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Lengthening of the carbon chain of sugars by the $CH(NO_2) \cdot CH(OEt)_2$ fragment. A route to higher 2-amino-2-deoxyaldoses †

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ABSTRACT

Nitroaldol (Henry) reactions promoted by trialkylsilyl chlorides have been applied to the preparation of chain-extended nitro and amino sugars. The one-pot reaction of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**1**) with 1,1-diethoxy-2-nitroethane in the presence of Et_3N, $Bu_4NF \cdot 3H_2O$, and $^tBuMe_2SiCl$ yielded 7-deoxy-1,2:3,4-di-*O*-isopropylidene-7-nitro-L-*threo*-α-D-*galacto*-octodialdo-1,5-pyranose diethyl acetal (**3a**) and a diastereoisomer in the ratio 4:1. The structure of **3a** was established by a single crystal X-ray diffraction study. Hydrogenation of **3a** (Ni, H_2) afforded the corresponding 7-amino-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-L-*threo*-α-D-*galacto*-octodialdo-1,5-pyranose diethyl acetal (**4a**). Conversion of the latter compound into a *trans*-oxazoline derivative demonstrated that the L-*threo* configuration had been retained. Likewise, reaction of the aldehydo sugar **1** with 1-nitropropane was carried out in order to compare the efficiency of the new nitroaldol procedure here applied with that reported using trialkylsilyl nitronic esters as intermediates.

INTRODUCTION

In spite of the chemical and biological importance of 2-amino-2-deoxyaldoses, relatively few efficient procedures are available for their preparation, and particularly for the higher carbon 2-amino-2-deoxyaldoses[1]. The most efficient and often used routes (such as the Kiliani–Fischer–Kuhn method[2]) to the latter compounds

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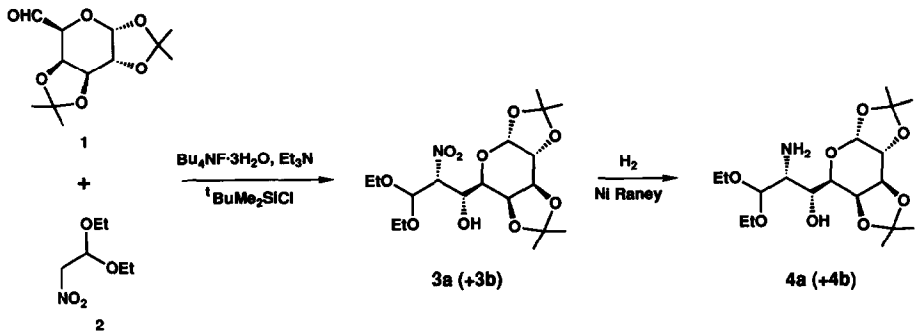
depend on elongation of the carbon chain by one carbon at a time and are tedious if the carbon chain is to be elongated by several atoms. Additions of a unit of two or more carbon atoms have been accomplished by the base-catalyzed aldol reaction of aldehydo aldoses with activated glycine derivatives[3], or by nitroaldol (Henry) reactions, catalyzed either by base or fluoride ion, of aldoses or *O*-protected aldehydo aldoses with suitable nitro compounds[4,5], followed by hydrogenation of the resulting nitroalcohol[5b]. The latter procedure has the disadvantages (often low yields and long reaction times, reversibility of the reaction) inherent in the Henry reaction. The Seebach modification[6] of the Henry reaction, the reaction of silyl nitronates with aldehydes catalyzed by anhydrous Bu_4NF, which has been extended to aldehydo sugars[7], has the drawback of being a multistep procedure which requires stringent conditions, and is too cumbersome to be applied to large-scale preparations. We have recently described[8] a one-step, simple variation of the Henry reaction in which the aldehyde and the nitro compound react in the presence of Et_3N, $Bu_4NF \cdot 3H_2O$, and $^tBuMe_2SiCl$; under these conditions, the reaction does not proceed through the intermediacy of trialkylsilyl nitronic esters, and the nitroalcohols are obtained directly, usually in high yields and with improved stereoselectivity. We have now extended the procedure to the carbohydrate field, in particular to the synthesis of 2-amino-2-deoxyaldoses, using as building blocks *O*-protected aldehydo sugars and the readily available 1,1-diethoxy-2-nitroethane[9] (**2**); hydrogenation of the higher 2-deoxy-2-nitroaldose diethyl acetal thus obtained would then afford the target amino sugar. As an example, we report the synthesis of 7-amino-7-deoxy-1,2:3,4-di-*O*-isopropylidene-L-*threo*-α-D-*galacto*-octodialdo-1,5-pyranose diethyl acetal (**4a**) via the nitro compound **3a**. Deprotection of **4a** would yield the corresponding 2-amino-2-deoxyoctodialdose. 2-Amino-2-deoxyaldoses could be obtained starting from the appropriate *O*-protected aldehyde and **2**.

