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# SECOIRIDOID DI-GLYCOSIDES FROM *OSMANTHUS ILICIFOLIUS*

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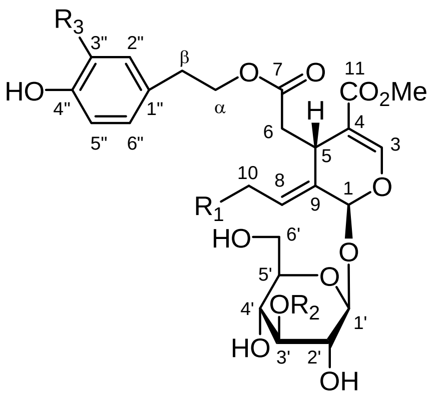
**Abstract** − Four new secoiridoid di-glycosides, 3′-*O*-β-D-glucopyranosyl ligustroside (**1**), 3′-*O*-β-D-glucopyranosyl 10-acetoxyligustroside (**2**), 3′-*O*-β-D-glucopyranosyl oleuropein (**3**) and 3′-*O*-β-D-glucopyranosyl 10-acetoxyoleuropein (**4**) were isolated from the leaves of *Osmanthus ilicifolius*. Their structures were established on the basis of chemical and spectral data. Furthermore, the structure of hiiragilide, previously elucidated to be 2′-*O*-β-D-glucopyranosyl 10-hydroxyligustroside, was revised as 3′-*O*-β-D-glucopyranosyl 10-hydroxyligustroside (**5**).

As the part of our continued studies on the constituents of oleaceous plant, we previously reported the isolation and identification of two bis-iridoid glycosides[1] along with three known secoiridoid glycosides[2] and ten known lignan glycosides[2,3] from the leaves of *Osmanthus ilicifolius* (Oleaceae: Japanese name, hiiragi). The leaves of this plant has been used in Japan as an herbal drug for vitiligo vulgaris.[4] In the course of further studies on the constituents of this plant, four new secoiridoid di-glycosides have been isolated. This paper deals with the structural elucidation and identification of these compounds.




**1** : $R_1$=$R_3$=H, $R_2$=β-D-glc*p*
**2** : $R_1$=OAc, $R_2$=β-D-glc*p*, $R_3$=H
**3** : $R_1$=H, $R_2$=β-D-glc*p*, $R_3$=OH
**4** : $R_1$=OAc, $R_2$=β-D-glc*p*, $R_3$=OH
**5** : $R_1$=OH, $R_2$=β-D-glc*p*, $R_3$=H
**6** : $R_1$=$R_2$=$R_3$=H
**7** : $R_1$=OAc, $R_2$=$R_3$=H
**8** : $R_1$=$R_2$=H, $R_3$=OH
**9** : $R_1$=OAc, $R_2$=H, $R_3$=OH
**10** : $R_1$=OH, $R_2$=$R_3$=H

Furthermore, we previously reported the isolation of a secoiridoid di-glycoside, named hiiragilide, from the same plant and characterized as 2′-*O*-β-D-glucopyranosyl 10-hydroxyligustroside.[5] In the present study, we have isolated one more secoiridoid di-glycoside (**5**), and direct comparison of the spectral data

This paper is dedicated to Professor Emeritus Keiichiro Fukumoto on the occasion of his 75th birthday.

of the acetate (**5a**) and hiiragilide nonaacetate, led to the conclusion that the structure of hiiragilide should be revised to 3′-*O*-β-D-glucopyranosyl 10-hydroxyligustroside (**5**).

