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Note

Selenoxides of D-xylose and D-ribose derivatives

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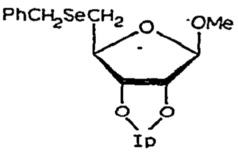
Selenides are oxidized to selenoxides by sodium periodate, hydrogen peroxide, and ozone[1]. Oxides of seleno sugars have not been reported thus far. This paper presents the results of the oxidation of a number of seleno sugars (**1**–**5**), now available[2], and the properties of the resulting selenoxides.



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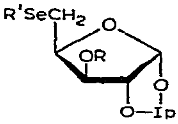
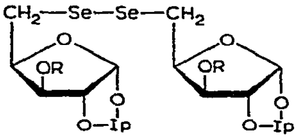
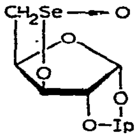


2 R = H, R' = CH_2Ph
3 R = Me, R' = CH_2Ph
4 R = R' = Me
5 R = H, R' = Me
6 R = Ac, R' = Me



7 R = H
9 R = Me



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Although all the just mentioned oxidizing agents gave the desired selenoxides, ozone proved to be the most convenient oxidant, giving complete conversion into the selenoxides as shown by t.l.c. of the freshly ozonized solution. All the selenoxides decomposed on warming, some even readily at room temperature. Thermal degradation was studied by heating the selenoxides in ethyl acetate solution under reflux. The resulting degradation products consisted mainly of the original selenides (**1**, **2**, **4**). In the case of the selenoxide of 5-*Se*-benzyl-1,2-*O*-isopropylidene-5-seleno-α-D-xylofuranose (**2**), the product was benzaldehyde and bis(5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)diselenide (**7**). All selenoxides were easily reduced by lithium aluminum hydride to their corresponding selenides. The methylation of the diselenide **7** with methyl iodide and various bases gave 1,2-*O*-isopropylidene-3-*O*-methyl-5-5-*Se*-methyl-seleno-α-D-xylofuranose (**4**); however, when sodium hydrogen carbonate was used as the base, 1,2-*O*-isopropylidene-5-*Se*-methyl-5-seleno-α-D-xylofuranose (**5**) was obtained. Treatment of **5** with ozone gave an oxide which rapidly decomposed at room temperature into the starting material and a crystalline compound. The latter compound was shown to be a selenoxide because it liberated iodine from iodide and was reduced by lithium aluminum hydride into **5**. Acetylation of **5** at elevated temperature gave the acetate **6**, whereas the acetylation at 0–5° gave the acetate of the selenoxide. The n.m.r. spectrum of this crystalline selenoxide in deuterochloroform showed the H-1 signal as a complex and the *Se*-methyl group signal as a doublet peak. When the spectrum was reexamined in deuterium oxide, the H-1 signal appeared as the expected doublet and the *Se*-methyl group as a singlet peak. These data are interpreted in the formation by **5** of two isomeric selenoxides, one of these being more stable than the other. The simplification of the n.m.r. spectrum in deuterium oxide is explained by the fast racemization of the isomeric selenoxides *via* the symmetrical selenoxide hydrate. Recently[3], two isomeric steroidal selenoxides were separated and characterized. All attempts at a separation of our product failed. In one other case, namely compound **3**, the n.m.r. spectrum of the selenoxide also showed a complex H-1 absorption and a doublet for the *O*-methyl group.

Oxidation of the diselenide (**7**) with hydrogen peroxide gave a stable, crystalline compound, the i.r. spectrum of which showed no hydroxyl group absorption. The compound liberated iodine and was titrated with alkali. The mass spectrum showed a peak at 252, caused by the loss of an oxygen atom from the molecular ion. These data indicate that the compound is an internal seleninic ester (**8**). An attempt to methylate **8** with methyl iodide gave, as only compound identified, bis(1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranos-5-yl) diselenide (**9**). However, during the isolation it was noted that acidification of the strongly alkaline reaction mixture liberated a large amount of iodine. This observation suggests the presence of 3-*O*-methyl seleninic acid which oxidized iodide to iodine and was itself reduced to the diselenide (**9**).

EXPERIMENTAL

Melting points were determined on a Fisher–Johns apparatus and are uncorrected. Column chromatography was performed on silica gel (60–200 mesh). I.r. spectra were determined on a Perkin–Elmer 700 spectrophotometer and n.m.r. spectra on a Varian T-60 spectrometer, chemical shifts being recorded in p.p.m. units with tetramethylsilane as the internal standard. Mass spectra were determined with a Hitachi–Perkin–Elmer RMU-7 mass spectrometer. Evaporations were conducted under diminished pressure at a bath temperature below 50°.

