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# Studies on the Constituents of Asclepiadaceae Plants. LVI.[1] Isolation of New Antitumor-Active Glycosides from *Dregea volubilis* (L.) BENTH.

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Seven new glycosides were isolated from the stem of *Dregea volubilis* (L.) BENTH. The structures of dregeosides $A_{p1}$ (**1**), $A_{01}$ (**2**), $A_{a1}$ (**3**), $A_{11}$ (**4**), $C_{11}$ (**5**), $K_{p1}$ (**6**), and $K_{a1}$ (**7**) were deduced on the basis of chemical and spectral evidence as drevogenin A 3-*O*-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-oleandropyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside, drevogenin A 3-*O*-β-D-glucopyranosyl-(1→4)-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-oleandropyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside, drevogenin A 3-*O*-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside, drevogenin A 3-*O*-β-D-glucopyranosyl-(1→4)-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside, drevogenin C 3-*O*-β-D-glucopyranosyl-(1→4)-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside, drebyssogenin $K_2$ 3-*O*-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-oleandropyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside, and drebyssogenin $K_2$ 3-*O*-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside, respectively. Among them, **1** and **2** were active against Ehrlich carcinoma (solid type), and the latter was also active against melanoma B-16.

**Keywords**——dregeoside $A_{p1}$; dregeoside $A_{01}$; dregeoside $A_{a1}$; dregeoside $A_{11}$; dregeoside $C_{11}$; dregeoside $K_{p1}$; dregeoside $K_{a1}$; *Dregea volubilis* (L.); Asclepiadaceae; antitumor activity

A crude drug prepared from the plant *Dregea volubilis* (L.) BENTH., native to Southeast Asia, has been used as an antifebrile and emetic.

In 1965 and 1966, Reichstein and his co-workers studied the components of the seed of this plant and confirmed the structures of drevogenins A (**8**), B, D, and P.[2,3] In 1969, Mitsuhashi *et al.*, studied the components of the stem of this drug and reported the structure of dregoside A.[4] In this paper, we describe the isolation and structures of seven new glycosides from the stem of this plant. These glycosides consist of C/D-*cis*-polyoxypregnane derivatives as the aglycone, and mainly 3-*O*-methyl-2,6-dideoxy sugars. Among them, dregeosides $A_{p1}$ (**1**)[5] and $A_{01}$ (**2**) showed antitumor activities against Ehrlich carcinoma (solid type), and the latter also showed activity against melanoma B-16.

The glycosides were isolated from methanolic extract of the stem of this plant, obtained from Thailand, as shown in Chart 1. The crude glycoside mixture was subjected to repeated silica gel and reversed phase gel column chromatography with various solvent systems to give **1**, **2**, and dregeosides $A_{a1}$[6] (**3**), $A_{11}$[6] (**4**), $C_{11}$ (**5**), $K_{p1}$ (**6**), and $K_{a1}$ (**7**) (yields: 0.016, 0.022, 0.035, 0.027, 0.005, 0.048, and 0.048% from the dried crude drug, respectively) as amorphous white powders. They showed positive Liebermann–Burchard and Keller–Kiliani[7] reactions, which suggest the presence of a $\Delta^5$ steroid with a 2-deoxy sugar moiety in each molecule.

Dregeoside $A_{p1}$[5] (**1**) has the molecular formula $C_{56}H_{90}O_{20}$ on the basis of its elemental

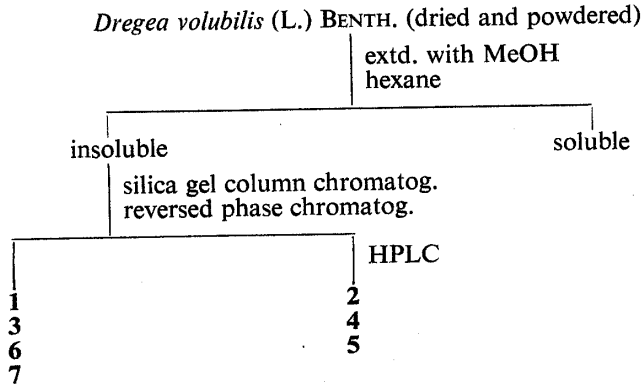
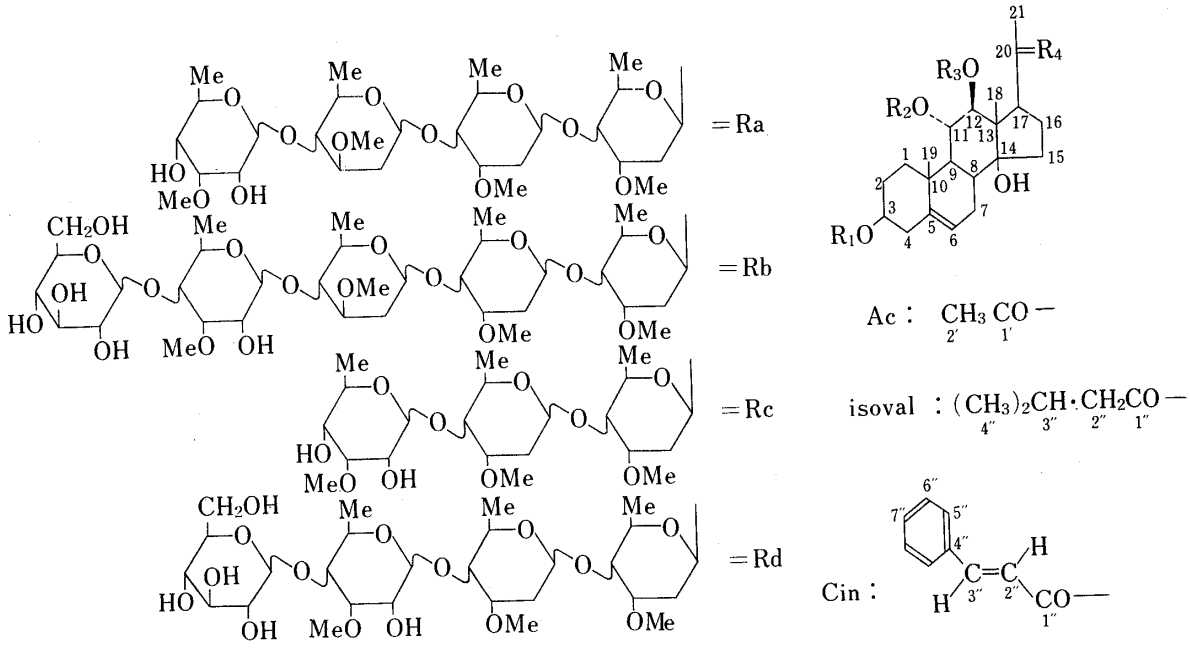



Chart 1. Extraction and Isolation of Glycosides

analysis. Molecular secondary ion mass spectrometry (SIMS) gave ion peaks at $m/z$ 1150 $[(M+Na)]^+$. The 400 MHz proton nuclear magnetic resonance ($^1$H-NMR) spectrum of **1** in deuterochloroform ($CDCl_3$) showed the methyl groups of the aglycone moiety at $\delta$ 1.01 (6H, d, $J=6.8$ Hz, 4″-$CH_3$), 1.07 (3H, s, 18-$CH_3$), 1.11 (3H, s, 19-$CH_3$), 1.97 (3H, s, 2′-$CH_3$), and 2.18 (3H, s, 21-$CH_3$) and the secondary methyl groups of 6-deoxy sugars at $\delta$ 1.21, 1.22, 1.26, and 1.35. The $\beta$-linkages of the sugars were revealed by the coupling constants of four anomeric proton signals at $\delta$ 4.48 (1H, dd, $J=10$, 2 Hz), 4.75 (1H, dd, $J=10$, 2 Hz), 4.795 (1H, d, $J=8$ Hz), and 4.83 (1H, dd, $J=10$, 2 Hz) in the $^1$H-NMR spectrum of **1**. From the $^{13}$C nuclear magnetic resonance ($^{13}$C-NMR) spectrum of **1** in pentadeuteropyridine ($C_5D_5N$) (Table I), **1**




| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| **1** | $R_a$ | Ac | isoval | O |
| **2** | $R_b$ | Ac | isoval | O |
| **3** | $R_c$ | Ac | isoval | O |
| **4** | $R_d$ | Ac | isoval | O |
| **5** | $R_d$ | Cin | Ac | O |
| **6** | $R_a$ | H | H | O-isoval |
| **7** | $R_c$ | H | H | O-isoval |

Chart 2

contained drevogenin A[3] (**8**) as the aglycone moiety and four monosaccharide units, two cymaropyranoses (**9**), one oleandropyranose (**10**), and one 3-*O*-methyl-6-deoxy-allopyranose (**11**) in that order. The glycosidation shifts[8] of the aglycone carbons for **1** were observed at C-2 (−2.2 ppm), C-3 (+6.6), and C-4 (−4.0) (Table I.) so that the sugar moiety is linked to the C-3 hydroxyl group of the aglycone. The glycosidation shifts[8] of the aglycone carbons for the

