Russian Journal of Organic Chemistry, Vol. 40, No. 10, 2004, pp. 1441–1449. Translated from Zhurnal Organicheskoi Khimii, Vol. 40, No. 10, 2004, pp. 1492–1499.
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Transformations of Caryophyllene Diepoxides in Various Acidic Media

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Received November 11, 2003

Abstract—Transformations of diepoxy derivatives of caryophyllene, a widely spread natural sesquiterpene, were studied in various acidic media under conditions of both homogeneous and heterogeneous catalysis. A number of previously unknown compounds were isolated. The experimental data were compared with the results of computer simulation of the most probable transformation pathways using molecular-mechanics and quantum-chemical methods.

In the modern literature, little attention is given to the synthesis of diepoxy derivatives of terpenoids and their reactions in the presence of acid catalysts [1–6]; presumably, the reason is high reactivity of these compounds and their strong ability to undergo polymerization [6–8]. Studies of acid-catalyzed reactions of diepoxides derived from terpenoids in a wide range of acid media should provide information on the effect of the acidity of the medium on the direction of cationoid rearrangements, and comparison of the results with analogous data for transformations of initial dienes and their monoepoxy derivatives should elucidate how the mode of formation of cationic center is related to structure of the final products [9]. Studies in this field are also important from the synthetic viewpoint, taking into account that diepoxy derivatives of terpenoids are obtained from accessible and renewable starting materials and that new transformation products possessing oxygen-containing functional groups may be expected to exhibit biological activity.

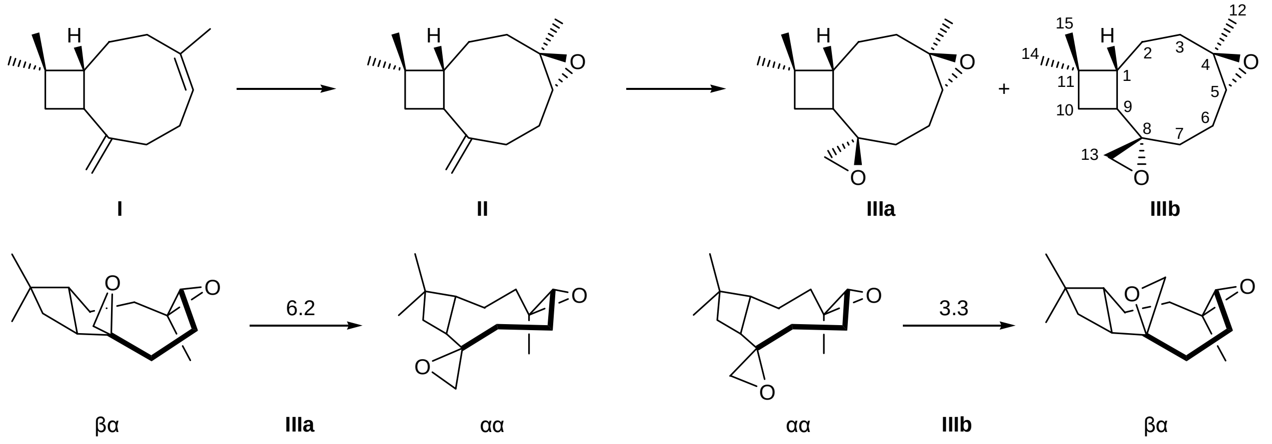
Caryophyllene (**I**) occupies a specific place among sesquiterpenoids due to diversity of its transformations. Acid-catalyzed reactions of caryophyllene give rise to compounds having clovane, caryolane, neoclovane, panasensane, and other skeletons [10–13].

Treatment of diene **I** with peroxy acids leads to formation of epimeric epoxy derivatives as a result of oxidation of the endocyclic double bond: 4β,5α-epoxycaryophyllene (**II**) and its 4α,5β-isomer [13]. It should be noted that compound **II** is one of the most widely spread natural epoxides, and its transformations have been well documented [13, 14]. Compound **II** can be isolated fairly readily (by crystallization) from a mixture of monoepoxy derivatives; repeated epoxidation gives a mixture of diastereoisomeric diepoxides **IIIa** and **IIIb** [15] (Scheme 1); transformations of the latter both over solid acid catalysts and in liquid acidic media have been reported.

We calculated the most stable conformations of diepoxy derivatives **IIIa** and **IIIb**, which coincided with the previously described αα and βα conformations of caryophyllene [16, 17]. The conformations were analyzed using Dreiding's models and molecular dynamics, and their stabilities were estimated by the molecular-mechanics method. The heats of formation of conformers were calculated in terms of the PM3 semiempirical approximation, and the most stable conformers (within 5 kcal/mol) were analyzed by the DFT method (B3LYP/6-31G*). Scheme 1 shows the best conformers (within 2 kcal/mol) according to the DFT calculations: the βα configuration of the 8,13-epoxy group determines the most stable conformer of both diepoxides **IIIa** and **IIIb**. It should be noted that the conformational barriers are low; therefore, conformational control is excluded almost completely.

The synthesis of caryophyllene diepoxides **IIIa** and **IIIb** and their transformations in nucleophilic media were described in [15]. It was shown that in alkaline medium 8,13-diols are formed due to stability of the 4,5-epoxy ring; these compounds undergo intramolecular ring closure with formation of a tricyclic ether.

Scheme 1.



I II IIIa IIIb

βα IIIa αα αα IIIb βα

ΔE = 0.0 (E = –735.924454) 1.3

ΔH_f^0(PM3) = –42.6 –40.7

ΔE = 0.0 (E = –735.924218) 0.5

ΔH_f^0(PM3) = –40.6 –43.1

The behavior of diepoxides **IIIa** and **IIIb** in acidic media was not studied.

