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Note

Preparation of 2,6-anhydro-aldose acylhydrazones, -semicarbazones and -oximes from 2,6-anhydro-aldononitriles (glycosyl cyanides)

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Abstract

Reductive transformation of per-*O*-acylated 2,6-anhydro-aldononitriles (glycopyranosyl cyanides of the D-*galacto*, D-*gluco*, D-*xylo*, and D-*arabino* configuration) with Raney-nickel–NaH_2PO_2 in pyridine–AcOH–water solvent mixture in the presence of benzoylhydrazine, ethyl carbazate, and semicarbazide gave the corresponding anhydro-aldose benzoylhydrazones, -ethoxycarbonylhydrazones, and -semicarbazones, respectively. Acid catalyzed transimination of the semicarbazones with thiosemicarbazide, hydroxylamine, and *O*-benzylhydroxylamine, resulted in the formation of anhydro-aldose thiosemicarbazones, and *E*/*Z* mixtures of anhydro-aldose oximes, and *O*-benzyl-(anhydro-aldose)-oximes, respectively.

Keywords: *C*-Glycosyl compounds; Hydrazones; Oximes

1. Introduction

Azomethines constitute a densely populated class of compounds readily available by condensation of a carbonyl compound with an ammonia derivative.[1,2] Their widespread application in organic synthesis is based on the sensitivity of the C=N double bond towards attacks by nucleophiles and radicals, and on additional various possibilities offered by substituents on the nitrogen especially when they are of heteroatomic nature.[2–8] Such derivatives are very well known among open chain carbohydrates as well and lend themselves to several ensuing transformations.[9] At variance, because of the more limited availability of 2,6-anhydro-aldoses (*C*-glycosyl aldehydes)[10] azomethine derivatives attached through carbon to the anomeric centre of pyranoid sugar rings are less frequent: *C*-glycosyl azomethines have been represented by anhydro-aldoximes,[11–14] nitrones,[15] and nitronates[16] of anhydro-aldoses; as well as *C*-glycosyl imidoyltellurides obtained from glycosyl tellurides.[17] For *N*-glycopyranosyl azomethines, see a recent work[18] by Györgydeák and co-workers and references cited therein.

Recently, we have elaborated a method for the preparation of tosylhydrazones from nitriles by Raney-nickel–NaH_2PO_2 reduction of the cyano group and in situ trapping of the intermediate with tosylhydrazine.[19] The application of this protocol to glycosyl cyanides (anhydro-aldononitriles, Scheme 1, **1**–**4**) led to the till then unknown anhydro-aldose tosylhydrazones (e.g., **5**) which opened a new way to *exo*-glycals via their aprotic Bamford–Stevens reaction.[20,21]

Studies on the Raney-nickel catalyzed conversion of nitriles to aldehydes in hydrogen atmosphere showed that the intermediate (probably an imine) had to be trapped to avoid formation of the corresponding methylamine.[22–25] 1,2-Dianilino-ethane and semicarbazide as trapping agents proved very efficient, phenylhydrazine was less effective, and tosyl- and benzoylhydrazine as well as hydroxylamine were reported to deliver no useful results.[22–25] For the conversion of glycosyl cyanides to the corresponding aldehydes, a modified protocol was used (Raney-nickel and NaH_2PO_2 in a mixture of AcOH and pyridine) with 1,2-dianilino-ethane,[26,27] while in the absence of a trapping agent a 1-formyl-glycal could be isolated.[28,29] Since our experiences with the formation of tosylhydra-

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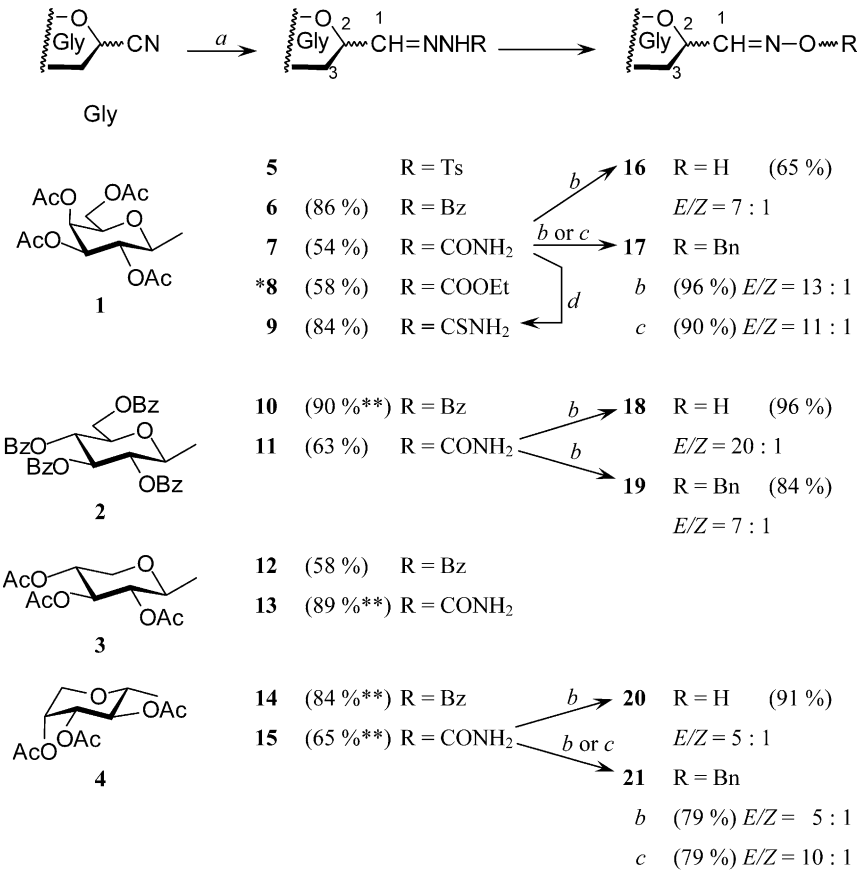

* Room temp.
** Yield of the crude product

Scheme 1. (a) Raney-Ni, NaH_2PO_2, $RNHNH_2$, pyridine, AcOH, water, 40 °C; (b) $NH_2OR \cdot HCl$, abs. pyridine, abs. CH_3CN, rt; (c) $NH_2OBn \cdot HCl$, AcOH, rt; (d) $NH_2NHCSNH_2$, AcOH, 40 °C.

zones from nitriles[19,20] contradicted the earlier observations,[22–25] we started a systematic investigation with respect to the trapping agent. Here we disclose our results on the scope and limitations of the above reductive transformation as to the preparation of new *C*-glycosyl azomethine derivatives.

