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# Reaction of 5,6-cyclic sulfates derived from glycofuranoses with bases. A one-pot synthesis of 6-deoxy-hexofuranos-5-ulose derivatives

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**Abstract**

Methyl 2,3-*O*-isopropylidene-5,6-*O*-sulfuryl-α-D-mannofuranoside **1** reacted with nitrogen bases to give the corresponding aminosulfates. Strong bases such as sodium *tert*-butoxide or *n*-butyllithium afforded methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hexofuranos-5-uloside **7**. The reaction was optimized with sodium *tert*-butoxide and applied to three other 5,6-cyclic sulfates derived from aldofuranosides to give the corresponding keto-aldoses in good yields. 

The cyclic sulfates of *vic*-diols are well known and have been used as electrophiles in a variety of nucleophilic displacement reactions.[1] Such sulfates are obtained by catalytic oxidation of cyclic sulfites with ruthenium trichloride and sodium periodate.[2]

We have already reported the regioselective synthesis of 6-*O*-alkyl and 6-alkynyl-6-deoxy compounds via a 5,6-cyclic sulfate derived from mannofuranose. This method has been extended to pseudo-di or trisaccharides and pseudo-*C*-disaccharides.[3–5]

More recently, it has been shown that 1,2-*O*-sulfuryldecane failed to generate C–C bonds with some carbon nucleophiles. For example, 1,2-*O*-sulfuryldecane reacted with *n*-butyllithium to give, unexpectedly, dodecanal in 99% yield.[6]

We herein report on the reactivity of 5,6-cyclic sulfates of glycofuranoses towards various organic and inorganic bases.

The results of the reaction of methyl 2,3-*O*-isopropylidene-5,6-*O*-sulfuryl-α-D-mannofuranoside **1**[3] with bases are illustrated in Table 1.

As expected, the use of weak bases such as pyridine (entry 1), triethylamine (entry 2) or DBU (entry 3), gave the corresponding aminosulfates **2**,[7] **3**[8] and **4**[9] in quantitative yields. Similarly, reactions with strong nitrogen bases such as sodium amide (entry 5) and LDA (entry 6) with the 5,6-cyclic sulfate **1** also gave the expected substitution products **5**[10] and **6**,[11] respectively (Scheme 1).

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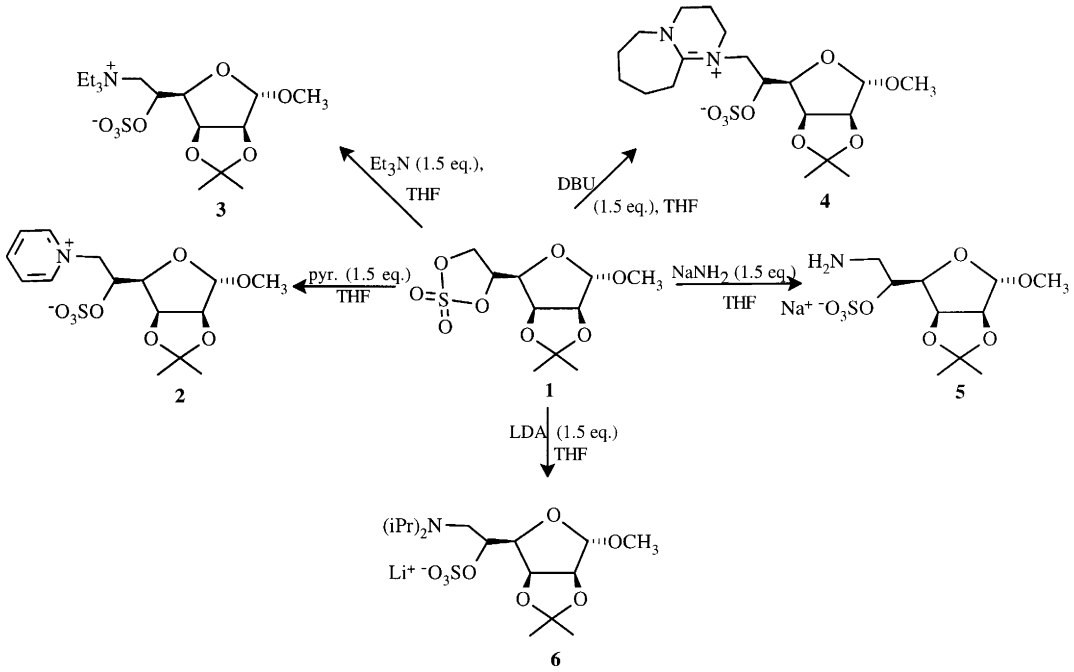
Table 1
Reaction of the cyclic sulfate derivative **1** with basic reagents

