ELSEVIER

www.elsevier.nl/locate/carres

Carbohydrate Research 322 (1999) 147–150

CARBOHYDRATE RESEARCH

Note

Solution and solid-state structure of 2,6-anhydro-1,1-bis(ethylsulfonyl)-1-deoxy-D-talitol

Peter Norris *, Timothy R. Wagner

Department of Chemistry, Youngstown State University, 410 Wick Avenue, Youngstown, OH 44555, USA

Received 20 May 1999; accepted 2 August 1999

Abstract

D-Galactose diethyl dithioacetal can be oxidized with *m*-chloroperoxybenzoic acid to produce the previously described highly crystalline bis(ethylsulfone), the structure of which has now been confirmed by nuclear magnetic resonance spectroscopy and X-ray crystallography. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: *C*-Glycoside, bis(sulfone); D-Galactose diethyl dithioacetal; X-ray crystallography

Carbohydrate-derived dithioacetals are among the most useful acyclic derivatives in terms of their utility in characterization and synthesis [1]. The MacDonald–Fischer chain degradation process relies upon an exhaustive oxidation of the dithioacetal group, followed by base-promoted cleavage of the bis(sulfone) group via a retro-aldol type reaction [2], and complements other chain descent processes such as the Wohl degradation.

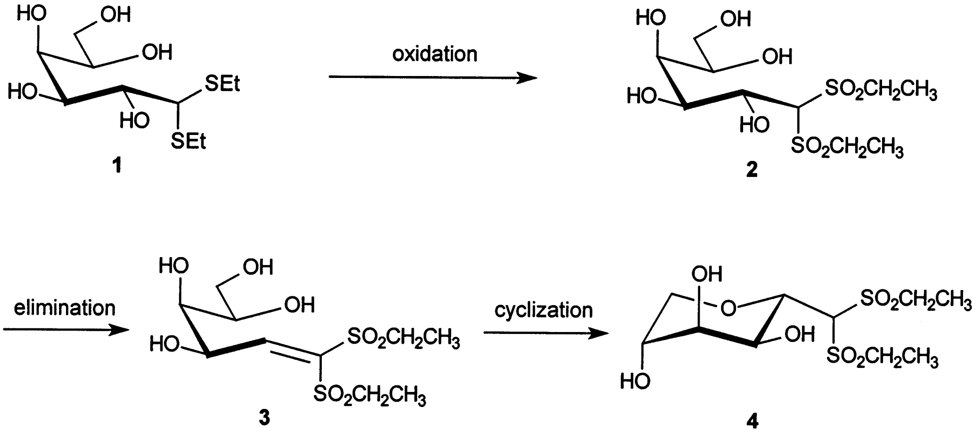
The effects of oxidation on carbohydrate dithioacetals have been investigated in depth by, amongst others, Zinner and Falk [3]. Later Hough and Taylor [4] observed that the outcome of exhaustive oxidation to the bis(sulfone) state is dependent upon the structure of the sugar involved. Zinner and Falk initially isolated the pentahydroxy bis(ethylsulfone) **2** (Scheme 1) after oxidizing D-galactose diethyl dithioacetal (**1**) using hydrogen peroxide and ammonium molybdate at 0 °C. However, Hough and Taylor later repeated this experiment and claimed that **2** converts to pyran **4** upon recrystallization, where **4** was the product of a sequence involving elimination of water from **2** to generate a ketene dithioacetal bis(sulfone) **3**. Highly electron-deficient alkene **3** is subsequently trapped in a 6-*exo*-trig type cyclization to afford **4** (Scheme 1). Although these later workers discovered that the oxidation outcome depends greatly on dithioacetal structure, in the aldohexose series the diethyl dithioacetals of D-mannose, D-glucose, and D-galactose were each found to undergo the oxidation–elimination–cyclization sequence, resulting in *C*-glycosyl bis(ethylsulfones) isolated in the pyran forms [4].

These earlier reports appeared before the routine application of nuclear magnetic resonance spectroscopy in carbohydrate chemistry, and the possibility of a ring closure from O-5, to form a furan ring, could not be completely discounted. We were interested in using sugar-derived bis(sulfones) in *C*-glycoside synthesis and therefore required more rigor-

---

* Corresponding author. Fax: + 1-330-742-1579.

