Carbohydrate Research, 58 (1977) 488–493

Note

Formation of 2,5-anhydropentose dibenzyl dithioacetals from pentose dibenzyl dithioacetals in acid solution

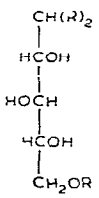
THEODORUS VAN ES

Department of Biochemistry, Rutgers University, New Brunswick, New Jersey 08903 (U S A)

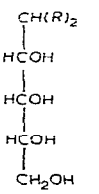
(Received August 23rd 1976, accepted for publication in revised form, December 20th, 1976)

Treatment of dialkyl dithioacetals of D- or L-arabinose with 1 mol equiv of *p*-toluenesulfonyl chloride in pyridine at low temperature gave the 5-*p*-toluenesulfonate of D- or L-arabinose, whereas similar treatment of D-ribose, D-xylose, and D-lyxose dithioacetals gave the 2,5-anhydropentose dithioacetals[1] A direct correlation was established[2] between the conformation of the pentose dithioacetals and their mode of reaction Intramolecular cyclisation of *p*-toluenesulfonyl derivatives of D-pentose dibenzyl dithioacetals led to the introduction of a sulfur atom into the ring[3,4], however, the formation of 2 5-anhydro-D-pentose derivatives was a major competing reaction This paper reports the anomalous formation of 2,5-anhydro-D-pentose derivatives directly from D-pentose dibenzyl dithioacetals

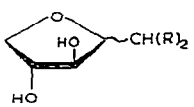
Zinner *et al*[5] have reported the formation, in low yield, of 2,5-anhydro-D-xylose dibenzyl dithioacetal by treatment of D-xylose dibenzyl dithioacetal with *p*-toluenesulfonyl chloride A re-examination, by high-pressure liquid chromatography, of the reaction products of D-xylose (**1**) and D-ribose (**5**) dibenzyl dithioacetals with various amounts of *p*-toluenesulfonyl chloride showed that the respective yields of 2,5-anhydro-D-xylose (**7**) and 2,5-anhydro-D-ribose (**13**) dibenzyl dithioacetals increased to ~90% when 2 mol equiv of *p*-toluenesulfonyl chloride were used With 1 mol equiv , however, the main product was the unreacted dithioacetal **1** or **5**, and the 2,5-anhydro compounds **7** or **13** were obtained in 30–40% yield



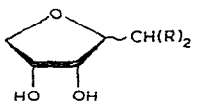
1 R = SBzl, R = H
2 R = SEt R = H
3 R = SEt R = Ts
4 R = SBzl R = Ts



5 R = SBzl
6 R = SEt

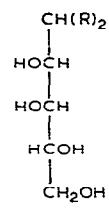


7 D-*xylo* R = SBzl
8 D-*lyxo* R = SBzl
9 D-*xylo* R = OMe
10 D-*lyxo* R = OMe
11 D-*xylo* R = SEt
12 D-*lyxo* R = SEt

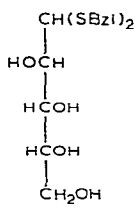


13 D-*ribo* R = SBzl
14 D-*arabino* R = SBzl
15 D-*ribo*, R = OMe
16 D-*ribo*, R = SEt

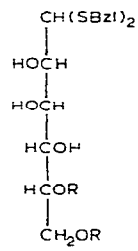
Treatment of pentose dibenzyl dithioacetals with 1 mol equiv of mercuric chloride in aqueous acetone unexpectedly gave 2,5-anhydropentose dibenzyl dithioacetals Under the same conditions, however, the corresponding diethyl dithioacetals gave no anhydro compounds but mainly unchanged starting material and isopropylidene derivatives of the dithioacetals Treatment of the xylose derivative[5] **1** gave 25% of the starting material **1** and 75% of a mixture of 2,5-anhydro-D-xylose (**7**) and 2,5-anhydro-D-lyxose (**8**) dibenzyl dithioacetals in the ratio of 2 3 To establish the composition of this mixture, the acetylated mixture of **7** and **8** was treated with mercuric chloride in neutral methanol to give a mixture of the acetates of 2,5-anhydro-D-xylose[1] (**9**) and 2,5-anhydro-D-lyxose (**10**) dimethyl acetals Compounds **9** and **10** were prepared, for comparison, from D-xylose diethyl dithioacetal (**2**) and D-lyxose diethyl dithioacetal[6] (**17**), respectively, by treatment with *p*-toluenesulfonyl chloride followed by reaction of the resultant 2,5-anhydro compounds **11** and **12** with mercuric chloride in neutral methanol



