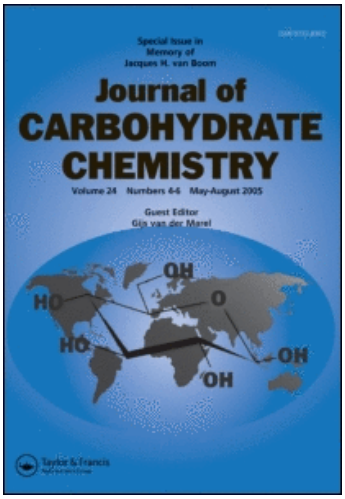


Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Benzyl-2,4-Diacetamido-2, 4,6-Tri-Deoxy-α(β) -D-Galactopyranoside

J. P. G. Hermans[a]; C. J. J. Elie[a]; G. A. van der Marel[a]; J. H. Van Boom[a]
[a] Gorlaeus Laboratories, Department of Organic Chemistry, RA Leiden, The Netherlands

To cite this Article Hermans, J. P. G. , Elie, C. J. J. , van der Marel, G. A. and Van Boom, J. H.(1987) 'Benzyl-2,4-Diacetamido-2, 4,6-Tri-Deoxy-α(β) -D-Galactopyranoside', Journal of Carbohydrate Chemistry, 6: 3, 451 — 462
To link to this Article: DOI: 10.1080/07328308708057932
URL: http://dx.doi.org/10.1080/07328308708057932

J. CARBOHYDRATE CHEMISTRY, 6(3), 451-462 (1987)

BENZYL-2,4-DIACETAMIDO-2,4,6-TRIDEOXY-α(β)-D-GALACTOPYRANOSIDE: A MODEL COMPOUND FOR THE PREPARATION OF FRAGMENTS OF THE N-ACETYL COMPLEX POLYSACCHARIDE OF STREPTOCOCCUS PNEUMONIAE

J. P. G. Hermans, C. J. J. Elie, G. A. van der Marel,*
and J. H. van Boom*

Gorlaeus Laboratories, Department of Organic Chemistry
P. O. Box 9502, 2300 RA
Leiden, The Netherlands

Received March 19, 1987 - Final Form June 2, 1987

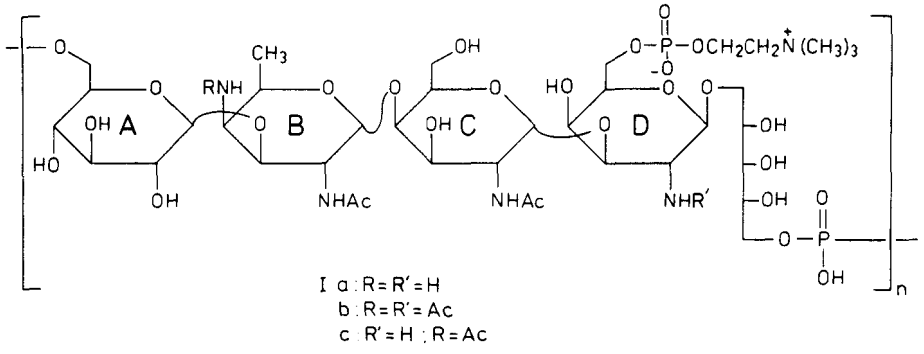
ABSTRACT

Benzyl-2,4-diacetamido-2,4,6-trideoxy-α(β)-D-galactopyranoside **6c** was synthesized from 1,6-anhydro-2,3-*O*-(4-methoxybenzylidene)-β-D-mannopyranose **1a**. The azide group at C-4, which is a precursor for the acetamido function, was introduced by substitution of the 4-O-triflate group with lithium azide. After regioselective oxidative acetal ring opening the other C-2 azide function was obtained by the same substitution procedure. Acetolysis of the 1,6-anhydro bridge and α(β)-coupling with benzyl alcohol gave the 2,4-diazido derivative **4b**. After base treatment the azide groups were reduced and subsequently acetylated. Selective protection of the primary hydroxyl by the phenyl thionocarbonyl group followed by reduction afforded the title compound.

