

Acid-Catalysed Isomerization of Caryophyllene Oxide in the Presence of SiO₂ and Al₂O₃ Impregnated with Sulphuric Acid

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Abstract

Catalytic activities of silica gel H⁺-SiO₂ and aluminum oxide H⁺-Al₂O₃ impregnated with sulphuric acid in reaction of acid catalysed caryophyllene oxide isomerization have been studied. It was established, that the activity of H⁺-SiO₂ is much higher than that for H⁺-Al₂O₃ being comparable in value with the activity of concentrated sulphuric acid. For H⁺-SiO₂ silica gel, dependence has been revealed between catalytic activity and silica gel particle size.

INTRODUCTION

Caryophyllene oxide **1** is among the most widespread sesquiterpenoid species available in the nature. This substance is contained in many ethereal oils and various extracts from plant raw material and serves as a source substrate for the synthesis of caryophyllene derivatives as well as of a series related compounds.

The unique feature of caryophyllene oxide consists in the fact that it is very readily (just like its precursor caryophyllene) is subjected to various rearrangements of the carbon skeleton. This fact is connected with a specific character of the structure of this sesquiterpenoid such as a significantly strained molecule due to the transannulation of a nonane carbon cycle with two minor cycles, which could stimulate the reorganization of the molecular skeleton as well as the formation of a set of more stable bicyclic and tricyclic systems. As the result of the contact with the sorbents of acidic nature, caryophyllene oxide readily undergoes isomerization under the conditions of the gas-liquid [1] and the column chromatography [2, 3], which in recent times caused the analysis and isolation of this compound to be substantially complicated.

For the first time the acid-catalysed isomerization of caryophyllene oxide was investigat-

ed in 1953 [4] during the determination of caryophyllene structure. Nevertheless, the interest of researchers with respect to the interaction of epoxide species **1** with acids due to a variety of possible transformations of this substrate under the conditions of acid catalysis does not weaken after a number of years, as demonstrated by the fact that novel works in this field are being published [5–9]. As an extension of the works concerning the studies on the behaviour of caryophyllene oxide in the presence of sorbents for chromatography [1–3], the isomerization of this sesquiterpenoid on the surface of solid acids was investigated [10]. It should be noted that since the authors of the works mentioned above identified only the predominant components of the mixture of the reaction products, there is an inconsistency in the literature data available from different sources against a background of significant dependence of the reaction mixture composition on the conditions of the reaction process.

The aim of the present work consisted in the studies on the behaviour of caryophyllene oxide **1** in the presence of Al₂O₃ and SiO₂ impregnated with sulphuric acid as compared to homogeneous systems. Similar sorbents impregnated with acids were successfully used as catalysts in the reactions of substituted benzene

nitration [11, 12], esterification of organic acids [13] which the sorbents exhibited higher activity and selectivity as compared to corresponding mineral acids.

RESULTS AND DISCUSSION

The catalysts for the isomerization process were prepared through the applying H_2SO_4 aqueous solution onto the sorbent (Al_2O_3 or SiO_2) with the subsequent removal of water. The mass fraction of the acid was varied within the range from 1 to 20 % ($H^+-Al_2O_3^{(1\%)}$, $H^+-Al_2O_3^{(5\%)}$, $H^+-Al_2O_3^{(10\%)}$, $H^+-Al_2O_3^{(20\%)}$, $H^+-SiO_2^{(1\%)}$, $H^+-SiO_2^{(5\%)}$). Under the preparation of H^+-SiO_2 the particle size of silica gel used was also varied (ranging within 0.140–0.315 mm for $H^+-SiO_2^{(1\%)}$ and $H^+-SiO_2^{(5\%)}$ and 0.002–0.040 mm for $H^+-SiO_2^{(5\% - sm)}$). The process of caryophyllene oxide isomerization was carried out *via* the interaction of caryophyllene oxide solution in hexane with a sorbent impregnated with acid; the substrate solution-to-catalyst contact time value was varied within the range from 5 min up to 72 h, the temperature of the reaction process was maintained at either 20 or 68 °C. The results of the experiments on caryophyllene oxide **1** isomerization in the presence of $H^+-Al_2O_3$ and H^+-SiO_2 are presented in Table 1.

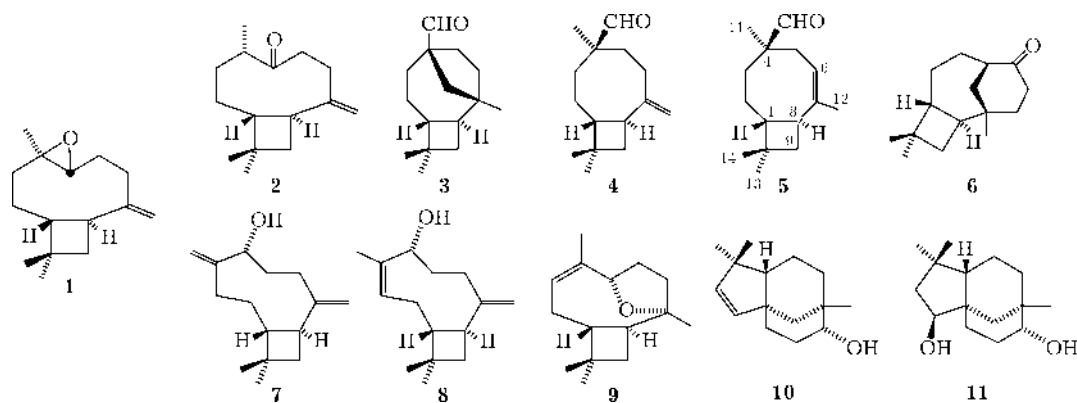
When the process of epoxy-caryophyllene **1** isomerization carrying out on the surface of acid-impregnated aluminum oxide $H^+-Al_2O_3$ was carried out (Scheme 1), the mixture of compounds such as **2–11** was observed to be formed, which the mixture was separated to

isolate individual components with the use of a column chromatography as well as preparative-scale gas-liquid chromatography techniques. The structure of compounds such as **2** [14], **3** [15], **4** [14], **6** [16], **7** [17], **8** [17], **9** [7], **10** [10] and **11** [8] was confirmed through the comparison of their NMR spectral parameters with those described in the literature.

The accumulation of caryophylla-4(12),8(13)-diene-5 α -ol **7** to a considerable extent is observed only with the use of the sorbent with a low acid content. So, for the reaction carried out in the presence of $H^+-Al_2O_3^{(1\%)}$ the prevailing product is allyl alcohol **7**: after 24 h of proceeding the reaction the content of this product in the mixture amounted to 54 % against the conversion level of the source epoxide species equal to 62 %. Simultaneously, caryophylla-4(12),8(13)-diene-5-one [19] is observed in the mixture which the substance, apparently, represents the product of allyl alcohol **7** oxidation by atmospheric oxygen. The yield of this compound may be as much as 20 % ($H^+-Al_2O_3^{(1\%)}$, for 8 h at 68 °C). With the use of the sorbent with higher acid content the alcohol **7** is observed to be present in the mixture only at low values of the solution-catalyst contact time parameter.

The accumulation of the second allyl alcohol such as caryophylla-3,8(13)-diene-5 α -ol **8** is also a time-limited process: a long duration contact of the reacting solution with the catalyst results in decreasing the content of this alcohol in the mixture of reaction products.

The most obvious pathway for the consumption of alcohol **8** consists in its cyclization re-



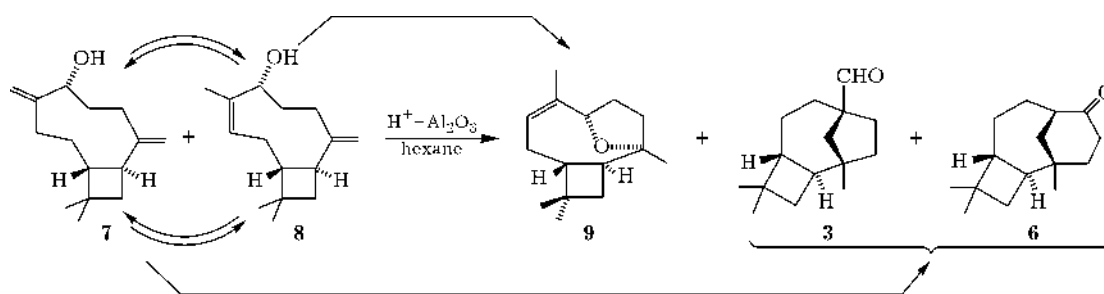
Scheme 1.