2. Results and discussion

Using benzoylhydrazine under the above mentioned Raney-nickel–NaH_2PO_2 reductive conditions at room temperature brought about no transformation of **1**. However, a slight enhancement of the reaction temperature to 40 °C resulted in a rather clean transformation of each glycosyl cyanide **1**–**4** to benzoylhydrazones **6**, **10**, **12**, and **14**, respectively, in 58–90% yields (Scheme 1). Ethyl-carbazate also served as a suitable trapping agent at room temperature to give **8** (58%). Only a partial transformation of **1** could be observed at room temperature with semicarbazide, but at 40 °C the reaction was complete in 1 h to give **7** as a crystalline crude product in 82% yield. Semicarbazones **11**, **13**, and **15** were obtained in 63–89% yields.

Trials to use other ammonia derivatives as trapping agents like phenylhydrazine, hydroxylamine, *O*-benzylhydroxylamine, aniline, and benzylamine were successful neither at room temperature nor at 40 °C. In the reaction of **1** with phenylhydrazine and aniline complex reaction mixtures unseparable with column chromatography were formed, with hydroxylamine, its *O*-benzyl derivative, and also with benzylamine 1-formyl-galactal[28,29] was isolated in 15–69% yield. These experiences together with the preparation[19,20] of tosylhydrazones like **5** indicated that a direct transformation of the nitrile group in glycosyl cyanides into imine derivatives was restricted to hydrazines substituted with electron withdrawing acyl or analogous groups.

In order to get other *C*-glycosyl azomethines, acid catalyzed transimination reactions of the hydrazone derivatives were investigated next. Thus semicarbazones **7**, **11**, and **15** were reacted at room temperature in a mixture of acetonitrile and pyridine with hydrochlorides of hydroxylamine and *O*-benzylhydroxylamine to give the corresponding oximes **16**, **18**, and **20** and their *O*-

benzylated derivatives **17**, **19**, and **21**, respectively, as mixtures of *E* and *Z* isomers (see below) generally in good yields. Under the same conditions, attempted reactions of **7** with hydrochlorides of aniline and benzylamine, hydrazine sulfate, and tosylhydrazine in the presence of catalytic or stoichiometric amounts of trifluoroacetic acid or *p*-toluenesulfonic acid gave not even a trace of the expected transimination products. Tosylhydrazone **5** also resisted transformations with *O*-benzylhydroxylamine.

Performing the reaction of **7** and **15** with $BnONH_2 \cdot HCl$ in glacial AcOH gave the expected **17** and **21**, respectively, in very good yields. On the contrary, no reaction occurred in this solvent with hydrochlorides of aniline and benzylamine, while with tosylhydrazine and $NH_2OH \cdot HCl$ multicomponent mixtures were formed. Compound **7** was also transformed with thiosemicarbazide both in acetonitrile–pyridine (at room temperature 85% conversion) and in AcOH at 40 °C the latter giving higher yield of **9** (84% vs. 43%) with a complete conversion of the starting material.

Structural elucidation of the new products was straightforward by NMR spectroscopy. In the ^1H NMR spectra, characteristic doublets ($J_{1,2} = 4.9–7.4$ Hz) appeared at $\delta \sim 7.4–7.5$ ppm for H-1 of benzoylhydrazones **6**, **10**, **12**, **14**, and at $\delta \sim 7.0–7.2$ ppm for semicarbazones **7**, **11**, **13**, **15**, ethoxycarbonylhydrazone **8**, and thiosemicarbazone **9**. In the ^{13}C spectra, resonances for C-1 were visible at $\delta \sim 145–146$ ppm for **6**, **10**, **12**, **14**, at $\delta \sim 137–138$ ppm for **7**, **11**, **13**, **15**, at $\delta =$ 142 ppm for **8**, and $\delta = 140$ ppm for **9**. In these spectra only one set of signals was to be observed indicating that no significant isomerization around the C=N double bond took place. The configuration of the C=N bond was not investigated in detail in these derivatives: it can be assumed that these are *E* as demonstrated with tosylhydrazones.[19,21] For the oximes, both the ^1H and ^{13}C spectra exhibited two sets of signals suggesting the presence of *E* and *Z* isomers. In keeping with the literature[13], H-1 in *E* diastereomers resonated at lower field ($\delta \sim 7.3–7.5$ ppm, for **16***E*, **18***E*, and **20***E*, $\delta \sim$ 6.8–6.9 ppm for **16***Z*, **18***Z*, and **20***Z*, $J_{1,2} = 6.7$ Hz for each; $\delta \sim 7.3–7.5$ ppm for **17***E*, **19***E*, and **21***E*, $\delta \sim 6.8–$ 6.9 ppm for **17***Z*, **19***Z*, and **21***Z*, $J_{1,2} = 6.7–7.3$ Hz for each). The signals for C-1 appeared around 146–147 ppm for each oxime **16**–**21**.

