# The Reactions of β- and α-Pyranose Peracetates with $PCl_5$, and Utilization of the Products to Construct Sarsasapogenin Glycosides

Setsuo SAITO,*[,a] Koki ICHINOSE,[a] Yuka SASAKI,[a] and Shigeya SUMITA[b]

*Faculty of Pharmaceutical Sciences, Josai University,[a] Keyakidai 1-1, Sakado, Saitama 350-02, Japan and Shiratori Pharmaceutical Co., Ltd.,[b] Tsudanuma 6-11-24, Narashino, Chiba 275, Japan.* *Received May 15, 1992*

**The reactions of β- and α-pyranose peracetates with $PCl_5$ gave products regioselectively chlorinated. The reactions of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (5) and -β-D-galactopyranose (6) with $PCl_5$ in $CCl_4$ and that of methyl 2,3,4-tri-*O*-acetyl-β-D-glucuronatopyranose (7) with $PCl_5$ in toluene gave 2-*O*-trichloroacetyl-β-D-pyranosyl chlorides 4, 12 and 14, respectively, as major products, and α-D-pyranosyl chlorides 11, 13 and 15, respectively, as minor products. On the other hand, the reactions of compounds 8 and 9 which were α-anomers of 5 and 6, respectively, with $PCl_5$ gave as major products transformed acetyl groups at C-6 to $-C(Cl)=CCl_2$ or $-C(Cl)_2-CCl_3$ group (16 and 17 from 8 and 18 from 9). The same reaction of 10, which was α-anomer of 7, gave α-chloride 15 as a major product. The glycosidation of sugar derivative 4 with sarsasapogenin 23 gave β-glycoside 24 (29.1%) and α-glycoside 25 (46.9%), and that of 12 with 23 gave β-glycoside 26 (24.0%) and α-glycoside 27 (40.8%). The improvement of the yields of β-glycosides 24 and 26 (66.9 and 62.1% for 24 and 26, respectively) in the glycosidations were accomplished by the employment of α-bromides 28 and 29 obtained from 4 and 6, respectively. The glycosidations of monoglycosides 30 and 31 obtained by the treatment 24 and 26, respectively, with ammonia-saturated ether with sugar acetate bromides 32 and 34 gave diglycoside derivatives 35 and 33, respectively.**

**Keywords** β-D-pyranose peracetate; α-D-pyranose paracetate; regioselective product; 2-*O*-trichloroacetyl-β-D-pyranosyl chloride; sarsasapogenin; glycosidation; sarsasaponin glycoside

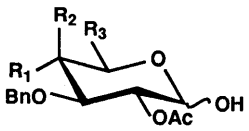
In a previous paper,[1] we reported the synthesis of glycyrrhetic acid glycosides having various β(1→2)-linked disaccharides. In the synthesis, pyranose benzyl derivatives (**1**—**3**) were used as starting materials for glycosidation with glycyrrhetic acid methyl ester. However, the synthesis of these benzyl derivatives from the corresponding pyranose peracetates required several steps. Brigl[2] and Lemieux and Huber[3] obtained 2-*O*-trichloroacetyl-β-D-glucopyranosyl chloride (**4**) in one step by the reaction of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**5**) with $PCl_5$ in $CCl_4$. The compound **4** seems to be more convenient for constructing various glycosides having β(1→2)-linked disaccharides, since the trichloroacetyl group at C-2 on **4** is easily removable and the resulting OH group can be linked by glycosidation with another pyranose derivative. In this paper, we will report the detailed investigation of the reactions of not only **5** but also 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose (**6**) and methyl 1,2,3,4-tetra-*O*-acetyl-β-D-glucuronatopyranose (**7**) with $PCl_5$ in $CCl_4$ or toluene. Also, we report the reactions of compounds **8**, **9** and **10** which are the α-isomers of **5**, **6** and **7**, respectively, with $PCl_5$ in $CCl_4$ or toluene. The synthesis of sarsasapogenin glycoside derivatives having β(1→2)-linked disaccharides is further reported.

The reaction of **5**[4] with $PCl_5$ in $CCl_4$ according to the method of Lemieux and Huber[3] gave compound **4** as a major product (55.1% yield) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl chloride (**11**) as a minor one (14.9% yield). Compound **4** was identified with the authentic sample[3] by the proton nuclear magnetic resonance ($^1$H-NMR) spectrum and thin-layer chromatography (TLC). Compound **11** exhibits signals assignable to an anomeric proton at δ 6.30 (d, $J$=4.0 Hz) and four acetyl groups in the $^1$H-NMR spectrum (Table I). The electron impact mass spectrum (EI-MS) of **11** shows a fragment ion peak at $m/z$ 331 ($M^+-Cl$). Compound **6**[5] was heated under reflux with $PCl_5$ in $CCl_4$ to give a major product (**12**) in 54.8% yield and a minor one (**13**) in 16.0% yield. The $^1$H-NMR spectrum of **12** shows the signals of an anomeric proton at δ 5.41 (d, $J$=9.0 Hz) and three acetyl groups at δ 1.99, 2.07 and 2.20. The EI-MS of **12** shows a fragment ion peak at $m/z$ 433 ($M^+-Cl$). These spectral data, together with the elemental analysis, suggest that compound **12** is 2-*O*-trichloroacetyl-3,4,6-tri-*O*-acetyl-β-D-galactopyranosyl chloride. The suggestion was comfirmed by the reaction of **12** with ammonia-saturated ether[3] to give 3,4,6-tri-*O*-acetyl-β-D-galactopyranosyl chloride which exhibited an H-2 signal at a higher field (δ 4.02) than that of **12** (δ 5.40) in the $^1$H-NMR

TABLE I. $^1$H-NMR Spectral Data for Compounds Obtained by the Reactions of β-Pyranose Peracetates with $PCl_5$

| | 4 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|
| H-1 | 5.42 (d, 8.4) | 6.30 (d, 4.0) | 5.41 (d, 9.0) | 6.38 (d, 4.0) | 5.53 (d, 8.5) | 6.34 (d, 4.0) |
| H-2 | 5.24 (dd, 9.2, 8.4) | 5.02 (dd, 9.9, 4.0) | 5.40 (dd, 9.0, 9.0) | 5.25 (dd, 10.8, 4.0) | 5.28 (dd, 9.5, 8.5) | 5.04 (dd, 9.9, 4.0) |
| H-3 | 5.38 (dd, 9.2, 9.2) | 5.56 (dd, 9.9, 9.9) | 5.20 (dd, 9.0, 3.7) | 5.41 (dd, 10.8, 2.7) | 5.48 (dd, 9.5, 9.5) | 5.61 (dd, 9.9, 9.9) |
| H-4 | 5.20 (dd, 9.2, 9.2) | 5.14 (dd, 9.9, 9.9) | 5.48 (d, 3.7) | 5.52 (d, 2.7) | 5.34 (dd, 9.5, 9.5) | 5.22 (dd, 9.9, 9.9) |
| H-5 | 3.89 (ddd, 9.2, 4.8, 2.2) | 4.30 (m) | 4.09 (dd, 5.6, 3.7) | 4.53 (dd, 7.0, 6.0) | 4.27 (d, 9.5) | 4.61 (d, 9.9) |
| H-6 | 4.13 (dd, 12.5, 4.8) | 4.33 (dd, 10.4, 4.8) | 4.25 (dd, 12.0, 3.7) | 4.10 (dd, 11.5, 7.0) | — | — |
| H-6′ | 4.19 (dd, 12.5, 2.2) | 4.13 (dd, 10.4, 3.3) | 4.13 (dd, 12.0, 5.6) | 4.18 (dd, 11.5, 6.0) | — | — |
| Acetyl | 2.02, 2.04, 2.12 | 2.04, 2.05, 2.10, 2.10 | 1.99, 2.07, 2.20 | 2.01, 2.06, 2.12, 2.16 | 2.04, 2.05 | 2.06, 2.06, 2.10 |
| $OCH_3$ | — | — | — | — | 3.79 | 3.77 |

Coupling constants ($J$ in Hz) are given in parentheses. The signal assignments were based on the decoupling method.

