THE NEUTRAL SUBSTANCES OF THE OLEORESIN OF ABIES SIBIRICA

II. The Structure of the Diterpene Hydroxy Ketone

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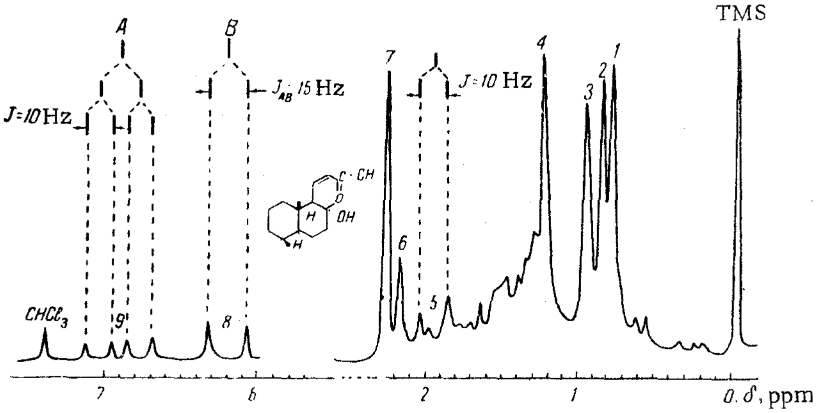
In studying the neutral oxygen-containing substances of Abies sibirica Ledb. (the oleoresin of the Siberian fir) we have isolated a crystalline diterpene hydroxy ketone $C_{18}H_{30}O_2$ [1].

On dehydrogenation the hydroxy ketone is converted into 1, 2, 5-trimethylnaphthalene and is therefore a bicyclic diterpene derivative [2]. The hydroxy ketone contains one double bond. Its IR spectrum has absorption bands at 990 and 1630 cm^{-1} corresponding to a trans-disubstituted double bond. Absorption at 1680 cm^{-1} can be assigned to a carbonyl group and that at 1080 and 3590 cm^{-1} to a tertiary hydroxy group [3].

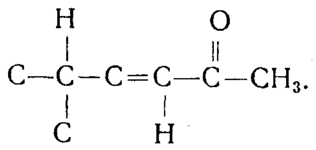
Absorption maxima in the UV spectrum at 234 and 310 mμ (log ε 4.13 and 1.95, respectively) confirm the presence of a carbonyl group in conjugation with a double bond [4].



NMR spectrum of the hydroxy ketone (I).

In the NMR spectrum of the hydroxy ketone (in $CDCl_3$ in a GPT-S-60 radiospectrometer, Table 1, figure), signals 1, 2, and 3 show the presence of three methyl groups located at C-4 and C-10. The chemical shift of signal 4 corresponds in intensity to one methyl group C-8 and shows the propinquity of an oxygen-containing function [5]; the absence of resolution of this signal shows the tertiary nature of the hydroxyl. Consequently, signal 4 belongs to a methyl group located on the same carbon atom as the carboxyl, the signal of which appears at 2.18 ppm (checked thermally). Protons of a methyl group attached to a carbonyl group absorb at 2.26 ppm.

Signals 8 and 9 in the weak field region are due to two protons at a double bond. The nonequivalence of the protons is due to a neighboring carbonyl group [6]. By interacting with one another, the protons give an AB spectrum (J = 15 Hz), and the splitting of the doublet A to form a quadruplet (J = 10 Hz) is due to the presence of one neighboring proton having a signal at 1.95 ppm (J = 10 Hz). Thus, the molecule must contain the moiety



$$C-\underset{\overset{|}{C}}{\overset{\overset{H}{|}}{C}}-C=\underset{\overset{|}{H}}{C}-\overset{\overset{O}{\|}}{C}-CH_3.$$

Signal number	Chemical shift, ppm	Nature of signal	Assignment of signal
1	0.78	Singlet	CH_3 at C-4
2	0.85		CH_3 at C-4
3	0.95		CH_3 at C-10
4	1.24		CH_3 at C-8
5	1.95	Doublet	H at C-9
6	2.18	Singlet	OH at C-8
7	2.26		CH_3 at C-13
8	6.20	Doublet	H at C-12
9	6.90	Quadruplet	H at C-11

In the mass spectrum of the hydroxy ketone (MKh-1303 mass spectrometer), a peak with m/e 278 corresponds to the molecular ion. The main peak with m/e 43 is probably due to the fragment