*5-*Se*-Benzyl-1,2-*O*-isopropylidene-3-*O*-methyl-5-seleno-α-D-xylofuranose* (**3**). — To a stirred solution of 5-*Se*-benzyl-1,2-*O*-isopropylidene-5-seleno-α-D-xylofuranose (**2**, 5.0 g) in dry tetrahydrofuran (50 ml) was added powdered potassium hydroxide (5.0 g) and dimethyl sulfate (5 ml). The mixture was stirred overnight and heated for 2 h at 50°. The excess of dimethyl sulfate was removed by the addition of ammonium hydroxide solution (10 ml). The solution was extracted with chloroform and the extracts were washed with water and dried over sodium sulfate. The solution was evaporated to give **3** (5.0 g) which was crystallized from petroleum ether (40–60°), m.p. 65–66°; $[\alpha]_D^{25}$ $-107°$ (*c*, 1.14, chloroform); n.m.r. data (chloroform-*d*): δ 1.40 (6-proton doublet, *J* 9.3 Hz, CMe_2), 2.67–2.90 (2-proton complex), 3.40 (3-proton singlet, OMe), 3.74 (1-proton doublet, *J* 3.2 Hz), 3.84 (2-proton singlet, $CH_2C_6H_5$), 4.04–4.40 (1-proton complex), 4.53 (1-proton doublet, *J* 3.9 Hz, H-2), 5.86 (1-proton doublet, *J* 3.9 Hz, H-1), and 7.30 (5-proton singlet, C_6H_5).

Anal. Calc. for $C_{16}H_{22}O_4Se$: C, 53.80; H, 6.16. Found: 53.82; H, 6.15.

*1,2-*O*-Isopropylidene-3-*O*-methyl-5-*Se*-methyl-5-seleno-α-*D*-xylofuranose* (**4**). — A solution of bis(5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl) diselenide (**7**, 1.0 g) in liquid ammonia (50 ml) was treated with sodium until the blue color persisted for 15 min. Methyl iodide (5 ml) was added and the solution was kept overnight at room temperature. The residue was extracted with chloroform and water. The chloroform extract was dried over sodium sulfate and evaporated to a syrup (1.1 g), which was applied to a column of silica gel in 1:99 methanol–benzene solution. Elution with the same solvent gave **4** as a syrup, $[\alpha]_D^{25}$ −22° (*c* 0.7, methanol); n.m.r. data (chloroform-*d*): δ 1.33 (6-proton doublet, *J* 10.3 Hz, CMe_2), 2.00 (3-proton singlet, SeMe), 2.67 (2-proton doublet, *J* 8.0 Hz), 3.40 (3-proton singlet, OMe), 3.67 (1-proton doublet, *J* 3.2 Hz), 4.06–4.34 (1-proton complex), 4.45 (1-proton doublet, *J* 3.9 Hz, H-2), and 5.75 (1-proton doublet, *J* 3.9 Hz, H-1); m.s. data: 282 (280) (M^+), 267 (265) ($M^+ - Me$).

Anal. Calc. for $C_{10}H_{18}O_4Se$: C, 42.71; H, 6.40. Found: C, 42.75; H, 6.39.

*1,2-*O*-Isopropylidene-5-*Se*-methyl-5-seleno-α-*D*-xylofuranose* (**5**). — A solution of the diselenide (**7**, 2.0 g) in *N,N*-dimethylformamide (15 ml) and methyl iodide (3 ml) was stirred with sodium hydrogen carbonate (6.0 g) overnight at room temperature. The mixture was evaporated and the residue extracted with chloroform. The extracts were washed with a sodium thiosulfate solution and water, dried over sodium sulfate, and evaporated to a solid (2.0 g), which crystallized from ethyl acetate–petroleum ether (40–60°), m.p. 97–98°; $[\alpha]_D^{25}$ −95° (*c* 1.18, chloroform); n.m.r. data (chloroform-*d*): δ 1.43 (6-proton doublet, *J* 11.5 Hz, CMe_2), 2.08 (3-proton singlet, SeMe), 2.42–2.65 (1-proton multiplet), 2.78 (2-proton doublet, *J* 8.0 Hz), 4.15–4.35 (2-proton complex), 4.51 (1-proton doublet, *J* 3.9 Hz, H-2), and 5.91 (1-proton doublet, *J* 3.9 Hz, H-1); m.s. data: 268 (266) (M^+); 253 (251) ($M^+ - Me$).

