A STUDY OF THE PROPERTIES AND ^{13}C NMR SPECTRA OF PINIFOLIC ACID AND ITS DERIVATIVES

I. I. Bardyshev, A. S. Degtyarenko,
T. I. Pekhk, and S. A. Makhnach

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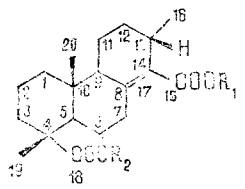
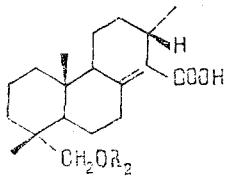
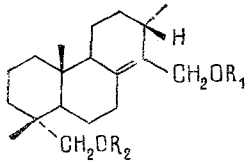
The properties and ^{13}C NMR spectra of pinifolic acid (13S-labd-8,17-ene-15,18-dioic acid), its monomethyl ester, its dimethyl ester, its dicyclohexylammonium salt, dihydropinifolic acid, 18-hydroxy-13S-labd-8(17)-en-15-oic acid, the cyclohexylammonium salt of the monomethyl ester, the bis(diethylammonium) salt, pinifodiol (13S-labd-8(17)-ene-15,18-diol), the acetate of 18-hydroxy-13S-labd-8(17)-en-15-oic acid, and the diacetate of pinifodiol have been studied.

Pinifolic (13S-labd-8(17)-ene-15,18-dioic) acid (I) was first isolated from the needles of *Pinus sylvestris* L. growing in Sweden [1]. Derivatives of it have been obtained: the monomethyl ester (II), the dimethyl ester (III), the dicyclohexylammonium salt (IV), dihydropinifolic acid (IV) and 18-hydroxy-13S-labd-8(17)-en-15-oic acid (VI). The IR and mass spectra of these compounds have been studied and their spatial structures have been established [1].







VI. $R_2 = H$; X. $R_2 = CH_3CO$

IX. $R_1 = R_2 = H$; XI. $R_1 = R_2 = CH_3CO$

I. $R_1 = R_2 = H$; II. $R_1 = H$, $R_2 = CH_3$

III. $R_1 = R_2 = CH_3$; IV. $R_1 = R_2 = C_6H_{11}\overset{+}{N}H_3$

VII. $R_1 = C_6H_{11}\overset{+}{N}H_3$; $R_2 = CH_3$; VIII. $R_1 = R_2 = C_2H_5\overset{+}{N}H_3$

Later [2] from the needles of trees of the same species growing in Belorussia, the monomethyl ester of pinifolic acid was isolated and its cyclohexylammonium salt (VII) was obtained, and to confirm their structure the IR, mass, and PMR spectra of these substances and of the synthesized compounds (I), (III), and (IV) were studied.

In the present communication we give the properties, including the IR and mass spectra, of the newly synthesized bis(diethylammonium) salt (VIII), of pinifodiol (13S-labd-8(17)-ene-15,18-diol) (IX), and of the acetates of 18-hydroxy-13S-labd-8(17)-en-15-oic acid (X) and of pinifodiol (XI), and the ^{13}C NMR spectra of compounds (I-XI).

The ^{13}C NMR spectra of compounds (I-XI) confirm the spatial structures of these substances deduced previously [1, 2]. The chemical shifts of the C_{19} and C_{20} atoms of compounds (I-XI) range from 17.0 to 18.1 ppm and from 14.9 to 15.4 ppm, respectively, i.e., approximately within the same limits as for the similarly oriented C_{19} and C_{20} groups of compounds of the labdane series related to them [3, 4], pimarane and isopimarane [5]. Consequently, the C_{19} and C_{20} methyl groups are oriented in the axial β position. If they were oriented in the equatorial α position, the values of their shifts should be approximately 30 ppm.

The alkyl chain at C_9 is in the equatorial β position, the chemical shift for C_{11} being the same as for C_{11} of sclareol (labd-14-ene-8,13-diol) [4].

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TABLE 1. Chemical Shifts of ^{13}C Nuclei of the Compounds, σ, TMS, ppm

