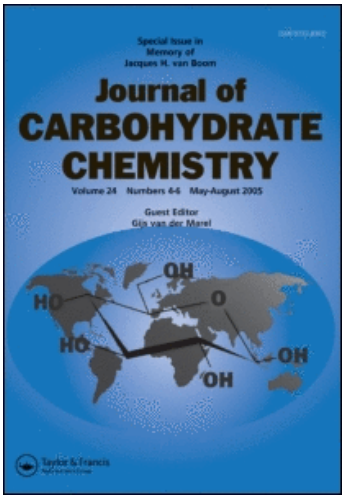

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Lin Yan[a]; Feng-Wu Liu[a]; Jian-Li Yang[a]; Hong-Min Liu[a]
[a] New Drug Research & Development Center, Zhengzhou University, Zhengzhou, P. R. China

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Synthesis of Novel Caged Intramolecular Ketals of β-*C*-Glycopyranosidic Ketones

Lin Yan, Feng-Wu Liu, Jian-Li Yang, and Hong-Min Liu

New Drug Research & Development Center, Zhengzhou University, Zhengzhou, P. R. China

Novel caged intramolecular ketals of β-*C*-glycosidic ketones were prepared from pyranoses. The structures of the new compounds were elucidated by NMR and HRMS spectral analysis. Preliminary studies revealed that the intramolecular ketal could be used to protect 3- and 6-hydroxyl groups of β-*C*-glycosidic ketones.

Keywords Caged molecule, β-*C*-Glycosidic ketone, Intramolecular ketal, Protecting group

INTRODUCTION

The ketal group is one of the most widely used carbohydrate protecting groups[1,2] commonly employed for the protection of vicinal hydroxyl groups. However, there is no case of protecting 3- and 6-hydroxyl groups on a sugar molecule by a ketal group as reported herein for the preparation of novel caged intramolecular ketals from β-*C*-glycosidic ketones through an intramolecular ketal reaction. The utility of these new caged compounds is similar to those of *myo*-inositol orthoesters, which are a class of important intermediates for the synthesis of phosphoinositols[3] and other molecules with interesting properties.[4] Gathering a number of specific properties such as caged structure, chirality, rigidity, and relative stability in one polycyclic system, these new *C*-glycoside derivatives may be useful intermediates for synthesis of a variety of 2- and 4-substituted pyranose derivatives.

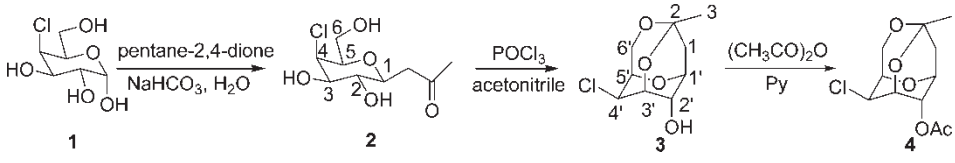
Address correspondence to Hong-Min Liu, New Drug Research & Development Center, Zhengzhou University, Zhengzhou 450052, P. R. China. E-mail: liuhm@zzu.edu.cn

The development of synthetic methodology for *C*-glycosides is largely stimulated by their occurrence as building blocks in a variety of biologically important natural products[5] and by the fact that they may serve as promising biological tools and potential therapeutics.[6] A number of recent reviews have been devoted to this subject.[7] Control of anomeric stereochemistry in the course of glycosylation is a key consideration in the synthesis of *C*-glycoside. Recently, Lubineau and coworkers reported a convenient, one-pot synthesis of β-*C*-glycosidic ketones in aqueous media.[8] Following this attractive method, we attempted to convert other free sugars to β-*C*-glycoside and further to prepare more elaborate *C*-glycoside derivatives.

RESULTS AND DISCUSSION

In our previous papers, we reported the preparation of 1′,4′:3′,6′-dianhydro-4-chloro-4-deoxy-galacto-sucrose by using sucralose as the starting material[9] and further hydrolysis to afford 4-chloro-4-deoxy-α-D-galactopyranose (**1**).[10] Condensation of the new unnatural sugar **1** with pentane-2,4-dione in aqueous alkaline solution by following the procedures in the literature[8] gave 1-(4-chloro-4-deoxy-β-D-galactopyranosyl)-propan-2-one (**2**) in an almost quantitative yield (Sch. 1). The structure of ketone **2** was confirmed by spectral analysis. The large coupling constants between H-1 and H-2 ($J_{1,2} =$ 9.3 Hz) revealed a β-configuration.

