Carbohydrate Research, 36 (1974) 408–411

Note

The *Se*-benzyl group as a participating group

THEODORUS VAN ES AND JOSE RABELO

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

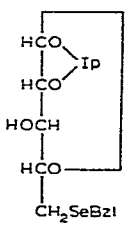
(Received January 14th, 1974; accepted in revised form, April 22nd, 1974)

During our work on seleno sugars, the methanolysis of 5-*Se*-benzyl-1,2-*O*-isopropylidene-5-seleno-α-D-xylofuranose (**1**) was investigated. When **1** was treated with acid-containing methanol, two main fractions were isolated by chromatography. The faster-moving component (**A**) contained no hydroxyl groups, whereas the slower-moving component (**B**) contained two adjacent hydroxyl groups, as shown by periodate oxidation. Spectral evidence showed the presence of dimethyl acetal, isopropylidene, methoxyl, and *Se*-benzyl groups in **A** and suggested that it be a mixture. **B** differed from **A** by the absence of the isopropylidene group, but could be converted into **A** by treatment with acidic acetone and copper sulfate. These results suggested a number of isomeric structures for **A**, among them **2–5**; **2**, **3**, and **5** were shown to be present.

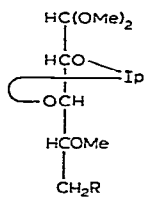
Reductive removal of selenium from **A** gave a mixture of three compounds as shown by gas-chromatography. These were identified as **7**, **8**, and **10** by synthesis and gas-chromatographic comparison.

Compounds **7** and **8** were synthesized from the corresponding pentose dialkyl dithioacetals by tosylation at O–6, formation of the dimethyl acetal with methanol in the presence of mercuric chloride and cadmium carbonate, reduction with lithium aluminum hydride, and methylation with dimethyl sulfate. The absence of **9** in the mixture obtained by reduction of **A** was shown by comparison with **9** obtained by a sequence of reactions similar to that just described, but starting from 3,4-*O*-isopropylidene-D-xylose dimethyl dithioacetal.

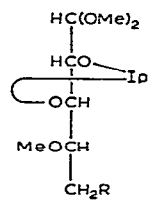
The formation of the isomers **2** and **3** may be explained by the formation of the dimethylacetal 2,3-isopropylidene derivative of **1** and participation and migra-



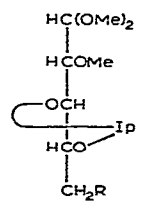
1



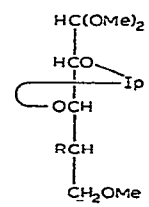
2 R = SeBzl
7 R = H



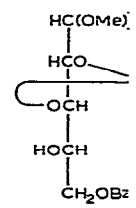
3 R = SeBzl
8 R = H



4 R = SeBzl
9 R = H



5 R = SeBzl
10 R = H



6

tion of a methoxyl group from C-1 to C-4 to give **3**, and by participation of the *Se*-benzyl group to give the 4,5-episelenonium intermediate which is opened by a methoxyl group from C-1 to give **2**. The episelenonium intermediate can also be opened by methanol to give **5**.

The deoxy derivative **10** was synthesized by a modification of a method reported by Kochetkov and Usov[3] starting from **6**, and **8** and **10** were shown to be present in the mixture obtained by reduction of **A**.

This participating reaction is unique to sugars containing a *Se*-benzyl group at C-5 since methanolysis of 5-*S*-benzyl-1,2-*O*-isopropylidene-5-thio-α-D-xylofuranose gave, as only products, the expected anomeric glycosides.

EXPERIMENTAL

General. — Solutions were evaporated at 40° under diminishes pressure. N.m.r. spectra were recorded with a Varian T-60 spectrometer, tetramethylsilane being the internal standard and chemical shifts quoted in p.p.m. The structures of all compounds were confirmed from their n.m.r. spectra. Mass spectra were determined with a Hitachi RMU7 mass spectrometer. G.l.c. analysis was performed with a Bendix gas chromatography 2600 equipped with a column (1.8 m) containing 10% EGSS-X on Gas-Chrom P (Applied Science Labs., State College, Pa. 16801) at 115°, with nitrogen as carrier gas.

