[Chem. Pharm. Bull. 32(7)2809—2814(1984)]

(1*R*, 5*R*,8*S*,9*S*)-Deoxyloganic Acid from *Nepeta cataria*

FUJIO MURAI,*,[a] MOTOKO TAGAWA,[a] SØREN DAMTOFT,[b]
SØREN ROSENDAL JENSEN,[b]
and BENT JUHL NIELSEN[b]

Laboratory of Chemistry, Aichi Medical University,[a] Nagakute, Aichi 480–11, Japan and Department of Organic Chemistry, Technical University of Denmark,[b] DK-2800, Lyngby, Denmark

(Received February 7, 1984)

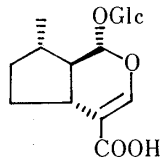
On the basis of exhaustive ^{1}H- and ^{13}C-nuclear magnetic resonance (NMR) spectral studies and chemical transformations, the structure of an iridoid glucoside formerly designated as 5-epideoxyloganic acid, isolated from *Nepeta cataria* L., has been revised to (1*R*, 5*R*, 8*S*, 9*S*)-deoxyloganic acid, which is renamed 1,5,9-epideoxyloganic acid. The absolute configuration of this glucoside was established by its chemical conversion to an antipode of boschnialactone.

Keywords——*Nepeta cataria*; Lamiaceae; iridoid glucoside; structural revision; 1,5,9-epideoxyloganic acid; antipode; boschnialactone; 8-epideoxyloganic acid

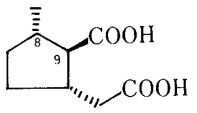
Nepeta cataria L. (Lamiaceae) (Chikumahakka in Japanese) has been used in Chinese medicine as an antifebrile, a diuretic and also as a remedy for stomach-ache and dropsy. The plant, which is similar to *Actinidia polygama* MIQ. (Actinidiaceae) (Matatabi in Japanese) and *Boschniakia rossica* HULT. (Orobanchaceae) (Oniku in Japanese), also attracts felids and causes them to show unusual behavior. In the previous paper,[1] we described the isolation of an iridoid glucoside, named 5-epideoxyloganic acid, from this plant. In addition, the tentative structure of the glucoside (**1a**) was suggested on the basis of its degradation with 10% sulfuric acid followed by oxidation with potassium permanganate to give 8*S*-*trans*, *trans*-boschnialinic acid (**2**). However, further study of the structure of the glucoside obliged us to reinvestigate the stereochemistry of the aglucone moiety. This paper describes further work leading to the revision of the absolute stereostructure to formula **1**.

The iridoid glucoside (**1**), $C_{16}H_{24}O_9$, mp 106 °C (dec.), $[\alpha]_D$ +85.1° (MeOH), was obtained as colorless needles. On an exhaustive comparison of the ^{13}C-nuclear magnetic resonance (NMR) spectra[1] of the acetate (**3**), 8-epideoxyloganic acid tetraacetate (**4**) and deoxyloganic acid tetraacetate (**5**), we noticed that the spectrum of **3** has a striking resemblance to that of **4**. Recently, we also obtained 8-epideoxyloganic acid (**6**),[2] $C_{16}H_{24}O_9 \cdot 1/2C_2H_5OH$, mp 219—220 °C, $[\alpha]_D$ −110.0° (MeOH), from the mechanolic extract of the whole plant of *Boschniakia rossica* HULT. along with the known glucoside boschnaloside[3] and boschnaside (8-epiiridodial glucoside),[2,3] The absolute structure of **6** was determined on the basis of the following chemical evidence: conventional acetylation of **6** gave the acetate, $C_{24}H_{32}O_{13}$, mp 186—187 °C, $[\alpha]_D$ −97.8° ($CHCl_3$), which was identical with **4** obtained on oxidation of boschnaloside tetraacetate (**7**) with potassium bichromate in acetic acid.[2,4]