When compound **2** was treated with sulfuric acid in refluxing THF for several hours, a small amount of intramolecular ketal **3** was obtained and more than half the amount of **2** was left unchanged. The product **3** was separated from **2** by column chromatography on silica gel. The disappearance of the signal of the carbonyl group at δ 212.5 and the appearance of a signal at δ 99.8 in the ^{13}C NMR spectrum of **3** indicated the formation of a new ketal carbon. At the same time, the ^{1}H signal of the methyl group shifted from δ 2.19 in **2** to δ 1.53 in **3**. Two-dimensional NMR analysis (COSY, HSQC, and HMBC) confirmed the structure showing correlations of H-1′ (δ 4.01), H-3′ (δ 4.13), and H-6′ (δ 4.07, 4.27) to C-2 (δ 99.8) (Fig. 1). Acetylation of **3** with acetic anhydride in pyridine generated product **4**. Both ^{1}H and ^{13}C NMR spectral data indicated that **4** had only one acetyl group.



Scheme 1

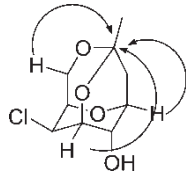


Figure 1: HMBC correlations for compound **3**.

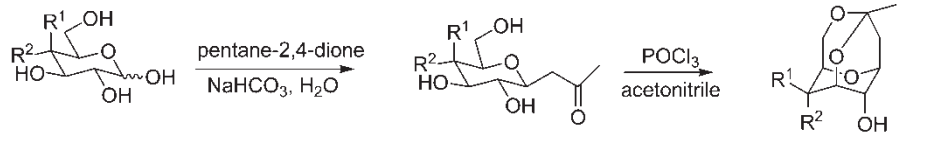
As the preliminary yield of the ketal was disappointing, we attempted optimization of the reaction conditions. Pleasantly, we found that employment of acetonitrile as a solvent and phosphoryl trichloride as an acid catalyst in the reaction not only afforded the product in reasonable yield (82%), but also made purification easier.

When glucose (**5**) and galactose (**6**) were used as starting materials, the corresponding β-*C*-glycosidic ketones **7** and **8** were generated. Subsequent treatment of the ketones with acid afforded intramolecular ketal compounds **9** and **10** (Sch. 2).

The formation of intramolecular ketals caused conversion of the conformation of the pyranose rings from $^4C_1$ to $^1C_4$ in the structure and upfield shifts of ^{13}C signals to different degrees for most of the carbons compared to that of the corresponding β-*C*-glycosidic ketones. In all conversions C-6′ signals shifted downfield by 3.6 to 8.3 ppm.

The newly formed compounds consist of four rings including two seven-membered and two six-membered rings, which gives a rigid and stable caged structure and forms a cavity in the molecule. The newly formed stereogenic center (C-2) has a fixed *S*-configuration. To the best of our knowledge, this novel structure has never been reported so far.

We performed the conversion of 4′-chloro-4′-deoxy-β-D-galactopyranosyl-propan-2-one-3′,6′-ketal (**3**) to the corresponding *O*-tosyl derivative **11**, an important precursor to introduce various substituents. Treatment of ketal **11** with aqueous trifluoroacetic acid at rt overnight furnished *C*-glycosidic ketone derivative **12** in 94% (Sch. 3).