Table 1. $^{13}C$ NMR Chemical Shifts of **1**–**5**

| Carbon | **1** | **2** | **3** | **4** | **5** |
|---|---|---|---|---|---|
| 1 | 95.2 | 94.3 | 95.3 | 94.4 | 94.6 |
| 3 | 155.1 | 154.9 | 155.1 | 154.9 | 155.0 |
| 4 | 109.5 | 109.2 | 109.5 | 109.3 | 109.3 |
| 5 | 31.9 | 32.5 | 31.8 | 32.5 | 32.4 |
| 6 | 41.1 | 41.1 | 41.3 | 41.1 | 41.2 |
| 7 | 173.2 | 172.9 | 173.2 | 172.9 | 173.1 |
| 8 | 124.9 | 124.4 | 124.9 | 124.4 | 129.5 |
| 9 | 130.1 | 133.9 | 130.5 | 134.0 | 130.0 |
| 10 | 13.6 | 61.8 | 13.6 | 61.9 | 59.3 |
| 11 | 168.7 | 168.3 | 168.7 | 168.4 | 168.5 |
| 11-$CO_2\underline{C}H_3$ | 51.9 | 52.0 | 52.0 | 52.0 | 52.0 |
| $\underline{C}OCH_3$ | — | 172.6 | — | 172.6 | — |
| $CO\underline{C}H_3$ | — | 20.8 | — | 20.8 | — |
| 1′ | 100.5 | 100.5 | 100.6 | 100.6 | 100.5 |
| 2′ | 74.1 | 74.2 | 74.2 | 74.1 | 74.2 |
| 3′ | 87.6 | 87.5 | 87.6 | 87.5 | 87.6 |
| 4′ | 70.0 | 70.0 | 70.0 | 69.9 | 70.0 |
| 5′ | 78.2 | 78.2 | 78.3 | 78.3 | 78.3 |
| 6′ | 62.7 | 62.7 | 62.7 | 62.7 | 62.7 |
| 1‴ | 105.3 | 105.3 | 105.3 | 105.3 | 105.3 |
| 2‴ | 75.6 | 75.6 | 75.6 | 75.6 | 75.6 |
| 3‴ | 77.9 | 77.9 | 77.9 | 77.9 | 77.9 |
| 4‴ | 71.6 | 71.6 | 71.7 | 71.6 | 71.6 |
| 5‴ | 78.2 | 78.2 | 78.1 | 78.2 | 78.2 |
| 6‴ | 62.7 | 62.7 | 62.7 | 62.6 | 62.7 |
| α | 66.9 | 67.0 | 66.9 | 67.0 | 66.9 |
| β | 35.2 | 35.2 | 35.5 | 35.4 | 35.2 |
| 1″ | 130.5 | 130.0 | 130.8 | 130.7 | 131.0 |
| 2″ | 131.0 | 131.0 | 117.1 | 117.1 | 131.0 |
| 3″ | 116.3 | 116.3 | 146.3 | 146.3 | 116.4 |
| 4″ | 157.1 | 157.1 | 145.0 | 145.0 | 157.1 |
| 5″ | 116.3 | 116.3 | 116.5 | 116.5 | 116.4 |
| 6″ | 131.0 | 131.0 | 121.4 | 121.4 | 131.0 |

Compound **1** was obtained as an amorphous powder, $[\alpha]_D$ –138.2 ° (MeOH). The molecular formula of **1**, $C_{31}H_{42}O_{17}$, was confirmed by HR-FAB-MS. The $^{13}C$ NMR spectrum of **1** was almost identical to that of **6** (ligustroside) isolated from the same plant,[5] except for the presence of an additional hexosyl moiety. In the $^{1}H$ NMR spectrum of **1**, the coupling constant of the anomeric proton signal of the additional hexosyl moiety was 7.8 Hz [$\delta_H$ 4.58 (H-1‴)]. Acid hydrolysis proved that both of two sugars in **1** are D-glucose. The location of the additional β-D-glucopyranosyl moiety in **1** was deduced to be at 3′-OH of **6**, because the signal due to C-3′ was markedly displaced downfield at $\delta_C$ 87.6 (+ 9.1 ppm), when comparing the $^{13}C$ NMR spectrum of **1** with that of **6**. This deduction was supported by the $^{1}H$-dedected heteronuclear multiple bond correlation (HMBC) between H-1‴ and C-3′. Consequently, the structure of **1** was determined to be 3′-*O*-β-D-glucopyranosyl ligustroside.

