Triterpenoids from *Abies* sp.

17.* Detection of stereoselective ethylidenation of ring A on the alkali fragmentation of 3,23-dioxo-7,24-lanostadien-26-oic acids

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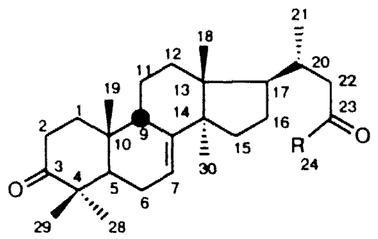
3,23-Dioxo-7,24-lanostadien-26-oic acids, components of a natural mixture of triterpenoids from Siberian fir needles, undergo fragmentation of the side-chain as well as condensation with piruvic acid formed in the reaction in boiling alcoholic alkali and give the 2-ethylidene derivative of the fragmentation product; the structure of the latter was established by NMR spectra and supported by X-ray analysis of its photoisomerization product.

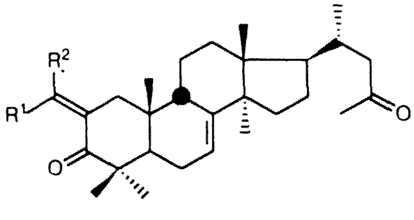
Key words: triterpenoids; aldol condensation; ethylidenation; NMR spectra; X-ray analysis.

Needles of Siberian fir (*Abies sibirica* Ledb.) contain a large amount of triterpene acids; firmanic acid (**1**) and its (24*Z*)-isomer are typical representatives of them.[2] When these acids are heated in ethanolic alkali, cleavage of their side chains occurs and the same methyl ketone **2** is formed (see Ref. 3).



1: R = $CH=C(CH_3)COOH$

2: R = CH_3



3: R^1 = H; R^2 = CH_3

4: R^1 = CH_3; R^2 = H

In continuation of our studies on the composition of the mixture of methyl ketones formed during the alkaline treatment of a native mixture of triterpene acids from Siberian fir needles intended to accelerate the formation of methyl ketones, we carried out this treatment under more drastic conditions *vs.* those described in Ref. 1 (refluxing on a water bath instead of heating at 60 °C). Unexpectedly, a new component (*ca.* 5%) was revealed in the product mixture, which was isolated by column chromatography on SiO_2.

The molecular formula of the new compound is $C_{29}H_{44}O_2$ (high-resolution mass spectrometry); two oxygen atoms are involved in the carbonyl groups, one of which is conjugated with a double bond (IR and UV spectra). The ^{1}H NMR spectrum of the compound obtained is similar to that of methyl ketone **2** but differs in the presence of signals of protons of the ethylidene group, which is presumably located in the molecule at C(2) according to IR and UV spectra. In fact, the protons of the $CH_3CH=C$ group reveal long-range spin coupling interaction with the protons of the $C(1)H_2$ groups in the ^{1}H NMR spectrum; one of these protons (pseudoaxial) interacts through four σ-bonds with the protons of the angular CH_3 group.

The data make it possible to propose structure **3** or **4** for the compound studied. The proof of this assumption and the choice between two variants were made as follows. Upon high-pressure mercury lamp irradiation of a solution of the studied compound in a mixture of hexane and ether, an equilibrium mixture of the initial methyl ketone and its photoisomer is formed (10:17, ^{1}H NMR). The latter compound was prepared in crystalline form using chromatography on SiO_2; it was established by X-ray analysis that the structure of the isomer is **4** (Fig. 1).

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* For Part 16 see Ref. 1.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 3, pp. 752—755, March, 1996.