Anal. Calc. for $C_9H_{16}O_4Se$: C, 40.45; H, 5.99. Found: C, 40.50; H, 5.97.

*3-*O*-Acetyl-1,2-*O*-isopropylidene-5-*Se*-methyl-5-seleno-α-*D*-xylofuranose* (**6**). — Compound **5** was treated with pyridine and acetic anhydride to give **6** as a syrup; $[\alpha]_D^{25}$ −51° (*c* 2.36, chloroform); n.m.r. data (chloroform-*d*): δ 1.42 (6-proton doublet, *J* 12.3 Hz, CMe_2), 2.05 (3-proton singlet, SeMe), 2.10 (3-proton singlet, OAc), 2.70 (2-proton doublet, *J* 8.0 Hz), 4.30–4.67 (2-proton complex), 5.23 (1-proton doublet, *J* 3.5 Hz), and 5.90 (1-proton doublet, *J* 3.9 Hz, H-1).

Oxidation of compounds **1–5** *to* **10–14** *with ozone.* — A solution of each compound (1.0 g) in ethyl acetate (50 ml) was cooled to −10° and ozone was passed through the solution until an excess was present. The solution was evaporated at 0°. The resulting selenoxides **10–13** of compounds **1–4** were decomposed by heating a solution in ethyl acetate for 2 h under reflux.

*Methyl 5-benzylseleninyl-2,3-*O*-isopropylidene-β-*D*-ribofuranoside* (**10**). — M.p. 114–115°; $[\alpha]_D^{25}$ +73° (*c* 1.21, chloroform); equiv. wt. (iodometric[4]) 185 (calc. 187);

n.m.r. data (chloroform-*d*): δ 1.53 (6-proton doublet, *J* 9.3 Hz, CMe_2), 2.68–3.08 (2-proton complex), 3.12 (3-proton singlet, OMe), 3.35 (1-proton singlet), 4.07 (2-proton singlet, $CH_2C_6H_5$), 4.65 (2-proton singlet), 4.97 (1-proton doublet, *J* 2.5 Hz, H-1), and 7.40 (5-proton singlet, C_6H_5).

5-Benzylseleninyl-1,2-O-isopropylidene-α-D-xylofuranose (**11**). — M.p. 123–125°; $[\alpha]_D^{25}$ +65° (*c* 1.0, methanol); equiv. wt. 181 (calc. 180); n.m.r. data could not be determined because of the poor solubility of this compound in deuterated acetone, chloroform, dimethyl sulfoxide, pyridine, or water.

5-Benzylseleninyl-1,2-O-isopropylidene-3-O-methyl-α-D-xylofuranoside (**12**). — M.p. 65–66°; $[\alpha]_D^{25}$ −25° (*c* 0.4, chloroform); equiv. wt. 193 (calc. 187); n.m.r. data (chloroform-*d*): δ 1.39 (6-proton, *J* 10.7 Hz, CMe_2), 2.50–3.17 (2-proton complex), 3.33 (3-proton doublet, *J* 2.0 Hz, OMe), 3.54–3.77 (1-proton complex), 4.07 and 4.17 (2-proton singlets, $CH_2C_6H_5$), 4.37–4.74 (2-proton complex), 5.80–6.00 (1-proton complex, H-1), and 7.37 (5-proton singlet, C_6H_5).

1,2-O-Isopropylidene-3-O-methyl-5-methylseleninyl-α-D-xylofuranoside (**14**). — Syrup; $[\alpha]_D^{25}$ −1° (*c* 2.6, chloroform); equiv. wt. 158 (calc. 149); n.m.r. data (chloroform-*d*): δ 1.42 (6-proton doublet, *J* 10.0 Hz, CMe_2), 2.64 [3-proton singlet, Se(O)Me], 3.07–3.40 (2-proton complex), 3.49 (3-proton singlet, OMe), 3.67–3.87 (1-proton complex), 4.64 (2-proton doublet, *J* 4.0 Hz), 5.90 (1-proton doublet, *J* 4.0 Hz), and 5.90 (1-proton doublet, *J* 4.0 Hz, H-1).

