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Structure of a Guaioxide-type Sesquiterpene from "San-shion"[1]

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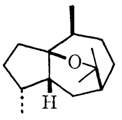
The structure including absolute stereochemistry of "LB", one of the volatile constituents of "San-shion" (the roots of *Ligularia* species), was found to be (1*S*,4*R*,5*S*,7*R*,10*R*)-5,11-epoxyguaiane.

In connection with chemical investigations on plants of the genus *Ligularia* (Compositae),[2] we examined the constituents of a Chinese drug "San-shion," the roots of a *Ligularia* genus,[3,4] and isolated five volatile constituents named tentatively LA-LE,[4] along with furanoligularenone[3] and ligularenolide.[5] Four of the volatile constituents, LA, LC, LD, and LE, were found to be identical with cyperene, liguloxide, *p*-cymene, and limonene, respectively.[4a,b] The identity of LB with ogarukaya-ether A, isolated from *Cymbopogon Goeringii* (Steud.) A. Camus, was confirmed by Fujita and Fujita,[6] structure **1** being proposed for ogarukaya-ether A based on biogenetic considerations.[6b] This paper deals with the structure determination leading to **2** for LB.

The molecular formula $C_{15}H_{26}O$ of LB was determined by elemental analysis and the appearance of a molecular ion peak at *m/e* 222 in the mass spectrum.[4a] The IR spectrum showed neither hydroxyl nor carbonyl absorption, the NMR spectrum suggesting the presence of two secondary and two tertiary methyl groups and the absence of olefinic proton (Experimental). The absence of unsaturated carbon–carbon linkage was revealed by treatment of LB with trifluoroperacetic acid which showed no consumption of the reagent. Thus, LB is a tricyclic saturated sesquiterpene containing an oxygen atom as a part of ether linkage. The absence of $-O-\overset{|}{C}\underline{H}-$ signal in the NMR spectrum suggests that both carbon atoms attached to the ether oxygen should be tertiary. Dehydrogenation of LB with palladium–charcoal gave *S*-guaiazulene as a major product and *Se*-guaiazulene as a minor one.[4a,b] Thus, two alternative structures (**A** and **B**; without stereochemical consideration) relating to a guaiane skeleton (**3**) can be suggested for LB.[4]



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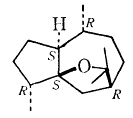

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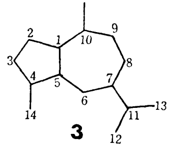

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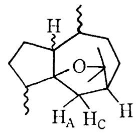
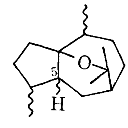


A



B

In the NMR spectrum of 1-epiguaioxide (**4**),[7,8] a double doublet signal due to $C_{(6\beta)}$–H (H_A; J=13 and J=6 Hz) appeared at δ 2.32 with small splittings (J=*ca.* 2 Hz). INDOR experiments[9] showed the presence of ABC-type spin-spin couplings for **4** (Fig. 1); the H_A proton couples with both the H_B proton (δ 1.87, dd, J=8 and J=6 Hz; $C_{(7\alpha)}$–H) and the H_C proton (δ 1.63, d, J=13 Hz; $C_{(6\alpha)}$–H). The small splittings are due to a W-letter long-range coupling between H_A and a proton on $C_{(8\beta)}$. The H_B proton couples further with the vicinal $C_{(8\beta)}$–proton (J=8 Hz). The presence of the same ABC-type spin-spin couplings was revealed for LB by INDOR experiments (Fig. 2). The H_A proton (δ 2.28, dd, J=13 and J=6.5 Hz; $C_{(6\beta)}$–H[10]) was found to couple with both the H_B proton (δ 1.96, dd, J=9[11] and J=6.5 Hz; $C_{(7\alpha)}$–H[10]) and the H_C proton (δ 1.69, d, J=13 Hz; $C_{(6\alpha)}$–H[10]); the coupling constant between H_B and H_C was almost null. The structure **A** can only account for these results, excluding the structure **B** with a $C_{(5)}$–proton for LB.

