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CYCLIZATION OF SOME LABDANE ALCOHOLS WITH A HYDROXY GROUP AT C-13 BY A SUPERACID

P. F. Vlad, N. D. Ungur,
A. N. Barba, D. V. Korchagina,
I. Yu. Bagryanskaya, Yu. V. Gatilov,
V. P. Gatilova, and V. A. Barkhash

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On the superacid cyclization of the labdane alcohols manool, isomanool, and sclareol the tetracyclic hydrocarbon (1S,2R,11S,12R,15R)-2,7,7,11,15-pentamethyltetracyclo[$10.2.1.0^{2,11}.0^{3,8}$]pentadec-3(8)-ene with a new carbon skeleton is formed.

It was established previously [1] that on the superacid cyclization of a number of labdane alcohols with a tertiary hydroxy group at C-13 [manool (I), isomanool (II), and sclareol (III)] a mixture of two new tetracyclic hydrocarbons was formed. The structure of one of them – (1R,2S,7S,11S,12R,13R)-2,6,6,11,13-pentamethyltetracyclo[$10.2.1.0^{1,10}.0^{2,7}$]-pentadec-9-ene (IV) – was shown by x-ray structural analysis. The structure of the second, liquid, hydrocarbon remained unelucidated.

In the present communication we give the results of an investigation of this new compound, which is (1S,2R,11S,12R,15R)-2,7,7,11,15-pentamethyltetracyclo[$10.2.1.0^{2,11}.0^{3,8}$]-pentadec-3(8)-ene (V).

When hydrocarbon (V) was ozonized it gave a mixture of a crystalline diketone and a liquid epoxide. The structure of the diketone was determined by x-ray structural analysis. It proved to be (1S,2R,11S,12R,15R)-2,7,7,11,15-pentamethyltricyclo[$10.2.1.0^{2,11}$]pentadecane-3,8-dione (VI). Consequently, the initial hydrocarbon possessed the structure shown in formula (V). The absolute configuration of the latter followed from the fact that on the migration of a methyl group from the C-10 to the C-9 position of the labdane skeleton it remains on the β-side of the molecule. The structure of hydrocarbon (V) was also confirmed by ^{13}C NMR results (see [1]).

The second product of the oxidation of hydrocarbon (V) by ozone was (1S,2R,11S,12R,15R)-2,7,7,11,15-pentamethyl-3α,8α-epoxytetracyclo[$10.2.1.0^{2,11}.0^{3,8}$]pentadecane (VII). Its

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Institute of Chemistry, Moldavian SSR Academy of Sciences, Kishinev. Novosibirsk Institute of Organic Chemistry, Siberian Branch, USSR Academy of Sciences. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 198-203, March-April, 1988. Original article submitted July 3, 1987.

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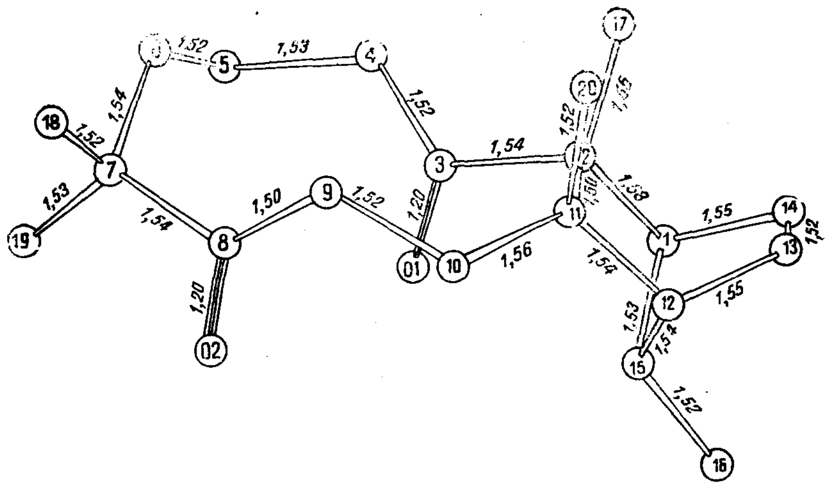
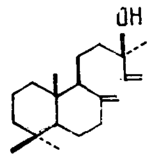


Structure of (1S, 2R, 12R, 15R)-2,7,7,11,15-pentamethyltricyclo [10.2.1.O^{2,11}]-pentadecane dione-3,8 (VI).

structure was confirmed by the fact that it was formed on the oxidation of hydrocarbon (V) by p-methoxycarbonylperbenzoic acid. The approach of the oxidant from the β-side of the molecule of compound (V) is sterically hindered by the methyl groups at C-2 and C-7, and therefore the epoxide ring must have the α-configuration.



