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Synthetic Studies on Acorane-Alaskane Sesquiterpenes. II.[1] Total Synthesis of (±)-Acorenone[2]

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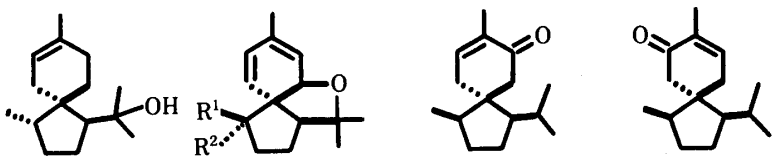
The metal-ammonia reduction of the cyclopenta[*c*]benzofuran derivative (**2b**) afforded a mixture of 4-*epi*-β-acorenol (**5**), a disubstituted olefin (**8**) as the main product, and a perhydro compound (**9**). Compound **8** was converted to **5** *via* the *exo*-diene (**15**). Dehydration of **5** afforded the 4-*epi*-β-acoradiene (**6**), selective reduction of which gave the monoolefin (**7**), and then the allylic oxidation of **7** gave (±)-acorenone (**3**) in good yield.

Keywords——acorane-alaskane sesquiterpene; acorenone; cyclopenta[*c*]benzofuran; total synthesis; 4-*epi*-β-acorenol; 4-*epi*-α-acorenol; 4-*epi*-β-acoradiene; metal–ammonia reduction; conjugate reduction; terminal olefin reduction

In our synthetic studies on acorane-alaskane sesquiterpenes, we have already reported the synthesis of (±)-β-acorenol (**1**) by the reductive C–O bond fission of the cyclopenta[*c*]benzofuran derivative (**2a**).[1] In this paper, we describe the synthesis of (±)-acorenone (**3**), one of the 1,4-*cis* series of acorane-alaskane sesquiterpenes, starting from **2b**.

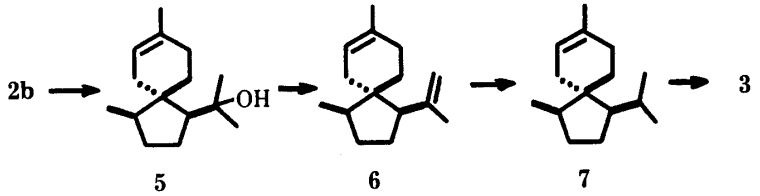
Acorenone (**3**) was isolated by Šorm *et al.* in 1961,[3] and the structure was determined by Zalkow *et al.* in 1968[4] in connection with the structure elucidation of acorenone B (**4**), thereby proving that **3** and **4** are epimers with respect to the spirocarbon. Their absolute structures were determined by the syntheses of the optically active compounds in 1977[5] and 1978.[6]

For the synthesis of acorenone (**3**),[7] if we obtained 4-*epi*-β-acorenol (**5**) from **2b** by the same method[1] as used for the synthesis of (±)-β-acorenol (**1**) from **2a**, the subsequent manipulation for the synthesis of (±)-acorenone (**3**) as shown in the synthetic plan would be easy.



1 **2a** : R^1=H, R^2=Me; **2b** : R^1=Me, R^2=H **3** **4**

synthetic plan



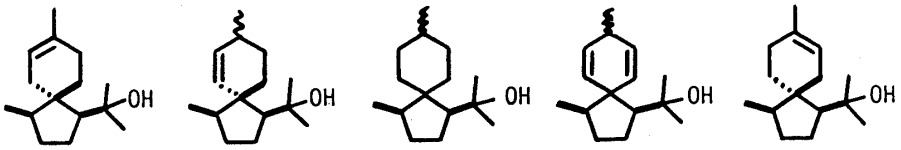
5 **6** **7**

Chart 1

Metal–Ammonia Reduction of 2b

First of all, we tried the reductive C–O bond fission of **2b** under the same conditions (20 eq of Li/NH_3/tetrahydrofuran (THF)/*tert*-BuOH/−40 °C/3 h) as those in the synthesis of **1** from **2a**. Unexpectedly, although the reduction of **2a** to **1** progressed exclusively (81% yield), the transformation of **2b** to **5** proved tricky (Table I, run 1); the yield of the desired product (**5**) was only 10%, the main product was a disubstituted olefin (**8**)[8] (66% yield), and the perhydro compound (**9**)[8] was also obtained in 20% yield. We examined many other conditions,[9] but the yield of **5** was 25% at most [Na (8 eq)/NH_3/THF/*tert*-BuOH/−20 °C/1.5 h] (run 2). When **2b** was treated with Li (4 eq) in liquid NH_3 at −78 °C for 4 min (run 3), the unstable nonconjugated diene (**10**)[8] was obtained as the main product along with small amounts of **2b** and **8**. Compound **10** could exclusively be transformed to **8** (20 eq of Li/NH_3/THF/*tert*-BuOH/−78 °C/2.5 h) (run 4). When the reaction was quenched after 30 min (run 5), a small amount of 4-*epi*-α-acorenol (**11**)[10] was contained in the crude product, which consisted mainly of **5**, **8**, and **9**. However, after 3 h (run 6), compound **11** was no longer detected, and the disubstituted olefin (**8**) was obtained in 71% yield along with small amounts of **5** and **9**. These results can be explained in terms of the ease of reduction of 4-*epi*-α-acorenol (**11**) rather than 4-*epi*-β-acorenol (**7**). Namely, as the double bond of **11** is located nearer to the hydroxyl group than that of **5**, the former is reduced much faster than the latter.[11] In addition, surprising results were obtained in the reduction of the conjugated dienes (**12** and **15**), whose synthesis will be described later (Chart 3). Although the metal–ammonia reduction of **15** afforded **5** as expected (run 7), the reduction of **12** at below −40 °C gave exclusively the disubstituted olefin (**8**) (run 8), while at elevated temperature a mixture of **5**, **8**, and **9** was obtained. Even at this temperature, the main product was **8** (run 9).

