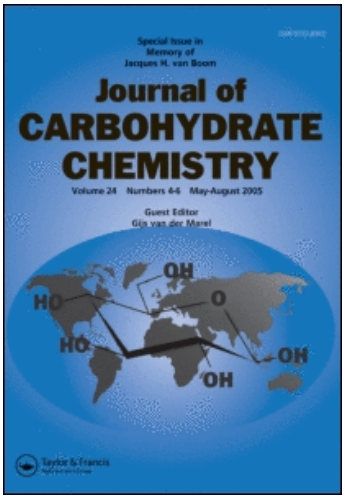

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Synthesis of *O*-[4,6-Di-*O*-Acetyl-4-*O*-(2,3,4,6-Tetra-*O*-Acetyl-β-D-Galactopyranosyl)-2-Deoxy-2-Hydroxyimino-D-Arabino-Hexopyranosyl]-*N*-Benzyloxycarbonyl-L-Serine Methyl Esters And Their Transformations

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SYNTHESIS OF *O*-[4,6-DI-*O*-ACETYL-4-*O*-(2,3,4,6-TETRA-*O*-ACETYL-β-D-GALACTOPYRANOSYL)-2-DEOXY-2-HYDROXYIMINO-D-ARABINO-HEXOPYRANOSYL]-*N*-BENZYLOXYCARBONYL-L-SERINE METHYL ESTERS AND THEIR TRANSFORMATIONS[1]

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ABSTRACT

3,6-Di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-deoxy-2-hydroxyimino-α- and -β-D-*arabino*-hexopyranosides of *N*-benzyloxycarbonyl-L-serine methyl ester as well as of ethanol have been synthesised from D-lactal hexaacetate via nitrosyl chloride, followed by condensation with L-serine derivatives and ethanol, respectively. The compounds of L-serine thus obtained were modified at C-2 and C-3 to afford L-serine derivatives attached to disaccharides containing terminal α-D-*gluco*-, 2-acetamido-α-D-*gluco*-, β-D-*manno*, 2-acetamido-β-D-*manno*-pyranosyl, 3-azido-2-hydroxyimino-α-D-*arabino*-, and α-D-*ribo*-hexopyranosyl residues.

INTRODUCTION

Previously we have reported on the synthesis, via the nitroso chloride procedure,[2,3] of the *O*-glycosyl derivatives of some hydroxy-L-α-amino acids from *O*-acetyl-2-deoxy-2-nitroso-α-D-*gluco*-,[4] α-D-*galacto*-,[5] and β-D-arabinopyranosyl chlorides.[6]

Following that route, it was the purpose of this endeavour to synthesise compounds containing disaccharides linked to L-serine

starting from D-lactal hexaacetate. Lactose was chosen as the starting reagent owing to its accessibility, and to its occurrence. In addition the *N*-acetyllactosamine residue is a building unit of the oligosaccharide portion of many *O*-linked glycoproteins.[5]

The synthesis of the lactosamine, L-serine and L-threonine glycosides have been previously described.[6] The saccharide residue was also obtained from D-lactal hexaacetate, but in a different way.[6] The method adopted here is interesting inasmuch as it can be employed for the preparation of *O*-glycosyl derivatives in which the first sugar residue can be modified at C-2 and C-3. This enables preparation of derivatives of the aforementioned amino acids linked to new oligosaccharide units, because as it has been shown, the hydroxyimino derivatives of the sugars[2,3,9-15] are very useful for the preparation of a wide range of new and important mono-[2,3,9-12] and oligosaccharide[13-15] structures.

The corresponding glycosides of ethanol have also been synthesised because inspection of their ^{1}H NMR spectra enabled identification of some signals in the spectra of L-serine derivatives. Furthermore we wanted to prove whether the differences in spatial structure of the compounds used as aglycons have an influence on the stereospecificity of the glycosidation.

RESULTS AND DISCUSSION

The methyl ester of *O*-[3,6-di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-2-deoxy-2-hydroxyimino-β-D-*arabino*-hexopyranosyl]-*N*-benzyloxycarbonyl-L-serine (3) and its α-anomer (4) were obtained by condensation of chloride (1) with the L-serine derivative (2) in *N,N*-dimethylformamide in the presence of $CaSO_4$ at ~20 °C. The overall yield was ~80%. In the absence of $CaSO_4$ as the water binding agent, 3,6-di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-deoxy-2-hydroxyimino-D-*arabino*-hexopyranose (5, ~10%) was obtained along with 3 and 4. Again, the reaction of 1 with ethanol in the same solvent, both in the presence and absence of $CaSO_4$, afforded only the corresponding glycosides 6 and 7. In this case, as with the reactions of monosaccharide chlorides with hydroxy-L-α-amino acids,[4-6] the product with a free OH group at C-1 was missing. This indicates that 1 reacts

less readily with compounds of more branched structures than do the corresponding monosaccharide chlorides.