1066-5285/96/4503-0713 $15.00

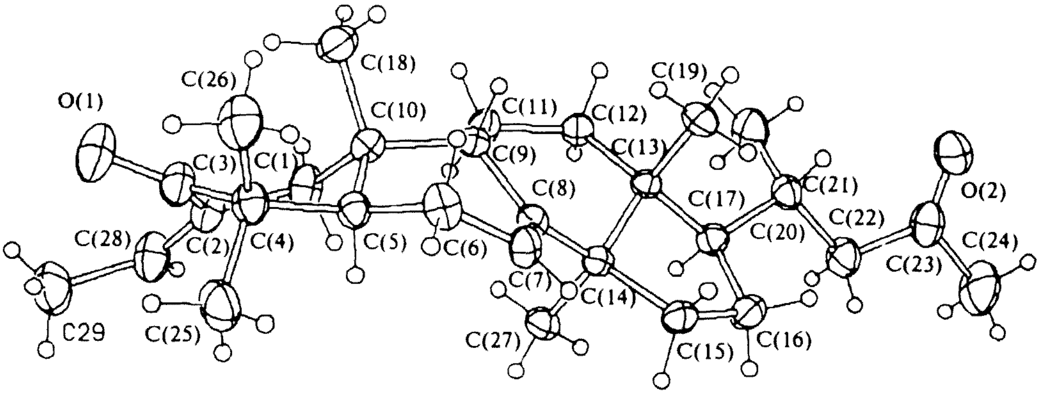
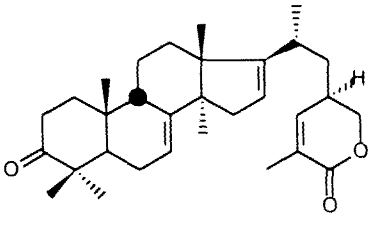


Fig. 1. Molecular structure of **4**.

The bond lengths in molecule **4** are close to the standard values.[4] The $C_{sp^3}-C_{sp^3}$ bond lengths in the polycyclic part of the molecule are within the 1.526 to 1.580 Å interval characteristic of strained steroid systems.[5] As can be seen from Fig. 1, all of the six-membered rings of the molecule of methyl ketone **4** possess rarely observed conformations (Table. 1). Possibly,[6] this conformational state is characteristic of the molecule of 9β-lanost-7-ene derivatives. It is interesting to note that despite the presence of the 2-ethylidene group, the conformation of ring A of methyl ketone **4** coincides with the conformation "*twist-Γ*" calculated for ring A of the molecule of the model 9β-lanost-7-en-3-one derivative 5.[6]



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According to our calculations (program MMX), the chair-like conformation of ring A of molecule **4** is more strained (by 2.1 kcal/mol) than the "crystalline" *twist*-form. In ring B of the molecule of methyl ketone **4**, the deviations of the C(5) and C(10) atoms to one side of the plane of the double bond are 1.209(3) and 0.882(4) Å, respectively, exceeding the corresponding values by 0.957 and 0.476 Å for derivative **5**. The conformation of ring C (distorted *twist*-form) is close to the conformation of that ring in the molecule of ketone **5**.

Thus, the product formed during alkaline treatment of acidic extract of Siberian fir needles possesses structure **3**.

The ^{13}C NMR spectral data on methyl ketones **3** and **4** are presented in Table 2 (the literature data[3] on compound **2** are given here as a reference).

Table 1. Intracyclic torsion angles (φ/deg) of the molecule of compound **4**

Ring	Angle	φ
A	C(10)C(1)C(2)C(3)	4.6
	C(1)C(2)C(3)C(4)	−42.8
	C(2)C(3)C(4)C(5)	21.7
	C(3)C(4)C(5)C(10)	34.5
	C(4)C(5)C(10)C(1)	−70.3
	C(5)C(10)C(1)C(2)	47.4
B	C(10)C(5)C(6)C(7)	−65.2
	C(5)C(6)C(7)C(8)	43.0
	C(6)C(7)C(8)C(9)	10.1
	C(7)C(8)C(9)C(10)	−42.8
	C(8)C(9)C(10)C(5)	17.8
	C(10)C(5)C(6)C(7)	33.8
C	C(11)C(9)C(8)C(14)	6.6
	C(9)C(8)C(14)C(13)	44.9
	C(8)C(14)C(13)C(12)	−61.8
	C(14)C(13)C(12)C(11)	26.3
	C(13)C(12)C(11)C(9)	25.0
	C(12)C(11)C(9)C(8)	−42.8
D	C(13)C(14)C(15)C(16)	−37.3
	C(14)C(15)C(16)C(17)	12.5
	C(15)C(16)C(17)C(13)	17.1
	C(16)C(17)C(13)C(14)	−39.4
	C(17)C(13)C(14)C(15)	48.0

