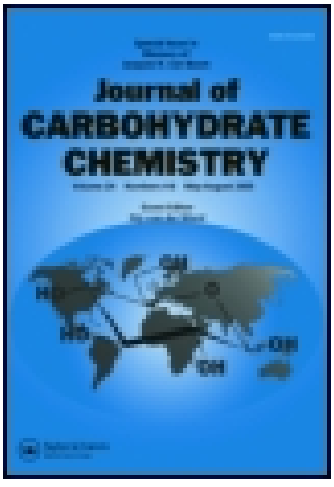


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# Effective Conversion of Three Diacetyl-*C*-(β-D-Glycopyranosyl) Phloroglucinols to Spiroketal Derivatives by Refluxing in Water

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Refluxing of diacetylphloroglucinol *C*-β-D-gluco-, -galacto-, and -allopyranosides in water for 1 d gave two kinds of spiroketal derivatives in total yields of 77%, 74%, and 64%, respectively. The structure and stereochemistry of the six new spiro(benzofuran-[2*H*]pyran and -[2*H*]furan) derived from galactoside and alloside were verified by NMR analysis. The production ratios of the spiro derivatives were measured by HPLC analysis at regular time intervals. Since the majority of spiro(benzofuran-[2*H*]furan) were produced after 8 to 12 h of refluxing and most spiro(benzofuran-[2*H*]pyran) produced after 2 d of refluxing, it is assumed that formation of spirofuran and spiropyran is a kinetic- and thermodynamic-controlled reaction, respectively.

**Keywords** Diacetylphloroglucinol *C*-β-D-glycopyranoside, Spiro(benzofuran-[2*H*] furan), Spiro(benzofuran-[2*H*]pyran), Kinetic-controlled product, Thermodynamic-controlled product

## INTRODUCTION

Recently, two novel kinds of flavone *C*-glycosides have been isolated from plants. Based on their structures, these compounds may form by a dehydration reaction between the *ortho*-hydroxyl group of the phenol moiety and the 2-hydroxyl group

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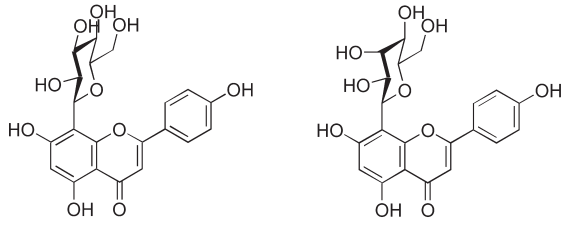
of the *C*-glycosyl moiety, followed by ring closure of the sugar moiety. One of these novel flavone *C*-glycosides, which has been extracted from oolong tea in trace amounts, shows potent anti-inflammatory activity, while its precursor, flavone 6-*C*-*β*-D-glucopyranoside (isovitexin), does not (Figs. 1 and 2).[1]

The other compound is composed of four trace constituents, pinnatifides A to D, which have been isolated from plants used in Chinese folk medicine. This compound contains novel flavone *C*-glycosides, including a spiro(benzofuran-[2*H*]furan) structure, which also seems to result from ketalization via a 1,2-hydride shift of the sugar moiety followed by ring closure with dehydration (Fig. 3).[2] Unfortunately, because only small amounts of these novel flavones have been isolated, the biological activity of these compounds is yet to be determined. On the other hand, chalcone *C*-glycoside, including a spiro(benzofuran-[2*H*]pyran), has been isolated as an acid-hydrolysate of chalcone *C*-*β*-D-glucopyranoside (Fig. 4).[3]

To the best our knowledge only a few reports describing the isomerization of polyphenol *C*-glycosides by internal-dehydration with 1,2-hydride shift have been published. The resistance to acid-hydrolysis of a *C*-glycoside differs from that of the corresponding *O*-glycoside. In addition, since the C-C bond of a *C*-glycoside is not cleaved in cells, the biological activity of a *C*-glycoside[4] occasionally differs from that of the *O*-glycoside and its aglycone. Furthermore, since the C-C bond cannot be cleaved by heat treatment, it can be assumed that this dehydrated isomerization occurs in flavonoid *C*-glycosides. However, synthesis of this novel polyphenol *C*-glycoside has been reported only for the above-mentioned flavone *C*-glycoside[1] and not for spiro-type polyphenol *C*-glycosides, except for bis-spiro fructodisaccharides.[5]

In a previous study, phloroacetophenone *C*-glucopyranoside and *C*-galactopyranoside (**1** and **3**) were successfully converted to the corresponding spiro(-benzofuran-[2*H*]pyran) derivatives (**2** and **4**) by refluxing in water in the presence of *p*-tolunensulfonic acid (*p*-TsOH) (Sch. 1, equations (1) and (2)).[6]

Recently, diacetylphloroglucinol *C*-*β*-D-glucopyranoside (**5**) also was converted to the spiro(benzofuran-[2*H*]furan) derivative (**7**), in 9.8% yield, by refluxing in water without any catalysts (Sch. 2).[7]




flavone 8-*C*-β-D-glucopyranoside (vitexin)

flavone 8-*C*-β-D-allopyranoside

**Figure 1:** Naturally occuring flavone *C*-glycosides.

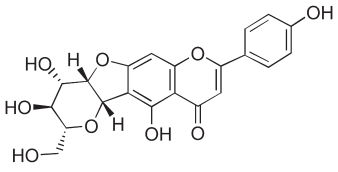


**Figure 2:** Novel flavone *C*-glycoside.



Following up on these studies, this paper describes the conversion of diacetylphloroglucinol *C*-*β*-D-glucopyranoside (**5**), -galactopyranoside (**8**), and -allopyranoside (**9**) to the corresponding spiro derivatives, especially spirofuran compound. In addition, the product ratio during the reaction was measured at regular intervals by HPLC analysis and the effective production of the desired spiro(benzofuran-[2*H*]furan) or spiro(benzofuran-[2*H*]pyran) was explored. And the mechanism for conversion reaction to these spiro derivatives was considered.

