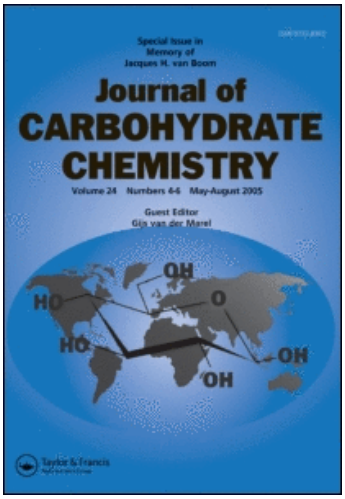

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NAPHTHALENE DISACCHARIDE FRAGMENTS AS BUILDING BLOCKS FOR ANGUCYCLINE SYNTHESIS

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Dedicated to Prof. W. Bartmann on the occasion of his 70th birthday

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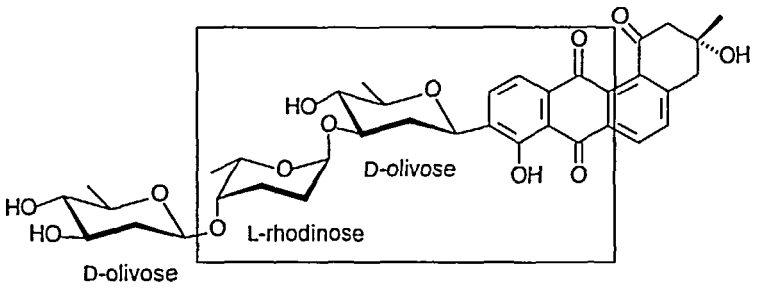
ABSTRACT

Methods for the construction of naphthalene oligodeoxy disaccharide fragments, common structural elements of the angucycline antibiotics, are investigated. The triphenylphosphonium bromide- or scandium triflate-catalyzed addition of rhodinal to 4-OH silyl-protected olivoses affords the required 3-*O*-α-oligodeoxy disaccharides selectively and in high yields.

INTRODUCTION

The angucyclines form a large group of quinoid antibiotics with benzo[*a*]anthracene as the angularly condensed aromatic aglycone skeleton (reviews[1,2]). Another very common structural element is the *C*-glycosidically linked olivose at C-9 as shown in urdamycine B (**1**)[3] (Figure 1). In most cases the sugar directly attached to *O*-3 of olivose

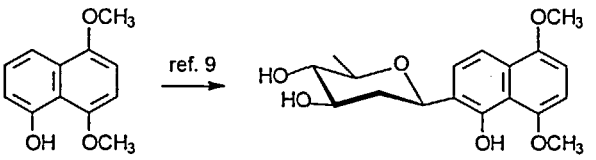


urdamycine B (1)

Figure 1

is rhodinose as found in urdamycine B (1) (Figure 1).[1] A number of syntheses of the aromatic benzo[*a*]anthracene derived aglycones have been published[2] and also two syntheses of the *C*-glycosides such as urdamycinone B,[4,5] or the antibiotic C104.[6] However, with the exception of the synthesis of a C3 trisaccharide component of the antibiotic PI-080 by Sulikowski et al.,[7] little work has been done on angucycline oligosaccharide synthesis. Thus, the goal of the present paper is to study systematically the optimum methods (review[8]) for the synthesis of naphthalene and naphthoquinone disaccharide fragments with several 2,6-dideoxy and 2,3,6-trideoxy sugars as shown in the framed part of urdamycine B (**1**). Particular attention is paid to the α- to β-glycoside ratio and the selective attachment to *O*-3 of the *C*-glycosidically bound olivose.

A direct electrophilic substitution of potential *C*-glycosyl donors with the electron-deficient naphthoquinones is not possible. Therefore, *C*-glycoside formation according to an electrophilic mechanism is usually performed with the corresponding naphthols.[6,9–11] 1-Hydroxy-5,8-dimethoxynaphthalene (**2**)[12,13] was taken to prepare the corresponding olivose *C*-glycoside **3**.[9] The naphthoquinone prepared by oxidation of **3** was previously used to prepare *C*-glycosidic angucyclinones employing a Diels-Alder reaction.[10] The disaccharides reported in this study can thus be regarded as precursors of the more complex angucyclines (review[2]).



2 3

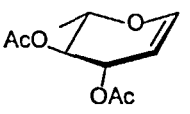
Scheme 1

The problem of regioselective (*O*-3 versus *O*-4) glycoside formation was addressed in two ways. First, the direct selectivity of the *O*-glycosylation step was studied and then a selectively 4-OH protected derivative of the olivose *C*-glycoside **3** was investigated. For both ways, different methods of glycosylation to form deoxyglycosides with different glycal derivatives [3,4-di-*O*-acetyl-L-rhamnal (**4**), 3,4-di-*O*-acetyl-L-fucal (**5**), 4-*O*-acetyl-L-amicetal (**6**), 4-*O*-benzoyl-L-rhodinal (**7**)] were tested: the Ferrier rearrangement,[15] the direct acid-catalyzed addition to glycals,[16] and the *N*-iodo succinimide (NIS) assisted addition to glycals[17] (general reviews[18,19]).

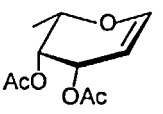
DISACCHARIDES FROM THE OLIVOSE *C*-GLYCOSIDE

It is known that olivose derivatives can be selectively converted to their 3-*O*-*tert*-butyldimethylsilyl ethers due to the slightly increased steric hindrance around 4-OH.[6] It was thus worthwhile to see if this selectivity could also be observed in the various *O*-glycosylations with the diol **3**. The results of the reactions of different glycals with the unprotected olivose *C*-glycoside derivative **3** are listed in Table 1.

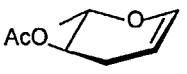
We first investigated the Ferrier rearrangement[15] of **3** with the 3,4-di-*O*-acetyl-L-rhamnal **4**[20] followed by hydrogenation of the resulting double bond. The procedure has the advantage that the desired **tri**deoxy glycosides are formed directly resulting from the allylic displacement reaction, and the more readily available **di**deoxy glycals can be used as glycosyl donors. BF_3 etherate and montmorillonite K-10[21,22] were used as the catalysts (entries 1 and 2). With BF_3 etherate (entry 1) the two 3-*O*- and 4-*O* α-glycosides **8** and **9** were formed in low yield and a ca. 2:1 selectivity. Montmorillonite K-10 was recently



3,4-di-O-acetyl-L-rhamnal (**4**)



3,4-di-O-acetyl-L-fucal (**5**)



4-O-acetyl-L-amicetal (**6**)

4-O-benzoyl-L-rhodinal (**7**)

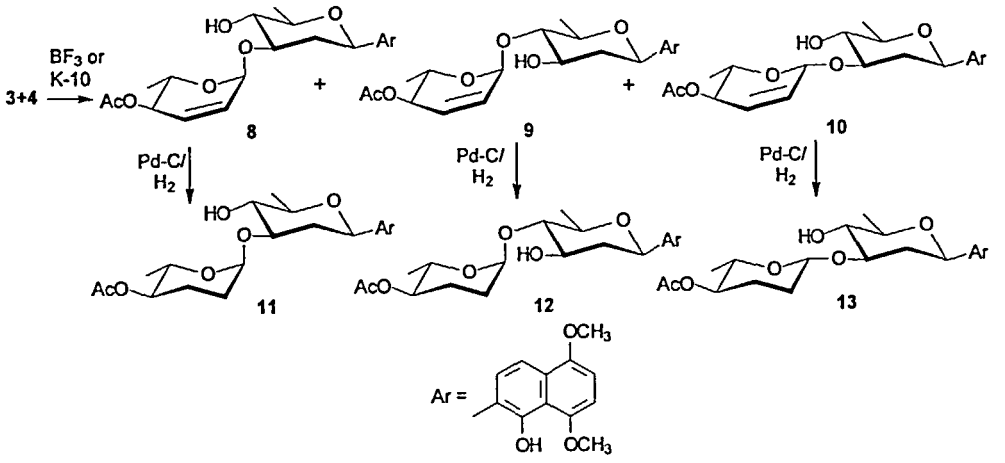
Figure 2

Table 1. Reaction of different glycals with the olivose *C*-glycoside derivative **3**

Entry	Sugar	Catalyst	Conditions	Solvent	Products (yields %)
1	rhamnal **4**	BF_3-Et_2O	0 °C	MeCN	**8** (14), **9** (8)
2	rhamnal **4**	K-10	0 – 22 °C	CH_2Cl_2	**8** (30), **9** (18), **10** (15)
3	fucal **5**	K-10	0 – 22 °C	CH_2Cl_2	**14** (17)
4	fucal **5**	$SnCl_4$	22 °C	CH_2Cl_2	**16** (23), **17** (15)
5	fucal **5**	$Sc(OTf)_3$	0 – 22 °C	CH_2Cl_2	**16** (18), **17** (12)
6	amicetal **6**	TPHB	0 – 22 °C	CH_2Cl_2	**11** (26), **12** (10) **13** (5)
7	rhodinal **7**	TPHB	0 – 22 °C	CH_2Cl_2	**18** (31), **20** (24)
8	rhodinal **7**	NIS	22 °C	MeCN	**19** (22)

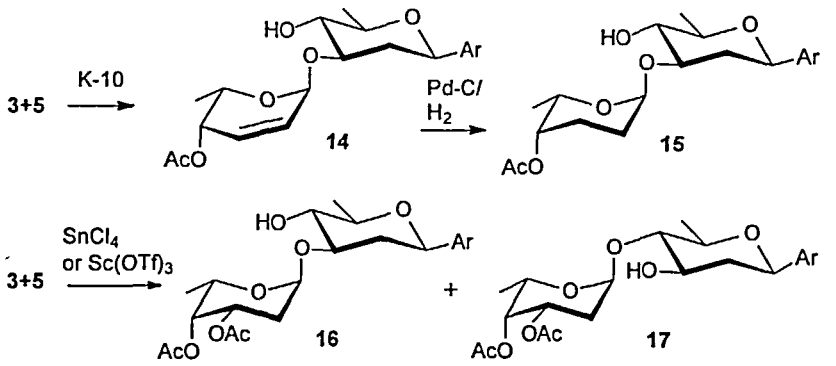
proposed as a Lewis acid for glycosylations,[21] and much better yields with the same 3-*O*:4-*O* selectivity were obtained with this catalyst (overall yield 62 %). In addition, the 3-*O*-β-glycoside **10** was also isolated in 15 % yield (entry 2, Table 1). The three compounds **8** – **10** were hydrogenated to the corresponding 2,3-dideoxy disaccharides **11** – **13**. At this stage an unambiguous assignment of the respective 3-*O* or 4-*O* glycosides could be made by comparison of the corresponding ^{13}C NMR shifts of C-3 and C-4 with structurally related natural angucyclines.[23] α- and β-Glycosides were easily distinguished by the absence (α-glycosides) or presence (β-glycosides) of a 1,2-diaxial relationship of the low field anomeric protons.

