Note

3,6-Anhydro-osazones of higher monosaccharides

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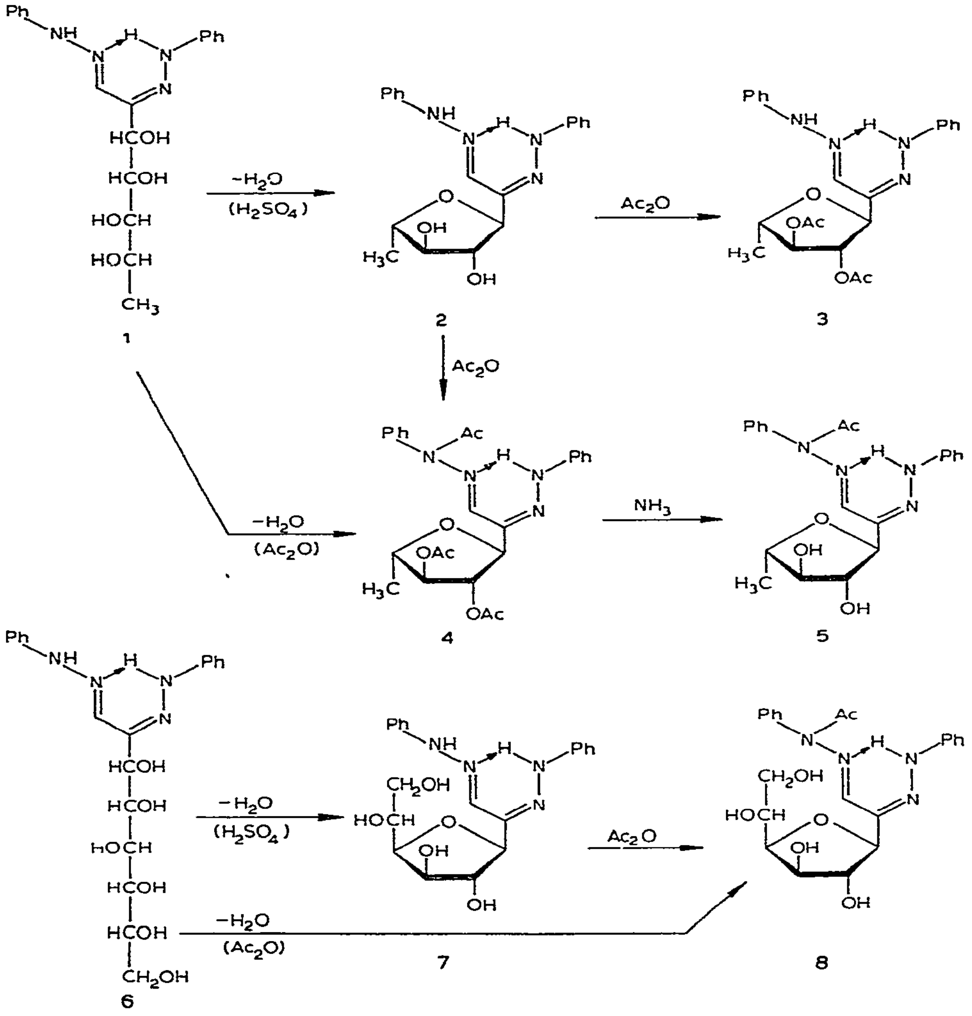
(Received December 19th, 1970)

Comparison of the circular dichroism (c.d.) spectra of osazones and their 3,6-anhydro derivatives revealed that inversion at C-3 takes place during anhydro-osazone formation when the hydroxyl groups on C-3 and C-4 of the parent osazone are "*trans*"-oriented to one another in the Fischer projection formula, but not when they are "*cis*"-oriented[1]. Continuing our work[2] on osazones from higher monosaccharides, we now describe the synthesis of two 3,6-anhydro-osazones that had been discussed in this c.d. study. These are 3,6-anhydro-7-deoxy-L-*manno*-heptulose phenylosazone (**2**) and 3,6-anhydro-D-*glycero*-D-*gulo*-octulose phenylosazone (**6**), as well as their acetyl derivatives. The dehydration was carried out either with methanolic sulfuric acid or with boiling acetic anhydride, and the configuration of the resulting anhydro compounds was found to be independent of the dehydrating agent used.

Thus, by starting with L-rhamnose and ascending the series, we prepared 7-deoxy-L-*manno*-heptulose phenylosazone (**1**) which, on dehydration with methanolic sulfuric acid, yielded 3,6-anhydro-7-deoxy-L-*manno*-heptulose phenylosazone (**2**). Compound **2** consumed one mole of periodate per mole and, on acetylation with acetic anhydride in pyridine, afforded the di-*O*-acetyl derivative (**3**), the i.r. spectrum of which showed the expected ester band at 1740 cm^{-1}. Refluxing of osazone **1** or its 3,6-anhydro derivative **2** with acetic anhydride yielded the same *N*-acetyl-di-*O*-acetyl-3,6-anhydro-7-deoxy-L-*manno*-heptulose phenylosazone (**4**), denoting that the configuration of the 3,6-anhydro ring formed by methanolic sulfuric acid or by acetic anhydride was the same. The i r. spectrum of compound **4** showed the Amide I band at 1695 and the ester band at 1740 cm^{-1}, and on selective hydrolysis of the *O*-acetyl groups with methanolic ammonia, compound **4** afforded *N*-acetyl-3,6-anhydro-7-deoxy-L-*manno*-heptulose phenylosazone (**5**), the i.r. spectrum of which showed only one carbonyl band, at 1660 cm^{-1} (O=CN).