Reaction on 1 with both the L-serine derivative and with ethanol is not stereospecific and results in a mixture of α and β anomers (α/β=2:1). A similar lack of stereospecifity of the glycosidation reaction has been noted previously.[4-6,16] In view of these results, a paper reporting on the reaction of 1 with benzyl alcohol to give only the α-configured product is noteworthy.[14]

The structures of 3-7 were established on the basis of the spectroscopic (^{1}H NMR and IR) and polarometric measurements. The 2-deoxy-2-hydroxyimino fragment was indicated by the structure of the H-1 (s) and H-3 (d) signals, the intensity of the signals of the methyl groups corresponding to the six acetyl groups and the bands of the OH groups (δ~ 9 and 3330 cm^{-1}). The D-*arabino** structure (* this refers to the configuration on the first sugar residue) was established from the $J_{3,4}$~ $J_{4,5}$~ 9 Hz values. The larger chemical shifts of H-1 for 4 and 6 (δ 5.85 and 5.91) as compared to δ H-1 for 3 and 7 (δ 5.64 and 5.15) is due respectively to the equatorial and axial orientation of H-1.
Also the $[\alpha]_D$ values for 4 and 6 (+18° and +15°, resp) and for 3 and 7 (-26° and +3°) support the α and β configurations, respectively.

The known influence on the configuration of the orientation of the oxime hydroxyl group on the chemical shifts in the ^{1}H NMR spectra[2,9,17,18] indicate that the hydroxyimino group in both the α and β anomers has the *Z* configuration.

Compounds 3, 4, and 6 were subjected to chemical transformations in the following sequence: deoximation with acetaldehyde, reduction of the resulting ketone with sodium borohydride and acetylation (conversion of 2-C=N-OH to 2-COAc). In this way, 9, 8, and 10, respectively, were obtained. Reduction of the 2-C=O group was highly stereospecific and the configuration of C-2 of the product depended on the configuration of the anomeric carbon atom. Reduction of the ketone with the α-D-*arabino** configuration gave exclusively the α-D-*gluco** isomer (8 and 10, $J_{1,2}$~ $J_{2,3}$~ $J_{3,4}$~ 9Hz), a product of the axial addition of the hydride ion to the C-2 carbonyl. On the other hand, the reduction of the β-D-*arabino** derivative gave the β-D-*manno** isomer (9, $J_{1,2}$~ 2, $J_{2,3}$~ 3, $J_{3,4}$~ 9 Hz). This addition occured from the "equatorial" side. These results are compatible with predictions based on the analyses of both the steric and

electrostatic effects influencing the course of the reaction of the carbonyl group in the sugar molecule.[19]

In 3 and 4 the hydroxyimino group was acetylated and then reduced to the amino group by the Ipaktschi procedure,[20] with sodium borohydride in methanol at ~ -30 °C in the presence of $NiCl_2 \cdot 6H_2O$. The reaction time was ~8 h and the yield was ~65%. The choice of this particular procedure was substantiated elsewere.[5] The products of reduction, after acetylation, were isolated as chromatographically homogeneous compounds. Their structures were established from the ^1H NMR data. The reduction of the acetoxyimino function of 4 stereocontrolled by the α-D-*arabino** moiety afforded the 2-amino-2-deoxy-α-D-glucopyranosyl* derivative (11), whereas the β-D-*arabino** isomer (3) gave β-D-*manno** isomer (12).