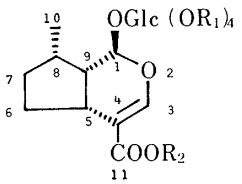
In the ^{1}H-NMR spectra (CD_3OD) of **1** and **6**, the only major difference is in the chemical shifts of H-1 (δ 5.27 in **1**, δ 5.46 in **6**) and H-1′ (δ 4.58 in **1**, δ 4.69 in **6**); the remaining chemical shifts and coupling constants are almost identical. Furthermore, the ^{13}C-NMR spectral data of **1**[5] and **6** are virtually identical, except for the signals attributed to C-1 (δ 101.49 in **1**, δ 97.06 in **6**) and C-1′ (δ 103.49 in **1**, δ 99.55 in **6**) (Table I).[2]



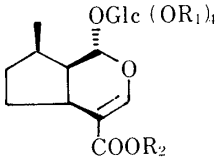
1a



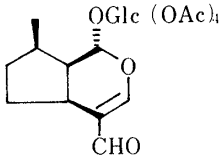
2



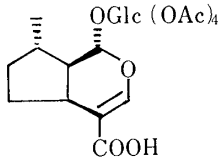
1 : $R_1=R_2=H$
3 : $R_1=COCH_3$, $R_2=H$
8 : $R_1=H$, $R_2=CH_3$



6 : $R_1=R_2=H$
4 : $R_1=COCH_3$, $R_2=H$
9 : $R_1=H$, $R_2=CH_3$



7



5

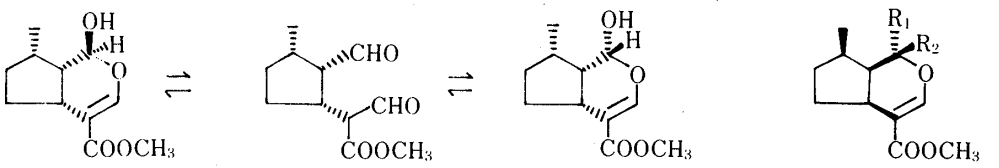
Fig. 1

TABLE I. ^{13}C-NMR Data for 1,5,9-Epideoxyloganic Acid (**1**) and 8-Epideoxyloganic Acid (**6**) (in D_2O)

Carbon	1	6
1	101.49 d	97.06 d
3	153.57 d	153.35 d
4	113.36 s	113.75 s
5	33.58 d	33.12 d
6	32.09 t	31.97 t
7	33.38 t	33.51 t
8	36.82 d	36.55 d
9	43.89 d	43.79 d
10	17.08 q	16.79 q
11	172.09 s	172.14 s
1′	103.49 d	99.55 d
2′	74.42 d	73.91 d
3′	76.96 d	76.91 d
4′	70.57 d	70.74 d
5′	77.54 d	77.42 d
6′	61.95 t	61.94 t

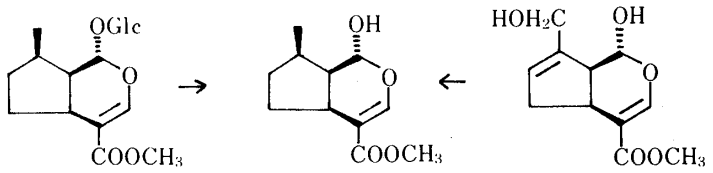
Chemical shifts in ppm relative to external $(CH_3)_4Si$ (in a capillary).

On treatment with diazomethane both **1** and **6** gave the corresponding methyl esters (**8**), $C_{17}H_{26}O_9 \cdot C_2H_5OH$, mp 94—95 °C (dec.), $[\alpha]_D$ +96.4° (MeOH), and (**9**), $C_{17}H_{26}O_9$, mp 147—148 °C, $[\alpha]_D$ −108.6° (MeOH). The ^{1}H-NMR spectra (CD_3OD) of these compounds showed signals due to the carbomethoxyl group at δ 3.68. The ^{13}C-NMR spectra (D_2O) of the methyl esters (**8**) and (**9**) are also quite similar to each other except for the chemical shifts at C-1 and C-1′, as seen in the case of **1** and **6** (Table I). These features can be accounted for by assuming that the aglucones of **1** and **6** are enantiomeric. Analogous data have been reported in the spectra of β-D-glucopyranosides of *d*- and *l*-menthol.[6] Furthermore, the coupling constants $J_{1,9}$ (J=4.0 Hz) of **1** and **6** are identical, suggesting that the two compounds have the same relative configuration. Thus, we prepared compounds **10a** and **11a**[7] by enzymatic



