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Synthetic Studies on Acorane-Alaskane Sesquiterpenes. I. Total Synthesis of (±)-β-Acorenol[1)]

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(±)-β-Acorenol (**2**) was synthesized by the metal-ammonia reduction of (1*R**,3a*R**,5a*R**,9a*R**)-2,3,3a,4-tetrahydro-1,4,4,7-tetramethyl-1*H*,5a*H*-cyclopenta[*c*]benzofuran (**11a**), which was prepared from the spirodienone **9a** or **10a** by reaction with methyllithium and subsequent Lewis acid treatment.

Keywords——acorane-alaskane sesquiterpene; β-acorenol; β-acoradiene; 4-*epi*-acorenone; cyclopenta[*c*]benzofuran; spirodienone; total synthesis; metal–ammonia reduction; allylic ether bond reductive fission; conjugated diene 1,4-reduction

A number of spiro[4.5]decane skeletal sesquiterpenes can be divided into five classes according to the substitution modes of alkyl groups on the carbon skeleton: acorane-alaskane, spirovetivane, spirolaurane, spiroaxane, and vitrane.[2)] Among these sesquiterpenes, the acorane-alaskane family is the largest group, and is important as its members are intermediates in terpene biogenesis and constituents of essential oils; α- (**1**)[3)] and β-acorenol (**2**),[3c)] α- (**3**)[3,4)] and β-acoradiene (**4**),[3c)] α- (**5**)[3c,5a)] and β-alaskene (**6**),[3c,5a)] acorenone (**7**),[6)] and acorenone B (**8**)[7)] are representative compounds of this family. Compound **1**, **3**, and **5** are representative compounds of biogenesis of cedrene, and **2**, **4**, and **6** are intermediates for prezizaene and zizaene.[3b,d,5)] Although total syntheses of acorenone (**7**) and acorenone B (**8**) have been reported by several researchers,[8)] there are few examples of the synthesis of other members of this group.[9)] Only two research groups have synthesized compounds bearing a tertiary hydroxyl group, *e.g.*, α- (**1**) and β-acorenol (**2**).[8a,9g,h)]

In this paper, we describe a synthesis of the cyclopenta[*c*]benzofuran derivatives **11a** and **11b** *via* the spirodienones (**9a** and **10a**, and **9b** and **10b**), and a total synthesis of (±)-β-acorenol (**2**) *via* **11a**.

Our synthetic strategy was as follows. First, we selected the *trans*- and *cis*-spirodienone esters (**9a** and **9b**) and ketones (**10a** and **10b**) as the initial key intermediates; the 1,4-*trans* compounds—**9a** and **10a**—would be transformed to **1**, **2**, **3**, and **4**, and the 1,4-*cis* compounds—**9b** and **10b**—would be converted to **7** and **8**. Second, we synthesized the cyclopenta[*c*]benzofuran derivatives **11a** and **11b** in which an asymmetry is introduced at the spiro center of **9** and **10**. Finally, compounds **11a** and **11b** were converted to the natural products by suitable fissions of the allylic ether bond.

The spirodienone esters **9a** and **9b** have already been synthesized by Corey *et al.*[10)] However, they made an error in the assignment of the *trans*- and *cis*-isomers, which we corrected in our previous paper.[11)] Next, we synthesized the spirodienones **10a** and **10b** as follows. The protected phenolic ester (**12**), which was prepared from *p*-methoxyacetophenone