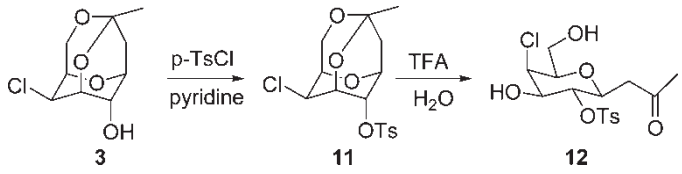


5: R^1 = H, R^2 = OH
6: R^1 = OH, R^2 = H

7: R^1 = H, R^2 = OH
8: R^1 = OH, R^2 = H

9: R^1 = H, R^2 = OH
10: R^1 = OH, R^2 = H

Scheme 2



Scheme 3

In summary, we have found that *β-C*-glycosidic ketones readily prepared from reducing sugars undergo acid-catalyzed intramolecular ketal formation leading to new caged ketal derivatives. Based on the intramolecular ketal reactions, a new method for protection of nonvicinal hydroxyls of sugar was developed, which broadened the methodology for derivation of carbohydrate compounds. The application of these caged compounds to synthesize a variety of 2- and 4-substituted carbohydrate analogs is under way.

EXPERIMENTAL

General Methods

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE DPX-400 spectrometer with tetramethylsilane as internal standard and using D_2O or $CDCl_3$ as solvent. Chemical shifts (δ) were expressed in ppm downfield from internal TMS. IR spectra were recorded on a Nicolet IR 200 spectrophotometer. Elemental analyses were carried out on a MOD 1106 analyzer. HRMS (high-resolution mass spectra) were taken with a Q-Tof Micromass spectrometer. Thin-layer chromatography (TLC) was performed on glass plates precoated with silica gel (5 to 40 μm) to monitor the reactions and certify the purity of the reaction products. Visualization was accomplished by spraying the chromatograms with 10% ethanolic sulfuric acid and charring them on a hot plate. Column chromatography was carried out on silica gel (200 to 300 mesh).

1-(4-Chloro-4-deoxy-β-D-galactopyranosyl) -propan-2-one (2)

To a solution of 4-chloro-4-deoxy-*α*-D-galactose (**1**, 198 mg, 1 mmol) in water (4 mL) were added sodium bicarbonate (126 mg, 1.5 mmol) and pentane-2,4-dione (120 mg, 1.2 mmol). After stirring at 90°C for about 8 h, followed by concentration to dryness under diminished pressure and fractionation by chromatography with 8:1 $CHCl_3$-MeOH, **2** was afforded as a syrup (223 mg, 94%): IR (KBr): 3393, 2912, 1708, 1362, 1084 cm^{-1}; ^{1}H NMR (D_2O, 400 MHz): δ 4.41 (dd, 1H, $J_{4,5} = 0.6$ Hz, $J_{4,3} = 3.8$ Hz, H-4), 3.86 (m, 1H, H-5), 3.84 (m, 1H, H-3), 3.73 (dt, 1H, $J_{1,1'a} = 3.1$ Hz, $J_{1,1'b}$, $J_{1,2} = 9.3$ Hz,

H-1), 3.66 (dd, 1H, $J_{6a,5} = 7.0$ Hz, $J_{6a,6b} = 11.7$ Hz, H-6a), 3.59 (dd, 1H, $J_{6b,5} = 5.4$ Hz, $J_{6b,6a} = 11.7$ Hz, H-6b), 3.49 (t, 1H, $J = 9.3$ Hz, H-2), 2.96 (dd, 1H, $J_{1'a,1} = 3.1$ Hz, $J_{1'a,1'b} = 16.8$ Hz, H-1′a), 2.70 (dd, 1H, $J_{1'b,1} = 9.3$ Hz, $J_{1'b,1'a} = 16.8$ Hz, H-1′b), 2.19 (s, 3H, H-3′); ^{13}C NMR (D_2O, 100 MHz): δ 212.5 (C-2′), 77.3 (C-5), 76.1 (C-1), 72.5 (C-3), 69.7 (C-2), 62.3 (C-4), 61.0 (C-6), 45.2 (C-1′), 29.6 (C-3′); HRMS (ESI): Calcd. for $C_9H_{15}ClO_5$: 238.0608. Found: 261.0506 $[M + Na]^+$. Anal. Calcd. for $C_9H_{15}ClO_5$: C, 45.29; H, 6.33. Found: C, 45.31; H, 6.36.