RESULTS AND DISCUSSION

Reaction of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**1**) with **2** in the presence of Et_3N, $Bu_4NF \cdot 3H_2O$, and $^tBuMe_2SiCl$ * afforded a mixture of 7-deoxy-1,2:3,4-di-*O*-isopropylidene-7-nitro-L-*threo*-α-D-*galacto*-octodialdo-1,5-pyranose diethyl acetal (**3a**) and a diastereoisomer **3b** in the ratio 4:1. The reaction proceeded at room temperature without any need of an inert atmosphere, and was complete (100% conversion, NMR monitoring) in 5 min. Fractionation of the reaction mixture afforded crystalline **3a** (58%), and a mixture of **3a** and **3b** (17%; 1:4 **3a**:**3b** ratio).

* Nitro compound **2**, aldehyde **1**, Et_3N, and $^tBuMe_2SiCl$ have to be added sequentially in this order to a solution of $Bu_4NF \cdot 3H_2O$ in THF.



A single crystal X-ray diffraction study * of **3a** provided evidence for the complete stereochemistry. The bond lengths and angles are listed in Table I, and Fig. 1 shows an ORTEP drawing of the molecule with the numbering scheme. The diffraction data revealed that the chirality at both C-6 and C-7 was *R*, thus defining the L-*threo*-α-D-*galacto* configuration of the compound. The C-4–C-8 fragment adopts a planar, zigzag disposition [maximum deviation from the mean plane, 0.026(3) Å]. The hydrogen atom of HO-6 is bonded to O-71 of the NO_2 group by an intramolecular hydrogen bond (O-6 · · · O-72 = 2.834 Å), thus helping to keep the planarity of C-4–C-8; this plane is twisted by 25.6(2)° from the mean plane of the twist-boat pyranose ring.

The $J_{6,7}$, $J_{7,8}$, and $J_{6,OH}$ coupling constant values measured for **3a** (2.3, 7.3, and 8.9 Hz, respectively) are in accordance with those observed for the fragment R · C(1)HOH · C(2)HNO_2 · C(3)H$(OEt)_2$ of *threo* isomers in simple model compounds[10].

The stereochemical outcome of the reaction can be rationalized by assuming that, according to Cram's rule, **2** attacks the carbonyl group of **1** at the less hindered *re* face in the conformation shown in Fig. 2, where the carbonyl double bond nearly eclipses H-5 and has its *si* face shielded by the isopropylidene group at position 3,4. This would lead to two isomers with the 6*R* configuration (**3a** and **3b**), differing in the chirality at C-7.

In order to compare the efficiency of the procedure here described to extend the sugar chain with the Seebach silyl nitronate method as applied by Martin et al.[7], aldehyde **1** was treated with 1-nitropropane under the conditions indicated above for **2**. Reaction was complete (100% conversion) in 5 min and two nitrononoses **5a** and **5b** were obtained in a single step in 85% yield after bulb-to-bulb distillation (diastereoisomeric ratio **5a** : **5b**, 1.5 : 1). The mixture of diastereoisomers

* Lists of the observed and calculated structure factors, isotropic thermal parameters, and nonhydrogen and hydrogen atomic coordinates are deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/542, *Carbohydr. Res.*, 247 (1993) 239–248.

