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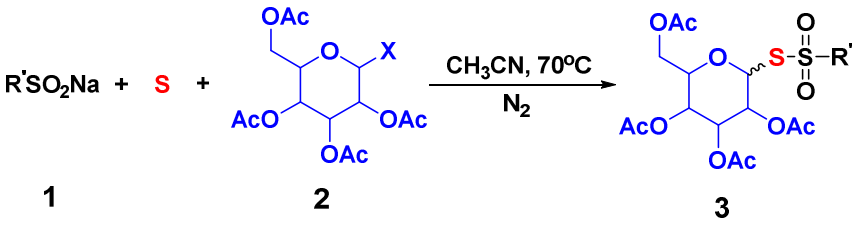
**Graphic Abstract**

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# One-pot Synthesis of Glycosyl Phenylthiosulfonates from Sulfinate, S and Glycosyl Bromides

Chunlai Feng,[a] Jin Wang,[a] Qiujie Tang,[a] Zijian Zhong,[a] Shusen Qiao,[a] Xingyu Liu,[a] Can Chen,[a] Aihua Zhou*[a]

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ABSTRACT

Glycosyl phenylthiosulfonates are reagents which are valuable for the S-glycosylation decoration of organic compounds and proteins. Here, one-pot multiple-component synthesis of glycosyl phenylthiosulfonates from sulfinate, sulfur powder and glycosyl bromides is reported. The reactions afford glycosyl phenylthiosulfonates in good yields under mild conditions. Further application and exploration of glycosyl phenylthiosulfonates are still on underway in our group.

## 1. Introduction

Thiosulfonates which possess R-$SSO_2$-R'(R, R'= Alkyl, Ar) structures have wide applications in organic synthesis and industry[1] Their strong sulfenylating power has been extensively utilized in organic syntheses for making sulfides and disulfides.[2] Thiosulfonates also have shown biological activities because they can block the normal metabolism of the microorganisms by sulfenylation of the enzyme's thiol groups with SR (R= alkyl, aryl).[3] Normally, thiosulfonates are made by reacting R′$SO_2$Na,[4] R′$SO_2$Cl,[5] R′$SO_2NHNH_2$ [6]or R′SSR′[7] with thiols or disulfides (Scheme 1).

In recent years, with the rapid development of sugar chemistry in the field of biochemistry, the synthesis of glycosides has received more and more attention from chemists.[8] Glycosyl phenylthiosulfonate are special thiosulfonates in which R (R-$SSO_2$-R') is replaced by different monosaccharides. Like normal thiosulfonates, glycosyl phenylthiosulfonate are also good reagents for chemically connecting S-sugar residues with functional groups of organic compounds and proteins,[9] this process can be called S-glycosylation. Although S-glycosylation is not as common as O-glycosylation, many examples of the decoration of oranic compounds and proteins with S-glycoside residues exist in the nature.[10] Compared with O-glycosides, S-glycosides are less susceptible to acid and enzymatic hydrolysis. They have different conformational preferences than O-glycosides, which can influence their biological properties.[11] Thus, any synthetic methods or reagents for conveniently attaching S-glycoside residues to drugs or proteins are pretty useful to medicinal chemists (Fig. 1). Compared with other reported S-glycosylation methods, the use of glycosyl phenylthiosulfonates as S-glycosylation reagent is more conveniennt and less odorless, and this S-glycosylation reaction can be carried out at room temperature which is also critical for generating S-glycosylation derivatives of some proteins.[12] Therefore, new synthetic method of using glycosyl phenylthiosulfonate as S-glycosylation agent is valued in drug discovery.[13]

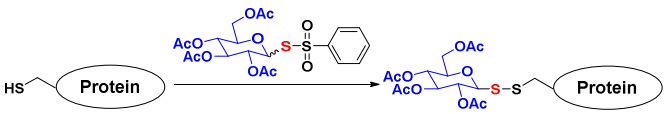


**Fig. 1.** Decoration of protein with glycosyl phenylthiosulfonate

Despite there is one report of using R′$SO_2$Na, S and RX to make thiosulfonates in literature, [14] but RX reagents used were alkyl halides and reactions had to undergo two seperate steps in order to generate thiosulfonates. Instead of using alkyl halides, we have improved the reaction by using acetylated glycosyl bromides and combined the two seperate reactions into a one-pot multiple-component reaction, our reactions are carried out under mild reaction conditions without any toxic additives or metal catalysts invovled, additionally, the yields of products are high.