4′-Chloro-4′-deoxy-β-D-galactopyranosyl-propan-2-one-3′,6′-ketal (3)

To a solution of 1-(4-chloro-4-deoxy-β-D-galactosyl)-propan-**2**-one (**2**, 238 mg, 1 mmol) in dry acetonitrile (10 mL) was added a catalytic amount of phosphoryl trichloride. The mixture was stirred at 60°C while the progress of the reaction was monitored by TLC with 12:1 $CHCl_3$-MeOH; after about 6 h, the starting material was no longer detectable, and the acid present was then removed by stirring for 30 min with anhydrous sodium carbonate. The solution was filtered and concentrated. The residue was dissolved in EtOAc, and the solution was washed with satd aq $NaHCO_3$ (5 mL × 2) and water (5 mL × 3), dried over anhydrous Na_2SO_4, and concentrated, affording **3** (180 mg, 82%) as an oil: IR (KBr): 3504, 2938, 1184, 1057 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.75 (dd, 1H, $J_{4',5'} = 2.8$ Hz, $J_{4',3'} = 6.8$ Hz, H-4′), 4.33 (m, 1H, H-5′), 4.27 (dd, 1H, $J_{6a',5'} = 4.4$ Hz, $J_{6a',6b'} = 13.6$ Hz, H-6′a), 4.13 (m, 1H, H-3′), 4.07 (d, 1H, $J_{6b',6a'} = 13.6$ Hz, H-6′b), 4.01 (m, 1H, H-1′), 3.92 (m, 1H, H-2′), 2.43 (dd, 1H, $J_{1a,1'} = 3.2$ Hz, $J_{1a,1b} = 15.6$ Hz, H-1a), 2.19 (dd, 1H, $J_{1b,1'} = 3.2$ Hz, $J_{1b,1a} = 15.6$ Hz, H-1b), 1.53 (s, 3H, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 99.8 (C-2), 76.1 (C-5′), 72.3 (C-3′), 69.2 (C-6′), 68.7 (C-1′), 68.4 (C-2′), 54.8 (C-4′), 39.1 (C-1), 29.5 (C-3); HRMS (ESI): Calcd. for $C_9H_{13}ClO_4$: 220.0502. Found: 243.0405 $[M + Na]^+$. Anal. Calcd. for $C_9H_{13}ClO_4$: C, 48.99; H, 5.94. Found C, 49.01; H, 5.93.

2′-Acetyl-4′-chloro-4′-deoxy-β-D-galactosyl-propan-2-one-3′,6′-ketal (4)

Compound **3** (150 mg, 0.68 mmol) was mixed with pyridine (1 mL), Ac_2O (0.5 mL), and a catalytic amount of DMAP. The mixture was stirred at ambient temperature and monitored by TLC. After the disappearance of starting sugar, absolute EtOH (2 mL) was added. The mixture was continued to stir for 20 min, then partitioned by EtOAc and H_2O. The EtOAc layer was washed with water (5 mL × 2), dried over anhydrous Na_2SO_4, and evaporated, affording compound **4** as an oil (167 mg, 94%): IR (KBr): 2939, 1744, 1367, 1213, 1187, 1056 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.92 (dd, 1H, $J_{2',1'} = 2.0$ Hz, $J_{2',3'} = 4.4$ Hz, H-2′), 4.63 (dd, 1H, $J_{4',5'} = 2.8$ Hz, $J_{4',3'} = 6.4$ Hz, H-4′), 4.34

(m, 1H, H-5′), 4.30 (dd, 1H, $J_{6'a,5'} = 4.4$ Hz, $J_{6'a,6'b} = 13.2$ Hz, H-6′a), 4.16 (m, 1H, H-3′), 4.14 (dd, 1H, $J_{1',2'} = 2.0$ Hz, $J_{1',1a} = J_{1',1b} = 3.2$ Hz, H-1′), 4.10 (d, 1H, $J_{6'b,6'a} = 13.2$ Hz, H-6′b), 2.43 (dd, 1H, $J_{1a,1'} = 3.2$ Hz, $J_{1a,1b} =$ 15.2 Hz, H-1a), 2.16 (dd, 1H, $J_{1b,1'} = 3.2$ Hz, $J_{1b,1a} = 15.2$ Hz, H-1b), 2.16 (s, 3H, H-*CH*$_3$), 1.54 (s, 3H, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.8 (C═O), 100.3 (C-2), 75.9 (C-5′), 70.4 (C-2′), 69.9 (C-3′), 69.3 (C-6′), 66.2 (C-1′), 54.9 (C-4′), 39.3 (C-1), 29.6 (C-3), 21.0 (C-*CH*$_3$); HRMS (ESI): Calcd. for $C_{11}H_{15}ClO_5$: 262.0608. Found: 285.0510 $[M + Na]^+$. Anal. Calcd. for $C_{11}H_{15}ClO_5$: C, 50.29; H, 5.76. Found C, 50.31; H, 5.78.

