Tetrahedron Vol. 49, No. 20, pp. 4183-4192, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00
Pergamon Press Ltd

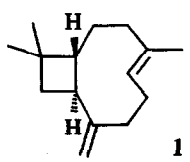
New Members of the Caryophyllene Family via Biomimetic π-Cyclizations and Consecutive Transformations.

Carsten E. Sowa, Ulrike Eggert and H. Martin R. Hoffmann*
Department of Organic Chemistry, University of Hannover,
Schneiderberg 1 B, D-3000 Hannover, Germany

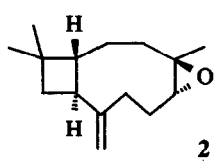
(*Received in Germany* 15 *October* 1992)

A series of derivatives from caryophyllene oxide have been prepared in enantiomerically pure form, including bicyclic, tricyclic and tetracyclic sesquiterpenes and sesquiterpenoids. A key intermediate is the unsaturated, chiral (pro 1S,8Z)-bridgehead carbocation **5** and its monobrominated derivative **5a**.

Caryophyllene (**1**) and its oxide **2** are naturally occurring sesquiterpenes which have fascinated organic chemists for a long time. Owing to the presence of the strained, *trans*-fused four-membered ring, the conformationally mobile nine-membered ring and the highly reactive *trans* double bond, **1** and its derivatives enter into a wide variety of unusual transformations and deep-seated rearrangements.[1,2] Caryophyllene derivatives containing osmophoric groups are also important in perfumery. For example, allylic alcohol **3** described below has a pleasant ambergris note.[3] The 5-methyl ketone derivative,[4] which has been prepared from caryophyllene and acetyl tetrafluoroborate by an ene reaction,[5] is commercially available under the name of Lignofix®.[3] We here report new facets of caryophyllene chemistry, resulting from the synthesis of the tricyclic [6.3.2.$0^{2,5}$] skeleton from caryophyllene oxide **2** in three stages.

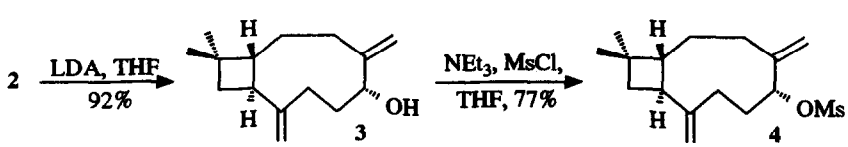


1



2

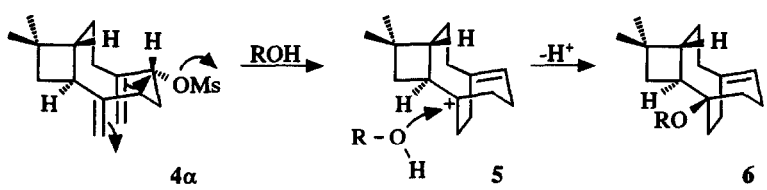
Results. Base-induced (LDA) opening of caryophyllene oxide **2** in refluxing THF gave allylic alcohol **3** in a clean regio- and stereoselective reaction in 92% isolated yield. A low temperature mesylation afforded sensitive mesylate **4** (77%, 12.7 g), which was isolated and crystallized from Et_2O/PE (2:1) at -20 °C.[6,7]



Scheme 1.

Solvolysis of allylic mesylate **4** was carried out in solvents with high and low ionizing power (Table 1). In this fashion, alcohol **6a** and also **6b-d** were prepared. Triphyllene (phyllon, Gr. leaf) skeleton **6** contains a bridgehead olefin and a second bridgehead carbon, which is oxyfunctionalized. Triphyllenol **6a** has independently been detected by a Japanese group[8] in oil of hops and oil of cloves, used for flavoring beer.

Table 1. Solvolytic Tricyclization of Allylic Mesylate **4α**.

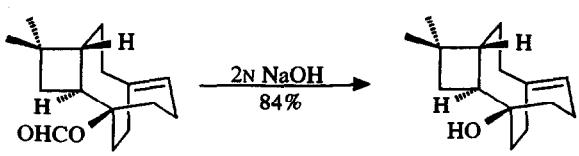


4α **5** **6**

	OR
6a	OH
6b	OCHO
6c	OAc
6d	OMe

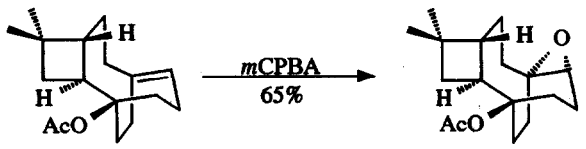
Protic Solvent R-OH	**Product**	**Yield [%]**
THF/H_2O (1:5), r.t.	**6a**	56
THF/H_2O (10:1), r.t.	**6a**	53
pyridine/HCOOH (1:2), r.t.	**6b**	53
pyridine/HCOOH (1:1), 0 °C	**6b**	44
pyridine/HCOOH (2:1), r.t.	**6b**	30
pyridine/HOAc (1:2), r.t.	**6c**	43
pyridine/HOAc (1:1), r.t.	**6c**	42
pyridine/HOAc (1:2), 0 °C	**6c**	40
MeOH	**6d**	39
CH_2Cl_2/MeOH (10:1), r.t.	**6d**	14
H_2O, NaOAc (saturated)	**6a, 6c**	15 (of **6a**) 0 (of **6c**)
THF/$PhCH_2NH_2$	---	0
CH_3CN/NaN_3	---	0
HCOOH	---	0

Formolysis and acetolysis of mesylate **4** gave the esters **6b** and **6c**, which were accompanied by one unidentified formate and acetate, respectively, and difficult to purify. However, a simple hydrolysis in the case of the formate (**6b** → **6a**) and epoxidation in the case of acetate (**6c** → **7**) allowed us to isolate pure tricyclic alcohol **6a** and pure tetracyclic acetate **7**.