Eight diastereomers (**2** and **4**—**10**) can be present for structure **A** without consideration of their enantiomers. Six of them, 1-epiguaioxide (**4**),[7,8] guaioxide (**5**),[12] bulnesoxide (**6**),[13] liguloxide (**7**),[8] 10-epiliguloxide (**8**),[8] and 1-epiliguloxide (**9**),[14] have so far been reported. None of the spectral data of the six known

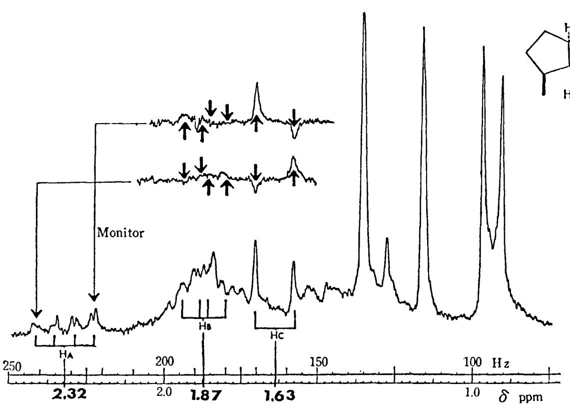


Fig. 1. INDOR experiments (100 MHz) for 1-epiguaioxide (**4**) in $CDCl_3$.

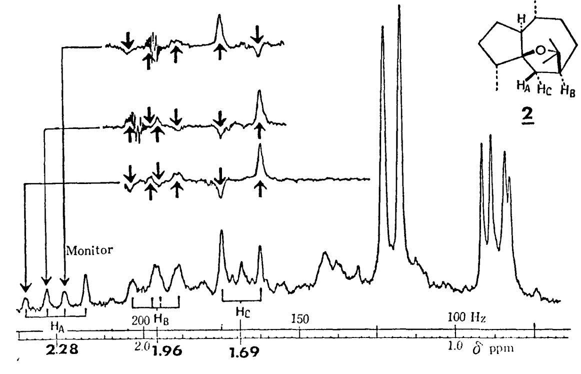
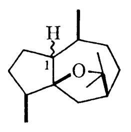
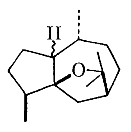


Fig. 2. INDOR experiments (100 MHz) for LB (**2**) in $CDCl_3$.

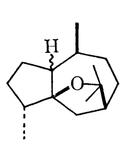
isomers are identical with those of LB. Thus, the structure of LB should be represented by either **2** or **10**, or by one of their enantiomers; the $C_{(1)}$–hydrogen atom and the $C_{(10)}$–methyl group are both oriented to the side opposite to the ether bridge for each of these structures.



5 1β-H
4 1α-H



6 1β-H
10 1α-H



7 1β-H
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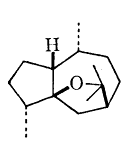

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Treatment of guaioxide (**5**) with *N*-bromosuccinimide (NBS) gave 4-bromoguaioxide which in turn afforded 3-dehydroguaioxide.[15] When LB was heated with 1.1—1.5 equivalent mol of NBS in carbon tetrachloride under reflux, a monobromide (**11**; $C_{15}H_{25}OBr$) and the unchanged LB were obtained in 8—17% and 67—83% yields, respectively. The NMR spectrum of **11** showed the presence of a secondary methyl and three tertiary methyl groups. One of the tertiary methyl signals appearing at δ 1.76 is due to $\underline{\mathrm{CH_3}}\text{–}\overset{|}{\underset{|}{\mathrm{C}}}\text{–Br}$. The bromide (**11**) was heated under reflux with potassium hydroxide in ethanol to give an olefin (**12**; $C_{15}H_{24}O$) in 76% yield. Hydroboration of **12** afforded an alcohol (**13**, $C_{15}H_{26}O_2$; 75% yield), which was oxidized with Jones reagent to give a ketone (**14**, $C_{15}H_{24}O_2$) in 81% yield. The IR spectrum ($\nu_{C=O}$ 1740 cm^{-1}) of **14** indicated the presence of five-membered ring ketone. This shows that the bromination of LB took place on $C_{(4)}$. The ketone (**14**) isomerized on a column of alumina into a hydroxy α,β-unsaturated ketone [**15**; λ_{max} 242 nm (ε 16700)] in 93% yield.[16] The NMR spectrum of **15** showed the presence of an olefinic methyl group (δ 1.70) and the absence of olefinic proton. The formation of the conjugated cyclopentenone derivative with an α-methyl group (**15**) from the ketone (**14**) provides further support for the location of an ether oxygen atom between $C_{(5)}$ and $C_{(11)}$ (structure **A**) rather than between $C_{(1)}$ and $C_{(11)}$ (structure **B**) for LB.

