TRITERPENOIDS FORM SPECIES OF Abies.

XI. READY FRAGMENTATION IN THE SIDE CHAINS OF THE MOLECULES OF TRITERPENE α,β-UNSATURATED γ-KETO ACIDS

V. A. Raldugin, S. A. Shevtsov,
and T. V. Leibyuk

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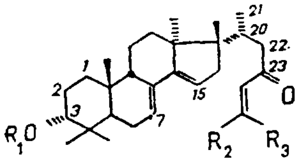
The structure of new trinortriterpene netural compounds formed as the result of the fragmentation of the side chains during the saponification of methyl esters of α,β-unsaturated γ-keto acids under the action of alcoholic alkali have been established by physicochemical methods.

Triterpene α,β-unsaturated γ-ketoacids with various carbon skeletons are the main components of the mixture of triterpene acids of an extract of the needles of the Siberian fir [1]. In an investigation of the chemical properties of the methyl ester (I) we found that its modification on heating with an ethanolic solution of potassium hydroxide took place ambiguously and led to a mixture of 3-O-deacyl acids isomeric at the Δ^{24}-double bond and unidentified products the amount of which rose with an increase in the time of the reaction [1].



	I	II	III
R_1	Ac	H	H
R_2	CH_3	CH_3	$COOCH_3$
R_3	$COOCH_3$	$COOCH_3$	CH_3

In order to elucidate the structures of the compounds formed, we have again performed saponification under severe conditions, using the esters (II) and (III) as the initial compounds. This showed that in both cases the stepwise accumulation of one and the same neutral product took place in the reaction mixture (monitoring by TLC), and with an increase in the reaction time to 4 h it became practically the only isolatable compound, while the proportion of acidic components decreased considerably. This product crystallized well and, according to its ^{13}C NMR spectrum, contained in its molecule 27 carbon atoms, two of which were linked with a nonconjugated carbonyl group (208.85 ppm, singlet) and with a secondary hydroxy group (76.36 ppm, doublet), respectively. The presence of these groups was confirmed by the IR spectrum (1730, 3645 cm^{-1}), and in the light of the results obtained and the mass of the molecular ion in the mass spectrum (m/z 398) the empirical formula $C_{27}H_{42}O_2$ was deduced for the product under investigation. Its PMR spectrum differed appreciably from those of the initial esters only by the absence of signals corresponding to the protons of a $-CH{=}C(CH_3)COOCH_3$ grouping and by the presence of a singlet signal of the protons of a methyl ketone group (2.10 ppm, 3 H). In a consideration of the ^{13}C NMR spectrum it was established that all the signals of the carbon atoms of the cyclic part of the molecule (up to C-22) coincided with those for the ester (III) [2], while the signal for the C-22 atom was somewhat shifted (47.43 ppm, triplet). The appearance in the spectrum of a quartet signal at 30.44 ppm, a displacement of the signal for the C-23 atom to the 208.85 ppm position, and the absence of signals due to the carbon atoms of the above-mentioned grouping permitted the conclusion that the molecule of the compound under investigation contained a methyl group in place of this fragment, and its structure was expressed by formula (IV). The absence of conjugation in the side chain permitted the observation of a maximum in the UV spectrum at 228 nm due to the partially conjugated [3] mariessiadiene system.

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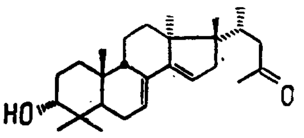
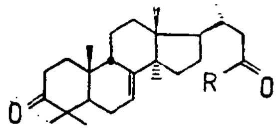


IV

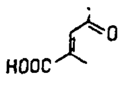


V. $R=(Z)\text{-}CH=C(CH_3)COOCH_3$
VI. $R=CH_3$

It must be mentioned that the saponification of the ester (V) took place similarly. The diketone (VI) then obtained was the only neutral product formed on the prolonged heating in an ethanolic solution of alkali both of the ester (V) and of its 24E isomer (methyl firmanoate [4, 5]).