Compound **2** was obtained as an amorphous powder, $[\alpha]_D$ –174.4 ° (MeOH). The molecular formula of **2**, $C_{33}H_{44}O_{19}$, was confirmed by HR-FAB-MS. The $^{13}C$ NMR spectrum of 2 was almost identical to that of **7** (10-acetoxyligustroside) isolated from the same plant,[5] except for the presence of an additional hexosyl moiety and difference in the chemical shift at C-3′ [$\delta_C$ 87.5 (+ 9.1 ppm)]. Acid hydrolysis proved that both of two sugars in **2** are D-glucose. The location of the additional β-D-glucopyranosyl moiety [$\delta_H$ 4.59 (1H, d, *J*=7.8 Hz, H-1‴)] in **2** was deduced to be at 3′-OH of **7**, because the $^{13}$C NMR chemical shifts due to glycosyl moieties in **2** was closely similar to that of **1**. This deduction was supported by the HMBC between H-1‴ and C-3′. Consequently, the structure of **2** was determined to be 3′-*O*-β-D-glucopyranosyl 10-acetoxyligustroside.

Compound **3** was obtained as an amorphous powder, $[\alpha]_D$ –122.6 ° (MeOH). The molecular formula of **3**, $C_{31}H_{42}O_{18}$, was confirmed by HR-FAB-MS. Acid hydrolysis of **3** yielded D-glucose. The $^1$H and $^{13}$C NMR spectra of **3** were almost identical to those of **8** (oleuropein) isolated from the same plant,[5] except for the presence of an additional β-glucopyranosyl group [$\delta_H$ 4.58 (1H, d, *J*=7.3 Hz, H-1‴)]. The location of the additional β-D-glucopyranosyl moiety in **3** was deduced to be at 3′-OH of **8**, because the $^{13}$C NMR chemical shifts due to glycosyl moieties in **3** was closely similar to that of **1**. This deduction was supported by the HMBC between H-1‴ and C-3′ ($\delta_C$ 87.6). Consequently, the structure of **3** was determined to be 3′-*O*-β-D-glucopyranosyl oleuropein.

Compound **4** was obtained as an amorphous powder, $[\alpha]_D$ –125.0 ° (MeOH). The molecular formula of **4**, $C_{33}H_{44}O_{20}$, was confirmed by HR-FAB-MS. Acid hydrolysis of **4** yielded D-glucose. The $^1$H and $^{13}$C NMR spectra of **4** were almost identical to those of **9** (10-acetoxyoleuropein) isolated from the same plant,[5] except for the presence of an additional β-glucopyranosyl group [$\delta_H$ 4.59 (1H, d, *J*=7.3 Hz, H-1‴)]. The location of the additional β-D-glucopyranosyl moiety in **4** was deduced to be at 3′-OH of **9**, because the $^{13}$C NMR chemical shifts due to glycosyl moieties in **4** was closely similar to that of **1**. This deduction was supported by the HMBC between H-1‴ and C-3′ ($\delta_C$ 87.5). Consequently, the structure of **4** was determined to be 3′-*O*-β-D-glucopyranosyl 10-acetoxyoleuropein.

We previously reported the isolation of a secoiridoid di-glycoside, named hiiragilide, from the same plant.[5] In the present study, we have isolated one more secoiridoid di-glycoside (**5**: 3′-*O*-β-D-glucopyranosyl 10-hydroxyligustroside), and direct comparison of the spectral data of the acetate (**5a**) and hiiragilide nonaacetate, led to the conclusion that the two are identical. Accordingly, the structure of hiiragilide, previously elucidated to be 2′-*O*-β-D-glucopyranosyl 10-hydroxyligustroside, was revised as **5**. The structure of **5** ($[\alpha]_D$ –115.7°, $C_{31}H_{42}O_{18}$) was determined as follows. Acid hydrolysis of **5** yielded D-glucose. The $^1$H and $^{13}$C NMR spectra of **5** were almost identical to those of **10** (10-hydroxy ligustroside) isolated from the same plant,[5] except for the presence of an additional β-D-glucopyranosyl moiety [$\delta_H$ 4.59 (1H, d, *J*=7.8 Hz, H-1‴)] and difference in the chemical shift at C-3′ [$\delta_C$ 87.6 (+ 9.1 ppm)]. The location of the additional β-D-glucopyranosyl moiety in **5** was deduced to be at 3′-OH of **10** by the HMBC between H-1‴ and C-3′. The structure of **5** was determined to be 3′-*O*-β-D-glucopyranosyl 10-hydroxyligustroside.

