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A Facile Synthesis of 1-Thiopentofuranoside

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Abstract : β-1-Thio-2,3,5-tribenzylarabinofuranoside and α-1-thio-2,3,5-tribenzylxylopyranoside were easily prepared using ethanethiol or benzenethiol in the presence of *conc.* hydrochloric acid at room temperature, while a dithioacetal was obtained from the corresponding 2,3,4-tribenzylpyranose.

1-Thioglycosides have been used not only as versatile glycosyl donors in the glycosidation reaction but also as key intermediates for the preparation of 1-fluoroglycosides. Various reagents, such as $PhSSiMe_3$ / ZnI_2 / Bu_4NI[1], Bu_3SnSMe / $SnCl_4$[2], Me_3SiSMe /BF_3 Et_2O[3], and $Bu_3Sn(SR)_2$ / $BuSn(OTf)_2$[4] have been used in the preparaton of 1-thioglycosides. The nucleophilicity of these thioalkoxylation reagents was reduced by interacting with stannane or silane to prevent excessive thioalkylation. Actually when unprotected arabinose, galactose and glucose were treated with ethanethiol and hydrochloric acid in dioxane, diethyl dithioacetals were predominantly produced[5].

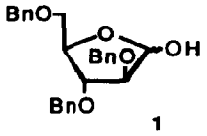
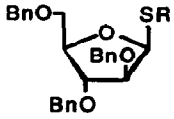
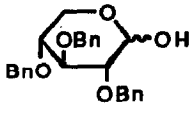
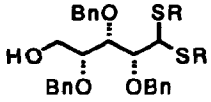
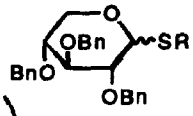
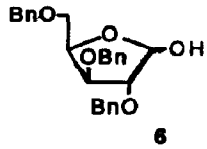
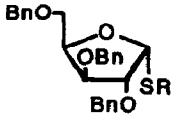
We herein report that the classical thioglycosidation with thiols and a catalytic amount of hydrochloric acid is a convenient method to prepare the thioglycosides of 2,3,5-tribenzylpentofuranoses without any production of dithioacetals. While sulfurization of arabinose with ethanethiol in the presence of *conc.* HCl forms arabinose diethyl dithioacetals, 2,3,5-tribenzylarabinofuranose (**1**) was converted to ethyl β-thio-2,3,5-tribenzylarabinofranoside[6] in 95 % yield. The β-configuration of **2a** was confirmed by NOE observed between H-1 and H-2 in the ^{1}H-NMR spectrum. The same treatment of **1** with thiophenol gave phenyl β-thio-2,3,5-tribenzylarabinofranoside **2b** in 86 % yield[7]. Both **2a** and **2b** can be used as arabinose donors for the synthesis of hydroxyprolylarabinosides which were found in the lectins from egg plant family plants, *e.g.* *Solanum tuberosum* and *Datura stramonium*[8].

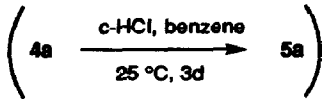
Interestingly, 2,3,4-tribenzylxylopyranose (**3**) reacted with ethanethiol in the same condition as mentioned above to afford only diethyl dithioacetal (**4a**, 90 %)[9] which was slowly converted to ethyl 1-thio-2,3,4-tribenzylxylopyranoside (**5a**, 80 %) in 3 days upon treating with *conc.* HCl in benzene at room

temperature, while 2,3,5-tribenzylxylofuranose (**6**) was rapidly converted to ethyl α-1-thio-2,3,4-tribenzylxylofuranoside (**7a**, 95 %)[10]. In addition, upon treating compound **3** with benzenethiol in the presence of *conc.* HCl, phenyl 1-thio-xylopyranoside **5b** (62 %) as well as diphenyl dithioacetal **4b** (22 %) were generated, while the application of the same condition to compound **6** solely afforded phenyl α-1-thio-2,3,5-tribenzylxylofuranoside (**7b**, 86 %)[11].

