Synthesis and Utility of 2-(Benzoyloxyimino)-2-deoxy-α-D-*lyxo*-hexopyranosyl Bromide as a Novel α-D-Talosaminide Building Block

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A novel α-D-talosaminyl donor, 2-(benzoyloxyimino)-2-deoxy-α-D-*lyxo*-hexopyranosyl bromide has been synthesized in a total yield of 32% over 6 steps from D-galactose. The utility of the donor was evaluated for the elaboration of α-D-TalNAc-(1→6)-α-D-Gal, α-D-TalNAc-(1→6)-α-D-Glc, and α-D-TalNAc-(1→3)-L-serine derivatives by a simple 3-step sequence, comprising α-selective glycosylation of appropriately protected acceptors of D-galactose, D-glucose, and L-serine, *talo*-selective hydroboration of the oxyimino function to an amino group, and *N*-acetylation.

Key words 2-ulose oxime; TalNAc building block; α-D-talosaminide; glycosylation; hydroboration

2-Amino-2-deoxy-D-talose (**1**, D-talosamine) has been found as a constituent of ovine[1] and bovine[2] cartilage, while 2-amino-2,6-dideoxy-L-talose (**2**, pneumosamine) is a component of the capsular polysaccharide from *Streptococcus pneumoniae* type **5**.[3] The availability of amino sugars from natural sources is limited, and hence, considerable efforts have been made to achieve synthetic access to **1** and **2**,[4] for structural studies on natural talosamine-containing oligosaccharides.

In our continuing studies to develop a synthetic vaccine based on the bacterial capsular polysaccharides[5] and lipopolysaccharides,[6] we required a practical synthetic method of *N*-acetyl-D-talosamine (D-TalNAc) for the construction of antigenic oligosaccharides, as well as chemically modified forms, elicited from the pneumococcal capsular polysaccharides.

The usual access to D-talosamine derivatives utilizes Kuhn's amino nitrile procedure,[7] a configurational inversion of 2-amino-2-deoxy-D-idose at C-3,[8] and a reduction of 2-(oxyimino)-2-deoxyglycosides with $LiBH_4$–Me_3SiCl.[9] However, neither of the former two approaches meets practical preparative criteria, inasmuch as they entail very low stereoselectivity[7] or multistep transformations from D-galactose.[8] The last approach, *i.e.*, the oxyiminoglycosyl procedure, appears to be most promising with respect to facility and stereoselectivity,[9] but the accessibility of the intermediary α-D-oxyiminoglycosides is rather poor, requiring Lemieux's nitrosoglycal method[10] or Stevens' method[11] *via* 2-ulose intermediates for the preparation of even simple alkyl 2-deoxy-2-(methoxyimino)-α-D-*lyxo*-hexopyranosides.

We here disclose a general, straightforward methodology using a versatile α-D-TalNAc donor, namely 2-(benzoyloxyimino)-2-deoxy-α-D-*lyxo*-hexopyranosyl bromide (**7**), which allows glycosylation of some glycosyl acceptors and subsequent reduction of the 2-benzoyloxyimino function to a 2-amino group, yielding α-D-TalNAc-containing oligosaccharides in a stereoselective fashion.

Results and Discussion

Preparations of 2-(Benzoyloxyimino)-2-deoxy-glycosyl Bromide (7) and Diethyldithiocarbamate (8) Based on our previous studies,[12] 2-(benzoyloxyimino)-2-deoxy-α-D-*erythro*-hexopyranosyl bromide can be utilized for practical assembly of oligosaccharides containing *N*-acetyl-β-D-mannosamine[13] and its α-D-analogue[5] associated with *Streptococcus pneumoniae* type 19F capsular polysaccharide. Accordingly, an α-D-TalNAc sugar unit may be formed stereoselectively from 2-(benzoyloxyimino)-2-deoxy-glycosyl bromide with α-D-*lyxo*-configuration, which should be readily accessible by a simple, 3-step conversion of a 2-hydroxy-D-galactal **4**. At first, the galactal **4** was prepared in 70% yield from 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide (**3**) by the use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in *N*,*N*-dimethylformamide (DMF). Oximation of **4** with excess hydroxylamine hydrochloride in pyridine afforded the 1,5-anhydro-D-tagatose oxime **5** in 73% yield. Subsequent *O*-benzoylation of **5** with benzoyl chloride in pyridine gave the *O*-benzoylated oxime **6** in 81% yield. The concluding photobromination with *N*-bromosuccinimide (NBS) proceeded smoothly to furnish the desired 2-(benzoyloxyimino)-2-deoxy-α-D-*lyxo*-hexopyranosyl bromide **7** in 90% yield. Conventional dithiocarbamoylation of **7** with sodium *N*,*N*-diethyldithiocarbamate readily gave an alternative TalNAc donor **8** in 84% yield. Both donors were stable, crystalline substances storable in a refrigerator for months without decomposition.

Syntheses of α-D-TalNAc-(1→6)-D-Gal (12a), α-D-TalNAc-(1→6)-D-Glc (12b), and α-D-TalNAc-(1→3)-L-serine (12c) Derivatives The utility of the donors **7** and **8** was first evaluated for stereoselective glycosylation of some glycosyl acceptors with a free hydroxyl group based on D-galactose (**9a**),[14] D-glucose (**9b**),[15] and L-serine (**9c**),[16] and then for stereoselective reduction of the 2-benzoyloxyimino function to a 2-amino group. The results of glycosylation of **9** with the donors **7** and **8** under several reaction conditions are summarized in Table 1.

