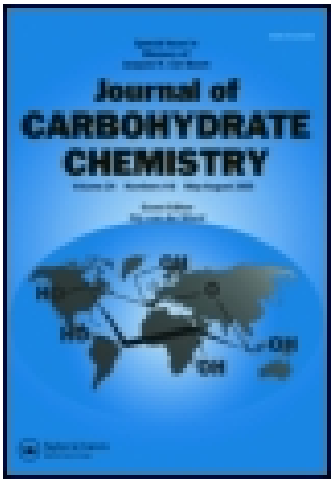

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Studies on the Synthesis of the C-Glycosidic Part of Nogalamycin, Part 1

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STUDIES ON THE SYNTHESIS OF THE *C*-GLYCOSIDIC PART OF NOGALAMYCIN, PART 1

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Dedicated to Prof. D. Seebach on the occasion of his 60th birthday

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ABSTRACT

Studies aimed at the construction of the *C*-glycosidic part of nogalamycin (**1**) and menogarol (**2**) are described. The stereochemistry of the addition of aryl lithiums to 4-acetyl-1,3-dioxolane **16**, prepared from D-glucose via **10a–15**, was studied. The major isomers were the (*S*)-isomers **17a** and **17b** as shown by X-ray analysis of **17a** with the unnatural configuration. The adduct **17a** was further converted to the anomeric naphthoquinones **22a** and **22b** by acetal cleavage, ozonolysis, acetalization and Diels-Alder reaction with 1-methoxybutadiene.

INTRODUCTION

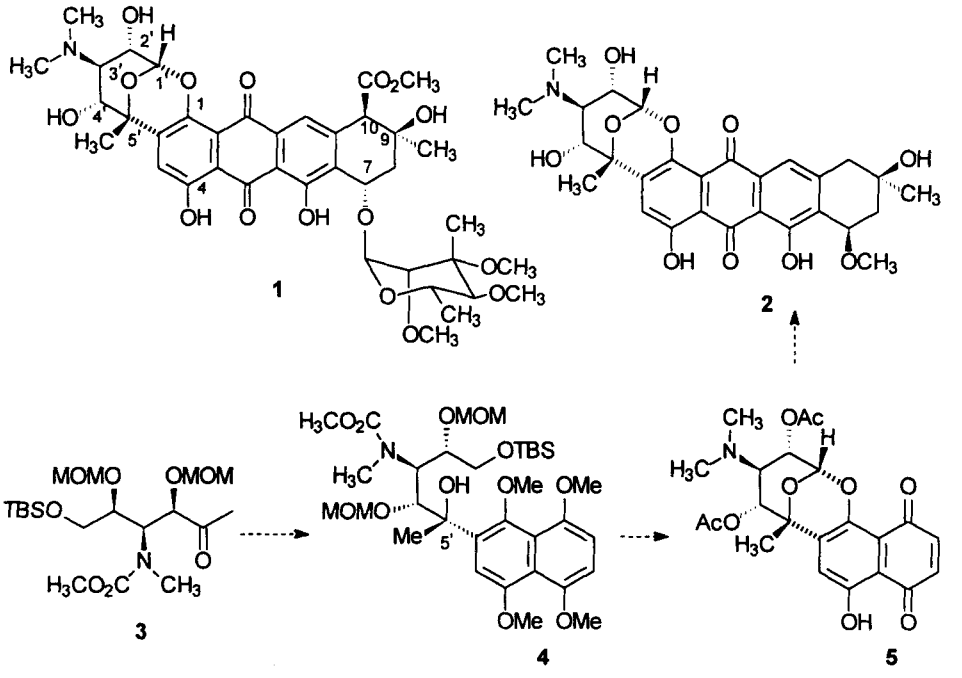
The anthracycline antibiotic nogalamycin (**1**) was isolated in 1968 by Wiley et al.[1,2] from *Streptomyces nogalater var. nogolate* sp. n. The compound belongs to a group

of related anthracyclines with a characteristic benzoxocin ring system such as decilorubicin,[3] avidinorubicin,[4] viriplanin,[5] arugomycin[6] and the respinomycins.[7] Of particular pharmological importance is the semisynthetic derivative (+)-7-*con*-*O*-methylnogarol (menogarol) (**2**).[8] The antitumor spectrum of menogarol (**2**) is comparable to that of doxorubicin but the cardiotoxicity is relatively low[9] and the antitumor drug is now in clinical test phase III.[10–12]

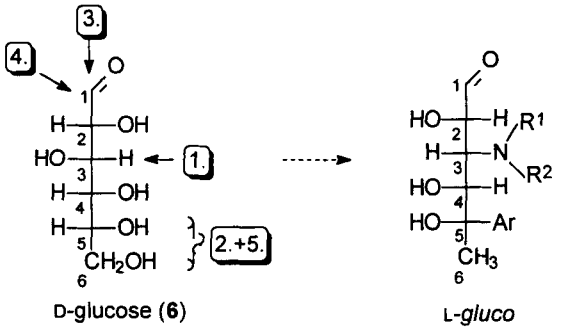
A number of model studies for the construction of the DEF-ring system of **1** are known.[13–18] The racemic sugar-free aglyon of nogalamycin was prepared in our group by a biomimetic type synthesis.[19] A total synthesis of racemic menogarol (**2**) was published by Hauser et al.[20] and Terashima et al. succeeded in the synthesis of the optically pure material.[21,22] The synthesis of Terashima et al.[21] relied on the stereoselective addition of the lithiated tetramethoxynaphthalenes to the open chain ketone **3** (obtained from D-arabinose) to generate the *C*-glycosidic tertiary alcohol **4**. The target molecule **2** was then prepared via the quinone **5** by Diels-Alder reactions.

The high stereoselectivity favoring the isomer **4** (14:1) was obtained after careful optimization under very special experimental conditions.[21] Several years ago, we started an extensive research program to investigate a more general approach to the stereoselective generation of the *C*-glycoysidic bond based on the addition of a **cyclic** system obtainable from inexpensive D-glucose in contrast to the open chain sugar derivative **3**. However, the aminosugar attached *C*-glycosidically to the anthraquinone in nogalamycin (**1**) has L-*gluco* configuration. Symmetry considerations revealed that the synthesis of the L-gluco-amino sugar from D-glucose could be achieved by the following five operations: (1) Addition of an amino substituent at C-3 with retention of configuration; (2) elimination of the hydroxy functions at C-5 and C-6 with formation of a double bond; (3) extension of the chain at C-1 by one carbon atom (a methyl group); (4) stereoselective formation of the aryl-*C*-glycosidic bond; (5) shortening of the chain by one carbon atom by cleavage of the double bond generating the required aldehyde function of the L-sugar.

The decisive step of the entire synthesis is the stereoselective formation of the *C*-glycosidic bond. Our strategy was based on previous results of Horton et al.,[23] who investigated the stereochemistry of the addition of phenylmagnesium bromide to the acetyl



Scheme 1



Scheme 2

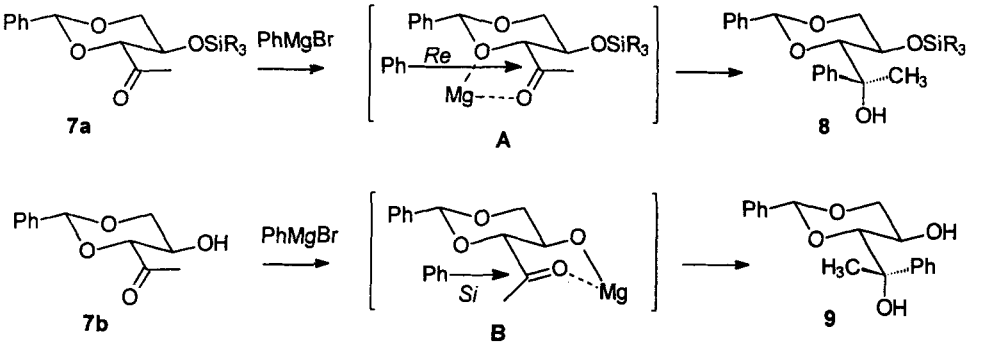
side chain of the 1,3-dioxolanes **7a** (R_3 = *t*-Bu, 2 Me) and **7b** (Scheme 3). The attack of the phenyl group occurred from the *Re*-side in the silyl ether **7a**, presumably via chelate **A** to yield the *tert*-alcohol **8** with (*R*)-configuration. The opposite stereochemical outcome was observed in the reaction of the unprotected alcohol **7b** via chelate **B** to form (*S*)-**9**.[23]