INTRODUCTION

Structural determination of many cell wall-associated antigens revealed the presence of several minor sugar derivatives like mono- and diamino sugars,[1] some of which have an additional 6-deoxy function. For instance, it has been established that a cell wall-associated polysaccharide antigen of the Complex Polysaccharide, C-Substance, from Streptococcus pneumoniae type 1 contains a 2-acetamido-4-amino-2,4,6-

trideoxy-D-galactose (Sug) residue,[2] the preparation of which has been reported.[3] Further, an appropriately protected Sug derivative has been used for the assemblage[4] of a methyl glycoside of the disaccharide α-D-GalpA-(1->3)-α-Sug p. The latter dimer is a structural element[5] of the capsular polysaccharide antigen of the same microorganism.



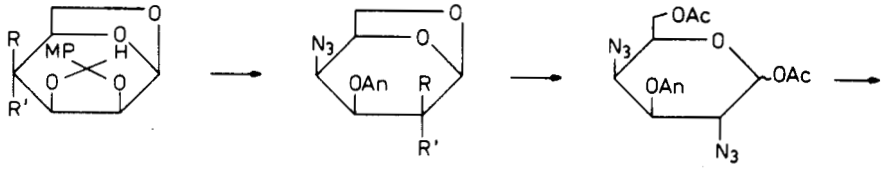
I a: R=R'=H
b: R=R'=Ac
c: R'=H; R=Ac

As part of a programme to study the immunochemical properties of naturally occurring and modified elements of the C-substance (**Ia, b** or **c**, n=1), we report on the preparation of 1,6-di-*O*-acetyl-3-*O*-anisoyl-2,4-diazido-2,4-dideoxy-α(β)-D-galactopyranoside (**3**). Evidence will also be given that compound **3** may open the way for the formation of an α-linkage between a fully *N*-acetylated Sug derivative and the C-4 position of 2-acetamido-2-deoxy-D-galactose in **Ib,c**.

RESULTS AND DISCUSSION

Previously we showed[6] that the easily accessible 1,6-anhydro-2,3-*O*-(4-methoxybenzylidene)-β-D-mannopyranose (**1a**) was a versatile starting compound in the synthesis of disaccharides. The presence of a free hydroxyl group at C-4 together with the possibility to open the 2,3-*O*-(4-methyoxybenzylidene)-acetal function regioselectively[6] at C-2 allow the performance of simultaneous or stepwise substitution reactions at the 4- and 2-positions. Furthermore, acetolysis of the 1,6-anhydro bridge affords a 1,6-di-*O*-acetyl intermediate, the anomeric centre of which can be activated for the introduction of an interglycosidic linkage. In addition, the C-6 position may be further processed

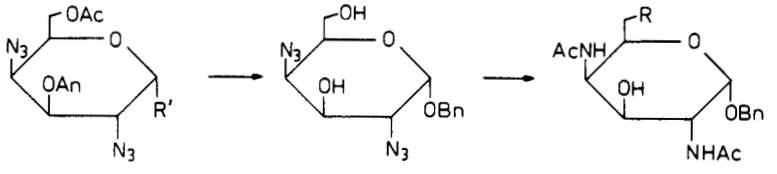
to give after deoxygenation the target molecule. The above mentioned features of compound **1a** indicate that the preparation of the required sugar derivative **6c** can in principle be realized by two approaches which have in common that the last step consists of introducing the 6-deoxy-function.



1a: R=H; R'=OH
b: R=H; R'=OTfl
c: R=N_3; R'=H
(MP=4-methoxyphenyl)

2a: R=OH; R'=H
b: R=OTfl; R'=H
c: R=H; R'=N_3
(An=Anisoyl)