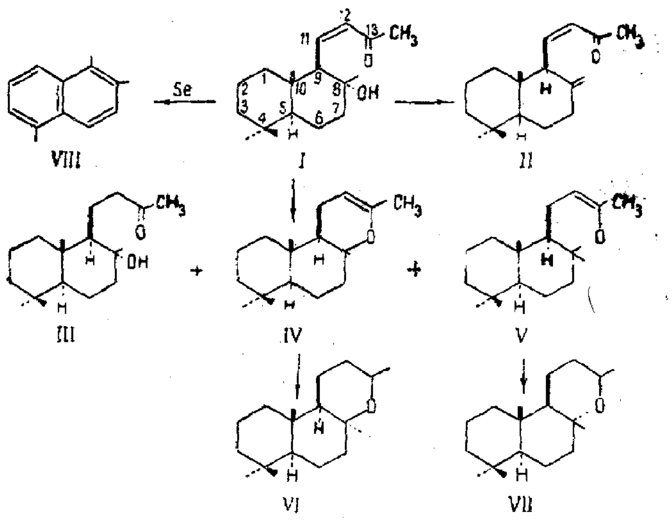
($COCH_3$) arising by the rupture of the C-12–C-13 bond. The peak with m/e 260 is produced from the molecular ion by the loss of water, which is confirmed by the metastable peak (m^*) at 243.3 ($278^+ \rightarrow 260^+ + 18$). These results enable us to propose structure (I) for the hydroxy ketone.

The hydroxy ketone was not esterified under the usual conditions; on dehydration with acetic anhydride it gave a ketone $C_{18}H_{28}O$ (II). The IR spectrum of (II) showed, in addition to the bands of a trans-disubstituted double bond, bands characteristic for an exomethylene double bond (890, 1630, 3085 cm^{-1}), the presence of which was shown by the production of formaldehyde on ozonization.

The hydrogenation of the hydroxy ketone (I) gave a mixture of products (4 : 1 : 1): a saturated hydroxy ketone $C_{18}H_{32}O_2$ (III) with mp 91°–92° C, and two isomeric oxides of composition $C_{18}H_{30}O$ with mp 46° C (IV) and 86° C (V). From its melting point and IR spectrum, the saturated hydroxy ketone was identical to a known hydroxy ketone obtained by the oxidation of sclareol [7, 8].

Ruzicka et al., [9] have reported that the saturated hydroxy ketone is unstable and readily dehydrates forming oxides. From their melting points and IR spectra, the compounds (IV) and (V) that we isolated are identical to known unsaturated oxides [7–10]. The hydrogenation of substances (IV) and (V) led to the corresponding saturated oxides (VI) and (VII) [7, 11]; their melting points also corresponded with those reported.

All these transformations confirm structure (I) for the hydroxy ketone, and consequently it can be assigned to the labdan group of compounds and may be called 14,15-bis-nor-8α-hydroxylabd-11-en-13-one



Experimental

The oxygen-containing diterpene compounds (70.0 g) were chromatographed on neutral alumina (activity grade II, III) at a ratio of 1 : 40. Ether eluted a crystalline substance (5.7 g). After rechromatography and three recrystallizations from ether, 2.2 g of a hydroxy ketone with mp 126° C (Kofler block) and $[\alpha]_D^{20}$ ±0° (c 3.0; chloroform) was obtained.

Found, %: C 77.81; H 11.82; H^* 0.44; mol. wt. 278 (mass spectrometry). Calculated for $C_{18}H_{30}O_2$, %: C 77.65; H 11.86; H^* 0.36; mol. wt. 278.42.

The hydroxy ketone (12.82 mg) was hydrogenated in glacial acetic acid on Pd/C. Hydrogen consumption was 1.5 ml (0° C, 760 mm), which corresponds to one double bond (theoretical consumption of hydrogen for one double bond 1.03 ml).

Dehydrogenation of the hydroxy ketone (I). A mixture of the hydroxy ketone (500 mg) and selenium (825 mg) was kept at 300°–320° C for 20 hr. The dehydrogenation product was chromatographed on alkaline alumina (activity grade I, II). Petroleum ether eluted an aromatic hydrocarbon with n_D 1.5810 giving a styphnate with mp 130°–131° C and a picrate with mp 139.5°–140° C. Mixtures of the styphnate and picrate of the aromatic hydrocarbon (VIII) with authentic samples of the styphnate and picrate of 1,2,5-trimethylnaphthalene gave no depression of the melting points (130° and 140° C, respectively).

The UV spectrum of the hydrocarbon obtained had maxima at 230, 290, and 324 mμ (log ε 4.75, 3.66, and 2.78, respectively), agreeing with literature data for 1,2,5-trimethylnaphthalene [10].