TABLE 1

Bonds lengths (Å) and bond angles (°) for **3a** [a]

O–C-1	1.415(4)	C-1–O–C-5	113.6(2)
O–C-5	1.424(3)	C-1–O-1–C-12	110.7(2)
O-1–C-1	1.412(4)	C-2–O-2–C-12	106.8(2)
O-1–C-12	1.436(3)	C-3–O-3–C-34	106.5(2)
O-2–C-2	1.429(3)	C-4–O-4–C-34	108.6(2)
O-2–C-12	1.431(4)	C-8–O-81–C-81	110.7(3)
O-3–C-3	1.422(3)	C-8–O-82–C-82	116.7(3)
O-3–C-34	1.418(4)	O-71–N-7–O-72	124.6(2)
O-4–C-4	1.425(4)	O-72–N-7–C-7	116.9(2)
O-4–C-34	1.427(5)	O-71–N-7–C-7	118.5(2)
O-6–C-6	1.416(4)	O–C-1–O-1	109.4(3)
O-71–N-7	1.219(4)	O-1–C-1–C-2	104.1(2)
O-72–N-7	1.223(3)	O–C-1–C-2	114.2(2)
O-81–C-8	1.396(3)	O-2–C-2–C-1	103.6(2)
O-81–C-81	1.441(6)	C-1–C-2–C-3	114.5(2)
O-82–C-8	1.406(4)	O-2–C-2–C-3	108.1(2)
O-82–C-82	1.441(4)	O-3–C-3–C-2	107.6(2)
N-7–C-7	1.500(4)	C-2–C-3–C-4	114.8(3)
C-1–C-2	1.528(4)	O-3–C-3–C-4	103.9(2)
C-2–C-3	1.509(4)	O-4–C-4–C-3	104.1(2)
C-3–C-4	1.547(5)	C-3–C-4–C-5	111.6(3)
C-4–C-5	1.512(4)	O-4–C-4–C-5	110.2(2)
C-5–C-6	1.531(5)	C-4–C-5–C-6	114.2(2)
C-6–C-7	1.532(4)	O–C-5–C-6	105.8(2)
C-7–C-8	1.538(5)	O-6–C-6–C-5	111.3(2)
C-12–C-121	1.513(6)	C-5–C-6–C-7	111.3(2)
C-12–C-122	1.512(6)	O-6–C-6–C-7	114.2(3)
C-34–C341	1.514(5)	N-7–C-7–C-6	111.0(2)
C-34–C-342	1.514(4)	C-6–C-7–C-8	113.6(2)
C-81–C-811	1.487(6)	N-7–C-7–C-8	105.9(2)
C-82–C-821	1.468(9)	O-82–C-8–C-7	112.4(2)
		O-81–C-8–C-7	105.0(3)
		O-81–C-8–O-82	113.3(2)
		O-1–C-12–O-2	104.1(2)
		O-2–C-12–C-122	111.1(3)
		O-2–C-12–C-121	108.2(3)
		O-1–C-12–C-122	110.3(3)
		O-1–C-12–C-121	108.7(3)
		C-121–C-12–C-122	113.9(3)
		O-3–C-34–O-4	104.5(2)
		O-4–C-34–C-342	109.0(3)
		O-4–C-34–C-341	111.5(3)
		O-3–C-34–C-342	108.7(3)
		O-3–C-34–C-341	110.9(3)
		C-341–C-34–C-342	111.9(3)
		O-81–C-81–C-811	108.7(4)
		O-82–C-82–C-821	108.7(4)

[a] Esds in parentheses.

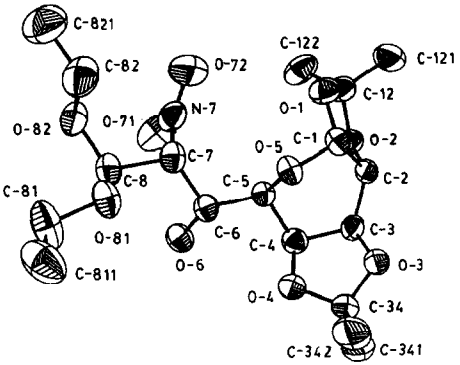
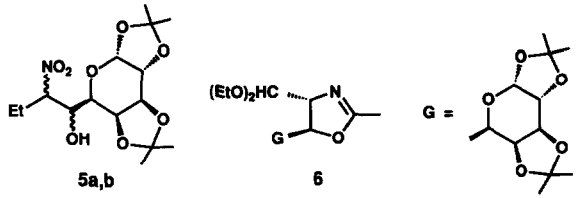


Fig. 1. ORTEP drawing of compound **3a**. For clarity, the hydrogen atoms are not shown.

5a and **5b** could be resolved (80% yield) using an alternative purification by column chromatography. The overall yield (three steps from 1-nitropropane) of **5**, as an unspecified mixture of diastereoisomers, reported[7] using 1-*aci*-nitropropane trimethyl silyl ester is 50%.