TABLE 1
Results of the experiments on caryophyllene oxide **1** isomerization

Catalyst	Conditions	T, °C	Mixture composition (according to GLC data), %															
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Others
H ⁺ -Al ₂ O ₃ (1%)	15 h	20	73.5	-	-	-	-	-	24.1	-	-	-	-	-	-	-	-	1.6 ^a
H ⁺ -Al ₂ O ₃ (1%)	24 h	20	38.4	-	-	-	-	-	54.2	-	-	-	-	-	-	-	-	7.4 ^a
H ⁺ -Al ₂ O ₃ (1%)	8 h	68	-	-	-	-	-	-	54.8	11.5	-	-	-	-	-	-	-	19.9 ^a
H ⁺ -Al ₂ O ₃ (5%)	1 h	20	16.6	3.1	2.0	16.6	2.2	-	43.3	7.8	-	-	-	-	-	-	-	-
H ⁺ -Al ₂ O ₃ (5%)	15 h	20	1.5	3.6	10.6	13.7	4.0	3.6	31.8	12.4	-	-	-	-	-	-	-	-
H ⁺ -Al ₂ O ₃ (10%)	5 min	20	12.4	6.8	7.3	12.4	3.3	5.8	23.6	14.1	-	-	-	-	-	-	-	-
H ⁺ -Al ₂ O ₃ (10%)	1 h	20	-	8.9	19.0	10.4	8.3	5.6	22.2	13.7	0.6	8.2	-	-	-	-	-	-
H ⁺ -Al ₂ O ₃ (10%)	15 h	20	-	-	40.3	-	15.1	9.3	-	8.1	5.1	12.1	1.9	-	-	-	-	-
H ⁺ -Al ₂ O ₃ (20%)	5 min	20	11.5	8.6	18.2	11.6	4.8	11.8	-	11.4	0.8	10.4	-	-	-	-	-	-
H ⁺ -Al ₂ O ₃ (20%)	1 h	20	-	-	41.5	4.0	14.4	8.6	-	4.9	4.5	13.8	0.8	-	-	-	-	-
H ⁺ -Al ₂ O ₃ (20%)	15 h	20	-	-	36.6	-	19.6	8.8	-	3.8	9.1	16.9	1.4	-	-	-	-	-
H ⁺ -Al ₂ O ₃ (20%)	72 h	20	-	-	30.6	-	13.5	8.7	-	-	9.6	18.2	8.4	-	-	-	-	-
H ⁺ -Al ₂ O ₃ (20%)	10 h	68	-	-	9.8	-	-	19.3	-	-	-	-	-	34.7	4.5	-	-	4.4
H ⁺ -SiO ₂ (5%)	5 min	20	-	-	9.0	-	-	7.0	-	-	4.8	-	-	22.7	21.4	1.7	7.1	-
H ⁺ -SiO ₂ (5%)	72 h	20	-	-	-	-	-	21.3	-	-	-	-	-	22.4	-	15.2	20.4	-
H ⁺ -SiO ₂ (5%)	3 h	68	-	-	-	-	-	22.3	-	-	-	-	-	11.5	-	32.6	13.1	-
H ⁺ -SiO ₂ (1%)	5 min	20	-	17.6	-	7.9	15.2	-	-	17.9	4.2	15.0	3.5	1.0	2.6	-	-	5.6 (17)
H ⁺ -SiO ₂ (1%)	3 h	68	-	-	16.0	-	-	4.9	-	-	-	-	-	18.4	30.9	-	-	7.0
H ⁺ -SiO ₂ (5% - sm)	5 min	20	-	15.4	-	10.9	8.8	-	-	16.1	1.3	16.2	8.4	-	-	-	-	1.5 (17)
H ⁺ -SiO ₂ (5% - sm)	72 h	20	-	-	15.1	-	5.9	4.5	-	-	8.4	19.5	7.4	-	14.8	-	-	3.7
H ⁺ -SiO ₂ (5% - sm)	3 h	68	-	-	9.6	-	-	11.0	-	-	-	-	-	25.2	22.3	-	-	6.9
H ₂ SO ₄ ^b	1 h	20	10.6	2.2	-	-	-	-	11.5	24.8	-	10.7	27.2	-	-	-	-	9.1 (17)
H ₂ SO ₄ ^b	3 h	20	-	4.3	-	2.8	1.9	-	-	16.3	3.8	2.3	41.5	-	-	-	-	18.0 (17)
H ₂ SO ₄ ^b	2 h	56	-	-	6.9	-	4.9	4.0	-	-	14.8	4.3	39.1	-	-	-	-	4.1 (17), 4.3 (19)
H ₂ SO ₄ ^c	3 h	20	-	7.0	7.2	5.0	4.7	2.5	-	-	12.3	-	-	30.9	7.0	11.0	3.8	-
H ₂ SO ₄ ^c	3 h	68	-	-	-	-	-	4.1	-	-	-	-	-	32.4	4.1	31.9	5.9	-

^a Caryophylla-4(12),8(13)-diene-5-one.

^{b,c} Solvents: acetone and hexane, respectively.



Scheme 2.

sulting in the formation of $5\alpha,8\alpha$ -epoxycryophyll-3-ene **9** that was also found out in the mixture of the products of caryophyllene oxide isomerization. At the same time the isomeric alcohol **7** under the conditions of the reaction does not undergo heterocyclization to result in the formation of a corresponding cyclic ether – $5\alpha,8\alpha$ -epoxycryophyll-4(12)-ene, but it is subjected to transformation into (1*S*,2*S*,5*R*,8*S*)-1,4,4-trimethyltricyclo[6.2.1.0^{2,5}]undecane-8-carbaldehyde **3** and isocaryolane-9-one **6** (Scheme 2).

The formation of carbonyl compounds such as **3** and **6** from allyl alcohol **7** may be described within the framework of the transformation of a tricyclic carbocation that could be formed as an intermediate product. The 1,2-shift of C^6-C^7 bond within this cation would result in the formation of aldehyde **3**, whereas a 1,2-hydride shift will provide the formation of ketone **6**. The obtaining of carbonyl compounds such as **3** and **6** from the alcohol **7** was described for $H_2SO_4/MeOH$, H_2SO_4/Et_2O , and tetracyanoethylene/MeOH systems [15].

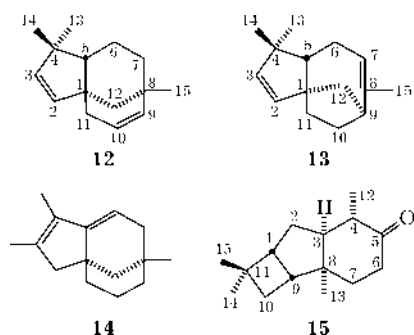
It should be noted, that there could be a fast interconversion of alcohols under the conditions of the reaction process.

Besides aldehyde **3** produced due to the rearrangement of allyl alcohol **7**, during the process of caryophyllene oxide isomerization, the products such as (1*R*,4*R*,8*S*)-4,10,10-trimethyl-7-methylenebicyclo[6.2.0]decane-4-carbaldehyde (**4**) and (1*R*,4*R*,8*S*)-4,7,10,10-tetramethylbicyclo[6.2.0]dec-6-ene-4-carbaldehyde **5** are formed those differ from each other only by the double bond position. The aldehydes such as **3** and **4** were described earlier as corresponding dinitrophenylhydrazones, formed in the process of acid-catalysed caryophyllene oxide

isomerization in the presence of 2,4-dinitrophenylhydrazine [5].

The aldehyde **4** is formed as the result of C^6-C^7 bond migration within the parent caryophyllene oxide molecule. Basing on the spectral data of this aldehyde, it is difficult to establish unambiguously the configuration of C^4 atom in this compound, however, according to the postulated mechanism of the reaction of cycles narrowing [20] the migration of C^6-C^7 bond should proceed with the conservation of a mutual position of the methyl groups at C^4 atom and C^4-C^5 bond, *i. e.* with the conservation of C^4 atom configuration.

With high solution-catalyst contact time values, as well as with the use of a catalyst with high acid content, there are only two aldehydes such as **3** and **5** in the mixture of reaction products. Apparently, under the conditions of the reaction process, an isomerization of aldehyde **4** to give aldehyde **5** occurs as the result of the migration of exocyclic double bond of aldehyde **4** inwards the cycle. The validity of this assumption is supported by the comparison of heat of formation values for aldehydes **4** and **5**, which indicates a lower thermodynamic stability of aldehyde **4** as compared to its isomer **5**. The formation of aldehyde **4** in significant amounts points to the fact that there is a kinetic control of products distribution occurring at the initial stage of the reaction. Further the process switches to the mode of thermodynamic control presented by slow transformation of aldehyde **4** to produce a more isomer such as **5**. Since aldehyde **5** represents the product of aldehyde **4** isomerization, it should exhibit the same mutual spatial arrangement of the substituents at C^4 atom as its precursor.