10a 10b 11a : R_1=OH, R_2=H
11b : R_1=H, R_2=OH

Fig. 2



9 11a 12

Fig. 3

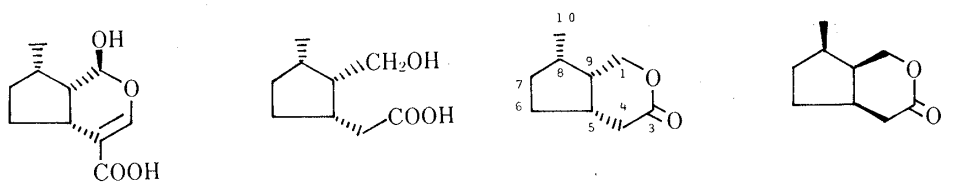
hydrolysis of the methyl esters **8** and **9** with β-glucosidase.

The aglucone (**10a**),[8] $C_{11}H_{16}O_4$, mp 84—86 °C, $[\alpha]_D$ +5.9° (MeOH), was obtained as colorless needles. It showed characteristic infrared (IR) bands at 3450 (hydroxy group), 1690, 1680, 1630 cm^{-1} (α,β-unsaturated ester). In addition, the ^{1}H-NMR ($CDCl_3$) spectrum of **10a** has a doublet at δ 1.10 (J=7.0 Hz) due to a secondary methyl group, a singlet at δ 3.60 due to a carbomethoxy group and a singlet at δ 7.30 due to an olefinic proton. On addition of D_2O, the doublet at δ 4.34 (J=4.0 Hz) due to the hydroxyl group disappeared, and the signals at δ 4.98 (br t) (Hα) and 5.42 (br t) (Hβ) due to the C-1 proton changed to two doublets (J=8.0 and 4.0 Hz, respectively). The ^{1}H-NMR spectrum also indicates the presence of **10a** and **10b** (relative ratio: **10a**–**10b** 5:2), which must be produced on epimerization at C-1. The mutarotation of **10a** was observed as follows: the value of the initial specific rotation (+123.2°) at 405 nm in chloroform changed to +25.3° after 22 h (**10a**⇌**10b**).

The aglucone (**11a**), $C_{11}H_{16}O_4$, mp 85—86 °C, $[\alpha]_D$ −4.1° (MeOH), was obtained as colorless needles. The melting point and IR, ^{1}H- and ^{13}C-NMR spectra of **11a** are identical with those of **10a**. However, the circular dichroism (CD) curves of **10a** and **11a** in methanol are opposite to each other. On the other hand, the aglucone (**11a**) of the glucoside (**9**) was identical with an authentic sample of 10-deoxy-7,8-dehydrogenipin which had been obtained by catalytic hydrogenation of genipin (**12**) over PtO_2, together with several other hydrogenation products.[4,7,8] Therefore, the absolute configuration of 8-epideoxyloganic acid (**6**) from *Boschniakia rossica* HULT. was further confirmed to be 8*R-cis, cis*.[2]

As the aglucones (**10a**) and (**11a**) have been proved to be enantiomeric, the absolute stereostructure of the glucoside (**1**) was established as (1*R*, 5*R*, 8*S*, 9*S*)-deoxyloganic acid. In order to confirm the absolute configuration of **1** in relation to that of boschnialactone (**13**),[9] we carried out the following chemical reaction. Enzymatic hydrolysis of **1** with β-glucosidase gave an aglucone (**14**), which was further treated with 2 N potassium hydroxide, resulting in decarboxylation followed by Cannizzaro reaction to provide an acid (**15**).[10] After addition of 10% sulfuric acid to **15**, the solution was heated at 80 °C for 30 min to give the corresponding lactone (**16**), $[\alpha]_D$ +25.1° ($CHCl_3$), whose IR, ^{1}H- and ^{13}C-NMR spectra and retention time (t_R) of gas chromatography (GLC) were identical with those of **13**, $[\alpha]_D$ −18.2° ($CHCl_3$). Therefore, the lactone (**16**) was determined to be an antipode of **13**.[10]

