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1,2,4-Triazole기를 가지고 있는 S-glycoside들의 합성 및 항균활성시험

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Synthesis and Antibacterial Activities of New S-glycosides Bearing 1,2,4-Triazole

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요약. 5-Aryl-3-(β-D-glucopyranosylthio)-1,2,4-triazole 화합물들을 합성하였으며, 합성한 화합물들에 대한 항균활성시험을 수행하였다.

주제어: S-glycosides, 1,2,4-Triazole, Glycosylation, 항균활성

ABSTRACT. Several new 5-aryl-3-(β-D-glucopyranosylthio)-1,2,4-triazoles have been synthesized. The structures of these new compounds were confirmed by ^{1}H NMR, ^{13}C NMR and elemental analyses.The antibacterial activities of the compounds were also evaluated.

Keywords: S-glycosides, 1,2,4-Triazole, Glycosylation, Antibacterial activities

INTRODUCTION

1,2,4-Triazoles are very important organic compounds with wide-ranging biological activities. These compounds are reported to possess significant antiviral,[1] antibacterial,[2] antifungal,[3] antiasthmatic,[4] antidepressant[5] and anti-inflammatory[6-7]activities.

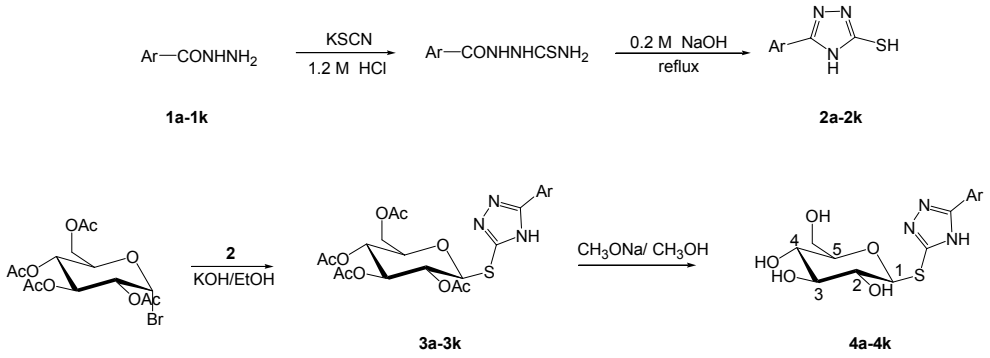
Glycosides have extensively existed in the animals and plants and taken on an important biological function.[8] Many active ingredients in natural drugs and Chinese traditional drugs belong to glycosides. Significant antibacterial and anticaner activities of glycosides have attracted many workers to attempt to improve the biological activity of these compounds by the glycosylation in order to increase their solubility in water and guidance quality.[9-11]

Since the recognized biological properties of ribavirin,[12] 1-β-D-ribofuranosyl-1,2,4-triazole-3-caroboxamide, the synthesis of N-glycosides and C-glycosides as well as their acyclic analogues possessing a 1,2,4-triazole moiety has attracted many workers[13-14] in this field to try to enhance the biological activity of these compounds. During past decades, a great deal of modified N-glycosides,[15-16] C-glycosides[17-19] and S-glycosides have been emphasized,[20-21] but only a few S-glycosides bearing 1,2,4-triazole have been reported.[21] In view of this, we turned our attention to the synthesis of novel S-glycosides possessing 1,2,4-triazole from 3-aryl-5-mercapto-1,2,4-triazole and tetra-*O*-acetyl-α-D-glucopyanosyl bromide. The antibacterial activities were also evaluated.

RESULTS AND DISCUSSIONS

The synthetic route for the target compounds is outlined in *Scheme* 1. 3-Aryl-5-mercapto-1,2,4-triazoles (**2a~2k**) were prepared via the reaction of acylhydrazines with potassium thiocyanate in the presence of 1.2 M hydrochloric acid and subsequent intramolecular dehydration of the precipitate arylthiosemicarbazides in 8% sodium hydroxide solution. The final recrystallization from 95% ethanol affords pure **2a~2k**.[22] 5-Aryl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (**3a~3k**) were obtained by the direct glycosylation of (**2a~2k**) with tetra-*O*-acetyl-α-D-glucopyanosyl bromide in ethanol in the presence of potassium hydroxide. The deacetylation of **3a~3k** using sodium methoxide in methanol gave the corresponding 5-aryl-3-(β-D-glucopyranosylthio)-1,2,4-triazoles (**4a~4k**) in good yields.

