CHEMISTRY LETTERS, pp. 1941-1944, 1993.

Catalytic Synthesis of β-D-Ribofuranosides from D-Ribofuranose and Alcohols

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Catalytic synthesis of β-D-ribofuranosides from C-1 free ribofuranose, 2,3,5-tri-O-benzyl-D-ribofuranose, and alcohols is efficiently performed by combined use of silver salts and Lawesson's reagent, [2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide], or silver salts and diphenyltin sulfide ($Ph_2Sn=S$) under mild conditions.

Glycosyl halides, 1-O-acylsugars, methyl glycosides, thioglycosides, and so on are usually used for glycosyl donors in most glycosylation reactions, and the coupling with various nucleophiles is carried out by activating the C-1 leaving groups of sugars with a suitable catalyst or promoter.

We have recently reported an efficient method for stereoselective synthesis of β-D-ribofuranosides from 2,3,5-tri-O-benzyl-1-O-iodoacetyl-D-ribofuranose and alkyl trimethylsilyl ethers by combined use of 10 mol% of silver salts and 20 mol% of diphenyltin sulfide ($Ph_2Sn=S$).[1] In the present experiment, it was also found that Lawesson's reagent could be used instead of $Ph_2Sn=S$ as a partner of silver salts in the above reaction (Table 1).

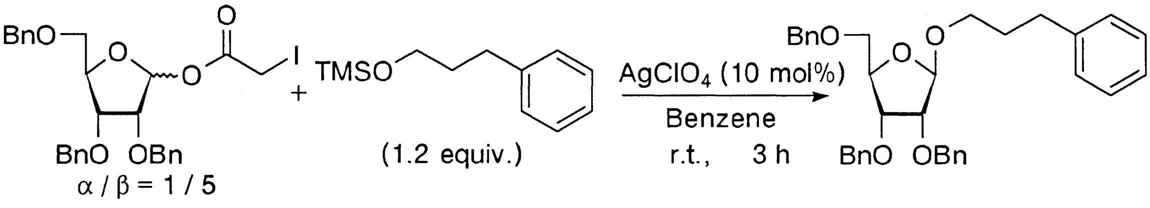


Table 1. Synthesis of β-D-Ribofuranoside

Entry	Partner of $AgClO_4$ / mol%		Yield / %[a)]	α / β [b)]
1	$Ph_2Sn=S$	20	91	5 / 95
2	Lawesson's reagent	10	91	5 / 95

a) Isolated yield. b) Determined by HPLC analysis.

In order to find a more convenient glycosylation method, a direct coupling of C-1 free ribofuranose, glycosyl donors, and free alcohols was studied since C-1 free ribofuranose is undoubtedly simple starting materials.[2] The glycosylation reaction of C-1 free ribofuranose and alcohols was tried with the consideration that C-1 hydroxy group of ribofuranose could be successfully activated under the conditions.

Concerning glycosylation reaction of C-1 free sugars with alcohols, it was recently reported that combined use of $Yb(OTf)_3$ and methoxyacetic acid effectively promoted the reaction in CH_2Cl_2 or 1,2-dichloroethane.[3]

First, the reaction of 2,3,5-tri-O-benzyl-D-ribofuranose and cyclohexanol (1.2 equiv.) was tried in the presence of 20 mol% of $AgClO_4$ alone in benzene at room temperature, however, the starting ribofuranose was recovered. On the other hand, when the reaction was carried out in the coexistence of $AgClO_4$ (20 mol%) and $Ph_2Sn{=}S$ (40 mol%) or Lawesson's reagent (10 mol%), the corresponding ribofuranoside was obtained in moderate yield ($Ph_2Sn{=}S$: y. 72%, α/β = 4/96, Lawesson's reagent: y. 73%, α/β = 5/95).

Next, several molecular sieves (MS) were added to the reaction mixture in order to remove water formed during the reaction to increase the yield, and actually good results were given when MS-3A was used (Table 2). When the experiments were carried out after stirring the mixture of $AgClO_4$, molecular sieves, and Lawesson's reagent for 60 min in benzene, the yields decreased irrespective of the kind of molecular sieves. The results suggested that the catalyst might be decomposed by stirring with molecular sieves for a long time. After screening several solvents in the presence of MS-3A, it was made clear that toluene and benzene were the solvents of choice with respect to chemical yield and stereoselectivity (Table 2).