## RESULTS AND DISCUSSION

Diacetylphloroglucinol *C*-*β*-D-glycopyranosides (**5**, **8**, and **9**) were synthesized by direct C-glycosylation of diacetylphloroglucinol with the unprotected sugars in the low yields of 32%, 25%, and 6.4%, respectively. Although most

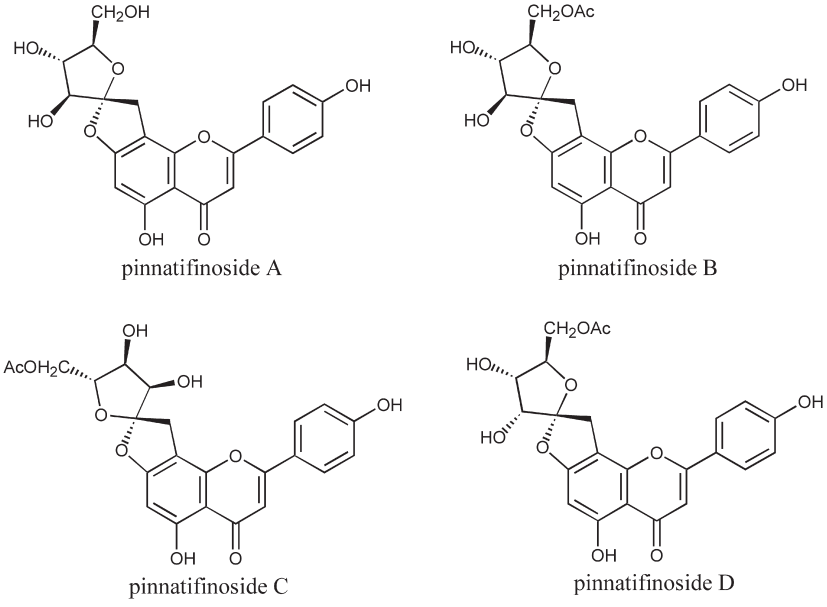



**Figure 3:** Naturally occuring novel flavone *C*-glycosides having a spiro-structure.

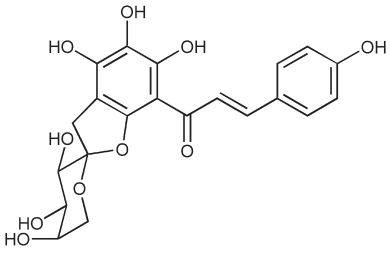
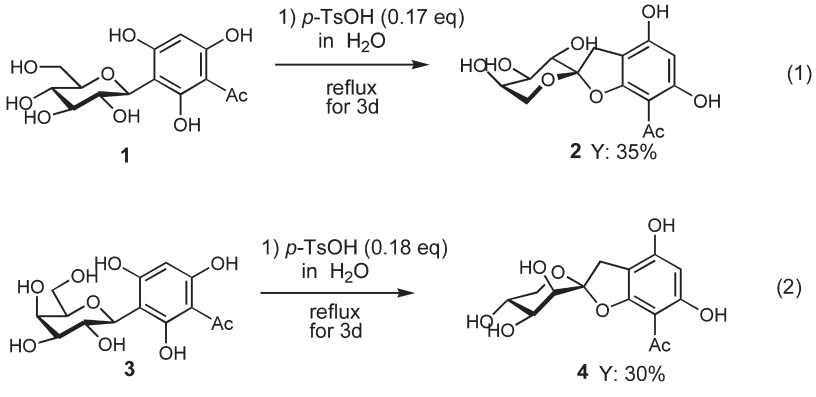


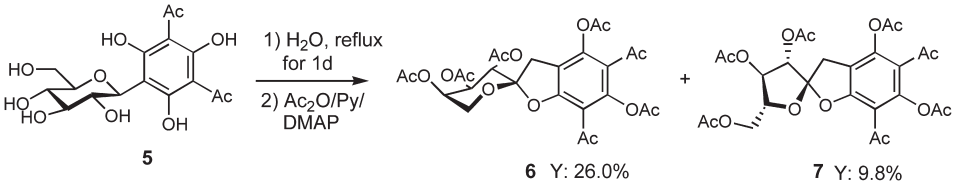
**Figure 4:** Novel chalcone *C*-glycosides having a spiro-structure.

of the starting materials were recovered under these reaction conditions, small amounts of some spiro derivatives were yielded with the desired *C*-glycosides. The reaction yields were low because of the relatively low reactivity of diacetylphloroglucinol (Sch. 3).[8] C-Glycosylation of diacetylphloroglucinol with D-galactose gave *C*-*β*-D-galactofuranoside (**10**) along with *C*-*β*-D-galactopyranoside (**8**) in the ratio of **8**:**10** = 14:1. A mixture of compounds **8** and **10** was used in the next conversion reaction.

Next, each of the *C*-glycopyranosides was refluxed in water without catalysts until the substrate nearly disappeared; durations ranged from overnight to 1 d. Twenty-four-hour refluxing of **5** followed by acetylation [$Ac_2O$/pyridine/4-dimethylaminopyridine (DMAP)] and separation by silica gel column chromatography gave a pyran-type spiro derivative (**6**) and a furan-type spiro derivative (**7**) in 49% and 28% yields, respectively (Sch. 4). Twenty-one-hour refluxing of a mixture of **8** and **10** followed by acetylation gave a pyran-type spiro derivative (**11**) in 70% yield and a furan-type spiro derivative (**12**) in 4% yield (Sch. 5). Sixteen-hour refluxing of **9** also gave furan-type spiro derivatives **13** and **14** in 35% and 25% yield, respectively (Sch. 6, equation (1)). Additional 34-h




**Scheme 1:** Conversion reaction of phloroacetophenone C-*β*-D-glucopyranoside and -galactopyranside (**1** and **3**) in refluxing water in the presence of catalytic amounts of p-TsOH.