The structure assignments of **3a~3k** and **4a~4k** were based on ^{1}H NMR, ^{13}C NMR and elemental analyses. In ^{1}H NMR spectrum of **3a~3k**, four singlets in the region of δ 1.96-2.13 were attributed to four acetyl groups. Seven protons of



***Scheme* 1.** Ar=Ph(a), *o*-CH_3Ph(b), *p*-CH_3Ph(c), *o*-ClPh(d), *p*-ClPh(e), *m*-ClPh(f), *o*-BrPh(g), *p*-BrPh(h), *o*-OHPh(i), *o*-OMePh(j), *p*-OMePh(k)

***Table* 1.** Antibacterial activity of compounds **4a-4k**

Compound	**4a**	**4b**	**4c**	**4d**	**4e**	**4f**	**4g**	**4h**	**4i**	**4j**	**4k**
E.coli	-	-	+	-	+	+	-	+	++	-	-
Streptococcus	-	+	-	+	++	+	-	+	++	-	-
B.subtilis	+	-	-	-	-	-	-	-	+++	-	-
S.aureus	-	+	+	-	+	-	+	+	++	-	-

Zone diameter of growth inhibition: < 10 mm (-), 10 - 13 mm (+), 14 - 17 mm (++) and 18 - 21 mm (+++). Diameter of the cup = 8 mm.

the sugar moiety exhibited the multiplets at δ 3.76-5.52. The aryl groups were found in the region of δ 6.91-8.28. While in the ^{1}H NMR spectrum of **4a~4k**, the disappearance of four sharp singlets around δ 2.00 could be mainly due to successful deacetylation of **3a~3k**. Seven protons of the sugar moiety exhibited the multiplets at δ 3.15-4.84. Only β-anomer was obtained as judged by a doublet at δ 4.70-4.84 ($J_{H1,H2}$ = 8.7-9.9 Hz) of the anomeric proton (H-1) in the sugar moiety.

Antibacterial Activity

Compounds **4a~4k** were screened for their antibacterial activity against *Escherichia coli*, *Streptococcus*, *Bacillus subtilis*, and *Staphylococus aureu* employing the cup-plate method at the concentration of 200 μg/mL in nutrient agar media. The zone of the growth inhibition of bacteria, produced by diffusion of the compounds from the cup into the surrounding medium, was measured after 24 h. The results are listed in *Table* 1. The antibacterial activity showed that most of the compounds were active against microorganisms. It is worthwhile to notice that compound **4i** showed a good inhibitory effect to these bacteria, but **4j~4k** do not express antibacterial activity.

The investigation on the sructure-activity relationship shows that hydroxy group enhances the antibacterial action of the title compounds. Further investigation on the biological activity of these compounds is in progress.

EXPERIMENTAL SECTION

The melting points were taken on an X-4 microscopic melting point apparatus and are uncorrected. All the ^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature on a Varian Mercury-300 MHz spectrometer with TMS as internal standard. Elemental analysis was performed on an Elementar Vario EL apparatus. All reagents of analytical grade were used without purification. 3-Aryl-5-mercapto-1,2,4-triazole (**2a-2k**) were synthesized according to the literature.[21]

General procedure for preparation of 5-aryl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3a~3k)

3-Aryl-5-mercapto-1,2,4-triazole (**2a~2k**) (1 mmol) was dissolved in the solution of KOH (1 mmol) in ethanol (10 mL). The mixture was stirred at room temperature for 30 min. Compound of tetra-*O*-acetyl-α-D-glucopyanosyl bromide (1 mmol, 0.41 g) was then added to the solution, which was stirred at room temperature for 12 h. The mixture was filtered and washed with water. The crude product was purified by flash column chromatography on silica gel with petroleum ether/ethyl acetate as eluent.

5-Phenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3a): Yield: 49%. mp 149 - 151 °C;

$[\alpha]_D$ -43° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.96 (s, 3 H, CH_3C=O), 1.97 (s, 3 H, CH_3C=O), 1.98 (s, 3 H, CH_3C=O) 2.00 (s, 3 H, CH_3C=O), 3.76-3.82 (m, 1 H, Glc-H-5), 4.14-4.16 (m, 2 H, Glc-H-6), 5.04-5.14 (m, 2 H, Glc-H-2, H-4), 5.23-5.29 (m, 2 H, Glc-H-1, H-3), 7.36-7.39 (m, 3 H, ArH), 7.94-7.98 (m, 2 H, ArH); ^{13}C NMR ($CDCl_3$): δ 20.39, 61.75, 67.96, 69.89, 73.52, 75.95, 83.27, 126.30, 128.15, 128.71, 130.07, 169.33, 169.53, 169.99, 170.90; Anal. Calcd. for $C_{22}H_{25}N_3O_9S$: C, 52.06; H, 4.97; N, 8.28; Found: C, 52.21; H, 4.94; N, 8.16.