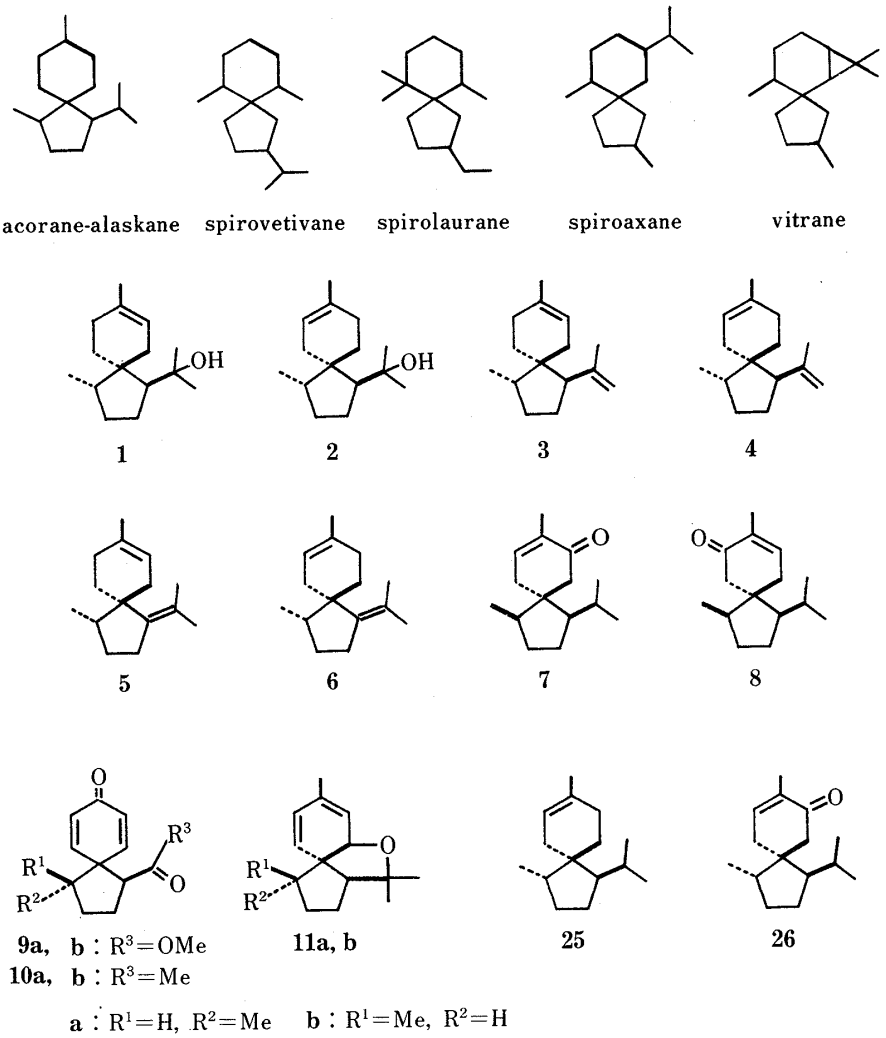
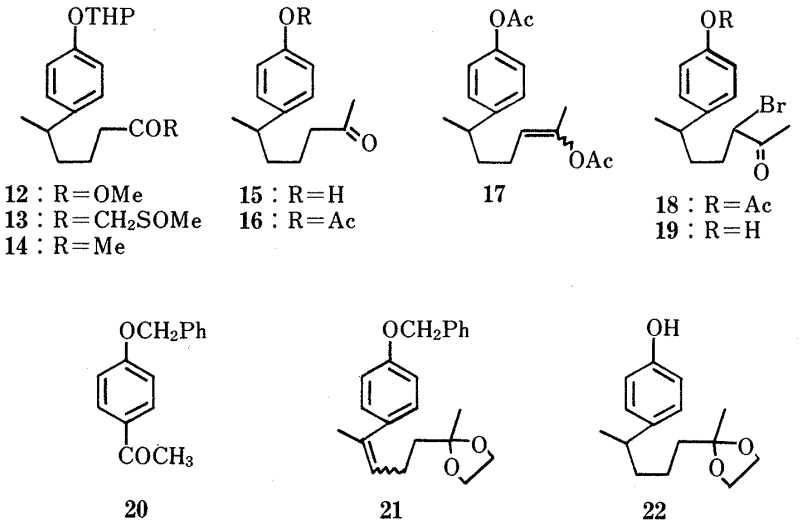


Chart 1

in 5 steps in *ca.* 35% yield,[10] was selected as a starting material. The ester (**12**) was transformed to the α-methanesulfinyl ketone (**13**) by reaction with methylsulfinyl carbanion (dimsyl anion)[12] at room temperature. Aluminum amalgam reduction of **13** in tetrahydrofuran (THF)–water (9 : 1) gave the methyl ketone (**14**) in 72% yield from **12**. Acid treatment of **12** afforded the phenolic ketone (**15**), which was acetylated to give **16** in quantitative yield (overall yield *ca.* 25% from *p*-methoxyacetophenone). The acetate (**16**) was treated with isopropenyl acetate in the presence of sulfuric acid[13] to give the enol acetate (**17**) as a mixture of *E* and *Z* isomers in 71% yield. The reaction of **17** with bromine in carbon tetrachloride in the presence of potassium carbonate[14] produced the bromo ketone (**18**), which was converted to the phenolic α-bromo ketone (**19**) by acid treatment in 86% yield from **17**. Compound **19** was treated with potassium *tert*-butoxide in *tert*-butanol (Ar_1^--5 participating spiroannelation)[15] at 60 °C for 3.5 h to give the desired spirodienones (**10a** and **10b**) in 25% yield (**10a** : **10b** = 1 : 4) with recovery of the starting material (39%).[16] As this route required many steps to obtain the target compound, we investigated a shorter synthetic route to compound **15**. The Wittig reaction of 4-benzyloxyacetophenone (**20**)[17] with the ylide prepared from 3-(2-methyl-1,3-dioxolan-2-yl)propyltriphenylphosphonium bromide[18] and *n*-butyllithium in THF afforded the olefin (**21**) as a mixture of *E* and *Z* isomers in 30% yield. Compound **21** was hydrogenated in the presence of 10% palladium on carbon in ethyl alcohol under 5 atm of hydrogen to yield the phenolic ketal (**22**) in 91% yield, and **22** was hydrolyzed to give **15** in

quantitative yield (overall yield *ca.* 27% from **20**).