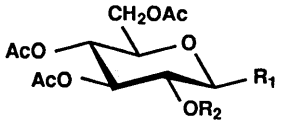


1 : $R_1$ = OBn, $R_2$ = H, $R_3$ = $CH_2OBn$

2 : $R_1$ = H, $R_2$ = OBn, $R_3$ = $CH_2OBn$

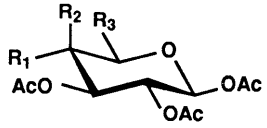
3 : $R_1$ = OBn, $R_2$ = H, $R_3$ = COOBn

Ac : $COCH_3$, Bn : $CH_2C_6H_5$



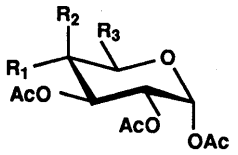
4 : $R_1$ = Cl, $R_2$ = $COCCl_3$

5 : $R_1$ = OAc, $R_2$ = Ac



6 : $R_1$ = H, $R_2$ = OAc, $R_3$ = $CH_2OAc$

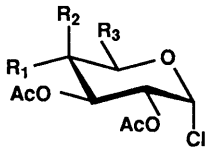
7 : $R_1$ = OAc, $R_2$ = H, $R_3$ = $COOCH_3$



8 : $R_1$ = OAc, $R_2$ = H, $R_3$ = $CH_2OAc$

9 : $R_1$ = H, $R_2$ = OAc, $R_3$ = $CH_2OAc$

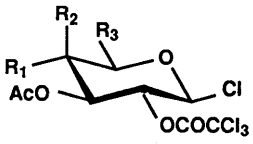
10 : $R_1$ = OAc, $R_2$ = H, $R_3$ = $COOCH_3$



11 : $R_1$ = OAc, $R_2$ = H, $R_3$ = $CH_2OAc$

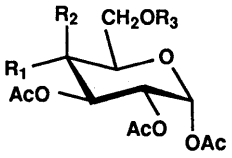
13 : $R_1$ = H, $R_2$ = OAc, $R_3$ = $CH_2OAc$

15 : $R_1$ = OAc, $R_2$ = H, $R_3$ = $COOCH_3$



12 : $R_1$ = H, $R_2$ = OAc, $R_3$ = $CH_2OAc$

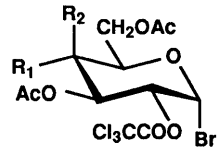
14 : $R_1$ = OAc, $R_2$ = H, $R_3$ = $COOCH_3$



16 : $R_1$ = OAc, $R_2$ = H, $R_3$ = $C(Cl)=CCl_2$

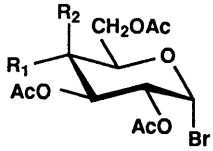
17 : $R_1$ = OAc, $R_2$ = H, $R_3$ = $C(Cl)_2CCl_3$

18 : $R_1$ = H, $R_2$ = OAc, $R_3$ = $C(Cl)=CCl_2$



28 : $R_1$ = OAc, $R_2$ = H

29 : $R_1$ = H, $R_2$ = OAc



32 : $R_1$ = H, $R_2$ = OAc

34 : $R_1$ = OAc, $R_2$ = H

Chart 1

spectrum. Compound **13** exhibits a doublet due to an anomeric proton at $\delta$ 6.38 ($J$=4.0 Hz) and four singlets due to acetyl groups at $\delta$ 2.01, 2.06, 2.12 and 2.16 in the $^1$H-NMR spectrum, and a fragment ion peak at $m/z$ 331 ($M^+-Cl$) in the EI-MS. Although compound **7** was recovered unchanged under the same conditions, the reaction using toluene instead of $CCl_4$ under refluxing condition gave compound (**14**) as a major product (52.9% yield) and compound (**15**) as a minor product (17.2% yield). In the $^1$H-NMR spectrum of **14**, signals due to an anomeric proton ($\delta$ 5.53, d, $J$=8.5 Hz), protons of a single methoxy ($\delta$ 3.79) and two acetyl groups ($\delta$ 2.04 and 2.05) are observed. The EI-MS of **14** shows the molecular ion peak at $m/z$ 454. Treatment of **14** with ammonia-saturated ether gave methyl 3,4-di-*O*-acetyl-$\beta$-D-glucuronatopyranosyl chloride which exhibited an H-2 signal at a higher field ($\delta$ 3.95) than that of **14** ($\delta$ 5.28) in the $^1$H-NMR spectrum. These spectral and chemical data suggest that **14** is methyl 2-*O*-trichloroacetyl-3,4-di-*O*-acetyl-$\beta$-D-glucuronatopyranosyl chloride. Compound **15** exhibits signals due to an anomeric proton ($\delta$ 6.34, d, $J$=4.0 Hz) and protons of a single methoxy ($\delta$ 3.77) and three acetyl groups ($\delta$ 2.06, 2.06 and 2.10) in the $^1$H-NMR spectrum and a molecular ion peak at $m/z$ 352 in the EI-MS. These spectral data suggest that **15** is methyl 2,3,4-tri-*O*-acetyl-$\alpha$-D-glucuronatopyranosyl chloride.

The results of these experiments indicate that $\beta$-isomers of sugar pyranose peracetates, **5**, **6** and **7**, give 2-*O*-trichloroacetyl $\beta$-D-pyranosyl chlorides, **4**, **12** and **14**, respectively, as major products and $\alpha$-chlorides, **11**, **13** and **15**, respectively, as minor products. In the major products, only an acetyl group at the C-2 position of the starting materials was transformed to a trichloroacetyl group; the other acetyl groups were intact. These results may be explained as follows (Fig. 1): In the reaction of **5** with $PCl_5$, the oxygen of an acetyl carbonyl group at C-2 takes part in the neighboring-group participation to the anomeric carbon to afford an intermediate such as A. The methyl group on the dioxolane cation of A is active enough to remove a proton giving an enolate intermediate B. The vinyl methylene of B reacts with a cation, $Cl^+$, to give an intermediate C which further reacts with $Cl^+$ to afford trichloromethyl dioxolane cation intermediate D. The anomeric carbon of D may finally be attacked by an anion, $Cl^-$, from a $\beta$-site to obtain 2-*O*-trichloroacetyl-$\beta$-D-pyranosyl chloride **4**, and accordingly, no other transformation of acetyl groups at C-3, 4 and 6 to the trichloroacetyl group occurred. In addition, the minor product **11** was obtained by the attack of $Cl^-$ at the anomeric carbon from the $\alpha$-site of an intermediate E which might be derived from A.

