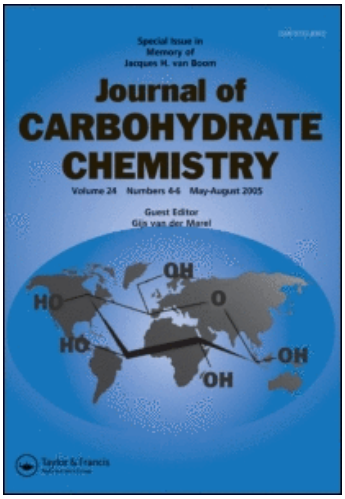

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Synthesis and Polycondensation of *Galacto*-Configurated Monomers *Via* the Trityl-cyano-ethylidene-Procedure

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SYNTHESIS AND POLYCONDENSATION OF *GALACTO*-CONFIGURATED MONOMERS *VIA* THE TRITYL-CYANO-ETHYLIDENE-PROCEDURE[1]

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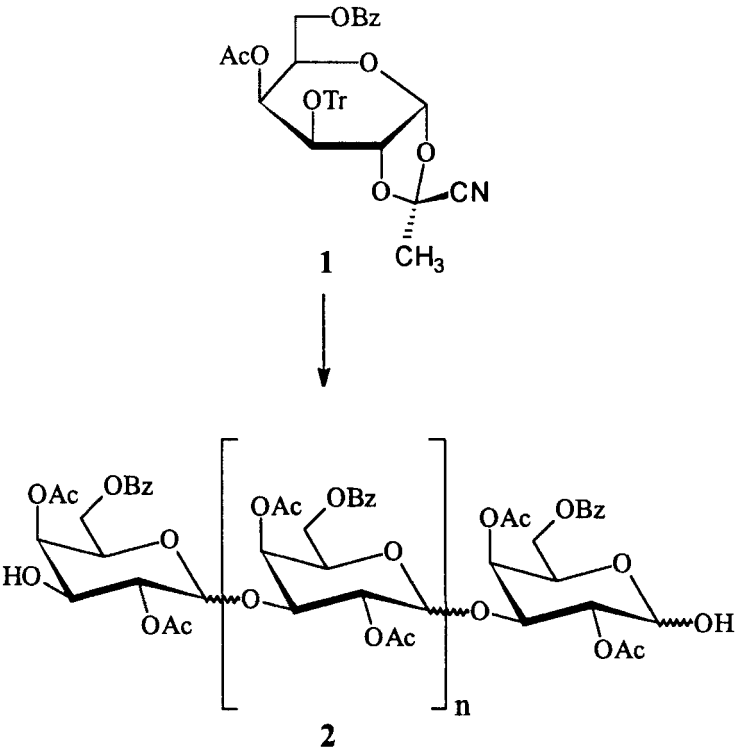
ABSTRACT

4-*O*-Acetyl-1,2-[1-(*exo*-cyano)ethylidene]-3-*O*-trityl-α-**D**-fucopyranose (**13**) and methyl 4-*O*-acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-3-*O*-trityl-α-**D**-galactopyranuronate (**14**) were synthesised. Trityl-cyanoethylidene condensation of the monomer **14** gave protected β-**D**-Gal*p*A-(1→3)-**D**-Gal*p*A-oligosaccharide derivatives with high stereoselectivity and a degree of polymerisation (d.p.) of eight. In the case of the **D**-fucose monomer **13**, the yield of oligomers is surprisingly low and the d.p. does not exceed seven. This result is in contrast to the d.p. 20 - 60 obtained with other 6-deoxy-sugars, as previously described by Kochetkov and coworkers.

INTRODUCTION

As part of our investigation on the synthesis of D-galacturonic acid oligomers[2,3] and fucose derivatives[4] we tested the scope of the trityl-cyanoethylidene-condensation (TCC)[5] as applied to *galacto*-configurated precursors. A study of the polymerisation of the 3-*O*-trityl-1,2-*O*-cyanoethylidene-D-galactose monomer **1** has shown[6] that the reaction gave only oligosaccharides with a limited average chain-length of eight glycoside units (n = 6).

SCHEME 1



Although absolute stereoselectivity (1,2-*trans*-glycosidic bonds) has often been observed, in this case the stereoregularity of the product **2** was low. The signals and coupling constants of ^{1}H NMR spectra and the signals of ^{13}C NMR spectra indicated more than 30% of α-glycosidic linkage between the D-galactose units.[6] In order to

evaluate the behaviour of further *galacto*-configurated monomers and the influence of the substitution pattern under the condition of the polycondensation, 3-*O*-trityl ethers of 1,2-*O*-cyanoethylidene derivatives (CED) of D-fucose and D-galacturonic acid were investigated.

RESULTS AND DISCUSSION

The glycosylation procedure using TCC requires 1,2-*O*-cyanoethylidene derivatives as donor molecules. The D-fucosyl bromide **5** as an intermediate was prepared in the following manner: D-Fucose derivative **3**, obtained from 6-deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose by reduction with Raney nickel,[7] was treated with acetic anhydride and perchloric acid as catalyst to give, after chromatographic purification, 80% of crystalline tetraacetate **4**. Its subsequent processing with 40% hydrogen bromide in chloroform gave **5** in 90% yield. Then, the bromide **5**, with an *O*-acetyl group at C-2, was reacted with cyanide ions in acetonitrile with rigorous exclusion of moisture and light. The *in situ* epimerisation to the β-fucosyl bromide was promoted by tetrabutylammonium bromide. A mixture of the *endo*- and *exo*-isomers **6** and **7** was formed (ratio 1 : 3) in 79% yield. These isomers could be easily separated by column chromatography.