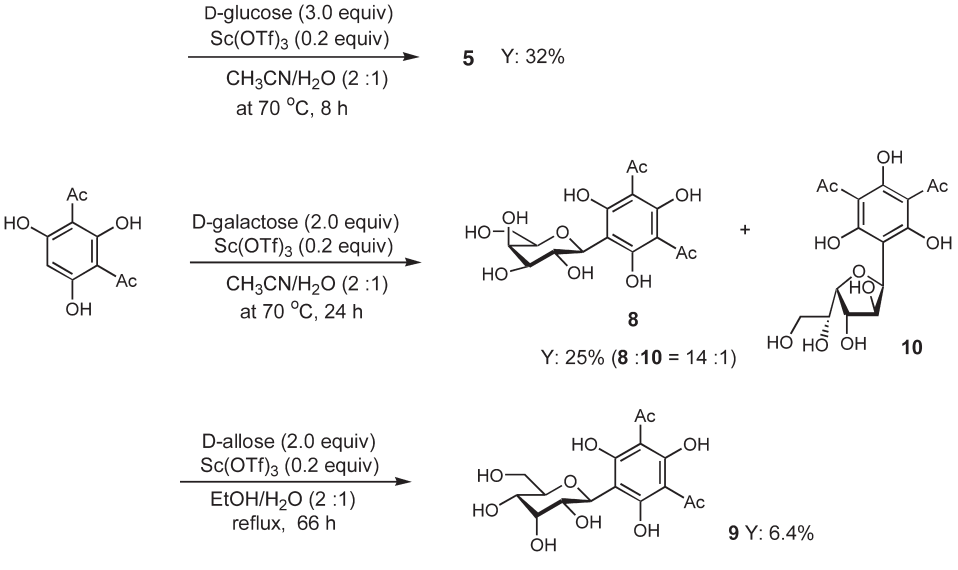



**Scheme 2:** Conversion reaction of diacetylphloroglucinol C-$\beta$-D-glucopyranoside (**5**) in refluxing water.

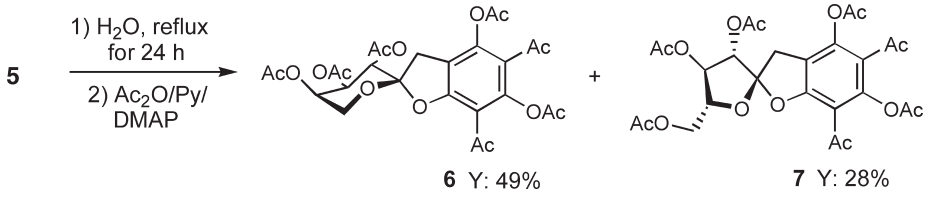


refluxing of **9** also gave furan-type spiro derivatives **13** and **14** in 23% and 15% yield, in addition to pyran-type spiro derivatives **15** and **16** in 19% and 6.4% yield, respectively (Sch. 6, equation (2)).

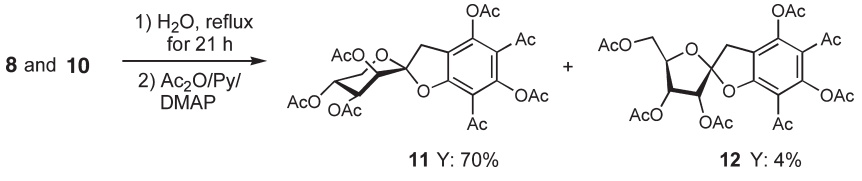
Structures of the spiro derivatives were elucidated by $^{1}H$ and $^{13}C$ NMR spectroscopy. Furthermore, the stereochemistry of the spiro-quaternary carbon was determined by NOESY measurement.[6,7] The characteristic differences in $^{1}H$ NMR spectra between spiropyran- and spirofuran-type compounds (see Table 1) were as follows: (a) a chemical shift of H-5′ in spiropyran was observed at lower field ($\delta$ 5.14–5.47 ppm) and chemical shifts of H-6′ab in spirofuran at lower field (H-6′a: $\delta$ 4.24–4.43 ppm, H-6′b: $\delta$ 4.15–4.29 ppm), and (b) two methylene protons at C-1′ in spiropyran were observed as one singlet peak or as two doublet peaks in close proximity; however, the two methylene protons in spirofuran were observed as two distinct pairs of doublet peaks. Stereochemistry of the spiro-quaternary carbon of each spiropyran- and spirofuran-type compounds



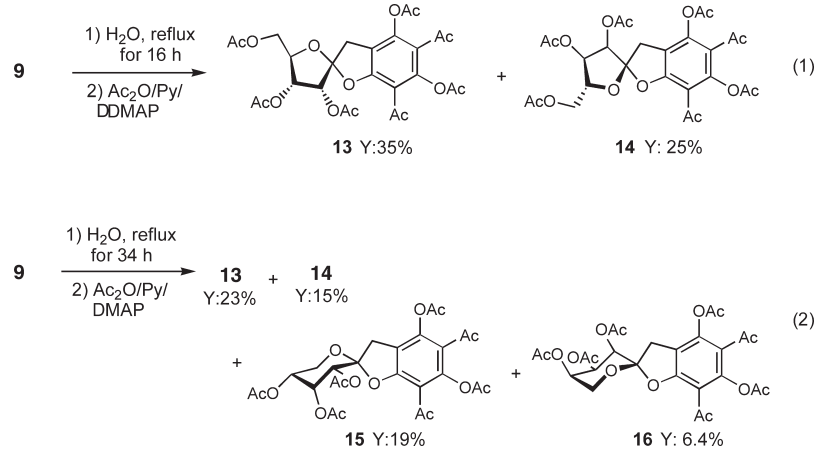

**Scheme 3:** Synthesis of three diacetylphloroglucinol C-$\beta$-D-glycopyranosieds.




**Scheme 4:** Conversion reaction of diacetylphloroglucimol C-$\beta$-D-glucopyranoside (**5**) to spiro-compound.




**Scheme 5:** Conversion reaction of diacetylphloroglucinol C-$\beta$-D-glactopyranosides (**8** and **10**) to spiro-compound.




**Scheme 6:** Conversion reaction of diacetylphloroglucinol C-$\beta$-D-allopyranoside (**9**) to spiro-compound.

(**11**, **12**, **13**, **14**, **15**, and **16**), which were isolated for the first time in the present study, was elucidated by NOESY measurement (Figs. 5, 6, and 7).

The stereochemistry of the quaternary carbon of the spiro(benzofuran-[2*H*]pyran) (**11**) formed from galactosides (**8** and **10**) was determined to be *R* from the NOE correlation between an acetyl-methyl group and H-4′, and an acetyl-methyl group and H-6′b. In addition, the pyran moiety was a $^5C_2$ form of the H-5′ axial from $J_{5'6'b} = 10$ Hz. The stereochemistry of the other