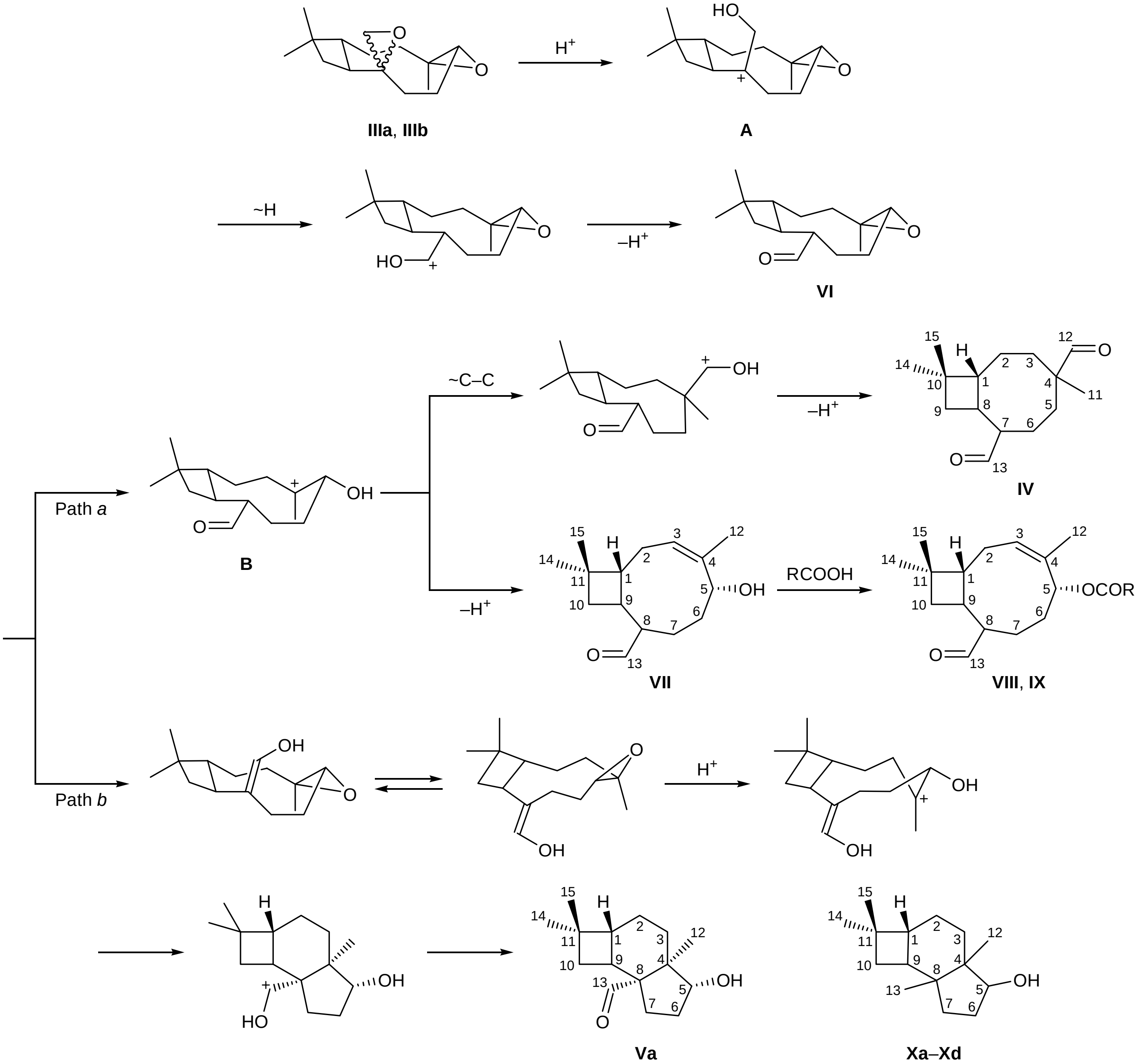
We have found that isomerization of compounds **IIIa** and **IIIb** over solid catalysts, such as β-zeolite, askanite–bentonite, K-10 synthetic clay, and solid superacid TiO_2/SO_4^{2-}) leads to formation of dialdehyde **IV** and tricyclic hydroxy aldehyde **V** (Scheme 2). The ratio of products **IV** and **V** depends on the catalyst nature (Table 1). The isomerization of **IIIa** and **IIIb** in fluorosulfonic acid (HSO_3F–**IIIa**/**IIIb** molar ratio 15:1; SO_2FCl–HSO_3F volume ratio 4:1; –110°C; quenching with acetone–water, 5:1) also gave dialdehyde **IV** and tricyclic hydroxy aldehyde **Va** (Table 1). Raising the temperature to –75°C and subsequent quenching afforded the same products (**IV** and **Va**) at the same ratio.

Ratios of transformation products (GLC) obtained from compounds **IIIa** and **IIIb** (2:1) in the presence of acid catalysts

Acid catalyst	IV	V	VII	VIII	IX
TiO_2/SO_4^{2-}	2	1	–	–	–
β-Zeolite	3	2	–	–	–
Askanite–bentonite	1	1	–	–	–
K-10	1	1	–	–	–
HSO_3F–SO_2FCl	2	1	–	–	–
CF_3COOH	2	1	–	–	1
HCOOH	2	1	–	4	–
HCOOH–dioxane	1	2	2	–	–