Hydrogenation of **3a** (H_2, Raney-Ni, 5 atm, 20°C) afforded, after column chromatography, 7-amino-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-L-*threo*-α-D-*galacto*-octodialdo-1,5-pyranose diethyl acetal (**4a**; 55%), and a mixture of **4a** and a diastereoisomer **4b** (6%). The conversion of **4a** into the *trans*-oxazoline **6** demonstrated that the L-*threo* configuration of **3a** had been retained. The configuration of **6** at C-6 and C-7 was assigned on the basis of the $J_{6,7}$ value (4.5 Hz), which is consistent with a *trans* disposition of H-6 and H-7, but too small for a *cis*-oxazoline[11].



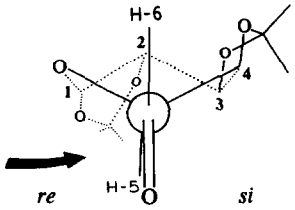


Fig. 2. Diagrammatic view of **1** along the C-5–C-6 bond in the reactive conformation.

EXPERIMENTAL

General methods.—Evaporations were conducted in vacuo at < 40°C (bath). Melting points were determinated with a Gallenkamp MFB-595 melting-point apparatus and are uncorrected. Elemental analyses were carried out at the Instituto de Química Orgánica General, C.S.I.C. (Madrid). Optical rotations were measured at room temperature with a Perkin–Elmer 241 MC polarimeter. IR spectra were recorded for KBr pellets or films, using an FT-IR Bomen MB-120 spectrophotometer. NMR spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si), using a Varian XL-200 (200 MHz), Bruker AC 200 (200 MHz), or Bruker AMX 500 (500 MHz) spectrometer. APT, COSY, and XHCORR spectra were obtained to assist in signal assignments. EI-mass spectra were obtained at 70 eV, using an MS-80 RFA Kratos instrument, an ionising current of 100 μA, an accelerating voltage of 4 kV, and a resolution of 1000 or 10000 (10% valley definition). The reactions were monitored by ^{1}H NMR spectroscopy and TLC (Kieselgel 60 F_{254}, Merck). Purifications of the products were carried out by column chromatography (Silica Gel 60, 0.063–0.200 nm, Merck) or by bulb-to-bulb distillation using a Büchi GKR-51 apparatus; boiling points refer to air-bath temperatures.

*7-Deoxy-1,2 : 3,4-di-*O*-isopropylidene-7-nitro-*L-threo-*α*-D-*galacto-octodialdo-1,5-pyranose diethyl acetal* (**3a**) *and its diastereoisomer* **3b**.—To a stirred solution of $Bu_4NF \cdot 3H_2O$ (1.4 g, 4.5 mmol) in THF (8 mL), cooled at 0°C, were sequentially added 1,1-diethoxy-2-nitroethane (**2**; 2.93 g, 18 mmol), a solution of 1,2 : 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**2**; 3.10 g, 12 mmol) in THF (6 mL), Et_3N (1.7 mL, 12 mmol), and a solution of ^{t}BuMe$_2$SiCl (2.71 g, 18 mmol) in THF (10 mL). After 5 min (100% conversion by ^{1}H NMR monitoring), the suspension was filtered. The filtrate was poured into 1 : 3 ether–hexane (290 mL), and washed with water (2 × 24 mL). The organic layer was separated, dried ($MgSO_4$), and evaporated, giving a residue containing **3a** and a diastereoisomer (**3b**) in the ratio 4 : 1 (^{1}H NMR spectroscopy). Crystallization from 1 : 1 EtOH–H_2O yielded **3a** (2.55 g). Column chromatography (1 : 3 ether–hexane) of the material in the mother liquor afforded a mixture of **3a** and **3b** (0.86 g, 17%) in the ratio 1 : 4, and an additional amount (0.37 g) of **3a** (total yield of **3a**, 58%).

