CRYSTAL STRUCTURE OF KORAIOL — A SESQUITERPENE ALCOHOL WITH A
NEW TYPE OF CARBON SKELETON FROM THE OLEORESIN OF *Pinus koraiensis*

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An x-ray structural investigation has been made of a new sesquiterpene alcohol — koraiol — in the form of its complex with pyridine (2:1). The cyclobutane rings are nonplanar and the foldings of rings A and B amount to 17 and 31°, respectively. The seven-membered ring has the chair form.

From the neutral fraction of the oleoresin of the Korean pine (*Pinus koraiensis* Sieb. et Zucc.) we have isolated a crystalline sesquiterpene alcohol with mp 92.5-93°C, $[\alpha]_D^{20}$ +31.7°, which we have called koraiol.

The PMR spectrum of koraiol contains the signals of four methyl groups (0.86, 1.13, 1.16, 1.20 ppm, singlets with intensities of 3 H each) and the signal of a proton at 2.52 ppm (triplet, J = 9 Hz). The IR spectrum also shows the absorption of methyl groups (ν = 1365, 1377 cm^{-1}) and in dilute solution the absorption of a tertiary hydroxy group appears (ν = 3610 cm^{-1}).

The molecular ion M^{+} = 222 corresponds to the empirical formula $C_{15}H_{26}O$. The strongest lines in the mass spectrum correspond to the splitting out of H_2O (204), of H_2O and $-CH_3$ (189), of $-CH(CH_3)_2$ (179), of $-CH(CH_3)_2$ and CH_3 (164), and of H_2O and $-CH(CH_3)_2$ (161). The ^{13}C NMR spectrum confirms the presence of a tertiary hydroxy group (singlet, 73.7 ppm) and also shows the absence of unsaturated carbon atoms from the molecule. Thus, the combination of spectral characteristics indicates the presence of a tricyclic system and of four angular methyl groups in the tertiary alcohol.

The dehydration of koraiol with thionyl chloride in pyridine led to two hydrocarbons X and Y, in a ratio of 1:1 (PMR). In the PMR spectrum of product X, the signal of the methyl group at 1.20 ppm had disappeared and the signals of an exomethylene group (4.48 and 4.78 ppm, 2 H) had appeared, which shows the presence in koraiol of the fragment $HO-\overset{|}{\underset{|}{C}}-CH_3$. The signal of a methyl group at 1.13 ppm had shifted upfield (0.98 ppm); in the initial alcohol it was probably subjected to the descreening influence of the hydroxy group. The IR spectrum also shows the absorption of a $=CH_2$ group (ν = 890, 1645, 3076 cm^{-1}). The spectral characteristics of product Y show that dehydration took place either with the formation of a tetrasubstituted double bond or with further cyclization or rearrangement of the hydrocarbon skeleton. The PMR spectrum lacked the signals of olefinic protons and the region of the signals of methyl groups had greatly changed. The spectral characteristics of koraiol and the hydrocarbons obtained from it on dehydration did not agree with those for known sesquiterpenoids.

The crystallization of koraiol from pyridine yielded crystals which were studied by the method of x-ray structural analysis. It was found that koraiol forms a complex with pyridine through hydrogen bonds. The structure and relative configuration of the koraiol molecule is shown in Fig. 1. The bond lengths and valence angles are given in Fig. 2. In actual fact, the koraiol (I) molecule consists of a tricyclic system. To a seven-membered ring are attached two four-membered rings in cis (ring A) and trans (ring B) linkage. The two crystallographically independent molecules of koraiol differ from one another somewhat; thus, some torsion angles differ by 8°:

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Angle	Koraiol I	Koraiol II
C (9) C (1) C (2) C (5)	47,8°	50,8°
C (1) C (2) C (5) C (6)	19,3	13,8
C (2) C (5) C (6) C (7)	− 81,7	−74,3
C (5) C (6) C (7) C (8)	82,4	76,9
C (6) C (7) C (8) C (9)	− 53,8	− 50,4
C (7) C (8) C (9) C (1)	67,1	63,7
C (8) C (9) C (1) C (2)	− 86,7	− 85,8
C (5) C (2) C (3) C (4)	−14,5	−9,9
C (2) C (3) C (4) C (5)	14,8	19,8
C (3) C (4) C (5) C (2)	−14,5	−10,0
C (4) C (5) C (2) C (3)	14,4	9,7
C (11) C (1) C (9) C (10)	23,2	23,0
C (1) C (9) C (10) C (11)	−23,3	− 23,8
C (9) C (10) C (11) C (1)	24,0	23,6
(10) C (11) C (1) C (9)	−-23,4	−23,7