3



4a: R'=Br
b: R'=OBn

5

6a: R=OH
b: R=PhOCSO
c: R=H

In the first or simultaneous approach to the introduction of the 2,4-diazido functions, 1,6-anhydro-3-*O*-anisoyl-β-**D**-mannopyranose[7] was triflated with excess trifluoromethanesulphonic anhydride.[8] Work-up of the reaction mixture yielded the 2,4-di-*O*-triflyl-β-**D**-mannopyranose derivative. Unfortunately, every attempt to convert both triflate functions by Walden inversion with lithium azide[9] failed. As expected, substitution of the 2-*O*-triflate group proceeded rapidly[7] but no reaction was observed at C-4 (Experimental details not given here). We therefore decided to investigate the stepwise introduction of the azide at C-4 followed by C-2. Thus, treatment of **1a** with trifluoromethanesulphonic anhydride in the presence of pyridine at low temperature afforded **1b** in a quantitative yield. Substitution of the 4-*O*-triflate group by LiN_3 in DMF was carried out at different temperatures and optimum conditions were obtained at 80 °C. Nonetheless the reaction

was accompanied by a considerable amount of elimination. Oxidative[10] opening of the acetal function in **1c** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[11] afforded **2a**.

Triflation of the 2-hydroxyl function, as described for **1a**, yielded **2b**, the triflate group of which could be smoothly substituted, at room temperature by azide to give **2c** in high yield. The 1,6-anhydro bridge was now opened by acetolysis[12] with trifluoroacetic acid and acetic anhydride at 50 ^{o}C to afford, after work-up and purification, compound **3**. The latter was converted at room temperature into the bromide **4a** with titanium tetrabromide[13] in dichloromethane. The bromide, which appeared to be rather stable, probably due to the deactivating influence of the azide and acyl functions, could be purified by silica gel column chromatography and crystallized from dry ether.

The presence of the non-participating azide function[14] at C-2 opens the way for the formation of an α-interglycosidic bond between residues B and C in **Ib,c**. For the time being, however, benzyl alcohol was chosen to function as the aglycon. Thus, coupling of **4a** with benzyl alcohol could be realized in the presence of $HgBr_2$, $Hg(CN)_2$[15] and using molecular sieves as acid scavenger.

Work-up and purification afforded the 1-*O*-benzyl derivative **4b** (α/β mixture 7/1). Reduction of the azide functions in compound **4b** with hydrogen sulfide[16] in pyridine/water may be accompanied by migration of acyl groups to the newly formed amino functions. In order to circumvent this possible side-reaction we first subjected **4b** to base treatment to give, after column chromatography, compound **5**, the azide functions of which were then reduced under the above mentioned conditions. Compound **6a** was obtained by complete acetylation of the 2,4-diamino derivative with acetic anhydride in pyridine and subsequent deacetylation of the 3- and 6-acyl functions under Zemplen conditions. The final step in the synthesis consists of converting the 6-hydroxyl group of **6a** into the 6-deoxy analogue **6c**. Earlier findings[17] have indicated that substitution reactions at the 6-position of galactose derivatives are difficult to conduct as a result of the presence of axially orientated substituents at C-4. The latter fact rules out the possibility to substitute commonly used leaving groups at C-6 such as bromide, iodide,[18,19] *p*-toluenesulphonyl and methanesulphonyl by

hydride ions. In addition, the presence of hydride ions does not exclude the possible formation of a 3,6-anhydro function. To overcome this problem, **6a** was treated with an equimolar amount of phenyl chlorothionocarbonate[20] in acetonitrile in the presence of 4-di-methylaminopyridine to give mainly the 6-*O*-phenyl thionocarbonyl derivative **6b**. Compound **6b** was converted, under radical-mediated conditions, into the target molecule **6c** by adding tri-*n*-butyltin hydride and a catalytic amount of 2,2'-azo*bis*-(2-methylpropionitrile) to a solution of **6b** in toluene and refluxing the mixture for 1 h. Spectroscopic data of **6c** thus obtained were in accordance with those reported for the pure α-isomer which was prepared earlier[21] starting from benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-4-*O*-(methylsulfonyl)-α- D-galactopyranoside.[22]

In conclusion, the results presented in this paper indicate that the 2,4-diazido derivative **3** may be a possible intermediate for the preparation of a repeating unit[23] of the Complex Polysaccharide **Ib,c**.