5-*o*-Methylphenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3b): Yield: 53%; mp 100 - 102 °C; $[\alpha]_D$ -31° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.98 (s, 3 H, CH_3C=O), 1.99 (s, 3 H, CH_3C=O), 2.00 (s, 3 H, CH_3C=O), 2.02 (s, 3 H, CH_3C=O), 2.53 (s, 3 H, $ArCH_3$), 3.78-3.82 (m, 1 H, Glc-H-5), 4.17-4.21 (m, 2 H, Glc-H-6), 5.06-5.19 (m, 2 H, Glc-H-2, H-4), 5.24-5.32 (m, 2 H, Glc-H-1, H-3), 7.19-7.30 (m, 3 H, ArH), 7.65-7.67 (m, 1 H, ArH); ^{13}C NMR ($CDCl_3$): δ 20.45, 21.03, 29.56, 61.84, 68.03, 69.84, 73.66, 76.04, 83.27, 125.95, 129.03, 129.86, 131.28, 137.05, 169.39, 169.51, 170.08, 170.83; Anal. Calcd. for $C_{23}H_{27}N_3O_9S$: C, 52.97; H, 5.22; N, 8.06; Found: C, 53.04; H, 5.61; N, 8.21.

5-*p*-Methylphenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3c): Yield: 33%; mp 150 - 152 °C; $[\alpha]_D$ -46° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.98 (s, 3 H, CH_3C=O), 1.99 (s, 3 H, CH_3C=O), 2.00 (s, 3 H, CH_3C=O), 2.01 (s, 3 H, CH_3C=O), 2.35 (s, 3 H, $ArCH_3$), 3.78-3.81 (m, 1 H, Glc-H-5), 4.15-4.18 (m, 2 H, Glc-H-6), 5.06-5.15 (m, 2 H, Glc-H-2, H-4), 5.24-5.27 (m, 2 H, Glc-H-1, H-3), 7.20 (d, 2 H, J = 8.1 Hz, ArH), 7.85 (d, 2 H, J = 8.1 Hz, ArH); ^{13}C NMR ($CDCl_3$): δ 20.43, 21.29, 61.78, 68.01, 69.93, 73.58, 75.98, 83.37, 129.46, 136.30, 140.39, 169.36, 169.57, 170.05, 170.92; Anal. Calcd. for $C_{23}H_{27}N_3O_9S$: C, 52.97; H, 5.22; N, 8.06; Found: C, 52.70; H, 5.21; N, 8.09.

5-*o*-Chlorophenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3d): Yield: 34%; mp 133 - 135 °C; $[\alpha]_D$ -19° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.01 (s, 3 H, CH_3C=O), 2.02 (s, 3 H, CH_3C=O), 2.03 (s, 3 H, CH_3C=O), 2.05 (s, 3 H, CH_3C=O), 3.79-3.85 (m, 1 H, Glc-H-5), 4.18-4.23 (m, 2 H, Glc-H-6), 5.14-5.23 (m, 2 H, Glc-H-2, H-4), 5.31 (t, 1 H, $J_{H2,H3}$ = 9.3 Hz, Glc-H-3), 5.38 (d, 1 H, $J_{H1,H2}$ = 10.5 Hz, Glc-H-1), 7.38-7.41 (m, 2 H, ArH), 7.47-7.49 (m, 1 H, ArH), 8.14-8.18 (m, 1 H, ArH); ^{13}C NMR ($CDCl_3$): δ 20.51, 61.45, 67.61, 69.58, 73.44, 76.47, 83.18, 122.47, 127.16, 130.97, 131.26, 132.94, 161.36, 164.69, 169.31, 169.42, 169.94, 170.55; Anal. Calcd. for $C_{22}H_{24}ClN_3O_9S$: C, 48.76; H, 4.46; N, 7.75; Found: C, 48.44; H, 4.57; N, 7.78.

5-*p*-Chlorophenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3e): Yield: 53%; mp 86 - 88 °C; $[\alpha]_D$ -55° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.99 (s, 3 H, CH_3C=O), 2.01 (s, 3 H, CH_3C=O), 2.04 (s, 3 H, CH_3C=O), 2.05 (s, 3 H, CH_3C=O), 3.80 (ddd, $J_{H4,H5}$ = 9.9 Hz, Glc-H-5), 4.17 (dd, $J_{H5,H6'}$ = 4.5 Hz, Glc-H-6'), 4.24 (dd, 1 H, $J_{H5,H6}$ = 2.4 Hz, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 5.05-5.16 (m, 3 H, Glc-H-2, H-3, H-4), 5.24-5.30 (m, 1 H, Glc-H-1), 7.37 (d, 2 H, J = 8.4 Hz, ArH), 7.95 (d, 2 H, J = 8.4 Hz, ArH); ^{13}C NMR ($CDCl_3$): δ 20.46, 20.66, 61.78, 67.96, 69.95, 73.40, 76.21, 83.12, 127.68, 128.96, 135.84, 169.38, 169.57, 170.03, 171.05; Anal. Calcd. for $C_{22}H_{24}ClN_3O_9S$: C, 48.76; H, 4.46; N, 7.75; Found: C, 48.59; H, 4.39; N, 7.71.

