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Carbohydrate Research 320 (1999) 147–160

CARBOHYDRATE RESEARCH

Synthesis of di- and trisaccharides incorporating a crown ether macrocycle☆,☆☆

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Received 17 October 1998; revised 10 May 1999; accepted 24 May 1999

Abstract

Di- and trisaccharides incorporating a non-reducing hexopyranose residue linked to a sugar bearing a 18-crown-6-ether were synthesized by the trichloroacetimidate method. Mainly β-glycosides were isolated when secondary alcohols were used as acceptors in the presence of $(C_2H_5)_2O{\cdot}BF_3$. Deprotection left four novel structures which were on one hand able to complex cationic species and on the other hand were able to be recognized by lectins. They are the first representatives of a new class of water-soluble cation vectors. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Trichloroacetimidates; Crown ethers; Glycosylation; Lectin recognition

1. Introduction

Lectins are widespread carbohydrate-binding proteins found in plants and vertebrate tissues [1]. They interact with the cell wall and with glycoproteins of the plasma membrane in order to mediate cell recognition, the aggregation process, and signal transduction [2]. This specificity for simple and complex oligosaccharidic structures plays a crucial role in recognition between putative biotic and target cells [3]. According to their biological status, lectins [4] and selectins [5], which are likely to be involved in the progression of complicated diseases such as chronic inflammation [6], are gaining more and more importance as cellular adhesion models [7]. For some years we have been interested in the development of sugar-derived crown ethers as complexing agents for cationic species. Thus, crown ethers were suitably modified in the sugar ring to accept catecholamines as guests [8,9]. One may expect that such macrocyclic hosts may also complex other types of biomolecules and interact directly with a number of RNA sequences via a 1,3-hydroxyamine functionality [10]. The next step should be the targeting of the supramolecular assembly of the macrocycle and its guest to a selected type of cell able to recognize a specific marker linked to the crown ether. In this regard, lectins (or selectins) expressed on the target cell should interact specifically with mono- or oligosac-

☆ Part 1 of the series: Lectin-targeted crown ethers.

☆☆ Part of the University Thesis of B. Dumont-Hornebeck (Nancy, 1997), presented in part at the 16th International Lectin Meeting (Interlec 16) held in Toulouse, France, August 8–13, 1995, Abstr. B 127.

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PII: S0008-6215(99)00151-2

charides attached to the supramolecular assembly [11]. On this basis, we recently embarked on the synthesis of glycosylated crown ethers to be tested against a galactose-specific lectin associated with the cell wall of *K. bulgaricus* [12]. This paper describes the details of the chemical synthesis of oligosaccharidic crown ethers using the trichloroacetimidate methodology [13].

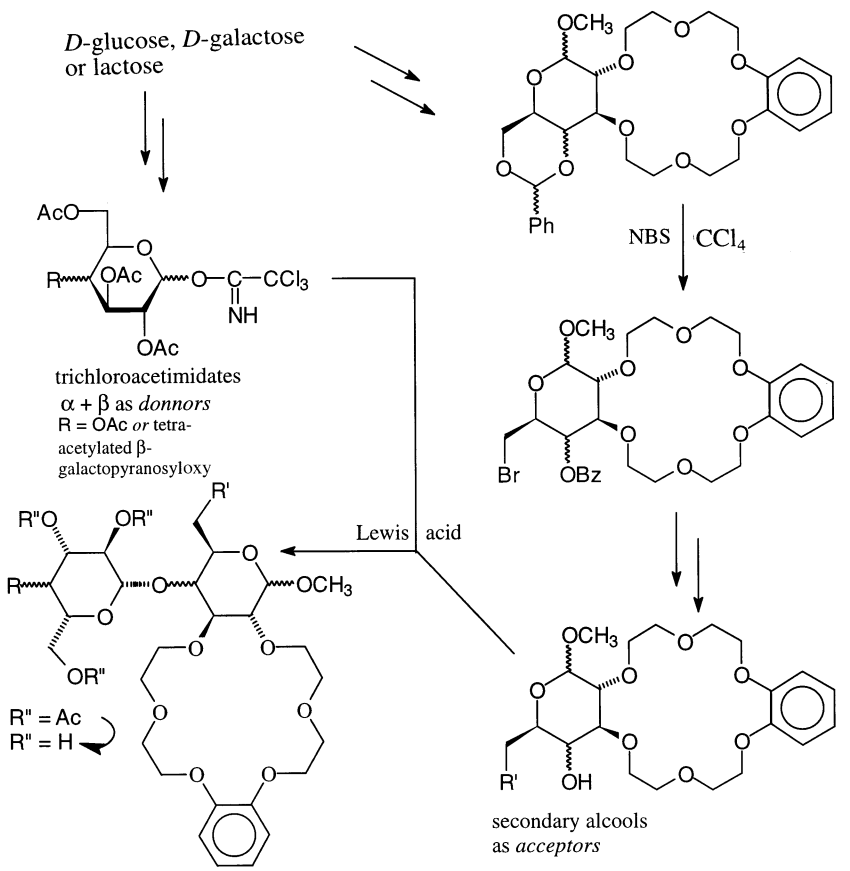
2. Results and discussion

The imidate method initiated by Pougny and Sinaÿ [14] and developed by Schmidt and co-workers [15] was employed throughout this work for the convergent synthesis of novel oligosaccharidic crown ethers. This strategy is outlined in Scheme 1.

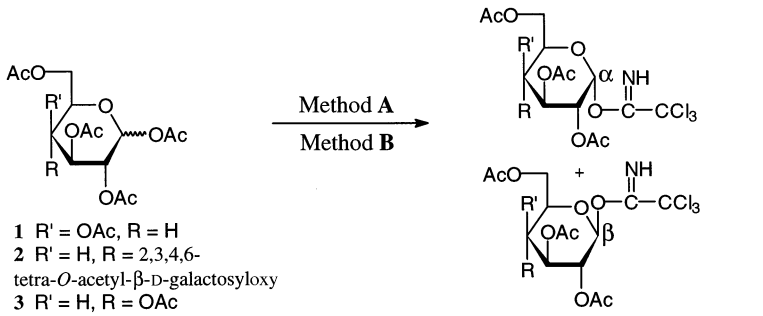
Trichloroacetimidates were prepared as stable crystalline mixtures of anomers by two methods from per-*O*-acetylated D-galactose (**1**), lactose (**2**), and D-glucose (**3**) (Scheme 2).

The anomeric ratio and the overall yields for the syntheses of trichloroacetimidates **4** [16], **5** [17], and **6** [18] are summarized in Table 1.

Hydrazine acetate in dimethylformamide instead of ammonia in THF at 0 °C allowed an easier 1-*O*-deacetylation control; cesium carbonate as a base (method B, M = Cs) led to shorter reaction times, cleaner reaction mixtures and a better yield in **4**. We gave up trying to isolate the thermodynamically favored α-imidates, since both anomers were believed to mainly yield the sole β-glycosidic linkage as expected from the neighboring-group participation of the 2-*O*-acetyl group [13,14]. However, an attempt with the primary alcohol **13** [19] as acceptor and the trichloroacetimidates **4** as donors in the presence of a catalytic amount of trimethylsilyl triflate [20] and finely ground molecular sieves (MS) in dichloromethane yielded after 2 h at 0 °C a mixture of α- and β-D-galactopyranosyl-(1 → 6)-α-D-glucopyranosides (3:1, 57%,



Scheme 1. Synthesis of glycosylated crown ethers from D-glucose, D-galactose or lactose.



1 R' = OAc, R = H
2 R' = H, R = 2,3,4,6-tetra-*O*-acetyl-β-D-galactosyloxy
3 R' = H, R = OAc

4 R' = OAc, R = H
5 R' = H, R = 2,3,4,6-tetra-*O*-acetyl-β-D-galactosyloxy
6 R' = H, R = OAc

Method **A**: i) NH_3, (3:7 MeOH/THF), 0 °C; ii) Cl_3CCN, K_2CO_3, CH_2Cl_2, rt.

Method **B**: i) $H_2N\text{-}NH_2$, AcOH, DMF, 50 °C; ii) Cl_3CCN, Cs_2CO_3, CH_2Cl_2, rt.

Scheme 2. Syntheses of trichloroacetimidates.

not represented here) according to the 400 MHz ^{1}H NMR. One must admit that this Lewis acid involves a rapid in situ anomerization of the donor in dichloromethane and that the displacement of the β-trichloroacetimidate by more reactive nucleophiles (such as primary alcohols) acquires a leading S_N2 character [21].

The synthesis of secondary alcohols **10** and **14** from **9** [19] has already been reported [13]. The acceptor **16** could be obtained either by nucleophilic displacement of bromine from **10** by an excess of sodium azide (99%) or from **9** by the same reaction followed by saponification of the intermediate **15** (aq NaOH, toluene, room temperature). In the same way, the nucleophilic displacement of the bromine atom by potassium phthalimide in dimethylformamide yielded the phthalimidate **17** (97%) from **10**. In the galactose series, the reduction of bromide **11** with lithium aluminum hydride yielded a separable mixture of alcohols **12** and **19** (14 and 56.5%, respectively) beside a trace of the ester **18** ($\sim$ 4%). The formation of both by-products **12** and **18** was ascribed to the bulky cis-substituents which hinder the approach of aluminohydride ion aggregates toward the galactose β-side (Scheme 3).

