[Chem. Pharm. Bull. 22(2) 280—285 (1974)]

UDC 547.913.6.02 : 581.192

Terpenoids. XXVI.[1] Structures of Lasiokaurinol and Lasiokaurinin, Two Novel Diterpenoids of *Isodon lasiocarpus* (Hayata) Kudo

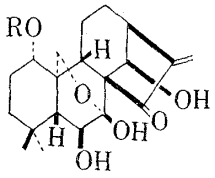
Eiichi Fujita, Manabu Taoka, and Tetsuro Fujita

Institute for Chemical Research, Kyoto University[2]

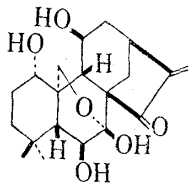
(Received March 30, 1973)

On the basis of chemical and spectroscopic evidence, the structure and absolute configuration of lasiokaurinol isolated from *Isodon lasiocarpus* (Hayata) Kudo were established as *ent*-1β-acetoxy-7β,20-epoxy-16-kaurene-6α,7α,14α,15α-tetraol (**9**). The structure of another minor diterpenoid, lasiokaurinin, was proposed as **10** on the basis of spectroscopic evidence. Some chemical reactions confirmed its structure and relative stereochemistry as **10**.

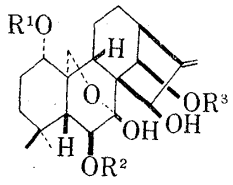
We have previously isolated oridonin (**1**),[3] lasiokaurin (**2**),[4] and lasiodonin (**3**)[4] from *Isodon lasiocarpus* (Hayata) Kudo (Japanese name: Taiwan-hikiokoshi), and determined their structures. We report here studies on two novel diterpenoids, lasiokaurinol and lasiokaurinin, which establish their structures.



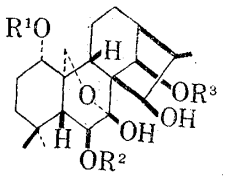
1: R=H
2: R=Ac



3



4: $R^1=R^2=R^3=H$
8: $R^1=R^2=R^3=Ac$
9: $R^1=Ac$, $R^2=R^3=H$



5: $R^1=R^2=R^3=H$
6: $R^1=Ac$, $R^2=R^3=H$
7: $R^1=R^2=R^3=Ac$

Lasiokaurinol, mp 143—147° and 218—221°, $[\alpha]_D^{27}$ -12°, was isolated as needles from the ethereal extract of the same plant. Its molecular formula was determined as $C_{22}H_{32}O_7$ on the basis of the high resolution mass spectrum. A close similarity between the structures of lasiokaurinol and lasiokaurin ($C_{22}H_{30}O_7$) (**2**) was shown by their nuclear magnetic resonance (NMR) spectra. Lasiokaurinol on treatment with lithium aluminum hydride gave a deacetylated product, whose infrared (IR) spectrum was superimposable with that of the known enmenol (**4**).[5] The melting point was also the same with the datum reported, and the dihydro-derivative of this compound was identical with the known oridonin tetrahydro-derivative (**5**).[3,5] Acetylation of lasiokaurinol dihydro-derivative (**6**) afforded the known triacetate (**7**)[3,5] of oridonin tetrahydro-derivative. Finally, the reduction of lasiokaurin (**2**) with sodium borohydride at 0° gave lasiokaurinol itself as a minor product accompanied by a major tetrahydro-derivative.

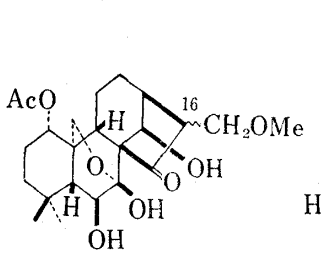
Thus, the structure and absolute configuration of lasiokaurinol were established as *ent*-1β-acetoxy-7β,20-epoxy-16-kaurene-6α,7α,14α,15α-tetraol (**9**). The acetylation product of lasiokaurinol was determined as **8**.

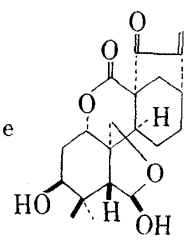
1) Part XXV: E. Fujita, M. Taoka, Y. Nagao, and T. Fujita, *J. C. S. Perkin I*, **1973**, 1760.
2) Location: *Uji, Kyoto, 611, Japan.*
3) E. Fujita, T. Fujita, H. Katayama, M. Shibuya, and T. Shingu, *J. Chem. Soc.* (*C*), **1970**, 1674.
4) E. Fujita and M. Taoka, *Chem. Pharm. Bull.* (Tokyo), **20**, 1752 (1972).
5) S. Mori, K. Shudo, T. Ageta, T. Koizumi, and T. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 871 (1970).

