MONO- AND SESQUITERPENOIDS OF THE OLEORESIN OF *Abies nephrolepis*. CRYSTAL STRUCTURE OF (+)-β-CEDROL

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The composition of the mono- and sesquiterpenoids from the oleoresin of the Khingan fir has been studied. Thirteen monoterpenoids have been identified — bornyl acetate, α-terpenyl acetate, geranyl acetate, citronellyl acetate, α-fenchyl acetate, linalool, geraniol, terpineol-4, α-terpineol, α-fenchol, borneol, sabinene hydrate and thymol methyl ether; and 19 sesquiterpenoids — α-longipinene, longicyclene, longifolene, α-copaene, α-ylangene, sibirene, β- and α-selinenes, δ- and γ-cadinenes, γ-muurolene, caryophyllene, α-humulene, β- and γ-bisabolenes, ar-curcumene, nerolidol, bisabolol, and β-cedrol. The crystal structure of β-cedrol has been investigated by x-ray structural analysis.

We have previously reported an investigation of the monoterpene hydrocarbons [1] and resin acids [2] of the oleoresin of *Abies nephrolepis* Maxim (Khingan fir). Continuing the study of the oleoresin of this species, we have determined the composition of the sequiterpene hydrocarbons and of the oxygen-containing mono- and sesquiterpenoids. The oleoresin of the Khangan fir which was collected again in the Khabarov krai in 1981 contained 24.4% of monoterpenoids and 6.7% of sesquiterpenoids. The monoterpene compounds consisted mainly of hydrocarbons (21.5%), while the sesquiterpenoids were uniformly distributed between hydrocarbons (3.5%) and oxygen-containing compounds (3.2%).

The composition of the monoterpenes of the oleoresin differed only slightly from that publishdd previously [1].

The bulk of the oxygen-containing monoterpenoids consisted of acetates — bornyl acetate, α-terpenyl acetate, geranyl acetate, citronellyl acetate, and α-fenchyl acetate. Alcohols were also found in small amount — linalool, geraniol, terpineol-4, α-terpineol, borneol, α-fenchol, and sabinene hydrate, and also thymol methyl ether. The dominating component of this fraction was bornyl acetate.

By adsorption chromatography, the sesquiterpene hydrocarbons yielded longifolene, α-longipinene, sibirene, ar-curcumene, δ- and γ-cadinenes, γ-muurolene, β-selinene, β- and γ-bisabolenes, caryophyllene, and α-humulene. In addition to these, α-copaene, α-ylangene, longicyclene, and α-selinene were identified by analytical GLC from their relative retention times and by the method of additives. As in the oleoresin of other Far Eastern species of fir [3], the sesquiterpenoids of *Abies nephrolepis* Maxim. are characterized by a high content of bisabolane compounds — β- and γ-bisabolenes and α-bisabolol — which, together with nerolidol, dominate in the sesquiterpene alcohol fraction. From this fraction a small amount of a crystalline alcohol with a tertiary hydroxy group was isolated the spectral characteristics of which agreed with literature information for β-cedrol [4]. However, the melting point of the alcohol isolated (82-84°C) differed somewhat from the melting point of natural (86-87°C) [5]) and synthetic (94-96°C [4]) cedrol. An x-ray structural analysis confirmed that the alcohol isolated was (+)-β-cedrol.

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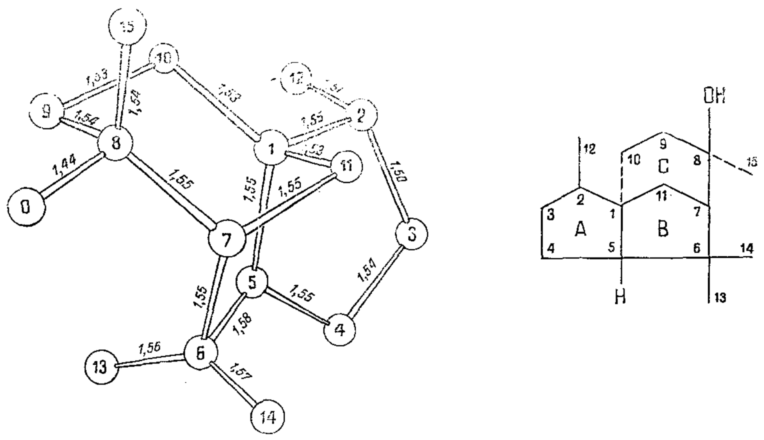