In the *cis*-ester (**9b**), the C_1-$COOCH_3$ (δ 3.48) and C_4-methyl (δ 0.79) signals appeared at higher fields than in the *trans*-ester (**9a**) (δ 3.59 and 0.86) in the proton nuclear magnetic resonance (^{1}H-NMR)spectra. On the other hand, the C_1-H signals (δ 3.01) in **9b** appeared at a lower field than in **9a** (δ 2.91), as described in the preceding paper.[11] It is readily predictable from these trends that **10a** [δ 0.83 (C_4-Me), 3.11 (C_1-H), 1.96 ($COCH_3$)] is *trans* and **10b** (δ 0.77, 3.18, and 1.86) is *cis*.



12 : R=OMe
13 : R=CH_2SOMe
14 : R=Me

15 : R=H
16 : R=Ac

17

18 : R=Ac
19 : R=H

20 **21** **22**

Chart 2

As the next step, it is important to introduce an asymmetry at the spiro center. For this purpose, we tried to link one of the C–C double bonds in the cyclohexadienone moiety with the side chain on the cyclopentane ring. We succeeded in converting **9** and **10** to the cyclopenta[*c*]benzofuran derivatives (**11a** and **11b**), which are versatile intermediates for the acorane-alaskane sesquiterpenes. The reductive fission of the allylic ether bond and the 1,4-reduction of the conjugated diene of **11a** would provide (±)-β-acorenol (**2**), and the metal–ammonia system should be suitable for these two reductions.

The esters (**9a** and **9b**) were each treated with excess methyllithium to give the unstable diols (**23a** and **23b**, respectively). Though the treatment of **23b** with magnesium perchlorate gave **11b** in 90% yield accompanied by the rearranged product (**24b**) (<5%), the same treatment of **23a** yielded mainly the rearranged product (**24a**) (40%), and the yield of **11a** was 27%. However, the yield of **11a** was somewhat improved (37%) by the treatment of **23a** with silica gel instead of magnesium perchlorate. The location of the methyl group on the benzene ring of the rearranged products (**24a** and **24b**) is clear from the coupling patterns of the aromatic protons. The signals of C_8-H appeared at the lowest field (δ 7.15 for **24a** and 7.24 for **24b**), affected by the C_1-isopropanol group, as a doublet (J=8 Hz, *ortho* coupling). Accordingly, it is evident that the methyl groups are located at C_6.

Though the spirodienone ketones (**10a** and **10b**) were subjected to the same reactions (methyllithium and subsequent Lewis acid treatment) to afford results similar to those of the esters (**9a** and **9b**), the treatment with methylmagnesium iodide under refluxing conditions directly gave **11a** (15%) together with **24a** (50%), and **11b** (55%) accompanied by **24b** (10%), respectively.

The A–C ring junction of **11b** is *cis*, on the basis of the reaction mechanism and the coupling constant of the allylic methine proton (C_{5a}-H). The attack of the hydroxy group of the C_1-substituent on the double bond (C_6)[19] (**23B** in Chart 3) would certainly result in the

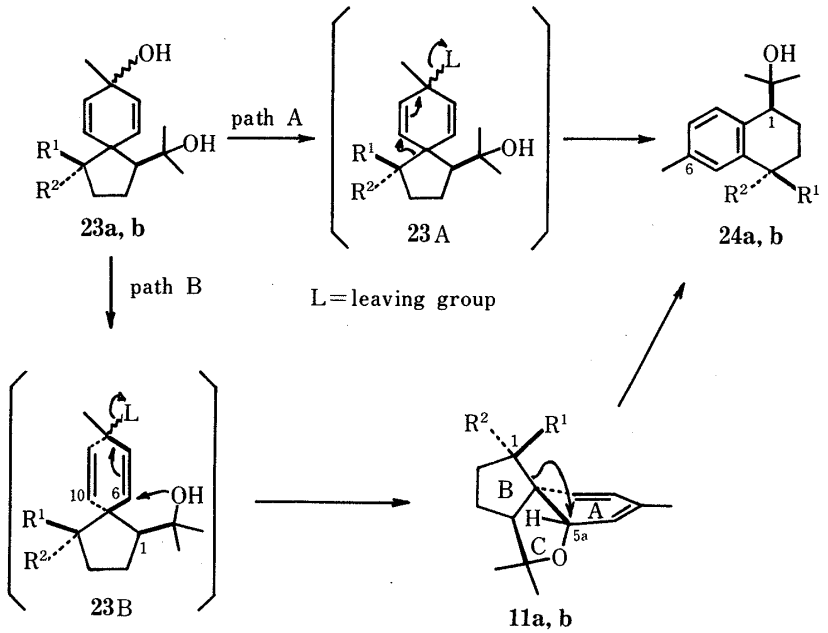


Chart 3

formation of an A–C *cis* compound. Though C_{5a}-H in the A–C *cis* compound can be both quasi-equatorial and quasi-axial, this proton in the A–C *trans* compound can only be quasi-axial. The *J* value (5 Hz) of C_{5a}-H of **11b** shows that this proton is quasi-equatorial.[20] Accordingly, the A–C ring junction can be concluded to be *cis*. Although the *J* value of this proton of **11a** is uncertain, the A–C ring fusion would be expected to be *cis* as in **11b**.