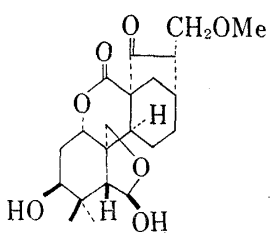
Lasiokaurinin, another minor diterpenoid, was isolated as crystals of mp 219—222° (decomp.), $[\alpha]_D^{27}$-14°. The molecular formula was determined as $C_{23}H_{34}O_8$. The NMR spectrum pattern suggested it to belong to a kaurane-type 7-hemiacetal-6-ol which is common among all the diterpenoids found hitherto in this plant. A comparison of its NMR spectrum with that of lasiokaurin (**2**), the known major diterpenoid, suggested the presence of an equatorial acetoxy group at C-1 and of a secondary hydroxy group at C-14 having such a same relative stereochemistry as **2**. It was very characteristic that any signals assignable to exocyclic methylene protons at C-17 which were common to all the kaurene-type diterpenoids found hitherto in *Isodon* species were not found, but instead, a doublet (2H, J=7 Hz) at δ 3.93 and a singlet (3H) at δ 3.27 which were attributable to a methoxymethyl group like isodotricin[6] were observed in the NMR spectrum in pentadeuteriopyridine (D_5-pyridine). The configuration of this methoxymethyl group was assigned to "*exo*" because of an intramolecular hydrogen-bonding between 14-hydroxy and 17-methoxy groups. This hydrogen-bonding was recognized by the following NMR observations: (i) The 17-methylene protons appeared as the AB part of an ABX type at δ 3.50—3.90 in deuteriochloroform ($CDCl_3$), but they changed to a doublet in D_5-pyridine. (ii) The 14-proton was observed as a multiplet in $CDCl_3$, and changed to a broad singlet by treatment with deuteroxide. (iii) The 14-hydroxy proton was observed as a doublet (J=10 Hz) at δ 5.72 in $CDCl_3$. The rate of deuterium exchange was considerably slow.

The remaining question is an additional oxygen atom, which is assumed to be present at C-15 as a ketone by analogy with the diterpenoids found hitherto. The IR absortipon at 1720 cm^{-1} is regarded as an overlap of absorptions due to acetate and ketone. This IR shift to lower wavenumber for a cyclopentanone is reasonably explained by an intramolecular hydrogen-bonding between the ketone and the 6-hydroxy group just as in oridonin.[3] This hydrogen-bonding is confirmed by the following NMR data. (i) The exchange rate of the 6-hydroxy proton (δ^{CDCl_3} 6.30, br. s) to deuterium was slow. (ii) The broad doublet in $CDCl_3$ due to the 6-proton changed to a more sharp doublet by deuteroxide. The structure and stereochemistry of lasiokaurinin were, thus, presented as **10** (or its antipode).

In order to confirm this proposal, the following reactions were carried out. Lasiokaurin (**2**) on treatment with methanol in the presence of *p*-toluenesulfonic acid under reflux gave a methanol adduct **11**, which was different from lasiokaurinin, but had the same molecular formula, and showed very similar NMR, IR, and mass spectra, when compared with lasiokaurinin. As reported[6] previously, enmein (**12**) on same treatment as above followed by acidic hydrolysis gave isodotricin (**13**), whose 16-methoxymethyl group was proved to have an *endo- i.e.* α-configuration. The foregoing methanol adduct also should have an *endo- i.e.* β-methoxymethyl group at C-16 as shown in formula **11**.





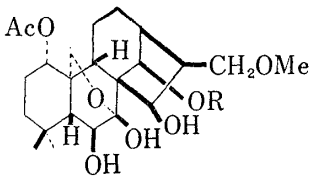


10: α-CH_2OMe, β=H at C-16
11: α-H, β-CH_2OMe at C-16

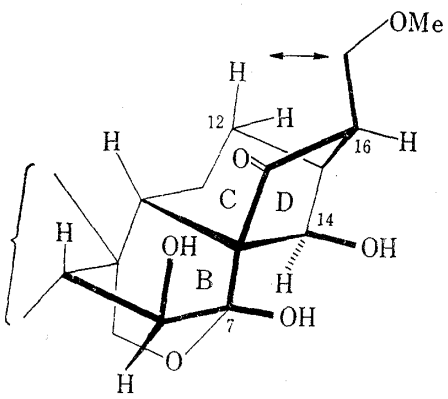
12 **13**

6) E. Fujita, T. Fujita, Y. Okada, S. Nakamura, and M. Shibuya, *Chem. Pharm. Bull.* (Tokyo), **20**, 2377 (1972).