Although the selectivity was not very high, the desired 3-*O*-α-glycoside **11** could be isolated in 26 % yield including the hydrogenation step. However, usually the second sugar in angucyclines is not L-amicetose as shown in **11** but L-rhodinose with inverted



Scheme 2

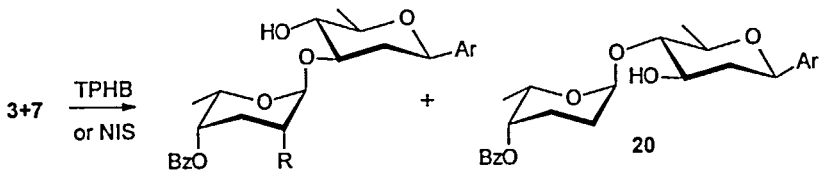
stereochemistry at C-4. Unfortunately, the required 3,4-di-*O*-acetyl-L-fucal (**5**) (see procedure of Reichstein et al.[24]) is not as readily available as the rhamnal **4**. Three catalysts, montmorillonite K-10, $SnCl_4$, and $Sc(OTf)_3$ were used in the glycosylation reaction of **5** with the diol **3**. Only a very moderate yield (17 %) of the Ferrier product **14** was attained with montmorillonite K-10, and hydrogenation yielded the desired disaccharide fragment **15** as present in angucyclines such as urdamycine B (**1**) (Figure 1, assignment of 3-*O*- and 4-*O*-glycosides by comparison of the ^{13}C NMR spectra with structurally related natural angucyclines[3,25,26] and by analysis of the HMBC NMR spectrum of **15**). $SnCl_4$ was successfully used by Grynkiewicz et al.[27] in Ferrier rearrangements with glucal derivatives. However, in our case only traces of the unsaturated rearrangement product **14** could be detected by TLC. The major products were the acid-catalyzed addition products **16** (23 %) and **17** (15 %) (Scheme 3; Table 1, entry 4). Scandium triflate has recently been proposed as an efficient reagent in many Lewis acid-catalyzed reactions[28–31] but has never been used as a catalyst for glycosylations. Similarly as with $SnCl_4$, only the addition products **16** and **17** were obtained (Table 1, entry 5).



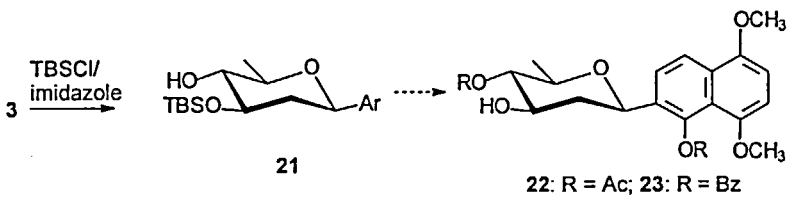
Scheme 3

2,3,6-Trideoxy glycals such as amicetal **6** or the rhodinal **7** have to be used in acid-catalyzed additions of alcohols to arrive at the desired angucycline trideoxydisaccharide fragments. To test this possibility, the easily prepared amicetal **6**[32] and the diol **3** were reacted with triphenylphosphonium bromide (TPHB) (Table 1, entry 6), which was used as an efficient catalyst for the addition of alcohols to glycals.[17] In fact, all four possible isomers could be detected by TLC. But only three of these (**11** – **13**), which were already known from the hydrogenation of the Ferrier products **8** – **10** (Scheme 2, Table 1, entry 2), were isolated.

Encouraged by these results, the rhodinal derivative **7**, prepared according to a procedure of Kirschnig et al.,[33] was reacted with **3** and TPHB as the catalyst (Scheme 4; Table 1, entry 7). The 3-*O*- and 4-*O*-α-glycosides **18** and **20** were isolated in 31 and 24 % yield, respectively, a result comparable to that of the Ferrier rearrangement with rhamnal **4** (entry 2). Finally, the NIS-assisted addition of **3** to rhodinal **7** according to the method of Thiem et al.[18,19] was tested. The selectivity towards glycosylation of 3-OH was much higher, but the product **19** could only be isolated in moderate yield (22 %, Scheme 24, Table 1, entry 8). We presume that the reaction of the electron-rich naphthol with the oxidant NIS decreased the yield of **19** by formation of various colored oxidized phenols as confirmed by TLC analysis.



Scheme 4



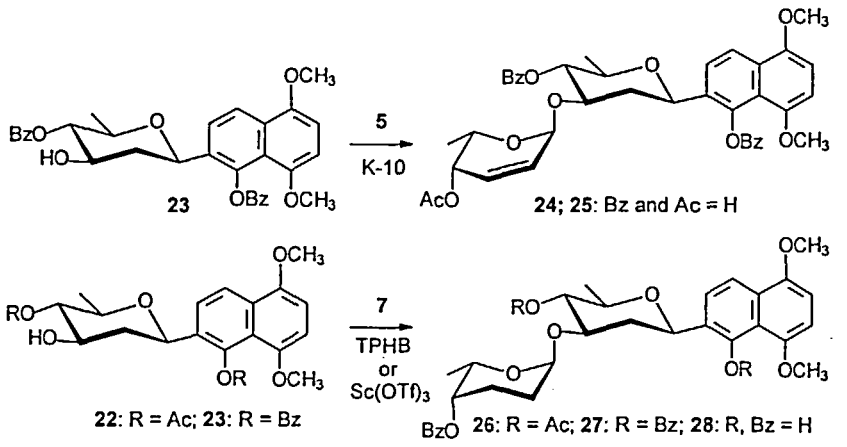
Scheme 5

REACTION WITH 4-*O* PROTECTED OLIVOSES

The successful selective protection of 3-OH in related olivose derivatives as a *tert*-butyldimethylsilyl ether[6] encouraged us to try this strategy in the preparation of disaccharide angucycline building blocks. Accordingly, the silylation was performed with the derivative **3** to yield the silyl ether **21**. The ether was acetylated or benzoylated at 4-OH and at the phenolic group and subsequently desilylated with aqueous HF to yield the desired diacetate **22** and the dibenzoate **23** (Scheme 5).

A number of glycosylation reactions were then performed on these selectively protected olivose derivatives **22** and **23** paying special attention to possible transacylation reactions during *O*-glycosylation. It must further be mentioned that acylation of the phenolic group also facilitates the subsequent selective oxidation to juglone derivatives for use in future Diels-Alder reactions. The results of the glycosylation of **22** and **23** with the fucal **5** and the rhodinal **7** (Scheme 6) that both lead to desired stereochemistry at C-4" are summarized in Table 2.

The reaction of the fucal **5** with **23** afforded the Ferrier rearrangement product **24** in only 18 % yield (in addition to 67 % of recovered starting material **23**) but no transacylation reactions were observed under the Lewis acid catalysis (Scheme 6, Table



Scheme 6

Table 2. 4-*O*-Glycosylation of 4-OH protected olivose derivatives **22** and **23**

Entry	Sugar/aglycon	Catalyst	Conditions	Solvent	Products (yields %)
1	fucal **5/23**	K-10	0 – 22 °C	CH_2Cl_2	**24** (18), **23** (67)
2	rhodinal **7/22**	TPHB	0 – 22 °C	CH_2Cl_2	**26** (52), **22** (36)
3	rhodinal **7/23**	TPHB	0 – 22 °C	CH_2Cl_2	**27** (71), **23** (16)
4	rhodinal **7/22**	$Sc(OTf)_3$	0 °C	CH_2Cl_2	**26** (62), **22** (38)

2, entry 1). The NMR spectra of all acylated phenols such as **24** showed many double signals due to hindered rotation of the phenolic acyl groups. For unambiguous identification, the products were reductively deacylated with LAH. Thus, the deacylated olefin **25** proved to be identical with the saponification product obtained from the previously prepared acetate **14** (Scheme 3).

Next, the TPHP-catalyzed addition of the acetate **22** and the benzoate **23** to the glycal **7** was studied yielding 52 and 71 % of the desired deoxy-α-glycosides **26** (R = Ac) and **27** (R = Bz) (Scheme 6; Table 2, entries 2 and 3). Again, no transacylation was observed and unreacted starting material was recovered. The deacylation product **28** was identical with the alcohols obtained from the acetate **15** and monobenzoate **18** prepared earlier (Schemes 3 and 4). Scandium triflate also proved to be an effective catalyst in the reaction of **22** with **7** affording 62 % of **26** in addition to 38 % of starting material **22**

(Scheme 6, Table 2, entry 4). The acylated disaccharides can be oxidized regioselectively and in high yields to the requisite naphthoquinones and used as angucycline precursors as will be communicated shortly.

In summary, the comparison of different methods for the attachment of oligodeoxyglycosides to the naphthalene core showed that selective protection of 4-OH by acylation followed by TPHB or scandium triflate-catalyzed addition of rhodinal selectively gave the desired α-glycoside in good conversion (52-71 %) and nearly quantitative yields. The method may be of general importance for the large group of olivose-containing oligodeoxysaccharides.

EXPERIMENTAL

For general procedures and instrumentation see reference 34.

2-(2,6-Dideoxy-β- D-*arabino*-hexopyranosyl)-1-hydroxy-5,8-dimethoxynaphthalene (3). To a suspension of the 3',4'-diacetate of **3**[10] (500 mg, 1.20 mmol) in dry methanol (40 mL) was added a small piece of sodium (ca. 20 mg), and the mixture was stirred for 2 h at 22 °C. The solution was neutralized by addition of 1 M HCl and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (100 mL), washed with water (50 mL), dried (Na_2SO_4), and concentrated under reduced pressure to ca. 2 mL. The product **3** precipitated as a yellow solid (312 mg, 78 %): mp 214 °C (dec). $[\alpha]_D^{20}$ = 72.9 (*c* 0.048 in CH_3OH). IR (KBr): $\tilde{\nu}$ = 3352 cm^{-1}, 2943, 2912, 1390. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.65 (dd, $J_{1',2'ax}$ = 11.3 Hz, $J_{2'eq,2'ax}$ = 12.5 Hz, 1 H, 2'-H_{ax}), 2.53 (dd, $J_{2'eq,2'ax}$ = 12.5 Hz, $J_{2'eq,3'}$ = 5.1 Hz, 1 H, 2'-H_{eq}), 2.84 (br s, 2 H, 2 x OH), 3.16 (dd, *J* = 9.5 Hz, 1 H, 4'-H), 3.39–3.58 (m, 1 H, 5'-H), 3.72–3.84 (m, 1 H, 3'-H), 3.97, 4.01 (2 x s, 2 x 3 H, 2 x OMe), 5.06 (d, $J_{1',2'ax}$ = 11.3 Hz, 1 H, 1'-H), 6.62, 6.69 (2 x d, $J_{6',7'}$ = 8.5 Hz, 2 x 1 H, 6-H, 7-H), 7.57, 7.72 (2 x d, $J_{3',4'}$ = 8.7 Hz, 2 x 1 H, 3-H, 4-H), 9.82 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.31 (q, C-6'), 56.12, 56.78 (2 x q, 2 x OMe), 71.85 (d, C-1'), 73.52 (d, C-3'), 76.44 (d, C-5'), 78.11 (C-4'), 103.29, 104.06 (2 x d, C-6, C-7), 113.47, 125.13 (2 x d, C-3, C-4), 115.49, 123.67, 127.91 (3 x s, C-2, C-4a, C-8a), 150.21, 150.46, 150.57 (3 x s, C-1, C-5, C-8). MS (GC-MS, 70 eV): *m/z* (%) = 334 (9) [M^+], 333 (77), 241 (100), 210 (46), 187 (25), 115 (20), 43 (15).

Anal. Calcd for $C_{18}H_{22}O_6Si$ (334.37): C, 64.66; H, 6.63. Found: C, 64.38; H, 6.49.

Reaction of rhamnal 4 with *C*-glycoside 3. A solution of **3** (40 mg, 0.12 mmol) and 3,4-Di-*O*-acetyl-L-rhamnal (**4**) (22 mg, 0.10 mmol) in dry CH_2Cl_2 (0.5 mL) was treated at 0 °C under argon with montmorillonite K-10[22] (7 mg). The suspension was stirred for 8 h at 22 °C, filtered, and the filtrate concentrated at reduced pressure. The residue was separated by column chromatography on silica gel (CH_2Cl_2/EtOAc 90:10 or 3 % MeOH/CH_2Cl_2) to afford the disaccharides **8** (15 mg, 30 %), **9** (9 mg, 18 %), and **10** (7 mg, 15 %) as yellow oils.

