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STEREOSELECTIVE SYNTHESES OF 1,2-TRANS *p*-MePh AND 2-PYRIDYL 1-THIOGLYCOSIDES CATALYZED BY ZIRCONIUM(IV) CHLORIDE

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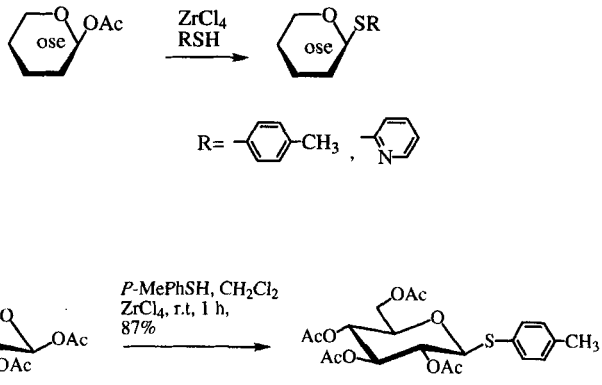
ABSTRACT: 1-Thioglycosides including per-*O*-acetyl *p*-MePh and 2-pyridyl 1-thioglycosides were chemically synthesized with high complete stereoselectivity by using $ZrCl_4$ as catalyst.

The acid-mediated thiolysis of peracetylated sugars is a well-established route for the synthesis of alkyl 1-thioglycosides.[1] However, when applied to the synthesis of aryl 1-thioglycopyranoside using stannic chloride or zinc chloride as Lewis acid catalyst, the reaction results in an anomeric mixture.[2] Even with boron trifluoride the reaction is not totally stereoselective and yields a small proportion of the 1,2-*cis* anomer.[3]



Scheme 1

Recently, zirconium(IV) chloride was used as a Lewis acid catalyst for the synthesis of 1,2-*trans* alkyl 1-thioglycopyranosides with complete stereoselectivity.[4] We here report the application of this methodology to the syntheses of some 1,2-*trans p*-MePh-1-thioglycopyranosides which were used as excellent donors in oligosaccharides library synthesis[5] and one spot oligosaccharides synthesis.[6]

Peracetylated glycopyranoses **1-5** were treated with *p*-toluenethiol and zirconium(IV) chloride, affording *p*-tolyl 1-thio-β-D-glycopyranosides **6-10** in yields of 81-95%. The ^{13}C NMR spectra of the crude reaction mixtures showed complete conversion of the starting material to the corresponding *p*-tolyl 1-thioglycopyranosides, and the signals at 84-87 ppm indicated that only 1,2-*trans* 1-thioglycopyranosides were formed.

This method was then extended to the preparation of 2-pyridyl 1-thioglycopyranosides **11** and **12**, which have been used as donors in the

Table 1
Yields and physical constants of *p*-MePh (**6**, **7**, **8**, **9**, **10**) and 2-pyridyl (**11**, **12**) per-*O*-acetyl 1-thioglycopyranosides

		Yield%	M.p (°C)	M.p (°C, lit.)	$[\alpha]_D$ ($CHCl_3$)	$[\alpha]_D$ (lit.)	ref.
Peractyl 4-Methylphenyl 1-thio-							
β-D-Glucopyranoside	(**6**)	87	115	118	-19.05 (c 0.21)	-21	11
β-D-Galactopyranoside	(**7**)	90	117-118	117-118.5	6.5 (c 0.92)		10
β-D-Xylopyranoside	(**8**)	81	107	108-109	-65.45 (c 3.3)	-65.4	10
β-D-Maltopyranoside	(**9**)	95	132-133	133-134	40.81 (c 0.50)	47.4	12
β-D-Lactopyranoside	(**10**)	95	155-156	120-123	-19.18 (c 0.37)	-18.3	12
Peractyl 2-Pyridyl 1-thio-							
β-D-Glucopyranoside	(**11**)	79	123-124	120-123	-4.08 (c 0.98)	-2.9	7
β-D-Galactopyranoside	(**12**)	73	77-78		15.76 (c 6.6)	2.0	7

Table 2
^{13}C NMR chemical shifts for *p*-MePh (**6**, **7**, **8**, **9**, **10**) and 2-pyridyl (**11**, **12**) per-*O*-acetyl 1-thioglycopyranosides

Compounds		Chemical shifts											
		C-1	C-2	C-3	C-4	C-5	C-6	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'
Peracetyl 4-Methylphenyl 1-thio-													
β-D-Glucopyranoside	(**6**)	85.57	69.73	73.84	68.01	75.48	61.94						
β-D-Galactopyranoside	(**7**)	86.65	67.17	71.91	67.17	74.19	61.42						
β-D-Xylopyranoside	(**8**)	86.21	69.40	72.09	68.31	65.14							
β-D-Maltopyranoside	(**9**)	84.97	70.79	76.59	72.89	76.06	61.78	95.76	70.21	69.51	68.38	68.38	62.93
β-D-Lactopyranoside	(**10**)	85.08	70.79	75.99	76.42	73.77	62.12	100.61	69.07	70.19	66.74	70.32	60.76
Peractyl 2-Pyridyl 1-thio-													
β-D-Glucopyranoside	(**11**)	81.08	69.09	75.56	67.89	75.33	61.48						
β-D-Galactopyranoside	(**12**)	81.61	66.43	71.52	66.96	74.01	60.86						

At 50.3 MHz in $CDCl_3$.

stereoselective syntheses of 1,2-*cis*-linked oligosaccharides[7] and *C*-glycosides.[8]

The present methodology is limited in that the desired products were not observed with *p*-nitrothiophenol, due presumably to the reduced nucleophilicity of this reagent.

Experimental

Melting points were measured in capillary tubes with a Büchi 535 apparatus and were corrected. Optical rotations were determined with a Jobin-Yvon "Digital Micropolarimeter". ^{13}C NMR spectra were recorded with a Bruker 200 spectrometer in $CDCl_3$. Mass spectra were record on a Finnigan MAT 288 mass spectrometer. The reaction were monitored by TLC on Silica Gel plates F-254 (E. Merck). Silica Gel 60 (E. Merck) was used for column chromatography.

General procedure for the preparation of peracetyl p-*tolyl 1,2*-trans *1-thioglycopyranosides* (**6, 7, 8, 9** and **10**).—To a solution of 1,2-*trans* per-*O*-acetyl glycopyranose (2.5 mmol) in dry CH_2Cl_2 (10 mL) was added $ZrCl_4$ (2 eq.) and *p*-toluenethiol (1.5 eq.). After stirring the mixture at room temperature for 1 h, 100 mL CH_2Cl_2 was added. The mixture was then washed with iced $NaHCO_3$ solution and dried with Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography (1:1, hexane/ethyl acetate) to afford the desired product.

General procedure for the preparation of peracetyl 2-pyridyl 1,2-trans *1-thioglycopyranosides* (**11** and **12**).—To a solution of 1,2-*trans* per-*O*-acetyl

glycopyranose (2.5 mmol) in 1,2-dichloroethane (20 mL) was added $ZrCl_4$ (2 eq.) and 2-thiopyridine (2 eq.). The reaction mixture was stirred at 60°C for 15 hours, cooled to room temperature, and 100 mL dichloromethane was added. The mixture was washed with iced $NaHCO_3$ solution. After drying (Na_2SO_4) and evaporation of the solvent, the residue was purified by column chromatography (1:1, hexane / ethyl acetate) to afford the product.

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