Scheme 3.

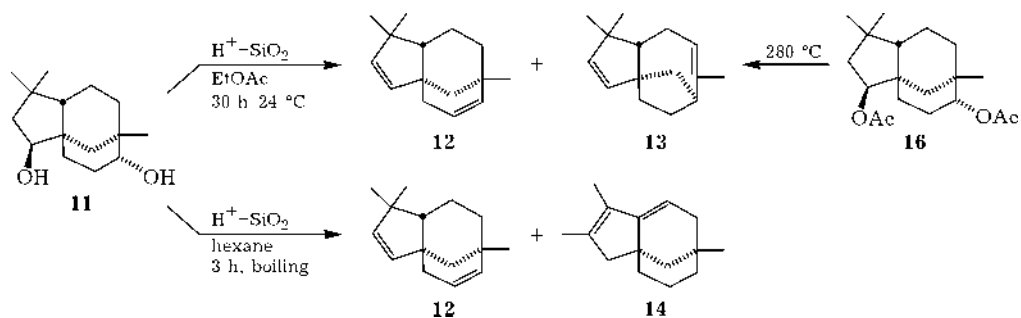
One more group of rearrangement products of epoxy caryophyllene is formed by the compounds with a clovane carbon skeleton such as clovane-9 α -ol **10** and clovane-2 β ,9 α -diol **11**. Diol **11**, apparently, could be formed as the result of the influence either of a residual water amount contained in $\text{H}^+ - \text{Al}_2\text{O}_3$ or of atmospheric moisture on intermediate species formed, and this product is observed only after a long duration contact of the reaction mixture with the catalyst.

The composition of the mixture obtained from the process of epoxide **1** isomerization in the presence of acid-impregnated silica gel $\text{H}^+ - \text{SiO}_2$ (5%) (Scheme 3), substantially differs from the composition of the mixture obtained with the use of $\text{H}^+ - \text{Al}_2\text{O}_3$. The greater part of the reaction products with the use of this catalyst is presented by hydrocarbons with the molecular mass equal to 202 that may be formally corresponding to dehydration products of the parent oxygen-containing sesquiterpenoid (with the molecular weight amounting to 220). Three dominating species among the reaction products are clovane-2,9-diene **12**, (1*R*,5*S*,9*S*)-4,4,8-trimethyltricyclo[7.2.1.0^{1,5}]dodeca-2,7-diene **13** and (1*R*,8*R*)-3,4,8-trimethyltricyclo[6.3.1.0^{1,5}]-

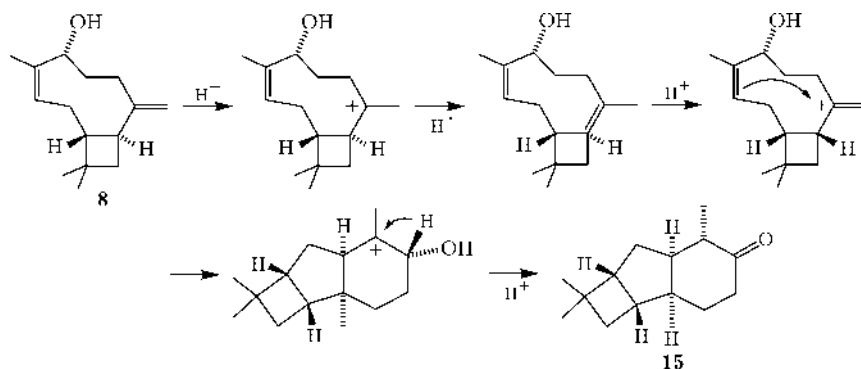
dodeca-3,5-diene **14** with the total content in the mixture of volatile components up to 40–50 %.

The diene **14** was described earlier as the product of transformation of clovane-2,9-diol **11** in superacidic media [21]. The structure of dienes such as **12** and **13** established with the use of two-dimensional NMR spectra ($^{13}\text{C} - ^1\text{H}$ correlation for direct and long-range SSIC, homonuclear correlation $^1\text{H} - ^1\text{H}$), allows assuming, that their precursor also is clovane-2,9-diol **11**. Indeed, the interaction of diol **11** with $\text{H}^+ - \text{SiO}_2$ results in the formation of dienes such as **12–14** (Scheme 4). The mixture of dienes **12** and **13** was also obtained through the reaction of thermal deesterification of clovane-2,9-diol diacetate **16**. These data confirm the validity of the conclusion about the structure of dienes **12** and **13** as well as about the configuration of their asymmetric centres made on the basis of NMR spectra analysis.

Except for the hydrocarbons, there are two carbonyl compounds in the mixture of the products of epoxide **1** rearrangement on $\text{H}^+ - \text{SiO}_2$ surface, such as isocaryolane-9-one **6** and (1*R*,3*S*,4*S*,8*S*,9*R*)-4,8,11,11-tetramethyltricyclo[7.2.0.0^{3,8}]undecane-5-one **15**. The structure of ketone **15** was established with the use of NMR spectra and then it was confirmed basing on the comparison of the ketone NMR spectra with corresponding spectra of (1*R*,3*S*,8*S*,9*R*)-4,8,11,11-tetramethyltricyclo[7.2.0.0^{3,8}]undec-4-ene formed *via* the action of an acid on caryophyllene hydrochloride [22], caryophyllene [23] or on the other isomeric dienes with a caryophyllene skeleton [24]. The configuration of the asymmetric centers of ketone **15** was established basing on spin-spin interaction constants: $^3J_{1-2\alpha} = 0$, $^3J_{3-4} = 6.5$ and $^4J_{3-7\alpha} = 2.1$.



Scheme 4.



Scheme 5.

The most obvious precursor of ketone **15** seems to be allyl alcohol **8** (Scheme 5), as demonstrated by the obtaining of ketone **15** when the sum of allyl alcohols was admitted into the interaction with H^+-SiO_2 . The *cis*-annulation of four- and five-membered cycles within the molecule of ketone **15** is caused by the migration of C^8-C^{13} exocyclic double bond in a parent alcohol **8** inward the cycle to the C^8-C^9 position. A cation formed as the result of β -addition of a proton to C^9 atom of caryophylla-3,8(9)-diene-5 α -ol, undergoes an attack of 3,4-double bond and a subsequent 1,2-hydride shift, which results in the formation of ketone **15**. The formation of an epimeric ketone with a *trans*-annulation of two minor cycles is considered to be impossible.