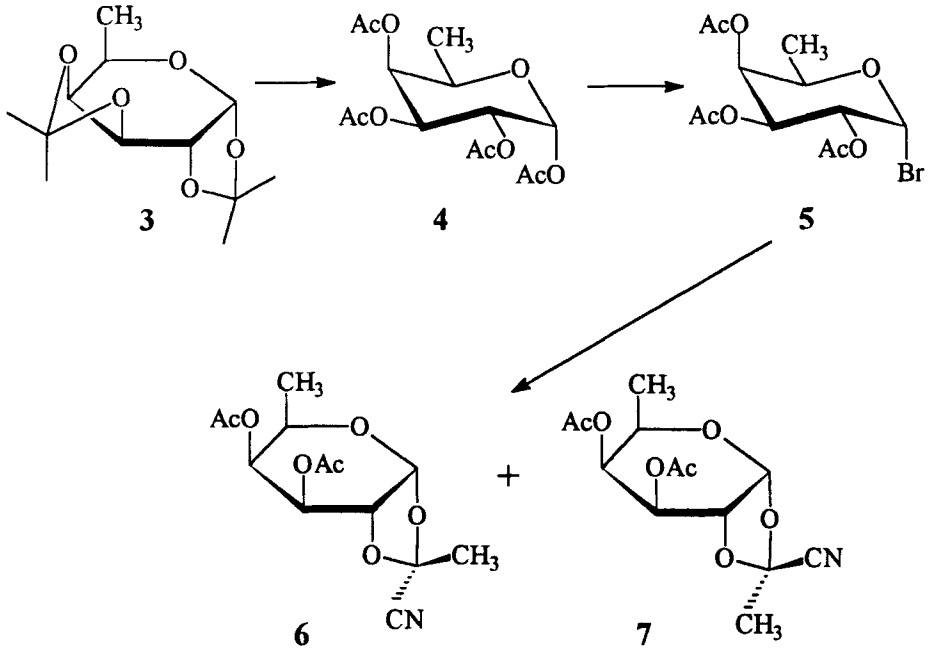
X-Ray and ^{1}H NMR studies[8] have dealt with the absolute configuration of the cyano group in peracetylated 1,2-*O*-(1-cyanoethylidene)-α-D-glycopyranoses. From these results it could be concluded that for cyanoethylidene derivatives with the methyl group in an *endo*-orientation (*R*-configuration), the proton signal from this methyl group appeared downfield (δ > 1.80 ppm) in comparison to those from a methyl group in an *exo*-orientation (*S*-configuration; δ < 1.80 ppm). Owing to the observed values for **6** [δ 1.79 ppm, $C\underline{H}_3(CN)C$] and **7** [δ 1.82 ppm, $C\underline{H}_3(CN)C$], the configuration of the 1,2-*cis*-fused five membered ring could be described as *endo*- and *exo*-cyanoethylidene group, respectively.

The synthesis of uronic acid CED is known[9] and was recently improved.[10] Thus, methyl 3,4-di-*O*-acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-α-D-galactopyranuronate (**8**) was prepared from the 6-*O*-trityl-CED of the corresponding neutral sugar by Jones oxidation with subsequent esterification.[10] In order to simplify monitoring, the *exo*-isomers **7** and **8** were used exclusively, in the following reaction steps.

Removal of the acetyl groups of **7** and **8** was achieved with sodium methoxide in anhydrous chloroform in 80% and 52% yield, respectively. Tritylation of diols **9** and **10** with triphenylmethylium perchlorate in the presence of 2,4,6-collidine regioselectively led

to derivatives **11** (55%) and **12** (83%). The subsequent acetylation (acetic anhydride / pyridine) with *N,N*-dimethyl-4-aminopyridine as a catalyst afforded the desired monomers **13** and **14** in an overall yield of 47% and 61% from **9** and **10**, respectively. The lower yield of the fucose derivative **11** may be caused by the formation of several *O*-trityl side products which were not further characterised.

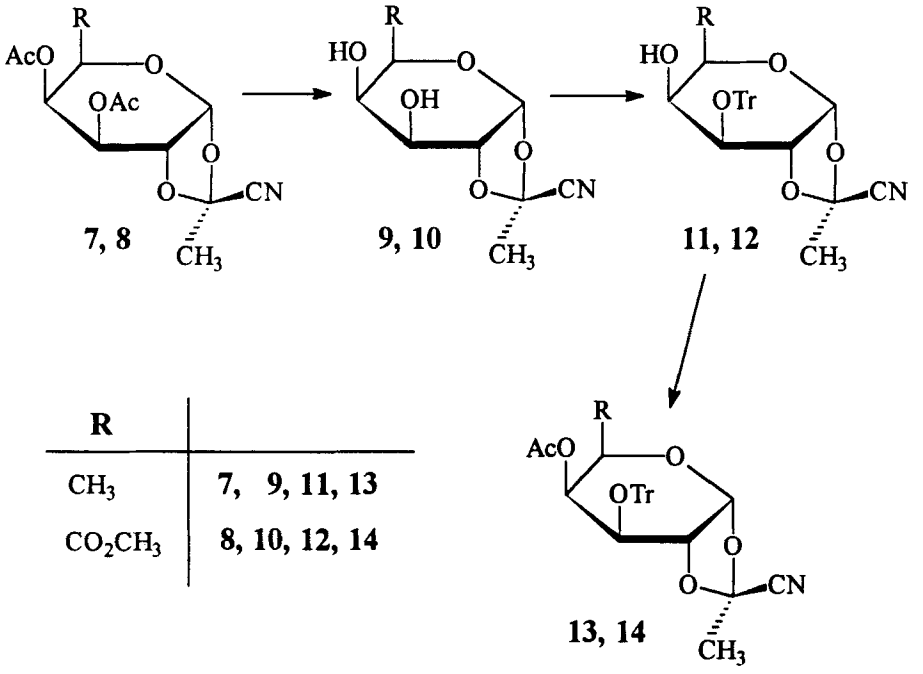
SCHEME 2



The ^{1}H and ^{13}C NMR spectra of compounds **10** - **14** were fully consistent with the assigned structures. The conversion of the diacetates **7** and **8** into the 3-*O*-trityl derivatives **11** and **12** via the diols **9** and **10** is evident from the considerable upfield shift of the H-3 and H-4 signals (H-3, δ 4.90 to 3.79 and 5.10 to 3.99 ppm; H-4, δ 5.19 to 2.30 and 5.76 to 2.29 ppm, respectively). Additionally, the acetylation of **11** and **12** at the *O*-4 position caused a significant downfield shift (δ > 1.60 ppm) for the H-4 signal in compounds **13** and **14**. As expected, tritylation of the *O*-3 position of the diol **10** to **12** has a negligible influence on the chemical shift of H-3 (δ 3.72 to 3.99 ppm). The smaller values

of $J_{2,3}$ (5.0 ± 1 Hz) for **11** - **14** could indicate a distortion of the $^4C_1$ towards the $^OS_2$ conformation.[11]