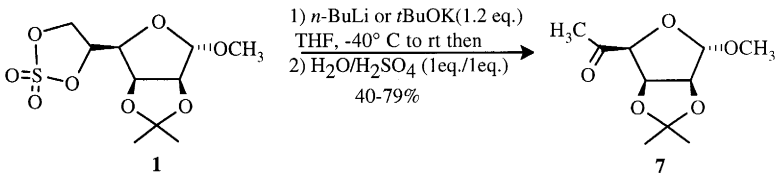
| Entry | Base (or nucleophile) 1.5 eq. | Reaction time | Temperature | Yield % | Product |
|---|---|---|---|---|---|
| 1 | $C_5H_5N$ | overnight | rt | 95 | **2** |
| 2 | $Et_3N$ | overnight | rt | 95 | **3** |
| 3 | DBU | overnight | rt | 92 | **4** |
| 4 | $(CH_3)_3COK$ | 25 min | 0° C then rt | 79 | **7** |
| 5 | $NaNH_2$ | overnight | rt | 70 | **5** |
| 6 | $(iPr)_2NLi$ | 1 h | - 40° C | 92 | **6** |
| 7 | *n*-BuLi | 20 min | - 40° C then rt | 40 | **7** |
| 8 | *tert*-BuLi | 10 min | - 40° C | - | complex mixture |
| 9 | NaH | 16 h | rt then 70°C | - | complex mixture |




Scheme 1.

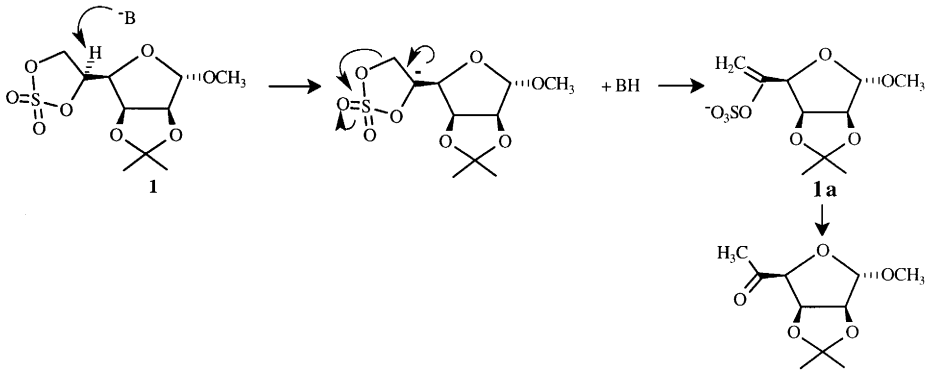
In contrast, reaction of the 5,6-cyclic sulfate **1** with *n*-butyllithium (entry 7) followed by acidic hydrolysis gave the ketone compound methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hexofuranos-5-uloside **7**[12,13] in 40% yield and no substitution product was detected (Scheme 2). Some degradation of the 5,6-cyclic sulfate **1** was observed which could explain the relatively low yield of **7**.

The optimum yield (79%) obtained for the methyl hexofuranos-5-uloside compound **7** was when **1** reacted with sodium *tert*-butoxide (entry 4, Scheme 2). It was found that treatment with stronger bases such as NaH and *tert*-BuLi resulted in degradation of **1** (Table 1). A mechanism for the formation of **7** is given in Scheme 3.




1 7

Scheme 2.



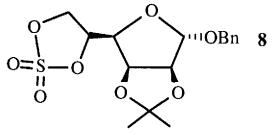
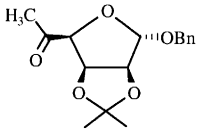
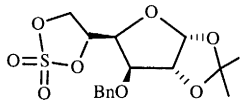
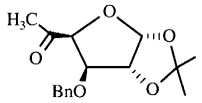
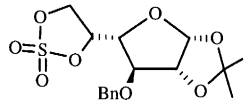
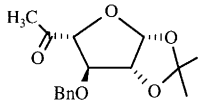

1 1a

Scheme 3.

It is proposed that base catalyses elimination and generates the olefin **1a** which hydrolyses to the ketone **7**.