Scheme 2 shows a probable mechanism of the above transformations. In the initial step, protonation of the 8,13-epoxy ring gives cation **A** which undergoes rearrangement to epoxy aldehyde **VI**. Compound **VI** is then transformed according to two paths, *a* and *b*, leading, respectively, to dialdehyde **IV** and hydroxy aldehyde **Va**. Path *a* includes protonation of the 4,5-epoxy ring and formation of cation **B**; C–C shift in the latter is accompanied by contraction of the 9-membered ring, and the subsequent elimination of proton yields compound **IV**. According to path *b*, enolization of the aldehyde group is followed by opening of the oxirane ring and recyclization to afford a tricyclic skeleton. Opening of the 4,5-epoxy ring in the keto–enol tautomerization products (ΔH_f^0 = –68.3 and –68.0 kcal/mol), and the subsequent transannular cyclization and elimination of proton result in formation of tricyclic hydroxy aldehydes. Taking into account flexibility of the 9-membered ring, the cyclization could give rise to four isomers **Va**–**Vd**; however, *trans*-cyclization products are less stable (Scheme 3). The proposed mechanism involving initial opening of the 8,13-epoxy ring, is supported by the following experimental data. By column chromatography on silica gel we succeeded in separating a mixture of diepoxides **IIIa** and **IIIb** into isomer **IIIa** and a mixture of **IIIa** and **IIIb** at a ratio of 0.9:1 (GLC). Transformations of each of the isolated samples over β-zeolite, clay, and solid superacid TiO_2/SO_4^{2-} afforded compounds **IV** and **Va** at the same ratio (2:1) as in the reactions with diepoxide mixture **IIIa**/**IIIb**. Thus, in the first step, both diepoxides give rise to the same cation **A** which is then converted into compounds **IV** and **Va** according to Scheme 2.

Scheme 2.

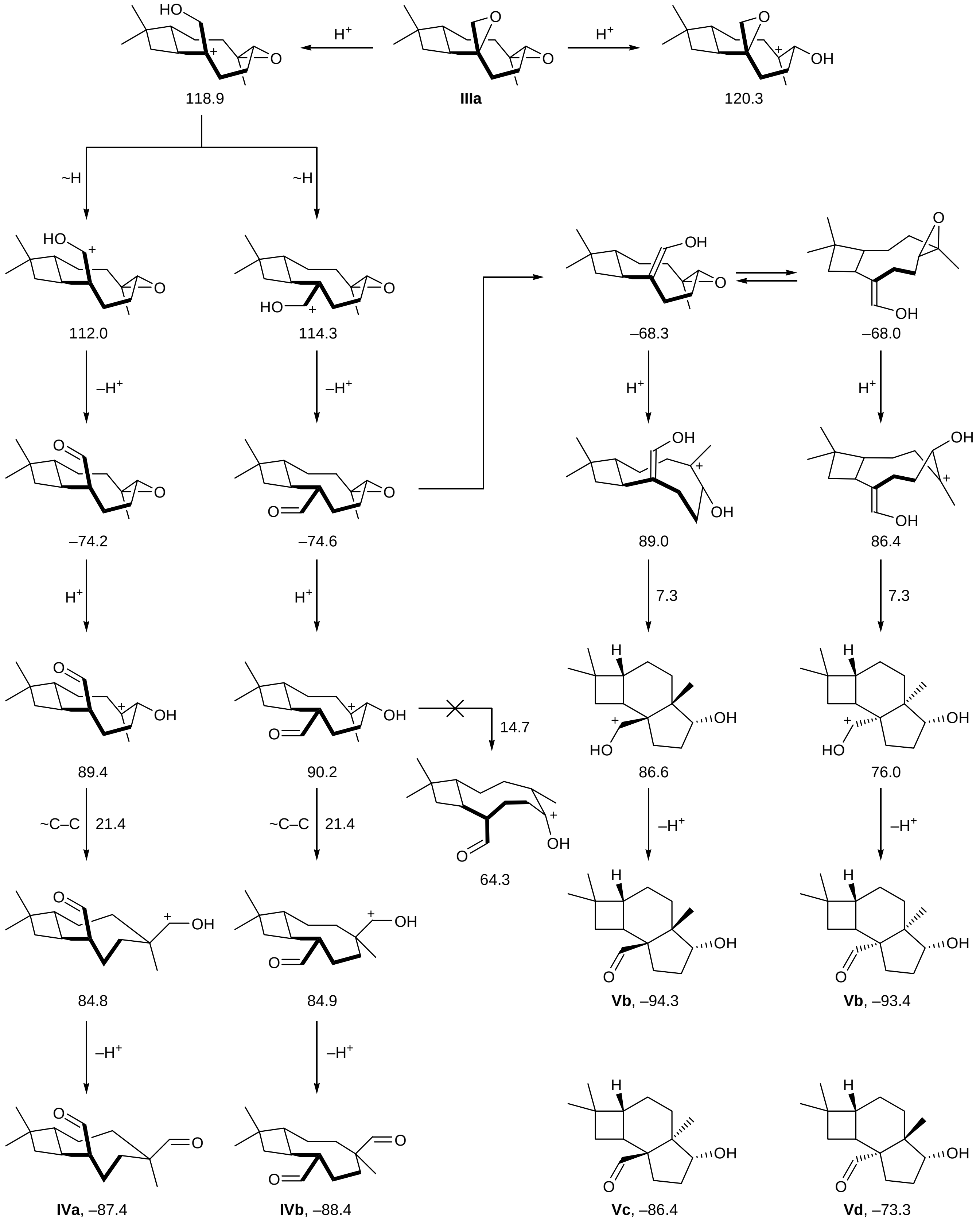


VIII, R = H; **IX**, R = CF_3; **X**, α-$C^{12}H_3$, α-OH, α-$C^{13}H_3$ (**a**); α-$C^{12}H_3$, β-OH, α-$C^{13}H_3$ (**b**); β-$C^{12}H_3$, α-OH, β-$C^{13}H_3$ (**c**); β-$C^{12}H_3$, β-OH, β-$C^{13}H_3$ (**d**).

Dissolution of compounds **IIIa** and **IIIb** in liquid acid systems [HCOOH–dioxane (1 : 1, by volume), HCOOH, CF_3COOH], apart from products **IV** and **Va**, gave unsaturated hydroxy aldehyde **VII** and the corresponding esters **VIII** and **IX**. The mechanism of formation of compound **VII** is shown in Scheme 2. Proton abstraction from cation **B** leads to formation of double bond, and the subsequent esterification yields esters **VIII** and **IX**.

