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A FACILE SYNTHESIS OF α-GLUCOSIDES AND α-RIBOSIDES FROM THE CORRESPONDING 1-O-ACYL SUGARS AND ALCOHOLS IN THE PRESENCE OF TRITYL PERCHLORATE

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In the presence of trityl perchlorate, 1-O-bromoacetyl-β-D-glucose stereoselectively reacts with alcohols to give the corresponding α-glucosides in good yields. The similar reaction of 1-O-acetyl-β-D-ribose affords the corresponding β-ribosides exclusively, while in the presence of molecular sieves 4A and lithium perchlorate, α-ribosides are prepared predominantly in good yields.

In the previous paper,[1] we have shown that 1-O-acyl-β-D-glucopyranoses are stereoselectively synthesized by the reaction of a 1-hydroxy glucose with acyl fluorides by utilizing cesium fluoride as an accelerator and an acid captor.

In the course of our continuous investigation on the development of stereoselective glycosylation reactions, it was also found that triphenylmethyl perchlorate (trityl perchlorate)[2] is an effective reagent for the activation of acyloxy groups on the anomeric center of 1-O-acyl sugars.

These facts prompted us to explore new synthetic reactions of glycosyl compounds starting from 1-O-acyl sugars and various nucleophiles. In this communication, we wish to describe a convenient method for the preparation of α-glucosides and α-ribosides by the reaction of the corresponding 1-O-acyl sugars with alcohols in the presence of trityl perchlorate, an activator. A stereoselective synthesis of β-ribosides is also described.

First, preparation of a variety of 1-O-acyl-β-D-glucopyranoses was achieved by treating 2,3,4,6-tetra-O-benzyl-D-glucopyranose with acyl chlorides in the presence of cesium fluoride or potassium fluoride. Of 1-O-acylglucoses thus prepared, the effect of acyl substituents and the reaction conditions, such as activators and solvents, were screened taking 3β-cholestanol as a model alcohol, and it was found that the combination of 1-O-bromoacetyl-β-D-glucose and trityl perchlorate in ether gave the best result; namely, 2,3,4,6-tetra-O-benzyl-1-O-bromoacetyl-β-D-glucopyranose (1)[3] reacted with 3β-cholestanol under mild conditions to give the corresponding α-glucoside in high stereoselectivity (See Table 1).

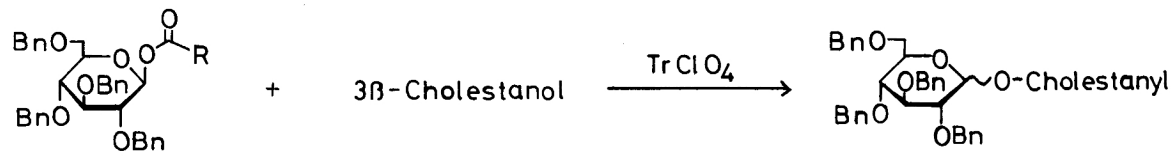

Table 1. Effect of Acyl Groups

R	Yield/%	α/β
$-CHCl_2$	57	91/9
$-CH_2Br$	75	96/4
$-CH_2I$	89	86/14

The following is a typical procedure for the reaction of 1 with 3β-cholestanol: the mixture of 1 (0.3 mmol), 3β-cholestanol (0.2 mmol) and trityl perchlorate (0.3 mmol) in ether (5 ml) was stirred at 0 °C. After the reaction was completed, aqueous sodium hydrogen carbonate was added and the organic layer was dried. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel to give 3β-cholestanyl 2,3,4,6-tetra-O-benzyl-α-D-glucopyranoside (72%) and β-anomer (3%).

Similarly, the reactions with 1-octadecanol and cyclohexanol afforded the corresponding α-glucosides stereoselectively (See Table 2).

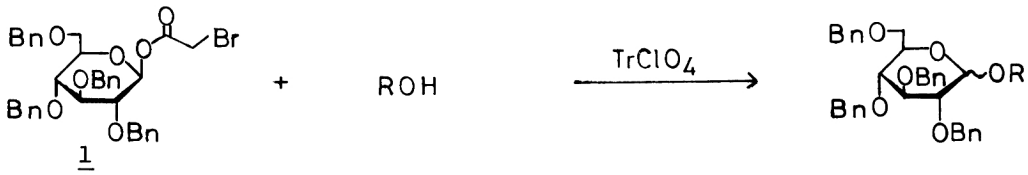

Table 2. Synthesis of α-Glucosides

Alcohol	Yield/%	α/β
1-Octadecanol	75	94/6
Cyclohexanol	86	92/8
3β-Cholestanol	75	96/4

Next, we applied the present method to the synthesis of α-ribosides, however, the reactions of 1-O-acetyl-2,3,5-tri-O-benzyl-β-D-ribofuranose (2)[4] with alcohols under the same reation conditions[5] as described above afforded the β-ribosides exclusively (See Table 3).

