NEW ROUTE FOR THE SYNTHESIS OF 3-DEOXYALDOS-2-ULOSES*†

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ABSTRACT

3-Deoxy-D-erythro- and 3-deoxy-D-threo-hexos-2-uloses, 3-deoxy-D-glyceropentos-2-ulose, and 4-hydroxy-2-oxobutyraldehyde ("3-deoxytetros-2-ulose") were obtained in about 20% net yields by heating aqueous solutions of D-glucose, Dgalactose, D-xylose, and D-erythrose, respectively, with benzoylhydrazine and ptoluidine and decomposing the resultant 3-deoxyaldos-2-ulose bis(benzoylhydrazones) with benzaldehyde. Several 3-deoxyaldos-2-ulose bis(benzoylhydrazones) and psubstituted bis(benzoylhydrazones) are described for the first time.

INTRODUCTION

Treating aqueous solutions of monosaccharides with benzoylhydrazine in the presence of aromatic amines^{2,3} for relatively short periods of time affords the aldos-2ulose bis(benzoylhydrazones). In the present work, we report conditions that lead to the formation in high yields, from the appropriate aldoses and aroylhydrazines, of bis(benzoylhydrazones) and p-substituted bis(benzoylhydrazones) of a 3-deoxyheptos-2-ulose, two 3-deoxyhexos-2-uloses, a 3,6-dideoxyhexos-2-ulose, a 3-deoxypentos-2ulose, and 4-hydroxy-2-oxobutyraldehyde ("3-deoxytetros-2-ulose"). The 3-deoxyaldos-2-ulose bis(benzoylhydrazones) constitute excellent starting materials for the preparation of the free 3-deoxyaldos-2-uloses. 3-Deoxy-D-erythro- and -D-threo-hexos-2-uloses, 3-deoxy-D-glycero-pentos-2-ulose, and the new "3-deoxytetros-2-ulose" were obtained in high yields by removal of the benzoylhydrazine residues with benzaldehyde. The preparation of 3-deoxyaldosuloses by this simple route is an improvement over existing methods, both in yields and in the purity of the products; for example, 3-deoxy-D-erythro-hexos-2-ulose (3) is obtained in 25% overall yield in two simple steps from D-glucose, whereas the conventional procedure involves two columnchromatographic separations that are quite tedious.

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Carbohyd. Res., 17 (1971) 183-192

The chemistry of the 3-deoxyaldos-2-uloses is of considerable intrinsic interest, and there have been several suggestions⁴⁻⁶ that compounds of this type are involved in preparations having carcinostatic activity. Studies on these derivatives are also important in understanding the detailed course of the non-enzymic browning (Maillard) reaction⁷⁻⁹ between sugars and amino acids that leads to deterioration of certain foodstuffs. The simple, preparative route here described makes the 3-deoxy-aldos-2-uloses of various chain-lengths and stereochemical configurations readily available in quantity.

DISCUSSION

It is known that, when aldoses react with arylamines, the N-substituted glycosylamines first formed undergo a series of rearrangements leading to Amadori compounds (1-arylamino-1-deoxyketoses) and thence to the 3-deoxyaldos-2-uloses¹⁰. It might therefore be supposed that, on prolonged heating, a mixture of an aldose or ketose, an aroylhydrazine, and an arylamine could yield a 3-deoxyaldos-2-ulose bis(arovlhydrazone), especially should such a derivative possess low solubility and good crystallizing properties. To evaluate this supposition, a number of aldoses and ketoses were treated for periods of up to 7 h with various aroylhydrazines in the presence of aromatic amines, and it was found that the desired 3-deoxyaldos-2-ulose bis(aroylhydrazones) crystallized out of the solutions on cooling. Thus, 3-deoxy-Derythro-hexos-2-ulose bis(benzoylhydrazone) (1a) was obtained in 35% yield by boiling an aqueous solution of D-glucose with an excess of benzoylhydrazine and p-toluidine for 7 h. D-Mannose, on similar treatment, also afforded 1a, but in lower yield (18%), and, in some experiments, another product, of lower melting point, was obtained; this product is under further investigation. The product obtained from D-glucose was identified as 3-deoxy-D-erythro-hexos-2-ulose bis(benzoylhydrazone) by comparing its m.p., i.r. spectrum, and X-ray powder diffraction diagram with those of an authentic specimen prepared directly from benzoylhydrazine and 3-deoxy-Derythro-hexos-2-ulose^{10,11} (3). Upon periodate oxidation, compound 1a consumed two moles of oxidant per mole and yielded a product giving acceptable analytical, as well as i.r. and n.m.r. spectral, data for the expected aldehyde (2).

