Rearrangement of (−)-β-Caryophyllene. A Product Analysis and Force Field Study

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Abstract: The rearrangement of (−)-β-caryophyllene (**1**) with sulfuric acid in ether has been reinvestigated. In the early stage, a multitude of products is formed. Of these, fourteen hydrocarbons (**3**, **4**, **6**−**17**) and four alcohols (**5**, **18**−**20**) were obtained pure. From the very beginning, the tricycloundecenes **15**−**17** accumulate quickly. This indicates that a previously unknown rearrangement of **1** by protonation of the exocyclic double bond followed by transannular ring closure is a main reaction, and that the conformation βα is involved. Three hydrocarbons (**3**, **4**, **8**) and three alcohols (**5**, **18**, **19**) proved to be stable. They are the main components in the late stage. A complete rearrangement scheme followed from a force field analysis using MMP2. First, all conformations up to 4 kcal above the global minimum of each product and each carbenium ion necessary for its formation were detected automatically using the search program HUNTER. Second, the conformation favoring a specific transformation was searched for. For transannular cyclizations, the conformation with the shortest distance between the atoms to be bound and, for ring openings and 1,2-shifts, the conformation with the smallest dihedral angle between the empty p-orbital and the bond to be broken were selected. In all cases, the selection criteria proved valid: The stereochemistry of the conformations selected matched the stereochemistry of the products observed. On the basis of the results presented, a fully automated search program for favorable rearrangement paths may be developed.

Introduction

(−)-β-Caryophyllene (**1**) plays a central role in sesquiterpene chemistry. It is ubiquitous in nature and has been proposed as a biogenetic precursor of several tricyclopentanoid sesquiterpenes, thought to be formed via rearrangement routes including transannular cyclizations.[1]

Known since 1834,[2] (−)-β-caryophyllene (**1**) was first isolated in nearly pure state and rearranged in 1892 by Wallach.[3] Treatment with sulfuric acid in acetic acid[3] or ether[4,5] yielded a hydrate and a tricyclic sesquiterpene, ultimately recognized in 1954 by Barton[6] as (1*R*,2*S*,5*R*,8*R*)-4,4,8-trimethyltricyclo-[6.3.1.0^{2,5}]dodecan-1-ol (β-caryolanol) (**5**) and (1*S*,5*S*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{1,5}]dodec-2-ene (clovene) (**4**), respectively. In 1965, Raphael[7] detected a third rearrangement product, (1*R*,6*S*,7*S*)-2,6,8,8-tetramethyltricyclo[5.2.2.0^{1,6}]undec-2-ene (α-neoclovene) (**3**).

According to ^{13}C DNMR experiments[8] (−)-β-caryophyllene (**1**) exists at room temperature in solution as a 76:24 mixture of two conformers separated by a low barrier of inversion ($\Delta G^{\ddagger}$ = 16.25 ± 0.11 kcal/mol). According to force field calculations using MM1[8] these conformers are βα (75%) and ββ (21%), the population of two other conformers, αα (3%) and αβ (<1%), being low (Scheme 1). Recently, a ^{1}H DNMR study[9] in connection with low temperature NOE experiments gave further evidence that the major conformer is βα (75%), and that the barrier of inversion to ββ (25%) is correct ($\Delta G^{\ddagger}$ = 16.1 ± 0.3 kcal/mol). As neither clovene (**4**) nor β-caryolanol (**5**) may be derived from βα, it is currently accepted[10] that most of the material is pumped over to αα and ββ, where protonation of the endocyclic double bond and transannular ring closure yield **4** and **5**, respectively. To explain the formation of α-neoclovene (**3**), an initial *exo*−*endo* isomerization to **2** followed by protonation and transannular ring closure has been proposed.[7] Interestingly, any product formation originating from protonation of the exocyclic double bond followed by direct ring closure has been declared "hardly possible".[11] We now report that this is a main reaction. Moreover, based on a thorough product analysis in conjunction with force field calculations using MMP2,[12] a complete mechanistic rationale of the sulfuric acid induced rearrangement of (−)-β-caryophyllene (**1**) will be given.

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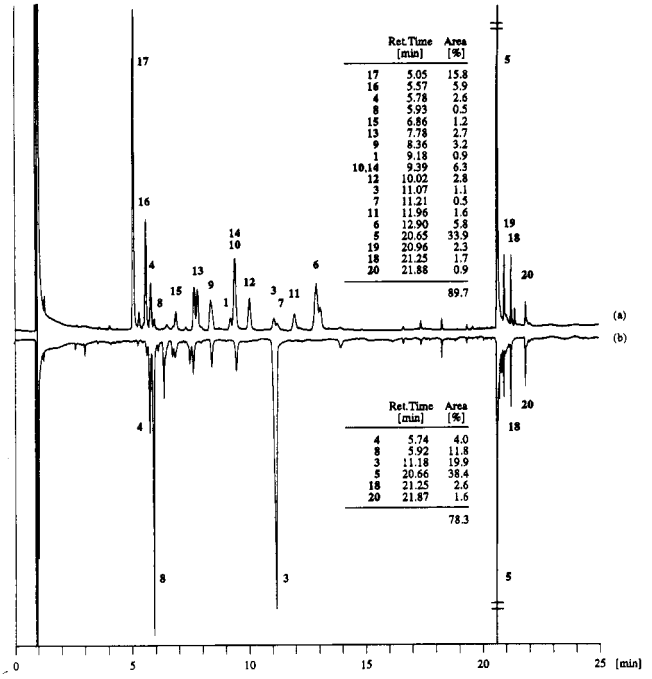
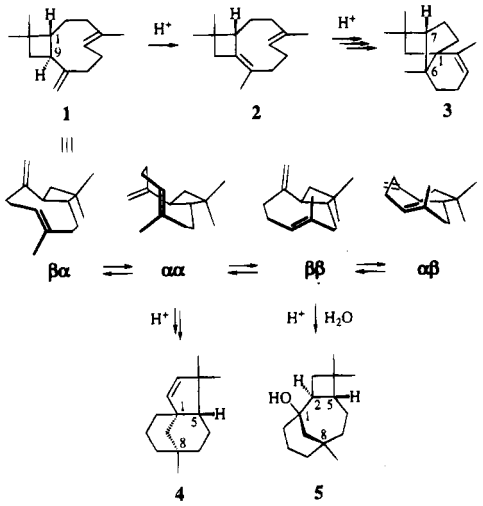


Figure 1. Capillary gas chromatograms (30 m × 0.32 i.d. deactivated fused-silica capillary column coated with 0.25 μm DB FFAP; 15 min 90 °C, 20 °C/min, to 220 °C; 10 min 220 °C; carrier gas 0.6 bar of H_2). Product distribution after rearrangement of **1** with 3 equiv of concentrated H_2SO_4 in ether at 20 °C: (a) after 30 min, (b) after 3 days.

Scheme 1

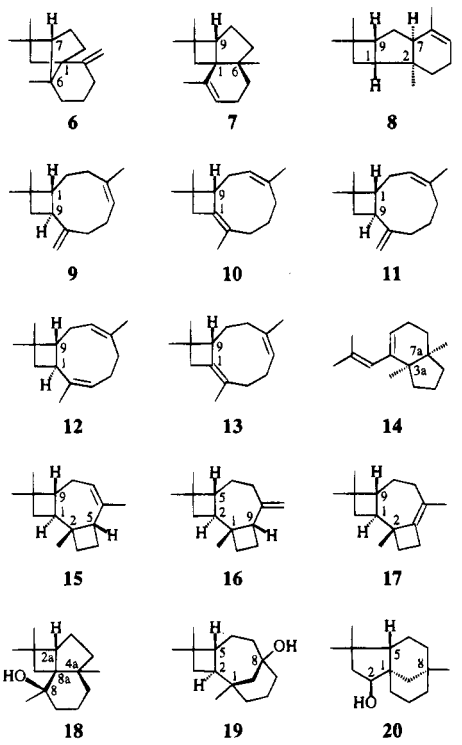


Results and Discussion

Product Analysis. When (−)-β-caryophyllene (**1**) was treated with 3 equiv of concentrated sulfuric acid in ether at 0−20 °C, a multitude of products emerged. After 30 min at least eighteen hydrocarbons and four alcohols were present (yields ≥0.5%, Figure 1a), but after 3 days only three hydrocarbons and three alcohols were left (yields ≥2%, Figure 1b). Separation could be achieved by a combination of chromatography on silica gel, chromatography on silica gel impregnated with 10% (w/w) silver nitrate, and preparative gas chromatography. Fourteen hydrocarbons and four alcohols (Schemes 1 and 2) were obtained pure and in sufficient quantities to run ^1H and ^{13}C NMR spectra and to record $^1H-^1H$ and $^1H-^{13}C$ correlation spectra, if necessary.

Reported ^1H NMR data of α-neoclovene (**3**),[7,13] clovene (**4**),[14] β-neoclovene (**6**),[13b] α-panasinsene (**7**),[13b] **8**,[15] and **20**[16] and reported ^{13}C NMR data of isocaryophyllene (**9**),[17] **10**−**12**,[17]

Scheme 2



β-caryolanol (**5**),[18] and isocaryolanol (**19**)[18d] allowed us to identify nine hydrocarbons and three alcohols as known. The structures of diene **13** and alcohol **18** were determined by chemical correlation (Scheme 3). The structure of **13** followed from the fact that it proved identical with one of the three dehydration products (**23**, **9**, **13**) of alcohol **22**, itself obtained by stereospecific addition of methyllithium to ketone **21**.[19] Similarly, the structure of **18** resulted from the fact that dehydration yielded α-panasinsene (**7**),[13b] β-panasinsene (**24**),[13b,20] and α-neoclovene (**3**).[7,13] Alcohol **18** proved to be a stereoisomer of the stereochemically unassigned alcohol **26**,[21] previously obtained by addition of methylmagnesium iodide to ketone **25** and rearranged to α-neoclovene (**3**) by treatment with acid. Our stereochemical assignment relies on mechanistic consid-

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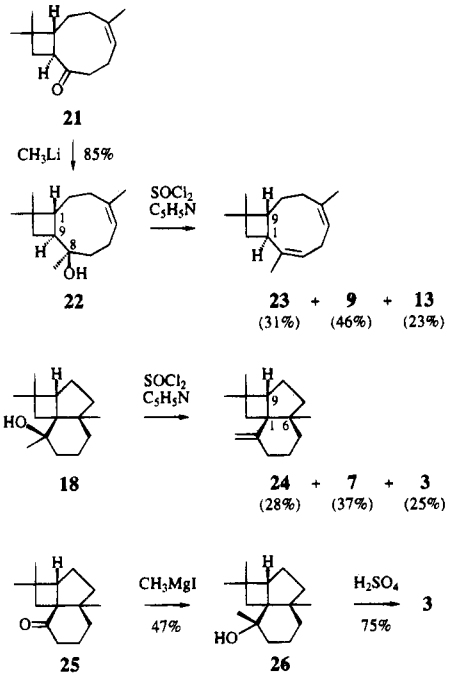
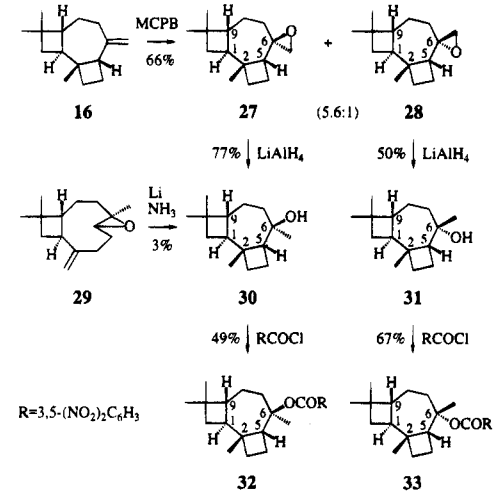
Scheme 3



Scheme 4



erations and will be discussed below. Of the remaining four hydrocarbons, **14** was identified by an analysis of the ^1H and ^{13}C NMR spectra in connection with $^1H-^1H$ and $^1H-^{13}C$ correlation spectra.