Secondary alcohols **10**, **12**, **14**, **16**, **17**, and **19** were glycosylated by different donors to give di- or trisaccharides **20**, **22**, **23**, **24**, **27**, **29**, **30**, **32**, **33**, and **35**. More precisely, glycosylation of **14** with 1.5 equivalents of **4** yielded the first target compound **20** (44%) after 5 h at room temperature in the presence of a large excess of boron trifluoride etherate in dichloromethane. The disaccharide **22**, which could not be detected in the reaction medium of **10** with **1** [22] in the conditions of Paulsen and Paal [23] after 2 h at room temperature, was readily obtained (62%) from the trichloroacetimidate **4** as donor with two equivalents of boron trifluoride etherate as 'catalyst'. This yield could even be raised up to 84% with the same β-selectivity if one equivalent of dried potassium tetrafluoroborate was added to the reaction mixture prior to addition of the donor. It has been established that the complexation of a potassium cation by similar crown ethers induces significant conformational changes of the fused sugar moiety [24]. Moreover, weaker interactions between the Lewis acid and the oxygen atoms of the crown ether should exist in its complex with the potassium cation involving altogether a better reactivity of the system.

In the same way, but without potassium tetrafluoroborate as the template agent, coupling **16** with two equivalents of **4** for 17 h at room temperature gave the expected disaccharide **23**, but only in 11% yield, and the disaccharide **24** in 23% yield from acceptor **17**. In all cases, the β-(1 $\rightarrow$ 4)-glycosidic linkage could be ascertained by ^{1}H NMR ($J_{1-2} \geq 7.0$ Hz) of the major product isolated after one or two chromatographic sequences on silica gel (see Section 3). The two disaccharides **27** and **29**, which displayed the β-D-galactopyranosyl-

(1→4)-β-D-galactopyranosyl linkage, were obtained in lower yields than their corresponding epimers **20** and **22**. In the same way, coupling the donor **5** with acceptors **14**, **10**, and **16** gave the trisaccharides **30**, **32**, and **33** (in 14, 55, and 14% yields, respectively). Here again, a unique β-(1→4)-glycosidic linkage was observed in the isolated reaction products. At least, coupling the donor **6** with the alcohol **10** afforded the disaccharide **35** in a fair yield (55%) after purification. The glycosylation yield seemed to be more dependent on the nature of the acceptor than on the nature of the donor: e.g., the azido group at C-6 of the 6-deoxysugar lowered the glycosylation rates and yields which became rather good (> 52%) when R′ was a bromine atom whatever the donor engaged. All acetylated disaccharides could be fully characterized by ^{1}H NMR, 2D-COSY and mass spectrometry. On the other hand, deacetylated oligosaccharides bearing a free amino function at C-6 of the sugar scaffold displayed ^{1}H NMR spectra with very poor resolution, suggesting a high level of self-association. Some transformations were performed on these oligosaccharides to isolate the target compounds **21**, **26**, **28**, **31**, and **39**. For example, disaccharides **22** and **35** could be reacted with an excess of sodium azide in dimethylformamide near 100 °C to give the azido compounds **23** and **36** (∼ 80%). The azide group was then hydrogenated over palladium to give the amines **25** and **38**, which were finally fully deacylated under the Zemplén conditions to yield the deprotected compounds **26** and **39**. As for **23** and **36**, the azide **33** could be reduced by hydrogen in the presence of palladium on charcoal in methanol to give the trisaccharide **34**. Alternatively we embarked on Gabriel synthesis from **22** and **35**, which were converted to the phthalimides **24** and **37**, and then deprotected to the previously isolated amino alcohols **26** and **39**. The overall yields were rather improved in this way; however, it did not allow us to isolate the pure intermediates **25** and **38**, which were recovered partially deacetylated by hydrazine after this penultimate step. For that reason, we did not apply the Gabriel synthesis to bromides **29** and **32**.

In summary, ten new acetylated oligosaccharides incorporating either a non-reducing galactose residue (compounds **20**, **22**, **23**, **24**, **27**, **29**, **30**, **32**, and **33**) or a glucose residue (disaccharide **35**) have been synthesized in acceptable yields by the trichloroacetimidate method. Mainly, if not solely, β-glycosides were isolated when secondary alcohols were used as acceptors. These glycosylated crown ethers may find applications in drug delivery. The in vitro recognition by a specific lectin of four selected deprotected oligosaccharides (**21**, **26**, **28**, and **31**) will be discussed in Part II of this series [25].

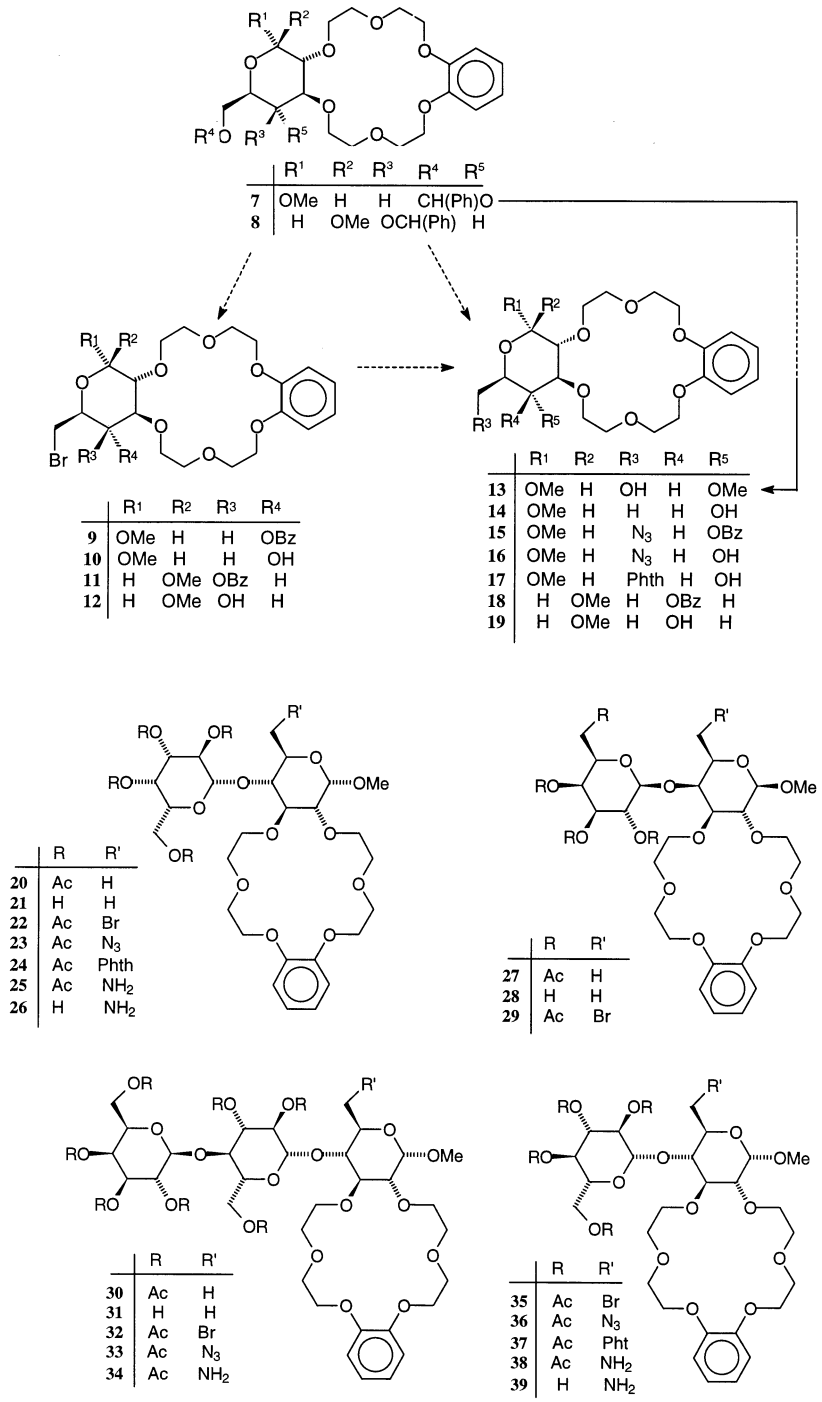
3. Experimental

General methods.—All reactions (except two-phase systems) were carried under a dried argon atmosphere. Chemicals were from Aldrich (France) and solvents from Prolabo (France). Methanol was distilled over Mg, toluene and THF over Na/benzophenone.

Table 1
Synthesis of trichloroacetimidates **4**–**6**

Starting material and method	Reaction time (h)		Product	Overall yield (%)	α:β ratio [a]
	i	ii (equiv of CCl_3CN/M_2CO_3)			
1 A	0.7	24 (*2.0*/*2.0*)	**4**	52	3:1
1 B	1.8	19 (*1.5*/*0.1*)	**4**	15	1:1
1 B		4.5 (*1.5*/*1.5*)	**4**	70	9:1
1 B		0.7 (*2.0*/*2.0*)	**4**	85	13:1
2 A	1.0	5.5 (*2.0*/*2.0*)	**5**	70	14:1
2 B	2.0	1.0 (*1.5*/*1.5*)	**5**	68	20:1
3 A	1.0	24 (*2.0*/*2.0*)	**6**	72	13:1
3 B	0.5	5 (*1.5*/*1.5*)	**6**	66	16:1

[a] By comparison of ^{1}H NMR NH signals between 8.5 and 9.0 ppm.



Scheme 3.