EXPERIMENTAL

General methods and materials. Pyridine, dichloromethane and 1,2-dichloroethane were dried by refluxing with CaH_2 for 16 h and then distilled. Pyridine and dichloromethane were stored over molecular sieves 4Å, 1,2-dichloroethane was stored over basic alumina. *N,N*-Dimethylformamide was stirred with CaH_2 for 16 h and then distilled under reduced pressure and stored over molecular sieves 4Å. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was purchased from Janssen (Belgium). DDQ was dissolved in hot dichloromethane, filtered to remove $DDQH_2$ and crystallized at 0 °C. Schleicher and Schull DC Fertigfolien F 1500 LS 254 were used for TLC analysis. Sugar compounds were visualized by UV light or by spraying with conc. H_2SO_4/methanol (2/8, v/v) followed by charring at 140 °C for a few minutes. Column chromatography was carried out on Merck Kieselgel 60 (230-400 mesh, ASTM). Evaporations were carried out below 40 °C under reduced pressure (15 mm or 0.5 mm Hg). Optical rotations were measured at 25 °C using a Perkin-Elmer 141 Polarimeter. ^1H NMR spectra were measured at 200 MHz using a Jeol JNM-FX 200 spectrometer or at 300 MHz using a Bruker WM-300 spectrometer, equipped with an Aspect-2000 computer, operating in the Fourier transform mode. ^{13}C NMR spectra were measured

at 25.15 MHz using a Jeol JNMPFT 100 spectrometer equipped with an EC-100 computer, operating in the Fourier transform mode. Chemical shifts are given in ppm (δ) relative to tetramethylsilane (TMS) as internal standard.

1,6-Anhydro-4-azido-2,3-O-(4-methoxybenzylidene)-4-deoxy-β-D-talopyranose (1b). To a stirred and cooled (-10 °C) solution of pyridine (0.67 mL, 8.37 mmol) in dry 1,2-dichloroethane (40 mL) was added trifluoromethanesulfonic anhydride (1.21 mL, 7.19 mmol). After 10 min, compound **1a** (1.0 g, 3.60 mmol) in dry 1,2-dichloroethane (10 mL) was added and stirring was continued until TLC analysis (CH_2Cl_2) showed complete conversion of the starting material (Rf 0.00) into the 4-*O*-triflate derivative (Rf 0.58). An aqueous 10% $NaHCO_3$ solution was added and the mixture was stirred for 20 min at room temperature. After the addition of dichloromethane, the organic layer was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residual yellowish oil was coevaporated twice with toluene and dissolved in dry DMF (50 mL). Lithium azide (2.13 g, 36 mmol) was added and the reaction mixture was stirred overnight at 80 °C. TLC analysis (CH_2Cl_2) indicated the formation of **1b** (Rf 0.34) together with a by-product (Rf 0.41). The solution was concentrated to dryness and the residue was taken up in a water/dichloromethane mixture. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The resulting oil was applied to a column of silica gel. Elution with dichloromethane afforded pure **1b** in 38% yield. IR (neat): 2110 cm^{-1} (ν N_3). 200 MHz ^1H NMR ($CDCl_3$): δ 3.70-3.76 (m, H4); 3.77 (s, 3H, CH_3O); 4.01 (dd, $H6_{exo}$, $J_{6,6'}$ = 9 Hz, $J_{5,6}$ = 1.5 Hz); 4.09 (dd, H2, $J_{1,2}$ = 3 Hz, $J_{2,3}$ = 6 Hz); 4.29 (dd, $H6_{endo}$); 4.39-4.46 (m, 2H, H3+H5); 5.40 (d, H1); 5.73 (s, H7); 6.90, 7.62 (2xd, 2x2H, H3+H5, H2+H6, methoxybenzyl arom.). ^{13}C [^1H]NMR ($CDCl_3$): δ 55.0 (s, CH_3O); 57.3 (s, C4); 63.9 (s, C6); 71.7, 73.9, 74.0 (s, C2, C3, C5); 98.9 (s, C1); 105.3 (s, C7); 113.5, 129.0 (s, methoxybenzyl arom.).