SCHEME 3

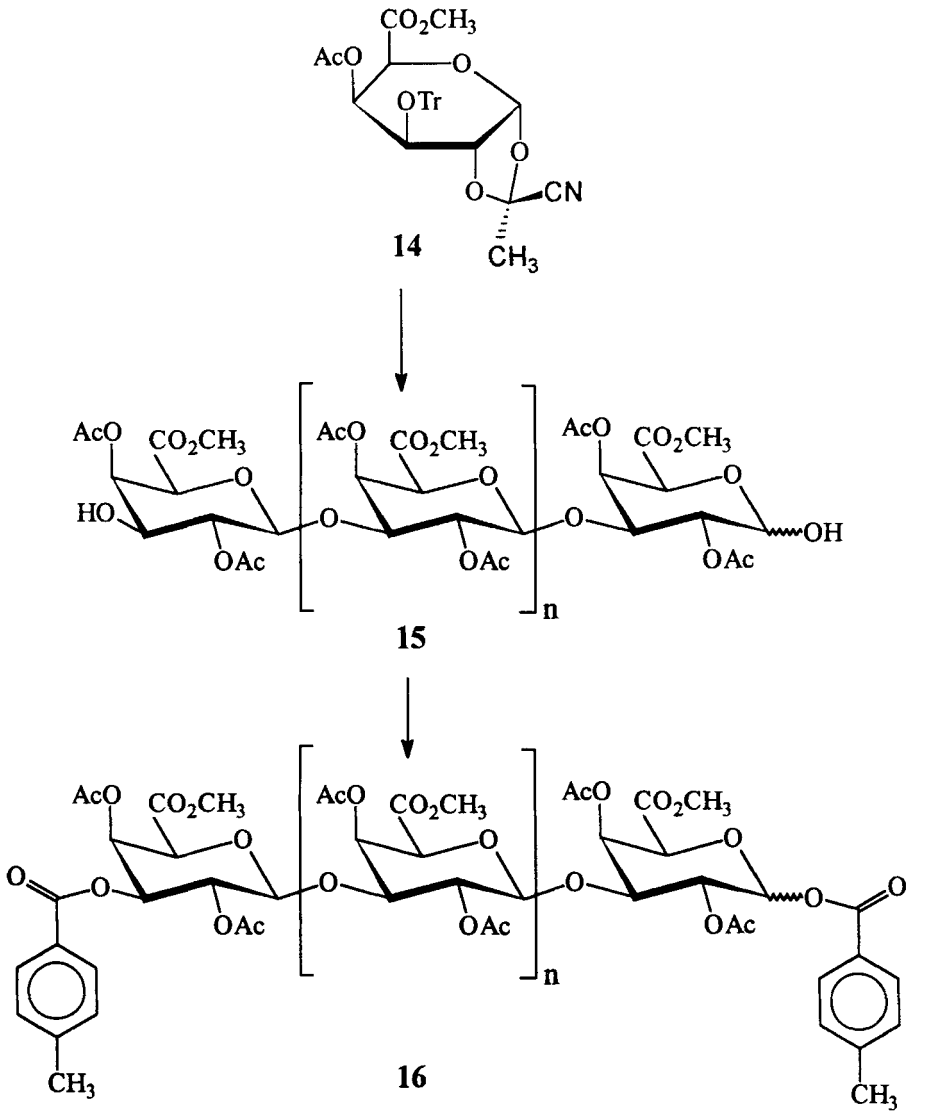


R	
CH_3	**7, 9, 11, 13**
CO_2CH_3	**8, 10, 12, 14**

Because the $J_{1,2}$ and $J_{4,5}$ values within the pyranose ring of galacturonic acid derivatives **8**, **10**, **12**, and **14** were similar, coupling between pyranosyl proton resonances for **12** (as the key compound) was assigned by homonuclear correlated spectroscopy (COSY, 400 MHz). In agreement with the β-shift effect of *O*-alkylation in ^{13}C NMR spectra,[12] the signals of C-2 ($\delta > 3$ ppm) and C-4 ($\delta > 2$ ppm) appeared at lower field for **13** and **14** in comparison with the corresponding signals of **7** and **8**.

Polycondensation of the monomers **13** and **14** was performed in dichloromethane in the presence of 0.1 equivalent of triphenylmethylium perchlorate using the vacuum technique.[13] The polycondensation of the 3-*O*-trityl-1,2-*O*-cyanoethylidene-D-galactose derivative **1** gave oligosaccharides with average chain-length of eight galactose units and with low stereoselectivity. By comparison, galacturonic acid monomer **14** gave oligosaccharides with the same average chain-length (n = 6) but with high stereoselectivity.

SCHEME 4

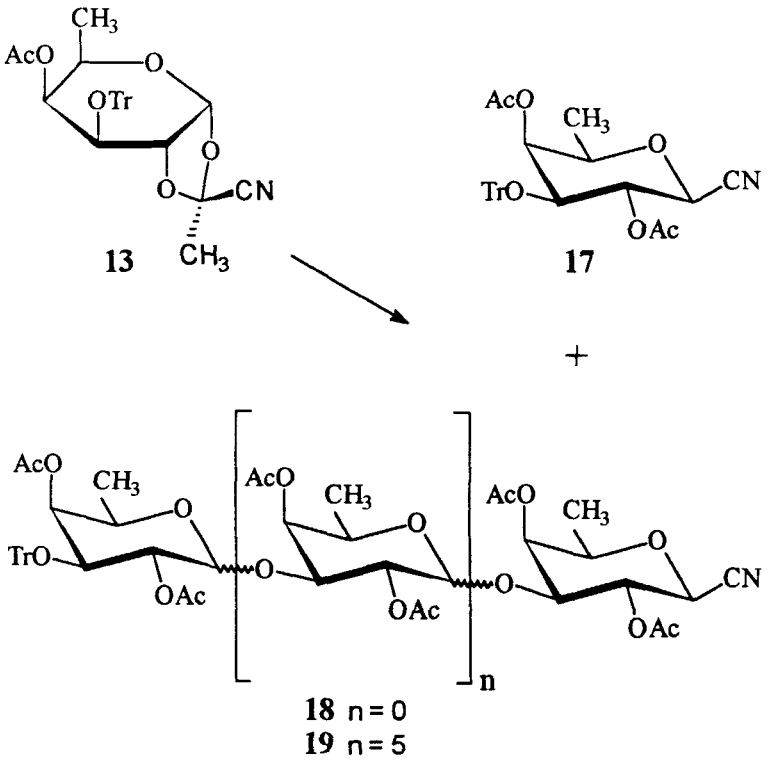


In order to estimate the degree of polymerisation, terminal groups in the chromatographically purified carbohydrate products (**15**) were treated with 4-methylbenzoyl chloride in pyridine.[14] The ratio of integral intensities to each other of the following signals in the ^{1}H NMR spectrum of **16** were determined: δ 2.0 - 2.2 (m, $C\underline{H}_3CO_2$) : 2.4 (s, $C\underline{H}_3$-C_6H_4) : 3.6-5.7 (m, <u>H-1</u> - <u>H-5</u>, $CO_2C\underline{H}_3$) : 7.3, 7.8 ppm (aromat. <u>H</u>). The ratio of comparable intensities of these signals was about 60 : 12.5 : 43 : 10, indicating an average chain length of eight linked galacturonic acid moieties (**16**, d.p. 8 in Scheme 4). A previous work on the synthesis of protected D-Gal*p*A-disaccharide units has shown[2] that values of 8.0 ± 0.1 Hz for $J_{1,2}$ in the ^{1}H NMR spectra and signals of δ 99.6 - 102.1 ppm for C-1 in ^{13}C NMR spectra indicate the β-glycosidic linkages whereas values of 3.4 ± 0.1 Hz for $J_{1,2}$ and signals of δ 95.7 - 96.9 ppm for C-1 are typical for β-glycosidic linkages. Because of the complexity of the ^{1}H NMR spectra of oligosaccharides, the β-glycosic linkage between the D-galacturonic acid units could only be assigned from signals in the ^{13}C NMR spectra. In the spectra of both oligomer mixtures (**15** and **16**) unambiguous signals for C-1 were only observed in a range of δ 99.0 - 102.0 ppm, suggesting a high stereoselectivity of the polycondensation. Nevertheless, preparation of unprotected D-galacturonic acid oligomers requires a new strategy of blocking groups, because attempts at deacetylation of **15** either under acidic or alkaline conditions was accompanied by considerable cleavage of glycosidic bonds.