Dimethylformamide was distilled over CaH_2 and CH_2Cl_2 over P_2O_5 and stored over 4 Å MS under argon. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck Silica Gel plates (60 F_{254}). Visualization was achieved under a UV lamp at 254 nm and development with a spray of H_2SO_4 solution (50% in MeOH) before heating at 270 °C. Anhydrous $MgSO_4$ was used to dry the organic solutions during work-up. Yields refer to pure isolated compounds after preparative chromatography on Silica Gel (E. Merck, particle size 40–63 μM). Melting points were taken in capillary tubes on a Büchi apparatus and are uncorrected. Unless otherwise stated, ^1H and ^{13}C

NMR spectra were recorded with a Bruker AC250 spectrometer in $CDCl_3$ or D_2O at respectively, 250 and 62.9 MHz at 298 K. EI mass spectra were recorded on a Nermag R-1010 spectrometer at 70 eV and ES mass spectra using a Micromass Platform II of the UHP-Nancy I. Elemental analyses and LSI HRMS were performed by the Service Central de Microanalyse du CNRS (Vernaison, France), LSI on a Micromass ZAB2-SEQ from a thioglycerol/NaCl matrix (ionization Cs^+ at 35 kV). CE — abbreviation for crown ether — is used throughout the experimental section. Optical rotations were measured on a Perkin–Elmer 141 automatic polarimeter in a 1 dm cell at ambient temperature. Water used for HPLC was deionized and distilled prior to use. The HPLC-grade MeCN solvent from Carlo Erba was used without further purification for the same purpose. The HPLC used a C_{18} column: Cosmosil®, 250 × 4.6 mm i.d., 5 μm particle size (ref. 378-62 from Promochem, Germany) with UV detection at 275 nm, 0.1 AUFS, flow rate of 1 mL/min.

*Methyl [2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-6-bromo-2,3,6-trideoxy-α-*D*-glucopyranoside* (**10**).—To a solution of methyl [2,3-*b*]-(11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-4-*O*-benzoyl-6-bromo-2,3,6-trideoxy-α-D-glucopyranoside (**9**) [19] (4.70 g, 7.68 mmol) in toluene (50 mL) was added 50% aq NaOH (50 mL), and the mixture was vigorously stirred for 16 h, the reaction was monitored by TLC (1:1 EtOAc–*n*-hexane). Chilled water (100 mL) was added and the aq phase was extracted with CH_2Cl_2 (3 × 50 mL). The organic phases were combined, washed with water until neutral, dried, and concentrated to a gum which solidified on standing. Preparative crystallization from Et_2O–*i*-PrOH gave the alcohol **10** (3.80 g, 97%) as a white solid: mp 104–105 °C; $[\alpha]_D + 50.1°$ (*c* 2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.82 (bs, 4 H, catechol), 4.77 (d, 1 H, H-1), 4.2–3.98 (m, 6 H, 3 × OCH_2), 3.96–3.58 (m, 12 H, 5 × OCH_2, H-3, -5), 3.5 (dd, 1 H, $J_{5-6'}$ 7.0, $J_{6-6'}$ 10.0 Hz, H-6′), 3.49 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 9.0 Hz, H-4), 3.39 (dd, 1 H, J_{5-6} 2.0 Hz, H-6), 3.36 (s, 3 H, OCH_3), 3.34 (dd, 1 H, J_{1-2} 3.0, J_{2-3} 9.0 Hz, H-2), 2.96 (bs, 1 H, OH); EIMS: *m*/*z* Calcd for $C_{21}H_{31}BrO_9$ 506. Found 506 $[^{79}BrM]^{\bullet+}$ and 508 $[^{81}BrM]^{\bullet+}$.

*Methyl [2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-4-O-benzoyl-6-bromo-2,3,6-trideoxy-β-*D*-galactopyranoside* (**11**).—To a stirred dispersion of methyl [2,3-b]-(11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-4,6-*O*-benzylidene-2,3-dideoxy-β-D-galactopyranoside (**8**) [19] (4.00 g, 7.5 mmol) in abs CCl_4 (200 mL) was added dry $CaCO_3$ (1.88 g, 2.5 equiv) and NBS (1.67 g, 1.25 equiv). The resulting dispersion was immediately heated to reflux by an incandescent 500 W lamp for 30 min, cooled to 5 °C, and filtered through a sintered glass under the fume board. The remaining succinimide and calcium salts were exhaustively rinsed with CH_2Cl_2 and the combined organic phases washed successively with 0.2 M $Na_2S_2O_5$ (10 mL), 5% aq $NaHCO_3$ (10 mL) and water (10 mL), dried, and finally evaporated under reduced pressure. The residue was chromatographed (2:1 → 1:1 *n*-hexane–EtOAc) to yield the bromide **11** (3.88 g, 85%) as white crystals: mp 119–120 °C (*i*-Pr_2O); $[\alpha]_D + 22.3°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.61–7.39 (m, 5 H, Ar), 6.88 (bs, 4 H, catechol), 5.76 (d, 1 H, J_{4-5} 3.0 Hz, H-4), 4.32 (d, 1 H, J_{1-2} 7.5 Hz, H-1), 4.25–3.63 (m, 17 H, 8 × OCH_2, H-5), 3.6 (s, 3 H, OCH_3), 3.54 (dd, 1 H, J_{2-3} 9.5, J_{3-4} 3.0 Hz, H-3), 3.48–3.39 (m, 3 H, H-2, -6, -6′); EIMS: *m*/*z* Calcd for $C_{28}H_{35}BrO_{10}$ 610. Found 610, $[^{79}BrM]^{\bullet+}$ and 612 $[^{81}BrM]^{\bullet+}$.

*Methyl [2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α-*D*-glucopyranoside* (**14**).—A solution of crown ether **9** [19] (3.35 g, 5.47 mmol) in THF (25 mL) was dropped over 20 min onto a stirred suspension of $LiAlH_4$ (0.88 g, 4 equiv) in THF (25 mL) at 0 °C. After 10 h of stirring at rt, the suspension was refluxed for 2 h, so that TLC (EtOAc) showed the complete reduction of the bromide **9**. EtOAc (5 mL) was dropped at rt to react with hydride excess and the hydrolysis was completed with satd aq Na_2SO_4 (1 mL). The solution was filtered through a sintered glass under the fume board and the remaining salts rinsed twice with THF (25 mL). The solution was concentrated under reduced pressure and the residue dissolved in CH_2Cl_2 (50 mL), washed twice with water (20 mL), dried, and concentrated to a syrup

which solidified on standing. Preparative crystallization from *i*-PrOH–*n*-hexane afforded the alcohol **14** (2.04 g, 87%) as a white solid: mp 126–128 °C, $[\alpha]_D + 52.8°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.89 (bs, 4 H, catechol), 4.74 (d, 1 H, H-1), 4.32–4.1 (m, 5 H, $2.5 \times OCH_2$), 4.03–3.71 (m, 11 H, $5.5 \times OCH_2$), 3.65 (m, 1 H, H-5), 3.52 (t, 1 H, J_{2-3} 9.0 Hz, H-3), 3.41 (dd, 1 H, J_{1-2} 3.5 Hz, H-2), 3.39 (s, 3 H, OCH_3), 3.17 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 9.0 Hz, H-4), 1.7 (bs, 1 H, OH), 1.26 (d, 3 H, J_{5-6} 5.5 Hz, CH_3); EIMS: *m*/*z* Calcd for $C_{21}H_{32}O_9$ 428. Found 428 $[M]^{\bullet+}$.

*Methyl 6-azido-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-4-O-benzoyl-2,3,6-trideoxy-α-*D*-glucopyranoside* (**15**).—To a stirred solution of crown ether **9** [19] (3.07 g, 5.0 mmol) in DMF (80 mL) was added NaN_3 (0.651 g, 2 equiv) and the solution was heated to 130 °C. The reaction, monitored by TLC (3:2, EtOAc–*n*-hexane), was complete after 45 min. The solvent was evaporated, the residue dissolved in CH_2Cl_2 (70 mL), washed twice with water (20 mL), dried, and concentrated. Chromatography of the residue (3:2, EtOAc–*n*-hexane) yielded the azide **15** (2.294 g, 80%) as a colorless gum: $[\alpha]_D + 12.6°$ (*c* 1, $CHCl_3$); IR (NaCl): *v* 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$): δ 8.13 (d, 2 H, H-1, -5, Ar), 7.59 (t, 1 H, H-3, Ar), 7.46 (t, 2 H, H-2, -4, Ar), 6.88 (bs, 4 H, catechol), 5.1 (t, 1 H, J_{4-5} 9.5 Hz, H-4), 4.9 (d, 1 H, H-1), 4.22–3.7 (m, 16 H, $8 \times OCH_2$), 3.78 (m, 1 H, H-5), 3.56 (t, 1 H, J_{3-4} 9.5 Hz, H-3), 3.52 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 9.5 Hz, H-2), 3.5 (s, 3 H, OCH_3), 3.37 (dd, 1 H, $J_{5-6'}$ 7.0 Hz, H-6′), 3.25 (dd, 1 H, J_{5-6} 3.0 Hz, H-6); EIMS: *m*/*z* Calcd for $C_{28}H_{35}N_3O_{10}$ 573. Found 573 $[M]^{\bullet+}$.

*Methyl 6-azido-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α-*D*-glucopyranoside* (**16**).—The procedure employed was exactly the same as for the synthesis of alcohol **10**. From azide **15** (0.94 g, 1.64 mmol) was obtained the alcohol **16** (0.732 g, 95%) as a white solid after preparative crystallization from $i\text{-}Pr_2O$–*i*-PrOH: mp 98–99 °C, $[\alpha]_D + 48.5°$ (*c* 1, $CHCl_3$); IR (KBr) *v* 2098 cm^{-1} (N_3), 3400 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 6.87 (bs, 4 H, catechol), 4.81 (d, 1 H, H-1), 4.3–4.1 (m, 5 H, $2 \times OCH_2$, H-5), 4.04–3.7 (m, 12 H, $6 \times OCH_2$), 3.55 (t, 1 H, H-3), 3.51 (dd, 1 H, J_{5-6} 2.5 Hz, H-6), 3.44 (d, 1 H, J_{1-2} 3.0, J_{2-3} 9.0 Hz, H-2), 3.43 (s, 3 H, OCH_3), 3.42 (bt, 1 H, J_{3-4} 9.0, J_{4-5} 7.5 Hz, H-4), 3.39 (dd, 1 H, $J_{5-6'}$ 6.0, $J_{6-6'}$ 13.0 Hz, H-6′), 3.15 (bs, 1 H, OH); EIMS: *m*/*z* Calcd for $C_{21}H_{31}N_3O_9$ 469. Found 469 $[M]^{\bullet+}$.