**Table 1:** $^{1}$H NMR data for *O*-acetylated spiro-compounds.

| | Compound no. | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Chemical shifts (ppm)** | **6** | **7** | **11** | **12** | **13** | **14** | **15** | **16** |
| H-1a | 3.14 | 3.38 | 3.05 | 3.39 | 3.31 | 3.33 | 3.08 | 3.16 |
| H-1b | 3.13 | 3.25 | | 3.13 | 3.24 | 3.16 | 3.02 | 3.10 |
| H-3′ | 5.63 | 5.59 | 5.59 | 5.64 | 5.24 | 5.57 | 5.17 | 5.46 |
| H-4′ | 5.30 | 5.44 | 5.41 | 5.75 | 5.35 | 5.53 | 5.75 | 5.44 |
| H-5′ | 5.47 | 4.36 | 5.33 | 4.65 | 4.49 | 4.45 | 5.14 | 5.28 |
| H-6′a | 4.18 | 4.43 | 4.06 | 4.24 | 4.34 | 4.36 | 4.15 | 4.22 |
| H-6′b | 3.92 | 4.21 | 3.76 | 4.21 | 4.29 | 4.15 | 3.80 | 4.01 |
| OAc × 3 | 2.05 | 2.05 | 2.02 | 2.08 | 2.08 | 2.06 | 2.04 | 2.03 |
| | 2.07 | 2.06 | 2.08 | 2.11 | 2.11 | 2.08 | 2.04 | 2.16 |
| | 2.11 | 2.07 | 2.22 | 2.15 | 2.13 | 2.14 | 2.15 | 2.21 |
| ArOAc | 2.26 | 2.26 | 2.27 | 2.27 | 2.27 | 2.18 | 2.26 | 2.27 |
| | 2.27 | 2.27 | 2.28 | 2.29 | 2.29 | 2.24 | 2.29 | 2.28 |
| Ac | 2.42 | 2.42 | 2.42 | 2.42 | 2.43 | 2.28 | 2.42 | 2.42 |
| | 2.62 | 2.61 | 2.63 | 2.54 | 2.63 | 2.40 | 2.74 | 2.58 |
| J value (Hz) | | | | | | | | |
| 1a,b | 17.0 | 17.0 | — | 17.3 | 17.1 | 17.3 | 16.8 | 16.8 |
| 3′,4′ | 10.5 | 7.0 | 3.2 | 4.7 | 6.6 | 4.6 | 3.4 | 3.6 |
| 4′,5′ | 3.5 | 6.0 | 10.4 | 5.5 | 6.6 | 7.2 | 3.2 | 3.6 |
| 5′,6′a | 1.5 | 4.0 | 5.7 | 4.7 | 3.2 | 3.5 | 11.0 | 2.1 |
| 5′,6′b | 2.0 | 7.5 | 10.3 | 7.5 | 4.1 | 6.0 | 5.3 | 2.0 |
| 6′a,b | 13.0 | 12.0 | 11.7 | 11.8 | 12.2 | 12.2 | 11.0 | 13.4 |
| | | | | | | | 3′,6′b 1.1 | 3′,5′ 1.0 |

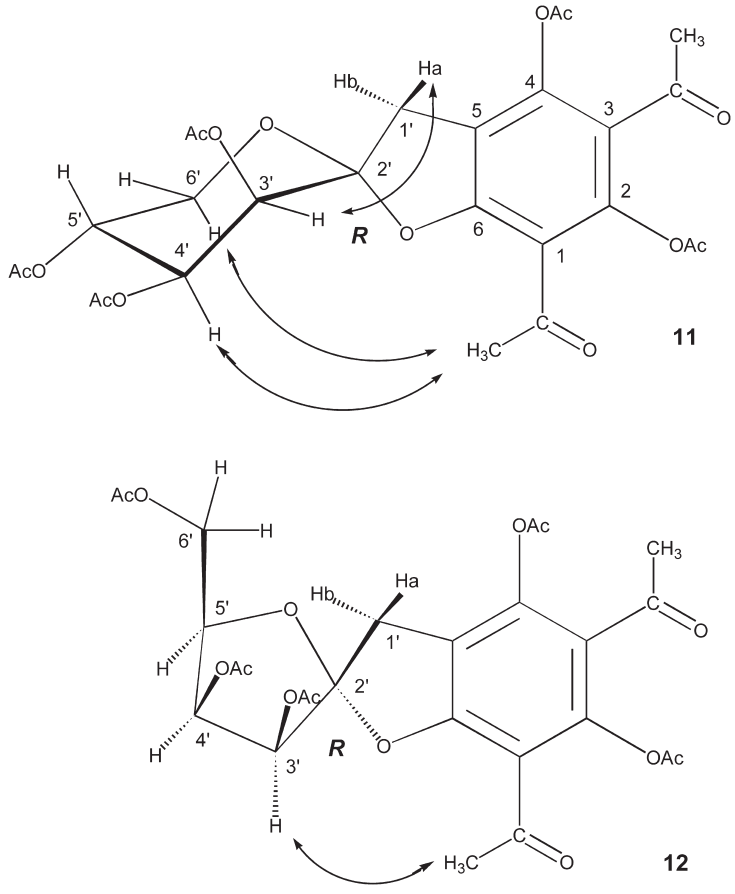



**Figure 5:** The NOESY correlation of spiro-compounds (**10** and **11**) synthesized from galactoside.

spiro(benzofuran-[2*H*]furan) (**12**) was *R* based on the NOE correlation between an acetyl-methyl group and H-3′ (Fig. 5). The stereochemistry of the two spiro (benzofuran-[2*H*]furan) (**13** and **14**) derived from alloside was determined to be *R* and *S*, respectively, from NOE correlations between H-3′ and H-1′ab for **13**, between H-3′ and an acetyl-methyl group, and H-3′ and H-6′ab for **14** (Fig. 6). The stereochemistry of the two spiro(benzofuran-[2*H*]pyran) (**15** and **16**) derived from alloside was determined to be *R* and *S*, respectively, because of NOE correlations between H-3′ and H-1′ab, H-6′a and an acetyl-methyl group for **15**, between an acetyl-methyl group and H-6'a, an acetyl-methyl group and H-4′, H-3′ and H-1′ab for **16**. The pyran moiety conformations for **15** and **16** were assumed to be ${}^5C_2$ and ${}^2C_5$, respectively, for **15**, $J_{5'6'a} = 11$ Hz and there was an NOE correlation between H-6′b and H-5′. For **16**, $J_{5'6'ab} = 2.1$ and 2.0 Hz and there was an NOE correlation between H-6′a and H-4′.