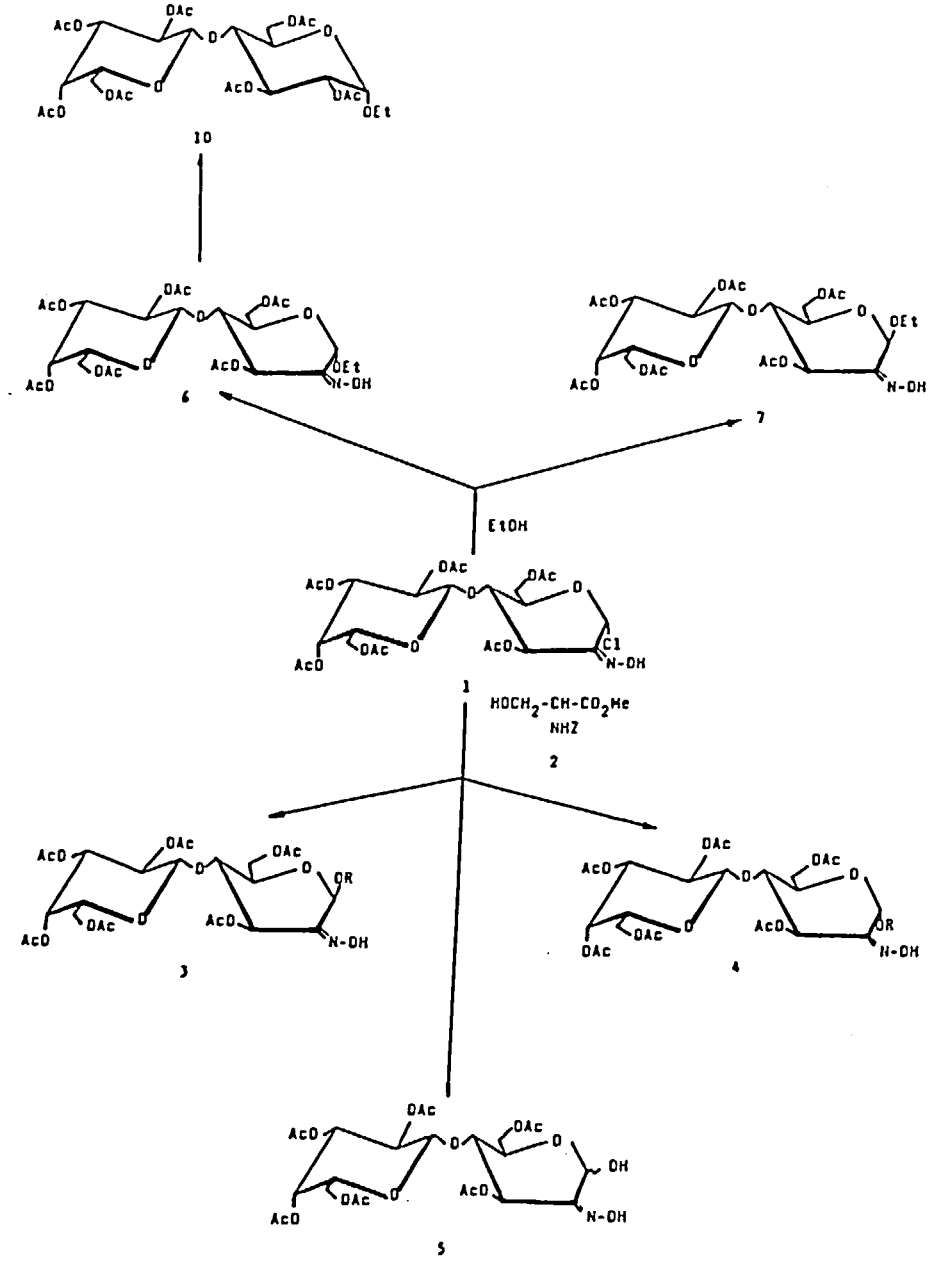
Use of the 3-OAc leaving group,[21-24] allowed modification of 4 at C-3. Refluxing 4 in ethanol in the presence of sodium azide, a sequence of elimination-addition reactions, led to substitution of 3-OAc by the azide residue and to formation of equatorial 13 (D-*arabino** isomer, $J_{3,4}$~ 9 Hz), and axial *Z*-isomer, 14 ($J_{3,4}$~ 3 Hz), and E-2-hydroxyimino-D-*ribo** isomer, 15 ($J_{3,4}$~ 3 Hz). The 13:14:15 ratio was 1:2:0.5.

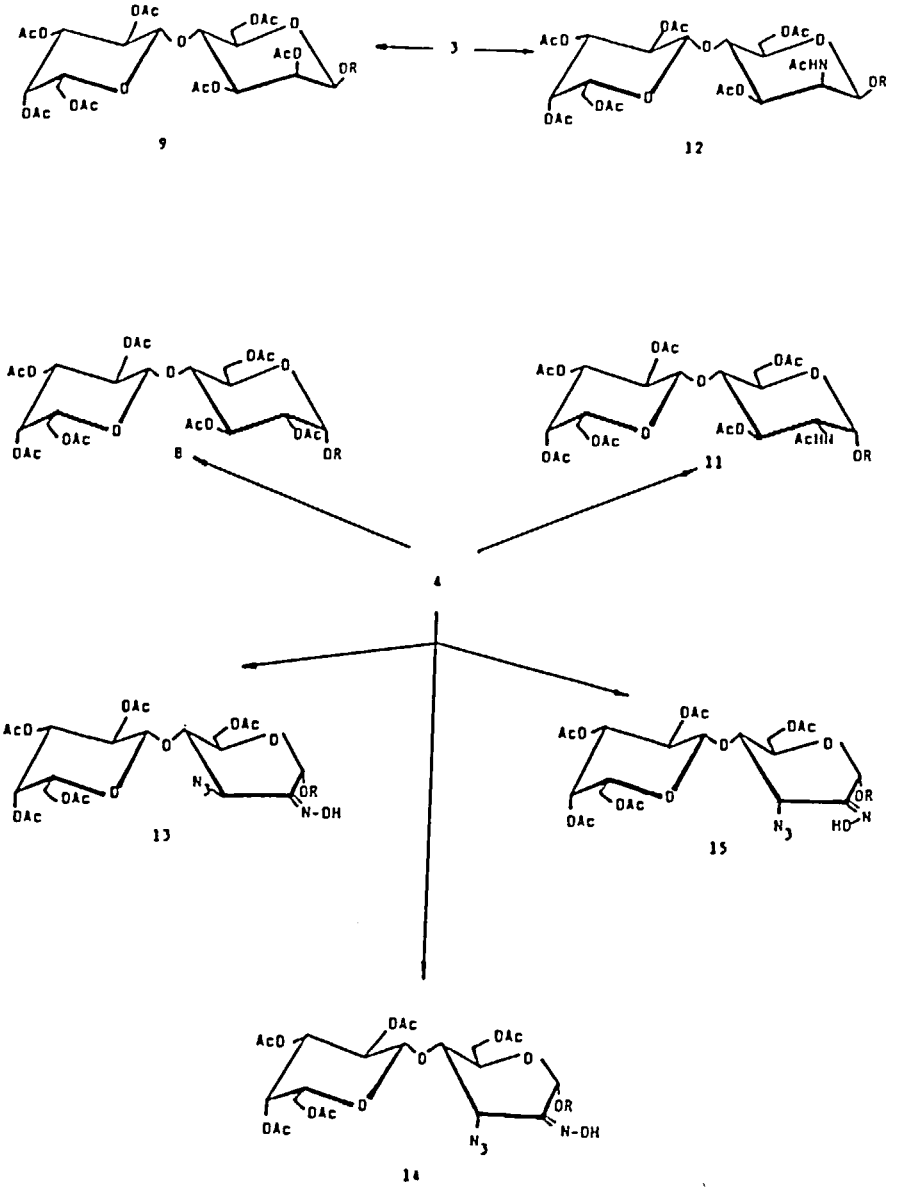
Compounds 13-15 are precursors of the corresponding 3-amino-2-hydroxyimino, 3-azido, and 2,3-diamino derivatives of serine.

