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Note

Peracetylated D-aldose semicarbazones*

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We have previously reported[1] that acetylation of D-glucose semicarbazone with a large excess of acetylating reagent (acetic anhydride–pyridine) leads to the 1-acetyl-1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)semicarbazide (**4**). This fully acetylated compound had been prepared in low yield by Wolfrom *et al.*[2] by treatment of D-glucose semicarbazone with moderate amounts of the acetylating mixture, but its structure had not been elucidated at that time. From the same reaction mixture, two other products had been obtained[2], namely the semicarbazone of 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-glucose (m.p. 155°) (**1**) and an isomeric pentaacetate that was thought to be a cyclic derivative (m.p. 171°). In the present paper we report evidence that "compound m.p. 171°" is 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-semicarbazide (**5**).

Wolfrom *et al.*[2] also reported that treatment of the semicarbazone of 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-glucose (**1**) ("compound m.p. 155°") with nitrous acid gave 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-glucose, and it was later demonstrated[1] that treatment with nitrous acid of 1-acetyl-1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)semicarbazide (**4**) produced 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide.

In the present work, we have investigated the structure of the compounds obtained by acetylating D-aldose semicarbazones. D-Mannose semicarbazone[3], D-galactose semicarbazone[3], D-xylose semicarbazone[3], and 2-deoxy-D-*arabino*-hexose semicarbazone were acetylated, as previously described for D-glucose semicarbazone[1], to give 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-mannose semicarbazone (**2**), 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-galactose 4-acetylsemicarbazone (**3**), 1-acetyl-1-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)semicarbazide (**6**), and 3,4,5,6-tetra-*O*-acetyl-*aldehydo*-2-deoxy-D-*arabino*-hexose semicarbazone (**7**), respectively. Compound **6**

*Dedicated to Professor V. Deulofeu, in honor of his 70th birthday.

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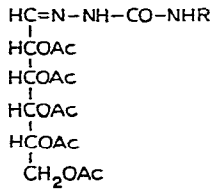

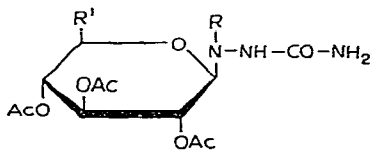

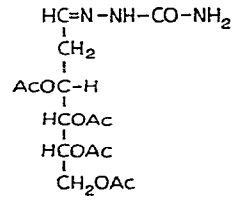

1 D-Gluco (R=H)
2 D-Manno (R=H)
3 D-Galacto (R=Ac)

4 R=Ac, R'=CH_2OAc
5 R=H, R'=CH_2OAc
6 R=Ac, R'=H

7

had been prepared by Major and Cook[4], but its structure was not elucidated at that time. On the other hand, compound **7** had been previously prepared by a different approach[5]. The structures of compounds **2**, **3**, **6**, and **7** were assigned by analysis of their respective p.m.r. spectrum (see Experimental).

DISCUSSION

The first examples of acetylated D-aldose semicarbazones were reported by Wolfrom *et al.*[2] who obtained three different acetylated products from D-glucose semicarbazone. These are now known to be the penta-*O*-acetyl acyclic semicarbazone **1**, the cyclic tetra-*O*-acetyl semicarbazide **5** (see Experimental), and a similar cyclic semicarbazide[1] having an additional *N*-acetyl group at position 1 (**4**). It seems that D-glucose semicarbazone is present, in solution, in the form of an equilibrium mixture of the acyclic and cyclic structures. This equilibrium can be displaced by the nature and amount of reagents employed in the acetylation reaction which accounts for the different results obtained by Wolfrom *et al.*[2] and by ourselves[1]. In the cases of D-mannose, D-galactose, and 2-deoxy-D-*arabino*-hexose semicarbazones, very few cyclic structures seem to be present since on acetylation, even using a many folds excess of acetylating reagents, only the open-chain acetylated semicarbazone structures **2**, **3**, and **7** were obtained. The only difference among these three products is that the D-galactose derivative has an additional *N*-acetyl group, which is assigned to N-4 because of the appearance of two NH signals and no NH_2 band on the p.m.r. spectrum, whereas the D-mannose and 2-deoxy-D-*arabino*-hexose derivatives lack this additional group. It is noteworthy that 2-deoxy-D-*arabino*-hexose behaves more like D-mannose than D-glucose. On the other hand, D-xylose semicarbazone resembles D-glucose semicarbazone, since on acetylation it produces the cyclic pyranoid structure with an acetyl group at N-1 (**6**).