The cycloheptane rings of molecules have a distorted chair conformation. The torsion angles of these rings (see above) are close to those calculated for cycloheptane [1], the mean valence angle for C—C—C in the rings being 116.2°, which also agrees with calculation, in spite of the distortion introduced by the small rings. A similar conformation of a cycloheptene ring has been found for a number of sesquiterpenoids [2]. The cyclobutane rings are nonplanar, the folding of ring B being considerably greater than that of ring A (33 and 17°, respectively). It may be mentioned that in the molecule of one caryophyllene derivative [3] an even greater folding of the ring, to 41°, has been found. The mean valence angle in the four-membered rings of koraiol is 88.4°, and the mean C—C bond length is 1.554 Å. These facts correspond to those given in the literature [3-5]. The geometry of the pyridine molecule is the usual one. Two molecules of koraiol and one molecule of pyridine are bound by N•••HO•••HO hydrogen bonds with the following distances: N•••H, 1.84; H•••O, 2.811; O•••H, 2.10; and O•••O, 2.844 Å. The N•••HO hydrogen bond lies in the plane of the pyridine molecule.

Thus, koraiol is the first representative of the sesquiterpenoids with a new type of carbon skeleton.

Starting from the established structure of koraiol it is easy to explain the formation of product X on its dehydration. The hydrocarbon X, which we have called β-koraiene (II) is formed by the elimination of a molecule of H_2O with the formation of an exocyclic double bond.
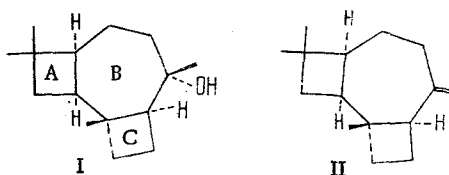
Although the structure of koraiol is externally similar to a caryophyllane structure, in the oleoresin it is apparently formed by different routes, since in koraiol rings A and B have the cis linkage and in caryophyllene and its derivatives the trans linkage. The difference most probably arises at the stage of the cyclization of an 11-membered humulane precursor. It has been shown [5] by an x-ray structural analysis of the complex of humulene with $AgNO_3$ that in humulene the C(2) and C(5) atoms and the C(1) and C(9) atoms are close (2.89 and 2.86 Å, respectively) which gives a possibility of ready cyclization. While cyclization with the participation of the C(2) and C(5) carbon atoms and the formation of trans-linked rings is observed frequently (caryophyllane [6] and bicyclohumulane [7] derivatives), koraiol is an example of cyclization at the C(1) and C(9) atoms and also of unusual cyclization at the C(2) and C(5) atoms.

Koraiol has also been found in the oleoresin of the Japanese stone pine (*Pinus pumila* (Pall.) Rgl.)