In conclusion, we have shown that anhydro-aldononitriles can readily be transformed into anhydro-aldose hydrazones by Raney-nickel–NaH_2PO_2 reduction in the presence of hydrazines bearing an electron withdrawing substituent (e.g., $-SO_2Ar$[19–21], –COR, $-CONH_2$). Anhydro-aldose semicarbazones are prone to acid catalysed transiminations with hydroxylamine, *O*-benzylhydroxylamine, or thiosemicarbazide to give the corresponding oximes and thiosemicarbazones, respectively. These new *C*-glycosyl azomethine derivatives can be valuable synthetic intermediates, and their ensuing reactions are currently being investigated in our laboratory.

3. Experimental

3.1. General methods

Melting points were measured on a Kofler hot-stage and are uncorrected. Optical rotations were determined with a Perkin–Elmer 241 polarimeter at room temperature. IR spectra were taken with a Perkin–Elmer 16 PC FT-IR spectrometer. NMR spectra were recorded with Bruker WP 360 SY (360/90 MHz for $^1H/^{13}C$). Chemical shifts are referenced to Me_4Si (^1H), to the residual solvent signals (^{13}C). TLC was performed on DC-Alurolle Kieselgel 60 F_{254} (Merck); the plates were visualized by gentle heating or with UV light. For column chromatography, Kieselgel 60 (E. Merck) was used. Organic solutions were dried on $MgSO_4$, and concentrated in vacuo at 40–50 °C (water bath).

3.2. General procedure I for the preparation of 2,6-anhydro-aldose hydrazones 6, 8, 10, 12, 14, and semicarbazones 7, 11, 13, 15

Raney-nickel (1.5 g, from an aq. suspension, E. Merck) was added at room temperature to a vigorously stirred solution of pyridine (5.7 mL), AcOH (3.4 mL), and water (3.4 mL, in case of **6**, **8**, **10**, **12**, and **14**, or 1.7 mL, in case of **7**, **11**, **13**, and **15**). Then NaH_2PO_2 (0.74 g, 8.4 mmol), benzoylhydrazine (0.23 g, 1.7 mmol, in case of **6**, **10**, **12**, and **14**), ethyl-carbazate (0.18 g, 1.7 mmol, in case of **8**), or an aq. sol. (1.7 mL) of semicarbazide (2 mmol, in case of **7**, **11**, **13**, and **15**) liberated from its hydrochloride (0.22 g) by 1.02 equivalent of KOH and the corresponding glycosyl cyanide **1**–**4** (1 mmol) were added to the mixture. The reaction was carried out at room temperature in case of **8**, or at 40 °C in case of **6**, **10**, **12**, and **14**, and **7**, **11**, **13**, and **15**. When the reaction was complete (TLC, 1:1 EtOAc–hexane) the insoluble materials were filtered off with suction, and washed with CH_2Cl_2 or EtOAc (10 mL). The organic layer of the filtrate was separated, washed with water (3 mL), 10% aq HCl solution (2×3 mL), cold, satd $NaHCO_3$ solution (2×3 mL), water (3 mL), (in case of **6** and **12** washing was performed with water only), and then dried. The solution was concentrated under reduced pressure, and traces of pyridine were removed by repeated co-evaporations with toluene. The residue was purified either by crystallization or column chromatography (1:1 or 1:2 EtOAc–hexane) as indicated with the description of the particular compounds.

3.3. General procedure II for the preparation of 2,6-anhydro-aldoximes 16–21

An anhydro-aldose semicarbazone (**7**, **11**, or **15**, 1 mmol) was dissolved in the mixture of dry acetonitrile (12.5 mL) and dry pyridine (4.2 mL). Hydroxylamine hydrochloride (278 mg, 4 mmol, in case of **16**, **18**, and **20**) or *O*-benzyl-hydroxylamine hydrochloride (638 mg, 4 mmol, in case of **17**, **19**, **21**) was added in one portion. The mixture was stirred at room temperature until disappearance of the starting material (TLC, 1:1 EtOAc–hexane). After dilution with EtOAc the solution was washed by 10% aq HCl solution (3 × 6 mL), cold, satd $NaHCO_3$ solution (3 × 6 mL), water (3 mL), then dried, and the solvent removed. The residue was purified either by crystallization or column chromatography (1:1 or 1:2 EtOAc–hexane) as indicated with the description of the particular compounds.

3.4. General procedure III for the preparation of *O*-benzyl-(2,6-anhydro-aldose)-oximes 17, 21

An anhydro-aldose semicarbazone (**7**, or **15**, 1 mmol) was dissolved in glacial AcOH (21 mL), and *O*-benzyl-hydroxylamine hydrochloride (638 mg, 4 mmol) was added in one portion. The mixture was stirred at room temperature until the starting material disappeared (TLC, 1:1 EtOAc–hexane), then poured onto ice-water, extracted with EtOAc (3 × 20 mL), the organic phase neutralized by cold, satd $NaHCO_3$ solution, dried, and the solvent removed. The residue was purified by column chromatography (1:2 EtOAc–hexane).

3.5. 3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptose benzoylhydrazone (6)

Colourless syrup; $[\alpha]_D$ −25° (*c* 1.05, $CHCl_3$); IR (KBr) 3422, 1750, 1372, 1226, 1166, 1052 cm^{-1}; ^1H NMR ($CDCl_3$): δ 10.52 (brs, 1 H, NH), 7.84 (d, 2 H, $J = 7.4$ Hz, Bz), 7.51 (t, 2 H, $J = 7.4$ Hz, Bz), 7.41 (d, 1 H, $J_{1,2} = 7.4$ Hz, H-1), 7.40 (t, 1 H, $J = 7.4$ Hz, Bz), 5.49–5.47 (m, 1 H, H-5), 5.25 (dd, 1 H, $J_{2,3} = 9.3$, $J_{3,4} = 10.1$ Hz, H-3), 5.15 (dd, 1 H, $J_{4,5} = 2.7$ Hz, H-4), 4.20–4.04 (m, 3 H, H-2, H-7, H-7′), 4.00 (dd, 1 H, $J_{5,6} < 1.0$, $J_{6,7} = 6.1$, $J_{6,7'} = 6.0$ Hz, H-6), 2.15, 2.02, 2.00 (3 s, 12 H, 4 × OAc); ^{13}C NMR (Me_2SO-d_6) δ 170.0, 169.7, 169.5, 163.2 (C=O), 145.7 (C-1), 132.9 (Bz quaterner), 131.9, 128.5, 127.7, 127.6 (Bz), 76.7, 73.4, 70.5, 67.9, 67.0 (C-2, C-3, C-4, C-5, C-6), 61.9 (C-7), 20.5, 20.4 (CH_3). Anal. Calcd for $C_{22}H_{26}N_2O_{10}$: C, 55.23; H, 5.48; N, 5.85; found: C, 55.31; H, 5.35; N, 5.74.