In view of their importance for mechanistic considerations, the structure and stereochemistry of the three tricyloundecenes **15**–**17** was ensured by an X-ray analysis of the 3,5-dinitrobenzoate **33**, prepared from **16**. Toward this end, **16** was subjected to a sequence of epoxidation, reduction, and esterification, yielding pairs of stereoisomeric epoxides (**27**, **28**), alcohols (**30**, **31**), and 3,5-dinitrobenzoates (**32**, **33**), respectively (Scheme 4). Alcohol **30**, obtained from the major epoxide **27**, proved to be identical with an alcohol formerly obtained in low yield by treatment of caryophyllene oxide **29** with lithium in liquid ammonia.[11] It may be biogenetically relevant that an alcohol with the same skeleton but with inverted configuration at C-1 and C-2 (koraiol) has been isolated from the oleoresins of Korean pines.[22] The 3,5-dinitrobenzoate **33** crystallized from acetone in rhombic crystals suitable for an X-ray analysis. This analysis confirmed the structure and configuration given, and hence the structure and configuration of **15**–**17**[23] and all products derived from **16**.

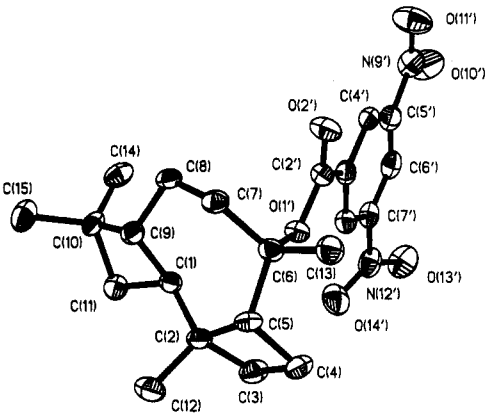


Figure 2. ORTEP plot of the X-ray crystal structure of **33** (hydrogen atoms omitted).

In the solid state, **33** adopts a chair conformation with the ester group in an *axial* position (Figure 2). The cyclobutane ring originating from **1** is *trans*-fused and moderately puckered ($\theta = 21.0-21.2°$); the newly formed cyclobutane ring is *cis*-fused and slightly puckered ($\theta = 9.1-9.4°$). Interestingly, the bond C-2–C-5 is considerably longer (159.0 pm) than all other bonds in the hydrocarbon part (150.6–156.6 pm). As will be shown later, this bond is cleaved during the ring opening of protonated **15**–**17**.

Some of the products formed by the sulfuric acid induced rearrangement of (−)-β-caryophyllene (**1**) have previously been obtained from other sources and/or with other reagents: The dienes **10**–**12**, obtained by hydrochlorination–dehydrochlorination of **1**, and isocaryophyllene (**9**) have been rearranged by treatment with sulfuric acid in ether, yielding mixtures of β-neoclovene (**3**) and **8**,[17] and isocaryolanol (**19**)[18b] and alcohol **20**[16] have been obtained by treatment of **1** with acidic alumina and aqueous chloroacetic acids, respectively. However, with the exception of **3**, none of these products has ever been observed during the sulfuric acid-catalyzed rearrangement of **1**. It is interesting to note that under superacid conditions[24] isocaryophyllene (**9**) yields an isomer of presilphiperfolenol,[25] and that in the present study no tricyclopentanoid sesquiterpene could be detected.

Force Field Studies. The most important finding of the present study is the fact that in the early stage of the rearrangement of **1** up to 40% of the hydrocarbon fraction consists of the formerly unobserved tricycloundecenes **15**–**17**. This indicates that initial protonation of the exocyclic double bond followed by transannular ring closure is a main reaction and that the major conformer $\beta\alpha$ is involved. To clarify this point and to develop a complete rearrangement scheme, we calculated the geometries and heats of formation of all products and all carbenium ions necessary for their formation using MMP2[12] in connection with the parameter set UNICAT2.[26] In

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(23) Originally deduced from $^1H-^1H$ and $^1H-^{13}C$ correlation spectra, the structural relation of **15** and **17** to **16** could also be proven chemically. Catalytic hydrogenation (1.1 atm of H_2, Pd/C, CH_3OH, 30 min at 25 °C) of pure **15**–**17** yielded identical mixtures (1.2:1) of two stereoisomeric saturated hydrocarbons (GC, ^1H NMR), indicating that the reduction had proceeded stepwise with formation of the same intermediate in all three cases. We thank one reviewer for suggesting this experiment.

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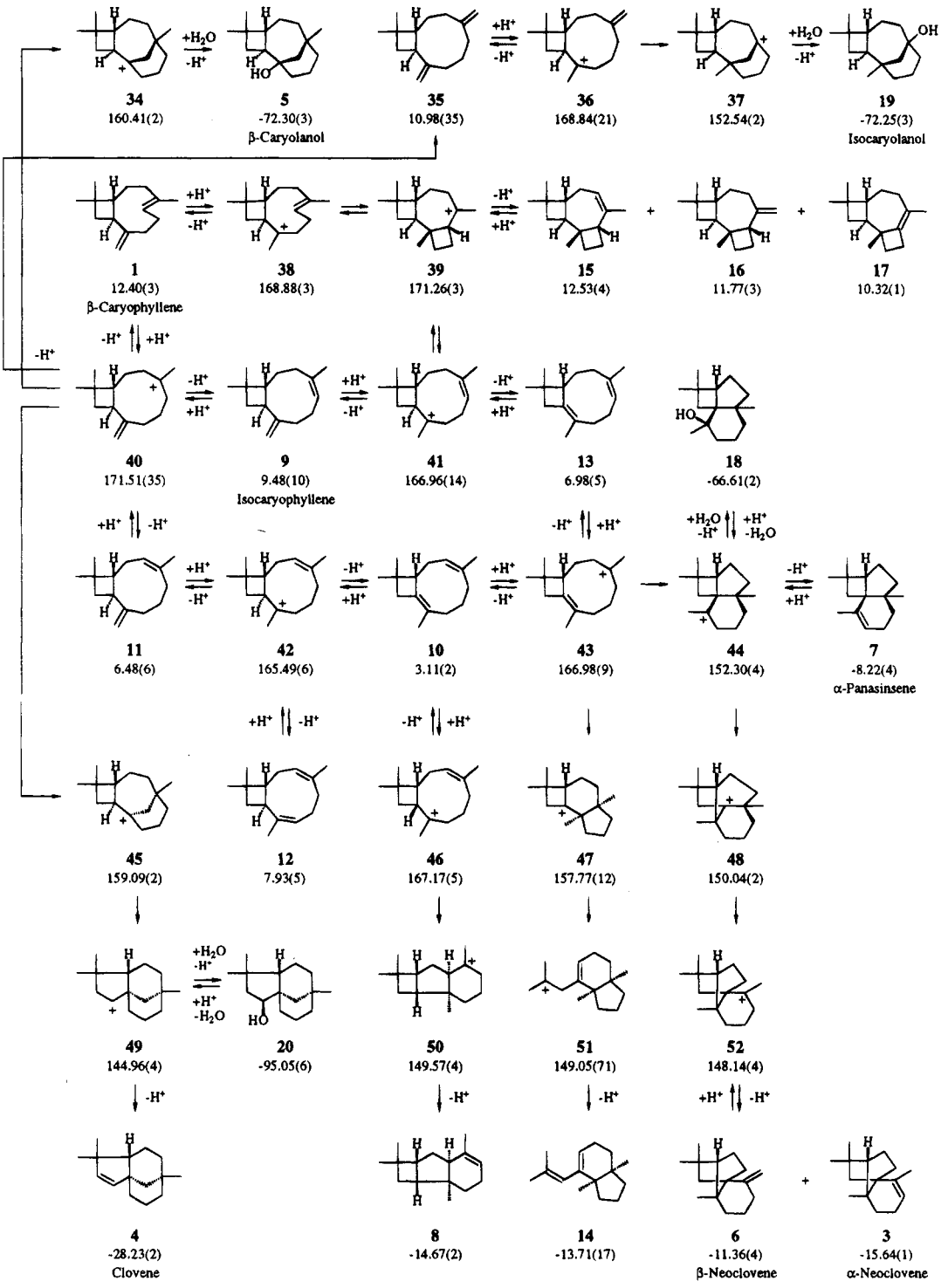
Scheme 5



each case, the global minimum and all conformations up to 4 kcal/mol higher in energy were detected automatically by the conformational search program HUNTER,[27] using a simulated annealing algorithm[28] in connection with a pertubation of the molecule by flapping the ring atoms[29] and rotating the side chains. The calculated heats of formation[30] of all global minima followed (in parentheses) by the number of conformations[31] detected are given in Scheme 5. Thermodynamically, the data for all neutral and charged species are in accord with the products observed.

(26) Müller, P.; Mareda, J. *Helv. Chim. Acta* **1987**, *70*, 1017−1024. Missing parameters involving atom types 2 ($C(sp^2)$) and 30 (C^+) were taken from MMX: Serena Software, P.O. Box 3076, Bloomington, IN 47402.

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(29) Goto, H.; Osawa, E. *J. Am. Chem. Soc.* **1989**, *111*, 8950−8951.

(30) Missing increments for the calculation of the heats of formation of carbenium ions were taken from Müller, P.; Blanc, C.; Mareda, J. *Chimia* **1985**, *39*, 234−235. To account for the stabilization of carbenium ions by β-alkyl branching, the calculated heats of formation were corrected as described by Engler, E. M.; Faracasiu, M.; Sevin, A.; Cense, J. M.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1973**, *95*, 5769−5771. Albeit values to two decimal places are given, quantitative precision is not intended.

(31) Two conformations were defined as different if at least one of the dihedral angles of the carbon skeleton differed by more than 2°.