RESULTS AND DISCUSSION

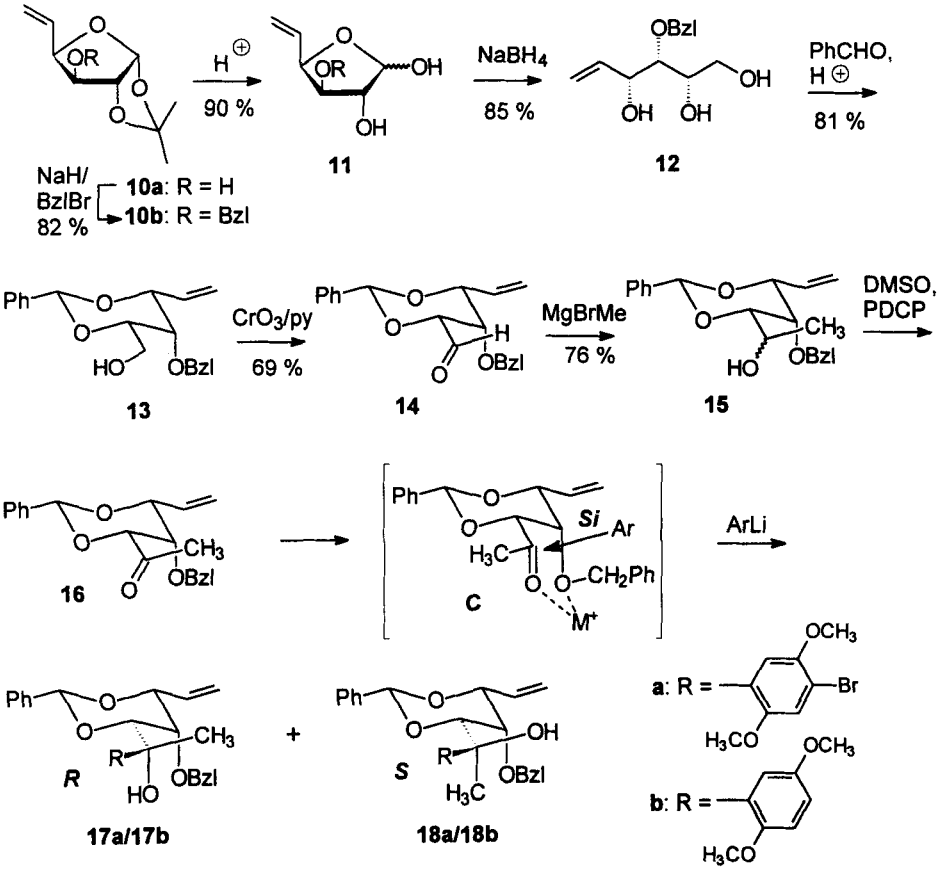
In our initial studies (part 1 and 2 of this series) we decided to introduce the dimethylamino group at a relatively late stage by a S_N2 process. Thus, the sugar precursor had to posess a leaving group (possibly a mesylate) of inverse configuration at 3' in **1** to give the correct stereochemistry of the amino group in the anticipated S_N2-process. These requirements were fulfilled by the ketone **16**.

The synthesis started from the known alcohol **10a**,[24] which was benzylated by treatment with sodium hydride and benzyl bromide to yield the benzyl ether **10b** in 82 % yield. The acetonide was cleaved with 4 % sulfuric acid in dioxane (2 h reflux) to afford the furanose **11** as the α,β-anomeric mixture (90 %). Reduction with sodium borohydride gave the triol **12** (85 %), which was converted to the six-membered benzylidene compound **13** upon treatment with benzaldehyde and trifluoroacetic acid. Freshly activated 3 Å molecular sieves in a reflux column were used for efficient trapping of the water formed during the acetalization. The exclusive reaction of the 1,3-diol in competition to the 1,2-diol to form the six-membered 1,3-dioxolane **13** was in agreement with expectation.[25] Several routes were tried to convert the hydroxymethyl group into the acetyl side chain. The most reliable one proved to be Collins oxidation of **13** to the aldehyde **14** (69 %), Grignard reaction with methylmagnesium bromide to yield the ethanol **15** followed by Swern oxidation to **16** (71 %).

The decisive addition of metalated aryl nucleophiles to **16** was tested by two reagents: 2-lithio-5-bromo-1,4-dimethoxybenzene and 2-lithio-1,4-dimethoxybenzene. The brominated adducts **17a/18a** were formed in good combined yield (89 %) in a ratio of 1:9 in favor of the less polar component (Scheme 4). Unambiguous assignment of the configuration of the newly generated quarternary center was not possible based on the NMR spectra alone but could be solved at a later stage (see below).



Scheme 3



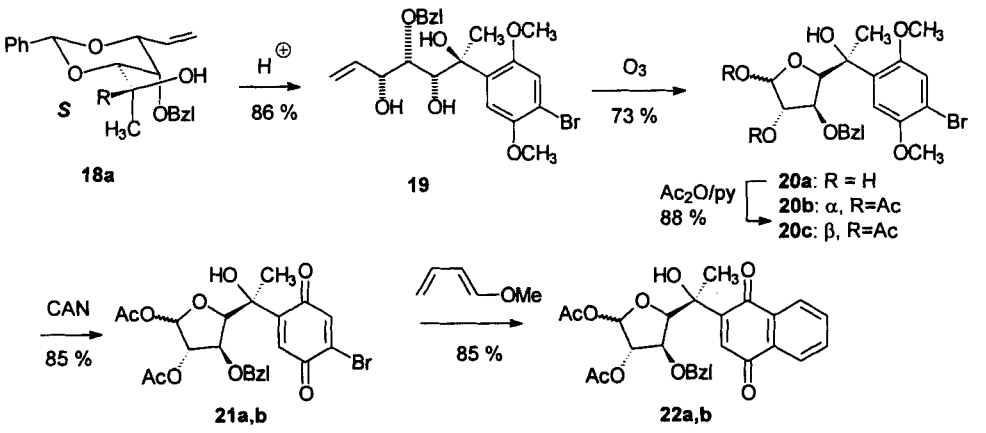
Scheme 4

DIELS-ALDER REACTION

Irrespective of the stereochemical result of the ArLi-addition to ketone **16**, we wished to test if the next step of our synthetic scheme towards nogalamycin was feasible (Scheme 5). For that purpose, the major isomer **18a** was treated with *p*-toluenesulfonic acid in methanol/water to cleave the benzylidene acetal. The resulting unsaturated diol **19** (86 %) was then subjected to ozonolysis to form the anomeric mixtures of the furanose **20a** (73 %) by reaction of the aldehyde with the secondary hydroxy group in preference to the tertiary hydroxy group forming a pyranose. Acetylation of **20a** afforded a separable mixture of the more polar α-diacetate **20b** and the ß-anomer **20c**. The assignment of the anomeric centers was confirmed by extensive NOE experiments of **20c** in addition to the analysis of the ^{1}H NMR coupling constants.

Oxidation of the anomeric mixture **20b/20c** with ceric ammonium nitrate (CAN) provided the bromobenzoquinones **21a/21b** (85 %), which could be separated by thin layer chromatography for characterization. The mixture **21a/21b** underwent a Diels-Alder reaction with 1-methoxybutadiene to afford, after base-catalysed elimination of HBr and CH_3OH, the naphthoquinones **22a** and **22b**. These latter transformations show that the anticipated cleavage of the double bond and the Diels-Alder reactions to construct the tetracyclic skeleton of **1** or **2** were, in principle, compatible with the functionalities of the *C*-glycoside.