Surprisingly, polycondensation of the D-fucose monomer **13** gave oligosaccharides with an average chain-length of seven saccharide units (n = 5) and with low overall yield (< 10%). This result is in contrast to the yield (> 80%) and the degree of polymerisation (d.p. > 40) of other synthetic 6-deoxy-glycans.[15] After standard work-up and chromatographic separation on silica gel, the main fraction of carbohydrate products was determined to be a mixture of β-cyanides of mono- and disaccharides. Furthermore, all compounds, including the higher oligomers, still showed the trityl ether function by TLC. Generally, the stereoregularity of the newly formed glycosidic bonds between saccharide moieties was low. Therefore, the 3-*O*-trityl-β-cyanide **17** was the only pure product isolated after chromatographic purification and crystallisation in 44% yield based on monomer **13**. The β-configuration of the glycosidic linkages was evident from the large coupling (10.0 Hz) of the H-1 doublet in the ^{1}H NMR spectra. The remaining NMR data also agreed with the structure of **17** represented. The structure of the β-linked disaccharide **18** was also characterised by NMR spectroscopy in the presence of traces of a second compound, probably the 1',2'-*cis*-isomer. The value of $J_{1',2'}$ in the ^{1}H NMR spectra (7.8 Hz) and the signal for C-1' in ^{13}C NMR spectra (100.8 ppm) proved the β-glycosidic linkage of **18**.

Because of the stability of the trityl ether group in the fucose derivatives, the low degree of polymerisation was indicated by comparison of the ratio of integral intensities from the following signals in the ^1H NMR: δ 0.9 - 1.2 (m, H-6) : 1.6 - 2.1 (m, CH_3CO_2) : 3.1 - 5.5 (m, H-1 - H-5) : 7.1 - 7.4 ppm (aromat. H). The ratio of intensities was about 22 : 40 : 33 : 15 and indicated an average chain length of seven linked D-fucose moieties (**19**, d.p. 7 in Scheme 5).

SCHEME 5



Summarising these results, we conclude that the application of the trityl-cyano-ethylidene condensation is strongly limited to *galacto*-configurated precursors. Generally, under the described conditions, degrees of polymerisation not higher then eight were observed. In the case of the galactose and fucose derivatives the stereoregularity of the

products was low. Furthermore, the formation of β-cyanides of mono- and oligosaccharides was the predominant reaction for the fucose derivative. These compounds still showed the trityl ether function but lost their ability to react as glycosyl donors. Therefore, only a small amount of higher oligomers could be obtained. In view of the stereoselectivity of the TCC the D-galacturonic acid monomer **14** gave the best results. Since the deacetylation of the obtained uronic acid oligomers is troublesome, unprotected galacturonic acid oligomers are not available by this method.

EXPERIMENTAL

General Procedures. Melting points were determined with Boetius micro apparatus BHMK05 (Rapido, Dresden) and were corrected. Optical rotations were measured for solutions in a 1-dm cell with an automatic polarimeter "Polamat A" (C. Zeiss, Jena) and DIP-360 (JASCO, Japan). NMR spectra were recorded with a Bruker spectrometer model WH-250 at 250 MHz for ^1H, and 62.89 MHz for ^{13}C, Bruker WH 270 at 270 MHz for ^1H, and 67.89 MHz for ^{13}C and Bruker WM-400 (400 MHz) for ^1H. Chemical shifts are given relative to the signal of internal tetramethylsilane. Key ^1H resonances were assigned by selective homonuclear resonance, and ^{13}C resonances by selective heteronuclear resonance. Thin-layer chromatography (TLC) on precoated plates of silica gel (Merck, Prod. No 5721) was performed with the following solvent-systems (v/v): (A_1) 2 : 1, (A_2) 3 : 1, (A_3) 4 : 1, (A_4) 10 : 1 and (A_5) 1 : 2 toluene-ethyl acetate; (B) 2 : 1 : 0.1 toluene-ethyl acetate-ethanol; (C) 14 : 1 chloroform-methanol, (D) 7 : 3 chloroform-acetone. Detection was effected by spraying with a mixture of methanol (40 mL), water (40 mL), concd H_2SO_4 (20 mL), H_2MoO_4 (1.0 g), and $Ce(SO_4)_2$ (1.0 g). The spots were made visible by charring for 3 - 5 minutes at 150 °C. Prior to charring, trityl derivatives gave bright-yellow spots. Preparative column chromatography was performed by gradient elution from columns of slurry-packed Silica Gel 60 (Merck, Prod. No. 7754, 0.063 - 0.2 mm, or Prod. No. 9385, 0.040 - 0.063 mm). Dichloromethane, chloroform, toluene, benzene, diethyl ether, acetonitrile, pyridine and 2,4,6-collidine were dried by heating with CaH_2 under reflux and were then distilled. Acetone was dried over P_2O_5 and then distilled from $KMnO_4$, acetic anhydride was freshly distilled before use. Nitromethane was distilled from urea at 100 mm Hg and then from CaH_2. Triphenylmethylium perchlorate ($TrClO_4$) was obtained and purified as described in ref. 12. Organic solutions were dried by filtration through cotton and then concentrated in vacuo at < 40 °C.