3.6. 3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptose semicarbazone (7)

White crystals from MeOH; mp 152–155 °C; $[\alpha]_D$ +2 (*c* 1.04, $CHCl_3$); IR (KBr) 3438, 1742, 1702, 1586, 1372, 1250, 1055 cm^{-1}; ^1H NMR (Me_2SO-d_6): δ 10.21 (brs, 1 H, NH), 7.01 (d, 1 H, $J_{1,2} = 6.1$ Hz, H-1), 6.40–6.00 (brs, 2 H, NH_2), 5.36–5.31 (m, 1 H, H-5), 5.26 (dd, 1 H, $J_{4,5} = 3.3$ Hz, H-4), 5.14 (dd, 1 H, $J_{3,4} = 10.1$ Hz, H-3), 4.27 (dd, 1 H, $J_{5,6} < 1.0$, $J_{6,7} = 6.0$, $J_{6,7'} = 6.0$ Hz, H-6), 4.21 (dd, 1 H, $J_{2,3} = 9.4$ Hz, H-2), 4.07–3.92 (m, 2 H, H-7, H-7′), 2.13, 2.00, 1.96, 1.93 (4 s, 12 H, 4 × OAc); ^{13}C NMR ($CDCl_3$): δ 170.3, 170.1, 170.0 (C=O), 157.7 ($NHCONH_2$) 137.8 (C-1), 77.1, 74.2, 71.6, 67.4, 66.4 (C-2, C-3, C-4, C-5, C-6), 61.6 (C-7), 20.7, 20.5 (CH_3). Anal. Calcd for $C_{16}H_{23}N_3O_{10}$: C, 46.04; H, 5.55; N, 10.07; found: C, 46.14; H, 5.69; N, 10.21.

3.7. 3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptose ethoxycarbonylhydrazone (8)

Colourless syrup; $[\alpha]_D$ +10° (*c* 0.98, $CHCl_3$); IR (KBr) 3274, 2982, 1732, 1538, 1372, 1230, 1056, 756; ^1H NMR ($CDCl_3$): δ 8.77 (brs, 1 H, NH), 7.13 (d, 1 H, $J_{1,2} = 5.2$ Hz, H-1), 5.49–5.47 (m, 1 H, H-5), 5.24 (dd, 1 H, $J_{2,3} = 9.4$, $J_{3,4} = 10.0$ Hz, H-3), 5.13 (dd, 1 H, $J_{4,5} = 3.2$ Hz, H-4), 4.33–3.94 (m, 6 H, H-2, H-6, H-7, H-7′, CH_2), 2.17, 2.05, 2.04, 2.01 (4 s, 12 H, 4 × OAc), 1.31 (t, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ 171.0, 170.7, 170.4, 170.2 (C=O), 141.7 (C-1), 78.6, 74.6, 71.3, 67.8, 67.4 (C-2, C-3, C-4, C-5, C-6), 62.0 (C-7, CH_2), 21.1, 20.9, 20.8, 14.7 (CH_3). Anal. Calcd for $C_{18}H_{26}N_2O_{11}$: C, 48.43; H, 5.87; N, 6.28; found: C, 48.30; H, 5.66; N, 6.05.

3.8. 3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptose thiosemicarbazone (9)

Semicarbazone **7** (30 mg, 0.07 mmol) was dissolved in glacial AcOH (1.5 mL), thiosemicarbazide (26 mg, 0.28 mmol) was added in one portion, and the mixture was stirred at 40 °C until disappearance of the starting material (TLC, 2:1 EtOAc–hexane). The solution was poured onto ice-water, extracted with EtOAc (3 × 4 mL), the organic phase neutralized by cold, saturated $NaHCO_3$ solution, dried, and the solvent removed. The residue was purified by column chromatography (1:2 to 1:1 EtOAc–hexane) to give **9** (84%). Colourless syrup; $[\alpha]_D$ −33° (*c* 1.00, $CHCl_3$); IR (KBr) 3456, 3336, 1748, 1600, 1254, 1224, 1050 cm^{-1}; ^1H NMR (Me_2SO-d_6): δ 11.4 (brs, 1 H, NH), 8.29, 7.51 (2 brs, 2 H, NH_2), 7.23 (d, 1 H, $J_{1,2} = 5.5$ Hz, H-1), 5.35–5.32 (m, 1 H, H-5), 5.28 (dd, 1 H, $J_{4,5} = 3.0$ Hz, H-4), 5.12 (dd, 1 H, $J_{3,4} = 10.3$ Hz, H-3), 4.29 (dd, 1 H, $J_{5,6} < 1.0$, $J_{6,7} = 6.7$, $J_{6,7'} = 6.1$ Hz, H-6), 4.23 (dd, 1 H, $J_{2,3} = 9.7$ Hz, H-2), 4.07–3.95 (m, 2 H, H-7, H-7′), 2.13, 2.00, 1.96, 1.93 (4 s, 12H, 4 × OAc); ^{13}C NMR ($CDCl_3$): δ 179.4 (C=S), 170.5,

170.3 (C=O), 139.6 (C-1), 76.9, 74.7, 71.7, 67.5, 66.4 (C-2, C-3, C-4, C-5, C-6), 61.8 (C-7), 21.1, 20.9, 20.7 (CH_3). Anal. Calcd for $C_{16}H_{23}N_3O_9S$: C, 44.34; H, 5.35; N, 9.69; found: C, 44.22; H, 5.49; N, 9.81.