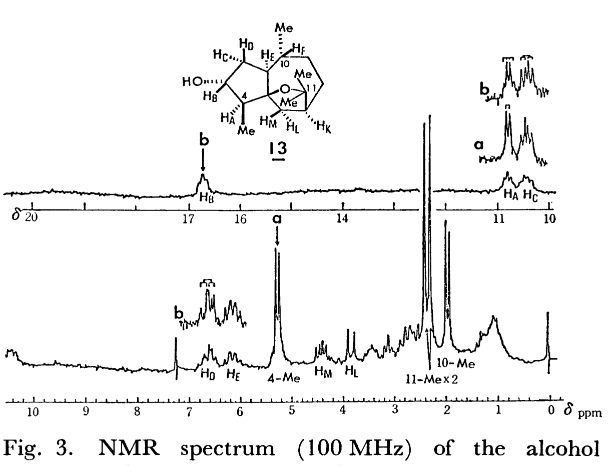
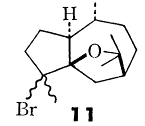


Fig. 3. NMR spectrum (100 MHz) of the alcohol (**13**) in $CDCl_3$ using Eu(fod)$_3$-d_{27} as a shift reagent [shift reagent/**13**=0.7 (M/M)]. NMDR experiments by irradiation of (a) $C_{(4)}$-CH_3 and (b) H_B are registered.

The hydroxy unsaturated ketone (**15**) was dehydrated to give an α,β: γ,δ-unsaturated ketone (**16**) quantitatively by refluxing with *p*-toluenesulfonic acid in benzene. The dienone (**16**) was found to be an enantiomer of known (1*R*,10*S*)-4,6-guaiadien-3-one (**17**)[15b)] derived from guaioxide (**5**). This leads to a (1*S*,10*R*)-stereochemistry for LB and its derivatives (**11**—**16**).



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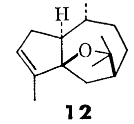

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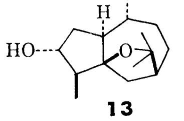

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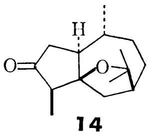

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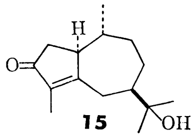

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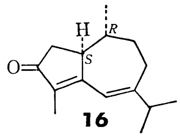

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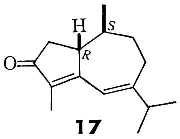

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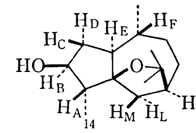

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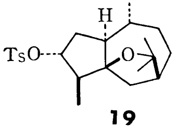

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The stereochemistry of the 3-hydroxy derivative (**13**) was determined as follows. Since a *cis*-relationship between the hydroxyl group and a hydrogen atom on $C_{(4)}$ is required by the mode of formation, two alternative structures, **13** and **18**, can be suggested for the alcohol. The NMR measurements using Eu(fod)$_3$-d_{27} as a shift reagent coupled with NMDR experiments lead to the assignment of signals as shown in Fig. 3, when a $C_{(2)}$–hydrogen atom *cis* to the hydroxyl group is designated as H_C. The coupling constants in a first-order approximation were determined to be $J_{A,14}=7$, $J_{A,B}=7$, $J_{B,C}=2$, $J_{B,D}=8.5$, $J_{C,D}=13.5$, $J_{C,E}=8$, $J_{D,E}=10.5$, and $J_{E,F}=10$ Hz. The structure of **13** rather than **18** is shown for the alcohol, since $J_{D,E}$ was found to be greater than $J_{C,E}$ and a large lanthanoid induced shift was observed for H_E. The structure **14** fits the ketone which exhibited a negative Cotton effect ($[\theta]_{295}-12900$), while 3-oxo-4-epiguaioxide (3-oxoliguloxide) showed a positive Cotton effect (a $+273$[12)]).