1,2,3,4-Tetra-*O*-acetyl-α-D-fucopyranose (4). To a solution of **3** (2.44 g, 10 mmol, prepared from 6-deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[7]), in acetic anhydride was added aq. 70% perchloric acid (0.13 mL) at -10 °C. The solution was kept for 12 h at that temperature (TLC, solvent A_1), methanol (6.7 mL) was added dropwise at 0 °C, and after 30 minutes the mixture was poured into ice-water (600 mL). The aqueous layer was extracted with chloroform (2 x 150 mL). The combined organic layers were washed successively with water (3 x 150 mL), sat. aq. $NaHCO_3$ (5 x 150 mL), and water (2 x 150 mL), dried, and concentrated. The crude material was purified by column chromatography (ethyl acetate gradient 15% → 50% in heptane) to yield **4** (2.66 g, 80%): mp 90 °C (from ethyl acetate-heptane); $[\alpha]_D^{21}$ +127.8° (*c* 1.02, acetone); lit.[16] mp 92-93 °C; $[\alpha]_D$ +129° (*c* 1.50, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.15 (d, 3 H, $J_{5,6}$ = 6.4 Hz, H-6), 2.01, 2.02, 2.16, 2.19 (4 s, 12 H, $C\underline{H}_3CO_2$), 4.27 (m, 1 H, H-5), 5.33 (m, 3 H, H-2, H-3, H-4), 6.33 (d, 1 H, $J_{1,2}$ = 2.6 Hz, H-1); ^{1}H NMR (C_6D_6) δ 0.90 (d, 3 H, $J_{5,6}$ = 6.4 Hz, H-6), 1.58, 1.62, 1.66, 1.73 (4 s, 12 H, $C\underline{H}_3CO_2$), 3.83 (m, 1 H, H-5), 5.42 (dd, 1 H, $J_{4,5}$ = 1.3 Hz, H-4), 5.60 (dd, 1 H, $J_{3,4}$ = 3.2 Hz, H-3), 5.71 (dd, 1 H, $J_{2,3}$ = 11.0 Hz, H-2), 6.75 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1); ^{13}C NMR ($CDCl_3$) δ 15.9 (C-6), 20.5, 20.8 (4 C, $\underline{C}H_3CO_2$), 66.4 (C-2), 67.2 (C-5), 67.8 (C-3), 70.5 (C-4), 89.9 (C-1), 169.1, 169.9, 170.1, 170.5 (4 C, $CH_3\underline{C}O_2$); ^{13}C NMR (C_6D_6) δ 15.9 (C-6), 19.9, 20.1, 20.3 (4 C, $\underline{C}H_3CO_2$), 67.1 (C-2), 67.5 (C-5), 68.3 (C-3), 70.9 (C-4), 90.3 (C-1), 168.9, 169.6, 169.8, 170.2 (4 C, $CH_3\underline{C}O_2$).

Anal. Calcd for $C_{14}H_{20}O_9$: C, 50.60; H, 6.07. Found: C, 50.72; H, 6.11.

3,4-Di-*O*-acetyl-1,2-*O*-[1-(*endo*- and *exo*-cyano)ethylidene]-α-D-fucopyranose (6 and 7). A solution of 40% HBr in acetic acid containing 5% acetic anhydride (11 mL; prepared by adding 33 mL of water to a mixture of 136 mL of acetyl bromide, 100 mL acetic acid, and 4 mL of acetic anhydride at -10 °C) was added to a stirred solution of crystalline **4** (3.32 g, 20 mmol) in dry chloroform (50 mL) at 0 °C. After 1 h at ambient temperature (TLC, solvent A_2) the reaction mixture was diluted with chloroform (10 mL) and hexane (120 mL) and then poured into ice-water (400 mL). The phases were separated, and the organic phase was washed successively with ice-water (60 mL), sat. aq. $NaHCO_3$ (2 x 60 mL) and ice-water (2 x 60 mL), dried, and concentrated. The syrupy 2,3,4-tri-*O*-acetyl-α-D-fucopyranosyl bromide **5** (3.18 g, 90% yield) was sufficiently pure for the next step.

The fucosyl bromide **5** (3.53 g, 10 mmol) in dry acetonitrile (30 mL) was stirred with dry, finely powdered sodium cyanide (2.67 g, 55 mmol) and tetrabutylammonium bromide (1.57 g, 5 mmol) for 30 h (TLC, solvent A_3). The mixture was then diluted with ethyl acetate (250 mL), washed with ethyl acetate saturated water (7 x 50 mL), and

concentrated to dryness. A solution of the residue in chloroform-light petroleum (1 : 2, 100 mL) was passed through a bed of silica gel to yield the *endo* / *exo* mixture, which was fractionated by chromatography on silica gel (ethyl acetate gradient 5% → 20% in heptane).

3,4-Di-*O*-acetyl-1,2-*O*-[1-(*endo*-cyano)ethylidene]-α-D-fucopyranose (6). (TLC, solvent A_2, R_f 0.25; 569 mg, 19%): mp 103-105 °C (from ethyl acetate-heptane); $[\alpha]_D^{20}$ +149.8° (*c* 1.02, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.23 (d, 3 H, $J_{5,6}$ = 6.4 Hz, H-6), 1.79 [s, 3 H, $C\underline{H}_3(CN)C$], 2.08, 2.15 (2 s, 6 H, $C\underline{H}_3CO_2$), 4.36 (m, 1 H, H-5), 4.36 (dd, 1 H, $J_{2,3}$ = 7.5 Hz, H-2), 5.35 (dd, 1 H, $J_{4,5}$ = 1.5 Hz, H-4), 5.46 (dd, 1 H, $J_{3,4}$ = 3.2 Hz, H-3), 5.71 (d, 1 H, $J_{1,2}$ = 4.7 Hz, H-1); ^{13}C NMR ($CDCl_3$) δ 16.2 (C-6), 20.6 (2 C, $\underline{C}H_3CO_2$), 27.3 [$\underline{C}H_3(CN)C$], 68.3 (C-5), 69.0 (C-4), 69.8 (C-3), 75.1 (C-2), 98.3 [$CH_3(CN)\underline{C}$], 99.2 (C-1), 117.8 [$CH_3(\underline{C}N)C$], 169.6, 170.1 (2 C, $CH_3\underline{C}O_2$).

Anal. Calcd for $C_{13}H_{17}NO_7$: C, 52.17; H, 5.73; N, 4.68. Found: C, 52.31; H, 5.80; N, 4.83.

3,4-Di-*O*-acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-α-D-fucopyranose (7). (TLC, solvent A_2, R_f 0.30; 1.79 g, 60%), syrup: $[\alpha]_D^{22}$ +1.05° (*c* 1.04, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.19 (d, 3 H, $J_{5,6}$ = 6.4 Hz, H-6), 1.82 [s, 3 H, $C\underline{H}_3(CN)C$], 2.04, 2.12 (2 s, 6 H, $C\underline{H}_3CO_2$), 4.23 (m, 1 H, H-5), 4.23 (dd, 1 H, $J_{2,3}$ = 7.2 Hz, H-2), 4.90 (dd, 1 H, $J_{3,4}$ = 3.4 Hz, H-3), 5.19 (dd, 1 H, $J_{4,5}$ = 1.5 Hz, H-4), 5.82 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1); ^{13}C NMR ($CDCl_3$) δ 16.0 (C-6), 20.4, 20.6 (2 C, $\underline{C}H_3CO_2$), 25.9 [$\underline{C}H_3(CN)C$], 66.2 (2 C, C-4, C-5), 71.7 (C-2), 72.0 (C-3), 96.6 [$CH_3(CN)\underline{C}$], 99.6 (C-1), 116.9 [$CH_3(\underline{C}N)C$], 169.8, 169.9 (2 C, $CH_3\underline{C}O_2$).

Anal. Calcd for $C_{13}H_{17}NO_7$: C, 52.17; H, 5.73; N, 4.68. Found: C, 51.95; H, 5.61; N, 4.49.