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were recorded using a Hilger-Watt polarimeter for solutions in chloroform. ^1H NMR spectra ($CDCl_3$, internal $MeSi_4$) were recorded with a Bruker MSL 300 (300.13 MHz) instrument. IR spectra were recorded as Nujol mulls with a Perkin-Elmer 257 spectrophotometer. Field desorption mass spectra were recorded on a MAT 711 mass spectrometer. TLC was performed on Merck Kieselgel 60 F-254 plates with carbon tetrachloride-acetone (3:1). Column chromatography was performed on Kieselgel (>0.08 mm) with carbon tetrachloride-acetone (3:1).

Hexa-*O*-acetyl-D-lactal mp 110-112 °C, $[\alpha]_D^{20}$ -18° (*c*, 0.5 chloroform); (lit.[25] mp 113-114 °C , $[\alpha]_D^{19}$ -12.27°) was prepared according to the literature procedure.[25]





Dimeric 3,6-Di-*O*-acetyl-4-*O*-(tetra-*O*-acetyl-β-D-galactopyranosyl)-2-deoxy-2-nitroso-α-D-glucopyranosyl Chloride (1), had mp 121-123 °C, $[\alpha]_D^{25}$ +68° (*c*, 0.5 $CHCl_3$), R_F 0.48; (lit.[26], mp 120-122 °C, $[\alpha]_D^{20}$ +66.7°(*c*, 1.0 $CHCl_3$)).

N-Benzyloxycarbonyl-L-Serine Methyl Ester (2), mp 89-90 °C; (lit.[27], mp 92-93 °C) was prepared by a literature procedure.[27]

O-[3,6-Di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-deoxy-2-hydroxyimino-β- and -α-D-*arabino*-hexopyranosyl]-*N*-benzyloxycarbonyl-L-serine Methyl Ester (3 and 4) and 3,6-di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-deoxy-2-hydroxyimino-α-D-*arabino*-hexopyranose (5).

a)To a solution of 1 (1.252 g, 2 mmol) in *N,N*-dimethylformamide (15 mL) was added 2 (2.2 mmol), and the mixture was kept for 48 h at ~20 °C. TLC then revealed the complete conversion of 1 into three products (R_F 0.17, 0.15, and 0.09). The mixture was then concentrated, the solution of the residue in dichloromethane (150 mL) was washed with saturated aq sodium hydrogencarbonate (5×20 mL) and water (3×20 mL), dried (Na_2SO_4), and concentrated. Column chromatography of the crude product afforded 3 (25%): mp 70-75 °C; $[\alpha]_D^{20}$ -26°; R_F 0.17; IR 3300 (OH), 1740 (ester CO), 1660 cm^{-1}(oxime CN); ^1H NMR δ 1.98, 2.04, 2.06, 2.08, 2.11, 2.13 (6s, 18H, 6AcO), 3.74 (s, 3H, CO_2Me), 3.96 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 4.62 (d, 1H, $J_{1',2'}$= 9 Hz, H-1'), 4.98 (dd, 1H, $J_{3',4'}$= 2.5 Hz, H-3'), 5.13 (dd, 1H, $J_{2',3'}$= 9 Hz, H-2'), 5.36 (dd, 1H, $J_{4',5'}$= 3.5 Hz,H-4'), 5.64 (s, 1H, H-1), 5.93 (d, $J_{3,4}$= 9 Hz, H-3), 6.20 (d, 1H, $J_{\alpha CHCN}$= 8.5 Hz, Ser-NH), 7.34-7.26 (m, 5H, Ph), 8.86 (brs, 1H, oxime H, exchangeable on deuteration); FD-mass spectrum: m/z 843 [M⁺ +1].

