DITERPENOIDS OF THE OLEORESIN OF *Pinus koraiensis*

THE STEREOCHEMISTRY OF NEOABIENOL

V. A. Raldugin and V. A. Pentegova

UDC 547.596

We have reported the isolation from the oleoresin of Pinus koraiensis Sieb. et Zucc. of cembrene, isocembrene, agathadiol, methyl lambertianate, methyl dehydroabietate, and dehydroabietinol [1], of pinusolide [2], and of neocembrene [3]. Continuing our study of the diterpenoids of the oleoresin of this species of Pinus, we have obtained a series of compounds belonging to the dehydroabietane and labdane structural groups.

The oxygen-containing diterpenoids of the oleoresin were separated into fractions chromatographically. From the monohydric alcohol fraction two diterpenoids were isolated, one of which, according to TLC and also its IR, UV, and NMR spectra, was identical with the neoabienol found in the oleoresin of Abies sibirica Ledb. [4]. Neoabienol is 11-trans-labda-11,13-dien-8α-ol [4]. The configuration of its trisubstituted double bond has not been determined.

It is known [5] that cis-α-ocimene and cis-β-ocimene isomerize on thermolysis into 4-trans-6-cis-2,6-dimethylocta-1,4,6-triene and 4-trans-6-cis-2,6-dimethylocta-2,4,6-triene, respectively. As suggested by Ohloff [5] and later shown by Sasaki [6] for cis-β-ocimene, the stereospecificity of these reactions is explained by the fact that the isomerization is a sigmatropic 1,5-hydride shift. The aliphatic part of the molecule of cis-abienol is similar to the corresponding parts of the molecules of the cis-ocimenes. Consequently, the occurrence of a similar intramolecular hydride shift in cis-abienol might be expected. In actual fact, the pyrolysis of cis-abienol (20 min in n-$C_{14}H_{30}$ in the presence of hydroquinone, 200-204°C) formed neoabienol. Synthetic neoabienol and a natural sample had similar constants and IR and NMR spectra. The ORD curves for the two samples coincided. Thus, the $C_{13}-C_{14}$ double bond in neoabienol possesses the cis configuration. The comparative ease of this transformation shows the possibility of the formation of neoabienol from cis-abienol (in the preparation of the initial diterpene fraction by distillation of the unsaponifiable substances of the oleoresin). This is the first time that the presence of a labdan-8-ol diterpenoid in the oleoresin of Pinus has been reported, which is of undoubted biogenetic and, possibly, chemotaxonomic interest.

The constants and spectra of the second monohydric alcohol were identical with those of 18-nordehydroabietan-4α-ol. We found one of the products of its dehydration – 19-nordehydroabiet-4(18)-ene – in the hydrocarbon diterpene fraction of the oleoresin. This is the first time that either of these norditerpenoids have been isolated from a natural source. They have been obtained previously by several workers through the oxidative decarboxylation of dehydroabietic acid [7, 8] and by the deamination of dehydroabietylamine [9].

The fraction of the polar hydroxyl-containing diterpenoids contained two compounds: a hydroxy aldehyde and a hydroxy ester. The hydroxy aldehyde was identified by its IR and NMR spectra as isoagatholal (15-hydroxylabda-8(20),13-diene-19-carbaldehyde) [10, 11], which was confirmed by its reduction to agathadiol. Isoagatholal is apparently an intermediate in the biosynthesis of the highly oxidized labdane diterpenoids pinusolide and methyl lambertianate.

Novosibirsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 595-597, September-October, 1971. Original article submitted May 18, 1971.

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The hydroxy ester with mp 82-83°C, $[\alpha]_D^{23}$ +52°, according to its spectra, is the methyl ester of 15-hydroxydehydroabietan-18-oic acid, which has recently been isolated from Agathis species by Carman [12].

EXPERIMENTAL

The melting points were determined on a Kofler block. The UV spectra were obtained on a Unicam SP 700C instrument, the IR spectra on a UR-20 instrument (in CCl_4), and the NMR spectra on Varian A56/60A and Varian HA-100 instruments (internal standard HMDS, the signal of which was taken as 0.05 ppm on the δ scale; solutions in CCl_4). The specific rotations were measured on a Zeiss polarimeter and on a Spectropol I spectropolarimeter, and the molecular weights were determined on an MKh-1303 instrument. The initial diterpene fraction of oxygen-containing diterpenoids was isolated from the oleoresin by a published method [13]* with a yield of 17%. The yields of diterpenoids are shown with respect to this fraction. The analyses of all the compounds corresponded to the calculated figures.

Neoabienol. The total oxygen-containing diterpenoids were chromatographed on air-dry silica gel. Petroleum ether containing gradually increasing amounts of diethyl ether eluted a fraction whose main component was isocembrol. Chromatography on SiO_2 +5% of $AgNO_3$ gave neoabienol (elution with a mixture of petroleum ether and 10% of diethyl ether). After additional purification on SiO_2, the analytical sample of neoabienol $C_{20}H_{24}O$ (yield 0.5%) had $[\alpha]_D^{24}$ 0° (c 8.10; chloroform), $[\alpha]_{300}^{20}$ −3.9°, $[\alpha]_{290}^{20}$ −10.6°, $[\alpha]_{270}^{20}$ −29.6° (c 0.775; chloroform). UV spectrum (in ethanol): λ_{max} 239 nm (log ε 4.35). NMR spectrum, ppm: 0.82, 0.88, and 0.91 (3H each, singlets, methyl groups at C_4 and C_{10}), 1.12 (3H, singlet, methyl group at C_8), 5.27 (1H, quartet, J=6.5 Hz, $C_{14}-H$), 5.53 (1H, B part of an AB system, doublet of doublets, J=15.5 and 10.0 Hz, $C_{11}-H$), 6.39 ppm (1H, A part of an AB system, doublet, J_{AB}=15.5 Hz, $C_{12}-H$).

