SUMMARY

Under the action of catalytic amounts of mineral acid, the pentaol obtained by the reduction of the norditerpenoid teucrin A with lithium tetrahydroaluminate undergoes an anionotropic rearrangement with the subsequent elimination of a molecule of water.

LITERATURE CITED

1. D. P. Popa and A. M. Reinbol'd, Khim. Prirodn. Soedin., 31 (1973).
2. C. Kaneko, T. Tsuchiya and M. Ishikawai, Chem. Pharm. Bull., 11, 271 (1963).
3. K. Nakanishi, Infrared Absorption Spectroscopy. Practical, Holden-Day, San Francisco (1962).

TRITERPENOIDS FROM THE LEAVES OF *Betula costata*

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Triterpenoids with a dammarane structure have been found in the leaves of various species of birch. Fischer and Seiler have isolated two previously unknown triterpenes — betulafolienetriol and betulafolienetetraol — from the leaves of the European species of birch *Betula alba* [1, 2] and have established their structure. Later, Japanese chemists showed the presence of new triterpenoids in the leaves of *Betula platyphylla* [3, 4].

Our aim was to search for sources rich in polycyclic alcohols of the dammarane series, which have been proposed for use as the starting material in the synthesis of glycosides [5]. We investigated the leaves of the far-eastern species *Betula costata*, since the presence of betulafolienetriol in them was known [6].

According to TLC, in the unsaponifiable part of an ethereal extract of the leaves of *Betula costata* (collected at the beginning of June, 1973, by G. P. Gorov) contained five triterpenes. We have isolated four individual substances — A, B, C, and D — so names in order of increasing polarity — and have determined their structures.

Triterpene A(I), $C_{30}H_{52}O_3$; the IR spectrum ($CHCl_3$) shows hydroxyl absorption at 3560 and 3620 cm^{-1}. Its PMR spectrum ($CDCl_3$) has the signals of the protons of eight tertiary methyl groups with δ (ppm) 0.77 (3H, s), 0.80 (3H, s), 0.88 (3H, s), 0.90 (3H, s), 1.0 (3H, s), 1.11 (3H, s), 1.57 (3H, s), 1.63 (3H, s) and the signal of a vinyl proton at C-24 with δ 5.09 ppm (1H, triplet), and also the signal of a C-3 proton at δ 3.32 ppm (1H, triplet, $J_{3,2} = J_{3,2} < 4$ Hz). The value of the constant shows the α configuration of the OH group at C-3. No signals of protons were observed in the 3.80-3.90 region, which permitted us to assume that there was no hydroxyl at C-12.

The mass spectrum of (I) contained the peak of the molecular ion M^+ 460, the peak of a tetracyclic fragment with m/e 333 and a peak with m/e 360. The absence of a hydroxyl at C-12 is responsible for the appearance of strong peaks of the side chain with m/e 128 and 110 as the result of cleavage between the fully substituted C-17 and C-20 atoms, since these peaks are the main ones in the mass spectrum of (I) taken at a low voltage (12 V).

Thus, for the triterpene acetate, A (I), the structure of dammar-24-ene-3α,17α,20-triol is proposed.

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Triterpene B (II), $C_{30}H_{52}O_3$, was identified as betula folienetriol by its physicochemical constants and by comparison with an authentic sample provided by Dr. N. Seiler.

Triterpene C (III), $C_{30}H_{52}O_5$; its IR spectrum ($CHCl_3$) showed hydroxyl absorption at 3420 cm^{-1} (independent of the concentration) and at 3610 cm^{-1} (free OH). The PMR spectrum of (III) had the signals of the protons of eight tertiary methyl groups, and also the signals of protons attached to carbon atoms bearing oxygen functions, with δ (ppm) 3.39 (1H, triplet, J = 2.2 Hz) and 3.80 (1H, sextet, J = 11 Hz, J = 7 Hz) — protons at C-3 and C-12, respectively; and a signal at δ 3.74 ppm (1H, triplet, J = 6.6 Hz) belonging to a C-24 proton.