TABLE I. Metal–Ammonia Reductions of **2b**, **10**, **12**, and **15**



5 **8** **9** **10** **11**

Run	Starting material	Conditions	Products (%)
1	**2b**	Li (20 eq), −40 °C, 3 h liq. NH_3/THF/*tert*-BuOH	**5** (10), **8** (66), **9** (20)
2	**2b**	Na (8 eq), −20 °C, 1.5 h liq. NH_3/THF/*tert*-BuOH	**5** (25), **8** (25), **9** (45)
3	**2b**	Li (4 eq), −78 °C, 4 min liq. NH_3/THF	**10** (>80),[a] **2b**, **8**
4	**10**	Li (20 eq), −78 °C, 2.5 h liq. NH_3/THF/*tert*-BuOH	**8** (>80)[a]
5	**2b**	Li (10 eq), −78 °C, 30 min liq. NH_3/THF/*tert*-BuOH	**5**, **8**, **9**, **11** (minor)
6	**2b**	Li (20 eq), −78 °C, 3 h liq. NH_3/THF/*tert*-BuOH	**8** (71), **5**, **9**
7	**15**	Li (20 eq), −40 °C, 3 h liq. NH_3/THF	**5** (82)
8	**12**	Li (10 eq), −40 °C, 2.5 h liq. NH_3/THF	**8** (>85)[a]
9	**12**	Li (10 eq), −33 °C, 2.5 h liq. NH_3/THF	**8** (main)[a] **5** (<20),[a] **9** (<20)[a]

a) By GC analysis.

A possible reaction pathway is presented in Chart 2. The protonation to the dianion (A) would produce three dienic intermediates (B, C, and D). Judging from the fact that the reduction of **12** afforded **8** as the main product, in the intermediates (B and D), the 1,4-reduction of the conjugated diene would compete with the reduction of the double bond near the hydroxyl group. The metal–amine reduction of a nonconjugated olefin generally needs vigorous conditions (*e.g.*, reflux in NH_3, 0 °C or room temperature in $EtNH_2$). However, a system in which one double bond is close to the other in a nonconjugated diene can accept electrons more easily,[12] so this system (compound **10**) can be reduced even at low (−78 °C) temperature with the assistance of the hydroxyl group. Accordingly, it is considered that compound **10** was easily reduced to produce **8** at low temperature.