6b **6a**

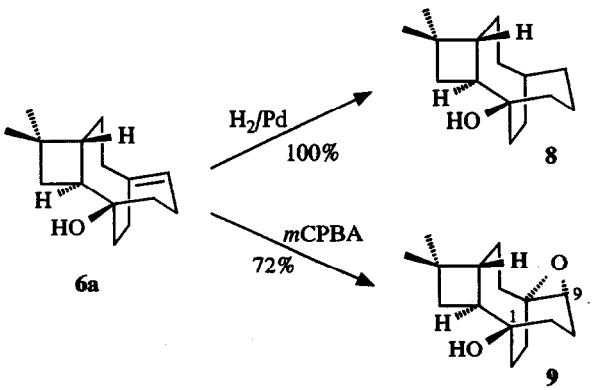
Scheme 2.



6c **7**

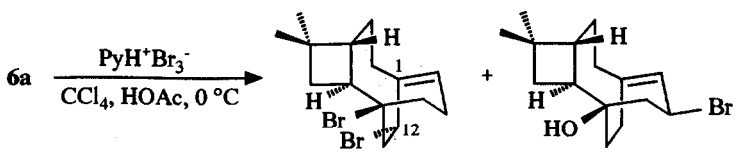
Scheme 3.

Triphyllenol **6a** was hydrogenated quantitatively to triphyllanol **8** and epoxidized to tetracyclic **9** in 72% yield.



Scheme 4.

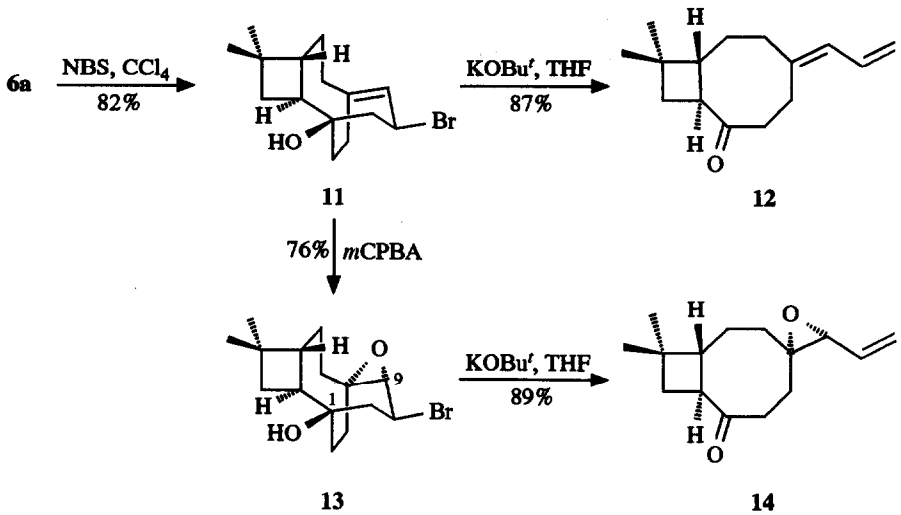
Bromination of tricyclic alcohol **6a** with $PyHBr_3$ left the double bond intact, giving dibromide **10** (major) and bromo-triphyllenol **11** (minor). Attempts to brominate the double bond of **6a** with other brominating agents such as elementary bromine were not successful.



10 (79%) **11** (15%)

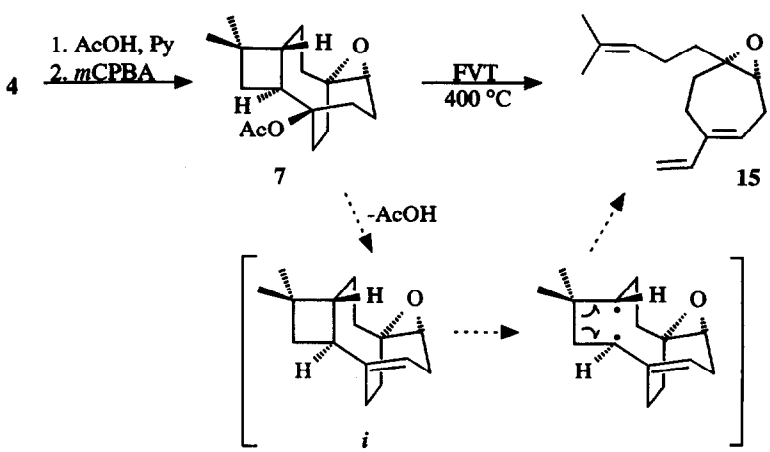
Scheme 5.

Bromo-triphyllenol **11** (15%) was accessible in high yield by treatment of triphyllenol **6a** with *N*-bromosuccinimide (NBS). Hydroxybromide **11** entered into facile, base-induced fragmentation, giving bicyclo-[6.2.0]decanone derivative **12**. Bromoalkenol **11** was also epoxidized to **13**, which was again submitted to base-induced fragmentation to yield diastereomerically pure spiro oxirane **14** (Scheme 6). Here, as in the sequel, diastereomeric purity also amounts to enantiomeric purity because of the *trans*-fused four-membered ring and its two chiral centres, which do not change their configuration.



Scheme 6.