Scheme 6

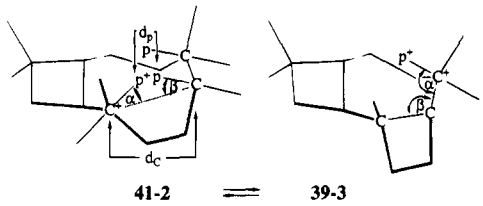


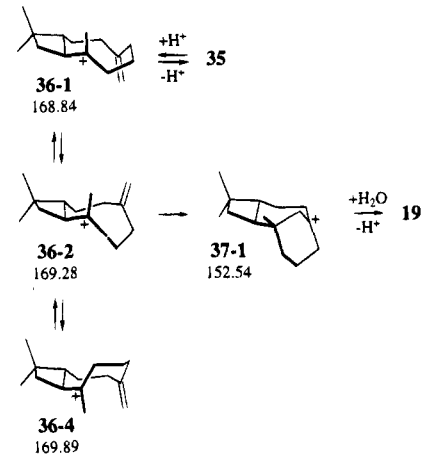
Table 1. Geometry of Selected Conformations of Carbenium Ions Involved in the Rearrangement of **1** As Determined by MMP2 Using the Parameter Set UNICAT2

selected conformation	$\Delta\Delta H_f$ (kcal/mol)	d_C (Å)	d_p (Å)	α (deg)	β (deg)	θ (deg)	product
			Methylene-Bridging				
36-2	0.44	3.23	0.85	13.2	22.9	105.1	**37-1**
36-4	1.05	3.21	0.86	5.5	25.1	178.6	
40-4	0.52	3.64	2.10	34.5	37.6	151.8	**45-1**
40-12	1.24	3.57	1.62	22.3	33.9	138.5	**34-1**
			Hypothetical Zero-Bridging				
36-2	0.44	3.09	0.59	15.6	15.9	85.4	
36-4	1.05	3.11	1.02	21.5	21.4	124.9	
40-4	0.52	3.02	0.87	20.4	16.5	128.3	
40-12	1.24	3.03	0.47	15.7	12.1	79.9	
			Zero-Bridging				
38-1	0.00	2.68	0.69	26.8	21.8	67.0	**39-2**
41-2	0.16	2.82	0.34	28.0	27.5	25.1	**39-3**
43-2	0.72	2.99	0.93	17.3	23.5	121.8	**44-1**
43-2	0.72	2.96	0.69	8.9	22.3	111.2	**47-1**
46-4	1.53	2.95	0.64	13.1	21.9	86.6	**50-1**
			1,2-Shifts				
44-1	0.00			92.7	116.2	27.1	**48-1**
45-1	0.00			84.7	106.4	0.1	**49-1**
48-1	0.00			79.5	103.6	2.3	**52-1**
			Ring-Openings				
39-2	0.42			89.0	114.5	8.1	**38-1**
39-3	3.17			88.0	118.2	24.9	**41-2**

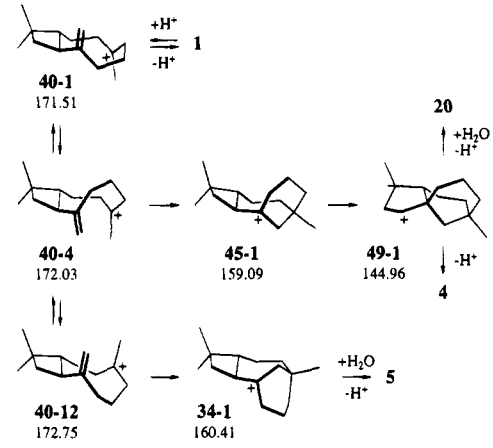
We next searched for the most favorable conformation of each intermediate carbenium ion with respect to the product formed by approaching each individual rearrangement step. Toward this end, all double bonds were defined as localized p-orbitals, and all p-orbitals (empty or filled) as orthogonal to the plane of the three neighboring carbon atoms with the center of each lobe arbitrarily set 1.5 Å from the origin. Then two selection criteria were used: for transannular cyclizations, we searched for the shortest distance (d_C) between the atoms to be bound, and for 1,2-shifts and ring openings—except for the nonclassical **47**—we searched for the smallest dihedral angle (θ) between the empty p-orbital and the bond to be broken. After this selection was done, further data describing the orientation of the orbitals involved were collected. For transannular cyclizations, we determined the distance p^+-p (d_p) and the angles p^+-C^+-C (α), C^+-C-p (β), and p^+-C^+-C-p (θ), and for 1,2-shifts and ring openings the angles p^+-C^+-C (α) and C^+-C-C (β). The meaning of the symbols is exemplified with **41-2** and **39-3** as selected conformations for the transannular cyclization of **41** and the ring opening of **39**, respectively (Scheme 6). All data are collected in Table 1, where the extension of the formula number indicates the conformation selected, and $\Delta\Delta H_f$ is the enthalpy difference to the global minimum.

As may be seen from Table 1, the shortest distances between the carbon atoms which undergo transannular cyclizations with formation of a methylene bridge are 3.23 Å in **36-2**, 3.64 Å in **40-4**, and 3.57 Å in **40-12**. These distances drop to 3.09 Å in **36-2**, 3.02 Å in **40-4**, and 3.03 Å in **40-12** if one considers a hypothetical zero bridge, which apparently does not form because a primary carbenium ion would be involved.[32] Interestingly, in all cases where zero-bridging is observed (**38-1**, **41-2**, **43-2**, **46-4**), the shortest distance between the cyclizing carbon atoms is in the same range. This indicates that the approach of the carbenium ion center to the double bond during methylene- and zero-bridging is roughly the same. The minimum conformations of **36** and **40** and the selected conformations leading to the formation of isocaryolanol (**19**) and clovene (**4**), **20**, and β-caryolanol (**5**), respectively, are given in Schemes 7 and 8. Note that **45-1** ($\theta = 0.1°$) easily rearranges to **49-1**, while **34-1** ($\theta = 80.3°$) does not rearrange further. No product derived from **36-4** has been observed, albeit the geometry for bridging is favorable ($d_C = 3.21$ Å). However, this may be due to the fact that some minor components remain unknown.

Scheme 7



Scheme 8

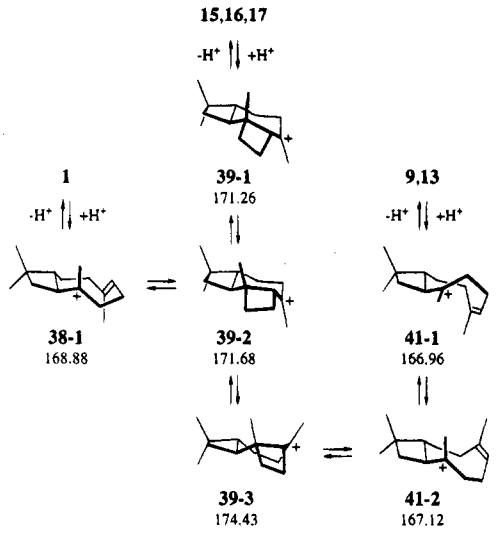


The shortest distance between two carbon atoms involved in a transannular cyclization is 2.68 Å in **38-1**. This corresponds to the fact that in the early stage of the rearrangement of **1** the formation of the formerly unknown hydrocarbons **15-17** is a main reaction. In the later stages, **15-17** are consumed through ring opening of **39-3** ($\Delta\Delta H_f = 3.17$ kcal/mol, $\theta = 24.9°$) to **41-2** with formation of **9** and/or **13** and, to a lesser extent, through ring opening of **39-2** ($\Delta\Delta H_f = 0.42$ kcal/mol, $\theta = -8.1°$) to **38-1** with formation of **1** (Scheme 9). This may be deduced from the fact that under the rearrangement conditions used for **1**, pure **16** yields largely α-neoclovene (**3**) (46%), **18** (9%), and **8** (5%), but only minor amounts of β-caryolanol (**5**) (9%) and clovene (**4**) (4%).[33] Further support comes from the

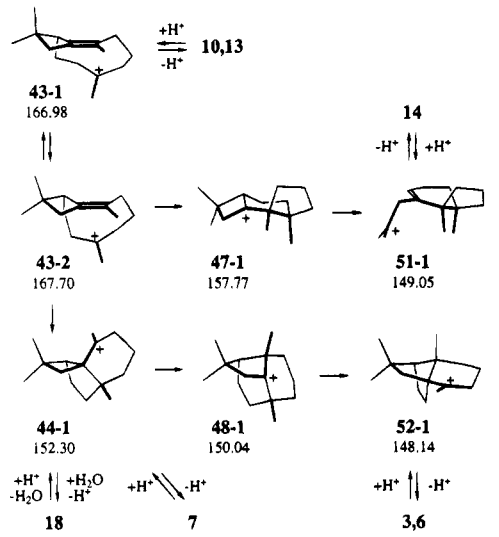
(32) Compare the heats of formation (kcal/mol) of the primary (201), secondary (183), and tertiary (166) butylcarbenium ion: Lossing, F. P.; Holmes, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 6917–6920 and references cited therein.

(33) We thank one reviewer for suggesting this experiment.

Scheme 9



Scheme 10



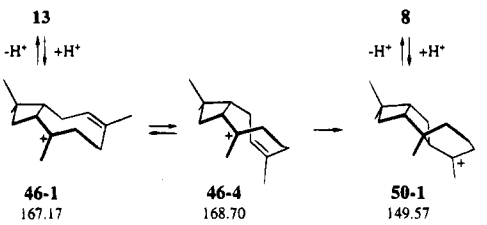
fact that the sulfuric acid induced rearrangement of isocaryophyllene (**9**) also yields α-neoclovene (**3**), but no β-caryolanol (**5**) and/or clovene (**4**).[34] It is interesting to note that **41-2** (d_C = 2.82 Å), as formed by protonation of **9** and/or **13**, could well cyclize to **39-3**. However, this possibility remains without consequences as only products uphill in energy could be formed.

A pecularity was found with **43**, where conformation **43-2** was selected twice: First, for the shortest distance for the cyclization to **44-1** (d_C = 2.99 Å) and, second, for the shortest distance for the cyclization to **47-1** (d_C = 2.96 Å). Of the products formed, **47-1** rearranges to the homoallylic carbenium ion **51-1** as the precursor of **14**, and **44-1** undergoes two 1,2-shifts with formation of **52-1** as the precursor of α-neoclovene (**3**) and β-neoclovene (**6**) (Scheme 10). Due to an unfavorable dihedral angle, the rearrangement of **44-1** (θ = 27.1°) to **48-1** (θ = 2.3°) is slow, and α-panasinsene (**7**) is formed as well. The cyclization of **46** is straightforward. In the selected conformation **46-4** the distance between the interacting carbon atoms is short (d_C = 2.95 Å), and the enthalpy gained by cyclization to **50-1** is large (Scheme 11).

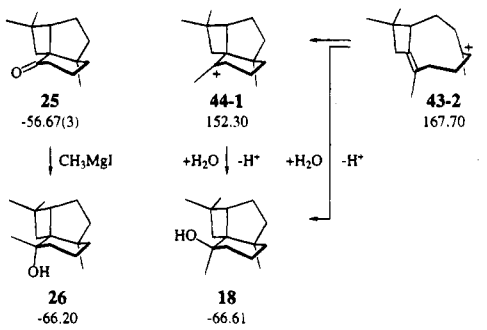
A comment should be made on the stereochemistry of **18** and its previously unassigned epimer **26**.[21] Our assignment takes account of the fact that the spatial relationships in the

(34) Gollnick, K.; Schade, G.; Cameron, A. F.; Hannaway, C.; Roberts, J. S.; Robertson, J. M. *Chem. Commun.* **1970**, 248−249.