TABLE I. $^{13}$C-NMR Chemical Shifts

| Aglycone moiety | **1** | **2** | **8** | Sugar moiety | **1** | **2** |
|---|---|---|---|---|---|---|
| C- 1 | 38.7 | 38.8 | 38.9 | Cym C-1 | 96.2 | 96.4 |
| 2 | 30.4 (−2.2) | 30.5 (−2.1) | 32.6 | 2 | 37.0[b] | 37.3[b] |
| 3 | 77.3[a] (+6.6) | 77.1[a] (+6.4) | 70.7 | 3 | 77.8[a] | 78.0 |
| 4 | 39.7 (−4.0) | 39.8 (−3.9) | 43.7 | 4 | 82.7[c] | 82.9[c] |
| 5 | 139.3 | 139.7 | 140.2 | 5 | 68.8 | 69.0 |
| 6 | 122.2 | 122.5 | 121.5 | 6 | 18.5[d] | 18.3[d] |
| 7 | 28.2 | 28.3 | 28.1 | 3-OMe | 58.7 | 58.9 |
| 8 | 37.1 | 37.2 | 37.2 | 1′ | 100.2 | 100.4 |
| 9 | 47.8 | 48.0 | 47.9 | 2′ | 37.0[b] | 37.6[b] |
| 10 | 39.3 | 39.5 | 39.3 | 3′ | 77.6[a] | 78.0 |
| 11 | 71.7 | 71.7 | 71.7 | 4′ | 82.9[c] | 83.1[c] |
| 12 | 77.6[a] | 77.5[a] | 77.3 | 5′ | 68.8 | 69.0 |
| 13 | 54.7 | 54.8 | 54.6 | 6′ | 18.6[d] | 18.5[d] |
| 14 | 83.8 | 83.9 | 83.8 | 3′-OMe | 58.7 | 58.9 |
| 15 | 34.5 | 34.6 | 34.5 | Ole C-1 | 101.7 | 101.8 |
| 16 | 23.9 | 24.0 | 23.9 | 2 | 37.1[b] | 37.3[b] |
| 17 | 58.2 | 58.3 | 58.2 | 3 | 79.0 | 79.6 |
| 18 | 11.5 | 11.4 | 11.4 | 4 | 83.1[c] | 83.3[c] |
| 19 | 19.2 | 19.3 | 19.3 | 5 | 71.9 | 71.9 |
| 20 | 213.4 | 214.0 | 213.4 | 6 | 18.6[d] | 18.6 |
| 21 | 31.8 | 31.9 | 31.8 | 3-OMe | 57.1 | 57.4 |
| 1′ | 169.7 | 170.1 | 170.1 | Allo C-1 | 101.7* | 101.8 |
| 2′ | 21.6 | 21.6 | 21.6 | 2 | 73.1* | 72.6 |
| 1″ | 172.6 | 173.0 | 172.2 | 3 | 83.6* | 83.1[c] (−0.5) |
| 2″ | 43.3 | 43.4 | 44.0 | 4 | 74.2* | 83.1[c] (+8.9) |
| 3″ | 25.6 | 25.7 | 25.9 | 5 | 70.8* | 69.5 (−1.3) |
| 4″ | 22.5 | 22.6 | 22.5 | 6 | 18.8 | 18.9 |
| | | | | 3-OMe | 61.9 | 61.7 |
| | | | | Glc C-1 | | 106.6* |
| | | | | 2 | | 75.5* |
| | | | | 3 | | 78.4* |
| | | | | 4 | | 71.9* |
| | | | | 5 | | 78.4* |
| | | | | 6 | | 63.0 |

$\delta$ ppm from internal TMS in $C_5D_5N$.

*a*), *b*), *c*), or *d*) in each column may be interchangeable.

* The chemical shifts with asterisks have the longest dipole–dipole relaxation times by PRFT measurements.

( ), glycosidation shifts.

Cym, $\beta$-D-cymaropyranosyl; Ole, $\beta$-D-oleandropyranosyl; Allo, 3-*O*-methyl-6-deoxy-$\beta$-D-allopyranosyl; Glc, $\beta$-D-glucopyranosyl.

other six glycosides described here were also observed at C-2, C-3, and C-4 (Tables I, III, V, and VI), and hence the sugar moiety was linked to the C-3 hydroxyl group of the aglycone in each case. The terminal 3-*O*-methyl-6-deoxy-allopyranosyl signals of **1** were easily distinguished from other sugar signals by PRFT measurements.[9] On mild acidic hydrolysis (0.05 N $H_2SO_4$–50% MeOH, 50 °C, 30 min), **1** afforded **8**, **9**, and sugar fragment-I (**12**). The former

two compounds were identified by thin layer chromatographic (TLC) comparison with authentic samples. The $^{13}$C-NMR signal pattern (Fig. 1) and $^{1}$H-NMR spectral data of **12** were the same as those of pachybiose[10,11] which was isolated from this drug. From these data, **10** was adjacent to **11**. Thus, the structure of **1** has been established as drevogenin A 3-*O*-3-*O*-methyl-6-deoxy-*β*-allopyranosyl-(1→4)-*β*-D-oleandropyranosyl-(1→4)-*β*-D-cymaropyranosyl-(1→4)-*β*-D-cymaropyranoside.

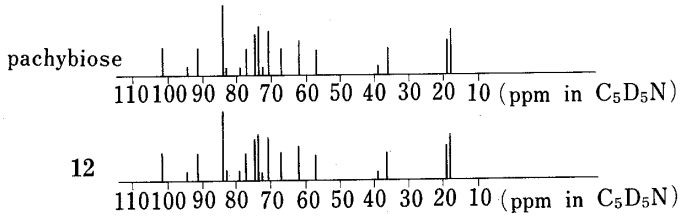



Fig. 1. $^{13}$C-NMR Spectra of **12** and Pachybiose

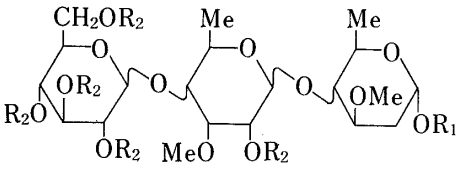
Dregeoside $A_{01}$ (**2**) has the molecular formula $C_{60}H_{100}O_{25}$ on the basis of its elemental analysis, and on mild acidic hydrolysis gave **8**, **9**, and sugar fragment-II (**13**), which were identified by TLC comparison with authentic samples. SIMS and the fast atom bombardment mass spectrum (FAB) of **2** gave ion peaks at *m/z*: 1267 $[(M+Na)^+]$ and *m/z*: 1283 $[(M+K)^+]$, respectively. The anomeric proton signals of **2** at *δ* 4.35 (1H, d, *J*=7.8 Hz), 4.49 (1H, dd, *J*=10, 2 Hz), 4.74 (1H, d, *J*=7.8 Hz), 4.76 (1H, dd, *J*=10, 2 Hz), and 4.84 (1H, dd, *J*=10, 2 Hz) showed *β*-glucosyl linkages by their coupling constants in the 400 MHz $^{1}$H-NMR ($CDCl_3$–$CD_3OD$ (9:1)). The $^{13}$C-NMR signals (Table I) indicated the presence of **8** as the aglycone moiety and five sugars; two **9**, one **10**, one **11**, and one glucopyranose (**14**). The PRFT measurements[9] of **2** showed that the terminal sugar was **14**. Compound **2** was hydrolyzed into deglucosyl-**2** (**15**) and **14** by snail *β*-glucosidase, and the latter was identified by high performance liquid chromatographic (HPLC) comparison with an authentic sample. The $^{1}$H-NMR and $^{13}$C-NMR (Table I) spectra of **15** were superimposable on those of **1**. On mild acidic hydrolysis, **15** gave **8**, **9**, and **12**. Thus **15** was identified as **1**. In order to clarify the glucosidic linkage in **2**, the trisaccharide (**13**), which was obtained by mild acidic hydrolysis of **2** an identified by TLC comparison with a sample from condurangoglycosides,[12] was investigated. The glycosidic linkage in **13** at C-4 of **11** was deduced from the glycosidation shifts.[12] This presumption was confirmed by 400 MHz $^{1}$H-NMR spin–spin decoupling experiments on the penta-*O*-acetate (**17**) of the methyl *α*-glycoside (**16**) of **13**. Owing to the acetylation, 2′-CH of **16** moved downfield to *δ* 4.59 (1H, dd, *J*=8.5, 2.9 Hz). Decoupling the proton at *δ* 5.05 (1H, d, *J*=8.5 Hz, 1′-CH) caused the double doublet (dd) at *δ* 4.59 to collapse to d. Irradiation of the proton at *δ* 4.59 caused the d at *δ* 5.05 and the dd at *δ* 3.96 (1H, dd, *J*=2.9, 2.5 Hz, 3′-CH) to collapse to s and d, respectively. Decoupling at *δ* 3.96 caused the dd at *δ* 4.59 to collapse to d (Fig. 2). Thus, the dd proton signal at *δ* 4.59 was assigned to 2′-CH of **17**. The hydroxyl group at C-2′ was acetylated, so that **14** is linked to the hydroxyl group at C-4′ of **13**. Therefore, the structure of **2** was confirmed as drevogenin A 3-*O*-*β*-D-glucopyranosyl-(1→4)-3-*O*-methyl-6-deoxy-*β*-D-allopyranosyl-(1→4)-*β*-D-oleandropyranosyl-(1→4)-*β*-D-cymaropyranosyl-(1→4)-*β*-D-cymaropyranoside.