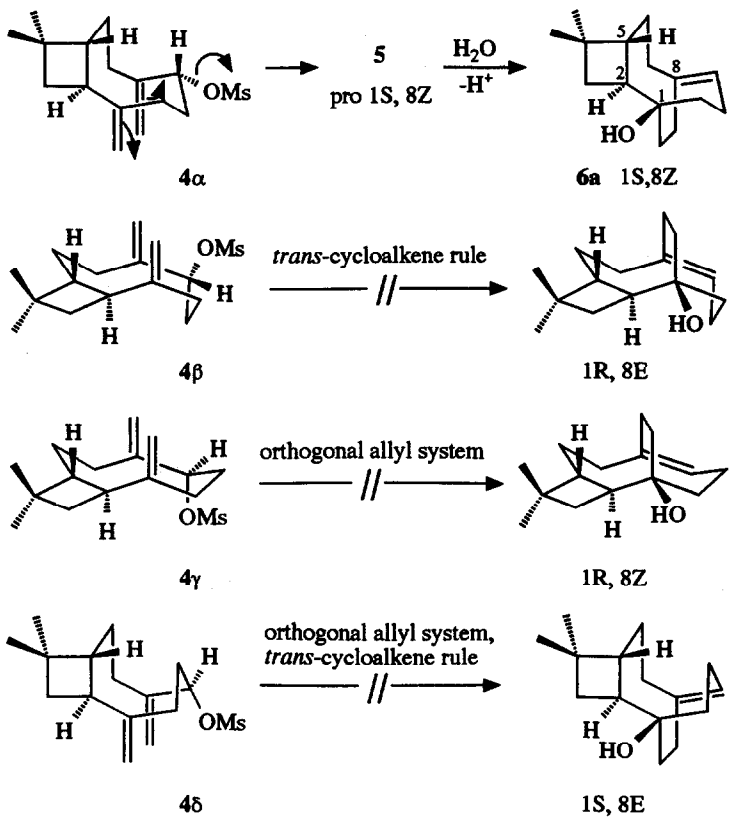
The easy fragmentation reactions (**11** → **12**, **13** → **14**) accord with the quasi equatorial position of the bromine leaving group, as formulated for **11** and **13** (Scheme 6). Independently, bicyclic dienone **12** was epoxidized regioselectively, but not stereoselectively to **14** and the diastereomeric β-epoxide *dia*-**14** (1:1). Epoxy acetate **7** was prepared conveniently in 2 steps from allylic mesylate (**4** → **6c** → **7**; 28% yield) rather than in 3 steps via triphyllenol **6a** (**4** → **6a** → **6c** → **7**; 33% yield).



Scheme 7.

Flash vapor thermolysis (FVT) of tetracyclic acetate **7** afforded cycloheptene oxide **15** (45%). Bridgehead olefin *i* is highly strained (MMX) and postulated as an intermediate, suffering stepwise [2+2] cycloreversion *en route* to **15** (Scheme 7).

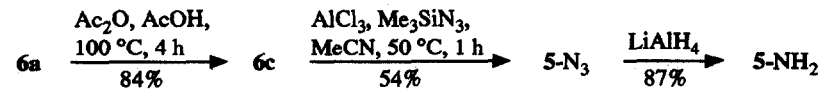
Discussion. A priori, four conformers 4α-δ of allylic mesylate **4** can be envisaged. However, only conformation 4α allows departure of mesylate in concert with transannular carbon-carbon bond making. All other conformers are unfavorable for cyclization, because either the *trans*-cycloalkene rule[9] is violated, giving a highly strained olefin, or formation of a planar allyl system is difficult. Thus, only 1S,8Z triphyllenol **6a** is expected on theoretical grounds (Scheme 8). Structural assignment and absolute stereochemistry of **6a** were corroborated by X-ray diffraction analysis.[6] Thus, the solvolytic cyclization is stereocontrolled, giving enantiomerically pure **6a**.[6-8]



Scheme 8.

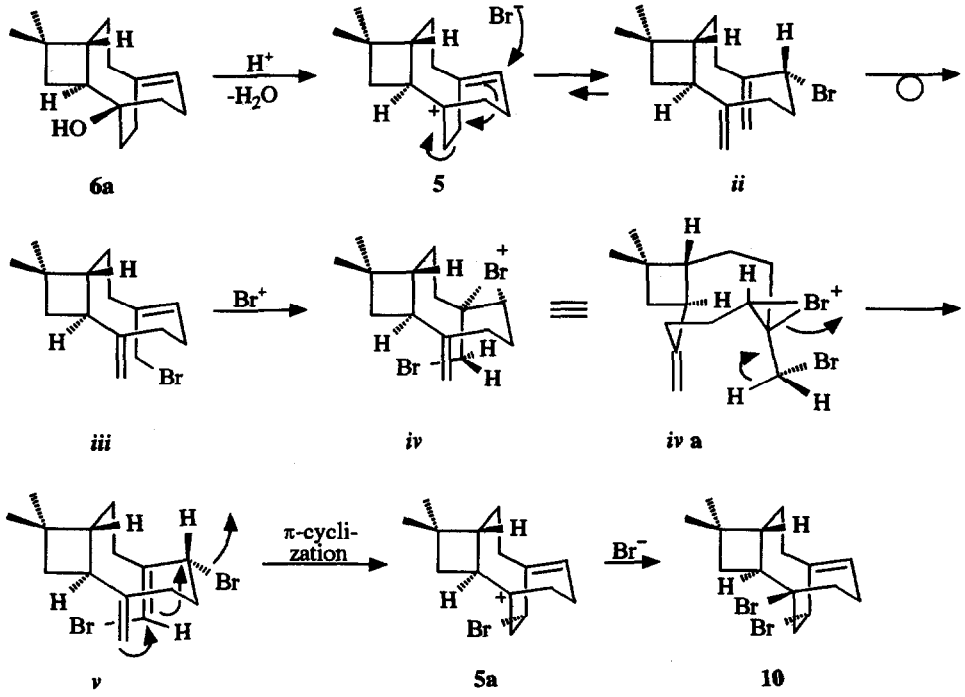
The yield of tricycle **6** correlates reasonably well with solvent polarity (Table 1). An S_N1-like heterolysis with *trans*annular participation of the double bond is likely. Optimum yields of **6a-d** are obtained at temperatures around 25 °C.

