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CYCLIZATION AND REARRANGEMENTS OF DITERPENOIDS. IX. ISOMERIZATION OF (1R,2S,7S,10S,11R,12S,13S)-2,6,6,10,12-PENTAMETHYLPENTACYCLO[10.2.1.$0^{1,10}$.$0^{2,7}$.$0^{11,13}$]PENTADECANE BY FLUOROSULFONIC ACID

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It has been shown that the opening of the cyclopropane ring in (1R, 2S, 7S, 10S, 11R, 12S, 13S)-2,6,6,10,12-pentamethylpentacyclo[10.2.1.$0^{1,10}$.$0^{2,7}$.$0^{11,13}$]pentadecane takes place under the action of fluorosulfonic acid at all three carbon–carbon bonds, but at low temperatures the main isomerization product is (1R, 2S, 7S, 10S, 12S, 13S)-2,6,6,10,12-pentamethyltetracyclo[10.2.1.$0^{1,10}$.$0^{2,7}$]pentadecan-13-ol, and at the ordinary temperature the main products are (1R, 2S, 7S, 11S, 12R, 13R)-2,6,6,11,13-pentamethyltetracyclo[10.2.1.$0^{1,10}$.$0^{2,7}$]pentadeca-9-ene and (1S, 2R, 11S, 12R, 15R)-2,7,7,11,15-pentamethyltetracyclo[10.2.1.$0^{2,11}$.$0^{3,8}$]pentadeca-3(8)-ene.

In an investigation of the dehydration by phosphorus oxychloride in pyridine of (1R, 2S, 7S, 10S, 12S, 13S)-2,6,6,10,12-pentamethyltetracyclo[10.2.1.$0^{1,10}$.$0^{2,7}$]pentadecan-13-ol (I) and its isomer (II) that are formed on the electrophilic cyclization of a number of labdane alcohols, we have established that one of the products is the pentacyclic hydrocarbon (1R, 2S, 7S, 10S, 11R, 12S, 13S)-2,6,6,10,12-pentamethylpentacyclo[10.2.1.$0^{1,10}$.$0^{2,7}$.$0^{11,13}$]pentadecane (III) [1, 2]. This hydrocarbon, containing a cyclopropane ring, is an analogue of trachylobane (IV) [3, 4]. As is known [3-5], under the action of acid, trachylobane and its derivatives isomerize into derivatives of ent-kaurane, ent-atisane, and ent-hibane, i.e., after the protonation of the cyclopropane ring each of the three of its C–C bonds undergoes cleavage.

In view of the accessibility of hydrocarbon (III) [1, 2], it appeared of interest to study its interaction with acids with the aim of obtaining tetracyclic substances with rearranged carbon skeletons.

In the present paper we give the results of the isomerization of hydrocarbon (III) by fluorosulfonic acid in 2-nitropropane at various temperatures. Isomerization was carried out for 5 min at a equimolar ratio of substrate and isomerizing agent.

When the reaction was performed at −100°C, the only reaction product was the alcohol (I) [6], the yield of which, with allowance for the initial compound (III) recovered, was 91%. Under these conditions only the cleavage of the C-11–C-13 bond of hydrocarbon (III) took place. At −75°C, the alcohol (I) was partially dehydrated with the formation of a small amount (∿13%) of the ether (V). At this temperature the formation of polymers also became more appreciable. The structure of ether (V) followed from its elementary and spectral analysis. Its molecular formula is $C_{40}H_{66}O$. In the IR spectrum there were maxima characteristic for C–O–C bonds at 1073 and 1091 cm^{-1}, and in its PMR spectra the signals of ten methyl groups at quaternary carbon atoms and of a proton at a carbon atom linked to ethereal oxygen. The structure of compound (V) was established definitively by independent synthesis from alcohol (I) by a known method [7].