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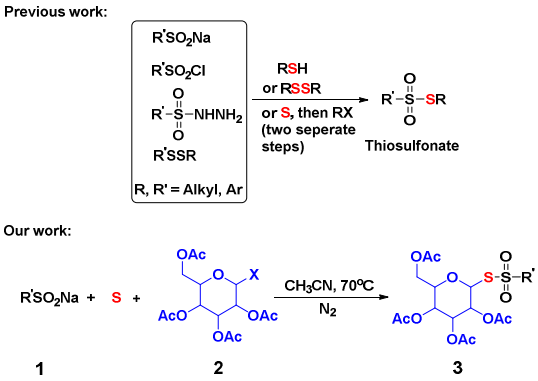
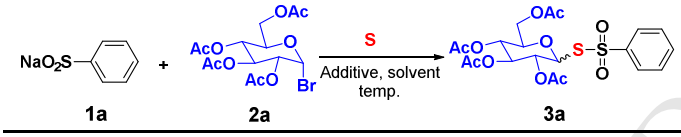



**Scheme 1.** Previous research and our work

## 2. Results and discussion

Screening to find a suitable reaction conditions for making glycosyl phenylthiosulfonates began with using sodium benzene sulfinate **1a** and S powder as representative reactants, and acetobromo-*α*-D-glucose **2a** was selected as the representative sugar part. Based on the literature and our previous research results,[14] different additives and solvents were screened at various temperatures. The experimental results are listed in Table 1.