Unsaturated tricyclic bridgehead cation **5** is the key reactive intermediate in these transformations. This chiral, nonracemic (pro 1S,8Z)-carbocation is not only generated in the solvolysis of allylic mesylate (Table 1), but also in the conversion of triphyllenol **6a** into the acetate **6c** (which requires heating in Ac_2O/AcOH to 100 °C and entails C-OH bond breaking) and, again, in the Lewis acid mediated conversion of the acetate **6c** into bridgehead azide **5**-N_3.[7]



Scheme 9.

Furthermore, we propose that bromination of triphyllenol **6a** to dibromide **10** might proceed via unsaturated bridgehead tricyclic cation **5** and its monobromo derivative **5a** (Scheme 10).



Scheme 10.

Fragmentation of cation **5** generates bicyclic allylic bromide *ii* (practically the microscopic reverse of the tricyclization of mesylate 4α → **5**, Scheme 8). Subsequent allylic rearrangement affords the thermodynamically more stable isomer (*ii* → *iii*). The required second bromination involves bromine-bridged cation *iv*, which suffers proton loss to furnish vinylic bromide *v*. In the preferred conformation (MMX) of the bromonium cation transannular and gauche interactions are minimized (cf. *iv*a), resulting in E-selective formation of *v*. Finally, bromoallylic bromide *v* is assumed to cyclize to **5a**, analogous to the tricyclization of **4** → **5** (Table 1). Termination occurs by nucleophilic capture of cation **5a** to dibromide **10**.

In view of the recent isolation of triphyllenol **6a** from essential oils[8] the tricyclizations described in this paper are undoubtedly biomimetic. Thus, one may speculate that the "violation of the Bredt rule" in forming tricycles **6a-d** is much older than the Bredt rule itself. To our knowledge, the direct preparation of **6a-d** from **4** is also the first stereoselective π-cyclization,[10] which is terminated by nucleophilic capture of an unsatura-

ted bridgehead cation and simultaneous formation of a bridgehead olefin.

EXPERIMENTAL

General Remarks. Melting points are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer FT 1710. Nuclear magnetic resonance (NMR) spectra were recorded with a Bruker WP 200 SY or a SMX 560. APT (attached proton test): Spin echo based selection of multiplicities of ^{13}C. Quaternary C and CH_2 carbon atoms give positive signals (↑), while CH and CH_3 give negative signals (↓). Mass spectral data (MS) were measured on a Finnigan MAT 312 (70 eV).

Allylic alcohol **3** and its mesylate **4** were prepared as described previously.[6,7]

(1R,2R,5S)-4,4-Dimethyltricyclo[6.3.2.0^{2,5}]tridec-8(9)-en-1-ol (**6a**). To a solution of mesylate **4** (12.72 g, 42.66 mmol) in THF (20 mL) and H_2O (100 mL) was added K_2CO_3 (2 g) and the mixture was stirred for 72 h at room temperature. THF was evaporated and the aqueous phase was extracted with MTBE (3 x 100 mL). The organic layer was washed with sat. aq. NH_4Cl solution, brine and water. After drying ($MgSO_4$) and removal of the solvent the crude product was recrystallized from PE/E (10:1) to afford **6a**, 5.4 g (56%), colorless needles. Spectroscopic data correspond with those of the literature.[6-8]

(1R,2R,5S)-4,4-Dimethyltricyclo[6.3.2.0^{2,5}]tridec-8(9)-en-1-yl formate (**6b**). To a solution of mesylate **4** (800 mg, 2.7 mmol) in pyridine (0.49 g, 0.5 mL, 6.2 mmol) was added conc. HCO_2H (0.57 g, 0.48 mL, 12.4 mmol) and the resulting mixture was stirred for 16 h at room temperature. Then Et_2O was added and the organic layer was washed with sat. aq. $NaHCO_3$ solution and water. The solvent was removed and the crude product was purified by chromatography (PE/E, 1:1) to yield a mixture of two formates, 490 mg (74%) (GC-analysis: 53.6% of tricyclic formate **6b**), colorless oil. Structural assignment was corroborated by saponification (2N NaOH, 4 mL) of the mixture and comparison with triphyllenol **6a**, prepared by the other route.[6,7] Spectroscopic data correspond with those of the literature.

(1R,2R,5S)-4,4-Dimethyltricyclo[6.3.2.0^{2,5}]-tridec-8(9)-en-1-yl acetate (**6c**). To a solution of mesylate **4** (170 mg, 0.57 mmol) in pyridine (0.49 g, 0.5 mL, 6.2 mmol) was added glacial acetic acid (0.75 g, 0.72 mL, 12.4 mmol) and the resulting mixture was stirred for 16 h at room temperature. Then Et_2O was added and the organic layer was washed with sat. aq. $NaHCO_3$ solution and water. The solvent was removed and the crude product was purified by chromatography (PE/E, 1:1) to yield a mixture of two inseparable acetates (GC-analysis: 43% of tricyclic acetate **6c**), colorless oil, which was assigned unambiguously from the spectroscopic data of the mixture and by saponification to **6a**.