Dregeoside $A_{a1}$[6] (**3**) has **8** as the aglycone moiety as determined by acidic hydrolysis and from the $^{13}$C-NMR spectrum (Table III). In the $^{1}$H-NMR spectrum of **3**, three *β*-linked anomeric proton signals were observed at *δ* 4.59 (1H, d, *J*=7.8 Hz), 4.76 (1H, dd, *J*=10, 2 Hz), and 4.83 (1H, dd, *J*=10, 2 Hz). In the $^{13}$C-NMR spectrum of **3** (Table II), anomeric carbon signals indicate the presence of three sugars; two **9** and one **11**. The terminal 3-*O*-methyl-6-deoxy-allopyranosyl signals of **3** were confirmed by PRFT measurements.[9] Mild acidic hydrolysis of **3** afforded **8**, **9**, and sugar fragment-III (**18**); the former two compounds were identified by TLC comparison with authentic samples. The $^{13}$C-NMR spectrum of **18**

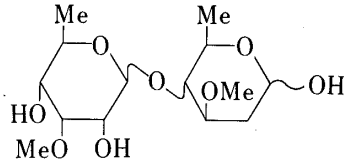
TABLE II. $^{13}$C-NMR Chemical Shifts

| Aglycone moiety | 15 | 20 | Sugar moiety | 15 | 20 |
|---|---|---|---|---|---|
| C- 1 | 38.7 | 38.7 | Cym C-1 | 96.4 | 96.4 |
| 2 | 30.3 | 30.5 | 2 | 37.1[b] | 36.9[b] |
| 3 | 77.1[a] | 77.1[a] | 3 | 77.8[a] | 78.0[c] |
| 4 | 39.8 | 39.8 | 4 | 82.8[c] | 83.2[d] |
| 5 | 139.7 | 139.7 | 5 | 68.9[d] | 69.0[e] |
| 6 | 122.5 | 122.5 | 6 | 18.5[e] | 18.6 |
| 7 | 28.3 | 28.2 | 3-OMe | 58.8[f] | 58.8 |
| 8 | 37.3 | 37.2 | 1′ | 100.4 | 100.4 |
| 9 | 48.0 | 48.0 | 2′ | 37.3[b] | 37.2[b] |
| 10 | 39.5 | 39.4 | 3′ | 77.8[a] | 78.1[c] |
| 11 | 71.9 | 71.9 | 4′ | 83.2[c] | 83.3[d] |
| 12 | 77.5[a] | 77.5[a] | 5′ | 69.0[d] | 69.3[e] |
| 13 | 54.8 | 54.8 | 6′ | 18.6[e] | 18.6 |
| 14 | 84.0 | 83.9 | 3′-OMe | 58.9[f] | 58.8 |
| 15 | 34.6 | 34.5 | Ole C-1 | 101.9 | |
| 16 | 24.0 | 24.0 | 2 | 37.5[b] | |
| 17 | 58.3 | 58.3 | 3 | 79.3 | |
| 18 | 11.4 | 11.4 | 4 | 83.3[c] | |
| 19 | 19.3 | 19.2 | 5 | 72.1 | |
| 20 | 214.0 | 214.0 | 6 | 18.6[e] | |
| 21 | 31.9 | 31.9 | 3-OMe | 57.1 | |
| 1′ | 170.1 | 170.0 | Allo C-1 | 101.9 | 104.2 |
| 2′ | 21.6 | 21.6 | 2 | 73.3 | 73.1 |
| 1″ | 173.0 | 173.0 | 3 | 84.0 | 83.9 |
| 2″ | 43.5 | 43.4 | 4 | 74.6 | 74.4 |
| 3″ | 25.6 | 25.6 | 5 | 71.0 | 70.7 |
| 4″ | 22.6 | 22.5 | 6 | 18.9 | 18.6 |
| | | | 3-OMe | 62.0 | 62.1 |

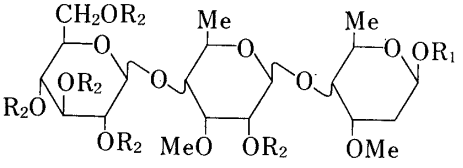
$\delta$ ppm from internal TMS in $C_5D_5N$.
*a*), *b*), *c*), *d*), *e*), or *f*) in each column may be interchangeable.
Cym, $\beta$-D-cymaropyranosyl; Ole, $\beta$-D-oleandropyranosyl; Allo, 3-*O*-methyl-6-deoxy-$\beta$-D-allopyranosyl.



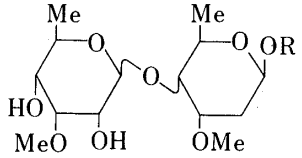

**13** : $R_1=R_2=H$
**16** : $R_1=Me$, $R_2=H$
**17** : $R_1=Me$, $R_2=Ac$




**12**




**21** : $R_1=R_2=H$
**22** : $R_1=Me$, $R_2=H$
**23** : $R_1=Me$, $R_2=Ac$




**18** : R=H
**19** : R=Me

Chart 3. Sugar Fragments

TABLE III. $^{13}$C-NMR Chemical Shifts

| Aglycone moiety | 3 | 4 | Sugar moiety | 3 | 4 |
|---|---|---|---|---|---|
| C- 1 | 38.7 | 38.7 | Cym C-1 | 96.4 | 96.4 |
| 2 | 30.5 (−2.1) | 30.5 (−2.1) | 2 | 36.9[b] | 37.1[b] |
| 3 | 77.1[a] (+6.4) | 77.1[a] (+6.4) | 3 | 78.0[c] | 78.0[c] |
| 4 | 39.8 (−4.1) | 39.8 (−4.1) | 4 | 83.3 | 83.0[d] |
| 5 | 139.7 | 139.7 | 5 | 69.0[d] | 69.0[e] |
| 6 | 122.5 | 122.4 | 6 | 18.6 | 18.2[f] |
| 7 | 28.2 | 28.2 | 3-OMe | 58.8 | 58.9[g] |
| 8 | 37.3 | 37.2 | 1′ | 100.4 | 100.4 |
| 9 | 48.0 | 48.0 | 2′ | 37.3[b] | 37.2[b] |
| 10 | 39.5 | 39.4 | 3′ | 78.1[c] | 78.1[c] |
| 11 | 71.9 | 71.9 | 4′ | 83.3 | 83.1[d] |
| 12 | 77.5[a] | 77.5[a] | 5′ | 69.3[d] | 69.2[e] |
| 13 | 54.8 | 54.7 | 6′ | 18.6 | 18.5[f] |
| 14 | 83.9 | 83.9 | 3′-OMe | 58.8 | 59.0[g] |
| 15 | 34.6 | 34.6 | Allo C-1 | 104.2* | 103.9 |
| 16 | 24.0 | 24.0 | 2 | 73.1* | 72.5 |
| 17 | 58.3 | 58.3 | 3 | 83.9* | 83.2[d] (−0.7) |
| 18 | 11.4 | 11.4 | 4 | 74.4* | 83.2[d] (+8.8) |
| 19 | 19.2 | 19.2 | 5 | 70.7* | 69.2[e] (−1.5) |
| 20 | 214.0 | 214.0 | 6 | 18.6 | 18.6[f] |
| 21 | 31.9 | 31.9 | 3-OMe | 62.1 | 61.7 |
| 1′ | 170.0 | 170.1 | Glc C-1 | | 106.5* |
| 2′ | 21.6 | 21.6 | 2 | | 75.4* |
| 1″ | 173.0 | 173.0 | 3 | | 78.3* |
| 2″ | 43.3 | 43.4 | 4 | | 71.9* |
| 3″ | 25.6 | 25.6 | 5 | | 78.3* |
| 4″ | 22.6 | 22.5 | 6 | | 63.0 |

$\delta$ ppm from internal TMS in $C_5D_5N$.

*a*), *b*), *c*), *d*), *e*), or *f*) in each column may be interchangeable.

* The chemical shifts with asterisks have the longest dipole–dipole relaxation times by PRFT measurements.

( ), glycosidation shifts.

Cym, β-D-cymaropyranosyl; Allo, 3-*O*-methyl-6-deoxy-β-D-allopyranosyl; Glc, β-D-glucopyranosyl.

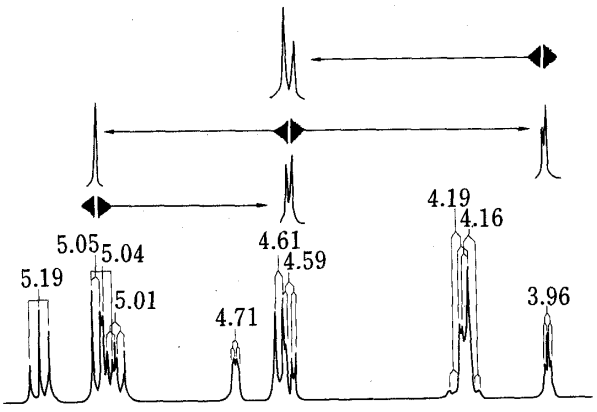



Fig. 2. Partial $^1$H-NMR Spectrum of **17** (400 MHz, $CDCl_3$)

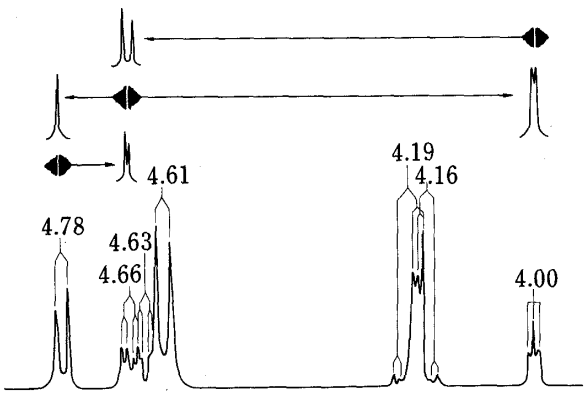



Fig. 3. Partial $^1$H-NMR Spectrum of **23** (400 MHz, $CDCl_3$)