Silver triflate (AgOTf)-promoted glycosylation of **9a** with the bromide **7** in CH_2Cl_2 afforded good α-selectivity (run 1, $\alpha:\beta=6:1$, 52% yield). Changing the solvent to CH_3CN or dioxane resulted in no superiority over CH_2Cl_2 (runs 2 and 3). Application of an insoluble silver catalyst such as Ag_2CO_3 resulted in only partial predominance of the β-anomer **11a** (run 4). Other acceptors (**9b** and **9c**) were similarly glycosylated with the bromide

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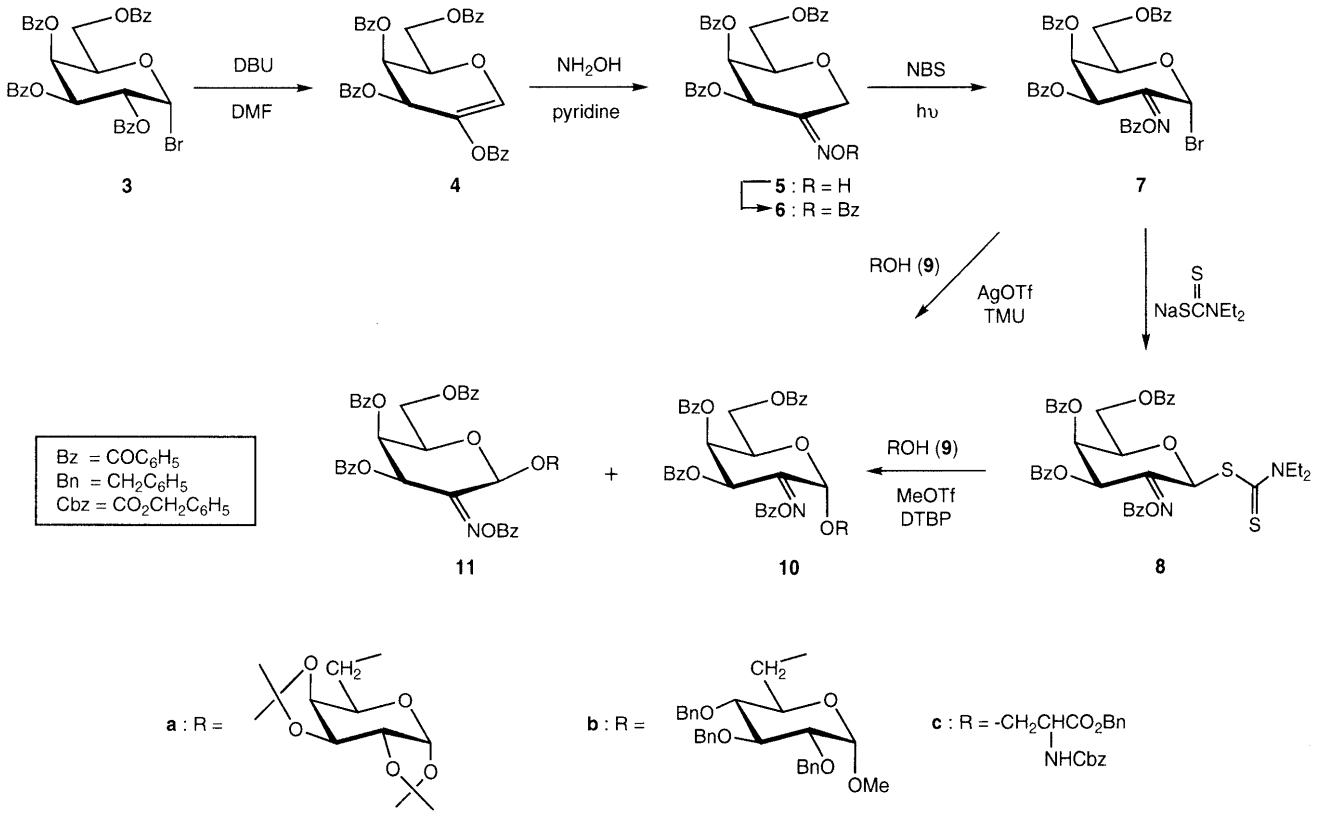

Chart 1

Table 1. Glycosylation of Alcohol Components (**9**) with Tri-*O*-benzoyl-2-(benzoyloxyimino)-2-deoxy-D-*lyxo*-hexopyranosyl Donors (**7** and **8**)

Run	Donor	Acceptor	Promoter	Solvent	Conditions		Products **10**:**11**[a]	Total yield (%)
					Temperature	Time (h)		
1	**7**	**9a**	AgOTf/TMU	CH_2Cl_2	r.t.	20	6:1	52
2	**7**	**9a**	AgOTf/TMU	CH_3CN	r.t.	20	3:2	27
3	**7**	**9a**	AgOTf/TMU	Dioxane	r.t.	20	2:1	10
4	**7**	**9a**	$AgCO_3/I_2$	CH_2Cl_2	r.t.	48	2:3	55
5	**7**	**9b**	AgOTf/TMU	CH_2Cl_2	r.t.	20	5:1	42
6	**7**	**9c**	AgOTf/TMU	CH_2Cl_2	r.t.	20	5:1[b]	59
7	**8**	**9c**	MeOTf/DTBP[c]	CH_2Cl_2	r.t.	2	2:1[b]	47

a) The **10**:**11** ratio was estimated by ^{1}H-NMR integration of the respective anomeric protons. *b*) The **10**:**11** ratio was determined from the isolated yields of the products. *c*) DTBP designates 2,6-di-*tert*-butylpyridine. r.t. = room temperature.

7, promoted by AgOTf/1,1,3,3-tetramethylurea (TMU), to give the α-anomers **10b** and **10c** in preference to the β-anomers (**11b** and **11c**) (runs 5 and 6). On the other hand, the use of glycosyl diethyldithiocarbamate **8** proved to afford less selectivity and efficiency than the bromide **7** (run 7).

The α-configuration of **10** was confirmed on the basis of the ^{1}H-NMR spectra, in which the signals of the anomeric protons (H-1′) invariably appeared at lower field (δ: 6.35, 6.35, and 6.23 for **10a**, **10b**, and **10c**, respectively), whereas the corresponding β-glycosides exclusively showed their anomeric proton signals at relatively higher field (δ: 5.97, 6.09, and 5.59 for **11a**, **11b**, and **11c**, respectively). Similar tendencies have been observed with respect to the anomeric chemical shifts of analogous compounds possessing a 2-benzoyloxyimino group.[17,18] In the ^{13}C-NMR spectra of **10** and **11**, the C-1′ signals appeared at δ: 91.87—92.35 (**10**) and 99.83 (**11c**), supporting the anomeric configurations described above.