We can conclude that the transformations of caryophyllene diepoxides **IIIa** and **IIIb** in acidic media lead to either contraction of the nonane ring to octane, as with 4β,5α-epoxy derivative [13], or formation of compounds having an allyl alcohol fragment, or rearrangement of the carbon skeleton. The latter process was not observed previously for caryophyllene and its monoepoxy derivatives in acidic media. Furthermore, introduction of two epoxy groups into the caryophyl-

Scheme 3.


HO
118.9
H+
IIIa
H+
120.3
OH
~H
~H
HO
112.0
114.3
HO
OH
–68.3
–68.0
OH
–H+
–H+
H+
H+
O
–74.2
–74.6
O
OH
89.0
86.4
OH
H+
H+
7.3
7.3
89.4
90.2
14.7
86.6
76.0
~C–C 21.4
~C–C 21.4
64.3
–H+
–H+
84.8
84.9
Vb, –94.3
Vb, –93.4
–H+
–H+
IVa, –87.4
IVb, –88.4
Vc, –86.4
Vd, –73.3

lene molecule is likely to change the site of initial protonation. According to published data [13], acid-catalyzed transformations of diene **I** begin with protonation of the C^4=C^5 double bond, whereas diepoxides **IIIa** and **IIIb** initially undergo opening of the 8,13-epoxy ring with formation of an aldehyde group.

The products obtained from diepoxides **IIIa** and **IIIb** in acidic media were not described previously. Their structure was established on the basis of the ^{1}H and ^{13}C NMR spectra. Multiplet signals from 2-H, 6-H, and 9-H in the ^{1}H NMR spectrum of **IIIb**, from 1-H and 3-H in the spectrum of **V**, from 1-H and 7'-H in the spectrum of **VII**, from 7'-H and 9-H in the spectrum of **VIII**, and from 1-H, 8-H, and 9-H in the spectrum of **IX** were assigned using two-dimensional ^{13}C–^{1}H correlation technique (direct ^{13}C–^{1}H coupling constants).

The complete ^{1}H and ^{13}C spectra of diepoxide **IIIa** were given in [18, 19]. For isomer **IIIb**, only chemical shifts of four protons [15] and four carbon nuclei [18] were reported. We now report more detailed ^{1}H and ^{13}C NMR spectra of compound **IIIb** (see Experimental), which were derived from the spectra recorded for a 0.9 : 1 mixture of isomers **IIIa** and **IIIb**; our data are very similar to those reported in the literature.

The orientation of protons (α or β) in molecule **IIIb** was determined by analogy with [18]. Our spectral data did not allow us to distinguish between stereoisomers **IVa** or **IVb**, i.e., to identify α- or β-orientation of the aldehyde group on C^7; likewise, the choice cannot be made on the basis of the calculation results: the difference between the enthalpies of formation of these isomers is less than 1 kcal/mol. However, the reaction yields only one stereoisomer. All the above stated also applies to compounds **VII–IX** (Scheme 3).

By comparing the ^{1}H and ^{13}C NMR spectra of compound **Va** with those reported for isomeric alcohols **Xa–Xd** [20] we assigned α-orientation to the substituents on C^4, C^5, and C^8. The chemical shifts of C^8, C^4, C^7, and C^9 in the ^{13}C NMR spectrum of **Va** differ from the corresponding values found for compound **Xa** due to effect of the formyl group on C^8. For compounds **VIII** and **IX**, direct ^{13}C–^{1}H coupling constants $^1J_{CH}$ are given; they were determined from the monoresonance spectra and are consistent with the assumed structures.

Thus we were the first to study reactions of caryophyllene diepoxides in acidic media and compare these transformations with the transformations of the initial diene and its 4β,5α-monoepoxy derivative under the same conditions; also, the behavior of diepoxides **IIIa** and **IIIb** in acidic and alkaline media was considered. The ratio of the transformation products depends on the nature of the medium.

EXPERIMENTAL

The purity of the initial compounds and reaction products was checked by GLC on a Biokhrom-1 chromatograph equipped with a flame ionization detector; SE-54 quartz capillary column, 13000 × 0.22 mm, and BS-30 (an analog of SE-30) quartz capillary column, 20000 × 0.27 mm, were used; carrier gas helium. The products were separated by column chromatography on silica gel (100–160 μm, Czechia). The specific optical rotations were measured on a Polamat A polarimeter. The elemental compositions were determined from the high-resolution mass spectra which were obtained on a Finnigan MAT-8200 spectrometer. Doubly distilled fluorosulfonic acid (bp 158–161°C) was used; SO_2FCl was purified by bubbling through sulfiric acid. The procedures for carrying out the reactions in superacids and quenching of the resulting solutions were described in [21]; a 5 : 1 (by volume) acetone–water mixture was used as nucleophilic medium for quenching. Askanite–bentonite clay (OST 113-12-86-82) was prepared by acid activation of bentonite clay from Askan deposit and was heated for 3 h at 110°C in a drying box just before use; K-10 synthetic clay was heated for 3 h at 110°C; titanium(IV) oxide sulfate (TiO_2/SO_4^{2-}) was calcined for 3 h at 400°C); wide-pore β-zeolite (SiO_2/Al_2O_3 22.4; pore diameter 0.75–0.80 nm; oxide concentrations, wt %: Na_2O 0.01, Al_2O_3 4.50, SiO_2 59.20, Fe_2O_3 0.08; produced by *Tseosit*, Novosibirsk) was calcined for 3 h at 500°C.

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer operating at 400.13 and 100.61 MHz, respectively, from solutions in CCl_4–$CDCl_3$ (1 : 1); the chemical shifts were measured relative to residual $CHCl_3$ (δ 7.24 ppm, δ_C 76.90 ppm). The structure of the products was established by analysis of the ^{1}H NMR spectra using double homonuclear resonance technique and ^{13}C NMR spectra using selective decoupling from protons, off-resonance technique, and two- (COSY, $^1J_{CH}$ = 135 Hz) and one-dimensional ^{13}C–^{1}H correlation techniques (LRJMD, J_{CH} = 10 Hz). In the NMR data listed below, the atom numbering corresponds to that given in Scheme 2.