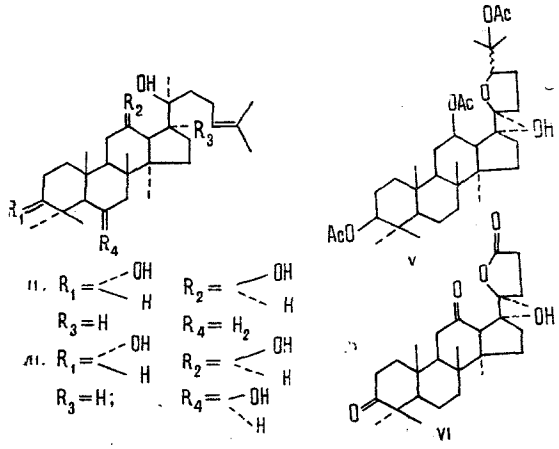
The mass spectra of (III) showed peaks with m/e 143 (100%) — corresponding to a fragment of the side chain ($C_8H_{15}O_2$) — and with m/e 59 [$(CH_3)_2\overset{+}{C}-OH$], which enables us to characterize the side chain of (III) as a substituted tetrahydrofuran ring [3] (Fig. 1b).

The molecule of (III) contains four hydroxyls, two of which, at C-3 and C-12, are readily esterified while the third hydroxyl is tertiary, is present in the side chain at C-25, and is acetylated under more severe conditions [7]. In the IR spectrum ($CHCl_3$) of the triacetate of compound C at C-3, C-12, and C-25 (V, Scheme) hydroxyl absorption is still observed at 3540 cm^{-1}. When (III) was oxidized by the Jones reagent in acetone, a trisnorhydroxydiketolactone (VI) having the same characteristics as the hydroxydiketolactone obtained by Fischer and Seiler from betulafolienetetraol [2] was obtained.

The results of the investigations performed show that triterpene C must be a derivative of betulafolienetetraol. When substance (III) was isolated for the first time [3], by analogy with betulafolienetriol the structure of an oxide of betulafolienetetraol [8] was proposed.

The triterpene D (IV), $C_{30}H_{52}O_4$, corresponds in its physicochemical properties to the betulafolienetetraol isolated previously [1]. The structure of (IV) was also confirmed by the results of a spectroscopic investigation of this compound. In the IR spectrum of (IV) ($CHCl_3$) hydroxyl absorption is observed at 3615 and 3370 cm^{-1}. The PMR spectrum of (IV) ($CDCl_3$) shows the signals of eight tertiary methyl groups at δ (ppm) 0.84 (3H, s), 0.89 (3H, s), 0.95 (3H, s), 0.98 (3H, s), 1.18 (3H, s), 1.21 (3H, s), 1.63 (3H, s), and 1.70 (3H, s), the signals of protons attached to carbon atoms bearing oxygen groups at δ (ppm) 3.40 (1H, triplet) and 3.85 (1H, triplet), corresponding to the protons at C-3 and C-12, and also the signal of a C-24 vinyl proton at δ 5.12 ppm (1H, triplet). The structure of betulafolienetriol as dammar-24-ene-3α,12β,20(S)-triol was established by Fischer and Seiler, and its mass spectrum was identical with the mass spectrum of the 6-hydroxy analog (VII) (Scheme) [9] according to the peak of the ions of the series a, b, d, s, and Sch. A distinguishing feature of the mass spectrum of (IV) is the presence of the peak of the molecular ion, M^+ 476, and of the peak of a tetracyclic fragment s with m/e 349, and the absence of ions of the *a* series with m/e 202 and m/e 216. This is due to the presence in (IV) of a hydroxy group at C-17 which, is also responsible for the formation of another type of ion $d'-d_1'$ with m/e 376.

It is easy to obtain (III) from the triterpene D (IV) (Fig. 1c): when a chloroform solution of (IV) was left in the light for a day, triterpene C (III) was formed [10]. When