Dehydration of the hydroxy ketone (I) [13]. The hydroxy ketone (100 mg), acetic anhydride (0.12 ml), and glacial acetic acid (0.12 ml) were heated on a water bath under reflux. The melting point of the dehydration product extracted in the usual way and purified on alkaline alumina (activity grade I, II) was 139.5°–141° C. The UV spectrum of the ketone (II) obtained had maxima at 234 and 310 mμ (log ε 4.3 and 1.89, respectively).

Found, %: C 82.81; H 11.90; mol. wt. 260 (mass spectrometry). Calculated for $C_{18}H_{28}O$, %: C 83.82; H 11.84; mol. wt. 260.

Determination of the methylene double bonds of ketone (III) [14]. The ketone (2.7 mg) was ozonized in propionic acid (3.0 ml) at −20° C for 30 sec. The amount of formaldehyde liberated (0.32 mg) corresponded to one methylene double bond (theoretical amount of formaldehyde for one methylene bond 0.32 mg).

Hydrogenation of the hydroxy ketone (I). The hydroxy ketone (I) (300 mg) was hydrogenated in ethyl acetate (5.0 ml) over a PtO_2 catalyst for 2 hr. The consumption of hydrogen was 29.4 ml (0° C, 760 mm), which corresponds to one double bond. The hydrogenation product was a glassy mass with n_D^{20} 1.5104 the treatment of which with petroleum ether separated it into two fractions: a readily soluble and a sparingly soluble fraction.

The sparingly soluble fraction gave a crystalline compound (III) (180 mg) with mp 91°–92° C (petroleum ether); the reaction with tetranitromethane was negative.

The IR spectrum had absorption bands at 1085, 1720, and 3604 cm^{-1}.

Found, %: C 77.07; H 11.77; mol. wt. 280 (mass spectrometry). Calculated for $C_{18}H_{32}O_2$, %: C 77.09; H 11.50; mol. wt. 280.

Preparation of the semicarbazone of compound (III) [15]. A methanolic solution of semicarbazide hydrochloride (60.8 mg) and sodium acetate (101.2 mg) were added to a methanolic solution of compound (III) (120 mg). The semicarbazone obtained was extracted with ether and chromatographed on neutral alumina (activity grade III/IV) at a 1 : 120 ratio. Ethanol eluted 90 mg of semicarbazone with mp 145°–146° C [7].

Found, %: C 67.80; H 10.45; N 12.18. Calculated for $C_{19}H_{35}O_2N_3$, %: C 67.78; H 10.50; N 12.50.

The readily soluble fraction consisted of a mixture of two components with different R_f values. The components were separated on alkaline alumina (activity grade I, II) and eluted with petroleum ether. The first fractions yielded 62 mg of a crystalline substance (IV) with mp 45°–46° C [7, 8].

Found, %: C 82.15; H 11.48; O 6.15; mol. wt. 262 (mass spectrometry). Calculated for $C_{18}H_{30}O$, %: C 82.38; H 11.52; O 6.15.

The later eluates deposited crystals of compound (V) (52 mg) with mp 86° C. Literature data: mp 86° C [10].

The IR spectra of (IV) and (V) had absorption bands at 870, 1670, and 3050 cm^{-1}.

Found, %: C 82.49; H 11.70; O 5.97; mol. wt. 262 (mass spectrometry). Calculated for $C_{18}H_{30}O$, %: C 82.38; H 11.52; O 6.15; mol. wt. 262.

Hydrogenation of compounds (IV) and (V). Compound (IV) (30 mg) was hydrogenated in ethyl acetate over a PtO_2 catalyst. A saturated product (VI) with mp 43° C was obtained. Literature data: mp 43° C [7].

Compound (V) (25 mg), on hydrogenation under the same conditions, gave a saturated substance (VII) with mp 83° C. Literature data: mp 83°–84° C [7].

The IR spectra of (VI) and (VII) had absorption bands at 1076, 1098, and 1117 cm^{-1}, which are characteristic for a saturated oxide ring [11].

The elementary analyses were carried out in the analytical laboratory of Novosibirsk Institute of Organic Chemistry. The IR spectra were taken on a UR-10 spectrophotometer and the UV spectra on a SF-4 spectrophotometer.

Summary

A new diterpene hydroxy ketone $C_{18}H_{30}O_2$, 14,15-bis-nor-8α-hydroxylabd-11-en-13-one has been isolated from *Abies sibirica* Ledb.

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