The iridoid glycoside which comprised an oleoside moiety as a framework is called oleoside-type secoiridoid glycoside, and this type occurs only in Oleaceae plant. Most of them isolated so far are the 1-*O*-mono-glycoside. To our knowledge, this is the second report of an oleoside-type secoiridoid 1-*O*-di-glycoside.[6]

## EXPERIMENTAL

**General** Optical rotation were taken with a JASCO DIP-360 digital polarimeter. UV spectra were recorded with a Beckman DU-64 spectrometer. The $^{1}H$ and $^{13}C$ NMR spectra were recorded with JEOL JNM-LA 400 (400 MHz, 100 MHz, respectively) spectrometer. Chemical shifts are given in a δ (ppm) scale with tetramethylsilane (TMS) as an internal standard. FAB-MS were recorded on a JEOL JMS-DX 303 mass spectrometer. Column chromatography was carried out on Kieselgel 60 (Merck; 230−400 mesh) and Sephadex LH-20 (Pharmacia Fine Chemicals). HPLC was carried out on a Tosoh HPLC system [pump, CCPS; detector, UV-8020; column, TSK gel ODS 120T (7.8 mm i.d. × 30 cm, Tosoh), TSK gel Amide-80 (7.8 mm i.d. × 30 cm, Tosoh) and Cosmosil 5SL (10 mm i.d. × 25 cm, Nacalai)].

**Material** The leaves of *O. ilicifolius* were collected in August, 2005 in Sendai, Miyagi prefecture, Japan, and identified by one of the authors (M. Kikuchi). A voucher specimen is held in the laboratory of M. Kikuchi.

**Extraction and Isolation** Fresh leaves of *O. ilicifolius* (2.6 kg) were extracted with MeOH at rt for eight months. The MeOH extract was concentrated under reduced pressure and the residue (466 g) was suspended in water. This suspension was successively extracted with $CHCl_3$, AcOEt, *n*-BuOH and $H_2O$. The *n*-BuOH-soluble fraction was concentrated under reduced pressure to produce a residue (167 g). The extract (74 g) was chromatographed on a silica gel column using $CHCl_3$−MeOH−$H_2O$ (50 : 10 : 1, 30 : 10 : 1, 10 : 10 : 1) and the eluate was separated into five fractions (frs. 1−5). Fr. 2 was chromatographed on a Sephadex LH-20 column using 50 % MeOH and the eluate was separated into twelve fractions (frs. 2-1−2-12). Part of the fr. 2-6 (1.5 g) was subjected to preparative HPLC [column, TSK gel ODS 120T; mobile phase, MeOH−$H_2O$ (2 : 3); UV detector, 205 nm; flow rate, 1.5 mL / min; column temperature, 40 °C] to give ten peaks (peaks 1−10). Peak 2 was subjected to preparative HPLC [column, TSK gel Amide-80; mobile phase, MeCN−$H_2O$ (9 : 1); UV detector, 205 nm; flow rate, 1.5 mL / min; column temperature, 40 °C] to give **10** (40.8 mg) and **5** (2.5 mg). Peak 3 was subjected to preparative HPLC [column, TSK gel Amide-80; mobile phase, MeCN−$H_2O$ (9 : 1); UV detector, 205 nm; flow rate, 1.5 mL / min; column temperature, 40 °C] to give **9** (70.8 mg) and **4** (7.0 mg). Peak 4 was subjected to preparative HPLC [column, TSK gel Amide-80; mobile phase, MeCN−$H_2O$ (9 : 1); UV detector, 205 nm; flow rate, 1.5 mL / min; column temperature, 40 °C] to give **8** (21.3 mg) and **3** (2.8 mg). Peak 8 was subjected to preparative HPLC [column, Cosmosil 5SL; mobile phase, $CHCl_3$−MeOH−$H_2O$ (50 : 10 : 1); UV detector, 230 nm; flow rate, 1.5 mL / min; column temperature, 40 °C] to give **7** (305.0 mg) and **2** (30.0 mg). Peak 10 was subjected to preparative HPLC [column, Cosmosil 5SL; mobile phase, $CHCl_3$−MeOH−$H_2O$ (50 : 10 : 1); UV detector, 230 nm; flow rate, 1.5 ml / min; column temperature, 40 °C] to give **6** (40.8 mg) and **1** (3.3 mg).