Hydrogenation of 3-dehydro LB (**12**) over platinum catalyst gave a saturated ether (4-epi LB) as the sole product in 60% yield, which was found to be not identical with LB; no LB was formed. The alcohol (**13**) was converted into a tosylate (**19**) in 90% yield. Treatment of **19** with lithium aluminium hydride gave a saturated ether (**10**) and the hydroxy ether (**13**) in 18 and 67% yields, respectively. Compound (**10**) was found to be identical with 4-epi LB mentioned above. Thus, the structure of 4-epi LB is shown by **10**, in which the $C_{(4)}$–methyl group should be in a $\beta(4S)$-configuration. This leads to the structure **2** with the $C_{(4)}$–methyl group in an $\alpha(4R)$-stereochemistry for LB.

In conclusion, the structures including absolute configuration of LB and 4-epi LB are found to be (1*S*,4*R*,5*S*,7*R*,10*R*)-5,11-epoxyguaiane (**2**) and (1*S*,4*S*,5*S*,7*R*,10*R*)-5,11-epoxyguaiane (**10**), respectively. Thus, all the diastereomers (**2** and **4**—**10**) represented by **A** (5,11-epoxyguaiane) have now been recorded.

Experimental

IR and UV spectra were measured with a Hitachi EPI-G2 spectrometer and a Hitachi 340 spectrophotometer, respectively, ^{1}H-NMR spectra with a JEOL PS-100 (100 MHz), a Varian HA-100 (100 MHz), or a Hitachi R-20B (60 MHz) spectrometer in deuteriochloroform solution containing tetramethylsilane as an internal standard, low resolution mass spectra with a Hitachi RMU-6-Tokugata mass spectrometer and high resolution mass spectra with a Hitachi RMH-2 or a JEOL D-300 mass spectrometer, with direct inlet system operating at 70 eV. CD spectra were carried out on a JASCO model J-20. For column chromatography Wakogel C-200 (Wako Pure Chemical Industries) was used. Thin-layer chromatography (TLC) was carried out on Kieselgel GF_{254} (E. Merck, Darmstadt) in 0.25 mm thickness, and vapor-phase chromatography (VPC) on a Shimadzu gas chromatograph model GC-2C.

Isolation of LB (2). LB (**2**; 340 mg) was isolated by the reported procedure[4a)] from the benzene extract of the drug (7.7 kg) in a 0.0046% yield: a colorless oil, $[\alpha]_{578}$ $-45°$ (*c* 2.0, $CHCl_3$); IR (film): 1380, 1365, 1160, 1150, 1100, 1020, 1010, 980, and 895 cm^{-1}; NMR: δ 0.87 (3H, d, $J=$ 5.5 Hz) and δ 0.89 (3H, d, $J=7.5$ Hz; $C_{(4)}$–CH_3 and $C_{(10)}$–CH_3), δ 1.18 and 1.24 [each 3H, s; $C_{(11)}$–$(CH_3)_2$].

Bromination of LB (2) with NBS. NBS (1.00 g; 5.62 mmol) was added to a solution of LB (**2**, 970 mg; 4.37 mmol) in carbon tetrachloride (15 ml), and the mixture was heated under reflux for 2.5 h with an infrared lamp. The reaction mixture was cooled and filtered. After removal of solvent under reduced pressure, the resulting residue was chromatographed on a column of silica gel. Elution with petroleum ether–benzene (*ca.* 4:1) gave a 4-bromo LB (**11**, 140 mg; 11% yield), an oil, IR (film): 1150, 1020, 1000, 895, and 805 cm^{-1}; NMR: δ 0.85—0.95 (3H, diffused d; $C_{(10)}$–CH_3), δ 1.20 and 1.22 [each 3H, s; $C_{(11)}$–$(CH_3)_2$], and δ 1.76 (3H, s; $C_{(4)}$–CH_3); MS: *m/e* 302 and 300 (relative abundance, each 15%; M^+), *m/e* 287 and 285 [each 100%; $(M-CH_3)^+$], and *m/e* 221 [40%; $(M-Br)^+$]. Found: *m/e* 302.1070. Calcd for $C_{15}H_{25}O^{81}Br$: M, 302.1069. Found: *m/e* 300.1115. Calcd for $C_{15}H_{25}O^{79}Br$: M, 300.1089. Successive elution with the same solvent mixture gave the starting compound (LB; **2**, 800 mg; 82.5%). Bromide (**11**), obtained in 8—17% yields, showed one spot on thin-layer chromatogram. The NMR spectrum showed methyl signals corresponding to one configurational isomer; the configuration at $C_{(4)}$ of **11** was left undetermined.

