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# Synthesis of 2,3-unsaturated thioglycopyranosides mediated by lithium tetrafluoroborate

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## Abstract:

Treatment of tri-*O* acetyl-**D**-glucal **1** with diverse thiols **2-7** in the presence of $LiBF_4$ in $CH_3CN$, furnished aryl/alkyl 2,3-unsaturated thioglycopyranosides **8-13** (56-72%).

***Keywords*** : Ferrier rearrangement, thioglycosides, glycosides, lithium fluoroborate, Lewis acid.

Thioglycosides are potential glycosyl donors[1] by virtue of activation by thiophilic agents and are useful intermediates in natural products synthesis. Catalysts such as $SnCl_4$,[2] have been used for the synthesis of 2,3-unsaturated thioglycosides. However, the $SnCl_4$ catalysed reaction of thiols with glycals is kinetically controlled, also forming the undesired 3-thioglycal. This problem was overcome by Dunkerton using $BF_3.Et_2O$[3] as catalyst and $(CH_3Si)_3SR$ as the nucleophile to afford 1-thio-hex-2-enopyranosides with stereo- and regioselectivity.

Lithium tetrafluoroborate, a mild Lewis acid, has been used for the deprotection of silyl ethers,[4] for the hydrolysis of acetals and as a Diels-Alder reaction catalyst.[5] $LiBF_4$ has also been used for the cleavage of β-trimethylsilyl protected glycosides and benzylidene acetals[6] and as supporting electrolyte for the electrochemical oxidation of phenylthioglycosides.[7]

We have now observed that lithium tetrafluoroborate in acetonitrile (LTAN) is an excellent catalyst for the synthesis of 2,3-unsaturated thioglycopyranosides using unactivated thiols through Ferrier rearrangement.[8] Reaction of tri-*O*-acetyl-**D**-glucal **1** with the thiophenol in LTAN at ambient temperature for 7 hours furnished 2,3-unsaturated thiophenyl glycopyranoside **8** in 65% yield with the α-anomer as the major product. Likewise, other thiols led to facile thioglycosidation upon reaction with tri-*O*-acetyl-**D**-glucal in LTAN affording the corresponding 2,3-unsaturated thioglucopyranosides in good yields.

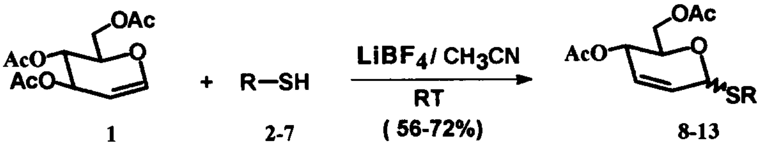

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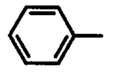
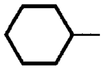
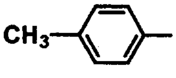
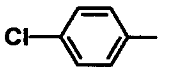
**Table 1**. $LiBF_4$/ $CH_3CN$ mediated glycosylation of thiols **2-7** with tri-*O*-acetyl-**D**-glucal **1**.

| Thiol ( RSH) R= | | Product (Time, yield, α:β)# | Thiol ( RSH) R= | | Product (Time, yield, α:β)# |
|---|---|---|---|---|---|
|  | 2 | **8** (7 h, 60%, 8:1) |  | 5 | **11** (7 h, 72%, 9:1) |
|  | 3 | 9 (7 h, 65%,4:1) | $CH_3CH_2$— | 6 | **12** (6 h, 64%, 4:1 ) |
|  | 4 | **10** (8 h, 56%, 6:1) | $CH_3(CH_2)_4CH_2$- | 7 | **13** (10 h, 62%, 4:1) |

# Isolated yields of pure products with compatible $^1H$ and $^{13}C$ NMR spectral data

We have also compared the efficacy of other fluoroborates such as $(C_6H_5CH_2)(C_6H_5)_3P$ $BF_4$, $(C_6H_5CH_2)(C_2H_5)_3N$ $BF_4$, $(n\text{-}Bu)_4N$ $BF_4$, $NaBF_4$, $KBF_4$/18 crown 6, $NH_4BF_4$ in $CH_3CN$. However, none of these salts was found to be effective. In summary, we have observed that $LiBF_4$ in $CH_3CN$ is a useful catalyst for the synthesis of 2,3-unsaturated aryl and alkyl thioglycopyranosides, otherwise difficultly accessed, under mild conditions. The isolated yields are good and the reaction is amenable for scale-up.

In a typical experiment, a mixture of tri-*O*-acetyl-D-glucal **1** (5 mmol), thiol (6 mmol) and anhydrous $LiBF_4$ (6 mmol) in dry $CH_3CN$ (5-6 mL) was stirred at ambient temp.. After completion (tlc), the reaction mixture was quenched by addition of water (25 mL) and extracted with $CH_2Cl_2$ (3 x 25 mL), dried, filtered and purified by flash chromatography on silica gel.

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