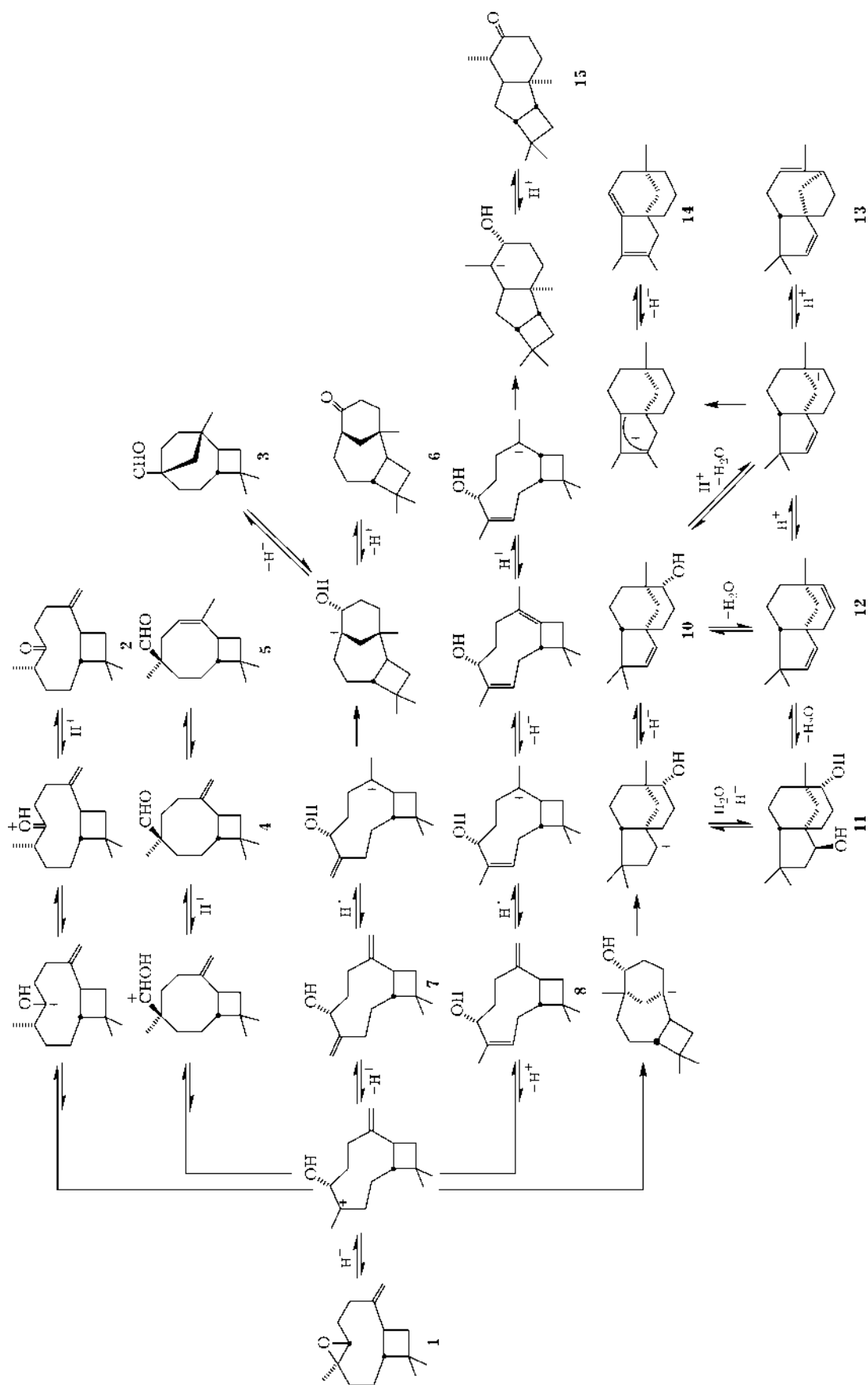
During the process of epoxide **1** isomerization in the presence of H^+-SiO_2 with low acid content ($H^+-SiO_2^{(1\%)}$) a mixture is formed that differs little in composition from typical mixtures obtained with the use of $H^+-Al_2O_3$ as a catalyst. However, the reaction rate on H^+-SiO_2 surface is much higher in comparison with $H^+-Al_2O_3$: already after 5 min of the reaction on $H^+-SiO_2^{(1\%)}$ surface at room temperature parent caryophyllene in the mixture being absent. With an increase either in the contact time of the reaction mixture with this catalyst or in the temperatures of the reaction process, such compounds as **6**, **12**, **13** and **15** appear in the mixture. This fact indicates the species **2–11** to serve as the precursors of these compounds. This is demonstrated by the obtaining of the mixture of compounds **6**, **12–15** through the interaction of the mixture formed due to $H^+-Al_2O_3$ catalysed epoxide **1** isomerization with $H^+-SiO_2^{(5\%)}$ (during 3 h at 68 °C).

The behaviour of H^+-SiO_2 with 5 % acid content prepared basing on silica gel with small (0.002–0.040 mm) particle size – so called $H^+-SiO_2^{(5\% - sm)}$ – is also similar to $H^+-SiO_2^{(1\%)}$ system.

The analysis of the data obtained in the studies on the isomerization of epoxide **1** on the surface of sorbents impregnated with acid allows one to conclude about the absence of a basic difference in the behaviour of H^+-SiO_2 and $H^+-Al_2O_3$ systems. All the observable differences in this case are connected only with different activities of these two catalysts in the reaction under investigation. Indeed, the process of epoxide **1** isomerization in the presence of $H^+-Al_2O_3$ under severe conditions ($H^+-Al_2O_3^{(20\%)}$, during 10 h at 68 °C) resulted in the formation of the mixture containing aldehyde **3**, ketones **6** and **15**, dienes **12** and **13**.

A higher catalytic activity of H^+-SiO_2 as compared to $H^+-Al_2O_3$ was demonstrated earlier by the example of sorbents impregnated either with phosphoric acid [25] or with phospho-tungstic acid [26]. Apparently, this fact is connected with a weaker interaction between impregnated acid and the surface of silica gel, as against the surface aluminium oxide [27, 28]. What is more, an essential contribution to the decrease of $H^+-Al_2O_3$ system activity is contributed by a partial solubility of the supporting medium when applying a strong mineral acid: for example, with the use 5 % H_2SO_4 for the preparation of the catalyst, as much as 30 % of impregnated acid is spent for Al_2O_3 dissolution, as a result of which the real content of the acid on the surface of the sorbent could be as low as 3.5 mass %.

General possible pathways of caryophyllene oxide isomerization process are presented in



Scheme 6.

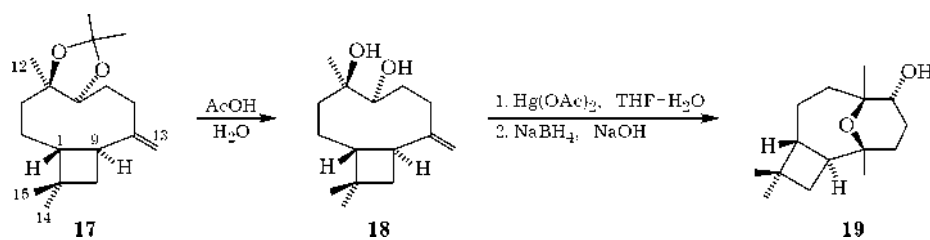
Scheme 6. The first stage of the interaction of a substrate with an acid catalyst consists in the coordination of a proton with an epoxide O atom, resulting in the disruption of the most substituted C⁴-O bond. Formed as the result of it the cation formed as the result of this process can undergo the following transformations. They are an 1,2-hydride shift with the formation of ketone such as **2**, a migration of C-C bond with the formation of aldehydes such as **4** and **5**, as well an elimination a proton with the formation of unsaturated alcohols such as **7** and **8**. When C⁸-C¹³ double bond within the molecules of the latter being protonated, an intramolecular cyclization could occur to result in the formation of tricyclic carbonyl compounds such as **3**, **6** and **15**. Another pathway of the reaction consists in the cyclization of the cation formed due to the opening of the epoxide cycle of the parent substrate **1** and the subsequent expansion of a four-membered cycle resulting in the formation of a clovane skeleton of compounds **10-12**. The rearrangements of the clovane skeleton as the result of a series of consecutive hydride ion or C-C bond shifts [21] result in the formation of isomeric skeletons of the compounds such as **13** and **14**. All the stages, except for ones resulting in the construction of a new carbon cycle, seem to be reversible.

A high catalytic activity of H⁺-SiO₂ as well as high reactivity of the compounds under formation result in significant resinification of the reaction mixture (20-30 % from overall product weight). One more manifestation event of high activity of H⁺-SiO₂ system as an acid catalyst could be presented by the formation of acylated clovane alcohols such as monoacetate and diacetate of alcohol **11** [18] as well as acetate of alcohol **10** when EtOAc was used for the elution of the products of reaction with H⁺-SiO₂. The overall content of these products

usually amounts to 3-4 % from the sum of volatile products. With the use of acetone as a polar solvent for the elution of the products of reaction with H⁺-SiO₂ there is a by-product of interaction with the solvent such as ketal **17** (as much as 5 %) formed, too.

For the comparison, a process was carried out for an acid-catalysed isomerization of caryophyllene oxide under homogeneous conditions. With the use of H₂SO₄-acetone system like the system described in [7] the formation of a set of products was observed similar to those obtained on the surface of H⁺-Al₂O₃. Under the conditions of incomplete transformation of the parent substrate (during 1 h at 20 °C), main products of the reaction are alcohols such as **7**, **8**, **10** and **11**. As the reaction temperature and processing time increased, the amount of allyl alcohols **7** and **8** reduced, whereas there are products of their isomerization such as nonsaturated epoxide **9**, aldehyde **3** and ketone **6** formed in the mixture.