3.9. 3,4,5,7-Tetra-*O*-benzoyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptose benzoylhydrazone (10)

Colourless syrup; $[\alpha]_D$ −43° (*c* 0.97, $CHCl_3$); IR (KBr) 3420, 1734, 1266, 1092, 708 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.32 (brs, 1 H, NH), 8.20–7.27 (m, 26 H, OBz, NHBz, H-1), 6.01, 5.73, 5.57 (3 pseudo t, 3 H, $J = 9.4$–10.0 Hz, H-3, H-4, H-5), 4.64–4.59 (m, 2 H, H-2, H-7), 4.47 (dd, 1 H, $J_{6,7'} = 5.3$, $J_{7,7'} = 12.1$ Hz, H-7′), 4.29–4.15 (m, 1 H, H-6); ^{13}C NMR ($CDCl_3$): δ 166.3, 165.9, 165.5, 164.3 (C=O), 145.1 (C-1), 132.5 (Bz quaterner), 133.8, 133.7, 133.5, 133.3, 130.0, 129.9, 129.1, 129.8, 128.6, 128.4, 127.5 (OBz, Bz), 129.5, 128.7 (OBz quaterners), 78.7, 76.4, 73.6, 71.0, 69.5 (C-2, C-3, C-4, C-5, C-6), 63.3 (C-7). Anal. Calcd for $C_{42}H_{34}N_2O_{10}$: C, 69.41; H, 4.72; N, 3.85; found: C, 69.52; H, 4.66; N, 3.76.

3.10. 3,4,5,7-Tetra-*O*-benzoyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptose semicarbazone (11)

Colourless syrup; $[\alpha]_D$ +41° (*c* 1.05, $CHCl_3$); IR (KBr) 3480, 1732, 1268, 1094, 708 cm^{-1}; ^1H NMR (Me_2SO-d_6): δ 10.23 (brs, 1 H, NH), 8.05–7.80 (6 H, OBz), 7.75–7.36 (m, 14 H, OBz), 7.20 (d, 1 H, $J_{1,2} = 5.4$ Hz, H-1), 6.11 (brs, 2 H, NH_2), 6.04, 5.71, 5.66 (3 pseudo t, 3 H, $J = 9.3$–10.1 Hz, H-3, H-4, H-5), 4.72 (dd, 1 H, $J_{2,3} =$ 10.1 Hz, H-2), 4.58–4.42 (m, 3 H, H-6, H-7, H-7′); ^{13}C NMR ($CDCl_3$): δ 166.2, 166.0, 165.9, 165.2 (C=O), 157.8 ($NHCONH_2$), 137.3 (C-1), 133.5, 133.3, 133.2, 129.8, 129.7, 128.4 (OBz), 129.5, 129.0, 128.8 (OBz quaterners), 77.0, 76.2, 74.2, 69.9, 69.5 (C-2, C-3, C-4, C-5, C-6), 63.2 (C-7). Anal. Calcd for $C_{36}H_{31}N_3O_{10}$: C, 64.96; H, 4.69; N, 6.31; found: C, 64.85; H, 4.77; N, 6.45.

3.11. 3,4,5-Tri-*O*-acetyl-2,6-anhydro-D-*gulo*-hexose benzoylhydrazone (12)

White crystals from MeOH; mp 225–227 °C dec.; $[\alpha]_D$ −43° (*c* 1.07, $CHCl_3$); IR (KBr) 1746, 1660, 1544, 1372, 1224, 772 cm^{-1}; ^1H NMR (acetone-d_6): δ 11.04 (brs, 1 H, NH), 7.91 (d, 2 H, $J = 7.4$ Hz, Bz), 7.57 (t, 2 H, $J =$ 7.4 Hz, Bz), 7.49 (d, 1 H, $J_{1,2} = 5.8$ Hz, H-1), 7.48 (t, 1 H, $J = 7.4$ Hz, Bz), 5.34 (dd, 1 H, $J_{3,4} = 9.7$ Hz, H-3), 5.03 (t, 1 H, $J_{4,5} = 9.7$ Hz, H-4), 4.95 (dd, 1 H, $J_{2,3} = 9.8$ Hz, H-2), 4.24–4.14 (m, 1 H, H-5), 4.11 (dd, 1 H, $J_{5,6} =$ 5.8, $J_{6,6'} = 11.2$ Hz, H-6), 3.56 (dd, 1 H, $J_{5,6'} = 10.7$ Hz, H-6′), 2.00, 1.96 (2 s, 9 H, 3× OAc); ^{13}C NMR (Me_2SO-d_6): δ 169.6, 169.5, 163.1 (C=O), 145.9 (C-1), 132.9 (Bz quaterner), 131.9, 128.4, 127.6 (Bz), 76.9, 72.3, 69.7, 68.7 (C-2, C-3, C-4, C-5), 65.4 (C-6), 20.4 (CH_3). Anal. Calcd for $C_{19}H_{22}N_2O_8$: C, 56.15; H, 5.46; N, 6.89; found: C, 56.22; H, 5.55; N, 6.98.