During the preparations of compounds **4**, **12** and **14**, it

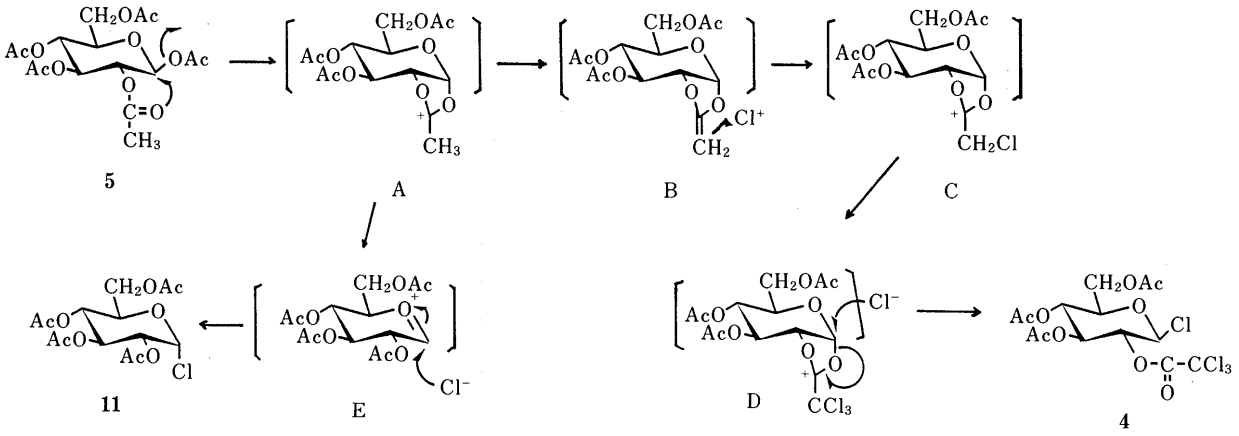


Fig. 1

TABLE II. $^1$H-NMR Spectral Data for Compounds **8**, **16** and **17**

| | **8** | **16** | **17** |
|---|---|---|---|
| H-1 | 6.32 (d, 4.0) | 6.35 (d, 3.7) | 6.35 (d, 3.7) |
| H-2 | 5.07 (dd, 9.8, 4.0) | 5.08 (dd, 10.3, 3.7) | 5.10 (dd, 9.9, 3.7) |
| H-3 | 5.45 (dd, 9.8, 9.8) | 5.47 (dd, 10.3, 9.5) | 5.47 (dd, 9.9, 9.9) |
| H-4 | 5.14 (dd, 9.8, 9.8) | 5.13 (dd, 10.3, 9.5) | 5.15 (dd, 9.9, 9.9) |
| H-5 | 4.14 (m) | 4.18 (ddd, 10.3, 4.6, 3.8) | 4.24 (m) |
| H-6 | 4.28 (dd, 14.3, 4.0) | 4.07 (dd, 14.6, 4.6) | 4.26 (m) |
| H-6′ | 4.07 (dd, 14.3, 2.8) | 4.05 (dd, 14.6, 3.8) | |
| Acetyl | 2.02, 2.04, 2.15, 2.11, 2.11 | 2.02, 2.04, 2.07, 2.19 | 2.02, 2.03, 2.05, 2.18 |

Coupling constants ($J$ in Hz) are given in parentheses. The signal assignments were based on the decoupling method.

TABLE III. $^1$H-NMR Spectral Data for Compounds **9** and **18**

| | **9** | **18** |
|---|---|---|
| H-1 | 6.38 (d,1.1) | 6.39 (d, 1.0) |
| H-2 | 5.34 | 5.34 |
| H-3 | | |
| H-4 | 5.51 (s) | 5.57 (s) |
| H-5 | 4.35 (dd, 6.6, 6.6) | 4.39 (dd, 6.6, 5.9) |
| H-6 | 4.13 (dd, 13.2, 6.6) | 4.05 (dd, 10.3, 6.6) |
| H-6′ | 4.08 (dd, 13.2, 6.6) | 3.97 (dd, 10.3, 5.9) |

Coupling constants ($J$ in Hz) are given in parentheses. The signal assignments were based on the decoupling method.

TABLE IV. $^{13}$C-NMR Spectral Data for Compounds **8**, **16** and **17**

| | **8** | **16** | **17** |
|---|---|---|---|
| C=O | 170.4, 170.0, 169.5, 169.3, 168.6 | 170.3, 169.5, 169.3, 168.6 | 170.3, 169.5, 168.9, 168.6 |
| $CH_3$ | 20.8, 20.6, 20.6, 20.5, 20.4 | 20.8, 20.7, 20.6, 20.4 | 20.8, 20.7, 20.6, 20.4 |
| C-1 | 89.0 | 88.8 | 89.0 |
| C-2 | 69.2 | 69.0 | 69.0 |
| C-3 | 69.8 | 69.8 | 70.1 |
| C-4 | 67.9 | 68.3 | 68.3 |
| C-5 | 69.8 | 71.0 | 69.4 |
| C-6 | 61.4 | 70.0 | 68.0 |
| C-1′ | — | 140.8 | 117.9 |
| C-2′ | — | 108.8 | 102.5 |

The signal assignments were based on $^1$H–$^{13}$C COSY method.

was found that when the starting sugar peracetates **5**, **6** and **7** were not sufficiently purified, the yields of the products decreased. Since it was thought that the impurities were **8**, **9** and **10**, which were α-isomers of **5**, **6** and **7**, respectively, the reactions of the α-isomers under the same reaction conditions were investigated. The reaction of **8**[7] with $PCl_5$ in $CCl_4$ gave, after separation by column chromatography, compounds **4** (2.6%), **11** (11.4%) and a mixture. The preparative HPLC ($H_2O$–acetone, 2 : 3) of the mixture gave compounds **16** (mp, 151—152 °C, 42.9%) and **17** (mp, 84—85 °C, 18.9%). The fast atom bombardment mass spectrum (FAB-MS) of **16** shows a pseudomolecular ion peak at $m/z$ 499 $[M+Na]^+$, and that of **17** a pseudomolecular ion peak at $m/z$ 569 $[M+Na]^+$. The $^1$H-NMR spectra of **16** and **17** were compared with that of the starting material **8** (Table II). The signals due to the protons of four acetyl groups and all seven protons on the pyranose rings in both compounds **16** and **17** were observed, and the chemical shifts and coupling constants of the protons of H-1, 2, 3 and 4 in both **16** and **17** were similar to those in **8**; on the other hand, those of the protons of H-6 and 6′ in **16** and **17** are different from those in **8**. In the $^{13}$C-NMR spectra (Table IV), the chemical shifts of the carbons at C-1, 2, 3, 4 and 5 in **16** and **17** were similar to the corresponding shifts in **8**; on the other hand, chemical shifts of the carbons at C-6 in **16** and **17** were different from that in **8**. Furthermore, two additional signals were observed at δ 108.8 and 140.8 in **16** and at δ 102.5 and 117.9 in **17** in each spectrum. These results indicate that the acetyl group at C-6 in **8** is converted to $-C(Cl)=CCl_2$ and $-C(Cl)_2-CCl_3$ to give **16** and **17**, respectively. The reaction of **9**[8] with $PCl_5$ in $CCl_4$ under a refluxing condition gave products **12** (4.2%), **13** (13.0%) and **18** (62.3%). Product **18** shows a pseudomolecular ion peak at $m/z$ 499 $[M+Na]^+$ in the FAB-MS. In comparing the $^1$H-NMR spectrum of **18** with that of **9** (Table III), both the chemical shifts and coupling constants of H-1, 2, 3, 4 and 5 in **18** were similar to those in **9**, whereas those of H-6 and 6′ in **18** were different from those in **9**. In the $^{13}$C-NMR spectrum (Table V), the chemical shifts of the carbons at C-1, 2, 3, 4 and 5 of **18** were similar to the corresponding shifts of **9**; on the other hand, the chemical shift of the carbon at C-6 of **18** was different from that of **9**. Two additional carbon signals at δ 109.3 and 140.5 were further observed. These spectral data indicate that the acetyl group at C-6 of **9** is converted to a

$-C(Cl)=CCl_2$ group to give **18**. On the other hand, the reaction of **10** with $PCl_5$ in toluene under a refluxing condition gave **15** as a major product (68.5%) and **14** as a minor one (5.3%). Thus, the reactions of the α-pyranoses **8**—**10** with $PCl_5$ gave different results from those of the β-isomers **5**—**7**. Although it has not yet been elucidated that only the acetyl groups at C-6 in **8** and **9** not those in **5** and **6** are converted to the substituent, $-C(Cl)=CCl_2$ or $-C(Cl)_2-CCl_3$, intermediates such as **19** and **20** (Fig. 2) may be favorably considered because in the 1C conformations, only the acetyl groups at C-6 are able to be activated.