Methyl 3,4-Di-*O*-acetyl 1,2-*O*-[1-(*exo*-cyano)ethylidene]-α-D-galactopyranuronate (8).[10] ^{1}H NMR ($CDCl_3$) δ 1.89 [s, 3 H, $C\underline{H}_3(CN)C$], 2.07, 2.09 (2 s, 6 H, $C\underline{H}_3CO_2$), 3.76 ($CO_2C\underline{H}_3$), 4.43 (dd, 1 H, $J_{2,3}$ = 5.8 Hz, H-2), 4.75 (d, 1 H, $J_{4,5}$ = 4.0 Hz, H-5), 5.10 (dd, 1 H, $J_{3,4}$ = 3.0 Hz, H-3), 5.76 (dd, 1 H, H-4), 5.94 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1); ^{13}C NMR ($CDCl_3$) δ 20.4, 20.6 (2 C, $\underline{C}H_3CO_2$), 25.8 [$\underline{C}H_3(CN)C$], 52.6 ($CO_2\underline{C}H_3$), 66.3 (C-4), 70.7 (C-3), 72.1 (C-5), 76.7 (C-2), 97.7 (C-1), 99.6 [$CH_3(CN)\underline{C}$], 116.7 [$CH_3(\underline{C}N)C$], 167.1 (C-6), 169.0, 169.7 (2 C, $CH_3\underline{C}O_2$).

Deacetylation of the diacetates 7 and 8. To a solution of the diacetates **7** (2.99 g, 10 mmol) or **8** (3.43 g, 10 mmol)[10] in dry chloroform (15 mL) were added dry methanol (31 mL) and 1 M sodium methoxide (1 mL) and the solution was kept for 30 minutes at ambient temperature (TLC, solvent A_1). The mixture was neutralised with 0.1 M acetic acid in methanol (about 10 mL) and concentrated. The residue was coevaporated with

toluene (4 x 60 mL) and processed by column chromatography (**7**, solvent C; **8**, solvent B).

1,2-*O*-[1-(*Exo*-cyano)ethylidene]-α-D-fucopyranose (9). (1.72 g, 80%): mp 119-120 °C (from ethyl acetate-heptane); $[\alpha]_D^{20}$ +108.0° (*c* 1.0, chloroform).

Anal. Calcd for $C_9H_{13}NO_5$: C, 50.23; H, 6.09; N, 6.51. Found: C, 49.92; H, 6.05; N, 6.49.

Methyl 1,2-*O*-[1-(*Exo*-cyano)ethylidene]-α-D-galactopyranuronate (10). (1.34 g, 52%): mp 129-131 °C (from ethyl ether-heptane); $[\alpha]_D^{25}$ +1.7° (*c* 1.0, chloroform); ^{1}H NMR (1 : 10, D_2O-DMSO-d_6) δ 1.84 [s, 3 H, C$\underline{H}_3$(CN)C], 3.67 ($CO_2C\underline{H}_3$), 3.72 (dd, 1 H, $J_{3,4}$ = 2.6 Hz, H-3), 4.08 (dd, 1 H, $J_{4,5}$ = 4.0 Hz, H-4), 4.17 (dd, 1 H, $J_{2,3}$ = 5.4 Hz, H-2), 4.64 (d, 1 H, H-5), 5.72 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1); ^{13}C NMR (1 : 3, CD_3OD-$CDCl_3$) δ 25.2 [$\underline{C}H_3$(CN)C], 51.9 ($CO_2\underline{C}H_3$), 66.8 (C-4), 69.2 (C-3), 73.6 (C-5), 80.1 (C-2), 97.2 (C-1), 99.4 [CH_3(CN)$\underline{C}$], 116.3 [$CH_3(\underline{C}N)$C], 168.0 (C-6).

Anal. Calcd for $C_{10}H_{13}NO_7$: C, 46.34; H, 5.06; N, 5.40. Found: C, 46.30; H, 5.11; N, 5.59.

Tritylation of the diols 9 and 10. To a solution of the diols **9** (2.15 g, 10 mmol) or **10** (2.59 g, 10 mmol) in dry dichloromethane (100 mL) were added in small portions 2,4,6-collidine (3.0 mL, 28 mmol) and tritylium perchlorate (6.5 g, 19 mmol), and the mixture was stirred at room temperature. When the reaction was complete (TLC, solvent A_4), the mixture was diluted with chloroform (300 mL). The organic solution was washed with water (3 x 150 mL), dried, and concentrated. The residue was purified by column chromatography (ethyl acetate gradient 5% → 20% in heptane, containing 0.1% pyridine).

1,2-*O*-[1-(*Exo*-cyano)ethylidene]-3-*O*-trityl-α-D-fucopyranose (11). (2.52 g, 55%): mp 157-160 °C (from ethyl ether-heptane); $[\alpha]_D^{23}$ +13.6° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.10 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6), 1.65 [s, 3 H, C$\underline{H}_3$(CN)C], 2.25 (dd, 1 H, $J_{OH,4}$ = 2.7 Hz, OH-4), 2.30 (ddd, 1 H, $J_{4,5}$ = 1.4 Hz, H-4), 3.57 (m, 1 H, H-5), 3.79 (dd, 1 H, $J_{3,4}$ = 3.6 Hz, H-3), 4.31 (t, 1 H, $J_{2,3}$ = 4.9 Hz, H-2), 5.75 (d, 1 H, $J_{1,2}$ = 4.9 Hz, H-1), 7.33, 7.56 [2 m, 15 H, C($\underline{C}_6H_5)_3$]; ^{13}C NMR ($CDCl_3$) δ 16.5 (C-6), 25.9 [$\underline{C}H_3$(CN)C], 68.0 (C-4), 68.6 (C-5), 74.2 (C-3), 76.2 (C-2), 88.5 [$\underline{C}(C_6H_5)_3$], 96.8 [CH_3(CN)$\underline{C}$], 99.1 (C-1), 117.4 [$CH_3(\underline{C}N)$C], 127.9, 128.3, 129.0, 144.0 [6 C, C($\underline{C}_6H_5)_3$].

Anal. Calcd for $C_{28}H_{27}NO_5$: C, 73.50; H, 5.95; N, 3.06. Found: C, 73.32; H, 6.11; N, 3.00.

Methyl 1,2-*O*-[1-(*Exo*-cyano)ethylidene]-3-*O*-trityl-α-D-galactopyranuronate (12). (3.65 g, 73%), syrup: $[\alpha]_D^{20}$ 0° (*c* 1.0, chloroform); ^{1}H NMR (1 : 20, D_2O-$CDCl_3$) δ 1.73 [s, 3 H, C$\underline{H}_3$(CN)C], 2.99 (t, 1 H, H-4), 3.99 (dd, 1 H, $J_{3,4}$ = 3.0 Hz, $J_{2,3}$

= 4.0 Hz, H-3), 4.02 (d, 1 H, $J_{4,5}$ = 3.7 Hz, H-5), 4.35 (t, 1 H, H-2), 5.79 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1), 7.23, 7.54 [2 m, 15 H, $C(C_6\underline{H}_5)_3$].

Anal. Calcd for $C_{29}H_{27}NO_7$: C, 69.45; H, 5.43; N, 2.79. Found: C, 69.71; H, 5.26; N, 2.64.