1,2-O-Isopropylidene-5-methylseleninyl-α-D-xylofuranoside (**15**). — Syrup; equiv. wt. 160 (calc. 142). The syrup was kept for 3 h at room temperature. The resultant product, consisting of three components as shown by t.l.c, was dissolved in 3:7 (v/v) methanol–benzene and the solution applied to a column of silica gel. Elution with the same solvent gave the following compounds: **5** (0.60 g), a crystalline compound (0.44 g) having m.p. 75–115°, and **8** (0.04 g).

The compound of m.p. 75–115° had an equiv. wt. of 144; $[\alpha]_D^{25}$ +9° (*c* 1.0, chloroform); n.m.r. data (chloroform-*d*): δ 1.45 (6-proton doublet, *J* 10.3 Hz, CMe_2), 2.75 [3-proton doublet, *J* 3.5 Hz, Se(O)Me], 3.20–3.57 (2-proton complex), 4.10–4.35 (1-proton complex), 4.50–4.64 (2-proton complex), 5.80–6.00 (1-proton complex, H-1); (deuterium oxide): δ 1.45 (6-proton doublet, *J* 10.3 Hz, CMe_2), 2.77 [3-proton singlet, Se(O)Me], 3.20–3.77 (2-proton complex), 4.20–4.34 (1-proton complex), and 6.00 (1-proton doublet, *J* 3.9 Hz, H-1).

The compound of m.p. 75–115° was treated with acetic anhydride overnight at 4°, and the solution evaporated at room temperature. The resultant syrup had $[\alpha]_D^{25}$ +99° (*c* 2.14, chloroform); n.m.r. data (chloroform-*d*): δ 1.45 (6-proton doublet, *J* 11.5 Hz, CMe_2), 1.95 (3-proton singlet, OAc), 3.10 [3-proton doublet *J* 4.5 Hz, Se(O)Me], 3.87–4.36 (2-proton complex), 4.50–4.70 (2-proton complex), 4.93–5.10 (1-proton complex), and 5.83–6.00 (1-proton complex). Heating of a solution of this acetate in ethyl acetate for 2 h under reflux gave **6** and **5**.

Oxidation of diselenide **7**. — A solution of the diselenide (**7**, 1.0 g) in methanol (40 ml) was treated with 30% hydrogen peroxide (1 ml). After 15 min at room temperature, the solution was evaporated and the residue (0.92 g) crystallized from methanol, m.p. 198–200°; $[\alpha]_D^{25°}$ +58° (*c* 1.38, water); equiv. wt. (iodometric) 90 (calc. for $C_8H_{12}O_5Se$: 90); equiv. wt. (base) 272 (calc. for $C_8H_{12}O_5Se$: 267).

Anal. Calc. for $C_8H_{12}O_5Se$: C, 35.95; H, 4.49. Found: C, 35.98; H, 4.52.

Methylation of **8**. — A solution of **8** (1.0 g) in dry tetrahydrofuran (40 ml) and methyl iodide (5 ml) was treated with sodium hydride (4.0 g). The solution was heated for 4 h under reflux with stirring and then cooled, and water slowly added to destroy the excess of sodium hydride. The alkaline solution was extracted with chloroform and the extracts were evaporated to a syrup (0.45 g) which consisted of a number of chromatographically similar compounds. The aqueous solution was acidified and extracted with chloroform. The extracts were evaporated to a syrup (0.40 g) which was applied to a column of silica gel in 1:39 (v/v) methanol–benzene solution. Elution with the same solvent gave **9**, $[\alpha]_D^{25}$ −175° (*c* 0.84, chloroform); n.m.r. data (chloroform-*d*): δ 1.43 (6-proton doublet, *J* 11.5 Hz, CMe_2), 3.17 (2-proton doublet, *J* 7.5 Hz), 3.44 (3-proton singlet, OMe), 3.74 (1-proton doublet, *J* 3.5 Hz), 4.34–4.54 (1-proton complex), 4.58 (1-proton doublet, *J* 4.0 Hz, H-2), 5.90 (1-proton doublet, *J* 4.0 Hz, H-1).

Anal. Calc. for $C_{18}H_{30}O_8Se_2$: C, 40.60; H, 5.64. Found: C, 40.69; H, 5.66.

An identical compound was formed when **3** was reduced with sodium in liquid ammonia.

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