Isomerization of cis-Abienol into Neoabienol. A mixture of 80 mg of cis-abienol [mp 40-41°C, $[\alpha]_D^{22}$ +22° (c 1.50), λ_{max} 238 nm (log ε 4.26)] and 5 ml of n-$C_{14}H_{30}$ containing 30 mg of hydroquinone was heated in an oil bath at 200-204°C for 20 min. After cooling, the reaction mixture was diluted with hexane. According to TLC, it contained cis-abienol, neoabienol, polymerization products, and a small amount of hydrocarbons. After the n-$C_{14}H_{30}$ and polymers had been separated on a column of deactivated SiO_2, 50 mg of a mixture of cis-abienol and neoabienol was obtained. From this by careful chromatography on SiO_2 was obtained 20 mg of neoabienol with $[\alpha]_D^{22}$ 0° (c 1.20); chloroform), identical with a natural sample with respect to IR and NMR spectra, TLC and ORD.

18-Nordehydroabietan-4α-ol. The fraction eluted immediately after the isocembrol and neoabienol consisted, according to the IR spectrum, of primary and tertiary alcohols. Its rechromatography on SiO_2 + 5% of $AgNO_3$ gave 18-nordehydroabietan-4α-ol with a yield of 2%, mp 90-91°C (from petroleum ether), $[\alpha]_D^{21}$ + 11.5° (c, 1.80; methanol). Mol. wt. 272 (mass spectrometry). According to the literature: mp 91.5-92.5°C [9], $[\alpha]_D^{25}$ +12° (c 0.34; methanol) [7]. The IR, UV, and NMR spectra correspond to those given by Bennet et al. [7].

Methyl 15-Hydroxydehydroabietan-18-oate. The fraction of polar diterpenoids eluted after the mixture of primary and tertiary alcohols was chromatographed on SiO_2 +5% of $AgNO_3$. Petroleum ether containing 15% of diethyl ether eluted pinusolide with mp 82-83°C, $[\alpha]_D^{24}$ +55° (c 1.09; chloroform). Then the mixture containing 25% of diethyl ether yielded methyl 15-hydroxydehydroabietan-18-oate $(C_{21}H_{30}O_3)_3 \cdot H_2O$ with a yield of 2%, mp 82-83°C, $[\alpha]_D^{23}$ +52° (c 0.77; ethanol). Literature data: mp 82-83°C, $[\alpha]_D$ +54°; (ethanol) [12]. IR spectrum, cm^{-1}: 3620 (OH); 1730, 1510, 1420, 1255, 1135, 1050, 835, 790, 730 (in KBr). The UV and NMR spectra corresponded to those given in the literature [12].

Isoagatholal. Further elution with a mixture of petroleum ether +35% of diethyl ether gave isoagatholal $C_{20}H_{34}O$ with a yield of 2%, n_D^{24} 1.5155, $[\alpha]_D^{20}$ + 19.3°, $[\alpha]_{363}^{20}$ 0°, $[\alpha]_{315}^{20}$ −330° (minimum), $[\alpha]_{300}^{20}$ 0°, $[\alpha]_{270}^{20}$ +720° (maximum). IR spectrum, cm^{-1}: 3630 (OH), 3090, 1655, 900 $\left(\rangle C=CH_2\right)$, 1730, 1040 (CHO). NMR spectrum, ppm: 0.55, 1.00, and 1.63 (3H each, singlets, methyl groups, at C_{10}, C_5, and C_{13}, respectively), 4.00 (2H, doublet, J=6.5 Hz, protons at C_{15}), 4.53 and 4.85 (1H each, narrow multiplets, protons of an exomethylene group), 5.30 (1H, triplet, J=6.5 Hz, $C_{14}-H$), and 9.65 (1H, singlet, CHO). The reduction of isoagatholal with lithium tetrahydroaluminate in diethyl ether formed agathadiol with mp 108-109°C, $[\alpha]_D^{25}$ +37.4° (c 0.67; chloroform), giving no depression of the melting point with an authentic sample.

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*As in Russian original. There is no reference 13 in the Literature Cited section – Publisher.

19-Nordehydroabiet-4(18)-ene. The diterpene hydrocarbons of Pinus koraiensis isolated in the usual way [13] were chromatographed on SiO_2 +5% of $AgNO_3$. The mixture of hydrocarbons eluted immediately after the cembrene was subjected to careful chromatographic separation on air-dry SiO_2 (eluent petroleum ether). This gave 19-nordehydroabiet-4(18)-ene (yield about 0.5% on the initial fraction of diterpene hydrocarbons) with n_D^{22} 1.5340, $[\alpha]_D^{24}$ +147° (c 0.88; methanol). Mol. wt. 254 (mass spectrometry). Literature data $[\alpha]_D^{25}$ +152° (c 0.2; methanol) [7]. The IR, UV, and NMR spectra corresponded to those given in the literature [7].

SUMMARY

1. Neoabienol, isoagatholal, 18-nordehydroabietan-4α-ol, 19-nordehydroabiet-4(18)-ene, and methyl 15-hydroxydehydroabietan-18-oate have been isolated from the oleoresin of Pinus koraiensis Sieb. et Zucc.

2. The trisubstituted double bond of neoabienol has the cis configuration. On thermolysis, cis-abieno rearranges stereospecifically into neoabienol.

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