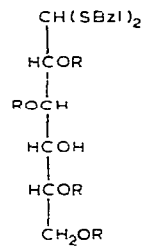
17 R = SEt
18 R = SBzl



19



20 R = H
21 R = CMe_2

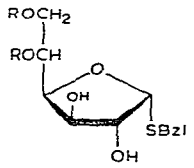


22 R = R = H
23 R R = R R = CMe_2
24 R R = CMe_2, R′ = H

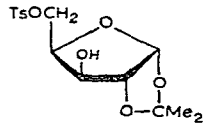
Treatment of D-lyxose dibenzyl dithioacetal (**18**) with mercuric chloride gave, in 80% yield, a mixture of **7** and **8** in the ratio of 1 3 The same treatment of D-ribose dibenzyl dithioacetal (**5**) gave mainly unchanged starting material and, in 10% yield, a mixture of 2,5-anhydro-D-ribose dibenzyl dithioacetal (**13**) and probably 2,5-anhydro-D-arabinose dibenzyl dithioacetal (**14**) in the ratio of 1 2 Finally, treatment of D-arabinose dibenzyl dithioacetal (**19**) with mercuric chloride gave **13** as the only 2,5-anhydro compound Treatment of acetylated **13** with mercuric chloride in neutral methanol gave the *O*-acetyl derivative of 2,5-anhydro-D-ribose dimethyl acetal (**15**) Compound **15** was also prepared, for comparison, by treatment of D-ribose diethyl dithioacetal (**6**) with *p*-toluenesulfonyl chloride, and treatment of the resultant 2,5-anhydro-D-ribose diethyl dithioacetal (**16**) with mercuric chloride in neutral methanol

On treatment with mercuric chloride, hexose dibenzyl dithioacetals gave no 2,5-anhydro compounds, the main products being isopropylidene derivatives D-Mannose dibenzyl dithioacetal[7] (**20**) gave the starting material and 5,6-*O*-isopropylidene-D-mannose dibenzyl dithioacetal[7 8] (**21**) in the ratio of 3 7 D-Glucose

dibenzyl dithioacetal[9] (**22**) gave 2,3 5,6-di-*O*-isopropylidene-D-glucose dibenzyl dithioacetal[9] (**23**), benzyl 5,6-*O*-isopropylidene-1-thio-α-D-glucofuranoside (**25**), benzyl 1-thio-α-D-glucofuranoside[10] (**26**), and 5,6-*O*-isopropylidene-D-glucose dibenzyl dithioacetal (**24**) in the ratio of 9 7 2 3 Compound **25** was prepared directly by treatment of **26** with acetone and anhydrous copper sulfate



25 R = CMe_2
26 R = H



27

The formation of the 2,5-anhydro derivatives by treatment of D-pentose dibenzyl dithioacetals with mercuric chloride in acetone is probably caused by an acid-catalyzed dehydration between C-2 and C-5 This interpretation was confirmed by the observation that treatment of the dithioacetal **1** under the same reaction conditions with hydrochloric acid instead of mercuric chloride gave the anhydro compounds **7** and **8** in approximately equal amounts

For the reaction leading to 2,5-anhydrides from dithioacetals, it has been proposed that either dehydration occurs without passage through an intermediate sulfonic ester or the intramolecular displacement of the 5-sulfonate group by O-2 Dehydration of dithioacetals can occur under different reaction conditions, in the limited case of pentose dibenzyl dithioacetals, as our results show The second reaction is the more likely, because we observed that 5-*O*-*p*-tolylsulfonyl-D-xylose diethyl dithioacetal (**3**) or the corresponding dibenzyl dithioacetal (**4**), when dissolved in pyridine at room temperature, gave the anhydro compounds **7** and **11** rapidly as the only products Compounds **3** and **4** were formed, as unstable, crystalline compounds, by treatment of 1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-xylofuranose (**27**) with ethanethiol and phenylmethanethiol, respectively, and trifluoroacetic acid The n m r spectra of **3** and **4** and their acetates were in agreement with the structures assigned

EXPERIMENTAL

General methods — Column chromatography was performed on Merck Silica gel (60–200 mesh) N m r spectra were determined with a Varian T-60 spectrometer, tetramethylsilane being the internal standard G l c analysis was performed with a Bendix Gas Chromatograph 2600, equipped with a column (1 8 m × 2 0 mm) containing 10% EGSS-X on Gas-Chrom P (Applied Science Labs , State College, PA 16801) with nitrogen as the carrier gas High-pressure liquid chromatography (h p l c) was performed on a column (3 2 × 250 mm) of Lichrosorb (5 μm Merck) at 160 atm, with 973 20 7 hexane–dichloromethane–2-propanol as eluent and detection at 254 nm with an Altex detector