Niwa *et al.*[9] reported that timosaponin A-III (**21**), isolated from the roots of *Anemarrhena asphodeloides* BUNGE (Liliaceae), was not hydrolyzed by emulsin. In the $^{13}C$-NMR spectrum, they assigned the sugar carbon signals of **21** as shown in Table VI, in which a glycosidation shift[10] was observed at the C-2 carbon of glucopyranose, not that of galactopyranose. These enzymic and spectral studies seemed to indicate that the structure of the saponin was **22** rather than **21**. Therefore, the structure of the saponin was confirmed by synthesis using sarsasapogenin **23** as a aglycon and the sugar derivatives **4** and **12**. The reaction of **23** with **4** in the presence of silver trifluoromethane sulfonate (Ag-OTf), 1,1,3,3-tetramethyl urea (TMU) and Drierite in $CH_2Cl_2$ gave compounds **24** (29.1%) and **25** (46.9%). Both compounds **24** and **25** show a pseudomolecular ion peaks at $m/z$ 873 $[M+Na]^+$. In the $^1H$-NMR spectra (Table VII), compounds **24** and **25** exhibit anomeric proton signals at $\delta$ 4.67 and 5.01 with the coupling constants of 7.8 and 3.7 Hz, respectively. The same reaction of **23** with **12** gave compounds **26** (24.0%) and **27** (48.0%). The FAB-MS of

TABLE V. $^{13}C$-NMR Spectral Data for Compounds **9** and **18**

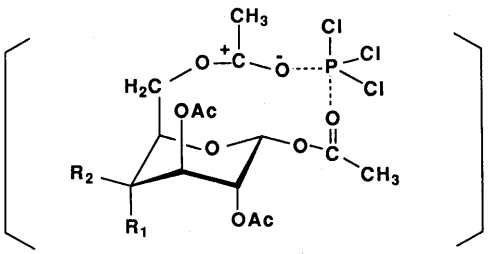
| | **9** | **18** |
|---|---|---|
| C=O | 170.3, 170.1, 170.1, 169.8, 168.9 | 170,0, 169,9, 169.8, 169.8 |
| $CH_3$ | 20.9, 20.8, 20.6, 20.6, 20.5 | 20.8, 20.6, 20.5, 20.5 |
| C-1 | 89.7 | 89.5 |
| C-2 | 66.4 | 66.3 |
| C-3 | 67.3 | 67.7 |
| C-4 | 67.3 | 67.3 |
| C-5 | 68.8 | 69.0 |
| C-6 | 61.1 | 69.5 |
| C-1′ | — | 140.5 |
| C-2′ | — | 109.3 |

The signal assignments were based on $^1H$–$^{13}C$ COSY method.

TABLE VI. $^{13}C$-NMR Spectral Data for Sugar Moieties of Compound **21**

| | Chemical shifts listed in literature[10] | Chemical shifts assigned in this study[a] |
|---|---|---|
| Galactose | | |
| C-1 | 105.9 | 102.4 |
| C-2 | 75.4 | 81.8 |
| C-3 | 77.9 | 76.5 |
| C-4 | 71.6 | 69.7 |
| C-5 | 78.2 | 76.8 |
| C-6 | 62.7 | 62.1 |
| Glucose | | |
| C-1 | 102.4 | 105.7 |
| C-2 | 81.6 | 75.1 |
| C-3 | 76.7 | 78.2 |
| C-4 | 69.7 | 71.8 |
| C-5 | 76.4 | 77.9 |
| C-6 | 62.1 | 62.8 |

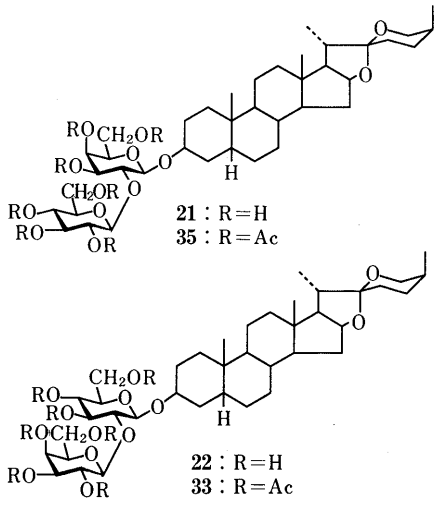
*a*) The spectrum was obtained in $d_5$-pyridine. The signal assignments were based on previously published papers.[1,13]



**19** : $R_1$ = OAc, $R_2$ = H

**20** : $R_1$ = H, $R_2$ = OAc

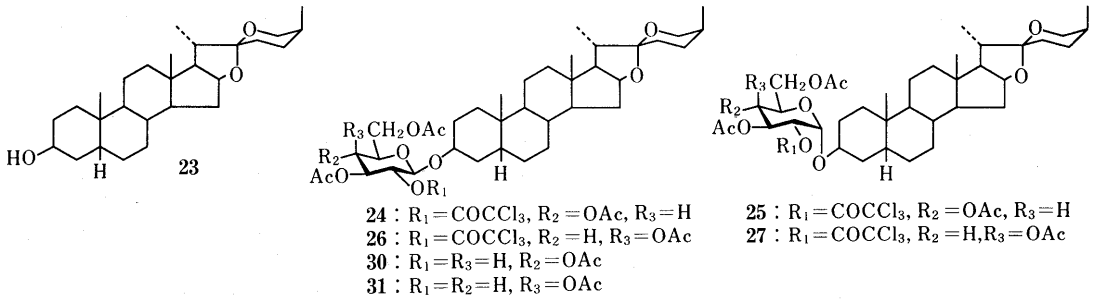
Fig. 2



**21** : R=H
**35** : R=Ac

**22** : R=H
**33** : R=Ac

Chart 2



**24** : $R_1$=$COCCl_3$, $R_2$=OAc, $R_3$=H
**26** : $R_1$=$COCCl_3$, $R_2$=H, $R_3$=OAc
**30** : $R_1$=$R_3$=H, $R_2$=OAc
**31** : $R_1$=$R_2$=H, $R_3$=OAc

**25** : $R_1$=$COCCl_3$, $R_2$=OAc, $R_3$=H
**27** : $R_1$=$COCCl_3$, $R_2$=H, $R_3$=OAc

Chart 3

TABLE VII. $^1$H-NMR Spectral Data for Compounds **24**—**27**, **30**, **31**, **33** and **35**[a]

| | **24** | **25** | **26** | **27** |
|---|---|---|---|---|
| Aglycon | | | | |
| 3-H | 4.01 (br s) | 3.96 (br s) | 4.04 (br s) | 3.95 (br s) |
| 16-H | 4.38 (br dd, 13.5, 7.0) | 4.39 (br dd, 13.5, 7.0) | 4.39 (br dd, 13.6, 7.0) | 4.40 (br dd, 13.9, 7.3) |
| 18-$CH_3$ | 0.78 (s) | 0.76 (s) | 0.74 (s) | 0.75 (s) |
| 19-$CH_3$ | 0.92 (s) | 0.93 (s) | 0.93 (s) | 0.95 (s) |
| 21-$CH_3$ | 1.08 (d, 7.0) | 1.08 (d, 7.0) | 1.07 (d, 7.0) | 1.08 (d, 6.8) |
| 26-H | 3.95 (dd, 11.0, 2.6) | 3.95 (dd, 11.0, 2.6) | 3.93 (dd, 11.0, 2.6) | 3.94 (dd, 10.6, 2.6) |
| 26-H′ | 3.29 (d, 11.0) | 3.29 (d, 11.0) | 3.29 (d, 11.0) | 3.22 (d, 10.6) |
| 27-$CH_3$ | 0.95 (d, 7.0) | 0.95 (d, 7.0) | 0.98 (d, 6.6) | 0.99 (d, 6.6) |
| Acetyl | 2.00, 2.03, 2.09 | 2.04, 2.05, 2.09 | 1.98, 2.05, 2.18 | 2.05, 2.07, 2.14 |
| Inner sugar | | | | |
| H-1 | 4.67 (d, 7.8) | 5.01 (d, 3.7) | 4.66 (d, 7.3) | 5.05 (d, 4.2) |
| H-2 | 5.04 (dd, 9.5, 7.8) | 4.95 (dd, 9.5, 3.7) | 5.24 (dd, 7.3, 7.3) | 5.09 (dd, 8.4, 4.2) |
| H-3 | 5.38 (dd, 9.5, 9.5) | 5.62 (dd, 9.5, 9.5) | 5.23 (dd, 7.3, 3.3) | 5.22 (dd, 8.4, 3.0) |
| H-4 | 5.09 (dd, 9.5, 9.5) | 5.22 (dd, 9.5, 9.5) | 5.43 (d, 3.3) | 5.41 (d, 3.0) |
| H-5 | 3.73 (ddd, 9.5, 4.8, 2.5) | 3.67 (ddd, 9.5, 4.8, 2.5) | 3.92 (dd, 6.6, 6.6) | 3.95 (dd, 6.5, 6.5) |
| H-6 | 4.29 (dd, 12.2, 4.8) | 4.29 (dd, 12.0, 4.8) | 4.20 (dd, 11.0, 6.6) | 4.13 (dd, 11.2, 6.5) |
| H-6′ | 4.13 (dd, 12.2, 2.5) | 4.03 (dd, 12.0, 2.5) | 4.12 (dd, 11.0, 6.6) | 4.04 (dd, 11.2, 6.5) |
| Outer sugar | | | | |
| H-1 | | | | |
| H-2 | | | | |
| H-3 | | | | |
| H-4 | | | | |
| H-5 | | | | |
| H-6 | | | | |
| H-6′ | | | | |