EXPERIMENTAL

General methods. — Melting points were determined by the capillary method and are uncorrected. I.r. spectra were determined with a Perkin–Elmer Model 137

"Infracord" spectrophotometer for mulls in Nujol. P.m.r. spectra were recorded with a Varian A-60 n.m.r. spectrometer. Solvents were removed under diminished pressure with an outside temperature kept below 50°. All compounds were recrystallized until a constant melting point was reached.

Preparation of D-*aldose semicarbazone. General procedure.* — Free sugar (500 mg), semicarbazide hydrochloride (500 mg), and sodium acetate trihydrate (800 mg) were dissolved in water (1 ml), and the solution was clarified by filtration. The solution was kept for 2–3 h at room temperature, treated with ethanol (10 ml), and kept overnight at room temperature. The crystalline precipitate was then collected by filtration and dried.

D-*Galactose semicarbazone.* — The crude product was recrystallized from water to give 426 mg, m.p. 188° (dec.), $[\alpha]_D^{20}$ +8.0→+20.0° (after 24 h, *c* 1, water); lit.[3]: m.p. 200–202°, $[\alpha]_D$ +3.1→+15.6° (after 24 h, *c* 4, water).

D-*Mannose semicarbazone.* — It was recrystallized from 80% ethanol to give 445 mg, m.p. 105°, $[\alpha]_D^{20}$ −62.0→−40.0° (24 h, *c* 1.11, water); lit.[3]: m.p. 108°, $[\alpha]_D$ −53→−43° (24 h, *c* 4, water).

D-*Xylose semicarbazone.* — It was recrystallized from 80% ethanol to give 337 mg, m.p. 185°, $[\alpha]_D^{20}$ −35.0→−28.0° (24 h, *c* 0.92, water); lit.[3]: m.p. 202–204°, $[\alpha]_D$ −38.8→−26.3° (24 h, *c* 4, water).

2-*Deoxy*-D-arabino-*hexose semicarbazone.* — It was recrystallized from 80% ethanol to give 305 mg, m.p. 165–166°, $[\alpha]_D^{20}$ +6.7° (*c* 1.04, water); i.r. data: ν_{max}^{Nujol} 3250, 3150, 1680, 1600, 1575 cm^{-1}; n.m.r. data (deuterium oxide): τ 2.59 (t, 1 H, *J* 5.5 Hz, H-1), 5.60–6.80 (m, 5 H, H-3, H-4, H-5, H-6), 7.60–8.80 (m, 2 H, $-CH_2-$).

Anal. Calc. for $C_7H_{15}N_3O_5$: C, 37.99; H, 6.83; N, 19.00. Found: C, 38.11; H, 6.96; N, 19.14.

2,3,4,5,6-Penta-O-*acetyl*-aldehydo-D-*glucose semicarbazone* (**1**). — It was prepared according to Wolfrom *et al.*[2]. Our product had m.p. 154–155°, $[\alpha]_D^{20}$ +90° (*c* 1.1, chloroform) after recrystallization from ethanol; i.r. data: ν_{max}^{Nujol} 3400, 3240, 3120, 1740, 1670, 1620, 1560 cm^{-1}; n.m.r. data (chloroform-*d*): τ 3.00 (d, 1 H, *J* 4 Hz, H-1), 4.50–4.65 (m, 3 H, H-3, H-4, H-5), 4.92 (d, 1 H, *J* 4 Hz, H-2), 5.80 (m, 2 H, H-6), 7.87, 7.90, 7.92, 7.94, 7.95 (five sharp singlets, 15 H, Ac groups); the signals at τ 0.90 (NH) and 4.40 (NH_2) disappeared on treatment with deuterium oxide.