3.12. 3,4,5-Tri-*O*-acetyl-2,6-anhydro-D-*gulo*-hexose semicarbazone (13)

White crystals from MeOH; mp 190–192 °C; $[\alpha]_D$ −43° (*c* 0.96, MeOH); IR 3434, 1750, 1702, 1250, 1226, 1036 cm^{-1}; ^1H NMR (Me_2SO-d_6): δ 10.19 (brs, 1 H, NH), 7.01 (d, 1 H, $J_{1,2} = 5.9$ Hz, H-1), 6.20 (brs, 2 H, NH_2), 5.25 (dd, 1 H, $J_{3,4} = 9.4$ Hz, H-3), 5.03 (dd, 1 H, $J_{4,5} =$ 10.1 Hz, H-4), 4.88 (ddd, 1 H, $J_{5,6} = 5.3$, $J_{5,6'} = 10.7$ Hz, H-5), 4.11 (dd, 1 H, $J_{2,3} = 9.3$ Hz, H-2), 3.97 (dd, 1 H, $J_{6,6'} = 10.7$ Hz, H-6), 3.50 (t, 1 H, H-6′), 1.98, 1.97, 1.93 (3 s, 9 H, 3× OAc); ^{13}C NMR (Me_2SO-d_6): δ 169.9, 169.6 (C=O), 156.5 ($NHCONH_2$), 137.0 (C-1), 76.7, 72.7, 69.5, 68.8 (C-2, C-3, C-4, C-5), 65.6 (C-7), 20.5, 20.4 (CH_3). Anal. Calcd for $C_{13}H_{19}N_3O_8$: C, 45.22; H, 5.55; N, 12.17; found: C, 45.44; H, 5.78; N, 12.29.

3.13. 3,4,5-Tri-*O*-acetyl-2,6-anhydro-D-*manno*-hexose benzoylhydrazone (14)

Colourless syrup; $[\alpha]_D$ −5° (*c* 0.95, $CHCl_3$); IR (KBr) 3442, 1748, 1662, 1374, 1226, 1052 cm^{-1}; ^1H NMR ($CDCl_3$): δ 10.14 (brs, 1 H, NH), 7.82 (d, 2 H, $J = 6.9$ Hz, Bz), 7.52 (t, 2 H, $J = 6.9$ Hz, Bz), 7.44–7.38 (m, 2 H, Bz, H-1), 5.37–5.36 (m, 1 H, H-5), 5.27 (dd, 1 H, $J_{3,4} =$ 10.0 Hz, H-3), 5.13 (dd, 1 H, $J_{4,5} = 2.1$ Hz, H-4), 4.11 (dd, 1 H, $J_{1,2} = 6.4$, $J_{2,3} = 9.6$ Hz, H-2), 4.02 (d, 1 H, $J_{5,6} < 1.0$, $J_{6,6'} = 12.9$ Hz, H-6), 3.74 (d, 1 H, $J_{5,6'} < 1.0$ Hz, H-6′), 2.15, 2.02 (2 s, 9 H, 3× OAc); ^{13}C NMR ($CDCl_3$): δ 170.3, 170.1, 164.5 (C=O, Bz), 145.8 (C-1), 132.5 (Bz quaterner), 129.1, 127.6 (Bz), 78.7, 70.9, 68.6, 67.5 (C-2, C-3, C-4, C-5), 68.0 (C-6), 21.0, 20.7 (CH_3). Anal. Calcd for $C_{19}H_{22}N_2O_8$: C, 56.15; H, 5.46; N, 6.89; found: C, 56.23 H, 5.39; N, 6.94.

3.14. 3,4,5-Tri-*O*-acetyl-2,6-anhydro-D-*manno*-hexose semicarbazone (15)

White crystals from EtOAc–hexane; mp 141.5–142.5 °C; $[\alpha]_D$ −16° (*c* 1.04, $CHCl_3$); IR (KBr) 3474, 1744, 1698, 1582, 1372, 1228, 1054 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.95 (brs, 1 H, NH), 7.08 (d, 1 H, $J_{1,2} = 4.9$ Hz, H-1), 6.02 (brs, 2 H, NH_2), 5.48 (pseudo t, 1 H, $J_{3,4} = 9.8$ Hz, H-3), 5.35–5.33 (m, 1 H, H-5), 5.11 (dd, 1 H, $J_{4,5} = 3.2$ Hz, H-4), 4.04 (d, 1 H, $J_{5,6} < 1.0$, $J_{6,6'} =$ 13.6 Hz, H-6), 3.98 (dd, 1 H, $J_{2,3} = 9.8$ Hz, H-2), 3.72 (d, 1 H, $J_{5,6'} < 1.0$ Hz, H-6′), 2.17, 2.03, 2.01 (3 s, 9 H, 3× OAc); ^{13}C NMR ($CDCl_3$): δ 170.3, 170.2, 170.1 (C=O), 157.7 ($NHCONH_2$), 137.9 (C-1), 77.5, 71.2, 68.5, 66.8 (C-2, C-3, C-4, C-5), 67.8 (C-7), 20.8, 20.5 (CH_3). Anal. Calcd for $C_{13}H_{19}N_3O_8$: C, 45.22; H, 5.55; N, 12.17; found: C, 45.29; H, 5.68; N, 12.24.

3.15. 3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptose oxime (16)

White crystals from CH_2Cl_2–hexane; mixture of *E* and *Z* isomers; IR: 3332, 1748, 1720, 1376, 1262, 1244, 1218, 1064, 958 cm^{-1}; Lit. [13] IR: 3332 cm^{-1}. **16***E*: ^1H NMR ($CDCl_3$): δ 8.65 (brs, 1 H, OH), 7.37 (d, 1 H, $J_{1,2} = 6.7$ Hz, H-1), 5.48–5.45 (m, 1 H, H-5), 5.29 (dd, 1 H, $J_{3,4} =$ 10.4 Hz, H-3), 5.11 (dd, 1 H, $J_{4,5} = 3.7$ Hz, H-4), 4.15–4.09 (m, 2 H, H-7, H-7′), 4.05 (dd, 1 H, $J_{2,3} = 9.8$ Hz, H-2), 3.98 (dd, 1 H, $J_{5,6} < 1.0$, $J_{6,7} = 6.7$, $J_{6,7'} = 6.1$ Hz, H-6), 2.18, 2.06, 2.03, 2.00 (4 s, 12 H, 4 × OAc); ^{13}C NMR ($CDCl_3$): δ 170.7, 170.4, 170.3, 170.1 (C=O), 147.1 (C-1), 76.3, 74.4, 71.4, 67.6, 66.9 (C-2, C-3, C-4, C-5, C-6), 61.7 (C-7), 20.8 (CH_3). Recognizable signals for **16***Z*: ^1H NMR ($CDCl_3$): δ 8.92 (s, 1 H, OH), 6.78 (d, 1 H, $J_{1,2} =$ 6.7 Hz, H-1), 5.21 (dd, 1 H, $J_{3,4} = 10.4$ Hz, H-3), 5.17 (dd, 1 H, $J_{4,5} = 3.0$ Hz, H-4), 4.88 (1 H, dd, $J_{2,3} = 9.2$ Hz, H-2); ^{13}C NMR ($CDCl_3$): δ 71.3, 69.8, 67.1 (sugar carbons).