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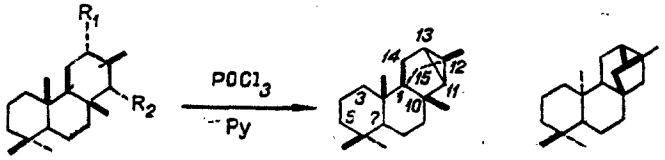
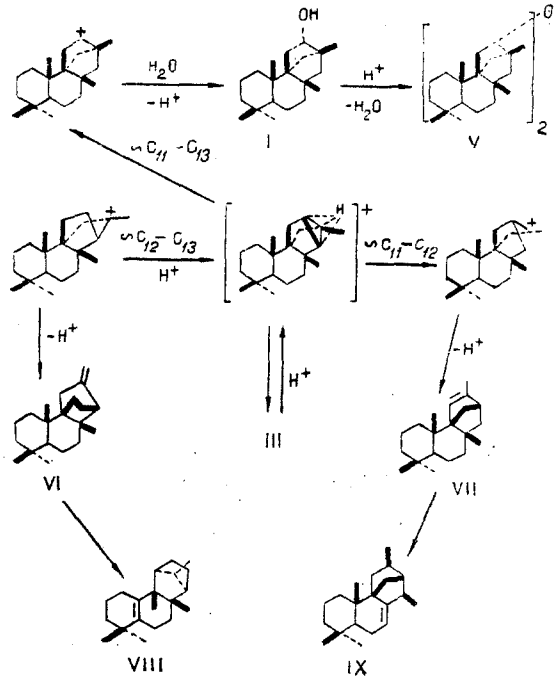


I. R_1=OH; R_2=H
II. R_1=H; R_2=OH

III IV

When the temperature of isomerization was raised to −50°C, the composition of the products became more complicated. In addition to the alcohol (I) (60%) and the ether (V) (10.5%), a small amount of hydrocarbons (VI) (6%) [2] and (VII) (2%) [1] was formed. The first of them was obtained as the result of the cleavage of the C-12–C-13 bond in hydrocarbon (III), and the second by the cleavage of the C-11–C-12 bond. Under these conditions the cleavage of the cyclopropane ring took place in all three possible directions, although the main direction remained the cleavage of the C-11–C-13 bond.



When isomerization was carried out at room temperature (22°C, see Table 1), the reaction products became the known hydrocarbons (VIII) (54%) and (IX) (18%), the yield of the first of them being far higher. They were the products of the further isomerization of the carbocations that gave compounds (I), (V), and (VI), at low temperatures.

Thus, the superacid isomerization of hydrocarbon (III) with fluorosulfonic acid in 2-nitropropane at low temperatures take place mainly with the cleavage of the C-11–C-13 bond and leads to compounds with the tetracyclo[10.2.1.$0^{1,10}$.$0^{2,7}$]pentadecane skeleton, and at the ordinary temperature the primary carbon cations generated as the result of the cleavage of the cylopropane ring of hydrocarbon (III) undergo further isomerization, leading to compounds with tetracyclo[10.2.1.$0^{1,10}$.$0^{2,7}$]- and tetracyclo[10.2.1.$0^{2,11}$.$0^{3,8}$]pentadecane carbon skeletons.

EXPERIMENTAL

For the general part, see [1].

Isomerization of Hydrocarbon (III) by Fluorosulfonic Acid. To a solution of 1.04 g of hydrocarbon (III) in 30 ml of 2-nitropropane cooled to −100°C was added, dropwise with stirring, a solution of 380 mg of fluorosulfonic acid in 10 ml of 2-nitropropane cooled to the same temperature. Stirring at this temperature was continued for another 5 min, the reaction mixture was frozen by the addition of liquid nitrogen, and then, with slow thawing

TABLE 1. Isomerization of Hydrocarbon (III) by Fluorosulfonic Acid in 2-Nitropropane*

Fraction No.	Temperature, °C	Initial product, %	Yield, %**						
			alcohol	the ether (V)	hydrocarbons				polymer
					VI	VII	VIII	IX	
1	—100	64,7	91	—	—	—	—	—	9
2	—75	4,2	73,5	12,9	—	—	—	—	15,6
3	—50	1,9	64,2	10,6	6,4	1,9	—	—	16,9
4	+22	—	—	—	—	—	54	18	27

*The molar ratio of hydrocarbon (III) to FSO_3H was 1:1, and the reaction time 5 min.

**The yields were determined by the column-chromatographic separation of the oxygen-containing compounds and by analyzing the hydrocarbon fractions by the GLC method, for the conditions of which, see [1].

out and vigorous stirring a 20% solution of caustic potash (50 ml) was added to it. The mixture was extracted with ether (3 × 15 ml), the extract was washed with water to neutrality, dried, and filtered, and the solvent was distilled off. The residue (1.03 g) was chromatographed on a column containing 15.5 g of silica gel. Petroleum ether eluted 673 mg of the initial hydrocarbon (III), and a mixture of petroleum ether and ethyl acetate (9:1) eluted 356 mg of the alcohol (I), mp 159-160.5°C (petroleum ether) which was identified by comparison with an authentic sample [6].

