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Synthesis of a set of sulfated and/or phosphorylated oligosaccharide derivatives from the carbohydrate–protein linkage region of proteoglycans

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Abstract—The synthesis of a set of various sulfoforms and/or phosphoforms as 7-methoxy-2-naphthyl glycosides of β-D-Xyl*p*, β-D-Gal*p*-(1→4)-β-D-Xyl*p*, and β-D-Gal*p*-(1→3)-β-D-Gal*p*-(1→4)-β-D-Xyl*p*, structures encountered in the common carbohydrate–protein linkage region of proteoglycans, is reported for the first time. These molecules will serve as probes for systematic studies of the substrate specificity of the glycosyltransferases involved in the early steps of the biosynthesis of proteoglycans. A straightforward divergent preparation was achieved using key intermediates, which were designed as common precursors.

Keywords: Proteoglycans; Linkage region; Sulfoforms; Phosphoforms

1. Introduction

Proteoglycans (PGs) are complex macromolecules composed of glycosaminoglycan (GAG) chains covalently linked to a core protein. They are ubiquitously distributed on the cell surface and in the extracellular matrix. They are important regulators of many fundamental biological processes,[1] and the elucidation of their biosynthesis pathways becomes an attractive challenge because of their implication in many pathologies and their potential as pharmaceutical targets. The construction of GAG chains is initiated by the synthesis of a common GAG–protein linkage structure, namely β-D-Glc*p*A-(1→3)-β-D-Gal*p*-(1→3)-β-D-Gal*p*-(1→4)-β-D-Xyl*p*-(1→O) which is linked to L-serine residues of the core protein.[2] This region is formed by a sequential stepwise addition of each sugar unit by respective *O*-glycosyltransferases (Fig. 1), and is a key step in the assembly of PGs. Occasionally, this linkage region may be modified by sulfation at C-4 and/or C-6 of the D-Gal*p* units, as well as by phosphorylation at C–2 of the D-Xyl*p* residue.[3]

The biological significance of these modifications is still not yet fully deciphered, although it has been suggested[4] that they could act as biosynthetic signals. To shed light on the role of these unique substituents, the substrate specificity of the human galactose β-(1→3)-glucuronyltransferase (GlcAT-1) was recently analyzed[5] with various synthetic[6] sulfoforms of the disaccharide β-D-Gal*p*-(1→3)-β-D-Gal*p*-(1→OMP), underlining the critical influence of the sulfate group located at C-6 of the reducing D-Gal*p* unit. This result suggests that sulfation on this position is a critical feature that determines the ability of a molecule to serve (or not) as a substrate for GlcAT-1. The synthetic corresponding glucuronylated trisaccharide derivatives were also prepared[7] to identify unambiguously the transfer products. In addition, it has been demonstrated[5] that the xylose β-(1→4)-galactosyltransferase (GalT-1) does not exhibit

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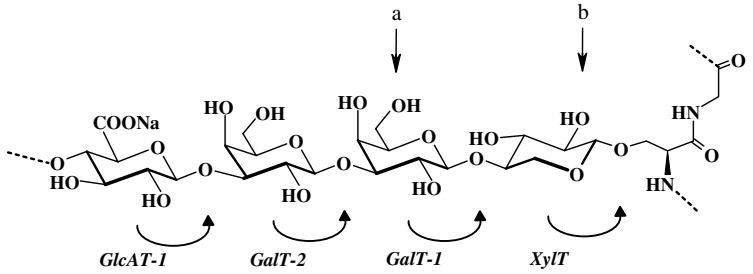
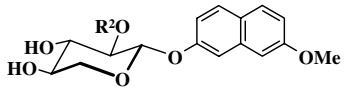


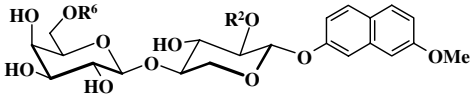
Figure 1. The carbohydrate–protein linkage region of proteoglycans and the glycosyltransferases involved in its biosynthesis. The arrows indicate relevant substitutions with a sulfate (a) or a phosphate (b) group.

in vitro activity toward a C-2 phosphorylated xyloside, suggesting that the presence of this modification prevents recognition and/or transfer of the first D-Gal*p* unit onto the xyloside derivative. However, this does not mean that this phosphate group is introduced before the transfer of the first D-Gal*p* unit by GalT-1. In fact, it has been reported[8] that this phosphorylation should be a transient phenomenon involved only in the very early steps of the biosynthesis.