Data for 2-[3-*O*-(4-*O*-Acetyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (8): $[\alpha]_D^{20}$ = 16.3 (*c* 0.16 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3373 cm^{-1}, 2925, 1738, 1614, 1461. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.30 (d, $J_{5'',6''}$ = 6.3 Hz, 3 H, 6''-H), 1.45 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.68 (dd, $J_{1',2'ax}$ = 11.5 Hz, $J_{2'ax,2'eq}$ = 12.8 Hz, 1 H, 2'-H_{ax}), 2.09 (s, 3 H, CH_3, OAc), 2.38 (ddd, $J_{1',2'eq}$ = 1.8 Hz, $J_{2'ax,2'eq}$ = 12.8 Hz, $J_{2'eq,3'}$ = 5.0 Hz, 1 H, 2'-H_{eq}), 3.26 (dd, *J* = 8.7 Hz, *J* = 8.8 Hz, 1 H, 4'-H), 3.52–3.60 (m, 1 H, 5'-H), 3.67–3.90 (m, 1 H, 3'-H), 3.93, 4.00 (2 x s, 2 x 3 H, 2 x OCH_3), 4.04–4.14 (m, 1 H, 5''-H), 5.00–5.17 (m, 3 H, 1'-H, 1''-H, 4''-H), 5.73–5.78 (m, 1 H, 2''-H or 3''-H), 5.87 (d, $J_{2'',3''}$= 10.2 Hz, 1 H, 2''-H or 3''-H), 6.61, 6.68 (2 x d, $J_{6,7}$ = 8.4 Hz, 2 H, 6-H, 7-H), 7.59, 7.72 (2 x d, $J_{3,4}$ = 8.7 Hz, 2 H, 2-H, 3-H), 9.77 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.63 (q, C-6''), 18.29 (q, C-6'), 20.82 (q, CH_3, OAc), 37.48 (t, C-2'), 55.52, 56.21 (2 x q, 2 x OCH_3), 65.50 (d, C-5''), 70.15, 71.24, (2 x d, C-1', C-4''), 76.49 (d, C-4', C-5'), 82.65 (d, C-3'), 94.01 (d, C-1''), 102.58, 103.45 (2 x d, C-6, C-7), 112.93, 125.27 (2 x d, C-3, C-4), 114.96, 123.77, 127.98 (3 x s, C-2, C-4a, C-8a), 127.24, 129.54 (2 x d, C-2'', C-3''), 149.62, 149.90, 150.09 (3 x s, C-1, C-5, C-8), 170.24 (s, OAc). MS (70 eV): *m/z* (%) = 488 (15) [M^+], 334 (13), 241 (11), 230 (14), 217 (11), 155 (11), 95 (100), 43 (50).

HRMS Anal. Calcd for $C_{26}H_{32}O_9$ (488.2046) Found: 488.2044.

Data for 2-[4-*O*-(4-*O*-Acetyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (9). $[\alpha]_D^{20}$ = −12.5 (*c* 0.40 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3380 cm^{-1}, 2956, 2925, 2854, 1738, 1615, 1519, 1446. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.30 (d, $J_{5'',6''}$ = 6.3 Hz, 3 H, 6''-H), 1.38 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.58–1.76 (m, 1 H, 2'-H_{ax}), 2.11 (s, 3 H, CH_3, OAc), 2.42 (ddd, $J_{1',2'eq}$ = 1.8 Hz, $J_{2'ax,2'eq}$ = 13.2 Hz, $J_{2'eq,3'}$ = 5.3 Hz, 1 H, 2'-H_{eq}), 3.18 (dd, *J* = 8.6 Hz, *J* = 8.7 Hz, 1 H, 4'-H), 3.44–3.69 (m, 1 H, 5'-H), 3.80–3.97 (m, 1 H, 3'-H), 3.93, 4.01 (2 x s, 2 x 3 H, 2 x OCH_3), 4.07–4.19 (m, 1 H, 5''-H), 4.44 (s, 1 H, OH), 5.00–5.17

(m, 3 H, 1'-H, 1"-H, 4"-H), 5.77–6.03 (m, 2 H, 2"-H, 3"-H), 6.61, 6.68 (2 x d, $J_{6,7}$ = 8.5 Hz, 2 H, 6-H, 7-H), 7.57, 7.72 (2 x d, $J_{3,4}$ = 8.8 Hz, 2 H, 2-H, 3-H), 9.76 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.19, 18.89 (2 x q, C-6", C-6'), 21.49 (q, CH_3, OAc), 39.40 (t, C-2'), 56.16, 56.84 (2 x q, 2 x OCH_3), 66.44, 70.61, 71.71, 72.10, 74.90 (5 x d, C-1', C-3', C-5', C-4", C-5"), 89.97 (d, C-4'), 96.98 (d, C-1"), 103.22, 104.05 (2 x d, C-6, C-7), 113.52, 125.27 (2 x d, C-3, C-4), 115.62, 123.77, 127.98 (3 x s, C-2, C-4a, C-8a), 127.28, 130 35 (2 x d, C-2", C-3"), 150.45, 150.55, 150.69 (3 x s, C-1, C-5, C-8), 170.87 (s, OAc). MS (70 eV): *m/z* (%) = 488 (5) [M^+], 376 (11), 334 (57), 259 (20), 241 (63), 230 (59), 215 (45), 95 (56), 57 (25), 43 (100), 28 (20).

HRMS Anal. Calcd for $C_{26}H_{32}O_9$ (488.2046) Found: 488.2049.

Data for 2-[3-*O*-(4-*O*-Acetyl-2,3,6-trideoxy-β-L-*erythro*-hex-2-enopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (10). $[\alpha]_D^{20}$ = –52.0 (*c* 0.35 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3371 cm^{-1}, 2956, 2924, 2853, 1736, 1631, 1614, 1518, 1451. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.38 (d, $J_{5",6"}$ = 6.3 Hz, 3 H, 6"-H), 1.43 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.76 (dd, $J_{1',2'ax}$ = 11.5 Hz, $J_{2'ax,\,2'eq}$ = 12.8 Hz, 1 H, 2'-H_{ax}), 2.06 (s, 3 H, CH_3, OAc), 2.29 (ddd, $J_{1',2'eq}$ = 1.8 Hz, $J_{2'ax,2'eq}$ = 12.8 Hz, $J_{2'eq,3'}$ = 5.2 Hz, 1 H, 2'-H_{eq}), 3.27 (dd, *J* = 8.8 Hz, *J* = 8.8 Hz, 1 H, 4'-H), 3.50–3.67 (m, 1 H, 5'-H), 3.80–3.95 (m, 2 H, 3'-H, 5"-H), 3.94, 4.02 (2 x s, 2 x 3 H, 2 x OCH_3), 4.07–4.19 (m, 1 H, 5"-H), 4.44 (s, 1 H, OH), 5.01 (dd, $J_{1',2'ax}$ = 11.3 Hz, $J_{1',2'eq}$ = 1.8 Hz,1 H, 1'-H), 5.14 (dd, $J_{4",\,5"}$ = 7.8 Hz, $J_{3",4"}$ = 1.9 Hz, 1 H, 4"-H), 5.47 (br s, 1 H, 1"-H), 5.86 (d, $J_{2",3"}$ = 10.3 Hz, 1 H, 2"-H or 3" H), 5.99 (d, $J_{2",3"}$ = 10.3 Hz, 1 H, 2"-H or 3" H), 6.62, 6.69 (2 x d, $J_{6,7}$ = 8.5 Hz, 2 H, 6-H, 7-H), 7.59, 7.72 (2 x d, $J_{3,4}$ = 8.8 Hz, 2 H, 2-H, 3-H), 9.77 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.74 (q, C-6"), 18.92 (q, C-6'), 21.45 (q, CH_3, OAc), 39.37 (t, C-2'), 56.14, 56.81 (2 x q, 2 x OCH_3), 70.20 (d, C-4"), 71.76 (d, C-1'), 72.45 (d, C-5"), 76.14 (d, C-4'), 76.73 (d, C-5'), 78.65 (d, C-3'), 96.21 (d, C-1"), 103.19, 104.03 (2 x d, C-6, C-7), 113.56, 125.27 (2 x d, C-3, C-4), 115.60, 123.85, 127.97 (3 x s, C-2, C-4a, C-8a), 129.78, 131.13 (2 x d, C-2", C-3"), 150.32, 150.54, 150.71 (3 x s, C-1, C-5, C-8), 170.78 (s, OAc). MS (70 eV): *m/z* (%) = 488 (51) [M^+], 334 (40), 259 (14), 230 (33), 215 (28), 155 (13), 95 (100), 71 (17), 57 (27), 43 (60), 28 (15).

HRMS Anal. Calcd for $C_{26}H_{32}O_9$ (488.2046) Found: 488.2044.

Hydrogenation of the unsaturated disaccharides 8–10. A suspension of **8–10** in dry 2-propanol (1 mL) and palladium on charcoal (5 %, 5 mg) was stirred for 3 h at 22 °C under an atmosphere of hydrogen. The suspension was filtered, and the solvent was removed at reduced pressure to yield the saturated disaccharides **11–13** as oils.

Alternatively, the products **11–13** were obtained by reaction of amicetal **6** with **3** with TPHB-catalysis (yields see Table 1).

2-[3-*O*-(4-*O*-Acetyl-2,3,6-trideoxy-α-L-*erythro*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (11). 15 mg, (0.031 mmol) of **8** yielded 13 mg (87 %) of **11**. $[\alpha]_D^{20}$ = 1.0 (*c* 0.50 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3370 cm^{-1}, 2956, 2927, 1737, 1615, 1456. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.26 (d, $J_{5'',6''}$ = 6.2 Hz, 3 H, 6''-H), 1.48 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.60–1.98 (m, 5 H, 2'-H_{ax}, 2''-H, 3''-H), 2.10 (s, 3 H, CH_3, OAc), 2.39 (ddd, $J_{1',2'eq}$ = 1.8 Hz, $J_{2'ax,2'eq}$ = 12.8 Hz, $J_{2'eq,3'}$ = 5.0 Hz, 1 H, 2'-H_{eq}), 3.30 (dd, *J* = 8.6 Hz, *J* = 8.8 Hz, 1 H, 4'-H), 3.51–3.65 (m, 1 H, 5'-H), 3.73–3.87 (m, 1 H, 3'-H), 3.97, 4.05 (2 x s, 2 x 3 H, 2 x OCH_3), 4.07–4.18 (m, 1 H, 5''-H), 4.50–4.60 (m, 1 H, 4''-H), 5.00 (s, 1 H, 1''-H), 5.06 (dd, $J_{1',2'ax}$ = 11.4 Hz, $J_{1',2'eq}$ = 1.8 Hz, 1 H, 1'-H), 6.65, 6.72 (2 x d, $J_{6,7}$ = 8.4 Hz, 2 H, 6-H, 7-H), 7.62, 7.76 (2 x d, $J_{3,4}$ = 8.7 Hz, 2 H, 2-H, 3-H), 9.76 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.29, 18.95 (2 x q, C-6'', C-6'), 21.61 (q, CH_3, OAc), 24.22, 29.88 (2 x t, C-2'', C-3''), 37.91 (t, C-2'), 56.17, 56.85 (2 x q, 2 x OCH_3), 68.23 (d, C-5''), 71.84 (d, C-1'), 73.50 (d, C-4''), 76.45, 76.76 (2 x d, C-4', C-5'), 82.20 (d, C-3'), 96.30 (d, C-1''), 103.16, 104.03 (2 x d, C-6, C-7), 113.54, 125.14 (2 x d, C-3, C-4), 115.59, 123.97, 127.94 (3 x s, C-2, C-4a, C-8a), 150.26, 150.52, 150.69 (3 x s, C-1, C-5, C-8), 170.72 (s, OAc). MS (70 eV): *m/z* (%) = 490 (5) [M^+], 334 (100), 259 (27), 243 (23), 241 (55), 230 (53), 215 (47), 187 (15), 81 (15), 57 (22), 43 (55), 29 (17).

HRMS Calcd for $C_{26}H_{34}O_9$ (490.2203) Found: 490.2198.