The methanol adduct **11** on sodium borohydride reduction gave an alcohol (**14**) whose NMR spectrum suggested a *cis*-relationship between the C-15 and C-16 substituents (1H, doublet, J=10 Hz, C-15-H). Since the 15-hydroxy-group should be β-oriented by an attack of the hydride reagent from the less-hindered α-side, the 16-methoxymethyl group must be β-oriented. The same conclusion was also obtained from an NMR investigation of the acetate **15**. The foregoing facts confirmed the stereochemistry **11** for the methanol-adduct of lasiokaurin. Accordingly, lasiokaurinin must be the 16-epimer of lasiokaurin methanol-adduct.



14: R=H
15: R=Ac



16

A comparison of the NMR spectra (Fig. 1) in D_5-pyridine of lasiokaurinin and lasiokaurin methanol-adduct (**11**) indicated a characteristic difference on signals of 16- and 17-protons. As described above, the 17-methylene protons were observed as a doublet (J=7 Hz) at δ 3.93 in lasiokaurinin, while the 16- and 17-protons in **11** appeared as an AB_2 at δ 3.78. The 16-hydrogen of **11** is surrounded by three oxygen atoms as shown in formula **16**. As the methoxymethyl group at C-16 is pushed out, in order to relieve a spacial crowd, especially the *endo*-steric interaction[7] with the axial 12-hydrogen, the 16-hydrogen results in getting more close to 14- and 7-hydroxy-groups. Presumably, this is why the 16-proton signal caused such a characteristic paramagnetic shift. On the other hand, the methoxy group gets close to 14-hydroxy group in lasiokaurinin, which results in the foregoing intramolecular hydrogen-bonding between them. These facts well supports the epimeric relationship of both compounds. Furthermore, their mass spectra show a similar fragmentation as shown in Table I.

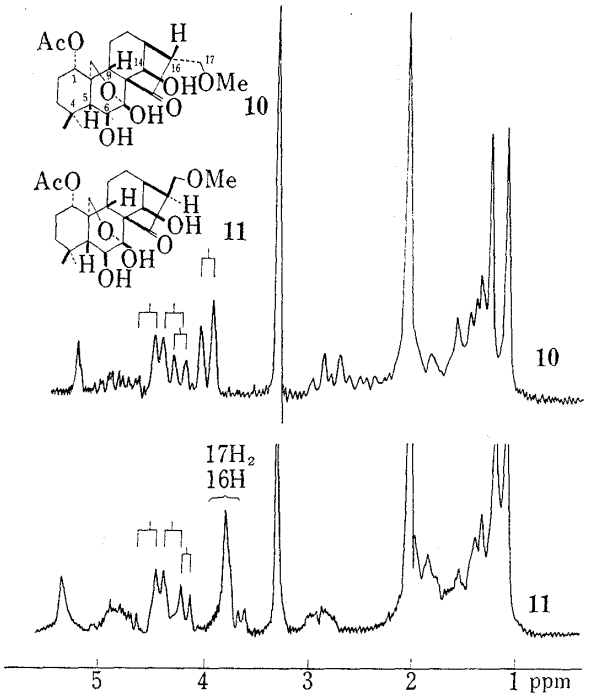


Fig. 1. NMR (D_5-pyridine) Spectra of **10** and **11**

7) Cf. J. MacMillan and E.R.H. Walker, *J. C. S. Perkin I*, **1972**, 1272.

Table I. Mass Spectra of **10** and **11**

m/e	438 (M^+)	420	410	406	392	388	378	360	346	342	332	328	310	300
10(%)	5	4	3	8	66	5	13	100	8	13	19	16	8	21
11(%)	14	5	24	80	48	24	11	100	48	20	24	48	28	56

Subsequently, lasiokaurinin was treated with *p*-toluenesulfonic acid in absolute methanol for a long time. A chromatography of the mixture on a silica gel column succeeded in separation of lasiokaurin (**2**) or its antipode and lasiokaurinin 16-epimer (**11** or its antipode) as crystals. Because of very small amount of the materials, the establishment of the absolute configuration of lasiokaurinin was not accomplished, but its structure and stereochemistry were, thus, established as **10**.