Reaction of dibenzyl dithioacetals with mercuric chloride — Dibenzyl dithioacetals **1**, **5**, **18**, **19**, **20**, and **22** (0 01 mol) were dissolved in aqueous acetone (100 ml, 90%) and mercuric chloride (0 01 mol) or hydrochloric acid (0 01 mol) dissolved in the same solvent was added The reaction mixture was kept at room temperature overnight and the precipitated mercury salts were filtered off The filtrate was neutralized with ammonium hydroxide and the precipitate filtered off The filtrate was evaporated and the residue acetylated with pyridine and acetic anhydride for 12 h at room temperature The resultant acetates were analyzed by h p l c The reference compounds were the acetylated dibenzyl dithioacetals **1**, **5**, **18**, **19**, **20**, **21**, **22**, **23**, and **24**, the 2,5-anhydro-D-pentose dibenzyl dithioacetals **7**, **8**, and **13** and the benzyl 1-thio-α-D-glucofuranosides **25** and **26**

p-*Toluenesulfonylation of dithioacetals* — Dithioacetals **1**, **2**, **5**, **6**, **17**, and **18** (0 01 mol) were dissolved in pyridine (10 ml) To the magnetically stirred solution at −10° was slowly added solid *p*-toluenesulfonyl chloride (11 mmol, or 20 mmol for **1** and **5**) After 2 h at −10°, the solution was kept for 24 h at room temperature and acetic anhydride (10 ml) added The solution was kept for a further 24 h, poured onto ice, and extracted with chloroform The chloroform extracts were washed successively with ice-cold. dilute hydrochloric acid saturated sodium hydrogencarbonate solution and water, dried (sodium sulfate), and evaporated to give a syrup The syrup was dissolved in methanol (50 ml) and deacetylated with a catalytic amount of sodium methoxide The solution was stored for 18 h at room temperature and evaporated to a syrup Column chromatography with 1 4 (v/v) methanol–benzene gave the 2 5-anhydro compounds **7**, **8**, **11**, **12**, **13**, and **16**

3,4-Di-O-acetyl derivative of 2,5-anhydro-D-xylose dibenzyl dithioacetal (**7**) — Yield 90%, $[\alpha]_D^{20}$ +145° (*c* 1 23, chloroform)

Anal Calc for $C_{23}H_{26}O_5S_2$ C, 61 9, H 5 8 Found C, 61 9 H, 5 7

3,4-Di-O-acetyl derivative of 2,5-anhydro-D-xylose diethyl dithioacetal (**11**) — Yield 75%, $[\alpha]_D^{20}$ −18° (*c* 2 94, chloroform)

Anal Calc for $C_{13}H_{22}O_5S_2$ C, 48 4, H, 6 8 Found C, 48 6 H, 6 9

3,4-Di-O-acetyl derivative of 2,5-anhydro-D-lyxose diethyl dithioacetal (**12**) — Yield 72%, $[\alpha]_D^{20}$ +12° (*c* 3 20, chloroform)

Anal Calc for $C_{13}H_{22}O_5S_2$ C, 48 4, H, 6 8 Found C 48 4, H, 7 0

3,4-Di-O-acetyl derivative of 2,5-anhydro-D-ribose dibenzyl dithioacetal (**13**) — Yield 90%, $[\alpha]_D^{20}$ −89° (*c* 1 7, chloroform)

Anal Calc for $C_{23}H_{26}O_5S_2$ C, 61 9, H, 5 8 Found C, 61 7, H, 5 9

3,4-Di-O-acetyl derivative of 2,5-anhydro-D-ribose diethyl dithioacetal (**16**) — Yield 78%, $[\alpha]_D^{20}$ −74° (*c* 1 16 chloroform)

Anal Calc for $C_{13}H_{22}O_5S_2$ C, 48 4, H, 6 8 Found C, 48 3, H, 6 8

3,4-Di-O-acetyl-2,5-anhydro-D-pentose dimethyl acetals — Dithioacetals (mixture of acetates of **7** and **8**, or acetates of **11**, **12**, **13**, or **16**) (1 0 g) were heated under reflux for 12 h with cadmium carbonate (5 0 g), mercuric chloride (2 0 g), and methanol (40 ml) The mixture was filtered and the residue thoroughly washed with chloroform The filtrate was washed with water, dried, and evaporated to a syrup