| | **30** | **31** | **33** | **35** |
|---|---|---|---|---|
| Aglycon | | | | |
| 3-H | 4.04 (br s) | 4.05 (br s) | 3.99 (br s) | 4.00 (br s) |
| 16-H | 4.41 (br dd, 13.5, 7.0) | 4.40 (br dd, 13.5, 7.0) | 4.40 (br dd, 13.4, 7.0) | 4.41 (br dd, 13.0, 6.9) |
| 18-$CH_3$ | 0.76 (d) | 0.76 (s) | 0.76 (s) | 0.76 (s) |
| 19-$CH_3$ | 0.95 (s) | 0.96 (s) | 1.01 (s) | 1.00 (s) |
| 21-$CH_3$ | 1.08 (d, 7.0) | 1.08 (d, 7.0) | 1.08 (d, 6.9) | 1.08 (d, 7.0) |
| 26-H | 3.95 (dd, 11.0, 2.2) | 3.95 (dd, 11.0, 2.6) | 3.95 (dd, 10.8, 2.4) | 3.95 (dd, 11.0, 2.6) |
| 26-H′ | 3.30 (d, 11.0) | 3.30 (d, 11.0) | 3.30 (d, 10.8) | 3.30 (d, 11.0) |
| 27-$CH_3$ | 0.99 (d, 7.0) | 0.99 (d, 7.0) | 0.99 (d, 7.0) | 0.99 (d, 7.0) |
| Acetyl | 2.03, 2.07, 2.07 | 2.04, 2.04, 2.13 | 1.97, 2.00, 2.03, 2.05, 2.06, 2.08, 2.14 | 1.99, 2.00, 2.01, 2.02, 2.06, 2.07, 2.14 |
| Inner sugar | | | | |
| H-1 | 4.41 (d, 7.7) | 4.38 (d, 7.7) | 4.46 (d, 7.9) | 4.44 (d, 7.9) |
| H-2 | 3.57 (dd, 9.5, 7.7) | 3.79 (dd, 10.3, 7.7) | 3.74 (dd, 9.7, 7.9) | 3.85 (dd, 10.0, 7.9) |
| H-3 | 5.14 (dd, 9.5, 9.5) | 4.95 (dd, 10.3, 3.3) | 5.17 (dd, 9.5, 9.5) | 4.96 (dd, 10.3, 7.9) |
| H-4 | 5.02 (dd, 9.5, 9.5) | 5.37 (d, 3.3) | 4.95 (dd, 9.5, 9.5) | 5.30 (d, 3.3) |
| H-5 | 3.66 (ddd, 9.5, 5.1, 2.6) | 3.89 (dd, 6.6, 6.6) | 3.67 (ddd, 9.5, 5.0, 2.1) | 3.83 (dd, 6.6, 6.6) |
| H-6 | 4.26 (dd, 12.1, 5.1) | 4.17 (dd, 11.0, 6.6) | 4.26 (dd, 12.2, 5.0) | 4.13 (dd, 11.4, 6.6) |
| H-6′ | 4.18 (dd, 12.1, 2.6) | 4.11 (dd, 11.0, 6.6) | 4.07 (dd, 12.2, 2.1) | 4.06 (dd, 11.4, 6.6) |
| Outer sugar | | | | |
| H-1 | | | 4.68 (d, 8.0) | 4.78 (d, 8.0) |
| H-2 | | | 5.08 (dd, 10.5, 8.0) | 4.89 (dd, 9.2, 8.0) |
| H-3 | | | 4.95 (dd, 10.5, 3.2) | 5.14 (dd, 9.2, 9.2) |
| H-4 | | | 5.36 (d, 3.2) | 5.05 (dd, 9.2, 9.2) |
| H-5 | | | 3.87 (dd, 6.7, 6.7) | 3.71 (ddd, 9.2, 5.1, 2.6) |
| H-6 | | | 4.16 (dd, 11.3, 6.7) | 4.33 (dd, 12.5, 5.1) |
| H-6′ | | | 4.13 (dd, 11.3, 6.7) | 4.07 (dd, 12.5, 2.6) |

a) Only assignable signals on aglycons are listed.[14] Coupling constants ($J$ in Hz) are given in parentheses. The signal assignments were based on the decoupling method.

compounds **26** and **27** show the same pseudomolecular ion peak at $m/z$ 873 $[M+Na]^+$. The $^1$H-NMR spectra of **26** and **27** exhibit anomeric proton signals at $\delta$ 4.66 and 5.05 with the coupling constants of 7.3 and 4.2 Hz, respectively. In this glycosidation, $\alpha$-glycosides were obtained roughly twice as frequently as $\beta$-glycosides. However, it is known that in compound **21** and most naturally occurring triterpenoidal saponins, D-pyranoses which link directly at the C-3 position of the aglycons arrange in a $\beta$-configuration. Therefore, we attempt to obtain $\beta$-glycosides as major products in the glycosidations. Compounds **4** and **12** reacted with 20% HBr in AcOH[11] for 12 h at room temperature to give bromides (**28**) and (**29**) in the yields of 90.3 and 85.9%, respectively. Both compounds **28** and **29**

TABLE VIII. $^1$H-NMR Spectral Data for Compounds **28** and **29**

| | **28** | **29** |
|---|---|---|
| H-1 | 6.65 (d, 4.4) | 6.71 (d, 4.0) |
| H-2 | 4.98 (dd, 9.8, 4.4) | 5.19 (dd, 9.0, 4.0) |
| H-3 | 5.70 (dd, 9.8, 9.8) | 5.16—5.22 |
| H-4 | 5.17 (dd, 9.8, 9.8) | |
| H-5 | 4.34 (ddd, 9.8, 4.0, 1.5) | 4.54 (dd, 6.2, 6.2) |
| H-6 | 4.39 (dd, 10.6, 4.0) | 4.22 (dd, 11.5, 6.2) |
| H-6′ | 4.15 (dd, 10.6, 1.5) | 4.14 (dd, 11.5, 6.2) |
| Acetyl | 2.02, 2.07, 2.11 | 2.00, 2.07, 2.18 |

Coupling constants ($J$ in Hz) are given in parentheses. The signal assignments were based on the decoupling method.