Acetylation of the trityl derivatives 11 and 12. Compounds **11** (4.58 g, 10 mmol) or **12** (5.40 g, 10 mmol) were dissolved in a mixture of dry pyridine (24 mL), acetic anhydride (8 mL), and *N,N*-dimethyl-4-aminopyridine (1.22 g, 10 mmol) and kept for 24 h at ambient temperature (TLC, solvent A_4). Water (24 mL) was added dropwise at 0 °C, and after 20 minutes the mixture was diluted with chloroform (60 mL) and hexane (120 mL) and poured into ice-water. The phases were separated, and the aqueous phase was extracted with a mixture of chloroform and hexane (1 : 2, 120 mL). The combined organic solutions were washed with cold sat. aq. $NaHCO_3$ (2 x 100 mL), ice-water (2 x 100 mL), dried, and concentrated. Traces of pyridine were removed by evaporation with repeated addition of toluene. The residue was purified by column chromatography (ethyl acetate gradient 0% → 20% in heptane, containing 0.1% pyridine).

4-*O*-Acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-3-*O*-trityl-α-D-fucopyranose (13). (4.25 g, 85%): mp 145-146 °C (from ethyl ether-hexane); $[\alpha]_D^{28}$ +43.2° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.99 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6), 1.55 [s, 3 H, $C\underline{H}_3(CN)C$], 2.21 (s, 3 H, $C\underline{H}_3CO_2$), 3.69 (m, 1 H, H-5), 3.79 (dd, 1 H, $J_{3,4}$ = 3.3 Hz, H-3), 4.22 (dd, 1 H, $J_{4,5}$ = 1.9 Hz, H-4), 4.34 (dd, 1 H, $J_{2,3}$ = 5.9 Hz, H-2), 5.69 (d, 1 H, $J_{1,2}$ = 4.7 Hz, H-1), 7.32, 7.50 [2 m, 15 H, $C(\underline{C}_6H_5)_3$]; ^{13}C NMR ($CDCl_3$) δ 16.4 (C-6), 20.8 ($\underline{C}H_3CO_2$), 25.7 [$\underline{C}H_3(CN)C$], 69.0 (C-5), 70.5 (C-4), 72.5 (C-3), 76.4 (C-2), 88.0 [$\underline{C}(C_6H_5)_3$], 96.9 [$CH_3(CN)\underline{C}$], 98.6 (C-1), 117.2 [$CH_3(\underline{C}N)C$], 127.5, 127.8, 129.1, 143.7 [6 C, $C(\underline{C}_6H_5)_3$], 169.8 ($CH_3\underline{C}O_2$).

Anal. Calcd for $C_{30}H_{29}NO_6$: C, 72.13; H, 5.85; N, 2.80. Found: C, 72.40; H, 5.61; N, 3.03.

Methyl 4-*O*-Acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-3-*O*-trityl-α-D-galactopyranuronate (14). (4.50 g, 83%): mp 157-158 °C (from ethyl ether-hexane); $[\alpha]_D^{23}$ +50.0° (*c* 2.5, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.65 [s, 3 H, $C\underline{H}_3(CN)C$], 2.11 (s, 3 H, $C\underline{H}_3CO_2$), 3.63 (s, 3 H, $CO_2C\underline{H}_3$), 3.95 (dd, 1 H, $J_{3,4}$ = 2.7 Hz, H-3), 4.15 (d, 1 H, H-5), 4.37 (dd, 1 H, $J_{2,3}$ = 5.0 Hz, H-2), 4.65 (dd, 1 H, $J_{4,5}$ = 3.8 Hz, H-4), 5.83 (d, 1 H, $J_{1,2}$ = 3.8 Hz, H-1), 7.31, 7.47 [2 m, 15 H, $C(\underline{C}_6H_5)_3$]; ^{13}C NMR ($CDCl_3$) δ 20.7 ($\underline{C}H_3CO_2$), 25.7 [$\underline{C}H_3(CN)C$], 52.4 ($CO_2\underline{C}H_3$), 68.3 (C-2), 71.6 (C-3), 72.3 (C-5), 80.2 (C-4), 88.7 [$\underline{C}(C_6H_5)_3$], 97.2 (C-1), 99.1 [$CH_3(CN)\underline{C}$], 116.9 [$CH_3(\underline{C}N)C$], 127.7, 128.0, 129.0, 143.4 [6 C, $C(\underline{C}_6H_5)_3$], 167.9 (C-6), 168.7 ($CH_3\underline{C}O_2$).

Anal. Calcd for $C_{31}H_{29}NO_8$: C, 68.50; H, 5.38; N, 2.58. Found: C, 68.40; H, 5.41; N, 2.59.

General procedure of the polycondensation. Solutions of the monomers **13** or **14** in dry benzene (2 mL / mmol) and $TrClO_4$ (10 mol% of the amount of the monomer) in dry nitromethane (1 mL / 0.1 mmol) were placed in separate limbs of a tuning-fork-shaped tube. The reaction components were dried by two fold lyophilisation (0.4 Pa) with dry benzene and kept for 2 h at 50 °C under high vacuum (0.2 Pa). Then the components were dissolved in dichloromethane (about 2 mL / mmol monomer) under reduced pressure, mixed, and kept overnight at ambient temperature in the dark. When the reaction was complete (TLC, solvent A_5), pyridine (0.05 mL / mmol, 2% water) was added. The mixture was filtered, diluted with chloroform (50 mL), and washed with water (3 x 30 mL), aq. 5% $NaHSO_4$ (2 x 30 mL), and water (2 x 30 mL). The organic phase was dried and concentrated. The crude material was purified by column chromatography (acetone gradient 0% → 100% in toluene).

Polycondensation of monomer 14. Reagents: Monomer **14** (435 mg, 0.8 mmol); initiator: $TrClO_4$ (27 mg, 0.08 mmol), TLC solvent D; R_f 0.0 - 0.7. The crude material (200 mg, amorphous powder) was submitted to column chromatography (acetone gradient 0% → 100% in chloroform) which afforded **15** (130 mg), amorphous white solid: ^1H NMR ($CDCl_3$) δ 2.0 - 2.2 (m, $C\underline{H}_3CO_2$), 3.7 - 5.7 (m, H-1 - H-5, $CO_2C\underline{H}_3$); ^{13}C NMR ($CDCl_3$) δ 20.6 ($\underline{C}H_3CO_2$), 52.6 ($CO_2\underline{C}H_3$), 69.4 - 76.0 (C-2 - C-5), 100.1 (C-1), 166.4 - 169.8 ($CH_3\underline{C}O_2$, C-6).

