Available online at www.sciencedirect.com
ScienceDirect
Carbohydrate Research 342 (2007) 520–528
Carbohydrate RESEARCH

Synthesis of a cyanoethylidene derivative of 3,6-anhydro-D-galactose and its application as glycosyl donor

Christian Vogel,[a,*] Galina Morales Torres,[a] Helmut Reinke,[a] Dirk Michalik[b] and Alice Voss[a]

[a] *University of Rostock, Institute of Chemistry, Albert-Einstein-Str. 3a, D-18059 Rostock, Germany*
[b] *Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Str. 29a, D-18059 Rostock, Germany*

Received 27 June 2006; received in revised form 18 September 2006; accepted 18 September 2006
Available online 23 October 2006

Dedicated to the memory of Professor Nikolay K. Kochetkov

Abstract—Starting from 1,2,4-tri-*O*-acetyl-3,6-anhydro-α-D-galactopyranose, 4-*O*-acetyl-3,6-anhydro-1,2-*O*-(1-cyanoethylidene)-α-D-galactopyranose (**7**) was synthesized by treatment with cyanotrimethylsilane. Additionally, 3,4-di-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-6-*O*-tosyl-α-D-galactopyranose was prepared from the corresponding bromide and both cyanoethylidene derivatives were used as donors in glycosylation reactions. The coupling with benzyl 2,4,6-tri-*O*-acetyl-3-*O*-trityl-β-D-galactopyranoside provided exclusively the β-linked disaccharides in approximately 30% yield. The more reactive methyl 2,3-*O*-isopropylidene-4-*O*-trityl-α-L-rhamnopyranoside gave with donors **3** and **7** the corresponding disaccharides in nearly 60% yield. Furthermore, the synthesis of 3,6-anhydro-4-*O*-trityl-1,2-*O*-[1-(*endo*-cyano)ethylidene]-α-D-galactopyranose, which can be used as a monomer for polycondensation reaction is described.

Keywords: 3,6-Anhydro-galactose; Cyanoethylidene derivatives; Glycosylation; X-ray structure

1. Introduction

Pursuing a program directed at the synthesis of oligosaccharide fragments by the modular design principle,[1] we were interested in elucidating the scope and limitations of 3,6-anhydro-galactose derivatives subjected to glycosylation reaction. To the best of our knowledge, there are only two report where applications of this type of sugar as glycosyl acceptor or donor have been described. A methyl α-carrabioside has been synthesized *via* glycosylation of methyl 3,6-anhydro-2-*O*-benzyl-α-D-galactopyranoside by Bernabé et al.,[2] whereas 4-*O*-acetyl-3,6-anhydro-α-D-galactopyranose 1,2-(methyl orthoacetate) (**5**) prepared by Bochkov and Kalinevitch[3] was coupled with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose to give the corresponding β-linked disaccharide in 70% yield. Unfortunately, the sugar orthoester **5** was not used for a condensation with glycosyl acceptor bearing a secondary hydroxyl group. In the course of the further development of this type of glycosylation, in many cases the trityl-cyanoethylidene condensation (TCC)[4] has been turned out to be superior compared with the orthoester procedure. Therefore, we now report the preparation of a 1,2-*O*-cyanoethylidene 3,6-anhydro-D-galactose derivative (**7**) utilized as a donor in glycosylation reaction. Furthermore, the synthesis of a corresponding monomer (**20**) carrying both cyanoethylidene as well as trityl function on the same molecule is described.

2. Results and discussion

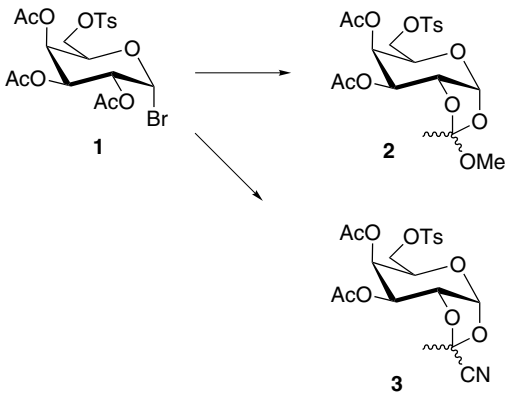
For the synthesis of the cyanoethylidene 3,6-anhydro derivative **7** (Scheme 2), two alternative routes have

* Corresponding author. Tel.: +49 381 6430; fax: +49 381 6412; e-mail: Christian.vogel@uni-rostock.de

0008-6215/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2006.09.015

been considered. Both pathways started from the acetylated 6-*O*-tosyl galactosyl bromide **1**,[5] which was prepared from 1,2,3,4-tetra-*O*-acetyl-6-*O*-tosyl-D-galactopyranose[6] according to a procedure reported by Rashid and Mackie.[7]

Following Bochkov's route,[3] bromide **1** was converted into orthoester **2** (Scheme 1), which was then subsequently cyclized to the 3,6-anhydro derivative **4** by treatment with sodium methoxide (Scheme 2). Acetylation of compound **4** provided derivative **5**, whereas treatment of the orthoester structure **4** with AcOH and acetic anhydride in pyridine led to an α/β-mixture (6:1) of the simple 3,6-anhydro triacetate **6**, which is surprisingly not described in the literature yet. Because attempted preparations of the corresponding bromide under various conditions failed, presumably due to the low stability of the pyranose ring under acidic conditions,[5] the 1,2-*O*-cyanoethylidene function was introduced by a procedure reported by Utimoto et al.[8] The treatment of compound **6** with trimethylsilyl cyanide and stannous chloride in dry MeCN provided the desired 3,6-anhydro cyanoethylidene derivative **7** in excellent 96% yield (Scheme 2). Surprisingly, the stereoselectivity of the reaction was low since an *exo–endo* mixture in a ratio of 1.0:1.5 was observed. X-ray and ^{1}H NMR studies were employed to address the absolute configuration of the cyano group in compound **7**. In ^{1}H spectra the proton signal for the methyl group of the *exo-cyano* derivative $\mathbf{7_{exo}}$ (*S*-configuration) appeared at δ 1.91 ppm downfield shifted in comparison to those from the methyl group of $\mathbf{7_{endo}}$ (*R*-configuration) at δ 1.79 ppm.[9]



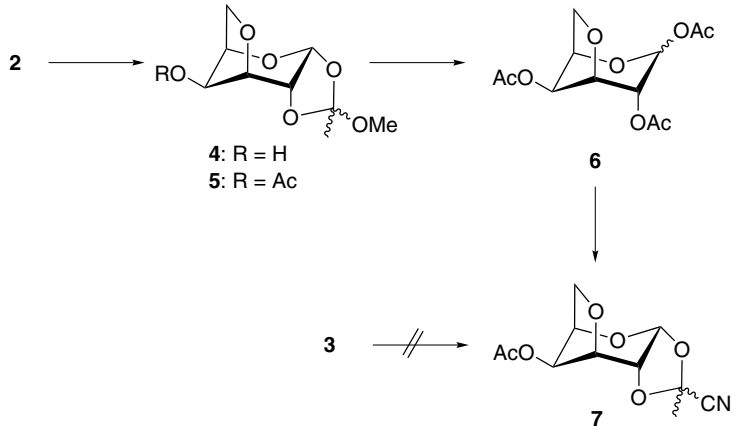
Scheme 1. Synthesis of cyanoethylidene glycosyl donor **3** by the treatment of bromide **1** with sodium cyanide and tetrabutylammonium bromide in dry MeCN.

Finally, the X-ray diffraction studies (Fig. 1) established the structure of compound $\mathbf{7_{exo}}$ and confirmed the $^1C_4$ conformation of this condensed and bridged pyranose ring.

In parallel, an alternative route for the synthesis of compound **7** *via* the cyanoethylidene derivative **3** (Scheme 1) was investigated. The treatment of bromide **1** with carefully powdered potassium cyanide, tetra-*n*-butylammonium bromide in dry MeCN[10] provided the exo/endo mixture of **3** in 96% yield. Both diastereomers could be separated by flash chromatography. Owing to the observed values for methyl groups of $\mathbf{3_{exo}}$ [δ 1.83 ppm, C(CN)CH_3] and $\mathbf{3_{endo}}$ [δ 1.76 ppm, C(CN)CH_3], the configurations of the 1,2-cis-fused five member rings could be described as having *endo*- and *exo*-cyano-ethylidene groups, respectively.