The basic differences of the composition of the products obtained in this case from the products obtained in the case of a heterogeneous catalyst are connected with the use of acetone as a solvent. First, the amount of clovanediol **11** formed considerably increases. In the case of the use of H₂SO₄-acetone system the content of diol **11** in the mixture of reaction products is as much as 30-40 %, whereas for the isomerization process on H⁺-Al₂O₃ or H⁺-SiO₂ surface this value ranges, as a rule, from 0 to 10 %. Second, there is a product of caryophyllane-4,5-diol condensation with acetone in the mixture of reaction products such as ketal **17**. A similar ketal was obtained earlier via the interaction of caryophyllene oxide with acetone in the presence of ascanite-bentonite clay [14]. NMR spectra of ketal **17** are in good coincidence with corresponding spectra described in the literature, however the NMR spectral data



Scheme 7.

do not allow one to make an unequivocal conclusion about the configuration of C⁴ and C⁵ atoms, which was also not successful for the authors of [14]. The aforesaid concerns also diol **18** obtained *via* hydrolysis of ketal **17**. There are 4β,5α- [18, 29] and 4α,5α-[6] dihydroxycaryophyllenes described in the literature. The NMR spectra of isomeric diols presented in these works demonstrate a good coincidence with NMR spectra of diol **18**, however, just like as in the case of the parent ketal, it was rather difficult to determine unambiguously the configurations of C⁴ and C⁵ atoms basing on NMR spectral data.

In order to establish the structure of diol **18** we subjected this substance to cyclization with the use of a mercuration-demercuration method [30] (Scheme 7). The analysis of constants ³J_{5,6} (*J*_{5,6β} = 11.6, *J*_{5,6α} = 5.0) in the ¹H MMR spectrum of epoxy alcohol **19** obtained in such a fashion and the comparison of its NMR spectra with corresponding spectra described for 4β,8β-epoxycaryophyllane-5-ol [7] as well as for 4α,8α-epoxycaryophyllane-5α-ol and 4β,8β-epoxycaryophyllane-5β-ol [31] allow one to make a conclusion about the configuration of C⁴ and C⁵ atoms of the compound obtained, and, accordingly, for parent diol **18** and ketal **17**.

The diol **18** itself is also present in the mixture of the reaction products, though in small proportion (the content in the mixture being less than 1 %). The low content of diol **18** in the mixtures could be connected with its fast condensation with acetone, the formation of ketal **17** and the cyclization to produce an epoxy alcohol such as **19**.

For the process of epoxide **1** isomerization in H₂SO₄-hexane system, after 3 h of the reaction proceeding at 20 °C, the compounds **6**, **12–15** are prevailing in the mixture of products, and at the increased process temperature they are almost the only products of the reaction. A high conversion level of the isomerization process under the present conditions may be connected with a two-phase nature of the system used, which provides a high concentration of acid within the region where the reaction occurs. Such a similar behaviour of the reaction under investigation for both H₂SO₄ and H⁺-SiO₂ systems is in a good agreement with data from the literature concerning the commensura-

bility of catalytic activities for concentrated sulfuric acid and H⁺-SiO₂ system with the acid mass fraction ranging from 20 to 50 % [12, 13].

EXPERIMENTAL

Caryophyllene oxide **1** with m.p. at about 62–63 °C (from methanol) was synthesized according to a technique described in [32]. For the preparation of sorbents impregnated with sulphuric acid, aluminum oxide (standard specifications TU 6-09-3916-75) and KSK silica gel with particle size of 0.002–0.040 or 0.140–0.315 mm were used. All the solvents used were as distilled.

The analysis of reaction mixtures by the method of chromatography-mass spectrometry was carried out using a Hewlett Packard G1081A device consisting of a series II HP 5890 gas chromatograph and an HP MSD 5971 mass selective detector; ionising electron energy being 70 eV. There was a HP5 column (5 % of diphenyl, 95 % of dimethylsiloxane, 30 m × 0.25 mm × 0.25 μm) used. Helium was used as a carrier gas with flow rate of 1 mL/min. The column temperature programming mode was as it follows: holding for 2 min at 50 °C, then heating at a rate of 4 °C/min up to 240 °C and subsequent heating at a rate of 20 °C/min up to 280 °C. The temperature of an ion source was at 173 °C; data were collected at a rate of 1.2 scan/s within a mass scanning range of 30–650 amu. The identification of the components of mixtures under investigation was performed basing on a comparison of the mass spectrometry data and retention time values obtained with corresponding data for reference compounds. The content of the components in mixtures were determined basing on peak area values with no use of correction coefficients.

The registration of NMR spectra was performed using a Bruker DRX-500 spectrometer (¹H registering at 500.132 MHz, ¹³C registering at 125.758 MHz) at room temperature (25 °C) for samples dissolved in CDCl₃ with the content of 25–50 mg/mL. A signal of solvent δ_H 7.24 ppm (CHCl₃) and δ_C 76.90 ppm (CDCl₃) was used as an internal reference. The assignment of signals was carried out with the use of ¹³C NMR spectra registered in a *J*-modulation

mode, as well as according to two-dimensional NMR spectra as it follows: 1) for ^1H - ^1H homonuclear correlation; 2) for ^{13}C - ^1H heteronuclear correlation on direct spin-spin coupling constants ($J = 135$ Hz); 3) for ^{13}C - ^1H heteronuclear correlation on long-range spin-spin coupling constants ($J = 10$ Hz).

Infrared spectra were registered using a Bruker Vector-22 IR spectrometer for 2 % solutions in CHCl_3 .

Mass spectra were registered with the use of a Finnigan MAT 8200 mass spectrometer (50–100 °C, electron impact ionisation, 70 eV).

Optical rotation angles were measured using a Polamat A polarimeter at $\lambda = 578$ nm.

The separation of the components of mixtures obtained was carried out with the use of the following techniques: 1) a column chromatography on a KSK silica gel with the particle size ranging within 0.140–0.315 mm, activated at 130 °C during 6 h; 2) a column chromatography on a silica gel, impregnated with 10 % of AgNO_3 ; 3) a preparative gas chromatography based on a column packed with 15 % OV-101/N-AW-DMCS or with 15 % of apiezon L/Chromaton N-AW, 4.5 m \times 6 mm in size; nitrogen as a carrier gas with flow rate of 60 mL/min, the temperature of a column being within a range of 150–220 °C.

The analytical thin layer chromatography procedure was performed using Sorbfil plates with a fixed sorbent layer. The spots corresponding to the components of a reaction mixture were developed to be visualized by spraying the plates with an alcoholic solution of vanillin (0.5 g of vanillin and 5 mL of concentrated H_2SO_4 dissolved in 100 mL of EtOH).

Preparation of H^+ - Al_2O_3 . For the preparation of H^+ - Al_2O_3 with 5 % acid content, to 10.0 g of Al_2O_3 was added 10.0 g of 5 % aqueous solution of H_2SO_4 . The mixture obtained was stirred at room temperature within 30 min. Water was distilled away using a rotary evaporator. The catalyst obtained was dried at 130 °C during 10 h. The samples of H^+ - Al_2O_3 with the acid content amounted to 1, 10 or 20 % were prepared in a similar fashion with the use of 1, 10 or 20 % aqueous solution of H_2SO_4 , respectively.

Preparation of H^+ - SiO_2 . For the preparation of H^+ - SiO_2 with 5 % acid content, to 10.0 g of SiO_2 was added 20.0 g of 2.5 % aqueous

solution of H_2SO_4 . The mixture obtained was stirred at room temperature within 30 min. Water was distilled away using a rotary evaporator. The catalyst obtained was dried at 130 °C during 10 h. Silica gel H^+ - SiO_2 with the acid content amounted to 1 % were prepared in a similar way with the use of 0.5 % aqueous solution of H_2SO_4 .

General technique for isomerization of caryophyllene oxide (1) on the surface of H^+ - Al_2O_3 or H^+ - SiO_2 . A chromatographic column (5 mm in diameter), containing 0.50 g of H^+ - Al_2O_3 or H^+ - SiO_2 , was applied with a solution of 25.0 mg (0.113 mmol) caryophyllene oxide in 0.8 mL of hexane. After keeping at 20 °C the column was washed out with 5 mL of hexane and 5 mL of EtOAc (in the case of H^+ - Al_2O_3) or acetone (in the case of H^+ - SiO_2). The experiments where the contact time value for the solution of compound **1** with a catalyst exceeds 24 h, as well as the experiments with the temperature increased were carried using a flat-bottomed flask under stirring (the volume of solvent being equal to 2.5 mL). The solution obtained was washed out successively with water (2 times \times 1 mL), with 1 M NaHCO_3 solution (2 times \times 1 mL), then again with water (2 times \times 1 mL) and then it was dried above MgSO_4 . After removal of the solvent the mass of the samples for the experiments with H^+ - Al_2O_3 and H^+ - SiO_2 amounted to about 23–25 and 17–22 mg, respectively. The results of the experiments (the composition of mixtures according to GLC data) are presented in Table 1.