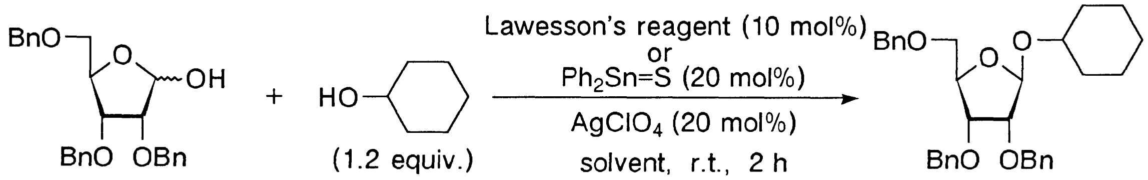


Table 2. Effects of MS and Solvents

Entry[a]	MS	Solvent	Preparation of Catalyst / min	Yield / %[b]	α/β[c]
1	3A	Benzene	15	**94**	**5/95**
2	3A	Benzene	60	57	14/86
3	4A	Benzene	15	29	33/67
4	4A	Benzene	60	5	52/48
5	5A	Benzene	15	88	7/93
6	5A	Benzene	60	20	37/63
7	3A	Toluene	15	**95**	**4/96**
8	3A	CH_2Cl_2	15	91	7/93
9	3A	1,2-Dichloroethane	15	91	5/95
10	3A	Et_2O	15	70	15/85
11	3A	CH_3CN	15	N.R.	—
12	3A	Benzene	2	**92**	**4/96**
13	3A	Toluene	2	88	4/96
14	3A	1,2-Dichloroethane	2	82	6/94
15	3A	Benzene	15	**91**	**4/96**

a) Entries 1-11: Lawesson's reagent was used; Entries 12-15 : Diphenyltin sulfide was used. b) Isolated yield. c) Determined by HPLC analysis.

Next, $Ph_2Sn{=}S$ was used as a partner of $AgClO_4$ in the above reaction. On the basis of the above data, subsequent experiments (Table 2, Entries 12-15; Table 3, Entries 1-5) were carried out by adding MS-3A to the stirred mixture of $AgClO_4$ and its partner in suitable solvent. In the case of $Ph_2Sn{=}S$, benzene was the solvent of choice with respect to chemical yield and stereoselectivity (Table 2). Similar results were obtained when the reactions were carried out after stirring $AgClO_4$ and $Ph_2Sn{=}S$ in benzene for 2 min or 15 min (Table 2).

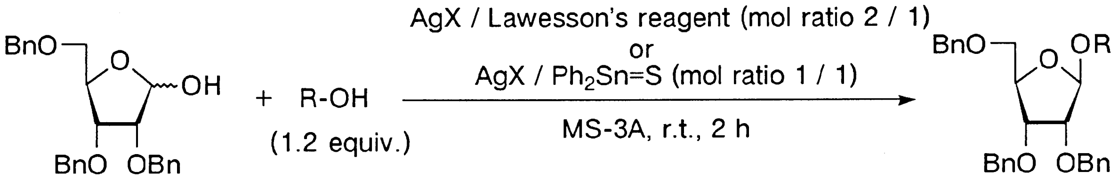
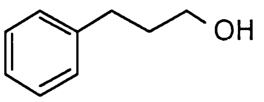
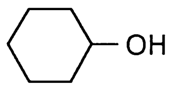
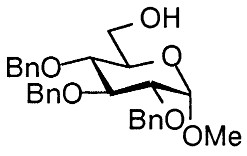


Table 3. Synthesis of β-D-Ribofuranosides from D-Ribofuranose and Alcohols

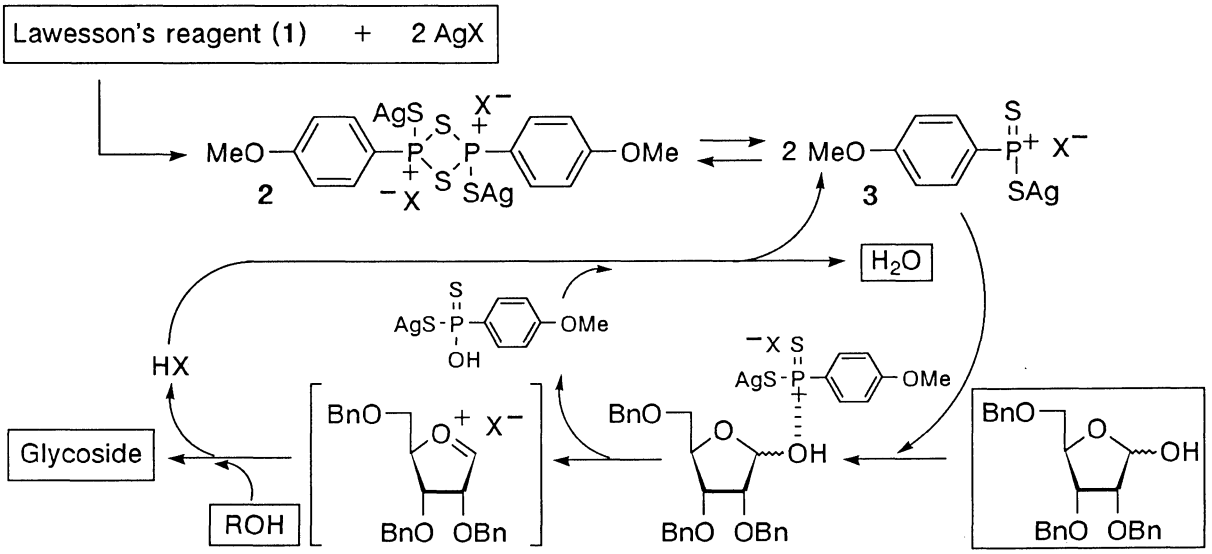
Entry	Alcohol	AgX / mol%		Method A[a]		Method B[b]	
				Yield / %[c]	α / β[d]	Yield / %[c]	α / β[d]
1		$AgClO_4$	20	97	5 / 95	95	4 / 96
2		$AgClO_4$	20	93	5 / 95	92	4 / 96
3		$AgSbF_6$	20	85	4 / 96	77	4 / 96
4	3β-Cholestanol	$AgClO_4$	20	90	4 / 96	90	4 / 96
5		$AgClO_4$	20	79	24 / 76	89	13 / 87