In a typical procedure, compound **1** (300 mg, 0.71 mmol) was mixed with ethandithiol (300 μl) and *conc.* HCl (100 μl), and the mixture was stirred at room temperature for 2h. The product was isolated by silica gel chromatography to give **2a** (315 mg) in 95 % yield. The same result was obtained when benzene or $CHCl_3$ was used as solvent (3.0 ml) in the presence of ethanethiol (300 μl).

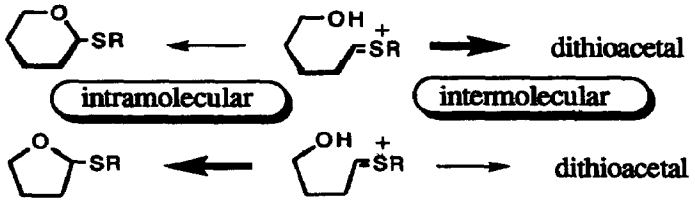
Table 1 Thioglycosidation of tribenzylpentoses with thiols in the presence of *conc.* HCl

tribenzylpentose	conditions	products	yield (α : β)
 **1**	RSH, *c*-HCl r. t. 2 h (**2a**) 1 d (**2b**)		**2a** : R = Et 95 % **2b** : R = Ph 86 % (1:13)
 **3**	RSH, *c*-HCl r. t. 1 h (**4a**) 3d (**4b**, **5b**)	 + 	**4a** : R = Et 90 % **4b** : R = Ph 22 % **5a** : R = Et **5b** : R = Ph 62 % (1: 5)
 **6**	RSH, *c*-HCl r. t. 0.5 h (**7a**) 18 h (**7b**)		**7a** : R = Et 95 % (12:1) **7b** : R = Ph 86 % (15:1)



The results can be explained as follows. 1-Thioglycosidation takes place first in the same way as the usual glycosidation reaction, followed by protonation on the ring oxygen and ring-opening to generate the thionium intermediate in both cases of pyranoses and furanoses. In the case of 2,3,4-tribenzylpyranoses, a nucleophilic attack of thiols is favoured. On the other hand, the intramolecular 5-exo-cyclization is more favorable than the intermolecular nucleophilic attack of thiols in the case of 2,3,5-tribenzylfuranoses. Also 1,2-*cis*-stereochemistry was predominant since the intramolecular attack is controlled by the steric effect of neighbouring benzyloxy group.

Interestingly, though protected pentpyranoses were easily convered to dithioacetals, and pentfuranoses to 1,2-*cis*-thioglycosides, neither 2,3,4,6-tetrabenzylglucose nor 2,3,4,6-tetrabenzylgalactose reacted with ethanethiol in the presence of *conc.* hydrochloric acid, and the starting materials were recovered.



Scheme 1 Reaction mechanism for the sulfurization of tribenzylpentose

Acknowledgement

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References

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3) K. C. Nicolaou, S. P. Seitz, D. P. Papahatjis, *J. Am. Chem. Soc.*, **105**, 2430 (1983).
4) T. Sato, Y. Fujita, J. Otera, H. Nozaki, *Tetrahedron Lett.*, **33**, 239 (1992).
5a) E. Fischer, *Chem. Ber.*, **27**, 673 (1894).
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6) ^{1}H-NMR ($CDCl_3$) δ : 7.35 - 7.24 (15H, m), 5.41 (1H, d, J = 4.9 Hz, H-1), 4.62 - 4.43 (6H, m, $PhCH_2$), 4.17 (1H, dd, J = 3.6, 3.9 Hz, H-2), 4.15 (1H, dd, J = 3.9, 6.6 Hz, H-4), 4.04 (1H, dd, J = 3.6, 3.9 Hz, H-3), 3.73 (1H, dd, J = 6.6, 9.9 Hz, H-5), 3.63 (1H, dd, J = 6.6, 9.9 Hz), 2.69 (2H,

q, J = 7.6 Hz, Et), 1.29 (3H, t, J = 7.6 Hz, Et). ^{13}C-NMR δ : 138.1, 137.8, 137.5, 128.4, 128.3, 128.2 (2C), 127.7, 127.6, 86.8 (C-1), 84.2 (C-4), 83.7 (C-3), 82.1 (C-2), 73.3, 72.3 71.8, 71.3 (C-5), 24.9, 15.1.