Isomerization of the sum of allyl alcohols (7 and 8). 1. A column containing 0.28 g of H^+ - Al_2O_3 (20 %), was applied with a solution of 14.0 mg (0.064 mmol) of a mixture of alcohols **7** and **8** (in the ratio of 20 : 80, respectively) in 0.3 mL of hexane. After keeping at 20 °C during 1 h, the column was washed out with 5 mL of EtOAc. After removal of the solvent, 13.0 mg of a mixture was obtained containing, according to GLC data, 37 % of caryophyllene-3 α -ol, 10 % of alcohol **8**, 27 % of cyclic ether **9**, 21 % of aldehyde **3** and 6 % of ketone **6**.

2. To a solution of 19 mg (0.086 mmol) of the mixture of alcohols **7** and **8** (in the ratio of 20 : 80, respectively) in 1 mL of hexane was added 0.10 g of H^+ - SiO_2 (5 %). The mixture was stirred at 20 °C during 3 h. The catalyst was

filtered, and then washed out with 2 mL of hexane and with 3 mL of acetone. After removal of the solvent, 17 mg of a mixture was obtained containing, according to GLC data, 27.8 % of ketone **15**, 22.3 % of aldehyde **3**, 14.7 % of ketone **6**.

(1R,4R,8S)-4,7,10,10-tetramethylbicyclo[6.2.0]dec-6-ene-4-carbaldehyde (5). A mixture of 5.0 g of H⁺-Al₂O₃ (5 %) and 0.25 g (1.1 mmol) caryophyllene oxide in 25 mL of hexane was boiled under intense stirring during 3 h. The catalyst was filtered, and then washed out with 20 mL of hexane and with 20 mL of ethyl acetate. After removal of the solvent, 0.24 g of a mix was obtained containing, according to GLC data, 10 % of ether **10**, 32 % of aldehyde **3**, 26 % of aldehyde **5**, 15 % of alcohol **10** and 11 % of ketone **6**. The fraction of aldehydes (0.12 g) was isolated with the use of a column chromatography technique (SiO₂, hexane as an eluent). Aldehyde **5** (38 mg) was separated from aldehyde **3** (52 mg) using a column chromatography technique (AgNO₃/SiO₂, hexane as an eluent). ¹H NMR spectrum (δ, ppm, J, Hz): 0.98 s (C¹¹H₃), 1.00 s (6H, C¹³H₃ и C¹⁴H₃), 1.54 d (H⁹, J_{9,8} = 10.0), 1.56 d (H^{9'}, J_{9',8} = 10.0), 1.62 dd (H¹, J_{1,8} = 10.0, J = 8.0), 1.65 s (C¹²H₃), 2.14 dd (H^{5α}, J_{5α,5β} = 14.3, J_{5α,6} = 10.0), 2.23 dd (H^{5β}, J_{5β,5α} = 14.3, J_{5β,6} = 6.5), 2.82 ddd (H⁸, J_{8,1} = 10.0, J_{8,9} = 10.0, J_{8,9'} = 10.0), 5.10 dddq (H⁶, J_{6,5α} = 10.0, J_{6,5β} = 6.5, J_{6,8} = 1.7, J_{6,12} = 1.7), 9.42 s (CHO). ¹³C NMR spectrum (δ, ppm): 53.8 (C¹), 22.3 (C²), 30.9 (C³), 52.2 (C⁴), 32.5 (C⁵), 118.0 (C⁶), 142.7 (C⁷), 38.7 (C⁸), 36.3 (C⁹), 35.2 (C¹⁰), 21.8 (C¹¹), 20.9 (C¹²), 21.3 (C¹³), 29.7 (C¹⁴), 206.5 (CHO). IR spectrum (cm⁻¹): 1721. Mass spectrum: m/z 220.18281 (220.18270 for C₁₅H₂₄O) (M⁺, 2), 164 (64), 149 (24), 138 (32), 136 (20), 135 (26), 133 (10), 131 (14), 123 (26), 122 (10), 121 (49), 119 (12), 111 (20), 110 (13), 109 (33), 108 (62), 107 (74), 106 (11), 105 (23), 96 (11), 95 (53), 94 (35), 93 (63), 91 (34), 83 (11), 82 (19), 81 (100), 80 (15), 79 (57), 77 (24), 69 (47), 68 (11), 67 (19), 55 (28), 53 (16), 43 (16), 41 (40), 39 (12).

Clovane-2,9-diene (12). A mixture of H⁺-SiO₂ (5 %) and 1.0 g (4.5 mmol) caryophyllene oxide in 50 mL of hexane were boiled during 2 h. The catalyst was filtered and washed out with 30 mL of hexane and 50 mL of diethyl ether. After removal of the solvent, 0.63 g of a mixture was obtained containing, according to GLC

data, 27 % of diene **12**, 10 % of diene **14**, 18 % of ketone **6**, 10 % of ketone **15**. Clovadiene **12** (96 mg) was isolated from the mixture using a preparative GLC technique (15 % of OV-101/N-AW-DMCS, column temperature being at 200 °C). ¹H NMR spectrum (δ, ppm, J, Hz): 0.96 s (C¹⁵H₃), 1.003 s (C¹⁴H₃), 1.005 c (C¹³H₃), 1.37 dd (H^{12α}, J_{12α,12β} = 12.2, J = 2.4), 1.50 m (H⁵), 1.75 dddd (H^{11β}, J_{11β,11α} = 17.5, J_{11β,10} = 4.8, J_{11β,9} = 1.7, J = 1.7), 2.26 ddd (H^{11α}, J_{11α,11β} = 17.5, J_{11α,10} = 2.5, J_{11α,9} = 2.5), 5.24 dddd (H⁹, J_{9,10} = 9.8, J_{9,11α} = 2.5, J_{9,11β} = 1.7, J = 1.7), 5.44 d (H², J_{2,3} = 5.6), 5.50 d (H³, J_{3,2} = 5.6), 5.71 ddd (H¹⁰, J_{10,9} = 9.8, J_{10,11β} = 4.8, J_{10,11α} = 2.5). ¹³C NMR spectrum (δ, ppm): 50.1 (C¹), 137.9 (C²), 140.1 (C³), 48.2 (C⁴), 52.6 (C⁵), 20.0 (C⁶), 34.6 (C⁷), 29.6 (C⁸), 135.1 (C⁹), 126.5 (C¹⁰), 40.7 (C¹¹), 43.6 (C¹²), 24.2 (C¹³), 30.1 (C¹⁴), 29.4 (C¹⁵). Mass spectrum: m/z 202 (M⁺, 74), 188 (11), 187 (71), 173 (20), 161 (12), 160 (47), 159 (100), 146 (12), 145 (36), 133 (13), 131 (33), 129 (12), 128 (13), 121 (15), 120 (45), 119 (22), 117 (15), 115 (16), 108 (46), 107 (18), 106 (10), 105 (48), 95 (12), 94 (15), 93 (43), 91 (41), 79 (26), 77 (23), 41 (15). [α]_D²⁰ -98.2 (c 4.97 CCl₄).

(1R,5S,9S)-4,4,8-trimethyltricyclo[7.2.1.0^{1,5}]dodeca-2,7-diene (13). A mixture of 10.0 g of H⁺-SiO₂ (5 % - sm) and 0.75 g (3.4 mmol) caryophyllene oxide in 30 mL of hexane was stirred at room temperature during 72 h. The catalyst was filtered and washed out with 100 mL of hexane and 50 mL of CH₂Cl₂. The fraction of hydrocarbons (91 mg) was isolated from the mixture of the reaction products with the use of a column chromatography technique (SiO₂, hexane as an eluent). Diene **13** (53 mg) was isolated from the mixture of hydrocarbons using a preparative GLC technique (15 % of OV-101/N-AW-DMCS, column temperature being at 150 °C). ¹H NMR spectrum (δ, ppm, J, Hz): 0.75 s (C¹³H₃), 0.97 ddd (H¹¹, J_{11,11'} = 12.8, J_{11,10} = 12.8, J_{11,10'} = 5.5), 1.00 s (C¹⁴H₃), 1.06 dddd (H¹⁰, J_{10,10'} = 12.8, J_{10,11} = 12.8, J_{10,11'} = 4.0, J_{10,9} = 0.5), 1.25 m (H⁵), 1.33 dddd (H^{11'}, J_{11',11} = 12.8, J_{11',10} = 4.0, J_{11',10'} = 4.0, J = 0.5), 1.43 m (H⁶), 1.52 m (H¹²), 1.59 dd (H^{6'}, J_{6',6} = 12.0, J = 5.0), 1.69 m (H^{12'}), 1.72 d (C¹⁵H₃, J_{15,7} = 1.5), 1.81 m (H^{10'}), 2.31 dddd (H⁹, J = 7.5, 6.6, 1.0, 0.5), 5.33 dq (H⁷, J_{7,6} = 1.5, J_{7,15} = 1.5), 5.39 dd (H², J_{2,3} = 5.6, J = 0.5), 5.49 d (H³,