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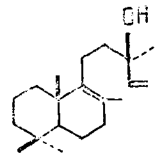

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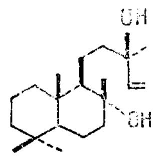

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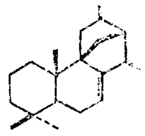

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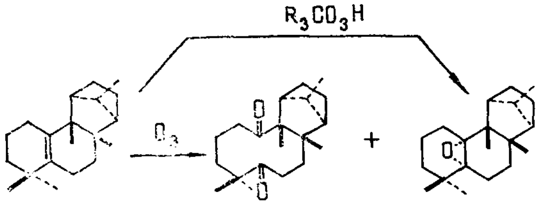
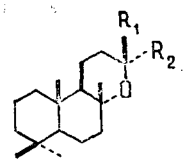


V VI VII



VIII. R_1=CH=CH$_2$; R_2=CH$_3$

IX. R_1=CH$_3$; R_2=CH$_2$=CH$_2$

The total yield of hydrocarbons (IV) and (V) on the cyclization of alcohols (I)-(III) by fluorosulfonic acid in sulfuryl chloride fluoride was low (15.6-21.3%). In spite of the fact that the reaction was performed at a fairly low temperature (−115°C), a polymeric product was predominating. It was shown with sclareol (III) as an example that roughly the same results were obtained when cyclization was carried out in nitropropane at −75 to −80°C. It can be seen from Table 1 that both the yield and the composition of the hydrocarbon fraction in the cyclization of sclareol (III) depend on the ratio of cyclizing agent to substrate (at a constant concentration of cyclizing agent). With a decrease in this ratio from 25:1 to 10:1 the yield of hydrocarbon fraction rose, reaching 39.2%, with a simultaneous decrease in the amount of polymeric material. A further decrease in the amount of cyclizing agent to 5 moles per 1 mole of sclareol (III) substantially suppressed the formation of polymeric material, but, at the same time, the composition of the reaction products changed. The predominating product became a mixture (1:1) of manoyl oxide (VIII) and 13-epimanoyl oxide (IX) (66.8%), and the total yield of hydrocarbons (IV) and (V) was only 13.7% (see Table 1).

As has been shown previously [1], hydrocarbons (IV) and (V) are formed in high yield (53.7%) on the prolonged reaction of the alcohols (I)-(III), of the mixture of diene acetates

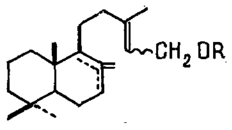
TABLE 1. Cyclization of Sclareol (III) by Fluorosulfonic Acid in 2-Nitropropane at −75 to −80°C

FSO_3H:sclareol ratio, molar	Yield of reaction products, %			
	hydrocarbon (IV)	hydrocarbon (V)	oxides (VIII) + (IX)	polymeric product
25:1	11,0	13,2	—	75,8
10:1	9,8	29,4	—	60,8
5:1	4.1	9.6	66.8	19.5

TABLE 2. Coordinates of the Nonhydrogen Atoms of Diketone (VI) ($\times 10^4$, in fractions of the cell)