Determination of degree of polymerisation of 15. A solution of **15** (130 mg), 4-methylbenzoyl chloride (0.2 mL, 1.5 mmol), dry pyridine (0.25 mL, 3.0 mmol) in dry acetonitrile (1 mL) was kept for 12 h at ambient temperature (TLC, solvent A_5). Methanol (0.03 mL) was added at 0 °C, and, after 1 h, the mixture was concentrated. The residue was dissolved in chloroform (50 mL), the organic layer was washed with water (3 x 30 mL), aq. 5% $NaHSO_4$ (2 x 30 mL), water (30 mL), aq. $NaHCO_3$ (2 x 30 mL), water (2 x 30 mL), dried, and concentrated. Column chromatography (acetone gradient 0% → 100% in chloroform) was performed to give **16** (130 mg), $[\alpha]_D^{26}$ +58° (*c* 3.2, chloroform). The ratio of integral intensities to each other of the following signals of the ^1H NMR ($CDCl_3$) spectrum was determined: δ 2.0 - 2.2 (m, $C\underline{H}_3CO_2$) : 2.4 (s, $C\underline{H}_3$-C_6H_4) : 3.6 - 5.7 (m, H-1 - H-5, $CO_2C\underline{H}_3$) : 7.3, 7.8 (2 m, CH_3-$C_6\underline{H}_4$). The ratio of comparable intensities of these signals was about 60 : 12.5 : 43 : 10; d.p. 8. ^{13}C NMR ($CDCl_3$) δ 20.6 ($\underline{C}H_3CO_2$), 52.6 ($CO_2\underline{C}H_3$), 69.5 - 75.3 (C-2 - C-5), 100.2 (C-1), 126.4 - 129.2 (C_6H_4), 166.4 - 169.8 ($CH_3\underline{C}O_2$, C-6).

Polycondensation of monomer 13. Reagents: Monomer **13** (500 mg, 1.0 mmol); initiator: $TrClO_4$ (34 mg, 0.1 mmol), TLC, solvent A_3; R_f 0.0 - 0.2, 0.5, and 0.7; spraying with sulphuric acid produced bright-yellow coloration of all the spots darkening upon heating, indicating the presence of a triphenylmethyl group in the substances. The crude material (417 mg, amorphous powder) was submitted to column chromatography

(ethyl acetate gradient 0% → 100% in toluene) which afforded **17** (TLC, solvent A_3, R_f 0.7; 220 mg, 44% with regard to **13**): mp 173-175 °C (from ethyl acetate-dioxane); $[\alpha]_D^{20}$ +51.9° (*c* 1.7, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.99 (d, 3 H, $J_{5,6}$ = 6.4 Hz, H-6), 1.83. 2.32 (2 s, 6 H, $C\underline{H}_3CO_2$), 3.19 (m, 1 H, H-5), 3.55 (dd, 1 H, $J_{3,4}$ = 3.1 Hz, H-3), 3.88 (d, 1 H, $J_{1,2}$ = 10.0 Hz, H-1), 4.46 (m, 1 H, $J_{4,5}$ < 0.5 Hz, H-4), 5.73 (t, 1 H, $J_{2,3}$ = 9.9 Hz, H-2), 7.3, 7.4 [2 m, 15 H, $C(C_6\underline{H}_5)_3$]; ^{13}C NMR ($CDCl_3$) δ 16.8 (C-6), 20.9, 21.2 (2 C, $\underline{C}H_3CO_2$), 67.4 (C-1), 67.7 (C-2), 72.5 (C-4), 73.1 (C-3), 75.2 (C-5), 88.6 [$\underline{C}(C_6H_5)_3$], 115.3 (CN), 127.7, 128.0, 129.2, 144.1 [$C(\underline{C}_6H_5)_3$], 169.4, 170.3 (2C, $CH_3\underline{C}O_2$).

Anal. Calcd for $C_{30}H_{29}NO_6$: C, 72.13; H, 5.85; N 2.80. Found: C, 72.00; H, 5.76; N, 2.79.

Column chromatography also gave the slightly impure disaccharide **18** (TLC, solvent A_3, R_f 0.5; 58 mg, 16% with regard to **13**); ^{1}H NMR ($CDCl_3$) δ 0.97 (d, 3 H, $J_{5,6}$ = 6.7 Hz, H-6), 1.17 (d, 3 H, $J_{5',6'}$ = 6.4 Hz, H-6'), 1.75, 2.10, 2.17, 2.30 (4 s, 12 H, $C\underline{H}_3CO_2$), 3.18 (m, 1 H, H-5), 3.45 (dd, 1 H, $J_{3',4'}$ = 3.1 Hz, H-3'), 3.99 (dd, 1 H, $J_{3,4}$ = 3.3 Hz, H-3), 4.70 (m, 1 H, H-5'), 4.19 (d, 1 H, $J_{1',2'}$ = 7.8 Hz, H-1'), 4.44 (m, 1 H, $J_{4',5'}$ < 0.5 Hz, H-4'), 4.98 (d, 1 H, $J_{1,2}$ = 6.2 Hz, H-1), 5.40 (dd, 1 H, $J_{2,3}$ = 10.5 Hz, H-2), 5.29 (m, 1 H, $J_{4,5}$ < 0.5 Hz, H-4), 5.33 (dd, 1 H, $J_{2',3'}$ = 10.3 Hz, H-2'), 7.28, 7.40 [2 m, 15 H, $C(C_6\underline{H}_5)_3$]; ^{13}C NMR ($CDCl_3$) δ 16.3 (C-6'), 16.6 (C-6), 20.7, 21.1, 21.3 (4 C, $\underline{C}H_3CO_2$), 65.7 (C-1), 67.3 (C-2), 70.3 (C-5), 70.7 (2 C, C-2', C-4), 71.6 (C-5'), 72.6 (2 C; C-3', C-4'), 73.5 (C-3), 100.8 (C-1'), 115.1 (CN), 127.5, 127.9, 129.1, 144.4 [$\underline{C}(C_6H_5)_3$], 170.0 (4 C, $CH_3\underline{C}O$).

Finally, column chromatography afforded the oligomer **19** (TLC, solvent A_3, R_f 0.0 - 0.2; 60 mg). The relative ratio of integral intensities of the following signals in the ^{1}H NMR ($CDCl_3$) spectrum were determined: δ 0.9 - 1.2 (m, H-6) : 1.6 - 2.1 (m, $C\underline{H}_3CO_2$) : 3.1 - 5.5 (m, H-1 - H-5,) : 7.1 - 7.4 (m, aromat. H). The ratio of comparable intensities of these signals was about 22 : 40 : 33 : 15; d.p. 7. ^{13}C NMR ($CDCl_3$) δ 16.3 (C-6), 20.8 - 21.3 ($\underline{C}H_3CO_2$), 65.8 - 76.7 (C-2 - C-5), 88.1 [$\underline{C}(C_6H_5)_3$], 94.1 - 94.8 (C-1α; very small intensities), 100.7 - 100.9 (C-1β), 115.0 (CN) 127.5 - 129.5, 144.5 (C_6H_5), 168.6 - 170.7 ($CH_3\underline{C}O_2$).

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