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Reductive Elimination of Glycosyl Phenyl Sulfones by SmI_2-HMPA : A Convenient Synthesis of Substituted Pyranoid Glycals[1]

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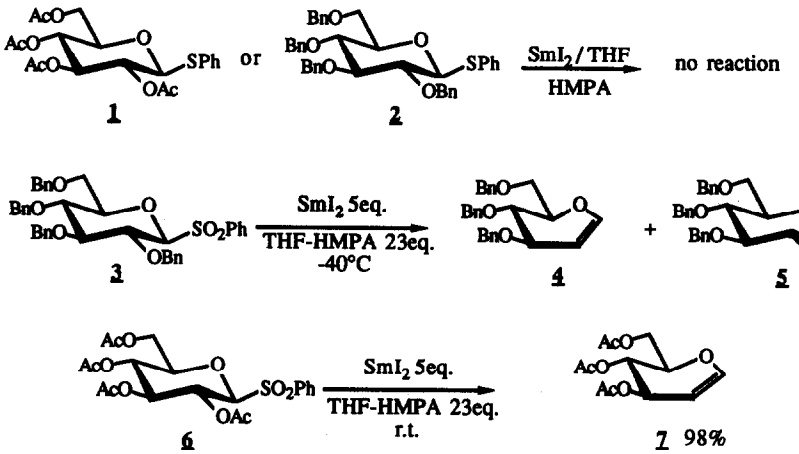
Abstract : A series of substituted glycosyl phenyl sulfones was converted into glycals after reductive samariation with SmI_2 in the presence of hexamethylphosphoric triamide, followed by elimination of the substituent at C-2. Practically quantitative yields were obtained when the leaving group was an acetate, as illustrated here with seven substrates.

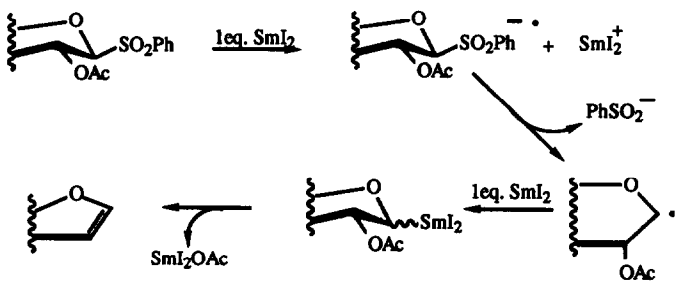
Glycals are versatile intermediates in carbohydrate chemistry[2]. Of particular importance is their conversion into efficient glycosyl donors for stereoselective synthesis of either 2-amino-2-deoxy-D-glycopyranosides[3] or 2-deoxy-α-and β-D-glycopyranosides[4]. Peracetylated glycals are usually prepared by modifications[5] 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[6] to convert glycosyl halides into glycals.

We have achieved[7] 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[8] by us that treatment of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (acetobromoglucose) with a solution of samarium diiodide[9] 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 SmI_2 was investigated and is presented in this letter[1]. Thiophenyl glycosides **1**[10] and **2**[11] remained intact when reacted with the efficient electron transfer system of SmI_2-THF-HMPA. On the other hand tetra-*O*-benzyl-β-D-glucopyranosyl phenyl sulfone **3**[12] was converted at -40°C into a mixture of tri-*O*-benzyl-D-glucal **4**[13](56%) and the known tetrahydropyran derivative **5** [14](33%). Tetra-*O*-acetyl-β-D-glucopyranosyl phenyl sulfone **6**[15] 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 β– 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.