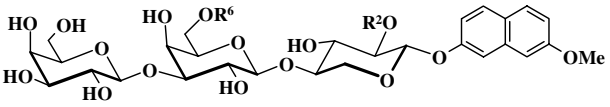
Thus, it is now relevant to study the substrate specificity of the galactose β-(1→3)-galactosyltransferase 6 (GalT-2) and the GlcAT-1 toward a as diverse as possible set of sulfated and phosphorylated structures. A chemical synthesis of several sulfated and/or phosphorylated glycosyl serine derivatives has been described,[9] but no biological assays were reported for these molecules. We now report for the first time the systematic preparation of a set of sulfoforms and/or phosphoforms of various oligosaccharide derivatives from the linkage region (Fig. 2) which should be useful to gain further insight into the substrate specificity of the glycosyltransferase involved. All target compounds were prepared as their 7-methoxy-2-naphthyl glycosides in which the naphthyl group will be useful for the detection of the products in transfer assays, and the methoxy group will serve as a marker to check the purity of the synthetic products by NMR spectroscopy.



1 R = H
2 R = PO_3Na_2



3 $R^2 = R^6 = H$
4 $R^2 = PO_3Na_2$, $R^6 = H$
5 $R^2 = H$, $R^6 = SO_3Na$
6 $R^2 = PO_3Na_2$, $R^6 = SO_3Na$



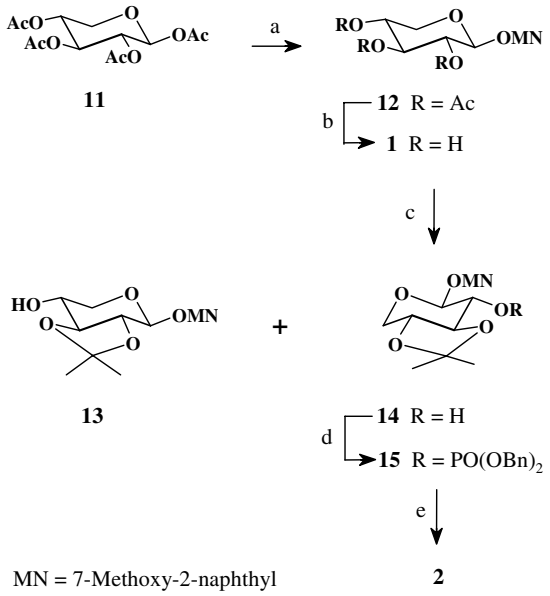
7 $R^2 = R^6 = H$
8 $R^2 = PO_3Na_2$, $R^6 = H$
9 $R^2 = H$, $R^6 = SO_3Na$
10 $R^2 = PO_3Na_2$, $R^6 = SO_3Na$

Figure 2. Target molecules.

2. Results and discussion

For the synthesis of the target molecules **1**–**10** (Fig. 2), all derivatives were planned to be obtained from common precursors to reduce the number of transformations. Advantage was taken of the rather low regioselectivity observed[10] in the acetalation reaction of xylosides. The 3,4-substituted regioisomer **14** (Scheme 1) would allow short access to phosphoform **2**, whereas its 2,3-substituted analog **13** could be used as an acceptor for elongation of the chain. The D-Gal*p* moiety, containing 1,2-*trans* linkages, was constructed by means of 2-O-benzoylated glycosyl units activated as their trichloroacetimidates.[11] In the di- and trisaccharide structures, the phosphate group could be introduced or not after construction of a suitably protected oligomer derivative.