Another key step for the construction of α-D-TalNAc is the stereocontrolled transformation of the benzoyloxyimino function into the *talo*-oriented acetamido group. We showed previously that the reduction of 2-(benzoyloxyimino)-α-D-glycosides by hydroboration is dependent on the kind of aglycons employed, yielding either α-D-mannosaminide[5] or α-D-glucosaminide.[17,19] Although the mechanism of the stereoselectivity remains to be resolved, the present stereochemical outcome is such that 2-(benzoyloxyimino)-2-deoxy-α-D-*erythro*-hexopyranosides with a simple alkyl or benzyl aglycon are transformed into α-D-glucosaminides,[17-19] and the analogues with a sterically hindered glycosyl aglycon[5] gave rise to α-D-mannosaminides. Accordingly, the reduction of the disaccharides **10a** and **10b** by hydroboration would be expected to form α-D-talosaminides (**12**) rather than α-D-galactosaminides (**13**).

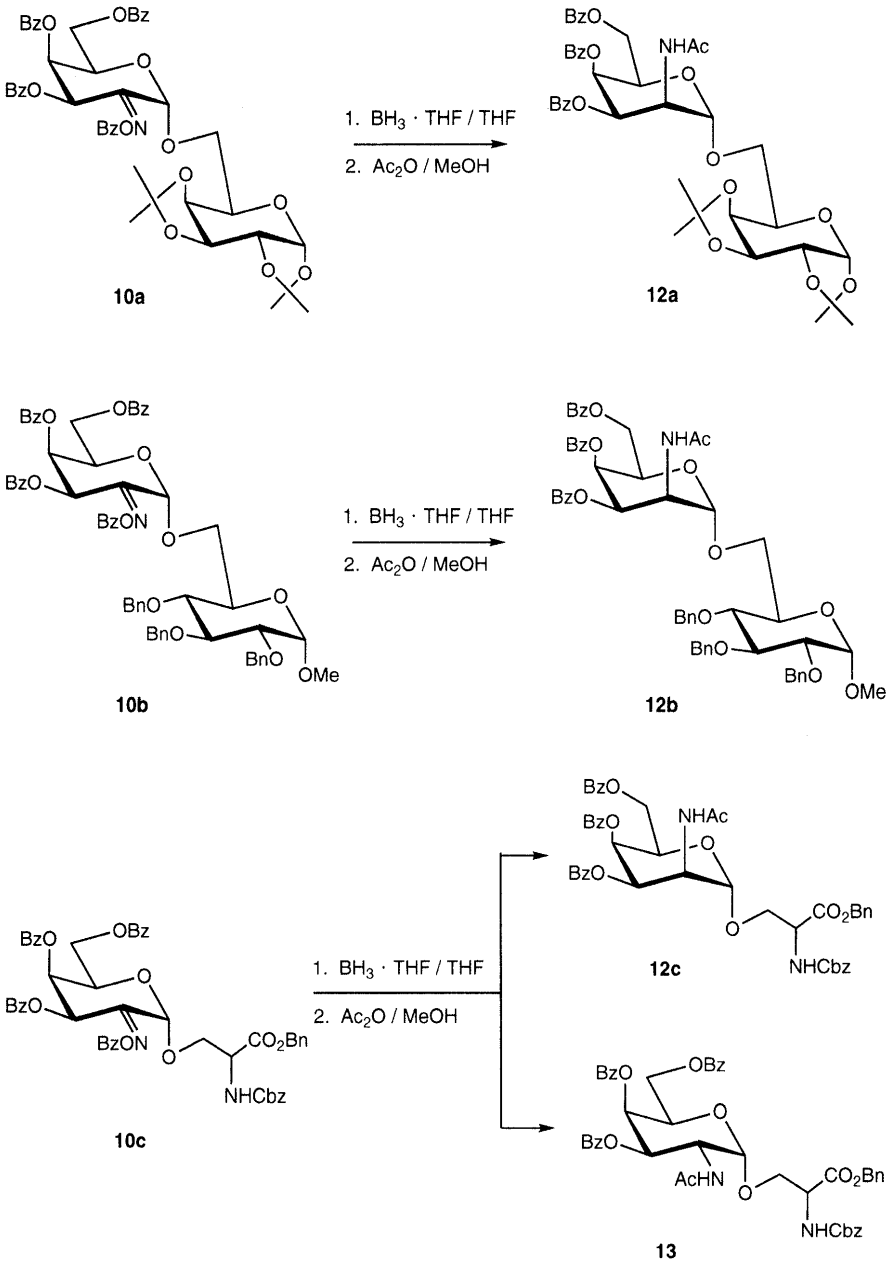

Chart 2

In fact, hydroboration of **10a** and **10b** with a twelve molar excess of borane tetrahydrofuran (THF) complex in THF followed by *N*-acetylation (Ac_2O/pyridine) led to the desired 2-acetamido-2-deoxy-α-D-talosaminides **12a** and **12b** in yields of around 40%. Although the reduction of **10**→**12** is still unsatisfactory with respect to the efficiency, the yields were improved by recycling the unreacted starting materials (31% and 51% recoveries of **10a** and **10b**, respectively); in this way, the overall yield for the conversion **10**→**12** amounted to 57% for **12a** and 60% for **12b** after one recycling process. On the other hand, the L-serine glycoside **10c** was reduced to form a mixture of α-D-talosaminide **12c** and α-D-galactosaminide **13** in a ratio of 4:3.

At this stage we have no decisive evidence that the *talo* selectivity is elicited by the stereochemical demand of the sugar aglycons of **10a** and **10b** as compared with the amino acid aglycon of **10c**. Hence, a variety of 2-(benzoyloxyimino)-2-deoxy-α-D-glycosides of type **10** having various kinds of aglycons are being prepared for the elucidation of the reduction mechanism of the 2-acyloxyimino group. The results will be reported elsewhere.

