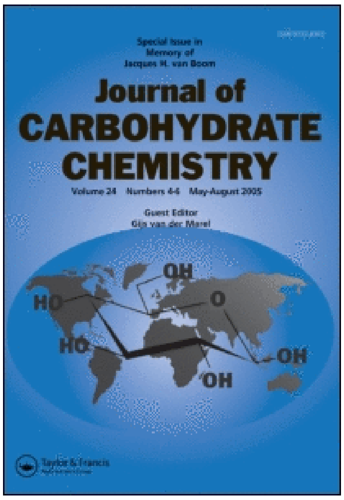


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Novel Route to 4-Thiofuranosides. Synthesis of Methyl 4-Thio-α-D-Talofuranoside

Björn Classon[a]; Per J. Garegg[a]; Bertil Samuelsson[a]; Zhengchun Liu[a]
[a] Department of Organic Chemistry, Arrhenius Laboratory. University of Stockholm, Stockholm, Sweden

To cite this Article Classon, Björn , Garegg, Per J. , Samuelsson, Bertil and Liu, Zhengchun(1987) 'Novel Route to 4-Thiofuranosides. Synthesis of Methyl 4-Thio-α-D-Talofuranoside', Journal of Carbohydrate Chemistry, 6: 4, 593 — 597
To link to this Article: DOI: 10.1080/07328308708058888
URL: http://dx.doi.org/10.1080/07328308708058888

J. CARBOHYDRATE CHEMISTRY, 6(4), 593-597 (1987)

NOVEL ROUTE TO 4-THIOFURANOSIDES. SYNTHESIS OF METHYL 4-THIO-α-D-TALOFURANOSIDE

Björn Classson*, Per J. Garegg, Bertil Samuelsson and Zhengchun Liu

Department of Organic Chemistry, Arrhenius Laboratory,
University of Stockholm, S-106 91 Stockholm, Sweden.

Received May 11, 1987 - Final Form September 14, 1987

ABSTRACT

Treatment with triiodoimidazole and triphenylphosphine of 2,3,5,6-tetra-O-benzyl-D-mannose diethyl dithioacetal, obtained in three standard reaction steps from methyl α-D-mannofuranoside, gave ring closure to ethyl 2,3,5,6-tetra-O-benzyl-1,4-dithio-α-D-talofuranoside, with sulfur in the furanose ring.

INTRODUCTION

Carbohydrates with sulfur in the furanose ring are of potential biological interest, e.g. as glycoside inhibitors. Their synthesis has been reviewed.[1,2]

In general, these syntheses have involved displacement of a leaving group at C-4 of a suitably protected carbohydrate using a nucleophilic reagent, e.g. thiocyanate, thiolacetate or thiolbenzoate. We now report on a synthesis of methyl 4-thio-α-D-talofuranoside, illustrating a novel use of the triphenylphosphine-triiodoimidazole reagent system, previously used, inter alia, for converting hydroxy into deoxyiodo compounds.[3]

RESULTS AND DISCUSSION

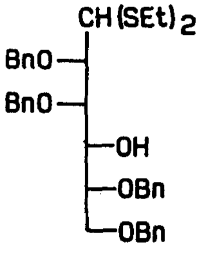
Methyl α-D-mannofuranoside[4] was benzylated and the product was hydrolysed to give 2,3,5,6-tetra-O-benzyl-D-mannopyranose, which was converted into the diethyl dithioacetal 1. Treatment of 1 with triphenylphosphine and triiodoimidazole afforded ethyl 2,3,5,6-tetra-O-benzyl-1,4-dithio-α-D-talopyranoside (2) in 86% yield. The corresponding α- or β-D-mannopyranoside were not observed.

The *talo* configuration of 5 was deduced from coupling constants. Thus, an analogous D-manno compound, 1,2,3,5,6-tetra-O--acetyl-4-thio-α-D-mannofuranose[5] has $J_{3,4}$ = 3.9 Hz and $J_{4,5}$ = 10.0 Hz whereas the corresponding coupling constant for 5 are 8.9 and 4.5 Hz respectively.

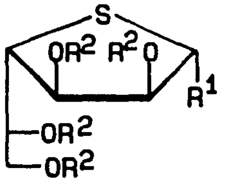
The thioglycoside 2 was converted into the methyl α-D-glycoside 3 by treatment with bromine in methanol, followed by catalytic hydrogenolysis to yield the compound 4.