The assignment of the configuration of the tertiary alcohols **17/18** formed in the addition reaction of **16** remained to be solved. Fortunately, the ß-anomer **20c** formed suitable crystals allowing X-ray structure analysis. There are two independent molecules in the asymmetric unit, which are closely similar except for the orientation of the benzyl groups. The five-membered rings adopt an envelope conformation, in which C-2 lies out of the plane of the other four atoms. An intramolecular hydrogen bond is observed from OH-7 to O-6 (Figure 1). The ORTEP-plot of **20c** shows that, unfortunately, the wrong (*S*)-isomer **18a** was formed predominantly in the addition reaction of **16** and the aryllithium. Evidently, the attack of ArLi occurred from the *Si*-side of the chelate **C** (Scheme 4). A similar result was observed by the addition of 2-lithio-1,4-dimethoxy-benzene on **16** to yield the isomers **17b/18b** in a 1:8 ratio in 73 % combined yield.



Scheme 5

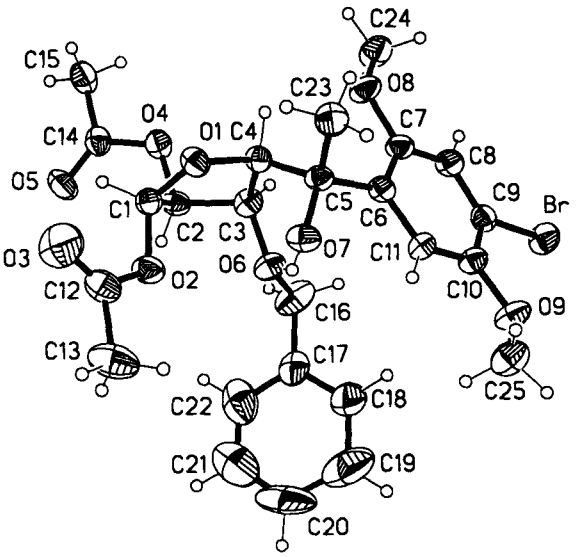


Figure 1. One of the two independent molecules of compound **20c** in the asymmetric unit. Ellipsoids represent 50% probabilitiy levels. H atom radii are arbitrary.

In conclusion, the formation of chelates similar to **C** had to be avoided and the stereochemistry of the benzyloxy group was inverted in future studies (see subsequent paper, part 2).

EXPERIMENTAL

For general procedures and instrumentation see reference 26. All reactions were carried out under an atmosphere of nitrogen.

5,6-Dideoxy-1,2-*O*-isopropyliden-α-D-*xylo*-hex-5-enofuranose (10a). A solution of 5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methanesulfonyl-α-D-*xylo*-hex-5-enofuranose[27] (1.00 g, 3.78 mmol) in dry methanol (20 mL) containing sodium methoxide (from 0.175 g of Na) was heated under reflux for 16 h. After cooling, water (5 mL) was added followed by 1 N HCl (2 mL). The methanol was evaporated and the resulting aqueous oily residue was extracted with dichloromethane (3 x 30 mL). The combined organic phases were washed with water (20 mL), dried (Na_2SO_4), filtered and concentrated to afford an oily residue of **10a** (0.67 g, 96 %), which crystallized on standing overnight at 5 °C: mp 167–168 °C; $[\alpha]_D^{25}$ –58.7 ° (*c* 0.31, $CHCl_3$); IR (KBr) 3430 cm^{-1} (br, OH), 1165, 990, 940; MS (EI) *m/z* (%) 171 (100) [M^+ –15], 129 (18), 115 (76), 111 (24), 71 (45), 69 (58) 59 (75), 57 (46), 56 (38); ^1H NMR (400 MHz, $CDCl_3$) δ 1.33, 1.51 (s, 6 H, $C(CH_3)_2$), 1.76 (br, 1 H, OH), 4.10 (d, J = 2.6 Hz, 1 H, 3-H), 4.58 (d, J = 3.7 Hz, 1 H, 2-H), 4.75 (m, 1 H, 4-H) 5.42 [dt, J = 1.6 Hz, J = 10.6 Hz, 1 H, CH=CH_2 (H_{cis})], 5.55 (dt, J = 1.6 Hz, J = 17.3 Hz, 1 H, CH=CH_2 (H_{trans})], 5.80–5.98 (m, 1 H, C*H*=CH_2), 5.95 (d, J = 3.7 Hz, 1 H, 1-H).

3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (10b). A suspension of NaH (0.26 g, 64.0 mmol) was reacted in dry DMF (10 mL) at –10 °C with **10a** (1.00 g, 5.3 mmol) for 10 min. After the complete evolution of H_2 (20 min), benzyl bromide (1.26 mL, 10.6 mmol) was added at rt over a period of 5 min and the mixture was stirred at rt for 1.5 h. After addition of EtOH (2 mL), the reaction mixture was poured into water (50 mL) and the aqueous phase was extracted with ether (2 x 30 mL). The combined organic phases were washed with water (2 x 25 mL), brine (1 x 25 mL), dried (Na_2SO_4), filtered and concentrated to afford 2.06 g of an oily residue. Purification by column chromatography (SiO_2, 30 g, dichloromethane/30 % petroleum ether) produced **10b** (1.22 g, 82 %) as a colorless liquid that was directly reduced in the next step (see below).

3-*O*-Benzyl-5,6-dideoxy-α,β-D-*xylo*-hex-5-enofuranose (11). (For related reactions see references 28,29). A solution of **10b** (1.00 g, 3.6 mmol) in 1,3-dioxane (10 mL)

was treated with sulfuric acid (4 %, 10 mL) and refluxed for 2 h. After cooling to rt the reaction mixture was neutralised with 1 N NaOH and concentrated to dryness under reduced pressure. The resulting residue was dissolved in dichloromethane (40 mL), filtered, washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure to give **11** (0.77 g, 90 %) as colorless needles (diethyl ether/pentane) (ratio of α/β = 2:1 by NMR): mp 70–75 °C, $[\alpha]_D^{25}$ +23.72° (*c* 0.118, $CHCl_3$); IR (KBr) 3270 cm^{-1} (br, OH), 1130; ^1H NMR (400 MHz, $CDCl_3$) δ 1.84, 2.66 (br, 4 H, 4 x OH), 3.36 [d, *J* = 4.9 Hz, 1 H, 1-OH (α-anom.)] 3.51 [d, *J* = 11.5 Hz, 1 H, 1-OH (β-anom.)], 3.88–3.92 [m, 1 H, 3-H (β-anom.)], 3.98 [dd, *J* = 3.1 Hz, *J* = 4.8 Hz, 1 H, 3-H (α-anom.)], 4.22–4.27 [m, 1 H, 2-H (α-anom.)], 4.30 [br, 1 H, 2-H (β-anom.)], 4.57–4.68 (m, 4 H, 2 x OCH_2Ph), 4.69–4.77 (m, 2 H, 2 x 4-H), 5.15 (d, *J* = 11.5 Hz, 1 H, 1-H (β-anom.)], 5.27–5.49 (m, 4 H, 2 x CH=CH_2), 5.53 (bt, becomes doublet with *J* = 4.3 Hz after exchange with D_2O, 1 H, 1-H, α-anom.)], 5.99 (ddd, *J* = 7.3 Hz, *J* = 10.3 Hz, *J* = 17.3 Hz, 1 H, C*H*=CH_2 (α-anom.)], 6.09 (ddd, *J* = 7.3 Hz, *J* = 10.3 Hz, *J* = 17.3 Hz, 1 H, C*H*=CH_2 (β-anom.)], 7.28–7.39 (m, 10 H, Ar-H).

Anal. Calcd for $C_{13}H_{16}O_4$ (236.27): C, 66.10; H, 6.77. Found: C, 65.98; H, 6.68.