Carbon atom	Compound									
	I	II	III	IV	VI	VII	VIII	IX	X*	XI†
1	39,4	39,1	39,1	39,6	39,5	39,2	39,4	39,7	38,6	38,5
2	19,6	19,3	19,3	19,8	19,6	19,3	19,7	19,7	18,6	18,6
3	38,3	38,0	37,9	39,1	38,3	37,4	39,0	36,4	35,9	35,3
4	48,4	48,7	48,6	‡	38,7	‡	48,8	38,8	36,9	36,8
5	51,1	51,0	50,9	51,3	49,3	51,1	51,1	49,5	49,6	49,5
6	28,0	27,7	27,7	27,9	25,9	27,8	27,9	25,1	24,4	24,3
7	39,1	38,8	38,8	38,7	38,8	38,9	38,5	39,0	38,1	38,1
8	149,4	148,8	145,8	151,0	149,4	149,2	149,5	149,8	147,9	148,0
9	58,8	58,4	58,4	58,9	58,2	58,7	58,7	58,6	57,3	57,3
10	40,1	39,9	39,9	40,0	40,3	40,0	39,9	40,5	39,6	39,6
11	22,0	21,7	21,7	22,0	21,8	21,9	21,9	21,9	21,1	20,8
12	37,0	36,7	36,7	37,6	36,8	38.	37,3	37,4	36,0	36,0
13	32,2	31,9	32,0	32,8	31,8	32,6	32,7	31,3	30,9	30,6
14	42,5	42,2	42,0	‡	42,2	‡	45,8	40,5	41,4	35,0
15	176,9	176,4	174,5	181,7	176,5	181,3	180,8	61,1	178,5	170,7
16	20,4	20,3	20,3	20,4	20,3	20,5	20,6	20,3	20,0	19,7
17	107,5	107,5	107,4	106,7	106,8	107,4	106,8	106,7	106,8	106,6
18	182,5	180,2	179,9	186,2	71,9	180,4	184,8	72,1	171,1	170,7
19	17,2	17,1	17,0	18,0	18,0	17,0	17,7	18,1	17,5	17,5
20	15,2	15,2	15,2	15,0	15,4	15,1	15,1	15,4	14,9	14,9

Note. According to its ^{13}C NMR Spectrum, compound (V) is a mixture of stereoisomers.
Solvents: CD_3OD; *) $CHCl_3$; †) $CDCl_3$; ‡) lines under strong solvent lines.

The chemical shifts of C_8 and C_{17}, linked by an ethylenic bond, have values characteristic for such atoms [3, 5]. The chemical shifts of C_{15} and C_{18} in the acids, methyl esters, and amine salts have characteristic values in the low field. Reduction of the carboxy groups to hydroxymethyl groups lead to a pronounced upfield shift of the C_{15} and C_{18} signals. Such a change in the groups of C_{18} is also reflected appreciably in the values of the signals of the neighboring C_4 and C_3 atoms, while a similar change of groups at C_{15} has little effect on the values of the signals of the neighboring C_{14}. These facts can be successfully to establish the structures of mono derivatives of pinifolic acid.

EXPERIMENTAL

The ^{13}C NMR spectra of the substances were taken on a Bruker WH-90 spectrometer with a resonance frequency for ^{13}C of 22.62 MHz. Specific rotations were determined on a Jasco J-20 spectropolarimeter. Melting points were determined on a Boëtius stage. IR spectra were recorded on a UR-20 instrument, and mass spectra on a Varian MAD-311 instrument.

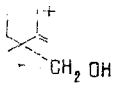
Preparation of Pinifolic Acid and Its Monomethyl Ester. Air-dry pine needles that had been ground in a ball mill were extracted with acetone in a ratio of 1 : 2 (by volume) three times (for six days each time). The acetone was distilled off, the residue was extracted with diethyl ether, and the resulting solution, in its turn, was extracted with 2% aqueous NaOH. The neutral substances were extracted from the solution of salts with diethyl ether, and then a 5% solution of CH_3COOH (in slight excess) was added to the solution. The free acids were extracted with petroleum ether—diethyl ether (10 : 1). The evaporated extract of the acids was chromatographed on a column filled with silica gel L 40/100 μ.

Elution with petroleum ether gave fractions 1 (higher fatty acids) and 2 (monobasic resin acids). Elution with diethyl ether—petroleum (1 : 50) yielded fraction 3 (solution of the monomethyl ester), and elution with the same solvents in a ratio of 1 : 20 gave fraction 4 (solution of linifolic acid). The subsequent purification of compounds (I) and (II) was performed by crystallization of their cyclohexylamine salts from ethanol. mp of (II) 72-74°C; $[\alpha]_D$ + 22.6° (c 1.0; chloroform). It must be mentioned that the crystallization of the monomethyl ester from ethanol at 0°C takes place very slowly (20-30 days).

The Amine Salts (IV, VII, and VIII). At 50°C, 1 g of the acid was dissolved in 50 ml of acetone, a 50% solution of the amine in the same solvent heated to 50°C and slowly added, with vigorous stirring, until a weakly alkaline reaction had been achieved. The salts were crystallized from acetone. The bis(diethylammonium) salt (VIII) had mp 124-127°C; $[\alpha]_D$ + 16.2° (c 1.0; ethanol), ν_{max}^{KBr} (cm^{-1}): 1370, 1515 (COO^-), 1630, 3040 (C=C).