Compound **3a** had: mp 114–117°C; $[\alpha]_D^{25}$ −56° (*c* 1, $CHCl_3$); ν_{max} 3508 (OH), 1553 and 1385 (NO_2), 1098 and 1065 cm^{-1} (C–O). MS data: *m/z* 406 (3%), 376 (1), 243 (63), 199 (20), 185 (25), 171 (15), 141 (100), 113 (40), 103 (44), 90 (45), and 71 (83); HRMS: *m/z* 406.1694 (Obsd), *m/z* 406.1713 (Calcd for $C_{17}H_{28}NO_{10}$, $[M - CH_3]^+$). ^{1}H NMR data: δ 5.50 (d, 1 H, $J_{1,2}$ 5.1 Hz, H-1), 5.19 (d, 1 H, $J_{7,8}$ 7.3 Hz, H-8), 5.00 (dd, 1 H, $J_{6,7}$ 2.3 Hz, H-7), 4.65 (dd, 1 H, $J_{2,3}$ 2.6, $J_{3,4}$ 8.0 Hz, H-3), 4.44 (dd, 1 H, $J_{4,5}$ 2.1 Hz, H-4), 4.33 (dd, 1 H, H-2), 4.27 (dd, 1 H, $J_{5,6}$ ~ 0, $J_{6,OH}$ 8.9 Hz, H-6), 3.8–3.5 (m, 4 H, 2 OCH_2CH$_3$), 3.72 (d, 1 H, H-5), 3.14 (d, 1 H, OH), 1.50, 1.46, 1.38, 1.32 (4 s, each 3 H, 4 CCH_3), 1.25 and 1.18 (2 t, each 3 H, 2 OCH$_2$CH_3); ^{13}C NMR data: δ 109.4, 108.9 [2 *C*(Me)$_2$], 99.2 (C-8), 96.0 (C-1), 86.6

(C-7), 70.4 (C-2,3), 70.2 (C-4), 67.7 (C-6), 66.8 (C-5), 63.7, 63.0 (2 OCH_2CH_3), 25.7, 25.5, 24.7, 24.3 (4 CCH_3), 15.0 and 14.8 (2 OCH_2CH_3). Anal. Calcd for $C_{18}H_{31}NO_{10}$: C, 51.30; H, 7.41; N, 3.32. Found: C, 51.50; H, 7.53; N, 3.40.

Data for **3b**. ^{1}H NMR: δ 5.47 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 5.19 (d, 1 H, $J_{7,8}$ 7.3 Hz, H-8), 4.86 (dd, 1 H, $J_{6,7}$ 2.9, H-7), 4.63 (dd, 1 H, $J_{2,3}$ 2.3, $J_{3,4}$ 8.0 Hz, H-3), 4.39 (dd, 1 H, $J_{4,5}$ 1.8 Hz, H-4), 4.30 (dd, 1 H, H-2), 4.30 (ddd, 1 H, $J_{5,6}$ 9.1, $J_{6,OH}$ 5.4 Hz, H-6), 4.06 (dd, 1 H, H-5), 3.8–3.5 (m, 4 H, 2 OCH_2CH_3), 3.05 (d, 1 H, OH), 1.44, 1.36, 1.33, 1.32 (4 s, each 3 H, 4 CCH_3), 1.22 and 1.17 (2 t, each 3 H, 2 OCH_2CH_3). ^{13}C NMR: δ 109.1, 108.8 [2 $C(Me)_2$], 100.1 (C-8), 95.9 (C-1), 88.7 (C-7), 70.3 (C-2,3), 70.2 (C-4), 69.5 (C-6), 66.8 (C-5), 64.7, 63.4 (2 OCH_2CH_3), 25.6, 25.5, 24.6, 24.2 (4 CCH_3), 15.0 and 14.9 (2 OCH_2CH_3).

7-Amino-7-deoxy-1,2 : 3,4-di-O-*isopropylidene*-L-threo-α-D-galacto-*octodialdo-1,5-pyranose diethyl acetal* (**4a**).—Freshly prepared Raney-Ni (0.4 g) was added to a solution of **3a** (250 mg, 0.6 mmol) in EtOH (15 mL). The suspension was shaken in a pressure reactor under 5 atm H_2 for 30 h at 20°C. The mixture was filtered through Celite and the filtrate evaporated to dryness. Column chromatography (60 : 1 CH_2Cl_2–MeOH) of the residue gave **4a** (128 mg, 55%), and a mixture of **4a** and a diastereiosomer **4b** (14 mg, 6%), which was not ressolved.

