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An efficient method for the preparation of 2-hydroxy- and 2-aminoglycals from glycosyl sulfoxides

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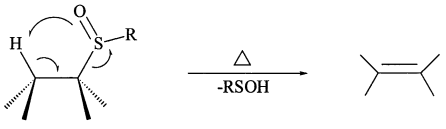
Abstract—A new and efficient route to 2-hydroxy- and 2-aminoglycals from glycosyl sulfoxides has been developed.

2-Hydroxy- and 2-aminoglycals are useful synthons for a variety of chemical reactions. They can serve as efficient 'indirect' β-D-mannosyl and β-D-mannosaminyl donors.[1] They are also excellent precursors to pyranoid enollactones[2] and *C*-glycosides.[3] In addition, 2-hydroxy- and 2-aminoglycals have been used in the synthesis of glycosidase inhibitors.[4]

To date, most reported methods for the preparation of 2-hydroxy- and 2-aminoglycals are through glycosyl halides under strong basic or acidic conditions.[5] The yields of such conversions are, however, relatively low. Here we report an efficient method for the synthesis of 2-hydroxy- and 2-aminoglycals through β-elimination of glycosyl sulfoxides.

The β-elimination of sulfoxides is well documented.[6] As shown in Scheme 1, it proceeds through a five-membered Ei mechanism with the stereoselective *syn*-elimination under heated conditions. This β-elimination reaction has been used in the preparation of α,β-unsaturated carbonyl derivatives for its mild condition. The dienes can also be prepared from the β-elimination of allylic sulfoxides.[7]



Scheme 1. β-Elimination of sulfoxides.

We had examined the utility of the β-elimination reaction of sulfoxides in the preparation of 2-hydroxy- and 2-aminoglycals from glycosyl sulfoxides, and the results of representative reactions are shown in Table 1.

After refluxing in toluene overnight, both protected 2-hydroxy- (entries **1**–**3**) and 2-amino (entries **4**, **5**) glycosyl sulfoxides afforded respective glycals in high yields. The glycals of sialic acid (entries **5**, **6**) were also prepared through this method in good yields.[8] Although it has been reported that a basic environment would be helpful for accelerating the reaction, we found that the neutral condition in refluxing toluene was enough to give satisfying conversion (more than 80% after 12 h in most cases). Thus, both acidic and basic labile functional groups are tolerated in the elimination process.

Using this strategy to make 2-hydroxy- and 2-aminoglycals has the following advantages: (1) thioglycosides are stable and easily synthesized. Actually, they are extensively used building blocks in carbohydrate chemistry; (2) the oxidation of thioglycosides with MCPBA and other oxidants to sulfoxides is a very efficient and high yield reaction; (3) the reaction was under neutral conditions and many functional groups can be tolerated; (4) the experiment is easy to be carried out and no complicated workup procedure is needed. Side products are negligible in those reactions.

In brief, the method described here for the synthesis of 2-substituted glycals is quite straightforward and should find use in many transformations.

Keywords: glycals; sulfoxides; thioglycosides.

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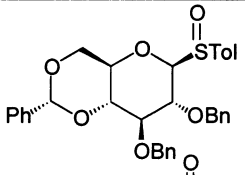
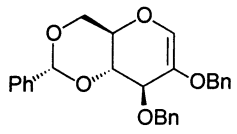
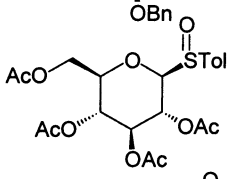
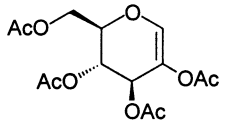
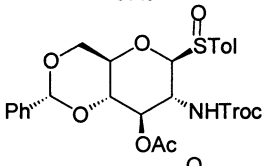
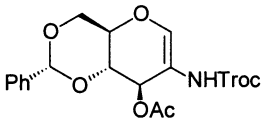
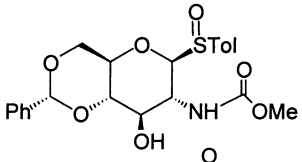
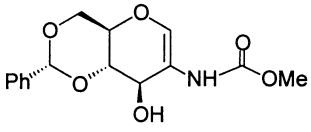
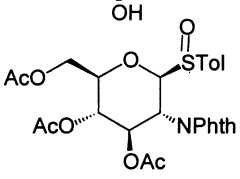
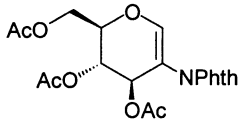
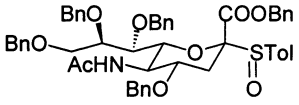
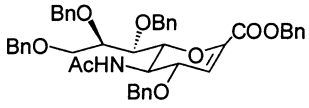
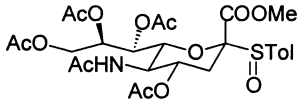
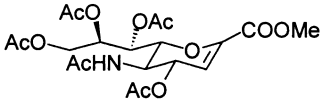
Table 1. Preparation of 2-hydroxy, 2-aminoglycals through β-elimination of glycosyl sulfoxides

entry	sulfoxides	product	yield (%)
1			80
2			85
3			85
4			74
5			87
6			64
7			62

Acknowledgements

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8. All compounds gave satisfactory ^{1}H, ^{13}C NMR and MS. Selected ^{1}H NMR (500 MHz, $CDCl_3$) spectroscopic data of products: **2** 6.63 (1H, s), 5.85 (1H, d, $J=4.1$ Hz), 5.49 (1H, dd, $J=1.8$, 4.1 Hz), 4.39 (m, 1H), 4.31 (1H, dd, $J=6.6$, 9.9 Hz), 4.24 (1H, dd, $J=4.1$, 9.9 Hz), 2.14 (3H, s), 2,12 (3H, s), 2.09 (3H, s), 2.05 (3H, s); **5**. 7.88 (2H, m), 7.75 (2H, m), 5.60 (1H, d, $J=3.7$ Hz), 5.33 (1H, t, $J=4.4$ Hz), 4.54 (2H, m), 4.38 (1H, dd, $J=3.7$, 11.7 Hz), 2.16 (3H, s), 2.14 (3H, s), 1.94 (3H, s); **6**. 7.34–7.17 (25H, m), 6.14 (1H, d, $J=4.0$ Hz), 5.25 (3H, m), 4.67–4.40 (10H, m), 4.24 (1H, dd, $J=5.5$, 12.8 Hz), 4.15 (1H, ddd, $J=1.9$, 4.4, 6.6 Hz), 3.96 (1H, dd, $J=4.4$, 9.9 Hz), 3.88 (1H, dd, $J=5.5$, 9.9 Hz), 3.68 (1H, dd, $J=4.4$, 9.9 Hz), 1.74 (3H, s).