TABLE IV. $^{13}$C-NMR Chemical Shifts

| | 18 | 19 |
|---|---|---|
| C-1-OMe | | 55.9 |
| 1 | 92.6 | 99.3 |
| 2 | 38.4 | 36.2 |
| 3 | 78.5 | 77.9 |
| 4 | 83.9 | 83.3 |
| 5 | 69.3 | 69.3 |
| 6 | 18.6 | 18.6 |
| 3-OMe | 58.6 | 58.5 |
| 1′ | 104.2 | 104.1 |
| 2′ | 73.2 | 73.0 |
| 3′ | 83.8 | 83.9 |
| 4′ | 74.5 | 74.4 |
| 5′ | 70.5 | 70.6 |
| 6′ | 18.9 | 18.6 |
| 3′-OMe | 62.1 | 62.1 |

$\delta$ ppm from internal TMS in $C_5D_5N$.

corresponded to that of α-methyl asclepobioside (**19**) (Table IV). The 400 MHz $^1$H-NMR spectrum of **18** also supported this conclusion. Thus, **18** was identified as asclepobiose.[10,13] According to these data, the structure of **3** has been established as drevogenin A 3-*O*-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside.

Dregeoside $A_{11}$[6] (**4**) has the molecular formula $C_{55}H_{88}O_{22}$ from the elemental analysis. The 400 MHz $^1$H-NMR ($CDCl_3$–$CD_3OD$ (9 : 1)) spectrum of **4** showed four anomeric proton signals at $\delta$ 4.35 (1H, d, $J$=7.8 Hz), 4.57 (1H, d, $J$=7.8 Hz), 4.75 (1H, dd, $J$=10, 2 Hz), and 4.84 (1H, dd, $J$=10, 2 Hz). From the $^{13}$C-NMR spectrum, **4** contained **8** as the aglycone moiety, and two **9**, one **11**, and one **14** (Table III). The PRFT measurements[9] of **4** indicated that the terminal sugar was **14**. Compound **4** was hydrolyzed into deglucosyl-**4** (**20**) and **14** by β-glucosidase, and the latter product was identified by HPLC comparison with an authentic sample. The $^1$H- and $^{13}$C-NMR (Table II) spectra of **20** were identical with those of **3**. On mild acidic hydrolysis, **20** gave **8**, **9**, and **18**, which were identified by TLC comparison with authentic samples. Thus, **20** identified as **3**. Acidic hydrolysis of **4** afforded sugar fragment-IV (**21**). The acetylation of the methyl β-glycoside (**22**) of **21** gave the penta-*O*-acetate (**23**). After the acetylation, 2′-CH of **23** moved downfield to $\delta$ 4.66 in the 400 MHz $^1$H-NMR spectrum. Decoupling the proton d at $\delta$ 4.78 (1H, d, $J$=8.3 Hz, 1′-CH) caused the dd at $\delta$ 4.66 (1H, dd, $J$=8.3, 2.9 Hz) to collapse to d. Irradiation of the proton at $\delta$ 4.66 caused the d at $\delta$ 4.78 and triplet (t) at $\delta$ 4.00 (1H, t, $J$=2.9 Hz, 3′-CH) to collapse to s and d, respectively. Decoupling the proton at $\delta$ 4.00 caused the dd at $\delta$ 4.66 to collapse to d. Thus, the dd proton signal at $\delta$ 4.66 was assigned to 2′-CH of **23**. The hydroxyl group at C-2′ was acetylated, and accordingly **14** was linked to the hydroxyl group at C-4′ of **21**. Consequently, the structure of **4** was deduced to be drevogenin A 3-*O*-β-D-glucopyranosyl-(1→4)-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside.

Dregeoside $C_{11}$ (**5**) has the molecular formula $C_{59}H_{86}O_{22}$ on the basis of elemental analysis. The 400 MHz $^1$H-NMR, infrared (IR), and ultraviolet (UV) spectra of **5** indicated the presence of acetyl and cinnamoyl ester moieties in the molecule. The β linkage of sugars was revealed by the coupling constants of four anomeric proton signals at $\delta$ 4.36 (1H, d, $J$=7.3 Hz), 4.57 (1H, d, $J$=7.8 Hz), 4.75 (1H, dd, $J$=10, 2 Hz), and 4.83 (1H, dd, $J$=10, 2 Hz) in the 400 MHz $^1$H-NMR spectrum of **5**. The $^{13}$C-NMR signals (Table V) indicated the presence of drevogenin C[14] (**24**) as the aglycone moiety and four sugars; two **9**, one **11**, and one **14**. The

Table V. $^{13}$C-NMR Chemical Shifts

| Aglycone moiety | 5 | 25 | 24 | Sugar moiety | 5 | 25 |
|---|---|---|---|---|---|---|
| C- 1 | 38.8 | 38.7 | 39.0 | Cym C-1 | 96.4 | 96.4 |
| 2 | 30.5 (−2.2) | 30.5 (−2.2) | 32.7 | 2 | 37.1 | 37.3 |
| 3 | 77.2 (+6.5) | 77.2 (+6.5) | 70.7 | 3 | 78.0[a] | 78.0[a] |
| 4 | 39.8 (−3.9) | 39.8 (−3.9) | 43.9 | 4 | 83.1[b] | 83.3 |
| 5 | 139.7 | 139.7 | 140.3 | 5 | 69.0[c] | 69.0[b] |
| 6 | 122.5 | 122.5 | 121.6 | 6 | 18.2[d] | 18.6 |
| 7 | 28.2 | 28.2 | 28.1 | 3-OMe | 58.9[e] | 58.8 |
| 8 | 37.4 | 37.5 | 37.5 | 1′ | 100.4 | 100.4 |
| 9 | 48.0 | 48.0 | 47.9 | 2′ | 37.1 | 37.3 |
| 10 | 39.5 | 39.5 | 39.3 | 3′ | 78.1[a] | 78.2[a] |
| 11 | 72.0 | 72.0 | 71.9 | 4′ | 83.1[b] | 83.3 |
| 12 | 78.0 | 78.0 | 77.9 | 5′ | 69.3[c] | 69.3[b] |
| 13 | 54.8 | 54.8 | 54.7 | 6′ | 18.5[d] | 18.6 |
| 14 | 84.1 | 84.1 | 83.9 | 3′-OMe | 59.0[e] | 58.8 |
| 15 | 34.6 | 34.6 | 34.6 | Allo C-1 | 104.0 | 104.2 |
| 16 | 24.0 | 24.1 | 24.0 | 2 | 72.5 | 73.1 |
| 17 | 58.3 | 58.3 | 58.2 | 3 | 83.3[b] | 83.9 |
| 18 | 11.5 | 11.5 | 11.6 | 4 | 83.3[b] | 74.5 |
| 19 | 19.3 | 19.3 | 19.4 | 5 | 69.3[c] | 70.7 |
| 20 | 213.8 | 213.8 | 213.2 | 6 | 18.6[d] | 18.6 |
| 21 | 31.9 | 31.9 | 31.8 | 3-OMe | 61.7 | 62.1 |
| 1″ | 167.0 | 166.0 | 166.7 | Glc C-1 | 106.5* | |
| 2″ | 118.0 | 118.0 | 117.7 | 2 | 75.5* | |
| 3″ | 146.5 | 146.5 | 146.2 | 3 | 78.3* | |
| 4″ | 134.5 | 134.5 | 134.4 | 4 | 72.0* | |
| 5″ | 129.4 | 129.4 | 129.1 | 5 | 78.3* | |
| 6″ | 128.2 | 128.8 | 128.6 | 6 | 63.0 | |
| 7″ | 131.0 | 131.0 | 130.7 | | | |
| 1′ | 170.2 | 170.2 | 170.3 | | | |
| 2′ | 21.4 | 21.4 | 21.4 | | | |

$\delta$ ppm from internal TMS in $C_5D_5N$.
*a*), *b*), *c*), *d*), or *e*) in each column may be interchangeable.
* The chemical shifts with asterisks have the longest dipole–dipole relaxation times by PRFT measurements.
( ), glycosidation shifts.
Cym, $\beta$-D-cymaropyranosyl; Allo, 3-*O*-methyl-6-deoxy-$\beta$-D-allopyranosyl; Glc, $\beta$-D-glucopyranosyl.

terminal glucose carbon signals of **5** were distinguished from those of other sugar moieties by PRFT measurements.[9] The sugar carbon signals of **5** were compatible with those of **4** (Table III). Compound **5** was hydrolyzed into deglucosyl-**5** (**25**) and **14** by $\beta$-glucosidase, and the latter was identified by HPLC comparison with an authentic sample. The $^{13}$C-NMR spectrum (Table V) of the sugar moiety of **25** agrees with that of **3** (Table III). On mild acidic hydrolysis, **25** gave **24**, **9**, and **18**, which were identified by TLC comparison with authentic samples. Thus, the structure of **5** has been established to be drevogenin C 3-*O*-$\beta$-D-glucopyranosyl-(1→4)-3-*O*-methyl-6-deoxy-$\beta$-D-allopyranosyl-(1→4)-$\beta$-D-cymaropyranosyl-(1→4)-$\beta$-D-cymaropyranoside.