a) Method A: The reactions were carried out by using [silver salts/Lawesson's reagent] (2/1) combined catalyst in toluene for 2 h. b) Method B: The reactions were carried out by using [silver salts/$Ph_2Sn=S$] (1/1) combined catalyst in benzene for 2 h. c) Isolated yield. d) Determined by HPLC analysis.

Further, the effects of the ratios of (1) $AgClO_4$ to Lawesson's reagent and (2) $AgClO_4$ to $Ph_2Sn=S$ were examined; (1) when the reactions were carried out by using catalyst system composed of $AgClO_4$/Lawesson's reagent 2/1, 4/1, 6/1, and 8/1, the corresponding ribofuranoside was obtained in nearly the same yield. Then, the ratio of $AgClO_4$ to Lawesson's reagent 2/1 was chosen as a typical experimental condition. (2) When the above reactions were carried out by using catalyst system composed of $AgClO_4$/$Ph_2Sn=S$ 1/2, 1/1, and 2/1, the corresponding ribofuranoside was obtained in almost same yield. In the case of using catalyst system composed of $AgClO_4$/$Ph_2Sn=S$ 2/1, black precipitation, probably Ag_2S, was observed, and the formation of $Ph_2Sn(ClO_4)_2$ in situ was suggested.[4] This active species was considered to be a stronger Lewis acid than $[Ph_2Sn^+\text{-}SAg\cdot{}^-ClO_4]$ which might be formed by mixing $AgClO_4$ and $Ph_2Sn=S$ in a ratio of 1:1 or 1:2. Accordingly, the $AgClO_4$/$Ph_2Sn=S$ ratio 1/1 was chosen.

Some alcohols were applied to the above reaction by using the 20 mol% catalyst system and the corresponding glycosides were obtained in good yields (Table 3). Silver hexafluoroantimonate could also be used instead of $AgClO_4$ in the above glycosylation, but the desired ribofuranoside was obtained in rather lower yield (Table 3).

At present, the reaction is considered to be catalyzed by the promotion of the new active species (2 and/or 3) generated from silver salts and Lawesson's reagent as shown in the following scheme.[5]



The following is a typical procedure for the preparation of cyclohexyl 2,3,5-tri-O-benzyl-D-ribofuranoside; to a stirred solution of $AgClO_4$ (0.03 mmol) in toluene (1 ml) was added a suspension of Lawesson's reagent (0.015 mmol) in toluene (1.5 ml) at room temperature. After stirring for 15 min, MS-3A (30 mg) was added and a solution of 2,3,5-tri-O-benzyl-D-ribofuranose (0.15 mmol) and cyclohexanol (0.18 mmol) in toluene (3.5 ml) was immediately added to the suspension at room temperature and kept stirring for 2 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. Usual work up and separation by TLC afforded the corresponding β-D-ribofuranoside (88%) and α-D-ribofuranoside (5%).

Thus, starting from C-1 free ribofuranose, 2,3,5-tri-O-benzyl-D-ribofuranose, and free alcohols, stereoselective preparation of various β-D-ribofuranosides is successfully carried out under mild conditions by using catalytic amount of [silver salt/Lawesson's reagent] or [silver salt/Ph_2Sn=S] combined system.

The present research is partially supported by Grant-in-Aids for Scientific Research on Priority Areas (No. 03242104) from Ministry of Education, Science and Culture.

References

1) T. Mukaiyama and N. Shimomura, *Chem. Lett.*, **1993**, 781.

2) B. Fischer, A. Nudelman, M. Ruse, J. Herzig, and H. E. Gottlieb, *J. Org. Chem.*, **49**, 4988 (1984); K. Toshima, G. Matsuo, T. Ishizuka, M. Nakata, and M. Kinoshita, *J. Chem. Soc., Chem. Commun.*,**1992**, 1641.

3) J. Inanaga, Y. Yokoyama, and T. Hanamoto, *J. Chem. Soc., Chem. Commun.*, **1993**, 1090.

4) In the cases of using catalyst system composed of $AgClO_4/Ph_2Sn$=S 1/1 and 1/2, the mixture were brown suspension in each case.

5) The active species of [silver salt/Ph_2Sn=S] combined catalyst system is already referred in 1).

(Received July 23, 1993)