In the course of our previous study[1] the glucoside (**1**) was proved to be readily degraded



14 15 16 13

Fig. 4

to give only 8*S-trans, trans*-boschnialinic acid (**2**). Thus, treatment of **1** with 10% sulfuric acid gave the dialdehyde which was further subjected to oxidation with potassium permanganate to afford **2**. However, we have found that some epimerization can take place at C-9 quite easily even on much milder acid treatment than that used above.[4] In this light, the formation of **2** from **1** is not wholly unexpected.

In conclusion, the *Nepeta* glucoside should have the absolute stereostructure depicted in **1**, corresponding to 1,5,9-epideoxyloganic acid. This is the first naturally occurring iridoid glucoside with stereochemistry deviating from the usual (1*S*, 5*S*, 9*R*) pattern.

Experimental

Melting points were determined on a Thomas Hoover apparatus and are uncorrected. IR and ultraviolet (UV) spectra were recorded on a JASCO IR-G spectrophotometer and a Hitachi EPS-3T grating spectrophotometer, respectively. Optical rotations were determined on a JASCO DIP-180 digital polarimeter. CD spectra were recorded on a JASCO J-20 spectropolarimeter. ^{1}H- and ^{13}C-NMR spectra were recorded on JNM-MH-100 and JNM-FX-100 spectrometers, respectively. Tetramethylsilane (TMS) was used as an internal standard in CD_3OD and $CDCl_3$, but as an external one (in a capillary) with D_2O. GLC analyses were performed on a NEVA model 1700 gas chromatograph (column, 5′ × 1/4″, 20% Apiezon L on Chromosorb W 100—120 mesh) using the following conditions: flow rate, 17 ml/min (He); column temperature, 180 °C; injection block temperature, 200 °C. Column chromatography was carried out on Silica gel BW-80 (Fuji Davison). For thin layer chromatography (TLC), Silica gel 60 F_{254} (Merck) was used and spots were detected by spraying the plates with anisaldehyde–H_2SO_4 reagent.

1,5,9-Epideoxyloganic Acid (1)——mp 106 °C (dec.). $[\alpha]_D^{28}$ +85.1° (*c*=1.1, MeOH), IR, UV and ^{1}H-NMR.[1] ^{13}C-NMR (Table I).

1,5,9-Epideoxyloganic Acid Tetraacetate (3)——mp 169—170 °C. $[\alpha]_D^{27}$ +49.4° (*c*=1.1, MeOH). IR, UV, ^{1}H- and ^{13}C-NMR.[1]

8-Epideoxyloganic Acid (6)[2]——The glucoside (**6**) was isolated from *Boschniakia rossica* HULT. as colorless plates, mp 219—220 °C. $[\alpha]_D^{22}$ −110.0° (*c*=1.4, MeOH). IR ν_{max} (Nujol): 3500—2500, 1680, 1640 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.08 (3H, d, *J*=6.6 Hz, CH_3), 4.69 (1H, d, *J*=7.6 Hz, 1′-H), 5.46 (1H, d, *J*=4.0 Hz, 1-H), 7.43 (1H, d, $^4J_{3,1}$=0.7 Hz, H-3). *Anal.* Calcd for $C_{16}H_{24}O_9 \cdot 1/2C_2H_5OH$: C, 53.25; H, 7.10. Found: C, 53.23; H, 7.42. ^{13}C-NMR (Table I).