Condensation of 1,2,3,4-tetra-*O*-acetyl-β-D-xylopyranose **11**[12] with 7-methoxy-2-naphtol in dichloromethane, in the presence of trimethylsilyl triflate (TMS-OTf), gave crystalline **12** in 77% yield (Scheme 1), which was transesterified with methanolic sodium methoxide to afford the crystalline target molecule **1** in 94% yield. Treatment of **1** with 2-methoxypropene and 10-camphorsulfonic acid in *N*,*N*-dimethylformamide gave the crystalline minor 3,4-*O*-isopropylidene derivative **14** (23%) along with the 2,3-*O*-isopropylidene isomer **13** (69%). Phosphorylation at O-2 was then achieved by



Scheme 1. Reagents and conditions: (a) 7-methoxy-2-naphtol, TMSOTf, 4 Å mol. sieves, CH_2Cl_2, 0 °C, 2 h; (b) MeONa, MeOH, rt, 1 h; (c) 2-methoxypropene, CSA, DMF, rt, 90 min; (d) Ipr_2N-$P(OBn)_2$, 1-*H*-tetrazole, CH_2Cl_2, rt, 1 h; then *m*-CPBA, −10 °C, 30 min; (e) H_2, 10% Pd/C, AcOH, EtOAc/MeOH/H_2O, rt, 24 h.

treatment of **14** with dibenzyl *N*,*N*-diisopropylphosphoramidite and 1-*H*-tetrazole in dichloromethane, followed by in situ oxidation[13] of the intermediary phosphite derivative with *m*-chloroperbenzoic acid to give the crystalline 2-phosphate **15** in 87% overall yield. The ^{1}H NMR spectra of **15** (Table 1) showed, in the signal for Xyl*p* H-2, the expected additional coupling $^3J_{H,P} = 9.0$ Hz. Full deprotection of **15** was achieved through catalytic hydrogenation (Pd/C) in an aqueous mixture of solvents, in the presence of acetic acid, to give directly the target molecule **2** in 80% overall yield. The ^{1}H (Table 4) and ^{13}C NMR data (Table 5) of **2** are in full agreement with the expected structure, and showed the $^3J_{H,P} = 9.0$ and $^2J_{C,P} = 5.0$ Hz coupling, respectively, in the signals for Xyl*p* H-2 and Xyl*p* C-2, respectively.

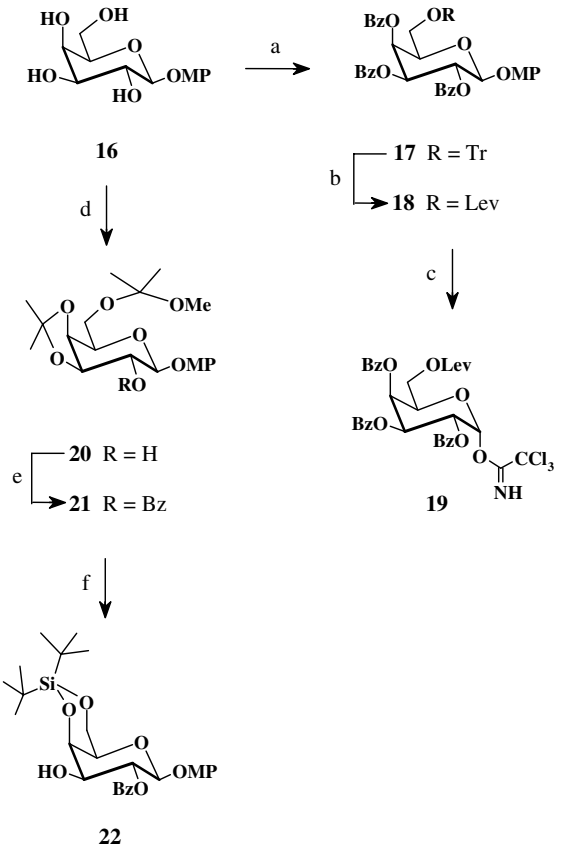
For the preparation of the target disaccharide derivatives **3**–**6** according to our proposed strategy, an activated derivative of D-galactose equipped with a robust temporary protection at O-6 was needed. To this end, easily available 4-methoxyphenyl β-D-galactopyranoside **16**[14] was submitted to conventional tritylation–benzoylation process to give crystalline **17** in 90% yield (Scheme 2). Exchange of the protection at O-6 was then achieved through treatment of **17** with boron trifluoride diethyletherate and methanol[15] in dichloromethane, a cleaner reaction than those by classical acid hydrolysis, followed by levulinoylation with 4-oxopentanoic acid (levulinic acid), 1,3-dicyclohexylcarbodiimide and 4-dimethylaminopyridine in dichloromethane to give **18** in 93% overall yield. Oxidative removal of the 4-methoxyphenyl group in **18** with ceric ammonium nitrate (CAN) followed by imidoylation with trichloroacetonitrile and 1,8-diazabicyclo[5,4,0]-undec-7-ene (DBU) afforded the α-imidate **19** in 78% overall yield. The ^{1}H NMR data of **19** (Table 1) were in agreement with the expected structure.