Heating of the bis(benzoylhydrazone) with benzaldehyde in ethanol in the way described for the preparation of D-*arabino*-hexosulose¹² afforded benzaldehyde benzoylhydrazone and amorphous 3-deoxy-D-*erythro*-hexos-2-ulose (3) in 75% yield. The latter was characterized by conversion into the known^{10,11} bis[(2,4-dinitro-phenyl)hydrazone] and into a new, crystalline bis(phenylhydrazone).

Prolonged heating of D-glucose and p-toluoylhydrazine in the presence of p-toluidine as for the reaction with benzoylhydrazine afforded crystalline 3-deoxy-Derythro-hexos-2-ulose bis(p-toluoylhydrazone) (1b).

Treatment of D-galactose with benzoylhydrazine and *p*-toluidine in the same way afforded the expected 3-deoxy-D-*threo*-hexos-2-ulose bis(benzoylhydrazone) (4a), which was converted with benzaldehyde into 3-deoxy-D-*threo*-hexos-2-ulose (5) in 65% yield. The latter was identified by conversion into the known bis[(2,4-dinitro-



Carbohyd. Res., 17 (1971) 183-192

phenyl)hydrazone]^{10,11}. Under similar conditions, L-sorbose gave the enantiomorphic 3-deoxy-L-*threo*-hexos-2-ulose bis(benzoylhydrazone) (6a), having the same m.p. as 4a and equal but opposite rotation. With *p*-toluoylhydrazine, D-galactose and L-sorbose afforded the enantiomorphic 3-deoxy-D- and -L-*threo*-hexos-2-ulose bis(*p*-toluoylhydrazones) (4b and 6b), respectively.

In the pentose series, 3-deoxy-D-glycero-pentosulose bis(benzoylhydrazone) (7a) was obtained both from D-arabinose and D-xylose. The former pentose, however, gave lower yields and, in certain experiments, it also gave D-arabinose benzoyl-hydrazone. The bis(benzoylhydrazone) 7a reacted with benzaldehyde to give, in 55% yield, 3-deoxy-D-glycero-pentos-2-ulose (8), which was characterized by conversion into the known¹¹ bis[(2,4-dinitrophenyl)hydrazone]. Similarly, with p-toluoyl-hydrazine, D-arabinose gave the expected 3-deoxy-D-glycero-pentos-2-ulose bis(p-toluoylhydrazone) (7b).

L-Rhamnose was similarly converted into 3,6-dideoxy-L-erythro-hexos-2-ulose bis(benzoylhydrazone) (9a) and bis(p-anisoylhydrazone) (9c).

On treatment with benzoylhydrazine, D-erythrose gave the optically inactive 4-hydroxy-2-oxobutyraldehyde bis(benzoylhydrazone) (10) which, on reaction with benzaldehyde, afforded the free "3-deoxytetros-2-ulose" (11), characterized by conversion into its bis[(2,4-dinitrophenyl)hydrazone].

The reaction is not restricted to lower monosaccharides, and D-glycero-Dgulo-heptose readily afforded 3-deoxy-D-arabino-heptos-2-ulose bis(benzoylhydrazone) (12) under similar treatment.

Like the aldosulose bis(aroylhydrazones)², the 3-deoxyaldos-2-ulose bis(aroylhydrazones) that separate from the reaction mixtures are solvated, even after recrystallization. Upon prolonged heating under diminished pressure, they may be converted into hemihydrates; the anhydrous forms are obtained only under very drastic conditions of drying.

