SUMMARY

In a study of the acetylation of lagochilin by PMR spectroscopy, it has been established that the reactivities of the hydroxy groups decrease in the following sequence: $C_{15} > C_{16} > C_{18} > C_3$.

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REFINEMENT OF THE STRUCTURES OF TRITERPENES FROM THE LEAVES OF Betula ermanii

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From the unsaponifiable part of an ethereal extract of the leaves of Betula ermanii two previously unknown triterpenes (II) and (I) have been isolated to which, previously, the structures of 20, 24-epoxydammarane-3β,6α,25-triol and its 6α-acetate were erroneously ascribed. A further study of the ^1H and ^{13}C spectra of compounds (II) and (I), and also the spectra of their derivatives – the diketone (III) and the epimer of the triterpene (II) at C^{11} (IV) – has shown that the triterpene (II) has the structure of 20(S),24(R)-epoxydammarane-3β,11α,25-triol, and the triterpene (I) is its 11α-acetate. Triterpenes (I) and (II) are the first examples of natural 11-hydroxylated C_{30}-triterpenes of the dammarane type.

In a preceding communication [1], for the triterpenese (II) and (I) that we had isolated from the leaves of Betula ermanii the structures of 20,24-epoxydammarane-3β,6α-25-triol and its 6α-acetate were proposed. A careful study of the ^1H and ^{13}C spectra of compounds (I) and (II) has, however, shown that the structures suggested previously are incorrect. To broaden the possibilities of structural correlations, triterpene (II) was oxidized with CrO_3 in pyridine to the diketone (III) [1], which, on reduction with $LiAlH_4$ in ether, gave an epimer of the triterpene (II). On similar oxidation, the epimeric triterpene (I) also gave the diketone (III).

In the ^1H spectra of compounds (I-IV), multiplets in the 3.0-4.0 ppm region are of particular interest. A triplet at 3.73 ppm with J = 6.5 Hz in the spectrum of each of these compounds can be assigned unambiguously to H^{24}, since it is detected also in the ^1H spectra of ocotillol (V), ocotillone* (VI) and other dammarane triterpenes with a side chain of the ocotillone type [2, 3]. The same analogies permit the triplet at 3.18 ppm with J = 6.8-7.2 Hz in the ^1H spectra of compounds (I), (II), and (IV) to be assigned to H^3. The values of δ and J for the H^3 signal show the β-configuration of the OH group at C^3.

A sextet at 3.80 ppm with J = 10.0 and 5.1 Hz (ΣJ = 25.1 Hz) in the ^1H spectrum of the triterpene (II) relates to an axial proton at a C atom bearing a hydroxyl function, the position of which was to be determined. In

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TABLE 1. ^{13}C Chemical Shifts of Compounds (I-VI) (ppm Relative to TMS)

