_4 and in benzene [2]. The value of $\Delta_{CCl_4} - \delta_{C_6H_6}$ for the angular methyl was very small (+4.2 Hz). A confirmation of the equatorial position of the C_4 hydroxy group is the fact that the dehydration of ajanol monoacetate (II) forms the unsaturated acetate (V), as well as the isomer (VI).

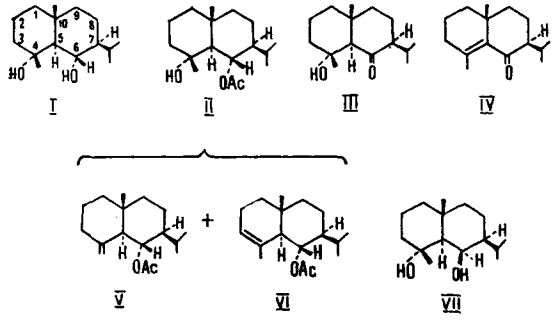
The hydrogenation of the hydroxy ketone (III) in acetic acid (PtO_2) [3] led to epiajanol (VII), with mp 84-85°C and $[\alpha]_D$ + 18°, having an axial secondary hydroxy group. The equatorial proton at C_6 of epiajanol (VII) resonates in a weaker field (4.30 ppm) than the corresponding axial proton of ajanol (3.66 ppm). The half-width of the signal of this proton in epiajanol (6 Hz) is considerably less than in ajanol (22 Hz), which agrees well with the axial nature of the secondary hydroxy group of epiajanol [4].

As shown in Table 1, in the NMR spectrum of epiajanol (VII) the signal of the angular methyl group is found at 1.26 ppm in CCl_4 and 1.06 ppm in benzene. This difference between the chemical shifts (+12 Hz) is due to the 1,3-diaxial arrangement of the angular methyl group and the hydroxy group at C_6 [2].

The angular proton at C_5 in the NMR spectrum of the hydroxy ketone (III) resonates at 2.10 ppm in CCl_4 solution and 1.78 ppm in benzene. The positive sign of Δ (+19 Hz) on passing from CCl_4 to benzene shows that the proton at C_5 is axial [2]. Consequently, in ajanol (I) the rings are trans-linked.

The absolute configuration of ajanol (I) was established from an analysis of the optical rotatory dispersion (ORD) curves and the circular dichroism (CD) of the hydroxy ketone (III) (Fig. 2a). The sign and molecular amplitude (a = +22.50) of the Cotton effect (CE) correspond to the β orientation of all the alkyl groups of ajanol (I). For the α,β-unsaturated ketone (IV) two CEs can be seen on the ORD and CD curves (Fig. 2b) at 316 and 236.5 nm for the $n-\pi^*$ and $\pi \rightarrow \pi^*$ transitions, respectively (R and K bands). The sign of the CE in the region of the R band coincides with that of a steroid analog – cholest-4-en-6-one [5]. The large value of the positive CE in the region of the $\pi \rightarrow \pi^*$ transition [6] corresponds to a right-hand helix of the bonds of the C = C–C = O group of atoms.

According to the chemical transformations described and the characteristics of its spectra, the structure and absolute configuration of ajanol can be illustrated by formula (I).