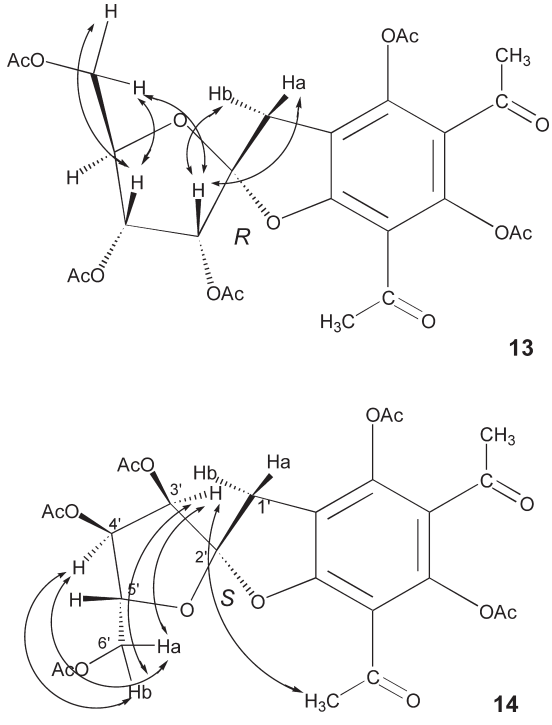



**Figure 6:** The NOESY correlation of spirofuran compounds (**13** and **14**) synyhesized from alloside.

Next, the product ratios were measured at regular time intervals by HPLC. For HPLC analysis, small amounts of hydroxy-free spiro compounds (**6′**, **7′**, **11′**, **12′**, **13′**, **14′**, **15′**, and **16′**) were prepared by each de-*O*-acetylation of acetates [NaOMe and then Dowex ($H^+$) resin treatment]. HPLC analysis of the product ratio at regular time intervals during the 90-h refluxing reaction of **5** in water showed that the production of spiro(benzofuran-[2*H*]furan) (**7′**) was maximal (ratio = 33%) after 8 h and gradually reduced. In contrast, the production of spiro(benzofuran-[2*H*]pyran) (**6′**) gradually increased after 8 h and reached the maximum (ratio = 78%) after 48 h. HPLC analysis of the product ratio for a 90-h reflux reaction in water of a mixture of **8** and **10** showed results similar to those obtained for **5**. The production of spiro(benzofuran-[2*H*]furan) (**12′**) was maximal after 8 h (ratio = 12%). The production of spiro(benzofuran-[2*H*]pyran) (**11′**) reached the maximum after 90 h and the product ratio was 70%. Reactions of both glucoside and galactoside gave either an *R*- or an *S*-diastereomer of spiropyran- and spirofuran-type compounds, respectively. Similarly, HPLC analysis of the product ratio of **9** showed different results from those of **5** and a mixture of **8** and **10** as follows: both spiropyran- and spirofuran-type compounds were composed of a

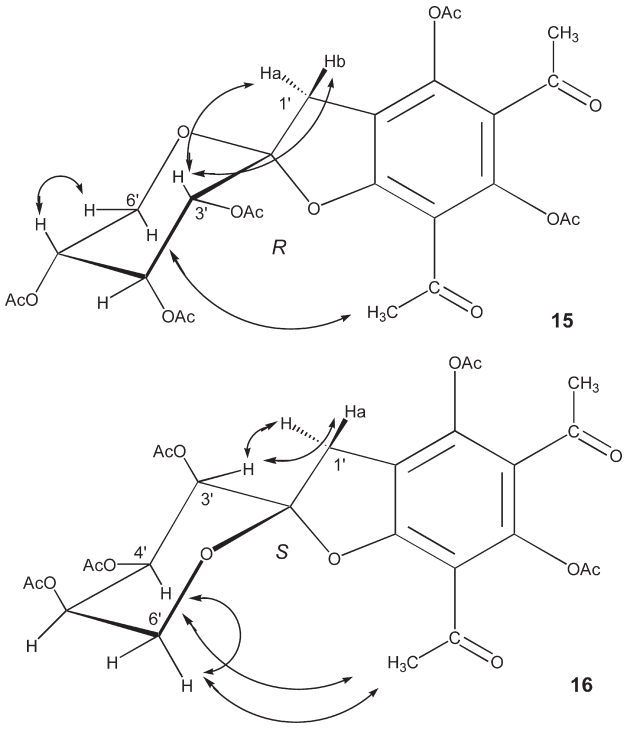



**Figure 7:** The NOESY correlation of spiropyran compounds (**15** and **16**) synthesized from alloside.

mixture of *R*- and *S*-diastereomers. Productions of the spirofuran-type compounds **13**′ and **14**′ were maximal after 12 h (production ratios = 38% and 30% for **13**′ and **14**′, respectively). Productions of the spiropyran-type compounds **15**′ and **16**′ reached maximum values after 48 h (production ratios = 27% and 11%, for **15**′ and **16**′, respectively) (Figures 8, 9, and 10).

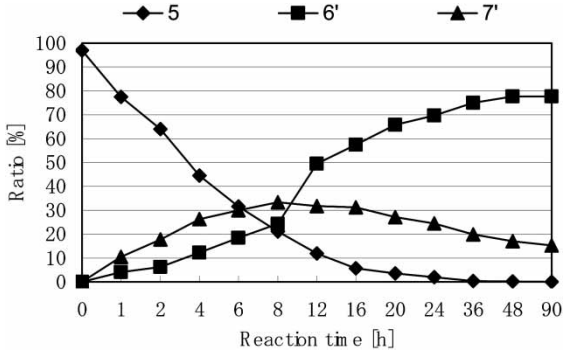



**Figure 8:** Conversion ratio at time intervals on the reflux reaction of diacetylphloroglucinol *C*-β-D-glucopyranoside (**5**) in water.

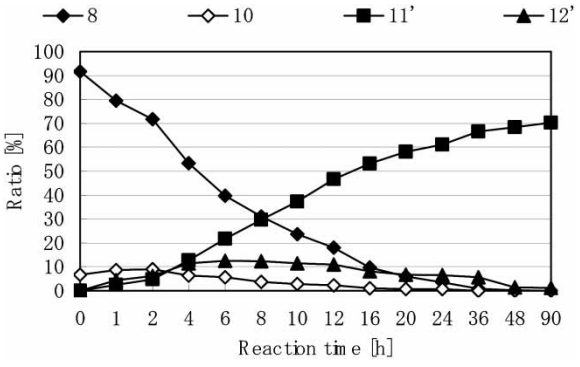



**Figure 9:** Conversion ratio at time intervals on the reflux reaction of diacetylphloroglucinol *C*-β-D-galactopyranosides (**8** and **10**) in water.