In view of the great variety of products formed when monosaccharides are treated with benzoylhydrazine in the presence of bases, it is recommended that, for the preparation of the 3-deoxy-aldos-2-ulose bis(benzoylhydrazones), the prescibed experimental conditions be followed closely, especially with regard to the time of reaction and the proportions of water and acetic acid used. It is also preferable to employ D-glucose and D-xylose instead of their 2-epimers in the reaction with benzoyl-hydrazine. For the preparation of the previously^{2,3} described products of the reaction [namely, the hexosulose bis(aroylhydrazones), which require shorter reaction periods], we suggest a further decrease in the reaction times earlier^{2,3} suggested, to avoid contamination of the products with 3-deoxyaldos-2-ulose bis(aroylhydrazones).

EXPERIMENTAL

General methods. — Melting points were determined with a Thomas-Hoover "Unimelt" apparatus and are uncorrected. I. r. spectra were recorded with a Perkin-Elmer Model 137 i.r. spectrophotometer. Optical rotations were measured in 1-dm tubes with a Perkin-Elmer Model 141 polarimeter. N.m.r. spectra were recorded at 60 and 100 MHz with Varian A-60 and HA-100 n.m.r. spectrometers. Chemical shifts are given on the τ scale, with tetramethylsilane ($\tau = 10.00$) as the internal standard. Microanalyses were performed by W. N. Rond. X-Ray powder diffraction data give interplanar spacings, Å, for CuK α radiation. Relative intensities were estimated visually: m, moderate; s, strong; v, very; w, weak. The strongest lines are numbered (1, strongest), and double numbers indicate approximately equal intensities. The camera diameter was 114.59 mm.

3-Deoxy-D-erythro-hexos-2-ulose bis(benzoylhydrazone) (1a). — A solution of D-glucose (2.5 g), benzoylhydrazine (3.2 g), and p-toluidine (1 g) in ethanol (50 ml) containing water (10 ml) and acetic acid (0.5 ml) was boiled under reflux for 7 h. The product, which separated after 24 h, was filtered off, washed successively with ethanol and ether, and dried, to give a monohydrate; yield 1.9 g (35%). It was recrystallized from ethanol as needles of the anhydrous form, m.p. 191–192° (dec.), $[\alpha]_D^{25} + 20.0°$ (c 0.2, pyridine); ν_{max}^{KBr} 1660 (CONH) and 3350 cm⁻¹ (OH); n.m.r. data (100 MHz, methyl sulfoxide- d_6 , signals exchangeable on deuteration, only, given) τ -2.16, -2.45 (NH), 3.55, 4.63, 5.16 (4,5,6-OH); X-Ray powder diffraction data: 16.61 s (2), 9.59 vw, 8.49 m, 7.48 m, 6.69 w, 5.32 m, 4.85 w, 4.46 vs (1), 4.09 m, 3.74 s (2,2), 3.09 s (2,2), and 3.15 vw.

Anal. Calc. for $C_{20}H_{22}N_4O_5 \cdot H_2O$: C, 58.0; H, 5.3; N, 13.5. Found: C, 57.8; H, 5.7; N, 13.6.

Anhydrous form:

Anal. Calc. for C₂₀H₂₂N₄O₅: C, 60.3; H, 5.5; N, 14.1. Found: C, 60.1; H, 5.7; N, 13.9.

Authentic 3-deoxy-D-erythro-hexos-2-ulose bis(benzoylhydrazone). — A solution of 3-deoxy-D-erythro-hexos-2-ulose¹¹ (0.12 g) and benzoylhydrazine (0.16 g) in water (10 ml) was heated for a few minutes on a boiling-water bath. The product that separated was filtered off, washed, and dried; yield 0.2 g (71%). It was recrystallized from methanol as needles, m.p. 191° (dec.), $[\alpha]_D^{25} + 18^\circ$ (c 0.15, pyridine); ν_{max}^{KBr} 1660 (CONH) and 3350 cm⁻¹ (OH). The product gave an X-ray powder pattern identical with that recorded for the preceding product.