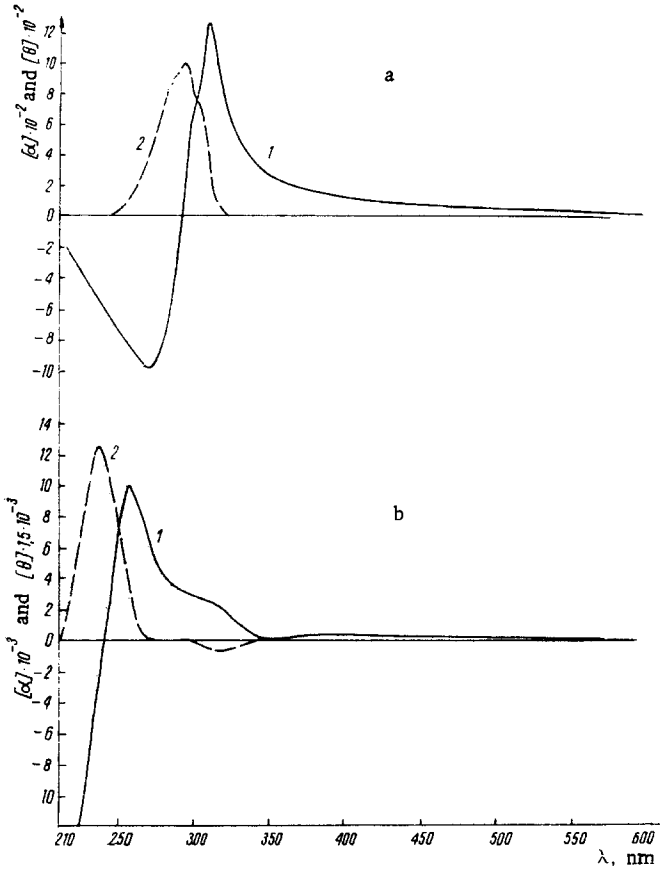


Fig. 2. ORD curve, c 0.410 (1), and CD curve, c 0.0148 (2) of the hydroxy ketone (III) in n-heptane (a), and ORD curve, c 0.270 (1) and CD curve, c 0.00042 (2) of the ketone (IV) in n-heptane (b).

EXPERIMENTAL

The ORD and CD curves were taken on a Spectropol spectropolarimeter, the IR spectra on a UR-20 instrument (CCl_4), and the NMR spectra on Varian HA-60 and HA-100 instruments (internal standard TMS). The molecular weights were determined mass spectrometrically on an MKh-1303 instrument. Gas–liquid chromatography was performed on a "Khrom-2" instrument with 10% of 1,2,3-tris(2-cyanoethoxy)propane on Chromosorb W in a column 3.4 m long at a column temperature of 160°C with nitrogen as the carrier gas.

Isolation of Ajanol (I). The fraction of oxygen-containing sesquiterpenes of the oleoresin of the Yeddo spruce (50 g) obtained by the usual method [7] was distilled through a fractionating column. The fraction boiling at 120-160°C (12 mm Hg) by repeated chromatography on silica gel yielded ajanol (I) (0.8 g) with mp 59-60°C, $[\alpha]_D^{20}$ −34.8° (c 0.855; dioxane). IR spectrum, cm^{-1}: 870, 900, 940, 960, 980, 1050, 1150, 1185, 1380, 1465, and 3620.

Found %: C 75.56; H 11.74. $C_{15}H_{28}O_2$. Calculated %: C 74.95; H 11.74. Mol. wt. 240.

The melting point of ajanol tosylate was 70°C.

Attempted Hydrogenation of Ajanol. A solution of 50 mg of ajanol in 50 ml of alcohol was treated with hydrogen over PtO_2 (10 mg) for 5 h. No absorption of hydrogen was observed. After the usual working up, the initial diol (I) was recovered (45 mg).

Dehydrogenation of (I). A mixture of 120 mg of ajanol (I) and 150 mg of selenium was heated at 270-300°C for 6 h. The dehydrogenation product was purified in the usual way. This gave 40 mg of eudalene; melting point of the picrate 91-92°C. A mixture with an authentic sample of eudalene picrate gave no depression of the melting point (91°C).

Acetylation of (I). A mixture of 240 mg of ajanol in 1.5 ml of pyridine and 1.8 ml of acetic anhydride was heated in the water bath for 2 h. Then the reaction mixture was diluted with water and extracted with ether. The extract was washed with water, HCl solution (5%), and water again. Then it was dried over Na_2SO_4 and the ether was distilled off. The residue (210 mg), by preparative TLC (SiO_2 + gypsum), gave ajanol monoacetate (II) (180 mg), mp 72-73°C, $[\alpha]_D^{20}$ −70° (c 0.248; n-heptane). IR spectrum, cm^{-1}: 925, 970, 1030, 1050, 1105, 1150, 1188, 1215, 1260, 1380, 1470, 1728, and 3535.