In the early stage, only **11a** was formed in the reaction of **23a** with magnesium perchlorate, but the amount of rearranged product (**24a**) increased with the reaction time, and finally **24a** became the main product. On the other hand, **23b** exclusively gave **11b**. The isolated **11a** was subjected to reaction with magnesium perchlorate to afford **24a**, but **11b** remained unchanged. Furthermore, **23a** and **23b** exclusively afforded **24a** and **24b**, respectively, under strongly acid conditions (*p*-TsOH). From the above results, it is thought that **11a**, **b** and **24a**, **b** are formed from **23a**, **b** through paths A and B as shown in Chart 3. Under strongly acid conditions, path A—dienol–benzene rearrangement (**23A**)—would be the main process, while under Lewis acid conditions, path B would become the main route. Compound **11a** is different from **11b** only in the configuration of the methyl group at C_1. This difference obviously reflects the instability of **11a**, namely the ease of rearrangement. In the case of **11b**, the C_1-methyl group covering the cyclohexadiene ring probably sterically disturbs the rearrangement in the transition state.

The cyclopenta[*c*]benzofuran derivative (**11a**) afforded (±)-*β*-acorenol (**2**) in one step in 81% yield when treated with 20 eq of lithium in liquid ammonia containing *tert*-butanol at −40 °C. *β*-Acorenol (**2**) was further transformed to 4-*epi*-acorenone (**26**)[8h] *via* (±)-*β*-acoradiene (**4**) as follows. Dehydration of **2** with alumina–pyridine[3,8a,9g,21] at 200 °C afforded **4** in 50% yield. Selective reduction of the terminal olefin of **4** with excess lithium in ethylamine at 0 °C[22] gave the mono olefin (**25**), which was oxidized with selenium dioxide in refluxing 95% ethyl alcohol to give **26**.

Compound, **2**, **4**, and **26** were identified by comparison of their infrared (IR) and ^{1}H-NMR spectra with those of authentic samples.

Experimental

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, q = quartet, 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) and silica gel column chromatography, Merck Kieselgel PF_{254} and Merck Kieselgel 60 (70—230 mesh) were used, respectively.

6-[4-(2-Tetrahydropyranyloxy)phenyl]-2-heptanone (14)——Dimethyl sulfoxide (DMSO) (13 ml) was added under N_2 to sodium hydride [a 50% dispersion in mineral oil (1.26 g), previously washed with pentane and dried *in vacuo*]. The mixture was stirred for 30 min at 70—80 °C to afford the dimsyl anion–DMSO solution. A solution of **12** (1.0 g) in THF (2 ml) was added dropwise to the anion solution (4 ml) diluted with THF (3 ml). After the mixture had been stirred for 50 min, it was poured into a satd. $NaHCO_3$ solution. The mixture was extracted with ether, and the extract was washed, dried, and evaporated to give the crude methanesulfinyl ketone (**13**) as a pale yellow oil (1.00 g). ^{1}H-NMR (CCl_4) δ: 1.18 (3H, d, J=6.5 Hz, C_7-H), 2.47 (3H, s, $SOCH_3$), 5.26 (1H, br s, anomeric H), 6.5—7.1 (4H, AA′BB′-type aromatic H). Aluminium chips (384 mg) were soaked in 2% $HgCl_2$ solution for 15 s, and the resulting aluminum amalgam was washed with EtOH, then ether. This amalgam was added to a solution of crude **13** (498 mg) in THF–water (9 : 1) (30 ml), and the mixture was stirred for 6.5 h at room temperature. After filtration of the reaction mixture, the filtrate was evaporated. Water was added to the residue, and the mixture was extracted with ether. The extract was washed, dried, and evaporated to give the crude product (436 mg), which was purified by PTLC (ether : petr. ether = 1 : 4) to afford **14** (341 mg) as a pale yellow oil in 72% yield from **12**. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725, 1615, 1590, 1510. ^{1}H-NMR (CCl_4) δ: 1.18 (3H, d, J=7 Hz, C_7-H), 1.93 (3H, s, C_1-H), 5.26 (1H, br s, anomeric H), 6.5—7.0 (4H, AA′BB′-type aromatic H). MS m/z: 290 (M^+). *Anal.* Calcd for $C_{18}H_{26}O_3$: C, 74.44; H, 9.03. Found: C, 74.09; H, 9.16.

6-(4-Hydroxyphenyl)-2-heptanone (15)——Conc. HCl (2.5 ml) was added to a solution of **14** (227 mg) in EtOH (10 ml), and the mixture was stirred at room temperature for 1 h. The mixture was poured into ice-water, and extracted with AcOEt. The extract was washed with satd. $NaHCO_3$ and water, then dried and evaporated. The residue was purified by PTLC ($CHCl_3$) to give **15** (161 mg) (100%) as a pale yellow oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720, 1620, 1600, 1520. ^{1}H-NMR (CCl_4) δ: 1.16 (3H, d, J=7 Hz, C_7-H), 1.3—1.6 (4H, m, C_4- and C_5-H), 2.01 (3H, s, C_1-H), 2.28 (2H, t-like, J=7 Hz, C_3-H), 2.54 (1H, m, C_6-H), 6.5—6.9 (4H, AA′BB′-type aromatic H). MS m/z: 206 (M^+). *Anal.* Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.99; H, 8.96.