5-*m*-Chlorophenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3f): Yield: 31%; mp 138 - 140 °C; $[\alpha]_D$ -54° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.01 (s, 3 H, CH_3C=O), 2.04 (s, 3 H, CH_3C=O), 2.08 (s, 3 H, CH_3C=O), 2.13 (s, 3 H, CH_3C=O), 3.82 (ddd, $J_{H4,H5}$ = 9.9 Hz, Glc-H-5), 4.16 (dd, $J_{H5,H6'}$ = 5.1 Hz, Glc-H-6'), 4.34 (dd, 1 H, $J_{H5,H6}$ = 2.4 Hz, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 5.04-5.14 (m, 3 H, Glc-H-2, H-3, H-4), 5.25-5.32 (m, 1 H, Glc-H-1), 7.35-7.39 (m, 2 H, ArH), 7.92-7.99 (m, 1 H, ArH), 8.07 (s, 1 H, ArH); ^{13}C NMR ($CDCl_3$): δ 20.51, 20.75, 61.78, 67.93, 69.93, 73.28, 76.30, 82.94, 124.42, 126.48, 129.74, 129.98, 131.38, 134.71, 169.38, 169.57, 170.02, 171.16; Anal. Calcd. for $C_{22}H_{24}ClN_3O_9S$: C, 48.76; H, 4.46; N, 7.75; Found: C, 48.94; H, 4.47; N, 7.73.

5-*o*-Bromophenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3g): Yield: 71%; mp 132 - 134 °C; $[\alpha]_D$ -18° (c 1, CH_2Cl_2; ^{1}H NMR ($CDCl_3$): δ 1.99 (s, 3 H, CH_3C=O), 2.01 (s, 3 H, CH_3C=O), 2.02 (s, 3 H, CH_3C=O), 2.04 (s, 3 H, CH_3C=O), 3.82 (ddd, $J_{H4,H5}$ = 9.9 Hz, Glc-H-5), 4.14 (dd, $J_{H5,H6'}$ = 2.4 Hz, Glc-H-6'), 4.22 (dd, 1 H, $J_{H5,H6}$ = 5.1 Hz, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 5.11 (d, 1 H, $J_{H2,H3}$ = 9.9 Hz, Glc-H-2), 5.17 (t, 1 H, $J_{H4,H5}$ = 9.9 Hz, Glc-H-4), 5.29 (d, 1 H, $J_{H3,H4}$ = 9.6 Hz,Glc-H-3), 5.36 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz,Glc-H-1), 7.28 (t, 1 H, J = 7.8 Hz, ArH), 7.40 (t, 1 H, J = 7.8 Hz, ArH), 7.65 (d, 1 H, J = 7.8 Hz, ArH), 7.98 (d, 1 H, J = 7.8 Hz, ArH); ^{13}C NMR ($CDCl_3$): δ 20.51, 61.87, 68.06, 69.87, 73.69, 76.08, 83.37, 120.75, 127.74, 131.35, 131.86, 133.89, 169.34, 169.45, 170.06, 170.76; Anal. Calcd. for $C_{22}H_{24}BrN_3O_9S$: C, 45.06; H, 4.13;

N, 7.17; Found: C, 44.97; H, 4.16; N, 7.40.

5-*p*-Bromophenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3h): Yield: 55%; mp 159 - 161 °C; $[\alpha]_D$ -48° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.01 (s, 3 H, CH_3C=O), 2.03 (s, 3 H, CH_3C=O), 2.07 (s, 3 H, CH_3C=O), 2.10 (s, 3 H, CH_3C=O), 3.80 (ddd, $J_{H4,H5}$ = 9.9 Hz, Glc-H-5), 4.17 (dd, $J_{H5,H6'}$ = 5.1 Hz, Glc-H-6'), 4.30 (dd, 1 H, $J_{H5,H6}$ = 2.4 Hz, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 5.06-5.14 (m, 3 H, Glc-H-2, H-3, H-4), 5.25-5.28 (m, 1 H, Glc-H-1), 7.55 (d, 2 H, *J* = 8.1 Hz, ArH), 7.92 (d, 2 H, *J* = 8.4 Hz, ArH); ^{13}C NMR ($CDCl_3$): δ 20.51, 20.75, 61.77, 67.93, 69.92, 73.32, 76.25, 83.00, 127.92, 131.92, 169.39, 169.60, 170.06, 171.16; Anal. Calcd. for $C_{22}H_{24}BrN_3O_9S$: C, 45.06; H, 4.13; N, 7.17; Found: C, 45.10; H, 3.94; N, 7.08.