Dregeosides $K_{p1}$ (**6**) and $K_{a1}$ (**7**) have the same aglycone moiety. On mild acidic hydrolysis, **6** gave drebyssogenin $K_2$[15,16] (**26**), **9**, and **12**, which were identified by TLC comparison with authentic samples, while **7** gave **26**, **9**, and **18**, which were identified in the same manner as in the case of **6**. In the 400 MHz $^1$H-NMR spectrum of **6**, the C-11 and C-12 proton signals were seen at $\delta$ 3.68 (1H, t, $J$=10 Hz) and 3.18 (1H, d, $J$=10 Hz), respectively,

TABLE VI. $^{13}$C-NMR Chemical Shifts

| Aglycone moiety | 6 | 7 | 26 | Sugar moiety | 6 | 7 |
|---|---|---|---|---|---|---|
| C- 1 | 39.8 | 39.7 | 39.9 | Cym C-1 | 96.3 | 96.3 |
| 2 | 30.6 (−2.2) | 30.6 (−2.2) | 32.8 | 2 | 36.9[a] | 36.9[a] |
| 3 | 77.8 (+6.3) | 77.8 (+6.3) | 71.5 | 3 | 77.8[b] | 78.0[b] |
| 4 | 40.0 (−4.0) | 40.0 (−4.0) | 44.0 | 4 | 83.1[c] | 83.2[c] |
| 5 | 140.9 | 140.9 | 141.4 | 5 | 68.9[d] | 69.0[d] |
| 6 | 122.1 | 122.1 | 121.1 | 6 | 18.5[e] | 18.6 |
| 7 | 28.1 | 28.1 | 28.1 | 3-OMe | 58.8[f] | 58.8 |
| 8 | 38.2 | 38.2 | 38.2 | 1′ | 100.2 | 100.4 |
| 9 | 49.9 | 49.8 | 49.8 | 2′ | 37.3[a] | 37.3[a] |
| 10 | 39.5 | 39.5 | 39.4 | 3′ | 78.1[b] | 78.1[b] |
| 11 | 71.7 | 71.6 | 71.5 | 4′ | 83.4[c] | 83.4[c] |
| 12 | 79.8 | 79.8 | 79.6 | 5′ | 69.1[d] | 69.3[d] |
| 13 | 53.7 | 53.7 | 53.6 | 6′ | 18.6[e] | 18.6 |
| 14 | 84.9 | 84.9 | 84.8 | 3′-OMe | 58.9[f] | 58.8 |
| 15 | 33.2 | 33.2 | 33.2 | Ole C-1 | 101.9 | |
| 16 | 25.1 | 25.1 | 25.0 | 2 | 37.6[a] | |
| 17 | 50.8 | 50.8 | 50.7 | 3 | 79.3[b] | |
| 18 | 10.7 | 10.7 | 10.7 | 4 | 82.0[c] | |
| 19 | 19.0 | 19.0 | 19.1 | 5 | 72.1 | |
| 20 | 73.8 | 73.7 | 73.6 | 6 | 18.6[e] | |
| 21 | 19.6 | 19.6 | 19.6 | 3-OMe | 57.2 | |
| 1″ | 172.4 | 172.4 | 172.4 | Allo C-1 | 102.0* | 104.2* |
| 2″ | 44.1 | 44.1 | 43.7 | 2 | 73.3* | 73.1* |
| 3″ | 25.7 | 25.7 | 25.7 | 3 | 84.0* | 83.9* |
| 4″ | 22.5 | 22.5 | 22.5 | 4 | 74.6* | 74.4* |
| | | | | 5 | 71.0* | 70.7* |
| | | | | 6 | 18.9[e] | 18.6 |
| | | | | 3-OMe | 62.1 | 62.1 |

$\delta$ ppm from internal TMS in $C_5D_5N$.
*a*), *b*), *c*), *d*), *e*), or *f*) in each column may be interchangeable.
* The chemical shifts with asterisks have the longest dipole–dipole relaxation times by PRFT measurements.
( ), glycosidation shifts.
Cym, $\beta$-D-cymaropyranosyl; Ole, $\beta$-D-oleandropyranosyl; Allo, 3-*O*-methyl-6-deoxy-$\beta$-D-allopyranosyl.

TABLE VII. Antitumor Activity of **1** and **2**

| | | |
|---|---|---|
| Tumor: | Ehrlich carcinoma (solid type) | |
| Host: | ddY mouse male 6 weeks | |
| Sample | Dose (*i.p.*) | *T/C* (%) |
| Mitomycin C | 0.75 mg/kg/d × 10 | 26.3 |
| **1** | 10.0 | 22.5 |
| **2** | 3.0 | 46.5 |
| Tumor: | Melanoma B-16 | |
| Host: | $BDF_1$ mouse male 6 weeks | |
| Sample | Dose (*i.p.*) | *T/C* (%) |
| **2** | 5 mg/kg/d × 10 | 43.4 |

while in that of **7**, the C-11 and C-12 proton signals were seen at $\delta$ 3.68 (1H, t, $J$ = 10 Hz) and 3.14 (1H, d, $J$ = 10 Hz), respectively. Either the C-11 or C-12 proton signals of **6** and **7** were moved upfield in comparison with those of **1**—**5**, which contained ester moieties at C-11 and C-12. The $^{13}$C-NMR signals (Table VI) of the aglycone moiety of **6** and **7** indicated the

presence of **26**, and those of the sugar moiety of **6** and **7** (Table VI) were compatible with those of **1** and **3**, respectively. Consequently, the structures of **6** and **7** were deduced to be drebyssogenin $K_2$ 3-*O*-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-oleandropyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside and drebyssogenin $K_2$ 3-*O*-3-*O*-methyl-6-deoxy-β-D-allopyranosyl-(1→4)-β-D-cymaropyranosyl-(1→4)-β-D-cymaropyranoside, respectively.

Compounds **1**—**4** were tested for antitumor activities against Ehrlich carcinoma (solid type) and melanoma B-16 *in vivo*. The results are summarized in Table VII. Compounds **1** and **2** showed antitumor activity against Ehrlich carcinoma (solid type), while **2** was also active against melanoma B-16, whereas **1** was not. Compounds **3** and **4** showed no antitumor activities against these tumors.

## Experimental

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 digital polarimeter at room temperature. UV spectra were obtained in ethanol with a Shimadzu UV-220 spectrometer, and absorption maxima are given in nm. IR spectra were recorded on a JASCO A-102 spectrometer. $^1$H-NMR spectra were run on a JEOL FX-500 (400 MHz) or FX-100 (100 MHz) spectrometer in $CDCl_3$ or in a mixture of $CDCl_3$–$CD_3OD$, and $^{13}$C-NMR spectra on a FX-200 (50 MHz) or FX-100 (25 MHz) machine in $C_5D_5N$ solution with tetramethylsilane as an internal standard. *Rf* values in TLC on silica gel (Kiesel gel 60 $F_{254}$, Merck) refer to the following solvent systems: $Rf_1$ $CHCl_3$–MeOH (95 : 5, v/v), $Rf_2$ $CHCl_3$–MeOH (9 : 1), $Rf_3$ acetone–benzene (3 : 5). Column chromatography was carried out on Wakogel C-200 (200 mesh), Wakogel C-100 (100 mesh), and Lobar column Lichroprep RP-8 (reversed phase). HPLC was conducted with a Waters 244 compact model, using a column of Radial PAK $C_{18}$ (solvent: $H_2O$–MeOH (2 : 8 v/v) or Radial PAK μBondapak $NH_2$ ($H_2O$–$CH_3CN$ (1 : 9)) with the radial compression separation system.

**Extraction and Isolation of Glycosides**——Ground stems of *Dregea volubilis* (L.) BENTH. (11 kg), obtained from Thailand, were dried, pulverized, and percolated with MeOH at room temperature. A dark yellow tar (900 g), obtained by evaporation of MeOH *in vacuo*, was dissolved in $CHCl_3$ and the precipitates were filtered off. The dark yellow tar (409.5 g) obtained by evaporation of the $CHCl_3$ *in vacuo* was dissolved in $CHCl_3$ (500 ml) again and the solution was poured into hexane (1600 ml). Finally a yellow crude glycoside mixture (359.3 g), which showed positive Liebermann–Burchard and Keller–Kiliani reactions, was obtained. The crude glycosides mixture (100.02 g) was subjected to column chromatography on silica gel, with solvents of increasing polarity from $CHCl_3$ to $CHCl_3$–MeOH (1 : 1 v/v) to separate fraction 2 (41.98 g: a mixture of **1**, **3**, **6**, and **7**) and fraction 4 (22.71 g: a mixture of **2**, **4**, and **5**). Fraction 2 (4.75 g) was rechromatographed on silica gel with solvents of increasing polarity from $CHCl_3$–MeOH (98 : 2) to $CHCl_3$–MeOH (92 : 8) to separated fraction B (1.65 g: a mixture of **1** and **3**) and fraction D (1.31 g: a mixture of **6** and **7**). Fraction B was rechromatographed on silica gel with acetone–hexane (1 : 9) to separate fraction I (127 mg: mainly **1**) and fraction II (327 mg: mainly **3**). Fraction D was rechromatographed on silica gel with acetone–hexane (4 : 6) to separate fraction III (279.3 mg: mainly **6**), and fraction IV (162.6 mg: mainly **7**). Fractions I (127 mg), II (327 mg), III (279.3 mg), and IV (162.6 mg) were each rechromatographed on reversed phased gel (solvent $H_2O$–MeOH (2 : 8)) to afford chromatographically pure **1** (54.7 mg), **3** (124.4 mg), **6** (37.5 mg), and **7** (30.1 mg), respectively. Fraction 4 (10.06 g) was rechromatographed on silica gel with $CHCl_3$–MeOH–hexane (9 : 2 : 15) to separate fraction α (1.8 g: a mixture of **2**, **4**, and **5**). Fraction α was rechromatographed on reversed phase gel (solvent $H_2O$–MeOH (2 : 8)) to separate fraction a (433.1 mg: mainly **2**) and fraction b (433.1 mg: a mixture of **4** and **5**). Fractions a (458 mg) and b (358 mg) were each further separated by HPLC (using a Radial PAK $C_{18}$ column) furnishing **2** (179.0 mg), **4** (217.8 mg), and **5** (41.8 mg).