Unfortunately, all attempts to convert compound **3** into a three-ring system (**7**) were unsuccessful (Scheme 2). Obviously, the cyano group is not stable enough under basic conditions essential for the formation of the 3,6-anhydro structure. Nevertheless, intermediate **3** represents also a suitable glycosyl donor for the introduction of a galacto-3,6-anhydro moiety into oligosaccharides as shown in Schemes 4 and 5.

Next, a *galacto*-configurated glycosyl acceptor carrying a trityl ether function at the 3-O-position (**10**) was synthesized. Selective tritylation of benzyl 2,6-di-*O*-acetyl-β-D-galactopyranoside (**8**)[11] with tritylium perchlorate in the presence of 2,4,6-collidine led to the 3-*O*-trityl



Scheme 2. Synthesis of 4-*O*-acetyl-3,6-anhydro-1,2-*O*-(1-cyanoethylidene)-α-D-galactopyranose (**7**) by the treatment of the corresponding triacetate **6** with cyanotrimethylsilane.

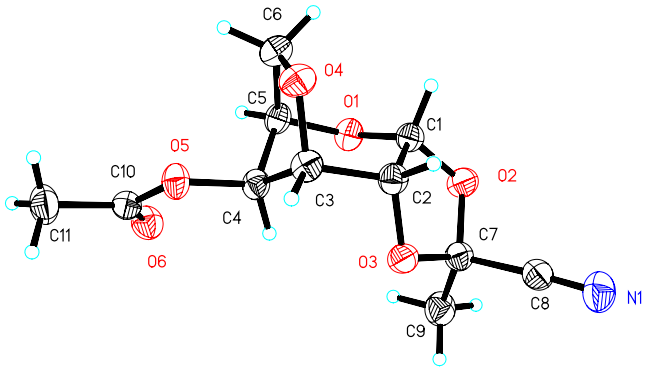
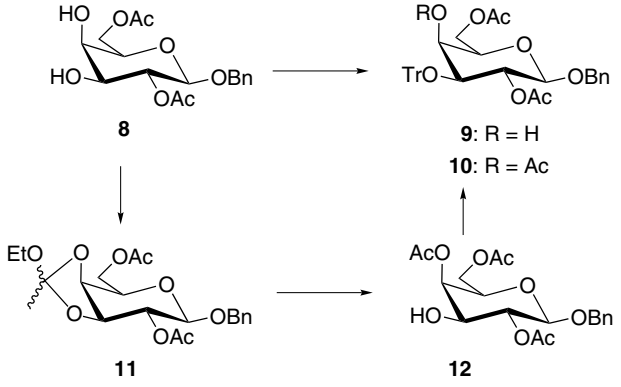


Figure 1. An ORTEP diagram of compound $\mathbf{7}_{exo}$.

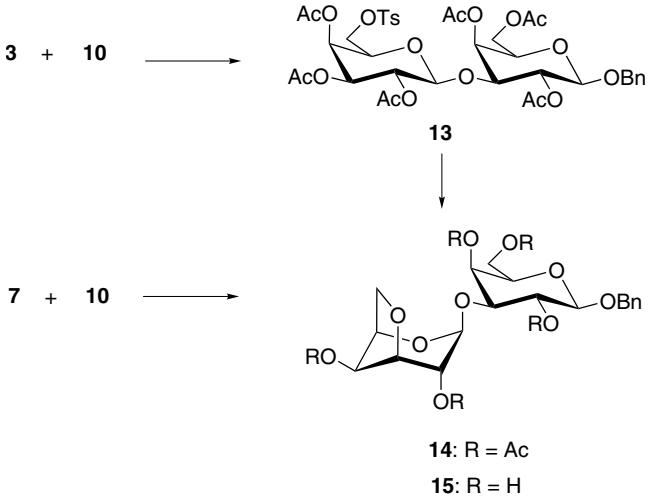
derivative **9** (72%, Scheme 3). Acetylation (Ac_2O/pyridine) catalyzed by *N*,*N*-dimethyl-4-aminopyridine gave then the full protected trityl ether **10** in 81% yield. HMBC correlation between H-3 of the pyranose ring and the quaternary carbon atom of the trityl group confirms its position at O-3. An alternative route to glycosyl acceptor **10** started from compound **8** *via* cyclic orthoester **11**, which was treated without further structural characterization with aq AcOH to form triacetate **12** in 75% overall yield. The structure of compound **12** is in accordance with the NMR spectra as well as the data from literature.[12] Finally, tritylation under conditions described above gave acceptor **10** in 75% yield. Altogether this pathway is a little favourable in comparison with the route *via* intermediate **9**.

Besides **10**, the rhamnose derivative **16**[13] was used as a model compound for a glycosyl acceptor (Scheme 5). The following synthesis of disaccharides was carried out in the presence of tritylium perchlorate in dichloromethane using vacuum technique under the standard conditions of the TCC.[13]

The coupling of the 6-*O*-tosyl donor **3** with acceptor **10** gave the expected β-(1→3)-linked disaccharide **13** in 28% isolated yield (Scheme 4). A similar outcome was



Scheme 3. Synthesis of *galacto*-configurated glycosyl acceptor **10** by two alternative routes.

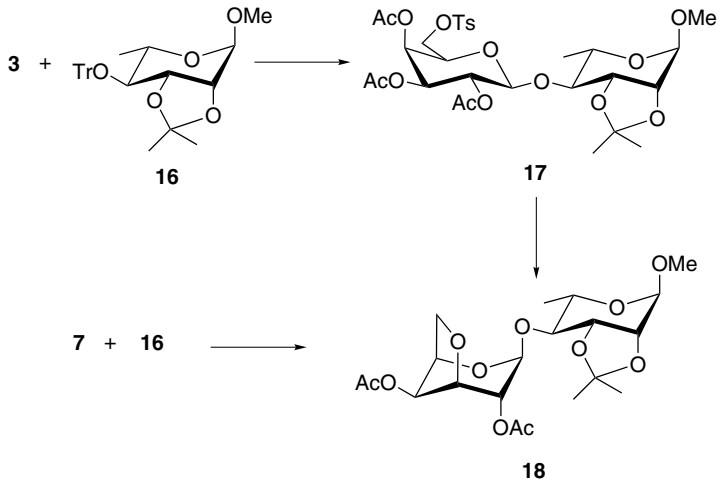


Scheme 4. Two alternative routes for the synthesis of β-(1→3)-linked 3,6-anhydro-D-galactopyranosyl-D-galactopyranoside **15**.

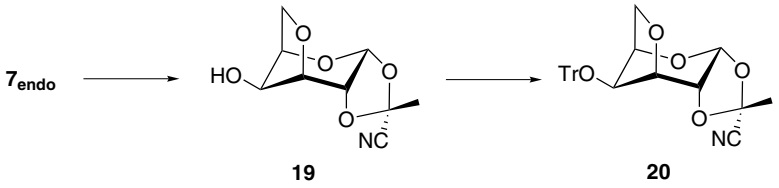
observed by the use of 3,6-anhydro donor **7** (32% yield of **14**). The NMR data secure the β-linkage between galactose moieties in compound **13**. Thus, the stereochemistry of the glycosidic linkage was assigned based on the large vicinal coupling constants $^3J_{1',2'} = 8.0$ Hz in the ^{1}H NMR and on the resonances of C-1′ at δ 101.2 in the ^{13}C NMR spectra of **13**. Determination of the stereochemistry at the anomeric centre of the anhydro residue in disaccharide **14** is not a simple task because the $^1C_4$ conformation of this ring system resulted in small coupling constants for both α- and β-linked glycosides. But, the observed coupling constant with a value almost zero argued for a trans-glycosidic linkage.