Anal. Calc. for $C_{20}H_{22}N_4O_5$: C, 60.3; H, 5.5; N, 14.1. Found: C, 60.0; H, 5.8; N, 13.8.

3-Deoxy-D-erythro-hexos-2-ulose bis(p-toluoylhydrazone) (1b). — A solution of D-glucose (2 g), p-toluoylhydrazine (3.5 g), and p-toluidine (1 g) in ethanol (50 ml) containing water (10 ml) and acetic acid (1 ml) was boiled under reflux for 7 h. The procedure used for preparing 1a gave 1b (yield 1.5 g, 32%); it was recrystallized from ethanol as needles, m.p. 237–238° (dec.); $[\alpha]_D^{25} + 59^\circ$ (c 0.1, pyridine).

Anal. Calc. for $C_{22}H_{26}N_4O_5 \cdot H_2O$: C, 59.5; H, 6.3; N, 12.6. Found: C, 59.7; H, 6.7; N, 12.2.

Periodate oxidation of 1a to give 2-oxobutanedial 1,2-bis(benzoylhydrazone) (2). — A suspension of 3-deoxy-D-erythro-hexos-2-ulose bis(benzoylhydrazone) (1a, 0.3 g) in a solution of metaperiodic acid dihydrate (HIO₄·2H₂O) (0.7 g) in water (50 ml) was shaken for 24 h at room temperature. The suspension was filtered, and the filtrate was diluted with water (500 ml), treated with an excess of arsenite, and then back-titrated against iodine (consumption of periodic acid, 1.9 moles per mole of **1a**). The precipitate was washed with water (yield 0.2 g, 80%), and recrystallized from water-ethanol, to give **2** as needles, m.p. 212° (dec.); $v_{\text{max}}^{\text{KBr}}$ 1660 (CONH) and 1700 cm⁻¹ (CHO); n.m.r. data (60 MHz, methyl sulfoxide- d_6): $\tau 2.8-3.5$ (10-proton multiplet, aryl), 4.71 (1-proton quartet, CHO), 7.45 (1-proton quartet, $J_{\text{B,X}}$ 7 Hz, Hb of methylene group), 8.01 (1-proton quartet, $J_{\text{A,X}}$ 2 Hz, $J_{\text{A,B}}$ 19 Hz, Ha of methylene group), and signals observed for NH protons below $\tau -2$.

Anal. Calc. for C₁₈H₁₆N₄O₃: C, 64.3; H, 4.7; N, 16.7. Found: C, 64.4; H, 4.6; N, 16.9.

3-Deoxy-D-erythro-hexos-2-ulose (3). — A solution of 3-deoxy-D-erythro-hexos-2-ulose bis(benzoylhydrazone) (1a, 2 g) in ethanol (60 m!), water (100 ml), acetic acid (2.4 ml), and freshly distilled benzaldehyde (3.2 ml) was boiled under reflux for 6 h; after 3 h, benzaldehyde benzoylhydrazone started to separate. Ethanol was removed by evaporating off 60 ml of the solution, with simultaneous dropwise addition of 100 ml of water. After 18 h, the precipitated benzaldehyde benzoylhydrazone was removed, and the filtrate was concentrated to 40 ml, washed with six 25-ml portions of ether, clarified with charcoal, and evaporated to a thick syrup. A solution of this product in water (10 ml) was mixed with hot ethanol (20 ml), filtered, and shaken consecutively with Amberlite IR-120 (H⁺) and Amberlite IR-4B (OH⁻) ion-exchange resins; the suspension was filtered and the filtrate evaporated (at 35–40°) to dryness, to give syrupy 3; yield 0.6 g (73%), $[\alpha]_D^{25} + 1.6^\circ$ (c 6, water) (after equilibration) (lit.¹⁰ $[\alpha]_D - 2.6 \rightarrow + 1.2^\circ$; and¹¹ $[\alpha]_D - 2.5 \rightarrow + 1.5^\circ$).