Methylation of 1,5,9-Epideoxyloganic Acid (1)——The glucoside (**1**) (200 mg) was methylated with ethereal CH_2N_2 to afford a crystalline solid, which was recrystallized from EtOH to yield the methyl ester (**8**) (125 mg) as colorless needles, mp 94—95 °C (dec.). $[\alpha]_D^{20}$ +96.4° (*c*=1, MeOH). IR ν_{max} (Nujol): 3400, 3250, 1690, 1635 cm^{-1}. ^{1}H-NMR (D_2O) δ: 1.06 (3H, d, *J*=7.3 Hz, CH_3), 3.68 (s, $COOCH_3$), 4.59 (1H, d, *J*=7.1 Hz, 1′-H), 5.31 (1H, d, *J*=4.0 Hz, 1-H), 7.40 (1H, d, $^4J_{3,1}$=0.7 Hz, 3-H). ^{13}C-NMR (D_2O) δ: 101.42 (d, C(1)), 153.11 (d, C(3)), 113.58 (s, C(4)), 33.53 (d, C(5)), 32.12 (t, C(6)), 33.41 (t, C(7)), 36.80 (d, C(8)), 43.89 (d, C(9)), 17.03 (q, C(10)), 170.92 (s, C(11)), 52.93 (q, $COO\underline{C}H_3$), 103.52 (d, C(1′)), 74.45 (d, C(2′)), 76.98 (d, C(3′)), 70.59 (d, C(4′)), 77.56 (d, C(5′)), 61.95 (t, C(6′)). *Anal.* Calcd for $C_{17}H_{26}O_9 \cdot C_2H_5OH$: C, 54.27; H, 7.67. Found: C, 53.77; H, 7.40.

Methylation of 8-Epideoxyloganic Acid (6)——The glucoside (**6**) (250 mg) was methylated with ethereal CH_2N_2 to afford a crystalline solid, which was recrystallized from EtOH to yield the methyl ester (**9**) (137 mg) as colorless needles, mp 147—148 °C (dec.). $[\alpha]_D^{22}$ −108.6° (*c*=1.1, MeOH). IR ν_{max} (Nujol): 3400, 1715, 1635 cm^{-1}: ^{1}H-NMR (CD_3OD) δ: 1.08 (3H, d, *J*=6.4 Hz, CH_3), 3.68 (3H, s, $COOCH_3$), 4.70 (1H, d, *J*=7.3 Hz, 1′-H), 5.45 (1H, d, *J*=4.0 Hz, 1-H), 7.42 (1H, s, H). ^{13}C-NMR (D_2O): δ: 97.04 (d, C(1)), 152.94 (d, C(3)), 113.95 (s, C(4)), 33.34 (d, C(5)), 32.12 (t, C(6)), 33.58 (t, C(7)), 36.70 (d, C(8)), 43.89 (d, C(9)), 16.89 (q, C(10)), 170.82 (s, C(11), 52.88 (q, $COO\underline{C}H_3$), 99.64 (d, C(1′)), 74.01 (d, C(2′)), 77.03 (d, C(3′)), 70.84 (d, C(4′)), 77.52 (d, C(5′)), 62.09 (t, C(6′)). *Anal.* Calcd for $C_{17}H_{26}O_9$: C, 54.54; H, 7.00. Found: C, 54.58; H, 7.02.

Enzymatic Hydrolysis of 1,5,9-Epideoxyloganin (8)——A 1% aqueous β-glucosidase (from almonds, Sigma)

solution (10 ml) was added to a solution of the glucoside (**8**) (2.96 g) in aqueous 0.1 N CH_3COOH–0.07 N CH_3COONa (12 ml, pH 4.6) and the mixture was allowed to stand at 36 °C for 24 h. It was then extracted with Et_2O, dried over Na_2SO_4, and concentrated to afford a crystalline solid, which was recrystallized from Et_2O–*n*-pentane to yield an aglucone (**10a**) (500 mg) as colorless needles, mp 84—86 °C. $[\alpha]_D^{21}$ +5.9°; $[\alpha]_{577}$ +7.3°; $[\alpha]_{546}$ +9.7°; $[\alpha]_{435}$ +33.2°; $[\alpha]_{405}$ +48.4° ($c=1.1$, MeOH). In chloroform solution ($c=1.5$) the initial rotation was considerably larger $[\alpha]_{405}^{21}$ +123.2°, declining to +25.3° after 22 h. CD ($c=0.02$, MeOH) $\Delta\varepsilon^{26}$: +4.4 (229) (positive maximum). IR ν_{max} (Nujol): 3450, 1690, 1680, 1630 cm^{-1}. ^{1}H-NMR (the compound was dissolved in $CDCl_3$ and allowed to stand for 24 h, and then the spectrum was measured) δ: 1.10 (3H, d, $J=7.0$ Hz, CH_3), 2.80 (1H, m, 5-H), 3.60 (3H, s, $COOCH_3$), 4.34 (1H, d, $J=4.0$ Hz, 1-OH), 4.98 (5/7H, br t, 1-H), 5.42 (2/7H, br t, 1-H in **10b**), 7.30 (1H, s, 3-H). The signal of 1-OH (δ 4.34) disappeared on addition of D_2O and two H-1 signals of the α and β forms appeared clearly at δ 4.98 (d, $J=8.0$ Hz) and at δ 5.42 (d, $J=4.0$ Hz), respectively. From the relative peak areas, the ratio **10a** : **10b** was suggested to be *ca.* 5 : 2. *Anal.* Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 61.95; H, 7.77.