Scheme 11



Scheme 12



geometry optimized structures of **44-1** and **25** are nearly the same. Addition reactions should therefore proceed with the same stereochemistry. Anticipating steric control and hence an equatorial attack of the reagent,[35] the products derived from **44-1** and **25** are **18** and **26**, respectively (Scheme 12). This assignment is in accord with an eventual formation of **18** by backside attack of water during the cyclization of **43-2**.

As demonstrated above, searching for the shortest distance between the atoms participating in transannular cyclizations, and searching for the smallest dihedral angle between the empty p-orbital and the bond to be broken in ring openings and 1,2-shifts, is a rough but appropriate means to select a reactive conformation. As may be seen from Table 1, most of the other data point in the same direction. In the case of favorable transannular cyclizations, a short distance d_C (<3 Å) is always connected with a short distance d_p (<1 Å) and small angles α (<30°) and β (<30°). This means that the p-orbitals are preoriented such that their axes lie within a narrow cone around the axis of the bond to be formed. The dihedral angles θ only describe the relative orientation of the p-orbitals within these cones. For favorable ring openings and 1,2-shifts, the dihedral angle θ must be small (<30°), and in this case, α and β are less decisive.

A final remark concerns the population of the different conformations of (−)-β-caryophyllene (**1**) as determined by ^{1}H and ^{13}C NMR measurements, and by MM1[8], MMP2,[12,36] and MM3[37] calculations (Table 2). On the basis of ^{1}H NMR measurements at −40 °C[9] and ^{13}C NMR spectra at room temperature,[8] it has been reported that in solution the only detectable conformations of **1** are βα (75%) and ββ (25%). In excellent agreement, MM1[8] favors βα (75%) over ββ (21%) and αα (3%), but MM2 favors ββ (58%) over βα (39%) and αα (3%), and MM3 αα (44%) over βα (29%) and ββ (26%). Especially the data from MM3 are in sharp contrast to what has been deduced from NMR measurements. However, while

(35) Due to the presence of an axial methyl group in the β-position, an axial approach should be hindered: Dauben, W. G.; Fonken, G. J.; Noyce, D. S. *J. Am. Chem. Soc.* **1956**, *78*, 2579−2582.

(36) For MM2 (77) and MMX calculations on (−)-β-caryophyllene, see: Hinkley, S. F. R.; Perry, N. B.; Weavers, R. T. *Phytochemistry* **1994**, *35*, 1489−1494 and ref 7, respectively.

(37) Allinger, N. L.; Yuh, Y. H.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8551−8566. The MM3 (89) program was obtained from the Technical Utilization Corp. Inc., 235 Glen Village Ct., Powell, OH 43065.

Table 2. Population of the Different Conformations of (−)-β-Caryophyllene (**1**) at 298 K As Determined by ^1H and ^{13}C NMR Spectra and by Force Field Calculations Using MM1, MM2, and MM3

	βα		αα		ββ		αβ
	ΔH_f	(%)	ΔH_f	(%)	ΔH_f	(%)	ΔH_f
^1H NMR		(76)				(24)	
^{13}C NMR		(75)				(25)	
MM1	12.94	(75)	14.78	(3)	13.69	(21)	16.94
MM2	12.63	(39)	14.17	(3)	12.40	(58)	17.25
MM3	18.54	(29)	18.23	(44)	18.56	(26)	21.83

the equilibrium βα ⇄ ββ ($\Delta G^{\ddagger}$ = 16.2 kcal/mol) is certainly within the slow exchange limit at the temperature employed (−40 °C), the equilibrium βα ⇄ αα with an unknown barrier of inversion may not be. In this case, the conformation assigned as βα may in fact be a rapidly interconverting mixture of βα and αα as indicated by MM3. The NOEs reported[9] are valid for both conformations. Any comment on the quality of MM3 must therefore await clarification of this point.

Summary and Conclusions

The rearrangment of (−)-β-caryophyllene (**1**) with sulfuric acid in ether has been reinvestigated. Instead of the two hydrocarbons (**3**, **4**) and one alcohol (**5**) reported, fourteen hydrocarbons (**3**, **4**, **6**−**17**) and four alcohols (**5**, **18**−**20**) were found. In the early stage, the new tricycloundecenes **15**−**17** accumulate to more than 40% of the hydrocarbons formed. This indicates that protonation of the *exocyclic* double bond followed by transannular ring closure is a primary reaction, and that the major conformer βα is involved. This is in sharp contrast to what was believed before. As the rearrangement proceeds, **15**−**17** are consumed through ring opening of **39** to **41** with formation of **9** and/or **13** and, to a lesser extent, through ring opening of **39** to **38** with formation of **1**. All products which follow are formed by an initial protonation of the *endocyclic* double bond. At the very end, all bicyclic dienes (**9**−**13**) formed in between have disappeared and only three hydrocarbons (**3**, **4**, **8**) and three alcohols (**5**, **18**, **19**) remain.

A complete rearrangement scheme resulted from a force field analysis using the conformational search program HUNTER[27] in connection with MMP2[12] and the parameter set UNICAT2.[26] We first calculated the geometries and heats of formation of all conformations up to 4 kcal above the global minimum for all products and all carbenium ions necessary for their formation. Then the conformations favoring each individual rearrangement step were extracted. For transannular cyclizations, we searched for the shortest distance (d_C) of the participating atoms, and for ring openings and 1,2-shifts we searched for the smallest dihedral angle (θ) between the empty p-orbital and the bond to be broken. In all cases these simple selection rules proved valid. The stereochemistry of the conformations selected matched the stereochemistry of the products observed.

We believe that the values for d_C and θ obtained from the analysis of the rearrangement of **1** may also be used in an *a priori* search for favorable rearrangement paths in other systems. These values are d_C = 3.2−3.6 Å for methylene-briding, d_C = 2.7−3.0 Å for zero-bridging, and θ = 0−30° for ring-openings and 1,2-shifts and will be tentatively used in an automated search program, CARESY,[38] which we are currently developing. CARESY is based on the conformational search program HUNTER[27] in conjunction with MM3[37] and is devised for an educt- and/or product-oriented search for synthetically useful rearrangement routes. A parameter set for carbenium ions, missing in MM3, has already been developed.[39]

(38) Weiser, J.; Fitjer, L. To be published.

Experimental Section

IR spectra were recorded on a Perkin-Elmer 298 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained with a Bruker AMX 300, Varian VXR 200, or Varian VXR 500 spectrometer. For standards other than TMS the following chemical shifts were used: $\delta_H(CHCl_3)$ = 7.24 ppm, $\delta_C(CDCl_3)$ = 77.00 ppm. Some of the ^{13}C spectra were studied by APT (attached proton test) to determine the number of protons attached to each carbon. Mass spectra were determined with a Varian MAT 311 A or 701 instrument operated at 70 eV. Preparative GC was carried out on a Carlo-Erba GC 6000 Vega Series 2 instrument employing a thermal conductivity detector and hydrogen as the carrier gas. Analytical gas chromatography was performed on a Carlo-Erba GC 6000 Vega Series 2 instrument employing a split/splitless injector, a FID 40 detector, and hydrogen as the carrier gas. Product ratios were not corrected for relative response. R_f values are quoted for Macherey & Nagel Polygram SIL G/UV254 plates. Colorless substances were detected by oxidation with 3.5% alcoholic molybdophosphoric acid (Merck) and subsequent warming. Impregnated TLC plates were prepared by dipping the plates into a solution of 10% (w/w) silver nitrate in methanol/water (2:1, v/v) and drying for 1 h at 110 °C.[40] The silica gel impregnated with 10% (w/w) silver nitrate for column chromatography was prepared by adding the appropriate amount of silica gel to a solution of silver nitrate in acetonitrile, evaporating the solvent on a rotary evaporator, and drying the residue for 48 h at 80 °C, 0.5 Torr, prior to use. Melting points were observed on a Reichert microhotstage and are not corrected. Microanalytical determinations were done at the Microanalytical Laboratory of the Institut of Organic Chemistry, Göttingen.

Rearrangement of (−)-β-Caryophyllene (1). A. Early Stage. (1*R*,2*S*,5*R*,8*R*)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-ol (β-Caryolanol) (5), (2a*S*,4a*R*,8*R*,8a*S*)-2,2,4a,8-Tetramethyldecahydrocyclobut[*c*]inden-8-ol (18), (1*S*,2*S*,5*R*,8*S*)-1,4,4-Trimethyltricyclo-[6.3.1.0^{2,5}]dodecan-8-ol (Isocaryolanol) (19), (1*S*,2*S*,5*S*,8*S*)-4,4,8-Trimethyltricyclo[6.3.1.0^{1,5}]dodecan-2-ol (20), (1*R*,6*S*,7*S*)-2,6,8,8-Tetramethyltricyclo[5.2.2.0^{1,6}]undec-2-ene (α-Neoclovene) (3), (1*S*,5*S*,8*S*)-4,4,8-Trimethyltricyclo[6.3.1.0^{1,5}]dodec-2-ene (Clovene) (4), (1*R*,6*S*,7*S*)-6,8,8-Trimethyl-2-methylenetricyclo[5.2.2.0^{1,6}]undecane (β-Neoclovene) (6), (1*S*,6*S*,9*S*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{1,6}]-undec-2-ene (α-Panasinsene) (7), (1*R*,2*S*,7*S*,9*R*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{2,7}]undec-5-ene (8), (1*R*,4*Z*,9*S*)-4,11,11-Trimethyl-8-methylenebicyclo[7.2.0]undec-4-ene (Isocaryophyllene) (9), (1*Z*,6*Z*,9*S*)-2,6,10,10-Tetramethylbicyclo[7.2.0]undeca-1,6-diene (10), (1*R*,3*Z*,9*S*)-4,11,11-Trimethyl-8-methylenebicyclo[7.2.0]undec-3-ene (11), (1*S*,2*Z*,6*Z*,9*R*)-2,6,10,10-Tetramethylbicyclo[7.2.0]undeca-2,6-diene (12), (1*Z*,5*Z*,9*S*)-2,6,10,10-Tetramethylbicyclo[7.2.0]undeca-1,5-diene (13), (3a*R*,7a*R*)-3a,7a-Dimethyl-4-(2-methyl-1-propenyl)-2,3,3a,6,7,7a-hexahydro-1*H*-indene (14), (1*S*,2*R*,5*R*,6*Z*,9*R*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{2,5}]undec-6-ene (15), (1*R*,2*S*,5*R*,9*S*)-1,4,4-Trimethyl-8-methylenetricyclo[7.2.0.0^{2,5}]undecane (16), and (1*S*,2*R*,5*Z*,9*R*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{2,5}]undec-5-ene (17). To a solution of (−)-β-caryophyllene (**1**) (5.00 g, 24.5 mmol) in ether (25 mL) was added at 0 °C with stirring a solution of 96% sulfuric acid (7.51 g, 73.5 mmol) in ether (25 mL). The mixture was allowed to warm to room temperature, and after 30 min a saturated solution of sodium bicarbonate (150 mL) was added. The mixture was extracted with ether (3 × 150 mL), the combined organic layers were dried ($MgSO_4$), and the solvent was evaporated (bath temperature 20 °C, 20 Torr) to yield 5.20 g of a colorless solid. According to capillary GC [30 m × 0.32 mm i.d. deactivated fused-silica capillary column coated with 0.25 μm DB FFAP; 15 min 90 °C, 20 °C/min, to 220 °C; 10 min 220 °C; 0.6 bar of H_2; retention times (min): 5.19 (**17**), 5.71 (**16**), 5.92 (**4**), 6.06 (8), 7.01 (**15**), 7.97 (**13**), 8.54 (**9**), 9.37 (**1**), 9.63 (**10** and **14**), 10.21 (**12**), 11.26 (**3**), 11.41 (**7**), 12.15 (**11**), 13.13 (**6**), 20.66 (**5**), 20.94 (**19**), 21.24 (**18**), 21.84 (**20**)], this solid contained the hydrocarbons **3** (1%), **4** (3%), **6** (3%), **7** (1%), **8** (1%), **9** (2%), **10** and **14** (7%), **11** (1%), **12** (2%), **13** (2%), **15** (1%), **16** (4%), and **17** (12%), and the alcohols **5** (44%), **18** (3%), **19** (3%), and **20** (2%). Filtration through silica gel with pentane (column 14 × 3 cm) yielded 1.80 g of

(39) Strobl, D.; Weiser, J.; Fitjer, L. To be published.