6-(4-Acetoxyphenyl)-2-heptanone (16)——Acetic anhydride (0.54 ml) was added to a solution of **15** (161 mg) in pyridine (2 ml), and the mixture was stirred overnight. The reaction mixture was poured into ice-water, and extracted with AcOEt. The extract was washed with 2% HCl, water, satd. $NaHCO_3$, and water, then dried and evaporated. The residue was purified by PTLC (ether : petr. ether = 2 : 3) to give **16** (194 mg) (100%) as a pale yellow oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770, 1730, 1605, 1510. ^{1}H-NMR (CCl_4) δ: 1.22 (3H, d, J=7 Hz, C_7-H), 1.94 (3H, s, CH_3COO), 2.17 (3H, s, C_1-H), 6.7—7.3 (4H, AA′BB′-type aromatic H). MS m/z: 248 (M^+). High MS m/z: 248. 141 (Calcd for $C_{15}H_{20}O_3$: 248.141).

2-Acetoxy-6-(4-acetoxyphenyl)-2-heptene (17)——Compound **16** (2.0 g) was dissolved in isopropenyl acetate (8 ml), and a few drops of conc. H_2SO_4 were added at 0 °C. The mixture was stirred for 7 h at room temperature, and neutralized by the addition of triethylamine. The mixture was evaporated, and the residue was purified by silica gel column chromatography (benzene : chloroform = 3 : 1) to give **17** as an *E,Z* mixture (a pale yellow oil) in 71% yield with recovery of **16** (12%). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770, 1760, 1510. ^{1}H-NMR (CCl_4) δ: 1.21, 1.24 (3H, each d, J=6.5 Hz, C_7-H), 1.79 (3H, br s, C_1-H), 1.89, 1.97 (3H, each s, C_2-$OCOCH_3$), 2.18 (3H, s, Ar-$OCOCH_3$), 2.4—2.9 (1H, m, C_6-H), 4.5—5.0 (1H, m, C_3-H), 6.7—7.3 (4H, AA′BB′-type aromatic H). MS m/z: 290 (M^+). High MS m/z: 290.151 (Calcd for $C_{17}H_{22}O_4$: 290.152).

6-(4-Acetoxyphenyl)-3-bromo-2-heptanone (18)——A solution of bromine (0.8 ml) in CCl_4 (5 ml) was added dropwise to a mixture of **12** (2.94 g), CCl_4 (53 ml), and anhydrous K_2CO_3 (5.62 g) with stirring at 0 °C until the color of the bromine persisted for more than 5 min. Satd. $Na_2S_2O_3$ solution was added to the mixture, then the organic layer was separated. The water layer was extracted with CCl_4. The combined organic layer and the extract were washed with satd. $NaHCO_3$ and water, then dried, and evaporated to give crude **18** as an oil, which was used for the next reaction without purification. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1775, 1730, 1510. ^{1}H-NMR (CCl_4) δ: 1.23 (3H, d, J=6.5 Hz, C_7-H), 2.15 (6H, s, C_1-H and CH_3COO), 2.3—2.9 (1H, m, C_6-H), 3.5—4.2 (1H, m, C_3-H), 6.7—7.2 (4H, AA′BB′-type aromatic H). MS m/z: 328 (0.66), 326 (0.67). High MS m/z: 326.052 (Calcd for $C_{15}H_{19}BrO_3$: 326.052).

3-Bromo-6-(4-hydroxyphenyl)-2-heptanone (19)——A 2% solution of HCl (20 ml) was added to a solution of crude **18** (3.41 g) in EtOH (150 ml), and the mixture was heated at 80 °C with stirring for 1 h. After cooling, the mixture was poured into ice-water, and extracted with $CHCl_3$. The extract was washed with satd. $NaHCO_3$ and water, then dried and evaporated. The residue was purified by column chromatography (ether : petr. ether = 1 : 2) to give **19** as an oil in 86% yield from **17**. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 3430, 1725, 1615, 1520. ^{1}H-NMR (CCl_4) δ: 1.20 (3H, d, J=6.5 Hz, C_7-H), 1.4—2.1 (4H, m, C_4- and C_5-H), 2.24 (3H, s, C_1-H), 2.4—2.9 (1H, m, C_6-H), 3.7—4.3 (1H, m, C_3-

H), 5.66 (1H, m, OH), 6.6—7.0 (4H, AA'BB'-type aromatic H). MS *m/z*: 284 (2.1), 286 (2.0). High MS *m/z*: 284.042 (Calcd for $C_{13}H_{17}BrO_2$: 284.041).