A possible mechanism for ketalization of the phloroglucinol *C*-glycopyranosides is as follows (Sch. 7): (i) phloroglucinol *C*-β-glycopyranoside causes the pinacol-typed 1,2-hydride shift via a quinone methide form to afford a ring-opened ketose, (ii) an *ortho*-hydroxyl group of the phloroglucinol moiety attacks the ketose to afford a benzodihydrofuran, and (iii) dehydration from the benzodihydrofuran resulting from subsequent attacking of a 6-hydroxyl (a) or a 5-hydroxyl (b) group produces a spiropyran or a spirofuran derivative. This reaction was catalyzed by Brönsted acid such as a *p*-TsOH or Lewis acid such as a scandium(III) trifluoromethanesulfonate [$Sc(OTf)_3$]; however, in that case it yielded many products. Use of alcohol or dioxane in place of water as a solvent yielded also many products. Just a simple reaction, 8- to 10-h refluxing in water of diacetylphloroglucinol *C*-glycoside produced mainly the corresponding spirofuran derivatives, and over 2-d refluxing mainly the corresponding spiropyran derivatives. On the other hand, the

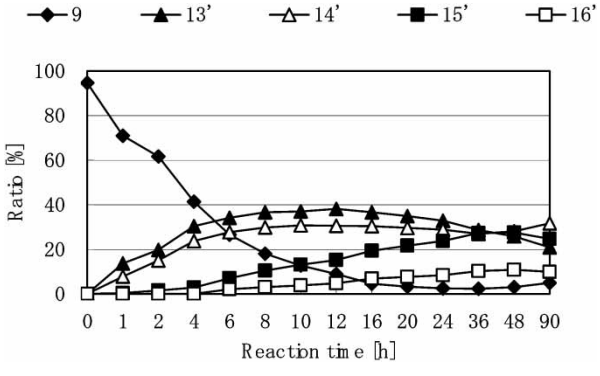
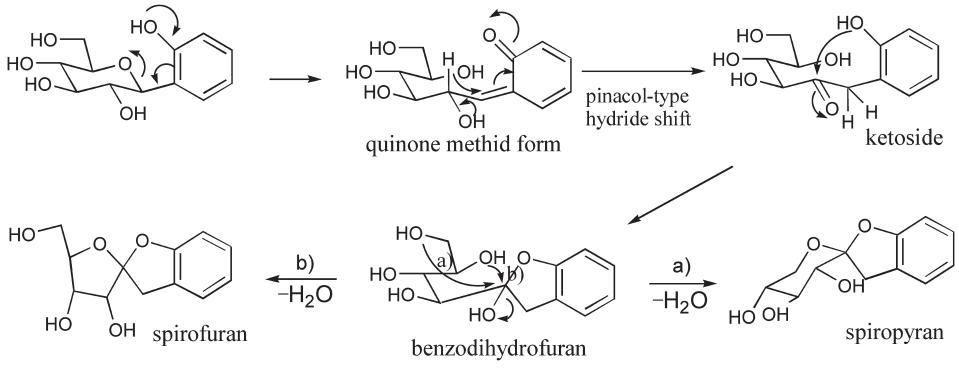



**Figure 10:** Conversion ratio at time intervals on the reflux reaction of diacetylphloroglucinol *C*-β-D-allopyranoside (**9**) in water.




**Scheme 7:** Possible mechanism for the spiroketalization of polyphenol *C*-glycoside.

conversion reaction of mono-acetylphloroglucinol *C*-glycopyranoside produced only the spiropyran derivative in the yield of 30% or 35% (Sch. 1).[6]

## CONCLUSION

A conversion reaction of three diacetylphloroglucinol *C*-*β*-D-glycopyranosides by refluxing in water was carried out and the conversion ratios of the resulting spiro derivatives were determined by HPLC analysis at regular time intervals. In each reaction, the production of spirofuran-type compound reached to maximal after 8 to 10 h, while that of spiropyran-type compound took over 2 d. The results of this study demonstrate that spirofuran is a kinetic-controlled product and spiropyran is a thermodynamic-controlled product. It was found that two kinds of spiro compounds can be selectively prepared by refluxing time. It was assumed that the formation of two kinds of spiro compounds is caused by internal ketalization via pinacol-type rearrangement of a hydride ion. However, it is obscure that the conversion reaction of galactosides **8** and **10** or alloside **9** formed preferentially *R*-spiropyran and *R*-spirofuran but that of glucoside **5** only *S*-diastereomers.[5c] Naturally occurring products, pinnatifinosides A and B are *R*-spirofuran compounds derived from glucoside, and pinnatifinosides C and D are *S*- and *R*-spirofuran compounds derived from alloside. We here had *S*-spirofuran (**7**) derived from glucoside and *R*- and *S*-spirofurans (**13** and **14**) derived from alloside in hand. Further studies will attempt the total synthesis of pinnatifinosides A to D based on the results of the present study.

## EXPERIMENT

Water used in this study was purified by distillation of deionized water using a Yamato Auto Still model WO-41 instrument. Reactions were monitored by TLC

on 0.25-mm silica gel F254 plates (E. Merck) using UV light, and either a 5% ethanolic solution of ferric chloride or a 7% ethanolic solution of phosphomolybdic acid with heat to visualize the bands. For separation and purification, flash column chromatography was performed on silica gel (230–400 meshes, Fuji-Silysia Co. Ltd., BW-300). Melting points were determined on an AS ONE ATM-01 melting point apparatus and were not corrected. Optical rotations were recorded on a JASCO DIP-370 polarimeter. IR spectra were recorded on a Horiba FT-720 IR spectrometer in the form of KBr disks. NMR spectra were recorded on a Varian Inova 500 spectrometer using $Me_4Si$ as the internal standard. Mass spectral data were obtained by fast-atom bombardment (FAB) using glycerol or *m*-nitrobenzylalcohol (NBA) as the matrix on a JEOL JMS-AX505HA instrument. Elemental analyses were performed on a Perkin-Elmer PE 2400 II instrument. HPLC was performed on a Hitachi L-7100 and L-4200H system using the following conditions: column: GL Sciences Inc., Inertsil ODS-3 column (4.6 × 250 mm); solvent: MeOH-$H_2O$-AcOH = 60:38:2; flow rate: 1 mL/min; wavelength: UV254 nm.

## Diacetylphloroglucinol *C*-β-D-galactopyranoside and -furanoside (8 and 10)

A solution of diacetylphloroglucinol (500 mg, 2.38 mmol), D-galactose (857 mg, 4.76 mmol), and $Sc(OTf)_3$ (234 mg, 0.476 mmol) in $CH_3CN$-$H_2O$ (2:1 10 mL) was stirred at 70°C in an oil bath for 1 d. After the reaction mixture was evaporated to remove $CH_3CN$, 100 mL of water was added and the resulting solution was absorbed to a Diaion-CHP20P gel (50 mL) column, washed with 200 mL of water, and eluted with acetone-water (200 mL 1:1) and acetone-MeOH (200 mL 1:1). The eluate was evaporated to dryness. The residue including the desired products and unreacted diacetylphloroglucinol was separated by silica gel column chromatography (10:1 $CHCl_3$-MeOH) to give a mixture of **8** and **10** (255 mg, 28.8%, **8**:**10** = 14:1). Pure **10** was afforded by recrystallization from MeOH, and the filtrate was separated by silica gel column chromatography with toluene-AcOEt-AcOH (5:2:0.2) and recrystallized from EtOH to give pure **8**.