3-Deoxy-D-erythro-hexos-2-ulose bis[(2,4-dinitrophenyl)hydrazone]. — A solution of the aldosulose 3 (0.2 g) and (2,4-dinitrophenyl)hydrazine (0.4 g) in 50 ml of 2M hydrochloric acid was boiled under reflux for 2 h, and the product was filtered off while hot. It was recrystallized from ethyl acetate as red needles; yield 0.3 g (46%), m.p. and mixed m.p. $265-266^{\circ}$ (dec.)¹¹.

Anal. Calc. for C₁₈H₁₈N₈O₁₁: C, 41.4; H, 3.4; N, 21.5. Found: C, 41.7; H, 3.6; N, 21.2.

3-Deoxy-D-erythro-hexos-2-ulose bis(phenylhydrazone). — A solution of the aldosulose 3 (0.3 g), phenylhydrazine (0.3 g), and 1 drop of acetic acid in water (10 ml) was kept for 1 h at 40°. The osazone (0.2 g, 31%) that separated was filtered off, washed successively with ethanol and ether, and recrystallized from ethanol-water as yellow needles, m.p. 190° (dec.), $[\alpha]_D^{25} - 73.1^\circ$ (c 0.15, pyridine).

Anal. Calc. for C₁₈H₂₂N₄O₃: C, 63.2; H, 6.4; N, 16.4. Found: C, 63.6; H, 6.7; N, 16.0.

3-Deoxy-D-threo-hexos-2-ulose bis(benzoylhydrazone) (4a). — A solution of Dgalactose (2.5 g), benzoylhydrazine (3.2 g), and p-toluidine (1 g) in ethanol (50 ml) containing 1 ml of acetic acid was boiled under reflux for 5 h, and cooled. The product that separated after 18 h was filtered off, washed successively with ethanol and ether, and dried; yield 1.5 g (27%). It was recrystallized from ethanol as needles, m.p. 204– 206° (dec.), $[\alpha]_D^{25} - 52.5°$ (c 0.8, pyridine); ν_{max}^{KBr} 1660 (CONH) and 3445 cm⁻¹ (OH).

Carbohyd. Res., 17 (1971) 183-192

Anal. Calc. for C₂₀H₂₂N₄O₅·0.5H₂O: C, 59.0; H, 5.7; N, 13.8. Found: C, 58.9; H, 5.9; N, 13.7.

3-Deoxy-D-threo-hexos-2-ulose bis(p-toluoylhydrazone) (4b). — A solution of D-galactose (2 g), p-toluoylhydrazine (3.5 g), and p-toluidine (1 g) in ethanol (50 ml) containing 1 ml of acetic acid was boiled under reflux for 5 h, and the product was isolated as for 4a; yield 1.4 g (30%). It crystallized from ethanol as needles, m.p. 240-241° (dec.), $[\alpha]_D^{25} - 86.3^\circ$ (c 0.1, pyridine).

Anal. Calc. for C₂₂H₂₆N₄O₅·0.5H₂O: C, 60.6; H, 6.2; N, 12.9. Found: C, 60.9; H, 6.2; N, 12.7.

3-Deoxy-D-threo-hexos-2-ulose (5). — To a solution of 3-deoxy-D-threohexosulose bis(benzoylhydrazone) (4a, 2g) in ethanol (60 ml) were added water (100 ml), acetic acid (2.4 ml), and benzaldehyde (3.2 ml), and the mixture was boiled under reflux for 6 h. The product was isolated as for compound 3; the syrup obtained [yield 0.53 g (65%), $[\alpha]_{D}^{25} + 10.5^{\circ}$ (c 6, water) (after equilibration), lit.¹⁰ $[\alpha]_{D} + 18 \rightarrow$ $+12.7^{\circ}$] was converted into the known 3-deoxy-D-threo-hexos-2-ulose bis[(2,4dinitrophenyl)hydrazone], m.p. 258° (lit.^{10,11} m.p. 258–259°).