Compound **4a** had: $[\alpha]_D^{25}$ −55° (*c* 1, $CHCl_3$); ν_{max} 3700–3400 (OH, NH) and 1089 cm^{-1} (C–O). MS data: *m/z* 391 (1%), 376 (5), 346 (12), 330 (20), 316 (10), 288 (90), 271 (18), 243 (8), 230 (20), 171 (12), 149 (18), 132 (10), 103 (100), 86 (23), and 75 (38); HRMS: *m/z* 391.2247 (Obsd), *m/z* 391.2206 (Calcd for $C_{18}H_{33}NO_8$, $[M]^+$). ^{1}H NMR data: δ 5.51 (d, 1 H, $J_{1,2}$ 5.1 Hz, H-1), 4.63 (dd, 1 H, $J_{2,3}$ 2.3, $J_{3,4}$ 8.0 Hz, H-3), 4.52 (d, 1 H, $J_{7,8}$ 4.8 Hz, H-8), 4.48 (dd, 1 H, $J_{4,5}$ 1.9 Hz, H-4), 4.31 (dd, 1 H, H-2), 4.00 (dd, 1 H, $J_{5,6}$ 9.1 $J_{6,7}$ 1.6 Hz, H-6), 3.80 (dd, 1 H, H-5), 3.8–3.5 (m, 4 H, 2 OCH_2CH_3), 3.16 (dd, 1 H, H-7), 1.8-1.6 (br, 3 H, OH and NH_2), 1.56, 1.47, 1.38, 1.33 (4 s, each 3 H, 4 CCH_3), and 1.22 (t, 6 H, 2 OCH_2CH_3); ^{13}C NMR data: δ 108.9, 108.4 [2 $C(Me)_2$], 104.6 (C-8), 96.3 (C-1), 70.6 (C-2,3), 70.5 (C-4), 67.9 (C-6), 66.7 (C-5), 63.7, 62.5 (2 OCH_2CH_3), 51.7 (C-7), 25.8, 24.8, 24.2 (4 CCH_3), 15.2 and 15.1 (2 CH_2CH_3).

Data for **4b**. ^{1}H NMR: δ 5.56 (d, 1 H, $J_{1,2}$ 5.1 Hz, H-1), 4.66 (d, 1 H, $J_{7,8}$ 4.1 Hz, H-8), 4.63 (dd, 1 H, $J_{2,3}$ 2.2, $J_{3,4}$ 8.1 Hz, H-3), 4.54 (dd, 1 H, $J_{4,5}$ 1.6 Hz, H-4), 4.32 (dd, 1 H, H-2), 3.95 (dd, 1 H, $J_{5,6}$ 7.9, $J_{6,7}$ 5.6 Hz, H-6), 3.84 (dd, 1 H, H-5), 3.8–3.5 (m, 4 H, 2 OCH_2CH_3), 3.04 (dd, 1 H, H-7), 2.1–1.8 (br, 3 H, OH and NH_2), 1.55, 1.46, 1.34, 1.33 (4 s, each 3 H, 4 CCH_3), 1.23 (t, 6 H, 2 OCH_2CH_3); ^{13}C NMR data: δ 108.9, 108.1 [2 $C(Me)_2$], 103.6 (C-8), 96.5 (C-1), 70.9 (C-6), 70.5 (C-2,3), 70.3 (C-4), 67.6 (C-5), 64.0, 63.7 (2 OCH_2CH_3), 55.5 (C-7), 25.8, 24.7, 24.4 (4 CCH_3), 15.3 and 15.2 (2 CH_2CH_3).

7,8,9-Trideoxy-1,2 : 3,4-di-O-*isopropylidene-7-nitro*-α-D-galacto-*nonoaldo-1,5-pyranoses* **5a** + **5b**.—To a stirred solution of $Bu_4NF \cdot 3H_2O$ (0.7 g, 2.2 mmol) in THF (4 mL), cooled at 0°C, were sequentially added 1-nitropropane (0.8 mL, 9 mmol), a solution of 1,2 : 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**1**; 1.55 g, 6 mmol) in THF (3 mL), Et_3N (0.8 mL, 6 mmol), and a

solution of $^{t}BuMe_2SiCl$ (1.36 g, 9 mmol) in THF (5 mL). After 5 min (100% conversion by ^1H NMR monitoring), the suspension was filtered. The filtrate was poured into 1:3 ether–hexane (160 mL), and washed with water (2 × 12 mL). The organic layer was separated, dried ($MgSO_4$), and evaporated to dryness. Purification of the crude product was carried out by two alternative procedures: (*A*) bulb-to-bulb distillation gave **5** (1.77 g, 85%) as a mixture of two diastereoisomers (**5a**:**5b**, 60:40); bp 120°C/0.04 mbar; (*B*) column chromatography (1:5 ether–hexane) gave **5b** (0.35 g, 17%), a mixture of **5a** and **5b** (0.56 g, 27%; ratio **5a**:**5b**, 4:5), and **5a** (0.75 g, 36%).