1,6-Anhydro-3-O-anisoyl-4-azido-4-deoxy-β-D-talopyranose (2a). Compound **1b** (0.30 g, 1 mmol) was dissolved in a mixture of dichloromethane/water (5.5 mL, 5:0.5, v/v) and DDQ (0.34 g, 1.5 mmol) was added in portions. The mixture was stirred overnight at room temperature under the exclusion of light. TLC analysis (CH_2Cl_2/MeOH, 96:4, v/v)

showed almost complete conversion of the starting material (Rf 0.83) into product **2a** (Rf 0.65). The reaction mixture was taken up in dichloromethane, washed with aqueous 10% $NaHCO_3$ and water, dried ($MgSO_4$) and concentrated to dryness. The crude product was purified by column chromatography (silica gel, eluent CH_2Cl_2/MeOH, 98:2, v/v) after which **2a** was obtained as a white solid in 87% yield. $[\alpha]_D^{25}$ -165° (c 1, $CHCl_3$). 200 MHz ^1H NMR ($CDCl_3$): δ 3.81-3.87 (m, 2H, H2+H4); 3.88 (s, 3H, CH_3O); 4.07 (d, $H6_{exo}$, $J_{6,6'}$ = 9 Hz, $J_{5,6}$ = 1 Hz); 4.41 (d, $H6_{endo}$); 4.47-4.51 (m, 2H, H3+H5); 5.42 (s, H1); 6.97, 8.04 (2xd, 4H, H3+H5, H2+H6, anisoyl arom.). $^{13}C[^1H]$NMR ($CDCl_3$): δ 55.2 (s, CH_3O); 58.4 (s, C4); 65.3 (s, C6); 68.1, 68.5, 72.9 (s, C2, C3, C5); 101.4 (s, C1); 113.7, 131.7 (s, anisoyl arom.); 163.6 (s, C=O anisoyl).

1,6-Anhydro-3-O-anisoyl-2,4-diazido-2,4-dideoxy-β-D-galactopyranose (2b). Compound **2a** (0.32 g, 0.97 mmol) was triflated as described for **1a**. A solution of the 2-O-triflate derivative and lithium azide (0.59 g, 10 mmol) in dry DMF (6.5 mL) was stirred overnight at ambient temperature. TLC analysis (CH_2Cl_2) indicated complete conversion of the starting material (Rf 0.81) into **2b** (Rf 0.54). The mixture was concentrated to dryness and the residue taken up in dichloromethane/-water. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Silica gel chromatography (CH_2Cl_2) afforded pure **2b** in 72% yield. $[\alpha]_D^{25}$ -40.5° (c 1, $CHCl_3$). IR (neat): 2110 cm^{-1} (ν N_3). 200 MHz ^1H NMR ($CDCl_3$): δ 3.66-3.71 (m, H2); 3.80-3.84 (m, H4); 3.85 (s, 3H, CH_3O); 4.16 (d, $H6_{exo}$, $J_{6,6'}$ = 8 Hz); 4.42 (d, $H6_{endo}$); 4.50-4.54 (m, 2H, H3+H5); 5.52 (m, H1); 6.94, 8.00 (2xd, 4H, H3+H5, H2+H6, anisoyl arom.). $^{13}C[^1H]$NMR ($CDCl_3$): δ 55.3 (s, CH_3O); 56.1 (s, C4); 61.2 (s, C2); 64.6 (s, C6); 68.3, 73.0 (s, C3, C5); 99.8 (s, C1); 113.7, 131.7 (s, anisoyl arom.); 163.8 (s, C=O anisoyl).