Experimental

Melting points were taken on a micro hot-stage and are uncorrected. Unless otherwise stated, IR spectra were recorded in KBr discs on a Hitachi model EPI-S2 spectrometer and NMR spectra with a Varian T-60 spectrometer in deuteriochloroform; signals are reported in ppm from TMS as internal standard. The mass spectra were determined on a JMS-OISG double-focusing mass spectrometer. Specific rotations were measured by Jasco DIP-180 Automatic Polarimeter. Extracts were dried over Na_2SO_4. Mallinckrodt silicic acid or Kieselgel 0.05—0.2 mm (Merck) was used for column chromatography, and Kieselgel G nach Stahl (Merck) for thin-layer chromatography (TLC).

Lasiokaurinol (**9**)——Rechromatography of the residue, which left after isolation[4] of oridonin, lasiokaurin, and lasiodonin, on silica gel column led to isolation of lasiokaurinol and lasiokaurinin. Lasiokaurinol was obtained from MeOH as colorless needles which first melted at 143—147°, resolidified, and finally melted again at 218—221° under decomposition, $[\alpha]_D^{27}$ −12° (c=0.085, MeOH). Yield: 40 mg from 3 kg of the dried plant. *Anal.* Calcd. for $C_{22}H_{32}O_7$: M 408.214, M-H_2O 390.204. Found: M^+ 408.209, M^+-H_2O 390.204. IR ν_{max} cm^{-1}: 3560, 3360, 3250, 1712, 1260. NMR δ (D_5-pyridine): 1.13, 1.14 (each 3H, s, C-4 Me_2), 1.65 (1H, d, J=6, C-5-H), 2.00 (3H, s, OAc), 2.7—3.1 (2H, m, C-9-H, C-13-H), 4.22 (1H, m, changed to d, J=6, by D_2O. C-6-H), 4.35, 4.57 (each 1H, AB-type, J=10, C-20 H_2), 4.88 (1H, dd, J=8, 10 Hz, C-1-H), 5.05 (1H, s, C-14-H), 5.33 (1H, br. s, C-15-H), 5.65 (2H, br. s, C-17 H_2), 6.43, 7.97, 8.45 (each 1H, br. s, 3×OH).

Enmenol (**4**) **from Lasiokaurinol** (**9**)——To a solution of 21 mg of lasiokaurinol in 10 ml of a mixture (1: 1) of ether and tetrahydrofuran was added slowly a suspension of 21 mg of $LiAlH_4$ in dry ether, and the mixture was refluxed for 30 minutes. After 50 ml of moistened ether was added to the cooled mixture to decompose an excess of the reagent, the mixture was washed with water. The ethereal layer was treated as usual left 18 mg of residue, which was chromatographed on silica gel column (CH_2Cl_2: acetone=4: 1) to isolate 13 mg of a crude product. Purification (MeOH) gave colorless prisms, mp 242—243°, IR ν_{max} cm^{-1}: 3320, 1100—1000. NMR δ (D_5-pyridine): 1.20, 1.23 (each 3H, s, C-4 Me_2), 3.73 (1H, t, J=7.5, C-1-H), 4.26 (1H, d, J=6, C-6-H), 4.80, 4.40 (each 1H, AB-type, J=10 Hz, C-20 H_2), 5.12 (1H, s, C-14-H), 5.36 (1H, br. s, C-15-H), 5.69 (2H, br. s, C-17 H_2). The IR spectrum was identical with that of enmenol (**4**).

Oridonin Tetrahydro-derivative (**5**)——A mixture of 12 mg of the foregoing product **4**, a catalytic amount of PtO_2 in 10 ml of MeOH was shaken in an atmosphere of hydrogen for 20 hr. The catalyst was filtered off and the filtrate was evaporated *in vacuo* to leave 13 mg of a crystalline residue, which was chromatographed (CH_2Cl_2: acetone=4: 1) on a silica gel column to isolate 12 mg of a product. Its recrystallization from MeOH yielded colorless prisms, mp 220—225° (lit.[3] 210—220°, lit.[5] 225—230°), IR ν_{max} cm^{-1}: 3400, 3340, 1055, 1025. The IR spectrum and the *Rf* value of TLC coincided with those of an authentic sample of oridonin tetrahydro-derivative (**5**).[5]