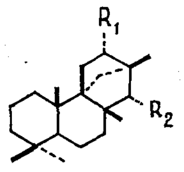
Atom	*x*	*y*	*z*
C-1	0883 (16)	—0276 (10)	4266 (4)
C-2	1854 (12)	—1188 (7)	3837 (3)
C-3	0817 (11)	—1033 (8)	3281 (3)
C-4	0463 (17)	—2168 (8)	2917 (4)
C-5	0237 (15)	—1913 (9)	2306 (3)
C-6	2070 (14)	—2110 (7)	1966 (3)
C-7	3225 (12)	—0933 (6)	1792 (3)
C-8	3910 (12)	—0133 (7)	2280 (3)
C-9	4817 (14)	—0774 (8)	2766 (3)
C-10	4669 (13)	—0004 (8)	3290 (3)
C-11	4062 (11)	—0694 (6)	3825 (3)
C-12	4038 (14)	0296 (8)	4282 (3)
C-13	3685 (19)	—0321 (10)	4849 (4)
C-14	1522 (22)	—0652 (11)	4851 (4)
C-15	2046 (14)	0931 (8)	4185 (3)
C-16	1530 (20)	2037 (12)	4552 (5)
C-17	1648 (18)	—2576 (10)	4025 (5)
C-18	1983 (18)	—0146 (10)	1399 (4)
C-19	5060 (20)	—1322 (12)	1485 (5)
C-20	5606 (17)	—1690 (10)	3922 (4)
O-1	0216 (8)	—0034 (5)	3133 (2)
O-2	3797 (9)	0989 (4)	2255 (2)

(X), and of the tetracyclic alcohols (XI) and (XII) with a mixture of 99% formic acid and concentrated sulfuric acid (20°C, 48 h). They are also obtained in small amount (∼1%) on the superacid cyclization of the mixture of alcohols (XIII).



X. R = Ac

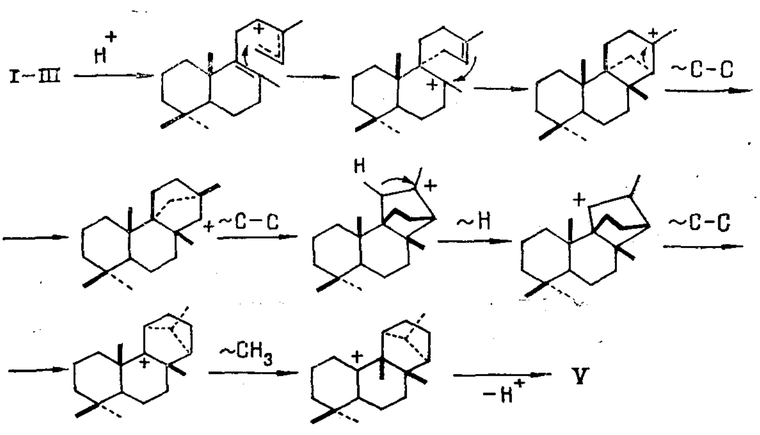
XIII. R = H



XI. R_1 = OH; R_2 = H

XII. R_1 = H; R_2 = OH

The formation of hydrocarbon (V) from alcohols (I)-(III) can be represented by the scheme



The same scheme explains the formation of alcohols (XI) and (XII).

EXPERIMENTAL

For the general part, see [1].

Cyclization by Fluorosulfonic Acid in Sulfuryl Chloride Fluoride: a) manool (I). To a solution of 1.88 g of fluorosulfonic acid in 4.5 ml of sulfuryl chloride fluoride was added 250 mg of crystalline manool (I) (molar ratio 25:1). The mixture was stirred at −115°C for 15 min and was frozen by the addition of liquid nitrogen, and then, as it thawed out, was added dropwise to a stirred mixture of 4.8 ml of ether and 12 ml of methanol. With continued stirring, 45 ml of a 17% solution of sodium carbonate and 50 ml of water were added to the reaction solution. The mixture was extracted three time with ether, and the extract was washed with water, dried with anhydrous sodium sulfate, and filtered, and the solvent was distilled off. The residue (192 mg) was chromatographed on a column with 5 g of silica gel. Petroleum ether eluted 49.8 mg (21.3%) of a mixture of hydrocarbons (IV) and (V) in a ratio of 1.2:1 (GLC results; Chrom-4 chromatograph, glass column, 3 mm × 2.5 m, 5% of SE-30 on Chromaton N-AW DMCS (0.160-0.200 mm), carrier gas helium, V = 60 ml/min, column temperature 170°C, evaporator temperature 250°C).