Anal. Calc. for $C_{17}H_{26}N_3O_{11}$: acetyl, 48.1. Found: acetyl, 47.9.

2,3,4,5,6-Penta-O-*acetyl*-aldehydo-D-*mannose semicarbazone* (**2**). — To a mixture of dry pyridine (16 ml) and acetic anhydride (21.4 ml), D-mannose semicarbazone (880 mg) was added, and the reaction mixture was stirred until complete dissolution (almost 1 h). After 24 h at room temperature the solution was poured into ice–water (50 ml) and the mixture was extracted with chloroform (3 × 30 ml). The organic extract was washed with 10% sulfuric acid, saturated sodium hydrogen carbonate solution, and water, and dried with sodium sulfate. The syrup obtained after evaporation of the solvent was crystallized from ethanol to give 480 mg, m.p. 180–181°, $[\alpha]_D^{23}$ +15.5° (*c* 0.48, chloroform); i.r. data: ν_{max}^{Nujol} 3350, 3150, 3050, 1745, 1670, 1610, and 1560 cm^{-1}; n.m.r. data (chloroform-*d*): τ 2.88 (d, 1 H, *J* 5.5 Hz, H-1).

4.20–5.00 (m, 6 H, H-2, H-3, H-4, H-5, and NH_2), 5.77 (m, 2 H, H-6), 7.90, 7.94, 7.99 (three sharp singlets, 15 H, acetyl groups). The signals from NH_2 and NH (τ 0.02) disappeared on treatment with deuterium oxide.

Anal. Calc. for $C_{17}H_{25}N_3O_{11}$: C, 45.64; H, 5.59; N, 9.39; acetyl, 48.1. Found: C, 45.71; H, 5.78; N, 9.55; acetyl, 48.7.

*2,3,4,5,6-Penta-*O*-acetyl-*aldehydo-D-*galactose 4-acetylsemicarbazone* (**3**). — D-Galactose semicarbazone (880 mg) was acetylated as just described for **2**. Stirring for 4 h at room temperature was needed to achieve complete dissolution, and the crude residue was recrystallized from ethanol to give 896 mg of product **3**, m.p. 198° (dec.), $[\alpha]_D^{20}$ +79.0° (*c* 0.74, chloroform); i.r. data: ν_{max}^{Nujol} 3380, 3200, 3080, 1740, 1675, 1630, and 1565 cm^{-1}; n.m.r. data (chloroform-*d*): τ 0.00 and 0.47 (two NH bands; they disappeared on treatment with deuterium oxide), 3.07 (d, 1 H, *J* 4 Hz, H-1), 4.50 (m, 4 H, four sugar protons), 5.90 (m, 2 H, H-6), 7.85, 7.87, 7.89, 7.91, 7.93, and 7.95 (six sharp singlets, 18 H, acetyl groups).

Anal. Calc. for $C_{19}H_{27}N_3O_{12}$: C, 46.62; H, 5.56; N, 8.59; acetyl, 51.6. Found: C, 46.77; H, 5.60; N, 8.53; acetyl, 51.6.