(2*S*,3*S*,4*R*)-3-Benzyloxy-5-hexen-1,2,4-triol (12). To a solution of **11** (1.86 g, 7.89 mmol) in dry ethanol (25 mL), was added $NaBH_4$ (2.98 g, 78.7 mmol) in small portions over a period of 10 min. During this addition the reaction temperature was maintained between 0–5 °C. The resulting suspension was then allowed to stir at rt for two days. After cooling to 10 °C, acetic acid (25 mL) was added, the inorganic salts were filtered off and the filtrate was concentrated. The residue was dissolved in dichloromethane (15 mL) and chromatographed on silica gel (20 g, dichloromethane/1 % CH_3OH) to yield **12** (1.59 g, 85 %) as needles (diethyl ether/pentane): mp 58–62 °C. $[\alpha]_D^{20}$ + 32.2 ° (*c* 0.21, $CHCl_3$); IR (KBr) 3320 cm^{-1} (br, OH), 2910, 1090, 930; MS (CI/NH_3, pos.) *m/z* (%) 256 (100) [M^+ + NH_4], 239 (9) [M^+ + H], 221 (6), 198 (3), 185 (2), 161 (2), 91 (9); ^1H NMR (400 MHz, $CDCl_3$) δ 2.42 (br, 3 H, OH), 3.54 (dd, *J* = 3.4 Hz, *J* = 4.2 Hz, 1 H, 3-H), 3.63 (dd, *J* = 3.6 Hz, *J* = 11.4 Hz, 1 H, 1-H), 3.77 (dd, *J* = 4.2 Hz, *J* = 11.4 Hz, 1 H, 1-H), 3.78–3.85 (m, 1 H; 4-H), 4.35–4.42 (m, 1 H, 2-H), 4.62 (d, J = 11.2 Hz, 1 H, CH_2Ph), 4.73 (d, *J* = 11.2 Hz, 1 H, OCH_2Ph), 5.26 (dt, *J* = 10.6 Hz, 1 H, olefin-H), 5.40 (dt, *J* = 1.4 Hz, 1 H, olefin-H), 5.98 (ddd, *J* = 5.3, 10.6, 17.1 Hz, 1 H, olefin-H), 7.30–7.41 (m, 5 H, Ar-H).

Anal. Calcd for $C_{13}H_{18}O_4$ (238.28): C, 65.54; H, 7.56. Found: C, 65.50; H, 7.49.

(2*R*,4*S*,5*S*,6*R*)-(5-Benzyloxy-2-phenyl-6-vinyl-[1,3]dioxan-4-yl)-methanol (13). A solution of **12** (30.00 g, 126 mmol) in dry $CHCl_3$ (350 mL) was treated with freshly distilled benzaldehyde (16.6 mL, 164 mmol) and trifluoroacetic acid (4 mL, 52 mmol). The mixture was refluxed for 7 h and the water generated in the reaction was removed by

trapping with freshly activated 3 Å molecular sieves placed in a dropping funnel used as a reflux column. The reaction mixture was then washed with a saturated solution of $KHCO_3$ (50 mL) and brine (50 mL), dried (Na_2SO_4), filtered and concentrated to give an oily residue (42 g), which was subjected to column chromatographic separation (SiO_2, 500 g, petroleum ether/0.5 % ethyl acetate). The first fraction gave **13** (32.90 g, 80 %) as colourless crystals: mp 107–108 °C. Further elution (petroleum ether/50 % ethyl acetate, finally pure ethyl acetate) gave the unreacted starting material **12** (4.42 g, 15%). Data for **13**: $[\alpha]_D^{25}$ + 35.69 ° (*c* 0.156, $CHCl_3$); IR (KBr) 3330 cm^{-1}(br, OH), 1100, 1030; MS (FD-3KV) *m/z* (%) 326 (100) [M^+], 325 (8), 164 (6); ^1H NMR (400 MHz, $CDCl_3$) δ 1.62 (dd, J = 3.9 Hz, J = 8.7 Hz, 1 H, exchanges with D_2O, OH), 3.49 (t, J = 1.7 Hz, 1 H, 5-H), 3.57 (ddd, J = 5.1 Hz, J = 8.7 Hz, J = 11.4 Hz, 1 H, C*H*$_2$OH), 3.86 (ddd, J = 3.9 Hz, J = 7.1 Hz, J = 11.4 Hz, 1 H, C*H*$_2$OH), 4.00 (ddd, J = 1.7 Hz, J = 5.1 Hz, J = 7.1 Hz, 1 H, 4-H), 4.41–4.46 (m, 1 H, 6-H), 4.57 and 4.79 (AB-signal $J_{A,B}$ = 11.7 Hz, 2 H, OCH_2Ph), 5.31 (dt, J = 1.4 Hz, J = 10.6 Hz, 1 H, CH=C*H*$_2$ (H_{cis})], 5.51 (dt, J =1.4 Hz, J = 17.3 Hz, 1 H, CH=C*H*$_2$ (H_{trans})], 5.67 (s, 1 H, 2-H), 6.10 (ddd, J = 6.1 Hz, J = 10.6 Hz, J = 17.3 Hz, 1 H, C*H*=CH_2), 7.28–7.41 (m, 8 H, Ar-H), 7.50–7.59 (m, 2 H, Ar-H).

Anal. Calcd for $C_{20}H_{22}O_4$ (326.39): C, 73.69; H, 6.74. Found C, 73.67; H, 6.84.

(2*R*,4*R*,5*S*,6*R*)-(5-Benzyloxy-2-phenyl-6-vinyl-[1,3]dioxan-4-yl)-carbaldehyde (14). Powdered CrO_3 (1.85 g, 18 mmol) was added to a solution of dry pyridine (2.89 mL, 36 mmol) in dry CH_2Cl_2 (30 mL). After stirring for 15 min, a solution of **13** (0.74 g, 2.27 mmol) in dry CH_2Cl_2 (3 mL) and acetic anhydride (1.69 mL, 18 mmol) were added. After stirring for 10 min, the reaction was found to be completed (TLC) The reaction mixture was transferred to the top of a short column of silica gel in ethyl acetate, with a layer of ethyl acetate above the gel to precipitate chromium compounds. The eluate was concentrated to dryness under reduced pressure and the pyridine was removed by azeotropic distillations with toluene (20 mL, repeated twice). The oily residue (0.69 g) was chromatographed on silica gel to yield the aldehyde **14** (0.50 g, 68 %) which was immediately subjected to Grignard reaction (see below).

1-[(2*R*,4*S*,5*S*,6*R*)-5-Benzyloxy-2-phenyl-6-vinyl-[1,3]dioxan-4-yl]ethanol (15). To a solution of MeMgBr [prepared from MeBr (0.39 mL, 6.3 mmol)] and Mg turnings (0.16 g, 6.29 mmol)] was added dropwise at 5 °C a solution of **14** (0.502 g, 1.55 mmol) in dry THF (10 mL). The reaction mixture was allowed to warm to rt, stirred for 16 h and hydrolysed by addition of saturated NH_4Cl solution (10 mL). The organic phase was separated and the aqueous phase extracted with Et_2O (2 x 20 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to yield **15** as a mixture of diastereomers (0.40 g, 76 %, ratio 1: 0.8) which crystallized from Et_2O/pentane: mp 79–84 °C. IR (KBr) 3430 cm^{-1} (OH), 1450, 1100, 1030; MS (FD 3

kV) *m/z* (%) 340 (100) [M^+], 107 (7), 106(71); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (d, *J* = 6.3 Hz, 3 H, CH_3), 1.29 (d, *J* = 4.3 Hz, 3 H, CH_3), 1.54 (s, exchanges with D_2O, 1 H, OH), 3.41 (s, exchanges with D_2O, 1 H, OH), 3.54 (dd, *J* = 1.6 Hz, *J* = 8.3 Hz, 1 H, 4-H), 3.62 (d, *J* =1.6 Hz, 1 H, 4-H), 3.71 (t, *J* = 1.6 Hz 1 H, 5-H), 3.83 (t, *J* =1.6 Hz, 1 H, 5-H), 3.93–4.02 (m, 2 H, 1'-H), 4.39–4.45 (m, 2 H, 6-H), 4.65 and 4.86 (AB-signal, $J_{A,B}$ =11.8 Hz, 2 H, OCH_2Ph), 4.67 and 4.88 (AB-signal, $J_{A,B}$ = 11.0 Hz, 2 H, OCH_2Ph), 5.27–5.35 (m, 2 H, CH=CH_2), 5.51 (dt, *J* = 1.5 Hz, *J* = 11.6 Hz, 1 H, CH=CH_2 (H_{cis})], 5.56 (dt, *J* = 1.5 Hz, *J* = 11.6 Hz, 1 H, CH=CH_2 (H_{cis})], 5.63 (s, 1 H, 2-H), 5.69 (s, 1 H, 2-H), 6.06–6.20 (m, 2 H, C*H*=CH_2) 7.28–7.43 (m, 16 H, Ar-H), 7.50–7.62 (m, 4 H, Ar-H).