The generality of this reaction was exemplified by treatment of sodium *tert*-butoxide with the related substrates **8**,[4] **10**[14] and **12**[15] to give the ketones **9**[16] (77%), **11**[17] (73%) and **13**[18] (72%), respectively (Table 2).

Table 2
Reaction of 5,6-cyclic sulfate glycofuranoses with sodium *tert*-butoxide

| Substrate | | Product | | Yield % |
|---|---|---|---|---|
|  | **8** |  | **9** | 77 |
|  | **10** |  | **11** | 73 |
|  | **12** |  | **13** | 72 |

In conclusion, we described a one-pot synthesis of manno, gluco and galactofurano-5-ulose derivatives in 72–79% yields by treatment of corresponding 5,6-*O*-sulfuryl compounds with sodium *tert*-butoxide. It is envisaged that 5,6-deoxy-5-oxo derivatives are potential precursors of aminosugars and cyclitols.

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6. Hoye, T. R.; Crawford, K. B. *J. Org. Chem.* **1994**, *59*, 520.
7. Data for **2**: $^{13}$C NMR ($CDCl_3$) $\delta$ 148.9 (C-4′), 147.9 (C-2′, C-6′), 130.4 (C-3′, C-5′), 116.1 ($C(CH_3)_2$), 109.1 (C-1), 86.3 (C-2), 81.4 (C-3), 81.1 (C-4), 77.0 (C-5), 62.7 (C-6), 56.6 ($OCH_3$), 27.1, 25.7 ($C(CH_3)_2$).
8. Data for **3**: $^{13}$C NMR ($CDCl_3$) $\delta$ 112.3 ($C(CH_3)_2$), 106.5 (C-1), 84.1 (C-2), 81.2 (C-3), 79.7 (C-4), 68.8 (C-5), 56.3 (C-6), 54.3 ($OCH_3$), 53.7 (3 $CH_2$), 25.4, 23.4 ($C(CH_3)_2$), 7.1 (3 $CH_3$).
9. Data for **4**: $^{13}$C NMR ($CDCl_3$) $\delta$ 170.1 (C-10′), 115.9 ($C(CH_3)_2$), 108.7 (C-1), 86.1 (C-2), 82.3 (C-3), 81.8 (C-4), 77.1 (C-5), 57.4 ($CH_2$), 57.1 ($OCH_3$), 55.9 ($CH_2$), 51.4 (C-6), 50.7 (C-9′), 30.5 (2 $CH_2$), 27.6 ($CH_2$), 27.1, 25.5 ($C(CH_3)_2$), 24.8, 21.7 ($CH_2$).
10. Data for **5**: $^{13}$C NMR ($D_2O$) $\delta$ 115.3 ($C(CH_3)_2$), 108.8 (C-1), 86.4 (C-2), 82.9 (C-3), 82.2 (C-4), 76.1 (C-5), 56.9 ($OCH_3$), 51.7 (C-6), 27.7, 26.3 ($C(CH_3)_2$).
11. Data for **6**: $^{13}$C NMR ($CDCl_3$) $\delta$ 112.4 ($C(CH_3)_2$), 106.8 (C-1), 84.3 (C-2), 80.1 (C-3), 79.7 (C-4), 69.9 (C-5), 59.7 (C-6), 54.8 ($OCH_3$), 44.8 (2 CH), 25.7 ($C(CH_3)_2$), 23.8 ($C(CH_3)_2$, 4 $CH_3$).
12. Data for **7**: IR: C=O (1719 $cm^{-1}$); $^1$H NMR ($CDCl_3$) $\delta$ 4.98 (s, 1H, H-1, $J_{1,2}$ 0), 4.94 (dd, 1H, H-3, $J_{2,3}$ 5.8, $J_{3,4}$ 4.1), 4.50 (d, 1H, H-2), 4.37 (d, 1H, H-4), 3.28 (s, 3H, $OCH_3$), 2.19 (s, 3H, H-6a,b,c), 1.35 (s, 3H, $C(CH_3)_2$), 1.21 (s, 3H, $C(CH_3)_2$); $^{13}$C NMR ($CDCl_3$) $\delta$ 204.2 (C-5), 113.0 ($C(CH_3)_2$), 107.4 (C-1), 84.8 (C-4), 84.2 (C-2), 80.7 (C-3), 54.8 ($OCH_3$), 27.7 (C-6), 25.7, 24.5 ($C(CH_3)_2$).