Epoxy acetate (**7**). Acetate **6c** (400 mg of the mixture) was treated with *m*CPBA (85%) (173 mg, 1.2 mmol) in CH_2Cl_2 (10 mL) and sat. aq. $NaHCO_3$ solution. After 3 h at room temperature the solvent was removed. The residue was diluted with Et_2O, washed with water, evaporated and purified by chromatography to afford **7**, 301 mg (71%): $[\alpha]_D^{22}$ = 62.7 (c 0.44, CH_2Cl_2); IR ($CHCl_3$) 2952, 2864, 1720, 1600, 1460, 1368, 1268, 1240, 1128, 1088, 1048, 1016, 968, 952 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ 2.86 - 1.30 (m, 17 H), 1.90 (s, 3 H, OAc), 1.02 (s, 6 H, CH_3); 50 MHz ^{13}C NMR ($CDCl_3$) δ 170.41 (↑, C=O), 87.02 (↑, C-1), 64.92 (↓, C-9), 59.02(↑, C-8), 47.29 (↓) and 44.54 (↓) (C-2, C-5), 35.67 (↑), 34.11 (↑), 33.85 (↑), 29.88 (↓, CH_3), 28.92 (↑), 28.66 (↑), 25.83 (↑), 25.69(↑), 24.20 (↑), 22.47 (↓, CH_3CO), 21.50 (↓, CH_3); MS (70 eV, r.t.) *m/z* (relative intensity) 278 (12), 263 (2), 235 (20), 218 (90), 190 (100), 176 (37), 161 (32), 148 (32), 148 (56), 132 (56), 105 (53), 91 (65), 79 (55).

Triphyllanol [(1R,2R,5S)-4,4-Dimethyltricyclo[6.3.2.0^{2,5}]tridecan-1-ol] (**8**). Triphyllenol **6a** (220 mg, 1 mmol) in THF (10 mL) was hydrogenated with Raney-Ni (from 0.3 g of alloy) as catalyst. After complete reaction the mixture was filtered and the solvent was evaporated to afford triphyllanol **8** quantitatively, colorless neddles (acetone), m.p. 151-152 °C: $[\alpha]_d^{22}$ = 94.6 (c 1.245, MeOH); IR (KBr) 3387, 2952, 2916, 2897, 1460, 1361, 1301, 1252, 1035, 1003, 866 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ 2.53 - 2.31 (m, 1 H) 2.26 - 1.15 (m, 19 H), 0.99 (s, 6 H, CH_3); ^{13}C NMR ($CDCl_3$, APT) δ 75.01 (↑, C-1), 46.80 (↓) and 45.78 (↓) (C-2, C-5), 40.86(↑), 39.09(↑), 34.24(↑), 33.43(↑), 30.68 (↑), 30.02 (↓, C-8), 29.99 (↓, CH_3), 29.41(↑), 24.57(↑), 21.41(↑), 20.87(↑), 20.29 (↓, CH_3); MS (70 eV, r.t.) *m/z* (relative intensity) 222 (11), 205 (63), 189 (39), 164 (100), 149 (13), 135 (34), 121 (46), 107 (44), 95 (61), 81 (81), 67 (65), 59 (90), 41 (95). Anal. calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.70. Found: C, 80.75; H, 11.68.

Triphyllenol oxide (**9**). To a solution of triphyllenol **6a** (220 mg, 1 mmol) in CH_2Cl_2 (4 mL) was added $NaHCO_3$ (168 mg, 2 mmol) in H_2O (2 mL) and *m*CPBA (85%) (207 mg, 1 mmol) in CH_2Cl_2 (3 mL) and the mixture was stirred for 20 h at room temperature. Et_2O was added and the organic layer was washed with 0.6N NaOH (3x) and water. After drying ($MgSO_4$) and removal of the solvent the crude product was purified by chromatography to give epoxide **9**, 180 mg (76%), m.p. 209 - 211 °C: $[\alpha]_D^{22}$ = 68.7 (c 0.76, CH_2Cl_2); IR (KBr) 3352, 2954, 2860, 1458, 1447, 1364, 1349, 1286, 1265, 1251, 1233, 1201, 1094, 1053, 1039, 1025, 998, 987, 951, 931, 923, 893, 845, 821, 754 cm^{-1}; 200 MHz ^1H NMR (CD_2Cl_2) δ 3.4 (s, 1 H, OH), 2.73 (dd, J = 9 Hz, J = 6 Hz, 1 H), 2.45 - 1.10 (m, 15 H), 1.02 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.82 (dt, J = 8 Hz, J = 12 Hz, 1 H); ^{13}C NMR (CD_2Cl_2, APT) δ 74.91 (↑, C-1), 64.96 (↓, C-9), 59.33 (↑, C-8), 50.50(↓) and 45.96 (↓) (C-2, C-5), 36.45 (↑), 35.25 (↑), 33.83 (↑), 33.79 (↑), 32.07 (↑), 29.94 (↓, CH_3), 27.09 (↑), 26.06 (↑), 24.63 (↑), 21.51 (↓, CH_3); MS (70 eV, 120 °C) *m/z* (relative intensity) 236 (2), 218 (19), 203 (6), 189 (4), 165 (25), 149 (15), 134 (21), 109 (34), 97 (50), 81 (78), 67 (50), 55 (54), 41 (100). Anal. calcd. for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.13; H, 10.22.