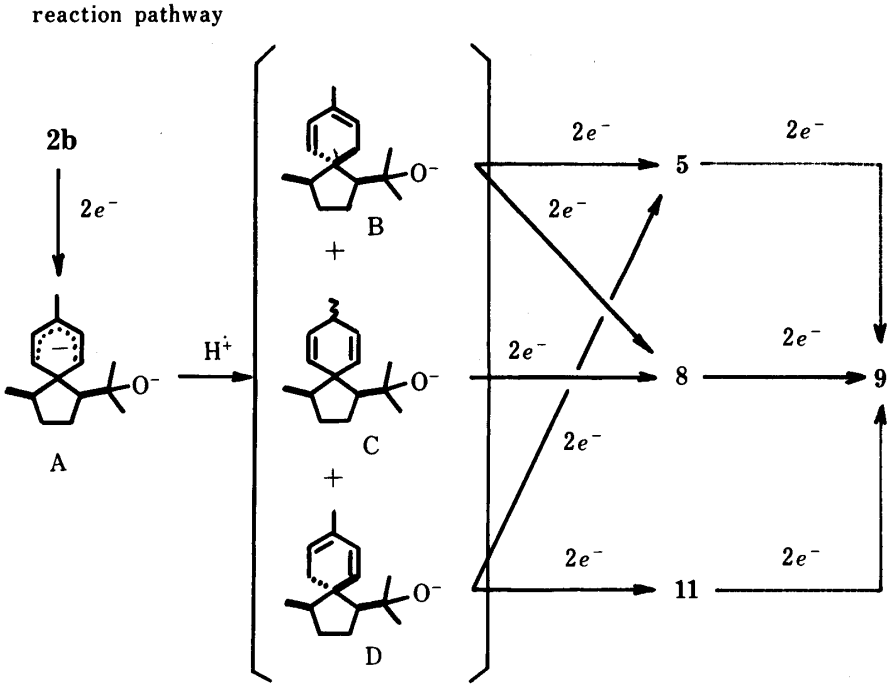


Chart 2

Thus, the disubstituted olefin (**8**) was easy to produce at lower temperature. In order to obtain **5** in a moderate yield, this reduction had to be done at higher temperature (*e.g.*, −30 °C), but at higher temperature the amount of the perhydro compound (**9**) was also increasing. As we could not obtain **5** as the main product, we turned our efforts to the conversion of **8** to **5**.

Conversion of the Disubstituted Olefin (8) to 4-*epi*-β-Acorenol (5)

Bromination of **8** gave the dibromide (**13**), and subsequent dehydrobromination of **13** afforded the allylic bromide (**14**)[8] in 63% yield from **8** under the conditions used [diazabicycloundecene (DBU) in THF]. All attempts at direct conversion of **14** to **5** proved abortive.[13] Thus, we tried to obtain the conjugated diene (**12** or **15**), 1,4-reduction of which would afford 4-*epi*-β-acorenol (**5**). We tried further dehydrobromination of **14** under various conditions.[14] Although there were differences in the reaction rates and yields, the *endo*- and *exo*-dienes (**12** and **15**) were obtained under all conditions examined. Compound **14** was treated with sodium iodide in dimethylformamide (DMF) containing pyridine to afford **12** and **15** (**12**/**15** = 55/45) in 59% yield as the best result, but in the absence of pyridine, the ratio (**12**/**15**) was 84—100/16—0, and moreover the yield was low (20—30%). Metal–ammonia reduction of the *exo*-diene (**15**) afforded the desired compound (**5**) exclusively, but the *endo*-diene (**12**) gave **8** as the main product as mentioned above.

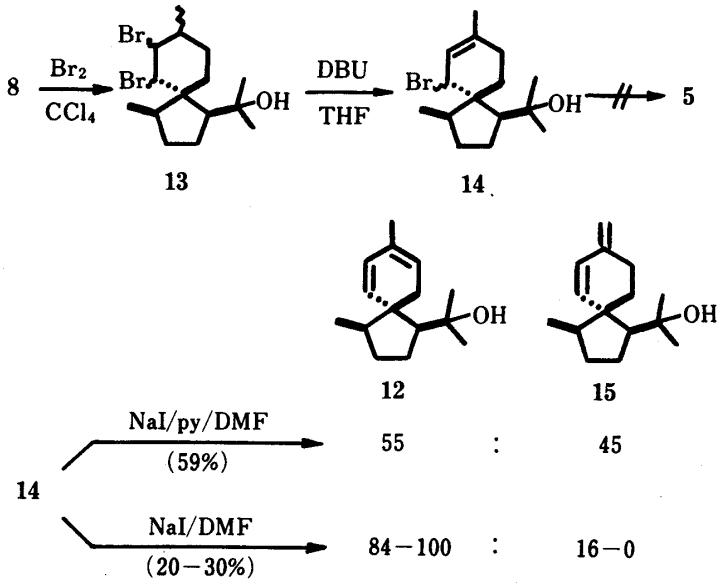
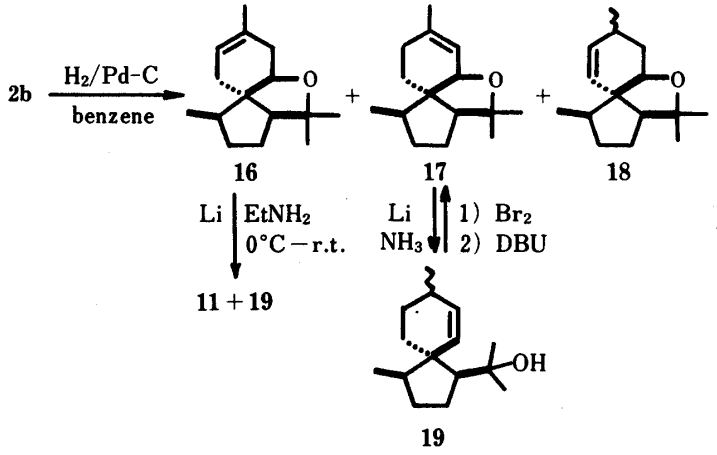