3-Deoxy-L-threo-hexos-2-ulose bis(benzoylhydrazone) (6a). — A solution of L-sorbose (2.5 g), benzoylhydrazine (3.2 g), and p-toluidine (1 g) in ethanol (50 ml) containing 1 ml of acetic acid was boiled under reflux for 6 h, and cooled. The product that separated after 24 h was filtered off, washed successively with ethanol and ether, and dried (yield 1.8 g, 32%); it was recrystallized from methanol as needles, m.p. 206° (dec.), $[\alpha]_D^{25} + 58^\circ$ (c 0.5, pyridine).

Anal. Calc. for C₂₀H₂₂N₄O₅·0.5H₂O: C, 59.0; H, 5.7; N, 13.8. Found: C, 59.0; H, 5.4; N, 13.3.

3-Deoxy-L-threo-hexos-2-ulose bis(p-toluoylhydrazone) (6b): — A solution of L-sorbose (2 g), p-toluoylhydrazine (3.5 g), and p-toluidine (1 g) in ethanol (50 ml) containing 1 ml of acetic acid was boiled under reflux for 6 h, and cooled. The product that separated after 24 h at room temperature was filtered off, washed successively with ethanol and ether, and dried (yield 1.5 g, 32%). Recrystallization from ethanol gave needles, m.p. 239–240° (dec.), $[\alpha]_D^{25} + 75.6°$ (c 0.1, pyridine).

Anal. Calc. for C₂₂H₂₆N₄O₅·H₂O: C, 59.5; H, 6.3; N, 12.6. Found: C, 59.6; H, 6.4; N, 12.1.

3-Deoxy-D-glycero-pentos-2-ulose bis(benzoylhydrazone) (7a). — A. From Dxylose. A solution of D-xylose (2.5 g), benzoylhydrazine (3.2 g), and p-toluidine (1 g) in ethanol (50 ml) containing 1 ml of acetic acid was boiled under reflux for 3 h, and cooled. The product (yield 2 g, 34%) that separated after 24 h was filtered off, washed successively with ethanol and ether, and recrystallized from ethanol to give needles, m.p. 228-230° (dec.), $[\alpha]_D^{25} - 18.5°$ (c 1, pyridine).

Anal. Calc. for C₁₉H₂₀N₄O₄: C, 62.0; H, 5.4; N, 15.2. Found: C, 61.5; H, 5.5; N, 15.3.

B. From D-arabinose. A solution of D-arabinose (2.5 g), benzoylhydrazine (3.2 g) and p-toluidine (1 g) in ethanol (50 ml) containing water (10 ml) and acetic acid (1 ml) was boiled under reflux for 5 h, and cooled. After 24 h, the product (yield

1.5 g, 25%) was isolated as in the preceding experiment; m.p. and mixed m.p. 230° (dec.), $[\alpha]_D^{25} - 19.1^\circ$ (c 1, pyridine).

Anal. Calc. for C₁₉H₂₀N₄O₄: C, 62.0; H, 5.4; N, 15.2. Found: C, 61.6; H, 5.7; N, 14.7.

3-Deoxy-D-glycero-pentos-2-ulose bis(p-toluoylhydrazone) (7b). — A solution of D-arabinose (2 g), p-toluoylhydrazine (3.5 g), and p-toluidine (1 g) containing water (10 ml) and acetic acid (1 ml) was boiled under reflux for 5 h, and cooled. After 24 h at room temperature, the product (yield 1.2 g, 27%) that had separated was filtered off, washed successively with ethanol and ether, and recrystallized from ethanol as needles, m.p. 270° (dec.), $[\alpha]_D^{25} - 38.6^\circ$ (c 0.1, pyridine).

Anal. Calc. for C₂₁H₂₄N₄O₄: C, 63.6; H, 6.1; N, 14.1. Found: C, 63.8; H, 6.1; N, 14.3.