**Dregeoside $A_{p1}$ (1)**——mp 118—120 °C, $[\alpha]_D$ +25.3° ($c$=1.01, MeOH). *Anal.* Calcd for $C_{56}H_{90}O_{20}\cdot H_2O$: C, 61.07; H, 8.42. Found: C, 60.91; H, 8.38. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3400 (OH), 1735 (C=O), 1715 (C=O), 1695 (C=O), 1160 (C–O–C). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 1.01 (6H, d, $J$=6.8 Hz, 4″-$CH_3$), 1.07 (3H, s, 18-$CH_3$), 1.11 (3H, s, 19-$CH_3$), 1.21, 1.22, 1.26, and 1.35 (each 3H, d, $J$=6.2, 5.9, 5.9, and 5.4, respectively, 6-$CH_3$ of sugar moiety), 1.97, 2.18 (each 3H, s, 2′- and 21-$CH_3$, respectively), 3.39, 3.44, 3.44, and 3.66 (each 3H, s, 3-$OCH_3$ of sugar moiety), 4.48 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.75 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.795 (1H, d, $J$=8 Hz, anomeric H), 4.804 (1H, d, $J$=10 Hz, 12-CHα), 4.83 (1H, dd, $J$=10, 2 Hz, anomeric H), 5.35 (1H, t, $J$=10 Hz, 11-CHβ), 5.47 (1H, d, $J$=5.4 Hz, 6-CH). $^{13}$C-NMR (25 MHz, $C_5D_5N$): see Table I.

**Acidic Hydrolysis of 1 and 3 with 0.05 N $H_2SO_4$–50% MeOH**——A solution of **1** (50 mg) in MeOH (25 ml) was treated with 0.1 N $H_2SO_4$ (25 ml), and the mixture was kept at around 50 °C for 30 min, then $H_2O$ (25 ml) was added and the whole was concentrated to 50 ml. The solution was warmed at around 50 °C for a further 30 min, then the solution was extracted with $Et_2O$ (50 ml). The aqueous layer was neutralized with 1% $Ba(OH)_2$, the precipitates were

filtered off and the solution was evaporated to dryness. The $Et_2O$ layer was washed with 5% $NaHCO_3$ (25 ml) and saturated NaCl (25 ml), then evaporated to dryness. The products were analyzed by TLC comparison with authentic samples. *Rf* value: $Et_2O$ layer; **8** ($Rf_1$: 0.5 and $Rf_3$: 0.65) and aqueous layer; **9** ($Rf_1$: 0.22 and $Rf_3$: 0.37) and **12** ($Rf_1$: 0.12 and $Rf_3$: 0.26). The mixture of **9** and **12** (23.7 mg) was separated by column chromatography on silica gel (solvent: $CHCl_3$–MeOH–$H_2O$ (10 : 2 : 1) lower layer) and furnished **12** (4.5 mg), $[\alpha]_D$ −8.5° ($c$=0.32, $H_2O$). $^1$H-NMR (100 MHz, $CDCl_3$–$CD_3OD$ (4 : 1)) $\delta$: 1.27, 1.34 (each 3H, d, $J$=6 Hz, 6 or 6′-$CH_3$), 1.59 (1H, ddd, $J$=13, 10.5, 4 Hz, 2-CH$\beta$), 2.21 (1H, ddd, $J$=13, 4, 2 Hz, 2-CH$\alpha$), 3.41, 3.64 (each 3H, s, 3 or 3′-$OCH_3$), 4.76 (1H, d, $J$=8 Hz, 1′-CH$\alpha$), 5.25 (1H, dd, $J$=4, 2 Hz, 1-CH$\beta$). **3** (51.7 mg) was acid-hydrolyzed by the procedure described above. The products were analyzed by TLC comparison with authentic samples. *Rf* value $Et_2O$ layer; **8** ($Rf_1$: 0.5 and $Rf_3$: 0.65) and aqueous layer; **9** ($Rf_1$: 0.22 and $Rf_3$: 0.37) and **18** ($Rf_1$: 0.13 and $Rf_3$: 0.22). The mixture of **9** and **18** (16.23 mg) was chromatographed on silica gel (solvent: $CHCl_3$–MeOH–$H_2O$ (10 : 2 : 1) lower layer) and furnished **18** (3.5 mg), $[\alpha]_D$ +28.2° ($c$=0.32, $H_2O$). $^1$H-NMR (400 MHz, $CDCl_3$–$CD_3OD$ (9 : 1)) $\delta$: 1.26, 1.33 (each 3H, d, $J$=6.4, 6.3 Hz, respectively, 6- or 6′-$CH_3$), 1.55 (1H, ddd, $J$=14, 10, 2 Hz, 2-CH$\beta$), 2.18 (1H, ddd, $J$=14, 4, 2 Hz, 2-CH$\alpha$), 3.22 (1H, dd, $J$=10, 4 Hz, 4′-CH), 3.31 (1H, dd, $J$=10, 3 Hz, 4-CH), 3.52, 3.67 (each 3H, s, 3 or 3′-$OCH_3$), 3.75 (1H, ddd, $J$=4, 3, 2 Hz, 3-CH), 4.21 (1H, dq, $J$=10, 6.4 Hz, 5-CH), 4.62 (1H, d, $J$=7.3 Hz, 1′-CH$\alpha$), 5.05 (1H, dd, $J$=10, 2 Hz, 1-CH$\alpha$). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table IV.

**Dregeoside $A_{01}$ (2)**——mp 149.5—151.5 °C, $[\alpha]_D$ +24.8° ($c$=1.00, MeOH). *Anal.* Calcd for $C_{62}H_{100}O_{25}\cdot 5/2H_2O$: 57.70; H, 8.20. Found: C, 57.88; H, 8.09. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3400 (OH), 1735, 1715, 1695 (C=O), 1160 (C–O–C). $^1$H-NMR (400 MHz, $CDCl_3$–$CD_3OD$ (9 : 1)) $\delta$: 1.02 (6H, d, $J$=6.3 Hz, 4″-$CH_3$), 1.07, 1.11 (each 3H, s, 18- and 19-$CH_3$, respectively), 1.22, 1.23, 1.30, and 1.37 (each 3H, d, $J$=5.9 Hz, respectively, 6-$CH_3$ of sugar moiety), 1.98, 2.20 (each 3H, s, 2′- and 21-$CH_3$, respectively), 3.37, 3.40, 3.44, and 3.61 (each 3H, s, 3-$OCH_3$ of sugar moiety), 4.35 (1H, d, $J$=7.8 Hz, anomeric H), 4.48 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.74 (1H, d, $J$=7.8 Hz, anomeric H), 4.76 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.82 (1H, d, $J$=10 Hz, 12-CH$\alpha$), 4.84 (1H, dd, $J$=10, 2 Hz, anomeric H), 5.36 (1H, t, $J$=10 Hz, 11-CH$\beta$), 5.49 (1H, d, $J$=4.9 Hz, 6-CH). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table I.

**Enzymatic Hydrolysis of 2, 4, and 5 with β-Glucosidase (Snail Enzyme)**——A suspension of **2** (38.2 mg) in 0.3 M NaOAc buffer adjusted to pH 5.5 was treated with a suspension (3 ml) of β-glucosidase prepared from a snail (*Fruticicola gainesil*). The mixture was allowed to stand at 37 °C for one week, then the solution was concentrated to dryness and the residue was extracted with MeOH. The insoluble precipitate was filtered off, and the filtrate was evaporated to dryness. The residue was extracted with acetone and the precipitate were filtered off, then the filtrate was evaporated to dryness. The precipitate was subjected to HPLC (column: Radial PAK μBondapak $NH_2$) analysis and identified as **14** by comparison with an authentic sample ($t_R$: 4.4 min). The residue was subjected to column chromatography on silica gel (increasing polarity of solvent from $CHCl_3$–MeOH (95 : 5, v/v)) to separate deglucosyl-**2** (**15**) (18 mg).