**Table 1**
Optimization of reaction conditions.

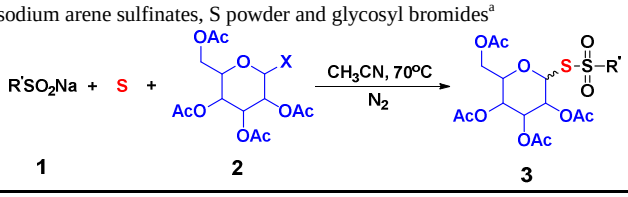


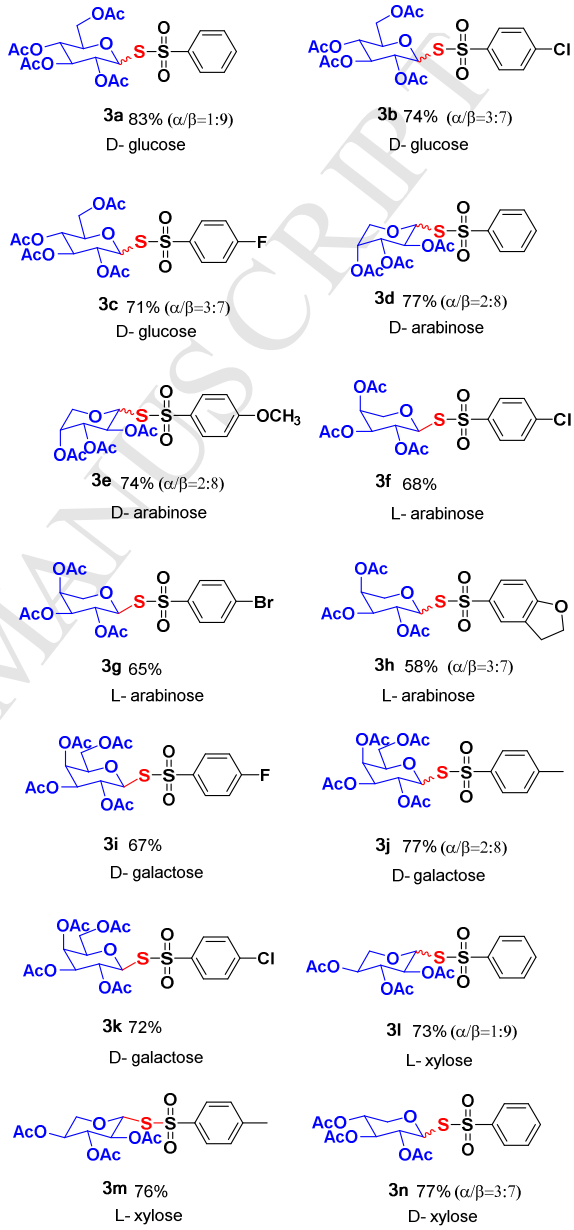

| Entry | Additive | Temp (°C) | Solvent | Yield of **3a** (%) |
|---|---|---|---|---|
| 1 | $Bu_4NBr$ | 50 | DMF | 0 |
| 2 | $Bu_4NI$ | 50 | DMF | 0 |
| 3 | $Bu_4NI$ | 70 | DMF | 0 |
| 4 | $Bu_4NI$ | 90 | $CH_3CN$ | 7 |
| 5 | --- | 25 | $H_2O$ | 0 |
| 6 | --- | 70 | $H_2O$/THF (1:1) | 0 |
| 7 | --- | 70 | $H_2O/CH_3CN$ (1:1) | 0 |
| 8 | --- | 25 | $CH_3CN$ | 0 |
| 9 | --- | 70 | DMSO | 0 |
| 10 | --- | 70 | Dioxane | 5 |
| 11 | --- | 70 | $CH_3CN$ | 62 |
| 12[b] | --- | 70 | $CH_3CN$ | 83 |
| 13 | --- | 70 | DCE | 0 |
| 14 | --- | 90 | $CH_3CN$ | 35 |

[a] Reaction conditions: sodium benzene sulfinate (2.0 equiv.), S (2 equiv.), acetobromo-D-glucose **2a** (1.0 equiv.), additive (0.2 equiv.), solvent (0.5 mL), reaction time 2 h. Isolated yields are based on reactant **2a.**
[b] Under $N_2$.

The screening started with using phase transfer catalyst $Bu_4NBr$ as an additive in DMF at 50 °C. This reaction failed to give expected product **3a** (Table 1, entry 1). Replacing $Bu_4NBr$ with $Bu_4NI$ as a phase transfer catalyst also didn't give any product (entry 2). Increasing the reaction temperature to 70°C still failed to give any **3a** (entry 3). Raising the temperature to 90 °C in $CH_3CN$, the reaction only generated a 7% yield of **3a** (entry 4). Using water as the solvent at 25°C didn't produce any **3a** (entry 5). Changing solvent from $H_2O$ to $H_2O$/THF(1:1) or $H_2O/CH_3CN$ (1:1) at 70 °C also didn't afford any **3a** (entries 6, 7). When $CH_3CN$ was solely employed, no **3a** was generated at 25°C (entry 8). Replacing $CH_3CN$ with DMSO as the solvent at 70 °C also didn't lead to any **3a** (entry 9). Employing dioxane gave a 5% yield of **3a** (entry 10). Using $CH_3CN$ as the solvent at 70 °C generated **3a** in 62% (entry 11). When this same reaction was performed under $N_2$, it afforded 83% of **3a** (entry 12). Using DCE as the solvent didn't give **3a** (entry 13). Using $CH_3CN$ as the solvent at 90 °C

**Table 2.** Synthesis of glycosyl phenylthiosulfonates using different sodium arene sulfinates, S powder and glycosyl bromides[a]

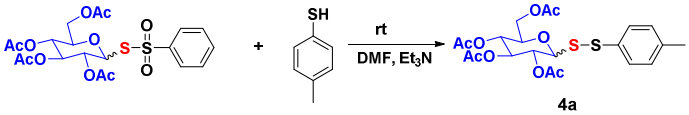



[a] Reaction conditions: sodium arene sulfinate (2.0 equiv.), S (2 equiv.), glycosyl bromide **2** (1.0 equiv.), additive (0.2 equiv.), solvent (0.5 mL), reaction time 2 h. Isolated yields are based on reactant **2**, under $N_2$.

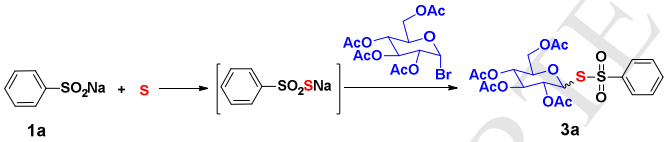
under air produced 35% of **3a** (entry 14). So the optimized reaction conditions selected using both S and an acetobromo-*α*-D-glucose **2a** to generate glycosyl phenylthiosulfonates are: the sodium benzene sulfinate (2.0 equiv.), S (2 equiv.), acetobromo-D-glucose **2a** (1.0 equiv.) in $CH_3CN$ at 70 °C under $N_2$ for 2h.