The barriers to conformational transformations were calculated by the PM3 method, and the heats of formation of carbocations and barriers to their rearrangements were calculated by the AM1 method; B3LYP/6-31G* calculations were performed using GAMESS program [22] at the Information Technology Department, Novosibirsk State University.

Caryophyllene was isolated from clove oil, $[\alpha]_{580}^{20}$ = –13.8° (c = 4.3, $CHCl_3$).

Caryophyllene diepoxides IIIa and IIIb were prepared by the procedure described in [15]. A 5-g portion of caryophyllene (**I**) was treated with monoperoxyphthalic acid, and recrystallization from MeOH gave 3 g of monoepoxy derivative **II**. The subsequent treatment of **II** with monoperoxyphthalic acid afforded 3.2 g of a mixture of diepoxides **IIIa** and **IIIb**. By column chromatography on silica gel (gradient elution with hexane–diethyl ether, 0 to 40% of the latter) we isolated 0.3 g of diepoxide **IIIa**, 0.4 g of a 0.9 : 1 mixture of **IIIa** and **IIIb**, and 1.5 g of a 1 : 0.8 mixture of **IIIa** and **IIIb**.

^{1}H NMR spectrum of **IIIb** (from the spectrum of mixture **IIIa**/**IIIb**, 0.9 : 1), δ, ppm (J, Hz): 0.87 s ($C^{15}H_3$), 0.89 s ($C^{14}H_3$), 1.25 s ($C^{12}H_3$), 1.60 d.d (1β-H, $J_{1,2}$ = 10, $J_{1,9}$ = 10), 1.38 m (2β-H), 1.59 m (2α-H), 0.91 d.d.d (3β-H, $J_{3\beta,3\alpha}$ = 13, $J_{3\beta,2\beta}$ = 13, $J_{3\beta,2\alpha}$ = 5), 2.08 d.t (3α-H, J = 13, $J_{3\alpha,2}$ = 4.5), 2.75 d.d (β-H, $J_{5\beta,6\alpha}$ = 10.5, $J_{5\beta,6\beta}$ = 4.5), 1.35 m (6α-H), 1.97 m (6β-H), 1.67 d.d.d (7α-H, $J_{7\alpha,7\beta}$ = 14.5, $J_{7\alpha,6\beta}$ = 9.5, $J_{7\alpha,6\alpha}$ = 5), 1.85 d.d.d (7β-H, J = 14.5, $J_{7\beta,6\alpha}$ = 6.5, $J_{7\beta,6\beta}$ = 5), 2.04 m (9α-H), 1.16 d.d (10β-H, $J_{10\beta,10\alpha}$ = 10, $J_{10\beta,9\alpha}$ = 10), 1.49 d.d (10α-H, J = 10, $J_{10\alpha,9\alpha}$ = 8), 2.53 d and 2.56 d (2H, 13-H, J = 5; *AB* system). ^{13}C NMR spectrum (from the spectrum of mixture **IIIa**/**IIIb**, 0.9 : 1), δ_C, ppm: 49.09 d (C^1), 27.21 t (C^2), 39.33 t (C^3), 59.25 s (C^4), 62.21 d (C^5), 24.64 t (C^6), 31.01 t (C^7), 58.44 s (C^8), 47.15 d (C^9), 35.53 t (C^{10}), 33.32 s (C^{11}), 16.15 q (C^{12}), 49.86 t (C^{13}), 21.90 q (C^{14}), 29.90 q (C^{15}). Found for **IIIa**/**IIIb** (2 : 1): m/z 236.11748 $[M]^+$. $C_{15}H_{24}O_2$. Calculated: M 236.11762.

Transformation of caryophyllene diepoxides IIIa/IIIb in $HSO_3F–SO_2FCl$. A solution of 0.05 g (0.0025 mol) of isomer mixture **IIIa**/**IIIb** (2 : 1) in 1.0 ml of methylene chloride was added at –110°C to a solution of 0.20 ml (0.0032 mol) of HSO_3F in 0.80 ml SO_2FCl, and the mixture was vigorously stirred for 15 min. It was then quenched with acetone–water (5 : 1, by volume) and extracted with diethyl ether, and the extract was dried over $MgSO_4$. We isolated 0.03 g of a mixture of compounds **IV** and **Va** at a ratio of 2 : 1 (GLC).

Isomerization of caryophyllene diepoxides IIIa/IIIb. *a. Over β-zeolite.* A solution of 0.5 g of isomer mixture **IIIa**/**IIIb** (2 : 1) in methylene chloride was added to 0.60 g of β-zeolite. The mixture was stirred for 30 min and filtered. According to the GLC data, the mixture contained compounds **IV** and **Va** at a ratio of 3 : 2. After removal of the solvent, the residue, 0.49 g, was subjected to column chromatography on silica gel (gradient elution with hexane–diethyl ether, 0 to 80% of the latter) to isolate 0.072 g (14.5%) of compound **IV** and 0.115 g (23%) of **Va**. Compounds **IV** and **Va** at a ratio of 3 : 2 (GLC) were also obtained under the same conditions from 0.01 g of diepoxide **IIIa** over 0.03 g of β-zeolite and from 0.01 g of mixture **IIIa**/**IIIb** (0.9 : 1) over 0.03 g of β-zeolite.