Anal. Calcd for $C_{36}H_{46}N_2O_{21}$: C, 51.30; H, 5.50; N, 3.32. Found: C, 51.20; H, 5.43; N, 3.32.

Eluted second was 4 (46%): mp 92-95 °C; $[\alpha]_D^{20}$ +18°; R_F 0.15; IR 3290 (OH), 1740 (ester CO), 1720 (urethane CO), and 1660 cm^{-1}(oxime CN); ^1H NMR δ 1.96, 2.03, 2.05, 2.08, 2.12, 2.15 (6s, 18H, 6AcO), 3.72 (s, 3H, CO_2Me), 3.95 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 4.56 (d, 1H, $J_{1',2'}$= 9 Hz, H-1'), 4.98 (dd, 1H, $J_{3',4'}$= 2.5 Hz, H-3'), 5.14 (dd, 1H, $J_{2',3'}$= 9 Hz, H-2'), 5.35 (dd, 1H, $J_{4',5'}$= 3 Hz, H-4'), 5.85 (s, 1H, H-1), 5.68 (d, 1H, $J_{3,4}$= 9.5 Hz, H-3), 6.22 (d, 1H, $J_{\alpha CHNH}$= 9 Hz, Ser-NH), 7.26-7.37 (m, 5H, Ph), 8.28 (brs, 1H, oxime H); FD-mass spectrum: m/z 843 [M⁺+1].

Found: C, 51.40; H, 5.60; N, 3.20.

Eluted third was 5 (12%), isolated as a syrup: $[\alpha]_D^{20}$+11°; R_F 0.9; IR 3340 (OH), 1740 (ester CO), and 1660 cm^{-1} (oxime CN); ^1H NMR δ 1.96, 2.00, 2.03, 2.08, 2.11, 2.15 (6s, 18H, 6AcO), 3.89 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 4.61 (d, 1H, $J_{1',2'}$= 10 Hz, H-1'), 4.93 (dd, 1H, $J_{3',4'}$= 3 Hz, H-3'), 5.16 (dd, 1H, $J_{2',3'}$= 9.5 Hz, H-2'), 5.36 (dd, 1H, $J_{4',5'}$= 3.5 Hz, H-4'), 5.80 (d, 1H, $J_{3,4}$= 9 Hz, H-3), 6.26 (s, 1H, H-1), 8.84 (brs, 1H, NOH), 9.20 (brs, 1H, C_1-OH); FD-mass spectrum: m/z 608 [M+ +1].

Anal. Calcd for $C_{24}H_{33}NO_{17}$: C, 47.45; H, 5.47; N, 2.31. Found: C, 47.25; H, 5.67; N, 2.18.

b) The chloride 1 (1 mmol, 0.626 g) was dissolved in *N,N*-dimethylformamide (10 mL), which contained 2 (1.1 mmol, 230 mg) and calcium sulfate (3 g). The mixture was protected from moisture and stirred for 48 h at 20 °C, after which time 1 was converted, as indicated by TLC into two products (R_F 0.17 and 0.15). Dichloromethane (75 mL) was added and the solid removed by filtration. The solution was processed as in (a) and column chromatography gave 3 (25%) and 4 (60%).

Ethyl 3,6-Di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-deoxy-2-hydroxyimino-α- and -β-D-*arabino*-hexopyranoside (6 and 7). A solution of 1 (313 mg, 0.5 mmol) and ethanol (0.5 mL) in *N,N*-dimethylformamide (8 mL) was kept at ~20 °C for 48 h and then processed as described for 3 and 4. Column chromatography of the crude product afforded, first 6 (75%): mp 114-116 °C; $[\alpha]_D^{20}$+25°; R_F 0.17; IR 3340 (OH), 1760 (ester CO), 1710 (urethane CO), and 1625 cm^{-1} (oxime CN); ^1H NMR δ 1.22 (t, 3H, Me), 2.00, 2.05, 2.07, 2.08, 2.10, 2.12 (6s, 18H, 6AcO), 3.72 (q, 2H, $EtCH_2$), 3.92 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 4.55 (d, 1H, $J_{1',2'}$= 8.5 Hz, H-1'), 4.88 (dd, 1H, $J_{3',4'}$= 3 Hz, H-3'), 5.12 (dd, 1H, $J_{2',3'}$= 9 Hz, H-2'), 5.31 (dd, 1H, $J_{4',5'}$= 3 Hz, H-4'), 5.72 (d, 1H, $J_{3,4}$= 9 Hz, H-3), 5.91 (s, 1H, H-1), 8.25 (brs, 1H, oxime H); FD-mass spectrum: m/z 635 [M+].

Anal. Calcd for $C_{26}H_{37}NO_{17}$: C, 49.13; H, 5.87; N, 2.20. Found: C, 49.55; H, 5.97; N, 2.30.