Chart 3

Structure Determination of the Reduction Products

The most important point in the structure determination of the compounds obtained here is how to determine the location of the double bonds. It would be effective for this purpose to synthesize and compare the isomers with respect to the location of the double bond; *e.g.*, α-,[15] β-, 4-*epi*-α-, and 4-*epi*-β-acorenols (**20**, **1**, **11**, and **5**), **8** and **19**. Catalytic hydrogenation of **2b** afforded **16**, **17**, and **18**[8] in 49, 27, and 16% yields, respectively. Metal–ammonia reduction of **17** provided the disubstituted olefin (**19**)[8] exclusively. Bromination of



^{1}H-NMR data (δ) for the C_4-methyl, *gem*-dimethyls, and olefinic protons of compounds **1**, **5**, **11**, and **20**

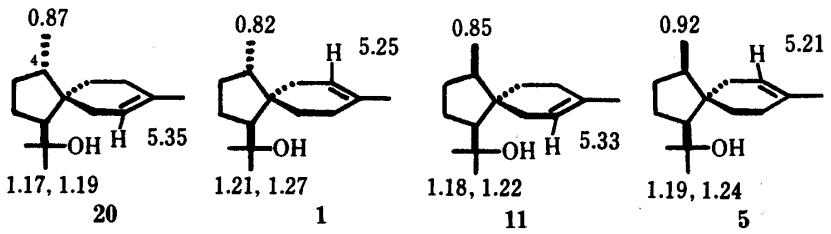


Chart 4

19 followed by DBU treatment regenerated the cyclic ether (**17**) in good yield. This different result from the cases of **8** and **14** shows that the double bond of **19** is on the same side as the hydroxyl group, thus confirming the location of the double bond of **8**. Treatment of the homoallylic ether (**16**) with lithium in ethylamine at room temperature afforded 4-*epi*-α-acorenol (**11**) and **19** in 12 and 26% yields, respectively.

As shown in Chart 4, in the four acorenols (**1**, **5**, **11**, and **20**[15]) the proton nuclear magnetic resonance (^{1}H-NMR) signals of the five-membered ring substituents located on the same side as the double bond (C_4-methyl of **1** and **11**) appear at higher fields than those of others due to the anisotropic effect. On the other hand, the signals of the olefinic protons near the hydroxyl group (**20**, **11**) appear at lower fields than those of the others.

Synthesis of (±)-Acorenone (3)

As the structure of **5** was revealed through the results described above, we set about the synthesis of (±)-acorenone (**3**) starting from **5**. Dehydration of **5** with alumina–pyridine at 200 °C[7b,15,16] provided 4-*epi*-β-acoradiene (**6**) in 78% yield. Treatment of **5** with thionyl chloride–pyridine afforded **6** and the *endo*-olefin (**21**) in 70 and 17% yields, respectively. Selective reduction of the terminal olefin of **6** under the conditions of Benkeser *et al.*[17] afforded the monoolefin (**7**) in quantitative yield. Selenium dioxide oxidation of **7** gave (±)-acorenone (**3**) in 75% yield; this product was identified by comparison of the physico-chemical data with the reported values.[7a]

Experimental

Infrared (IR) spectra were recorded on a Hitachi 215 or a Hitachi 260-10 spectrophotometer. ^{1}H-NMR spectra were recorded on a Hitachi R-22 (90 MHz) instrument with tetramethylsilane as an internal standard. The following abbreviations for the signal patterns are used: s = singlet, d = doublet, t = triplet, m = multiplet, and br = broad. Ultraviolet (UV) spectra were recorded on a Hitachi 124 spectrophotometer. Low- and high-resolution mass spectra (MS and High MS) were obtained with a JEOL JMS-D300 mass spectrometer. For preparative thin layer chromatography (PTLC), Merck Kieselgel 60 PF_{254} was used. High-performance liquid chromatography (HPLC) and gas chromatography (GC) were carried out on Waters and Shimadzu GC 4CM instruments, respectively.

General Procedure for Metal–Ammonia Reduction——A solution of the starting material in THF or THF/*tert*-BuOH was added to liquid NH_3, then an appropriate amount of metal was added, and the mixture was stirred for 4 min—3 h at an appropriate temperature. The reaction was quenched by the addition of NH_4Cl, and the NH_3 was allowed to evaporate at room temperature. Saturated $NaHCO_3$ was added to the residue, and then the whole was extracted with AcOEt. The extract was washed with water and brine, then dried, and evaporated.