The properties and spectral characteristics of compounds (IV) and (V) have been given in [1]. The remainder of the cyclization product consisted of polymeric materials;

b) isomanool (II). With stirring and cooling to the same temperature, a solution of 30 mg of isomanool (II) in 0.2 ml of SO_2FCl was added to a solution of 226 mg of FSO_3H in 0.5 ml of SO_2FCl (molar ratio of FSO_3H to isomanool 25:1), the mixture was stirred at −115°C for 15 min and was worked up as described above, and the residue (25.4 mg) was chromatographed on a column with 0.5 g of SiO_2. This gave 4.4 mg (15.6%) of a mixture of hydrocarbons (IV) and (V) in a ratio of 1.6:1;

c) sclareol (III). With stirring, 30 mg of crystalline sclareol was added to a solution of 224 mg of FSO_3H in 0.5 ml of SO_2FCl (molar ratio of FSO_3H to sclareol 25:1), and the mixture was stirred at −115°C for 15 min and was worked up as described above. The residue (25.1 mg) was chromatographed on a column with 0.5 g of silica gel. Hexane eluted 5.3 mg (20.0%) of a mixture of hydrocarbons (IV) and (V) in a ratio of 1.3:1.

Cyclization of Sclareol (III) with Fluorosulfonic Acid in 2-Nitropropane. a) With vigorous stirring at −75 to −80°C, 100 mg (0.32 mmole) of sclareol was added in one portion to a solution of 812 mg (8.12 mmole) of FSO_3H in 2 ml of 2-nitropropane (ratio of FSO_3H to sclareol 25:1) and the mixture was stirred at the same temperature for 15 min, after which 10 ml of a 30% solution of caustic potash was added to it. The resulting mixture was extracted three times with petroleum ether, the extract was washed with water to neutrality, dried with anhydrous sodium sulfate, and filtered, and the solvent was distilled off. The residue (78.6 mg) was chromatographed on a column with 2.5 g of silica gel. Petroleum ether eluted 21.6 mg (24.2% yield) of a mixture of hdyrocarbons (IV) and (V) in a ratio of 1:1.2 (GLC results).

b) In a similar manner to that described in a), 500 mg (1.62 mmole) of sclareol (III) was cyclized with a solution of 1.63 g (1.63 mmole) of FSO_3H in 4 ml of 2-nitropropane (FSO_3H: sclareol ratio 10:1). The residue (430 mg) was chromatographed on a column with 10 g of SiO_2, and 173.5 mg (39.2%) of a mixture of hydrocarbons (IV) and (V) in a ratio of 1:3 was isolated (GLC results, see Table 1).

c) As described in a), 150 mg (0.49 mmole) of sclareol (III) was cyclized with a solution of 244 mg (2.44 mmole) of FSO_3H in 3 ml of 2-nitropropane (FSO_3H:sclareol ratio 5:1). The reaction product (136.2 mg) was chromatographed on a column with 2.7 g of silica gel. Petroleum ether eluted 18.1 mg of a mixture of hydrocarbons (IV) and (V) in a ratio of 1:2.5, and a mixture of petroleum ether and ethyl acetate (19:1) eluted 94.4 mg of a mixture of manoyl and 13-epimanoyl oxides (VIII) and (IX) (1:1), identified by chromatographic comparison with authentic samples (GLC and TLC on $SiO_2 \cdot AgNO_3$).

Ozonization of the Hydrocarbon (V). At −70°C, a current of ozonized air was passed through a solution of 646 mg of the hydrocarbon (V) in 15 ml of dry methylene chloride and 0.5 ml of dry pyridine until the ozone broke through. The solution was acidified with 50 ml of 10% H_2SO_4 and was exhaustively extracted with ether. After the usual working up procedure, the residue (661 mg) was chromatographed on a column with 18 g of silica gel. Petroleum ether eluted 20 mg of the initial hydrocarbon (V), and petroleum ether—ethyl acetate (19:1) eluted 530 mg of the epoxide (VII): colorless viscous liquid, $[\alpha]_D^{19}$ +5.4° (c 3.0). IR spectrum (cm^{-1}): 1353, 1373 $[C(CH_3)_2]$, 912, 920, 974 $\left(\underset{\diagdown O \diagup}{>C-C<}\right)$. PMR spectrum ($CCl_4$, δ, ppm): 0.86 (d, J = 6 Hz, 3 H); 0.87 (s, 6H); 0.92 (s, 6H) (the signals of methyl groups). Found %: C 83.16; H 11.14. $C_{20}H_{32}O$. Calculated %: C 83.27; H 11.18.