1-(β-D-Glucopyranosyl)-propan-2-one (7)

The compound was prepared from **5** in 96% yields under the conditions described in **3.2**. IR (KBr): 3422, 2912, 1706, 1363, 1085 cm^{-1}; ^{1}H NMR (D_2O, 400 MHz): δ 3.76 (dd, 1H, $J_{6a,5} = 1.6$ Hz, $J_{6a,6b} = 12.4$ Hz, H-6a), 3.70 (dt, 1H, $J_{1,1'a} = 3.2$ Hz, $J_{1,1'b} = J_{1,2} = 9.2$ Hz, H-1), 3.59 (dd, 1H, $J_{6b,5} =$ 5.2 Hz, $J_{6b,6a} = 12.4$ Hz, H-6b), 3.40 (t, 1H, $J = 8.4$ Hz, H-3), 3.33 (m, 1H, H-5), 3.31 (m, 1H, H-4), 3.14 (t, 1H, $J = 9.2$ Hz, H-2), 2.94 (dd, 1H, $J_{1'a,1} =$ 2.8 Hz, $J_{1'a,1'b} = 16.4$ Hz, H-1′a), 2.63 (dd, 1H, $J_{1'b,1} = 9.2$ Hz, $J_{1'b,1'a} =$ 16.4 Hz, H-1′b), 2.19 (s, 3H, H-3′); ^{13}C NMR (D_2O, 100 MHz): δ 213.3 (C-2′), 79.5 (C-5), 77.2 (C-3), 75.3 (C-1), 73.1 (C-2), 69.7 (C-4), 60.7 (C-6), 45.6 (C-1′), 29.8 (C-3′); HRMS (ESI): Calcd. for $C_9H_{16}O_6$: 220.0947. Found: 243.0846 $[M + Na]^+$. Anal. Calcd. for $C_9H_{16}O_6$: C, 49.09; H, 7.32. Found C, 49.06; H, 7.34.

1-(β-D-Galacopyranosyl)-propan-2-one (8)

The compound was prepared from **6** in 92% yields under the conditions similar to those described in **3.2**. IR (KBr): 3381, 2923, 1706, 1364, 1088 cm^{-1}; ^{1}H NMR (D_2O, 400 MHz): δ 3.85 (d, 1H, $J_{4,3} = 3.3$ Hz, H-4), 3.63 (dt, 1H, $J_{1,1'a} = 3.0$ Hz, $J_{1,1'b} = J_{1,2} = 9.4$ Hz, H-1), 3.58 (dd, 1H, $J_{6a,5} =$ 8.4 Hz, $J_{6a,6b} = 11.0$ Hz, H-6a), 3.55 (dd, 1H, $J_{6b,5} = 8.7$ Hz, $J_{6b,6a} = 11.0$ Hz, H-6b), 3.54 (m, 1H, H-5), 3.51 (m, 1H, H-3), 3.35 (t, 1H, $J = 9.4$ Hz, H-2), 2.92 (dd, 1H, $J_{1'a,1} = 3.0$ Hz, $J_{1'a,1'b} = 16.7$ Hz, H-1′a), 2.64 (dd, 1H, $J_{1'b,1} =$ 9.4 Hz, $J_{1'b,1'a} = 16.7$ Hz, H-1′b), 2.17 (s, 3H, H-3′); ^{13}C NMR (D_2O, 100 MHz): δ 213.4 (C-2′), 78.5 (C-5), 75.6 (C-1), 73.8 (C-3), 70.4 (C-2), 69.1 (C-4), 61.1 (C-6), 45.7 (C-1′), 29.7 (C-3′); HRMS (ESI): Calcd. for $C_9H_{16}O_6$: 220.0947. Found: 243.0860 $[M + Na]^+$. Anal. Calcd. for $C_9H_{16}O_6$: C, 49.09; H, 7.32. Found C, 49.11; H, 7.34.