Run 1. Metal–Ammonia Reduction of *rac*-(1*R*,3a*S*,5a*S*,9a*S*)-2,3,3a,4-Tetrahydro-1,4,4,7-tetramethyl-1*H*,5a*H*-cyclopenta[*c*]benzofuran (2b)——**2b** (117 mg, 0.54 mmol) in THF/*tert*-BuOH (5 ml/1 ml), liquid NH_3 (20 ml) and Li (75 mg, 10.8 mg-atom) were used in this reaction. The mixture was stirred for 3 h at −40 °C. The crude product was purified by HPLC. Compound **8** was separated on μ-Porasil semiprep. (hexane : AcOEt = 20 : 1) (79 mg: 66% yield), and **5** and **9** were separated on μBondapac/C_{18} (MeCN : H_2O = 4 : 1) [**5**: 12 mg (10%), **9**: 24 mg (20%)]. **5**: A colorless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3440. ^{1}H-NMR (CCl_4) δ: 0.92 (1H, d, J = 7 Hz, C_4-Me), 1.19, 1.24 (each 3H, s, C_1-C<u>Me$_2$</u>OH), 1.62 (3H, br s, C_8-Me), 5.21 (1H, m, C_7-H). MS *m/z*: 204 ($M^+ - H_2O$). High MS *m/z*: 204.1877 [Calcd for $C_{15}H_{24}$ ($M^+ - H_2O$): 204.1878]. **8**: A colorless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 3575. ^{1}H-NMR (CCl_4) δ: 0.84 (3H, d, J = 6.3 Hz, C_4-Me), 0.96 (3H, d, J = 6.5 Hz, C_8-Me), 1.13, 1.22 (each 3H, s, C_1-C<u>Me$_2$</u>OH), 5.11, 5.44 (each 1H, br d, J = 10 Hz, C_6- and C_7-H). MS *m/z*: 222 (M^+). High MS *m/z*: 222.1979 (Calcd for $C_{15}H_{26}O$: 222.1984). **9**: Colorless crystals (mp 64—65 °C; soluble in petr. ether). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600, 3400. ^{1}H-NMR (CCl_4) δ: 0.83 (3H, d, J = 4 Hz, C_8-Me), 0.90 (3H, d, J = 7 Hz, C_4-Me), 1.17, 1.19 (each 3H, s, C_1-C<u>Me$_2$</u>OH). MS *m/z*: 206 ($M^+ - H_2O$). High MS *m/z*: 206.2022 [Calcd for $C_{15}H_{26}$ ($M^+ - H_2O$): 206.2036].

Run 2. Metal–Ammonia Reduction of 2b with Sodium——**2b** (105 mg, 0.48 mmol), Na (88 mg, 3.83 mg-atom), liquid NH_3 (20 ml) and THF/*tert*-BuOH (5 ml/1 ml) were used in this reaction at −20 °C (bath temperature). The reaction was quenched after 1.5 h. Yields: **5** (27 mg; 25%), **8** (27 mg; 25%), **9** (48 mg; 45%).

Run 3. Metal–Ammonia Reduction of 2b for 4 min——**2b** (63 mg, 0.29 mmol), Li (8 mg, 1.15 mg-atom), liquid NH_3 (10 ml) and THF (2 ml) were used in this reaction at −78 °C. The reaction was quenched after 4 min. The crude product contained **10** as the main product [over 80% by GC analysis (SE-30)] with small amounts of **8** and the starting material (**2b**). As **10** was unstable, the crude product was further reduced without purification. **10**: ^{1}H-NMR (CCl_4) δ: 0.69 (3H, d, J = 5.8 Hz, C_4-Me), 1.03, 1.16 (each 3H, s, C_1-C<u>Me$_2$</u>OH), 1.07 (3H, d, J = 7.5 Hz, C_8-Me), 2.5—

3.0 (1H, m, C_8-H), 5.18 (1H, dt, J=10, 1.8 Hz), 5.4—5.6 (2H, m), 5.71 (1H, br d, J=10 Hz).

Run 4——The crude product **10** was subjected to reaction with 20 eq of Li in liquid NH_3 containing THF/*tert*-BuOH at −78 °C to produce **8** in over 80% yield by GC analysis [column, SE-30 (2 m); column temperature, 125 °C; retention times, **10** (4 min), **2b** (5.6 min), **8** (7 min), **9** (8 min), **5** (9 min)].

Run 5. Quench after 30 min——On HPLC separation of the crude product by the same procedure as described above, it was proved by ^{1}H-NMR that compound **11** was present, but **11** and **5** could not be separated.

Run 6——The products obtained by the reaction with 20 eq of Li at −78 °C for 3 h were separated by HPLC by the same procedure as described above.

Run 7. *rac*-(1*R*,4*S*,5*R*)-1-(1-Hydroxy-1-methylethyl)-4,8-dimethylspiro[4.5]dec-7-ene (4-*epi*-β-Acorenol: 5) from the *exo*-Diene (15)——A solution of **15** (24 mg, 0.11 mmol) in THF (6 ml) was added to liquid NH_3 (20 ml) at −40 °C, then Li (15 mg, 2.16 mg-atom) was added, and the mixture was stirred for 3 h at that temperature. After usual work-up, the crude product was purified by PTLC (hexane : AcOEt = 15 : 1) to give **5** (20 mg; 82%).