Then the same mixture of solvents eluted from the column 80 mg of the diketone (VI), mp 148-149.5°C (from petroleum ether), $[\alpha]_D^{20}$ +45.5° (c 1.9). IR spectrum (cm^{-1}): 1353, 1373 $[C(CH_3)_2]$, 1678, 1686 ($>C{=}O$). PMR spectrum (CCl_4, δ, ppm): 0.91 (d, J = 6.6 Hz, 3H); 1.00 (s, 3H); 1.02 (s, 3H); 1.09 (s, 6H) (signals of methyl groups). Mass spectrum (m/z, %): 304 (M^+, 14), 276(44), 261(3), 248(4), 195(36), 137(93), 108(100), 95(64), 81(53). Found %: C 78.76; H 10.48. $C_{20}H_{32}O_2$. Calculated %: C 78.90; H 10.59.

Epoxidation of the Hydrocarbon (V). At room temperature, 124 mg of p-methoxycarbonylperbenzoic acid was added to a solution of 115 mg of compound (V) in 5 ml of chloroform, and the mixture was kept at the same temperature for 24 h. Then it was diluted with 15 ml of water and was exhaustively extracted with ether, the extract was worked up in the usual way, and the residue (110 mg) was chromatographed on a column with 3 g of silica gel. Petroleum ether eluted 15 mg of the initial olefin, and petroleum ether—ethyl acetate (19:1) eluted 85 mg of the epoxide (VII), identical with the product of the ozonization of hydrocarbon (V).

X-Ray Structural Results. The x-ray structural experiment was performed on a Syntex $P2_1$ automatic diffractometer using Mo radication with a graphite monochromator. Crystallographic characteristics of the diketone (VI): a = 6.838(I) Å, b = 10.682(4) Å, c = 24.397(6) Å, Z = 4, d_{calc} = 1.07 g/cm³, R 6.5%, R_W 4.5%, w^{-1} σ^2_F + (0.006 F)². The crystals of compound (VI) belong to the rhombic system, space group $P2_12_12_1$. The intensities of 1833 independent reflections were measured by the $2\theta/\omega$ scanning method in the range $2\theta \leq 50°$. The calculations made use of 1080 reflections with $I > 2\sigma$. The structure was refined by the MULTAN program. The positions of the hydrogen atom were calculated geometrically. The final refinement of the structure was done by the method of least squares in the full-matrix anisotropic-isotropic (for the H atoms) approximation. The coordinates of the atoms are given in Table 2.

The structure of the molecule of compound (VI) and the bond lengths are given in Fig. 1. The standard deviations for the bond lengths average 0.01 Å. In the molecule of the diketone (VI) a ten-membered ring is linked to a norbornyl system. The norbornyl fragment has the usual form. Within the 3σ range, the geometric magnitudes correspond to the usual values [2], with the exception of the length of the C-2—C-11 bond, which is extended to 1.601 Å.

SUMMARY

It has been established that on the interaction of a number of labdane alcohols having a tertiary allyl hydroxy group in the side chain (manool, isomanool, sclareol) with fluorosulfonic acid, a mixture of two tetracyclic hydrocarbons with new carbon skeletons is formed — (1R,2S,7S,11S,12R,13R)-2,6,6,11,13-pentamethyltetracyclo$[10.2.1.0^{1,10}.0^{2,7}]$pentadec-9-ene and (1S,2R,11S,12R,15R)-2,7,7,11,15-pentamethyltetracyclo$[10.2.1.0^{2,11}.0^{3,8}]$pentadec-3(8)-ene.

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