The α-D-*talo*-configuration of the amino sugar moiety of **12** was determined from the coupling constants $J_{1',2'}$ and $J_{2',3'}$ of *ca.* 2.0—3.0 and 4.0—5.0 Hz, which are in good agreement with those reported for α-D-TalNAc derivatives.[9] In contrast, the α-D-*galacto*-configuration of **13** was evidenced by the $J_{1',2'}$ and $J_{2',3'}$ values of 4.0 and 11.0 Hz, respectively.

In summation, a practical, straightforward reaction sequence has been developed for generating a useful α-D-TalNAc donor, 2-(benzoyloxyimino)-2-deoxy-α-D-*lyxo*-hexopyranosyl bromide **7**, in an overall yield of 32% for 6 steps from D-galactose. Its utility for assembly of α-D-TalNAc-containing oligosaccharides was demonstrated by α-glycosidation of **7**, followed by reduction of

the oxyimino function in a stereoselective manner. This approach will be applied to the synthesis of a variety of other α-D-TalNAc-containing oligosaccharides of biological significance.

Experimental

Melting points are uncorrected values obtained on a Yanagimoto micro melting point apparatus or Yamato MP-1 apparatus. Spectral measurements-$[\alpha]_D$: Jasco DIP-150; ^{1}H- and ^{13}C-NMR: Varian VXR-300 or XL-400; MS: JMS D-100 instrument. FAB-MS were measured with a PEG 400 or *meta*-nitrobenzoic acid (*m*-NBA) matrix in acetone. TLC: Merck Silica Gel F_{254} plastic sheets were used to monitor the reactions and to ascertain the purity of the products; solvent systems are given individually and were the same for TLC and column chromatography. Spots were visualized by UV light (254 nm) or by charring with 10% aqueous H_2SO_4. Column chromatography: Merck Silica gel 60 (70—230 mesh).

1,5-Anhydro-2,3,4,6-tetra-*O*-benzoyl-D-*lyxo*-hex-1-enitol (4) 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.40 ml, 2.7 mmol) was added dropwise to an ice-cooled stirred solution of 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide[20] (**3**) (1.0 g, 1.5 mmol) in DMF (1.0 ml). The mixture was left standing at room temperature for 3 h and then poured into ice-water (4 ml). The precipitates were collected, dried (P_2O_5), and purified by elution from a silica-gel column with MeC_6H_5–AcOEt (10 : 1). The major fraction was concentrated and crystallized from MeOH–H_2O to afford 610 mg (70%) of **4** as colorless crystals, mp 62—64 °C, $[\alpha]_D^{25}$ +36.6° (c=1.0, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.61 (1H, dd, H-6a), 4.84 (1H, ddd, H-5), 4.91 (1H, dd, H-6b), 6.05 (1H, dd, H-4), 6.39 (1H, d, H-3), 6.96 (1H, s, H-1), 7.24—8.15 (aromatic H); $J_{3,4}$=5.0, $J_{4,5}$=2.0, $J_{5,6a}$=4.0, $J_{5,6b}$=7.5, $J_{6a,6b}$=11.0 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 62.12 (C-6), 64.72 (C-3), 65.05 (C-4), 73.59 (C-5), 127.59 (C-2), 128.3—133.5 (C_6H_5), 139.49 (C-1), 165.23, 165.32, 165.59, 166.19 ($\underline{C}OC_6H_5$). FAB-MS *m/z*: 579 $(M+H)^+$, 601 $(M+Na+H)^+$. *Anal.* Calcd for $C_{34}H_{26}O_9$: C, 70.58; H, 4.53. Found: C, 70.56; H, 4.48.

Oxime of 1,5-Anhydro-3,4,6-tri-*O*-benzoyl-D-tagatose (5) A mixture of the galactal **4** (116 mg, 0.20 mmol) and hydroxylamine hydrochloride (76 mg, 1.1 mol) in dry pyridine (1.4 ml) was stirred at 40 °C for 20 h. After concentration of the mixture *in vacuo*, the residue was diluted with CH_2Cl_2 (15 ml) and washed with H_2O (15 ml). The organic phase was consecutively washed with 1 M HCl (15 ml), H_2O (15 ml), 5% aqueous $NaHCO_3$ (15 ml), and H_2O (3×15 ml). Drying (Na_2SO_4) and concentration *in vacuo* gave a residue, which was purified by elution from a silica-gel column with MeC_6H_5–AcOEt (10 : 1) to give 70.9 mg (73%) of **5** as a colorless syrup, $[\alpha]_D^{26}$ −11.9° (c=1.0, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.07 (1H, d, H_R-1), 4.33 (1H, m, H-5), 4.40 (1H, m, H-6a), 4.61 (1H, m, H-6b), 5.35 (1H, d, H_S-1), 6.01 (1H, dd, H-4), 6.03 (1H, d, H-3), 7.12—8.14 (aromatic H), 8.23 (1H, s, NOH); $J_{1,1}$=15.0, $J_{3,4}$=3.5, $J_{4,5}$=1.0, $J_{5,6a}$=4.5, $J_{5,6b}$=6.0, $J_{6a,6b}$=10.0 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 60.89 (C-1), 62.41 (C-6), 69.22 (C-3), 69.48 (C-4), 74.69 (C-5), 128.2—133.6 (C_6H_5), 149.40 (C-2), 165.05, 165.71, 166.12 ($\underline{C}OC_6H_5$). FAB-MS *m/z*: 490 $(M)^+$, 512 $(M+Na-H)^+$.