Fig. 1. Structure of β-cedrol.

TABLE 1. Valence Angles, deg

Angle	Valence	Angle	Valence
C(2)C(1)C(5)	106(1)	C(7)C(6)C(13)	116(1)
C(2)C(1)C(10)	116(1)	C(5)C(6)C(14)	113(1)
C(5)C(1)C(10)	110(1)	C(7)C(6)C(14)	106(1)
C(2)C(1)C(11)	113(1)	C(13)C(6)C(14)	106(1)
C(5)C(1)C(11)	102(1)	C(6)C(7)C(8)	117(1)
C(10)C(1)C(11)	107(1)	C(6)C(7)C(11)	100(1)
C(1)C(2)C(3)	102(1)	C(8)C(7)C(11)	108(1)
C(1)C(2)C(12)	114(1)	C(7)C(8)C(9)	111(1)
C(3)C(2)C(12)	110(1)	C(7)C(8)C(15)	109(1)
C(2)C(3)C(4)	105(1)	C(9)C(8)C(15)	111(1)
C(3)C(4)C(5)	102(1)	C(7)C(8)O	109(1)
C(1)C(5)C(4)	105(1)	C(9)C(8)O	109(1)
C(1)C(5)C(6)	105(1)	C(15)C(8)O	108(1)
C(4)C(5)C(6)	120(1)	C(8)C(9)C(10)	113(1)
C(5)C(6)C(7)	106(1)	C(1)C(10)C(9)	113(1)
C(5)C(6)C(13)	111(1)	C(1)C(11)C(7)	101(1)

The spatial structure of the (+)-β-cedrol molecule is given in Fig. 1, which also gives the mean bond lengths for the two independent molecules. Tables 1 and 2 give the mean valence angles and the Cremer—Pople parameters [6] characterizing the conformations of the rings. Among cedranes, the structure of α-bromonorketone-2,5-diepi-β-cedrene [sic] has been studied by x-ray structural analysis [7], and for this the authors reported a considerable internal strain and the boat form for ring C. In the case of cedrol, ring C has the chair form with an equatorial hydroxy group. A possible reason for the change in the form of ring C is the configuration of the C(5) atom.

EXPERIMENTAL

PMR spectra (δ scale, HMDS) were recorded on a Varian HA56/60 instrument for solutions in CCl_4. The ^{13}C NMR spectrum was obtained on a Bruker WP200SY instrument in $CDCl_3$. Optical rotations were measured on a Zeiss polarimeter for solutions in $CHCl_3$.

Analytical GLC was performed on a Biokhrom 01 instrument with a 52 m × 0.2 mm glass capillary column containing the stationary phase OV-101, the temperature of analysis being 100-160°C/2°C per minute and the rate of flow of carrier gas 3 ml/min.

Working Up of the Oleoresin. The oleoresin (300 g) of *Abies nephrolepis* Maxim., collected in July, 1981, in the flood plain of the R. Malampu, Khabarov krai, was treated with a 2% solution of NaOH (1.5 liters). The neutral substances were extracted with ether, and the extract was evaporated. The neutral fraction isolated (142 g, 47.3%) was separated by chromatography on air-dry silica gel (0.10-0.16 mm, 1.5 kg) into hydrocarbons (70 g) and oxygen-containing compounds (55 g).