1,6-Di-O-acetyl-3-O-anisoyl-2,4-diazido-2,4-dideoxy-D-galactopyranoside (3). Compound **2b** (0.35 g, 1 mmol) was dissolved in acetic anhydride (7 mL) and the solution was cooled at 0 °C. Trifluoroacetic acid (0.7 mL) was added under an atmosphere of nitrogen and the reaction mixture was stirred overnight at 50 °C. TLC analysis (toluene/-acetone, 97:3, v/v) indicated complete conversion of the starting material (Rf 0.44) into product **3** (Rf 0.16). The mixture was

coevaporated twice with toluene and the crude product was purified by column chromatography (silica gel, eluent CH_2Cl_2). Compound **3** was obtained as a white solid in 80% yield (mixture of anomers, α:β = 2:1). 200 MHz ^1H NMR ($CDCl_3$): δ 2.08 (s, CH_3 6-O-acetyl); 2.17, 2.19 (2xs, 2xCH_3 1-O-acetyl); 5.56 (d, H1α, $J_{1,2}$ 7.5 = Hz); 6.33 (d, H1β, $J_{1,2}$ = 4 Hz). $^{13}C[^1H]$NMR ($CDCl_3$): δ 20.6, 20.8 (s, 2xCH_3 acetyl); 90.3, 92.7 (s, Clβ, Clα); 164.2, 165.1, 168.5, 170.2 (s, C=O anisoyl, 3xC=O acetyl).

6-O-Acetyl-3-O-anisoyl-2,4-diazido-2,4-dideoxy-α-D-galactopyranosyl bromide (4a). To compound **3** (0.20 g, 0.45 mmol) was added $TiBr_4$ (2.25 mmol, 5.6 mL of a standard solution in dry dichloromethane, 0.15 g/mL) and ethyl acetate (1 mL). The dark-red solution was stirred overnight at room temperature under an atmosphere of dry nitrogen. TLC analysis (toluene/acetone, 97:3, v/v) showed complete conversion of the starting material (Rf 0.16) into the bromide **4a** (Rf 0.29). Dry sodium acetate was added until the solution became colourless. The mixture was taken up in dry toluene, filtrated over Celite and evaporated to dryness. This procedure was repeated until a clear oil was obtained (0.18 g, 0.38 mmol) which could be crystallized from dry ether, mp 95 °C. The mother liquor was purified by flash column chromatography (eluent CH_2Cl_2). 300 MHz ^1H NMR ($CDCl_3$): δ 2.09 (s, 3H, CH_3 acetyl); 3.85 (s, 3H, CH_3O); 4.20 (d, H2); 4.24 (m, H4); 4.25, 4.27 (dd, H6, $J_{6,6'}$ = 11.5 Hz, $J_{5,6}$ = 1.5 Hz); 4.37 (dd, H6'); 4.46 (t, H5, $J_{4,5}$ = 6 Hz); 5.61, 5.66 (dd, H3, $J_{2,3}$ = 10 Hz, $J_{3,4}$ = 3 Hz); 6.46 (d, H1, $J_{1,2}$ = 4 Hz); 6.95, 8.06 (2xd, 4H, H3+H5, H2+H6 anisoyl arom.). Anal. Calcd for $C_{16}H_{17}O_6N_6Br$: C, 41.0; H, 3.7; N, 17.9; Br, 17.0. Found: C, 40.9; H, 3.6; N, 17.5; Br, 17.2.

Benzyl-6-O-acetyl-3-O-anisoyl-2,4-diazido-2,4-dideoxy-α(β)-D-galactopyranoside (4b). Benzyl alcohol (47.6 mg, 0.44 mmol) was dissolved in dry dichloromethane (6.5 mL). $HgBr_2$ (78.6 mg, 0.22 mmol), $Hg(CN)_2$ (166.5 mg, 0.66 mmol) and molecular sieves 4Å (322 mg) were added and the mixture was stirred for 1 h at room temperature under nitrogen. **4a** (0.18 g, 0.38 mmol) in dry dichloromethane (2 mL) was added and the solution was stirred overnight at ambient temperature. TLC analysis (toluene/acetone, 97:3, v/v) indicated complete disappearance of **4a** and the formation of **4b** (Rf 0.51) together with a