Acetylation of Lasiokaurinol Dihydro-derivative (**6**) **to Oridonin Tetrahydro-derivative Triacetate** (**7**)——Crude lasiokaurinol (containing a small amount of lasiokaurin) was dissolved in MeOH and hydrogenated over PtO_2 for 24 hr. The catalyst was filtered off and evaporation of the solvent from the filtrate *in vacuo* left a residue. Twelve mg of the residue was dissolved in 1 ml of a mixture of Ac_2O and pyridine and allowed to stand at room temperature for 24 hr. After decomposing the excess of Ac_2O by EtOH, the solvent was evaporated off *in vacuo* to leave a residue, which was chromatographed on a silica gel column (CH_2Cl_2) to separate two substances. The first eluted substance (5 mg) was crystallized from a mixture of ether and acetone as needles, mp 158—161°, $[\alpha]_D^{28}$ −37° (c=0.14, $CHCl_3$), IR ν_{max} cm^{-1}: 3500, 3440, 3360, 1738, 1720, 1700. NMR δ: 0.83 (3H, s), 0.98 (3H, d, J=7, C-16-Me), 1.16 (3H, s), 2.00. 2.06. 2.12 (each 3H, s, 3×OAc), 2.80 (1H, d, J=3.5, C-15-OH), 4.20 (2H, s, C-20 H_2), 4.41 (1H, s, C-7-OH), 4.49 (1H, q, J=9, 3.5, C-15-H), 4.78 (1H, m, C-1-H), 5.25 (1H, d, J=5 Hz, C-6-H), 5.46 (1H, s, C-14-H). This compound was proved to be

identical with the authentic sample [mp 158—161°, $[\alpha]_D^{28}$ −35° (c=0.13, $CHCl_3$)] of oridonin tetrahydro-derivative triacetate (7) (m. mp, IR, NMR, $[\alpha]_D$, TLC). The secondly eluted substance (6 mg) was estimated as a mixture of lasiokaurinol dihydro-derivative 14-acetate and lasiokaurin dihydro-derivative 14-acetate formed from lasiokaurin contaminated in the original material.

Acetylation of Lasiokaurinol——Acetylation of 8.5 mg of crude lasiokaurinol by usual method and chromatography (CH_2Cl_2) on silica gel column gave 6 mg of a crystalline product, which was recrystallized from MeOH to give lasiokaurinol diacetate (**8**) as colorless prisms, mp 167—172°. *Anal.* Calcd. for $C_{26}H_{36}O_9$: 492.235 (M). Found: 492.235 (M^+). IR ν_{max} cm^{-1}: 3550, 1740, 1235. NMR δ: 0.83, 1.19 (each 3H, s, C-4 Me_2), 2.00, 2.05, 2.17 (each 3H, s, 3×OAc), 3.67 (1H, d, J=3, C-15-OH), 4.23 (2H, s, C-20 H_2), 4.50 (1H, s, C-7-OH), 4.6—4.9 (1H, m, C-1-H), 4.86 (1H, m, changed to a br. s, by D_2O. C-15-H), 5.19, 5.28 (each 1H, br. s, C-17 H_2), 5.35 (1H, d, J=6, C-6-H), 5.40 (1H, s, C-14-H).