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15. Data for **12**: $^1$H NMR ($CDCl_3$) $\delta$ 7.38–7.30 (m, 5H, CH(Ph)), 5.84 (d, 1H, H-1, $J_{1,2}$ 3.8), 4.99 (m, 1H, H-5), 4.69 (d, 1H, $CH_2$(Bn)), 4.65 (d, 1H, H-2), 4.54–4.43 (m, 3H, $CH_2$(Bn), H-6, H-6′), 4.06 (t, 1H, H-4, $J_{3,4}$ 5.1, $J_{4,5}$ 5.1), 3.92 (d, 1H, H-3), 1.52 (s, 3H, $C(CH_3)_2$), 1.35 (s, 3H, $C(CH_3)_2$); $^{13}$C NMR ($CDCl_3$) $\delta$ 136.3 ($C_{ipso}$), 128.7, 128.4, 128.1 (CH(Ph)), 114.6 ($C(CH_3)_2$), 105.3 (C-1), 84.8 (C-2), 81.5 (C-3), 81.1 (C-4), 79.9 (C-5), 72.3 ($CH_2$(Bn)), 68.9 (C-6), 27.4, 26.7 ($C(CH_3)_2$).
16. Data for **9**: IR: C=O (1721 $cm^{-1}$); $^1$H NMR ($CDCl_3$) $\delta$ 7.28 (m, 5H, CH(Ph)), 5.17 (s, 1H, H-1, $J_{1,2}$ 0), 4.99 (dd, 1H, H-3, $J_{2,3}$ 5.7, $J_{3,4}$ 4.2), 4.65 (t, 2H, $CH_2$(Bn)), 4.48 (d, 1H, H-2), 4.45 (d, 1H, H-4), 2.22 (s, 3H, H-6a,b,c), 1.38 (s, 3H, $C(CH_3)_2$), 1.23 (s, 3H, $C(CH_3)_2$); $^{13}$C NMR ($CDCl_3$) $\delta$ 204.1 (C-5), 136.9 ($C_{ipso}$), 128.4, 127.9 (CH(Ph)), 113.0 ($C(CH_3)_2$), 105.6 (C-1), 85.3 (C-4), 84.3 (C-2), 80.7 (C-3), 69.1 ($CH_2$(Bn)), 27.8 (C-6), 25.7, 24.5 ($C(CH_3)_2$).
17. Data for **11**: IR: C=O (1722 $cm^{-1}$); $^1$H NMR ($CDCl_3$) $\delta$ 7.32–7.18 (m, 5H, CH(Ph)), 6.04 (d, 1H, H-1, $J_{1,2}$ 3.5), 4.60–4.53 (m, 3H, H-3, H-4, CH(Bn)), 4.43 (d, 1H, $CH_2$(Bn)), 4.23 (d, 1H, H-3, $J_{3,4}$ 3.6), 2.18 (s, 3H, H-6a,b,c), 1.43 (s, 3H, $C(CH_3)_2$), 1.28 (s, 3H, $C(CH_3)_2$); $^{13}$C NMR ($CDCl_3$) $\delta$ 206.6 (C-5), 136.8 ($C_{ipso}$), 128.4, 127.9 (CH(Ph)), 112.2 ($C(CH_3)_2$), 105.8 (C-1), 85.4 (C-2), 83.6 (C-3), 81.7 (C-4), 72.3 ($CH_2$(Bn)), 29.6 (C-6), 26.8, 26.2 ($C(CH_3)_2$).
18. Data for **13**: IR: C=O (1718 $cm^{-1}$); $^1$H NMR ($CDCl_3$) $\delta$ 7.27 (m, 5H, CH(Ph)), 5.97 (d, 1H, H-1, $J_{1,2}$ 3.8), 4.59–4.53 (m, 3H, H-2, CH(Bn)), 4.43 (s, 2H, H-3, H-4), 2.27 (s, 3H, H-6a,b,c), 1.35 (s, 3H, $C(CH_3)_2$), 1.24 (s, 3H, $C(CH_3)_2$); $^{13}$C NMR ($CDCl_3$) $\delta$ 207.2 (C-5), 137.0 ($C_{ipso}$), 128.4, 127.9, 127.7 (CH(Ph)), 112.0 ($C(CH_3)_2$), 106.3 (C-1), 89.7 (C-4), 83.6 (C-2, C-3), 71.8 ($CH_2$(Bn)), 29.6 (C-6), 25.7, 25.6 ($C(CH_3)_2$).