In order to obtain information on the mechanism of the observed fragmentation, we performed the saponification of the ester (V) under mild conditions (at room temperature). It took place completely in the course of a day, but under these conditions no neutral product (VI) was formed. The resulting mixture of acid components regenerated from their sodium salts consisted, according to TLC, of three compounds. It was treated with an ethereal solution of diazomethane, and it was established by PMR spectroscopy that the resulting mixture of methyl esters consisted of the ester (V) together with methyl firmanoate and its $\Delta^{25(27)}$ isomer (methyl isofirmanoate [5, 6]) in a ratio of 4:10:1. Thus, on saponification not only the cis-trans isomerization in the side chain described previously [1] but also deconjugation (migration of the Δ^{24} double bond) had taken place.

On the prolonged boiling of an ethanolic solution of the mixture of acids obtained from the mild saponification of the ester (V), only traces of the diketone (VI) were detected. The latter was not formed in any appreciable amount whatever when the same mixture was heated in a saturated aqueous solution of sodium bicarbonate. Consequenlty, what is decisive for the formation of the diketone (VI) is the combination of a strongly alkaline medium and an elevated temperature, and the reaction apparently takes place in the manner of a retroaldol process. In this connection, it is interesting to observe that a process opposite in nature has been described in the literature – the acid (VII) is formed in low yield when a solution of acetone and pyruvic in 85% phosphoric acid is boiled for 70 h [2,7].



VII

The fragmentation in the side chains of the molecules of triterpene α,β-unsaturated γ-keto acids that has been detected is of interest as a method for obtaining tetracyclic trinortriterpene derivatives, since with its aid it is possible to convert the pair of photolabile [1] keto acids or their methyl esters into one and the same neutral compound. On the other hand, to avoid the formation of fragmentation products, the saponification of the methyl esters of keto acids under consideration and other, analogous, ones must be performed at room temperature.

EXPERIMENTAL

NMR spectra were recorded on a Bruker AC-200 instrument (50.3 MHz for ^{13}C and 200 MHz for ^{1}H) using solutions in deuterochloroform (δ scale, internal standard $CHCl_3$). Mass spectra were obtained on a Finnigan MAT 8200 instrument. UV spectra (for solutions in ethanol) and IR spectra (for solutions in CCl_4) were recorded on Specord UV-VIS and UR-20 instruments, respectively. Angles of optical rotation were determined for solutions in $CHCl_3$ on a Zeiss polarimeter. Melting points were determined on a Kofler stage.

Chromatography was conducted on elutriated air-dry silica gel of type KSK with a grain size of 0.00-0.14 mm, at a ratio of substance to sorbent of ~1:30. The alcohol used in the investigation was 95% ethanol (rectified spirit). The initial compounds were obtained from the mixture of triterpene acids in an extract of Siberian fir needles [1, 4].

3α-Hydroxy-25,26,27-trinor-7,14-mariessiadien-23-one (IV). Ester (II) (0.45 g) was dissolved with heating in 15 ml of 10% ethanolic NaOH, and the solution was heated at 70-80°C for another 4 h. After this, it was cooled, diluted with 50 ml of water, and extracted with 50 ml of diethyl ether. The ethereal extract was washed with 10 ml of water and was dried with sodium sulfate, and the solvent was driven off from it. This gave 0.37 g of the hydroxy ketone (IV) with mp 84-85°C (from pentane), $[\alpha]_D^{20}$ + 54.3° (c 3.5). Mass spectrum (m/z): 398.3154 (M^+, 100%; calculated for $C_{27}H_{42}O_2$ – 398.3185); 313 ($(M - \text{side chain})^+$ 80%). UV spectrum: λ_{max} 228 nm (log ε 3.76). PMR spectrum (ppm): 0.79 (3H, d, J = 6 Hz, Me-20), 0.84 (6H, s, tertiary Me groups), 0.89, 0.92 and 0.95 (3H each, singlets, tertiary Me groups), 2.10 (3H, s, $-C(O)-CH_3$) 3.42 (1H, m, $W_{\frac{1}{2}}$ = 6 Hz, H-3), 5.15 (1H, dt, J = 1.2, 1.5, and 1.5 Hz, H-15), 5.53 (1H, dd, J = 5.0, 2.5 Hz, H-7), ^{13}C NMR spectrum, ppm: singlets – 208.85; 152.66; 136.48; 51.48, 50.28; 36.97; 34.56 doublets – 120.61; 114.86; 76.37; 52.80; 37.79; 33.78, triplets – 47.43, 44.85; 33.38; 30.44; 25.13; 25.09; 22.51, quartets – 28.57; 28.05; 22.85; 22.14; 19.09; 16.89; 16.29.