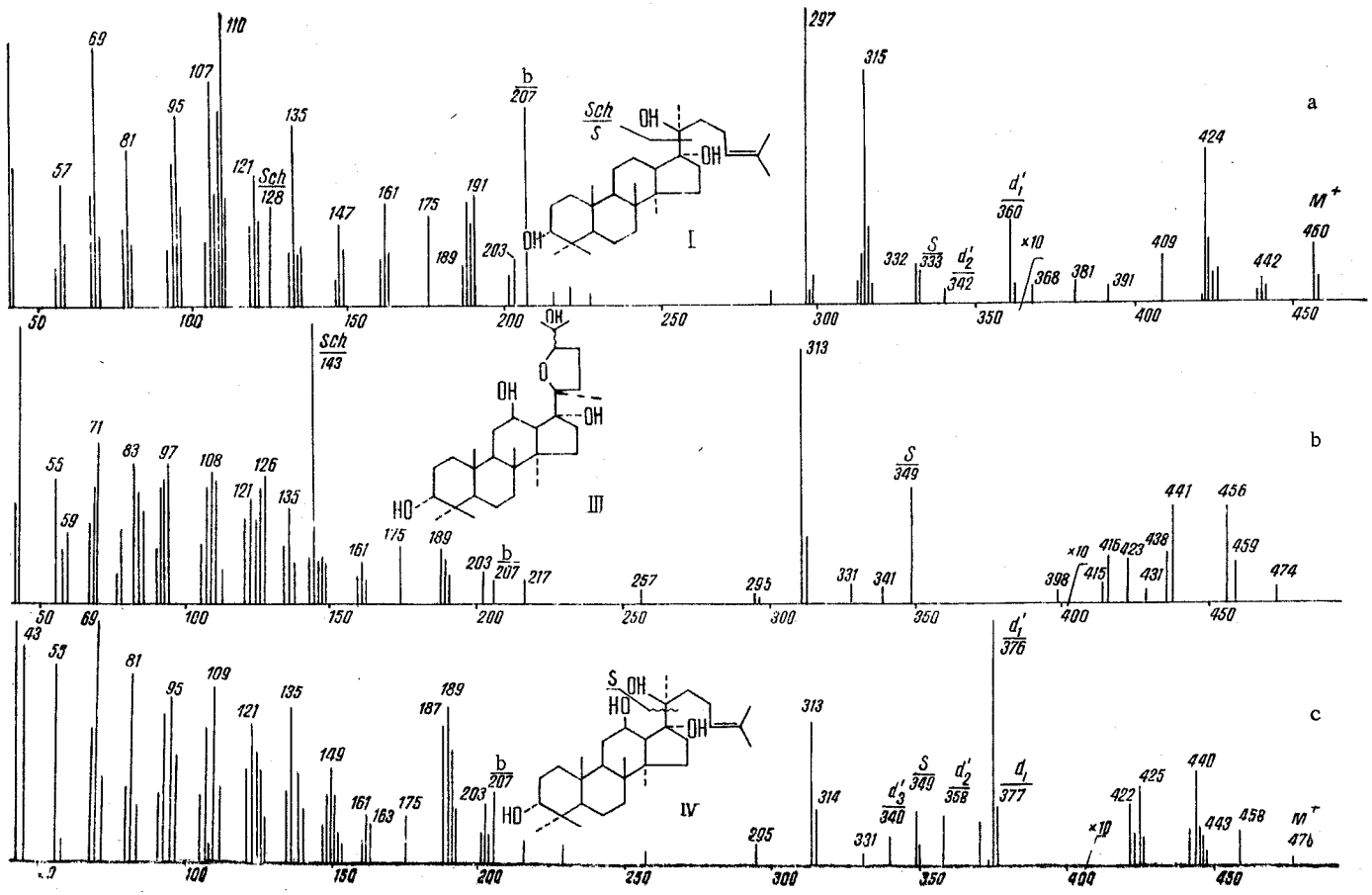


Fig. 1. Mass spectra of the triterpenoids A (I) — (a); C (III) — (b); and D (IV) — (c).

(IV) was oxidized with the Jones reagent, the trisnorhydroxydiketolactone (VI) was obtained, and the action of perbenzoic acid on (IV) [3] formed two substances, one of which was identical with (III). The other substance, (IIIa), had the same empirical formula ($C_{30}H_{52}O_5$) and its fragmentation in the mass spectrum was similar to that of (III). However, the IR and PMR spectra of (IIIa) differed substantially from the spectra of (III). Oxidation of the second product (IIIa) with the Jones reagent led to the formation of the trisnorhydroxydiketolactone (VI). Thus this substance (III) may be considered as the epimer of (III) at C-24.