The final evidence for this assessment was given by the transformation of the 6-*O*-tosyl residue in disaccharide **13** into a 3,6-anhydro structure. The deacetylation of compounds **13** and **14** under Zemplén conditions, but, in the case of disaccharide **13** with a 10-fold excess of sodium methoxide and extended reaction time compared to **14**, provided the same deesterified 3,6-anhydro derivative **15**.

Next, condensation of the cyanoethylidene derivatives **3** and **7** with rhamnosyl acceptor **16** provided quite better results and both disaccharides **17** and **18** were obtained in approximately 60% yield. The ^{1}H and ^{13}C NMR spectra of **17** and **18** were fully consistent with the assigned structures. The β-stereochemistry of the glycosidic linkage between galactose residue and rhamnose in disaccharide **17** was evident from the large coupling constant $^3J_{1',2'} = 7.8$ Hz in the ^{1}H NMR spectra. The signal for C-1′ of compound **17** appeared in the anomeric region at δ 100.3. The coupling constant at the anomeric centre for the 3,6-anhydro residue of compound **18** was zero and indicates a trans-glycosidic linkage.



Scheme 5. Two alternative routes for the synthesis of β-(1→4)-linked 3,6-anhydro-D-galactopyranosyl-L-rhamnopyranoside **18**.



Scheme 6. Synthesis of 3,6-anhydro-4-*O*-trityl-1,2-*O*-[1-(*endo*-cyano)ethylidene]-α-D-galactopyranose (**20**) as a potential monomer for polycondensation reactions.

The treatment of tosyl derivative **17** with sodium methoxide, followed by acetylation provided disaccharide **18** in 65% yield. Again, the stereochemistry of the anomeric centre of the 3,6-anhydro-galactopyranosyl residue was confirmed by an alternative synthetic route.

In summary it may be said that the supply of suitable glycosyl donors based on 3,6-anhydro-galactose until now is limited, but, the cyanoethylidene derivative **7**, which was obtained in an excellent yield provide β-linked disaccharides in moderate yields as these first experiments have shown. It is worth noting that we also synthesized monomer **20** for application in polycondensation reactions based on the same principle. For this purpose, compound **7** was deacetylated by treatment with 0.28 M methanolic hydrochloric acid (**19**), and subsequently tritylated with tritylium perchlorate (Scheme 6).

3. Experimental

3.1. General methods

Melting points were determined with a Boetius microheating plate BHMK 05 (Rapido, Dresden) and are uncorrected. Optical rotations were measured for solns in a 2-cm cell with an automatic polarimeter 'GYROMAT' (Dr. Kernchen Co.). ^{1}H NMR spectra (500.13 and 250.13 MHz) and ^{13}C NMR spectra (125.8 and 62.8 MHz) were recorded on Bruker instruments AVANCE 500 and AC 250, with $CDCl_3$ or Me_2SO-d_6 as solvents. The calibration of spectra was carried out on solvent signals ($CDCl_3$: $\delta^1H = 7.25$, $\delta^{13}C = 77.0$; Me_2SO-d_6: $\delta^1H = 2.50$, $\delta^{13}C = 39.7$). The ^{1}H and ^{13}C NMR signals were assigned by DEPT and two-dimensional ^{1}H,^{1}H COSY, ^{1}H,^{1}H NOESY and ^{1}H,^{13}C correlation spectra (HMBC and HSQC). The mass spectra were recorded on an AMD 402/3 spectrometer (AMD Intectra GmbH). Elemental analysis was performed on a Leco CHNS-932 instrument. For the X-ray structure determination of compound $\mathbf{7_{exo}}$, an X8Apex system with CCD area detector was used ($\lambda = 0.71073$ Å, graphite monochromator). The structure was solved by direct methods (Bruker-SHELXTL). The refinement calculations were done by the full-matrix least-squares method of Bruker SHELXTL, Vers.5.10, Copyright 1997, Bruker Analytical X-ray Systems. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were put into theoretical positions and refined using the riding model. CCDC 610435 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44

1223 336033; e-mail: deposit@ccdc.cam.ac.uk): All washing solns were cooled to ~5 °C. The $NaHCO_3$ and NaCl solns were saturated. Trityl perchlorate was obtained and purified as described in Ref. 4. All reactions were monitored by TLC (Silica Gel 60, F_{254}, E. Merck KGaA). The following solvent systems (v/v) were used: (A_1) 1:2, (A_2) 1:1, (A_3) 2:1, (A_4) 5:1 petroleum ether–EtOAc; (B_1) 1:3, (B_2) 1:1 toluene–EtOAc; (C_1) 3:1 $CHCl_3$–MeOH; (E_1) 5:1:1 toluene–heptane–EtOH. The spots were made visible by spraying with methanolic 10% H_2SO_4 soln and charring them for 3–5 min with a heat gun. The detection of benzyl derivatives was effected by UV fluorescence. Preparative flash chromatography was performed by elution from the columns of slurry-packed Silica Gel 60 (E. Merck, 63–200 or 40–63 μm). All solvents and reagents were purified and dried according to standard procedures.[14] After a classical work-up of the reaction mixtures, the organic layer as a rule, were dried over $MgSO_4$, and then concentrated under diminished pressure (rotary evaporator).

3.2. 3,4-Di-*O*-acetyl-1,2-*O*-[1-(*exo*-,*endo*-cyano)ethylidene]-6-*O*-tosyl-α-D-galactopyranose (3)

The heterogeneous mixture of freshly prepared 2,3,4-tri-*O*-acetyl-6-*O*-tosyl-α-D-galactopyranosyl bromide (**1**)[6] (1.042 g, 2.2 mmol), carefully powdered sodium cyanide (650 mg, 13.3 mmol) and tetrabutylammonium bromide (299 mg, 0.9 mmol) in dry MeCN (6 mL) was vigorously stirred at room temperature for 15 h in the dark (TLC, solvent A_3). The mixture was then diluted with $CHCl_3$ (60 mL), washed with water (7 × 20 mL), passed through a bed of silica gel and concentrated. The residue was then subjected to column chromatography (gradient EtOAc–toluene 30→60%) to yield **3** (96%), separated into fractions containing pure *exo*-isomer (470 mg), an *exo*-, *endo*-mixture (231 mg) and pure *endo*-isomer (198 mg).

The *exo*-isomer had: mp: 98–100 °C (from EtOAc–heptane); $[\alpha]_D^{25}$ +65 (*c* 1.0, $CHCl_3$); R_f 0.49 (solvent A_3); ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 7.79–7.72, 7.38–7.31 (2m, 4H, $SO_2C_6H_4CH_3$), 5.76 (d, 1H, $^3J_{1,2}$ 5.0 Hz, H-1), 5.35 (dd, 1H, $^3J_{4,5}$ 2.1 Hz, H-4), 4.94 (dd, 1H, $^3J_{3,4}$ 3.7 Hz, H-3), 4.30–4.25 (m, 2H, H-2, H-5), 4.15–4.00 (m, 2H, H-6a,6b), 2.45 (s, 3H, $SO_2C_6H_4CH_3$), 2.05 (s, 6H, 2 × CH_3CO, one signal is isochronic), 1.83 [s, 3H, CH_3(CN)C]; ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 169.74, 169.46 (2 × CH_3CO), 145.31, 132.25, 129.96, 128.02 ($SO_2C_6H_4CH_3$, two signals are isochronic), 116.65 [CH_3(*C*N)C], 98.65 (C-1), 97.41 [CH_3(CN)*C*], 72.74 (C-2), 70.63, 69.42 (C-3, C-5), 65.95 (C-6), 64.98 (C-4), 25.72 [*C*H_3(CN)C], 21.66 ($SO_2C_6H_4CH_3$), 20.56, 20.40 (2 × CH_3CO). Anal. Calcd for $C_{20}H_{23}NO_{10}S$ (469.46): C, 51.17; H, 4.94; N, 2.98; S, 6.83. Found: C, 51.07; H, 5.11; N, 2.48; S, 6.43.