Eluted second was 7 (15%): mp 80-84 °C; $[\alpha]_D^{20}$ +3°; R_F 0.15; IR 3320 (OH), 1750 (ester CO), 1710 (urethane CO), and 1620 cm^{-1} (oxime CN); ^{1} H NMR δ 1.14 (t, 3H, Me), 1.98, 2.00, 2.04, 2.06, 2.10, 2.12 (6s, 18H, 6AcO), 3.75 (q, 2H, $EtCH_2$), 3.95 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 4.57 (d, 1H,

$J_{1',2'}$= 9 Hz, H-1'), 4.87 (dd, 1H, $J_{3',4'}$= 3 Hz, H-3'), 5.12 (dd, 1H, $J_{2',3'}$= 9 Hz, H-2'), 5.15 (s, 1H, H-1), 5.33 (dd, 1H, $J_{4',5'}$= 3 Hz, H-4'), 6.20 (d, 1H, $J_{3,4}$= 8.5 Hz, H-3), 8.75 (brs, 1H, oxime H); FD-mass spectrum : m/z 635 [M+].

Found: C, 49.40; H, 6.00; N, 2.35.

***O*-[2,3.6-Tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)-α-D-glucopyranosyl]-*N*-benzyloxycarbonyl-L-serine Methyl Ester (8).** The solution of **4** (422 mg, 0.5 mmol), acetaldehyde (1.5 mmol), and **M** hydrochloric acid (0.5 mL) in acetonitrile (5 mL) was stirred at room temperature for 50 h, then cooled to 0 °C, and treated with sodium borohydride (2.5 mmol) in small portions. The resulting solution was stirred for 4 h at ~20 °C, then cooled to 0 °C, neutralized with acetic acid, and concentrated. The residue was treated with acetic anhydride-pyridine, and the product was subjected to column chromatography to give **8** (78%), isolated as a syrup: $[\alpha]_D^{\circ}$ +40°; R_F 0.26; IR 3320 (NH), 1765 (ester CO), and 1720 cm^{-1} (urethane CO); ^1H NMR δ 1.95, 2.00, 2.02, 2.04, 2.06, 2.10, 2.14 (7s, 21H, 7 AcO), 3.73 (s, 3H, CO_2Me), 3.87 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 4.44 (d, 1H, $J_{1',2'}$= 10 Hz, H-1'), 4.70 (dd, 1H, $J_{2,3}$= 9 Hz, H-2), 4.92 (d, 1H, $J_{1,2}$= 3 Hz, H-1), 4.96 (dd, 1H, $J_{3',4'}$= 3Hz, H-3'), 5.11 (dd, 1H, $J_{2',3'}$= 10 Hz, H-2'), 5.35 (dd, 1H, $J_{4',5'}$= 3Hz, H-4'), 5.78 (d, 1H, $J_{\alpha CHNH}$= 8.5 Hz, Ser-NH), 7.37-7.26 (m, 5H, Ph); FD-mass spectrum: m/z 872 [M+ +1].

Anal. Calcd for $C_{36}H_{49}NO_{22}$: C, 52.3; H, 5.7; N, 1.6. Found: C, 52.1; H, 5.6; N, 1.6.

Similar treatment of **3** gave ***O*-[2,3,6-Tri-*O*-acetyl-4-*O*-(-tetra-*O*-acetyl-β-D-galacopyranosyl)-β-D-mannopyranosyl]-*N*-benzyloxycarbonyl-L-serine Methyl Ester (9,** syrup 76%) $[\alpha]_D^{\circ}$ +11°; R_F 0.22; IR 3315 (NH), 1770 (ester CO), and 1710 cm^{-1} (urethane CO); ^1H NMR δ 1.96, 2.00, 2.03, 2.05, 2.07, 2.09, 2.14 (7s, 21H, 7AcO), 3.60 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 3.72 (s, 3H, CO_2Me), 4.52 (d, 1H, $J_{1',2'}$= 9 Hz, H-1'), 4.57 (d, 1H, $J_{1,2}$= 2Hz, H-1), 4.96 (dd, 1H, $J_{3',4'}$= 3 Hz, H-3'), 5.05 (dd, 1H, $J_{3,4}$= 9Hz, H-3), 5.14 (dd, 1H, $J_{3',4'}$= 9Hz, H-2'), 5,34 (dd, 1H, $J_{4',5'}$= 3Hz, H-4'), 5.35 (dd, 1H, $J_{2,3}$= 3H, H-2), 5.62 (d, 1H ,$J_{\alpha CHNH}$= 9 Hz, Ser-NH), 7.42-7.26 (m, 5H, Ph). FD-mass spectrum: m/z 872 [M+ +1].

Anal. Calcd for $C_{36}H_{49}NO_{22}$: C, 52.3; H, 5.7; N, 1.6. Found: C, 52.2; H, 5.5; N, 1.5.