3′-*O*-β-D-Glucopyranosyl ligustroside (**1**) An amorphous powder; $[\alpha]_D^{27}$ –138.2 ° (*c* 0.13, MeOH); UV $\lambda_{max}$ (MeOH) nm (log ε): 226 (4.2), 240sh (4.1), 276 (3.3); FAB-MS *m/z*: 709 $[M+Na]^+$; HR-FAB-MS *m/z*: 709.2318 (Calcd for $C_{31}H_{42}O_{17}Na$, 709.2320); $^1H$ NMR ($CD_3OD$) δ: 1.64 (3H, dd, *J*=7.3, 1.5 Hz, $H_3$-10), 2.44 (1H, dd, *J*=14.1, 9.3 Hz, H-$6_A$), 2.70 (1H, dd, *J*=14.1, 4.4 Hz, H-$6_B$), 2.82 (2H, br t, *J*=6.8 Hz, $H_2$-β), 3.53 (1H, dd, *J*=8.8, 7.8 Hz, H-2′), 3.61 (1H, dd, *J*=8.8, 8.3 Hz, H-3′), 3.63 (1H, dd, *J*=11.7, 5.9 Hz, H-$6'_A$), 3.67 (1H, dd, *J*=12.2, 6.0 Hz, H-$6'''_A$), 3.71 (3H, s, 11-$CO_2CH_3$), 3.89 (1H, dd, *J*=11.7, 2.4 Hz, H-$6'_B$), 3.90 (1H, dd, *J*=12.2, 2.0 Hz, H-$6'''_B$), 3.97 (1H, dd, *J*=9.3, 4.4 Hz, H-5), 4.10 (1H, dt, *J*=10.7, 6.8 Hz, H-$\alpha_A$), 4.22 (1H, dt, *J*=10.7, 6.8 Hz, H-$\alpha_B$), 4.58 (1H, d, *J*=7.8 Hz, H-1‴), 4.84 (1H, d, *J*=7.8 Hz, H-1′), 5.91 (1H, br s, H-1), 6.05 (1H, br q, *J*=7.3 Hz, H-8), 6.71 (2H, d, *J*=8.3 Hz, H-3″, 5″), 7.05 (2H, d, *J*=8.3 Hz, H-2″, 6″), 7.51 (1H, s, H-3); $^{13}C$ NMR ($CD_3OD$): Table 1.

3′-*O*-β-D-Glucopyranosyl 10-acetoxyligustroside (**2**) An amorphous powder; $[\alpha]_D^{27}$ –174.4 ° (*c* 1.21, MeOH); UV $\lambda_{max}$ (MeOH) nm (log ε): 226 (4.6), 230sh (4.4), 276 (3.6); FAB-MS *m/z*: 767 $[M+Na]^+$; HR-FAB-MS *m/z*: 767.2358 (Calcd for $C_{33}H_{44}O_{19}Na$, 767.2374); $^1H$ NMR ($CD_3OD$) δ: 2.01 (3H, s, 10-$COCH_3$), 2.49 (1H, dd, *J*=15.1, 9.8 Hz, H-$6_A$), 2.77 (1H, dd, *J*=15.1, 3.9 Hz, H-$6_B$), 2.83 (2H, br t, *J*=6.8 Hz, $H_2$-β), 3.54 (1H, dd, *J*=9.8, 7.8 Hz, H-2′), 3.62 (1H, br t, *J*=9.0 Hz, H-3′), 3.64 (1H, dd, *J*=11.7, 6.1 Hz, H-$6'_A$), 3.69 (1H, dd, *J*=12.2, 5.9 Hz, H-$6'''_A$), 3.72 (3H, s, 11-$CO_2CH_3$), 3.89 (1H, dd, *J*=11.7, 2.2 Hz, H-$6'_B$), 3.90 (1H, dd, *J*=12.2, 2.0 Hz, H-$6'''_B$), 4.00 (1H, dd, *J*=9.8, 3.9 Hz, H-5), 4.14 (1H, dt, *J*=10.7, 6.8 Hz, H-$\alpha_A$), 4.25 (1H, dt, *J*=10.7, 6.8 Hz, H-$\alpha_B$), 4.56 (1H, ddd, *J*=13.5, 6.1, 1.5 Hz, H-$10_A$), 4.59 (1H, d, *J*=7.8 Hz, H-1‴), 4.76 (1H, dd, *J*=13.5, 7.6 Hz, H-$10_B$), 4.87 (1H, d, *J*=7.8 Hz, H-1′), 5.98 (1H, br s, H-1), 6.06 (1H, br dt, *J*=6.1, 1.5 Hz, H-8), 6.71 (2H, d, *J*=8.8 Hz, H-3″, 5″), 7.05 (2H, d, *J*=8.8 Hz, H-2″, 6″), 7.53 (1H, s, H-3); $^{13}C$ NMR ($CD_3OD$): Table 1.

