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

V. A. Khan, Yu. V. Gatilov, Zh. V. Dubovenko, and V. A. Pentegova

UDC 539.26;547.597;547.642

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, [α]D +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 C₁₅H₂₀O. The strongest lines in the mass spectrum correspond to the splitting out of H₂O (204), of H₂O and −CH₃ (189), of −CH(CH₃)₂ (179), of −CH(CH₃)₂ and CH₃ (164), and of H₂O and −CH(CH₃)₂ (161). The ¹³C 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–CH₂. 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 −CH₃ 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°.
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-H--O hydrogen bonds with the following distances: N-H, 1.84; H-O, 2.81; O--H, 2.10; and O-O, 2.84 Å. The N-H 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-koralene (II) is formed by the elimination of a molecule of H₂O with the formation of an exocyclic double bond.

Although the structure of koraiol is externally similar to a caryophyllene 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 must probably arise 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 AgNO₃ 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, 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 ¹³C NMR spectrum was taken on a Brüker WP-80/DS, 20.115 MHz, instrument with CDCl₃, as internal standard at 76.9 ppm on the ¹³C δ scale.