(40) Wilson, W. K.; Schroepfer, G., Jr. *J. Org. Chem.* **1988**, *53*, 1713−1719.

hydrocarbons containing 26% **17**, 15% **10** and **14**, 9% **6**, 9% **16**, 6% **9**, 5% **4**, 5% **13**, 4% **12**, 3% **3**, 2% **8**, 2% **15**, 2% **11**, and 1% **14**. Subsequent elution with ether gave 2.20 g of alcohols containing 56% **5**, 9% **19**, 6% **18**, and 2% **20**.

The alcohols were chromatographed on silica gel (column 65 × 4.5 cm) using pentane/ether, 95:5 [R_f = 0.24 (**18**), 0.16 (**20**), 0.08 (**5**), 0.01 (**19**)], followed by pentane/ether, 80:20 [R_f = 0.32 (**5**), 0.23 (**19**)], and pentane/ether, 70:30. One hundred thirteen milligrams (2.1%) of **18**, 1.42 g (26.1%) of **5**, and 133 mg (2.5%) of **19** were pure, while 200 mg (3.7%) of **20** was obtained as a 1:9 mixture with **5**. This material was subjected to preparative GC [3 m × 1/4 in. all glass system, 15% OV-101 on Chromosorb W AW/DMCS, 60−80 mesh, 220 °C, relative retention times: 1.00 (**5**), 1.23 (**20**)], yielding 30 mg of **20** as a 1:3 mixture with **5**.

The hydrocarbons were chromatographed on silica gel (column 90 × 3 cm) in pentane, yielding fractions **A** (30 mg), **B** (880 mg), **C** (220 mg), **D** (90 mg), **E** (70 mg), and **F** (120 mg). According to capillary GLPC **A** contained **4** (25%), **16** (13%), **8** (11%), and **17** (7%), **B** contained **17** (47%), **16** (16%), **10** and **14** (10%), **4** (7%), **3** (5%), **15** (3%), **7** (2%), and **8** (2%), **C** contained **10** and **14** (72%), **15** (5%), **6** (2%), and **17** (2%), **D** contained **9** (48%), **11** (26%), and **13** (26%), **E** contained **13** (69%), **1** (14%), **9** (6%), **11** (4%), **6** (3%), and **12** (1%), and **F** contained **6** (63%), **12** (30%), **1** (3%), and **13** (3%). Chromatography of fraction **B** on silica gel impregnated with 10% silver nitrate (column 70 × 2.3 cm) in pentane/ether, 60:1, yielded fractions **B1** (20 mg), **B2** (120 mg), **B3** (150 mg), **B4** (80 mg), **B5** (80 mg), **B6** (50 mg), **B7** (20 mg), and **B8** (10 mg). According to capillary GLPC **B1** contained **8** (46%), **14** (24%), and **3** (24%), **B2** contained **17** (74%), **3** (23%), and **14** (3%), **B3** contained **17** (94%), **3** (3%), and **7** (3%), **B4** contained **17** (82%) and **7** (13%), **B5** contained **10** (71%), **16** (13%), and **17** (2%), **B6** contained **16** (94%), **10** (2%), and **15** (1%), **B7** contained **15** (46%), **16** (29%), and **4** (17%), and **B8** contained **4** (89%), **16** (3%), and **15** (1%). Fraction **A** was not considered further, while fractions **B1**−**B8**, **C**, and **F** were subjected to preparative GC on OV-101 [3 m × 1/4 in. all glass system, 15% OV-101 on Chromosorb W AW-DMCS 80/100 mesh, 150 °C (**B1**, **B4**, **B7**), 160 °C (**B2**, **B6**, **F**), 170 °C (**B3**, **B5**, **C**), 180 °C (**B8**)], and **D** and **E** on FFAP [3 m × 1/4 in. all glass system, 15% FFAP on Chromosorb W AW-DMCS 60/80 mesh, 160 °C], yielding (GC purity in parentheses) 6 mg of **3** (>95%), 5 mg of **4** (>95%), 1 mg of **6** (>92%), 3 mg of **7** (>95%), 12 mg of **8** (>95%), 10 mg of **9** (>97%), 68 mg of **10** (>95%), 8 mg of **11** (>93%), 2 mg of **12** (>95%), 2 mg of **13** (>90%), 6 mg of **14** (>90%), 2 mg of **15** (>90%), 12 mg of **16** (>95%), and 30 mg of **17** (>95%).

The ^{1}H NMR data of **3**,[7,13] **4**,[14] **5**,[18d] **6**,[13b] **7**,[13b] **8**,[15] **10**,[17] **11**,[17] **12**,[17] **19**,[18d] and **20**[16] and the ^{13}C NMR data of **5**,[18] **9**,[17] **10**,[17] **11**,[17] **12**,[17] and **19**[18d] were identical with literature data. However, the ^{1}H NMR data for **3**, **4**, and **6**−**8** were incomplete, and ^{1}H NMR data for **9** and ^{13}C NMR data for **3**, **4**, **6**−**8**, and **20** were missing. These data are given together with the data of the formerly unknown **13**−**18**.

Data for 3: ^{1}H NMR (500 MHz, $CDCl_3$, TMS int) δ 1.01 (d, 3, *J* = 1.5 Hz, H-13), 1.03 (s, 3, H-14), 1.17 (dd, 1, *J* = 12, 0.5 Hz, H-9), 1.19 (d, 3, *J* = 0.5 Hz, H-15), 1.29 (dd, 1, *J* = 12, 7.5 Hz, H-5), 1.43 (dt, 1, *J* = 12, 3 Hz, H-10), 1.45 (d, 1, *J* = 3.5 Hz, H-7), 1.56 − 1.66 (m, 2, H-10, H-11), 1.60 (ddd, 3, *J* = 4, 2, 1.5 Hz, H-12), 1.70 (dd, 1, *J* = 12, 3.5 Hz, H-9), 1.70 − 1.76 (m, 1, H-11), 1.89 (dtq, 1, *J* = 8, 12, 1.5 Hz, H-5), 2.00−2.08 (m, 1, H-4), 2.13−2.22 (m, 1, H-4), 5.10 (m, 1, H-3); ^{13}C NMR (50 MHz, $CDCl_3$, TMS int) δ 18.5 (q), 20.5 (q), 22.9 (t), 23.9 (t), 27.0 (t), 31.6 (q), 32.0 (q), 37.0 (s, C-8), 37.6 (t, C-5), 47.2 (t, C-9), 49.3 (s), 51.2 (s), 54.3 (d, C-7), 117.8 (d, C-3), 138.8 (s, C-2); MS *m/z* 204 (M^+), 189 (100).

Data for 4: ^{1}H NMR (500 MHz, $CDCl_3$, TMS int) δ 0.84 (s, 3), 0.93 (s, 3), 1.02 (dt, 1, *J* = 5.5, 13 Hz), 1.03 (s, 3), 1.22 (dt, 1, *J* = 12, 2.5 Hz), 1.29−1.41 (m, 7), 1.47 (dd, 1, *J* ≈ 8.5, 7 Hz), 1.47−1.52 (m, 1), 1.53−1.60 (m, 1), 1.63−1.75 (m, 1), 5.26 (d, 1, *J* = 5.5 Hz), 5.34 (d, 1, *J* = 5.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int) δ 20.5 (t), 21.4 (t), 24.7 (q), 30.0 (s, C-4), 32.2 (q), 33.1 (q), 34.4 (t), 39.0 (t), 39.2 (t), 43.7 (t, C-12), 47.9 (s), 50.0 (s), 50.1 (d, C-5), 137.2 (d), 138.8 (d).

Data for 6: ^{1}H NMR (500 MHz, $CDCl_3$, TMS int) δ 0.97 (d, 3, *J* = 1 Hz, H-13), 1.04 (s, 3, H-15), 1.09 (d, 1, *J* = 12 Hz, H-9) 1.11 (ddd, 1, *J* = 13, 9, 6.5 Hz, H-10), 1.21 (s, 3, H-14), 1.23 (m, 1, H-5), 1.50 (d, 1, *J* = 3.5 Hz, H-7), 1.59−1.85 (m, 5, H-4, H-5, H-11), 1.81 (dd, 1, *J* = 12, 3.5 Hz, H-9), 2.04 (ddt, 1, *J* = 13, 11.5, 3 Hz, H-10), 2.08 (ddt, 1, *J* = 14, 5, 2 Hz, H-3), 2.34 (dddt, 1, *J* = 14, 12.5, 6.5, 2 Hz, H-3), 4.45 (t, 1, *J* = 2 Hz, H-12), 4.72 (t, 1, *J* = 2 Hz, H-12); ^{13}C NMR (50 MHz, $CDCl_3$, $CDCl_3$ int) δ 18.59 (q), 23.11 (t), 23.14 (t), 30.03 (t), 30.24 (t), 31.76 (q), 31.84 (q), 32.67 (t), 36.33 (s), 47.83 (t), 52.58 (s), 54.24 (s), 55.76 (d), 106.76 (t), 151.32 (s).

Data for 7: ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.86 (s, 3, H-12), 0.92 (s, 3, H-15), 1.13−1.18 (m, 1, H-5), 1.19 (s, 3, H-14), 1.40−1.48 (m, 2, H-5, H-7), 1.53 (m, 1, H-8), 1.70−1.87 (m, 4, H-4, H-7, H-8, H-11), 1.91 (dd, 1, *J* = 12.5, 2 Hz, H-11), 1.95 (ddd, 3, *J* = 2, 1, 1 Hz, H-13), 1.99 (m, 1, H-4), 2.22 (br d, 1, *J* = 7.5 Hz, H-9), 5.45 (br d, 1, *J* = 6 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$, TMS int) δ 19.4 (q, C-12), 22.6 (t, C-4), 23.8 (q, C-13), 24.8 (q, C-15), 24.9 (t, C-8), 28.6 (s, C-10), 30.3 (q, C-14), 33.6 (t, C-5), 36.7 (t, C-11), 41.5 (s, C-6), 42.0 (t, C-7), 49.3 (s, C-1), 53.1 (d, C-9), 123.3 (d, C-3), 137.0 (s, C-2).