Runs 8 and 9——The crude products of the reaction of **12** with Li at under −40 °C and over −33 °C were analyzed by GC. At under −40 °C, over 85% of the product was **8**, and at reflux temperature, **5** and **9** were generated, but the yields were below 20%, and most of the remaining product was **8**.

***rac*-(1*R*,4*S*,5*R*)-6-Bromo-1-(1-hydroxy-1-methylethyl)-4,8-dimethylspiro[4.5]dec-7-ene (14)**——A solution of Br_2 (0.1 ml of Br_2/5 ml of CCl_4) was added dropwise to a solution of **8** (217 mg, 0.98 mmol) in CCl_4 (10 ml) at 0 °C unitl the color of Br_2 persisted for more than 5 min (1.5 ml). After 30 min, the reaction mixture was washed with a mixture of saturated $NaHCO_3$ and saturated $Na_2S_2O_3$, then with brine, dried, and evaporated to give the crude dibromide (**13**: 363 mg). A mixture of **13** (363 mg), DBU (0.8 ml, 5.3 mmol), and THF (2 ml) was refluxed with stirring for 4 h, then allowed to cool. Water (5 ml) was added, and then the whole was extracted with ether. The extract was washed with water and brine, then dried, and evaporated. The crude product was purified by alumina (Merck Aluminiumoxid 90) column chromatography (benzene) to give the allylic bromide (**14**: 185 mg; 63% yield from **8**) as a pale yellow oil. **14**: IR ν_{max}^{film} cm^{-1}: 3400, 1680. ^{1}H-NMR (CCl_4) δ: 0.93 (3H, d, J=6.3 Hz, C_4-Me), 1.16, 1.19 (each 3H, s, C_1-C<u>Me$_2$</u>OH), 1.68 (3H, s, C_8-Me), 3.55 (1H, br d, J=5.5 Hz, C_6-H), 5.42 (1H, m, C_7-H). MS m/z: 220 (M^+ − HBr). High MS m/z: 220.1827 [Calcd for $C_{15}H_{24}O$ (M^+ − HBr): 220.1827].

***rac*-(1*R*,4*S*,5*R*)-1-(1-Hydroxy-1-methylethyl)-4,8-dimethylspiro[4.5]deca-6,8-diene (12) and *rac*-(1*R*,4*S*,5*R*)-1-(1-Hydroxy-1-methylethyl)-4-methyl-8-methylenespiro[4.5]dec-6-ene (15)**——A mixture of **14** (63 mg, 0.21 mmol), DMF (2 ml), NaI (122 mg, 0.81 mmol), and dry pyridine (0.1 ml) was heated with stirring under N_2 at 100 °C for 6 h, then allowed to cool. Saturated $NaHCO_3$ (10 ml) was added, then the whole was extracted with AcOEt. The extract was washed with water and brine, then dried, and evaporated. The crude product was purified by PTLC (hexane: developed 4 times) followed by HPLC (μPorasil semiprep.; hexane : AcOEt = 20 : 1) to give **12** (15 mg) and **15** (12 mg) in 59% yield, as colorless oils. **12**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 3575, 3015, 1665, 1595. UV λ_{max}^{EtOH} nm (ε): 269 (7900). ^{1}H-NMR ($CDCl_3$) δ: 0.82 (3H, d, J=6 Hz, C_4-Me), 1.21, 1.29 (each 3H, s, C_1-C<u>Me$_2$</u>OH), 1.72 (3H, br s, C_8-Me), 1.99, 2.56 (2H, AB type, C_{10}-H), 5.1—5.4 (2H, m, olefinic H), 5.68 (1H, dd, J=9, 1.8 Hz, olefinic H). MS m/z: 220 (M^+). High MS m/z: 220.1829 (Calcd for $C_{15}H_{24}O$: 220.1827). **15**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 3595, 3015, 1640, 1595, 875. UV λ_{max}^{EtOH} nm (ε): 235 (12200). ^{1}H-NMR ($CDCl_3$) δ: 0.86 (3H, d, J=6 Hz, C_4-Me), 1.19, 1.26 (each 3H, s, C_1-C<u>Me$_2$</u>OH), 4.74 (2H, br s, C_8=C<u>H$_2$</u>), 5.34 (1H, br d, J=10 Hz, olefinic H), 6.16 (1H, d, J=10 Hz, olefinic H). MS m/z: 220 (M^+). High MS m/z: 220.1829 (Calcd for $C_{15}H_{24}O$: 220.1827).

The reaction without pyridine was done similarly to give a mixture of **12** and **15** in 20—30% yield; the ratio of **12**/**15** was 84—100/16—0 as determined by GC analysis.