Anal. Calcd for $C_{21}H_{24}O_4$ (340.42): C, 74.11; H, 7.05. Found: C, 74.40; H, 7.38.

1–[(2*R*,4*R*,5*S*,6*R*)–5–Benzyloxy–2–phenyl–6–vinyl–[1,3]dioxan-4-yl]-ethanone (16). To a solution of DMSO (3.55 mL, 50 mmol) in CH_2Cl_2 (100 mL) at –10 °C were added sequentially phenyl dichlorophosphate (PDCP) (4.48 mL, 30 mmol), triethylamine (7.02 mL, 50 mmol) and a solution of **15** (3.41 g, 10 mmol) in CH_2Cl_2 (45 mL). The reaction mixture was stirred for 2.5 h at rt. After addition of water (200 mL) the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated. The resulting oily residue was chromatographed (SiO_2, 100 g, CH_2Cl_2/petroleum ether) to yield **16** (2.41 g, 71 %) (colorless needles from EtAc/pentane): mp 113–114 °C; $[\alpha]_D^{25}$ +68.37 ° (*c* 0.175, $CHCl_3$); IR (KBr) 1726 cm^{-1} (C=O), 1110, 1065; MS (EI) *m/z* (%) 338 (0.2) [M^+], 296 (2), 295 (6), 265(5), 264 (20), 197 (23), 191 (46), 189 (39), 180 (19), 177 (46), 176 (100), 175 (40); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3 H, CH_3), 3.87 (t, *J* = 2.0 Hz, 1 H, 5-H), 4.35 (d, *J* = 2.0 Hz, 1 H, 4-H), 4.40–4.45 (m, 1 H, 6-H), 4.47 and 4.59 (AB-signal, $J_{A,B}$ = 11.1 Hz, 2 H, OCH_2Ph), 5.27 (dt, *J* = 1.1 Hz, *J* = 10.6 Hz, 1 H, CH=CH_2 (H_{cis})], 5.47 (dt, *J* =1.4 Hz, *J* = 17.3 Hz, 1 H, CH=CH_2 (H_{trans})], 5.67 (s, 1 H, 2-H), 5.99 (ddd, *J* = 6.2 Hz, *J* = 10.6 Hz, *J* = 17.4 Hz, 1 H, C*H*=CH_2), 7.27–7.41 (m, 8 H, Ar-H), 7.57–7.61 (m, 2 H, Ar-H).

Anal. Calcd for $C_{21}H_{22}O_4$ (338.40): C, 74.55; H, 6.50. Found C, 74.53; H, 6.58.

Reaction of ketone 16 with 2-lithio-5-bromo-1,4-dimethoxybenzene. A solution of 2,5-dibromo-1,4-dimethoxybenzene (0.414 g, 1.4 mmol) in dry THF (20 mL) was treated dropwise at –90 °C under N_2 within 3 min with *n*-BuLi (1.6M, 0.88 mL, 1.4 mmol). The reaction mixture was allowed to warm to –50 °C and maintained at this temperature for 15 min. To the suspension was then added dropwise within 10 min at –50 °C a solution of **16** (0.338 g, 1.0 mmol) in dry THF (10 mL). After warming up to 0 °C and stirring for 40 min the reaction was quenched at 5 °C by addition of a saturated solution of NH_4Cl (10 mL). The reaction mixture was diluted by addition of of Et_2O (20 mL), the organic phase was separated, the aqueous phase extracted with Et_2O (20 mL)

and the combined organic phases were washed with brine, dried (Na_2SO_4), filtered and concentrated to yield 0.727 g of an oily residue. Column chromatography on silica gel (CH_2Cl_2/petroleum ether 1:1) yielded three compounds: least polar fraction **18a** (0.441 g, 80 %), polar fraction **17a** (0.49 g, 9 %) and the starting ketone **16** (0.035 g, 10 %).

1-(*S*)-{(2*R*,4*S*,5*S*,6*R*)-5-Benzyloxy-2-phenyl-6-vinyl-[1,3]dioxan-4-yl}-1-(4-bromo-2,5-dimethoxyphenyl)ethanol (18a). Colorless plates (Et_2O/pentane): mp 160–162 °C, $[\alpha]_D^{25}$ +83.12 ° (*c* 0.276, $CHCl_3$); IR (KBr) 3460 cm^{-1} (OH), 1490, 1212; MS (EI) *m/z* (%) = 556/554 (2) [M^+], 261/259 (40), 260/258 (66), 245/243 (17), 181 (15), 180 (24), 107 (14), 105 (21), 91 (100), 77 (13), 55 (73); ^1H NMR (400 MHz, $CDCl_3$) δ 1.58 (s, 3 H, CH_3), 3.23 (br, 1 H, 5-H), 3.65, 3.86 (s, 6 H, 2 x OCH_3), 3.80 and 4.57 (A,B-spect., $J_{A,B}$ = 11.0 Hz, 2 H, OCH_2Ph), 4.31–4.38 (m, 1 H, 6-H), 4.72–4.76 (br, 2 H, 4-H, OH), 5.21 (bd, *J* = 10.6 Hz, 1 H, CH=CH_2 (H_{cis})], 5.47 (bd, *J* = 17.3 Hz, 1 H, CH=CH_2 (H_{trans})], 5.79 (s, 1 H, 2-H), 5.96 (ddd, *J* = 6.1 Hz, *J* = 10.6 Hz, *J* = 17.3 Hz, 1 H, C*H*=CH_2), 7.12 (s, 1 H, 3"-H), 7.20–7.45 (m, 9 H, Ar-H), 7.61–7.67 (m, 2 H, Ar-H).

Anal. Calcd for $C_{29}H_{31}BrO_6$ (555.47): C, 62.69; H, 5.58; Br, 14.40. Found: C, 62.59; H, 5.76; Br, 16.25.

1-(*R*)-{(2*S*,4*S*,5*S*,6*R*)-5-Benzyloxy-2-phenyl-6-vinyl-[1,3]dioxan-4-yl}-1-(4-bromo-2,5-dimethoxyphenyl)ethanol (17a). Mp 63–68 °C (pentane/diisopropyl ether); $[\alpha]_D^{25}$ −31.3 ° (*c* 0.15, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.64 (s, 3 H, CH_3), 3.79, 3.81 (s, 6 H, 2 x OCH_3), 3.96 (t, *J* =1.4 Hz, 1 H, 5-H), 4.44–4.48 (m, 1H, 6-H), 4.52 (d, *J* =1.4 Hz, 1 H, 4-H), 4.65 and 4.88 (A,B-signal, $J_{A,B}$ = 10.7 Hz, 2 H, OCH_2Ph), 4.94 (s, exchanges with D_2O 1 H, OH), 5.34 (dt, *J* =1.4 Hz, *J* = 10.6 Hz, 1 H, CH=CH_2 (H_{cis})], 5.53 (s, 1 H, 2-H), 5.59 (dt, *J* = 1.5 Hz, *J* = 17.3 Hz, 1 H, CH=CH_2 (H_{trans})], 6.16 (ddd, *J* = 5.8 Hz, *J* = 10.6 Hz, *J* = 17.3 Hz, C*H*=CH_2), 7.04 (s, 1 H, 3"-H), 7.21–7.45 (m, 10 H, Ar-H), 7.47 (s, 1H, Ar-H). HRMS Calcd for $C_{29}H_{31}BrO_6$ 554.1304. Found 554.1304 ± 2 ppm.