Data for **8**—Colorless prism. mp 137–138°C (EtOH). $[\alpha]_D^{21}$ +104 (*c* 0.98, MeOH). IR (KBr) $\nu$ 3396, 2931, 1620, 1427, 1365, and 1288 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$) $\delta$ 2.63 (3H, s, $CH_3$), 3.76 (1H, t, *J* 9.4 Hz, H-2′), 4.74 (1H, d, *J* 9.6 Hz, H-1′), 16.3 (1H, br.s, OH). $^{13}C$ NMR (DMSO-$d_6$) $\delta$ (galactose moiety) 60.6 (C-6′), 68.3, 69.7, 73.9, 74.0, 79.4, (diaetylphloroglucinol moiety) 32.7 ($COCH_3$ × 2), 103.4 (C-3,5), 104.1 (C-1), 166.7 (C-2,6), 170.2 (C-4), 204.6 ($COCH_3$ × 2). FAB-MS (glycerol, *m*/*z*) 373 $(M+H)^+$. Anal. Calcd for $C_{16}H_{20}O_{10}$: C, 51.61; H, 5.41. Found: C, 51.59; H, 5.45.

Data for **10**—Colorless prism. mp 166°C (MeOH). $[\alpha]_D^{21}$ − 132 (*c* 0.98, MeOH). IR (KBr) $\nu$ 3429, 2935, 1624, 1431, 1300, and 1066 $cm^{-1}$. $^1H$ NMR

(DMSO-$d_6$, at 80°C) $\delta$ 2.63 (3H, s, $COCH_3$), 3.90 (1H, t, $J$ 3.3 Hz, OH), 4.01 (1H, d, $J$ 3.2 Hz, OH), 4.07 (1H, d, $J$ 1.7 Hz, OH), 5.35 (1H, $J$ 3.2 Hz, H-1′), 16.1 (1H, br.s, OH). $^{13}$C NMR (DMSO-$d_6$) $\delta$ (galactose moiety) 62.8 (C-6′), 70.3, 77.4, 78.3, 80.0, 85.8, (diacetylphloroglucinol moiety) 32.6 and 32.7 ($COCH_3 \times 2$), 98.9 (C-3,5), 103.1 (C-1), 167.3 (C-2,6), 170.1 (C-4), 203.9 ($COCH_3 \times 2$). FAB-MS (glycerol, $m/z$) 373 $(M + H)^+$. Anal. Calcd for $C_{16}H_{20}O_{10}$: C, 51.61; H, 5.41. Found: C, 51.44; H, 5.33.

## Diacetylphloroglucinol *C*-β-D-allopyranoside (9)

A solution of diacetylphloroglucinol (500 mg, 2.38 mmol), D-galactose (857 mg, 4.76 mmol) and $Sc(OTf)_3$ (245 mg, 0.498 mmol) in $CH_3CN$-$H_2O$ (2:1 10 mL) was refluxed with stirring in an oil bath for 66 h. The reaction mixture was separated and purified in the same manner as the described above for the galactosides (**8** and **10**) to give **9** (55.4 mg, 6.25%) as colorless prisms.

Colorless prism. mp 166–167°C (EtOH). $[\alpha]_D^{21}$ +49.1 ($c$ 0.293, MeOH). IR (KBr) $\nu$ 3496, 3407, 3103, 2929, 1606, 1371, and 1278 $cm^{-1}$. $^1$H NMR $\delta$ 2.65 (3H, s, $CH_3$), 5.16 (1H, d, $J$ 10.0 Hz, H-1′), 12.9 (1H, br.s, OH), 16.3 (1H, br.s, OH). $^{13}$C NMR (DMSO-$d_6$) $\delta$ (allose moiety) 59.3 (C-6′), 65.9, 69.6, 70.0, 71.1, 76.2, (diacetylphloroglucinol moiety) 32.7 ($COCH_3 \times 2$), 102.9 (C-3,5), 103.5 (C-1), 167.2 (C-2,6), 170.1 (C-4), 204.0 ($COCH_3 \times 2$). FAB–MS (glycerol, $m/z$) 373 $(M + H)^+$. Anal. Calcd for $C_{16}H_{20}O_{10}$: C, 51.61; H, 5.41. Found: C, 50.39; H, 5.55.

## Conversion Reaction of Glycoside to Spiro Derivatives

A mixture of **8** and **10** (14:1, 100 mg) was dissolved in 100 mL of water and the resulting solution was refluxed for 1 d. The reaction mixture was evaporated to dryness. The residue was dissolved in pyridine (2 mL) and $Ac_2O$ (4 mL), and DMAP (5 mg) was added to the mixture. After stirring at rt for 1 d, the reaction mixture was poured into ice-cold water (50 mL) and extracted with AcOEt three times. The organic layers were combined, washed with water and saturated NaCl solution, dried with anhydrous $Na_2SO_4$, and then evaporated to dryness. The residue was separated and purified by silica gel column chromatography (3:1–1:1 hexane-AcOEt) to give **11** and **12**. Conversion reaction of glucoside **5** and alloside **9** and succeeding workups were carried out in the same manner as the described above for the galactosides, respectively.

*(2R,3′S,4′S,5′R)-3′4,4′,5′,6-Pentakis-acetoxy-5,7-diacetyl-3′,4′,5′,6′-tetrahydrospiro[benzofuran-2(3H),2′-[2H]pyran] (**11**)*

Colorless prism. mp 201°C (MeOH). $[\alpha]_D^{21}$ +66.7 ($c$ 1.025, $CHCl_3$). IR (KBr) $\nu$ 2993, 2941, 1778, 1751, 1697, 1622, 1431, and 1371 $cm^{-1}$. $^{13}$C NMR ($CDCl_3$) $\delta$

20.6, 20.7, 20.7, 20.8, 20.9, and 167.1, 168.9, 169.7, 169.7, 170.0 (OAc × 5), 36.7 (C-1′), 62.0 (C-6′), 65.3, 69.1, 70.0, 111.5 (C-2′), (aromatic moiety) 114.9, 117.5, 123.6, 145.9, 146.9, 158.0, 31.3 and 32.0 ($ArCOCH_3$ × 2), 195.1 and 197.2 ($ArCOCH_3$ × 2). FAB-MS (NBA, $m/z$) 565 $(M+H)^+$. Anal. Calcd for $C_{26}H_{28}O_{14}$: C, 55.32; H, 5.00. Found: C, 55.44; H, 5.05.