EXPERIMENTAL

The IR spectra were taken on a UR-20 instrument. The PMR spectra were recorded on a Varian HA 56/60 instrument (internal standard HMDS, δ 0.05 ppm). The mass spectra were obtained on a MS 902 instrument of the firm AEI using a glass inlet system (120°C, 70 eV). The ^{13}C NMR spectrum was taken on a Brüker WP-80/DS, 20.115 MHz, instrument with $CDCl_3$ as internal standard at 76.9 ppm on the ^{13}C δ scale.
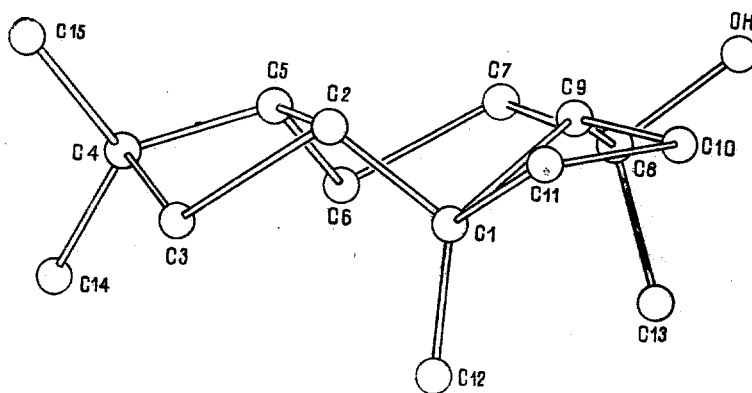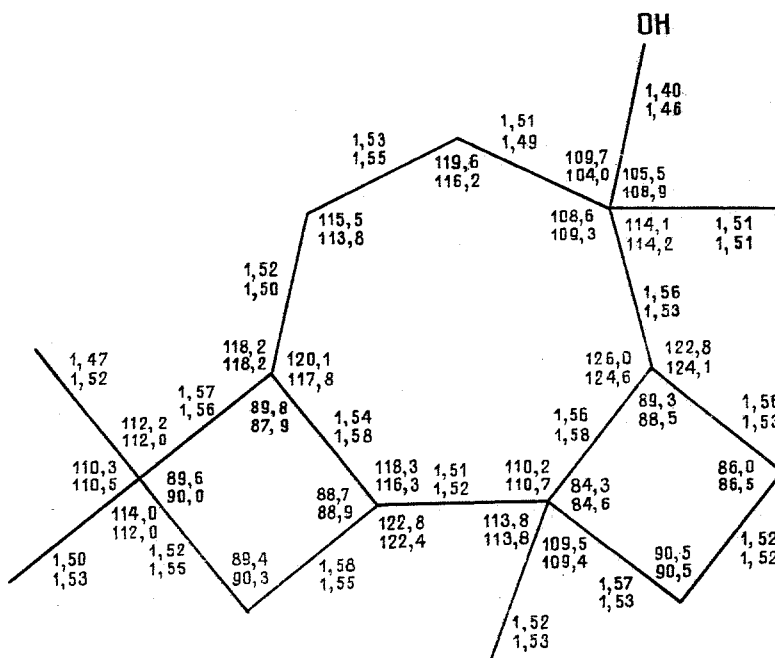
Fig. 1. Crystal structure of koraiol.

Fig. 2. Bond lengths (Å) and valence angles (°) of two crystal-
lographically independent koraiol molecules.

Isolation of Koraiol. The oleoresin of the Korean pine (10 kg) was treated with a 1%
solution of NaOH and the neutral fraction of the oleoresin was extracted with ether. Vacuum
distillation (110-160°C/3•10⁻² mm Hg) yielded a fraction of sesquiterpene compounds (100 g).
Chromatography on Al_2O_3 (neutral, activity grade I-II, ratio of substance to sorbent 1:20)
led to the separation of the hydrocarbons (60 g) from the oxygen-containing compounds (39 g).
Chromatography of the fraction of oxygen-containing compounds (10 g) on SiO_2 (0.100-0.140 mm,
250 g) with petroleum ether containing 20% of diethyl ether yielded a crystalline alcohol
(0.6 g).

The koraiol was recrystallized from pentane and diethyl ether. It had mp 92.5-93°C,
$[\alpha]_D^{20}$ +31.7° (c 11.5; $CHCl_3$). ¹³C NMR, ppm: 73.7 (singlet), 53.6; 50.7; 46.6; 43.1; 42.6
(singlet), 38.7; 34.2; 32.4 (singlet), 31.2; 24.2; 23.5; 22.4; 22.2; 18.8. Mass spectrum:
222 (M⁺, 4%), 204 (22%), 189 (17%), 179 (19%), 164 (16%), 161 (25%), 148 (53%), 133 (35%),
126 (44%), 121 (45%), 108 (98%), 93 (100%).

Recrystallization from pyridine yielded the complex of koraiol with pyridine, mp 89-90°C.

Dehydration of Koraiol. A solution of 0.25 g of koraiol in 1 ml of pyridine was added
to 0.5 g of $SOCl_2$ in 2 ml of pyridine. The mixture was left at 0°C for 16 h and then the ex-
cess of $SOCl_2$ was decomposed with ice and the reaction mixture was diluted with 10 ml of H_2O
and was extracted with ether. The solvent was distilled off and the products, which had res-

TABLE 1. Coordinates (×10⁴, ×10³ for the Hydrogens) and Temperature Factors (Å²) for the Atoms of the Molecules