EXPERIMENTAL

The PMR spectra were taken on a Brüker HX-90 E instrument in $CDCl_3$ with TMS as internal standard (δ scale), the mass spectra on an MKh-1303 spectrometer, and the IR spectra on a UR-20 spectrophotometer.

The individuality of the substances was checked by thin-layer chromatography on silica gel (KSK) in the following solvent systems: chloroform–ethanol (10:1) and petroleum ether–acetone (2:1). For detecting the triterpenes on the chromatograms we used a 10% solution of H_2SO_4 in methanol.

Isolation of the Triterpenes A, B, C, and D. The air-dry leaves of *Betula costata* (9 kg) were covered with diethyl ether and were exhaustively extracted at room temperature. The ethereal extract obtained was evaporated to dryness. The subsequent treatment was performed as described by Fischer and Seiler [1]. This gave 129 g of unsaponifiable ethereal extract, and 100 g of this was deposited on a column filled with silica gel (KSK) and eluted with various solvent systems. In the benzene–chloroform (2:3) systems, fractions containing triterpenes A and B were obtained; triterpene C (III) was eluted with chloroform, and D (IV) with chloroform–methanol (20:1). Then the pure crystalline triterpenoids A, B, C, and D were obtained by repeated purification on chromatographic columns and by recrystallization.

Triterpene A (I), composition $C_{30}H_{52}O_3$, yield 250 mg, mp 140-142°C (petroleum ether), $[\alpha]_D^{20}$ +4.80° (c 0.5; $CHCl_3$). Mass spectrum: M^+ 460, m/e 442 (M $-H_2O$), 424 (M $-2H_2O$), 409 (M $-2H_2O-CH_3$) 333 (M $-C_8H_{15}O$), 297 (333 $-2H_2O$), 207, 128, 110.

Triterpene B (II), 100 mg, mp 197-198°C (acetone), acicular crystals giving no depression of the melting point in a mixture with betulafolienetriol.

Triterpene C (III). Crystals (10.77 g) were obtained in the form of prisms with mp 250-251.5°C (acetone), $[\alpha]_D^{20}$ +6.00° (c 0.5, $CHCl_3$). Mass spectrum: m/e 474 (M $-H_2O$), 459 (M $-H_2O-CH_3$), 456 (M $-2H_2O$), 441 (M $-2H_2O-CH_3$), 349, 313, 143 (100%).

Triterpene D (IV), 9.3 g, mp 168-170°C (acetone), $[\alpha]_D^{20}$ +8.50 (c 0.5; $CHCl_3$). Mass spectrum: M^+ 476, m/e 458 (M $-H_2O$), 440 (M $-2H_2O$), 425 (M $-2H_2O-CH_3$), 422 (M $-3H_2O$), 376, 313.

Oxidation of Betulafolienetetraol Oxide. By the usual method [3], 200 mg of (III) in 16 ml of acetone was oxidized with the Jones reagent for 1.7 h. After the addition of dilute Na_2SO_3, the mixture was extracted with ether. The ethereal solution was washed 2-3 times with water, dried over calcined Na_2SO_4, and evaporated to dryness. The residue was recrystallized from methanol, giving colorless needles with mp 280-290°C (decomp.), the identity of which with the trisnorhydroxydiketolactone (VI) was shown by a mixed melting point and by a direct comparison of IR spectra.

Preparation of the Triacetate of Betulafolienetetraol Oxide at C-3, C-12, and C-25. A solution of 200 mg of (III) in 2 ml of pyridine was treated with 1 ml of acetic anhydride and the mixture was heated at 90°C for 24 h. The yield of chromatographically homogeneous noncrystalline triacetate of C (V) was 110 mg. IR spectrum, cm^{-1}: 1736 (–C(=O)–O–) and 3540 (OH). The PMR spectrum showed the signals of the protons of eight tertiary methyl groups with δ (ppm) 0.84 (3H), 0.88 (6H), 0.98 (3H), 1.15 (3H), 1.18 (3H), 1.26 (3H), and 1.33 (3H), the signals of the protons of acetate groups with δ (ppm) 1.96 (3H), 1.99 (3H), and 2.09 (3H), the signal of the proton of the C-17 hydroxy group at δ 2.9 ppm (1H), and the signals of C-3, C-12, and C-24 protons at, respectively, δ (ppm) 4.62 ($J_{3,2} = J_{3,2'} < 4$ Hz), 5.10 (J = 4 Hz; J = 10 Hz), and 3.76 (J = 8 Hz).