small amount of the β-isomer (Rf 0.44). The reaction mixture was filtrated over Celite, which was washed with dichloromethane. The solution was washed twice with 1 M KBr and water, dried ($MgSO_4$) and concentrated to dryness. Column chromatography (Kieselgel, eluent CH_2Cl_2) afforded **4b** as a colourless oil in 60% yield: (α/β mixture = 7/1). 300 MHz ^1H NMR ($CDCl_3$): δ 2.11 (s, 3H, CH_3 acetyl); 3.87 (s, 3H, CH_3O); 3.93-3.99 (dd, 1H, H2); 4.09-4.13 (dd, 1H, H4, $J_{3,4}$ = 3.5 Hz); 4.17-4.25 (dd, 1H, H6, $J_{6,6'}$ = 11.5 Hz); 4.33-4.39 (dd, H6'); 4.45 (t, 1H, H5); 4.65 (d, 1H, H1, $J_{1,2}$ = 3.5 Hz); 4.70, 4.95 (dd, AB, 2H, CH_2 benzyl); 5.59, 5.63 (dd, H3, $J_{2,3}$ = 10 Hz); 6.95 8.07 (2xd, 4H, H3+H5, H2+H6, anisoyl arom.); 7.38 (m, 5H, benzyl arom.).

Benzyl-2,4-diazido-2,4-dideoxy-α(β)-D-galactopyranoside (5). Compound **4b** (110 mg, 0.23 mmol) was dissolved in dry methanol (2 mL) and a catalytic amount of sodium methoxide (1 M in dry methanol) was added. After stirring for 1 h at room temperature, TLC analysis (CH_2Cl_2) showed complete conversion of the starting material (Rf 0.47) into **5** (Rf 0.0). The solution was neutralized by adding Dowex 50 W cation-exchange resin (100-200 mesh, H^+ form), the resin removed by filtration, and the solution concentrated to dryness. Column chromatography (silica gel, eluent CH_2Cl_2/MeOH, 95:5, v/v) afforded pure **5** as a white solid in 95% yield (α/β mixture).

Benzyl-2,4-diacetamido-2,4-dideoxy-α(β)-D-galactopyranoside (6a). Compound **5** (70 mg, 0.22 mmol) was dissolved in pyridine/water (10 mL, 4:1, v/v) and H_2S was led through the mixture with stirring at room temperature. After 24 h, TLC analysis (CH_2Cl_2/MeOH, 43:7, v/v) showed almost complete conversion of the starting material into the 2,4-diamino derivative (baseline). The reaction mixture was coevaporated twice with dry pyridine and dissolved in dry pyridine (5 mL). Acetic anhydride (0.5 mL) was added and the solution was stirred at room temperature for 1 h, after which TLC analysis (CH_2Cl_2) indicated the formation of the completely acetylated derivative (Rf 0.73). The reaction mixture was taken up in dichloromethane, washed with water and aqueous 10% $NaHCO_3$, dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography (Kieselgel, eluent CH_2Cl_2/MeOH, 98:2, v/v) and subsequently *O*-deacetylated as described for compound **4b**. After 1 h TLC analysis (CH_2Cl_2/MeOH, 92:8, v/v)

showed complete formation of **6a** (α/β mixture, Rf 0.11 and 0.21). The solution was neutralized with Dowex 50 W cation-exchange resin (100-200 mesh, H^+ form), the resin removed by filtration, and the solution concentrated to dryness to afford **6a** (0.18 mmol). 300 MHz ^{1}H NMR ($CDCl_3$/MeOD): δ 1.99, 2.10 (2xs, 2x3H, 2xCH_3 acetyl); 3.43-3.58 (m, 2H, H6+H6', $J_{6,6'}$ = 12 Hz); 3.96-4.09 (m, 2H, H3+H5, $J_{2,3}$ = 10 Hz); 4.11-4.15 (dd, 1H, H2, $J_{1,2}$ = 3.5 Hz); 4.38-4.42 (dd, 1H, H4); 4.40, 4.25 (dd, AB, 2H, CH_2 benzyl); 4.70 (d, 1H, H1); 6.95 (d, 1H, 2'NH); 7.30-7.40 (m, 5H, benzyl arom.); 7.63 (d, 1H, 4'NH). ^{13}C[^{1}H]NMR ($CDCl_3$/MeOD): δ 22.1, 22.5 (2xs, 2xCH_3 acetyl); 50.4, 50.8 (2xd, C2+C4); 60.5 (C6); 66.8, 69.5 (C3+C5); 69.6 (CH_2 benzyl); 96.5 (C1); 127.6, 128.3 (C arom. benzyl); 136.7 (C=O acetyl).