The syrup endo-isomer had: $[\alpha]_D^{23}$ +61.6 (*c* 1.0, $CHCl_3$); R_f 0.35 (solvent A_3); ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 7.79–7.72, 7.38–7.31 (2m, 4H, $SO_2C_6H_4CH_3$), 5.69 (d, 1H, $^3J_{1,2}$ 4.6 Hz, H-1), 5.47 (dd, 1H, $^3J_{4,5}$ 2.5 Hz, H-4), 5.32 (dd, 1H, $^3J_{3,4}$ 3.05 Hz, H-3), 4.36 (dd, 1H, $^3J_{2,3}$ 7.5 Hz, H-2), 4.32 (dd, 1H, $^3J_{5,6a}$ 6.2 Hz, H-5), 4.16–4.03 (m, 2H, H-6a,6b), 2.45 (s, 3H, $SO_2C_6H_4CH_3$), 2.08, 2.05 (2s, 6H, 2 × CH_3CO), 1.76 [s, 3H, CH_3(CN)C]; ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 169.46, 169.42 (2 × CH_3CO), 145.38, 132.24, 130.02, 128.01 ($SO_2C_6H_4CH_3$, two signals are isochronic), 117.39 [CH_3(*C*N)C], 98.68 [CH_3(CN)*C*], 98.49 (C-1), 76.26 (C-2), 69.65, 69.39 (C-3, C-5), 65.78 (C-6), 65.76 (C-4), 26.81 [*C*H_3(CN)C], 21.67 ($CH_3C_6H_4$), 20.55, 20.47 (2 × CH_3CO). Anal. Calcd for $C_{20}H_{23}NO_{10}S$ (469.46): C, 51.17; H, 4.94; N, 2.98; S, 6.83. Found: C, 51.33; H, 5.16; N, 3.07; S, 6.54.

3.3. 1,2,4-Tri-*O*-acetyl-3,6-anhydro-D-galactopyranose (6)

3,6-Anhydro-1,2-*O*-(1-methoxyethylidene)-α-D-galactopyranose (**4**)[3] (880 mg, 4 mmol) was dissolved in aq 90% AcOH (20 mL) at ambient temperature, and kept for 30 min under these conditions. After concentration, the residue was dissolved in dry pyridine (10 mL) and freshly distilled Ac_2O (6 mL) was added dropwise under an atmosphere of argon at 0 °C. After stirring for 2 h at room temperature (TLC, solvent B_2), the mixture was poured into ice water (100 mL). The aq layer was extracted with $CHCl_3$ (2 × 50 mL), the combined extracts were washed successively with ice water (2 × 50 mL), aq $NaHCO_3$ (2 × 50 mL) and ice water (2 × 50 mL), dried and concentrated. Traces of pyridine were removed by evaporation with repeated addition of toluene. The crude material was purified by column chromatography (solvent B_2) to yield **6** (976 mg, 84%, 6:1 ratio of the α,β anomers) as a colourless syrup: R_f 0.52 (solvent B_2); ^{1}H NMR of **6α** ($CDCl_3$, 250.13 MHz): δ 6.12 (d, 1H, $^3J_{1,2}$ 2.9 Hz, H-1), 5.44 (d, 1H, $^3J_{4,5}$ 1.8 Hz, H-4), 5.21 (dd, $^3J_{2,3}$ 5.5 Hz, H-2), 4.50 (br, 1H, H-5), 4.46 (d, 1H, H-3), 4.28 (d, 1H, $^2J_{6a,b}$ 10.6 Hz, H-6a), 4.03 (dd, 1H, $^3J_{5,6a}$ 3.1 Hz, H-6b), 2.17, 2.07, 2.06 (3s, 9H, 3 × CH_3CO); ^{13}C NMR of **6α** ($CDCl_3$, 62.8 MHz): δ 169.72, 169.54, 168.46 (CH_3CO), 87.83 (C-1), 76.71 (C-2), 75.92, 72.78 (C-3, C-5), 69.45 (C-6), 69.27 (C-4), 20.87, 20.70 (3 × CH_3CO, one signal is isochronic). Anal. Calcd for $C_{12}H_{16}O_8$ (288.25): C, 50.00; H, 5.59. Found: C, 50.23; H, 5.73.

3.4. 4-*O*-Acetyl-3,6-anhydro-1,2-*O*-[1-(*exo*-,*endo*-cyano)-ethylidene]-α-D-galactopyranose (7)

Trimethylsilyl cyanide (0.9 mL, 6.8 mmol) and stannous chloride (68.0 mg, 0.36 mmol) were added to a stirred soln of compound **6** (667 mg, 2.3 mmol) in dry MeCN (8 mL) under argon at room temperature. After stirring

for 6 h (TLC, solvent B_1), the mixture was diluted with $CHCl_3$ (50 mL). The organic layer was washed with water (5×20 mL), concentrated and toluene was coevaporated several times from the residue. Column chromatography (gradient EtOAc–toluene 30→60%) furnished compound **7** in 96% yield, separated into fractions containing pure *exo*-isomer (105 mg) as colourless needles, an *exo*-, *endo*-mixture (292 mg) and pure *endo*-isomer (168 mg) as colourless crystals.

The exo-isomer had: mp 105–109 °C (from EtOAc–heptane); $[\alpha]_D^{23}$ +10.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 5.62 (d, 1H, $^3J_{1,2}$ 3.2 Hz, H-1), 5.38 (d, 1H, $^3J_{4,5}$ 1.8 Hz, H-4), 4.54–4.49 (m, 2H, H-2, H-3), 4.47 (br, 1H, H-5), 4.08 (d, 1H, $^2J_{6a,b}$ 10.5 Hz, H-6b), 4.00 (dd, 1H, $^3J_{5,6a}$ 3.0 Hz, H-6a), 2.08 (s, 3H, CH_3CO), 1.91 [s, 3H, CH_3(CN)C]; ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 169.52 (CH_3CO), 116.45 [$CH_3(CN)$C], 101.68 [CH_3(CN)*C*], 96.48 (C-1), 79.53 (C-2), 76.38 (C-5), 75.38 (C-3), 71.92 (C-4), 71.01 (C-6), 25.98 [*C*H_3(CN)C], 20.79 (*C*H_3CO). Anal. Calcd for $C_{11}H_{13}NO_6$ (255.22): C, 51.77; H, 5.13; N, 5.49. Found: C, 51.72; H, 5.15; N, 5.34.

The endo-isomer had: mp 112–114 °C (from EtOAc–heptane); $[\alpha]_D^{23}$ +8.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 5.64 (d, 1H, $^3J_{1,2}$ 3.2 Hz, H-1), 5.50 (d, 1H, $^3J_{4,5}$ 1.8 Hz, H-4), 4.65–4.53 (m, 2H, H-3, H-5), 4.36 (dd, 1H, $^3J_{2,3}$ 5.0 Hz, H-2), 4.12 (d, 1H, $^2J_{6a,b}$ 10.5 Hz, H-6b), 4.07 (dd, 1H, $^3J_{5,6a}$ 3.0 Hz, H-6a), 2.08 (s, 3H, CH_3CO), 1.79 [s, 3H, CH_3(CN)C]; ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 169.31 (CH_3CO), 117.42 [$CH_3(CN)$C], 101.62 [CH_3(CN)*C*], 97.65 (C-1), 80.55 (C-2), 75.85 (C-5), 75.76 (C-3), 72.56 (C-4), 70.12 (C-6), 26.54 [*C*H_3(CN)C], 20.81 (*C*H_3CO). Anal. Calcd for $C_{11}H_{13}NO_6$ (255.22): C, 51.77; H, 5.13; N, 5. 49. Found: C, 51.75; H, 5.20; N, 5.31.