2-[4-*O*-(4-*O*-Acetyl-2,3,6-trideoxy-α-L-*erythro*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (12). 13 mg, (0.031 mmol) of **9** yielded 13 mg (99 %) of **12**. $[\alpha]_D^{20}$ = –29.0 (*c* 0.51 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3364 cm^{-1}, 2934, 1737, 1615, 1455. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.26 (d, $J_{5'',6''}$ = 6.2 Hz, 3 H, 6''-H), 1.40 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.68 (dd, $J_{1',2'ax}$ = 11.5 Hz, $J_{2'ax,2'eq}$ = 13.0 Hz, 1 H, 2'-H_{ax}), 1.87–2.09 (m, 4 H, 2''-H, 3''-H), 2.12 (s, 3 H, CH_3, OAc), 2.42 (ddd, $J_{1',2'eq}$ = 1.8 Hz, $J_{2'ax,2'eq}$ = 13.0 Hz, $J_{2'eq,3'}$ = 5.2 Hz, 1 H, 2'-H_{eq}), 3.13 (dd, *J* = 8.6 Hz, *J* = 8.6 Hz, 1 H, 4'-H), 3.55–3.69 (m, 1 H, 5'-H), 3.76–4.18 (m, 2 H, 3'-H, 5''-H), 3.96, 4.04 (2 x s, 2 x 3 H, 2 x OCH_3), 4.41–4.60 (m, 1 H, 4''-H), 4.69 (br s, 1 H, OH), 4.97 (s, 1 H, 1''-H), 5.07 (dd, $J_{1',2'ax}$ = 11.5 Hz, $J_{1',2'eq}$ = 1.5 Hz, 1 H, 1'-H), 6.62, 6.71 (2 x d, $J_{6,7}$ = 8.5 Hz, 2 H, 6-H, 7-H), 7.62, 7.76 (2 x d, $J_{3,4}$ = 8.8 Hz, 2 H, 2-H, 3-H), 9.79 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.18, 18.99 (2 x q, C-6'', C-6'), 21.60 (q, CH_3,

OAc), 24.15, 29.80 (2 x t, C-2", C-3"), 39.35 (t, C-2'), 56.20, 56.89 (2 x q, 2 x OCH_3), 68.80, 71.70, 72.27, 73.31, 74.85 (5 x d, C-1', C-3', C-5', C-4", C-5"), 89.85 (d, C-4'), 99.16 (d, C-1"), 103.21, 104.07 (2 x d, C-6, C-7), 113.50, 125.17 (2 x d, C-3, C-4), 115.65, 123.88, 127.99 (3 x s, C-2, C-4a, C-8a), 150.44, 150.57, 150.73 (3 x s, C-1, C-5, C-8), 170.66 (s, OAc). MS (70 eV): *m/z* (%) = 491 (20) [M^++1], 490 (71) [M^+], 446 (6), 360 (30), 334 (82), 260 (17), 259 (31), 241 (34), 231 (34), 230 (100), 217 (31), 215 (37), 157 (55), 57 (53).

HRMS Calcd for $C_{26}H_{34}O_9$ (490.2203). Found: 490.2206.

2-[3-*O*-(4-*O*-Acetyl-2,3,6-trideoxy-β-L-*erythro*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (13). 8 mg, (0.016 mmol) of **10** yielded 7 mg (87 %) of **13** $[\alpha]_D^{20}$ = 12.4 (*c* 0.15 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3384 cm^{-1}, 2929, 1736, 1615, 1452. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.23 (d, $J_{5",6"}$ = 6.2 Hz, 3 H, 6"-H), 1.45 (d, $J_{5',6'}$ = 6.0 Hz, 3 H, 6'-H), 1.60–2.26 (m, 5 H, 2'-H_{ax}, 2"-H, 3"-H), 2.08 (s, 3 H, CH_3, OAc), 2.39–2.48 (m, 1 H, 2'-H_{eq}), 2.92 (br s, 1 H, OH), 3.35 (dd, *J* = 8.8 Hz, *J* = 9.0 Hz, 1 H, 4'-H), 3.53–3.64 (m, 2 H, 5'-H, 5"-H), 3.84–3.91 (m, 1 H, 3'-H), 3.97, 4.05 (2 x s, 2 x 3 H, 2 x OCH_3), 4.40–4.53 (m, 1 H, 4"-H), 4.80 (dd, $J_{1",2"ax}$ = 9.1 Hz, $J_{1",2"eq}$ = 2.5 Hz, 1 H, 1"-H), 5.09 (dd, $J_{1',2'ax}$ = 11.6 Hz, $J_{1',2'eq}$ = 1.9 Hz, 1 H, 1'-H), 6.65, 6.72 (2 x d, $J_{6,7}$ = 8.4 Hz, 2 H, 6-H, 7-H), 7.61, 7.76 (2 x d, $J_{3,4}$ = 8.7 Hz, 2 H, 2-H, 3-H), 9.65 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.59, 18.91 (2 x q, C-6", C-6'), 21.59 (q, CH_3, OAc), 28.02, 30.38 (2 x t, C-2", C-3"), 39.08 (t, C-2'), 56.17, 56.88 (2 x q, 2 x OCH_3), 71.70 (d, C-1'), 73.05 (d, C-4"), 74.04 (d, C-5"), 76.34 (d, C-4'), 78.08 (d, C-5'), 81.25 (d, C-3'), 101.44 (d, C-1"), 103.20, 104.06 (2 x d, C-6, C-7), 113.62, 125.33 (2 x d, C-3, C-4), 115.65, 123.73, 127.98 (3 x s, C-2, C-4a, C-8a), 150.40, 150.53, 150.69 (3 x s, C-1, C-5, C-8), 170.68 (s, OAc). MS (70 eV): *m/z* (%) = 490 (11) [M^+], 360 (4), 334 (100), 272 (6), 259 (24), 241 (39), 230 (73), 215 (42), 187 (12), 81 (22).

HRMS Calcd for $C_{26}H_{34}O_9$ (490.2203). Found: 490.2202.

2-[3-*O*-(4-*O*-Acetyl-2,3,6-trideoxy-α-L-*threo*-hex-2-enopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (14). To a mixture of *C*-glycoside **3** (100 mg, 0.30 mmol) and 3,4-di-*O*-acetyl-L-fucal (**5**) (53 mg, 0.25 mmol) in dry CH_2Cl_2 (2 mL) was added under argon at 0 °C montmorillonite K-10 (19 mg). The suspension was stirred for 3 h at 22 °C and an additional amount montmorillonite K-10 (10 mg) was added. The suspension was filtered, the filtrate concentrated at reduced pressure, and the residue separated by TLC chromatography on

silica gel (3 % MeOH/CH_2Cl_2). HPLC analysis indicated a ratio of **14**: to the 4'-α-isomer of 9:5. The 4'-α-isomer could not be isolated in analytically pure state. Yield (21 mg, 17%). $[\alpha]_D^{20}$ = 91.2 (*c* 0.23 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3383 cm^{-1}, 2923, 1737, 1614, 1455. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.34 (d, $J_{5",6"}$ = 6.6 Hz, 3 H, 6"-H), 1.48 (d, $J_{5',6'}$ = 6.2 Hz, 3 H, 6'-H), 1.71 (q, $J_{1',2'ax}$ = 11.5 Hz, $J_{2'ax,2'eq}$ = 12.8 Hz, 1 H, 2'-H_{ax}), 2.15 (s, 3 H, CH_3, OAc), 2.43 (ddd, $J_{1',2'eq}$ = 1.7 Hz, $J_{2'ax,2'eq}$ = 12.8 Hz, $J_{2'eq,3'}$ = 5.0 Hz, 1 H, 2'-H_{eq}), 3.28 (dd, *J* = 8.6 Hz, *J* = 8.8 Hz, 1 H, 4'-H), 3.52–3.68 (m, 1 H, 5'-H), 3.74–3.91 (m, 1 H, 3'-H), 3.96, 4.04 (2 x s, 2 x 3 H, 2 x OCH_3), 4.41 (dq, $J_{5",6"}$ = 6.6 Hz, $J_{4",5"}$ = 2.2 Hz, 1 H, 5"-H), 4.98–5.09 (m, 2 H, 1'-H, 4"-H), 5.26 (d, $J_{1",2"}$ = 2.6 Hz, 1 H, 1"-H), 6.00 (dd, $J_{2",3"}$ = 10.0 Hz, *J* = 2.9 Hz, 1 H, 2"-H or 3"-H), 6.14 (dd, $J_{2",3"}$= 10.2 Hz, *J* = 5.3 Hz, 1 H, 2"-H or 3"-H), 6.65, 6.72 (2 x d, $J_{6,7}$ = 8.5 Hz, 2 H, 6-H, 7-H), 7.62, 7.76 (2 x d, $J_{3,4}$ = 8.8 Hz, 2 H, 2-H, 3-H), 9.62 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.47 (q, C-6"), 18.96 (q, C-6'), 21.30 (q, CH_3, OAc), 38.22 (t, C-2'), 56.15, 56.86 (2 x q, 2 x OCH_3), 65.12 (d, C-4"), 66.08 (C-5"), 71.83 (d, C-1'), 76.59 (d, C-4', C-5'), 83.70 (d, C-3'), 94.75 (d, C-1"), 103.16, 104.03 (2 x d, C-6, C-7), 113.58, 125.11, 126.30, 130.50 (4 x d, C-3, C-4, C-2", C-3"), 115.56, 123.84, 127.94 (3 x s, C-2, C-4a, C-8a), 150.25, 150.50, 150.68 (3 x s, C-1, C-5, C-8), 171.01 (s, OAc). MS (70 eV): *m/z* (%) = 488 (12) [M^+], 334 (26), 241 (16), 230 (26), 215 (17), 156 (13), 95 (100), 43 (43), 32 (23).

HRMS Calcd for $C_{26}H_{32}O_9$ (488.2046). Found: 488.2050.

2-[3-*O*-(4-*O*-Acetyl-2,3,6-trideoxy-α-L-*threo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (15). Hydrogenation of **14** (11 mg, 0.023 mmol) proceeded as described for **11** to yield **15** (9 mg, 81 %) as an oil. $[\alpha]_D^{20}$ = 3.8 (*c* 0.65 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3373 cm^{-1}, 2935, 1736, 1615, 1448. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.17 (d, $J_{5",6"}$ = 6.6 Hz, 3 H, 6"-H), 1.43 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.65 (dd, $J_{2'ax,2'eq}$ = 12.9 Hz, $J_{1',2'ax}$ = 11.4 Hz, 1 H, 2'-H_{ax}), 1.76–1.81, 2.03–2.15 (2 x m, 2 x 2 H, 2"-H, 3"-H), 2.12 (s, 3 H, CH_3, OAc), 2.36 (ddd, $J_{1',2'eq}$ = 1.9 Hz, $J_{2'ax,2'eq}$ = 12.9 Hz, $J_{2'eq,3'}$ = 5.1 Hz, 1 H, 2'-H_{eq}), 3.23 (dd, *J* = 8.6 Hz, *J* = 8.7 Hz, 1 H, 4'-H), 3.48–3.58 (m, 1 H, 5'-H), 3.73–3.78 (m, 1 H, 3'-H), 3.92, 4.00 (2 x s, 2 x 3 H, 2 x OCH_3), 4.25 (dq, $J_{4",5"}$ = 1.6 Hz, $J_{5",6"}$ = 6.6 Hz, 1 H, 5"-H), 4.85 (br s, 1 H, 4"-H), 5.01 (dd, $J_{1',2'ax}$ = 11.4 Hz, $J_{1',2'eq}$ = 1.9 Hz, 1 H, 1'-H), 5.05 (s, 1 H, 1"-H), 6.61, 6.71 (2 x d, $J_{6,7}$ = 8.4 Hz, 2 H, 6-H, 7-H), 7.58, 7.78 (2 x d, $J_{3,4}$ = 8.7 Hz, 2 H, 2-H, 3-H), 9.74 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.51 (q, C-6"), 18.93 (q, C-6'), 21.52 (q, CH_3, OAc), 23.12, 25.26 (2 x t, C-2", C-3"), 38.10 (t, C-2'), 56.12, 56.89 (2 x q, 2 x OCH_3),

66.63 (d, C-5"), 66.72 (d, C-4'), 71.84 (d, C-1'), 76.49 (d, C-5'), 76.84 (d, C-4"), 82.84 (d, C-3'), 97.49 (d, C-1"), 103.18, 104.07 (2 x d, C-6, C-7), 113.53, 125.15 (2 x d, C-3, C-4), 115.61, 124.00, 127.96 (3 x s, C-2, C-4a, C-8a), 150.27, 150.54, 150.73 (3 x s, C-1, C-5, C-8), 171.42 (s, OAc). MS (70 eV): *m/z* (%) = 490 (5) [M^+], 360 (11), 334 (100), 259 (19), 230 (45), 157 (21), 97 (27), 43 (55).