3′-*O*-β-D-Glucopyranosyl oleuropein (**3**) An amorphous powder; $[\alpha]_D^{27}$ –122.6 ° (*c* 0.11, MeOH); UV $\lambda_{max}$ (MeOH) nm (log ε): 202 (4.4), 230 (4.2), 280 (3.4); FAB-MS *m/z*: 725 $[M+Na]^+$; HR-FAB-MS *m/z*: 725.2256 (Calcd for $C_{31}H_{42}O_{18}Na$, 725.2268); $^1H$ NMR ($CD_3OD$) δ: 1.66 (3H, dd, *J*=7.3, 1.5 Hz, $H_3$-10), 2.44 (1H, dd, *J*=14.1, 8.8 Hz, H-$6_A$), 2.70 (1H, dd, *J*=14.1, 4.6 Hz, H-$6_B$), 2.76 (2H, br t, *J*=6.8 Hz, $H_2$-β), 3.52 (1H, dd, *J*=8.8, 7.8 Hz, H-2′), 3.61 (1H, br t, *J*=8.8 Hz, H-3′), 3.63 (1H, dd, *J*=11.7, 5.9 Hz, H-$6'_A$), 3.69 (1H, dd, *J*=12.2, 5.4 Hz, H-$6'''_A$), 3.71 (3H, s, 11-$CO_2CH_3$), 3.89 (1H, dd, *J*=11.7, 2.4 Hz, H-$6'_B$), 3.90 (1H, dd, *J*=12.2, 2.0 Hz, H-6‴$_B$), 3.97 (1H, dd, *J*=8.8, 4.6 Hz, H-5), 4.10 (1H, dt, *J*=10.7, 6.8 Hz, H-α$_A$), 4.20 (1H, dt, *J*=10.7, 6.8 Hz, H-α$_B$), 4.58 (1H, d, *J*=7.3 Hz, H-1‴), 4.87 (1H, d, *J*=7.8 Hz, H-1′), 5.91 (1H, br s, H-1), 6.06 (1H, br q, *J*=7.3 Hz, H-8), 6.54 (1H, dd, *J*=8.3, 2.0 Hz, H-6″), 6.66 (1H, d, *J*=2.0 Hz, H-2″), 6.68 (1H, d, *J*=8.3 Hz, H-5″), 7.51 (1H, s, H-3); $^{13}$C NMR ($CD_3OD$): Table 1.