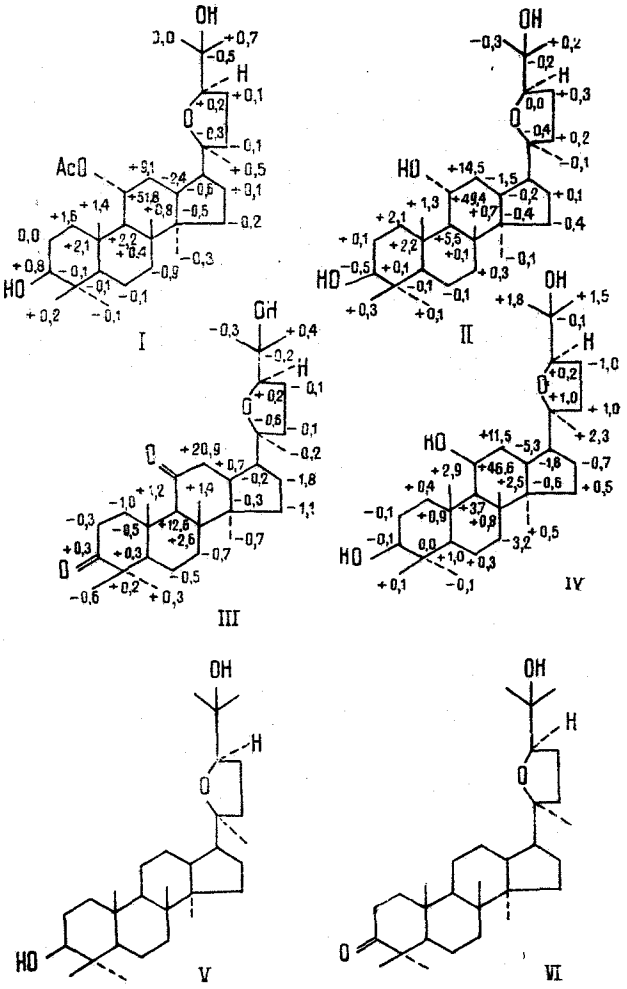
C atom	Compound					
	I	II	III	IV	V	VI
1	40.6	41.1	38.9	39.4	39.0	39.9
2	27.4[a]	27.5[a]	33.9	27.3	27.4	34.2
3	78.1	78.4	216.5	78.8	78.9	216.2
4	38.9	39.1	47.6	39.0	39.0	47.4
5	55.8	55.8	55.8	56.9	55.9	55.5
6	18.2	18.2	19.3	18.6	18.3	19.8
7	35.0	36.2	34.0	32.7	35.9[a]	34.7
8	41.1	40.8	43.0	41.5	40.7	40.4
9	52.9	56.2	62.9	54.4	50.7	50.3
10	39.5	39.6	36.4	38.3	37.4	36.9
11	73.4	71.0	211.0	68.2	21.6	22.2
12	34.6	40.0	46.6	37.0	25.5[b]	25.7
13	40.6	41.5	44.0	37.7	43.0	43.3
14	49.8	49.9	49.7	49.7	50.3	50.0
15	31.3	31.1	30.5	32.0	31.5	31.6
16	27.7[a]	27.7[a]	25.8	26.9	27.6	27.6
17	49.1	49.5	49.5	47.9	49.7	49.7
18	16.9	16.8	17.5[a]	18.6[a]	16.1[c]	16.1[a]
19	16.9	16.8	16.4[a]	18.4[a]	15.5[c]	15.2[a]
20	86.1	86.0	85.5	87.4	86.4	86.1
21	24.0	23.4	23.5	25.8	23.5	23.7
22	35.9	36.2	35.8	37.0	36.0[a]	35.9
23	26.1	26.3	26.2	25.0	26.0[b]	26.3
24	83.6	83.4	83.6	83.6	83.4	83.4
25	71.2	71.5	71.3	71.6	7 .7	71.5
26	26.1[b]	25.8[b]	27.3[b]	27.9[b]	26.1[d]	27.6[b]
27	25.0[b]	24.5[b]	24.8[b]	25.8[b]	24.3[d]	24.4[b]
28	28.3	28.4	26.3[b]	28.2	28.1	26.9
29	15.4	15.6	21.4	15.4	15.5[c]	21.1
30	16.3	16.5	15.7[a]	17.1	16.6[c]	16.4[a]
31	170.3	—	—	—	—	—
32	22.0	—	—	—	—	—

Note. The assignments of the signals in groups a, b, c, and d are uncertain.

the ^1H spectrum of the triterpene (IV) – the epimer of triterpene (II) at its asymmetric center – there was no signal at 3.80 ppm, but a multiplet had appeared at 4.32 ppm with $\Sigma J \simeq 12.0$ Hz, which indicates the equatorial position of the corresponding proton. Analysis of the ^1H spectra of the triterpenes (II) and (IV) permitted the hydroxy group with the unestablished location to be ascribed to several positions in the skeleton. Positions 2 and 16 are excluded, however, as the result of the oxidation of the triterpenes (II) and (IV), since the IR spectrum of the diketone (III) shows only one strong band of the stretching vibrations of a carbonyl group at 1697 cm^{-1}, just like the IR spectrum of ocotillone (VI). This could not apply in the case of a 2,3-diketone and, all the more, of a 3,16-diketone. Position 12 is excluded by a comparison of the ^1H and ^{13}C spectra of the triterpene (II) and of 12β-hydroxylated triterpenes of the dammarane series [4]. We made the choice between positions 6 and 11 in the skeleton by comparing the ^{13}C spectra of ocotillone (VI) [4] and of the diketone (III), and also of ocotillol (V) and the triterpenes (I), (II), and (IV).