*Methyl [2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-6-*N*-phthalimido-α-*D*-glucopyranoside* (**17**).—To a stirred solution of **10** (1.00 g, 1.97 mmol) in DMF (20 mL) was added potassium phthalimide (0.548 g, 1.5 equiv) and the reaction mixture was immediately heated to 135 °C. The reaction was monitored by TLC (1:1 EtOAc–*n*-hexane) and was complete after 5 h. The solvent was evaporated, the residue dissolved in CH_2Cl_2 (70 mL), washed twice with water (20 mL), dried, and concentrated to a gum (1.10 g, 97%) which solidified on standing: mp 137–139 °C (*i*-PrOH); IR (NaCl) *v* 1717 cm^{-1} (C=O); $[\alpha]_D + 56.7°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.9–7.7 (m, 4 H, Ar), 6.88 (bs, 4 H, catechol), 4.75 (d, 1 H, H-1), 4.3–3.7 (m, 20 H, $8 \times OCH_2$, H-4, -5, -6, -6′), 3.57 (t, 1 H, J_{3-4} 9.0 Hz, H-3), 3.46 (bs, 1 H, OH), 3.5, J_{2-3} 9.0 Hz, H-2), 3.34 (dd, 1 H, J_{1-2} 3.5 Hz, J_{2-3} 9.0 Hz, H-2), 3.31 (s, 3 H, OCH_3); EIMS: *m*/*z* Calcd for $C_{29}H_{35}NO_{11}$ 573. Found 573 $[M]^{\bullet+}$.

*Methyl [2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-β-*D*-galactopyranoside* (**19**).—The procedure was similar to that employed for the synthesis of alcohol **14** except that 8 equiv of $LiAlH_4$ (in two 0.25 g portions) were used and the reaction time was 6 days at reflux. From 1.00 g (1.635 mmol) of bromide **11** were successively isolated by gradient chromatography with 1:1 → 1:9 *n*-hexane–EtOAc: (i) 0.148 g (15%) of starting material **11**; (ii) 38 mg (4.4%) of methyl [2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-4-*O*-benzoyl-2,3,6-trideoxy-β-D-galactopyranoside (**18**) as a colorless gum: $[\alpha]_D + 21.5°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.09 (bd, 2 H, Ar), 7.56 (bt, 1 H, Ar), 7.43 (t, 2 H, Ar), 6.93–6.83 (m, 4 H, catechol), 5.5 (d, 1 H, H-4, $J_{4-5} < 1$ Hz), 4.28 (1 H, H-1), 4.23–4.0 (m, 5 H, $2.5 \times OCH_2$), 3.97–3.63 (m, 12 H, $5.5 \times OCH_2$, H-5), 3.57 (s, 3 H, OCH_3), 3.53 (dd, 1 H, J_{3-4} 3.5 Hz, H-3), 3.42 (dd, 1 H, J_{1-2} 7.5, J_{2-3} 9.5 Hz, H-2), 1.25 (d, 3 H, J_{5-6} 6.4 Hz, CH_3); EIMS:

m/z Calcd for $C_{28}H_{36}O_{10}$ 532. Found 532 $[M]^{\bullet+}$; (iii) 0.114 g (13.8%) of methyl [2,3-*b*](11,12 - benzo - 1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-6-bromo-2,3,6-trideoxy-β-D-galactopyranoside (**12**) as white crystals: mp 100–101 °C (*i*-Pr_2O); $[\alpha]_D - 3.0°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.9 (bs, 4 H, Ar), 4.19 (d, 1 H, H-1), 4.19–3.7 (m, 17 H, 8 × OCH_2, H-4) 3.65–3.5 (m, 3 H, H-5, -6, -6′), 3.52 (s, 3 H, OCH_3), 3.43 (t, 1 H, J_{1-2} 7.2 Hz, H-2), 3.34 (dd, 1 H, J_{2-3} 9.5, J_{3-4} 3.0 Hz, H-3), 2.55 (bs, 1 H, OH); EIMS: *m/z* Calcd for $C_{21}H_{31}BrO_9$ 506. Found 506 $[^{79}BrM]^{\bullet+}$ and 508 $[^{81}BrM]^{\bullet+}$; (iv) 0.395 g (56.5%) of target compound **19** as a white solid: mp 147–149 °C (*i*-PrOH–*n*-hexane), $[\alpha]_D - 1.0°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.88 (bs, 4 H, catechol), 4.23–4.05 (m, 5 H, H-1, 2 × OCH_2), 4.0–3.68 (m, 13 H, 6 × OCH_2, H-4), 3.50 (m, 1 H, H-5), 3.49 (s, 3 H, OCH_3), 3.36 (d, 1 H, J_{1-2} 6.5 Hz, H-2), 3.32 (dd, 1 H, J_{2-3} 6.5, J_{3-4} 3.0 Hz, H-3), 2.4 (bs, 1 H, OH), 1.33 (d, 3 H, J_{5-6} 6.7 Hz, CH_3); EIMS: *m/z* Calcd for $C_{21}H_{32}O_9$ 428. Found 428 $[M]^{\bullet+}$.

Methyl (2,3,4,6-tetra-O-*acetyl-β*-D-*galactopyranosyl) - (1→4) - [2,3*-b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α*-D-*glucopyranoside* (**20**).—To a solution of acceptor **14** (0.25 g, 0.58 mmol) and donor **4** (0.46 g, 1.5 equiv) in CH_2Cl_2 (6 mL) was added crushed 4 Å MS (~1 g, activated at 105 °C for 24 h and stored in vacuo over P_2O_5) and the suspension was magnetically stirred under argon for 30 min at rt. Boron trifluoride etherate (1.5 mL, 20 equiv) in CH_2Cl_2 (6 mL) was then added dropwise over a period of 15 min. The reaction was monitored by TLC (1:1, EtOAc–*n*-hexane) and was diluted after 5 h with CH_2Cl_2 (20 mL). The suspension was filtered and the filtrate neutralized by slow addition of satd $NaHCO_3$ (~20 mL) at 0 °C. The isolated organic phase was then washed twice with water (5 mL), dried with $MgSO_4$, and concentrated under reduced pressure. Chromatography (2:1, EtOAc–*n*-hexane) of the residue on silica gel afforded the disaccharide **20** (0.191 g, 44%) as a white solid: mp 167–168 °C (EtOAc), $[\alpha]_D + 38.5°$ (*c* 1, $CHCl_3$); ^1H 2D-NMR ($CDCl_3$): δ 6.95–6.82 (m, 4 H, catechol), 5.37 (d, 1 H, H-4 Gal), 5.18 (dd, 1 H, H-2 Gal), 5.02 (d, 1 H, J_{1-2} 8.0 Hz, H-1 Gal), 4.97 (dd, 1 H, J_{2-3} 10.3, J_{3-4} 3.2 Hz, H-3 Gal), 4.71 (d, 1 H, H-1 Glc), 4.25–3.6 (m, 16 H, 8 × OCH_2), 4.02 (m, 1 H, J_{4-5} 1.0 Hz, H-5 Gal), 3.74 (dd, 2 H, J_{5-6} 6.0 Hz, H-6, -6′ Gal), 3.71 (t, 1 H, J_{3-4} 9.0 Hz, H-3 Glc), 3.66 (m, 1 H, H-5 Glc), 3.4 (d, 1 H, J_{1-2} 3.5, J_{2-3} 9.0 Hz, H-2 Glc), 3.37 (s, 3 H, OCH_3), 3.28 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 9.0 Hz, H-4 Glc), 2.14, 2.06, 1.99, 1.98 (4 s, each 3 H, 4 × OAc), 1.17 (d, 3 H, J_{5-6} 6.3 Hz, CH_3 Glc); IEMS: *m/z* Calcd for $C_{35}H_{50}O_{18}$ 758. Found 758 $[M]^{\bullet+}$; Anal. Calcd for $C_{35}H_{50}O_{18}$ C, 55.40; H, 6.64. Found: C, 55.27; H, 6.59.

Methyl β-D-*galactopyranosyl-(1→4)-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α*-D-*glucopyranoside* (**21**).—To a solution of **20** (64 mg, 88 μmol) in abs MeOH (10 mL) under argon, was added MeONa (~20 mg) and the mixture was stirred at rt until TLC (1:1, EtOAc–*n*-hexane) showed that the deacetylation was complete (~30 min). The mixture was demineralized for 15 min with Dowex (H^+) cation-exchange resin (~0.8 mL) and filtered. The resin was washed with MeOH and the solvents evaporated under reduced pressure to yield **21** (49 mg, 98%) as a colorless solid: mp 145–147 °C (MeOH); $[\alpha]_D + 42.5°$ (*c* 0.2, H_2O); ^1H NMR (D_2O): δ 7.0–6.9 (m, 4 H, catechol), 4.7 (d, 1 H, J_{1-2} 3.0 Hz, H-1 Glc), 4.45 (d, 1 H, J_{1-2} 7.5 Hz, H-1 Gal), 4.16 (t, 3 H, 1.5 × OCH_2), 4.05–3.55 (m, 20 H, 6.5 × OCH_2, H-3, -4, -5 Glc, H-2, -3, -4, -5 Gal), 3.5–3.4 (m, 3 H, H-2 Glc, H-6, -6′ Gal), 3.32 (s, 3 H, OCH_3), 1.3 (d, 3 H, J_{5-6} 6.1 Hz, CH_3); ESMS: *m/z* Calcd for $C_{27}H_{42}O_{14}$ 590. Found 613 $[M + Na]^+$; Anal. Calcd for $C_{27}H_{42}O_{14}$ C, 54.90; H, 7.17. Found: C, 54.72; H, 7.20; t_r (HPLC) 14.6 min (4:1 water–MeCN as eluent).