Dehydrobromination of the 4-Bromo LB (11). The bromide (**11**; 170 mg; 0.56 mmol) in an ethanolic potassium hydroxide (KOH 350 mg, EtOH 8 ml) was heated under reflux for 1.5 h and the reaction mixture was treated in the usual way to give a residue which was chromatographed on a column of silica gel. Elution with petroleum ether–benzene (1:1) gave an olefin (3-dehydro LB; **12**; 95 mg; 76% yield), an oil, IR (film): 1155, 1010, 995, 885, and 820 cm^{-1}; NMR: δ 0.88 (3H, d, $J=6$ Hz; $C_{(10)}$–CH_3), δ 1.20 and 1.27 [each 3H, s; $C_{(11)}$–$(CH_3)_2$], δ 1.74 (3H, br s; $C_{(4)}$–CH_3), and δ 5.65 (1H, m; $C_{(3)}$–H); MS: *m/e* 220 (52%; M^+), *m/e* 205 [77%; $(M-CH_3)^+$], *m/e* 202 [66%; $(M-H_2O)^+$], *m/e* 187 [63%; $(C_{14}H_{19})^+$], and *m/e* 159 [100%; $(C_{12}H_{15})^+$]. Found: *m/e* 220.1824. Calcd for $C_{15}H_{24}O$: M, 220.1827.

Hydroboration of the 3-Dehydro LB (12). A solution of diborane (3 mmol) in tetrahydrofuran (3 ml) was added dropwise to a solution of the olefin (**12**, 62 mg; 0.28 mmol) in tetrahydrofuran (4 ml) under a nitrogen atmosphere. After the mixture had been stirred at room temperature for 40 min, a small quantity of water, 2 ml of 3 M aqueous solution of sodium hydroxide, and 2 ml of 30% aqueous hydrogen peroxide solution were added in succession. The resulting mixture was stirred at 50 °C for 1.5 h, and then treated in the usual way to give a residue which was chromatographed on a column of silica gel. Elution with benzene–ether (4:1) gave a 3α-hydroxy 4-epi LB (**13**, 49 mg; 75% yield), white crystals, mp 84—85 °C (crystallized from benzene); IR (KBr disk): 3250 (br), 1150, 1100, 1065, 990, 980, 890, 800, and 770 cm^{-1}; NMR: δ 0.85 (3H, diffused d; $C_{(10)}$–CH_3), δ 1.04 (3H, d, $J=7$ Hz; $C_{(4)}$–CH_3), δ 1.17 and 1.26 [each 3H, s; $C_{(11)}$–$(CH_3)_2$], and δ 3.93 (1H, m; $C_{(3)}$–H); the NMR spectrum with addition of $Eu(fod)_3$-d_{27} (Fig. 3); MS: *m/e* 238 (73%; M^+), *m/e* 223 [100%; $(M-CH_3)^+$], *m/e* 220 [28%; $(M-H_2O)^+$], and *m/e* 205 [64%; $(C_{14}H_{21}O)^+$]. Found: *m/e* 238.1920. Calcd for $C_{15}H_{26}O_2$: M, 238.1932.