5-*o*-Hydroxyphenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3i): Yield: 50%; mp 178 - 180 °C; $[\alpha]_D$ -49° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.99 (s, 3 H, CH_3C=O), 2.02 (s, 3 H, CH_3C=O), 2.04 (s, 3 H, CH_3C=O), 2.06 (s, 3 H, CH_3C=O), 3.82-3.85 (m, 1 H, Glc-H-5), 4.20-4.23 (m, 2 H, Glc-H-6), 5.07-5.17 (m, 3 H, Glc-H-2, H-3, H-4), 5.27-5.30 (m, 1 H, Glc-H-1), 6.91 (t, 1 H, *J* = 7.5 Hz, ArH), 7.01 (d, 1 H, *J* = 7.5 Hz, ArH), 7.31 (t, 1 H, *J* = 7.8 Hz, ArH), 7.82 (d, 1 H, *J* = 7.8 Hz, ArH), 10.71 (s, 1 H, Ar-OH); ^{13}C NMR ($CDCl_3$): δ 20.45, 20.54, 61.81, 67.92, 69.80, 73.54, 76.22, 83.11, 117.53, 119.63, 125.95, 132.15, 156.65, 169.44, 169.70, 170.11, 177.22.); Anal. Calcd. for $C_{22}H_{25}N_3O_{10}S$: C, 50.47; H, 4.81; N, 8.03. Found: C, 50.40; H, 4.96; N, 8.09.

5-*o*-Methoxyphenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3j): Yield: 34%; mp 157 - 158 °C; $[\alpha]_D$ -31° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 1.98 (s, 3 H, CH_3C=O), 2.00 (s, 3 H, CH_3C=O), 2.02 (s, 3 H, CH_3C=O), 2.04 (s, 3 H, CH_3C=O), 3.83 (ddd, $J_{H4,H5}$ = 9.9 Hz, Glc-H-5), 4.04 (s, 3 H, Ar-OCH_3), 4.10 (dd, $J_{H5,H6'}$ = 1.8 Hz, Glc-H-6'), 4.25 (dd, 1 H, $J_{H5,H6}$ = 4.5 Hz, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 5.12-5.52 (m, 3 H, Glc-H-2, H-3, H-4), 5.50 (d, 1 H, $J_{H1,H2}$ = 10.5 Hz,Glc-H-1), 7.05 (d, 1 H, *J* = 8.1 Hz, ArH), 7.11 (t, 1 H, *J* = 7.8 Hz, ArH), 7.44 (t, 1 H, *J* = 7.8 Hz, ArH), 8.28 (d, 1 H, *J* = 7.5 Hz, ArH); ^{13}C NMR ($CDCl_3$): δ 20.57, 56.00, 61.87, 68.07, 69.84, 73.93, 75.96, 83.67, 111.18, 114.66, 121.52, 129.52, 131.90, 153.82, 156.71, 156.87, 169.38, 169.45, 170.15, 170.67; Anal. Calcd. for $C_{23}H_{27}N_3O_{10}S$: C, 51.39; H, 5.06; N, 7.82; Found: C, 51.24; H, 4.99; N, 7.91.

5-*p*-Methoxyphenyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)-1,2,4-triazole (3k): Yield: 70%; mp 172 - 174 °C; $[\alpha]_D$ -23° (c 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 2.01 (s, 3 H, CH_3C=O), 2.02 (s, 3 H, CH_3C=O), 2.05 (s, 3 H, CH_3C=O), 2.09 (s, 3 H, CH_3C=O), 3.72-3.79 (m, 1 H, Glc-H-5), 3.83 (s, 3 H, $ArOCH_3$), 4.15-4.25 (m, 2 H, Glc-H-6), 5.07-5.19 (m, 2 H, Glc-H-2, H-4), 5.25-5.31 (m, 2 H, Glc-H-1, H-3), 6.94 (d, 2 H, *J* = 8.1 Hz, ArH), 7.93 (d, 2 H, *J* = 8.1 Hz, ArH); ^{13}C NMR ($CDCl_3$): δ 20.53, 20.68, 55.30, 61.78, 68.00, 69.92, 73.55, 76.07, 83.29, 114.17, 127.92, 161.10, 169.41, 169.62, 170.09, 171.02; Anal. Calcd. for $C_{23}H_{27}N_3O_{10}S$: C, 51.39; H, 5.06; N, 7.82; Found: C, 51.11; H, 5.00; N, 7.76.