Dibromide (**10**). To a solution of triphyllenol **6a** (1.0 g, 4.5 mmol) in CCl_4 (30 mL) was added $PyH^+Br_3^-$ (2.5 g, 7.8 mmol) and glacial acetic acid (15 mL) at 0 °C. After complete reaction (TLC control) Et_2O was added and the organic layer was washed with water and sat. aq. $NaHCO_3$ solution and dried ($MgSO_4$). The solvent was evaporated and the crude product was purified by chromatography (E/PE, 3:1) to yield dibromide **10** (major product) and bromotriphyllenol **11** (minor product). Data for **10**: 1.3 g (79%), colorless needles, m.p. 78 - 79 °C: $[\alpha]_D^{22}$ = -77.0 (c 0.53, CH_2Cl_2); IR ($CHCl_3$) 2957, 2921, 2860, 1657, 1473, 1460, 1442, 1360, 1177, 820, 773, 680, 465; 560 MHz ^1H NMR ($CDCl_3$) δ 5.59 (ddd, ^3J = 8 Hz, ^3J = 8.5 Hz, ^4J = 0.3 Hz, 1 H, H-2), 4.49 (ddd, ^3J = 9.9 Hz, ^3J = 9.1 Hz, ^4J = 0.3 Hz, 1 H, H-12), 3.31 (dd, ^3J = 9.1 Hz, ^2J = 14.3 Hz, 1 H, H_a-13), 3.15 (dd, ^3J = 9.9 Hz, ^2J = 14.3 Hz, 1 H, H_b-13), 2.75 (m, 1 H, H_a-3), 2.5 (m, 2 H, H-4), 2.31 (ddd, ^2J = 12.3 Hz, ^3J = 8.0 Hz, ^3J = 0.2 Hz, H, H_a-11), 2.29 (m, 1 H, H-6), 2.07 (dddd, ^2J = 12.5 Hz, ^3J = 8.0 Hz, ^3J = 3.0 Hz, ^3J = 4 Hz, 1 H, H_b-3), 1.80 (ddd, ^2J = 12.3 Hz, ^3J = 10.8 Hz, ^3J = 8.2 Hz, 1 H, H_b-11), 1.75 (dd, ^3J = 10.5 Hz, ^3J = 7.7 Hz, 1H, H_a-7), 1.63 (ddd, ^2J = 14.0 Hz, ^3J = 8.0 Hz, ^3J = 0.2 Hz, 1 H, H_a-10), 1.58 (m, 1 H, H_b-7), 1.50 (m, 1 H, H-9), 1.363 (dddd, ^2J = 14.0 Hz, ^3J = 10.8 Hz, ^3J = 7.8 Hz, ^3J = 8.0 Hz, 1 H, H_b-10), 0.98 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, APT) δ 138.44 (↑, C-1), 131.03 (↓, C-2), 73.89 (↓, C-5), 53.23 (↓, C-6), 52.21 (↑, C-13), 49.02 (↓, C-9), 47.05 (↓, C-12), 38.79 (↑, C-7), 36.82 (↑, C-4), 33.76 (↑, C-11), 31.73 (↑, C-8), 29.62 (↓, C-14), 25.36 (↑, C-10), 24.85 (↑, C-3), 21.59 (↓, C-15); MS (70 eV, 140 °C) *m/z* (relative intensity) 362 (5), 305 (6), 283 (47), 281 (49), 227 (28), 225 (28), 201 (70), 159 (40), 145 (64), 131 (50), 117 (58), 91 (100), 79 (54), 69 (90). Anal. Calcd for $C_{15}H_{22}Br_2$: C, 49.74; H, 6.14. Found: C, 49.89; H, 6.04. NOE-effect: H_a-3 with H-13 (11%).

Bromo-triphyllenol (**11**). To a solution of triphyllenol **6a** (100 mg, 0.45 mmol) in CCl_4 (2 mL) was added *N*-bromosuccinimide (81 mg, 0.45 mmol). The mixture was refluxed for 2 h and then cooled to -20 °C. After filtration and removal of the solvent the residue was taken up with Et_2O. The organic layer was washed with water and brine and dried ($MgSO_4$). The solvent was evaporated and the crude product purified by chromatography (E/PE, 1:1) to afford **11**, 110 mg (82%), colorless crystals, m.p. 113 - 116 °C: $[\alpha]_D^{22}$ = -168.8 (c, 0.65, CH_2Cl_2); IR ($CHCl_3$) 3592, 3000, 2952, 2860, 1660, 1444, 1364, 1292, 1172, 1048, 884, 824 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ 5.61 (m, 1 H, H-9), 4.52 (ddd, ^3J = 9.5 Hz, ^3J = 9.5 Hz, ^3J = 1.5 Hz, 1 H, H-10), 2.84 (dd, ^3J = 9.5 Hz, ^2J = 14 Hz, 1 H, H-11), 2.66 (m, 1 H, allyl H), 2.4 - 2.0 (m, 4 H, CH and allyl H), 2.0 - 1.2 (m, 10 H), 0.98 (s, 6 H, CH_3); ^{13}C NMR ($CDCl_3$,APT) δ 139.1 (↑, C-8), 131.63 (↓, C-9), 75.09 (↑, C-1), 50.77 (↓, C-2), 49.89 (↑, C-11), 49.73 (↓, C-5), 46.68 (↓, C-10), 34.29 (↑, CH_2), 29.85 (↓, CH_3), 26.11 (↑, CH_2), 23.54 (↑, CH_2), 21.79 (↓, CH_3); MS (70 eV, 80 °C) *m/z* (relative intensity) 299 (2), 297 (2), 282 (7), 280 (7), 219 (26), 202 (100), 173 (6), 159 (21), 145 (36), 131 (26), 119 (48), 107 (51), 105 (37), 91 (44). Anal. Calcd for $C_{15}H_{23}BrO$: C, 60.19; H, 7.76. Found: C, 59.98; H, 7.62.