HRMS Calcd for $C_{26}H_{34}O_9$ (490.2203). Found: 490.2197.

$SnCl_4$–catalyzed reaction of 3 with fucal 5. A solution of **3** (32 mg, 0.096 mmol) and fucal **5** (17 mg, 0.079 mmol) in dry CH_2Cl_2 (0.5 mL) was treated at 22 °C with a 0.1 M solution of $SnCl_4$ in CH_2Cl_2 (0.05 mL). The reaction was quenched by addition of aqueous $NaHCO_3$ (10 mL), and the aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic phases were washed with brine, dried (Na_2SO_4), and the solvent was removed at reduced pressure. The residue was separated by TLC on silica (3 % MeOH/CH_2Cl_2) to afford **16** (10 mg, 23 %) and **17** (6 mg, 15 %, not analytically pure) as oils. Alternatively, **3** (40 mg, 0.12 mmol) and **5** (25 mg, 0.12 mmol) were reacted at 0 °C with scandium triflate (5 mg, 0.01 mol) for 2 h to yield **16** (12 mg, 18 %) and **17** (7 mg, 12 %) (see Table 1).

2-[3-*O*-(3,4-Di-*O*-acetyl-2,6-dideoxy-α-L-*lyxo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (16). $[\alpha]_D^{20} = -1.3$ (*c* 0.30 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3377 cm^{-1}, 2927, 1743, 1615, 1387. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.24 (d, $J_{5",6"}$ = 6.5 Hz, 3 H, 6"-H), 1.47 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.58–1.92 (m, 2 H, 2'-H_{ax}, 2"a-H), 2.01, 2.20 (2 x s, 2 x 3 H, 2 x CH_3, OAc), 2.10–2.13 (m, 1 H, 2"b-H), 2.36 (dd, $J_{2'ax,2'eq}$ = 13.2 Hz, $J_{2'eq,3'}$ = 5.1 Hz, 1 H, 2'-H_{eq}), 3.28 (dd, *J* = 8.7 Hz, *J* = 8.5 Hz, 1 H, 4'-H), 3.50–3.85 (m, 2 H, 3'-H, 5'-H), 3.97, 4.05 (2 x s, 2 x 3 H, 2 x OCH_3), 4.37 (q, $J_{5",6"}$ = 6.5 Hz, 1 H, 5"-H), 4.85 (br s, 1 H, 4"-H), 5.05 (d, $J_{1',2'ax}$ = 9.6 Hz, 1 H, 1'-H), 5.24 (br s, 1 H, 1"-H), 5.28–5.36 (m, 2 H, 3"-H, 4"-H), 6.65, 6.72 (2 x d, $J_{6,7}$ = 8.5 Hz, 2 H, 6-H, 7-H), 7.62, 7.77 (2 x d, $J_{3,4}$ = 8.8 Hz, 2 H, 2-H, 3-H), 9.79 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.03 (q, C-6"), 18.92 (q, C-6'), 21.15, 21.39 (2 x q, 2 x CH_3, OAc), 30.92 (t, C-2"), 37.66 (t, C-2'), 56.19, 56.89 (2 x q, 2 x OCH_3), 66.05 (d, C-5"), 66.87, 70.09 (2 x d, C-3", C-4"), 71.80 (d, C-1'), 76.45, 76.66 (d, C-4', C-5'), 82.19 (d, C-3'), 97.28 (d, C-1"), 103.19, 104.09 (2 x d, C-6, C-7), 113.59, 125.14 (2 x d, C-3, C-4), 115.60, 123.86, 127.98 (3 x s, C-2, C-4a, C-8a), 150.25, 150.52, 150.74 (3 x s, C-1, C-5, C-8), 171.06 (2 x s, OAc). MS (70 eV): *m/z* (%) = 548 (24) [M^+], 334 (98), 316 (15), 259 (18), 230 (37), 95 (77), 43 (100).

HRMS Calcd for $C_{26}H_{34}O_9$ (548.2258): Found: 548.2260.

2-[4-*O*-(3,4-Di-*O*-acetyl-2,6-dideoxy-α-L-*lyxo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (17). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.27 (d, $J_{5'',6''}$ = 6.2 Hz, 3 H, 6''-H), 1.40 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.64–1.95 (m, 3 H, 2'-H_{ax}, 2''-H), 2.05, 2.22 (2 x s, 2 x 3 H, 2 x CH_3, OAc), 2.39-2.47 (m, 1 H, 2'-H_{eq}), 3.15 (dd, J = 8.4 Hz, J = 8.7 Hz, 1 H, 4'-H), 3.42–3.67 (m, 1 H, 5'-H), 3.79–3.91 (m, 1 H, 3'-H), 3.96, 4.00 (2 x s, 2 x 3 H, 2 x OCH_3), 4.37–4.47 (m, 1 H, 5''-H), 5.06 (d, $J_{1',2'ax}$ = 11.3 Hz, 1 H, 1'-H), 5.21–5.40 (m, 3 H, 1''-H, 3''-H, 4''-H), 6.65, 6.72 (2 x d, $J_{6,7}$ = 8.4 Hz, 2 H, 6-H, 7-H), 7.60, 7.76 (2 x d, $J_{3,4}$ = 8.7 Hz, 2 H, 2-H, 3-H), 9.88 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.96 (q, C-6''), 19.07 (q, C-6'), 21.17, 21.37 (2 x q, 2 x CH_3, OAc), 31.00 (t, C-2''), 39.37 (t, C-2'), 56.14, 56.83 (2 x q, 2 x OCH_3), 66.70, 69.96, 71.70, 72.28, 76.45, 74.75 (5 x d, C-1', C-3', C-5', C-3'', C-4'', C-5''), 90.12 (d, C-4'), 100.32 (d, C-1''), 103.22, 104.05 (2 x d, C-6, C-7), 113.48, 125.98 (2 x d, C-3, C-4), 115.63, 123.75, 127.98 (3 x s, C-2, C-4a, C-8a), 150.46, 150.57, 150.69 (3 x s, C-1, C-5, C-8), 170.63, 171.05 (s, OAc).

TPHB-catalyzed reaction of 3 with rhodinal 7. A solution of **3** (37 mg, 0.11 mmol) and 4-*O*-benzoyl-L-rhodinal (**7**) (29 mg, 0.133 mmol) in dry CH_2Cl_2 (0.8 mL) was treated under argon at 0 °C with TPHB (2 mg, 0.006 mmol) and the mixture was stirred for 20 min at 22 °C. The reaction was quenched by addition of CH_2Cl_2 (10 mL) and aqueous $NaHCO_3$ (8 mL). The aqueous phase was extracted with CH_2Cl_2 (2 x 5 mL), the combined organic phases were dried (Na_2SO_4), filtered, and the solvent removed at reduced pressure. The residue was separated by column chromatography on silica gel (3 % MeOH/CH_2Cl_2) to afford the disaccharides **18** (19 mg, 31 %) and **20** (15 mg, 24%) as oils.

2-[3-*O*-(4-*O*-Benzoyl-2,3,6-trideoxy-α-L-*threo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (18). $[\alpha]_D^{20}$ = 8.9 (*c* 0.37 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3377 cm^{-1}, 2935, 1716, 1614, 1518, 1450. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.25 (d, $J_{5'',6''}$ = 6.5 Hz, 3 H, 6''-H), 1.46 (d, $J_{5',6'}$ = 6.0 Hz, 3 H, 6'-H), 1.59–1.77 (m 2 H, 2'-H_{ax}, 2a''-H or 3a''-H), 1.90–2.19, (m, 3 H, 2a''-H or 3a''-H, 2''b-H, 3''b-H), 2.40 (dd, $J_{2'ax,2'eq}$ = 13.0 Hz, $J_{2'eq,3'}$ = 4.9 Hz, 1 H, 2'-H_{eq}), 3.27 (dd, J = 8.4 Hz, J = 8.6 Hz, 1 H, 4'-H), 3.52–3.63 (m, 1 H, 5'-H), 3.73–3.85 (m, 1 H, 3'-H), 3.93, 4.00 (2 x s, 2 x 3 H, 2 x OCH_3), 4.19 (s, 1 H, OH), 4.37 (q, $J_{5'',6''}$ = 6.6 Hz, 1 H, 5''-H), 5.05 (d, $J_{1',2'ax}$ = 11.4 Hz, 1 H, 1'-H), 5.12 (br s, 2 H, 1''-H, 4''-H), 6.61, 6.71 (2 x d, $J_{6,7}$ = 8.5 Hz,

2 x 1 H, 6-H, 7-H), 7.42–7.62 (m, 4 H, 3-H or 4-H, 3 H, benzoyl), 7.73 (d, $J_{3,4}$ = 8.7 Hz, 1 H, 3-H or 4-H), 8.11 (d, J = 7.1 Hz, 2 H, H, benzoyl), 9.77 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.72 (q, C-6"), 19.00 (q, C-6'), 23.24, 25.45 (2 x t, C-2", C-3"), 38.11 (t, C-2'), 56.17, 56.85 (2 x q, 2 x OCH_3), 66.90 (d, C-5"), 70.25 (d, C-4"), 71.88 (d, C-1'), 76.52 (d, C-5'), 76.85 (d, C-4'), 82.79 (d, C-3'), 97.51 (d, C-1"), 103.13, 104.01 (2 x d, C-6, C-7), 113.55 125.16 (2 x d, C-3, C-4), 115.58, 124.00, 127.93 (3 x s, C-2, C-4a, C-8a), 128.89, 130.12 (2 x d, 4x C, benzoyl), 130.64 (s, C, benzoyl), 133.55 (d, C, benzoyl), 150.27, 150.51, 150.67 (3 x s, C-1, C-5, C-8), 166.53 (s, C=O, benzoyl). MS (DCI, NH_3): *m/z* (%) = 551 (72) [M^+–1], 437 (4), 316 (54), 258 (18), 121 (100).

DCI-HRMS Calcd for $C_{31}H_{35}O_9$ (M^+–1) (551.2281). Found: 551.2250.