***O*-Benzoyloxime of 1,5-Anhydro-3,4,6-tri-*O*-benzoyl-D-tagatose (6)** Benzoyl chloride (1.2 ml, 10.2 mmol) was added dropwise to an ice-cooled, stirred solution of the oxime **5** (500 mg, 1.02 mmol) in dry pyridine (6.0 ml). The mixture was stirred at ambient temperature for 4 h, poured into ice-H_2O (100 ml), and extracted with CH_2Cl_2 (40 ml). The organic phase was washed with 1 M HCl (40 ml), 5% aqueous $NaHCO_3$ (40 ml), and H_2O (3×40 ml). Drying (Na_2SO_4) and concentration *in vacuo* gave a residue, which was eluted from a silica-gel column with MeC_6H_5–AcOEt (10 : 1). Evaporation of the eluate containing **6** (TLC) and trituration of the residue with Et_2O–pentane provided 490 mg (81%) of **6** as a colorless powder, mp 67—72 °C, $[\alpha]_D^{25}$ −8.8° (c=1.0, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.37 (1H, d, H_R-1), 4.39 (1H, dd, H-6a), 4.48 (1H, m, H-5), 4.69 (1H, dd, H-6b), 5.48 (1H, d, H_S-1), 6.14 (1H, dd, H-4), 6.23 (1H, d, H-3), 7.2—8.2 (aromatic H); $J_{1,1}$=15.0, $J_{3,4}$=3.5, $J_{4,5}$=1.0, $J_{5,6a}$=5.0, $J_{5,6b}$=6.5, $J_{6a,6b}$=10.0 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 62.10 (C-6), 62.34 (C-1), 69.26 (C-3), 69.49 (C-4), 74.98 (C-5), 128—134 (C_6H_5), 158.30 (C-2), 165.0, 165.5, 166.0 ($\underline{C}OC_6H_5$). FAB-MS *m/z*: 594 $(M)^+$, 616 $(M+Na-H)^+$. *Anal.* Calcd for $C_{34}H_{27}NO_9$: C, 68.80; H, 4.59; N, 2.36. Found: C, 68.61; H, 4.32; N, 2.64.

3,4,6-Tri-*O*-benzoyl-2-(benzoyloxyimino)-2-deoxy-α-D-*lyxo*-hexopyranosyl Bromide (7) A mixture of the benzoyloxime **6** (276 mg, 0.47 mmol) and *N*-bromosuccinimide (126 mg, 0.71 mmol) in dry CCl_4 (10 ml) was irradiated with a 250 W tungsten lamp such that gentle reflux was effected. After 30 min the resulting yellowish solution was cooled (0 °C), the precipitate (succinimide) was filtered off, and the filtrate was evaporated to dryness. The residue was partitioned between CH_2Cl_2 (30 ml) and H_2O (30 ml). The organic phase was washed with H_2O (2×25 ml), dried (Na_2SO_4), and concentrated *in vacuo* to give a syrup. Crystallization from Et_2O–pentane furnished 285 mg (90%) of **7** as a pale yellow powder, mp 68—72 °C, $[\alpha]_D^{20}$ +239° (c=1.2, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.48 (1H, dd, H-6a), 4.65 (1H, dd, H-6b), 4.96 (1H, ddd, H-5), 6.20 (1H, dd, H-4), 6.61 (1H, d, H-3), 7.72 (1H, s, H-1), 7.2—8.2 (aromatic H); $J_{3,4}$=3.5, $J_{4,5}$=1.0, $J_{5,6a}$=6.5, $J_{5,6b}$=7.0, $J_{6a,6b}$=12.0 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 61.57 (C-6), 66.42 (C-3), 68.22 (C-4), 72.17 (C-5), 74.03 (C-1), 128—134 (C_6H_5), 155.0 (C-2), 165.0, 165.5, 166.0 ($\underline{C}OC_6H_5$). FAB-MS *m/z*: 672 $(M)^+$. *Anal.* Calcd for $C_{34}H_{26}BrNO_9$: C, 60.71; H, 3.87; N, 2.08. Found: C, 61.13; H, 4.08; N, 2.15.

3,4,6-Tri-*O*-benzoyl-2-(benzoyloxyimino)-2-deoxy-β-D-*lyxo*-hexopyranosyl *N*,*N*-Diethyldithiocarbamate (8) A mixture of sodium *N*,*N*-diethyldithiocarbamate (450 mg, 2.0 mmol) and molecular sieves (3A, 1.0 g) in dry acetone (2.0 ml) was stirred at room temperature for 1 h. 2-(Benzoyloxyimino)-2-deoxyglycosyl bromide **7** (1.33 g, 2.0 mmol) was then added, and the mixture was further stirred for 0.5 h, filtered through a pad of Celite, and concentrated to dryness. The residue was diluted with CH_2Cl_2 (30 ml) and washed with H_2O (3×10 ml). Drying and concentration to dryness gave a syrup, which was eluted from a silica-gel column was MeC_6H_5–AcOEt (10 : 1). The major fraction was concentrated and crystallized from Et_2O–pentane to afford 1.24 g (84%) of **8** as colorless crystals, mp 165—169 °C, $[\alpha]_D^{25}$ −15.5° (c=0.83, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.18, 1.25 (3H each, t, $CH_2\underline{C}H_3$), 3.64, 3.74 (2H, q, $C\underline{H}_2CH_3$), 3.98, 4.05 (2H, q, $C\underline{H}_2CH_3$), 4.68 (1H, dd, H-6a), 4.85 (1H, dd, H-5), 4.87 (1H, dd, H-6b), 6.24 (1H, dd, H-4), 6.54 (1H, d, H-3); $J_{3,4}$=4.0, $J_{4,5}$=5.0, $J_{5,6a}$=3.0, $J_{5,6b}$=7.0, $J_{6a,6b}$=7.5 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 11.38, 12.62 (2×$CH_2\underline{C}H_3$), 47.08, 50.73 (2×$\underline{C}H_2CH_3$), 62.08 (C-6), 67.88 (C-4), 68.17 (C-3), 74.15 (C-5), 81.65 (C-1), 158.35 (C-2), 190.46 (C=S). FAB-MS *m/z*: 741 $(M+H)^+$, 763 $(M+Na)^+$. *Anal.* Calcd for $C_{39}H_{36}N_2O_9S_2$: C, 63.23; H, 4.90; N, 3.78. Found: C, 62.91; H, 4.66; N, 3.94.