Benzyl-6-O-phenylthionocarbonyl-2,4-diacetamido-2,4-dideoxy-α(β)-D-galactopyranoside (6b). To compound **6a** (102 mg, 0.29 mmol) in dry acetonitrile (2 mL) was added 4-dimethylaminopyridine (0.11 g, 0.58 mmol) and the mixture was stirred at -15 °C under an atmosphere of dry nitrogen. Phenyl chlorothionocarbonate (50 mg, 40 μL, 0.29 mmol) was added and the solution was allowed to warm up slowly to room temperature. After 1 h TLC analysis (CH_2Cl_2/MeOH, 92:8, v/v) indicated the formation of the monosubstituted product (Rf 0.49) together with a small amount of disubstitution (Rf 0.64). The reaction mixture was concentrated to dryness and the crude product was purified by column chromatography (Kieselgel, eluent CH_2Cl_2/MeOH, 98:2, v/v). The 6-*O*-phenylthionocarbonyl derivative was isolated as a colourless solid in about 60% yield. 300 MHz ^{1}H NMR ($CDCl_3$): δ 1.99, 2.09 (2xs, 2x3H, 2xCH_3 acetyl); 3.72-3.79 (m, 1H, H2, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10 Hz); 4.00 (d, 1H, H1); 4.02-4.10 (m, 1H, H3); 4.12 (d, 1H, H4); 4.16, 4.88 (dd, AB, 2H, CH_2 benzyl); 4.39-4.69 (m, 3H, H5, H6+H6'); 6.67 (d, 1H, NH); 7.18-7.39 (m, 10H, arom. benzyl and phenyl).

Benzyl-2,4-diacetamido-2,4,6-trideoxy-α(β)-D-galactopyranoside (6c). The 6-*O*-phenylthionocarbonyl derivative (28 mg, 50 μmol) was dissolved in dry toluene (1 mL) and tri-*n*-butyltinhydride (50 μL) together with a catalytic amount of 2,2'-azo*bis*(2-methylpropionitrile) was added. The reaction mixture was heated under reflux for 1 h after which TLC analysis (CH_2Cl_2/MeOH, 92:8, v/v) showed almost complete conversion of the starting material (Rf 0.49) into the 6-deoxy

derivative **6c** (Rf 0.37). The solution was cooled and concentrated to dryness. Column chromatography (Kieselgel, eluent CH_2Cl_2/MeOH 95:5, v/v) afforded **6c** in 92% yield. 200 MHz ^{1}H NMR ($CDCl_3$): δ 1.09 (d, 3H, CH_3, J_{5, CH_3} = 6 Hz); 1.93, 2.06 (2xs, 2x3H, 2 CH_3 acetyl); 3.54 (q, 1H, H5, $J_{4,5}$ = 2 Hz); 3.70 (m, 1H, H3); 4.08-4.28 (m, 2H, H2+H4); 4.52, 4.69 (2H, AB, CH_2 benzyl); 4.80 (d, 1H, H1, $J_{1,2}$ = 3.5 Hz); 5.61, 6.21 (2xd, 2H, 2xNH); 7.22-7.41 (m, 5H, benzyl arom.). ^{13}C[^{1}H]NMR ($CDCl_3$): δ 16.7 (CH_3); 20.3 (2xs, 2xCH_3 acetyl); 69.6 (CH_2 benzyl); 96.3 (C1); 127.9, 128.1, 128.5 (benzyl arom.).

ACKNOWLEDGMENT

The authors wish to thank Mr. C. Erkelens for recording the NMR spectra. This work was supported by the Netherlands Foundation for Chemical Research (S.O.N.) with financial aid from the Netherlands Organization for the Advancement of Pure Research (Z.W.O.).

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