Under the optimum conditions defined above, different sodium aromatic sulfinates with electron-withdrawing (-F, -Cl and -Br) and electron-donating substitutes (-$CH_3$, -$OCH_3$) and various acetated D- or L-glycosyl bromides (including acetyl-D-glucopyranosyl bromide, acetyl-D-arabinopyranosyl bromide, acetyl-L-arabinopyranosyl bromide, acetyl-D-galactopyranosyl bromide, acetyl-D-xylopyranosyl bromide and acetyl-L-xylopyranosyl bromide) were selected and tried in these reactions. Most reactions of sodium arene sulfinates with different glycosyl bromides proceeded well, giving good yields of glycosyl phenylthiosulfonates. The isolated yields of most reactions ranged from 69% to 90%, giving different ratios of *α*/*β* anomers (shown in Table 2). It was easily found that *β*-diastereoisomers were more favorable anomer products. But glycosyl bromides without any functions on the 2-position failed to give any expected products. Different ratios of α/β anomers of glycosyl phenylthiosulfonates were determined by H-NMR spectra. The resultant glycosyl phenylthiosulfonate reacted with *p*-methylbezenethiol in DMF at room temperature, generating disulfide **4a** in a good yield. Its NMR spectrum matched well the one previously reported in the literature.




**Scheme 2**. Reaction with PhSH

Based on previous reports,[14] a simple but plausible mechanism is proposed in Scheme 3, in which sodium benzene sulfinate reacted with S first to give sodium benzenesulfonothioate intermediate, then it further reacted with the glycosyl bromide to afford glycosyl phenylthiosulfonate.




**Scheme 3**. Possible reaction mechanism

## 3. Conclusion

In summary, we reported a convenient one-pot and multiple-component synthesis of glycosyl phenylthiosulfonates by using different sulfinates, S powder and glycosyl bromides as starting materials. Most reactions afforded good yields of glycosyl phenylthiosulfonates under mild conditions. Glycosyl phenylthiosulfonates have been proved to be valuable reagents for the S-glycosylation decoration of organic compounds and proteins. Further study to expand the application scope of glycosyl phenylthiosulfonates are still underway in our group.

## 4. Experimental

**General:** All reactions were carried out in sealed tubes; stirring was achieved with an oven-dried magnetic stirring bar. Solvents were purified by standard methods unless otherwise noted. Commercially available reagents were purchased from Aladdin Company in China and used throughout without further purification other than those detailed below. Flash column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by TLC analysis. Deuterated solvents were purchased from Cambridge Isotope laboratories.$^1$H and $^{13}$C NMR spectra were recorded on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz respectively. HRMS spectrometry (LC-HRMS) was recorded on a LXQ Spectrometer (Thermo Scientific) operating in the ESI-TOF mode (MeOH as a solvent).

**General procedure for the synthesis of compounds 3.**

(2R,3R,4S,5R)-2-(Acetoxymethyl)-6-bromotetrahydro-2H-pyran-3,4,5-triyl triacetate **2a** (0.5 mmol, 1.0 equiv.), S (2.0 equiv.) and sodium benzene sulfinate (2.0 equiv.) were added to round-bottom flasks with acetonitrile (0.5 mL) in it. Then the mixture was stirred at 70$^0$C. After 2 h, the reaction was cooled down to room temperature. The reaction mixture was quenched with water, then extracted with ethyl acetate, dried over anhydrous $Na_2SO_4$ and concentrated under vacuum. The residue was purified by silica gel flash chromatography (petroleum ether : EtOAc = 5: 1) to give product **3a** as a yellow oil in 83% yield. The same procedure was applied to the production of compound **3b-n**.

**General procedure for the synthesis of compounds 4a.**

2,3,4,6-Tetra-O-acetyl-*β*-D-glucopyranosyl phenylthiosulfonate (**3a**) (0.5 mmol, 1.0 equiv.), *p*-methylbezenethiol (1.5 equiv.), Triethylamine (1.5 equiv.) were added to DMF (1.0 mL) in round-bottom flasks under nitrogen atmosphere. The mixture was stirred at room temperature for 24 h. The reaction mixture was quenched with water, then extracted with ethyl acetate, dried over anhydrous $Na_2SO_4$ and concentrated under vacuum. The residue was purified by silica gel flash chromatography (petroleum ether : EtOAc = 10:1) to give product **4a** as a yellow oil in 76% yield.