6-*O*-[3,4,6-Tri-*O*-benzoyl-2-(benzoyloxyimino)-2-deoxy-α-D-*lyxo*-hexopyranosyl]-1,2 : 3,4-di-*O*-isopropylidene-α-D-galactopyranose (10a) 1,1,3,3-Tetramethylurea (TMU) (0.1 ml, 0.8 mmol) was added to a mixture of 1,2 : 3,4-di-*O*-isopropylidene-α-D-galactopyranose **9a**[14] (135 mg, 0.52 mmol) AgOTf (134 mg, 0.52 mmol), and the glycosyl bromide **7** (270 mg, 0.4 mmol) in dry CH_2Cl_2 (4 ml), containing powdered molecular sieves (3A, 200 mg). The mixture was stirred in the dark at room temperature for 20 h, then diluted with CH_2Cl_2 (30 ml), and filtered through a pad of Celite. The filtrate was washed successively with 5% aqueous $NaHCO_3$ (30 ml) and H_2O (3×30 ml), then dried (Na_2SO_4), and the solvent was removed *in vacuo* to give a residue, which was eluted from a silica-gel column with MeC_6H_5–AcOEt (5 : 1). The major fraction was concentrated to provide 177 mg (52%) of **10a** as a yellowish syrup, slightly contaminated with the corresponding β-anomer **11a** (**10a** : **11a**=6 : 1, estimated by ^{1}H-NMR), $[\alpha]_D^{18}$ +10.5° (c=1.0, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.20, 1.29, 1.34, 1.56 (3H each, s, 2×CMe_2), 4.00 (2H, dd, H-6a, 6b), 4.09 (1H, ddd, H-5), 4.25 (1H, dd, H-4), 4.32 (1H, dd, H-2), 4.40 (1H, dd, H-6′a), 4.60 (1H, dd, H-3), 4.63 (1H, dd, H-6′b), 4.96 (1H, ddd, H-5′), 5.53 (1H, d, H-1), 5.97 (1H, s, β-H-1′), 6.15 (1H, dd, H-4′), 6.35 (1H, s, α-H-1′), 6.41 (1H, d, H-3′ of the β-anomer), 6.44 (1H, d, H-3′ of the α-anomer), 7.2—8.2 (aromatic H); $J_{1,2}$=5.0, $J_{2,3}$=2.5, $J_{3,4}$=8.0, $J_{4,5}$=2.0, $J_{5,6a}$=$J_{5,6b}$=6.0, $J_{6a,6b}$=8.0, $J_{3',4'}$=3.0, $J_{4',5'}$=1.0, $J_{5',6'a}$=$J_{5',6'b}$=6.5, $J_{6'a,6'b}$=11.0 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 24.31, 24.86, 25.88, 26.11 (4×CH_3), 62.27 (C-6′), 66.59 (C-5), 67.60 (C-3′), 67.70 (C-4′), 67.87 (C-5′), 67.93 (C-6), 70.46 (C-2), 70.65 (C-3), 70.94 (C-4), 91.87 (C-1′), 96.32 (C-1), 108.80, 109.42 (2×$\underline{C}CH_3$), 128.3—133.5 (C_6H_5), 156.26 (C-2′), 162.64, 165.02, 165.82, 165.94 (4×$\underline{C}OC_6H_5$). FAB-MS *m/z*: 874 $(M+H)^+$, 957 $(M+DEA+H)^+$.

Methyl 6-*O*-[3,4,6-Tri-*O*-benzoyl-2-(benzoyloxyimino)-2-deoxy-α-D-*lyxo*-hexopyranosyl]-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (10b) Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**9b**)[15] (72.5 mg, 0.13 mmol) was glycosylated with the glycosyl bromide **7** (67.2 mg, 0.10 mmol) as described for **10a**. After general work-up the product was purified by column chromatography on silica gel with MeC_6H_5–AcOEt (10 : 1) to

afford 44.3 mg (42%) of a 5:1 mixture of **10b** and **11b** as a yellowish syrup, $[\alpha]_D^{22}$ +91.1° (c=0.8, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) of **10b** δ: 3.31 (3H, s, CH_3), 3.32 (1H, dd, H-2), 3.40 (3H, s, CH_3 of **11b**), 3.42 (1H, dd, H-4), 3.77 (1H, br d, H-5), *ca.* 3.8 (1H, m, H-3), 3.91 (1H, dd, H-6a), 3.94 (1H, dd, H-6b), 4.37 (1H, d, H-1), 4.43 (1H, dd, H-6'a), 4.55 (1H, dd, H-6'b), 4.6—5.0 (3 × PhC$\underline{H}_2$), 4.88 (1H, ddd, H-5'), 6.07 (1H, dd, H-4'), 6.09 (1H, s, H-1' of **11b**), 6.33 (1H, d, H-3'), 6.35 (1H, s, H-1'), 7.2—8.2 (aromatic H); $J_{1,2}$=3.5, $J_{2,3}=J_{3,4}=J_{4,5}=J_{5,6b}$=9.0, $J_{5,6a}$=4.5, $J_{6a,6b}$=10.0, $J_{3',4'}$=3.5, $J_{4',5'}$=1.0, $J_{5',6'a}=J_{5',6'b}$=5.0 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) of **10b** δ: 55.20 (OCH_3), 66.84 (C-6), 67.57 (C-3'), 67.82 (C-6'), 70.02 (C-5), 70.67 (C-4'), 63.24 (C-5'), 74.96, 75.53 (2 × Ph$\underline{C}H_2$), 77.24 (C-4), 80.21 (C-2), 81.91 (C-3), 91.95 (C-1'), 97.79 (C-4), 127—130, 134, 138 (C_6H_5), 157.2 (C-2'), 165—166 ($\underline{C}OC_6H_5$). FAB-MS m/z: 1055 $(M)^+$, 1079 $(M+Na+H)^+$.