3′-*O*-β-D-Glucopyranosyl 10-acetoxyoleuropein (**4**) An amorphous powder; $[\alpha]_D^{27}$ –125.0 ° (*c* 0.28, MeOH); UV $\lambda_{max}$ (MeOH) nm (log ε): 202 (4.5), 230 (4.2), 280 (3.5); FAB-MS *m/z*: 783 $[M+Na]^+$; HR-FAB-MS *m/z*: 783.2339 (Calcd for $C_{33}H_{44}O_{20}Na$, 783.2324); $^1$H NMR ($CD_3OD$) δ: 2.02 (3H, s, 10-$COCH_3$), 2.50 (1H, dd, *J*=14.6, 9.8 Hz, H-6$_A$), 2.77 (1H, dd, *J*=14.6, 3.9 Hz, H-6$_B$), 2.77 (2H, br t, *J*=6.8 Hz, H$_2$-β), 3.54 (1H, dd, *J*=9.3, 7.8 Hz, H-2′), 3.62 (1H, dd, *J*=9.3, 8.3 Hz, H-3′), 3.64 (1H, dd, *J*=12.0, 5.8 Hz, H-6′$_A$), 3.68 (1H, dd, *J*=12.2, 5.4 Hz, H-6‴$_A$), 3.72 (3H, s, 11-$CO_2CH_3$), 3.89 (1H, dd, *J*=12.0, 2.0 Hz, H-6′$_B$), 3.90 (1H, dd, *J*=12.2, 2.0 Hz, H-6‴$_B$), 4.00 (1H, dd, *J*=9.8, 3.9 Hz, H-5), 4.14 (1H, dt, *J*=10.7, 6.8 Hz, H-α$_A$), 4.22 (1H, dt, *J*=10.7, 6.8 Hz, H-α$_B$), 4.58 (1H, ddd, *J*=13.7, 5.8, 1.5 Hz, H-10$_A$), 4.59 (1H, d, *J*=7.3 Hz, H-1‴), 4.77 (1H, dd, *J*=13.7, 7.8 Hz, H-10$_B$), 4.88 (1H, d, *J*=7.8 Hz, H-1′), 5.97 (1H, br s, H-1), 6.07 (1H, br dt, *J*=7.8, 1.5 Hz, H-8), 6.54 (1H, dd, *J*=8.3, 2.4 Hz, H-6″), 6.66 (1H, d, *J*=2.4 Hz, H-2″), 6.68 (1H, d, *J*=8.3 Hz, H-5″), 7.53 (1H, s, H-3); $^{13}$C NMR ($CD_3OD$): Table 1.

Hiiragilide (**5**: 3′-*O*-β-D-Glucopyranosyl 10-hydroxyligustroside) An amorphous powder; $[\alpha]_D^{27}$ –115.7 ° (*c* 0.10, MeOH); UV $\lambda_{max}$ (MeOH) nm (log ε): 225 (4.2), 235sh (4.0), 275 (3.3); FAB-MS *m/z*: 725 $[M+Na]^+$; HR-FAB-MS *m/z*: 725.2290 (Calcd for $C_{31}H_{42}O_{18}Na$, 725.2269); $^1$H NMR ($CD_3OD$) δ: 2.49 (1H, dd, *J*=14.9, 9.8 Hz, H-6$_A$), 2.72 (1H, dd, *J*=14.9, 4.4 Hz, H-6$_B$), 2.82 (2H, br t, *J*=7.1 Hz, H$_2$-β), 3.54 (1H, dd, *J*=8.8, 7.8 Hz, H-2′), 3.61 (1H, dd, *J*=9.3, 8.8 Hz, H-3′), 3.65 (1H, dd, *J*=11.7, 5.9 Hz, H-6′$_A$), 3.66 (1H, dd, *J*=12.2, 6.3 Hz, H-6‴$_A$), 3.70 (3H, s, 11-$CO_2CH_3$), 3.89 (1H, dd, *J*=11.7, 2.5 Hz, H-6′$_B$), 3.90 (1H, dd, *J*=12.2, 1.8 Hz, H-6‴$_B$), 3.94 (1H, dd, *J*=9.8, 4.4 Hz, H-5), 4.21 (4H, m, H$_2$-10, H$_2$-α), 4.59 (1H, d, *J*=7.8 Hz, H-1‴), 4.86 (1H, d, *J*=7.8 Hz, H-1′), 5.96 (1H, br s, H-1), 6.13 (1H, br t, *J*=6.1 Hz, H-8), 6.71 (2H, d, *J*=8.3 Hz, H-3″, 5″), 7.04 (2H, d, *J*=8.3 Hz, H-2″, 6″), 7.52 (1H, s, H-3); $^{13}$C NMR ($CD_3OD$): Table 1.