3.5. Benzyl 2,6-di-*O*-acetyl-3-*O*-trityl-β-D-galactopyranoside (9)

Trityl perchlorate (0.96 g, 2.8 mmol) and 2,4,6-collidine (0.5 mL, 3.6 mmol) were added in portions to a soln of benzyl 2,6-di-*O*-acetyl-β-D-galactopyranoside (**8**)[11] (528 mg, 1.5 mmol) in CH_2Cl_2 (10 mL). After stirring for 15 min at room temperature under argon (TLC, solvent A_3), the mixture was diluted with $CHCl_3$ (60 mL) and the organic layer was washed with water (3×30 mL), dried and concentrated. The residue was purified by column chromatography (solvent A_3) to afford **9** (638 mg, 72%) as an amorphous colourless solid: mp 204–205 °C; $[\alpha]_D^{21}$ −26.5 (*c* 1.0, $CHCl_3$); R_f 0.55 (solvent A_3); ^{1}H NMR ($CDCl_3$, 500.13 MHz): δ 7.48, 7.32–7.23 (2m, 20H, C_6H_5, $CH_2C_6H_5$), 5.46 (dd, 1H, $^3J_{2,3}$ 9.8 Hz, H-2), 4.83, 4.55 (2d, 2H, ^2J 12.3 Hz, $CH_2C_6H_5$), 4.24 (d, 1H, $^3J_{1,2}$ 7.9 Hz, H-1), 4.16 (dd, 1H, $^2J_{6a,b}$ 11.4 Hz, $^3J_{5,6a}$ 6.9 Hz, H-6a), 4.01 (dd, 1H, $^3J_{5,6b}$ 6.0 Hz, H-6b), 3.71 (dd, 1H, $^3J_{3,4}$ 3.2 Hz, H-3), 3.21 (ddd, 1H, $^3J_{4,5}$ 1.2 Hz, H-5), 2.51 (br, 1H, H-4), 2.29 (br, 1H, OH-4), 2.00, 1.95 (2s, 6H, $2 \times CH_3CO$); ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 170.50, 169.64 ($2 \times CH_3CO$), 144.19, 137.23, 128.85, 128.29, 127.95, 127.66, 127.65, 127.47 [$C_6H_5CH_2$, $C(C_6H_5)_3$, 16 signals are isochronic], 99.69 (C-1), 87.70 [$C(C_6H_5)_3$], 74.26 (C-3), 71.46 (C-5), 70.42 (C-2), 69.90 ($C_6H_5CH_2$), 67.09 (C-4), 62.78 (C-6), 21.14, 20.80 ($2 \times COCH_3$). Anal. Calcd for $C_{36}H_{36}O_8$ (596.67): C, 72.47; H, 6.08. Found: C, 72.52; H, 6.21.

3.6. Benzyl 2,4,6-tri-*O*-acetyl-3-*O*-trityl-β-D-galactopyranoside (10)

Via **9**. Compound **9** (466 mg, 0.8 mmol) was added to a soln of *N*,*N*-dimethyl-4-aminopyridine (94 mg, 0.8 mmol) in Ac_2O (5 mL) and pyridine (4 mL). The reaction mixture was then kept for 24 h under argon at room temperature (TLC, solvent A_4). After adding EtOH (3 mL) at 0 °C stirring was continued for further 20 min at ambient temperature. The reaction mixture was then diluted with $CHCl_3$ (50 mL) and poured into ice water. The phases were separated, and the aqueous phase was extracted with $CHCl_3$ (2×25 mL). The combined organic soln was successively washed with ice water (2×50 mL), aq $NaHCO_3$ (2×50 mL), ice water (2×50 mL), dried and concentrated. Traces of pyridine were removed by evaporation with repeated addition of toluene. The residue was purified by column chromatography (solvent A_4) to yield **9** (405 mg, 81%) as a light-yellow syrup.

Via **12**. Trityl perchlorate (1.9 g, 5.5 mmol) and 2,4,6-collidine (0.9 mL, 6.5 mmol) were added to a soln of **12** (1.7 g, 4.3 mmol) in CH_2Cl_2 (32 mL). After stirring for 20 min at ambient temperature, an additional amount of 2,4,6-collidine (0.4 mL, 3.2 mmol) and trityl perchlorate (0.86 g, 2.6 mmol) was added and stirring was continued for 1 h (TLC, solvent A_3). The reaction mixture was then diluted with $CHCl_3$ (200 mL) and the organic layer was washed with water (3×60 mL), dried and concentrated. The residue was purified by column chromatography (solvent A_3) to give **10** (2.06 g, 75%) as a light-yellow syrup: $[\alpha]_D^{21}$ −9.7 (*c* 1.0, $CHCl_3$); R_f 0.25 (solvent A_3); ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 7.44–7.34, 7.33–7.20 (2m, 20H, C_6H_5,$CH_2C_6H_5$), 5.50 (dd, 1H, $^3J_{2,3}$ 9.9 Hz, H-2), 4.84, 4.53 (2d, 2H, ^2J 12.4 Hz, $CH_2C_6H_5$), 4.30 (d, 1H, H-4), 4.19 (d, 1H, $^3J_{1,2}$ 7.9 Hz, H-1), 3.90 (m, 2H, H-6a,6b), 3.62 (dd, 1H, $^3J_{3,4}$ 3.2 Hz, H-3), 3.21 (m, 1H, H-5), 2.20, 2.00, 1.80 (3s, 9H, $3 \times CH_3CO$); ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 170.29, 169.94, 169.80 ($3 \times CH_3CO$), 144.09, 137.03, 129.06, 128.32, 127.74, 127.69, 127.62, 127.35 [$C_6H_5CH_2$, $C(C_6H_5)_3$, 16 signals are isochronic], 100.17 (C-1), 87.85 [$C(C_6H_5)_3$], 72.61 (C-3), 71.32 (C-5), 70.52 (C-2), 70.22 ($C_6H_5CH_2$), 69.53 (C-4), 62.29 (C-6), 21.21, 21.09, 20.68

($3 \times CH_3CO$). Anal. Calcd for $C_{38}H_{38}O_9$ (638.70): C, 71.46; H, 6.00. Found: C, 71.42; H, 6.06.

3.7. Benzyl 2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (12)

Triethyl orthoacetate (5×2.6 mL, total 71 mmol) and anhyd *p*-toluenesulfonic acid (2×88 mg, total 0.94 mmol) were added in portions to a stirred soln of compound **8** (5.047 g, 11.9 mmol) in abs CH_2Cl_2 (83 mL) at room temperature. After stirring for 2 h (TLC, solvent A_1, R_f 0.54), Et_3N (40 mL) and CH_2Cl_2 (300 mL) were successively added and the organic layer was washed with water (2×150 mL), dried and concentrated. The residue (**11**) was dissolved in aq 80% AcOH (40 mL), and the reaction mixture was kept for 10 min at room temperature (TLC, solvent A_1), diluted then with toluene (50 mL) and evaporated. After repeated coevaporation with solvent E_1 (4×60 mL) crystalline compound **12** (3.5 g, 75%) was obtained: mp 130–133 °C (from diisopropyl ether), lit.[12] mp 133 °C; $[\alpha]_D^{22}$ −46.2 (*c* 1.0, $CHCl_3$), lit.[12] $[\alpha]_D$ −40 (*c* 0.82, $CHCl_3$); R_f 0.24 (solvent A_1); ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 7.37–7.26 (m, 5H, $CH_2C_6H_5$), 5.31 (dd, 1H, $^3J_{3,4}$ 3.8 Hz, $^3J_{4,5}$ 1.0 Hz, H-4), 5.04 (dd, 1H, $^3J_{2,3}$ 10.0 Hz, H-2), 4.89, 4.62 (2d, 2H, ^2J 12.5 Hz, $CH_2C_6H_5$), 4.47 (d, 1H, $^3J_{1,2}$ 8.0 Hz, H-1), 4.22–4.10 (m, 2H, H-3, H-5), 3.84–3.75 (m, 2H, H-6a,6b), 2.67 (br, 1H, OH), 2.14, 2.07 (2s, 9H, $3 \times CH_3CO$, one signal is isochronic); ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 171.12, 170.93, 170.50 ($3 \times CH_3CO$), 136.80, 128.40, 127.96, 127.76 ($C_6H_5CH_2$, two signals are isochronic), 99.41 (C-1), 72.69 (C-3), 71.34 (C-5), 70.98 (C-2), 70.63 ($C_6H_5CH_2$), 69.66 (C-4), 61.91 (C-6), 20.91, 20.73, 20.70 ($3 \times CH_3CO$). Anal. Calcd for $C_{19}H_{24}O_9$ (396.39): C, 57.57; H, 6.10. Found: C, 57.85; H, 6.23.