General procedure for preparation of 5-aryl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4a~4k)

The compound (**3a~3k**) (0.2 mmol) was added to NaOMe (5 M)-MeOH (3 mL) and then stirred at room temperature for 1 ~ 2 h. The solution was concentrated and the crude product was purified by flash column chromatography on silica gel.

5-Phenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4a): Yield: 93%; $[\alpha]_D$ +27° (c 1, MeOH); ^{1}H NMR (D_2O): δ 3.29-3.36 (m, 3 H, Glc-H-2, H-3, H-5), 3.49 (t, 1 H, $J_{H4,H5}$ = 8.7 Hz, Glc-H-4), 3.61 (dd, 1 H, $J_{H5,H6'}$ = 5.1 Hz, Glc-H-6'), 3.78 (dd, 1 H, $J_{H5,H6}$ = 1.8 Hz, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 4.77 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz, Glc-H-1), 7.31-7.43 (m, 3 H, ArH), 7.88 (d, 2 H, *J* = 7.8 Hz, ArH); ^{13}C NMR (D_2O): δ 49.00, 60.95, 69.54, 72.35, 77.37, 80.14, 86.85, 125.82, 129.06, 131.47, 153.72, 164.22; Anal. Calcd. for $C_{14}H_{17}N_3O_5S$: C, 49.55; H, 5.05; N, 12.38; Found: C, 49.39; H, 4.93; N, 12.18.

5-o-Methylphenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4b): Yield: 85%; $[\alpha]_D$ -5° (c 0.5, MeOH); ^{1}H NMR (D_2O): δ 2.33 (s, 1 H, $ArCH_3$), 3.30-3.41 (m, 3 H, Glc-H-2, H-3, H-5), 3.52 (t, 1 H, $J_{H4,H5}$ = 9.0 Hz, Glc-H-4), 3.65 (dd, 1 H, $J_{H5,H6'}$ = 5.1 Hz, Glc-H-6'), 3.83 (dd, 1 H, $J_{H5,H6}$ = 1.5 Hz, $J_{H6,H6'}$ = 12.6 Hz, Glc-H-6), 4.81 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz, Glc-H-1), 7.13-7.21 (m, 3 H, ArH), 7.48 (d, 1 H, *J* = 6.9 Hz, ArH); ^{13}C NMR (D_2O): δ 22.46, 63.55, 72.12, 74.87, 79.86, 82.73, 89.34, 128.45, 131.47, 132.12, 133.27, 134.77, 139.82, 155.42, 167.38; Anal. Calcd. for $C_{15}H_{19}N_3O_5S$: C, 50.98; H, 5.42; N, 11.89; Found: C, 50.81; H, 5.70; N, 12.12.

5-*p*-Methylphenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4c): Yield: 89%; $[\alpha]_D$ -90° (c 1, MeOH); ^{1}H NMR (D_2O): δ 2.17 (s, 1 H, $ArCH_3$), 3.24-3.35 (m, 3 H, Glc-H-2, H-3, H-5), 3.44 (t, 1 H, $J_{H4,H5}$ = 8.4 Hz, Glc-H-4), 3.57 (dd,

1 H, $J_{H5,H6'}$ = 8.1 Hz, Glc-H-6'), 3.75 (d, 1 H, $J_{H6,H6'}$ = 12.0 Hz, Glc-H-6), 4.72 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz, Glc-H-1), 7.14 (d, 2 H, *J* = 8.1 Hz, ArH), 7.71 (d, 2 H, *J* = 8.1 Hz, ArH); ^{13}C NMR (D_2O): δ 20.44, 60.95, 69.58, 72.14, 77.47, 80.14, 86.95, 125.74, 128.55, 129.56, 139.16, 153.55, 164.22; Anal. Calcd. for $C_{15}H_{19}N_3O_5S$: C, 50.98; H, 5.42; N, 11.89; Found: C, 51.22; H, 5.63; N, 12.15.