***2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl phenylthiosulfonate (3a)*** [3b]
Following the general procedure, isolated yield (83%) as a colorless oil; IR: 2945, 2361, 1750, 1375, 1331, 1228, 1146 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz):δ 8.05 – 7.86 (m, 2H), 7.76 – 7.44 (m, 3H), 5.32 – 5.18 (m, 2H), 5.11 – 4.96 (m, 2H), 4.11 (dd, *J* = 12.5, 4.5 Hz, 1H), 3.91 (dd, *J* = 12.5, 2.4 Hz, 1H), 3.79 – 3.69 (m, 1H), 2.16 – 1.96 (m, 12H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 170.35, 169.83, 169.29, 169.25, 145.85, 134.01, 129.23, 126.97, 86.65, 76.37, 73.42, 68.69, 67.72, 61.50, 20.66, 20.49,20.44.MS (ESI-TOF) m/z calculated for $C_{20}H_{24}NaO_{11}S_2^+$527.06(M+Na)$^+$, found 527.42.

***2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl p-chlorophenylthiosulfonate (3b)***
Following the general procedure, isolated yield (74%) as a colorless oil; IR: 3094, 2948, 1755, 1370, 1230, 1149 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz): δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.52 (d, *J* = 8.7 Hz, 2H), 5.35 – 5.21 (m, 2H), 5.17 – 4.98 (m, 2H), 4.18 – 4.07 (m, 1H), 4.01 (dd, *J* = 12.5, 2.4 Hz, 1H), 3.77 (ddd, *J* = 10.2, 4.6, 2.4 Hz, 1H), 2.13 – 1.97 (m, 12H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ170.51, 170.26, 169.79, 169.28, 169.26, 144.29, 140.66, 129.58, 129.49, 129.46, 128.47, 86.64, 73.42, 73.33, 68.65, 67.79, 67.74, 61.57, 61.49, 20.64, 20.56, 20.51, 20.48, 20.47, 20.45. MS (ESI-TOF) m/z calculated for $C_{20}H_{23}ClNaO_{11}S_2^+$561.02(M+Na)$^+$, found 561.50.

***2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl p-fluorophenylthiosulfonate (3c)***
Following the general procedure, isolated yield (71%) as a colorless oil; IR: 2953, 1756, 1588, 1493, 1228, 1145 cm$^{-1}$; 1H-NMR ($CDCl_3$, 400 MHz): δ 7.97 (dd, *J* = 9.0, 4.9 Hz, 2H), 7.22 (dd, *J* = 9.0, 8.1 Hz, 2H), 5.33 – 5.20 (m, 2H), 5.15 – 4.96 (m, 2H), 4.14 – 4.07 (m, 1H), 4.00 (dd, *J* = 12.6, 2.5 Hz, 1H), 3.81 – 3.71 (m, 1H), 2.11 – 1.98 (m, 12H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 170.25, 169.79, 169.28, 169.26, 131.06, 130.96, 130.03, 129.93, 116.60, 116.37, 86.62, 73.42, 73.32, 68.64, 67.75, 61.50, 20.62, 20.49, 20.47, 20.45. MS (ESI-TOF) m/z calculated for $C_{20}H_{23}FNaO_{11}S_2^+$545.05 (M+Na)$^+$, found 545.46.

***2,3,4-Tri-O-acetyl-β-D-arabinopyranosyl phenylthiosulfonate (3d)***
Following the general procedure, isolated yield (80%) as a colorless oil; IR: 2970, 2361, 1752, 1372, 1331, 1221, 1147 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz): δ 8.09 – 7.83 (m, 2H), 7.75 – 7.47 (m, 3H), 5.45 – 5.37 (m, 1H), 5.28 (d, *J* = 10.0 Hz, 1H), 5.20 (td, *J* = 10.0, 3.3 Hz, 1H), 5.12 (dd, *J* = 9.8, 3.3 Hz,

1H), 4.03 – 3.89 (m, 2H), 3.88 – 3.77 (m, 1H), 2.12 – 1.92 (m, 12H);$^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 170.16, 169.94, 169.69, 169.54, 145.93, 133.98, 129.29, 129.22, 127.95, 126.98, 87.25, 74.98, 71.46, 66.83, 65.87, 60.77, 20.64, 20.56, 20.54, 20.51, 20.47, 20.45. MS (ESI-TOF) m/z calculated for $C_{20}H_{24}NaO_{11}S_2^+$527.06 $(M+Na)^+$, found 527.38.