$J_{3,2} = 5.6$). ^{13}C NMR spectrum, (δ , ppm): 53.1 (C^1), 135.6 (C^2), 140.6 (C^3), 47.4 (C^4), 56.3 (C^5), 36.0 (C^6), 127.2 (C^7), 136.5 (C^8), 37.2 (C^9), 29.1 (C^{10}), 21.3 (C^{11}), 28.7 (C^{12}), 25.0 (C^{13}), 28.6 (C^{14}), 22.1 (C^{15}). Mass spectrum: m/z 202 (M^+ , 71), 187 (42), 175 (14), 174 (100), 173 (28), 160 (17), 159 (99), 146 (10), 145 (30), 131 (33), 129 (15), 128 (14), 119 (16), 117 (15), 115 (14), 105 (20), 91 (25), 79 (11), 77 (14). $[\alpha]_{578}^{23} -33.3$ (c 2.16 CCl_4).

(1R,8R)-3,4,8-trimethyltricyclo [6.3.1.0¹⁵]-dodeca-3,5-diene (14). This compound was synthesized with the use of a technique described in [21]. NMR spectra are in a good agreement with data from the literature [33]. Mass spectrum: m/z 202 (M^+ , 93), 187 (20), 173 (15), 161 (14), 160 (62), 159 (49), 146 (14), 145 (25), 133 (15), 131 (29), 129 (13), 128 (14), 121 (15), 120 (100), 119 (18), 117 (13), 115 (15), 105 (78), 91 (24), 77 (12). $[\alpha]_{578}^{20} -27.6$ (c 2.47 CCl_4) (data from the literature: $[\alpha]_{578}^{20} +2.8$ (c 2.96 CHCl_3) [33], $[\alpha]_{578}^{20} -38.4$ (c 8.95 CHCl_3) [21]).

(1R,3S,4S,8S,9R)-4,8,11,11-tetramethyltricyclo [7.2.0.0^{3,8}]undecane-5-one (15). A mixture of 5.0 g of H^+-SiO_2 (5%) and 1.0 g (4.5 mmol) of caryophyllene oxide in 50 mL of hexane was boiled during 2 h. The catalyst was filtered and washed out with 30 mL hexane and 50 mL of diethyl ether. After removal of the solvent, 0.63 g of a mixture was obtained containing, according to GLC data, 27% of diene **12**, 10% of diene **14**, 18% of ketone **6**, 10% of ketone **15**. Ketone **15** (49 mg) was isolated from the mixture with the use of a preparative GLC technique (15% of OV-101/N-AW-DMCS, column temperature being at 200 °C). ^1H NMR spectrum ($\text{C}_6\text{D}_6 + \text{CCl}_4$ (1 : 1), δ , ppm, J , Hz): 0.89 s (C^{14}H_3), 0.93 d (C^{12}H_3 , $J_{12,4} = 6.5$), 1.02 s (C^{13}H_3), 1.09 s (C^{15}H_3), 1.10 ddd ($\text{H}^{2\beta}$, $J_{2\beta,2\alpha} = 14.1$, $J_{2\beta,3} = 12.7$, $J_{2\beta,1} = 8.9$), 1.32 dddd ($\text{H}^{7\alpha}$, $J_{7\alpha,7\beta} = 13.8$, $J_{7\alpha,6\alpha} = 6.2$, $J_{7\alpha,6\beta} = 2.3$, $J_{7\alpha,3} = 2.1$), 1.35 dd ($\text{H}^{10\alpha}$, $J_{10\alpha,10\beta} = 12.2$, $J_{10\alpha,9} = 7.2$), 1.48 ddd ($\text{H}^{7\beta}$, $J_{7\beta,6\alpha} = 14.0$, $J_{7\beta,7\alpha} = 13.8$, $J_{7\beta,6\beta} = 4.5$), 1.53 ddd ($\text{H}^{10\beta}$, $J_{10\beta,10\alpha} = 12.2$, $J_{10\beta,9} = 8.8$, $J_{10\beta,1} = 2.5$), 1.62 dd ($\text{H}^{2\alpha}$, $J_{2\alpha,2\beta} = 14.1$, $J_{2\alpha,3} = 7.1$), 2.01 ddd ($\text{H}^{6\beta}$, $J_{6\beta,6\alpha} = 13.5$, $J_{6\beta,7\beta} = 4.5$, $J_{6\beta,7\alpha} = 2.3$), 2.10 ddd (H^1 , $J_{1,2\beta} = 8.9$, $J_{1,9} = 7.0$, $J_{1,10\beta} = 2.5$), 2.18 dddd (H^3 , $J_{3,2\beta} = 12.7$, $J_{3,2\alpha} = 7.1$, $J_{3,4} = 6.5$, $J_{3,7\alpha} = 2.1$), 2.20 ddd (H^9 , $J_{9,10\beta} = 8.8$, $J_{9,10\alpha} = 7.2$, $J_{9,1} = 7.0$), 2.25 ddd ($\text{H}^{6\alpha}$, $J_{6\alpha,7\beta} = 14.0$, $J_{6\alpha,6\beta} = 13.5$, $J_{6\alpha,7\alpha} = 6.2$), 2.46 dq

(H^4 , $J_{4,12} = 6.5$, $J_{4,3} = 6.5$). ^{13}C NMR spectrum, (δ , ppm): 44.6 (C^1), 28.0 (C^2), 52.7 (C^3), 42.3 (C^4), 209.9 (C^5), 37.4 (C^6), 34.8 (C^7), 41.2 (C^8), 44.3 (C^9), 34.4 (C^{10}), 32.1 (C^{11}), 13.3 (C^{12}), 17.9 (C^{13}), 24.0 (C^{14}), 31.9 (C^{15}). IR spectrum (cm^{-1}): 1705. Mass spectrum: m/z 220.18289 (220.18270 for $\text{C}_{15}\text{H}_{24}\text{O}$) (M^+ , 20), 166 (10), 165 (83), 164 (58), 149 (17), 147 (14), 136 (13), 135 (13), 121 (13), 109 (27), 108 (21), 107 (100), 105 (19), 95 (17), 93 (56), 92 (14), 91 (28), 86 (12), 84 (29), 82 (10), 81 (44), 80 (71), 79 (28), 77 (21), 69 (17), 67 (26), 55 (29), 53 (14), 43 (10), 41 (39). $[\alpha]_{578}^{23} -46.6$ (c 0.94 CCl_4). m.p. = 95–97 °C.

Isomerization of clovanediol (11) on the surface of H^+-SiO_2 . 1. A column containing 0.10 g of H^+-SiO_2 (5%) was applied with a solution of 7.5 mg (0.031 mmol) of clovanediol in 0.3 mL of EtOAc. After keeping at 24 °C during 30 h the column was washed out with 2 mL of EtOAc. After removal of the solvent, 6.8 mg of colorless oil was obtained. According to GLC data, the mixture obtained contained 6% of diene **12** and 5% of diene **13**, and the balance was presented by the sum of clovanediol monoacetate, clovanediol diacetate as well as clovenol acetate.

2. A mixture of 0.15 g H^+-SiO_2 (5%), 7.5 mg (0.031 mmol) of clovanediol and 1 mL of hexane was boiled under stirring for 3 h in a flat-bottomed flask supplied with a backflow condenser. The catalyst was separated with the use of decantation, it was washed out with 2 mL of hexane and 2 mL of acetone. Organic filtrates were joined together. After removal of the solvent we obtained 5.2 mg of oil containing, according to GLC data, 45% of diene **12** and 27% of diene **14**.

Thermal deesterification of clovanediol diacetate (16). Diacetate **16** (0.70 g, 2.17 mmol) was heated in a sealed ampoule during 3 h at the temperature of 280 °C. After cooling the reaction mixture was diluted with 5 mL of CH_2Cl_2 , then it was washed out with 0.5 M NaHCO_3 solution (3 times \times 2 mL) and with water (3 times \times 2 mL), and then it was dried above MgSO_4 . Oil obtained after removal of the solvent was separated with the use of a column chromatography technique (SiO_2 , hexane, and then CH_2Cl_2 being eluents). The fraction of hydrocarbons (0.13 g, 30%), according to GLC

data, contained 37 % of diene **12** and 41 % of diene **13**.