Anal. Calcd for $C_{29}H_{31}BrO_6$ (555.47): C, 62.69; H, 5.58. Found: C, 62.52; H, 5.57.

Reaction of ketone 16 with 2-lithio-1,4-dimethoxybenzene. A solution of 2-bromo-1,4-hydroquinone dimethyl ether (2.289 g, 1.33 mmol) in dry THF (20 mL) was treated at −78 °C with 1.6 M *n*-BuLi (0.83 mL, 1.3 mmol). The resulting solution was warmed to −50 °C, maintained at this temperature for 15 min and cooled to −78 °C within 10 min. A solution of **16** (0.322 g, 0.95 mmol) in dry THF (10 mL) was then added to the reaction mixture. After warming up to 0 °C within 3 h the reaction was quenched at 5 °C by additon of saturated solution of NH_4Cl (10 mL). After addition of Et_2O (30 mL), the organic phase was separated and the aqueous phase was extracted with Et_2O (2 x 20 mL). The combined organic phases were washed with brine (40 mL), dried

over Na_2SO_4, filtered and evaporated to dryness under reduced pressure [(1:7.83 mixture by HPLC analysis (CH_3OH: H_2O:75:25) on a RP-18 column)]. The residue (0.620 g) was separated by preparative TLC chromatography on silica gel (0.2 % CH_3OH: CH_2Cl_2) to yield the two diastereomeric products **17b** (0.038 g, 8 %) and **18b** (0.296 g, 65 %) in addition to starting material **16** (0.035 g, 11 %).

Reaction of ketone 16 with 2-magnesio-1,4-dimethoxybenzene. In a similar Grignard reaction of **16** (0.39 g, 1.150 mmol) in THF (10 mL) with 2-magnesio-1,4-dimethoxbenzene [prepared from 2-bromo-1,4-dimethoxybenzene (0.349 g, 1.61 mmol) and magnesium (0.054 g, 2.25 mmol)] 0.614 g of an oily mixture with a diastereomeric ratio of 1:8.68 (HPLC) was obtained. Isolated yields: **18b** (0.279 g, 51.04 %), **17b** (0.035 g, 6.38 %), unreacted ketone **16** (0.150 g, 38.5 %).

1–(*S*)–{(2*R*,4*S*,5*S*,6*R*)–5–Benzyloxy-2-phenyl-6-vinyl-[1,3]dioxan-4-yl}-1-(2,5-dimethoxyphenyl)ethanol (18b). mp 136–137 °C (colorless needles, diisopropyl ether/pentane), $[\alpha]_D^{25}$ + 66.0 ° (*c* 0.112, $CHCl_3$); IR (KBr) 3450 cm^{-1} (OH), 1480, 1270; MS (EI) *m/z* (%) 476 (2) [M^+], 314 (2), 299 (2), 206 (4), 180 (100), 165 (25), 151 (10), 105 (11), 91 (79), 77 (11), 57 (9), 43 (50); ^1H NMR (400 MHz, $CDCl_3$) δ 1.60 (s, 3 H, CH_3), 3.24 (t, *J* = 1.4 Hz, 1 H, 5-H), 3.67, 3.85 (s, 6 H, 2 x OCH_3), 3.83 and 4.50 (A,B-signal, $J_{A,B}$ = 10.9 Hz, 2 H, OCH_2Ph), 4.32–4.36 (m, 1 H, 6-H), 4.69 (s, 1 H, OH), 4.77 (d, *J* = 1.4 Hz, 1 H, 4-H), 5.20 (dt, *J* =1.3 Hz, *J* = 10.6 Hz, 1 H, CH=CH_2 (H_{cis})], 5.46 (dt, *J* = 1.4 Hz, *J* = 17.3 Hz, 1 H, CH=CH_2 (H_{trans})], 5.80 (s, 1 H, 2-H), 5.96 (ddd, *J* = 6.2 Hz, *J* = 10.6 Hz, *J* = 17.3 Hz, 1 H, C*H*=CH_2), 6.82 (dd, *J* =3.0 Hz, *J* = 8.8 Hz, 1 H, 4"-H), 6.88 (d, *J* = 8.8 Hz, 1 H, 3"-H), 7.21–7.41 (m, 8 H, Ar-H), 7.44 (d, *J* = 3.0 Hz, 1 H, 6"-H), 7.61–7.67 (m, 2 H, Ar-H).

Anal. Calcd for $C_{29}H_{32}O_6$ (476.57): C, 73.10; H, 6.72. Found: C, 73.14; H, 6.78.

1–(*R*)–{(2*R*,4*S*,5*S*,6*R*)–5–Benzyloxy-2-phenyl-6-vinyl-[1,3]dioxan-4-yl}-1-(2,5-dimethoxyphenyl)ethanol (17b). Mp 49–52 °C (diisopropyl ether/pentane); ^1H NMR (400 MHz, $CDCl_3$) δ 1.69 (s, 3 H, CH_3), 3.72 (s, 3 H, OCH_3), 3.80–3.83 (m, 4 H, OCH_3, 5-H), 4.41–4.47 (m, 1 H, 6-H), 4.56 and 4.82 (A,B-signal, *J* = 10.7 Hz, 2 H, OCH_2Ph), 4.58 (d, *J* = 1.5 Hz, 1 H, (4-H), 4.77 (s, 1 H, OH), 5.30 (dt, *J* = 1.4 Hz, 10.6 Hz, 1 H, CH=CH_2 (H_{cis})], 5.50–5.60 (m, 2 H, 2-H, CH=CH_2 (H_{trans})], 6.13 (ddd, *J* = 6.0 Hz, *J* = 10.6 Hz, *J* = 17.2 Hz, 1 H, C*H*=CH_2), 6.76 (dd, *J* = 3.0 Hz, *J* = 8.8 Hz, 1 H, 4"-H), 6.81 (d, *J* = 8.8 Hz, 1 H, 3"-H), 7.22–7.40 (m, 11 H, Ar-H). HRMS $C_{29}H_{32}O_6$ calcd for 476.2199. Found: 476.2199 ± 2 ppm.

Anal. Calcd for $C_{29}H_{32}O_6$ (476.57): C, 73.10; H,6.72. Found: C, 72.94, H, 6.76.