Atom	X	Y	Z	B	X	Y	Z	B
	Koraiol I				Koraiol II			
C(1)	1940(5)	3796(8)	2499(5)	4.9	9037(6)	7682(10)	2724(7)	4.8
C(2)	2355(5)	5187(7)	2715(6)	5.1	8394(7)	6230(10)	2846(7)	4.4
C(3)	2399(6)	5875(9)	3780(6)	5.3	9320(9)	5491(12)	3914(8)	7.1
C(4)	3557(6)	6385(8)	3768(6)	5.1	8227(7)	4785(10)	3777(7)	5.3
C(5)	3633(5)	5393(7)	2885(5)	4.6	7737(6)	5705(9)	2829(6)	4.6
C(6)	4354(6)	4227(7)	3164(6)	4.7	6829(7)	6639(10)	2939(7)	5.3
C(7)	4453(5)	3381(8)	2211(6)	5.9	6359(7)	7472(11)	1970(8)	5.6
C(8)	3554(5)	2429(7)	1838(5)	4.5	6994(7)	8637(9)	1721(7)	4.3
C(9)	2453(5)	3145(7)	1627(5)	4.0	8191(6)	8200(9)	1744(6)	5.1
C(10)	1347(6)	2488(11)	1192(6)	5.6	9081(8)	9154(12)	1514(9)	6.6
C(11)	0845(5)	3582(10)	1718(6)	5.9	9911(8)	8200(14)	2130(9)	6.5
C(12)	1963(8)	2995(10)	3487(6)	6.7	9121(10)	8448(14)	3732(8)	7.4
C(13)	3599(7)	1231(8)	2514(7)	6.3	6911(12)	9782(13)	2427(10)	7.6
C(14)	4392(9)	6268(13)	4815(8)	7.9	8298(13)	3429(14)	3450(11)	8.8
C(15)	3531(10)	7773(10)	3351(9)	8.0	7733(10)	4852(14)	4714(8)	6.4
O	3700(3)	2038(5)	0806(3)	5.4	6544(5)	9071(6)	0704(5)	5.5
H(2)	190(5)	574(6)	203(5)	6	911(6)	584(9)	228(6)	6
1H(3)	256(5)	513(7)	447(5)	6	1009(6)	486(8)	410(5)	1
2H(3)	192(5)	664(6)	384(5)	6	942(7)	606(9)	444(6)	6
H(5)	391(5)	582(7)	219(5)	6	795(6)	737(8)	114(6)	6
1H(6)	524(5)	459(6)	354(5)	6	618(6)	609(8)	313(5)	6
2H(6)	407(5)	364(6)	367(5)	6	719(6)	718(8)	360(6)	6
1H(7)	452(5)	406(6)	153(5)	6	626(6)	692(9)	137(6)	6
2H(7)	493(5)	298(7)	231(5)	6	563(7)	778(8)	199(6)	6
H(9)	250(4)	383(6)	103(4)	6	795(6)	737(8)	114(6)	6
1H(10)	136(5)	169(7)	157(5)	6	936(6)	942(9)	81(6)	6
2H(10)	111(6)	25(8)	053(5)	6	906(6)	1003(9)	187(6)	6
1H(11)	061(5)	441(7)	132(5)	6	1007(6)	741(8)	160(6)	6
2H(11)	029(5)	332(7)	205(4)	6	1056(6)	852(8)	243(6)	6
1H(12)	158(5)	204(7)	315(5)	6	831(6)	840(8)	413(6)	6
2H(12)	274(5)	287(6)	403(5)	6	930(6)	937(9)	351(6)	6
3H(12)	140(5)	343(6)	384(5)	6	996(7)	827(8)	419(6)	6
1H(13)	366(5)	132(3)	341(5)	3	713(6)	1065(9)	210(6)	6
2H(13)	284(5)	055(6)	238(5)	6	613(7)	999(8)	253(6)	6
3H(13)	427(5)	093(7)	240(5)	6	711(7)	967(9)	303(7)	6
1H(14)	454(5)	529(7)	508(5)	6	851(7)	323(9)	280(7)	6
2H(14)	509(6)	670(6)	464(5)	6	777(7)	284(9)	315(7)	6
3H(14)	419(5)	670(7)	541(5)	6	855(7)	282(9)	406(7)	6
1H(15)	319(5)	848(7)	361(5)	6	760(8)	555(9)	499(7)	6
2H(15)	310(5)	770(7)	259(5)	6	834(6)	427(8)	541(6)	6
3H(15)	431(5)	805(7)	340(5)	6	705(6)	426(8)	468(6)	6
H(0)	333(5)	124(7)	048(5)	6	678(7)	845(9)	036(7)	6