3.8. General procedure of glycosylations

The CED glycosyl donor (**3** or **7**) together with 10 mol % excess of trityl ether glycosyl acceptor (**10** or **16**) dissolved in dry NO_2Me (1 mL/mmol) and trityl perchlorate (10 mol % of the amount of CED glycosyl donor) likewise dissolved in dry NO_2Me (1 mL/0.1 mmol) were placed in separate limbs of a turning-fork-shaped tube, and both solns were freeze-dried. NO_2Me was then distilled (0.133 Pa) from CaH_2 into the limb containing the sugar derivatives, and lyophilization was repeated followed by drying of the residuals for several hours. CH_2Cl_2 was distilled (0.133 Pa) from CaH_2 into the tube and the solns were mixed and kept overnight at room temperature in the dark. The bright yellow coloured reaction mixture was treated with 1:1 MeOH–pyridine (0.05 mL/mmol), and the decolourized soln was diluted with $CHCl_3$ and washed with water. The organic phase was dried and evaporated. The crude material was purified by column chromatography (gradient EtOAc–toluene 30→60% with 1% Et_3N).

3.9. Benzyl 2,3,4-tri-*O*-acetyl-6-*O*-tosyl-β-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (13)

Reagents: CED glycosyl donor **3** (115 mg, 0.24 mmol); trityl ether glycosyl acceptor **10** (171 mg, 0.27 mmol); initiator trityl perchlorate (9 mg, 0.024 mmol); disaccharide **13** (57 mg, 28%): mp 73–75 °C (amorphous white solid); $[\alpha]_D^{22}$ −21.9 (*c* 1.0, $CHCl_3$); R_f 0.24 (solvent A_2); ^{1}H NMR ($CDCl_3$, 500.13 MHz): δ 7.75, 7.37–7.26 (2m, 9H, $CH_2C_6H_5$, $SO_2C_6H_4CH_3$), 5.41 (d, 1H, $^3J_{3,4}$ 3.5 Hz, H-4), 5.29 (d, 1H, $^3J_{3',4'}$ 3.5 Hz, H-4′), 5.24 (dd, 1H, $^3J_{2,3}$ 10.0 Hz, H-2), 5.02 (d, 1H, $^3J_{2',3'}$ 10.5 Hz, H-2′), 4.89–4.86 (m, 2H, H-3′, $CH_2C_6H_5$), 4.60 (d, 1H, ^2J 12.5 Hz, $CH_2C_6H_5$), 4.51 (d, 1H, $^3J_{1',2'}$ 8.0 Hz, H-1′), 4.40 (d, 1H, $^3J_{1,2}$ 8.2 Hz, H-1), 4.20–4.05 (m, 3H, H-6a,6b, H-6a′), 3.94–3.86 (m, 2H, H-5′, H-6b′), 3.85 (dd, 1H, H-3), 3.81 (m, 1H, $^3J_{5,6a} = {}^3J_{5,6b}$ 6.3 Hz, $^3J_{4,5}$ 0.8 Hz, H-5), 2.45 (s, 3H, $SO_2C_6H_4CH_3$), 2.12, 2.07, 2.04, 2.03, 1.99, 1.93 (6s, 18H, CH_3CO); ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 170.52, 170.12, 170.03, 170.00, 169.19, 168.97 ($6 \times CH_3CO$), 145.29, 136.87, 132.42, 130.02, 128.43, 127.93, 127.90, 127.74 ($C_6H_5CH_2$, $SO_2C_6H_4CH_3$, four signals are isochronic), 101.17 (C-1′), 99.41 (C-1), 75.64 (C-3), 71.32 (C-5), 71.11 (C-5′), 71.02 (C-2), 70.39 (C-3′), 70.30 ($C_6H_5CH_2$), 69.22 (C-4), 68.33 (C-2′), 66.77 (C-4′), 66.62 (C-6′), 62.10 (C-6), 21.63 ($SO_2C_6H_4CH_3$), 20.88, 20.75, 20.63, 20.51, 20.45, 20.43 ($6 \times COCH_3$). Anal. Calcd for $C_{38}H_{46}O_{19}S$ (838.83): C, 54.41; H, 5.53; S, 3.82. Found: C, 54.18; H, 5.57; S, 3.80.

3.10. Benzyl 3,6-anhydro-2,4-di-*O*-acetyl-β-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (14)

Reagents: CED glycosyl donor **7** (226 mg, 0.88 mmol); trityl glycosyl acceptor **10** (623 mg, 0.97 mmol); initiator trityl perchlorate (30 mg, 0.08 mmol); disaccharide **14** (177 mg, 32%): mp 61–63 °C (amorphous white solid); $[\alpha]_D^{22}$ −36.6 (*c* 1.1, $CHCl_3$); R_f 0.33 (solvent A_2); ^{1}H NMR ($CDCl_3$, 500.13 MHz): δ 7.34–7.26 (m, 5H, $CH_2C_6H_5$), 5.42 (d, 1H, $^3J_{3,4}$ 3.5 Hz, H-4), 5.26 (dd, 1H, $^3J_{2,3}$ 10.0 Hz, H-2), 5.18 (d, 1H, $^3J_{4',5'}$ 1.8 Hz, H-4′), 4.89 (d, 1H, $^3J_{2',3'}$ 4.7 Hz, H-2′), 4.88, 4.61 (2d, 2H, ^2J 12.5 Hz, $CH_2C_6H_5$), 4.66 (s, 1H, H-1′), 4.41 (d, 1H, $^3J_{1,2}$ 8.0 Hz, H-1), 4.32 (br, 1H, H-5′), 4.28 (d, 1H, H-3′), 4.23 (d, 1H, $^2J_{6a',6b'}$ 10.0 Hz, H-6a′), 4.14 (m, 2H, H-6a,6b), 3.81–3.76 (m, 3H, H-3, H-5, H-6b′), 2.17, 2.08, 2.07, 2.05, 2.03 (5s, 15H, CH_3CO); ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 170.48, 170.37, 169.86, 169.63, 169.41 ($5 \times CH_3CO$), 136.89, 128.41, 127.90, 127.78 ($C_6H_5CH_2$, two signals are isochronic), 99.67

(C-1), 99.67 (C-1′), 76.23 (C-3), 76.17 (C-3′), 75.42 (C-5′), 73.22 (C-2′), 73.22 (C-4′), 71.34 (C-5), 70.38 (C-6′), 70.35 ($C_6H_5CH_2$), 70.25 (C-2), 67.91 (C-4), 62.14 (C-6), 20.89, 20.84, 20.84, 20.78, 20.74 ($5\times COCH_3$). Anal. Calcd for $C_{29}H_{36}O_5$ (624.59): C, 55.77; H, 5.8. Found: C, 55.64; H, 5.75.

3.11. Benzyl 3,6-anhydro-β-D-galactopyranosyl-(1→3)-β-D-galactopyranoside (15)

Via **13**. A methanolic sodium methoxide soln (1.0 M, 0.5 mL) was added to a soln of compound **13** (47 mg, 0.056 mmol) in dry MeOH (5 mL). After stirring for 18 h at room temperature, the reaction mixture was neutralized with IRC-120 (H^+) resin, filtered, dried and concentrated. Column chromatography (solvent A_1) of the residue gave disaccharide **15** (19 mg, 83%) as a colourless syrup.