***2,3,4-Tri-O-acetyl-β-D-arabinopyranosyl p-methoxyphenylthiosulfonate (3e)***

Following the general procedure, isolated yield (77%) as a colorless oil; IR: 2966, 1751, 1372, 1334, 1220, 1145 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz):δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.44 – 7.28 (m, 2H), 5.42 (dd, *J* = 3.4, 1.0 Hz, 1H), 5.27 (d, *J* = 10.1 Hz, 1H), 5.20 (td, *J* = 10.1, 5.0 Hz, 1H), 5.11 (dd, *J* = 9.6, 3.3 Hz, 1H), 4.01 – 3.91 (m, 2H), 3.90 – 3.80 (m, 1H), 2.45 (d, *J* = 8.6 Hz, 3H), 2.19 – 1.91 (m, 12H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ170.17, 169.94, 169.71, 169.53, 145.80, 145.25, 143.14, 139.52, 129.86, 129.77, 128.04, 127.07, 89.34, 87.21, 75.08, 74.97, 71.50, 67.52, 66.95, 66.85, 65.90, 61.06,60.77, 60.32, 21.71, 21.63, 20.62, 20.55, 20.52, 20.48, 20.45. MS (ESI-TOF) m/z calculated for $C_{21}H_{26}NaO_{11}S_2^+$541.08 $(M+Na)^+$, found 541.47.

***2,3,4-Tri-O-acetyl-β-L-arabinopyranosyl p-chlorophenylthiosulfonate (3f)***

Following the general procedure, isolated yield (73%) as a colorless oil; IR: 2968, 1577, 1593, 1371, 1228, 1146 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz):δ 7.85 (d, *J* = 9.0 Hz, 2H), 6.99 (s, 2H), 5.40 (t, *J* = 3.9 Hz, 1H), 5.28 – 5.14 (m, 2H), 5.10 (dd, *J* = 9.5, 3.3 Hz, 1H), 4.18 – 3.99 (m, 1H), 4.00 – 3.91 (m, 2H), 3.88 (d, *J* = 7.3 Hz, 3H), 2.13 – 1.95 (m, 12H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 170.33, 170.21, 169.98, 169.77, 169.74, 169.56, 164.35, 163.92, 137.57, 130.39, 129.44, 114.37, 114.27, 87.14, 75.07, 74.91, 71.49, 66.87, 65.90, 60.81, 55.84, 55.81, 20.63, 20.58, 20.53, 20.46. MS (ESI-TOF) m/z calculated for $C_{21}H_{26}NaO_{12}S_2^+$557.07 $(M+Na)^+$, found 557.48.

***2,3,4-Tri-O-acetyl-β-L-arabinopyranosyl p-bromophenylthiosulfonate (3g)***

Following the general procedure, isolated yield (67%) as a colorless oil; IR: 2964, 1752, 1589, 1493, 1221, 1145 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz): δ 7.98 (dd, *J* = 9.0, 4.9 Hz, 2H), 7.23 (dd, *J* = 9.0, 8.1 Hz, 2H), 5.43 (dd, *J* = 3.4, 0.9 Hz, 1H), 5.31 (d, *J* = 10.1 Hz, 1H), 5.21 (t, *J* = 9.9 Hz, 1H), 5.13 (dd, *J* = 9.8, 3.3 Hz, 1H), 4.06 – 3.96 (m, 2H), 3.94 – 3.84 (m, 1H), 2.12 – 2.03 (m, 9H), 1.97 (s, 3H);$^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 170.17, 169.92, 169.69, 169.56, 166.94, 164.39, 142.02, 130.07, 129.97, 116.58, 116.35, 87.30, 75.14, 71.42, 66.88, 65.82, 60.94, 60.33,20.62,20.57, 20.51, 20.44. MS (ESI-TOF) m/z calculated for $C_{20}H_{23}FNaO_{11}S_2^+$ 545.05 $(M+Na)^+$, found 545.43.