0008-6215/99/$ - see front matter © 1999 Elsevier Science Ltd. All rights reserved.
PII: S0008-6215(99)00208-6



Scheme 1.

ous proof of the structure of several of these *C*-glycosyl bis(sulfones). We have now oxidized dithioacetal **1** and analyzed the crystalline product by NMR spectroscopy and X-ray diffraction in order to confirm the earlier results of Hough and Taylor.

Oxidation of **1** using excess *m*-chloroperoxybenzoic acid (*m*-CPBA) in dioxane without external cooling resulted in a highly exothermic reaction. After stirring for 24 h and filtration of the precipitate, crystallization of the residue from ethanol resulted in a crystalline solid that was suitable for X-ray diffraction analysis.

The solid, mp 180–185 °C[1], showed ten signals in its ^{13}C spectrum, the methylene carbons of the exocyclic bis(ethylsulfone) group appearing at 50.31 and 51.59 ppm, i.e., significantly downfield of the methylene carbons in the starting dithioacetal **1** (25.3 and 25.9 ppm). The ^{1}H NMR spectrum, taken in Me_2SO-d_6, showed signals for a total of 20 protons, including the OH groups. Upon the addition of a drop of D_2O, the four most downfield signals (4.82–5.05 ppm) disappeared, and these were therefore assigned to the OH groups on the pyran ring (4.82, 4.97, 5.05 ppm) and the acidic proton α to the two sulfone groups (4.95 ppm). The ring protons were assigned with the help of a COSY experiment as follows. With the acidic proton on the bis(ethylsulfonyl)methyl group established at 4.95 ppm, the adjacent proton on C-2 (see Fig. 1 for numbering scheme) appeared at 4.46 ppm ($J = 1.5$, 10.2 Hz). The multiplet at 4.23 ppm was assigned to the proton at C-3, and the multiplet at 3.75 ppm to the proton at C-4. The remaining ring protons were part of a seven-hydrogen multiplet that included the methylene signals from the bis(ethylsulfonyl) groups. It should be noted that the large coupling between H-2–H-3 (10.2 Hz) strongly supports the $^{1}C_{4}$ pyran structure of **4** proposed by Hough and Taylor. The $^{4}C_{1}$ form would have a much smaller coupling for these protons as the dihedral angle would approach 90°.

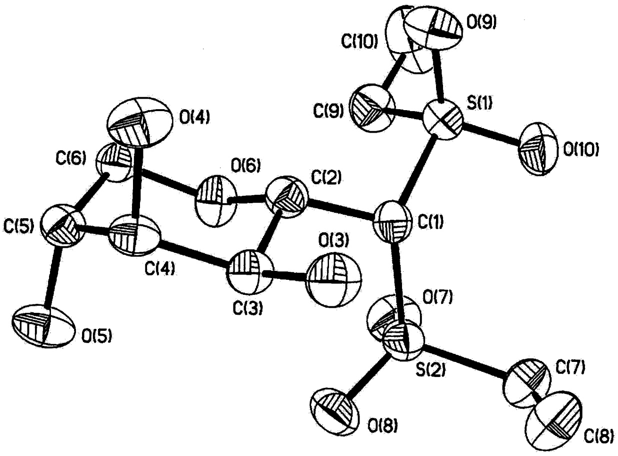


Fig. 1. ORTEP-type [5] representation of **4**. Selected bond lengths (Å) and bond angles (°): C(1)–C(2) = 1.527(3), C(2)–C(3) = 1.535(3), C(3)–C(4) = 1.523(3), C(4)–C(5) = 1.515(3), C(5)–C(6) = 1.500(3), O(6)–C(6) = 1.439(3), O(6)–C(2) = 1.420(3) Å; C(1)–C(2)–C(3) = 113.9(2), S(1)–C(1)–S(2) = 113.42(14)°.

---

[1] Hough and Richardson [4] have reported several melting points for **4**, the most recent being 193–195 °C, and claimed the value changes with such factors as the method used and the rate of heating the sample. The melting point reported herein is for a homogenous sample that was heated very slowly to its melting point.