Enzymatic Hydrolysis of 8-Epideoxyloganin (9)——The glucoside (**9**) (911 mg) was subjected to enzymatic hydrolysis with β-glucosidase in a manner similar to that described above, affording the crude product (380 mg), which was purified by silica gel (5 g) column chromatography with C_6H_6–AcOEt mixture of increasing AcOEt content as the eluent. The eluate with C_6H_6–AcOEt (97 : 3) was concentrated to afford a crystalline solid, which was recrystallized from Et_2O–*n*-pentane to give an aglucone (**11a**) (91 mg) as colorless needles, mp 85—86 °C. $[\alpha]_D^{22}$ −4.1°; $[\alpha]_{577}$ −5.6°; $[\alpha]_{546}$ −6.2°; $[\alpha]_{435}$ −23.8°; $[\alpha]_{405}$ −38.1° ($c=1.6$, MeOH). In chloroform solution ($c=1.1$) the initial rotation of **11a** was also considerably larger, $[\alpha]_{405}^{22}$ −119.8°, declining to −21.1° after 24 h. CD ($c=0.1$, MeOH) $\Delta\varepsilon^{26}$: −3.7 (229) (negative maximum). IR ν_{max} (Nujol): 3450, 1690, 1680, 1630 cm^{-1}. ^{1}H-NMR (the compound was dissolved in $CDCl_3$ and allowed to stand for 24 h, and then the spectrum was measured) δ: 1.14 (3H, d, $J=7.0$ Hz, CH_3), 2.84 (1H, m, 5-H), 3.70 (3H, s, $COOCH_3$), 4.24 (1H, br t, 1-OH), 5.03 (5/7H, t, $J=8.0$ Hz, 1-H), 5.47 (2/7H, t, $J=4.0$ Hz, 1-H in **11b**), 7.38 (1H, s, 3-H). Further, the signal of 1-OH (δ 4.24) disappeared on addition of D_2O and two 1-H signals of the β and α forms appeared clearly at δ 5.03 (d, $J=8.0$ Hz) and at δ 5.47 (d, $J=4.0$ Hz), respectively. The ratio **11a** : **11b** was suggested to be *ca.* 5 : 2 from the relative peak areas. *Anal.* Calcd for $C_{11}H_{16}O_4$: 62.25; H, 7.60. Found: C, 62.21; H, 7.87.