***2,3,4-Tri-O-acetyl-β-L-arabinopyranosyl 2,3-dihydrobenzofuranylthio-sulfonate (3h)***

Following the general procedure, isolated yield (72%) as a colorless oil; IR: 2966, 1752, 1581, 1371, 1222, 1149 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz): δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.51 (d, *J* = 8.8 Hz, 2H), 5.42 (dd, *J* = 3.2, 0.9 Hz, 1H), 5.31 (d, *J* = 10.0 Hz, 1H), 5.20 (t, *J* = 9.9 Hz, 1H), 5.13 (dd, *J* = 9.8, 3.3 Hz, 1H), 4.06 – 3.96 (m, 2H), 3.94 – 3.82 (m, 1H), 2.11 – 1.95 (m, 12H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 170.18, 169.92, 169.68, 169.57, 144.38, 140.59, 129.47, 128.51, 87.28, 75.16, 71.38, 66.90, 65.80, 60.99, 20.65, 20.57, 20.52,20.45.MS(ESI-TOF) m/z calculated for $C_{20}H_{23}ClNaO_{11}S_2^+$ 561.02 $(M+Na)^+$, found 561.50.

***2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl p-fluorophenylthiosulfonate (3i)***

Following the general procedure, isolated yield (69%) as a colorless oil; IR: 2973, 1749, 1367, 1227, 1151, 1069 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz):δ 7.87 – 7.79 (m, 2H), 7.70 (d, J = 8.7 Hz, 2H), 5.44 (dd, *J* = 3.4, 1.1 Hz, 1H), 5.31 (d, *J* = 10.2 Hz, 1H), 5.22 (t, *J* = 9.9 Hz, 1H), 5.13 (dd, *J* = 9.7, 3.3 Hz, 1H), 4.08 – 3.96 (m, 2H), 3.90 (dd, *J* = 10.1, 5.2 Hz, 1H), 2.13 – 1.98 (m, 12H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 170.19, 169.92, 169.69, 169.56, 144.94, 132.48, 129.23, 128.52, 87.34, 75.22,71.43, 66.87, 65.81, 60.97, 20.67, 20.58, 20.54, 20.46. MS (ESI-TOF) m/z calculated for $C_{20}H_{23}BrNaO_{11}S_2^+$604.97 $(M+Na)^+$, found 605.39.

***2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl p-tolylthiosulfonate (3j)***

Following the general procedure, isolated yield (74%) as a colorless oil; IR: 2977, 1751, 1593, 1477, 1369, 1221, 1141 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz):δ 7.96 – 7.73 (m, 2H), 6.99 (t, *J* = 9.2 Hz, 2H), 5.58 (d, *J* = 5.1 Hz, 1H), 5.24 – 5.07 (m, 3H), 3.89 (d, *J* = 6.3 Hz, 3H), 3.84 (dd, *J* = 12.2, 6.9 Hz, 1H), 3.68 – 3.55 (m, 1H), 2.13 – 2.00 (m, 9H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 169.77, 169.17, 169.13,164.28,163.80, 137.48, 130.48, 129.42, 114.32, 114.24, 86.42, 68.64, 68.21, 65.83, 55.83,55.77, 20.76, 20.70, 20.66, 20.62. MS (ESI-TOF) m/z calculated for $C_{18}H_{22}NaO_{10}S_2^+$485.05 $(M+Na)^+$, found 485.43.

***2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl p-chlorophenylthiosulfonate (3k)***

Following the general procedure, isolated yield (78%) as a colorless oil; IR: 2979, 1752, 1578, 1372, 1221, 1148 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz): δ 7.84 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 8.7 Hz, 2H), 5.62 (d, *J* = 4.9 Hz, 1H), 5.26 – 5.15 (m, 2H), 5.08 (dd, *J* = 5.9, 4.9 Hz, 1H), 3.78 (dd, *J* = 12.1, 6.9 Hz, 1H), 3.64 – 3.51 (m, 1H), 2.11 – 1.98 (m, 9H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 169.65, 169.12, 169.03, 144.24, 140.39, 129.49, 129.45, 128.49, 86.62, 68.66, 67.94, 65.60, 62.10, 20.64, 20.61, 20.58. MS (ESI-TOF) m/z calculated for $C_{17}H_{19}ClNaO_9S_2^+$489.00 $(M+Na)^+$, found 489.38.