Likewise 6 gave **Ethyl 2,3,6-Tri-*O*-acetyl-4-*O*-(-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranoside** (10, 65%, mp 126-128 °C); $[\alpha]_D^{20}$ +72°; IR 1750 cm^{-1} (ester CO); ^1H NMR δ 1.20 (t, 3H, Me), 1.95, 2.05, 2.07, 2.12 (4s, 21H, 7AcO), 3.75 (q, 2H, $EtCH_2$), 3.90 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 4.37 (dd, 1H, $J_{2,3}$= 10 Hz, H-2), 4.50 (dd, 1H, $J_{1',2'}$=9 Hz, H-1), 4.89 (d, $J_{1,2}$= 3 Hz, H-1), 4.98 (dd, 1H, $J_{2',3'}$= 9 Hz, H-2'), 5.00 (dd, 1H, $J_{3',4'}$= 2.5 Hz, H-3'), 5.12 (dd, 1H, $J_{3,4}$= 9 Hz, H-3), 5.34 (dd, 1H, $J_{4',5'}$= 3Hz, H-4').FD-mass spectrum: m/z 664 [M+].

Anal. Calcd for $C_{26}H_{41}O_{18}$: C, 50.60; H, 6.07. Found: C, 51.0; H, 6.2.

O-[2-Acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-(tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranosyl]-*N*-benzyloxycarbonyl-L-serine Methyl Ester (11). To a solution of 4 (422 mg, 0.5 mmol) in dichloromethane (15 mL) pyridine (0.75 mmol), acetic anhydride (0.75 mmol), and a catalytic amount of 4-dimethylaminopyridine (DMAP) were added. The mixture was stirred at ~20 °C until 4 disappeared (TLC, ~1.5 h), then washed with water (3×10 mL), dried ($MgSO_4$), and concentrated. A solution of the residue in methanol (10 mL) was stirred with a suspension of $NiCl_2 \times 6H_2O$ (1.25 mmol), cooled to -30 °C, treated with sodium borohydride (5 mmol) in small portions, and stirred for 8 h. TLC then indicated one main product. The solution was filtered and concentrated, and the residue was extracted with dichloromethane (30 mL). The extract was washed with water (2×10 mL), dried ($MgSO_4$) and concentrated, and the residue was treated conventionally with acetic anhydride-pyridine and a catalytic amount of DMAP. Column chromatography of the crude product afforded 11 (65%); mp 96-98 °C; R_F 0.20; IR 3270 (NH), 1760 (ester CO), 1705 (urethane CO), and 1655 cm^{-1} (amide CO); ^1H NMR δ 1.86 (s, 3H, AcN), 1.96, 2.03, 2.05, 2.10, 2.12 (5s, 18H, 6AcO), 3.42 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 3.69 (s, 3H, COMe), 4.32 (dd, 1H, $J_{2,3}$= 10 Hz, H-2), 4.54 (d, 1H, $J_{1',2'}$= 9 Hz, H-1'), 4.88 (d, 1H, $J_{1,2}$= 3 Hz, H-1), 4.98 (dd, 1H, $J_{3',4'}$= 3 Hz, H-3'), 5.16 (dd, 1H, $J_{2',3'}$= 10 Hz, H-2'), 5.30 (dd, 1H, $J_{3,4}$= 10 Hz, H-3), 5.36 (dd, 1H, $J_{4',5'}$= 3.5 Hz, H-4'), 5.65 (d, 1H, $J_{\alpha CHNH}$= 8 Hz, Ser-NH), 6.10 (d, 1H, $J_{\alpha CHNH}$= 8 Hz, AcNH), 7.40-7.28 (m, 5H, Ph). FD-mass spectrum: m/z 887 [M+].

Anal. Calcd for $C_{38}H_{50}N_2O_{22}$: C, 51.45; H, 5.68; N, 3.16. Found: C, 51.59; H, 5.72; N, 3.21.

Similar treatment of 3 gave ***O*-[2-Acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-(tetra-*O*-acetyl-β-D-mannopyranosyl]-*N*-benzyloxycarbonyl-L-serine Methyl Ester** (12, 60%): mp 82-85 °C; $[\alpha]_D^{25}$ -32°; R_F 0.36; IR 3300 (NH), 1775 (ester CO), 1710 (urethane CO), and 1640 cm^{-1} (amide CO). ^1H NMR δ 1.88 (s, 3H, AcN), 1.92, 2.03, 2.06, 2.09, 2.14 (5s,18H, 6AcO), 3.18 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 3.75 (s, 3H, CO_2Me), 3.90 (dd, 1H, $J_{3',4'}$= 3 Hz, H-3'), 4.47 (d, 1H, $J_{1,2}$= 2 Hz, H-1), 4.58 (d, 1H, $J_{1',2'}$= 9 Hz, H-1'), 4.90 (dd, 1H, $J_{2,3}$= 3 Hz, H-2), 4.98 (dd, 1H, $J_{3,4}$= 9 Hz, H-3), 5.10 (dd, 1H, $J_{2',3'}$= 9Hz, H-2'), 5,32 (dd, 1H, $J_{4',5'}$= 3 Hz, H-4'), 5.58 (d, 1H, $J_{\alpha CHNH}$= 8.5 Hz, Ser-NH), 6.15 (d, 1H, $J_{\alpha CHNH}$= 9 Hz, AcNH), 7.38-7.26 (m, 5H, Ph). FD-mass spectrum: m/z 888 [M+].