7) See Ref. 4). In their case α : β = 70 : 30.
^{1}H-NMR ($CDCl_3$) δ : 7.54 - 7.18 (20H, m), 5.67 (1H, d, J = 4.6, H-1), 4.66 - 4.52 (6H, m, $PhCH_2$), 4.26 (1H, dd, J = 3.3, 4.6 Hz, H-2), 4.22 (1H, ddd, J = 3.6, 6.3, 6.9 Hz, H-4), 4.10 (1H, dd, J = 3.3, 3.6 Hz, H-3), 3.77 (1H, dd, J = 6.3, 9.9 Hz, H-5), ^{13}C-NMR δ : 138.0, 137.6, 137.2, 135.3, 131.1, 130.7, 128.8, 128.4 (2C), 128.3, 127.8 (2C), 127.7, 127.5, 127.0, 126.7, 89.7 (C-1), 84.1 (C-2), 83.1 (C-3), 82.5 (C-4), 73.2 (C-5), 71.8, 70.9, 68.8 (C-5).

8) D. Ashford, *Biochem. J.*, **201**, 199 (1982).

9) ^{1}H-NMR ($CDCl_3$) δ : 7.40 - 7.23 (15H,m), 4.93 - 4.55 (6H, m, $PhCH_2$), 4.12 (1H, dd, J = 4.3, 6.3 Hz, H-3), 4.05 (1H, dd, J = 4.0, 6.3 Hz, H-2), 3.95 (1H, d, J = 4.0 Hz, H-1), 3.85 - 3.60 (3H, m, H-5, 4), 2.67, 2.57 (each 2H, q, J = 7.6 Hz), 1.19 (6H, t, J = 7.3 Hz), ^{13}C-NMR δ : 138.3, 138.0, 137.8, 128.4 (2C), 128.3, 128.2, 128.0, 127.8 (3C), 127.4, 82.1 (C-2), 80.0 (C-3), 78.1 (C-4), 74.9, 74.7, 71.9, 61.4 (C-5), 53.1 (C-1), 25.2, 25.1, 14.4.

10) ^{1}H-NMR ($CDCl_3$) δ : 7.26 - 7.10 (15H, m), 5.48 (1H, d, J = 5.3 Hz, H-1), 4.55 - 4.31 (7H, m), 4.05 (1H, dd, J = 5.6, 10.2 Hz, H-5), 3.59 (1H, dd, J = 6.0, 10.2 Hz, H-5), 2.59 (2H, q, J = 7.3 Hz), 1.21 (3H, t, J = 7.3 Hz). ^{13}C-NMR δ : 138.1, 137.7, 137.4, 128.3, 128.2, 127.8, 127.6, 127.5, 127.4, 86.9, 83.8, 81.9, 77.3, 73.2, 72.6, 72.1, 67.9, 24.6, 15.0.

11) ^{1}H-NMR ($CDCl_3$) δ : 7.55 - 7.03 (20H, m), 5.80 (1H, d, J = 5.0 Hz, H-1), 4.69 - 4.36 (7H, m, $PhCH_2$ and H-4), 4.22 (1H, dd, J = 2.3, 5.0 Hz, H-2), 4.09 (1H, dd, J = 2.3, 4.6 Hz, H-3), 3.80 (1H, dd, J = 6.1, 10.1 Hz, H-5), 3.71 (1H, dd, J = 5.8, 10.1 Hz, H-5), ^{13}C-NMR δ : 138.1, 137.7, 137.2, 135.6, 130.9, 128.7, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 126.6, 89.9 (C-1), 83.7 (C-2), 81.6 (C-3), 78.1 (C-4), 73.2, 72.9, 72.1, 67.7 (C-5).

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