Influence of the Phenylsulfonylethylidene (PSE) Acetal Clamp on the Glycosylation Involving Thioglycoside Donors

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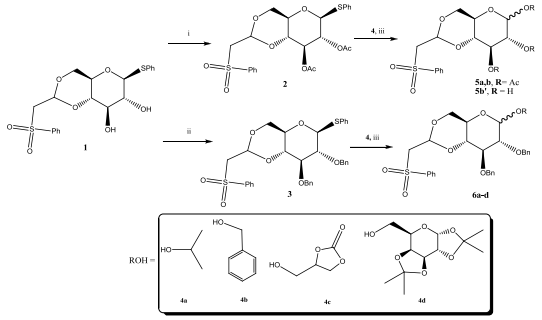
INTRODUCTION

The selective manipulation of the different hydroxyl groups on carbohydrate templates is the key to protecting group strategies. PSE acetals were recently introduced by us as protecting groups in glycochemistry for their remarkable stability under acidic conditions in opposition to conventional acetals.[1,2] We report here a study on the influence of a PSE acetal on a standard glycosylation reaction based on thio-β-D-glycopyranoside donors.[3]

RESULTS AND DISCUSSION

Phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside was converted in two steps into the thioglycoside **1** equipped with a 4,6-*O*-PSE clamp.[1] The thioglycoside donors **2** and **3** were then obtained through acetylation and benzylation, respectively (Scheme).

The methodology applied for glycosylation used NIS-TMSOTf as activating system.[3] The test reaction of **2** with isopropanol **4a** afforded the glucoside **5a** in moderate yields (entries 1-2). Using the more reactive acceptor alcohol **4b** results in poor yields of glucoside **5b** (entry 3), whereas reacting **4b** in large excess (4 equiv) only afforded the hydrolyzed β-glycoside **5b'** (R = H) in 31% yield (entry 4). This was probably formed via a 1,2-orthoester intermediate and transesterification process. The more reactive donor **3** led to glucosides **6a-b** with better yields (entries 5-6). Those results are in agreement with the armed-disarmed concept in glycosylation.[4] Next, other acceptors were reacted with the thio-donor **3** under optimized conditions. Thus, glycerol carbonate **4c** underwent glucosylation in dry dichloromethane to give **6c** in 75 % yield (entry 7). Finally, the disaccharide **6d** was obtained from **4d** in 60% yield and total α-selectivity (entry 6). Such stereoselectivity suggests the involvement of a S_N1 mechanism via an oxacarbenium ion to afford the α-glycoside also favored by the anomeric effect.[5]



Conditions: i)Ac_2O, DMAP, py, 12h (97%); ii) BnBr, NaH, 1 Equiv TBAB, -40 °C to r.t., 16h (87%); iii) NIS, TMSOTf, MS 4, DCM, 1h

Scheme

Table

Entry	Conditions donor:ROH:NIS:TMSOTf	Product	Yield % [a] (α:β ratio)[b]
1	1:2:1.5:0.15	**5a**	29 (2:1) [c]
2	1:2:1.5:0.30	**5a**	39 (3:2) [c]
3	1:2:2:0.30	**5b**	<10 (ND) [c]
4	1:4:2:0.30	**5b'**	31 β only [c,d]
5	1:2:2:0.20	**6a**	53 (3:1) [e]
6	1:2:2:0.20	**6b**	55 α only
7	1:2:2:0.20	**6c**	75 (16:1) [e]
8	1:2:2:0.20	**6d**	60 α only

[a] After column chromatography; [b] Determined by ^{1}H NMR; [c] Starting material recovered; [d] AcOBn was detected by ^{1}H NMR; [e] As ^{1}H NMR does not show the (α:β) ratio, a ^{13}C NMR experiment with d_1 = 10 s was used for integration of α-C_1 and β-C_1; ND = not determined.

CONCLUSION

In summary, we have shown the effect of a PSE acetal clamp on the glycosylation reaction involving a β-thioglycoside donor in the D-gluco series. NIS-TMSOTf activation of the reacting system affords glucosylated products with marked α-stereoselectivity.

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