Methyl (2,3,4,6-tetra-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-6-bromo-2,3,6-trideoxy-α-D-glucopyranoside* (**22**).—The same procedure was used as for the synthesis of **20** except 2 equiv of donor **4** (0.98 g) and catalyst $(C_2H_5)_2O{\cdot}BF_3$ (0.25 mL) were used. Yield after 21 h of reaction at rt from 0.507 g of **10** (1.0 mmol), similar work-up as **20**, and chromatography (1:1→9:1,

EtOAc–*n*-hexane) on silica gel: 0.517 g (62%) of **22** as a white solid: mp 153–155 °C (EtOAc); $[\alpha]_D + 46.8°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.9 (bs, 4 H, catechol), 5.38 (d, 1 H, $J_{4-5} < 1.0$ Hz, H-4 Gal), 5.17 (dd, 1 H, H-2 Gal), 5.06 (d, 1 H, J_{1-2} 8.0 Hz, H-1 Gal), 4.98 (dd, 1 H, J_{2-3} 10.0, J_{3-4} 3.5 Hz, H-3 Gal), 4.81 (d, 1 H, J_{1-2} 3.5 Hz, H-1 Glc), 4.3–3.4 (m, 25 H, 8 × OCH_2, H-2, -3, -4, -5, -6, -6′ Glc, H-5, -6, -6′ Gal), 3.38 (s, 3 H, OCH_3), 2.14, 2.1, 2.03, 1.97 (4 s, each 3 H, 4 × OAc); EIMS: *m*/*z* Calcd for $C_{35}H_{49}BrO_{18}$ 836. Found 836 $[^{79}BrM]^{\bullet+}$ and 838 $[^{81}BrM]^{\bullet+}$.

Methyl (2,3,4,6-tetra-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-6-azido-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α-*D*-glucopyranoside* (**23**).—The same procedure was used as for the synthesis of **20**. From 0.30 g (0.64 mmol) of acceptor **16**, after 17 h of reaction at rt, pyridine (1 mL) was added and the reaction mixture was diluted with CH_2Cl_2 (50 mL) to give, after the usual work-up and chromatography (1:1 → 9:1, EtOAc–*n*-hexane) on silica gel, the azide **23** (57 mg, 11%) as a pale-yellow gum: $[\alpha]_D + 50.2°$ (*c* 1, $CHCl_3$); IR (NaCl) *v* 2102 cm^{-1} (N_3); ^1H 2D-NMR ($CDCl_3$): δ 6.9 (bs, 4 H, catechol), 5.35 (dd, 1 H, $J_{4-5} < 2.0$ Hz, H-4 Gal), 5.11 (dd, 1 H, H-2 Gal), 5.03 (d, 1 H, J_{1-2} 7.5 Hz, H-1 Gal), 4.95 (dd, 1 H, J_{3-4} 3.0, J_{2-3} 9.8 Hz, H-3 Gal), 4.78 (d, 1 H, J_{1-2} 3.5 Hz, H-1 Glc), 4.25–3.7 (m, 22 H, 8 × OCH_2, H-6, -6′, -5 Gal, H-3, -4, -5 Glc), 3.46 (dd, 1 H, H-6′ Glc), 3.41 (d, 1 H, H-2 Glc), 3.4 (s, 3 H, OCH_3), 3.25 (dd, 1 H, $J_{6-6'}$ 12.0, J_{5-6} 3.0 Hz, H-6 Glc), 2.14–1.93 (4 s, each 3 H, 4 × OAc); EIMS: *m*/*z* Calcd for $C_{35}H_{49}N_3O_{18}$ 799. Found 799 $[M]^{\bullet+}$.

Methyl (2,3,4,6-tetra-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-6-*N*-phthalimido-2,3,6-trideoxy-α*-D-*glucopyranoside* (**24**).—This compound has been obtained by two methods. Method C: to a solution of bromine **22** (0.138 g, 0.164 mmol) in DMF (10 mL) was added potassium phthalimide (46 mg, 1.5 equiv) and the reaction mixture was heated for 1.5 h at 150 °C. Similar work-up as for **17** and chromatography (EtOAc → 9:1 CH_2Cl_2–EtOH) on silica gel yielded 0.105 g (71%) of **24** as a colorless gum: $[\alpha]_D + 40.4°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.95–7.7 (m, 4 H, Ar), 6.9 (bs, 4 H, catechol), 5.36 (t, 1 H, J_{4-5} 3.0 Hz, H-4 Gal), 5.22 (t, 1 H, H-2 Gal), 5.0 (dd, 1 H, J_{2-3} 9.5, J_{3-4} 3.0 Hz, H-3 Gal), 4.9 (d, 1 H, J_{1-2} 8.0 Hz, H-1 Gal), 4.63 (d, 1 H, H-1 Glc), 4.34 (dd, 1 H, J_{5-6} 2.0, $J_{6-6'}$ 11.5 Hz, H-6′ Gal), 4.25–3.6 (m, 22 H, 8 × OCH_2, H-3, -5, -6, -6′ Glc, H-5, -6 Gal), 3.54 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 9.0 Hz, H-4 Glc), 3.36 (dd, 1 H, J_{1-2} 3.0, J_{2-3} 9.0 Hz, H-2 Glc), 3.07 (s, 3 H, OCH_3), 2.2–1.9 (4 s, each 3 H, 4 × OAc); EIMS: *m*/*z* Calcd for $C_{43}H_{53}NO_{20}$ 903. Found 904 $[M + H]^+$. Method D: the same procedure was used as for the synthesis of **20**. From 0.250 g (0.43 mmol) of **17**, after 20 h of reaction at rt, usual work-up, and chromatography (1:1 → 9:1, EtOAc–*n*-hexane) on silica gel were isolated 29 mg (23%) of a gum with ^1H NMR spectrum identical to that described above.

Methyl (2,3,4,6-tetra-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-6-amino-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacy-clooctadeca-11-ene)-2,3,6-trideoxy-α-*D*-glucopyranoside* (**25**).—To a solution of the azide **23** (0.121 g) in 1:1 MeOH–EtOAc (20 mL) under argon was added palladium on activated charcoal (10% Pd, 100 mg) and the magnetically stirred suspension was saturated with H_2 ($\sim$780 Torr) at rt. The reaction was monitored by TLC (EtOAc) and was stopped after 30 h by filtration through a Celite 521 pad. The residue was purified by chromatography on deactivated silica gel (1:1 EtOAc–*n*-hexane then 9:1 → 1:9 EtOAc–EtOH) to yield the amine **23** (65 mg, 56%) as a pale-yellow solid: mp 57–60 °C, $[\alpha]_D + 38.5°$ (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.93–6.85 (m, 4 H, catechol), 5.37 (d, 1 H, $J_{4-5} < 2.0$ Hz, H-4 Gal), 5.17 (dd, 1 H, H-2 Gal), 5.06 (d, 1 H, J_{1-2} 8.0 Hz, H-1 Gal), 4.96 (dd, 1 H, J_{2-3} 10.0, J_{3-4} 3.6 Hz, H-3 Gal), 4.78 (d, 1 H, H-1 Glc), 4.25–3.62 (m, 23 H, 8 × OCH_2, H-6, -6′, -5 Gal, H-3, -5, -6, -6′ Glc), 3.45 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 9.3 Hz, H-4 Glc), 3.41 (s, 3 H, OCH_3), 3.37 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 9.5 Hz, H-2 Glc), 2.45 (d, 2 H, NH_2), 2.14, 2.05, 1.99, 1.97 (4 s, each 3 H, 4 × OAc); EIMS: *m*/*z* Calcd for $C_{35}H_{51}NO_{18}$ 773. Found 774 $[M + H]^+$.

*Methyl β-*D*-galactopyranosyl-(1→4)-6-amino-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-*

hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α-D-glucopyranoside (**26**).—Method E: to a suspension of K_2CO_3 (13.4 mg, 1.25 equiv) in MeOH (10 mL) was added hydrazine hydrochloride (13.2 mg, 2.5 equiv) and the mixture was stirred at rt as long as CO_2 evolved ($\sim$45 min). Then, 70 mg (0.8 mmol) of the disaccharide **24** was added to the resulting solution and this was heated to gentle reflux. The reaction was monitored by TLC (EtOAc) and was stopped after 2 h. The solvent was evaporated and the residue dissolved in CH_2Cl_2 (50 mL) and washed with 1% aq Li_2CO_3 (10 mL). The aq phase was extracted with CH_2Cl_2 (3 × 20 mL), the organic phases combined, dried, concentrated, and purified by chromatography on silica gel ($CH_2Cl_2 \rightarrow$ 9:1 CH_2Cl_2–EtOH) to afford 47 mg of partially deacetylated disaccharide, which was dissolved in MeOH (10 mL) and treated with 1 M methanolic MeONa (0.2 mL) for 2 h at rt. The solution was then demineralized for 15 min with Dowex (H^+) cation-exchange resin ($\sim$0.5 mL) and filtered. The beads were rinsed with MeOH and the solvents evaporated under reduced pressure to yield the target compound **26** (37 mg, 70% over two steps) as a pale-yellow gum: $[\alpha]_D + 38.1°$ (*c* 0.5, CH_3CN); ^1H NMR (D_2O): δ 7.05–6.95 (m, 4 H, catechol); 4.92 (d, 1 H, J_{1-2} 3.5 Hz, H-1 Glc), 4.45 (d, 1 H, J_{1-2} 7.5 Hz, H-1 Gal), 4.25–4.1 (m, 4 H, 2 × OCH_2), 4.05–3.2 (m, 27 H, H-6, -6′ Glc, OCH_3, H-5, -4, -3, -2 Glc, H-6, -6′, -5, -4, -3, -2 Gal, 6 × OCH_2); ^{13}C NMR (3:1 acetone-d_6–D_2O): δ 122.1 (C-4, -5 catechol), 114.3 (C-3 catechol), 114.0 (C-6 catechol), 104.2 (C-1 Gal), 97.4 (C-1 Glc), 79.4 (C-4 Glc), 78.5 (C-5 Gal), 74.0, 73.9 (C-5, -3 Glc), 72.1, 71.9 (C-4, -3 Gal), 71.3, 70.8, 70.6, 69.5 (OCH_2), 69.2 (C-2 Gal), 68.9 (C-2 Glc), 61.8 (C-6 Gal), 55.1 (OCH_3), 40.8 (C-6 Glc), LSIHRMS: *m*/*z* Calcd for $C_{27}H_{43}NO_{14}Na$ 628.2581. Found 628.2575 $[M + Na]^+$; t_r (HPLC) 14.1 min (H_2O as eluent). Method F: a solution of the amine **25** (40 mg, 0.05 mmol) was deacetylated in the Zemplén conditions (as for disaccharide **20**) for 24 h at rt, purified by elution on basic alumina (Fluka type 5016 A) with 7:3 CH_3CN–H_2O to yield **25** (31 mg, 99%) as a pale-orange gum identical in all aspects with the compound prepared by method E.

Methyl (2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-[2,3-b](11,12-benzo-1,4,7,-10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-β-D-galactopyranoside (**27**).—The same procedure was used as for the synthesis of the disaccharide **20**. From 0.230 g (0.56 mmol) of acceptor **19** and 2 equiv of donor **4**, after 24 h of reaction at rt, usual work-up, and chromatography on silica gel (1:1 → 9:1 EtOAc–*n*-hexane), was isolated 0.114 g (28%) of disaccharide **27** as a pale-yellow gum: $[\alpha]_D + 43.9°$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.94–6.87 (m, 4 H, catechol), 5.35 (dd, 1 H, $J_{4-5} < 1.0$ Hz, H-4 Gal), 5.19 (dd, 1 H, H-2 Gal), 5.02 (dd, 1 H, J_{2-3} 10.5, J_{3-4} 3.4 Hz, H-3 Gal), 4.64 (d, 1 H, J_{1-2} 7.8 Hz, H-1 Gal), 4.2–4.02 (m, 7 H, 2 × OCH_2, H-1 CE, H-6, -6′ Gal), 4.0–3.64 (15 H, 6 × OCH_2, H-4, -5 CE, H-5 Gal), 3.75 (s, 3 H, OCH_3), 3.55 (dd, 1 H, H-3 CE), 3.5 (t, 1 H, $J_{1-2} = J_{2-3} \sim$ 8.5 Hz, H-2 CE), 2.15, 2.03, 2.02, 1.98 (4 s, each 3 H, 4 × OAc), 1.29 (d, 3 H, J_{5-6} 6.5 Hz, CH_3); ^{13}C HMQC-NMR ($CDCl_3$): δ 169.5, 169.4, 168.9 (CH_3CO_2), 148.0, 147.8 (C-2, -1 catechol), 120.8, 120.6 (C-5, -4 catechol), 113.5, 113.0 (C-6, -3 catechol), 101.3 (C-1 Gal), 101.0 (C-1 EC), 77.3, 75.9, 74.3 (C-3, -5 Gal, C-3 EC), 70.3 (OCH_2), 69.9 (C-2 EC), 69.7 (OCH_2), 69.4 (C-5 EC), 68.9, 68.7, 68.6 (OCH_2), 68.2 (C-4 EC), 67.9 (OCH_2), 67.5, 66.1, 60.5 (C-4, -2, -6 Gal), 57.0 (OCH_3), 20.0, 19.8 (CH_3CO_2), 15.4 (C-6 EC); EIMS: *m*/*z* Calcd for $C_{35}H_{50}O_{18}$ 758. Found 758 $[M]^{\bullet+}$.

Methyl β-D-galactopyranosyl-(1→4)-[2,3-b](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-β-D-galactopyranoside (**28**).—The same procedure was used as for the deacetylation of **20**. Yield after 24 h of reaction at rt and usual work-up: 87 mg (99%) of disaccharide **28** as a pale-yellow gum: $[\alpha]_D + 37.2°$ (*c* 0.2, CH_3CN); ^1H NMR (D_2O): δ 7.0 (bs, 4 H, catechol), 4.5 (d, 1 H, J_{1-2} 7.0 Hz, H-1 Gal), 4.1–4.25 (m, 5 H, 2.5 × OCH_2), 4.0 (d, 1 H, J_{1-2} 7.5 Hz, H-1 CE), 3.9–3.4 (m, 24 H, OCH_3, H-6, -6′ Gal, 5.5 × OCH_2, H-2, -3, -4, -5 CE, H-2, -3, -4, -5 Gal), 1.2 (d, 3 H, J_{5-6} 6.0 Hz, CH_3); ^{13}C NMR (CD_3CN): δ 148.6 (C-1, -2 catechol), 122.5 (C-4, -5 catechol), 114.6, 113.2 (C-3, -6 catechol), 104.9, 103.6, (C-1 CE, C-1 Gal), 78.3,

76.1, 74.5, 73.9, 72.6, 69.6 (C-2, -3, -4, -5 CE, C-2, -3, -4, -5 Gal), 70.9, 70.6, 70.0, 69.9, 68.9, 68.4, 68.0 (OCH_2), 61.8 (C-6 Gal), 57.4 (OCH_3), 16.9 (C-6 CE); LSIHRMS: m/z Calcd for $C_{27}H_{42}O_{14}Na$ 613.2472. Found 613.2508 $[M + Na]^+$.

Methyl (2,3,4,6-tetra-O-*acetyl-β*-D-*galactopyranosyl)-(1→4)-[2,3*-b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-6-bromo-2,3,6-trideoxy-β*-D-*galactopyranoside* (**29**).—The same procedure was used as for the synthesis of the disaccharide **20**. From 75 mg (0.15 mmol) of acceptor **12** with 2 equiv of the donor **4**, after 16 h of reaction at rt, usual work-up, and chromatography on silica gel (1:1→9:1 EtOAc–*n*-hexane) 64 mg (52%) of the disaccharide **29** was isolated as a pale-yellow wax: $[\alpha]_D + 18.7°$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.9 (bs, 4 H, catechol), 5.35 (d, 1 H, H-4 Gal), 5.2 (dd, 1 H, $J_{4-5} < 1.5$ Hz, H-2 Gal), 5.02 (dd, 1 H, J_{2-3} 10.5, J_{3-4} 3.5 Hz, H-3 Gal), 4.64 (d, 1 H, J_{1-2} 7.5 Hz, H-1 Gal), 4.14 (d, 1 H, H-1 CE), 4.25–3.64 (m, 22 H, 8 × OCH_2, H-5, -6, -6′ CE, H-5, -6, -6′ Gal), 3.53 (dd, 1 H, H-3 CE), 3.5 (s, 3 H, OCH_3), 3.47 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 8.0 Hz, H-4 CE), 3.29 (t, 1 H, $J_{1-2} \sim J_{2-3}$ 7.0 Hz, H-2 CE), 2.12, 2.03, 2.02, 1.97 (4 s, each 3 H, 4 × OAc), EIMS: m/z Calcd for $C_{35}H_{49}BrO_{18}$ 836. Found 836 $[^{79}BrM]^{\bullet+}$ and 838 $[^{81}BrM]^{\bullet+}$.

Methyl (2,2′,3,3′,4′,6,6′-hepta-O-*acetyl-β-lactosyl)-(1→4)-[2,3*-b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α*-D-*glucopyranoside* (**30**).—To a solution of the acceptor **14** (0.84 g, 1.96 mmol) and donor **5** (2.14 g, 1.4 equiv) in CH_2Cl_2 (30 mL) was added crushed 4 Å MS (~1 g) and the suspension was magnetically stirred under argon for 30 min at rt. A solution of trimethylsilyl triflate (80 μL, ~0.2 equiv) in CH_2Cl_2 (10 mL) was then added dropwise over 45 min. The reaction was monitored by TLC (EtOAc), a new portion of **5** (0.77 g, 0.5 equiv) being added after 22 h of stirring. The reaction was definitively stopped after 46 h (total time) by addition of abs pyridine (3 mL). Usual work-up and chromatography on a silica gel column (EtOAc) afforded a partially deprotected trisaccharide according to ^1H NMR. Therefore, the material was reacetylated in 1:9 pyridine–Ac_2O (10 mL) at rt for 22 h with a crystal of 4-DMAP to afford, after chromatography (1:1 CH_2Cl_2–Et_2O) on silica gel, the trisaccharide **30** (0.290 g, 14%) as a white solid: mp 85–87 °C (EtOAc), $[\alpha]_D +$ 24.0° (*c* 1, $CHCl_3$); ^1H 2D-NMR ($CDCl_3$): δ 6.9–6.8 (m, 4 H, catechol), 5.31 (d, 1 H, J_{4-5} 3.0 Hz, H-4 Gal), 5.1 (t, 1 H, H-2 Glc), 5.07 (dd, 1 H, J_{2-3} 10.5 Hz, H-2 Gal), 4.93 (d, 1 H, H-1 Glc, J_{1-2} 8.0 Hz), 4.9 (dd, 1 H, J_{3-4} 3.7, J_{2-3} 10.3 Hz, H-3 Gal), 4.82 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 9.0 Hz, H-3 Glc), 4.68 (d, 1 H, H-1 CE), 4.42 (d, 1 H, J_{1-2} 7.6 Hz, H-1 Gal), 4.23–3.55 (m, 24 H, H-5 CE, 8 × OCH_2, H-4, -5, -6, -6′ Glc, H-5, -6, -6′ Gal,), 3.61 (t, 1 H, H-3 CE), 3.36 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 9.5 Hz, H-2 CE), 3.32 (s, 3 H, OCH_3), 3.21 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 9 Hz, H-4 CE), 2.11 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.0 (bs, 12 H, 4 × OAc), 1.93 (s, 3 H, OAc), 1.14 (d, 3 H, J_{5-6} 6.0 Hz, CH_3); ESMS: m/z Calcd for $C_{47}H_{66}O_{26}$ 1047. Found 1070 $[M + Na]^+$.