***O*^{3}-[3,4,6-Tri-*O*-benzoyl-2-(benzoyloxyimino)-2-deoxy-α-D-*lyxo*-hexopyranosyl]-*N*-benzyloxycarbonyl-L-serine Benzyl Ester (10c)** Method A (Use of the Glycosyl Bromide **7**): *N*-Benzyloxycarbonyl-L-serine benzyl ester **9c**[16] (41.1 mg, 0.125 mmol) was glycosylated with the glycosyl bromide **7** (67.2 mg, 0.10 mmol) in dry CH_2Cl_2 (1 ml) as described for **10a**. After general work-up, the crude syrupy product was eluted from a silica-gel column with MeC_6H_5–AcOEt (5:1). A faster-eluting fraction was concentrated to afford 45.6 mg (50%) of **10c**, and a slower-eluting one gave 8.7 mg (9%) of **11c**, each as a colorless syrup. **10c**: $[\alpha]_D^{21}$ +65.2° (c=0.6, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.17, 4.28 (1H each, dd, H-3), 4.52—4.59 (2H, m, H-5', 6'), 4.69 (1H, m, H-2), 5.91 (1H, d, NH), 5.97 (1H, dd, H-4'), 6.18 (1H, d, H-3'), 6.23 (1H, s, H-1'); $J_{3',4'}$=3.5, $J_{4',5'}$=1.0, $J_{2,NH}$=7.5 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 54.44 (C-2), 62.33 (C-6'), 67.44 (C-3'), 69.91 (C-3), 70.25 (C-4'), 77.20 (C-5'), 92.35 (C-1'), 155.41 (C-2'), 165.7 (C-1). FAB-MS m/z: 921 $(M+H)^+$, 943 $(M+Na)^+$.

11c: $[\alpha]_D^{21}$ +29.5° (c=1.0, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 4.17, 4.26 (1H each, dd, H-3), 4.34 (1H, dd, H-6'a), 4.54 (1H, dd, H-6'b), 4.59 (1H, ddd, H-5'), 4.71 (1H, td, H-2), 5.11, 5.15, 5.22, 5.33 (1H each, d, CH_2Ph), 5.59 (1H, s, H-1'), 5.89 (1H, dd, H-4'), 5.93 (1H, d, NH), 6.07 (1H, d, H-3'); $J_{3',4'}$=3.0, $J_{4',5'}$=1.0, $J_{5',6'a}$=5.0, $J_{5',6'b}$=6.0, $J_{6'a,6'b}$=10.0, $J_{2,NH}$=8.0, $J_{2,3a}$=3.0, $J_{2,3b}$=4.0, $J_{3a,3b}$=10.0 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 54.48 (C-2), 62.17 (C-6'), 67.19, 67.86 ($\underline{C}H_2$Ph), 68.96 (C-5'), 69.77 (C-3), 70.47 (C-3'), 71.12 (C-4'), 99.83 (C-1'), 155.04 (C-2'), 165.55 (C-1). FAB-MS m/z: 921 $(M+H)^+$, 943 $(M+Na)^+$.

Method B (Use of the Glycosyl Carbamate **8**): Methyl triflate (34.4 μl, 0.3 mmol) and 2,6-di-*tert*-butylpyridine (DTBP) (13.6 μl, 60.7 μmol) were added to a stirred solution of the carbamate **8** (50 mg, 67.5 μmol) and the suitably protected L-serine **9c** (22.2 mg, 67.5 μmol) in dry CH_2Cl_2 (1 ml) with molecular sieves (3 A, 100 mg). The mixture was stirred at room temperature for 2 h. Triethylamine (2 μl, 9.68 μmol) was added to the mixture, which was then filtered through a pad of Celite. The filtrate was evaporated to dryness and the residue was eluted from a silica-gel column with MeC_6H_5–AcOEt (5:1) to give 20.3 mg (33%) of **10c** and 8.7 mg (14%) of **11c**.

6-*O*-(2-Acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-α-D-talopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (12a) A 1 M solution of BH_3·THF complex in THF (4.1 ml) was added dropwise to a solution of the disaccharide **10a** (174 mg, 0.204 mmol) in THF (4 ml) at −10 °C under an atmosphere of N_2. The mixture was stirred at this temperature for 0.5 h, and then allowed to warm to room temperature. Stirring was continued for a further 2 h, then excess reductant was quenched with MeOH (3 ml). *N*-Acetylation was effected by stirring the mixture with Ac_2O (1 ml) at ambient temperature for 1 h. The resulting mixture was passed through a basic resin (Amberlite IR-45), which was washed with MeOH. The eluate was concentrated *in vacuo* and the residue was purified by elution from a silica-gel column with $CHCl_3$–AcOEt (1:1). The major fractions were concentrated to give 64.9 mg (41%) of **12a** and 67.5 mg (39% recovery) of the unreacted starting material. **12a**: a colorless syrup, $[\alpha]_D^{21}$ +26.9° (c=1.1, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.31, 1.34, 1.39, 1.56 (3H each, s, 4 × CH_3), 1.86 (3H, s, $COCH_3$), 3.81 (1H, dd, H-6a), 3.89 (1H, dd, H-6b), 4.04 (1H, ddd, H-5), 4.28 (1H, dd, H-4), 4.31 (1H, dd, H-2), 4.36 (1H, dd, H-6'a), 4.51 (1H, dd, H-6'b), 4.62 (1H, dd, H-3), 4.69 (1H, dd, H-2'), 4.75 (1H, ddd, H-5'), 5.02 (1H, d, H-1'), 5.52 (1H, d, H-1), 5.69 (1H, dd, H-3'), 5.96 (1H, dd, H-4'), 6.51 (1H, d, NH); $J_{1,2}$=5.1, $J_{2,3}$=2.3, $J_{3,4}$=7.2, $J_{4,5}$=2.0, $J_{5,6a}=J_{5,6b}$=6.0, $J_{6a,6b}$=9.8, $J_{1',2'}$=3.0, $J_{2',NH}$=9.5, $J_{2',3'}$=5.0, $J_{3',4'}$=3.5, $J_{4',5'}$=1.0, $J_{5',6'a}=J_{5',6'b}$=6.5, $J_{6'a,6'b}$=11.0 Hz. FAB-MS m/z: 775 $(M+H)^+$, 798 $(M+Na)^+$.