For the preparation of the target trisaccharide derivatives **7**–**10**, a suitably protected and activated digalactosyl block should be constructed for further coupling with acceptor **13**. Preparation of the central D-Gal*p* unit was achieved from the common precursor **16** as follows (Scheme 2). Treatment of **16** with 2,2-dimethoxypropane (neat) and 10-camphorsulfonic acid under thermodynamic control[16] gave directly the crystalline bis-acetal **20** in 75% yield along with the expected 2,6-diol (20%), which was retreated under the same conditions to afford an additional crop of **20**, raising the total yield to 90%. This procedure allowed direct access to a 3,4,6-trisubstitued derivative having its 2-hydroxy group free. Conventional benzoylation of **20** gave crystalline **21** in 94% yield. In the ^{1}H NMR spectra of **20** and **21** (Table 1), the *J* values observed strongly suggested a significant departure from the $^4C_1$ conformation in solution, probably due to the torsional effect of the 3,4-acetal group. Acid hydrolysis of **21** gave the corresponding crystalline triol derivative, which was treated with di-*tert*-butylsilyl

Table 1. ^{1}H NMR data: carbohydrate ring protons for monosaccharide derivatives **12**–**15** and **17**–**22**[a]

	12	13	14	15	17	18	19	20	21	22
H-1	5.27	5.45	5.05	5.28	5.16	5.24	6.88	4.66	4.95	4.97
$J_{1,2}$	6.5	7.5	6.5	5.5	8.0	8.0	3.5	8.2	7.5	8.0
H-2	5.29	3.70	3.75	4.79	5.91	6.01	6.03	3.82	5.48	5.59
$J_{2,3}$	8.0	ND	8.0	9.0	10.5	10.5	10.5	7.0	8.0	10.5
$J_{2,P}$	—	—	—	9.0	—	—	—	—	—	—
H-3	5.24	3.70	3.68	3.84	5.59	5.61	5.92	3.73	4.30	3.78
$J_{3,4}$	8.0	8.0	8.0	9.0	3.6	3.6	3.5	6.0	6.0	3.5
H-4	5.05	4.08	4.06	3.81	5.96	5.93	6.05	4.22	4.05	4.50
$J_{4,5}$					1.0	0.8	0.8	2.0	1.5	1.0
H-5	4.28	4.21	4.29	4.26	4.06	4.29	4.72	3.95	4.05	3.58
	3.59	3.51	3.65	3.74						
H-6					3.57	4.41	4.31	4.15	4.42	4.30
					3.33	4.29	4.25	3.72	3.76	4.27

[a] Chemical shifts (δ, in ppm) and coupling constants (*J*, in Hz) for solns in $CDCl_3$.