TABLE IX. Comparisons of Reaction Times and Yields of Products Obtained by the Glycosidation of **23** with Chlorides **4** and **12** and by Those of **23** with Bromides **28** and **29**

| Starting sugar derivative | Reaction time (h) | Products (yield, %) |
|---|---|---|
| **4** | 8.0 | **24** (29.1), **25** (46.9) |
| **12** | 10.0 | **26** (24.0), **27** (48.0) |
| **28** | 1.5 | **24** (66.9), **25** (19.1) |
| **29** | 2.0 | **26** (62.1), **27** (20.8) |

show the fragment ion peak at $m/z$ 433 ($M^+ - Br$) in the EI-MS. In the $^1$H-NMR spectra (Table VIII), **28** and **29** exhibited anomeric proton signals at $\delta$ 6.65 and 6.71 with the coupling constants of 4.4 and 4.0 Hz, respectively. When compounds **28** and **29** were used in the glycosidation with **23**, the yields of the $\beta$-glycosides **24** and **26** increased, accompanying a reduction in reaction time by about 2—2.5 times (Table IX). Treatment of **24** and **26** with ammonia-saturated ether gave compounds **30** and **31** in the yields of 93.5 and 91.8%, respectively. Both compounds **30** and **31** show pseudomolecular ion peaks at $m/z$ 727 $[M+Na]^+$. The $^1$H-NMR spectrum of **30** (Table VII) exhibits an anomeric proton signal at $\delta$ 4.41 (d, $J=7.7$ Hz) and the signals of three acetyl groups, together with the H-2 signal ($\delta$ 3.57) on the sugar moiety shifted at a higher field than that of 24 ($\delta$ 5.24). In the $^1$H-NMR spectrum of **31**, an anomeric proton signal ($\delta$ 4.38, d, $J=7.7$ Hz) and the signals of three acetyl groups were observed, and the signal of H-2 on the sugar moiety shifted at a higher field ($\delta$ 3.79) than that of **26** ($\delta$ 5.24). Glycosidation of **30** with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**32**) in the presence of Ag-OTf and TMU in $CH_2Cl_2$ gave compound (**33**) in the yield of 60.7% and recovered the starting material **30** (26.7%). The similar reaction of **31** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**34**) gave compound (**35**) in the yield of 68.1% and recovered the starting material **31** (19%). Both compounds **33** and **35** show pseudomolecular ion peaks at $m/z$ 1057 $[M+Na]^+$. In the $^1$H-NMR spectra, two anomeric protons of **33** are observed at $\delta$ 4.46 and 4.68 with coupling constants of 7.9 and 8.0 Hz, respectively, and those of **35** are at $\delta$ 4.44 and 4.78 with coupling constants of 7.9 and 8.0 Hz, respectively. These spectral data suggest that the glycosidation of **30** with **32** and that of **31** with **34** give only $\beta$-glycosides **33** and **35**, respectively, but no α-glycosides different from those of **23** with **4** and **12**. These results suggested that the acetyl groups at C-2 of **32** and **34** took part in neighboring-group participation, with anomeric carbons to release $Br^-$ resulting in the formation of dioxolane cations.[12] Compounds **30** and **31** predominantly attacked the anomeric carbons from the $\beta$-site to give $\beta$-glycosides **33** and **35**, respectively. The acetate of timosaponin A-III (**21**) was identified with compound **35**, not **33**, by $^1$H-NMR spectra and HPLC. Therefore, the structure of timosaponin A-III was confirmed as **21** not **22**, and the carbon signals of the sugar moieties of **21** in the $^{13}$C-NMR spectrum were reassigned as shown in Table VI.

## Experimental

**Measurements** Melting points were obtained on a Yanagimoto micro-melting point apparatus and are uncorrected. The TLC utilized Kieselgel $HF_{254}$ (Merck), and spots were detected by spraying with dilute $H_2SO_4$ followed by heating at 80 °C for 10 min. Column chromatography was carried out on Wakogel C-200. An SSC-6300 (Senshu Scientific Co., Ltd.) equipped with an SSC-3000 A was employed for analytical HPLC using ODS-1251-D (4.6 × 250 mm), and was further equipped with an SSC autoinjector 6310 and an SSC fraction collector 6320 for preparative HPLC using ODS-4521-D (10 × 250 mm). $^1$H- and $^{13}$C-NMR spectra were obtained with a JEOL JNM-GX NMR spectrometer at 270 and 67.8 MHz, respectively, and chemical shifts were given in ppm with tetramethylsilane as an internal standard. EI and FAB mass spectra were recorded on a JEOL JMS-DX 300 mass spectrometer. Optical rotations were measured with a JASCO J-20A spectropolarimeter.

**Reaction of 5 with $PCl_5$ in $CCl_4$** A suspension of **5** (78 g) and $PCl_5$ (117 g) in $CCl_4$ (400 ml) was refluxed for 5 h. The mixture was poured into ice water (800 ml) and extracted with $CH_2Cl_2$ (500 ml × 3). The combined organic extracts were successively washed with $H_2O$, saturated aqueous $NaHCO_3$, and $H_2O$, then dried over $Na_2SO_4$, and filtered. The filtrate was evaporated under reduced pressure at 40 °C to give a residue which was subjected to column chromatography (benzene–acetone, gradient up to 2%) to obtain **4** (52.3 g, 55.1%, mp 144—145 °C (lit. 140—142 °C)[3] after recrystallization from ether–*n*-hexane) and **11** (10.9 g, 14.9%). The EI-MS of **4** $m/z$ (rel. intensity): 468 (2, $M^+$), 433 (5, $M^+ - Cl$), 310 (11), 308 (25), 306 (20), 272 (7), 270 (6), 259 (13), 257 (11), 229 (10), 211 (28), 205 (7), 187 (18), 175 (9), 169 (100). *Anal.* Calcd for $C_{14}H_{16}Cl_4O_9$: C, 35.78; H, 3.43. Found: C, 35.65; H, 3.52. The EI-MS of **11** $m/z$ (rel. intensity): 331 (7, $M^+ - Cl$), 246 (7), 229 (13), 212 (7), 211 (55), 206 (19), 204 (56), 187 (19), 175 (6), 173 (7), 170 (10), 169 (100). *Anal.* Calcd for $C_{14}H_{19}ClO_9$: C, 45.85; H, 5.22. Found: C, 45.79; H, 5.30.

**Reaction of 6 with $PCl_5$ in $CCl_4$** A suspension of **6** (100 g) and $PCl_5$ (200 g) in $CCl_4$ (500 ml) was refluxed for 5 h. The reaction mixture was treated according to the preparative method of **4** to give a residue which was subjected to column chromatography (benzene–acetone, gradient up to 2%) to obtain products **12** (66.8 g, 54.8%) and **13** (15.0 g, 16.0%). EI-MS of **12** $m/z$ (rel. intensity): 433 (5, $M^+ - Cl$), 310 (9), 308 (21), 306 (17), 211 (31), 187 (6), 179 (11), 175 (5), 169 (100). *Anal.* Calcd for $C_{14}H_{16}Cl_4O_9$: C, 35.78; H, 3.43. Found: C, 35.74; H, 3.48. EI-MS of **13** $m/z$ (rel. intensity): 331 (3, $M^+ - Cl$), 211 (8), 200 (6), 187 (6), 171 (8), 169 (25), 162 (9), 157 (6), 145 (6), 144 (9), 140 (9), 127 (13), 126 (16), 115 (16), 113 (14), 112 (100). *Anal.* Calcd for $C_{14}H_{19}ClO_9$: C, 45.85; H, 5.22. Found: C, 45.81; H, 5.28.

**Detrichloroacetylation of 12** Compound **12** (13 g) was dissolved in ammonia-saturated ether (26 ml) and vigorously shaken for 10 min at 0 °C. The mixture was sucked for 5 min and evaporated to give a residue. The residue was subjected to column chromatography (benzene–acetone, gradient up to 4%) to obtain 3,4,6-tri-*O*-acetyl-β-D-galactopyranosyl chloride (7.8 g, 86.9%). EI-MS $m/z$ (rel. intensity): 289 (4, $M^+ - Cl$), 211 (8), 200 (6), 187 (6), 186 (10), 171 (8), 169 (25), 162 (9), 157 (6), 145 (6), 144 (9), 140 (9), 127 (13), 126 (16), 115 (16), 113 (14), 112 (100). $^1$H-NMR spectrum ($CDCl_3$) $\delta$: 2.06 (s, Ac × 2), 2.16 (s, Ac), 2.71 (br s, exchangeable with $D_2O$, OH), 3.97 (dd, $J=5.6$, 3.7 Hz, H-5), 4.02 (dd, $J=9.9$, 8.5 Hz, H-2), 4.12 (dd, $J=12.0$, 3.7 Hz, H-6), 4.17 (dd, $J=12.0$, 5.6 Hz, H-6′), 4.94 (dd, $J=9.9$, 3.3 Hz, H-3), 5.18 (d, $J=8.5$ Hz, H-1), 5.41 (d, $J=3.3$ Hz, H-4). *Anal.* Calcd for $C_{12}H_{17}ClO_8$: C, 44.39; H, 5.28. Found: C, 44.35; H, 5.33.