The other experiments on the isomerization of hydrocarbon (III) were performed in a similar manner, and their results are given in Table 1.

Synthesis of the Ether (V). A solution of 150 mg of the alcohol (I) in 10 ml of dichloroethane was treated with 135 mg of dry zinc chloride, and the mixture was boiled under reflux for 2.5 h [7]. The reaction mixture was cooled, washed with water to neutrality, dried, and filtered, and the solvent was distilled off. The residue (123 mg) was chromatographed on a column containing 1.8 g of silica gel. Petroleum ether eluted 96 mg of the ether (V), mp 54-55.5°C (from methanol), $[\alpha]_D^{20}$ +47° (c 3.3). IR spectrum (cm^{-1}): 1073, 1091 (C—O—C), 1377, 1383 [$C(CH_3)_2$]. PMR spectrum (δ, ppm): singlets of 6H each at 0.80, 0.85, 0.93, and 1.02 (CH_3 groups at quaternary carbon atoms); 3.02 (m, 2H, possibly one of the H-14 hydrogen atoms), 3.63 (m, 2H, H-13). Found, %: C 85.30; H 12.05. $C_{40}H_{66}O$. Calculated, %: C 85.34; H 11.81.

The compound obtained was identical with the product of the isomerization of hydrocarbon (III) (Table 1, experiments 2 and 3).

Then a mixture of petroleum ether and ethyl acetate eluted from the column 18 mg of the initial alcohol (I).

SUMMARY

It has been shown that the opening of the cyclopropane ring in (1R, 2S, 7S, 10S, 11R, 12S, 13S)-2,6,6,10,12-pentamethylpentacyclo[10.2.1.$0^{1,10}$.$0^{2,7}$.$0^{11,13}$]pentadecane takes place under the action of fluorosulfonic acid at all three carbon—carbon bonds, but at low temperatures the main isomerization product is (1R, 2S, 7S, 10S, 12S, 13S)-2,6,6,10,12-pentamethyltetracyclo[10.2.1.$0^{1,10}$.$0^{2,7}$]pentadecan-13-ol and at room temperature the main products are (1R, 2S, 7S, 11S, 12R, 13R)-2,6,6,11,13-pentamethyltetracyclo[10.2.1.$0^{1,10}$.$0^{2,7}$]pentadeca-9-ene and (1S, 2R, 11S, 12R, 15R)-2,7,7,11,15-pentamethyltetracyclo[10.2.1.$0^{2,11}$.$0^{3,8}$]pentadeca-3(8)-ene

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^{13}C NMR SPECTRA OF BIOLOGICALLY ACTIVE COMPOUNDS. VIII. STEREOCHEMISTRY OF A TRITERPENEGLYCOSIDE – GLYCYRRHIZIC ACID – AND ITS DERIVATIVES

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Details of the ^{13}C NMR spectra of glycyrrhizic acid and four of its derivatives are given, and on their basis the configurations of the anomeric centers of the carbohydrate chain have been redetermined and the β-configuration of the C-1' carbon atom has been suggested.

There is no information in the literature on the use of ^{13}C NMR spectroscopy to establish the structure of a triterpene glycoside – glycyrrhizic acid – the active principle of an extract of liquorice Glycyrrhiza glabra.

We have previously [1] reported the ^{13}C NMR spectra of derivatives of the aglycon – glycyrrhetic acid. In the present paper we give details of the ^{13}C NMR spectra of glycyrrhizic acid (I) and four of its esters (II-V) as the result of a study in which a stereochemical configuration of the carbohydrate moiety of the molecule is proposed.

The stereochemistry of the disaccharide moiety of glycyrrhizic acid was established by Lythgoe and Trippett [2] by hydrolysis and the subsequent methylation of the hydrolysis products with the use of optical rotation results. It was shown [2] that the bond between the glucuronic acids of the disaccharide part of glycyrrhizic acid has the β-configuration and the bond with the aglycon the α-configuration.

Thus, according to results of previous work [2-4], glycyrrhizic acid has the structure of 3β-[O-α-D-glucopyranuronosyl-(1 → 2)-β-D-glucopyranuronosyloxy]-11-oxo-(18βH)-olean-12-en-30β-oic acid.

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