Data for 8: ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.75 (s, 3), 0.87 (s, 3), 1.00 (ddd, 1, *J* = 13, 6, 1 Hz, H-3), 1.13 (s, 3, H-14), 1.26 (dt, 1, *J* = 6, 13 Hz, H-3), 1.36 (ddd, 1, *J* = 13, 10.5, 9 Hz, H-8), 1.49 (dd, 1, *J* = 12, 7.5 Hz, H-11), 1.56 (ddd, 1, *J* = 12, 8.5, 3, H-11), 1.69 (ddd, 3, *J* = 2, 1, 1 Hz, H-12), 1.88 (dtq, 1, *J* = 15.5, 6, 1.5 Hz, H-4), 1.98−2.04 (m, 2, H-4, H-7), 2.06 (ddd, 1, *J* = 13, 8, 0.5 Hz, H-8), 2.20 (dddd, 1, *J* = 9, 7, 3, 0.5 Hz, H-9), 2.25 (ddd, 1, *J* = 8.5, 7.5, 7 Hz, H-1), 5.23 (m, 1, H-5); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int) δ 17.4 (q, C-13), 23.1 (t, C-4), 23.8 (q, C-12), 24.3 (q, C-15), 29.5 (t, C-3), 31.7 (q, C-14), 32.1 (s, C-10), 34.1 (t, C-11), 34.3 (t, C-8), 40.6 (s, C-2), 44.9 (d, C-1), 45.8 (d, C-9), 49.4 (d, C-7), 118.5 (d, C-5), 136.7 (s, C-6).

Data for 9: ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.96 (s, 3, H-14), 0.98 (s, 3, H-15), 1.41 (dddd, 1, *J* = 13.5, 11.5, 7, 3.5 Hz), 1.46−1.54 (m, 1), 1.52 (t, 1, *J* = 10 Hz), 1.65 (m, 3, H-12), 1.70 (ddd, 1, *J* = 10.5, 8.5, 1 Hz), 1.82 (ddd, 1, *J* = 12, 9, 4.5 Hz), 1.98 (ddd, 1, *J* = 13, 7, 3.5 Hz), 2.08−2.24 (m, 5), 2.50 (q, 1, *J* = 9 Hz), 4.74 (m, 1, H-13), 4.82 (d, 1, *J* = 2 Hz, H-13), 5.24 (t, 1, *J* = 7.5 Hz, H-5).

Data for 13: ^{1}H NMR (500 MHz, $CDCl_3$, TMS int) δ 1.00 (s, 3), 1.06 (s, 3), 1.44 (br s, 3), 1.46−1.54 (m, 1), 1.55−1.60 (m, 1), 1.65−1.72 (m, 1), 1.69 (br s, 3), 1.89 (ddd, 1, *J* = 14, 9, 5 Hz), 1.96−2.04 (m, 2), 2.14−2.39 (m, 3), 2.09 (ddq, 1, *J* = 13, 3.5, 0.5 Hz, H-11), 2.41 (br d, 1, *J* = 13 Hz, H-11), 5.12 (br t, 1, *J* = 7.5 Hz, H-5); ^{13}C NMR (125 MHz, $CDCl_3$, TMS int) δ 19.0 (q), 23.2 (q), 23.9 (q), 25.8 (t), 27.5 (t), 29.5 (q), 31.0 (t), 33.5 (t), 33.8 (s), 41.9 (t), 52.3 (d), 123.5 (d), 125.7 (s), 132.7 (s), 136.5 (s); MS *m/z* 204 (17, M^+), 148 (100); HRMS *m/z* (M^+) calcd 204.1878, obsd 204.1878.

Data for 14: ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.89 (s, 3), 0.92 (s, 3), 1.33−1.41 (m, 2), 1.44−1.56 (m, 4), 1.64−1.69 (m, 1), 1.68 (d, 3, *J* = 1.5 Hz), 1.76 (d, 3, *J* = 1.5 Hz), 1.76−1.82 (m, 1), 2.06 (m, 2), 5.28 (dt, 1, *J* = 1.5, 4 Hz), 5.68 (m, 1); ^{13}C NMR (50 MHz, $CDCl_3$, $CDCl_3$ int) δ 19.26 (q), 20.20 (t), 21.28 (q), 22.55 (t), 24.31 (q), 26.09 (q), 30.54 (t), 36.02 (t), 36.89 (t), 42.41 (s), 47.24 (s), 123.72 (d), 125.53 (d), 133.31 (s), 141.94 (s).

Data for 15: IR (CCl_4) (C−H) 2950, 2920, 2860 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.99 (s, 3), 1.01 (s, 3), 1.09 (s, 3), 1.44−1.56 (m, 4, H-3, H-11), 1.53 (m, 3, H-12), 1.71 (q, 1, *J* = 10 Hz, H-4), 1.85 (dt, 1, *J* = 5.5, 10.5 Hz, H-9), 1.98−2.07 (m, 2, H-8), 2.14 (dddd, 1, *J* = 10.5, 8.5, 8.5, 2.5 Hz, H-4), 2.46 (dt, 1, *J* = 8.5, 10 Hz, H-5), 2.50 (br t, 1, *J* = 10.5 Hz, H-1), 5.17 (m, 1, H-7); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int) δ 22.99 (q), 24.09 (q), 24.77 (t), 26.17 (q), 30.16 (q), 30.32 (t), 30.68 (t), 33.71 (s), 34.34 (t), 40.59 (d), 42.39 (s), 43.73 (d), 51.19 (d), 120.66 (d), 136.67 (s); MS *m/z* 204 (4, M^+), 44 (100); HRMS *m/z* (M^+) calcd 204.1878, obsd 204.1878.

Data for 16: IR (neat) (C=C) 3070, 1630 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, TMS int) δ 0.98 (s, 3), 0.99 (s, 3), 1.14 (dt, 1, *J* = 3, 12.5 Hz, H-6), 1.17 (s, 3), 1.34 (t, 1, *J* = 10 Hz, H-3), 1.42 (ddd, 1, *J* = 10, 8, 0.8 Hz, H-3), 1.52−1.62 (m, 4, H-11, H-6, H-7), 1.65 (m, 1, H-5), 1.91 (dddd, 1, *J* = 12, 9.5, 7.5, 7.5 Hz, H-10), 2.12 (dddd, 1, *J* = 12, 9, 9, 6.5 Hz, H-10), 2.20 (dt, 1, *J* = 8, 10 Hz, H-2), 2.46 (m, 1, H-7), 2.58 (m, 1, H-9), 4.70 (dt, 1, *J* = 2, 1.5 Hz, H-12), 4.83 (t, 1, *J* = 2 Hz, H-12); ^{13}C NMR (50 MHz, $CDCl_3$, $CDCl_3$ int) δ 19.2 (t, C-10), 22.3 (q), 24.2 (q), 29.4 (t, C-11), 30.2 (q), 30.5 (t, C-6), 33.9 (s), 34.0 (t, C-3), 36.7 (t, C-7), 40.4 (s), 42.9 (d, C-2), 47.8 (d, C-5), 51.4 (d, C-9), 109.8 (t, C-12), 154.1 (s, C-8); MS *m/z* 204 (2, M^+), 93 (100); HRMS *m/z* (M^+) calcd 204.1878, obsd 204.1878.

Data for 17: IR (neat) (C−H) 2940, 2920, 2860 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.98 (s, 3), 0.99 (s, 3), 1.13 (ddd, 1, J = 12.5, 7.5, 3 Hz, H-8), 1.14 (s, 3), 1.32 (t, 1, J = 10 Hz, H-11), 1.40 (dd, 1, J = 10, 7.5 Hz, H-11), 1.38−1.44 (m, 1, H-8), 1.48 (ddd, 3, J = 2, 1, 1 Hz, H-12), 1.51 (dd, 1, J = 10, 3 Hz, H-3), 1.53−1.60 (m, 1, H-3), 1.65 (dt, 1, J = 2.5, 11 Hz, H-9), 1.87 (ddd, 1, J = 15, 5, 3 Hz, H-7), 1.99 (dt, 1, J = 7.5, 11 Hz, H-1), 2.06 (br t, 1, J = 15 Hz, H-7), 2.35 (m, 1, H-4), 2.57 (m, 1, H-4); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int) δ 18.09 (q), 21.03 (q), 21.41 (q), 24.89 (t), 27.67 (t), 30.00 (q), 30.21 (t), 34.22 (t), 35.23 (t), 36.03 (s), 47.43 (d), 47.83 (s), 49.79 (d), 125.93 (s), 143.01 (s); MS m/z 204 (46, M^+), 133 (100); HRMS m/z (M^+) calcd 204.1878, obsd 204.1878.

Data for 18: IR (neat) (O−H_{ass}) 3640−3200 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.87 (s, 3), 1.03 (br s, 3), 1.10−1.16 (m, 1), 1.19 (s, 3), 1.26 (br s, 3), 1.30 (br s, 1), 1.37−1.60 (m, 6), 1.68 (br d, 1, J = 14 Hz), 1.70−1.88 (m, 3), 1.93 (m, 1), 1.98 (d, 1, J = 14 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int) δ 21.88 (t), 24.66 (q), 26.30 (t), 28.59 (q), 29.12 (q), 33.64 (t), 34.36 (q), 34.49 (t), 34.58 (t), 35.47 (s), 38.34 (s), 45.40 (s), 48.18 (t), 57.18 (d), 83.09 (s); MS m/z 222 (8, M^+), 207 (100); HRMS m/z (M^+) calcd 222.1983, obsd 222.1983.

Data for 20: ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int) δ 19.08 (t), 25.63 (q), 30.10 (s), 31.64 (q), 32.01 (t), 32.96 (q), 33.43 (t), 34.39 (t), 37.30 (s), 40.59 (t), 43.17 (t), 44.60 (s), 47.81 (t), 50.85 (d), 81.14 (d).

B. Early Stage. Directed Isolation of (1*R*,2*S*,5*R*,9*S*)-1,4,4-Trimethyl-8-methylenetricyclo[7.2.0.0^{2,5}]undecane (16) and (1*S*,2*R*,5*Z*,9*R*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{2,5}]undec-5-ene (17). To a solution of (−)-β-caryophyllene (**1**) (5.00 g, 24.5 mmol) in ether (25 mL) was added at 0 °C with stirring a solution of 96% sulfuric acid (7.51 g, 73.5 mmol) in ether (25 mL). The mixture was allowed to warm to 15 °C, and after 30 min worked up as described above. The hydrocarbons (2.55 g) were chromatographed on silica gel (column 60 × 5 cm) in pentane, and only fraction **A** (572 mg), containing 7% **4**, 29% **16**, and 64% **17**, was separated further by chromatography on silica gel impregnated with 10% silver nitrate (column 36 × 2.5 cm) in pentane/ether, 60:1, yielding 123 mg (2%) of pure **16** and 229 mg (5%) pure of **17**. The ^1H NMR spectra were identical with those of authentic samples.