Compound **5a** had $[\alpha]_D^{25}$ −59° (*c* 1, $CHCl_3$); ν_{max} 3700–3500 (OH), 1551 and 1377 (NO_2), 1090 and 1069 cm^{-1} (C–O). MS data: *m/z* 333 (10%), 332 (58), 243 (76), 199 (23), 185 (32), 141 (100), 122 (18), 113 (46), 100 (51), 85 (36), and 71 (50); HRMS: *m/z* 332.1313 (Obsd), *m/z* 332.1346 (Calcd for $C_{14}H_{22}NO_8$, $[M-CH_3]^+$). ^1H NMR data: δ 5.49 (d, 1 H, $J_{1,2}$ 5.1 Hz, H-1), 4.77 (ddd, 1 H, $J_{6,7}$ 3.3, J_{7,CH_2} 5.3 and 9.6 Hz, H-7), 4.65 (dd, 1 H, $J_{2,3}$ 2.5, $J_{3,4}$ 7.9 Hz, H-3), 4.45 (dd, 1 H, $J_{4,5}$ 1.8 Hz, H-4), 4.32 (dd, 1 H, H-2), 4.00 (ddd, 1 H, $J_{5,6}$ 9.2, $J_{6,OH}$ 9.4 Hz, H-6), 3.66 (dd, 1 H, H-5), 3.01 (d, 1 H, OH), 2.3–1.9 (m, 2 H, CH_2CH_3), 1.49, 1.45, 1.37, 1.32 (4 s, each 3 H, 4 CCH_3), and 1.02 (t, 3 H, CH_2CH_3); ^{13}C NMR data: δ 109.4, 108.9 [2 $C(Me)_2$], 96.1 (C-1), 89.3 (C-7), 70.4 (C-2,3), 70.3 (C-4), 69.8 (C-6), 67.3 (C-5), 25.8, 25.6, 24.7, 24.2 (4 CCH_3), 24.0 (CH_2CH_3), and 10.3 (CH_2CH_3).

Compound **5b** had: $[\alpha]_D^{25}$ −69° (*c* 1, $CHCl_3$); ν_{max} 3700–3500 (OH), 1549 and 1379 (NO_2), 1090 (C–O). MS data: *m/z* 347 (1%), 333 (22), 332 (100), 274 (10), 243 (40), 185 (23), 141 (61), 122 (42), 113 (69), 100 (91), 85 (47), and 71 (48); HRMS: *m/z* 347.1615 (Obsd), *m/z* 347.1580 (Calcd for $C_{15}H_{25}NO_8$, $[M]^+$). ^1H NMR data: δ 5.50 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 4.70 (ddd, 1 H, $J_{6,7}$ 2.8, J_{7,CH_2} 3.0 and 10.7 Hz, H-7), 4.65 (dd, 1 H, $J_{2,3}$ 2.5, $J_{3,4}$ 7.9 Hz, H-3), 4.41 (dd, 1 H, $J_{4,5}$ 1.8 Hz, H-4), 4.38 (ddd, 1 H, $J_{5,6}$ 8.9, $J_{6,OH}$ 4.2 Hz, H-6), 4.34 (dd, 1 H, H-2), 3.69 (dd, 1 H, H-5), 3.09 (d, 1 H, OH), 2.6–1.8 (m, 2 H, CH_2CH_3), 1.52, 1.46, 1.37, 1.33 (4 s, each 3 H, 4 CCH_3), and 1.02 (t, 3 H, CH_2CH_3); ^{13}C NMR data: δ 109.5, 108.7 [2 $C(Me)_2$], 96.2 (C-1), 90.2 (C-7), 70.5, 70.4 (C-2,3), 70.3 (C-4), 70.0 (C-6), 66.4 (C-5), 25.8, 25.7, 24.7, 24.3 (4 CCH_3), 19.9 (CH_2CH_3), and 10.4 (CH_2CH_3).