2-[4-*O*-(4-*O*-Benzoyl-2,3,6-trideoxy-α-L-*threo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (20). $[\alpha]_D^{20}$ = 20.0 (*c* 0.31 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3376 cm^{-1}, 2935, 1716, 1614, 1518, 1450. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.25 (d, $J_{5",6"}$ = 6.6 Hz, 3 H, 6"-H), 1.38 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.59–2.23 (m, 5 H, 2'-H_{ax}, 2"-H, 3"-H), 2.41 (dd, $J_{2'ax,2'eq}$ = 13.1 Hz, $J_{2'eq,3'}$ = 5.2 Hz, 1 H, 2'-H_{eq}), 3.15 (dd, J = 8.5 Hz, J = 8.6 Hz, 1 H, 4'-H), 3.57–3.64 (m, 1 H, 5'-H), 3.80–4.05 (m, 1 H, 3'-H), 3.93, 4.01 (2 x s, 2 x 3 H, 2 x OCH_3), 4.41 (q, $J_{5",6"}$ = 6.6 Hz, 1 H, 5"-H), 4.80 (s, 1 H, OH), 5.02–5.13 (m, 3 H, 1'-H, 1"-H, 4"-H), 6.61, 6.68 (2 x d, $J_{6,7}$ = 8.5 Hz, 2 x 1 H, 6-H, 7-H), 7.44–7.66 (m, 4 H, 3-H or 4-H, 3 H, benzoyl), 7.73 (d, $J_{3,4}$ = 8.8 Hz, 1 H, 3-H or 4-H), 8.12 (d, J = 7.0 Hz, 2 H, H, benzoyl), 9.77 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.64 (q, C-6"), 19.08 (q, C-6'), 23.18, 25.52 (2 x t, C-2", C-3"), 39.35 (t, C-2'), 56.15, 56.83 (2 x q, 2 x OCH_3), 67.37 (d, C-5"), 70.16 (d, C-4"), 71.68 (d, C-1'), 72.32 (d, C-3'), 74.89 (d, C-5'), 89.93 (d, C-4'), 99.99 (d, C-1"), 103.18, 104.00 (2 x d, C-6, C-7), 113.50, 125.18 (2 x d, C-3, C-4), 115.63, 123.87, 127.97 (3 x s, C-2, C-4a, C-8a), 128.92, 130.13 (2 x d, 4 x C, benzoyl), 130.57 (s, C, benzoyl), 133.60 (d, C, benzoyl), 150.48, 150.56, 150.67 (3 x s, C-1, C-5, C-8), 166.52 (s, C=O, benzoyl). MS (DCI, NH_3): *m/z* (%) = 551 (39) [M^+–1], 437 (5), 228 (5), 257 (23), 243 (11), 147 (14), 146 (15), 121 (100).

DCI-HRMS Calcd for $C_{31}H_{35}O_9$ (M^+–1) (551.2281): Found: 551.2277.

2-[3-*O*-(4-*O*-Benzoyl-2-iodo-2,3,6-trideoxy-α-L-*threo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (19). A solution of **3** (40 mg, 0.12 mmol) and **7** (39 mg, 0.18) in dry CH_3CN (1.5 mL) was treated under argon with molecular sieves (4 Å, 35 mg). The suspension was stirred

45 min at 22 °C, NIS (54 mg, 0.24 mmol) was added and the mixture stirred for 15 h in the dark. The suspension was filtered, the solvent was removed at reduced pressure, the residue was redissolved in CH_2Cl_2 (30 mL), washed with $Na_2S_2O_3$ (10 %, 3 x 15 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to afford the iodide **19** (18 mg, 22%): mp 102 °C. $[\alpha]_D^{20}$ = –33.0 (*c* 0.60 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3359 cm^{-1}, 2924, 2851, 1724, 1621. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.38 (d, $J_{5'',6''}$ = 6.7 Hz, 3 H, 6''-H), 1.44 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.71 (dd, $J_{1',2'ax}$ = 11.7 Hz, $J_{2'ax,2'eq}$ = 12.8 Hz, 1 H, 2'-H_{ax}), 2.44–2.55 (m, 2 H, 2'-H_{eq}, 3a''-H), 2.79–287 (m, 1 H, 3b''-H), 3.28 (dd, *J* = 8.7 Hz, 1 H, 4'-H), 3.50–3.60 (m, 1 H, 5'-H), 3.70–3.80 (m, 1 H, 3'-H), 3.94, 4.03 (2 x s, 2 x 3 H, 2 x OCH_3), 4.05–4.11 (m, 1 H, 2''-H), 4.42–4.56 (m, 1 H, 5''-H), 5.06 (d, $J_{1',2'ax}$ = 10.1 Hz, 1 H, 1'-H), 5.19–5.24 (m, 1 H, 4''-H), 5.26 (d, $J_{1'',2''}$ = 4.5 Hz, 1 H, 1''-H), 6.63, 6.69 (2 x d, $J_{6,7}$ = 8.4 Hz, 2 x 1 H, 6-H, 7-H), 7.45–7.50, 7.57–7.62 (2 x m, 4 H, 3-H or 4-H, 3 H, benzoyl), 7.74 (d, $J_{3,4}$ = 8.7 Hz, 1 H, 3-H or 4-H), 8.16 (d, *J* = 7.1 Hz, 2 H, H, benzoyl), 9.79 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.56 (q, C-6''), 18.90 (q, C-6'), 19.37 (d, C-2''), 33.81 (t, C-3''), 37.81 (t, C-2'), 56.20, 56.83 (2 x q, 2 x OCH_3), 67.84 (d, C-5''), 68.97 (d, C-4''), 71.82 (d, C-1'), 76.48 (d, C-5'), 76.54 (d, C-4'), 83.34 (d, C-3'), 101.15 (d, C-1''), 103.23, 104.08 (2 x d, C-6, C-7), 113.61, 125.11 (2 x d, C-3, C-4), 115.59, 123.77, 127.98 (3 x s, C-2, C-4a, C-8a), 128.86, 130.09 (2 x d, 4x C, benzoyl), 130.44 (s, C, benzoyl), 133.70 (d, C, benzoyl), 150.25, 150.52, 150.70 (3 x s, C-1, C-5, C-8), 166.19 (s, C=O, benzoyl). MS (70 eV): *m/z* (%) = 678 (24) [M^+], 552 (16), 434 (39), 241 (18), 217 (29), 105 (100), 77 (26).

HRMS Calcd for $C_{31}H_{35}O_9I$ (678.1326): Found: 678.1324.

2-(3-*O*-*tert*-Butyldimethylsilyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-1-hydroxy-5,8-dimethoxynaphthalene (21). A solution of the diol **3** (500 mg, 1.50 mmol), imidazole (256 mg, 3.75 mmol), and TBSCl (339 mg, 2.25 mmol) in dry DMF (2 mL) was stirred for 2 h at 22 °C. The reaction was quenched by addition of water (40 mL) and Et_2O (30 mL), the organic phase was separated and the aqueous phase extracted with Et_2O (2 x 20 mL). The combined organic phases were dried ($MgSO_4$) and the solvent removed under reduced pressure. The crude product was purified by filtration through a short column of silica gel (Et_2O/PE 1:1) to yield the oily silyl ether **21** (597 mg, 89 %). $[\alpha]_D^{20}$ = 60.0 (*c* 0.39 in CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3387 cm^{-1}, 2955, 2930, 1618. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.13, 0.18 (2 x s, 2 x 3 H, 2 x CH_3 , TBDMS), 0.93 (s, 9 H,

$C(CH_3)_3$, TBDMS), 1.45 (d, $J_{5',6'}$ = 6.2 Hz, 3 H, 6'-H), 1.71 (m, 1 H, 2'-H_{ax}), 2.27 (ddd, $J_{1',2'eq}$ = 2.1 Hz, $J_{2'eq,2'ax}$ = 12.8 Hz, $J_{2'eq,3'}$ = 4.9 Hz, 1 H, 2'-H_{eq}), 2.38 (d, $J_{4',OH}$ = 2.0 Hz, 1 H, OH), 3.27 (ddd, $J_{3',4'}$ = 8.5 Hz, $J_{4',5'}$ = 8.5 Hz, $J_{4',OH}$ = 2.0 Hz, 1 H, 4'-H), 3.50–3.70 (m, 1 H, 3'-H), 3.76–3.92 (m, 1 H, 5'-H), 3.97, 4.05 (2 x s, 2 x 3 H, 2 x OMe), 5.07 (dd, $J_{1',2'eq}$ = 2.1 Hz, $J_{1',2'ax}$ = 11.3 Hz, 1 H, 1'-H), 6.65, 6.71 (2 x d, $J_{6,7}$ = 8.5 Hz, 2 x 1 H, 6-H, 7-H), 7.63, 7.76 (2 x d, $J_{3,4}$ = 8.7 Hz, 2 x 1 H, 3-H, 4-H), 9.79 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.83, –4.27 (2 x q, 2 x CH_3, TBDMS), 17.81 (s, $C(CH_3)_3$, TBDMS), 18.23 (q, C-6'), 25.59 (q, $C(CH_3)_3$, TBDMS), 40.40 (t, C-2'), 55.53, 56.20 (2 x q, 2 x OMe), 71.19, 74.71, 75.40, 77.96 (4 x d, C-1', C-3', C-4', C-5'), 102.60, 103.42 (2 x d, C-6, C-7), 112.93, 124.65 (2 x d, C-3, C-4), 115.00, 123.45, 127.34 (3 x s, C-2, C-4a, C-8a), 149.60, 149.93, 150.13 (C-1, C-5, C-8). MS (GC-MS, 70 eV): *m/z* (%) = 448 (17) [M^+], 402 (10), 373 (14), 299 (22), 255 (100), 243 (55), 217 (58), 117 (37), 75 (37).

Anal. Calcd for $C_{24}H_{36}O_6Si$ (488.63): C, 64.25; H, 8.09. Found: C, 63.99; H, 7.84.

1-Acetoxy-2-(4-*O*-acetyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-5,8-dimethoxynaphthalene (22). A solution of silyl ether **21** (330 mg, 0.73 mmol) in dry pyridine (5 mL) was treated at 22 °C with Ac_2O (0.42 mL, 4.41 mmol). The mixture was stirred for 16 h and then quenched by addition of ice-cold 1 M HCl (50 mL). The mixture was extracted with CH_2Cl_2 (3 x 30 mL) and the combined organic phases washed with 1 M HCl (50 mL), water (50 mL), aqueous $NaHCO_3$ (3 x 50 mL), and brine (30 mL). The solution was dried (Na_2SO_4) and concentrated under reduced pressure. Evaporation of the eluate afforded an oily diacetate (388 mg, quantitative). A solution of this TBDMS ether (200 mg, 0.38 mmol) in CH_3CN (2 mL) was treated at 22 °C with HF (0.2 mL, 40 % in water). After 3 h a saturated aqueous solution of $NaHCO_3$ (20 mL) was added, the mixture was extracted with Et_2O (3 x 15 mL), the organic phase was dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford the diacetate **22** as a yellow solid (133 mg, 85 %): mp 169–170 °C. $[\alpha]_D^{20}$ = 51.0 (*c* 0.50 in CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3490 cm^{-1}, 2940, 2900, 1769, 1740, 1604, 1420. ^{1}H NMR (200 MHz, $CDCl_3$) (mixture of rotamers): δ = 1.32 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.78–2.50 (m, 2 H, 2'-H_{ax}, 2'-H_{eq}), 2.20, 2.41 (2 x s, 2 x 3 H, 2 x CH_3, OAc), 3.47–3.71, 3.82–4.06 (2 x m, 2 x 1 H, 3'-H, 5'-H), 3.90, 3.97 (2 x s, 2 x 3 H, 2 x OCH_3), 4.65 (dd, *J* = 9.0 Hz, *J* = 9.3 Hz, 1 H, 4'-H), 4.80–5.06 (m, 1 H, 1'-H), 6.73, 6.79 (2 x d, $J_{6,7}$ = 8.6 Hz, 2 x 1 H, 6-H, 7-H), 7.66 (br s, 1 H, 3-H or 4-H), 8.21 (d, $J_{3,4}$ = 8.9 Hz, 1 H, 3-H or 4-H). ^{13}C NMR (75 MHz, $CDCl_3$)

(mixture of rotamers): δ = 18.51 (q, C-6'), 21.31, 21.06 (2 x q, 2 x CH_3, OAc), 40.97, 41.68 (2 x t, C-2'), 56.26, 56.99 (2 x q, 2 x OMe), 72.09, 72.81, 74.59, 79.32 (4 x d, C-1', C-3', C-4', C-5'), 104.61, 107.05 (2 x d, C-6, C-7), 121.12, 123.63, 124.27 (3 x d, C-3, C-4), 119.78, 128.26, 131.22 (3 x s, C-2, C-4a, C-8a), 142.72, 148.90, 149.43, (3 x s, C-1, C-5, C-8), 169.89 (s, 2 x OAc). MS (70 eV): *m/z* (%) = 418 (62) [M^+], 376 (100), 259 (40), 241 (87), 230 (60), 215 (37), 43 (25).