Oxidation of 3α-Hydroxy 4-Epi LB (13). A few drops of Jones reagent were added slowly to a stirred solution of the alcohol (**13**, 25 mg; 0.10 mmol) in acetone (1 ml) at 0—10 °C, and the mixture was further stirred for 10 min at the same temperature. The reaction mixture was treated in the usual way to give a residue which was chromatographed on a column of silica gel. Elution with benzene–ether (10:1) gave a ketone (3-oxo 4-epi LB; **14**; 20 mg; 81% yield), white crystals, mp 63—64 °C (crystallized from benzene); IR: (KBr disk): 1740, 1180, 1120, 1010, 995, 990, 890, 875, and 820 cm^{-1}; CD (*c* 1.17×10^{-3}, EtOH): $[\theta]_{330}$ ±0, $[\theta]_{295}$ -12900, $[\theta]_{250}$ ±0; NMR: δ 0.89 (3H, d, $J=6$ Hz; $C_{(10)}$–CH_3), δ 1.03 (3H, d, $J=7$ Hz; $C_{(4)}$–CH_3), δ 1.16 and 1.25 [each 3H, s; $C_{(11)}$–$(CH_3)_2$], and δ 2.20 (1H, q, $J=7$ Hz, $C_{(4\alpha)}$–H); MS: *m/e* 236 (90%; M^+), *m/e* 221 [100%; $(M-CH_3)^+$], *m/e* 218 [29%; $(M-H_2O)^+$], and *m/e* 203 [40%; $(C_{14}H_{19}O)^+$]. Found: *m/e* 236.1786. Calcd for $C_{15}H_{24}O_2$: M, 236.1776.

Isomerization of 3-Oxo 4-Epi LB (14) on Alumina. The ketone (**14**; 10 mg; 0.04 mmol) in a small amount of ether (*ca.* 3 ml) was placed on the top of a column of neutral alumina (5 g). After 4 h, elution with ether gave a hydroxy α,β-unsaturated ketone (**15**, 9.3 mg; 93% yield) as white crystals, mp 57—58.5 °C (crystallized from AcOEt); IR (KBr disk): 3450, 3250, 1675, 1610, 1140, and 970 cm^{-1}; UV (EtOH): λ_{max} 242 nm (ε 16700); NMR: δ 1.06 (3H, d, $J=5$ Hz; $C_{(10)}$–CH_3), δ 1.24 and 1.28 [each 3H, s; $C_{(11)}$–$(CH_3)_2$], and δ 1.70 (3H, s; $C_{(4)}$–CH_3); MS: *m/e* 236 (1%; M^+), *m/e* 221 [5%; $(M-CH_3)^+$], *m/e* 218 [100%; $(M-H_2O)^+$], and *m/e* 178 [18%; $(C_{12}H_{18}O)^+$]. Found: *m/e* 236.1783. Calcd for $C_{15}H_{24}O_2$: M, 236.1776.

Dehydration of the Hydroxy α,β-Unsaturated Ketone (15). *p*-Toluenesulfonic acid (18 mg; 0.10 mmol) was added to a solution of the hydroxy α,β-unsaturated ketone (**15**, 8.5 mg; 0.036 mmol) in benzene (5 ml) and the solution was heated under reflux for 1.5 h under a nitrogen atmosphere. The reaction mixture was treated in the usual way to give a single product, (1*S*, 10*R*)-4,6-guaiadien-3-one (**16**; 7.6 mg; quantitative yield), an oil; IR (film): 1690, 1625, 1590, 1340, 1285, 1055, and 875 cm^{-1}; UV (EtOH): λ_{max} 293 nm (ε 20800); CD (c 3.50×10^{-4}, EtOH): $[\theta]_{365}$ ±0, $[\theta]_{295}$ -20300, $[\theta]_{240}$ ±0; NMR: δ 1.06 (3H, d, J=6 Hz; $C_{(10)}$-CH_3), δ 1.09 [6H, d, J=7 Hz; $C_{(11)}$-$(CH_3)_2$], δ 1.75 (3H, s; $C_{(4)}$-CH_3), and δ 6.35 (1H, br s; $C_{(6)}$-H); MS: m/e 218 (100%; M^+), m/e 203 [27%; $(M-CH_3)^+$], and m/e 175 [37%; $(M-C_3H_7)^+$]. Found: m/e 218.1682. Calcd for $C_{15}H_{22}O$: M, 218.1671.