Methyl β-lactosyl-(1→4)-[2,3-b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α*-D-*glucopyranoside* (**31**).—To a solution of the trisaccharide **30** (0.233 g, 0.22 mmol) in abs MeOH (15 mL) under argon was added NaOMe (~25 mg) and the mixture was stirred at rt until TLC (EtOAc) showed that the Zemplén deacetylation was complete (2 h). The mixture was demineralized for 15 min with Dowex (H^+) cation-exchange resin (~0.8 mL) and filtered. The beads were rinsed with MeOH and solvents evaporated under reduced pressure to yield **31** (171 mg, 99%) as a white solid: mp 138–140 °C (MeOH); $[\alpha]_D + 33.5°$ (*c* 0.2, DMF); ^1H NMR (1:1 CD_3CN–D_2O): δ 7.0 (bs, 4 H, catechol), 4.75 (d, 1 H, J_{1-2} 3.0 Hz, H-1 CE), 4.44 (d, 1 H, J_{1-2} 7.5 Hz, H-l Gal), 4.08 (t, 4 H, 2 × OCH_2), 4.0–3.3 (m, 30 H), 3.28 (s, 3 H, OCH_3), 3.18 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 8.5 Hz, H-4 EC), 1.23 (d, 3 H, J_{5-6} 6.0 Hz, CH_3); ^{13}C NMR (1:1 CD_3CN–D_2O): δ 149.0 (C-1, -2 catechol), 122.7 (C-4, -5 catechol), 115.1, 114.9 (C-3, -6 catechol), 103.95 (C-1 Gal), 103.1 (C-1 Glc), 97.7 (C-1 CE), 72.7, 71.5, 71.05, 70.4, 70.0, 69.95, 69.7, 69.5 (8 × OCH_2), 82.6, 79.8, 79.6, 75.3 (C-2, -3, -5, -4 Glc), 80.6, 73.5, 71.8, 69.4 (C-2, -3, -4, -5 Gal), 76.2, 75.8, 74.4, 67.5, (C-4, -5, -3, -2 CE), 61.9, 61.3 (C-6 Glc, C-6 Gal), 55.5 (OCH_3), 17.7

(C-6 CE); FABMS: *m/z* Calcd for $C_{33}H_{52}O_{19}$: 752. Found 775 $[M+Na]^+$; Anal. Calcd for $C_{33}H_{52}O_{19}$ C, 52.66; H, 6.96. Found C, 52.45; H, 6.80; t_r (HPLC) 16.4 min (80:20 H_2O–CH_3CN as eluent).

Methyl (2,2′,3,3′,4′,6,6′-hepta-O-*acetyl-β-lactosyl)-(1→4)-[2,3-*b*](11,12-benzo-1,4,7,10,-13,16-hexaoxacyclooctadeca-11-ene)-6-bromo-2,3,6-trideoxy-α-*D*-glucopyranoside* (**32**).— The same procedure was used as for the synthesis of the disaccharide **20**. From 0.45 g (0.887 mmol) of acceptor **10** with 1.385 g (2 equiv) of the donor **5**, after 24 h of reaction at rt, usual work-up, and chromatography on silica gel (1:1 EtOAc–*n*-hexane), was isolated ~0.60 g of partially deacetylated trisaccharide as a gum according to ^{1}H NMR. Peracetylation of this mixture, as for **30**, afforded the trisaccharide **32** (0.549 g, 55%) as a colorless wax: $[\alpha]_D+44.1°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.87 (bs, 4 H, catechol), 5.5–4.9 (m, 5 H, Lac), 4.83 (d, 1 H, H-1 EC), 4.79 (t, 1 H, Lac), 4.47 (d, 1 H, J_{1-2} 8.0 Hz, H-1 Gal), 4.43 (d, 1 H, J_{1-2} 8.0 Hz, H-1 Glc), 4.2–3.6 (m, 25 H, 8 × OCH_2, H-3, -4, -5 CE, H-5, -6, -6′ Gal, H-5, -6, -6′ Glc), 3.48–3.33 (m, 5 H, $J_{5-6'}$ ~5, J_{1-2} 3.5 Hz, H-6′ CE, OCH_3, H-2 CE), 3.28 (dd, 1 H, $J_{6-6'}$ 11.5, J_{5-6} 8.0 Hz, H-6 CE), 2.15–1.9 (m, 21 H, 7 × OAc), ; EIMS: *m/z* Calcd for $C_{47}H_{65}BrO_{26}$ 1124. Found 1042 $[^{81}BrM-2C_2H_2O]^{\bullet+}$.

Methyl (2,2′,3,3′,4′,6,6′-hepta-O-*acetyl-β-lactosyl)-(1→4)-6-azido-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α-*D*-glucopyranoside* (**33**).— The same procedure was used as for the synthesis of the disaccharide **20**. From 0.47 g (1.0 mmol) of the acceptor **16** with 0.97 g (1.2 equiv) of the donor **5**, in the presence of 1.2 equiv (140 μL) of $(Et)_2O{\cdot}BF_3$, after 24 h of reaction at rt, usual work-up, and chromatography on silica gel (1:1 EtOAc–*n*-hexane), was isolated 0.15 g (14%) of the trisaccharide **33** as a pale-yellow wax: $[\alpha]_D+47.8°$ (*c* 0.5, $CHCl_3$); IR (NaCl) *ν* 2100 cm^{-1} (N_3), ^{1}H NMR ($CDCl_3$): δ 6.9 (bs, 4 H, catechol), 5.4–4.9 (m, 6 H, Lac), 4.82 (d, 1 H, H-1 CE), 4.47 (d, 1 H, J_{1-2} 8.0 Hz, H-1 Gal), 4.43 (d, 1 H, J_{1-2} 8.5 Hz, H-1 Glc), 4.3–3.6 (m, 25 H, 8 × OCH_2, H-3, -4, -5 CE, H-5, -6, -6′ Gal, H-5, -6, -6′ Glc), 3.57 (1 H, dd, $J_{5-6'}$ 6.0 Hz, H-6′ CE), 3.48 (dd, 1 H, J_{1-2} 3.5, $J_{2-3}\sim J_{3-4}$ 8.0 Hz, H-2 CE), 3.44 (s, 3 H, OCH_3), 3.41 (dd, 1 H, J_{5-6} 2.0, $J_{6-6'}$ 9.0 Hz, H-6), 2.17–1.95 (m, 21 H, 7 × OAc); EIMS Calcd for $C_{47}H_{65}N_3O_{26}$ 1087. Found 1087 $[M]^{\bullet+}$.

Methyl (2,2′,3,3′,4′,6,6′-hepta-O-*acetyl-β-lactosyl)-(1→4)-6-amino-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α-*D*-glucopyranoside* (**34**).— The same procedure was used as for the synthesis of the disaccharide **25**. From 70 mg (64 μmol) of the azide **33** after 18 h of reaction at rt, usual work-up, and chromatography on silica gel (EtOAc → 19:1 EtOAc–EtOH) was isolated 20 mg (30%) of the trisaccharide **34** as a yellow–orange gum: $[\alpha]_D+55.8°$ (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.87 (bs, 4 H, catechol), 5.37 (d, 1 H, J_{1-2} 7.0 Hz, H-4 Gal), 5.2–4.85 (m, 4 H Lac), 4.78 (d, 1 H, J_{1-2} 3.5 Hz, H-1 CE), 4.48 (d, 1 H, J_{1-2} 8.0 Hz, H-1 Gal), 4.3–3.5 (m, 25 H), 3.42 (t, 1 H, $J_{3-4}\sim J_{4-5}$ 9 Hz, H-4 CE), 3.4 (s, 3 H, OCH_3), 3.33 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 9.5 Hz, H-2 CE), 2.15 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.06 (bs, 12 H, 4 × OAc), 1.95 (s, 3 H, OAc), 1.8 (bs, 2 H, NH_2); LSIHRMS: *m/z* Calcd for $C_{47}H_{67}NO_{26}Na$ 1084.3849. Found 1084.3855.