(1*S*,8*R*)-5,9,9-Trimethylbicyclo[6.2.0]decane-2,5-dicarbaldehyde (IV). $[\alpha]_{580}^{20}$ = –4.8° (c = 2.1, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm (J, Hz): 0.92 s ($C^{11}H_3$), 0.95 s ($C^{14}H_3$), 0.96 s ($C^{15}H_3$), 1.84 m (1β-H), 1.30–1.38 m (2H, 2-H), 1.53 m (3-H, $J_{3,3'}$ = 15), 1.65 m (3'-H, J = 15), 1.45 m and 1.76 m (2H, 5-H), 1.41 m and 1.70 m (2H, 6-H), 2.19 d.d.d.d (7-H, $J_{7,8}$ = 11, $J_{7,6}$ = 8.5, $J_{7,6'}$ = 4, $J_{7,13}$ = 1.5), 2.08 d.d.d.d (8α-H, J = 11, $J_{8,1}$ = 9, $J_{8,9}$ = 9, $J_{8,9'}$ = 8), 1.36 d.d (9-H, $J_{9,9'}$ = 10, $J_{9,8}$ = 9), 1.84 d.d (9'-H, J = 10, 8), 9.35 s (12-H), 9.53 d (13-H, J = 1.5). ^{13}C NMR spectrum, δ_C, ppm: 49.19 d (C^1), 22.25 t (C^2), 30.38 t (C^3), 48.76 s (C^4), 28.02 t (C^5), 19.68 t (C^6), 59.25 d (C^7), 33.64 d (C^8), 39.45 t (C^9), 36.48 s (C^{10}), 22.52 q (C^{11}), 205.13 d (C^{12}), 202.67 d (C^{13}), 22.52 q (C^{14}), 30.38 q (C^{15}). Found: m/z: 236.11748 $[M]^+$. $C_{15}H_{24}O_2$. Calculated: M 236.11762.

(2a*R*,4a*R*,5*R*,7a*R*,7b*S*)-5-Hydroxy-2,2,4a-trimethyldecahydrocyclobuta[*e*]indene-7a-carbaldehyde (Va). $[\alpha]_{580}^{20}$ = –5.3° (c = 3.7, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.03 s ($C^{15}H_3$), 1.09 s ($C^{12}H_3$), 1.11 s ($C^{14}H_3$), 1.49 m (1β-H), 1.28–1.42 m (2H, 2-H), 1.17 m and 1.35 m (2H, 3-H), 3.58 d.d (5β-H, $J_{5,6'}$ = 5.5, $J_{5,6}$ = 1.5), 1.72 d.d.d.d (6-H, $J_{6,6'}$ = 14.5, $J_{6,7'}$ = 10, $J_{6,7}$ = 5, $J_{6,5}$ = 1.5), 2.31 d.d.d.d (6'-H, J = 14.5, $J_{6',7}$ = 12, $J_{6',7'}$ = 5.5, $J_{6',5}$ = 5.5), 1.87 d.d.d (7-H, $J_{7,7'}$ = 14, $J_{7,6'}$ = 12, $J_{7,6}$ = 5), 2.05 d.d.d (7'-H, J = 14, $J_{7',6}$ = 10, $J_{7',6'}$ = 5.5), 2.26 d.d.d (9α-H, $J_{9,1}$ = 12, $J_{9,10}$ = 11, $J_{9,10'}$ = 7), 1.21 d.d (10-H, $J_{10,9}$ = 11, $J_{10,10'}$ = 9.5), 1.58 d.d (10'-H, J = 9.5, $J_{10',9}$ = 7), 9.10 s (13-H). ^{13}C NMR spectrum, δ_C, ppm: 46.27 d

(C^1), 22.87 t (C^2), 36.63 t (C^3), 52.64 s (C^4), 81.25 d (C^5), 32.60 t (C^6), 23.17 t (C^7), 60.80 s (C^8), 35.03 d (C^9), 37.91 t (C^{10}), 39.03 s (C^{11}), 16.48 q (C^{12}), 207.47 d (C^{13}), 20.73 q (C^{14}), 30.25 q (C^{15}). Found: *m*/*z* 236.11748 $[M]^+$. $C_{15}H_{24}O_2$. Calculated: *M* 236.11762.

b. Over askanite–bentonite clay. Dry methylene chloride, 2 ml, was added to 0.02 g of askanite–bentonite clay, and 0.015 g of mixture **IIIa**/**IIIb** (2:1) was then added under stirring. The mixture was stirred for 20 min and filtered. According to the GLC data, the mixture contained compounds **IV** and **Va** at a ratio of 1:1. Compounds **IV** and **Va** at a ratio of 1:1 (GLC) were also obtained under the same conditions from 0.01 g of diepoxide **IIIa** over 0.015 g of askanite–bentonite and from 0.01 g of mixture **IIIa**/**IIIb** (0.9:1) over 0.015 g of askanite–bentonite.

c. Over K-10 clay. Dry methylene chloride, 2 ml, was added to 0.02 g of K-10 clay, and 0.015 g of mixture **IIIa**/**IIIb** (2:1) was then added under stirring. The mixture was stirred for 20 min and filtered. According to the GLC data, the mixture contained compounds **IV** and **Va** at a ratio of 1:1. Compounds **IV** and **Va** at a ratio of 1:1 (GLC) were also obtained under the same conditions from 0.01 g of diepoxide **IIIa** over 0.015 g of K-10 clay and from 0.01 g of mixture **IIIa**/**IIIb** (0.9:1) over 0.015 g of K-10 clay.

d. Over solid superacid TiO_2/SO_4^{2-} (AH). Dry methylene chloride, 2 ml, was added to 0.03 g of TiO_2/SO_4^{2-}, and 0.02 g of mixture **IIIa**/**IIIb** (2:1) was then added under stirring. The mixture was stirred for 20 min and filtered. According to the GLC data, the mixture contained compounds **IV** and **Va** at a ratio of 2:1. Compounds **IV** and **Va** at a ratio of 2:1 (GLC) were also obtained under the same conditions from 0.01 g of diepoxide **IIIa** over 0.03 g of TiO_2/SO_4^{2-} and from 0.01 g of mixture **IIIa**/**IIIb** (0.9:1) over 0.03 g of TiO_2/SO_4^{2-}.