Oxazoline **6**.—To a stirred solution of **4a** (60 mg, 0.15 mmol) in CH_2Cl_2 (1.2 mL), cooled at 0°C, was added ethyl iminoacetate hydrochloride (25 mg, 0.20 mmol). After 9 h, the mixture was treated with cold water (3 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 × 3 mL). The organic layers were combined, dried ($MgSO_4$), and evaporated, to give the pure oxazoline **6** (52 mg, 82%); $[\alpha]_D^{25}$ −136° (*c* 1, $CHCl_3$); ν_{max} (C=N), 1089 and 1072 cm^{-1} (C–O). MS data: *m/z* 415 (2%), 414 (3), 400 (11), 354 (4), 254 (9), 208 (10), 171 (10), 149 (13), 112 (21), 103 (100), and 75 (86); HRMS: *m/z* 415.2198 (Obsd), *m/z* 415.2206 (Calcd for $C_{20}H_{33}NO_8$, $[M]^+$. ^1H NMR data: δ 4.95 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 4.62 (dd, 1 H, $J_{2,3}$ 2.5, $J_{3,4}$ 7.8 Hz, H-3), 4.62 (dd, 1 H, $J_{5,6}$ 8.8 $J_{6,7}$ 5.0 Hz, H-6), 4.39 (d, 1 H, $J_{7,8}$ 4.0 Hz, H-8), 4.33 (dd, 1 H, $J_{4,5}$ 1.6 Hz, H-4), 4.32 (dd, 1 H, H-2), 4.17 (ddq, 1 H, $^5J_{7,Me}$ 1.3 Hz, H-7), 3.8–3.5 (m, 4 H, 2 OCH_2CH_3), 3.56 (dd, 1 H, H-5), 1.98 (d, 3

H, CH_3C=N), 1.44, 1.36, 1.31 (3 s, 12 H, 4 CCH_3), 1.21 and 1.18 (2 t, each 3 H, 2 OCH_2CH_3); ^{13}C NMR data: 165.1 (C=N), 109.3, 108.4 [2 $C(Me)_2$], 102.7 (C-8), 96.1 (C-1), 77.0 (C-6), 71.5 (C-7), 70.5 (C-2,3), 70.4 (C-4), 67.9 (C-5), 63.0, 62.8 (2 OCH_2CH_3), 25.9, 24.8, 24.7, 24.3 (4 CCH_3), 15.1, 15.0 (2 OCH_2CH_3), and 13.9 (CH_3C=N).

Crystal data for **3a**.—Crystals of $C_{18}H_{31}NO_{10}$ (M_r 421.45), monoclinic, space group $P2_1$ with $a = 11.980(1)$, $b = 9.178(1)$, $c = 10.891(1)$ Å, $\alpha = 112.57(1)°$, $V = 1105.8(2)$ Å^3, $Z = 2$, $D_c = 1.27$ g.cm^{-3}, μ(Mo$K\alpha$) = 0.097 mm^{-1}, and $F(000) = 452$. Unit-cell parameters were obtained from the least-squares refinement of values of 25 reflections ($2 < \theta < 14$), using an Enraf–Nonius CAD-4 diffractometer. Mo$K\alpha$ radiation, $\lambda = 0.71069$ Å (graphite monochromator). A total of 3357 reflections were scanned ($0 \le h \le 11$, $0 \le k \le 8$, $-10 \le l \le 10$), and measured in the $2\theta < 40°$ range, $\omega - 2\theta$ mode. Two standard reflections, monitored every 100 reflections, showed statistical fluctuations; 2584 observed reflections [$I \ge 2\sigma(I_0)$] were used for structure determination. Corrections were made for Lorentz and polarization factors; absorption and extinction were ignored. The structure was solved by direct methods using the MULTAN-80 programm[12] and Fourier synthesis. F was refined by full-matrix least squares. A difference Fourier synthesis up to $\sin\theta/\lambda = 0.48$ Å^{-1} revealed the H atoms. Further refinement of F with non-H atoms isotropically produced convergence with $R = 0.035$, $R_w = 0.035$ [$W^{-1} = \sigma^2(F)$]. The thermal parameters assigned to H atoms were equal to those of bonded atoms. A final difference Fourier synthesis showed $\Delta\rho = \pm 0.25$ eÅ^{-3}. Maximum least-squares shift to error for non-H atoms was 0.03 excepting some temperature factors for terminal C-811 and C-821. The XRAY-70 system[13] of computer programs was used. Atomic scattering factors were obtained from International Tables for X-Ray Crystallography[14].

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