3.16. *O*-Benzyl-(3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptose)-oxime (17)

Colourless syrup; mixture of *E* and *Z* isomers; IR (KBr) 1746, 1372, 1220, 1056 cm^{-1}. **17***E*: ^1H NMR (C_6D_6): δ 7.50 (d, 1 H, $J_{1,2} = 7.3$ Hz, H-1), 7.23–6.98 (m, 5 H, Bn), 5.62 (dd, 1 H, $J_{3,4} = 10.3$ Hz, H-3), 5.50–5.47 (m, 1 H, H-5), 5.17 (dd, 1 H, $J_{4,5} = 3.1$ Hz, H-4), 4.96 (d, 1 H, $J = 16.2$ Hz, CH_2–Bn), 4.93 (d, 1 H, CH_2–Bn), 4.07 (dd, 1 H, $J_{7,7'} = 11.0$ Hz, H-7), 4.02 (dd, 1 H, H-7′), 3.89 (dd, 1 H, $J_{2,3} = 9.8$ Hz, H-2), 3.28 (dd, 1 H, $J_{5,6} < 1.0$, $J_{6,7} =$ 6.7, $J_{6,7'} = 6.1$ Hz, H-6), 1.72, 1.60, 1.59, 1.55 (4 s, 12 H, 4 × OAc); ^{13}C NMR ($CDCl_3$): δ 170.4, 170.2, 170.0, 169.7 (C=O), 146.2 (C-1), 137.4 (Bn quaterner), 128.4, 128.1, 127.9 (Bn), 76.2 (CH_2–Bn), 76.4, 74.3, 71.3, 67.5, 66.7 (C-2, C-3, C-4, C-5, C-6), 61.6 (C-7), 20.7, 20.6, 20.5 (CH_3). Recognizable signals for **17***Z*: ^1H NMR (C_6D_6): δ 6.81 (d, 1 H, $J_{1,2} = 7.3$ Hz, H-1), 5.57 (t, 1 H, $J_{3,4} = 9.7$ Hz, H-3), 5.20 (dd, 1 H, $J_{4,5} = 3.6$ Hz, H-4), 4.84 (dd, 1 H, $J_{2,3} = 9.7$ Hz, H-2), 3.23 (dd, 1 H, $J_{5,6} <$ 1.0, $J_{6,7} = 6.7$, $J_{6,7'} = 6.1$ Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 146.0 (C-1), 75.2 (CH_2–Bn), 70.2, 66.9 (sugar carbons), 21.9 (CH_3).

3.17. 3,4,5,7-Tetra-*O*-benzoyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptose oxime (18)

Colourless syrup; mixture of *E* and *Z* isomers; IR: 3436, 1732, 1452, 1316, 1108, 1094, 1070, 708 cm^{-1}. **18***E*: ^1H NMR ($CDCl_3$): δ 8.29 (brs, 1H, OH), 8.05–7.75 (m, 8 H, OBz), 7.57–7.19 (m, 12 H, OBz), 7.32 (d, 1 H, $J_{1,2} =$ 6.7 Hz, H-1), 6.00, 5.75, 5.65 (3 pseudo t, 3 H, $J = 9.7$–9.8 Hz, H-3, H-4, H-5), 4.62 (dd, 1 H, $J_{6,7'} = 2.4$, $J_{7,7'} =$ 12.2 Hz, H-7′), 4.48 (dd, 1 H, $J_{2,3} = 9.8$ Hz, H-2), 4.44 (dd, 1 H, $J_{6,7} = 4.9$ Hz, H-7), 4.27–4.15 (m, 1 H, H-6); ^{13}C NMR ($CDCl_3$): δ 166.3, 166.1, 165.5, 165.3 (C=O), 146.8 (C-1), 133.6, 133.5, 133.4, 133.2, 129.9, 129.8, 128.5, 128.4 (OBz), 129.6, 129.0, 128.8 (OBz quaterners), 76.4, 76.3, 74.0, 70.5, 69.5 (C-2, C-3, C-4, C-5, C-6), 63.2 (C-7). Recognizable signals for **18***Z*: ^1H NMR ($CDCl_3$): δ 8.41 (s, 1 H, OH), 6.87 (d, 1 H, $J_{1,2} = 6.7$ Hz, H-1), 6.03, 5.69, 5.55 (3 pseudo t, 3 H, $J = 9.2$–9.7 Hz, H-3, H-4, H-5), 5.26 (dd, 1 H, $J_{2,3} = 9.7$ Hz, H-2); ^{13}C NMR ($CDCl_3$): δ 73.9, 70.7, 69.9, 69.8, 69.6 (sugar carbons).