TABLE 2. Cremer–Pople Parameters

Ring	S	S_2	θ	φ_2	Conformation
A		0 597		2.9	Twist
B		0 683		79,2	Distorted twist
C	1.207	0.218	169.5	149.3	Chair

TABLE 3. Coordinates of the Atoms ($\times 10^4$) of the Two Independent Molecules of (+)-β-Cedrol*

Atom	x	y	z	Atom	x	y	z
C (1)	0903 (11)	4093 (8)	7708 (8)	C (1′)	4001 (11)	2085 (8)	5341 (8)
C (2)	1834 (13)	3904 (9)	8422 (9)	C (2′)	3213 (12)	1274 (9)	5278 (9)
C (3)	2367 (14)	4784 (11)	8578 (10)	C (3′)	2468 (28)	1320 (17)	6048 (20)
C (4)	1352 (16)	5415 (10)	8521 (9)	C (3″)	3198 (54)	0835 (32)	6191 (34)
C (5)	0474 (11)	5031 (8)	7847 (8)	C (4′)	3381 (13)	1607 (10)	6744 (8)
C (6)	0396 (11)	5426 (8)	6938 (8)	C (5′)	3946 (11)	2371 (9)	6281 (8)
C (7)	0555 (11)	4659 (8)	6335 (7)	C (6′)	5239 (11)	2708 (8)	6520 (7)
C (8)	−0549 (12)	4087 (8)	6190 (8)	C (7′)	5881 (10)	2736 (8)	5651 (8)
C (9)	−1081 (11)	3766 (8)	7032 (8)	C (8′)	5666 (11)	3534 (8)	5081 (8)
C (10)	−0134 (13)	3479 (8)	7668 (8)	C (9′)	4332 (11)	3679 (8)	4952 (9)
C (11)	1504 (11)	4129 (8)	6837 (8)	C (10′)	3657 (12)	2857 (10)	4768 (9)
C (12)	1346 (15)	3508 (9)	9218 (9)	C (11′)	5325 (12)	1951 (8)	5220 (8)
C (13)	−0797 (12)	5961 (9)	6837 (9)	C (12′)	2363 (20)	1297 (15)	4520 (15)
C (14)	1447 (15)	6072 (10)	6698 (9)	C (12″)	1942 (41)	1109 (43)	5026 (45)
C (15)	−0198 (14)	3305 (8)	5636 (9)	C (13′)	5217 (11)	3541 (9)	7041 (7)
O	−1437 (7)	4563 (5)	5749 (5)	C (14′)	5897 (12)	2042 (9)	7074 (8)
				C (15′)	6366 (13)	3415 (9)	4257 (8)
				O′	6168 (8)	4290 (6)	5511 (5)

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*A table of thermal parameters can be obtained from the authors.

Fractional distillation of the hydrocarbons (67 g) gave 55 g of monoterpenes (60-110°C/10 mm Hg), 9 g of sesquiterpenes (80-120°C/2 mm Hg), and 2.6 g of diterpenes (still residue). Similarly, 35 g of oxygen-containing compounds yielded 5 g of monoterpenoids (60-100°C/2 mm Hg), 5.4 g of sesquiterpenoids (100-140°C/22 mm Hg), and 24 g of diterpenoids (still residue).

Sesquiterpene Hydrocarbons. The mixture of sesquiterpenes (2.5 g) was chromatographed on silica gel impregnated with 20% of silver nitrate (50 g). Petroleum ether with the gradient addition of diethyl ether eluted 9 fractions (I-IX). The compounds in the fractions were identified by means of their PMR spectra.

Fraction I (0.08 g) consisted of a mixture of α-longipinene and longifolene (1:2); fraction II (0.15 g) of longifolene; fraction III (0.18 g) of δ-cardinene; fraction IV (0.21 g) of a mixture of sibirene and ar-curcumene (2:1); fraction V (0.42) of γ-bisabolene; fraction VI (0.07 g) of a mixture of γ-cadinene and γ-muurolene (5:1); fraction VII (0.4 g) of β-bisabolene; fraction VIII (0.41 g) of a mixture of caryophyllene and β-selinene (1:1); and fraction IX (0.31 g) of α-humulene.