*1-(2,3,4,6-Tetra-*O*-acetyl-β-*D*-glucopyranosyl)semicarbazide* (**5**). — It was prepared from D-glucose semicarbazone according to the procedure of Wolfrom *et al.*[2] and recrystallized from water and from abs. ethanol, m.p. 170–171°, $[\alpha]_D^{20}$ +100° (*c* 1.04, chloroform); i.r. data: ν_{max}^{Nujol} 3420, 3310, 3200, 1745, 1660, and 1575 cm^{-1}; n.m.r. data (dimethyl sulfoxide-d_6): τ 4.60 (t, 1 H, *J* 9 Hz, H-4), 5.05 (t, 1 H, *J* 9 Hz, H-2 or H-3), 5.10 (t, 1 H, *J* 9 Hz, H-2 or H-3), 5.55 [q, 1 H, $J_{1,2}$ 9 Hz, $J_{1,NH}$ 8 Hz, H-1; on treatment with deuterium oxide the quartet collapsed into a doublet at τ 5.57 ($J_{1,2}$ 9 Hz)], 5.75–6.10 (m, 3 H, H-5 and H-6), 7.95, 7.98, 8.01, and 8.03 (four sharp singlets, 12 H, acetyl groups).

Anal. Calc. for $C_{15}H_{23}N_3O_{10}$: C, 44.44; H, 5.68; N, 10.37; acetyl, 42.5. Found: C, 44.58; H, 5.91; N, 10.41; acetyl, 40.0.

*1-Acetyl-1-(2,3,4-tri-*O*-acetyl-β-*D*-xylopyranosyl)semicarbazide* (**6**). — Acetylation of D-xylose semicarbazone (880 mg) by a procedure similar to the one described for the preparation of **2**, but with a 10-h stirring time, afforded compound **6** (210 mg) which was recrystallized from 80% ethanol, m.p. 248°, $[\alpha]_D^{20}$ +17.0° (*c* 0.47, methanol); lit.[4]: m.p. 232–233°, $[\alpha]_D^{20}$ +21° (*c* 1, methanol); i.r. data: ν_{max}^{Nujol} 3300, 3180, 3095, 1740, 1695, 1660, and 1510 cm^{-1}; n.m.r. data (chloroform-*d*): τ 4.10 [(d, 1 H, $J_{1,2}$ 9 Hz, H-1); the fact that the signal from the anomeric proton appeared as a doublet (instead of a triplet or quartet) clearly indicated the lack of a hydrogen atom on the nitrogen atom attached to C-1]; 4.30–5.00 [(m, 5 H, H-2, H-3, H-4, NH_2); treatment with deuterium oxide eliminated two protons simplifying the multiplet]; 5.77 (q, 1 H, J_{gem} 12 Hz, J_{vic} 6 Hz, H-5_{axial}), 6.40 (q, 1 H, J_{gem} 12 Hz, J_{vic} 2 Hz, H-5_{equat}), 7.82 (s, 3 H, *N*-acetyl group), 7.93 (s, 9 H, three *O*-acetyl groups).

Anal. Calc. for $C_{14}H_{21}N_3O_9$: N, 11.20; acetyl, 45.8. Found: N, 10.96; acetyl, 46.1.

*3,4,5,6-Tetra-*O*-acetyl-2-deoxy-*aldehydo-D-arabino-*hexose semicarbazone* (**7**). — 2-Deoxy-D-*arabino*-hexose semicarbazone (880 mg) was acetylated as previously

described for compound **2**; in this case the mixture had to be stirred for 10 h to obtain a clear solution. The crude product was recrystallized from ethanol to give 306 mg, m.p. 157–158°, $[\alpha]_D^{20}$ +53° (*c* 1.07, chloroform); lit.[5]: m.p. 158°, $[\alpha]_D^{16}$ +50° (*c* 1, chloroform); i.r. data: ν_{max}^{Nujol} 3300, 3200, 3090, 1745, 1675, 1650, 1590, and 1555 cm^{-1}; n.m.r. data (chloroform-*d*): τ 2.65 (t, 1 H, *J* 5 Hz, H-1), 4.50–5.00 (m, 3 H, H-3, H-4, H-5), 5.75 (m, 2 H, H-6), 7.30–8.00 (m, 2 H, $-CH_2-$), 7.83, 7.90, and 7.95 (three sharp singlets, 12 H, acetyl groups).

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