*Methanolysis of 5-*Se*-benzyl-1,2-*O*-isopropylidene-5-seleno-α-D-xylofuranose* (**1**). — A solution of **1** (1.0 g) in methanolic hydrogen chloride (1%, 40 ml) was kept at room temperature overnight. The solution was neutralized with lead carbonate and the filtered solution was evaporated to a syrup (0.95 g) which was applied to a column of silica gel with 1:19 (v/v) methanol–benzene as eluent. Two fractions, **A** (0.29 g) and **B** (0.39 g), were recovered. Alternatively, **A** can be prepared by heating under reflux the just mentioned solution for 45 min and then neutralizing with lead carbonate. The syrup, acetone (30 ml), anhydrous copper sulfate (3.0 g), and sulfuric acid (0.05 ml) were stirred at room temperature overnight. The suspension was filtered, and the filtrate neutralized with calcium hydroxide and filtered again. The filtrate was evaporated to a syrup (1.0 g) which, on chromatography, gave **A** (0.75 g); i.r. datum: OH absorption absent; n.m.r. data (chloroform-d): δ 1.43 [6-proton singlet, $C(CH_3)_2$], 3.27, 3.33, 3.36, 3.47 [total 9 protons, singlets, OCH_3 and $CH(OCH_3)_2$], 3.81 (2-proton singlet, $SeCH_2C_6H_5$), 7.28 (5-proton singlet, C_6H_5); m.s.: 404(402) ($M^{\ddagger}$), 389(387) ($M^{\ddagger}-Me$), 273(271) ($M^{\ddagger}-OMe$), very intense 91 and 75 [$CH(OMe)_2^+$].

Anal. Calc. for $C_{18}H_{28}O_5Se$: C, 53.60; H, 6.95. Found: C, 53.45; H, 7.10.

Fraction **B** consumed 1.08 moles of periodate; after 30 min at room temperature, no further uptake of periodate occurred; n.m.r. data (chloroform-*d*): δ 3.34, 3.38, 3.45 [total 9 protons, singlets, $C(OCH_3)_2$ and OCH_3], 3.81 (2-proton singlet, $SeCH_2C_6H_5$), and 7.28 (5-proton singlet, C_6H_5).

Anal. Calc. for $C_{15}H_{24}O_5Se$: C, 49.60; H, 6.61. Found: C, 49.76; H, 6.79.

Removal of selenium from compound **A**. — Compound **A** (1.60 g), ethanol (30 ml), and Raney nickel (approximately 8 g) were heated under reflux with stirring

overnight. The suspension was filtered and the nickel repeatedly washed with hot ethanol. The filtrate was evaporated to a syrup (0.70 g), which was applied to a column of silica gel and eluted with 1:49 methanol–benzene to give **C** (0.48 g). Analysis by gas chromatography showed three components with relative retention times of 356 (41%), 442 (27%), and 575 (32%); n.m.r. data (chloroform-*d*): δ 1.20, 1.21 (total 3 protons, two overlapping doublets, 5-CH_3), 1.43 [6-proton singlet, C(CH_3)$_2$], 3.35, 3.40, and 3.46 [total 9 protons, singlets, OCH_3 and CH(OCH_3)$_2$]; m.s.: 234 (M^+), 219 ($M^+ - Me$), 203 ($M^+ - OMe$), intense 75 [$CH(OMe)_2^+$].

Anal. Calc. for $C_{11}H_{22}O_5$: C, 56.41; H, 9.40. Found: C, 56.32; H, 9.51.

*5-Deoxy-2,3-O-isopropylidene-4-O-methyl-*D*-xylose dimethyl acetal* (**7**). — 2,3 *O*-Isopropylidene-D-xylose diethyl dithioacetal[1] (5.92 g) and pyridine (25 ml) were cooled to −10° and a solution of tosyl chloride (4.20 g) in chloroform (15 ml) was slowly added at such a rate that the temperature did not exceed 0°. The solution was kept overnight at room temperature, and then extracted with water and chloroform. The chloroform extracts were successively washed with ice-cold, dilute hydrochloric acid, a sodium hydrogen carbonate solution, and water, and then dried over sodium sulfate. The solution was evaporated to a syrup (9.29 g); $[\alpha]_D^{28}$ −31° (*c* 1.65, chloroform). The syrup slowly decomposed at room temperature and was not analyzed. Part of it (5.0 g), cadmium carbonate (15.0 g), and a solution of mercuric chloride (10.0 g) in methanol (70 ml) were heated under reflux for 4 h. The solution was filtered and the filtrate extracted with water and chloroform. The chloroform extracts were washed with a 10% solution of potassium iodide and water. The chloroform was evaporated to give 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-D-xylose dimethyl acetal (4.3 g) as a syrup which slowly decomposed at room temperature; $[\alpha]_D^{28}$ +16° (*c* 4.1, chloroform).

The compound just described (1.30 g), anhydrous ether (50 ml), and lithium aluminum hydride (0.60 g) were heated under reflux overnight. The excess of reducing agent was destroyed by careful addition of ice. The solution was diluted with chloroform and washed with ice-cold, dilute hydrochloric acid. The chloroform layer was washed with a sodium hydrogen carbonate solution, water, and dried over sodium sulfate. The solution was evaporated to a syrup (0.25 g). Chromatography of this syrup on silica gel with 1:19 methanol–benzene as eluent gave 5-deoxy-2,3-*O*-isopropylidene-D-xylose dimethyl acetal (0.21 g).