Replacement of a hydroxyl group by a deoxyiodo is known to proceed with inversion of configuration. Since 2 has the *talo*-configuration it seems probable, according to previous mechanistic proposals,[6] recently corroborated by ^{31}P NMR studies,[7] that one of the sulfur atoms in the dithioacetal 1 has intervened before nucleophilic attack of iodide anion can occur upon the presumed 4-phosphonium intermediate of 1.

Dialkyl dithioacetals of aldoses with a free 4-OH and benzyl groups in the other positions are readily obtained from glycofuranosides. The above formation of a 4-thiofuranoside, probably proceeding *via* an intermediate 4-phosphonium derivative represents a novel entry into the 4-thio-glycofuranoside series.



1



2 R^1=SEt R^2=Bn
3 R^1=OMe R^2=Bn
4 R^1=OMe R^2=OH
5 R^1=OMe R^2=OAc

EXPERIMENTAL

General methods. These were the same as those described before.[8]

2,3,5,6-Tetra-O-*benzyl*-D-*mannose diethyl dithioacetal* (1). Methyl α-D-mannofuranoside[4] (8.0 g) was benzylated at room temperature with benzyl bromide (63.2 g) and sodium hydride (8.9 g) in *N*,*N*-dimethyl formamide (250 mL). The product was worked up and purified by silica gel column chromatography (isooctane - ethyl acetate 10:3) to yield *methyl 2,3,5,6-tetra*-O-*benzyl*-α-D-*mannofuranoside* (19.1 g, 83%): α_D $+18^\circ$ (*c* 3.6, $CHCl_3$); δ_C (25 MHz, $CDCl_3$) 55.8 (OCH_3), 70.5 (C-6), 76.2 (C-5), 78.1 (C-3), 78.2 (C-2), 85.0 (C-4), 107.2 (C-1).

Anal. Calcd for $C_{35}H_{38}O_6$: C, 75.8; H, 6.9. Found: C, 75.8; H, 6.8.

The furanoside (10.0 g) was treated with 80% trifluoroacetic acid (20 mL) at 0 °C for 72 h. The solution was extracted with chloroform. The chloroform extract was washed with water, saturated aqueous sodium hydrogen carbonate and water, dried, filtered and concentrated. Silica gel column chromatography (toluene - ethyl acetate 85:15) gave *2,3,5,6-tetra*-O-*benzyl*-D-*mannose* (6.72 g, 69%): α_D -35° (*c* 3.2, $CHCl_3$); δ_C (25 MHz, $CDCl_3$) 69.7 (C-6), 77.3 (C-5), 77.9 (C-3), 78.1 (C-2), 79.8 (C-4), 96.1 (C-1).

Anal. Calcd for $C_{34}H_{36}O_6$: C, 75.5; H, 6.7. Found: C, 75.8; H, 6.7.

The tetrabenzyl mannose (6.5 g) was treated at room temperature with ethanethiol (2.99 g) in dichloromethane (80 ml) containing a catalytic amount of titanium(IV) chloride. The mixture was diluted with dichloromethane and the product was worked up as described above and then purified by silica gel column chromatography (isooctane - ethyl acetate 10:2) to yield 1 (6.8 g, 87%): α_D -32° (*c* 1, ethanol); δ_C 14.6 ($2xCH_3$), 25.2 and 26.2 ($2xSCH_2$), 53.8 (C-4), 70.0 (C-5), 70.7 (C-6), 77.5 (C-3), 78.7 (C-2), 83.2 (C-1).

Anal. Calcd for $C_{38}H_{46}O_5S_2$: C, 70.6; H, 7.2; S, 9.9. Found: C, 70.9; H, 7.3; S, 9.7.

Ethyl 2,3,5,6-tetra-O-benzyl-1,4-dithio-α-D-talofuranoside (2). Triphenyl phosphine (7.1 g) and triiodoimidazole (7.24 g) were added to a solution of 1 in toluene - acetonitrile (2:1, 60 ml) and the solution was kept at 90 °C for 24 h. After the usual work-up,[9] the product was purified by silica gel column chromatography (toluene - ethyl acetate 9:1) to yield 2 (2.8 g, 86%): α_D -15° (c 4.4, $CHCl_3$); δc (25 MHz, $CDCl_3$) 14.6 (CH_3), 26.4 (SCH_2), 50.7 and 50.9 (C-1 and C-4), 72.1 (C-6), 77.5 (C-5), 80.6 (C-3), 83.5 (C-2).

Anal. Calcd for $C_{36}H_{40}O_4S_2$: C, 72.0; H, 6.7; S, 10.7. Found: C, 72.4; H, 6.7; S, 9.9.