In the ^{13}C spectra of triterpenes of the dammarane series with a 3β-OH group and an oxygen function at C^{12} or without it, the C^5 signal is detected in a weaker field (~56.0 ppm) than the C^9 signal (~50.5 ppm), and the introduction of an OH group at position 6 causes a downfield shift of the C^5 signal (61.0 ppm) [4, 5]. The absence from the ^{13}C spectra of the triterpenes (I), (II), and (IV) in the 60.0 ppm region unambiguously indicates that the third OH group in these compounds is located at C^{11}. The presence of the C^9 signal in the ^{13}C spectrum of the triterpene (II) in a weaker field than the C^5 signal is explained by the β-effect of the 11α-OH group. The effects of the 11α-OH, 11α-OAc, and 11α-OH groups and the 11-keto group in the ^{13}C spectra of compounds (I-IV) shown in the structural formulas with respect to ocotillol (V) and ocotillone (VI), respectively, are, in the majority of cases, in good agreement with the effects of similar functional groups in triterpenoids and steroids [4-9]. The better agreement of the chemical shifts of the C^{21}, C^{22}, C^{24}, and C^{25} atoms in the ^{13}C spectra of compounds (I-III) with the chemical shifts of the corresponding C atoms in the spectra of 20(S),24(R)-ocotillol (V) and 20(S),24(R)-ocotillone (VI) [4] show a correspondence of the stereochemistries of the asymmetric centers C^{20} and C^{24} in compound (V and VI), on the one hand, and (I-III), on the other hand. The considerable change in the chemical shifts of the C^{20}, C^{21}, C^{22}, C^{23}, C^{26}, and C^{27} in the ^{13}C spectrum of the epimer (IV) as compared with the chemical shifts of the same C atoms in the ^{13}C spectra of (I-III, V, and VI) is most probably due not to

the change in the stereochemistry at C^{20} or C^{24} but to the influence of an intramolecular hydrogen bond formed between the 11β-OH group and the oxygen function at C^{25}.



Thus, the triterpene (II) has the structure of 20(S),24(R)-epoxydammarane-3β,11α,25-triol, and triterpene (I) is its 11α-acetate. Triterpene (IV) is, correspondingly, 20(S),24(R)-epoxydammarane-3β,11β,25-triol and (III) is 25-hydroxy-20(S),24(R)-epoxydammarane-3,11-dione. It must be mentioned that among natural triterpenes of the dammarane type isolated from higher plants only one 11-hydroxylated triterpene is known, but this contains 31 carbon atoms [10]. Triterpenes (I) and (II) are, therefore, the first natural 11-hydroxylated C_{30}-triterpenes of the dammarane type.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker HX-90E spectrometer with working frequencies of 90.0 MHz for ^1H and 22.63 MHz for ^{13}C in the Fourier regime at 30°C using 8% solutions of the substances in $CDCl_3$. The ^{13}C chemical shifts (Table 1) are given on the δ scale relative to TMS. The accuracy of measurement was $\pm$0.15 Hz for ^1H and $\pm$1.5 Hz for ^{13}C. The assignment of the signals in the ^{13}C spectra of compound (I-IV) was made by the method of selective double heteronuclear resonance on the basis of the PMR results by the method of off-resonance spin decoupling and on the basis of results on the effects of oxygen-containing substituents in six-membered rings [4-9]. To assign the signals in the ^{13}C spectra we also used a comparison of the experimental chemical shifts with the calculated values. The semiempirical calculation of the ^{13}C chemical shifts for compounds (I-IV) was carried out by two methods [11, 12].

Reduction of the Diketone (III) with $LiAlH_4$. A solution of 250 mg of the diketone (III) in 30 ml of absolute ether was added dropwise to a suspension of 500 mg of $LiAlH_4$ in 60 ml of absolute ether. The reaction mixture

was heated under reflux for 6 h. Then 0.5 ml of H_2O, 0.5 ml of 15% NaOH, and 1.5 ml of H_2O were added successively. The inorganic layer was separated off, and the ethereal layer was washed with water, dried over Na_2SO_4, and evaporated. The residue was separated on a column containing SiO_2. Elution by the petroleum ether–acetone (15:1) system gave 100 mg of 20(S),24(R)-epoxydammarane-3β,11β,25-triol (IV). mp 173-175°C (hexane), $[\alpha]_D$ +52.0 (c 1; chloroform).

Oxidation of the Triterpene (IV). To a solution of 45 mg of the triterpene (IV) in 1.5 ml was added 55 mg of CrO_3 in 1.5 ml of pyridine. The reaction mixture was stirred at 20°C for two days and was then diluted with 40 ml of water, and the aqueous solution was extracted with ether (4 × 15 ml). The combined ethereal extracts were washed with dilute $NaHCO_3$ solution and with water, and they were dried over Na_2SO_4 and evaporated. This gave 30 mg of the diketone (III) with mp 167-170°C. Crystallization from hexane gave 23 mg of the diketone (III) with mp 170-172°C, $[\alpha]_D$ +46° (c 0.5; chloroform).

SUMMARY

From the unsaponifiable part of an ethereal extract of the leaves of Betula ermanii we have isolated two new triterpenes having the structures of 20(S),24(R)-epoxydammarane-3β,11α,25-triol (II) and its 11α,O-acetyl derivative (I), and not 20,24-epoxydammarane-3β,6α,25-triol and its 6α-acetate, as suggested previously [1]. Triterpenes (I) and (II) are the first natural 11-hydroxylated C_{30}-triterpenes of the dammarane type.

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