Transformation of caryophyllene diepoxides IIIa and IIIb. *a. In the system HCOOH–dioxane (1:1, by volume).* Diastereoisomer mixture **IIIa**/**IIIb** (2:1), 0.50 g, was dissolved in a mixture of 0.5 ml HCOOH and 0.5 ml of dioxane. After 30 min, the resulting mixture was treated with a saturated solution of sodium carbonate and extracted with diethyl ether (3×30 ml), and the extract was dried over $MgSO_4$. According to the GLC data, the extract contained compounds **IV**, **Va**, and **VII** at a ratio of 1:2:2. Removal of the solvent gave 0.370 g of a mixture of **IV**, **Va**, and **VII**, which was subjected to column chromatography on silica gel (gradient elution with hexane–diethyl ether, 0 to 100% of the latter) to isolate 0.031 g (6%) of compound **VII**. Compounds **IV**, **Va**, and **VII** at a ratio of 1:2:2 (GLC) were also obtained under the same conditions from 0.02 g of diepoxide **IIIa** in 0.4 ml of HCOOH–dioxane and from 0.02 g of mixture **IIIa**/**IIIb** (0.9:1) in 0.4 ml of HCOOH–dioxane.

(1*S*,6*Z*,5*S*,9*R*)-5-Hydroxy-6,10,10-trimethylbicyclo[7.2.0]undec-6-ene-2-carbaldehyde (VII). $[\alpha]_{580}^{20}$ = –5.0° (*c* = 4.3, $CHCl_3$). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.95 s ($C^{14}H_3$), 0.99 s ($C^{15}H_3$), 1.62 br.s ($C^{12}H_3$), 2.17 m (1β-H), 2.02 d.d.d (2-H, $J_{2,2'}$ = 15.5, $J_{2,1}$ = 8.5, $J_{2,3}$ = 7.5), 2.24 m (2'-H, *J* = 15.5, $J_{2',1}$ = 6, $J_{2',3}$ = 5, $J_{2',12}$ = 1.5), 5.39 d.d.q (3-H, $J_{3,2}$ = 7.5, $J_{3,2'}$ = 5, $J_{3,12}$ = 1.5), 4.65 d.d (5β-H, *J* = 10, 5), 1.54–1.68 m (2H, 6-H), 1.23 d.d.d.d (7-H, $J_{7,7'}$ = 14, $J_{7,8}$ = 7, *J* = 12, 3.5), 1.82 m (7'-H), 2.05 m (8-H, $J_{8,9}$ = 11, $J_{8,7}$ = 7, $J_{8,13}$ = 2.2, $J_{8,7'}$ = 2), 1.93 d.d.d.d (9α-H, $J_{9,8}$ = 11, $J_{9,10}$ = 10, $J_{9,1}$ = 9.5, $J_{9,10'}$ = 8), 1.35 d.d (10-H, $J_{10,10'}$ = 10, $J_{10,9}$ = 10), 1.81 d.d (10'-H, *J* = 10, $J_{10',9}$ = 8), 9.47 d (13-H, *J* = 2.2). ^{13}C NMR spectrum, δ_C, ppm: 50.97 d (C^1), 27.43 t (C^2), 125.09 d (C^3), 136.38 s (C^4), 70.77 d (C^5), 33.39 t (C^6), 23.56 t (C^7), 59.25 d (C^8), 36.67 d (C^9), 38.98 t (C^{10}), 35.77 s (C^{11}), 17.26 q (C^{12}), 202.64 d (C^{13}), 22.58 q (C^{14}), 30.48 q (C^{15}). Found: *m*/*z* 236.11748 $[M]^+$. $C_{15}H_{24}O_2$. Calculated: *M* 236.11762.

b. In HCOOH. Diastereoisomer mixture **IIIa**/**IIIb** (2:1), 0.30 g, was dissolved in 3 ml of HCOOH. The mixture was stirred for 30 min, treated with a saturated solution of sodium carbonate, and extracted with diethyl ether (3×30 ml), and the extract was dried over $MgSO_4$. According to the GLC data, the extract contained compounds **IV**, **Va**, and **VIII** at a ratio of 2:1:4. Removal of the solvent gave 0.230 g of a mixture of products, which was subjected to column chromatography on silica gel (gradient elution with hexane–diethyl ether, 0 to 80% of the latter) to isolate 0.022 g (6%) of compound **VIII**.

(1*R*,3*Z*,5*S*,9*S*)-8-Formyl-4,11,11-trimethylbicyclo[7.2.0]undec-3-en-5-yl formate (VIII). $[\alpha]_{580}^{20}$ = –4.6° (*c* = 2.2, $CHCl_3$). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.97 s ($C^{14}H_3$), 1.04 s ($C^{15}H_3$), 1.62 br.s ($C^{12}H_3$), 2.30 m (1β-H), 2.02 d.d.d (2-H, $J_{2,2'}$ = 15.5, $J_{2,1}$ = 8, $J_{2,3}$ = 7.5), 2.36 d.d.d.q (2'-H, *J* = 15.5, $J_{2',1}$ = 6.5, $J_{2',3}$ = 5, $J_{2',12}$ = 1.5), 5.45 d.d.q (3-H, $J_{3,2}$ = 7.5, $J_{3,2'}$ = 5, $J_{3,12}$ = 1.5), 5.79 d.d (5-H, $J_{5,6'}$ = 11, $J_{5,6}$ = 4.5), 1.63 m (6-H, $J_{6,6'}$ = 14, $J_{6,7}$ = 12, $J_{6,5}$ = 4.5, $J_{6,7'}$ =