Table 1
Crystal data summary and refinement results for **4**

Structural formula	$C_{10}H_{20}O_8S_2$
Formula weight	332.38
Color	colorless
Crystal Size (mm)	$0.38 \times 0.23 \times 0.18$
Space group	$P2_1$ (No. 4)
Unit cell dimensions	
a (Å)	10.0985(5)
b (Å)	5.8282(3)
c (Å)	12.8031(5)
β (°)	104.224(3)
V (Å^3)	730.44(6)
Z	2
$D_{\text{calc.}}$ (g/cm^3)	1.511
λ (Cu K$_\alpha$) (Å)	1.54178
μ (mm^{-1})	3.637
θ Range for data collection (°)	3.56–57.15
Limiting indices	$-11 \leq h \leq 11$, $-5 \leq k \leq 6$, $-13 \leq l \leq 13$
Reflections collected	2253
Independent reflections	1916 ($R_{\text{int}} = 0.0192$)
Number of parameters	262
Refinement method	Full-matrix least-squares on F^2
Hydrogen atom positions	Refined
Final R indices [$I > 2\sigma(I)$]	$R_1(F)$ [a] $= 0.0263$, $wR_2(F^2)$ [b] $= 0.0722$
Final R indices (all data)	$R_1(F)$ [a] $= 0.0264$, $wR_2(F^2)$ [b] $= 0.0724$
Goodness-of-fit on F^2	1.041
Absolute structure parameter	0.018(14)
Extinction coefficient	0.0194(12)
Largest difference peak and hole (e Å^{-3})	0.206 and -0.233

[a] $R_1(F) = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ with $F_o > 4.0\sigma(F)$.

[b] $wR_2(F^2) = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$ with $F_o > 4.0\sigma(F)$, and $w^{-1} = \sigma^2(F_o)^2 + (WP)^2 + TP$, where $P = (\max(F_o^2, 0) + 2F_c^2)/3$, $W = 0.0561$, and $T = 0.05$.

The small coupling constant for the exocyclic bis(sulfone) proton (1.5 Hz) suggests that the bis(sulfone) group is oriented such that the H-1–C-1–C-2–H-2 dihedral angle is close to 90°. This might be expected, as the electron-rich sulfone groups would orient themselves to point away from the endocyclic oxygen in **4**, thus minimizing any electrostatic interactions. This is supported by the crystal structure of **4** (Fig. 1), which shows this to be the case in the solid state.

The X-ray diffraction study (Fig. 1, Tables 1 and 2) clearly showed the crystalline product to indeed be the pyran proposed by Hough and Taylor. The compound exists in the solid state in the $^1C_4$ conformation as predicted [4] in order for the bulky bis(ethylsulfone) group to be equatorial.

Table 2
Atomic coordinates ($\times 10^4$) [a] and equivalent isotropic displacement parameters (Å $\times 10^3$) for **4**

Atom	x	y	z	U_{eq} [b]
S(1)	3267(1)	756(1)	1816(1)	35(1)
S(2)	630(1)	3074(1)	2012(1)	37(1)
O(3)	752(2)	−1939(4)	3962(1)	41(1)
O(4)	3090(2)	−1806(3)	5777(1)	41(1)
O(5)	1900(2)	4049(3)	5929(2)	43(1)
O(6)	3048(2)	3006(3)	4140(1)	36(1)
O(7)	1253(2)	4992(3)	1615(2)	53(1)
O(8)	−93(2)	3525(4)	2823(1)	50(1)
O(9)	4140(2)	−1087(3)	2313(2)	50(1)
O(10)	2583(2)	554(4)	699(1)	51(1)
C(1)	1926(2)	905(5)	2543(2)	32(1)
C(2)	2482(2)	839(4)	3765(2)	31(1)
C(3)	1417(2)	146(4)	4380(2)	30(1)
C(4)	2096(2)	−5(4)	5580(2)	29(1)
C(5)	2843(2)	2213(4)	5957(2)	31(1)
C(6)	3774(2)	2873(5)	5256(2)	31(1)
C(7)	−503(3)	1703(6)	922(2)	51(1)
C(8)	−1291(3)	−261(7)	1247(3)	66(1)
C(9)	4221(3)	3331(6)	2026(2)	47(1)
C(10)	5261(5)	3342(10)	1371(4)	81(1)

[a] E.s.d are given in parentheses.

[b] U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

In summary, we have repeated the exhaustive oxidation of D-galactose dithioacetal (**1**) first studied by Zinner and Falk [3], and then by Hough and Taylor [4]. Using NMR spectroscopy and X-ray diffraction, we have confirmed the original assignment of the pyran structure of **4** made by Hough. We are now using compounds related to **4** for the synthesis of more elaborate *C*-glycosides.

1. Experimental

General methods.—Melting points were determined on a Mel-Temp apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 instrument at 400 and 100 MHz, respectively, as solutions in Me_2SO-d_6 with Me_4Si as the internal standard.