The Hydroxy Ketone (III). With stirring, 0.2 ml of the Jones reagent (2.67 g of CrO_3 and 2.3 ml of concentrated H_2SO_4 in 10 ml of water) was added to a solution of 120 mg of (I) in 5 ml of acetone at 0°C. Then water and ice were added to the reaction mixture and it was extracted with ether. The ethereal extract was washed to neutrality and dried over Na_2SO_4, and the solvent was distilled off. By preparative TLC 100 mg of (III) was isolated with n_D^{21} 1.4810, $[\alpha]_D^{20}$ + 28.4° (c 0.410; heptane). Mol. wt. 238. ORD: $[\alpha]_{319}$ + 1250°, $[\alpha]_{280}$ −1000° and CD: $[\Theta]_{302.5}$ + 1000° (Fig. 2a). IR spectrum, cm^{-1}: 965, 1050, 1060, 1070, 1135, 1197, 1210, 1270, 1390, 1465, 1703, and 3540.

The α,β-Unsaturated Ketone (IV). A mixture of 200 mg of the hydroxy ketone (III), 0.8 ml of pyridine, and 0.15 ml of thionyl chloride was kept at 0°C for 30 min. Then it was poured into water containing ice and was extracted with ether. The extract was washed with water, HCl solution (5%), and water again. Then it was dried over Na_2SO_4 and the ether was distilled off. By preparative TLC, the residue (130 mg) yielded 110 mg of (IV) with n_D^{22} 1.5005, $[\alpha]_D^{20}$ + 96.0° (c 0.270; n-heptane). IR spectrum, cm^{-1}: 948, 955, 1115, 1140, 1170, 1190, 1215, 1275, 1300, 1372, 1385, 1465, 1640, and 1696. UV spectrum: λ_{max} 248 nm (log ε 3.68). NMR spectrum (CCl_4): 1.63 ppm (3H; singlet, $>C=C\langle^{CH_3}$), 0.93 PPM (3H; singlet, $>C-CH_3$), and 0.91 and 0.86 ppm (6H; two doublets, $-CH\langle^{CH_3}_{CH_3}$). CD: $[\Theta]_{236}$ + 8500 and $[\Theta]_{316}$ − 710 (Fig. 2b).

Dehydration of the Monoacetate (II). A mixture of 150 mg of the acetate (II), 0.8 ml of pyridine, and 0.13 ml of thionyl chloride was kept at 0°C for 30 min. Then it was treated as described above. By preparative TLC, the residue (110 mg) yielded 60 mg of a mixture of (V) and (VI) (1 : 3, respectively, according to GLC and NMR) with n_D^{23} 1.4920, $[\alpha]_D^{20}$ + 2.2° (c 0.360; n-heptane). NMR spectrum (CCl_4): 5.30 ppm ($>C=C\langle^{H}$; singlet), 4.38-4.84 ppm (> C = CH_2; multiplet), 1.97 ppm ($-OCOCH_3$), 0.83 ppm ($>C-CH_3$; singlet), and 0.80 and 0.88 ppm ($-CH\langle^{CH_3}_{CH_3}$; two doublets, J = 6.5 Hz).

Epiajanol (VII). The hydroxy ketone (III) (40 mg) was hydrogenated in acetic acid (5 ml) over PtO_2 (60 mg). After the usual working up, preparative TLC on silica gel yielded epiajanol (VII) (16 mg) with mp 84-85°C, $[\alpha]_D^{20}$ +18.0° (c 0.222; dioxane) and mol. wt. 240. IR spectrum: 910, 930, 1000, 1030, 1110, 1160, 1190, 1210, 1380, 1470, 3540, 3615, and 3630.

CONCLUSIONS

From the neutral fraction of the oleoresin of Picea ajanensis Fisch. a new sesquiterpene diol of the selinane type has been isolated which we have called ajanol. It has been established that it is selinane-4α,6α-diol.

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