The origin of methyl ketone **3** may be explained as follows. Retroaldol cleavage of acid **1** affords methyl ketone **2** and piruvic acid. This reaction is reversible and the equilibrium is shifted to the product **2**.[3] The aldol condensation also proceeds at the C(2) position, and, possibly, at the C(22) position of the molecule of methyl ketone **2**, but the condensation at the $C(2)H_2$ group is irreversible due to decarboxylation of the reaction product. The formation of the ethylidene derivative **3** in the reaction of methyl ketone **2** with piruvic acid under conditions of the synthesis of compound **3** from the mixture of acids of fir needles confirms the above assumption. The reaction was carried out at incomplete

Table 2. ^{13}C NMR spectra of compounds **2**, **3**, and **4** ($CDCl_3$, tetramethylsilane, δ)

Atom	**2**	**3**	**4**
C(1)	33.93 t	38.01 t	43.31 t
C(2)	34.13 t	136.28 s	135.28 s
C(3)	218.43 s	209.22 s	210.44 s
C(4)	46.75 s	45.00 s	46.44 s
C(5)	52.19 d	53.50 d	53.01 d
C(6)	22.79 t	22.88 t	22.84 t
C(7)	121.37 d	121.78 d	121.64 d
C(8)	148.29 s	148.04 s	148.21 s
C(9)	45.24 d	43.40 d	44.14 d
C(10)	35.59 s	34.79 s	35.83 s
C(11)	20.57 t	20.11 t	20.36 t
C(12)	33.93 t	33.69 t	33.85 t
C(13)	43.85 s	44.13 s	44.05 s
C(14)	51.77 s	51.52 s	51.68 s
C(15)	32.84 t	32.94 t	32.96 t
C(16)	28.17 t	28.12 t	28.19 t
C(17)	52.77 d	52.71 d	52.79 d
C(18)	22.20 q	21.69 q	21.95 q
C(19)	22.89 q	22.97 q	23.10 q
C(20)	32.84 d	33.01 d	32.99 d
C(21)	19.21 q	19.31 q	19.31 q
C(22)	50.66 t	50.87 q	50.85 q
C(23)	208.89 s	208.90 s	209.18 s
C(24)	30.41 q	30.53 q	30.53 q
C(28)	27.78 q	29.65 q	28.17 q
C(29)	21.07 q	21.38 q	20.76 q
C(30)	27.15 q	25.64 q	26.35 q
C(31)	—	136.31 d	135.82 d
C(32)	—	13.71 q	15.27 q

conversion (34 %) of the starting compound **2**. GLC, TLC, and NMR did not reveal other products except ethylidene derivative **3**. The generality of the transformation found for 3-ketotriterpenoids is yet unclear. Ring A in the molecules of (9β)-lanost-7-en-3-one derivatives is conformationally flexible (the molecular mechanics calculations indicate the existence of three energetically close conformations of the ring, the chair conformation being not the major one[6]); this possibly determines the ability of methyl ketone **2** to react with piruvic acid at methylene group at C(2).

Experimental

Melting points were determined with a Kofler block. The IR spectrum was registered with a UR-20 instrument in KBr. The NMR spectra were recorded with a Bruker AM-400. MS (EI, 70 eV) was obtained with a Finnigan MAT 8200 instrument. The UV spectra were recorded with a Specord UV-VIS spectrophotometer. Optical rotations were measured with a Zeiss polarimeter in $CHCl_3$. GLC analyses were carried out with a Chrom-5 chromatograph (carrier gas N_2, 5% SE-30 on Chromaton N, 2500×3 mm column, linear temperature program from 210 to 265 °C (2 deg/min). Column chromatography was carried out on KSK silica gel, the substance:sorbent ratio was 1:20, and a hexane—ether (9:1) mixture was used as the eluent.

The total acidic extract from Siberian fir needles prepared by us previously[1] was used.