**15**: $[\alpha]_D$ +20.7° ($c$=0.61, MeOH). $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$: 1.02 (6H, d, $J$=6.3 Hz, 4″-$CH_3$), 1.07, 1.11 (each 3H, s, 18- and 19-$CH_3$), 1.21, 1.22, 1.26, and 1.35 (each 3H, d, $J$=6.4, 6.4, 5.9, and 5.4 Hz, respectively, 6-$CH_3$ of sugar moiety), 1.97, 2.18 (each 3H, s, 2′- and 21-$CH_3$, respectively), 3.39, 3.44, 3.44, and 3.66 (each 3H, s, 3-$OCH_3$ of sugar moiety), 4.48 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.75 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.795 (1H, d, $J$=8.3 Hz, anomeric H), 4.805 (1H, d, $J$=10 Hz, 12-CH$\alpha$), 4.84 (1H, dd, $J$=10, 2 Hz, anomeric H), 5.35 (1H, t, $J$=10 Hz, 11-CH$\beta$), 5.47 (1H, d, $J$=5.4 Hz, 6-CH). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table II. **4** (30 mg) was enzymatically hydrolyzed and chromatographed by the procedure described above. **14** was identified by HPLC (column: Radial PAK μBondapak $NH_2$) comparison with an authentic sample. After column chromatography, deglucosyl-**4** (**20**) (23.3 mg) was obtained.

**20**: $[\alpha]_D$ +32.5° ($c$=1.00, MeOH). $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$: 1.01 (6H, d, $J$=6.3 Hz, 4″-$CH_3$), 1.07, 1.11 (each 3H, s, 18- and 19-$CH_3$, respectively), 1.21, 1.26, 1.28 (each 3H, d, $J$=6.3, 6.4, and 5.9 Hz, respectively, 6-$CH_3$ of sugar moiety), 1.97, 2.18 (each 3H, s, 2′- and 21-$CH_3$, respectively), 3.21 (1H, dd, $J$=9.6, 2.9 Hz, 4-CH of sugar moiety), 3.27 (1H, dd, $J$=9.7, 2.9 Hz, 4-CH of sugar moiety), 3.42, 3.44, and 3.66 (each 3H, s, 3-$OCH_3$ of sugar moiety), 3.90 (1H, dq, $J$=9.6, 6.3 Hz, 5-CH of sugar moiety), 4.59 (1H, d, $J$=7.8 Hz, anomeric H), 4.76 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.80 (1H, d, $J$=10 Hz, 12-CH$\alpha$), 4.83 (1H, dd, $J$=10, 2 Hz, anomeric H), 5.35 (1H, t, $J$=10 Hz, 11-CH$\beta$), 5.47 (1H, d, $J$=5.6 Hz, 6-CH). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table II. When **5** (24.7 mg) was enzymatically hydrolyzed and chromatographed by the procedure described above, **14** was identified by HPLC (column: Radial PAK μBondapak $NH_2$) comparison with an authentic sample, and deglucosyl-**5** (**25**) (8.7 mg) was also obtained.

**25**: $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$: 1.14, 1.15 (each 3H, s, 18- and 19-$CH_3$, respectively), 1.21, 1.24, 1.28 (each 3H, d, $J$=5.9, 5.4, and 6.4 Hz, respectively, 6-$CH_3$ of sugar moiety), 1.89, 2.17 (each 3H, s, 2′- and 21-$CH_3$, respectively), 3.22 (1H, dd, $J$=9.5, 3 Hz, 4-CH of sugar moiety), 3.26 (1H, dd, $J$=9.8, 3 Hz, 4-CH of sugar moiety), 3.42, 3.44, 3.66 (each 3H, s, 3-$OCH_3$ of sugar moiety), 3.85 (1H, dq, $J$=9.5, 7 Hz, 5-CH of sugar moiety), 3.91 (1H, dq, $J$=9.8, 6 Hz, 5-CH of sugar moiety), 4.59 (1H, d, $J$=8.3 Hz, anomeric H), 4.76 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.83 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.92 (1H, d, $J$=10 Hz, 12-CH$\alpha$), 5.48 (1H, t, $J$=10 Hz, 11-CH$\beta$), 5.49 (1H, d, $J$=6 Hz, 6-CH), 6.47, 7.76 (2H, ABq, $J$=16 Hz, 2″-CH=3″-CH), 7.42 (3H, m, 5″- and 7″-CH), 7.58 (2H, m, 6″-CH). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table V.

**Acidic Hydrolysis of 2, 4—7, 15, 20, and 25**——A solution of one of the eight glycosides (1 mg) in MeOH (5 ml) was treated with 0.1 N $H_2SO_4$ (5 ml) and the mixture was kept at around 50 °C for 15 min, then $H_2O$ (5 ml) was added and the solution was concentrated to 10 ml. The solution was warmed at around 50 °C for a further 30 min, then neutralized with 1% $Ba(OH)_2$ and the precipitates were filtered off. The filtrate was evaporated to dryness, and the products were analyzed by TLC. When **2** was hydrolyzed, **8**, **9**, and **13** were identified by comparison with authentic samples. When **4** was hydrolyzed, **8**, **9**, and **20** were identified; when **5** was hydrolyzed, **24**, **9**, and **21** were identified; when **6** was hydrolyzed, **26**, **9**, and **12** were identified; when **7** was hydrolyzed, **26**, **9**, and **18** were identified; when **15** was hydrolyzed, **8**, **9**, and **12** were identified; when **20** was hydrolyzed, **8**, **9**, and **18** were identified; and when **25** was hydrolyzed, **24**, **9**, and **18** were identified, all by comparison with authentic samples. *Rf* values: **8** ($Rf_1$: 0.5, $Rf_3$: 0.65), **9** ($Rf_1$: 0.22, $Rf_3$: 0.37), **12** ($Rf_1$: 0.12, $Rf_3$: 0.26), **13** ($Rf_2$: 0.07, $Rf_3$: 0.04), **18** ($Rf_1$: 0.13, $Rf_3$: 0.22), **21** ($Rf_2$: 0.07, $Rf_3$: 0.24), **24** ($Rf_1$: 0.44, $Rf_3$: 0.63), and **26** ($Rf_1$: 0.15, $Rf_3$: 0.41).

**Acetylation of 16 and 22**——A solution of **16** (20 mg) or **22** (22 mg) in pyridine (1 ml) was treated with acetic anhydride (0.5 ml) and stirred at room temperature overnight. Usual work-up of the reaction mixture and column chromatography on silica gel (solvent : $CHCl_3$–MeOH (99 : 1, v/v) gave **17** (29.9 mg) or **23** (16.9 mg), respectively.

**17**: $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$: 1.20 (3H, d, $J$=6.4 Hz, 6′-$CH_3$), 1.24 (3H, d, $J$=6.4 Hz, 6-$CH_3$), 1.53 (1H, ddd, $J$=13.2, 11.0, 3.9 Hz, 2-CH$\beta$), 2.00, 2.03, 2.04, 2.08, and 2.10 (each 3H, s, –OAc), 2.22 (1H, ddd, $J$=13.2, 5.4, 1.5 Hz, 2-CH$\alpha$), 3.20 (1H, dd, $J$=9.3, 8.5 Hz, 4-CH), 3.24 (1H, dd, $J$=9.4, 2.5 Hz, 4′-CH), 3.28, 3.37, and 3.49 (each 3H, s, 1 or 3 or 3′-$OCH_3$), 3.60 (1H, ddd, $J$=11.0, 8.5, 5.4 Hz, 3-CH), 3.63 (1H, dq, $J$=9.0, 6.4 Hz, 5-CH), 3.74 (1H, ddd, $J$=9.8, 4.8, 3.4 Hz, 5″-CH), 3.90 (1H, dq, $J$=9.4, 6.4 Hz, 5′-CH), 3.96 (1H, dd, $J$=2.9, 2.5 Hz, 3′-CH), 4.16 (1H, dd, $J$=12.2, 3.4 Hz, 6″-CH), 4.19 (1H, dd, $J$=12.2, 4.8 Hz, 6″-CH), 4.59 (1H, dd, $J$=8.5, 2.9 Hz, 2′-CH), 4.61 (1H, d, $J$=7.8 Hz, 1″-CH), 4.71 (1H, dd, $J$=3.9, 1.5 Hz, 1-CH), 5.01 (1H, dd, $J$=9.8, 7.8 Hz, 2″-CH), 5.04 (1H, t, $J$=9.8 Hz, 4″-CH), 5.05 (1H, d, $J$=8.5 Hz, 1′-CH), 5.19 (1H, t, $J$=9.8 Hz, 3″-CH).

**23**: $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$: 1.18 (3H, d, $J$=6.3 Hz, 6′-$CH_3$), 1.24 (3H, d, $J$=5.9 Hz, 6-$CH_3$), 1.54 (1H, ddd, $J$=13.7, 9.8, 2.4 Hz, 2-CH$\beta$), 2.00, 2.03, 2.04, 2.07, and 2.08 (each 3H, s, –OAc), 2.15 (1H, ddd, $J$=13.7, 3.7, 2.0 Hz, 2-CH$\alpha$), 3.20 (1H, dd, $J$=9.5, 2.9 Hz, 4-CH), 3.25 (1H, dd, $J$=9.3, 2.9 Hz, 4′-CH), 3.41, 3.47, and 3.50 (each 3H, s, 1 or 3 or 3′-$OCH_3$), 3.74 (1H, ddd, $J$=9.8, 5.1, 4.4 Hz, 5″-CH), 3.77 (1H, ddd, $J$=3.7, 2.9, 2.7 Hz, 3-CH), 3.87 (1H, dq, $J$=9.5, 5.9 Hz, 5-CH), 3.91 (1H, dq, $J$=9.3, 6.3 Hz, 5′-CH), 4.00 (1H, t, $J$=2.9 Hz, 3′-CH), 4.16 (1H, dd, $J$=12.2, 4.5 Hz, 6″-CH), 4.19 (1H, dd, $J$=12.2, 5.1 Hz, 6″-CH), 4.61 (1H, d, $J$=8.3 Hz, 1″-CH), 4.63 (1H, dd, $J$=9.8, 2.0 Hz, 1-CH), 4.66 (1H, dd, $J$=8.3, 2.9 Hz, 2′-CH), 4.78 (1H, d, $J$=8.3 Hz, 1′-CH), 5.00 (1H, dd, $J$=9.8, 8.3 Hz, 2″-CH), 5.04 (1H, t, $J$=9.8 Hz, 4″-CH), 5.19 (1H, t, $J$=9.8 Hz, 3″-CH).