(1S,8R)-9,9-Dimethyl-5-propylidene-bicyclo[6.2.0]decan-2-one (**12**). To a solution of bromo-triphyllenol **11** (200 mg, 0.67 mmol) in THF (10 mL) was added KOBu^t (75 mg, 0.67 mmol) and the mixture was stirred for 2 h at r.t. Two drops of water were added and the solvent was removed. The residue was diluted with Et_2O and washed with water and brine. the organic layer was dried ($MgSO_4$) and evaporated. Chromatography (E/PE, 3:1) yielded starting material (15 mg) and **12**, 108 mg (80%), colorless oil: IR ($CHCl_3$) 2936, 2896, 2864, 1688, 1456, 1160, 1112, 1092, 908 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ 6.69 (dd, ^3J = 17 Hz, ^3J = 11 Hz, 1 H, H-12), 5.49 (m, 1 H, H-11), 5.39 (d, ^3J = 17 Hz, 1 H, H-13), 5.20 (dm, ^3J = 11 Hz, 1 H, H-13), 3.0 - 2.5 (m, 4 H, allyl H), 2.35 - 2.15 (m, 2 H), 2.05 - 1.45 (m, 6 H, CH_2), 1.02 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, APT) δ 216.18 (↑, C=O), 138.66 (↑, C-5), 113.48, 127.96 (↓, propylidene C), 114.27 (↑, terminal propylidene C), 52.64, 51.86 (↓, C-1, C-8), 29.68, 21.70 (↑, CH_2), 29.40 (↓, CH_3), 23.11 (↓, CH_3); MS (70 eV, r.t.) *m/z* (relative intensity) 218 (33), 203 (11), 189 (10), 175 (13), 162 (14), 147 (18), 133 (18), 119 (38), 105 (57), 91 (77), 79 (100).

Bromo-triphyllenol oxide (**13**). To a solution of bromo-triphyllenol **11** (300 mg, 1 mmol) in CH_2Cl_2 was added sat. aqu. $NaHCO_3$ solution (2 mL) and *m*CPBA (85%) (250 mg, 1.2 mmol) in CH_2Cl_2. The mixture was stirred for 16 h at r.t., evaporated and diluted with Et_2O. The organic layer was washed with 2N NaOH (3x) and water. After drying ($MgSO_4$), removal of the solvent and chromatography (E/PE, 1:1) **13** was isolated, 240 mg (76%), colorless crystals, m.p. 104 - 105 °C: $[\alpha]_D^{22}$ = -46.2 (c 0.26, CH_2Cl_2); IR ($CHCl_3$) 3592, 2952, 2864, 1716, 1612, 1460, 1368, 1300, 1124, 1088, 1052, 1000, 936, 872, 596 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ 4.48 (m, 1 H, H-10), 3.13 (m. 1 H, H-9), 2.60 (dd, ^2J = 14 Hz, ^3J =12 Hz, 1 H, H_a-11), 2.49 - 2.14 (m, 3 H, CH_2 and H-2), 2.05 (dd, ^2J = 14 Hz, ^3J = 8 Hz, 1 H, H_b-11), 1.87 - 1.36 (m, 7 H), 1.28 (s, 1 H, OH), 1.04 (s, 6 H, CH_3), 0.87 (m, 1 H); MS (70 eV, r.t.) *m/z* (relative intensity) 316 (10), 314 (10), 297 (21), 296 (24), 283 (8), 281 (8), 257 (5), 255 (7), 236 (37), 217 (59), 199 (11), 179 (36), 119 (55), 105 (39), 95 (68), 79 (86), 55 (100). Anal. Calcd for $C_{15}H_{23}BrO_2$: C, 57.14; H, 7.37. Found: C, 57.11; H, 7.19.

Spiro oxirane **14**. Bromo-triphyllene oxide **13** (130 mg, 0.41 mmol) in THF (10 mL) and $KOBu^t$ (45 mg, 0.40 mmol) were allowed to react as desribed for compound **12**. Chromatography (E/PE, 1:1) afforded starting material (10 mg) and **14**, 79 mg (89%), colorless solid, m.p. 43 °C: $[\alpha]_D^{22}$ = -148.6 (c 0.14, CH_2Cl_2); IR ($CHCl_3$) 2956, 2940, 2864, 1692, 1640, 1596, 1448, 1368, 1348, 1132, 1100, 992, 960, 936, 624 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ 5.96 (dd, $^3J_{trans}$ = 17 Hz, $^3J_{cis}$ = 11 Hz, 1 H, H-4'), 5.45 (dd, ^2J = 2 Hz, $^3J_{trans}$ = 17 Hz, 1 H, terminal Z-vinyl H), 5.36 (dd, ^2J = 2 Hz, $^3J_{cis}$ = 11 Hz, 1 H, terminal E-vinyl H), 3.05 (m, 1 H, H-1), 2.88 (dd, J = 10 Hz, J = 4 Hz, H-3'), 2.5 - 2.24 (m, 4 H), 2.16 - 1.88 (m, 2 H), 11.77 - 1.55 (m, 2 H), 1.45 (m, 1 H), 1.04 (s, 6 H, CH_3); ^{13}C NMR ($CDCl_3$, APT) δ 214.14 (↑, C=O), 132.55 (↓, vinyl C), 118.53 (↑, terminal vinyl C), 63.62 (↓, C-5), 60.66 (↑, allyl C), 52.60 and 51.93 (↓, C-6, C-9), 29.49 (↓, CH_3), 22.45 (↓, CH_3), 39.44 (↑), 36.65 (↑), 35.23 (↑), 34.63 (↑), 26.66 (↑), 24.20 (↑); MS (70 eV, r.t.) *m/z* (relative intensity) 234 (2), 219 (2), 205 (2), 191 (3), 179 (3), 165 (9), 149 (4), 137 (5), 119 (10), 109 (10), 96 (100), 55 (37). No other diastereomer (enantiomer, chiral shift reagent) was detectable by ^1H NMR.