**Reaction of 7 with $PCl_5$ in Toluene** A suspension of **7** (50 g) and $PCl_5$ (114 g) in toluene (200 ml) was refluxed for 18 h. The reaction mixture was treated according to the preparative method of **4** to give a residue which was subjected to column chromatography (benzene–acetone, gradient up

to 2%) to obtain products **14** (32.9 g, 52.9%) and **15** (8.05 g, 17.2%). EI-MS of **14** *m/z* (rel. intensity): 456 (3, $M^+ + 2$), 454 (3, $M^+$), 259 (18), 257 (17), 197 (17), 173 (45), 162 (12), 155 (100). *Anal.* Calcd for $C_{13}H_{14}Cl_4O_9$: C, 34.24; H, 3.09. Found: C, 34.19; H, 3.17. EI-MS of **15** *m/z* (rel. intensity): 354 (2, $M^+ + 2$), 352 (2, $M^+$), 312 (10), 310 (29), 215 (19), 214 (12), 197 (30), 180 (10), 173 (83), 162 (22), 157 (14), 155 (100). *Anal.* Calcd for $C_{13}H_{17}ClO_9$: C, 44.27; H, 4.86. Found: C, 44.20; H, 4.96.

**Detrichloroacetylation of 14** Compound **14** (4.0 g) was dissolved in ammonia-saturated ether (8 ml) with vigorous shaking for 10 min at 0 °C. The mixture was sucked for 5 min and evaporated to give a residue which was subjected to column chromatography (benzene–acetone, gradient up to 4%) to obtain methyl 3,4-di-*O*-acetyl-*β*-D-glucuronatopyranosyl chloride (2.3 g, 84.4%). EI-MS *m/z* (rel. intensity): 310 (3, $M^+$), 275 (10), 215 (30), 197 (14), 173 (21), 156 (11), 155 (100). $^1$H-NMR spectrum ($CDCl_3$) $\delta$: 2.06 and 2.11 (each s, Ac), 2.45 (d, $J$=4.0 Hz, exchangeable with $D_2O$, OH), 3.76 (s, $OCH_3$), 3.95 (ddd, $J$=9.5, 9.5, 4.0 Hz, exchanged to dd with addition of $D_2O$, H-2), 4.55 (d, $J$=9.5 Hz, H-5), 5.19 (dd, $J$=9.5, 9.5 Hz, H-4), 5.35 (d, $J$=9.5 Hz, H-1), 5.37 (dd, $J$=9.5, 9.5 Hz, H-3). *Anal.* Calcd for $C_{11}H_{15}ClO_8$: C, 42.52; H, 4.87. Found: C, 42.35; H, 4.90.

**Reaction of 8 with $PCl_5$ in $CCl_4$** A suspension of **8** (20 g) and $PCl_5$ (40 g) in $CCl_4$ (50 ml) was refluxed for 5 h. The reaction mixture was treated according to the preparative method of **4** to give a residue. The residue was subjected to column chromatography (benzene–acetone, gradient up to 2%) to give products **4** (410 mg, 2.6%) and **11** (1.9 g, 11.4%) and a mixture. The mixture was subjected to preparative HPLC ($H_2O$– acetone, 2:3) to obtain compounds **16** (10.5 g, 42.9%, mp 151—152 °C, after recrystallization from ether–*n*-hexane) and **17** (5.3 g, 18.9%, mp 84—85 °C, after recrystallization from ether–*n*-hexane). FAB-MS of **16** *m/z*: 499 $[M+Na]^+$. EI-MS *m/z* (rel. intensity): 417 (2, $M^+ - OCOCH_3$), 331 (24, $M^+ - C(Cl)=CCl_2$), 257 (5), 256 (6), 229 (9), 187 (8), 169 (79), 152 (7), 145 (12), 141 (19), 127 (78), 117 (6), 115 (26), 109 (89), 103 (26), 99 (58), 97 (11), 85 (13), 81 (100). *Anal.* Calcd for $C_{16}H_{19}Cl_3O_{10}$: C, 40.23; H, 4.01. Found: C, 40.22; H, 4.02. FAB-MS of **17** *m/z*: 569 $[M+Na]^+$. EI-MS *m/z* (rel. intensity): 487 (3, $M^+ - OCOCH_3$), 331 (22, $M^+ - C(Cl)_2 - CCl_3$), 318 (10), 316 (15), 314 (10), 229 (7), 187 (10), 169 (56), 157 (84), 155 (6), 149 (9), 145 (39), 141 (12), 127 (52), 117 (10), 115 (100). *Anal.* Calcd for $C_{16}H_{19}Cl_5O_{10}$: C, 35.03; H, 3.49. Found: C, 35.01; H, 3.52.

**Reaction of 9 with $PCl_5$ in $CCl_4$** A suspension of **9** (5 g) and $PCl_5$ (10 g) in $CCl_4$ (10 ml) was refluxed for 5 h. The reaction mixture was treated according to the preparative method of **4** to give a residue. The residue was subjected to column chromatography (benzene–acetone, gradient up to 2%) to give compounds **12** (0.25 g, 4.2%), **13** (0.61 g, 13.0%) and **18** (3.8 g, 62.3%). FAB-MS of **18** *m/z*: 499 $[M+Na]^+$. EI-MS *m/z* (rel. intensity): 331 (20, $M^+ - C(Cl)=CCl_2$), 256 (7), 229 (13), 187 (8), 169 (73), 152 (13), 145 (15), 141 (25), 127 (77), 117 (9), 109 (69), 103 (30), 99 (66), 97 (13), 85 (15), 81 (100). *Anal.* Calcd for $C_{16}H_{19}Cl_3O_{10}$: C, 40.24; H, 4.01. Found: C, 40.11; H, 4.08.

**Reaction of 10 with $PCl_5$ in Toluene** A suspension of 10 (20 g) and $PCl_5$ (40 g) in toluene (40 ml) was refluxed for 5 h. The reaction mixture was treated according to the preparative method of **4** to give **14** (1.28 g, 5.3%) and **15** (12.8 g, 68.5%).

**Synthesis of 10** Methyl glucuronatopyranose **7**[6] (5g) was dissolved in acetic anhydride (20 ml) containing zinc chloride (2 g) and heated for 20 min in a boiling steam bath. The mixture was poured into ice-water (100 ml) and extracted with $CH_2Cl_2$ (200 ml × 3). The combined extracts were washed successively with water, $NaCO_3$-saturated aqueous solution and water, dried over anhydrous $Na_2SO_4$, and evaporated to give a residue. The preparative HPLC of the residue (ODS-H-5251, 20 × 250 mm; solvent system, 40% $H_2O$ in acetone; flow rate, 4 ml/min, column temp. 35 °C) gave **10** (6.35 g, 63.5%). *Anal.* Calcd for $C_{15}H_{20}O_{11}$: C, 47.87; H, 5.36. Found: C, 47.80; H, 5.38. $^1$H-NMR ($CDCl_3$) $\delta$: 6.64 (d, $J$=3.6 Hz, H-1), 5.52 (dd, $J$=9.9, 9.9 Hz, H-3), 5.22 (dd, $J$=9.9, 9.9 Hz, H-4), 5.12 (dd, $J$=9.9, 3.6 Hz, H-2), 4.42 (d, $J$=9.9 Hz, H-5), 3.75 (3H, s, $OCH_3$), 2.02, 2.05, 2.05, 2.19 (each 3H, s, Ac).