(2(31)*E*,20*R*)-25,26,27-Trinor-2-ethylidene-9β-lanosta-2(31),7-diene-3,23-dione (3). Using the procedure of Ref. 1, replacing thermostatting at 60 °C by refluxing on a water bath, from 4.58 g acidic extract of Siberian fir needles, a mixture of methyl ketones (2.73 g) was obtained; by chromatography of the latter on SiO_2, compound **3** (0.11 g) was isolated, m.p. 190.5—191.5 °C (hexane); $[\alpha]^{18}{}_D$ +20.5° (*c* 1.95). IR (CCl_4), ν/cm^{-1}: 920, 1615 (C=C), 1680 (conjugated C=O), 1710 (C=O). UV (EtOH), λ_{max}/nm: 243 (ε 6200). ^{1}H NMR ($CDCl_3$) δ: 0.75 (s, 3 H, CH_3(18)); 0.811 (d, 3 H, $^4J_{19,1\alpha}$ = 1.0, CH_3(19)); 0.882 (d.d, 3 H, $^3J_{21,20}$ = 6.4, $^4J_{21,22a}$ = 0.6, CH_3(21)); 1.01 (s, 6 H, 2 × CH_3); 1.14 (s, 3 H, CH_3); 1.70 (d.d.d, 3 H, $^3J_{32,31}$ = 7.0, $^5J_{32,1\beta}$ = 1.8, $^5J_{32,1\alpha}$ = 1.1, CH_3(32)); 2.10 (d.m, 1 H, $^2J_{1\alpha,1\beta}$ = 16, H(1α)); 2.11 (s, 3 H, CH_3CO); 2,16 (d.d, 1 H, $^2J_{22b,22a}$ = 16.0, $^3J_{22b,20}$ = 10, H(22b)); 2.21 (d.m, 1 H, ^2J = 16, H(1β)); 2.48 (br.d, 1 H, $^2J_{22a,22b}$ = 16.0, $^3J_{22a,20}$ = 3.0, H(22a)); 5.66 (d.t, 1 H, J = 8.0 and 3.0, H(7)); 6.60 (q.d.d, 1 H, $^3J_{31,32}$ = 7.0, $^4J_{31,1\beta}$ = 2.2, $^4J_{31,1\alpha}$ = 2.8, H(31)). ^{13}C NMR is given in Table. 2. MS (m/z): 424.33353 $[M]^+$. Calculated for $C_{29}H_{44}O_2$: 424.33411. The relative GLC retention times for compounds **2** and **3** are 1.00 and 1.26, respectively.

(2(31)*Z*,20*R*)-25,26,27-Trinor-2-ethylidene-9β-lanosta-2(31),7-diene-3,23-dione (4). A solution of methyl ketone **3** (0.060 g) in a mixture of hexane and ether (5:1, 20 mL) was placed in a quartz cuvette and irradiated with a DRSh-1000 mercury lamp for 30 min. The solvent was removed and chromatography of the product gave compounds **4** and **3** successively (0.025 and 0.015 g, respectively). Methyl ketone **4**: m.p. 158—159 °C (hexane); $[\alpha]_D{}^{18}$ +85.7° (*c* 1.4). UV (EtOH), λ_{max}/nm: 244 (ε 5800). ^{1}H NMR ($CDCl_3$) δ: 0.77 (s, 3 H, CH_3(18)); 0.87 (d.d, 3 H, $^3J_{21,20}$ = 6.5 Hz, $^4J_{21,22a}$ =

Table 3. Coordinates (×10^4) and equivalent thermal factors (× 10^3/Å) of nonhydrogen atoms of compound **4**