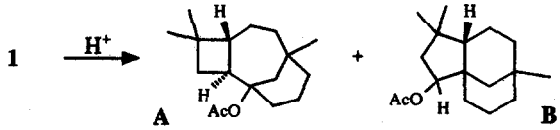
(1R,2R)-5-Vinyl-1-[4-methyl-3-pentenyl]-4-cyclohepten-1(2)-oxide (**15**). Epoxy acetate **7** (100 mg, 0.36 mmol) was heated in a thermolysis apparatus at 10^{-3} Pa to 120 °C. The thermolysis oven had a constant temperature of 400 °C. The product was collected in a trap (liquid N_2). Chromatography afforded **15** as major product, 35 mg (45%), colorless oil: IR ($CHCl_3$) 3092, 3000, 2968, 2928, 2856, 2732, 1720 1632, 1604, 1452, 1376, 1104, 988, 900, 848 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ 6.29 (dd, $^3J_{trans}$ = 17 Hz, $^3J_{cis}$ = 10 Hz, 1 H, ethenyl H), 5.60 (m, 1 H, 3-pentenyl H), 5.11 (d, $^3J_{trans}$ = 17 Hz, 1 H, ethenyl H), 5.07 (m, 1 H, H-4), 4.94 (dd, $^3J_{cis}$ = 10 Hz, J = 0.5 Hz, 1 H, ethenyl H), 3.03 (t, ^3J = 5 Hz, 1 H, H-2), 2.80 - 2.50 (m, 2 H, H-3), 2.40 - 2.25 (m, 2 H, allyl H), 2.15 - 1.90 (m, 4 H), 1.68 (s, 3 H, CH_3), 1.60 (s, 3 H, CH_3), 1.65 - 1.40 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 140.60 (s, cycloheptene C), 140.36 (d, vinyl C), 131.89 (s, pentene C), 126.55, 123.71 (d, pentene C, cycloheptene C), 110.60 (t, vinyl C), 62.04 (s, C-1), 60.61 (d, C-2), 36.95, 28.58, 28.23, 23.20, 22.94 (t, CH_2), 25.70 (q, CH_3), 17.66 (q, CH_3); MS (70 eV, r.t.) *m/z* (relative intensity) 218 (20), 204 (8), 220 (12), 189 (5), 175 (8), 157 (10), 132 (86), 117 (33), 105 (51), 91 (73), 79 (62), 69 (100). $[\alpha]_D^{20}$ = 39.7 (c = 0.61 in CH_2Cl_2).

Acknowledgments. We thank Prof. R. G. Boeckman Jr. for a discussion and the Fonds der Chemischen Industrie for support of this work.

REFERENCES

1. Nakanishi, K.; Goto, T.; Itô, S.; Natori, S.; Nozoe, S. (Ed.): *Natural Products Chemistry, Vol. 1*, p. 83, Academic Press, New York, **1974**; Simonsen, J. L.; Barton, D. H. R. *The Terpenes*, Vol. III, p. 39, Cambridge University Press, Cambridge, UK, **1952**; King, J. F.; de Mayo, P. in de Mayo, P. (Ed.): *Molecular Rearrangements, Vol. 2*, Wiley, New York **1964**, Chap. 13; Gatilova, V. P.; Korchagina, D. V.; Rybalova, T. V.; Gatilov, Y. V.; Dubovenko, Z. V.; Barkhash, V. A. *Zh. Org. Khim.* **1989**, *25*, 320.
2. Total synthesis: Corey, E. J.; Mitra, R. B.; Uda, H. *J. Am. Chem. Soc.* **1964**, *86*, 485.
3. Ohloff, G. *Riechstoffe und Geruchssinn. Die molekulare Welt der Düfte.* Springer, Heidelberg, **1990**.
4. Schulte-Elte, K.-H.; Joyeux, M.; Ohloff, G. *Ger. Offen.* 2 440 025, 13 March 1975; cf. *Chem. Abstr.* **1975**, *83*, 10519d.
5. (a) Hoffmann, H. M. R.; Tsushima, T. *J. Am. Chem. Soc.* **1977**, *99*, 6008; (b) Hoffmann, H. M. R. *Angew. Chem.* **1969**, *81*, 597; *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 556.
6. Vogt, U.; Eggert, U.; Slawin, A. M. Z.; Williams, D. J.; Hoffmann, H. M. R. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1456; *Angew. Chem.* **1990**, *102*, 1530.
7. Hoffmann, H. M. R.; Eggert, U. *Synlett* **1991**, 337.
8. Uchida, T.; Matsubara, Y.; Koyama, Y. *Agric. Biol. Chem.* **1989**, *53*, 3011; Uchida, T.; Matsubara, Y.; Adachi, A. *Agric. Biol. Chem.* **1986**, *50*, 1903.

9. See Maier, W. F.; Schleyer, P. von R. *J. Am. Chem. Soc.* **1981**, *103*, 1891; Mc Ewen, A. B.; Schleyer, P. von R. *J. Am. Chem. Soc.* **1986**, *108*, 3951.
10. For comparison, acetolysis of (-)-caryophyllene (**1**) in the presence of mineral acid, affords tricyclic esters **A** and **B** derived from caryolan-1-ol and clovan-2-ol, respectively.[11]



11. For a review of transannular π-cyclizations see Harrowven, D.; Pattenden, G. in Trost, B. M.; Fleming, I.; Pattenden, G. (Eds.): *Comprehensive Organic Synthesis, Vol. 3*, p. 379, Pergamon, Oxford, **1991**; Moriarty, R. M. in Eliel, E. L.; Allinger, N. L. (Eds.): *Top. Stereochem., Vol. 8*, p. 271, Interscience, N.Y., **1974**.