(1*R,4*R**)- and (1*R**,4*S**)-1-Acetyl-4-methylspiro[4.5]deca-6,9-dien-8-one (10a and 10b)**——Potassium *tert*-butoxide (100 mg) was added to a solution of **19** (260 mg) in anhydrous *tert*-BuOH (15 ml), and the mixture was heated at 60 °C for 3.5 h. After cooling, the reaction mixture was poured into satd. $NaHCO_3$ containing crushed ice, and extracted with benzene. The extract was washed, dried over a mixture of anhydrous Na_2SO_4 and $CaCO_3$, and evaporated. The residue was purified by PTLC (ether : petr. ether = 3 : 2, developed twice) to give **10a** (5%) and **10b** (20%) with recovery of **19** (39%). **10a** (colorless oil): IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720, 1670, 1630. UV λ_{max}^{EtOH} nm (ε): 244 (13200). ^{1}H-NMR (CCl_4) δ: 0.83 (3H, d, *J* = 6 Hz, C_4-Me), 1.96 (3H, s, $COCH_3$), 3.11 (1H, t, *J* = 7.3 Hz, C_1-H), 5.9—7.0 (4H, m, olefinic H). MS *m/z*: 204 (M^+). High MS *m/z*: 204.114 (Calcd for $C_{13}H_{16}O_2$: 204.115). **10b** (colorless oil): IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1715, 1670, 1630. ^{1}H-NMR (CCl_4) δ: 0.77 (3H, d, *J* = 7 Hz, C_4-Me), 1.86 (3H, s, $COCH_3$), 3.18 (1H, t, *J* = 8.5 Hz, C_1-H), 5.9—6.9 (4H, m, olefinic H). UV λ_{max}^{EtOH} nm (ε): 247 (12100). MS *m/z*: 204 (M^+). High MS *m/z*: 204.115 (Calcd for $C_{13}H_{16}O_2$: 204.115).

2-[4-(4-Benzyloxyphenyl)-3-pentenyl]-2-methyl-1,3-dioxolane (21)——A 15% *n*-BuLi–hexane solution (34 ml) was added dropwise to a suspension of 3-(2-methyl-1,3-dioxolan-2-yl)propyltriphenylphosphonium bromide (22 g) and THF (100 ml) under stirring. After 1 h, a solution of 4-benzyloxyacetophenone (**20**) (10 g) in THF (30 ml) was added to the ylide solution, and stirring was continued for 8 h at room temperature. After the addition of MeOH (2 ml), the mixture was poured into satd. $NaHCO_3$ solution, and extracted with ether. The extract was washed with water, dried and evaporated. The residue was purified with alumina column chromatography (Merck Aluminum Oxid 90) (benzene : hexane = 1 : 1) to give **21** as an *E*,*Z* mixture (pale yellow oil) in 30% yield with recovery of **20** (25%). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1610, 1510. ^{1}H-NMR (CCl_4) δ: 1.19, 1.29 (3H, each s, CH_3–C(O)(O)–), 1.98 (3H, s, CH_3–C=), 3.77, 3.85 (4H, each s, OCH_2CH_2O), 4.99 (2H, s, OCH_2Ph), 5.35, 5.63 (1H, each t-like, olefinic H), 6.6—7.4 (9H, m, aromatic H). MS *m/z*: 338 (M^+). *Anal.* Calcd for $C_{22}H_{26}O_3$: C, 78.07; H, 7.74. Found: C, 77.79; H, 7.73.

2-[4-(4-Hydroxyphenyl)pentyl]-2-methyl-1,3-dioxolane (22)——A mixture of 10% Pd–C (200 mg), **21** (400 mg), and EtOH (15 ml) was shaken under 5 atm of H_2. After 1 h, the catalyst was filtered off, and the filtrate was evaporated to give **22** as a pale yellow oil in 91% yield. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610, 3400, 1620, 1600, 1520. ^{1}H-NMR (CCl_4) δ: 1.20 (3H, d, *J* = 7 Hz, CH_3–CH<), 1.23 (3H, s, CH_3–C(O)(O)–), 1.2—1.7 (6H, m), 2.52 (1H, m, CH_3–CH<), 3.82 (4H, s, OCH_2CH_2O), 6.5—7.0 (4H, AA'BB'-type aromatic H). MS *m/z*: 250 (M^+). High MS *m/z*: 250.157 (Calcd for $C_{15}H_{22}O_3$: 250.157).