Found: C, 51.55; H, 5.78; N, 3.10.

***O*-[6-*O*-Acetyl-3-azido-2,3-dideoxy-2-hydroxyimino-4-*O*-(tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-*arabino*-hexopyranosyl]-*N*-benzyloxycarbonyl-L-serine Methyl Ester (13) and its (Z)- and (E)-2-Hydroxyimino-α-D-*ribo*-hexopyranosyl isomers (14 and 15).** Sodium azide (5 mmol) was added to a solution of **4** (421 mg, 0.5 mmol) in ethanol (15 mL). The resulting reaction mixture was stirred and boiled under reflux. TLC after 2 h showed complete conversion of **4** into three products. The solution was filtered and concentrated, and the residue was extracted with ether. The extract was filtered, diluted with chloroform (100 mL), washed with water (2×10 mL), dried (Na_2SO_4), and concentrated. Column chromatography of the resulting syrup gave first **13** (25%): mp 75-78 °C; $[\alpha]_D^{25}$ +36°; R_F 0.22; IR 3300 (OH), 2130 (N_3), 1740 (ester CO), and 1705 cm^{-1} (urethane CO); ^1H NMR δ 1.92, 2.00, 2.02, 2.09 (4s, 15H, 5AcO), 3.62, (s, 3H, CO_2Me), 4.30 (d, 1H, $J_{3,4}$= 9 Hz, H-3), 4.50 (d, 1H,$J_{1',2'}$= 9 Hz, H-1'), 4.56 (dd, 1H, $J_{4,5}$= 9Hz, H-4), 4.86 (dd, 1H, $J_{3',4'}$= 3 Hz, H-3'), 5.08 (dd, 1H, $J_{2',3'}$= 9Hz, H-2'), 5.39 (dd, 1H, $J_{4',5'}$= 3.5 Hz, H-4'), 5.78 (d, 1H, $J_{\alpha CHNH}$= 8.5 Hz, Ser-NH), 5.82 (s, 1H, H-1, 7.56-7.23 (m, 5H, Ph). FD-mass spectrum: m/z 826 [M+].

Anal. Calcd for $C_{34}H_{43}N_5O_{19}$: C, 49.45; H, 5.25; 8.48. Found: C, 49.60; H, 5.33; N, 8.58.

Eluted second was **14** (44%): mp 92-95 °C; $[\alpha]_D^{20}$ +64°; R_F 0.18; IR 3300 (OH), 2120 (N_3), 1740 (ester CO), and 1710 cm^{-1} (urethane CO). ^1H NMR δ 1.93, 2.01, 2.09 (4s, 15H, 5AcO), 3.65 (3, 3H, CO_2Me), 4.42 (dd,

1H, $J_{4,5}$= 8.5 Hz, H-4), 4.60 (d, 1H, $J_{3,4}$= 3 Hz, H-3), 4.81 (dd, 1H, $J_{3,4}$= 3 Hz, H-3), 4.81 (dd, 1H, $J_{3',4'}$= 3 Hz, H-3'), 5.19 (dd, 1H, $J_{2',3'}$= 9 Hz, H-2'), 5.33 (dd, 1H, $J_{4',5'}$= 3 Hz, H-4'), 5.55 (dd, 1H, $J_{1',2'}$= 9 Hz, H-1'), 5.71 (s, 1H, H-1), 5.87 (d, 1H, $J_{\alpha CHNH}$= 8 Hz, Ser-NH), 7.38-7.26 (m, 5H, Ph). FD-mass spectrum: m/z 826 [M⁺+1].

Found: C, 49.50; H, 5.38; N, 8.66.

Eluted third was 15 (11%) isolated as a syrup: $[\alpha]_D^{20}$ +42°; R_F 0.14; IR 3290 (OH), 2130 (N_3), 1730 (ester CO), and 1710cm^{-1} (urethane CO); ^{1}H NMH δ 1.92, 2.03, 2.10 (3s, 15H, 5AcO), 3.60 (s, 3H, CO_2Me), 4.36 (dd, 1H, $J_{4,5}$= 9 Hz, H-4), 4.48 (dd, 1H, $J_{1',2'}$= 9 Hz, H-1'), 4.93 (dd, 1H, $J_{3',4'}$= 3 Hz, H-3'), 5.12 (dd, 1H, $J_{2',3'}$= 9 Hz, H-2'), 5.25 (s, 1H, H-1), 5.38 (dd, 1H, $J_{4',5'}$= 3 Hz, H-4'), 5.50 (d, 1H, $J_{3,4}$= 3 Hz, H-3), 5.70 (d, 1H, $J_{\alpha CHNH}$= 8 Hz, Ser-NH), 7.40-7.25 (m, 5H, Ph). FD-mass spectrum: m/z 826 [M⁺+1].

Found: C, 49.58; H, 5.30; N, 8.65.

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