Sodium Borohydride Reduction of Lasiokaurin (2)——To a solution of 110 mg of lasiokaurin (2) in 15 ml of MeOH was slowly added 110 mg of $NaBH_4$ under ice-cooling and stirring. After 1 hr, a small amount of acetic acid was added, and then the mixture was evaporated *in vacuo* to leave a residue, which was suspended in AcOEt and washed with aq. NaCl. The AcOEt layer was treated as usual to give 109 mg of a crude product. When its solution in MeOH was allowed to stand, 7 mg of crystals, mp 145—148° and 220—223° (decomp.), $[\alpha]_D^{26}$ −10° (c=0.043, MeOH), precipitated. *Anal.* Calcd. for $C_{22}H_{32}O_7 \cdot H_2O$: C, 61.95; H, 8.04. Found: C, 62.10; H, 8.23. IR ν_{max} cm^{-1}: 3550, 3360, 3280, 1712, 1265, 875. This compound was proved to be identical with natural lasiokaurinol (**9**) (m. mp, $[\alpha]_D$, IR, NMR, TLC). The filtrate from the crystals of lasiokaurinol was evaporated *in vacuo* to leave *ca.* 100 mg of residue, which was chromatographed (CH_2Cl_2: acetone=4: 1) on a silica gel column to give lasiokaurin tetrahydro-derivative (**6**) as an oil. *Anal.* Calcd. for $C_{22}H_{34}O_7$: 410.230 (M), 392.220 (M-H_2O). Found: 410.231 (M^+), 392.220 (M^+-H_2O). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 3360, 1723, 1255, 1043. NMR δ (D_5-pyridine): 1.13 (6H, s, C-4 Me_2), 1.23 (3H, d, J=8, C-16-Me), 2.00 (3H, s, OAc), 4.10 (1H, d, J=4.5, C-6-H), 4.29, 4.50 (each 1H, AB-type, J=10, C-20 H_2), 4.90 (1H, m, C-1-H), 5.00 (1H, s, C-14-H), 5.22 (1H, d, J=10 Hz, C-15-H), 5.80—7.80 (OH).

Lasiokaurinin (10)——The crude crystals obtained from column-chromatography (see lasiokaurinol) was recrystallized from MeOH to yield pure lasiokaurinin as crystals, mp 219—222° (decomp.), $[\alpha]_D^{27}$ −14° (c=0.032, MeOH). Yield: 24 mg from 3 kg of the dried plant material. *Anal.* Calcd. for $C_{23}H_{34}O_8$: 438.225 (M). Found: 438.226 (M^+). IR ν_{max} cm^{-1}: 3350, 3225, 1720, 1240. NMR δ: 1.15 (6H, s, C-4 Me_2), 2.00 (3H, s, OAc), 3.40 (3H, s, OMe), 3.50—3.90 (2H, m, C-17 H_2), 3.93 (1H, br. d, J=7, C-6-H), 4.21 (2H, s, C-20 H_2), 4.5—5.0 (2H, m, C-1-H and C-14-H)*, 5.07 (1H, br. s, OH), 5.72 (1H, d, J=10 Hz, C-14-OH), 6.30 (1H, br. s, C-6-OH). *By D_2O-addition, br. s (C-14-H) appeared at δ 4.75. δ (D_5-pyridine): 1.08, 1.13 (each 3H, s, C-4 Me_2), 2.03 (3H, s, OAc), 3.27 (3H, s, OMe), 3.92 (2H, d, J=7, C-17 H_2), 4.20 (1H, d, J=6, C-6-H), 4.30 ,4.48 (each 1H, AB-type, J=10 Hz, C-20 H_2), 4.6—5.0 (1H, m, C-1-H), 5.15 (1H, br. s, C-14-H), 6.0—7.0 (3H, br. s, 3×OH).

Methanol Addition of Lasiokaurin (2) into Lasiokaurinin 16-Epimer (11)——Seven mg of oxalic acid was added into a solution of 155 mg of lasiokaurin (2) in 20 ml of abs. MeOH, and the mixture was heated under reflux for 100 hr. On cooling, 75 mg of the material (lasiokaurin) precipitated. Filtrate from lasiokaurin was evaporated off to leave a residue, which was chromatographed (SiO_2, CH_2Cl_2: acetone=9: 1) to separate 35 mg of lasiokaurin and 29 mg of lasiokaurinin 16-epimer (**11**) . Recrystallization of **11** from MeOH gave colorless needles, mp 201—203.5°. *Anal.* Calcd. for $C_{23}H_{34}O_8$: C, 62.99; H. 7.82, M 438.225. Found: C, 63.18; H, 7.86, M^+ 438.225. IR ν_{max} cm^{-1}: 3425, 3225, 1730, 1718, 1240. NMR δ (D_5-pyridine): 1.09, 1.19 (each 3H, s, C-4 Me_2), 2.02 (3H, s, OAc), 3.28 (3H, s, OMe), 3.78 (3H, m, C-17 H_2, C-16-H), 4.18 (1H, m, changed to d, J=6, by D_2O, C-6-H), 4.35, 4.52 (each 1H, AB-type, J=10 Hz, C-20 H_2), 4.7—5.0 (1H, m, C-1-H), 5.32 (1H, br. s, C-14-H), 6.0—7.0 (3H, br. s, 3×OH).