Acetylation with acetic anhydride in pyridine at 20°C gave the 3-O-acetate of the hydroxy ketone (IV) with mp 173-174°C (from a mixture of petroleum ether and diethyl ether). PMR spectrum (ppm): 4.65 (1H, d, J = 3 Hz, H-3), 2.03 (3H, s, $OCOC\underline{H}_3$), 2.10 (3H, s, $-C(O)-(C\underline{H}_3)$.

Compound (IV) was obtained analogously with the same yield from the ester (III), and also from the ester (I) with an alcoholic solution of KOH.

25,26,27-Trinor-9β-lanost-7-ene-3,23-dione (VI). This was obtained from 0.35 g of the ester (V) by the procedure described for the ester (II), the yield amounting to 0.29 g. Analogously, and with the same yield, the diketone (VI) was obtained from the 24E isomer of ester (V) (methyl firmanoate). Colorless crystals with mp 144.5-145.5°C (from petroleum ether), $[\alpha]_D^{22}$ + 31.7° (c 0.63). Mass spectrum (m/z): 398.3158 (M^+, 36%; calculated for $C_{27}H_{42}O_2$ – 398.3185); 383 ($(M-15)^+$, 100%); 325 ($(M-H-\text{Me side chain with cleavage at } C(20)-C(22))^+$, 80%). IR spectrum: 1720 cm^{-1} (C=O). PMR spectrum: 0.75, 0.92, 0.95, 1.01, and 1.02 (3H each, singlets, tertiary Me groups), 0.82 (3H, d, J = 6 Hz, Me-20), 2.05 3H, s, $-C(O)-C\underline{H}_3$), 2.36 (2H, dd, J = 8 and 6.5 Hz, 2H-2), 2.37 (1H, dd, J = 16 and 3 Hz H-22a), 5.60 (1H, ddd, J = 7, 3 and 3 Hz, H-7). ^{13}C NMR spectrum, (ppm): 50.7 (t, C-20); 208.99 (s, C-23); 30.43 (q, C-24); the other signals coincided with those for methyl firmanoate [5] – singlets: 218.53, 148.25, 51.73; 46.72, 43.81; 35.56, doublets – 121.34; 52.73; 52.14; 45.17; 32.79, triplets – 34.11; 33.89; 33.89; 32.83; 28.15; 22.75; 20.53, quartets – 27.15; 22.88; 22.19; 21.04; 19.19.

Saponification of the Ester (V) at Room Temperature. The ester (V) (0.20 g) was dissolved in 10 ml of hot ethanol, the solution was cooled to room temperature, and to it was added 10 ml of a 10% ethanolic solution of NaOH. After being kept at room temperature for 24 h, the reaction mixture was diluted with 30 ml of water, acidified with 5% hydrochloric acid to pH 2, and extracted with diethyl ether. The ethereal extract was washed with saturated aqueous sodium chloride and evaporated to dryness. This gave 0.19 g of a product part of which (0.04 g) was methylated with an ethereal solution of diazomethane. The ratio of the ester (V), methyl firmanoate, and methyl isofirmanoate in the mixture of methyl esthers obtained (4:10:1) was established from the relative integral intensities of the signals of the PMR spectrum at (ppm) 6.13 (H-24), 7.04 (H-24), and 6.32 (H-26), respectively.

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