Anal. Calcd for $C_{22}H_{26}O_8$ (418.44): C, 63.15; H, 6.26. Found: C, 63.40; H, 6.03.

1-Benzoyloxy-2-(4-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-5,8-dimethoxynaphthalene (23). A solution of the TBDMS ether **21** (see above, 300 mg, 0.67 mmol) in dry pyridine (5 mL) was benzoylated at 22 °C with BzCl (283 mg, 2.01 mmol). Workup proceeded as described for **22** to yield the dibenzoate as a white solid (383 mg, 85 %): mp 86–88 °C. A solution of this dibenzoate (240 mg, 0.37 mmol) in CH_3CN (4 mL) was treated at 22 °C with HF as described for **22** to yield the alcohol **23** (167 mg, 84 %): mp 102–105°C. $[\alpha]_D^{20}$ = 18.7 (*c* 0.38 in CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3456 cm^{-1}, 2951, 2934, 2855, 1734, 1725, 1603. ^1H NMR (200 MHz, $CDCl_3$) (mixture of rotamers): δ = 1.23–1.44 (m, 3 H, 6'-H), 1.78–2.06 (m, 1 H, 2'-H_{ax}), 2.22–2.37, 2.61–2.69, (2 x m, 1 H, 2'-H_{eq}), 3.51, 3.52, 3.99 (3 x s, 2 x 3 H, 2 x OCH_3), 3.60–4.18 (m, 2 x 1 H, 3'-H, 5'-H), 4.80–5.11 (m, 2 H, 1'-H, 4'-H), 6.74 (br s, 2 H, 6-H, 7-H), 7.38–8.35 (m, 12 H, 3-H, 4-H,10 benzoyl-H). ^{13}C NMR (50 MHz, $CDCl_3$) (mixture of rotamers): δ = 18.64 (q, C-6'), 41.21, 41.58 (2 x t, C-2'), 56.31 (q, 2 x OMe), 72.05, 72.23, 72.90, 74.54, 74.77, 79.87, 80.14 (7 x d, C-1', C-3', C-4', C-5'), 104.45, 104.73, 106.45, 106.71 (4 x d, C-6, C-7), 121.04, 121.31, 123.67, 124.33, 128.90, 129.02, 129.32, 130.24, 130.78, 133.74, 135.00 (8 x d, C-3, C-4, 10 C benzoyl), 119.85, 128.30, 129.92, 131.45, 131.76, 131.99, 132.27, (7 x s, C-2, C-4a, C-8a, 2 x C benzoyl), 143.05, 143.23, 149.56, 149.90, (4 x s, C-1, C-5, C-8), 167.86, (s, 2 x C=O benzoyl). MS (70 eV): *m/z* (%) = 542 (70) [M^+], 480 (5), 241 (29), 189 (6), 105 (100), 43 (7).

Anal. Calcd for $C_{32}H_{30}O_8$ (542.58): C, 70.84; H, 5.57. Found: C, 70.97; H, 5.82.

1-Benzoyloxy-2-[4-*O*-benzoyl-3-*O*-(4-*O*-acetyl-2,3,6-trideoxy-α-L-*threo*-hex-2-enopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-5,8-dimethoxynaphthalene (24). A solution of **23** (62 mg, 0.11 mmol) and 3,4-di-*O*-acetyl-L-fucal (**5**) (28 mg, 0.13 mmol) in dry CH_2Cl_2 (0.7 mL) was treated under argon at 0 °C with montmorillonite K-10 (9 mg) and the mixture was stirred for 3 h at 22 °C. Additional fucal **5** (15 mg, 0.07 mmol) and montmorillonite K-10 (5 mg) was added and stirring was

continued for 3 h at 22 °C. The suspension was filtered, the solvent removed at reduced pressure, and the residue separated by column chromatography on silica (3 % $MeOH/CH_2Cl_2$) to yield oily **24** (14 mg, 18%) and starting material **23** (40 mg). ^1H NMR (200 MHz, $CDCl_3$) (mixture of rotamers): δ = 0.73–0.80 (m, 3 H, 6"-H), 1.23–1.33 (m, 3 H, 6'H), 1.62–2.20 (m, 1 H, 2'-H_{ax}), 2.06, 2.07 (2 x s, 3 H, CH_3, OAc), 2.35–2.41, 2.61–2.67 (2 x m, 1 H, 2'-H_{eq}), 3.49, 3.51, 3.99 (3 x s, 2 x 3 H, 2 x OMe), 3.63–3.91 (m, 2 H, 5'-H, 5"-H), 4.09–4.28 (m, 1 H, 3'-H), 4.65–4.71 (m, 1 H, 4"-H), 4.82–5.18 (m, 3 H, 1'-H, 4'-H, 1"-H), 5.85–6.03 (m, 2 H, 2"-H, 3"-H), 6.74 (br s, 2 H, 6-H, 7-H), 7.43–8.36 (m, 12 H, 3-H, 4-H, 10 H, benzoyl). ^{13}C NMR (50 MHz, $CDCl_3$) (mixture of rotamers): δ = 16.00 (q, C-6"), 18.57 (q, C-6'), 21.22 (q, CH_3, OAc), 37.99, 38.49 (2 x t, C-2'), 56.32 (q, 2 x OMe), 65.12, 65.23, 72.46, 74.97, 75.17, 76.08 (6 x d, C-1', C-3', C-4', C-5', C-4", C-5"), 91.06 (d, C-1"), 104.50, 104.78, 106.32, 106.70 (4 x d, C-6, C-7), 121.15, 121.38, 123.79, 124.38, 126.24, 128.84, 129.03, 129.14, 130.07, 130.60, 130.86, 133.64 (12 x d, C-3, C-4, C-2", C-3", 10 C, benzoyl), 119.79, 128.45, 130.28, 130.59, 131.49, 131.81, 133.76 (7 x s, C-2, C-4a, C-8a, 2 C, benzoyl), 149.54, 149.77, 149.90 (3 x s, C-1, C-5, C-8), 166.14, 166.21 (2 x s, C=O, benzoyl), 170.93 (s, C=O, OAc).

2-[3-*O*-(2,3,6-Trideoxy-α-L-*threo*-hex-2-enopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (25). A solution of **24** (20 mg, 0.029 mmol) in dry THF (1.5 mL) at 0 °C was treated with LAH (10 mg, 0.26 mmol) and stirred for 30 min. The mixture was then diluted by addition of Et_2O (10 mL) and then filtered through a batch of celite. The filtrate was concentrated at reduced pressure and the residue purified by column chromatography on silica gel (3 % $MeOH/CH_2Cl_2$) to afford the oily deprotected disaccharide **25** (9 mg, 77 %). The product was identical with the saponification (K_2CO_3 /MeOH) product from **20**. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.37 (d, $J_{5",6"}$ = 6.5 Hz, 3 H, 6"-H), 1.45 (d, $J_{5',6'}$ = 6.0 Hz, 3 H, 6'-H), 1.58–1.77 (m, 1 H, 2'-H_{ax}), 2.43 (dd, $J_{2'ax,2'eq}$ = 13.2 Hz, $J_{2'eq,3'}$ = 5.2 Hz, 1 H, 2'-H_{eq}), 3.24 (dd, J = 8.6 Hz, J = 8.7 Hz, 1 H, 4'-H), 3.48–3.86 (m, 3 H, 3'-H, 5'-H, 4"-H), 3.93, 4.01 (2 x s, 2 x 3 H, 2 x OCH_3), 4.27 (q, $J_{5",6"}$ = 6.5 Hz, 1 H, 5"-H), 5.02 (d, $J_{1',2'ax}$ = 11.3 Hz, 1 H, 1'-H), 5.15 (br s, 1 H, 1"-H), 5.84 (dd, $J_{2",3"}$ = 10.0 Hz, J = 2.8 Hz, 1 H, 2"-H or 3"-H), 6.20 (dd, $J_{2",3"}$ = 10.0 Hz, J = 5.7 Hz, 1 H, 2"-H or 3"-H), 6.61, 6.68 (2 x d, $J_{6,7}$ = 8.5 Hz, 2 H, 6-H, 7-H), 7.58, 7.72 (2 x d, $J_{3,4}$ = 8.8 Hz, 2 H, 2-H, 3-H), 9.77 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.47 (q, C-6"), 18.96 (q, C-6'), 38.27 (t, C-2'), 56.18, 56.82 (2 x q, 2 x OCH_3), 64.15, 67.89, 71.85, 76.60 (4 x d, C-1', C-4', C-4", C-5"),

83.77 (d, C-3'), 95.16 (d, C-1"), 103.17, 104.04 (2 x d, C-6, C-7), 113.58, 125.13, 128.37, 130.57 (4 x d, C-3, C-4, C-2", C-3"), 115.36, 123.87, 127.95 (3 x s, C-2, C-4a, C-8a), 150.25, 150.51, 150.69 (3 x s, C-1, C-5, C-8).

1-Acetoxy-2-[4-*O*-acetyl-3-*O*-(4-*O*-benzoyl-2,3,6-trideoxy-α-L-*threo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-5,8-dimethoxynaphthalene (26). A solution of **22** (50 mg, 0.12 mmol) and 4-*O*-benzoyl-L-rhodinal (**7**) (50 mg, 0.23 mmol) in dry CH_2Cl_2 (1 mL) was treated under argon at 0 °C with TPHB (2 mg, 0.006 mmol). After stirring for 15 min at 22 °C CH_2Cl_2 (10 mL) and aqueous $NaHCO_3$ (10 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL), the combined organic phases were dried (Na_2SO_4), and the solvent was removed at reduced pressure. The residue was separated by column chromatography on silica gel (3 % MeOH/CH_2Cl_2) to yield **26** (40 mg, 52 %) mp 179 °C and starting material **22** (23 mg, 46 %). Alternatively, the glycosylation was catalyzed with $Sc(OTf)_3$ (3.5 mg, 0.007 mmol) as described for **20**. [**22**: (40 mg, 0.10 mmol) and 4-*O*-benzoyl-L-rhodinal (**7**) (31 mg, 0.14 mmol): **26** (38 mg, 63 %) and starting material **22** (15 mg, 37 %)]. $[\alpha]_D^{20}$ = –26.5 (*c* 4.00 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3005 cm^{-1}, 2934, 1770, 1743, 1705, 1607. ^1H NMR (200 MHz, $CDCl_3$) (mixture of rotamers): δ = 1.22 (d, $J_{5",6"}$ = 6.5 Hz, 3 H, 6"-H), 1.29 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.38–2.60 (m, 6 H, 2'-H, 2"-H, 3"-H), 2.14, 2.40 (2 x s, 2 x 3 H, 2 x CH_3, OAc), 3.57–3.74 (m, 1 H, 3'-H), 3.87, 3.94 (2 x s, 2 x 3 H, 2 x OCH_3), 3.84–4.15 (m, 2 H, 3'-H, 5"-H), 4.51–4.79 (m, 1 H, 4"-H), 4.89 (dd, *J* = 9.4 Hz, 1 H, 4'-H), 5.06–5.11 (m, 2 H, 1'-H, 1"-H), 6.70, 6.76 (2 x d, $J_{6',7'}$ = 8.6 Hz, 2 x 1 H, 6-H, 7-H), 7.36–7.72 (m, 4 H, 3-H or 4-H, 3 H, benzoyl), 8.11 (m, 3 H, 3-H or 4-H, 2 H, benzoyl). ^{13}C NMR (50 MHz, $CDCl_3$) (mixture of rotamers): δ = 17.73 (q, C-6"), 18.54 (q, C-6'), 21.37, 21.52 (2 x q, 2 x CH_3, OAc), 23.36, 24.74 (2 x t, C-2", C-3"), 37.58 (t, C-2'), 56.29, 56.89 (2 x q, 2 x OCH_3), 65.81 (d, C-5"), 70.33 (d, C-1'), 72.79 (d, C-4"), 73.52 (d, C-5'), 75.02 (d, C-3'), 75.99 (d, C-4'), 93.24 (d, C-1"), 104.12, 106.71, 107.09 (3 x d, C-6, C-7), 121.23, 123.76, 124.46, 128.97, 130.11, 133.50 (6 x d, C-3, C-4, 5 C, benzoyl), 119.82, 128.28, 130.70, 130.71 (4 x s, C-2, C-4a, C-8a, C, benzoyl), 149.47, 150.01, (2 x s, C-1, C-5, C-8), 166.56 (s, C=O, benzoyl), 169.75, 170.49 (2 x s, 2 x OAc). MS (70 eV): *m/z* (%) = 636 (95) [M^+], 592 (8), 444 (14), 376 (100), 219 (24), 105 (52), 43 (27).

