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Carbohydrate Research 326 (2000) 323–325

CARBOHYDRATE RESEARCH

Note

Synthesis of 5-thio-L-altrose☆

Neil A. Hughes *

Department of Chemistry, University of Newcastle upon Tyne, Newcastle upon Tyne, NE1 7RU, UK

Received 7 December 1999; accepted 2 February 2000

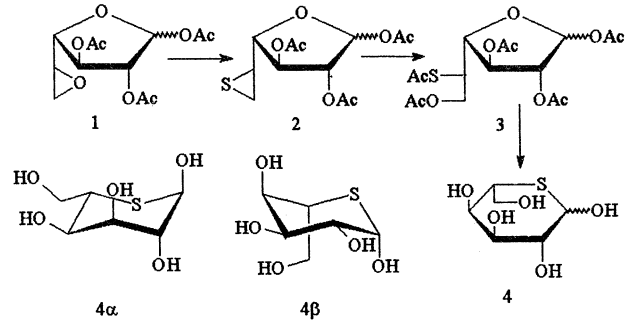
Abstract

Treatment of 1,2,3-tri-*O*-acetyl-5,6-anhydro-D-galactofuranose with thiourea gave 1,2,3-tri-*O*-acetyl-5,6-dideoxy-5,6-epithio-L-altrofuranose, acetolysis of which gave 1,2,3,6-tetra-*O*-acetyl-5-*S*-acetyl-5-thio-L-altrofuranose. Deacetylation of the latter gave 5-thio-L-altrose.

Keywords: 5,6-Anhydro-D-galactose, protected; Conformation: 5,6-Dideoxy-5,6-epithio-L-altrose, protected; 5-Thio-L-altrose; Thio sugar

1. Introduction

Earlier we reported the synthesis of 5-thio-D-altrose [2]; we now describe the synthesis of the L enantiomer by standard procedures. Treatment of a 2:3 α,β mixture of 1,2,3-tri-*O*-acetyl-5,6-anhydro-D-galactofuranose (**1**) [3] with thiourea in methanol gave the *altro*-episulfide **2** in modest yield, the reaction being accompanied by deacetylation. Acetolysis of **2** gave the pentaacetate **3**, which yielded 5-thio-L-altrose (**4**) on cleavage of the acetate groups. Compounds **2** and **3** were α,β mixtures (**2**, 2:1; **3**, 3:1) and in their ^{1}H NMR spectra the 1,2-*trans* α-forms were identified by the lack of coupling between H-1 and H-2 (see Table 1). The Table also shows differing values of $J_{2,3}$ for the α and β anomers of both **2** and **3**, suggesting that the α anomers have the E_2 and the β anomers the ^2E conformation. The ^{1}H NMR spectrum of 5-thio-L-altrose (**4**) itself in D_2O solution showed it to be a mixture of α- and β-pyranose forms, **4α** and **4β**. The major component **4β** adopted the $^4C_1$ conformation, with axial H-2 and H-3 ($J_{2,3}$ 9.5; $J_{4,5}$ 4.5; $J_{1,5}$ 0.9 Hz), while the minor component **4α** was largely in the $_4C^1$ conformation ($J_{2,3}$ 6.7; $J_{4,5}$ 7.0 Hz). Conformational preferences for 5-thio-altropyranose compounds were discussed at length in the earlier paper [2].



2. Experimental

General methods.—NMR spectra were recorded at 500 MHz (^{1}H) or 75 MHz (^{13}C) for solutions in $CDCl_3$ or D_2O. The petroleum

☆ 5-Thiopyranoses, Part 15. For Part 14, see Ref. [1].

* Tel.: +44-191-2227074; fax: +44-191-2226929.
E-mail address: n.a.hughes@ncl.ac.uk (N.A. Hughes)

0008-6215/00/$ - see front matter
PII: S0008-6215(00)00052-5

Table 1
^{1}H NMR data: chemical shifts (ppm) and coupling constants (Hz)