3.18. *O*-Benzyl-(3,4,5,7-tetra-*O*-benzoyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptose)-oxime (19)

Colourless syrup; mixture of *E* and *Z* isomers; IR (KBr) 1732, 1266, 1094, 708 cm^{-1}. **19***E*: ^1H NMR ($CDCl_3$): δ 8.05–7.75 (m, 8 H, OBz), 7.55–7.22 (m, 18 H, OBz, Bn, H-1), 5.95, 5.72, 5.60 (3 pseudo t, 3 H, $J = 9.4$–10.0 Hz, H-3, H-4, H-5), 4.91 (s, 2 H, CH_2–Bn), 4.64 (dd, 1 H, $J_{7,7'} = 12.3$ Hz, H-7), 4.46 (dd, 1 H, H-7′), 4.39 (dd, 1 H, $J_{1,2} = 7.0$, $J_{2,3} = 10.0$ Hz, H-2), 4.26 (ddd, 1 H, $J_{6,7} =$ 2.3, $J_{6,7'} = 4.7$ Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 166.3, 165.9, 165.5, 165.3 (C=O), 146.0 (C-1), 137.1 (Bn quaterner), 133.6, 133.5, 133.4, 133.3, 129.9, 129.8, 128.5, 128.4, 128.0 (OBz, Bn), 129.7, 129.1, 128.9, 128.8 (OBz quaterners), 76.6, 76.4, 73.8, 70.5, 69.5 (C-2, C-3, C-4, C-5, C-6), 76.3 (CH_2-Bn), 63.2 (C-7). Recognizable signals for **19***Z*: ^1H NMR ($CDCl_3$): δ 6.88 (d, 1 H, $J_{1,2} = 7.0$ Hz, H-1), 5.99, 5.70, 5.53 (3 pseudo t, 3 H, $J = 9.3$–10.0 Hz, H-3, H-4, H-5), 5.19 (dd, 1 H, $J_{2,3} = 10.0$ Hz, H-2); ^{13}C NMR ($CDCl_3$): δ 146.1 (C-1), 76.7 (CH_2–Bn), 76.2, 73.8, 70.7, 70.6 (sugar carbons).

3.19. 3,4,5-Tri-*O*-acetyl-2,6-anhydro-D-*manno*-hexose oxime (20)

Colourless syrup; mixture of *E* and *Z* isomers; IR 3416, 1746, 1372, 1226, 1058 cm^{-1}. **20***E*: ^1H NMR ($CDCl_3$): δ 8.41 (brs, 1 H, OH), 7.37 (d, 1 H, $J_{1,2} = 6.7$ Hz, H-1), 5.36–5.33 (m, 1 H, H-5), 5.32 (pseudo t, 1 H, $J_{3,4} = 9.8$ Hz, H-3), 5.11 (dd, 1 H, $J_{4,5} = 3.6$ Hz, H-4), 4.05 (dd, 1 H, $J_{5,6} = 1.9$, $J_{6,6'} = 13.4$ Hz, H-6), 3.97 (dd, 1 H, $J_{2,3} =$ 9.8 Hz, H-2), 3.72 (d, 1 H, $J_{5,6'} < 1.0$ Hz, H-6′), 2.17, 2.03 (2 s, 9 H, 3 × OAc); ^{13}C NMR ($CDCl_3$): δ 170.6, 170.4, 170.1 (C=O), 147.4 (C-1), 76.6, 71.2, 68.6, 67.3 (C-2, C-3, C-4, C-5), 68.1 (C-6), 21.1, 20.8 (CH_3). Recognizable signals for **20***Z*: ^1H NMR ($CDCl_3$): δ 8.69 (brs, 1 H, OH), 6.79 (d, 1 H, $J_{1,2} = 6.7$ Hz, H-1), 5.28 (pseudo t, 1 H, $J_{3,4} = 9.8$ Hz, H-3), 5.17 (dd, 1 H, $J_{4,5} = 3.7$ Hz, H-4), 4.78 (dd, 1 H, $J_{2,3} = 9.8$ Hz, H-2), 4.03 (dd, 1 H, $J_{5,6} = 2.5$, $J_{6,6'} = 12.8$ Hz, H-6′), 3.74 (d, 1 H, $J_{5,6'} < 1.0$ Hz, H-6′); ^{13}C NMR ($CDCl_3$): δ 70.9, 70.2, 67.8, 67.4 (sugar carbons).

3.20. *O*-Benzyl-(3,4,5-tri-*O*-acetyl-2,6-anhydro-D-*manno*-hexose)-oxime (21)

White crystals from diethyl ether–hexane; mixture of *E* and *Z* isomers; IR (KBr) 1748, 1372, 1220, 1058 cm^{-1}. **21***E*: ^1H NMR ($CDCl_3$): δ 7.41–7.25 (m, 6 H, Bn, H-1), 5.33 (brs, 1 H, H-5), 5.28 (dd, 1 H, $J_{3,4} = 10.4$ Hz, H-3), 5.07 (brs, 3 H, CH_2–Bn, H-4), 4.03 (dd, 1 H, $J_{5,6} = 2.5$ Hz, H-6), 3.92 (dd, 1 H, $J_{1,2} = 6.7$, $J_{2,3} = 9.8$ Hz, H-2), 3.68 (d, 1 H, $J_{5,6'} < 1.0$, $J_{6,6'} = 12.8$ Hz, H-6′), 2.16, 2.00, 1.82 (3 s, 9 H, 3 × OAc); ^{13}C NMR ($CDCl_3$): δ 170.4, 170.2, 169.8 (C=O), 146.4 (C-1), 137.5 (Bn quaterner), 128.5, 128.2, 128.0 (Bn), 76.3 (CH_2–Bn), 76.8, 71.1, 68.6, 67.2 (C-2, C-3, C-4, C-5), 68.1 (C-6), 21.1, 20.8, 20.6 (CH_3). Recognizable signals for **21***Z*: ^1H NMR ($CDCl_3$): δ 6.75 (d, 1 H, $J_{1,2} = 6.7$ Hz, H-1), 4.74 (dd, 1 H, $J_{2,3} = 9.2$ Hz, H-2), 2.15, 1.99, 1.85 (3 s, 9 H, 3 × OAc); ^{13}C NMR ($CDCl_3$): δ 70.8, 70.7, 67.7, 67.4 (sugar carbons).

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