C. Late Stage. (1*R*,2*S*,5*R*,8*R*)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]-dodecan-1-ol (β-Caryolanol) (5), (2a*S*,4a*R*,8*R*,8a*S*)-2,2,4a,8-Tetramethyldecahydrocyclobut[*c*]inden-8-ol (18), (1*S*,2*S*,5*R*,8*S*)-1,4,4-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-8-ol (Isocaryolanol) (19), (1*S*,2*S*,5*S*,8*S*)-4,4,8-Trimethyltricyclo[6.3.1.0^{1,5}]dodecan-2-ol (20), (1*R*,6*S*,7*S*)-2,6,8,8-Tetramethyltricyclo[5.2.2.0^{1,6}]undec-2-ene (α-Neoclovene) (3), (1*S*,5*S*,8*S*)-4,4,8-Trimethyltricyclo[6.3.1.0^{1,5}]dodec-2-ene (Clovene) (4), and (1*R*,2*S*,7*S*,9*R*)-2,6,10,10-Tetramethyltricyclo-[7.2.0.0^{2,7}]undec-5-ene (8). To a solution of (−)-β-caryophyllene (**1**) (10.00 g, 49.0 mmol) in ether (50 mL) was added at 0 °C with stirring a solution of 96% sulfuric acid (15.02 g, 147.0 mmol) in ether (50 mL). The mixture was allowed to warm to room temperature, and after 3 days a saturated solution of sodium bicarbonate (300 mL) was added with cooling. The mixture was extracted with ether (3 × 100 mL), the combined organic layers were dried ($MgSO_4$), and the solvent was evaporated (bath temperature 20 °C, 20 Torr) to yield 7.48 g of a colorless solid. According to capillary GC [30 m × 0.32 mm i.d. deactivated fused-silica capillary column coated with 0.25 μm DB FFAP; 15 min 90 °C, 20 °C/min, to 220 °C; 10 min 220 °C, 0.6 bar of H_2; retention times (min): 5.92 (**4**), 6.06 (**8**), 11.26 (**3**), 20.66 (**5**), 20.94 (**19**), 21.24 (**18**), 21.84 (**20**)], the solid contained the hydrocarbons **3** (18%), **4** (3%), and **8** (9%), and the alcohols **5** (38%), **18** (3%), **19** (4%), and **20** (2%). Chromatography on silica gel (column 80 × 4.5 cm) in pentane yielded 1.39 g of a mixture of 13% **4**, 33% **8**, and 48% **3**. Chromatography of this mixture on silica gel impregnated with 10% silver nitrate (column 55 × 2.5 cm) in pentane gave 105 mg of pure **8**, 169 mg of pure **3**, and 219 mg of a 1.2:1 mixture of **3** and **4**. The ^1H NMR data of **3**,[7,13] and **8**[15] were consistent with literature data.

(1*R*,4*Z*,8*R*,9*S*)-4,8,11,11-Tetramethylbicyclo[7.2.0]undec-4-en-8-ol (22). To a stirred solution of **21**[19] (404 mg, 1.96 mmol) in anhydrous ether (4 mL) under nitrogen at 0 °C was added a 1.60 M solution of methyllithium in ether (5.0 mL, 8.00 mmol). Stirring was continued for 45 min at 0 °C until the mixture was hydrolyzed with saturated ammonium chloride (4.5 mL) and extracted with ether (2 × 5 mL). The combined organic layers were dried (molecular sieves 3 Å), the solvent was evaporated (bath temperature 25 °C, 20 Torr), and the residue was chromatographed on silica gel in pentane/ether, 5:1 [column 30 × 3 cm, R_f = 0.36 (**21**), 0.28 (**22**)], yielding 371 mg (85%) of pure **22** as a colorless oil: IR (CCl_4) (O−H) 3610, (O−H_{ass}) 3540 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, TMS int) δ 0.95 (s, 3), 0.97 (s, 3), 0.98 (s, 3), 1.49−1.56 (m, 3), 1.58 (dd, 1, J = 5, 4 Hz), 1.64 (t, 1, J = 10 Hz), 1.68 (br d, 3, J = 1.5 Hz), 1.79 (dt, 1, J = 4, 9 Hz), 1.85 (br s, 1), 1.87 (ddd, 1, J = 14, 11, 4 Hz), 2.02 (q, 1, J = 9 Hz), 2.08−2.25 (m, 4), 5.29 (t, 1, J = 8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int) δ 23.09 (q), 23.23 (t), 25.63 (q), 26.03 (t), 27.76 (q), 29.63 (q), 31.63 (t), 32.77 (s), 35.11 (t), 41.89 (t), 45.09 (d), 45.88 (d), 72.86 (s), 125.10 (d), 135.87 (s); MS m/z 222 (<1, M^+), 108 (100); HRMS m/z (M^+) calcd 222.1983, obsd 222.1983.

Elimination of (1*R*,4*Z*,8*R*,9*S*)-4,8,11,11-Tetramethylbicyclo[7.2.0]-undec-4-en-8-ol (22). (1*R*,4*Z*,9*S*)-4,11,11-Trimethyl-8-methylene-bicyclo[7.2.0]undec-4-ene (Isocaryophyllene) (9), (1*Z*,5*Z*,9*S*)-2,6,10,-10-Tetramethylbicyclo[7.2.0]undeca-1,5-diene (13), and (1*S*,2*Z*,5*Z*,9*R*)-2,6,10,10-Tetramethylbicyclo[7.2.0]undeca-2,5-diene (23). To a stirred solution of **22** (73 mg, 0.33 mmol) in anhydrous pyridine (2.3 mL) under nitrogen at 0 °C was added over a period of 15 min a solution of thionyl chloride (150 mg, 1.26 mmol) in anhydrous pyridine (0.45 mL). The mixture was stirred for another 45 min until it was hydrolyzed with water (2.2 mL) and extracted with pentane (3 × 3 mL). The combined organic layers were dried (molecular sieves, 3 Å), and the solvent was evaporated (bath temperature 25 °C, 20 Torr). The residue was dissolved in pentane and filtrated through silica gel (column 5 × 1 cm), yielding 55 mg of a mixture of **9** (46%), **13** (23%), and **23** (31%) according to capillary GC [30 m × 0.32 mm i.d. deactivated fused-silica capillary column coated with 0.25 μm DB FFAP, 90 °C, 0.6 bar of H_2, retention times (min): 8.00 (**13**), 8.59 (**9**), 13.29 (**23**)]. Preparative GLPC [3 m × 1/4 in. all glass system, 15% FFAP on chromosorb W AW/DMCS, 60−80 mesh, 160 °C; relative retention times: 1.00 (**13**), 1.14 (**9**), 1.53 (**23**)] gave 9 mg (13%) of **13**, 8 mg (12%) of a mixture of **13** and **9**, 4 mg (6%) of **9**, and 19 mg (28%) of **23** as colorless liquids. **9** and **13** were identified by their ^1H NMR spectra.

Data for 23: ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.92 (s, 3), 0.94 (s, 3), 1.31 (dddd, 1, J = 13, 11, 11, 2.5 Hz, H-8), 1.51 (d, 1, J = 10 Hz, H-11), 1.55 (q, 3, J = 1 Hz, H-13), 1.59 (ddt, 1, J = 13, 7, 2.5 Hz, H-8), 1.66 (t, 3, J = 1.5 Hz, H-12), 1.85 (ddd, 1, J = 10, 9, 1 Hz, H-11), 1.98 (ddd, 1, J = 13, 7, 2.5 Hz, H-7), 2.01 (ddd, 1, J = 11, 9, 2.5 Hz, H-9), 2.27−2.36 (m, 2, H-4, H-7), 2.50 (br q, 1, J = 11 Hz, H-1), 2.93 (m, 1, H-4), 5.02 (m, 1, H-5), 5.38 (m, 1, H-3); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int) 22.64 (q), 23.06 (q), 23.99 (q), 26.03 (t), 28.51 (t), 30.28 (q), 31.39 (t), 33.17 (s), 39.37 (t), 40.84 (d), 49.63 (d), 121.02 (d), 122.54 (d), 132.47 (s), 141.54 (s); MS m/z 204 (22, M^+), 41 (100); HRMS m/z (M^+) calcd 204.1878, obsd 204.1878.

Elimination of (2a*S*,4a*R*,8*R*,8a*S*)-2,2,4a,8-Tetramethyldecahydrocyclobut[*c*]inden-8-ol (18). (1*S*,6*S*,7*S*)-2,6,8,8-Tetramethyltricyclo-[5.2.2.0^{1,6}]undec-2-ene (α-Neoclovene) (3), (1*S*,6*S*,9*S*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{1,6}]undec-2-ene (α-Panasinsene) (7), and (1*S*,6*R*,9*S*)-6,10,10-Trimethyl-2-methylenetricyclo[7.2.0.0^{1,6}]-undecane (β-Panasinsene) (24). To a stirred solution of **18** (16 mg, 0.07 mmol) in anhydrous pyridine (0.5 mL) under nitrogen was added at room temperature thionyl chloride (26 mg, 0.22 mmol). After 10 min the reaction was complete according to TLC [pentane/ether, 98:2; R_f = 0.68, 0.63, 0.06 (**18**)]. The mixture was hydrolyzed with water (0.2 mL) and extracted with pentane (3 × 1 mL). The combined organic layers were washed with saturated ammonium chloride (1 mL) and dried (molecular sieves, 3 Å), and the solvent was evaporated (bath temperature 20 °C, 20 Torr). According to capillary GC [30 m × 0.32 mm i.d. deactivated fused-silica capillary column coated with 0.25 μm DB FFAP, 90 °C, 0.6 bar of H_2, retention times (min): 6.5 (**24**), 11.0 (**3**), 11.2 (**7**), 13.9 (unidentified)], the residue consisted of 25% **3**, 37% **7**, 28% **24**, and 10% unidentified compound. **3**, **7**, and **24** were identified by comparing the ^1H and ^{13}C NMR data of the product mixture with the present experimental data for pure samples of **3** and **7** originating from the rearrangement of **1**, and with literature data for **24**.[13b,20]

(1*S*,2*R*,5*R*,6*S*,9*R*)-2,10,10-Trimethyltricyclo[7.2.0.0^{2,5}]undecane-6-spiro-1′-oxacyclopropane (27) and (1*S*,2*R*,5*R*,6*R*,9*R*)-2,10,10-Trimethyltricyclo[7.2.0.0^{2,5}]undecane-6-spiro-1′-oxacyclopropane (28).