(1*R,3a*R**,5a*R**,9a*R**)-2,3,3a,4-Tetrahydro-1,4,4,7-tetramethyl-1*H*,5a*H*-cyclopenta[*c*]benzofuran (11a) and (1*R**,4*S**)-1,2,3,4-Tetrahydro-1-(1-hydroxy-1-methyl)ethyl-4,6-dimethylnaphthalene (24a)**——An ether solution of MeLi (1 M, 6 ml) was added to a solution of **9a** (151 mg) in ether (6 ml) at 0 °C, and the mixture was stirred for 19 h at room temperature. After the addition of wet ether and crushed ice, the mixture was poured into satd. $NaHCO_3$ solution, and extracted with ether. The extract was washed, dried, and evaporated to give the crude dienic diol (**23a**), which was passed through a silica gel (Merck Kieselgel 60) column. The eluate was evaporated, the residue was purified by PTLC (ether : petr. ether = 1 : 10, developed twice) to give **11a** as a pale yellow oil (56 mg, 37% from **9a**) and **24a** as a colorless oil (53 mg, 35%). **11a**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3025, 1670. ^{1}H-NMR (CCl_4) δ: 0.87 (3H, d, *J* = 6.5 Hz, C_1-Me), 1.10, 1.13 (each 3H, s, C_4-Me_2), 1.77 (3H, br s, C_7-Me), 2.1—2.3 (1H, m, C_{3a}-H), 3.9—4.2 (1H, m, C_{5a}-H), 5.40 (1H, m, C_6-H), 5.5—5.8 (2H, AB q, C_8- and C_9-H). UV λ_{max}^{EtOH} nm (ε): 259 (4200). MS *m/z*: 218 (M^+). High MS *m/z*: 218.167 (Calcd for $C_{15}H_{22}O$: 218.167). **24a**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610, 3580, 1615. ^{1}H-NMR (CCl_4) δ: 1.01, 1.19 (each 3H, s, C_1-CMe_2OH), 1.26 (3H, d, *J* = 7 Hz, C_4-Me), 1.6—2.1 (4H, m), 2.26 (3H, s, C_6-Me), 2.5—3.0 (2H, m, C_1- and C_4-H), 6.78 (1H, br d, *J* = 8 Hz, C_7-H), 6.89 (1H, br s, C_5-H), 7.15 (1H, d, *J* = 8 Hz, C_8-H). MS *m/z*: 200 ($M^+ - H_2O$). High MS *m/z*: 200.156 (Calcd for $C_{15}H_{20}$: 200.157).

(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 (11b) and (1*R**,4*R**)-1,2,3,4-Tetrahydro-1-(1-hydroxy-1-methyl)ethyl-4,6-dimethylnaphthalene (24b)**——The crude dienic diol (**23b**) was obtained from **9b** in a manner similar to that described for the compound **23a**. A solution of crude **23b** in dry THF was stirred for 1 h with a small amount of magnesium perchlorate, and the mixture was poured into $NaHCO_3$ solution containing crushed ice, then extracted with AcOEt. The extract was washed, dried, and evaporated. The residue was purified by PTLC (ether : petr. ether = 1 : 10) to give **11b** as a pale yellow oil (90%) together with a small amount of **24b** as a colorless oil. **11b**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3025, 1675. ^{1}H-NMR (CCl_4) δ: 0.76 (3H, d, *J* = 6 Hz, C_1-Me), 1.09, 1.12 (each 3H, s, C_4-Me_2), 1.78 (3H, br s, C_7-Me), 2.1—2.4 (1H, m, C_{3a}-H), 4.02 (1H, br d, *J* = 5 Hz, C_{5a}-H), 5.4—5.6 (1H, m, C_6-H), 5.46 (1H, d, *J* = 9.5 Hz, C_9-H), 5.71 (1H, dd, *J* = 9.5 and 1 Hz, C_8-H). UV λ_{max}^{EtOH} nm (ε): 259 (3500). MS *m/z*: 218 (M^+). High MS *m/z*: 218.166 (Calcd for $C_{15}H_{22}O$: 218.167). **24b**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600, 3570, 1615. ^{1}H-NMR (CCl_4) δ: 1.12, 1.27 (each 3H, s, C_1-CMe_2OH), 1.31 (3H, d, *J* = 7 Hz, C_4-Me), 1.6—2.0 (4H, m), 2.25 (3H, s, C_6-Me), 2.5—3.0 (2H, m, C_1- and C_4-H), 6.77 (1H, br d, *J* = 8 Hz, C_7-H), 6.88 (1H, br s, C_5-H), 7.25 (1H, d, *J* = 8 Hz, C_8-H). MS *m/z*: 200 ($M^+ - H_2O$). High MS *m/z*: 200.155 (Calcd for $C_{15}H_{20}$: 200.157).

Similar results were obtained by the reaction of the ketones (**10a** and **10b**) with methyllithium followed by Lewis acid treatment. The reaction of the ketones (**10a** and **10b**) with methylmagnesium iodide was carried out as follows.

An ether solution of the ketones (**10a** and **10b**) was added at 0 °C to methylmagnesium iodide solution prepared from Mg and MeI in ether. The mixture was stirred at 0 °C for 1 h and refluxed for 2 h, then satd. NH_4Cl solution was added at 0 °C. The organic layer was separated, and the water layer was extracted with ether. The combined ether layer was washed with satd. $NaHCO_3$, and $Na_2S_2O_3$, then dried and evaporated. The residue was purified by PTLC to give **11a** (15%) and **24a** (50%) from **10a**, and **11b** (55%) and **24b** (10%) from **10b**.