HRMS Calcd for $C_{31}H_{36}O_9$ (636.2571). Found: 636.2570.

1-Benzoyloxy-2-[4-*O*-benzoyl-3-*O*-(4-*O*-benzoyl-2,3,6-trideoxy-α-L-*threo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-5,8-dimethoxynaphthalene (27). A solution of **23** (100 mg, 0.18 mmol) and 4-*O*-benzoyl-L-rhodinal (**7**) (44 mg, 0.20

mmol) in dry CH_2Cl_2 (1.5 mL) was treated with TPHB (4 mg, 0.012 mmol) as described for **26** to yield **26** (100 mg, 71 %): mp 103 °C and starting material **23** (18 mg, 18 %). $[\alpha]_D^{20}$ = –27.7 (*c* 0.30 in CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3066 cm^{-1}, 2935, 1740, 1734, 1719, 1603, 1450. ^1H NMR (200 MHz, $CDCl_3$) (mixture of rotamers): δ = 0.75, 0.81 (2 x d, $J_{5",6"}$ = 6.6 Hz, 3 H, 6"-H), 1.28 (d, $J_{5',6'}$ = 6.0 Hz, 3 H, 6'-H), 1.47–2.16 (m, 5 H, 2'-H_{ax}, 2"-H, 3"-H), 2.38, 2.64, (2 x d, $J_{2'\text{-ax},2'\text{eq}}$ = 13.1 Hz, 1 H, 2'-H_{eq}), 3.48, 3.50, 3.94 (3 x s, 2 x 3 H, 2 x OCH_3), 3.63–3.81 (m, 2 x 2 H, 5'-H, 5"-H), 3.99–4.16 (m, 1 H, 3'-H), 4.51 (br s, 1 H, 4"-H), 4.78–5.17 (m, 3 H, 1'-H, 4'-H, 1"-H), 6.69 (br s, 2 H, 6-H, 7-H), 7.41–8.34 (m, 17 H, 3-H, 4-H, 15 H, benzoyl). ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of rotamers): δ = 17.29, 17.77 (2 x q, C-6"), 18.48, 18.59 (2 x q, C-6'), 23.13, 23.35, 24.51, 24.70 (4 x t, C-2", C-3"), 37.49, 37.98 (2 x t, C-2'), 53.90, 56.30 (2 x q, 2 x OMe), 65.56 (d, C-5"), 70.23, 70.46 (2 x d, C-4"), 72.60, 72.59 (2 x d, C-1'), 73.45, 73.53 (2 x d, C-3'), 74.95, 75.06 (2 x d, C-5'), 76.26 (d, C-4'), 93.05, 93.18 (2 x d, C-1"), 104.49, 104.76, 106.38, 106.69 (4 x d, C-6, C-7), 121.16, 121.38, 123.84, 124.50, 128.80, 128.97, 129.02, 129.15, 129.98, 130.04, 130.15, 130.64, 130.90, 133.41, 133.75, 133.81 (16 x d, C-3, C-4, 15 C, benzoyl), 119.83, 128.32, 128.45, 130.22, 130.43, 131.46, 131.78 (7 x s, C-2, C-4a, C-8a, 3 C, benzoyl), 143.08, 143.27, 149.55, 149.77, 149.87 (5 x s, C-1, C-5, C-8), 165.51, 166.16, 166.24, 166.46 (3 x s, 3 x C=O, benzoyl). MS (DCI, NH_3): *m/z* (%) = 655 (100) [M^+ - benzoyl], 625, 579, 533, 437, 362, 315, 159 (all < 1), 121 (14).

DCI-HRMS Calcd for $C_{38}H_{39}O_{10}$ (M^+–benzoyl) 655.2549. Found: 655.2543.

2-[3-*O*-(2,3,6-Trideoxy-α-L-*threo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-1-hydroxy-5,8-dimethoxynaphthalene (28). Three methods gave identical samples of the deprotected oily disaccharide **28**: Saponification (K_2CO_3 /MeOH) of **20** (12 mg, 0.024 mmol) or LAH reduction of **26** (15 mg, 0.027 mmol) or **12 h** (20 mg, 0.031 mmol) as described for **25**. Yields 85, 72, and 77 %, respectively. $[\alpha]_D^{20}$ = 14.0 (*c* 1.60 in CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3385 cm^{-1}, 2976, 2924, 1616. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.26 (d, $J_{5",6"}$ = 6.5 Hz, 3 H, 6"-H), 1.45 (d, $J_{5',6'}$ = 6.1 Hz, 3 H, 6'-H), 1.50–2.05 (m, 5 H, 2'-H_{ax}, 2"-H, 3"-H), 2.38 (ddd, $J_{1',2'\text{eq}}$ = 1.7 Hz, $J_{2'\text{ax},2'\text{eq}}$ = 12.9 Hz, $J_{2'\text{eq},3'}$ = 4.9 Hz, 1 H, 2'-H_{eq}), 3.24 (dd, *J* = 8.7 Hz, 1 H, 4'-H), 3.49–3.88 (m, 3 H, 5'-H, 3'-H, 4"-H), 3.93, 4.01 (2 x s, 2 x 3 H, 2 x OCH_3), 4.16–4.24 (m, 1 H, 5"-H), 5.01–5.05 (m, 2 H, 1'-H, 1"-H), 6.62, 6.68 (2 x d, $J_{6,7}$ = 8.4 Hz, 2 H, 6-H, 7-H), 7.59, 7.72 (2 x d, $J_{3,4}$ = 8.7 Hz, 2 H, 2-H, 3-H), 9.76 (s, 1 H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.53 (q, C-6"), 18.95 (q, C-6'), 24.61, 25.98 (2 x t, C-2", C-3"), 38.10 (t, C-2'), 56.18, 56.81 (2 x q, 2

x OCH_3), 65.79, 67.68, 76.49, (3 x d, C-4', C-5', C-5"), 71.86 (d, C-1'), 82.81 (d, C-3'), 97.64 (d, C-1"), 103.16, 104.04 (2 x d, C-6, C-7), 113.52, 125.16 (2 x d, C-3, C-4), 115.60, 124.00, 127.94 (3 x s, C-2, C-4a, C-8a), 150.27, 150.53, 150.69 (3 x s, C-1, C-5, C-8). MS (70 eV): *m/z* (%) = 448 (17) [M^+], 360 (11), 334 (100), 259 (24), 241 (28), 230 (40), 215 (31), 115 (18), 69 (16), 57 (14).

HRMS Calcd for $C_{24}H_{32}O_8$ (448.2097). Found: 448.2097.

REFERENCES AND NOTES

1. J. Rohr and R. Thiericke, *Nat. Prod. Rep.*, **9**, 103 (1992).
2. K. Krohn and J. Rohr, *Top. Curr. Chem.*, 188, 127 (1997).
3. J. Rohr and A. Zeeck, *J. Antibiot.*, **40**, 459 (1987).
4. V. A. Boyd and G. A. Sulikowski, *J. Am. Chem. Soc.*, **117**, 8472 (1995).
5. M. Yamaguchi, T. Okuma, A. Horiguchi, C. Ikeura and T. Minami, *J. Org. Chem.*, **57**, 1647 (1992).
6. T. Matsumoto, T. Sohma, H. Yamaguchi, S. Kurata and K. Suzuki, *Synlett*, 263 (1995).
7. A. Sobti, K. Kim and G. A. Sulikowski, *J. Org. Chem.*, **61**, 6 (1996).
8. K. Toshima and K. Tatsuta, *Chem. Rev.*, **93**, 1503 (1993).
9. F. L. Andrews and D. S. Larsen, *Tetrahedron Lett.*, **35**, 8693 (1994).
10. G. Matsuo, Y. Miki, M. Nakata, S. Matsumura and K. Toshima, *J. Chem. Soc., Chem. Commun.*, 225 (1996).
11. G. Matsuo, S. Matsumura and K. Toshima, *J. Chem. Soc., Chem. Commun.*, 2173 (1996).
12. R. G. F. Giles, A. B. Hughes and M. V. Sargent, *J. Chem. Soc., Perkin Trans. I*, 1581 (1991).
13. G. M. L. Cragg, G. F. Giles and G. H. P. Roos, *J. Chem. Soc., Perkin Trans. I*, 1339 (1975).
14. V. A. Boyd, B. E. Drake and G. A. Sulikowski, *J. Org. Chem.*, **58**, 3191 (1993).
15. R. J. Ferrier and N. Prasad, *J. Chem. Soc. (C)*, 570 (1969).
16. V. Bolitt, C. Mioskowski, S.-G. Lee and J. R. Falck, *J. Org. Chem.*, **55**, 5812 (1990).
17. J. Thiem, H. Karl and J. Schwentner, *Synthesis*, 696 (1978).
18. J. Thiem and W. Klaffke, *Top. Curr. Chem.*, **154**, 285 (1990).
19. S. J. Danishefsky and M. T. Bilodeau, *Angew. Chem.*, **108**, 1482 (1996); *Angew. Chem. Int. Ed. Engl.*, **35**, 1380 (1996).
20. B. K. Shull, Z. Wu and M. Koreeda, *J. Carbohydr. Chem.*, **15**, 955 (1996).
21. K. Toshima. T. Ishizuka, G. Matsuto and M. Nakata, *Synlett*, 306 (1995).
22. P. Laszlo, *Science*, 1473 (1987).
23. N. Kawamura, R. Sawa, Y. Takahashi, T. Sawa, N. Kinoshita, H. Naganawa, M. Hamada and T. Takeuchi, *J. Antibiot.*, **48**, 1521 (1995).
24. B. Iselin and T. Reichstein, *Helv. Chim. Acta.*, **27**, 1200 (1944).
25. T. Uchida, M. Imoto, Y. Watanabe, K. Miura, T. Dobashi, N. Matsuda, T. Sawa, H. Naganawa, M. Hamada, T. Takeuchi and H. Umezawa, *J. Antibiot.*, **38**, 1171 (1985).

26. T. Henkel and J. Rohr, *J. Antibiot.*, **43**, 492 (1990).
27. G. Grynkiewicz, W. Priebe and A. Zamojski, *Carbohydr. Res.*, **68**, 33 (1979).
28. S. Kobayashi and S. Nagayama, *J. Org. Chem.*, **61**, 2256 (1996).
29. S. Kobayashi, M. Araki, H. Ishitani, S. Nagayama and I. Hachiya, *Synlett*, 233 (1995).
30. A. Kawada, S. Mitamura and S. Kobayashi, *Synlett*, 545 (1994).
31. S. Kobayashi, *Synlett*, 689 (1994).
32. A. Martin, M. Païs and C. Monneret, *Carbohydr. Res.*, **113**, 21 (1983).
33. A. Kirschning, S. Domann, G. Dräger and L. Rose, *Synlett*, 767 (1995).
34. K. Krohn, A. Michel, U. Flörke, H.-J. Aust, S. Draeger and B. Schulz, *Liebigs Ann. Chem.*, 1093 (1994).