Oxidation of Betulafolienetetraol (IV). 1. A solution of 100 mg of (IV) in 5 ml of acetone was oxidized with the Jones reagent for 17 h. The reaction mixture was worked up as described above. The residue was recrystallized from methanol, giving colorless needles (30.0 mg) with mp 280-290°C (decomp.), which were identical with the trisnorhydroxydiketolactone (VI).

2. Over 8 h, a solution of perbenzoic acid [11] (280 mg in 3.5 ml of $CHCl_3$) was added in small portions to a ice-cooled solution of (IV) (350 mg in 8 ml of chloroform). After 17 h, the reaction mixture was poured into a mixture of ice and Na_2CO_3. The organic layer was separated off, washed with water, and dried with calcined Na_2SO_4. After evaporation, the oily product was passed through a column of silica gel (KSK). The fractions eluted by the petroleum ether–acetone (20:1) system yielded a substance (140 mg) with mp 250-251.5°C identical with betulafolienetetraol oxide (IV). Evaporation of the fraction eluted by the petroleum ether–acetone (5:1) system yielded a crystalline residue (135 mg) which, after recrystallization from benzene, gave (IIIa) with mp 278-280°C, $[\alpha]_D^{20}$ −15.80° (c 0.5; $CHCl_3$), showing in the NMR spectra eight signals of tertiary methyl groups with δ (ppm) 0.84 (3H, 2), 0.90 (3H, s), 0.95 (3H, s), 1.00 (3H, s), 1.14 (3H, s), 1.21 (3H, s), 1.25 (3H, s), and 1.35 (3H, s), the signals of protons attached to carbon atoms bearing oxygen functions with δ 3.40 ppm (1H, triplet), the signal of a C-3 proton at δ 3.93 ppm (1H, sextet), the signal of the C-12 proton, and the signal of a C-24 proton at δ 3.83 ppm (1H, triplet).

SUMMARY

From the unsaponifiable part of an ethereal extract of the leaves of *Betula costata* four triterpenoids of the dammarane series have been isolated. For the previously unknown triterpenoids A and C the structures of dammar-24-ene-3α,17α,20-triol and of betulafolienetetraol oxide, respectively, have been proposed.

LITERATURE CITED

1. F. G. Fischer and N. Seiler, Ann. Chem., 626, 185 (1959).
2. F. G. Fischer and N. Seiler, Ann. Chem., 644, 146 (1961).
3. M. Nagai, N. Tanaka, and S. Ichikawa, Chem. Pharm. Bull., 21, 2061 (1973).
4. N. Ikekawa, A. Ohta, M. Seki, and A. Takahashi, Phytochem., 11, 3037 (1972).
5. N. I. Uvarova, G. I. Oshitok, and G. B. Elyakov, Abstracts of Papers at the Third Indo-Soviet Symposium on the Chemistry of Natural Compounds [in Russian], Tashkent (1973), p. 164.
6. P. G. Gorovoi, N. I. Uvarova, G. I. Oshitok, and G. B. Elyakov, Rast. Res., 11, 97 (1975).
7. R. Tschesche, G. Biernoth, and G. Snatzke, Ann. Chem., 674, 196 (1964).
8. N. I. Uvarova, G. V. Malinovskaya, V. V. Isakov, A. K. Dzizenko, Yu. N. El'kin, and G. B. Elyakov, Khim. Prirodn. Soedin., 549 (1975).
9. L. I. Strigina, T. M. Remennikova, Yu. N. El'kin, A. K. Dzizenko, V. V. Isakov, and G. B. Elyakov, Dokl. Akad. Nauk SSSR, 210, 727 (1973).
10. G. V. Malinovskaya, N. I. Uvarova, V. V. Isakov, Yu. N. El'kin, A. K. Dzizenko, and G. B. Elyakov, Abstracts of an All-Union Symposium on Bioorganic Chemistry [in Russian], Vladivostok (1975), p. 16.
11. V. Karnojitsky, Peroxydes Organiques, Hermann, Paris (1958).