Similarly, D-*glycero*-D-*gulo*-octulose phenylosazone (**6**) was prepared, and dehydrated with methanolic sulfuric acid to give the 3,6-anhydro derivative (**7**). To find out if dehydration with acetic anhydride would give the same type of 3,6-anhydro ring, compounds **6** and **7** were refluxed with acetic anhydride, and then subjected to partial hydrolysis; each yielded the same *N*-acetyl-3,6-anhydro-D-*glycero*-D-*gulo*-octulose phenylosazone (**8**), which showed only one carbonyl band, at 1670 cm^{-1} (O=CN).



It is interesting that, whereas in the pentose series, dehydration of osazones with acetic anhydride gives rise exclusively to dianhydro-osazones of the pyrazole type[3], and that, in the hexose series, the major product is the dianhydro-osazone accompanied by a small proportion of the *N*-acetyl-3,6-anhydro-osazone, in the heptose and octose series, the reverse is found; the *N*-acetyl-3,6-anhydro-osazones preponderate, and, out of four tested[2], only one heptulose osazone yielded a dianhydro-osazone. It seems that, as the series is ascended, the formation of 3,6-anhydro rings is favored and the formation of pyrazole rings inhibited.

EXPERIMENTAL

*3,6-Anhydro-7-deoxy-*L-manno-*heptulose phenylosazone* (**2**). — 7-Deoxy-L-*manno*-heptulose phenylosazone[4] (**1**) (1 g) was refluxed with methanolic sulfuric acid solution (20 ml containing 0.01 ml of conc. sulfuric acid) for 4 h on a hot-water bath. Hot water (20 ml) was added, and the methanol was evaporated off, on the water bath Compound **2** was filtered off, and dried (yield 0.4 g). It crystallized from dilute ethanol in yellow needles, m.p. 212–215°, ν_{max}^{KBr} 3250 cm^{-1} (OH); λ_{max}^{EtOH} 205, 229 (sh), 256, 310, and 394 nm (log ε 4.2, 4.1, 4.2, 3.9, and 4.2), λ_{min}^{EtOH} 217, 279, and 346 nm (log ε 4.0, 3.6, and 3.8); soluble in methanol or acetone, and insoluble in water.

Anal. Calc. for $C_{19}H_{22}N_4O_3$: C, 64.4; H, 6.3; N, 15.8. Found: C, 64.4; H, 6.4; N, 16.0.

*3,6-Anhydro-di-*O*-acetyl-7-deoxy-*L-manno*-heptulose phenylosazone* (**3**). — To a solution of 3,6-anhydro-7-deoxy-L-*manno*-heptulose phenylosazone (2 g) in dry pyridine (5 ml) was added acetic anhydride (5 ml); the mixture was kept overnight at room temperature, and poured onto crushed ice, and the solid obtained was filtered off, washed, and dried (yield 0.3 g). Compound **3** crystallized from methanol in yellow needles, m.p. 163–165°, that were soluble in methanol or acetone, and insoluble in water.

Anal. Calc. for $C_{23}H_{26}N_4O_5$: C, 63.0; H, 6.0; N, 12.8. Found: C, 63.2; H, 5.7; N, 12.6.

N*-Acetyl-di-*O*-acetyl-3,6-anhydro-7-deoxy-*L-manno*-heptulose phenylosazone* (**4**). — (*a*) *From 7-deoxy-*L-manno*-heptulose phenylosazone* (**1**). Compound **1** (1 g) was refluxed with acetic anhydride (10 ml) for 0.5 h, and the mixture was poured onto crushed ice. The oil obtained was repeatedly washed with water, and then kept in the refrigerator until it solidified. Compound **4** (yield 0.4 g) crystallized from dilute ethanol in yellow needles, m.p. 201–203°, ν_{max}^{KBr} 1740 (OAc) and 1695 cm^{-1} (NAc); λ_{max}^{EtOH} 207, 243, 270 (sh), and 378 nm (log ε 4.2, 4.4, 3.9, and 3.3), λ_{min}^{EtOH} 222 and 310 nm (log ε 4.2 and 3.2); soluble in methanol or ethanol, and insoluble in water.

Anal. Calc. for $C_{25}H_{28}N_4O_6$: C, 62.5; H, 5.9; N, 11.7. Found: C, 62 8; H, 6.0; N, 11.3.