Anal. Calc. for $C_{10}H_{20}O_5$: C, 54.55; H, 9.09. Found: C, 54.38; H, 9.18.

The compound just described (0.20 g), anhydrous tetrahydrofuran (10 ml), powdered potassium hydroxide (1.0 g), and dimethyl sulfate (1 ml) were stirred at room temperature overnight. Ammonia (3 ml) was added to destroy the excess of dimethyl sulfate, sufficient water was added to dissolve all the solids, and the solution was extracted with chloroform. The dried extract was evaporated to a syrup (0.21 g), which on chromatography on silica gel with 1:99 methanol–benzene gave the title compound **7** (0.14 g); $[\alpha]_D^{23}$ −1° (*c* 1.0, chloroform). Analysis by gas chromatography showed one peak, identical to one of the components in the reduction product **C**, with a relative retention time of 356.

Anal. Calc. for $C_{11}H_{22}O_5$: C, 56.41; H, 9.40. Found: C, 56.49; H, 9.29.

5-Deoxy-2,3-O-isopropylidene-4-O-methyl-L-arabinose dimethyl acetal (**8**). — The experiment was performed as described for the preparation of **7** except that the starting material was 2,3-*O*-isopropylidene-L-arabinose diethyl dithioacetal[2]. The structures of the intermediates were confirmed by n.m.r. The title compound was obtained as a syrup; $[\alpha]_D^{27}$ −2° (*c* 3.0, chloroform). Analysis by gas chromatography showed one peak, identical to one of the components obtained from the reduction of compound **A**, with a relative retention time of 442.

Anal. Calc. for $C_{11}H_{22}O_5$: C, 56.41; H, 9.40. Found: C, 56.32; H, 9.47.

5-Deoxy-3,4-O-isopropylidene-2-O-methyl-D-xylose dimethyl acetal (**9**). — From 3,4-*O*-isopropylidene-D-xylose dimethyl dithioacetal[2] as just described for the preparation of **7**. The title compound was obtained as a syrup; $[\alpha]_D^{20}$ +9° (*c* 0.8, chloroform). Analysis by gas chromatography showed one peak with a relative retention time of 259.

Anal. Calc. for $C_{11}H_{22}O_5$: C, 56.41; H, 9.40. Found: C, 56.41; H, 9.29.

5-O-Benzoyl-2,3-O-isopropylidene-L-arabinose dimethyl acetal (**6**). — 5-*O*-Benzoyl-2,3-*O*-isopropylidene-L-arabinose diethyl dithioacetal[3] (2.59 g), cadmium carbonate (8.0 g), and a solution of mercuric chloride (4.0 g) in methanol (20 ml) were heated under reflux for 6 h. The compound was isolated as previously described as a syrup (1.9 g). Chromatography on silica gel with 1:19 methanol–benzene as eluent gave the title compound; $[\alpha]_D^{20}$ −9° (*c* 5.1, chloroform).

Anal. Calc. for $C_{17}H_{24}O_7$: C, 60.00; H, 7.06. Found: C, 60.11; H, 7.01.

4-Deoxy-2,3-O-isopropylidene-5-O-methyl-L-threo-pentose dimethyl acetal (**10**) *and 5-deoxy-2,3-O-isopropylidene-4-O-methyl-L-arabinose dimethyl acetal* (**8**). — Compound **6** (1.5 g), triphenylphosphite methiodide[3] (2.0 g), and benzene (10 ml) were heated for 24 h at 50°. The solution was diluted with chloroform and washed with water. The chloroform was evaporated to a syrup (2.5 g). Since this crude product could not be separated from the triphenylphosphite, Raney nickel (approximately 15 g) and ethanol (30 ml) were added and the mixture was heated under reflux overnight. The product was isolated as described previously[3] and was treated, without further purification, with powdered potassium hydroxide (3.0 g), tetrahydrofuran (15 ml), and dimethyl sulfate (2 ml) for 2 h at 50°. The product was isolated as described for the preparation of **7**. Chromatography on silica gel with 1:99 methanol–benzene as the eluent gave a mixture of the title compounds as a syrup (0.20 g). Analysis by gas chromatography showed the presence of some triphenylphosphite and two other components, namely **8**, with a relative retention time of 442 (33%) and **10** with a relative retention time of 575 (67%). Both compounds were present in the reduction mixture **C**.

REFERENCES

1 D. G. Lance and J. K. N. Jones, *Can. J. Chem.*, 45 (1967) 1533.
2 H. Zinner and J. Milbradt, *Carbohyd. Res.*, 3 (1967) 389.
3 N. K. Kochetkov and A. I. Usov, *Tetrahedron*, 19 (1963) 973.