Sodium Borohydride Reduction of Lasiokaurinin 16-Epimer (11) to Alcohol 14——To a solution of 19 mg of **11** in 2 ml of MeOH was added 19 mg of $NaBH_4$ under ice-cooling, and the mixture was stirred at room temperature for 20 hr. After neutralization with 5% HCl, extracts with AcOEt were treated as usual to give 15 mg of a crude product, which was chromatographed (SiO_2, CH_2Cl_2: acetone=4: 1) to separate 12 mg of a crystalline compound. Its recrystallization from MeOH yielded pure alcohol **14** as needles, mp 205—206°. *Anal.* Calcd. for $C_{23}H_{36}O_8$: 440.241 (M). Found: 440.241 (M^+). IR ν_{max} cm^{-1}: 3450, 3280, 1730, 1250. NMR δ (D_5-pyridine): 1.12 (6H, s, C-4 Me_2), 2.01 (3H, s, OAc), 3.37 (3H, s, OMe), 3.90 (2H, d, J=7.5, C-17 H_2), 4.13 (1H, m, C-6-H), 4.30, 4.51 (each 1H, AB-type, J=10, C-20 H_2), 4.83 (1H, m, C-1-H), 4.93 (1H, br. s, OH), 5.01 (1H, s, C-14-H), 5.37 (2H, br. s, C-15-H, OH), 7.69, 8.23 (each 1H, br, s, 2×OH). By D_2O treatment: 4.13 (1H, d, J=5, C-6-H), 5.37 (1H, d, J=10 Hz, C-15-H).

Acetylation of 14 into 15——A solution of 10 mg of **14** in 2 ml of Ac_2O–pyridine (1: 1) was allowed to stand at room temperature for 7 hr. After addition of EtOH to decompose excess of the reagent, the solvent was evaporated off *in vacuo* to leave 11 mg of a residue, which was chromatographed (SiO_2, CH_2Cl_2: acetone= 9: 1) to separate 6 mg of a main product as an amorphous substance. *Anal.* Calcd. for $C_{25}H_{38}O_9$: 482.251 (M). Found: 482.253 (M^+). IR ν_{max} cm^{-1}: 3500, 3400, 1740, 1240—1250. NMR δ (D_5-pyridine): 1.07 (6H, s, C-4 Me_2), 1.99 (6H, s, 2×OAc), 3.35 (3H, s, OMe), *ca.* 3.93 (2H, m, C-17 H_2), 4.05 (1H, d, J=5, C-6-H), 4.26, 4.52 (each 1H, AB-type, d, J=10, C-20 H_2), *ca.* 5.00 (1H, m, C-1-H), 4.90—5.80 (3H, br. s, 3×OH), 5.28 (1H, d, J=10 Hz, C-15-H), 6.01 (1H, br. s, C-14-H).

Treatment of Lasiokaurinin with p-Toluenesulfonic Acid in Methanol——About 3 mg of *p*-toluenesulfonic acid was added into 3 mg of lasiokaurinin in 1 ml of abs. MeOH, and the mixture was refluxed for 10 hr, then the mixture was allowed to stand at room temperature for 1 month. A TLC test gave three spots (1: 1: 1). Neutralization with Na_2CO_3 aq., extraction with CH_2Cl_2, and usual treatment of the extract gave 3.5 mg of a mixture. UV λ_{max}^{MeOH}: 238.5 nm (ε 2800). The mixture was chromatographed (SiO_2, CH_2Cl_2: acetone=4: 1) to separate each about 0.5 mg of crystalline lasiokaurin (**2**) or its antipode and lasiokaurinin 16-epimer (**11** or its antipode). (Crystallized from MeOH.) Lasiokaurin: *Anal.* Calcd. for $C_{22}H_{30}O_7$: 406.199 (M). Found: 406.198 (M^+). The *Rf* value on TLC, IR (KBr disc. Infrared microscope was used.) spectrum, and the mass fragmentations coincided with those of an authentic sample of **2**. Lasiokaurinin 16-epimer *Anal.* Calcd. for $C_{23}H_{34}O_8$: 438.225, (M). Found: 438.221, (M^+). The *Rf* value on TLC and the mass fragmentations coincided with those of an authentic sample of **11**.

Acknowledgement We express our thanks to Prof. S.-T. Lu of Kaohsiung Medical College and Prof. W.-S. Kan of China Medico-Pharmaceutical College for collecting the plant material. Thanks are also due to Dr. S. Hayashi for micro IR measurement and to Miss Y. Izumi for mass spectra.