Pyridine

Atom	X	Y	Z	B
N	2828(8)	9570(10)	0167(6)	6.0
C(1)	1918(9)	8957(11)	0166(7)	6.3
C(2)	1797(9)	7660(12)	0002(8)	6.4
C(3)	2663(10)	6897(11)	−123(8)	6.1
C(4)	3633(9)	7539(12)	−127(7)	6.1
C(5)	3701(9)	8865(11)	014(8)	5.3
H(1)	137(7)	956(9)	029(6)	6
H(2)	101(7)	729(8)	009(6)	6
H(3)	267(6)	582(9)	−020(6)	6
H(4)	442(7)	705(9)	−031(6)	6
H(5)	443(7)	946(9)	009(6)	6

inified, were separated by chromatography on Al₂O₃ (neutral, activity grade I-II, 10 g), petroleum ether eluting 0.145 g of a mixture of hydrocarbons. This mixture of hydrocarbons (0.120 g) was separated by chromatography on SiO₂ (0.071-0.100 mm, 10 g) impregnated with 10% of AgNO₃. Petroleum ether eluted product Y (0.060 g) and further elution with the addition of 1% of diethyl ether yielded β-koraiene (0.055 g).

IR spectrum of Y, cm⁻¹: 1263, 1375, 1430, 1448, 1463. PMR spectrum, ppm: 0.90 (singlet, 3 H), 1.12 (singlet, 3 H), 1.40 (singlet, 6 H). Mass spectrum: 204 (M⁺ 38%), 189 (24%), 175 (39%), 161 (26%), 148 (50%), 133 (100%). IR spectrum of β-koraiene, cm⁻¹: 890, 1374, 1380, 1445, 1465, 1645, 3075. PMR spectrum, ppm: 0.86 (singlet, 3 H), 0.98 (singlet, 3 H), 1.16 (singlet, 3 H), 4.48 (singlet, 1 H), 4.78 (singlet, 1 H).

The X-ray structural experiment was performed on a Syntex $P2_1$ diffractometer using Mo radiation with a graphite monochromator. The crystals of the koraiol-pyridine complex belonged to the monoclinic system with $a = 12.550(3)$, $b = 10.258$ (2), $c = 13.105$ (3) Å, $\beta = 102.88$ (2)°, space group $P2_1$, $z = 2$ for $C_{35}H_{57}O_2N$, $d_{calc} = 1.06$ g/cm^3. The intensities of the reflections were measured by the $2\theta/\omega$ scanning method. Independent reflections numbering 1660 with $2\theta \leqslant 40°$ were measured, and 1528 reflections with $I > 2\sigma$ were used in the calculation. Absorption was not taken into account. Repeated attempts to determine the structure of koraiol with the aid of the MULTAN program were unsuccessful.

We found the structure by the method using the NQEST (x) function. The method consists in representing the phases of the 15 reflections included in the 14 quartets of the NQEST criterion [8] by magic integers [9]. Then all the values of NQEST (x) were calculated, running through x with some step Δx [10]. The phases for the 33 best values of NQEST (x) $\leqslant -0.55$ were used as the initial phases for the MULTAN program, the starting set of which thus consist of 18 reflections (three of them fix the origin of the coordinates of the cell).

From the peaks of the E-synthesis according to the phases of the variant having the best value of the criterion R_α [11] it was possible to isolate 24 out of the 38 atoms of the molecules of the complex. The remaining atoms were found from E-syntheses. The structure was refined in the anisotropic approximation to R = 0.054. The hydrogen atoms found from a difference synthesis were refined with fixed isotropic B = 6. The coordinates of the atoms are given in Table 1.

SUMMARY

1. A new sesquiterpene alcohol which has been called koraiol has been isolated from the oleoresins of *Pinus koraiensis* Sieb. et Zucc. and *Pinus pumila* (Pall.) Rgl.

2. The structure of koraiol has been determined by the x-ray structural analysis of a crystal of the complex of koreol with pyridine.

3. The dehydration of koraiol has given a new sesquiterpene hydrocarbon which has been called β-koraiene. Koraiol and β-koraiene possess a previously unknown type of carbon skeleton.

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