Methyl 2,3,5,6-tetra-O-benzyl-4-thio-α-D-talofuranoside (3). Compound 2 (2.5 g) was treated with a 3% (w/vol) solution of bromine in methanol (500 mL) at 0 °C for 1 h, worked up and purified as described above and then purified by silica gel chromatography (isooctane - ethyl acetate 10:2) to give 3 (1.64 g, 69%): α_D -16 (c 1, ethanol); δ_C (25 MHz, $CDCL_3$) 49.9 (C-4), 56.2 (OCH_3), 72.9 (C-6), 77.1 (C-5), 81.2 and 81.3 (C-2 and C-3), 89.3 (C-1).

Anal. Calcd for $C_{35}H_{38}O_5S$: C, 73.7; H, 6.7; S, 5.6. Found: C, 73.4; H, 6.8; S, 5.5.

Methyl 4-thio-α-D-talofuranoside (4). A solution of 3 (0.3 g) in 95% aqueous ethanol (50 mL) was hydrogenolysed with 10% palladium on carbon (1.01 g) at 400 KPa for 5 days, filtered and concentrated. Purification of the product by silica gel column chromatography (ethyl acetate - methanol - acetic acid - water 12:3:3:2) afforded 4 (56 mg, 51%): α_D +55° (c 1, H_2O); δ_C (25 MHz, $(CD_3)_2SO$) 51.8 (C-4), 55.7 (OCH_3), 65.6 (C-6), 71.1 (C-5), 74.3 (C-3), 78.1 (C-2), 91.3 (C-1). A satisfactory elemental analysis could not be obtained for this compound. Its purity was, however, demonstrated by TLC and the NMR was in agreement with the assigned structure. It was converted by conventional acetylation into methyl 2,3,5,6-tetra-O-acetyl-4-thio-α-D-talofuranoside (5) which had α_D +122° (c 0.13, $CHCl_3$): δ_C (25 MHz, $CDCl_3$) 20.7 and 20.9 ($4\times CH_3CO$), 47.2 (C-4), 56.6 (OCH_3), 64.2 (C-6), 69.8 (C-5), 73.7 (C-3), 76.7 (C-2) 89.2 (C-1); δ_H (400 MHz,

$CDCl_3$). 5.48 (dd, $J_{2,3}$ = 3.5 Hz, H-2), 5.33 (dd, $J_{3,4}$ = 8.9 Hz, H-3), 5.26 (m, H-5), 4.85 (d, $J_{1,2}$ = 1.7 Hz, H-1), 4.28 and 4.15 (H-6 and H-6'), 3.83 (dd, $J_{4,5}$ = 4.5 Hz, H-4).

Anal. Calcd for $C_{15}H_{22}O_9S$: C, 47.6; H, 5.9; O, 38.1; S, 8.5. Found: C, 47.1; H, 5.8; O, 38.0; S, 8.3.

ACKNOWLEDGEMENTS

This work was suppported by grants from the Swedish National Board for Technical Development and the Swedish Natural Science Research Council as well as by a maintenance grant from the Government of China (to Z. L.).

REFERENCES

1. D. Horton and J. Wander in The Carbohydrates, Vol. 1B; W. Pigman and D. Horton, Eds.; Academic Press, New York, N.Y., 1980, p. 799, and references therein.

2. H. Paulsen and K. Todt, Advan. Carbohyd. Chem., 23, 115 (1968).

3. P. J. Garegg, Pure Appl. Chem., 56, 845 (1984) and references therein.

4. D. F. Mowery, in Methods in Carbohydrate Chemistry, Vol. 2, R. L. Whistler and M. L. Wolfrom, Eds.; Academic Press, New York and London, 1963, p. 328.

5. R. H. Shah, J. L. Bese, and O. P. Bahl, Carbohydr. Res., 77, 107 (1979).

6. B. Classon, P. J. Garegg, and B. Samuelsson, Can. J. Chem., 59, 339 (1981).

7. P. J. Garegg, T. Regberg, J. Stawinski, and R. Strömberg, J. Chem. Soc., Perkin Trans. II, 271 (1987).

8. P. Ossowski, Å. Pilotti, P. J. Garegg, and B. Lindberg, J. Biol. Chem., 259, 11337 (1984).

9. P. J. Garegg, R. Johansson, C. Ortega, and B. Samuelsson, J. Chem. Soc. Perkin Trans. I, 681 (1982).