(2*S*,3*R*,4*S*,5*R*)–4–Benzyloxy–2–(4–bromo–2,5–dimethoxyphenyl)–hept–6–en–2,3,5-triol (19). A solution of **18a** (125 mg, 0.225 mmol) and *p*-toluenesulfonic acid (30 mg) in methanol/water (10 mL, CH_3OH:H_2O=10:1) was stirred at 50 °C for 24 h. The

solvent was removed under reduced pressure, the residue was dissolved in CH_2Cl_2 (25 mL) and the organic phase was washed sequentially with a $NaHCO_3$ solution (5 %, 10 mL), water (10 mL) and brine. The solution was dried (Na_2SO_4), the solvent removed at reduced pressure and the residue purified by column chromatography on silica gel (CH_2Cl_2) to yield **19** (90 mg, 86 %): mp 62–64 °C (diisopropyl ether/pentane); $[\alpha]_D^{25}$ + 75.86 ° (*c*, 0.087 $CHCl_3$); IR ($CHCl_3$) 3540 cm^{-1}, 3440 (OH), 1490, 1380, 1080; ^1H NMR (400 MHz, $CDCl_3$) δ 1.49 (s, 3 H, CH_3), 2.62 (br, 1 H, OH), 3.06 (bd, J = 9.4 Hz, 1 H, OH), 3.24 (dd, J = 1.8 Hz, J = 5.5 Hz, 1 H, 4-H), 3.71, 3.77 (s, 6 H, 2 x OCH_3), 3.95 and 4.78 (A,B-signal, $J_{A,B}$ = 11.0 Hz, 2 H, OCH_2Ph), 4.01 (br, 1 H, OH), 4.44 (bt, J = 5.7 Hz, 1 H, 5-H), 4.51 (bd, J = 8.3 Hz, 1 H, 3-H), 5.23 (dt, J = 1.5 Hz, J = 10.6 Hz, 1 H, CH=CH_2 (H_{cis})], 5.37 (dt, J = 1.5 Hz, J = 17.2 Hz, 1 H, CH=CH_2 (H_{trans})] 5.89 (ddd, J = 5.8 Hz, J = 10.6 Hz, J = 17.2 Hz, 1 H, C*H*=CH_2), 7.06 (s, 1 H, 7'-H), 7.21–7.38 (m, 6 H, Ar-H). HRMS calcd for $C_{22}H_{27}BrO_6$:.466.0991. Found: 466.099 ± 2 ppm.

Anal. Calcd for $C_{22}H_{27}BrO_6$ (467.36): C, 56.53; H, 5.78. Found: C, 56.48, H, 5.73.

3-*O*-Benzyl-6-deoxy-5-*C*-(4-bromo-2,5-dimethoxyphenyl)-α,β-D-*ido*hexofuranose (20a). Ozone was bubbled at −78 °C through a solution of **19** (1.40 g, 2.9 mmol) in CH_2Cl_2 (100 mL) containing Sudan-B (2 mg). After the reaction mixture became colorless, the flow of O_3 was stopped and the excess O_3 was removed by passing a stream of N_2 through the solution. The solution was then treated with Me_2S (2.20 mL, 29.8 mmol) and allowed to reach rt within 3 h. After stirring overnight, the solvent was removed at reduced pressure. The oily residue was purified by filtration through a short bed of SiO_2 (CH_2Cl_2) to afford **20a** (1.02 g, 73 %): mp 49–55 °C (diisopropyl ether/pentane), $[\alpha]_D^{25}$ +47.22 ° (*c* 0.108, $CHCl_3$); IR(KBr) 3430 cm^{-1} (OH), 1490, 1375, 1215; ^1H NMR (400 MHz, $CDCl_3$) δ 1.57, 1.58 (s, 6 H, 2 x CH_3), 2.92 (br, 1 H, OH), 3.61, 3.63 (s, 6 H, 2 x OCH_3), 3.67–3.73 (m, 2 H, 2 x 3-H), 3.76, 3.77 (s, 6 H, 2 x OCH_3), 3.84–3.94 (m, 3 H, 2-H, OH, OCH_2Ph), 3.96, 4.41 (A,B-signal, $J_{A,B}$ = 11.2 Hz, 2 H, OCH_2Ph), 4.11 (br, 1H, OH), 4.17 (bd, J = 2.9 Hz (becomes dd, J = 1.3 Hz, J = 4.1 Hz after D_2O exchange), 1 H, 2-H), 4.29 (br, 1 H, OH), 4.33 (d, J = 11.0 Hz, 1 H, OCH_2Ph), 5.20 (d, J = 3.9 Hz, 1 H, 4-H), 5.24 (d, J = 4.7 Hz, 1 H, 4-H), 5.32 (br, 1 H, 1-H), 5.73 (bd, J = 3.8 Hz, 1 H, 1-H), 7.01–7.06 and 7.20–7.30 (2 m, 14 H, Ar-H).
HRMS Calcd for $C_{21}H_{25}BrO_7$ (468.0784). Found: 468.078 ± 2 ppm.

Acetylation of 20a. To a solution of **20a** (1.00 g, 2.13 mmol) in dry pyridine (25 mL), DMAP (0.78 g, 6.39 mmol) and Ac_2O (2.01 mL, 21.0 mmol) was added. The mixture was stirred overnight at rt, water (50 mL) was added and the reaction mixture was extracted with Et_2O (2 x 60 mL). The combined organic phases were washed with 50 mL of 1 N HCl, water (2 x 50 mL) and brine and dried over Na_2SO_4. Filtration, removal

of Et_2O under reduced pressure and filtration through a short bed of SiO_2 yielded 1.12 g of a anomeric mixture of **20b/20c** (1.03 g, 87 %). IR (KBr) 3500 cm^{-1} (OH), 1750, 1490, 1375, 1240, 1215; MS (EI) *m/z* (%) 554 (3) [M^+ + 1], 552 (3) [M^+ – 1], 494, (9), 492 (9), 260 (100), 258 (91), 243 (17), 165 (4), 162 (9), 115 (3), 91 (48), 65 (3), 43 (45). 100 mg of the anomeric mixture **20b/20c** was separated by preparative TLC on silica gel (1 % CH_3OH:CH_2Cl_2) to afford from the less polar fraction 40 mg of β-anomer **20c** and from the polar fraction 46 mg of α-anomer **20b**.

1,2-Di-*O*-acetyl-3-*O*-benzyl-6-deoxy-5-*C*-(4-bromo-2,5-dimethoxyphenyl)-β-D-*ido*-hexofuranose (20c). Mp 107–108 °C; $[\alpha]_D^{25}$ +101.21 ° (*c* 0.33, $CHCl_3$), ^1H NMR (400 MHz, $CDCl_3$) δ 1.55 (s, 3 H, CH_3), 2.11, 2.13 (s, 6 H, 2 x $OCOCH_3$), 3.56, 3.75 (s, 6 H, 2 x OCH_3), 3.71 (d, J = 4.8 Hz, 1 H, 3-H), 3.88, 4.54 (A,B-signal, $J_{A,B}$ = 11.0 Hz, 2 H, OCH_2Ph) 4.11 (s, exchanges with D_2O, 1 H, OH), 5.20 (s, 1 H, 2-H), 5.23 (d, J = 4.8 Hz, 1 H, 4-H), 6.28 (s, 1 H, 1-H), 7.01–7.07 (m, 3 H, Ar-H), 7.19 (s, 1 H, 3'-H), 7.25-7.32 (m, 3 H, Ar-H).

Anal. Calcd for $C_{25}H_{29}BrO_9$ (553.40): C, 54.24; H, 5.24. Found: C, 54.10; H, 5.25.

1,2–Di–*O*–acetyl-3-*O*-benzyl-6-deoxy-5-*C*-(4-bromo-2,5-dimethoxyphenyl)-α-D-*ido*-hexofuranose (20b). Mp 113–114 °C; $[\alpha]_D^{25}$ –18.22 ° (*c* 0.439, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.56 (s, 3 H, CH_3), 2.06, 2.12 (s, 6 H, 2 x $OCOCH_3$), 3.62, 3.78 (s, 6H, 2 x OCH_3), 3.86 (dd, J = 2.3 Hz, J = 4.8 Hz, 1 H, 3-H), 3.92 and 4.43 (AB-signal, $J_{A,B}$ = 11.2 Hz, 2 H, OCH_2Ph), 4.00 (s, 1 H, OH), 5.20 (d, J = 4.8 Hz, 4-H), 5.36 (dd, J = 2.3 Hz, J = 4.6 Hz, 1 H, 2-H), 6.57 (d, J = 4.6 Hz, 1 H, 1-H), 6.92–6.98 (m, 2 H, Ar-H) 7.05 (s, 1H, 6'-H), 7.22 (s, 1 H, 3'-H), 7.24–7.30 (m, 3 H, Ar-H).

Anal. Calcd for $C_{25}H_{29}BrO_9$ (553.40): C, 54.24; H, 5.24. Found: C, 54.33; H, 5.66.