**Dregeoside $A_{a1}$ (3)**——mp 130.5—133 °C, $[\alpha]_D$ +35.2° ($c$=1.01, MeOH). *Anal.* Calcd for $C_{49}H_{78}O_{17}\cdot 3/2H_2O$: C, 60.91; H, 8.45. Found: C, 61.13; H, 8.23. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3400 (OH), 1735, 1715, 1695 (C=O), 1160 (C–O–C). SIMS $m/z$: 961 [(M+Na)$^+$]. $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$: 1.01 (6H, d, $J$=5.9 Hz, 4″-$CH_3$), 1.07, 1.11 (each 3H, s, 18- and 19-$CH_3$, respectively), 1.21, 1.26, 1.28 (each 3H, d, $J$=5.9, 6.4, and 5.9 Hz, respectively, 6-$CH_3$ of sugar moiety), 1.97, 2.18 (each 3H, s, 2′- and 21-$CH_3$, respectively), 3.21 (1H, dd, $J$=9.5, 2.7 Hz, 4-CH of sugar moiety), 3.27 (1H, dd, $J$=9.3, 2.9 Hz, 4-CH of sugar moiety), 3.42, 3.44, 3.66 (each 3H, s, 3-$OCH_3$ of sugar moiety), 3.91 (1H, dq, $J$=9.6, 6.3 Hz, 5-CH of sugar moiety), 4.59 (1H, d, $J$=7.8 Hz, anomeric H), 4.76 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.80 (1H, d, $J$=10 Hz, 12-CH$\alpha$), 4.83 (1H, dd, $J$=10, 2 Hz, anomeric H), 5.35 (1H, t, $J$=10 Hz, 11-CH$\beta$), 5.47 (1H, d, $J$=4.9 Hz, 6-CH). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table III.

**Dregeoside $A_{11}$ (4)**——mp 162.5—165 °C, $[\alpha]_D$ +33.0° ($c$=1.01, MeOH). *Anal.* Calcd for $C_{55}H_{88}O_{22}\cdot 3/2H_2O$: 58.54; H, 8.13. Found: C, 58.64; H, 8.03. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3400 (OH), 1735, 1715, 1695 (C=O), 1160 (C–O–C). SIMS $m/z$: 1123 [(M+Na)$^+$]. $^1$H-NMR (400 MHz, $CDCl_3$–$CD_3OD$ (9 : 1)) $\delta$: 1.02 (6H, d, $J$=5.9 Hz, 4″-$CH_3$), 1.07, 1.11 (each 3H, s, 18- and 19-$CH_3$, respectively), 1.23, 1.27, and 1.29 (each 3H, d, $J$=5.9, 4.9, 6.8 Hz, respectively, 6-$CH_3$ of sugar moiety), 1.98, 2.20 (each 3H, s, 2′- and 21-$CH_3$, respectively), 3.42, 3.44, 3.60 (each 3H, s, 3-$OCH_3$ of sugar moiety), 4.35 (1H, d, $J$=7.8 Hz, anomeric H), 4.57 (1H, d, $J$=7.8 Hz, anomeric H), 4.75 (1H, dd, $J$=10, 2 Hz, anomeric H), 4.81 (1H, d, $J$=10 Hz, 12-CH$\alpha$), 4.84 (1H, dd, $J$=10, 2 Hz, anomeric H), 5.35 (1H, t, $J$=10 Hz, 11-CH$\beta$), 5.49 (1H, d, $J$=3.4 Hz, 6-CH). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table III.

**Dregeoside $C_{11}$ (5)**——mp 142—145 °C, $[\alpha]_D$ +52.1° ($c$=1.02, MeOH). *Anal.* Calcd for $C_{59}H_{86}O_{22}\cdot 2H_2O$: C, 59.88; H, 7.67. Found: C, 59.86; H, 7.73. UV $\lambda_{max}^{ethanol}$ nm (log $\varepsilon$): 281 (4.17), 224 (4.03), 218 (4.09). IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3400 (OH), 1730, 1710 (C=O), 1635 (C=C–C=O), 1160 (C–O–C). $^1$H-NMR (400 MHz, $CDCl_3$–$CD_3OD$ (9 : 1)) $\delta$: 1.14 (6H, s, 18- and 19-$CH_3$), 1.22, 1.24, 1.29 (each 3H, d, $J$=6.4, 6.4, and 5.9 Hz, respectively, 6-CH of sugar moiety), 1.90, 2.18 (each 3H, s, 2′- and 21-$CH_3$, respectively), 3.42, 3.44, 3.60 (each 3H, s, 3-$OCH_3$ of sugar moiety), 4.36 (1H, d, $J$=7.3 Hz), 4.57 (1H, d, $J$=7.8 Hz), 4.75 (1H, dd, $J$=10, 2 Hz), 4.83 (1H, dd, $J$=10, 2 Hz) anomeric H, 4.93 (1H, d, $J$=10 Hz, 12-CH$\alpha$), 5.49 (1H, t, $J$=10 Hz, 11-CH$\beta$), 5.50 (1H, d, $J$=5.9 Hz, 6-CH), 6.48, 7.77 (2H, ABq, $J$=16.1 Hz, 2″-CH=3″-CH), 7.41 (3H, m, 5″- and 7″-CH), 7.60 (2H, m, 6″-CH). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table V.

**Dregeoside $K_{p1}$ (6)**——mp 125.5—128 °C, $[\alpha]_D$ +13.2° ($c$=1.00, MeOH). *Anal.* Calcd for $C_{54}H_{90}O_{19}\cdot H_2O$: C, 61.11; H, 8.74. Found: C, 61.08; H, 8.69. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3550 (OH), 1720 (COOR), 1160 (C–O–C). $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$: 0.94 (3H, s, 18-$CH_3$), 0.96 (6H, d, $J$=6.4 Hz, 4″-$CH_3$), 1.15 (3H, s, 19-$CH_3$), 1.21, 1.22, 1.28, 1.35 (each 3H, d, $J$=6.4, 5.4, 5.9, and 5.4 Hz, respectively, 6-$CH_3$ of sugar moiety), 1.26 (3H, d, $J$=6.4 Hz, 21-$CH_3$),

3.18 (1H, d, $J=10$ Hz, 12-CH$\alpha$), 3.39, 3.44, 3.44, 3.66 (each 3H, s, 3-$OCH_3$ of sugar moiety), 3.68 (1H, t, $J=10$ Hz, 11-CH$\beta$), 4.48 (1H, dd, $J=10$, 2 Hz), 4.75 (1H, dd, $J=10$, 2 Hz), 4.79 (1H, d, $J=7.8$ Hz), 4.85 (1H, dd, $J=10$, 2 Hz) anomeric H, 5.45 (1H, d, $J=5.0$ Hz, 6-CH). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table VI.

**Dregeoside $K_{a1}$ (7)**—— mp 131.5—135 °C, $[\alpha]_D$ +15.5° ($c=1.01$, MeOH). *Anal.* Calcd for $C_{47}H_{78}O_{16}\cdot 3/2H_2O$: 60.95; H, 8.82. Found: C, 60.76; H, 8.56. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3550 (OH), 1720 (COOR), 1160 (C–O–C). $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$: 0.94 (3H, s, 18-$CH_3$), 0.96 (6H, d, $J=6.4$ Hz, 4″-$CH_3$), 1.16 (3H, s, 19-$CH_3$), 1.24 (3H, d, $J=6.4$ Hz, 21-$CH_3$), 1.24, 1.26, 1.28 (each 3H, d, $J=6.4$, 6.8 and 5.9 Hz, respectively, 6-$CH_3$ of sugar moiety), 3.14 (1H, d, $J=10$ Hz, 12-CH$\alpha$), 3.22 (1H, dd, $J=9.3$, 2.9 Hz), 3.27 (1H, dd, $J=9.8$, 2.9 Hz) 4-CH of sugar moiety, 3.42, 3.44, 3.66 (each 3H, s, 3-$OCH_3$ of sugar moiety), 3.68 (1H, t, $J=10$ Hz, 11-CH$\beta$), 3.91 (1H, dq, $J=9.3$, 6.4 Hz, 5-CH of sugar moiety), 4.59 (1H, d, $J=8.3$ Hz), 4.76 (1H, dd, $J=10$, 2 Hz), 4.85 (1H, dd, $J=10$, 2 Hz) anomeric H, 5.45 (1H, d, $J=4.9$ Hz, 6-CH). $^{13}$C-NMR (50 MHz, $C_5D_5N$): see Table VI.

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