Enzymatic Hydrolysis of 1,5,9-Epideoxyloganoic Acid (1) with β-Glucosidase and Cannizzaro Reaction of the Aglucone (14)——An aqueous solution (18 ml) of the glucoside (**1**) (1.10 g) was treated with β-glucosidase (177 mg), and the mixture was allowed to stand at 37 °C for 24 h. The reaction solution was extracted with Et_2O, then the extract was dried over Na_2SO_4, and concentrated to give the crude product (**14**) (416 mg), which was mixed with 2 N KOH (16 ml) and EtOH (3 ml). The reaction mixture was refluxed under N_2 for 3 h, then Et_2O were added and whole was shaken. The H_2O layer was acidified with 10% H_2SO_4 and extracted with Et_2O. The extract was dried over Na_2SO_4, and concentrated to give the crude product. Next, 10% H_2SO_4 (3 ml) and EtOH (5 ml) were added to this product, and the mixture was refluxed for 30 min then extracted with Et_2O. The ethereal layer was washed with sat. $NaHCO_3$ soln. to remove the acid fraction. The ethereal layer was dried over Na_2SO_4, and concentrated to afford the residue (76 mg), which was subjected to silica gel (2 g) column chromatography using only $CHCl_3$ as the eluent. The eluate fractions which showed a spot at *Rf* 0.6 on TLC with $CHCl_3$–MeOH (50 : 1) were collected and concentrated. The residue was further purified by silica gel (5 g) column chromatography in a manner similar to that described above to give a lactone (**16**) (12 mg) as an oily substance, $[\alpha]_D^{21}$ +25.1° ($c=0.7$, $CHCl_3$), which was identified as an antipode of boschnialactone by direct comparison of the IR, ^{1}H- and ^{13}C-NMR spectra and t_R (GLC), 17.6 min, with those of an authentic sample of boschnialactone (**13**),[9] $[\alpha]_D^{26}$ −18.2° ($c=1.2$, $CHCl_3$) (an antipode of **16**). IR ν_{max} (neat): 1743 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.01 (3H, d, $J=6.0$ Hz, CH_3), 4.10, 4.18 (2H, d, $J=4.0$, 2.0 Hz, 1-H), ^{13}C-NMR ($CDCl_3$) δ: 67.51 (t, C(1)), 173.75 (s, C(3)), 32.87 (t, C(4)), 37.38 (d, C(5)), 34.98 (t, C(6)), 35.16 (t, C(7)), 32.87 (d, C(8)), 39.79 (d, C(9)), 14.68 (q, C(10)).

Acknowledgments We thank Novo Industries for access to NMR facilities, and the Danish National Research Council for financial assistance. We are also grateful to Dr. Niwa and the staff of the Analytical Center, Faculty of Pharmaceutical Science, Meijo University, for measurements of ^{13}C-NMR and CD spectra and for elemental analyses, respectively.

References and Notes

1) *a*) M. Tagawa and F. Murai, *Planta Medica*, **39**, 144 (1980); *b*) *Idem, ibid.*, **47**, 109 (1983).
2) F. Murai and M. Tagawa, Abstracts of Papers, the 27th Symposium on the Chemistry of Terpenes, Essential Oils and Aromatics, Nagasaki, 1983, p. 18.
3) F. Murai and M. Tagawa, *Planta Medica*, **46**, 1 (1982).
4) F. Murai and M. Tagawa, *Chem. Pharm. Bull.*, **28**, 1730 (1980).
5) In the previous paper,[1a] the signal at δ 23.5 in the ^{13}C-NMR (D_2O) spectrum of the glucoside (**1**) was incorrectly assigned to the C-7 carbon atom. In fact, the signal observed at δ 33.4 should be that due to the C-7 carbon atom.

6) S. Seo, Y. Tomita, K. Tori, and Y. Yoshimura, *J. Am. Chem. Soc.*, **100**, 3331 (1978).
7) C. Djerassi, T. Nakano, A. N. James, L. H. Zalkow, E. J. Eisenbraun, and J. N. Shoolery, *J. Org. Chem.*, **26**, 1192 (1961).
8) The configuration of the OH group at C-1 of 10-deoxy-7,8-dihydrogenipin was not clearly determined in the paper of Djerassi *et al.*[7] However, the crystalline aglucone of **9**, mp 85—86 °C, showed mutarotation after being dissolved in a solvent ($CDCl_3$), and hence the crystalline form might be only **11a**. By analogy it was thought that the crystalline aglucone of **8** might be **10a**.
9) T. Sakan, F. Murai, Y. Hayashi, Y. Honda, T. Shono, M. Nakajima, and M. Kato, *Tetrahedron*, **23**, 4635 (1967).
10) We attempted to produce the C_9-epimer of **15** by treatment under alkaline conditions, but so far we have not been able to obtain the compound or the C_9-epimer of **16**.