Via **14**. A methanolic sodium methoxide soln (1.0 M, 0.05 mL) was added to a soln of compound **14** (44 mg, 0.07 mmol) in dry MeOH (5 mL). After stirring for 2 h at ambient temperature, the reaction mixture was neutralized with IRC-120 (H^+) resin, filtered and dried and concentrated. Chromatographically, purification (solvent A_1) of the residue provided **15** (22 mg, 75%) as a colourless syrup: $[\alpha]_D^{22}$ −68.9 (*c* 0.89, MeOH); R_f 0.33 (solvent C_1); ^{1}H NMR (Me_2SO-d_6, 500.13 MHz): δ 7.40–7.26 (m, 5H, $C_6H_5CH_2$), 5.33 (d, 1H, $^3J_{2',OH}$ 4.7 Hz, OH-2′), 5.10 (d, 1H, $^3J_{4',OH}$ 4.0 Hz, OH-4′), 5.02 (d, 1H, $^3J_{2,OH}$ 5.4 Hz, OH-2), 4.80, 4.58 (2d, 2H, ^2J 12.3 Hz, $C_6H_5CH_2$), 4.68 (s, 1H, H-1′), 4.63 (br, 1H, OH-6), 4.43 (d, 1H, $^2J_{6a',6b'}$ 9.0 Hz, H-6a′), 4.34 (d, 1H, $^3J_{4,OH}$ 6.8 Hz, OH-4), 4.23 (d, 1H, $^3J_{1,2}$ 7.7 Hz, H-1), 4.12 (br, 1H, H-4′), 4.04 (br, 1H, H-5′), 3.89–3.86 (m, 3H, H-4, H-2′, H-3′), 3.68 (dd, 1H, $^2J_{6a',6b'}$ 9.0 Hz, $^3J_{5',6b'}$ 3.0 Hz, H-6b′), 3.58–3.47 (m, 3H, H-2, H-6a,6b), 3.35 (m, 1H, $^3J_{5,6a} = {}^3J_{5,6b}$ 6.3 Hz, $^3J_{4,5}$ 1.0 Hz, H-5), 3.31 (dd, 1H, $^3J_{2,3}$ 9.8 Hz, $^3J_{3,4}$ 3.4 Hz, H-3); ^{13}C NMR (Me_2SO-d_6, 125.8 MHz): δ 138.28, 128.25, 127.72, 127.45 ($C_6H_5CH_2$, two signals are isochronic), 104.39 (C-1′), 102.92 (C-1), 81.76 (C-3), 80.94 (C-2′), 77.46 (C-5′), 75.38 (C-5), 72.77 (C-3′), 69.81 (C-4′), 69.70 (C-2), 69.53 ($C_6H_5CH_2$), 69.27 (C-6′), 67.82 (C-4), 60.26 (C-6); MS, CI (*m*/*z*): 415 $[M]^+$.

3.12. Methyl 2,3,4-tri-*O*-acetyl-6-*O*-tosyl-β-D-galacto-pyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (17)

Reagents: CED glycosyl donor **3** (94 mg, 0.20 mmol) trityl glycosyl acceptor **16**[13] (100 mg, 0.22 mmol); initiator trityl perchlorate (6.9 mg, 0.02 mmol); disaccharide **17** (78 mg, 59%): $[\alpha]_D^{21}$ −17.4 (*c* 0.87, $CHCl_3$); R_f 0.27 (solvent A_3); ^{1}H NMR ($CDCl_3$, 500.13 MHz): δ 7.74, 7.32 (2m, 4H, $SO_2C_6H_4CH_3$), 5.33 (dd, 1H, $^3J_{4',5'}$ 1.0 Hz, H-4′), 5.07 (dd, 1H, $^3J_{2',3'}$ 10.4 Hz, H-2′), 5.00 (dd, 1H, $^3J_{3',4'}$ 3.4 Hz, H-3′), 4.87 (d, 1H, $^3J_{1',2'}$ 7.8 Hz, H-1′), 4.83 (d, 1H, $^3J_{1,2}$ 0.8 Hz, H-1), 4.07 (dd, 1H, $^2J_{6a',6b'}$ 10.0 Hz, $^3J_{5',6a'}$ 6.6 Hz, H-6a′), 4.05 (dd, 1H, $^3J_{2,3}$ 5.7 Hz, H-2), 4.00 (dd, 1H, $^3J_{3,4}$ 7.3 Hz, H-3), 4.00 (dd, 1H, $^2J_{6a',6b'}$ 10.0 Hz, $^3J_{5',6b'}$ 6.2 Hz, H-6b′), 3.89 (m, 1H, H-5′), 3.56 (dq, 1H, $^3J_{5,6}$ 6.2 Hz, H-5), 3.47 (dd, 1H, $^3J_{4,5}$ 10.0 Hz, H-4), 3.34 (s, 3H, OCH_3), 2.44 (s, 3H, $SO_2C_6H_4CH_3$), 2.04, 2.03, 1.95 (3s, 9H, CH_3CO), 1.47, 1.31 [2s, 6H, $C(CH_3)_2$], 1.23 (d, 3H, H-6); ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 169.98, 169.94, 169.65 ($3\times CH_3CO$), 145.21, 132.33, 129.98, 127.99 ($SO_2C_6H_4CH_3$, two signals are isochronic), 109.37 [$C(CH_3)_2$], 100.28 (C-1′), 97.83 (C-1), 80.15 (C-4), 77.98 (C-3), 75.94 (C-2), 70.69 (C-5′), 70.64 (C-3′), 68.92 (C-2′), 67.00 (C-4′), 66.19 (C-6′), 63.78 (C-5), 54.80 (OCH_3), 27.96, 26.29 [$2\times C(CH_3)_2$], 21.64 ($SO_2C_6H_4CH_3$), 20.79, 20.51, 20.50 ($3\times COCH_3$), 17.54 (C-6). Anal. Calcd for $C_{29}H_{40}O_{15}S$ (660.68): C, 52.72; H, 6.10; S, 4.85. Found: C, 52.68; H, 6.24; S, 4.40.

3.13. Methyl 3,6-anhydro-2,4-di-*O*-acetyl-β-D-galacto-pyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamno-pyranoside (18)

Reagents: CED glycosyl donor **7** (51.7 mg, 0.2 mmol); trityl glycosyl acceptor **16** (100 mg, 0.22 mmol); initiator trityl perchlorate (7 mg, 0.02 mmol); disaccharide **18** (54 mg, 60%).

Via **17**. A methanolic sodium methoxide soln (1.0 M, 1.25 mL) was added to a soln of compound **17** (245 mg, 0.37 mmol) in dry MeOH (5 mL). After stirring for 18 h at ambient temperature, the reaction mixture was neutralized with IRC-120 (H^+) resin, filtered and dried and concentrated. Ac_2O (2.0 mL) was added dropwise to a soln of the residue in dry pyridine (5 mL) under an atmosphere of argon at 0 °C. After stirring for 2 h at room temperature (TLC, solvent A_3), the mixture was poured into ice water (50 mL). The aqueous layer was extracted with $CHCl_3$ (2×25 mL), the combined extracts were washed successively with ice water (2×25 mL), aq $NaHCO_3$ (2×25 mL) and ice water (2×25 mL), dried and concentrated. Traces of pyridine were removed by evaporation with repeated additions of toluene. The crude material was purified by column chromatography (eluent gradient EtOAc 30→60% in toluene with 1% Et_3N) to yield **18** (108 mg, 65%) as a colourless syrup: $[\alpha]_D^{21}$ −57.5 (*c* 0.8, $CHCl_3$); R_f 0.46 (solvent A_3); ^{1}H NMR ($CDCl_3$, 500.13 MHz): δ 5.25 (d, 1H, $^3J_{4',5'}$ 1.8 Hz, H-4′), 5.18 (s, 1H, H-1′), 5.03 (d, 1H, $^3J_{2',3'}$ 4.8 Hz, H-2′), 4.82 (d, 1H, $^3J_{1,2}$ 0.6 Hz, H-1), 4.40 (m, 1H, H-5′), 4.37 (d, 1H, H-3′), 4.34 (d, 1H, $^2J_{6a',6b'}$ 9.8 Hz, H-6a′), 4.17 (dd, 1H, $^3J_{3,4}$ 7.0 Hz, H-3), 4.06 (dd, 1H, $^3J_{2,3}$ 5.7 Hz, H-2), 3.88 (dd, 1H, $^2J_{6a',6b'}$ 9.8 Hz, $^3J_{5',6b'}$ 3.2 Hz, H-6b′), 3.66 (dq, 1H, $^3J_{5,6}$ 6.3 Hz, H-5), 3.55 (dd, 1H, $^3J_{4,5}$ 9.8 Hz, H-4), 3.34 (s, 3H, OCH_3), 2.11, 2.07 (2s, 6H, CH_3CO), 1.50,