β-D-Glucopyranosyl-propan-2-one-3′,6′-ketal (9)

The compound was prepared from **7** in 76% yields under the conditions described in **3.3**. IR (KBr): 3420, 2926, 1178, 1068 cm^{-1}; ^{1}H NMR ($CDCl_3$,

400 MHz): δ 4.27 (d, 1H, $J_{5',6'} = 4.4$ Hz, H-5′), 4.14 (m, 1H, H-4′), 4.10 (m, 1H, H-1′), 4.05 (m, 1H, H-3′), 4.02 (dd, 1H, $J_{6'a,5'} = 4.4$ Hz, $J_{6'a,6'b} = 13.2$ Hz, H-6′a), 3.93 (dd, 1H, $J_{6'b,5'} = 4.4$ Hz, $J_{6'b,6'a} = 13.2$ Hz, H-6′b), 3.75 (m, 1H, H-2′), 2.44 (dd, 1H, $J_{1a,1'} = 3.2$ Hz, $J_{1a,1b} = 15.6$ Hz, H-1a), 2.13 (dd, 1H, $J_{1b,1'} = 3.2$ Hz, $J_{1b,1a} = 15.6$ Hz, H-1b), 1.44 (s, 3H, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 99.9 (C-2), 78.7 (C-5′), 69.7 (C-6′), 69.3 (C-4′), 69.1 (C-1′), 67.9 (C-3′), 66.6 (C-2′), 39.1 (C-1), 29.5 (C-3); HRMS (ESI): Calcd. for $C_9H_{14}O_5$: 202.0841. Found: 225.0737 $[M + Na]^+$. Anal. Calcd. for $C_9H_{14}O_5$: C, 53,46; H, 6.98. Found C, 53.45; H, 7.01.

β-D-Galactopyranosyl-propan-2-one-3′,6′-ketal (10)

The compound was prepared from **8** in 85% yields under the conditions described in **3.3**. IR (KBr): 3326, 2962, 1389, 1136, 1079 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.41 (d, 1H, $J_{4',3'} = 6.5$ Hz, H-4′), 4.36 (d, 1H, $J_{3',4'} = 6.5$ Hz, H-3′), 4.23 (t, 1H, $J = 2.6$ Hz, H-1′), 4.18 (t, 1H, $J = 5.3$ Hz, H-5′), 4.04 (m, 1H, H-2′), 3.87 (dd, 1H, $J_{6'a,5'} = 6.2$ Hz, $J_{6'a,6'b} = 11.2$ Hz, H-6′a), 3.77 (dd, 1H, $J_{6'b,5'} = 4.6$ Hz, $J_{6'b,6'a} = 11.2$ Hz, H-6′b), 2.07 (dd, 1H, $J_{1a,1'} = 2.3$ Hz, $J_{1a,1b} = 14.4$ Hz, H-1a), 1.97 (dd, 1H, $J_{1b,1'} = 3.3$ Hz, $J_{1b,1a} = 14.4$ Hz, H-1b), 1.49 (s, 3H, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 105.8 (C-2), 74.6 (C-4′), 73.1 (C-3′), 71.3 (C-1′), 70.7 (C-5′), 68.5 (C-2′), 64.7 (C-6′), 43.0 (C-1), 22.1 (C-3); HRMS (ESI): Calcd. for $C_9H_{14}O_5$: 202.0841. Found: 203.0927 $[M + H]^+$. Anal. Calcd. for $C_9H_{14}O_5$: C, 53.46; H, 6.98. Found C, 53.48; H, 6.96.