Acetylation of **5** Compound **5** (1.5 mg) was acetylated with $Ac_2O$-pyridine in the usual manner to give **5a** (2.0 mg). An amorphous powder; $[\alpha]_D^{27}$ –101.9 ° (*c* 0.12, MeOH); UV $\lambda_{max}$ (MeOH) nm (log ε): 207 (4.1), 216sh (4.1), 226 (4.1); FAB-MS *m/z*: 1103 $[M+Na]^+$; HR-FAB-MS *m/z*: 1103.3204 (Calcd for $C_{49}H_{60}O_{27}Na$, 1103.3219); $^1$H NMR ($CDCl_3$) δ: 2.01 (6H, s, $COCH_3$), 2.00, 2.04, 2.05, 2.06, 2.08, 2.11 (each 3H, s, $COCH_3$), 2.29 (3H, s, 4″-$COCH_3$), 2.41 (1H, dd, *J*=15.4, 9.3 Hz, H-6$_A$), 2.75 (1H, dd, *J*=15.4, 3.9 Hz, H-6$_B$), 2.90 (2H, br t, *J*=7.1 Hz, H$_2$-β), 3.68 (1H, ddd, *J*=9.8, 4.1, 2.2 Hz, H-5‴), 3.73 (1H, m, H-5′), 3.73 (3H, s, 11-$CO_2CH_3$), 3.95 (1H, dd, *J*=9.3, 3.9 Hz, H-5), 3.96 (1H, t, *J*=9.4 Hz, H-3′), 4.04— 4.40 (6H, m, H$_2$-α, H$_2$-6′, H$_2$-6‴), 4.63 (1H, d, *J*=8.1 Hz, H-1‴), 4.66 (1H, m, H-10$_A$), 4.77 (1H, dd, *J*=13.4, 7.1 Hz, H-10$_B$), 4.90 (1H, dd, *J*=9.5, 8.1 Hz, H-2‴), 4.92 (1H, d, *J*=8.3 Hz, H-1′), 4.99−5.17 (4H, m, H-2′, 4′, H-3‴, 4‴), 5.68 (1H, br s, H-1), 5.97 (1H, br t, *J*=6.1 Hz, H-8), 7.01 (2H, d, *J*=8.5 Hz, H-3″, 5″), 7.19 (2H, d, *J*=8.5 Hz, H-2″, 6″), 7.44 (1H, s, H-3); $^{13}$C NMR ($CDCl_3$) δ: 20.35, 20.37, 20.56, 20.58, 20.66, 20.90, 20.91, 21.12, 21.13 (CO$\underline{C}H_3$), 30.9 (C-5), 34.3 (C-β), 39.9 (C-6), 51.6 (11-$CO_2\underline{C}H_3$), 60.7 (C-10), 61.7 (C-6′), 61.8 (C-6‴), 65.0 (C-α), 68.0 (C-4′), 71.2 (C-2‴), 71.8 (C-5′), 72.2 (C-5‴), 72.4 (C-2′), 72.9 (C-3‴), 78.6 (C-3′), 92.6 (C-1), 96.8 (C-1′), 101.0 (C-1‴), 108.5 (C-4), 121.6 (C-3″, 5″), 124.3 (C-8), 129.8 (C-2″, 6″), 131.0 (C-9), 135.2 (C-1″), 149.4 (C-4″), 152.8 (C-3), 166.4 (C-11), 168.9, 169.1, 169.30, 169.34, 169.6, 170.4, 170.5, 170.66 ($\underline{C}OCH_3$), 170.7 (C-7).

**Acid Hydrolysis of 1−5**. Each of compounds (*ca*. 1.0 mg) was refluxed with 1M HCl (1 mL) for 5 h. The reaction mixture was neutralized with $Ag_2CO_3$ and filtered. The solution was concentrated *in vacuo* and dried to give a sugar fraction. The sugar fraction was analyzed by HPLC under the following conditions: column, TSK gel Amide-80 (7.8 mm i.d.× 30 cm, Tosoh); column temperature, 45 °C; mobile phase, MeCN−$H_2O$ (4 : 1); flow rate, 1.0 mL/min; chiral detection (JASCO OR-2090). Identification of D-glucose present in the sugar fraction was carried out by the comparison of the retention time and optical rotation with that of authentic sample; $t_R$ (min) 39.0 (D-glucose, positive optical rotation).

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