***2,3,4-Tri-O-acetyl-β-L-xylopyranosyl phenylthiosulfonate (3l)***

Following the general procedure, isolated yield (65%) as a colorless oil; IR: 2974, 1752, 1572, 1372, 1220, 1146 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz): δ 7.87 – 7.77 (m, 2H), 7.75 – 7.65 (m, 2H), 5.66 (d, *J* = 4.8 Hz, 1H), 5.23 (ddd, *J* = 9.5, 7.5, 3.3 Hz, 2H), 5.12 (dd, *J* = 5.9, 4.8 Hz, 1H), 3.82 (dd, *J* = 12.1, 7.1 Hz, 1H), 3.68 – 3.53 (m, 1H), 2.16 – 2.02 (m, 9H); $^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 169.71, 169.14, 169.06, 144.80, 132.47, 129.09, 128.51, 86.66, 68.71, 67.92, 65.55, 62.00, 20.69, 20.67, 20.63. MS (ESI-TOF) m/z calculated for $C_{17}H_{19}BrNaO_9S_2^+$532.95 $(M+Na)^+$, found 533.32.

***2,3,4-Tri-O-acetyl-β-L-xylopyranosyl p-tolylthiosulfonate (3m)***

Following the general procedure, isolated yield (73%) as a colorless oil; IR: 2923, 2852, 1746, 1373, 1211, 1144 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz):δ 8.11 – 7.82 (m, 2H), 7.76 – 7.43 (m, 3H), 5.68 (d, *J* = 5.2 Hz, 1H), 5.10 (t, *J* = 5.8 Hz, 1H), 4.90 (t, *J* = 5.4 Hz, 1H), 4.73 (td, *J* = 5.6, 3.6 Hz, 1H), 3.97 (dd, *J* = 12.7, 3.6 Hz, 1H), 3.43 (dd, *J* = 12.7, 5.4 Hz, 1H), 2.19 – 1.90 (m, 9H);$^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 169.60, 169.09, 168.80, 145.77, 133.90, 129.18, 127.04, 86.54, 68.21, 68.17, 66.86, 62.70, 20.73, 20.63, 20.58. MS (ESI-TOF) m/z calculated for $C_{17}H_{20}NaO_9S_2^+$455.04 $(M+Na)^+$, found 455.39.

***2,3,4-Tri-O-acetyl-β-D-xylopyranosyl phenylthiosulfonate (3n)***

Following the general procedure, isolated yield (76%) as a colorless oil; IR: 3435, 1763, 1748, 1218, 1140, 1067 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz):δ 7.99 – 7.67 (m, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 5.63 (d, *J* = 5.3 Hz, 1H), 5.08 (t, J = 5.8 Hz, 1H), 4.88 (t, *J* = 5.5 Hz, 1H), 4.75 – 4.64 (m, 1H), 3.96 (dd, *J* = 12.7, 3.6 Hz, 1H), 3.42 (dd, *J* = 12.7, 5.5 Hz, 1H), 2.42 (s, 3H), 2.15 – 1.95 (m, 9H);$^{13}$C-NMR ($CDCl_3$, 100 MHz)：δ 169.61, 169.09, 168.82,145.09, 142.97, 129.74, 127.08, 86.46, 68.29, 68.19,66.91, 62.77, 21.65, 20.72, 20.61, 20.57. MS (ESI-TOF) m/z calculated for $C_{18}H_{22}NaO_9S_2^+$469.06 $(M+Na)^+$, found 469.45.

***4-Tolylphenyl-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl) disulfide (4a)*** [16]

isolated yield (72%) as a colorless oil; 1H-NMR (CDCl3, 400 MHz): δ 7.51 (d, J = 8.2 Hz, 2H), 7.11 (d, J = 7.9 Hz, 2H), 5.42 – 5.21 (m, 2H), 5.21 – 5.03 (m, 1H), 4.74 – 4.50 (m, 1H), 4.20 (dd, J = 12.4, 4.6 Hz, 1H), 4.12 (dd, J = 12.4, 2.3 Hz, 1H), 3.76 (ddd, J = 10.0, 4.6, 2.4 Hz, 1H), 2.34 (s, 3H), 2.04 (d, J = 4.5 Hz, 12H). MS (ESI-TOF) m/z calculated for C21H26NaO9S2+ 509.09 (M+Na)+, found 509.31.

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**Highlights:**

One-pot Synthesis of Glycosyl Phenylthiosulfonates from Sulfinate，S and Glycosyl Bromides