Chromatography on silica gel with 1 40 (v/v) methanol–benzene gave the following 3,4-di-*O*-acetyl derivatives:

3,4-Di-O-acetyl derivative of 2,5-anhydro-D-xylose dimethyl acetal (**9**) — Yield 52%, $[\alpha]_D^{20}$ −14° (*c* 1 88, chloroform), g l c retention time (190°, EGSS-X) 9 53 min

Anal Calc for $C_{11}H_{18}O_7$ C, 50 4, H, 6 9 Found C, 50 2, H, 6 9

3,4-Di-O-acetyl derivative of 2,5-anhydro-D-lyxose dimethyl acetal (**10**) — Yield 42%, $[\alpha]_D^{20}$ +7° (*c* 1 87, chloroform), g l c retention time (190°, EGSS-X) 7 50 min

Anal Calc for $C_{11}H_{18}O_7$ C, 50 4, H, 6 9 Found C, 50 3, H, 6 8

3,4-Di-O-acetyl derivatives of 2,5-anhydro-D-ribose dimethyl acetal (**15**) — Yield 43% $[\alpha]_D^{20}$ −39° (*c* 2 61, chloroform), g l c retention time (190°, EGSS-X) 8 12 min

Anal Calc for $C_{11}H_{18}O_7$ C, 50 4, H, 6 9 Found C, 50 4, H, 6 8

3,4-Di-O-acetyl derivative of benzyl 5,6-O-isopropylidene-1-thio-α-D-glucofuranoside (**25**) — Thioglycoside **26** (1 0 g), acetone (50 ml), and anhydrous copper sulfate (5 0 g) were stirred overnight The reaction mixture was filtered and the filtrate evaporated to a syrup Chromatography on silica gel with 1 20 (v/v) methanol–benzene gave **25** (0 86 g), which was acetylated with pyridine and acetic anhydride, $[\alpha]_D^{20}$ +156° (*c* 1 07, chloroform)

Anal Calc for $C_{20}H_{26}O_7S$ C, 58 5, H, 6 3 Found C, 58 6, H, 6 3

5-O-p-Tolylsulfonyl-D-xylose diethyl dithioacetal (**23**) — Compound **27** (3 42 g), anhydrous chloroform (20 ml), ethanethiol (5 ml), and trifluoroacetic acid (4 ml) were kept for 3 h at room temperature The mixture was diluted with chloroform and washed with water and sodium hydrogencarbonate solution The chloroform extract was dried (sodium sulfate) and evaporated at room temperature to a syrup that crystallized from ethyl acetate–hexane (3 0 g), m p 58–59°, $[\alpha]_D^{20}$ +43° (*c* 1 15, chloroform)

5-O-p-Tolylsulfonyl-D-xylose dibenzyl dithioacetal (**4**) — This compound was synthesized as described for **3**, except that phenylmethanethiol (4 9 g) was used instead of ethanethiol (2 2 g), m p 68–69°, $[\alpha]_D^{20}$ −54° (*c* 0 69, chloroform)

2,5-Anhydro-D-xylose diethyl dithioacetal and dibenzyl dithioacetal (**11** *and* **7**) — Compound **3** or **4** (1 0 g) and pyridine (10 ml) were stirred for 3 h at room temperature Acetic anhydride (3 ml) was added and the solution kept overnight The sole products formed were the acetates of **11** and **7**, respectively, as shown by h p l c and spectral analysis

ACKNOWLEDGMENTS

The author thanks the Charles and Johanna Busch Foundation Fund for financial support and Mr Michael Merion for technical assistance

REFERENCES

1 J Defaye, *Adv Carbohydr Chem*, 25 (1970) 181–228
2 J Defaye and D Horton, *Carbohydr Res*, 14 (1970) 128–132
3 T van Es, *Carbohydr Res*, 37 (1974) 373–380

4 T VAN ES, *Carbohydr Res* 46 (1976) 237–244
5 H ZINNER, H BRANDHOFF, H SCHMANDKE, H KRISTEN, AND R HAUN, *Chem Ber*, 92 (1959) 3151–3155
6 H ZINNER, H BRANDNER, AND G REMBARZ, *Chem Ber*, 89 (1956) 800–813
7 E PACSU AND C U KARY, *Ber*, 62 (1929) 2811–2817
8 P A J GORIN, *Can J Chem*, 43 (1965) 2078–2084
9 E PACSU, *Ber*, 57 (1924) 849–853
10 J W GREEN AND E PACSU, *J Am Chem Soc*, 59 (1937) 1205–1210