

## Reductive Elimination of Glycosyl Phenyl Sulfones by $\text{SmI}_2$ -HMPA : A Convenient Synthesis of Substituted Pyranoid Glycals<sup>1</sup>

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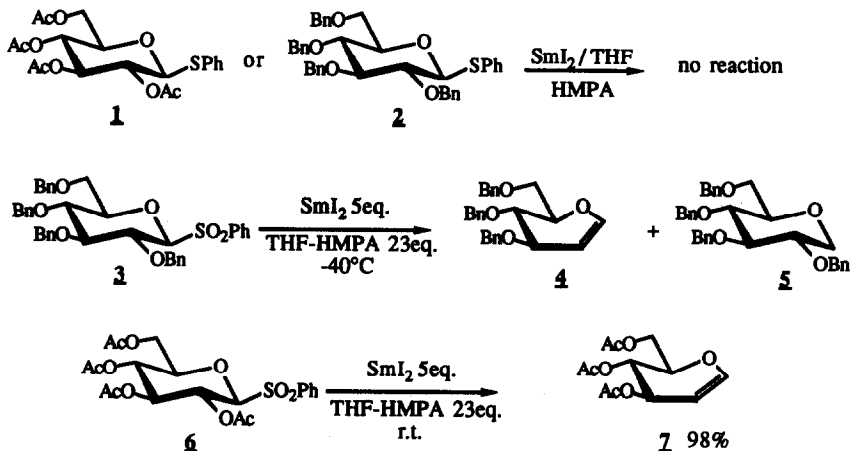
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**Abstract :** A series of substituted glycosyl phenyl sulfones was converted into glycals after reductive samariumation with  $\text{SmI}_2$  in the presence of hexamethylphosphoric triamide, followed by elimination of the substituent at C-2. Practically quantitative yields were obtained when the leaving group was an acetate, as illustrated here with seven substrates.

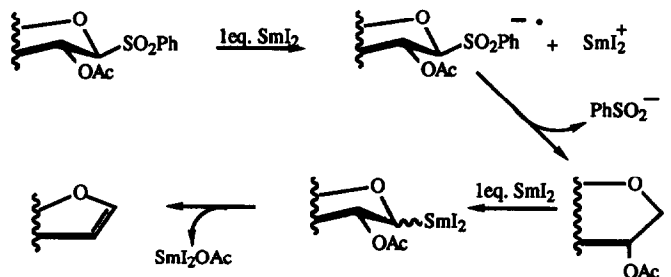
Glycals are versatile intermediates in carbohydrate chemistry<sup>2</sup>. Of particular importance is their conversion into efficient glycosyl donors for stereoselective synthesis of either 2-amino-2-deoxy-D-glycopyranosides<sup>3</sup> or 2-deoxy- $\alpha$ - and  $\beta$ -D-glycopyranosides<sup>4</sup>. Peracetylated glycals are usually prepared by modifications<sup>5</sup> of the classical Fischer's synthesis involving reduction of peracetylated glycosyl bromides with zinc dust. A variety of other reductive methods have also been reported<sup>6</sup> to convert glycosyl halides into glycals.

We have achieved<sup>7</sup> the efficient conversion of a variety of thiophenyl glycosides and glycosyl phenyl sulfones into glycal derivatives under reductive lithiation with lithium naphthalenide, followed by elimination of the substituent at C-2. Thiophenyl glycosides -and sulfones- are stable under a variety of reaction conditions (acylation, alkylation, acetalation) and have thus attracted considerable attention. Their direct conversion into a glycal derivative, under mild conditions, avoids the need for a glycosyl halide. However a potential disadvantage of this procedure is that concomitant *O*-debenzylation may occur, especially when running the reduction on a rather large scale. On the other hand, esters are usually not stable under these conditions.

It has recently been reported<sup>8</sup> by us that treatment of 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-glucopyranosyl bromide (acetobromoglucose) with a solution of samarium diiodide<sup>9</sup> in THF gave tri-*O*-acetyl-D-glucal in 90% yield. In order to benefit by the aforementioned advantage of thioglycosides and sulfones, their reactivity towards  $\text{SmI}_2$  was investigated and is presented in this letter<sup>1</sup>. Thiophenyl glycosides **1**<sup>10</sup> and **2**<sup>11</sup> remained intact when reacted with the efficient electron transfer system of  $\text{SmI}_2$ -THF-HMPA. On the other hand tetra-*O*-benzyl- $\beta$ -D-glucopyranosyl phenyl sulfone **3**<sup>12</sup> was converted at -40°C into a mixture of tri-*O*-benzyl-D-glucal **4**<sup>13</sup>(56%) and the known tetrahydropyran derivative **5**<sup>14</sup>(33%). Tetra-*O*-acetyl- $\beta$ -D-glucopyranosyl phenyl sulfone **6**<sup>15</sup> was transformed at room temperature into tri-*O*-acetyl-D-glucal **7**, in 98% yield.



In general, as shown in Table I, a quantitative reduction-elimination occurred in the case of glycosyl phenyl sulfones which are *O*-acetylated at C-2. A transient unstable anomeric organosamarium species is formed, which undergoes a very fast  $\beta$ -elimination of the acetate :



No glycal formation was observed when the C-2 position is *O*-allylated. Not unexpectedly, a reductive radical cyclisation took place. The anomeric radical formed by one-electron reduction of the sulfone undergoes a 5-exo-trig cyclisation, and the resulting intermediate radical is subsequently reduced to an organosamarium species which is then protonated.