2,6-Anhydro-1,1-bis(ethylsulfonyl)-1-deoxy-D-talitol (**4**).—D-Galactose diethyl dithioacetal (**1**, 2.0 g, 6.99 mmol) was dissolved in warm dioxane (40 mL), then *m*-CPBA (7.8 g, ~ 65% assay, ~ 30 mmol) was added portionwise over 10 min. The mixture became hot and was allowed to cool and then stirred for 24 h at room temperature. The resultant precipitate was filtered, then washed with cold dioxane and ether. Recrystallization from ethanol afforded **4** as colorless needles (2.0 g, 86%): mp 180–185 °C [4], $[\alpha]_D + 14°$ (*c*, 5.0, H_2O) [lit. [4] +19° (*c*, 2.17, H_2O)]; ^1H NMR: δ 1.21–1.26 (6 H, 2 × t, *J* 7.3 Hz, 2 × CH_2CH_3), 3.40–3.67 (7 H, m, H6,6′, 2 × CH_2CH_3), 3.75 (1 H, m, H-4), 4.23 (1 H, m, H-3), 4.46 (1 H, dd, *J* 1.5 Hz, 10.2, H-2), 4.82 (1 H, d, *J* 7 Hz, OH), 4.95 (1 H, d, *J* 1.5 Hz, H-1), 4.96 (1 H, d, *J* 5.6 Hz, OH), 5.05 (1 H, d, *J* 3.5 Hz, OH). ^{13}C NMR: δ 6.44 (CH_3), 7.24 (CH_3), 50.32 (CH_2), 51.59 (CH_2), 65.1 (CH), 69.1 (CH), 70.8 (CH), 71.1 (CH), 73.3 (CH), 79.3 (CH).

X-ray crystal structure of **4** *[5]*[2].—Diffraction data were collected using Cu K_α radiation (1.54178 Å) on a Bruker (i.e., Siemens) P4 diffractometer equipped with a graphite monochromator. The unit cell constants and orientation matrix found prior to data collection were obtained from least-squares refinement of 100 reflections, ranging from 7 to 56° in 2θ. A full sphere of intensity data was collected using $\theta/2\theta$ scans; three check reflections were collected every 97 reflections to monitor intensity decay. A total of 2253 reflections were measured, 1916 of which were independent. Reflection data were corrected for Lorentz-polarization and absorption effects using the ψ-scan method. Physical properties of the crystal and parameters for data collection are summarized in Table 1.

The structure was solved by direct methods, and refined by the full-matrix least-squares on F^2 technique for all of the data. The structure determination and refinement, as well as the ORTEP-type plot that appears in this paper were performed using SHELXTL 5.05 [5] on a Pentium PC. Positions for all non-hydrogen atoms were refined anisotropically, followed by isotropic refinement of all hydrogen positions. Finally, the extinction parameter was refined. Final refinement converged to $R = 0.0264$ and $wR_2 = 0.0724$ for all data. At this point, the Flack parameter was 0.018 with e.s.d. 0.014, so that the absolute configuration was taken as correct. Total parameters refined were 262, corresponding to 7.3 observations per parameter. Other refinement details are given in Table 1. Table 2 gives positional parameters for non-hydrogen atoms, and Fig. 1 lists selected bond lengths.

Acknowledgements

The purchases of the X-ray diffractometers at Youngstown State were supported by funds from the National Science Foundation (DMR-9403889). The Graduate School and the College of Arts and Sciences at Youngstown State are thanked for financial support during this work.

References

[1] D. Horton, P. Norris, in S. Hanessian (Ed.), *Preparative Carbohydrate Chemistry*, Marcel Dekker, New York, 1997, pp. 35–51.
[2] D.L. MacDonald, H.O.L. Fischer, *J. Am. Chem. Soc.*, 74 (1952) 2087–2090.
[3] H. Zinner, K.-H. Falk, *Chem. Ber.*, 12 (1953) 503.
[4] L. Hough, T.J. Taylor, *J. Chem. Soc.*, (1956) 970–980.
[5] G.M. Sheldrick, SHELXTL 5.05, Program for the Refinement of Crystal Structures, University of Göttingen, Germany, 1996.

---

[2] Tables of atomic coordinates, bond lengths and bond angles have been deposited with the Cambridge Crystallographic Data Centre. These tables may be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 IEZ, UK.