To a rapidly stirred mixture of **16** (400 mg, 1.96 mmol) in dichloromethane (20 mL) and 0.5 M aqueous potassium bicarbonate (5 mL) was added at room temperature 75% *m*-chloroperbenzoic acid (540 mg, 2.36 mmol). According to TLC [pentane/ether, 95:5; R_f = 0.72 (**16**), 0.46 (**28**), 0.30 (**27**)], the reaction was complete after 1 h. The layers were separated and the organic layer was washed with a 1 M solution of potassium hydroxide (3 × 15 mL) and water (2 × 15 mL) and dried ($MgSO_4$), and the solvent was evaporated (bath temperature 20 °C, 20 Torr). Chromatography of the residue (400 mg) on silica gel (column 60 × 1.6 cm) in pentane/ether, 95:5, yielded 239 mg (56%) of pure **27** and 45 mg (10%) of pure **28** as colorless liquids.

Data for 27: IR (neat) (OC−H_2) 3040−3000 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.96 (s, 3), 0.98 (s, 3), 1.18 (s, 3), 1.14−1.31 (m, 2), 1.40−1.59 (m, 7), 1.65−1.77 (m, 1), 1.90 (dq, 1, J = 13, 9 Hz), 2.10 (q, 1, J = 9 Hz), 2.26 (dd, 1, J = 9.5, 4 Hz), 2.64 (dd, 1, J = 4, 1 Hz), 2.89 (dd, 1, J = 4, 2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int) δ 14.64 (t), 22.50 (q), 23.84 (q), 26.01 (t), 30.13 (q), 32.76 (t), 33.83 (s), 34.11 (t), 38.49 (t), 38.71 (s), 45.32 (d), 46.74 (d), 49.16 (d), 49.74 (t), 59.51 (s); MS *m/z* 220 (1, M^+), 41 (100); HRMS *m/z* (M^+) calcd 220.1827, obsd 220.1827.

Data for 28: IR (neat) (OC−H_2) 3040−3000 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.97 (s, 3), 1.03 (s, 3), 1.12 (s, 3), 1.27−1.72 (m, 11), 2.30 (dd, 1, J = 9.5, 6.5 Hz), 2.35−2.47 (m, 3); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int) δ 12.91 (t), 22.35 (q), 24.19 (t), 24.24 (q), 29.50 (t), 30.22 (q), 33.75 (t), 33.80 (s), 34.47 (t), 39.93 (s), 42.93 (d), 47.05 (d), 48.78 (d), 52.44 (t), 58.76 (s); MS *m/z* (220 (1, M^+), 41 (100); HRMS *m/z* (M^+) calcd 220.1827, obsd 220.1827.

(1*S*,2*R*,5*R*,6*R*,9*R*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{2,5}]undecan-6-ol (30). To a stirred suspension of $LiAlH_4$ (87 mg, 2.30 mmol) in anhydrous ether (2 mL) under nitrogen was added within 2 min a solution of **27** (255 mg, 1.15 mmol) in anhydrous ether (6 mL). According to TLC [pentane/ether, 5:1; R_f = 0.16 (**30**)], the reaction was complete after 2.5 h. Water (87 μL), 15% aqueous potassium hydroxide (87 μL), and water (261 μL) were added, the liquid was decanted, and the residue was extracted with ether (10 × 2 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated (bath temperature 20 °C, 20 Torr). Chromatography of the residue (237 mg) on silica gel (column 60 × 1.4 cm) in pentane/ether, 5:1, gave 195 mg (77%) of pure **30** as a colorless solid: mp 112−113 °C (lit.[11] mp 111−112 °C); IR (CCl_4) (O−H) 3590, (O−H_{ass}) 3520−3020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.96 (s, 3), 0.97 (s, 3), 1.11 (s, 3), 1.20 (s, 3), 1.27−1.98 (m, 13), 2.29 (ddd, 1, J = 11, 9, 9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int) δ 18.58 (t), 22.46 (t), 22.56 (q), 24.92 (q), 27.13 (q), 30.22 (q), 31.95 (t), 34.20 (s), 34.28 (t), 38.49 (t), 40.59 (d), 41.07 (s), 44.83 (d), 57.60 (d), 75.64 (s); MS *m/z* 222 (1, M^+), 93 (100). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.78. Found: C, 81.03; H, 11.87.

(1*S*,2*R*,5*R*,6*S*,9*R*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{2,5}]undecan-6-ol (31). To a stirred suspension of lithium aluminum hydride (27 mg, 0.72 mmol) in anhydrous ether (1 mL) under nitrogen was added within 2 min a solution of **28** (80 mg, 0.36 mmol) in anhydrous ether (3 mL). According to TLC [pentane/ether, 5:1; R_f = 0.31 (**31**)], the reaction was complete after 2.5 h. Water (27 μL), 15% aqueous potassium hydroxide (27 μL), and water (81 μL) were added, the liquid was decanted, and the residue was extracted with ether (10 × 1 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated (bath temperature 20 °C, 20 Torr). Chromatography of the residue (63 mg) on silica gel (column 15 × 1.5 cm) in pentane/ether, 5:1, gave 40 mg (50%) of pure **31** as a colorless liquid: IR (neat) (O−H_{ass}) 3620−3200 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.95 (s, 3), 0.99 (s, 3), 1.03 (s, 3), 1.08 (s, 3), 1.19−1.69 (m, 9), 1.73 (dd, 1, J = 10, 5 Hz), 1.76−1.89 (m, 2), 2.00 (dddd, 1, J = 12, 9.5, 9.5, 8 Hz), 2.43 (q, 1, J = 9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int) δ 16.19 (t), 22.36 (q), 23.57 (t), 24.78 (q), 30.21 (q), 30.62 (q), 32.33 (t), 33.96 (s), 34.33 (t), 40.61 (t), 40.83 (d), 43.68 (d), 46.64 (s), 55.56 (d), 74.55 (s); MS *m/z* 222 (1, M^+), 93 (100). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.78. Found: C, 80.89; H, 12.33.

3′,5′-Dinitrobenzoic Acid (1*S*,2*R*,5*R*,6*R*,9*R*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{2,5}]undec-6-yl Ester (32). To a stirred solution of **30** (50 mg, 0.23 mmol) in 1.5 mL of pyridine was added at room temperature 3,5-dinitrobenzoyl chloride (104 mg, 0.45 mmol), and the mixture was heated to 55 °C. According to TLC [CH_2Cl_2, R_f = 0.84 (**16**), 0.75 (**32**), 0.20 (**30**)], the reaction was complete after 6 h. The mixture was hydrolyzed with water (4 mL) and extracted with ether (1 × 3 mL, 2 × 2 mL). The combined organic layers were washed with 1 N H_2SO_4 (2 mL) and water (2 × 2 mL) and dried (molecular sieves, 3 Å), and the solvent was evaporated (bath temperature 20 °C, 20 Torr). Chromatography of the residue (130 mg) on silica gel (column 18 × 1.6 cm) in pentane/ether, 15:1 [R_f = 0.34 (**32**)], gave 47 mg (49%) of pure **32** as a pale yellow oil: IR (CCl_4) (Ar−H) 3090, (C=O) 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.89 (s, 3), 0.97 (s, 3), 1.20 (s, 3), 1.32−1.65 (m, 6), 1.51 (s, 3), 1.72−1.95 (m, 3), 2.13 (ddd, 1, J = 14.5, 11, 6 Hz), 2.24 (ddd, 1, J = 14.5, 5, 3 Hz), 2.40 (ddd, 1, J = 11, 10, 8.5 Hz), 2.61 (t, 1, J = 10 Hz), 9.11 (d, 2, J = 2 Hz), 9.19 (t, 1, J = 2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int) δ 19.41 (t), 21.79 (t), 22.78 (q), 24.61 (q), 25.05 (q), 30.42 (q), 30.55 (t), 30.69 (t), 33.47 (t), 34.11 (s), 37.17 (d), 42.76 (s), 42.85 (d), 54.60 (d), 91.76 (s), 121.93 (d), 129.18 (d), 135.71 (s), 148.69 (s), 161.16 (s); MS *m/z* 417 (<0.1, M^+), 93 (100).

3′,5′-Dinitrobenzoic Acid (1*S*,2*R*,5*R*,6*S*,9*R*)-2,6,10,10-Tetramethyltricyclo[7.2.0.0^{2,5}]undec-6-yl Ester (33). To a stirred solution of **31** (26 mg, 0.12 mmol) in pyridine (0.5 mL) was added at room temperature 3,5-dinitrobenzoyl chloride (55 mg, 0.24 mmol), and the mixture was heated to 55 °C. According to TLC [pentane/ether, 15:1; R_f = 0.32 (**33**)], the reaction was complete after 25 h. The mixture was hydrolyzed with water (1.5 mL) and extracted with ether (1 × 1.5 mL, 2 × 1 mL). The combined organic layers were washed with 1 N H_2SO_4 (1 mL) and water (2 × 1 mL) and dried (molecular sieves, 3 Å), and the solvent was evaporated (bath temperature 20 °C, 20 Torr). TLC chromatography of the residue (45 mg) in pentane/ether, 15:1, gave 32 mg (67%) of pure **33** as a colorless solid: mp 136 °C; IR (CCl_4) (Ar−H) 3090, (C=O) 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int) δ 0.74 (s, 3), 0.93 (s, 3), 0.96−1.09 (m, 1), 1.21 (s, 3), 1.33−1.54 (m, 5), 1.51 (s, 3), 1.69−1.79 (m, 1), 1.86−2.09 (m, 3), 2.16−2.31 (m, 1), 2.39 (dd, 1, J = 10, 9 Hz), 2.80−2.91 (m, 1), 9.23 (s, 3); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int) δ 16.69 (t), 22.26 (q), 24.33 (t), 24.50 (q), 24.95 (q), 29.97 (q), 32.63 (t), 34.05 (t), 34.23 (t), 37.58 (s), 41.07 (s), 44.19 (d), 46.92 (d), 56.91 (d), 90.97 (s), 122.03 (d), 129.23 (d), 135.62 (s), 148.78 (s), 161.19 (s); MS *m/z* 417 (<0.1, M^+), 93 (100). Anal. Calcd for $C_{22}H_{28}N_2O_6$: C, 63.45; H, 6.78; N, 6.73. Found: C, 63.50; H, 6.75; N, 6.61.

X-ray Crystallographic Analysis. 33 (molecular formula $C_{22}H_{28}N_2O_6$, M = 416.5) formed rhombic crystals from acetone, space group $P2_12_12_1$, a = 828.3(2) pm, b = 1294.7(3) pm, c = 1992.6(4) pm, α = β = γ = 90°, V = 2.1369(8) nm^3, Z = 4, D_{calc} = 1.295 g cm^{-3}. A total of 2958 reflections with 3.56° < θ < 25.00° were measured on a Stoe four-circle diffractometer using graphite-monochromated radiation Mo Kα; of these 2710 independent reflections were used for the structure determination and refinement. The structure was solved by direct methods. The anisotropic refinement against F^2 with geometrically positioned H atoms (riding model: d(C−H) = 96 pm, ∠(HCH) = 109.5°) converged at R_1 = 0.0637 (wR_2 = 0.1418). All calculations were performed with the program SHELXL-93.[41]

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Supporting Information Available: ^1H NMR spectra of **3**, **4**, **6**−**9**, **13**−**18**, **22**, **23**, **27**, **28**, and **30**−**33** and tables of X-ray crystal data, atomic coordinates, bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates, and isotropic displacement parameters (25 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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