Catalytic Hydrogenation of 2b to Give *rac*-(1*R*,3a*S*,5a*S*,9a*R*)-2,3,3a,4,6,9-Hexahydro-1,4,4,7-tetramethyl-1*H*,5a*H*-cyclopenta[*c*]benzofuran (16), *rac*-(1*R*,3a*S*,5a*S*,9a*R*)-2,3,3a,4,8,9-Hexahydro-1,4,4,7-tetramethyl-1*H*,5a*H*-cyclopenta[*c*]benzofuran (17), and *rac*-(1*R*,3a*S*,5a*S*,9a*S*)-2,3,3a,4,6,7-Hexahydro-1,4,4,7-tetramethyl-1*H*,5a*H*-cyclopenta[*c*]benzofuran (18)——A mixture of **2b** (308 mg, 1.41 mmol), 10% Pd–C (20 mg), and benzene (20 ml) was stirred under H_2 (1 atom) for 1.5 h. After removal of the catalyst by filtration, the filtrate was concentrated. The residue was purified by PTLC (ether : petr. ether = 1 : 10) to give **16** (47%), **17** (27%), and **18** (16%) as colorless oils. **16**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3035, 1125, 810. ^{1}H-NMR (CCl_4) δ: 0.93 (3H, br d, J=5.5 Hz, C_1-Me), 1.09, 1.17 (each 3H, s, C_4-Me$_2$), 1.66 (3H, br s, C_7-Me), 3.81[18] (1H, br t, J=3.3 Hz, C_{5a}-H), 5.39[18] (1H, m, C_8-H). MS m/z: 220 (M^+). High MS m/z: 220.1831 (Calcd for $C_{15}H_{24}O$: 220.1827). **17**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3020, 1675, 1130. ^{1}H-NMR (CCl_4) δ: 0.89 (3H, d, J=5.5 Hz, C_1-Me), 1.11, 1.18 (each 3H, s, C_4-Me), 1.70 (3H, br s, C_7-Me), 3.73[18] (1H, br d, J=5.5 Hz, C_{5a}-H), 5.48[18] (1H, m, C_8-H). MS m/z: 220 (M^+). High MS m/z: 220.1816 (Calcd for $C_{15}H_{24}O$: 220.1827). **18**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1125, 660. ^{1}H-NMR (CCl_4) δ: 0.88 (3H, br d, J=6 Hz, C_1-H), 1.08, 1.17 (each 3H, s, C_4-Me$_2$), 3.81 (1H, m, C_{5a}-H), 5.17 (1H, br d, J=10 Hz, C_9-H), 5.59 (1H, dd, J=10, 4.5 Hz, C_8-H). MS m/z: 220 (M^+). High MS m/z: 220.1822 (Calcd for $C_{15}H_{24}O$: 220.1827).

Metal–Ammonia Reduction of 17 and Regeneration of 17 from *rac*-(1*R*,4*S*,5*R*)-1-(1-Hydroxy-1-methylethyl)-4,8-dimethylspiro[4.5]dec-6-ene (19)——A solution of **17** (55 mg, 0.25 mmol) in THF (1.5 ml) was added to a blue-colored mixture of Li (18 mg, 2.59 mg-atom) in liquid NH_3 (10 ml) at −78 °C, and the whole was stirred for 30 min. After usual work-up, the crude product was purified by PTLC (hexane : AcOEt = 15 : 1) to give **19** (46 mg; 83%) as a colorless oil. **19**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3590, 3020. ^{1}H-NMR (CCl_4) δ: 0.87 (3H, d, J=6 Hz, C_4-Me), 0.98 (3H, d, J=6 Hz,

C_8-Me), 1.10, 1.22 (each 3H, s, C_1-C$\underline{Me}_2$OH), 5.62 (2H, br s, olefinic H). MS *m/z*: 204 ($M^+ - H_2O$). High MS *m/z*: 204.1873 [Calcd for $C_{15}H_{24}$ ($M^+ - H_2O$): 204.1878].

Bromination and DBU treatment of **19** as described for **13** and **14** regenerated **17** (25 mg; 63% yield).

Metal–Amine Reduction of 16——A solution of **16** (50 mg, 0.23 mmol) in THF (1.5 ml) was added to a blue-colored mixture of Li (75 mg, 10.8 mg-atom) and $EtNH_2$ (50 ml) at 0 °C, and the whole was stirred for 3 h at room temperature. After usual work-up, the crude product was purified by PTLC (ether : petr. ether = 1 : 10, developed 3 times) to give 4-*epi*-α-acorenol (**11**: 6 mg; 12%) as a colorless oil and **19** (13 mg; 26%). **11**: IR ν_{max}^{film} cm^{-1}: 3455. ^{1}H-NMR (CCl_4) δ: 0.85 (3H, br d, *J* = 7 Hz, C_4-Me), 1.18, 1.22 (each 3H, s, C_1-C$\underline{Me}_2$OH), 1.61 (br s, C_8-Me), 2.5 (1H, br d, *J* = 17 Hz, C_6-H), 5.33 (1H, m, C_7-H). MS *m/z*: 204 ($M^+ - H_2O$). High MS *m/z*: 204.1878 [Calcd for $C_{15}H_{24}$ ($M^+ - H_2O$): 204.1878].