3), 1.79 d.d.d.d (6'-H, J = 14, $J_{6',5}$ = 11, $J_{6',7'}$ = 5, $J_{6',7}$ = 2.5), 1.23 d.d.d.d (7-H, $J_{7,7'}$ = 14, $J_{7,6}$ = 12, $J_{7,8}$ = 7, $J_{7,6'}$ = 2.5), 1.92 m (7'-H), 2.12 d.d.d.d (8-H, $J_{8,9}$ = 10.5, $J_{8,7}$ = 7, $J_{8,7'}$ = 2, $J_{8,13}$ = 2), 1.91 m (9α-H), 1.44 d.d (10-H, $J_{10,10'}$ = 10, $J_{10,9}$ = 10), 1.85 d.d (10'-H, J = 10, $J_{10',9}$ = 8), 9.49 d (13-H, $J_{13,8}$ = 2), 7.98 d (16-H, $J_{16,5}$ = 1). ^{13}C NMR spectrum, δ_C, ppm ($^1J_{CH}$, Hz): 51.06 d (C^1, J = 129), 27.48 t (C^2, J = 124), 127.51 d (C^3, J = 159), 132.11 s (C^4), 73.00 d (C^5, J = 149), 30.54 t (C^6, J = 130), 23.19 t (C^7, J = 126), 58.80 d (C^8, J = 124), 37.04 d (C^9, J = 131), 39.00 t (C^{10}, J = 138), 36.07 s (C^{11}), 17.80 q (C^{12}, J = 126), 201.42 d (C^{13}, J = 170), 22.78 q (C^{14}, J = 125), 30.58 q (C^{15}, J = 124), 159.75 d (C^{16}, J = 224). Found: m/z 219.11752 $[M - OCHO]^+$. $C_{15}H_{23}O$. Calculated: $(M - OCHO)$ 219.11762.

c. In CF_3COOH. Diastereoisomer mixture **IIIa/IIIb** (2:1), 2.5 g, was dissolved in 25 ml of trifluoroacetic acid. The mixture was stirred for 30 min, treated with a saturated solution of sodium carbonate, and extracted with diethyl ether (3×30 ml), and the extract was dried over $MgSO_4$. According to the GLC data, the extract contained compounds **IV**, **Va**, and **IX** at a ratio of 2:1:1. Removal of the solvent gave 1.20 g of a mixture of products, which was subjected to column chromatography on silica gel (gradient elution with hexane–diethyl ether, 0 to 80% of the latter) to isolate 0.100 g (6%) of compound **IX**.

(1*R*,3*Z*,5*S*,9*S*)-8-Formyl-4,11,11-trimethylbicyclo[7.2.0]undec-3-en-5-yl trifluoroacetate (IX). $[\alpha]_{580}^{20}$ –5.2° (c = 3.8, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.00 s ($C^{15}H_3$), 1.07 s ($C^{14}H_3$), 1.58 br.s ($C^{12}H_3$), 1.59 m (1β-H), 1.95 d.d.d (2-H, $J_{2,2'}$ = 14, $J_{2,3}$ = 8, $J_{2,1}$ = 2), 2.23 br.d.d.d (2'-H, J = 14, $J_{2',1}$ = 13, $J_{2',3}$ = 8), 5.67 d.d.q (3-H, $J_{3,2}$ = 8, $J_{3,2'}$ = 8, $J_{3,12}$ = 1.5), 5.78 d.d (5-H, $J_{5,6'}$ = 12, $J_{5,6}$ = 6.5), 1.62 d.d.d.d (6-H, $J_{6,6'}$ = 14, $J_{6,7}$ = 12.5, $J_{6,5}$ = 6.5, $J_{6,7'}$ = 2), 1.78 d.d.d.d (6'-H, J = 14, $J_{6',5}$ = 12, $J_{6',7'}$ = 7, $J_{6',7}$ = 2), 1.36 d.d.d.d (7-H, $J_{7,7'}$ = 15, $J_{7,6}$ = 12.5, $J_{7,8}$ = 5, $J_{7,6'}$ = 2), 2.03 d.d.d.d (7'-H, J = 15, $J_{7',6'}$ = 7, $J_{7',8}$ = 2.5, $J_{7',6}$ = 2), 2.25 d.d.d (8-H, $J_{8,9}$ = 11.5, $J_{8,7}$ = 5, $J_{8,7'}$ = 2.5), 2.34 d.d.d.d (9α-H, $J_{9,8}$ = 11.5, $J_{9,10}$ = 8.5, $J_{9,10'}$ = 8, $J_{9,1}$ = 8), 1.28 d.d (10-H, $J_{10,10'}$ = 11, $J_{10,9}$ = 8.5), 2.09 d.d.d (10'-H, J = 11, $J_{10',9}$ = 8, $J_{10',1}$ = 1), 9.59 s (13-H). ^{13}C NMR spectrum, δ_C, ppm ($^1J_{CH}$, Hz): 49.95 d (C^1, J = 128), 28.07 t (C^2, J = 126), 129.98 d (C^3, J = 154), 131.90 s (C^4), 76.41 d (C^5, J = 148), 25.80 t (C^6, J = 128), 21.15 t (C^7, J = 127), 58.46 d (C^8, J = 125), 36.11 d (C^9, J = 131), 41.01 t (C^{10}, J = 134), 35.17 s (C^{11}), 15.78 q (C^{12}, J = 127), 201.88 d (C^{13}, J = 169), 22.85 q (C^{14}, J = 125), 30.36 q (C^{15}, J = 125), 156.30 q (C^{16}, $^2J_{CF}$ = 42), 114.56 q (C^{17}, $^1J_{CF}$ = 286). Found: m/z 332.11571 $[M]^+$. $C_{17}H_{23}O_3F_3$. Calculated: M 332.11662.

The authors thank the Russian Foundation for Basic Research (project no. 00-03-32721) for providing access to the STN database through the STN Center at the Novosibirsk Institute of Organic Chemistry, as well as post-graduate student A.A. Romanenko (Parallel Calculation Department) and student of the Novosibirsk State University V.P. Vysotskii for their help in performing the calculations.

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