Monoterpenoids. The oxygen-containing monoterpenoids (2.4 g) were chromatographed on silica gel (0.07-0.10 mm, 60 g), and gradient elution (petroleum-ether–diethyl ether) led to the isolation of eight fractions (I-VIII) the compositions of which were determined by PMR spectroscopy. Fraction I (0.04 g) contained thymol methyl ether; fraction II (0.35 g) α-fenchyl acetate, $[\alpha]_D^{22}$ −35° (*c* 18) ; fraction III (0.91 g) bornyl acetate and α-terpenyl acetate (3:1); fraction IV (0.26 g) citronellyl acetate and geranyl acetate (1:3); fraction V (0.13 g) terpineol-4 and linalool (1:2); fraction VI (0.12 g) borneol; fraction VII (0.18 g) α-terpineol, α-fenchol, and geraniol (5:1:2); and fraction VIII (0.05 g) sabinene hydrate.

Sesquiterpenoids. The oxygen-containing sesquiterpenoids (2 g) were chromatographed on silica gel (0.07-0.10 mm, 50 g), and the fractions obtained were rechromatographed on silica gel impregnated with 20% of silver nitrate. This led to the isolation of bisabolol (0.9 g, $[\alpha]_D^{21}+70.5°$ (*c* 1.7)); nerolidol (0.8 g, $[\alpha]_D^{22}-6.8°$ (in the pure form)), and β-cedrol (0.05 g, mp 82-84°C (petroleum ether), $[\alpha]_D^{22}+11.8°$(*c* 30.0)).

^{1}H NMR of β-cedrol (ppm): 0.82 (3 H, doublet, J = 6 Hz); 0.96 (3 H, singlet); 1.17 (3 H, singlet); 1.26 (3 H, singlet).

^{13}C NMR (ppm): quartets at 15.47, 27.55, 28.83, and 30.12; triplets at 25.29, 31.55, 35.31, 36.94, and 41.92; doublets at 41.42, 54.49, and 61.02; singlets at 43.34, 54.04, and 75.02.

X-Ray Structural Analysis. The experiments was performed on a Syntex $P2_1$ diffractometer at −65°C. The crystals of β-cedrol were rhombic: a = 11.220(4), b = 15.554(5), c = 15.837(6) Å; space group $P2_12_12_1$, z = 8, d_{calc} = 1.07 g/cm^3. The intensities of 2759 independent reflections were measured by the 2θ/ω scanning method in the range of $2\theta \leqslant 50°$ (λ Mo K_α, graphite monochromator). The calculations were performed on 1531 reflections with $I \geqslant 3\sigma$ without correction for absorption. The structure was interpreted by the direct method using the MULTAN-XTL program with expansion of the starting set to 10 reflections and the use of magic numbers (Fibonacci series [7]). The positions of the H atoms were calculated geometrically. Finally, the structure was refined by the method of least squares in the full-matrix anisotropic variant (the parameters of the H atoms were not refined) to R = 0.099 and R_ω = 0.108, where $\omega^{-1} = \sigma_F^2 + (0.04F)^2$. The coordinates of the nonhydrogen atoms are given in Table 3. As an F synthesis showed, ring A of the second crystallographically independent molecule is present in two conformations (ratio 7:3) differing by the positions of C(3') and C(12') (and C(3") and C(12") in Table 3). In the crystal, the molecules are bound by O...O and O'...O' hydrogen bonds.

SUMMARY

1. The composition of the oxygen-containing monoterpenoids and the sesquiterpene compounds of the oleoresin of *Abies nephrolepis* Maxim. has been studied.

2. The crystal structure of β-cedrol has been investigated by x-ray structural analysis.

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