(*b*) *From 3,6-anhydro-7-deoxy-*L-manno*-heptulose phenylosazone* (**2**). — Compound **2** (0.2 g) was refluxed with acetic anhydride (5 ml) for 0.5 h, and the mixture processed as in (*a*). Compound **4** (yield 0.05 g) crystallized from methanol in pale-yellow needles, m.p. 200–202° alone or mixed with product from (*a*).

N*-Acetyl-3,6-anhydro-7-deoxy-*L-manno*-heptulose phenylosazone* (**5**). — Compound **4** (1 g) was hydrolyzed with 20% methanolic ammonia (30 ml) overnight at room temperature. Compound **5** separated out, and was filtered off, washed, and dried (yield 0.2 g). It crystallized from dilute methanol in yellow needles, m.p. 224–227°, ν_{max}^{KBr} 3400 (OH) and 1660 cm^{-1} (NAc); λ_{max}^{EtOH} 207, 243, 270 (sh), and 378 nm (log ε 4.2, 4.3, 3.9, and 4.3), λ_{min}^{EtOH} 222 and 310 nm (log ε 4.1 and 3.1); soluble in methanol or ethanol, and insoluble in water.

Anal. Calc. for $C_{21}H_{24}N_4O_4$: C, 63.5; H, 5.8; N, 14.1. Found: C, 63 9; H, 6 1; N, 14.2.

D-glycero-D-gulo-*Octulose phenylosazone* (**6**). — To a mixture of D-*erythro*-L-*galacto*- and D-*erythro*-L-*talo*-octose[5] (5 g) in water (200 ml) were added phenylhydrazine (10 ml) and glacial acetic acid (10 ml), and the mixture was heated for 3 h on a boiling-water bath, and cooled. The osazone was collected, washed with dilute ethanol, and dried (yield 4.5 g). It crystallized from dilute ethanol in yellow needles, m.p. 222–224°, $[\alpha]_D$ $-86°$ (*c* 0.8 pyridine), ν_{max}^{KBr} 3400 cm^{-1} (OH); soluble in methanol, ethanol, or acetone, and insoluble in ether or water.

Anal. Calc. for $C_{20}H_{26}N_4O_6$: C, 57.4; H, 6.3; N, 13.4. Found: C, 57.2; H, 6.0; N, 13.0.

*3,6-Anhydro-*D-glycero-D-glulo-*octulose phenylosazone* (**7**). — Compound **6** (1 g) was refluxed with methanolic sulfuric acid solution (60 ml, containing 0.03 ml of conc. sulfuric acid) for 12 h on a boiling-water bath. Hot water (20 ml) was then added, and the solution was concentrated on the water bath, and cooled. Compound **7** separated; it was filtered off, washed, and dried (yield 0.6 g). It crystallized from dilute ethanol in yellow needles, m.p. 192–194°; ν_{max}^{KBr} 3400 cm^{-1} (OH); soluble in methanol, ethanol, or acetone, and insoluble in water.

Anal. Calc. for $C_{20}H_{24}N_4O_5 \cdot H_2O$: C, 57.4; H, 6.3; N, 13.4. Found: C, 57.4; H, 6.6; N, 13.7.

N-*Acetyl-3,6-anhydro-*D-glycero-D-gulo-*octulose phenylosazone* (**8**). — (*a*) *From* D-glycero-D-gulo-*octulose phenylosazone* (**6**). Compound **6** (1 g) was refluxed with acetic anhydride (10 ml) for 0.5 h, and poured onto crushed ice. The oil obtained was repeatedly washed with water and then kept in a refrigerator for 3 days, whereupon it solidified. It was filtered off, washed, dried, and hydrolyzed with 20% methanolic ammonia (20 ml) overnight at room temperature. Compound **8** separated; it was filtered off, washed, and dried (yield 0.2 g). It crystallized from dilute methanol in pale-yellow needles, m.p. 262–265°, ν_{max}^{KBr} 3400 (OH) and 1670 cm^{-1} (NAc), λ_{max}^{EtOH} 213, 220, 303 (sh), and 358 nm (log ε 4.1, 4.2, 3.7, and 4.4), λ_{min}^{EtOH} 225 and 310 nm (log ε 4.1 and 3.6); soluble in methanol, ethanol, or acetone, and insoluble in water.

Anal. Calc. for $C_{22}H_{26}N_4O_6$: C, 59.7; H, 5.9; N, 12.7. Found: C, 60.2; H, 5.8; N, 13.0.

(*b*) *From 3,6-anhydro-*D-glycero-D-gulo-*octulose phenylosazone* (**7**) Compound **7** (0.2 g) was refluxed with acetic anhydride (5 ml) for 0 5 h, and poured onto crushed ice; the oil obtained was washed repeatedly with water, and hydrolyzed with 20% methanolic ammonia (20 ml) overnight at room temperature. The solution was concentrated on a water bath, and cooled, whereupon compound **8** separated; it was filtered off, washed, and dried (yield 0.05 g). Compound **8** crystallized from methanol in pale-yellow needles, m.p. 260–262° alone or mixed with the product from (*a*).

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