**Glycosidation of 23 with 4** To a solution of **23** (5.0 g) in dry $CH_2Cl_2$ (40 ml), Ag-OTf (5.0 g), Drierite (5.0 g), TMU (1.9 ml) and **4** (5.0 g) were added, and the mixture was stirred for 6 h at room temperature. The reaction mixture was filtered, and the filtrate was poured into ice-water (200 ml) and extracted with $CH_2Cl_2$ (200 ml × 3). The combined organic extracts were washed successively with $NaHCO_3$-saturated aqueous solution and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue which was subjected to column chromatography (benzene–EtOAc, gradient up to 2%) to give **24** (2.97 g, 29.1%) and **25** (4.79 g, 46.9 %). FAB-MS of **24** *m/z*: 873 $[M+Na]^+$. *Anal.* Calcd for $C_{41}H_{59}Cl_3O_{12}$: C, 57.92; H, 6.99. Found: C, 55.77; H 6.80. FAB-MS of **25** *m/z*: 873 $[M+Na]^+$. *Anal.* Calcd for $C_{41}H_{59}Cl_3O_{12}$: C, 57.92; H, 6.99. Found: C, 57.68; H, 7.01.

**Glycosidation of 23 with 12** To a solution of **23** (4.0 g) in dry $CH_2Cl_2$ (35 ml), Ag-OTf (4.0 g), Drierite (4.0 g), TMU (1.51 ml) and **12** (4.0 g) were added, and the mixture was stirred for 5 h at room temperature. The reaction mixture was treated according to the preparative method of **24** and **25** to give compounds **26** (3.92 g, 48.0 %) and **27** (1.96 g, 24.0%). FAB-MS of **26** *m/z*: 873 $[M+Na]^+$. *Anal.* Calcd for $C_{41}H_{59}Cl_3O_{12}$: C, 57.92; H, 6.99. Found: C, 57.78; H, 7.01. FAB-MS of **27** *m/z*: 873 $[M+Na]^+$. *Anal.* Calcd for $C_{41}H_{59}Cl_3O_{12}$: C, 57.92; H, 6.99. Found: C, 57.81; H, 7.03.

**Reaction of 4 with HBr** To a solution of **4** (25 g) in AcOH (50 ml), 20% HBr in AcOH (100 ml) was added at 0 °C, and stirred overnight at room temperature. The reaction mixture was poured into ice-water (300 ml) and extracted with $CH_2Cl_2$ (250 ml × 3). The combined organic extracts were washed successively with an $NaHCO_3$-saturated aqueous solution and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue which was subjected to column chromatography (benzene–acetone, gradient up to 2%) to give **28** (24.7 g, 90.3%). EI-MS *m/z*: (rel. intensity): 433 (2, $M^+ - Br$), 354 (10), 352 (14), 350 (8), 307 (6), 273 (14), 271 (15), 170 (6), 169 (100). *Anal.* Calcd for $C_{14}H_{16}BrCl_3O_9$: C, 32.68; H, 3.13. Found: C, 32.54; H, 3.23.

**Reaction of 12 with HBr** To a solution of **12** (20 g) in AcOH (50 ml), 20% HBr in AcOH (90 ml) was added and stirred overnight at room temperature. The reaction mixture was treated according to the preparative method of **28** to give **29** (18.1 g, 85.9%). EI-MS *m/z* (rel. intensity): 433 (2, $M^+ - Br$), 354 (6), 352 (11), 350 (8), 307 (7), 273 (15), 271 (16), 170 (8), 169 (100). *Anal.* Calcd for $C_{14}H_{16}BrCl_3O_9$: C, 32.68; H, 3.13. Found: C, 32.48; H, 3.31.

**Glycosidation of 23 with 28** To a solution of **23** (3.0 g) in dry $CH_2Cl_2$ (40 ml), **28** (3.0 g), AgOTf (4.0 g), Drierite (3.0 g) and TMU (1.13 ml) were added, and the mixture was stirred for 1.5 h at room temperature. The reaction mixture was treated according to the glycosidation of **23** with **4** to give **24** (4.1 g, 66.9%) and **25** (1.17 g, 19.1%).

**Glycosidation of 23 with 29** To a solution of **23** (3.5 g) in dry $CH_2Cl_2$ (32 ml), **29** (3.5 g), AgOTf (3.6 g), Drierite (3.0 g) and TMU (1.16 ml) were added, and the mixture was stirred for 2.0 h at room temperature. The reaction mixture was treated according to the glycosidation of **23** with **4** to give **26** (4.0 g, 62.1%) and **27** (1.34 g, 20.8%).

**Detrichloroacetylation of 24** Ammonia-saturated ether (50 ml) was cooled at 0 °C, and **24** (2.0 g) was added. The mixture was shaken vigorously for 10 min at 0 °C. The mixture was sucked for 5 min and evaporated to give a residue which was subjected to column chromatography (benzene–EtOAc, gradient up to 5%) to give **30** (1.56 g, 93.5%). FAB-MS of **30** *m/z*: 727 $[M+Na]^+$. *Anal.* Calcd for $C_{39}H_{60}O_{11}$: C, 66.45; H, 8.58. Found: C, 66.41; H, 8.60.

**Detrichloroacetylation of 26** Ammonia-saturated ether (50 ml) was cooled at 0 °C, and **26** (1.5 g) was added. The mixture was shaken vigorously for 10 min at 0 °C. The reaction mixture was treated according to the preparative method of **30** to give **31** (1.18 g, 91.8%). FAB-MS of **31** *m/z*: 727 $[M+Na]^+$. *Anal.* Calcd for $C_{39}H_{60}O_{11}$: C, 66.45; H, 8.58. Found: C, 66.29; H, 8.69.

**Glycosidation of 30 with 32** To a solution of **30** (1.2 g) and **32** (1.0 g) in dry $CH_2Cl_2$ (30 ml), Ag-OTf (0.44 g), Drierite (1.0 g) and TMU (0.23 ml) were added, and the mixture was stirred for 5 h at room temperature and filtered. The filtrate was poured into ice-water (200 ml) and extracted with $CH_2Cl_2$ (100 ml × 3). The combined organic extracts were washed successively with $NaHCO_3$-saturated aqueous solution and water, dried over $MgSO_4$, and evaporated to give a residue. The residue was subjected to column chromatography (benzene–acetone, gradient up to 3%) to give product **35** (1.07 g, 60.7%) and the starting material **30** was recovered (0.32 g, 26.7%). FAB-MS of **35** *m/z*: 1057 $[M+Na]^+$. $[\alpha]_D^{16}$ −45.2° ($c$=0.44, $CHCl_3$). *Anal.* Calcd for $C_{53}H_{78}O_{20}$: C, 61.49; 7.60. Found: C, 61.38; H, 7.70.

**Glycosidation of 31 with 34** To a solution of **31** (1.0 g) and **34** (1.0 g) in dry $CH_2Cl_2$ (25 ml), Ag-OTf (0.36 g), Drierite (1.0 g) and TMU (0.2 ml) were added, and the mixture was stirred for 5h at room temperature. The reaction mixture was treated according to the preparative method of **35** to give **33** (0.85 g, 68.1%) and the starting material **31** was recovered (0.19 g, 19.0%). FAB-MS of **33** *m/z*: 1057 $[M+Na]^+$. $[\alpha]_D^{16}$ −38.4° ($c$=0.76, $CHCl_3$). *Anal.* Calcd for $C_{53}H_{78}O_{20}$: C, 61.49; H, 7.60. Found: C, 61.25; H, 7.73.

**Acetylation of 21** Saponin **21** (50 mg) was dissolved in pyridine (1 ml) and $Ac_2O$ (1 ml), and the mixture was allowed to stand overnight at room temperature. The reaction mixture was coevaporated 3 times with toluene

(50 ml) to give a product. In the HPLC (ODS-1251-D; solvent system, 20% $H_2O$ in acetone; flow rate, 0.2 ml/min; column temp., 35 °C), the product showed a peak with a retention time of 36.5 min, which was in accord with that of **35**. Furthermore, the $^1$H-NMR spectrum of the product is completely consistent with that of **35**, not that of **33** (Table VII).

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