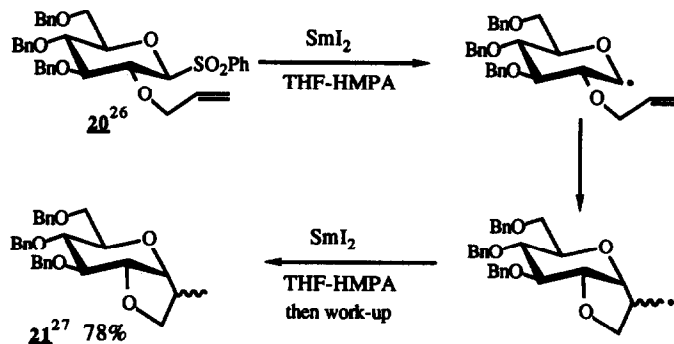
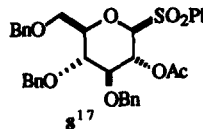
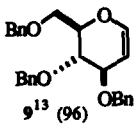
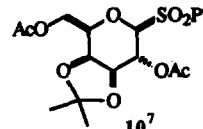
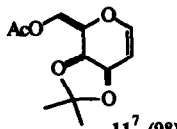
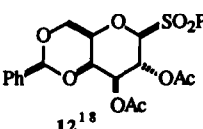
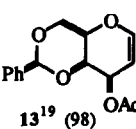
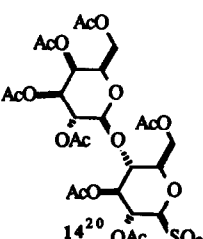
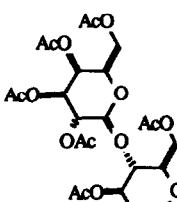
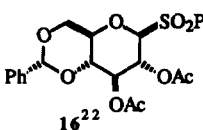
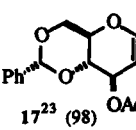
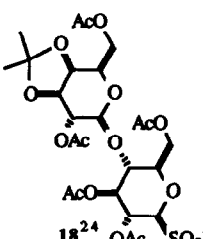
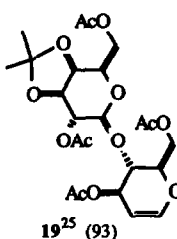


Table I16. Conversion of glycosyl phenyl sulfones into glycals.

Substrate	Product (yield %)	Substrate	Product (yield %)
			
			
			

**Experimental procedure:** A 0.1M solution of  $\text{SmI}_2$  in THF (Seq., 5ml), prepared according to Kagan's procedure<sup>9</sup>, was added to a sulfone (0.1mmol) at room temperature under argon. HMPA (23eq., 400 $\mu$ l) was added to start the reaction. The solution becomes purple. The mixture was stirred for about 15-20 min. until the color of the solution changed to yellow brown. After dropwise addition of an aqueous saturated solution of  $\text{NH}_4\text{Cl}$ , the reaction mixture was extracted twice with ether, dried ( $\text{MgSO}_4$ ), and purified by flash chromatography (cyclohexane/EtOAc).

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  - 16 All new compounds gave satisfactory microanalytical and spectral data.
  - 17 <sup>1</sup>H N. M. R. (400 MHz, CDCl<sub>3</sub>) δ : 5.23 (1H, dd, J<sub>1,2</sub> 10Hz, J<sub>2,3</sub> 9Hz, H-2), 4.83-4.42 (6H, OCH<sub>2</sub>-Ph), 4.45 (1H, d, H-1), 2.10 (3H, s, OAc); [α]<sub>D</sub> -3 (c 1.06 CHCl<sub>3</sub>); m. p. 114°C (ethanol).
  - 18 <sup>1</sup>H N. M. R. (250 MHz, CDCl<sub>3</sub>) δ : 5.44 (1H, dd, J<sub>1,2</sub>=J<sub>2,3</sub> 9.8Hz, H-2), 5.00 (1H, dd, J<sub>3,4</sub> 3.3Hz, H-3), 4.61 (1H, d, H-1); [α]<sub>D</sub> -10 (c 1.15 CHCl<sub>3</sub>).
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  - 24 <sup>1</sup>H N. M. R. (400 MHz, CDCl<sub>3</sub>) δ : 5.30 (1H, dd, J<sub>1,2</sub>=J<sub>2,3</sub> 9Hz, H-2), 4.84 (1H, dd, J<sub>1',2'</sub> 8Hz, J<sub>2',3'</sub> 10Hz, H-2'), 4.47 (1H, d, H-1), 4.34 (1H, d, H-1'); [α]<sub>D</sub> -17 (c 1.10 CHCl<sub>3</sub>).
  - 25 <sup>1</sup>H N. M. R. (400 MHz, CDCl<sub>3</sub>) δ : 6.43 (1H, dd, J<sub>1,2</sub> 6Hz, J<sub>1,3</sub> 1Hz, H-1), 4.98 (1H, dd, J<sub>1',2'</sub> 8Hz, J<sub>2',3'</sub> 7Hz, H-2'), 4.86 (1H, dd, J<sub>2,3</sub> 3.5Hz, H-2), 4.56 (1H, d, H-1'); [α]<sub>D</sub> +10 (c 1.35 CHCl<sub>3</sub>); m. p. 138-139°C (ethanol).
  - 26 <sup>1</sup>H N. M. R. (400 MHz, CDCl<sub>3</sub>) δ : 6.00 (1H, dt, J<sub>trans</sub> 17Hz, J<sub>cis</sub> 10.5Hz, CH=), 5.34 (1H, dd, J<sub>gem</sub> 1.7Hz, CH<sub>2</sub>=), 5.21 (1H, dd, CH<sub>2</sub>=), 4.55 (1H, d, J<sub>1,2</sub> 9Hz, H-1), 4.37 (2H, d, OCH<sub>2</sub>-CH=CH<sub>2</sub>); [α]<sub>D</sub> -21 (c 1 CHCl<sub>3</sub>); m. p. 107°C (ethanol).
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