Dihydropinifolic acid (V) was obtained by the hydrogenation of an ethanolic solution of pinifolic acid in the presence of platinum black. mp 223-225°C; $[\alpha]_D$ + 36.5° (c 1.0; ethanol). According to the literature: mp 218-219°C; $[\alpha]_D$ + 30.0° (c 1.5; ethanol). Mass spectrum, m/z (%): M^+ 318 (3), 292 ($M^+ - COOH$, 69), 277 ($M^+ - COOH - CH_3$, 29), 223 (47), 195 (99), 177 (45), 163 (40), 123 (100).

18-Hydroxy-13S-labd-8(17)-en-15-oic Acid and Pinifodiol. A solution of 13 g of the monomethyl ester of pinifolic acid in 150 ml of dry ether was reduced with a solution of 5 g of $LiAlH_4$ in 100 ml of the same solvent. The reaction mixture was heated at 35°C for 4 h. The excess of hydride was decomposed with water, and then the mixture was neutralized with 3 N aqueous CH_3COOH. The ethereal solution of the product was washed with water and extracted with 2% aqueous NaOH. By the usual method, 6.5 g of (VI) was obtained from the aqueous solution, and 5.6 g of pinifodiol (IX) from the ethereal solution.

Properties of (VI): n_D^{25} 1.5901; $[\alpha]_D$ + 33.8° (c 1.0; ethanol). According to the literature [1]: n_D^{25} 1.508; $[\alpha]_D$ + 33.0°(c 0.8; chloroform). ν_{max}^{KBr} (cm^{-1}): 1042 (C—O), 1645 (C = C), 1709 (C = O), 3360 (OH). Mass spectrum, m/z (%): M^+ 322 (4), 291 ($M^+ - CH_2OH$, 100), 277 ($M^+ - COOH$, 23), 207 ($M^+ - C_6H_{11}O_2$ 8), 210 (28), 176 (16), 149 (29), 135 (33); fragment 153 

(8), fragment 121  (68). The mass and ^{13}C NMR spectra unambiguously show the position of the hydroxymethyl group at C_4.

Properties of (IX): mp 82-84°C; $[\alpha]_D$ + 48.2° (c 1.0; ethanol). ν_{max}^{KBr} (cm^{-1}): 1042, 1052 (C—O), 1645, 3045 (C = C), 3350 (OH). Mass spectrum m/z (%): M^+ 308 (8), 277 ($M^+ - CH_2OH$, 100), 264 (33), 253 (20) 221 (11), 207 ($M^+ - C_6H_{13}O$, 23), 195 (32), 176 (35), 161 (41), 153 (15), 149 (61), 135 (64), 121 (85).

Diacetate of Pinifodiol (XI). A mixture of 1 g of pinifodiol (IX), 5 g of acetic anhydride, and 0.4 g of freshly-fused sodium acetate was heated at 140°C for 1 h. Then the solution was cooled to 0°C, 15 ml of water has added, and the mixture was heated in the boiling water bath with stirring for 15 min. After this, it was repeatedly extracted with saturated NaCl solution and then with water. The oil, n_D^{25} 1.5114, $[\alpha]_D$ + 25.5° (c 1.0; ethanol) was purified by chromatography on silica gel 40/100 μ with elution by pentane. ν_{max}^{film} (cm^{-1}): 1240 (C—O), 1642, 3082 (C=C), 1740 (C=O). Mass spectrum, m/z (%): M^+392(5), 332(82): 319 ($M^+ - CH_2OCOCH_3$, 50) 272 (27), 254 (35), 249 ($M^+ - C_8H_{15}O_2$, 14), 190 (51), 175 (100), 135 (100), 121 (100).

The acetate of 18-hydroxy-13S labd-8(17)-en-15-oic acid (X) was obtained by the acetylation of (VI) by the same method, but only half the amount of acetylating agent was used. Oil, n_D^{25} 1.5122, $[\alpha]_D$ + 25.0° (c 1.0; ethanol); it was purified in the same way as (XI).

ν_{max}^{film} (cm^{-1}): 1240 (C—O), 1643, 3085 (C=C), 1710, 1740 (C=O). Mass spectrum, m/z (%): M^+ 364 (3), 319 ($M^+ - COOH$, 8), 304 (41), 291 ($M^+ - CH_2OCOCH_3$, 46), 249 ($M^+ - C_6H_{11}O_2$, 7), 175 (54), 135 (100), 121 (100).

SUMMARY

Pinifolic acid and its monomethyl ester have been isolated from the needles of *Pinus sylvestris* L. and derivatives of them have been obtained. The properties and ^{13}C NMR spectra of these compounds have been studied.

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