The IR, UV, NMR, and mass spectra of **16** were found to be identical with those of known (1*R*, 10*S*)-4,6-guaiadien-3-one (**17**).[15b] The dienone (**16**) exhibits a negative Cotton effect and **17** a positive CD maximum ($[\theta]_{295}$ $+18300$).[15b]

Hydrogenation of 3-Dehydro LB (12). 3-Dehydro LB (**12**, 15 mg; 0.07 mmol) and platinum catalyst (prepared from platinum oxide; 10 mg) in a mixture of ethyl acetate (5 ml) and acetic acid (0.3 ml) were stirred under a hydrogen atmosphere at room temperature for 5 h. The catalyst was removed by filtration and the solvents evaporated to give a residue, which was purified by chromatography on a column of silica gel. Elution with petroleum ether–benzene (5:1) gave 4-epi LB (**10**, 9 mg; 60% yield). No LB (**2**) was obtained. On VPC examination (7% SE-30; 2.3 m; 125 °C; N_2 50 ml/min), the retention time of 4-epi LB (**10**) was found to be 12.3 min, and that of authentic LB (**2**) 11.1 min under the same conditions. 4-Epi LB (**10**), an oil; IR (film): 1150, 1140, 1020, 995, and 895 cm^{-1}; NMR: δ 0.85 (3H, diffused d) and δ 0.95 (3H, d, J=6 Hz; $C_{(4)}$-CH_3 and $C_{(10)}$-CH_3), δ 1.19 and 1.29 [each 3H, s; $C_{(11)}$-$(CH_3)_2$], and δ 2.15 (1H, dd, J=5 Hz and 12 Hz; $C_{(6\beta)}$-H); MS: m/e 222 (20%; M^+), m/e 207 [100%; $(M-CH_3)^+$], m/e 189 [40%; $(C_{14}H_{21})^+$], and m/e 164 [45%; $(C_{12}H_{20})^+$]. Found: m/e 222.1948. Calcd for $C_{15}H_{26}O$: M, 222.1983.

Tosylation of 3α-Hydroxy 4-Epi LB (13). A mixture of the alcohol (**13**, 49 mg; 0.21 mmol) and *p*-toluenesulfonyl chloride (100 mg; 0.53 mmol) in dry pyridine (1 ml) was left at 0 °C for 72 h under a nitrogen atmosphere. After the usual treatment, a tosylate (**19**, 75 mg; 90% yield) was obtained as white crystals. 3α-Tosyloxy 4-epi LB (**19**), mp 119—121 °C (dec.) (crystallized from MeOH–$CHCl_3$); IR (KBr disk): 1640 (w), 1335, 1175, 1100, 985, 955, and 865 cm^{-1}; NMR: δ 0.82 (3H, d, J=4 Hz) and δ 0.83 (3H, d, J=7 Hz; $C_{(4)}$-CH_3 and $C_{(10)}$-CH_3), δ 1.14 and 1.28 [each 3H, s; $C_{(11)}$-$(CH_3)_2$], δ 2.46 (3H, s; aromatic CH_3), δ *ca.* 4.5 (1H, m; $C_{(3\beta)}$-H), and δ 7.37 and 7.84 (each 2H, d, J=8.5 Hz; aromatic H's); MS: m/e 392 (1%; M^+), m/e 377 [2%; $(M-CH_3)^+$], m/e 237 [95%; $(C_{15}H_{25}O_2)^+$], m/e 220 [49%; $(C_{15}H_{24}O)^+$], and m/e 205 [100%; $(C_{14}H_{21}O)^+$]. Found: m/e 392.2021. Calcd for $C_{22}H_{32}O_4S$: M, 392.2021.

Reaction of the Tosylate (19) with Lithium Aluminium Hydride. A mixture of the tosylate (**19**, 20 mg; 0.05 mmol) and lithium aluminium hydride (50 mg; 1.3 mmol) in dry tetrahydrofuran (6 ml) was heated under reflux for 10 h under a nitrogen atmosphere. The reaction mixture was treated in the usual way to give a residue, which was chromatographed on a column of silica gel. Elution with benzene gave 4-epi LB (**10**, 2 mg; 18% yield), identical [TLC, VPC (SE-30), IR, and MS] with an authentic specimen. Successive elution with benzene-ether (2:1) gave 3α-hydroxy 4-epi LB (**13**, 8 mg; 67% yield).

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