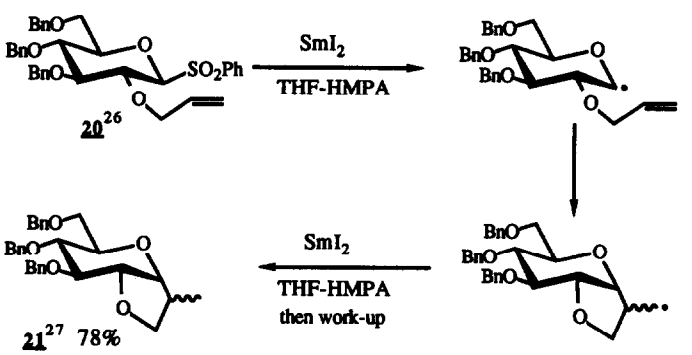
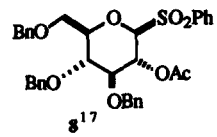
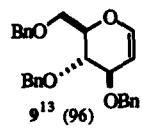
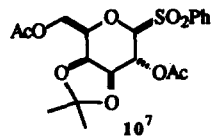
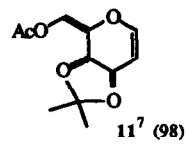
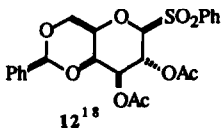
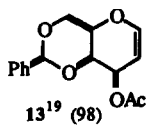
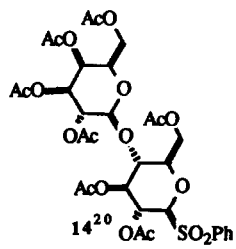
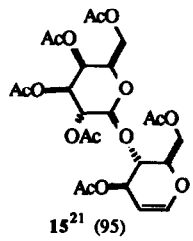
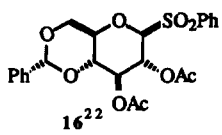
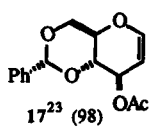
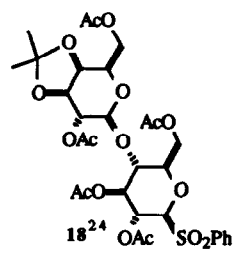
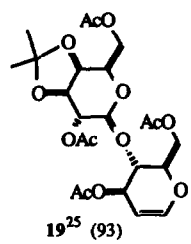


Table I[16]. Conversion of glycosyl phenyl sulfones into glycals.

Substrate	Product (yield %)	Substrate	Product (yield %)
 **8**[17]	 **9**[13] (96)	 **10**[7]	 **11**[7] (98)
 **12**[18]	 **13**[19] (98)	 **14**[20]	 **15**[21] (95)
 **16**[22]	 **17**[23] (98)	 **18**[24]	 **19**[25] (93)

Experimental procedure: A 0.1M solution of SmI_2 in THF (5eq., 5ml), prepared according to Kagan's procedure[9], was added to a sulfone (0.1mmol) at room temperature under argon. HMPA (23eq., 400µl) 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 NH_4Cl, the reaction mixture was extracted twice with ether, dried ($MgSO_4$), and purified by flash chromatography (cyclohexane/EtOAc).

References and Notes

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16 All new compounds gave satisfactory microanalytical and spectral data.

17 ^{1}H N. M. R. (400 MHz, $CDCl_3$) δ : 5.23 (1H, dd, $J_{1,2}$ 10Hz, $J_{2,3}$ 9Hz, H-2), 4.83-4.42 (6H, OCH_2-Ph), 4.45 (1H, d, H-1), 2.10 (3H, s, OAc); $[\alpha]_D$ -3 (c 1.06 $CHCl_3$); m. p. 114°C (ethanol).

18 ^{1}H N. M. R. (250 MHz, $CDCl_3$) δ : 5.44 (1H, dd, $J_{1,2}$=$J_{2,3}$ 9.8Hz, H-2), 5.00 (1H, dd, $J_{3,4}$ 3.3Hz, H-3), 4.61 (1H, d, H-1); $[\alpha]_D$ -10 (c 1.15 $CHCl_3$).

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24 ^{1}H N. M. R. (400 MHz, $CDCl_3$) δ : 5.30 (1H, dd, $J_{1,2}$=$J_{2,3}$ 9Hz, H-2), 4.84 (1H, dd, $J_{1',2'}$ 8Hz, $J_{2',3'}$ 10Hz, H-2'), 4.47 (1H, d, H-1), 4.34 (1H, d, H-1'); $[\alpha]_D$ -17 (c 1.10 $CHCl_3$).

25 ^{1}H N. M. R (400 MHz, $CDCl_3$) δ : 6.43 (1H, dd, $J_{1,2}$ 6Hz, $J_{1,3}$ 1Hz, H-1), 4.98 (1H, dd, $J_{1',2'}$ 8Hz, $J_{2',3'}$ 7Hz, H-2'), 4.86 (1H, dd, $J_{2,3}$ 3.5Hz, H-2), 4.56 (1H, d, H-1'); $[\alpha]_D$ +10 (c 1.35 $CHCl_3$); m. p. 138-139°C (ethanol).

26 ^{1}H N. M. R. (400 MHz, $CDCl_3$) δ : 6.00 (1H, dt, J_{trans} 17Hz, J_{cis} 10.5Hz, CH=), 5.34 (1H, dd, J_{gem} 1.7Hz, CH_2=), 5.21 (1H, dd, CH_2=), 4.55 (1H, d, $J_{1,2}$ 9Hz, H-1), 4.37 (2H, d, OCH_2-CH=CH_2); $[\alpha]_D$ -21 (c 1 $CHCl_3$); m. p. 107°C (ethanol).

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