Methyl 6-*O*-(2-Acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-α-D-talopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (12b) A solution of the disaccharide **10b** (44.2 mg, 0.042 mmol) in dry THF (0.84 ml) was treated with a 1 M solution of BH_3·THF complex in THF (0.84 ml) as described for **10a**→**12a**. Termination with MeOH (0.6 ml) and subsequent *N*-acetylation with Ac_2O (0.2 ml) followed by processing of the mixture as described for **12a** gave a syrup, which was eluted from a silica-gel column with $CHCl_3$–AcOEt (3:1). The major fractions were concentrated to give 16.5 mg (40%) of **12b** and 22.6 mg (51% recovery) of recovered **10b**. **12b**: A colorless syrup, $[\alpha]_D^{23}$ +73.9° (c=0.3, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.86 (3H, s, $COCH_3$), 3.40 (3H, s, OCH_3), 3.33—3.44 (2H, m, H-4, H-5), 3.45 (1H, dd, H-2), 3.72—3.85 (2H, m, H-3, H-6a), 3.98 (1H, dd, H-6b), 4.35 (1H, d, H-1), 4.62 (1H, dd, H-2'), 4.5—5.0 (3 × PhC$\underline{H}_2$), 4.88 (1H, ddd, H-5'), 5.00 (1H, d, H-1'), 5.60 (1H, dd, H-3'), 5.87 (1H, dd, H-4'), 6.47 (1H, d, NH); $J_{1,2}$=3.5, $J_{2,3}$=9.0, $J_{1',2'}$=2.5, $J_{2',NH}$=9.5, $J_{2',3'}$=5.0, $J_{3',4'}$=3.5, $J_{4',5'}$=1.0, $J_{5',6'a}=J_{5',6'b}$=5.0 Hz. FAB-MS m/z: 1002 $(M+Na)^+$.

***O*^{3}-(2-Acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-α-D-talopyranosyl)-*N*-benzyloxycarbonyl-L-serine Benzyl Ester (12c) and *O*-(2-Acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-α-D-galactopyranosyl)-*N*-benzyloxycarbonyl-L-serine Benzyl Ester (13)** A solution of the *O*-glycosyl-L-serine ester **10c** (92.0 mg, 0.10 mmol) in dry THF (1.3 ml) was treated with 1 M BH_3·THF complex (1.3 ml) as described for **12a**. After general work-up, purification on a silica-gel column with $CHCl_3$–AcOEt (2:1) provided 17.7 mg (21%) of **12c** and 12.7 mg (15%) of **13** as a colorless syrup. **12c**: $[\alpha]_D^{22}$ +66.5° (c=1.2, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.86 (3H, s, $COCH_3$), 4.03, 4.04 (1H each, dd, H-3), 4.26 (1H, dd, H-6'a), 4.42 (1H, ddd, H-5'), 4.56 (1H, ddd, H-2'), 4.58 (1H, dd, H-6'b), 4.63 (1H, ddd, H-2), 4.92 (1H, d, H-1'), 5.10, 5.24 (1H each, s, $C\underline{H}_2$Ph), 5.48 (1H, dd, H-3'), 5.83 (1H, dd, H-4'), 5.84 (1H, d, NH-2), 6.45 (1H, d, NH-2'); $J_{1',2'}$=2.0, $J_{2',3'}$=4.0, $J_{3',4'}$=3.0, $J_{4',5'}$=1.0, $J_{5',6'a}$=5.0, $J_{5',6'b}$=7.5, $J_{2',NH}$=9.0, $J_{2,3a}$=3.50, $J_{2,3b}$=5.0, $J_{2,NH}$=8.5 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 23.21 ($CO\underline{C}H_3$), 48.72 (C-2'), 54.39 (C-2), 62.59 (C-6'), 65.50 (C-3'), 67.16, 67.81 (4 × CH_2Ph), 67.29 (C-5'), 68.33 (C-4'), 69.24 (C-3), 100.47 (C-1'), 164.67, 164.81, 165.99, 169.48, 169.52 (5 × C=O). FAB-MS m/z: 845 $(M)^+$, 867 $(M+Na)^+$.

13: $[\alpha]_D^{22}$ +42.3° (c=0.6, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.81 (3H, s, $COCH_3$), 3.98, 4.06 (1H each, dd, H-3), 4.28 (1H, dd, H-6'a), 4.36 (1H, ddd, H-5'), 4.51 (1H, dd, H-6'b), 4.64 (1H, ddd, H-2), 4.70, 5.12 (1H each, s, C$\underline{H}_2$Ph), 4.85 (1H, ddd, H-2'), 4.98 (1H, d, H-1'), 5.42 (1H, dd, H-3'), 5.77 (1H, d, NH-2), 5.78 (1H, d, NH-2'), 5.81 (1H, dd, H-4'); $J_{1',2'}$=4.0, $J_{2',3'}$=11.0, $J_{3',4'}$=3.0, $J_{4',5'}$=1.0, $J_{5',6'a}$=6.0, $J_{5',6'b}$=6.5, $J_{6'a,6'b}$=10.5, $J_{2',NH}$=9.0, $J_{2,3a}$=3.0, $J_{2,3b}$=3.5, $J_{2,NH}$=8.0 Hz. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 22.13 ($CO\underline{C}H_3$), 48.22 (C-2'), 54.48 (C-2), 62.59 (C-6'), 65.41, 67.33, 67.75 (4 × CH_2Ph), 67.75 (C-5'), 68.19 (C-4'), 69.13 (C-3'), 69.49 (C-3), 99.15 (C-1'), 165.56, 165.99, 166.37, 170.14 (5 × C=O). FAB-MS m/z: 845 $(M)^+$, 867 $(M+Na)^+$.

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