Oxidation of 20b/20c with ceric ammonium nitrate. A solution of **20b/20c** (0.320 g, 0.57 mmol) in CH_3CN/H_2O (5 mL, 8:2) was treated at 0 °C with a solution of ceric ammonium nitrate (0.951 g, 1.73 mmol) in CH_3CN/H_2O (6 mL, 1:1). After stirring for 2 h at 20 °C the reaction mixture was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phases were washed with water (10 mL), dried (Na_2SO_4), filtered and evaporated to dryness under reduced pressure to yield the anomeric mixture of the bromoquinones **21b/21c** (0.320 g) as an oily residue. The mixture was separated by preparative TLC chromatography on silica gel (2 % CH_3OH/CH_2Cl_2) to yield from the less polar fraction the β-anomer **21c** (0.151 g, 50.1 %) and from the polar fraction the α-anomer **21b** (0.105 g, 35 %).

1,2-Di-*O*-acetyl-5-*C*-[5'-bromo-1',4'-benzoquinone-2'-yl]-3-*O*-benzyl-ß-L-*ido*-hexofuranose (21a). ^1H NMR ($CDCl_3$) δ 1.44 (s, 3 H, CH_3), 2.11 (s, 3 H, $OCOCH_3$),

2.15 (s, 3 H, $OCOCH_3$), 3.80 (d, J = 5.0 Hz, 1 H, (3-H), 3.81 (s, exchanges with D_2O, 1 H, OH), 4.36 (d, J = 11,6 Hz, 1H, OCH_2Ph), 4.67 (d, J = 11,6 Hz, 1H -OCH_2Ph), 4.99 (d, J = 5.0 Hz, 1 H, C4-H), 5.25 (s, 1 H, 2-H), 6.26 (s, 1 H, 1-H), 6.97 (s, 1H, 6'-H), 7.08–7.15 (m, 2 H, Ar-H), 7.16 (s, 1 H, 3'-H), 7.20–7.39 (m, 3 H, Ar-H)

1,2-Di-*O*-acetal-5-*C*-[5'-bromo-1',4'-benzoquinone-2'-yl]-3-*O*-benzyl-α-L-*ido*-hexofuranose (21b). ^1H NMR ($CDCl_3$) δ 1.46 (s, 3 H, CH_3), 2.09 and 2.11 (2 s, 2 x 3 H, 2 $OCOCH_3$), 3.53 (s, 1H, OH), 4.04 (dd, J = 3.7, J = 5.6 Hz, 1 H, 3-H), 4.24 (d, J = 11.3 Hz, 1 H, OCH_2Ph), 4.62 (s, J = 3 Hz, 1 H, OCH_2Ph), 5.67 (d, J = 5.6 Hz, 1 H, 4-H), 5.36 (dd, J = 3.7, 4.6 Hz, 1 H, 2-H), 6.53 (d. J = 4.6 Hz, 1 H, 1-H), 6.98 (s, 1 H, 6'-H), 7.00–7.10 (m, 2 H, Ar H), 7.11 (s. 1H, 3'-H), 7.27–7.37 (m, 3H, Ar-H); IR (KBr) 3490 cm^{-1} (OH), 1745, 1665, 1370, 1220, 1020.

Crystal structure analysis of compound 20c.[30]

Crystal data: $C_{25}H_{29}BrO_9$, M_r = 553.39, monoclinic, $P2_1$, a = 1063.5(5), b = 2264.7(9), c = 1064.8(5) pm, β = 91.40(4)°, V = 2564 nm^3, Z = 4, D_x = 1.434 Mg m^{-3}, $F(000)$ = 1144, λ(Mo $K\alpha$) = 71.073 pm, μ = 1.64 mm^{-1}, T = –95 °C. **Data collection and reduction**: Colourless prism 0.7 x 0.45 x 0.4 mm, Siemens R3 diffractometer, 6141 intensities to $2\theta_{max}$ 55°, 5923 independent (R_{int} 0.028). **Structure solution**: direct methods. **Structure refinement**: anisotropic on F^2 (program SHELXL-93, G.M. Sheldrick, University of Göttingen); H atoms with riding model or rigid methyl and hydroxy groups; $wR(F^2)$ 0.118 (all refl.), $R(F)$ 0.034 ($F > 4\sigma(F)$) for 643 parameters and 607 restraints (to light atom U components); max. Δρ 526 e nm^{-3}, max. Δ/σ 0.001, S = 1.08. The absolute configuration was confirmed by an x refinement (H.D. Flack, *Acta Cryst.* **A39** (1981) 876–881), with x = –0.023(9).

Diels-Alder reaction of 21a/21b with 1-methoxybutadiene. A solution of **21a/21b** (0.065 g, 0.124 mmol) in dry C_6H_6 (2 mL) was treated with 1-methoxybuta-1,3-diene (neat, 0.016 mL, 0.1552 mmol). After stirring overnight at rt, 2 drops of triethylamine were added and the reaction mixture was stirred further for 2 h. The reaction mixture was diluted with CH_2Cl_2 (15 mL), washed with 1 N HCl (5 mL), water (2 x 10 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated . The oily residue was purified by preparative TLC on silica gel (2 % CH_3OH/CH_2Cl_2) to yield from the less polar fraction the β-anomer **22a** (0.025, 41 %) and from the polar fraction the α-anomer **22b** (0.026 g, 43 %).

1,2-Di-*O*-acetyl-5-*C*-[1',4'-naphthoquinone-2'-yl]-3-*O*-benzyl-ß-L-*ido*-hexo-furanose (22a). Mp 54–56 °C (diisopropyl ether/pentane); $[\alpha]_D^{25}$ +58.8 ° (*c* 0.085, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.55 (s, 3 H, CH_3), 2.11 and 2.15 (2 s, 2 x 3 H, 2 $OCOCH_3$), 3.85 (d, J = 5.0 Hz, 1 H, (C3-H), 3.87 (s, 1H, OH), 4.29 (d, J = 11.3 Hz, 1 H, OCH_2Ph), 4.63 (d, J = 11.3 Hz, 1 H, OCH_2Ph), 5.23–5.29 (m, 2 H, 2-H and 4-H), 6.28

(s, 1 H, 1-H), 7.06–7.10 (m, 4 H, Ar–H), 7.27-7.41 (m, 2 H, Ar-H), 7.70 and 7.80 (m, 2 H, 5'-H and 8'-H), 7.95–8.00 (m, 1H, Ar-H), 8.03–9.02 (m, 1H, Ar-H); MS (CI-Isob) 494 (100) [M^+].

1,2-Di-*O*-acetyl-5-*C*-[1',4'-naphthoquinone-2'-yl]-3-*O*-benzyl-α-L-*ido*-hexofuranose (22b). Mp 62–68 ° C (diisopropyl ether/pentane); $[\alpha]_D^{25}$ −15.62 ° (*c* 0.013, $CHCl_3$); IR (KBr) 3485 cm^{-1} (OH), 1750, 1650, 1370, 1220, 1050; ^1H NMR ($CDCl_3$) δ 1.57 and 2.07 (2 s, 2 x 3 H, 2 $OCOCH_3$), 3.68 (s, 1 H, OH) 4.05 (dd, *J* = 3.3, 5.4 Hz, 1 H, 3-H), 4.20 (d, *J* = 11.4 Hz, 1 H, OCH_2Ph), 4.56 (d, *J* = 11.4 Hz, 1 H, OCH_2Ph), 5.24 (d, *J* = 5.4 Hz, 1 H, 4-H), 5.37 (dd, *J* = 3.2, 4.7 Hz, 1 H, 2-H), 6.56 (d, *J* = 4.7 Hz, 1 H, 1-H), 6.92–7.10 (m, 4 H, Ar-H), 7.29–7.40 (m, 2H, Ar-H), 7.70–7.78 (m, 2 H, 5'-H and 8'-H), 7.96–8.09 (m, 2 H, Ar-H).

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30. Full details have been deposited at: Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, 76344 Eggenstein-Leopoldshafen, whence this material can be obtained on quoting a full literature citation and the deposition number CSD 406634.