5-*o*-Chlorophenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4d): Yield: 88%; $[\alpha]_D$ +8° (c 1, MeOH); ^{1}H NMR (D_2O): δ 3.26-3.35 (m, 3 H, Glc-H-2, H-3, H-5), 3.47 (t, 1 H, $J_{H4,H5}$ = 9.0 Hz, Glc-H-4), 3.59 (dd, 1 H, $J_{H5,H6'}$ = 5.4 Hz, Glc-H-6'), 3.77 (dd, 1 H, $J_{H5,H6}$ = 1.8 Hz, $J_{H6,H6'}$ = 12.6 Hz, Glc-H-6), 4.75 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz, Glc-H-1), 7.29-7.32 (m, 2 H, ArH), 7.44-7.61 (m, 2 H, ArH); ^{13}C NMR (D_2O): δ 32.31, 60.88, 69.74, 72.20, 77.28, 80.11, 86.69, 127.06, 130.08, 131.16, 153.05, 162.59; Anal. Calcd. for $C_{14}H_{16}ClN_3O_5S$: C, 44.98; H, 4.31; N, 11.24; Found: C, 44.72; H, 4.59; N, 10.95.

5-*p*-Chlorophenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4e): Yield: 90%; $[\alpha]_D$ +7° (c 1, MeOH); ^{1}H NMR (D_2O): δ 3.31-3.44 (m, 3 H, Glc-H-2, H-3, H-5), 3.53 (t, 1 H, $J_{H4,H5}$ = 9.0 Hz, Glc-H-4), 3.67 (dd, 1 H, $J_{H5,H6'}$ = 2.4 Hz, Glc-H-6'), 3.84 (d, 1 H, $J_{H6,H6'}$ = 12.6 Hz, Glc-H-6), 4.83 (d, 1 H, $J_{H1,H2}$ = 9.0 Hz, Glc-H-1), 7.49 (d, 2 H, *J* = 8.1 Hz, ArH), 7.88 (d, 2 H, *J* = 8.1 Hz, ArH); ^{13}C NMR (D_2O): δ 60.94, 69.53, 72.31, 77.33, 80.11, 86.88, 127.06, 128.83, 129.96, 133.71, 153.62, 163.23; Anal. Calcd. for $C_{14}H_{16}ClN_3O_5S$: C, 44.98; H, 4.31; N, 11.24; Found: C, 44.84; H, 4.53; N, 11.50.

5-*m*-Chlorophenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4f): Yield: 89%; $[\alpha]_D$ +3° (c 1, MeOH); ^{1}H NMR (D_2O): δ 3.27-3.41 (m, 3 H, Glc-H-2, H-3, H-5), 3.49 (t, 1 H, $J_{H4,H5}$ = 8.1 Hz, Glc-H-4), 3.61 (dd, 1 H, $J_{H5,H6'}$ = 5.1 Hz, Glc-H-6'), 3.79 (dd, 1 H, $J_{H5,H6}$ = 1.2 Hz, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 4.75 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz, Glc-H-1), 7.18-7.27 (m, 2 H, ArH), 7.67 (d, 1 H, *J* = 7.5 Hz, ArH), 7.73 (s, 1 H, ArH); ^{13}C NMR (D_2O): δ 30.27, 60.84, 69.38, 72.15, 77.10, 80.02, 86.67, 123.91, 125.41, 128.42, 130.34, 133.03, 134.08, 153.65, 162.80; Anal. Calcd. for $C_{14}H_{16}ClN_3O_5S$: C, 44.98; H, 4.31; N, 11.24; Found: C, 44.66; H, 4.22; N, 11.19.

5-*o*-Bromophenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4g): Yield: 90%; $[\alpha]_D$ +8° (c 0.5, MeOH); ^{1}H NMR (D_2O): δ 3.25-3.39 (m, 3 H, Glc-H-2, H-3, H-5), 3.45 (t, 1 H, $J_{H4,H5}$ = 8.1 Hz, Glc-H-4), 3.60 (dd, 1 H, $J_{H5,H6'}$ = 5.1 Hz, Glc-H-6'), 3.77 (dd, 1 H, $J_{H5,H6}$ = 1.8 Hz, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 4.76 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz, Glc-H-1), 7.26 (t, 1 H, *J* = 7.5 Hz, ArH), 7.34-7.44 (m, 2 H, ArH), 7.65 (d, 1 H, *J* = 7.5 Hz, ArH); ^{13}C NMR (D_2O): δ 60.95, 69.62, 72.37, 77.57, 80.24, 86.85, 122.19, 127.58, 130.49, 131.03, 133.13, 133.62, 153.07, 163.87; Anal. Calcd. for $C_{14}H_{16}BrN_3O_5S$: C, 40.20; H, 3.86; N, 10.05; Found: C, 40.02; H, 3.70; N, 10.19.