3-Deoxy-D-glycero-pentos-2-ulose (8). — A solution of 3-deoxy-D-glyceropentos-2-ulose bis(benzoylhydrazone) (7a, 2 g) was treated with benzaldehyde in the usual way. The product 8 (yield 0.55 g, 75%) was converted into the crystalline bis[(2,4-dinitrophenyl)hydrazone], m.p. 258° (lit.¹¹ m.p. 257–258°).

3,6-Dideoxy-L-erythro-hexos-2-ulose bis(benzoylhydrazone) (9a). — A solution of L-rhamnose (2.5 g), benzoylhydrazine (3.2 g), and p-toluidine (1 g) in ethanol (50 ml), water (10 ml), and acetic acid (0.5 ml) was refluxed for 5 h, and cooled. The product (yield 1.2 g, 21%) that separated after 24 h was filtered off, washed successively with ethanol and ether, and recrystallized from ethanol as needles, m.p. 234° (dec.), $[\alpha]_{\rm D}^{25} - 85^{\circ}$ (c 0.2, pyridine).

Anal. Calc. for C₂₀H₂₂N₄O₄: C, 62.9; H, 5.8; N, 14.7. Found: C, 63.1; H, 5.9; N, 14.7.

3,6-Dideoxy-L-erythro-hexos-2-ulose bis(p-anisoylhydrazone) (9c). — A solution of L-rhamnose (2 g), *p*-anisoylhydrazine (3.5 g), and *p*-toluidine (1 g) in ethanol (50 ml), water (10 ml) and acetic acid (1 ml) was refluxed for 5 h. The product was isolated as for 9a; needles, m.p. 225–227° (dec.), $[\alpha]_D^{25} - 68.6°$ (c 0.1, pyridine).

Anal. Calc. for C₂₂H₂₆N₄O₆: C, 59.7; H, 5.9; N, 12.7. Found: C, 59.5; H, 6.2; N, 12.8.

4-Hydroxy-2-oxobutyraldehyde bis(benzoylhydrazone) (10). — A solution of D-erythrose¹³ (2 g), benzoylhydrazine (3.2 g), and p-toluidine (1 g) in ethanol (100 ml), water (10 ml), and acetic acid (1 ml) was refluxed for 4 h and cooled. The product (yield 0.55 g, 10%) that separated after 24 h at room temperature was filtered off, washed successively with ethanol and ether, and recrystallized from methanol as needles, m.p. 233° (dec.), $[\alpha]_D^{25} \pm 0^\circ$ (c 0.4, pyridine).

Anal. Calc. for C₁₈H₁₈N₄O₃: C, 63.9; H, 5.3; N, 16.6. Found: C, 63.7; H, 5.4; N, 16.2.

4-Hydroxy-2-oxobutyraldehyde ("3-deoxytetros-2-ulose") (11). — A solution of "3-deoxytetros-2-ulose" bis(benzoylhydrazone) (10, 2 g) was treated with benzaldehyde in the usual way. The product (yield 0.5 g, 18%) was converted into the crystalline bis[(2,4-dinitrophenyl)hydrazone], m.p. 264° (dec.). Anal. Calc. for C₁₆H₁₄N₈O₉: C, 41.6; H, 3.0; N, 24.2. Found: C, 42.0; H, 3.4; N, 24.1.

3-Deoxy-D-arabino-heptos-2-ulose bis(benzoylhydrazone) (12). — A solution of D-glycero-D-gulo-heptose¹⁴ (1 g), benzoylhydrazine (1.5 g), and p-toluidine (1 g) in ethanol (50 ml), water (10 ml), and acetic acid (1 ml) was refluxed for 4 h and cooled. The product (yield 0.7 g, 35%) that separated after 24 h was filtered off, washed successively with ethanol and ether, and recrystallized from methanol as needles, m.p. 183° (dec.), $[\alpha]_D^{25} - 98.9^\circ$ (c 0.4, pyridine).

Anal. Calc. for $C_{21}H_{24}N_4O_6 \cdot 0.5H_2O$: C, 57.6; H, 5.8; N, 12.7. Found: C, 58.1; H, 6.3; N, 12.9.

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Carbohyd. Res., 17 (1971) 183-192