(±)-β-Acorenol (2)——Lithium (52 mg) was added to a solution of **11a** (105 mg) in THF–*tert*-BuOH–liq. NH_3 (5/1/20 ml) at −40 °C under N_2, and the mixture was stirred at −40 °C for 3 h. After decomposition of lithium by the addition of NH_4Cl, the NH_3 was evaporated off. Satd. $NaHCO_3$ solution was added to the residue, and the whole was extracted with AcOEt. The extract was washed, dried, and evaporated. The residue was purified by PTLC (*n*-hexane : AcOEt = 10 : 1, developed 3 times) to give **2** as a colorless oil (87 mg) in 81% yield. IR ν_{max}^{film} cm^{-1}: 3410. ^{1}H-NMR (CCl_4) δ: 0.82 (3H, d, J = 7 Hz, C_4-Me), 0.96 (1H, br s, OH), 1.21, 1.27 (each 3H, s, C_1-C<u>Me</u>$_2$OH), 1.60 (3H, br s, C_8-Me), 2.36 (1H, br d, J = 16 Hz, C_6-H), 5.25 (1H, m, C_7-H). MS *m/z*: 204 ($M^+ - H_2O$). High MS *m/z*: 204.187 (Calcd for $C_{15}H_{24}$: 204.188).

(±)-β-Acoradiene (4)——A mixture of **2** (30 mg), Al_2O_3 (Woelm, neutral, activity I) (780 mg), and pyridine (1 ml) was heated at 200 °C in a sealed tube for 5 h. After cooling of the mixture, MeOH was added, and the whole was filtered. The filtrate was evaporated, then the residue was purified by PTLC (*n*-hexane) to give **4** (14 mg) in 50% yield. As this reaction sometimes failed and the yield was not constant, we performed the dehydration of **2** with thionyl chloride–pyridine. $SOCl_2$ (0.07 ml) was added to a solution of **2** (35 mg) in pyridine (1.6 ml) at 0 °C, and the mixture was stirred for 10 min. Na_2CO_3 (130 mg) in H_2O (1 ml) was added to the mixture, and the whole was extracted with AcOEt. The extract was washed with satd. tartaric acid solution, satd. $NaHCO_3$ solution, and satd. NaCl solution, then dried and evaporated. The residue was purified by PTLC (*n*-hexane) to give a mixture of **4** and β-alaskene (**6**) (unidentified) (*ca.* 10 : 1) in 96% yield, and this mixture was separated by HPLC (Waters, μ-Porasil semiprep. ×2, *n*-hexane, recycled 4 times) to give **4** in 75% yield. IR ν_{max}^{film} cm^{-1}: 1640. ^{1}H-NMR (CCl_4) δ: 0.84 (3H, d, J = 7 Hz, C_4-Me), 1.58 (3H, br s, C_1-C<u>Me</u>=CH_2), 1.71 (3H, br s, C_8-Me), 4.57, 4.71 (each 1H, br s, =CH_2), 5.23 (1H, m, C_7-H). MS *m/z*: 204 (M^+). High MS *m/z*: 204.189 (Calcd for $C_{15}H_{24}$: 204.188).

(1*R,4*S**,5*S**)-1-Isopropyl-4,8-dimethylspiro[4.5]dec-7-ene (25)**——A solution of **4** (18 mg) in THF–*tert*-BuOH (1 ml/0.3 ml) was added to the blue solution prepared from $EtNH_2$ (5 ml) and Li (50 mg) under N_2, and the mixture was stirred at room temperature for 30 min. After decomposition of Li by adding NH_4Cl to the reaction mixture, $EtNH_2$ was evaporated off. Satd. $NaHCO_3$ solution was added to the residue, and the whole was extracted with ether. The extract was washed, dried, and evaporated. The residue was purified by PTLC (*n*-hexane) to give **25** (17 mg) as a colorless oil in 94% yield. ^{1}H-NMR (CCl_4) δ: 0.81, 0.86, 0.93 (each 3H, d, J = 7 Hz, C_1-CH<u>Me</u>$_2$ and C_4-Me), 1.63 (3H, br s, C_8-Me), 5.24 (1H, m, C_7-H). MS *m/z*: 206 (M^+). High MS *m/z*: 206.203 (Calcd for $C_{15}H_{26}$: 206.204).

(1*R,4*S**,5*S**)-1-Isopropyl-4,8-dimethylspiro[4.5]dec-8-en-7-one (4-*epi*-Acorenone) (26)**——SeO_2 (17 mg) in 95% EtOH (1 ml) was added to a refluxing solution of **25** (10 mg) in 95% EtOH (1 ml), and the mixture was refluxed for 10 h. After cooling, the mixture was filtered, then the filtrate was evaporated. The residue was purified by PTLC (*n*-hexane : AcOEt = 10 : 1) to give **26** (7 mg) in 66% yield. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1675. ^{1}H-NMR (CCl_4) δ: 0.83, 0.85, 0.92 (each 3H, d, J = 6.5 Hz, C_1-CH<u>Me</u>$_2$ and C_4-Me), 1.75 (3H, br s, C_8-Me), 2.28, 2.46 (2H, AB q, C_6-H_2), 2.1—2.4 (2H, m, C_{10}-H_2), 6.59 (1H, m, C_9-H). UV λ_{max}^{EtOH} nm (ε): 238 (6700). MS *m/z*: 220 (M^+). High MS *m/z*: 220.183 (Calcd for $C_{15}H_{24}O$: 220.183).

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