Isomerization of caryophyllene oxide (1) in H₂SO₄-acetone system. To a solution of caryophyllene oxide (100 mg, 0.45 mmol) in the mixture of acetone (0.4 mL) with 60 mL of water, was added H₂SO₄ (10 mL, 0.19 mmol). The mixture was intensively stirred at 20 °C or under boiling conditions. Acetone was evaporated in the vacuum of a water-jet air pump, and then to the residue obtained, diethyl ether (4 mL) was added. The solution was washed out successively with water (0.5 mL), with 1 M NaHCO₃ aqueous solution (2 times × 0.5 mL), again with water (2 times × 0.5 mL) and then it was dried above MgSO₄. The mass of the samples after removal of the solvent amounted to about 90–100 mg. The results of the experiments are presented in Table 1.

Dihydrocaryophyllene-4β,5α-diol acetone (17). To a solution of caryophyllene oxide (1.0 g, 4.5 mmol) in 10 mL of acetone was added H₂SO₄ (0.1 mL, 1.9 mmol). The mixture was stirred at room temperature during 3 h, then 2 mL of water, 2 mL of hexane and 4 mL of diethyl ether were added. The organic layer was separated; the aqueous layer was extracted with diethyl ether (3 times × 2 mL). The organic fractions joined together were washed out with 1 M NaHCO₃ solution and with water, and then they were dried above MgSO₄. The mass of the sample after removal of the solvent amounted to 0.98 g. Using a column chromatography technique (SiO₂, hexane-CH₂Cl₂ mixture being as an eluent with a gradient of CH₂Cl₂ concentration from 0 up to 100 %) we isolated 0.34 g of a fraction containing, according to GLC data, ketone **2**, cyclic ether **9** and ketal **17**. Ketal **17** (95 mg) was isolated from the mixture with the use of a preparative GLC technique (15 % of apiezon L/Chromaton N-AW, the temperature of a column being at 220 °C). ¹H and ¹³C NMR spectra of ketal **17** are in a good agreement with data from the literature [10]. Mass spectrum: 278 (*M*⁺, 3), 263 (35), 207 (16), 205 (15), 203 (35), 177 (26), 164 (23), 163 (20), 161 (15), 151 (24), 149 (37), 147 (69), 138 (30), 137 (18), 136 (26), 135 (32), 133 (28), 131 (18), 124 (15), 123 (60), 122 (28), 121 (67), 119 (32), 111 (18), 110 (26), 109 (79), 108 (41), 107 (64), 106 (53), 105 (54), 97 (15), 96 (25), 95 (68), 94 (31),

93 (71), 91 (55), 85 (23), 83 (26), 82 (24), 81 (50), 80 (17), 79 (67), 77 (31), 71 (19), 69 (55), 67 (35), 59 (33), 55 (42), 53 (19), 43 (100), 41 (58).

[α]₅₇₈²² -22.0 (c 3.00 CCl₄) (data from the literature:

[α]₅₇₈¹⁹ -40.5 (c 8.9 CHCl₃) [14], m.p. = 56–58 °C.

Dihydrocaryophyllene-4β,5α-diol (18). A mixture of ketal **17** (33.5 mg, 0.120 mmol) with 80 % acetic acid (1.5 mL) was conditioned at 20 °C during 100 h. After reaction, water (1.5 mL) was added to the reaction mixture, and then the latter was extracted diethyl ether (5 times × 1 mL). The ethereal extracts joined together were washed out with a solution of 0.5 M NaHCO₃ (2 times × 1 mL) and with water (2 times × 1 mL), and then they were dried above MgSO₄. The mass of the sample after removal of the solvent amounted to 28.0 mg. Diol **18** (23.0 mg, 80 %) was isolated from the mixture obtained using a column chromatography (SiO₂, CH₂Cl₂ as an eluent). ¹H and ¹³C NMR spectra of **18** are in a good agreement with data from the literature [18, 29]. [α]₅₇₈²⁰ -224 (c 1.43 CCl₄) (data from the literature: [α]_D -260 (c 2.5 CHCl₃) [18], [α]_D²⁵ -30 (c 1.27 CHCl₃) [29]).

4β,8β-Epoxycaryophyllane-5α-ol (19). To a suspension obtained through the addition of 150 μL of THF to a solution of Hg(II) acetate (7.8 mg, 0.0245 mmol) in 150 μL of water, was dropwise added a solution of diol **18** (5.8 mg, 0.0243 mmol) in 250 μL of THF. The reaction mixture was stirred at 20 °C during 3 h. Then 28 μL of 3 M NaOH aqueous solution and 28 μL of 3 M NaOH solution containing 1 mg (0.0264 mmol) NaBH₄ were added. The mixture was conditioned at 20 °C during 1 h under intense stirring. The reaction mixture was saturated with sodium chloride, then the organic layer was separated, and the aqueous layer was extracted with hexane (5 times × 0.3 mL). The organic fractions joined together were washed out with water (3 times × 0.2 mL) and then were dried above anhydrous NaSO₄. The mass of the sample after removal of the solvent amounted to 5.0 mg. With the use of a column chromatography (SiO₂, CH₂Cl₂ as an eluent), 2.5 mg (43 %) of 4β,8β-epoxycaryophyllane-5α-ol **19** was isolated from the mixture obtained. ¹H NMR spectrum (CDCl₃, δ, ppm, *J*, Hz): 0.98 s (C¹⁴H₃), 0.99 s (C¹³H₃), 1.01 s (C¹²H₃), 1.17 s (C¹⁵H₃),

2.07 m (H^1), 2.50 ddd (H^9), 3.43 dd (H^5 , $J_{5,6\beta} = 11.6$, $J_{5,6\alpha} = 5.0$). ^{13}C NMR spectrum for epoxy alcohol **19** is in a good agreement with data from the literature [7].

Isomerization of caryophyllene oxide (1) in H_2SO_4 -hexane system. To a solution of 25.0 mg (0.113 mmol) caryophyllene oxide in 2 mL of hexane was added H_2SO_4 (5 mL, 0.09 mmol). The mixture was intensively stirred during 3 h at 20 °C or at boiling. The hexane solution was separated; the residue was washed out with hexane (2 times \times 1 mL) and with ether (2 times \times 1 mL). The organic fractions joined together were washed out with water and dried over $MgSO_4$. The mass of the samples after removal of the solvent amounted to about 18–23 mg. The results of the experiments are presented in Table 1.

Linear retention indices for caryophyllene oxide and the products of its isomerization (in ascending order of value): **12** – 1340, **13** – 1360, **14** – 1455, **9** – 1518, **2** – 1554, **3** – 1555, **5** – 1562, **1** – 1586, **4** – 1587, **10** – 1589, **15** – 1606, **19** – 1633, **6** – 1641, **7** – 1641, **8** – 1662, **17** – 1707, **18** – 1789, **11** – 1876.

CONCLUSIONS

The analysis of the results obtained during the studies on the behaviour of caryophyllene oxide in the presence of SiO_2 and Al_2O_3 impregnated with sulphuric acid allows one to conclude about the efficiency of the use of these catalysts in order to obtain various isomerization products from the source sesquiterpenoid. The reaction in the presence of H^+-SiO_2 и $H^+-Al_2O_3$ proceeds under mild conditions and is distinguished by a simplified technique of products isolation as compared to similar homogeneous reactions.

The determining factor in the reaction process with the use of H^+-SiO_2 and $H^+-Al_2O_3$ could be represented not only by the reactants concentration on the adsorbent surface, but also by the nature of the latter. In this connection, the variation of the nature of the sorbent used for the preparation of the catalyst, allows the composition of reaction product mixtures to be substantially varied. However, we have established that all the observable discrepancies are

connected only with rather different activities of H^+-SiO_2 and $H^+-Al_2O_3$ with respect to the reaction under investigation. The higher catalytic activity of H^+-SiO_2 as compared to $H^+-Al_2O_3$ could be caused, apparently, by a weaker interaction of impregnated acid with the surface of silica gel as against the surface of aluminum oxide. The catalytic activity of H^+-SiO_2 system with respect to the reaction under investigation is revealed to be quite commensurable with the activity of concentrated sulphuric acid (in two-phase H_2SO_4 /hexane system).

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