Compounds	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,4}$)	H-4 ($J_{4,5}$)	H-5 ($J_{5,6a}$)	H-6a ($J_{5,6b}$)	H-6b ($J_{6a,6b}$)	Other signals
2α [a]	6.19	5.17	5.24	3.87	3.09	2.56	2.32	2.14, 2.12, 2.11 (3 × Ac)
	(0.0)	(1.4)	(4.3)	(7.8)	(6.1)	(5.2)	(1.6)	
2β [a]	6.38	5.31	5.69	3.55	3.09	2.55	2.25	2.13, 2.10, 2.09 (3 × Ac)
	(4.5)	(6.9)	(5.4)	(8.5)	(6.4)	(5.1)	(1.6)	
3α [a]	6.21	5.10	5.17	4.34	4.04	4.38	4.31	2.18, 2.13, 2.12, 2.07 (4 × OAc);
	(0.0)	(0.0)	(3.9)	(8.3)	(4.6)	(4.9)	(11.6)	2.38 (SAc)
3β [a]	6.38	5.28	5.49	4.17	4.07	4.37	4.30	2.20, 2.10, 2.09, 2.07 (4 × OAc);
	(4.5)	(6.4)	(4.8)	(9.8)	(4.4)	(4.4)	(11.6)	2.38 (SAc)
4α [b]	4.82	3.99	4.11	3.75	3.18	3.82	3.75	
	(6.6)	(6.7)	(2.9)	(7.0)	(5.5)	(6.7)	(11.9)	
4β [b]	5.00	3.92	4.01	4.28	3.04	4.00	3.82	
	(3.0)	(9.5)	(2.9)	(4.5)	(7.6)	(6.4)	(11.9)	($J_{1,5}$ 0.9 Hz)

[a] In $CDCl_3$.
[b] In D_2O.

ether (PE) used had a boiling range of 60–80 °C. Kieselgel 60 was used for thin-layer chromatography (TLC) (E. Merck 5554) and column chromatography (Prolabo 200–400 mesh); elution was with EtOAc–petroleum ether mixtures.

1,2,3-Tri-O-*acetyl-5,6-dideoxy-5,6-epithio*-L-*altrofuranose* (**2**).—A solution of 5,6-anhydro-1,2,3-tri-*O*-acetyl-D-galactofuranose (**1**) [3] (830 mg, 2.88 mmol) and thiourea (800 mg, 10.05 mmol) in MeOH (10 mL) was left at room temperature (rt) for 20 h. The solvent was removed in vacuo and the residue partitioned between CH_2Cl_2 and water. The organic extract was dried ($MgSO_4$) and concentrated to leave a residue, which was chromatographed on silica gel and eluted with 3:1 petroleum ether–EtOAc. Early fractions contained the episulfide **2** (210 mg, 0.69 mM, 24%), mass spectrum: *m/z* 304.061440 ($C_{12}H_{16}O_7S$ Calcd. 304.061675 for M^+). A later fraction contained partially deacetylated material, which on reacetylation (Ac_2O–pyridine) gave a further quantity of **2** (173 mg, 0.57 mM, 20%).

1,2,3,6-Tetra-O-*acetyl-5*-S-*acetyl-5-thio*-L-*altrofuranose* (**3**).—A mixture of **2** (280 mg, 0.92 mmol), NaOAc (300 mg), Ac_2O (3 mL), and HOAc (0.3 mL) was heated with stirring under reflux for 6 h. Water (20 mL) was added to the cooled mixture and after 2 h the mixture was extracted with CH_2Cl_2. The extract was washed with dilute $KHCO_3$, dried ($MgSO_4$) and concentrated. The residue was chromatographed in silica, eluting with 2:1 petroleum ether–EtOAc to yield the pentaacetate **3** as a syrup (250 mg, 0.62 mmol, 67%), mass spectrum: *m/z* 347.079765 ($C_{16}H_{22}O_{10}S$ calcd. 347.080065 for $M^+ - COCH_3$).

5-Thio-L-*altrose* (**4**).—Under an N_2 atmosphere the pentaacetate **3** (250 mg, 0.61 mmol) was dissolved in MeOH (2 mL) containing NaOMe [(from Na (30 mg, 1.3 mmol)]. After 10 min at rt, CO_2 was passed into the mixture which was then evaporated to dryness, dissolved in water (2 mL) and passed through Zerolit-225-H^+. The eluate was evaporated and the residue dissolved in EtOH and reevaporated. Recrystallization of the final residue from EtOH gave 5-thio-L-altrose (**4**, 60 mg, 0.31 mmol, 51%), m.p. 175–179 °C, $[\alpha]_D$ + 63° → + 58° (final) (*c* 1.0, H_2O) (lit. for the D enantiomer, m.p. 177–178 °C, $[\alpha]_D$ − 68° → − 48° (H_2O) [2])^{13}C NMR (D_2O) **4α**: 75.6 (C-1), 74.3, 73.5, 70.3 (C-2, C-3, C-4), 63.0 (C-6), 45.3 (C-5); **4β**: 75.4 (C-1), 72.5, 71.9, 69.2 (C-2, C-3, C-4), 65.0 (C-6), 49.2 (C-5). Anal. Calcd. For $C_6H_{12}O_5S$: C, 36.72; H, 6.17. Found: C, 36.61; H, 5.98.

Acknowledgements

The author thanks L. Cook and M.N.S. Hill for the NMR data, D. Dunbar for the elemental analyses and S. Addison for the MS data.

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