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A Convenient 2-Deoxy-α-D-glucopyranosylation Reaction Using Dimethylphosphinothioate Method

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Several 2-deoxy-α-glucosides were obtained in good yields with high stereoselectivity by glycosylation reaction of the corresponding alcohols with 3,4,6-tri-O-benzyl-2-deoxy-β-D-glucopyranosyl dimethylphosphinothioate in the presence of a catalytic amount of triphenylmethylium perchlorate or an equivalent amount of silver perchlorate.

2-Deoxy-glycosides are widely found in natural products, and especially sugar-containing substances related to the macrolide and anthracycline groups are biologically important in the field of antibiotics.[1] Although many syntheses of 2-deoxy-glycosides have been studied, to our best knowledge, successful examples of direct glycosylation reactions of 2-deoxy aldoses are rare[2] except those having any auxiliary groups. The absence of neighboring groups and the high reactivity of the anomeric position due to the inductive effect of the deoxy-link gave non-stereospecific glycosylation and required the electron withdrawing groups as the protection of functions, such as p-nitrobenzoyl and trifluoroacetyl groups, for the glycosyl donor's stability.

We have already reported the glycosylation reactions of the glucopyranose and N-protected 2-amino-2-deoxy-D-glucopyranose using their

dimethylphosphinothioates (Mpt) derivatives.[3] Through these reactions the Mpt derivatives were proved to be very stable glycosyl donors. In this study we tried further application of the Mpt method to the glycosylation of 3,4,6-tri-O-benzyl-2-deoxy-D-glucopyranose (**1**)[4] as a representative of 2-deoxy-aldoses.

3,4,6-Tri-O-benzyl-2-deoxy-β-D-glucopyranosyl dimethylphosphinothioate (**2**)[5] was obtained in 74% yield by the acylation reaction of lithium salt

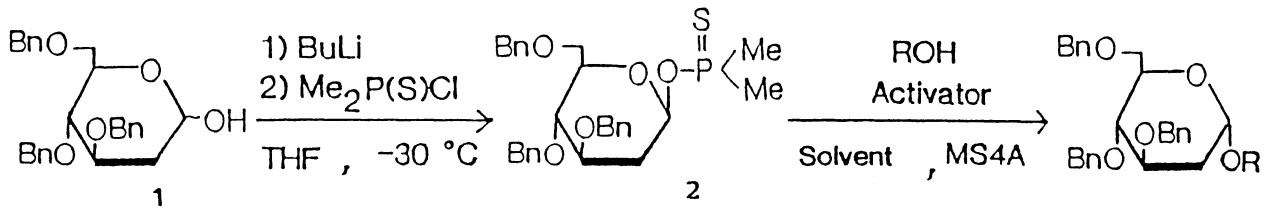


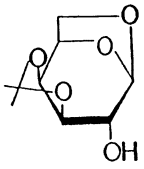
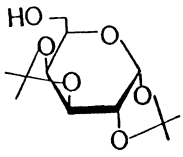
Table 1. The glycosylation reaction between **2** and 3β-cholestanol[a]

Entry	Activator(equiv.)	Solvent	Yield /%	α/β[b]
1	$AgClO_4$ (1)	PhH	53	40/1
2	$TrtClO_4$ (1)	PhH	62	20/1
3	$TrtClO_4$ (0.3)	PhH	68	20/1
4	$TrtClO_4$ (0.2)	PhH	69	15/1
5	$TrtClO_4$ (0.1)	PhH	72	8/1
6	$TrtClO_4$ (0.05)	PhH	49	3/2
7	$TrtClO_4$ (0.1)	PhH	35	2/1
8	$TrtClO_4$ (0.1)+$LiClO_4$ (1)	PhH	62	7/1
9	$TrtSbCl_6$ (0.3)	PhH	64	5/1
10	$TrtBF_4$ (0.3)	PhH	63	4/1
11	$TrtSnCl_5$ (0.3)	PhH	45	8/1
12	$TrtClO_4$ (0.3)	CH_2Cl_2	62	5/1
13	$TrtClO_4$ (0.3)	CH_3CN	No reaction	

a)Trt=triphenylmethylium. Molar ratio; **2**:alcohol=1:1.
b)The ratios were determined by ^{13}C NMR spectrosocopy.

of **1** with dimethylphosphinothioyl chloride in THF at -30 °C as described previously.[3] As expected **2** was obtained as a stable material. As summarized in Table 1, the high stereoselective glycosylation reactions between **2** and 3β-cholestanol were achieved under the conditions using more than 30 mol% of triphenylmethylium perchlorate or an equivalent amount of silver perchlorate (Entries 1,2,and 3). Also, the other alcohols gave the corresponding 2-deoxy-α-glucosides in good yields with high stereoselectivity as shown in Table 2. This glycosylation reaction would be explained by S_N2 type substitution mechanism.

Table 2. The glycosylation reaction of several alcohols using **2**[a]

Entry	Alcohol	Yield/%	α/β[b]
1	3β-Cholestanol	68	20/1
2	n-Octanol	64	12/1
3		64	5/1
4		62	8/1

a)The glycosylation reaction was carried out in the presence of 30 mol% triphenylmethylium perchlorate in benzene. Molar ratio; **2**:alcohol=1:1. b)The ratios were determined by ^{13}C NMR spectrosocopy.

Typical experimental procedure was as follows; compound **2** (107 mg, 0.2 mmol), 3β-cholestanol (80 mg, 0.2 mmol), triphenylmethylium perchlorate (21 mg, 0.06 mmol), and powdered 4A molecular sieves (ca. 100 mg) were stirred in benzene (2 ml) for 2 h at room temperature. After addition of 5% sodium

hydrogen carbonate (5 ml), the reaction mixture was filtered and extracted with dichloromethane. The organic layer was dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The crude product was purified by thin-layer chromatography (developing solvent; AcOEt:hexane= 1:4) to give the corresponding 2-deoxy-glucoside (112 mg, 68%).

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5) Compound **2**: ^{13}C NMR ($CDCl_3$) 23.7(d, J_{cp}=79.4 Hz, P-CH_3), 25.3(d, J_{cp}=68.4 Hz, P-CH_3), 37.1(d, J_{ccop}=7.3 Hz, C-2), 93.7(d, J_{cop}=6.1 Hz, C-1).

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