***rac*-(1*R*,4*R*,5*S*)-1-Isopropenyl-4,8-dimethylspiro[4.5]dec-7-ene (4-*epi*-β-Acoradiene: 6)**——A mixture of **5** (88 mg, 0.40 mmol), Al_2O_3 (Woelm, neutral, activity I; 2.2 g), and pyridine (3 ml) was heated at 200 °C in a sealed tube for 5 h. After cooling, MeOH was added, and the whole was filtered. The solids were washed with ether. The combined filtrate was evaporated, and the residue was purified by PTLC (hexane) to give **6** (63 mg; 78%) as a colorless oil.

Thionyl Chloride–Pyridine Procedure——Thionyl chloride (0.05 ml) was added to a solution of **5** (25 mg, 0.11 mmol) in pyridine (1.1 ml) at 0 °C, and the whole was stirred for 10 min. Saturated $NaHCO_3$ was added, then the whole was extracted with ether. The extract was washed with saturated tartaric acid, saturated $NaHCO_3$, and brine, then dried, and evaporated. The residue was purified by PTLC (hexane) to give a mixture of **6** and α-alaskene (**21**) (unidentified), which was separated by HPLC (μ-Porasil semiprep., hexane, recycled 4 times) to give **6** (16 mg; 70%) and **21** (4 mg: 17%) as colorless oils. **6**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3070, 3010, 1640, 895. ^{1}H-NMR (CCl_4) δ: 0.95 (3H, d, *J* = 6 Hz, C_4-Me), 1.59 (6H, br s, C_8-Me and C_1-C($\underline{Me}$)=CH_2), 4.68, 4.77 (2H, each br s, =CH_2), 5.24 (1H, m, C_7-H). MS *m/z*: 204 (M^+). High MS *m/z*: 204.1847 (Calcd for $C_{15}H_{24}$: 204.1879). **21**: ^{1}H-NMR (CCl_4) δ: 0.88 (3H, d, *J* = 7 Hz, C_4-Me), 1.57 (3H, s, C_8-Me), 1.69, 1.71 (each 3H, s, =CMe_2), 5.33 (1H, m, C_7-H). MS *m/z*: 204 (M^+). High MS *m/z*: 204.1879 (Calcd for $C_{15}H_{24}$: 204.1897).

Benkeser Reduction of 6 to Give *rac*-(1*R*,4*R*,5*S*)-1-Isopropyl-4,8-dimethylspiro[4.5]dec-7-ene (7)——A solution of **6** (17 mg, 0.08 mmol) in THF/*tert*-BuOH (1.1 ml/0.26 ml) was added dropwise to a blue-colored mixture of Li (44 mg, 6.34 mg-atom) and $EtNH_2$ (5 ml), and the mixture was stirred at 15 °C for 30 min. After usual work-up, the crude product was purified by PTLC to give **7** (17 mg, quant.). ^{1}H-NMR (CCl_4) δ: 0.84 (3H, d, *J* = 6 Hz, C_4-Me), 0.91 (6H, d, *J* = 6 Hz, C_1-CH$\underline{Me}_2$), 5.27 (1H, m, C_7-H). MS *m/z*: 206 (M^+). High MS *m/z*: 206.2059 (Calcd for $C_{15}H_{25}$: 206.2036).

(±)-Acorenone (3)——A solution of SeO_2 (17 mg, 0.15 mmol) in 95% EtOH (0.5 ml) was added to a solution of **7** (17 mg, 0.08 mmol) in 95% EtOH (1 ml), then the whole was refluxed for 9 h. After filtration, the filtrate was evaporated. The residue was purified by PTLC (hexane : AcOEt = 10 : 1) to give (±)-**3** (8 mg; 75%). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1675, 1382, 1369. ^{1}H-NMR (CCl_4) δ: 0.82, 0.85, 0.96 (each 3H, d, *J* = 6 Hz, C_1-CH$\underline{Me}_2$ and C_4-Me), 1.69 (3H, br s, C_8-Me), 2.20 (2H, s, C_6-H), 2.09, 2.55 (2H, AB type, C_{10}-H), 6.45 (1H, m, C_9-H). MS *m/z*: 220 (M^+). High MS *m/z*: 220.1824 (Calcd for $C_{15}H_{24}O$: 220.1827).

References and Notes

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10) Compound **11** was detected in the HPLC separation procedure (see Experimental) by ^{1}H-NMR, but could not be isolated.
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18) In compound **17**, irradiation of the signals at δ 5.48 transformed the signals at δ 3.73 to a singlet, but in compound **16**, irradiation at δ 3.81 had no effect on the signals at δ 5.39, thereby confirming the location of the double bond in **16** and **17**.