5-*p*-Bromophenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4h): Yield: 95%; $[\alpha]_D$ +3° (c 1, MeOH); ^{1}H NMR (D_2O): δ 3.27-3.42 (m, 3 H, Glc-H-2, H-3, H-5), 3.49 (t, 1 H, $J_{H4,H5}$ = 9.0 Hz, Glc-H-4), 3.62 (dd, 1 H, $J_{H5,H6'}$ = 5.4 Hz, Glc-H-6'), 3.79 (dd, 1 H, $J_{H5,H6}$ = 1.8 Hz, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 4.77 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz, Glc-H-1), 7.46 (d, 2 H, *J* = 8.4 Hz, ArH), 7.67 (d, 2 H, *J* = 8.4 Hz, ArH); ^{13}C NMR (D_2O): δ 60.88, 69.42, 72.22, 77.19,80.05, 86.75, 122.10, 127.36, 130.35, 131.85, 153.75, 163.38; Anal. Calcd. for $C_{14}H_{16}BrN_3O_5S$: C, 40.20; H, 3.86; N, 10.05; Found: C, 45.87; H, 4.05; N, 10.25.

5-*o*-Hydroxyphenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4i): Yield: 85%; $[\alpha]_D$ -10° (c 0.6, MeOH); ^{1}H NMR (D_2O): δ 3.15-3.30 (m, 3 H, Glc-H-2, H-3, H-5), 3.36 (t, 1 H, $J_{H4,H5}$ = 8.4 Hz, Glc-H-4), 3.51 (dd, 1 H, $J_{H5,H6'}$ = 5.1 Hz, Glc-H-6'), 3.67 (d, 1 H, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 4.84 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz, Glc-H-1), 6.63-6.72 (m, 2 H, ArH), 7.08 (t, 1 H, *J* = 7.5 Hz, ArH), 7.52 (d, 1 H, *J* = 7.5 Hz, ArH); ^{13}C NMR (D_2O): δ 60.83, 69.36, 72.09, 77.21, 80.14, 86.47, 117.55, 118.28, 127.62, 130.60, 152.94, 159.69, 162.80; Anal. Calcd. for $C_{14}H_{17}N_3O_6S$: C, 47.32; H, 4.82; N, 11.82; Found: C, 47.41; H, 4.64; N, 11.98.

5-*o*-Methoxyphenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4j): Yield: 87%; $[\alpha]_D$ +9° (c 0.5, MeOH); ^{1}H NMR (D_2O): δ 3.25-3.37 (m, 3 H, Glc-H-2, H-3, H-5), 3.47 (t, 1 H, $J_{H4,H5}$ = 8.7 Hz, Glc-H-4), 3.61 (dd, 1 H, $J_{H5,H6'}$ = 5.1 Hz, Glc-H-6'), 3.78 (d, 1 H, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6), 3.76 (s, 3 H, $ArOCH_3$), 4.76 (d, 1 H, $J_{H1,H2}$ = 9.9 Hz, Glc-H-1), 7.02 (t, 1 H, *J* = 7.5 Hz, ArH), 7.10 (d, 1 H, *J* = 8.7 Hz, ArH), 7.39 (t, 1 H, *J* = 8.7 Hz, ArH), 7.82 (d, 1 H, *J* = 7.8 Hz, ArH); ^{13}C NMR (D_2O): δ 56.08, 62.60, 71.12, 73.77, 79.24, 82.06, 87.89, 112.62, 121.22, 121.69, 131.10, 131.79, 154.26, 158.58, 159.10; Anal. Calcd. for $C_{15}H_{19}N_3O_6S$: C, 48.77; H, 5.18; N, 11.38; Found: C, 48.53; H, 5.34; N, 11.49.

5-*p*-Methoxyphenyl-3-(β-D-glucopyranosylthio)-1,2,4-triazole (4k): Yield: 89%; $[\alpha]_D$ -37° (c 1, MeOH); ^{1}H NMR (D_2O): δ 3.24-3.35 (m, 3 H, Glc-H-2, H-3, H-5), 3.44 (t, 1 H, $J_{H4,H5}$ = 8.7 Hz, Glc-H-4), 3.56 (m, 1 H, Glc-H-6'), 3.60 (s, 1 H, $ArOCH_3$), 3.74 (d, 1 H, $J_{H6,H6'}$ = 12.3 Hz, Glc-H-6),

4.70 (d, 1 H, $J_{H1, H2}$ = 9.6 Hz, Glc-H-1), 6.82 (d, 2 H, J = 8.1 Hz, ArH), 7.71 (d, 2 H, J = 8.4 Hz, ArH); ^{13}C NMR (D_2O): δ 55.30, 60.83, 69.39, 72.19, 77.16, 80.00, 86.73, 114.22, 124.51, 127.19, 153.22, 159.11, 163.93; Anal. Calcd. for $C_{15}H_{19}N_3O_6S$: C, 48.77; H, 5.18; N, 11.38; Found: C, 48.44; H, 5.36; N, 11.20.

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