Methyl (2,3,4,6-tetra-O-*acetyl-β-*D*-glucopyranosyl)-(1→4)-[2,3-*b*](11,12-benzo-1,4,7,10,-13,16-hexaoxacyclooctadeca-11-ene)-6-bromo-2,3,6-trideoxy-α-*D*-glucopyranoside* (**35**).— The same procedure was used as for the synthesis of **20** except that 2 equiv of the donor **6** (4.07 g) and catalyst ($(Et)_2O{\cdot}BF_3$, 1.0 mL) were engaged. After 4 h of reaction at rt from 2.10 g of **10** (4.13 mmol), similar work-up, and chromatography (1:1 EtOAc–*n*-hexane) on silica gel: 1.843 g (53%) of **35** as a white solid: mp 141–142 °C (*i*-PrOH), $[\alpha]_D+35.5°$ (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.89 (bs, 4 H, catechol), 5.21–5.05 (m, 2 H, H-2, -3 Glc), 4.97–4.92 (m, 2 H, H-1,-4 Glc), 4.8 (d, 1 H, H-1 EC), 4.3 (dd, 1 H, J_{5-6} 4.0, $J_{6-6'}$ 12.0 Hz, H-6 Glc), 4.23–4.02 (m, 7 H, 3 × OCH_2 CE, H-5 Glc), 3.98–3.75 (m, 12 H, 5 × OCH_2, H-5 CE, H-6′ Glc), 3.7 (t, 1 H, H-3 CE), 3.68 (dd, 1 H, $J_{5-6'}$ 7.0 Hz, H-6′ CE), 3.65 (t, 1 H, $J_{3-4}\sim J_{4-5}$ 9.5 Hz, H-4 CE), 3.53 (dd, 1 H, J_{5-6} 4.0, $J_{6-6'}$ 11.0 Hz, H-6 CE), 3.41 (s, 3 H, OCH_3), 3.39 (dd, 1 H, J_{1-2} 3.0, J_{2-3} 9.5 Hz, H-2 CE), 2.13–1.97 (4 s, each 3 H, 4 × OAc);

EIMS: Calcd m/z for $C_{35}H_{49}BrO_{18}$ 836. Found 836 $[^{79}BrM]^{\bullet+}$ and 838 $[^{81}BrM]^{\bullet+}$.

*Methyl (2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-(1→4)-6-azido-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α-*D*-glucopyranoside* (**36**).—To a solution of 0.40 g (0.477 mmol) of bromide **35** in abs DMF (10 mL) under argon were added NaN_3 (62 mg, 2 equiv) and NH_4Cl (100 mg, ~4 equiv). The mixture was then heated at 130/135 °C for 2 h so that TLC (EtOAc) showed no more starting material. The solvent was evaporated and the residue dissolved in CH_2Cl_2 (50 mL), washed with water (2 × 20 mL), dried, and concentrated to yield, after chromatography, the azide **36** (0.296 g, 78%) as a colorless gum which crystallized on standing: mp 63–65 °C (EtOAc); $[\alpha]_D + 52.1°$ (*c* 1, $CHCl_3$); IR (KBr): ν 2099 cm^{-1} (N_3); ^1H NMR ($CDCl_3$): δ 6.89 (bs, 4 H, catechol), 5.2–4.85 (m, 4 H, H-1, -2, -3, -4 Glc), 4.77 (d, 1 H, H-1 CE), 4.27 (dd, 1 H, J_{5-6} 4.0, $J_{6-6'}$ 12.5 Hz, H-6′ Glc), 4.22–3.6 (m, 22 H, 8 × OCH_2, H-3, -4, -5, -6′ CE, H-5, -6 Glc), 3.39 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 9.0 Hz, H-2 CE), 3.38 (s, 3 H, OCH_3), 3.23 (dd, 1 H, J_{5-6} 3.5, $J_{6-6'}$ 13.0 Hz, H-6 CE), 2.08–1.95 (4 s, each 3 H, 4 × OAc); ^{13}C NMR ($CDCl_3$): δ 170.8, 170.3, 169.6, 169.5 (CH_3CO_2), 148.9, 148.8 (C-1, -2 catechol), 121.7, 121.5 (C-4, -5 catechol), 114.2, 114.0 (C-3, -6 catechol), 100.5 (C-1 Glc), 97.6 (C-1 EC), 80.7 (C-3 CE), 80.6 (C-4 EC), 79.7 (C-5 EC), 78.1 (C-2 EC), 73.2 (C-3, -5 Glc,), 72.7 (OCH_2), 72.2 (C-5 EC), 71.9 (OCH_2), 71.7 (C-4 EC), 70.9, 70.8, 70.0, 69.8, 69.6 (OCH_2), 69.5 (C-2 Glc), 69.3 (OCH_2), 68.0 (C-4 Glc), 61.9 (C-6 Glc), 55.4 (OCH_3), 50.6 (C-6 EC), 20.8, 20.7, 20.6 (CH_3CO_2); EIMS: m/z Calcd for $C_{35}H_{49}N_3O_{18}$ 799. Found 799 $[M]^{\bullet+}$.

*Methyl (2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-(1→4)-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-*N*-phthalimido-α-*D*-glucopyranoside* (**37**).—The same procedure was used as for the synthesis of the acceptor **17**. To a stirred solution of the bromide **35** (0.23 g, 0.274 mmol) in abs DMF (10 mL) was added potassium phthalimide (76 mg, 1.5 equiv) and the reaction mixture was heated to 135 °C. The reaction was monitored by TLC (EtOAc) and was complete after 2 h. The solvent was evaporated, the residue dissolved in CH_2Cl_2 (70 mL), washed twice with water (20 mL), dried, concentrated, and chromatographed (1:1 EtOAc–*n*-hexane) to yield the disaccharide **37** (0.143 g, 65%) as a white foam: $[\alpha]_D + 37.5°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.9–7.65 (m, 4 H, Ar), 6.9 (bs, 4 H, catechol), 5.02 (d, 1 H, J_{1-2} 8.0 Hz, H-1 Glc), 5.22–4.95 (m, 3 H, H-2, -3, -4 Glc), 4.65 (d, 1 H, H-1 CE), 4.33 (dd, 1 H, J_{5-6} 4.0, $J_{6-6'}$ 12.0 Hz, H-6′ Glc), 3.98 (m, 1 H, J_{5-6} 3.5, $J_{5-6'}$ 8.0 Hz, H-5 CE), 4.25–3.7 (m, 20 H, 8 × OCH_2, H-6, -6′ CE, H-5, -6 Glc), 3.68 (t, 1 H, H-3 CE), 3.53 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 9.0 Hz, H-4 CE), 3.35 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 9.0 Hz, H-2 CE), 3.1 (s, 3 H, OCH_3); 2.15–2.0 (m, 12 H, 4 × OAc); EIMS: m/z Calcd for $C_{43}H_{53}NO_{20}$ 903. Found 904 $[M + H]^+$.

*Methyl (2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-(1→4)-6-amino-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α-*D*-glucopyranoside* (**38**).—The same procedure was used as for the synthesis of **25** except that a 1:1 mixture of MeOH–EtOAc (20 mL) was used as the solvent. From 0.200 g (0.25 mmol) of azide **36** in the presence of 0.100 g of 10% Pd/C after 14 h of reaction at rt under 780 Torr of H_2, was obtained after usual work-up and chromatography on deactivated silica (1% NEt_3) 0.112 g (58%) of the amine **38** as a yellow–orange gum: $[\alpha]_D + 23.0°$ (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.9 (bs, 4 H, catechol), 5.2–4.9 (m, 3 H, H-2, -3, -4 Glc), 4.85 (d, 1 H, H-1 Glc, J_{1-2} 8.0 Hz), 4.73 (d, 1 H, H-1 CE), 4.3–3.62 (m, 22 H, 8 × OCH_2, H-5, -6, -6′ CE, H-5, -6, -6′ Glc), 3.51 (t, 1 H, H-3 CE), 3.4 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 9.0 Hz, H-4 CE), 3.38 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 9.0 Hz, H-2 CE), 3.37 (s, 3 H, OCH_3), 2.15–2.0 (4 s, each 3 H, 4 × OAc), 1.27 (bs, 2 H, NH_2); EIMS: m/z Calcd for $C_{35}H_{51}NO_{18}$ 773. Found 774 $[M + H]^+$.

*Methyl β-*D*-glucopyranosyl-(1→4)-6-amino-[2,3-*b*](11,12-benzo-1,4,7,10,13,16-hexaoxacyclooctadeca-11-ene)-2,3,6-trideoxy-α-*D*-glucopyranoside* (**39**).—A first attempt at Gabriel synthesis from the phthalimide **37** failed. Thus, the same procedure was used as for the synthesis of **26**. From 100 mg (0.129 mmol) of the acetylated precursor **38** after 24

h stirring were isolated 112 mg (> 99%) of the target compound **39** as a pale-yellow gum: $[\alpha]_D + 16.6°$ (*c* 0.2, H_2O); ^1H NMR (D_2O): δ 7.03–6.93 (m, 4 H, catechol), 4.88 (d, 1 H, H-1 CE), 4.41 (d, 1 H, J_{1-2} 7.7 Hz, H-1 Glc), 4.14 (bt, 4 H, $2 \times OCH_2$), 4.0–3.3 (m, 22 H, H-3, -5, -6, -6 CE, H-2, -3, -5, -4, -6, -6′ Glc, $6 \times OCH_2$), 3.3 (dd, 1 H, J_{1-2} 3.4 Hz, J_{2-3} 9.0 Hz, H-2 CE), 3.29 (s, 3 H, OMe), 3.19 (t, 1 H, $J_{3-4} \sim J_{4-5}$ 8.7 Hz, H-4 CE); ^{13}C NMR (D_2O): δ 148.9 (C-1, -2 catechol), 122.7 (C-4, -5 catechol), 115.0, 114.8 (C-3, -6 catechol), 102.5 (C-1 Glc), 98.6 (C-1 CE), 71.1, 70.9, 70.8, 69.8, 69.7, 69.2 (OCH_2), 80.2, 79.2, 76.8, 76.3, 76.2, 74.4, 70.1, 69.4 (C-4, -5, -3, -2 CE, C-5, -4, -3, -2 Glc), 61.5 (C-6 Glc), 55.3 (OCH_3), 41.5 (C-6 CE); LSIHRMS: *m/z* Calcd for $C_{27}H_{43}NO_{14}Na$ 628.2581. Found 628.2577 $[M + Na]^+$; t_r (HPLC) 14.7 min (H_2O as eluent).

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