2′-*O*-Tosyl-4′-chloro-4′-deoxy-β-D-galactosyl-propan-2-one-3′,6′-ketal (11)

Compound **3** (238 mg, 1 mmol) was dissolved in dry pyridine (1 mL) and toluene 4-sulfonyl chloride (285 mg, 1.5 mmol) was added. The reaction mixture was stirred at rt for 24 h. After the disappearance of starting sugar, distilled water (2 mL) was added. The mixture was continued to stir for 20 min, then partitioned between EtOAc and H_2O. The EtOAc layer was washed with water (5 mL × 2), dried over anhydrous Na_2SO_4, and evaporated, affording compound **11** as an oil (340 mg, 91%): IR (KBr): 2924, 1598, 1367, 1190, 1177 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (d, 2H, $J = 8.2$ Hz, H-Ar), 7.37 (d, 2H, $J = 8.2$ Hz, H-Ar), 4.61 (m, 1H, H-4′), 4.57 (dd, 1H, $J_{2',1'} = 2.5$ Hz, $J_{2',3'} = 6.6$ Hz, H-2′), 4.31 (m, 1H, H-5′), 4.25 (dd, 1H, $J_{6'a,5'} = 4.4$ Hz, $J_{6'a,6'b} = 13.6$ Hz, H-6′a), 4.05 (m, 3H, H-3′, H-6′b, H-1′), 2.47 (s, 3H, Ar-*CH*$_3$), 2.40 (dd, 1H, $J_{1a,1'} = 3.4$ Hz, $J_{1a,1b} = 15.4$ Hz, H-1a), 2.18 (dd, 1H, $J_{1b,1'} = 2.9$ Hz, $J_{1b,1a} = 15.4$ Hz, H-1b), 1.49 (s, 3H, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.0 (C-Ar), 133.8 (C-Ar), 130.6 (2C-Ar), 128.2 (2C-Ar), 100.6 (C-2), 76.4 (C-5′), 76.3 (C-2′), 70.4 (C-3′), 69.7 (C-6′), 66.9 (C-1′), 54.4 (C-4′), 40.1 (C-1), 29.9 (C-3), 22.1 (C-*CH*$_3$); HRMS (ESI): Calcd. for $C_{16}H_{19}ClO_6S$:

374.0591. Found: 397.0484 $[M + Na]^+$. Anal. Calcd. for $C_{16}H_{19}ClO_6S$: C, 51.27; H, 5.11. Found C, 51.30; H, 5.10.

1-(4-Chloro-4-deoxy-2-*O*-tosyl-β-D-galactopyranosyl)-propan-2-one (12)

A mixture of ketal **11** (300 mg, 0.80 mmol), trifluoroacetic acid (0.5 mL), and water (0.5 mL) was stirred at rt overnight. The solvents were evaporated under diminished pressure. The residue was dissolved in EtOAc, and the solution was washed with satd aq $NaHCO_3$ (5 mL × 2) and water (5 mL × 3). The organic layer was dried over anhydrous Na_2SO_4 and evaporated, affording **12** (295 mg, 94%) as an oil: IR (KBr): 3447, 2925, 1715, 1599, 1359, 1178 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.83 (d, 2H, $J = 8.2$ Hz, H-Ar), 7.36 (d, 2H, $J = 8.2$ Hz, H-Ar), 4.62 (t, 1H, $J = 9.4$ Hz, H-2), 4.43 (d, 1H, $J = 3.6$ Hz, H-4), 3.92 (m, 2H, H-5, H-3), 3.78 (m, 1H, H-1), 3.64 (dd, 1H, $J_{6a,5} = 7.2$ Hz, $J_{6a,6b} = 11.6$ Hz, H-6a), 3.11 (dd, 1H, $J_{6b,5} = 5.6$ Hz, $J_{6b,6a} = 11.6$ Hz, H-6b), 2.73 (m, 2H, H-1′), 2.46 (s, 3H, Ar-*CH*$_3$), 2.15 (s, 3H, H-3′); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.4 (C-2′), 145.5 (C-Ar), 133.2 (C-Ar), 129.9 (2C-Ar), 128.1 (2C-Ar), 79.4 (C-5), 77.7 (C-2), 73.9 (C-1), 72.1 (C-3), 63.1 (C-4), 62.2 (C-6), 45.0 (C-1′), 30.8 (C-3′), 21.7 (C-*CH*$_3$); HRMS (ESI): Calcd. for $C_{16}H_{21}ClO_7S$: 392.0697. Found: 415.0580 $[M + Na]^+$. Anal. Calcd. for $C_{16}H_{21}ClO_7S$: C, 48.92; H, 5.39. Found C, 48.89; H, 5.40.

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