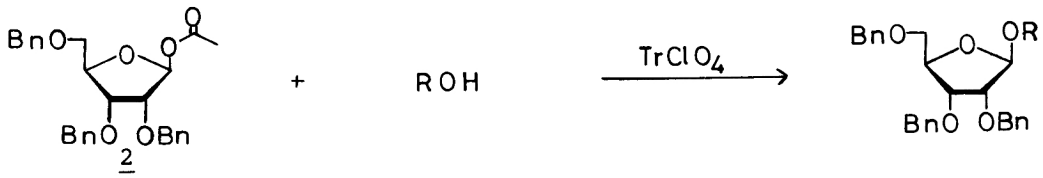

Table 3. Synthesis of β-Ribosides

Alcohol	Yield/%	α/β
1-Octadecanol	73 (95)[a]	0/100
Cyclohexanol	83	0/100
3β-Cholestanol	88	0/100

a) Three molar amounts of alcohol was used (yield based on 2).

As a result of examination of the reaction mixture by thin layer chromatography, the isomerization of α-riboside to the corresponding β-anomer was detected. Therefore, it may be explained that the initially formed α-riboside isomerized to the β-anomer by the interaction with trityl perchlorate. Then, it was postulated that the isomerization would be suppressed when the reaction was carried out in the presence of appropriate bases. On the basis of this hypothesis, we examined various basic additives and finally found that the combined use of molecular sieves 4A[6] and lithium perchlorate[7] suppressed the isomerization and desired α-ribosides were produced preferentially (See Table 4).

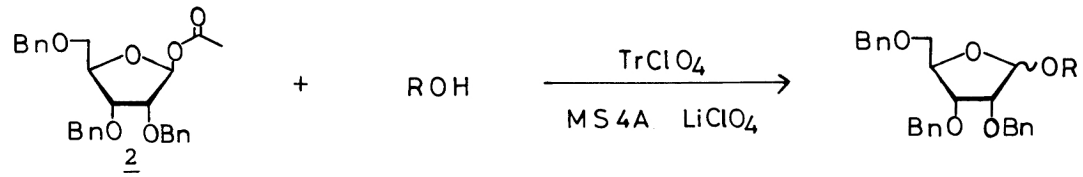

Table 4. Sythesis of α-Ribosides

Alcohol	Yield/%	α/β
2-Propanol	91[a]	73/27
Cyclohexanol	86[a]	70/30
3β-Cholestanol	75	79/21

a) Three molar amounts of alcohol was used (yield based on 2).

A typical procedure is described for the reaction of 2 with 3β-cholestanol: the mixture of 2 (0.3 mmol), 3β-cholestanol (0.2 mmol), trityl perchlorate (0.3 mmol), 4A molecular sieves (200 mg), and lithium perchlorate (0.3 mmol) was stirred at 0 °C. Usual work up and separation by TLC afforded 3β-cholestanyl 2,3,5-tri-O-benzyl-α-D-ribofuranoside (59%) and β-anomer (16%).

There have been reported several methods for the syntheses of glycosides from 1-O-acyl sugars and alcohols using rather strong Lewis acids such as $BF_3 \cdot OEt_2$, $FeCl_3$ and $SnCl_4$, etc.[8] In these reactions, 1,2-trans-glycosides are obtained by

utilizing neighbouring effect of C-2 acyloxy group of sugars, whereas, in the absence of neighbouring participation, a mixture of anomers is obtained.[9]

It is noted that, according to the present method, 1,2-cis-glycosides are prepared preferentially in good yields by the reactions of various readily available 1-O-acyl sugars with alcohols by using trityl perchlorate as an activator.

Further study for the synthesis of C-nucleosides using 1-O-acyl sugars is now in progress.

References

1) S. Shoda and T. Mukaiyama, Chem. Lett., 1982, 861.
2) H. J. Dauben, Jr., L. R. Honnen, and K. M. Harmon, J. Org. Chem., 25, 1442 (1960).
3) This compound was prepared by the reaction of 2,3,4,6-tetra-O-benzyl-D-glucopyranose with bromoacetyl chloride in the presence of potassium fluoride and easily purified by recrystallization from 2-propanol. ^{1}H NMR ($CDCl_3$) 5.6 (H-1, J_{12}=7.2 Hz) ^{13}C NMR ($CDCl_3$) 95.3 (C-1), $[\alpha]_D^{20}$ + 2.0° (c 0.64, $CHCl_3$), mp 105.0–105.5°C.
4) This compound was prepared by the reaction of 2,3,5,-tri-O-benzyl-D-ribofuranose with acetic anhydride in pyridine. ^{1}H NMR ($CDCl_3$) 6.1 (H-1, J_{12}=0 Hz) ^{13}C NMR ($CDCl_3$) 98.9 (C-1), $[\alpha]_D^{26}$ + 59° (c 1.0, $CHCl_3$).
5) 1,2-dimethoxyethane (DME) was used as a solvent.
6) When molecular sieves 3A or 5A were used as additive, a good result could not be obtained.
7) The reaction was slow unless lithium perchlorate was added as an additive.
8) For example, S. Hanessian and J. Banoub, Carbohydr. Res., 59, 261 (1977); M. Kiso and L. Anderson, Carbohydr. Res., 72, C12 (1979).
9) G. Wulff and G. Rohle, Angew. Chem., Int. Ed. Engl., 13, 157 (1974).

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