1.30 [2s, 6H, $C(CH_3)_2$], 1.33 (d, 3H, H-6); ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 169.89, 169.55 ($2\times CH_3CO$), 109.35 [$C(CH_3)_2$], 98.06 (C-1), 97.24 (C-1′), 78.17 (C-4), 77.88 (C-3), 76.45 (C-3′), 75.91 (C-2), 75.36 (C-5′), 74.40 (C-2′), 73.50 (C-4′), 70.54 (C-6′), 63.87 (C-5), 54.78 (OCH_3), 27.81, 26.28 [$2\times C(CH_3)_2$], 20.94, 20.88 ($2\times COCH_3$), 18.15 (C-6). Anal. Calcd for $C_{20}H_{30}O_{11}$ (446.45): C, 53.81; H, 6.77. Found: C, 53.64; H, 6.36.

3.14. 3,6-Anhydro-1,2-*O*-[1-(*endo*-cyano)ethylidene]-α-D-galactopyranose (19)

Compound $\mathbf{7_{endo}}$ (150 mg, 0.58 mmol) was dissolved in methanolic HCl (0.28 M, 12.25 mL, prepared by adding 0.25 mL acetyl chloride to 12 mL of ice cold dry MeOH) and the soln was stirred for 9 h at room temperature (TLC, solvent A_2). The reaction mixture was then neutralized by filtration through a layer of alkaline alumina and concentrated. The residue was purified by column chromatography (solvent A_2) to furnish compound **19** (76 mg, 62%) as a colourless syrup: $[\alpha]_D^{21}$ +58,7 (*c* 0.98, $CHCl_3$); R_f 0.39 (solvent A_2); ^1H NMR ($CDCl_3$, 250.13 MHz): δ 5.62 (d, 1H, $^3J_{1,2}$ 3.2 Hz, H-1), 4.65 (br, 1H, H-4), 4.48–4.43 (m, 2H, H-3, H-5), 4.35 (dd, 1H, $^3J_{2,3}$ 5.0 Hz, H-2), 4.14 (dd, 1H, $^3J_{5,6a}$ 3.1 Hz, H-6a), 4.05 (d, 1H, $^2J_{6a,b}$ 10.5 Hz, H-6b), 2.70 (d, 1H,$^3J_{4,OH}$ 4.5 Hz, OH-4), 1.77 [s, 3H, CH_3(CN)C]; ^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 117.75 [$CH_3(CN)$C], 101.37 [CH_3(CN)*C*], 97.49 (C-1), 80.81 (C-2), 77.95 (C-5), 77.76 (C-3), 70.43 (C-4), 69.68 (C-6), 26.51 [CH_3(CN)C]. Anal. Calcd for $C_9H_{11}NO_5$ (213.19): C, 50.70; H, 5.20; N, 6.57. Found: C, 50.45; H, 5.16; N, 6.11.

3.15. 3,6-Anhydro-4-*O*-trityl-1,2-*O*-[1-(*endo*-cyano)ethylidene]-α-D-galactopyranose (20)

Trityl perchlorate (157 mg, 0.57 mmol), 2,4,6-collidine (70 μL, 0.52 mmol) and *N*,*N*-dimethyl-4-aminopyridine (16 mg, 0.13 mmol) were added to a soln of compound **19** (50 mg, 0.23 mmol) in dry CH_2Cl_2 (5 mL). After stirring overnight under an inert atmosphere at room temperature (TLC, solvent A_4), the mixture was diluted with CH_2Cl_2 (10 mL), and successively washed with cold aq 15% $NaHSO_4$ (2×5 mL), ice water (3×5 mL), dried and concentrated. The residue was purified by column chromatography (solvent A_4) to yield **20** (85 mg, 80%) as a colourless syrup: $[\alpha]_D^{22}$ −3.7 (*c* 1.0, $CHCl_3$); R_f 0.28 (solvent A_4); ^1H NMR ($CDCl_3$, 500.13 MHz): δ 7.49–7.46, 7.35–7.25 (2m, 15H, C_6H_5), 5.46 (d, 1H, $^3J_{1,2}$ 3.2 Hz, H-1), 4.56 (d, 1H, $^3J_{4,5}$ 1.5 Hz, H-4), 4.21 (dd, 1H, $^3J_{2,3}$ 5.0 Hz, H-2), 4.16 (d, 1H, H-3), 4.10 (dd, 1H, $^3J_{5,6a}$ 3.2 Hz, H-6a), 3.90 (d, 1H, $^3J_{6a,b}$ 10.1 Hz, H-6b), 3.29 (br, 1H, H-5), 1.67 [s, 3H, CH_3(CN)C]; ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 143.69, 128.70, 128.09, 127.48 [$C(C_6H_5)_3$, 14 signals are isochronic], 117.42 [$CH_3(CN)$C], 101.19 [CH_3(CN)*C*], 97.61 (C-1), 88.14 [$C(C_6H_5)_3$], 81.18 (C-2), 77.28 (C-5), 77.23 (C-3), 73.15 (C-4), 70.31 (C-6), 26.59 [CH_3(CN)C]. Anal. Calcd for $C_{28}H_{25}NO_5$ (455.50): C, 73.83; H, 5.53; N, 3.08. Found: C, 73.54; H, 5.79; N, 2.89.

References

1. For a short review see: Vogel, C.; Nolting, B.; Kramer, S.; Steffan, W.; Ott, A.-J. Synthesis of pectin fragments by modular design principle. In *Advances in Pectin and Pectinase Research*; Vorhagen, F., Schols, H., Visser, R., Eds.; Kluwer Academic: Dordrecht, 2003; pp 209–220.
2. Parra, E.; Caro, H.-N.; Jiménez-Barbero, J.; Martin-Lomas, M.; Bernabé, M. *Carbohydr. Res.* **1990**, *208*, 83–92.
3. Bochkov, A. F.; Kalinevitch, V. M. *Carbohydr. Res.* **1974**, *32*, 9–14.
4. Kochetkov, N. K.; Betaneli, V. I.; Ovchinnikov, M. V.; Backinowsky, L. V. *Tetrahedron* **1981**, *37*, 149–156.
5. Haworth, W. N.; Jackson, J.; Smith, F. *J. Chem. Soc.* **1940**, 620–632.
6. Györgydeák, Z.; Szilágyi, L. *Liebigs Ann. Chem.* **1987**, 235–241.
7. Rashid, A.; Mackie, W. *Carbohydr. Res.* **1992**, *223*, 147–155.
8. Utimoto, K.; Wakabayashi, Y.; Horiie, T.; Inoue, M.; Shishiyama, Y.; Obayashi, M.; Nozaki, H. *Tetrahedron* **1983**, *39*, 967–973.
9. Cano, F. H.; Foces-Foces, C.; Bernabé, M.; Jiménez-Barbero, J.; Martin-Lomas, M.; Penades-Ullate, S. *Tetrahedron* **1985**, *41*, 3875–3886.
10. Betaneli, V. I.; Ovchinnikov, M. V.; Backinowsky, L. V.; Kochetkov, N. K. *Carbohydr. Res.* **1979**, *68*, C11–C13.
11. Levy, A.; Flowers, H. M.; Sharon, N. *Carbohydr. Res.* **1967**, *4*, 305–311.
12. Lee, E. E.; Bruzzi, A.; O'Brien, E.; O'Colla, P. S. *Carbohydr. Res.* **1974**, *35*, 103–109.
13. Betaneli, V. I.; Ovchinnikov, M. V.; Backinowsky, L. V.; Kochetkov, N. K. *Carbohydr. Res.* **1979**, *76*, 252–256.
14. Perrin, D. D.; Amarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: Oxford, 1988.