*(2R,3′S,4′S,5′R)-3′,4,4′,6,6′-Pentakis-acetoxy-5,7-diacetyl-5′-acetoxymethylspiro[benzofuran-2(3H),2′-(2H)furan] (**12**)*

Colorless amorphous solid. $[\alpha]_D^{21}$ +76.0 ($c$ 0.995, $CHCl_3$). IR (KBr) $\nu$ 3004, 2941, 1772, 1750, 1697, 1618, 1431, and 1373 $cm^{-1}$. $^{13}C$ NMR ($CDCl_3$) $\delta$ 20.3, 20.4, 20.7, 20.8, 21.0, and 167.3, 168.9, 168.9, 169.3, 170.5 (OAc × 5), 33.6 (C-1′), 62.3 (C-6′), 70.9, 74.8, 76.5, 114.4 (C-2′), (aromatic moiety) 117.6, 118.5, 123.0, 145.7, 146.8, 158.0, 31.4 and 31.9 ($ArCOCH_3$ × 2), 195.5 and 197.3 ($ArCOCH_3$ × 2). FAB–MS (NBA, $m/z$) 565 $(M+H)^+$. Anal. Calcd for $C_{26}H_{28}O_{14}$: C, 55.32; H, 5.00. Found: C, 55.30; H, 5.29.

*(2R,3′R,4′R,5′R)-3,4,4′,6,6′-Pentakis-acetoxy-5,7-diacetyl-5′-acetoxymethylspiro[benzofuran-2(3H),2′-(2H)furan] (**13**)*

Colorless amorphous solid. $[\alpha]_D^{21}$ −54.6 ($c$ 1.065, $CHCl_3$). IR (KBr) $\nu$ 3004, 2941, 1776, 1751, 1697, 1622, 1431, and 1373 $cm^{-1}$. $^{13}C$ NMR ($CDCl_3$) $\delta$ 34.1 (C-1′), 63.3 (C-6′), 69.7, 72.3, 82.4, 113.8 (C-2′), 20.4, 20.6, 20.7, 20.8, 21.0, 167.2, 169.0, 169.7, 17.0, 170.3 (OAc × 5), (aromatic moiety) 31.4 and 31.7, 195.3 and 197.4 ($ArCOCH_3$ × 2), 116.3, 117.5, 122.9, 145.8, 147.0, 159.2. FAB-MS (NBA, $m/z$) 565 $(M+H)^+$. Anal. Calcd for $C_{26}H_{28}O_{14}$: C, 55.32; H, 5.00. Found: C, 55.27; H, 5.14.

*(2S,3′R,4′R,5′R)-3,4,4′,6,6′-Pentakis-acetoxy-5,7-diacetyl-5′-acetoxymethylspiro[benzofuran-2(3H),2′-(2H)furan] (**14**)*

Colorless amorphous solid. $[\alpha]_D^{21}$ +84.6 ($c$ 0.475, $CHCl_3$). IR (KBr) $\nu$ 2941, 1775, 1749, 1697, 1621, 1436, and 1371 $cm^{-1}$. $^{13}C$ NMR ($CDCl_3$) $\delta$ 33.5 (C-1′), 63.7 (C-6′), 71.1, 74.5, 79.3, 114.4 (C-2′), 20.4, 20.5, 20.7, 20.7, 21.0, 167.2, 168.9, 169.1, 169.4, 170.4 (OAc × 5), (aromatic moiety) 31.4 and 32.0, 195.3 and 197.3 ($ArCOCH_3$ × 2), 117.3, 119.0, 123.1, 145.7, 146.9, 157.8. FAB-MS (NBA, $m/z$) 565 $(M+H)^+$. Anal. Calcd for $C_{26}H_{28}O_{14}$: C, 55.32; H, 5.00. Found: C, 55.27; H, 5.07.

*(2R,3′R,4′R,5′R)-3,4,4′,5′,6-Pentakis-acetoxy-5,7-diacetyl[benzofuran-2(3H),2′-(2H)pyran] (**15**)*

Colorless amorphous solid. $[\alpha]_D^{21}$ +110 ($c$ 1.045, $CHCl_3$). IR (KBr) $\nu$ 2981, 2956, 1778, 1758, 1691, 1618, 1434, and 1371 $cm^{-1}$. $^{13}C$ NMR ($CDCl_3$) $\delta$ 36.7 (C-1′), 58.7 (C-6′), 67.0, 67.8, 65.1, 110.0 (C-2′), 20.5 (×2), 20.6, 20.8, 20.9, 167.1, 169.0, 169.3, 169.7, 170.1 (OAc × 5), (aromatic moiety) 31.3 and 31.9, 195.3 and 197.3 ($ArCOCH_3$ × 2), 114.3, 117.5, 123.4, 145.9, 146.9, 159.5.

FAB-MS (NBA, *m/z*) 565 $(M + H)^+$. Anal. Calcd for $C_{26}H_{28}O_{14}$: C, 55.32; H, 5.00. Found: C, 55.23; H, 4.80.

*(2S,3′R,4′R,5′R)-3,4,4′,5′,6-Pentakis-acetoxy-5,7-diacetyl[benzofuran-2(3H), 2′-(2H)pyran] (**16**)*

Colorless prism (from EtOAc). mp 143°C. $[\alpha]_D^{21}$ −92.5 (*c* 0.990, $CHCl_3$). IR (KBr) $\nu$ 3020, 2940, 1774, 1751, 1697, 1617, 1430, and 1373 $cm^{-1}$. $^{13}C$ NMR ($CDCl_3$) $\delta$ 36.9 (C-1′), 63.9 (C-6′), 65.5, 65.7, 68.2, 112.1 (C-2′), 20.6, 20.7 (×2), 20.9 (×2), 167.2, 168.9, 169.4, 169.7, 170.1 (OAc × 5), (aromatic moiety) 31.3 and 31.9, 195.0 and 197.3 ($ArCOCH_3$ ×2), 115.0, 117.7, 123.5, 145.9, 146.8, 158.1. FAB-MS (NBA, *m/z*) 565 $(M + H)^+$. Anal. Calcd for $C_{26}H_{28}O_{14}$: C, 55.32; H, 5.00. Found: C, 55.14; H, 4.80.

## HPLC Analysis

Each sample for HPLC analysis was prepared by de-*O*-acetylation in the scale of several milligrams. Retention time (min) of each sample shows as follows: (glucosides) **5**: 7.03, **6′**: 7.72, **7′**: 11.42. (galactosides) **8**: 7.42, **10**: 10.88, **11′**: 14.91, **12′**: 13.00. (allosides) **9**: 7.96, **13′**: 11.72, **14′**: 10.20, **15′**: 17.19, **16′**: 16.44.

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