Atom	*x/a*	*y/b*	*z/c*	U_{eq}
C(1)	117(7)	5873(4)	3412(2)	58(2)
C(2)	−492(8)	5994(5)	3925(2)	66(2)
C(3)	1165(9)	6009(5)	4255(2)	66(2)
C(4)	2584(8)	6931(5)	4130(2)	62(2)
C(5)	3100(7)	6850(4)	3602(2)	47(1)
C(6)	4535(7)	7737(4)	3443(2)	52(1)
C(7)	5261(7)	7463(5)	2957(2)	58(2)
C(8)	3739(7)	7386(4)	2584(2)	43(1)
C(9)	2184(6)	6592(4)	2752(2)	42(1)
C(10)	1443(7)	6817(4)	3249(2)	45(1)
C(11)	1405(8)	5830(4)	2453(2)	59(2)
C(12)	1790(9)	5739(4)	1932(2)	61(2)
C(13)	2780(7)	6828(4)	1768(2)	47(1)
C(14)	4458(6)	7039(4)	2098(2)	47(1)
C(15)	5554(8)	7933(5)	1813(2)	67(2)
C(16)	5140(8)	7572(5)	1313(2)	68(2)
C(17)	3683(8)	6893(4)	1281(2)	54(1)
C(18)	348(8)	7967(4)	3207(2)	64(2)
C(19)	1342(8)	7811(4)	1771(2)	63(2)
C(20)	2811(9)	6353(4)	851(2)	61(2)
C(21)	3419(13)	5096(5)	796(2)	98(2)
C(22)	3309(11)	7002(5)	404(2)	77(2)
C(23)	2338(11)	8143(5)	363(2)	72(2)
C(24)	3244(15)	9028(6)	66(3)	120(3)
C(28)	4348(10)	6715(8)	4431(2)	89(2)
C(29)	1816(13)	8102(5)	4287(2)	92(2)
C(30)	5654(8)	5946(5)	2134(2)	69(2)
O(1)	2063(6)	4897(4)	4245(1)	80(1)
O(2)	869(7)	8325(4)	556(1)	90(2)

0.6, $CH_3(21)$); 0.92 (d, 3 H, $^4J_{19,1\alpha} = 0.8$ Hz, $CH_3(19)$); 0.99 (d, 3 H, $^4J_{30,15\beta} = 1.1$ Hz, $CH_3(30)$); 1.02 (s, 3 H, CH_3); 1.09 (s, 3 H, CH_3); 2.10 (s, 3 H, CH_3CO); 2.15 (d.d, 1 H, $^2J_{22b,22a} = 16.0$ Hz, $^3J_{22b,20} = 10$ Hz, H(22b)); 2.19 (br.d, 1 H, $^2J = 15$ Hz, H(1β)); 2.32 (br.d, 1 H, $^2J = 15$ Hz, H(1α)); 2.47 (br.d.d, 1 H, $^3J_{32,31} = 7.1$ Hz, $^5J_{32,1\alpha} = 2.3$ Hz, $^5J_{32,1\beta} = 1.5$ Hz, H(32)); 5.63 (d.t, 1 H, $J = 8.0$ and 3.0 Hz, H(7)); 5.80 (q.d.d, 1 H, $^3J_{31,32} = 7.1$ Hz, $^4J_{31,1\alpha} = 2.2$ Hz, $^4J_{31,1\beta} = 1.5$ Hz, 3 H(32)). ^{13}C NMR is given in Table 2.

X-ray analysis of compound 4 was carried out with a Syntex $P2_1$ diffractometer (Cu-Kα radiation, graphite monochromator). The crystals were of rhombic syngony: $a = 7.526(2)$, $b = 13.863(3)$, $c = 24.116(5)$ Å, $V = 2516.1(7)$ Å^3, space group $P2_12_12_1$, $Z = 4$, $C_{29}H_{44}O_2$, $\mu = 0.49$ mm^{-1}, $d_{calc} = 1.121$ g/cm^3. The intensities of 2453 independent reflections with $2\theta < 130°$ were measured by $\theta/2\theta$-scanning of the crystal (2.70×0.55×0.45 mm^3). After correction for the absorption and the real form of the crystal (transmission 0.68—0.83), the structure was solved using the SHELX-86 program by the direct method and refinement was carried out by the least-square method in full-matrix anisotropic-isotropic (for hydrogen atoms) approximation using the SHELXL-93 program to $wR_2 = 0.1195$, $S = 1.0$ for 1248 reflections with $I > 2\sigma$. The positions of hydrogen atoms were calculated geometrically. The coordinates of nonhydrogen atoms are presented in Table 3.

Reaction of methyl ketone 2 with piruvic acid. Piruvic acid (0.16 g) and a 10 % alcoholic NaOH (15 mL) solution were added to compound **2** (0.08 g) in EtOH (2 mL). The mixture was refluxed for 4 h on a water bath. After the treatment,[1] a mixture of compounds **2** and **3** (66 : 34 according to GLC and ^1H NMR, 0.07 g) was isolated.

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Received August 2, 1995