

1,2-cis- β -Mannopyranoside Formation
by the Dimethylphosphinothioate Method

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1,2-cis- β -Mannopyranosides were obtained predominantly by reactions of mannopyranosyl dimethylphosphinothioate derivatives with several alcohols in the presence of iodine and a catalytic amount of triphenylmethyl perchlorate as the activator in benzene.

In carbohydrate chemistry, a highly stereoselective O-glycosidation is very significant for the synthesis of complex oligosaccharides. In recent years new methods for stereospecific glycosidation have been reported.¹⁾ However the formation of 1,2-cis- β -mannopyranosidic linkage in the carbohydrate chain of N-glycoproteins remains a serious problem owing to its steric repulsion and anomeric effect.²⁾

Although several examples of 1,2-cis- β -mannopyranosylation reaction have been reported, such as S_N2 reaction using insoluble silver silicate³⁾ and intramolecular glycosylation,^{4,5)} they seem not to be easy to apply to the synthesis of oligosaccharides.

Mannopyranosylation could be assumed as follows. Although 1,2-cis- β -mannopyranosides could be produced even by most reported glycosidation methods, 1,2-cis- β -mannopyranosides would be immediately converted to 1,2-trans- α -mannopyranosides by acidic components from the activators. Certain 1,2-cis- β -mannopyranosides could be obtained without anomerization under

the conditions reducing acid as little as possible.

We previously reported glycosidation using glycosyl dimethylphosphinothioate in the presence of iodine and a catalytic amount of triphenylmethyl perchlorate (TrtClO_4) as the activator.⁶⁾ Attention was directed to the catalytic amount of TrtClO_4 in the glycosidation, and 1,2-cis- β -mannopyranoside synthesis was attempted by this method.

First, we examined reactions of 2,3,4-tri-O-benzyl-6-deoxy-L-mannopyranosyl dimethylphosphinothioate (**1**) and 3 β -cholestanol (**2**) with various amounts of TrtClO_4 .⁷⁾ Although only 3 β -cholestanyl 1,2-trans- α -mannopyranoside (**3- α**) was obtained using 50 mol% amount of TrtClO_4 (entry 1), **3- β** was synthesized predominantly following reduction of TrtClO_4 to 5 mol% (entry 3). The time-course of the anomer ratio of the reaction mixture was measured by HPLC, but no anomerization could be detected. Unfortunately **3- α** was predominantly obtained by the reaction using a still smaller amount of TrtClO_4 (entries 4 and 5).

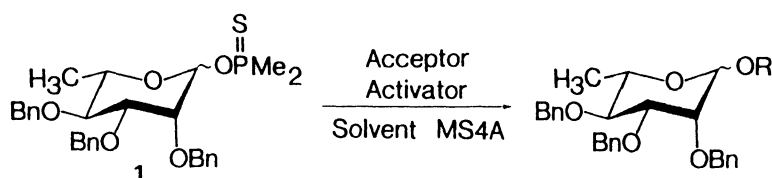
Iodine was found essential for this reaction. Iodide anion appeared to be related in some manner to the selectivity (entries 5-11).

Further we examined this reaction using several solvents, such as benzene, toluene, fluorobenzene and dichloromethane. Benzene and fluorobenzene were particularly effective (entries 3 and 8). It was of interest that the molecular size of effective solvents were similar.

Based on the above results, the reaction mechanism except for entries 4 and 5 was considered to be as follows. Mannosyl perchlorate, possibly generated by the reaction of **1** and TrtClO_4 , immediately reacted with iodide ion to afford α -mannosyl iodide containing solvent molecule. The reaction of alcohol and this intermediate might give the β -mannoside predominantly without anomerization.

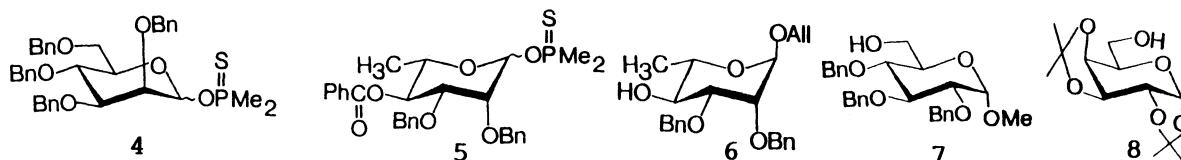
Other β -mannosides were obtained using various acceptors. Similarly 2,3,4,6-tetra-O-benzyl-D-mannopyranosyl dimethylphosphinothioate (**4**) gave the corresponding 1,2-cis- β -mannoside predominantly (entry 15).

On the other hand, 4-O-acyl mannosyl donors were known to increase

Table 1. a) Mannopyranosylation reactions using I_2 -cat.TrtClO₄

Entry	Acceptor	Activator(equiv.)	Solvent	Yield/%	α/β^b
1	3 β -Cholesterol(2)	$\text{I}_2(1)$ -TrtClO ₄ (0.5)	PhH	94	α
2	2	$\text{I}_2(1)$ -TrtClO ₄ (0.1)	PhH	93	60/40
3	2	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhH	76	40/60
4	2	$\text{I}_2(1)$ -TrtClO ₄ (0.023)	PhH	84	80/20
5	2	$\text{I}_2(1)$	PhH	79	α
6	2	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	CH ₂ Cl ₂	71	α
7	2	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhCH ₃	78	90/10
8	2	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhF	76	38/62
9	2	$\text{I}_2(0.5)$ -TrtClO ₄ (0.05)	PhH	52	61/39
10	2	$\text{I}_2(0.25)$ -TrtClO ₄ (0.05)	PhH	33	53/47
11	2	NaI(1)- $\text{I}_2(0.25)$ -TrtClO ₄ (0.05)	PhH	18	37/63
12	6	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhH	46	69/31
13	7	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhH	50	45/55
14	8	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhH	69	50/50
15 ^{c)}	2	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhH	67	30/70
16 ^{d)}	2	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhH	85	18/82
17 ^{d)}	6	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhH	47	43/57
18 ^{d)}	7	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhH	52	23/77
19 ^{d)}	8	$\text{I}_2(1)$ -TrtClO ₄ (0.05)	PhH	61	35/65

a) Molar ratio ; 1 : acceptor = 1 : 1. b) The anomer ratios were determined by HPLC and ¹H NMR. c) Compound 4 was used as a donor. d) Compound 5 was used as a donor.



β -selectivity by through-bond interactions and/or participation of the 4-O-acyl group.^{2,8)} The reactions of the 4-O-benzoyl derivative 5 with various acceptors were consequently carried out to afford 1,2-cis- β -

mannosides in high selectivity up to $\alpha/\beta=18/82$ (entry 16).

More detailed research is presently being conducted.

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