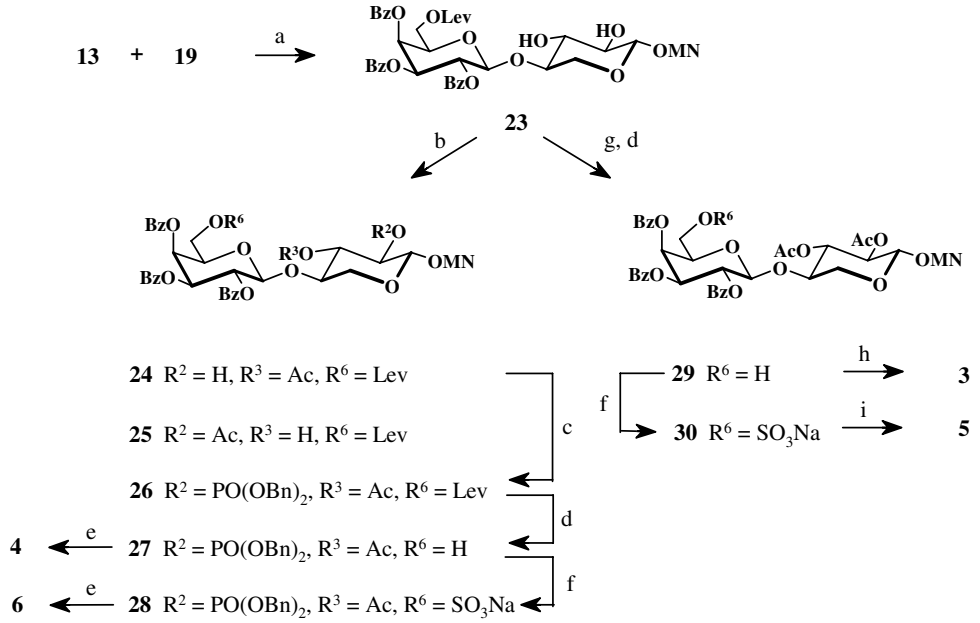


Scheme 2. Reagents and conditions: (a) TrCl, pyridine, 60 °C, 6 h; then PhCOCl, rt, 15 h; (b) $BF_3{\cdot}Et_2O$, MeOH, CH_2Cl_2, rt, 30 min; then LevOH, DCC, DMAP, CH_2Cl_2, rt, 1 h; (c) CAN, toluene/MeCN/H_2O, rt, 20 min; then CCl_3CN, DBU, CH_2Cl_2, rt, 30 min; (d) 2,2-dimethoxypropane (neat), CSA, rt, 48 h; (e) PhCOCl, pyridine, 0 °C, 1 h; (f) 90% TFA, rt, 10 min; then DTBS ditriflate, *sym*-collidine, CH_2Cl_2, 0 °C, 90 min.

ditriflate[17] and *sym*-collidine in dichloromethane to afford the acceptor **22** in 80% overall yield. The convenience of the 4,6-di-*tert*-butylsilylene acetal in oligosaccharide synthesis, compared to its 4,6-benzylidene congener, was recently highlighted.[7]

Preparation of the target disaccharide derivatives **3**–**6** was then achieved as follows (Scheme 3). Condensation of imidate **19** (1 equiv) with alcohol **13** (1 equiv) in dichloromethane, in the presence of trimethylsilyl triflate, followed by mild acid hydrolysis of the 2,3-isopropylidene acetal afforded the common intermediate **23** in 71% overall yield. Previous studies of our group on the regioselective acylation of 2,3-unsubstituted xylopeptide derivatives[18] showed that major substitution could be achieved at O-3 through the tin procedure.[19] Thus, treatment of the 2,3-dibutylstannylene acetal derived from **23** with acetic anhydride (1.05 equiv) gave the 3-acetate **24** in 71% overall yield, along with its regioisomer **25** (18%), the structures of which were easily deduced from their ^{1}H NMR spectra (Table 2). Phosphorylation of **24**, as described for the preparation of **15**, gave **26** in 91% yield, whose ^{1}H NMR data (Table 2) were in full agreement with the expected structure. This intermediate was later treated with hydrazine acetate in pyridine to give **27** (93% yield), a common intermediate that could be either directly deprotected or sulfonated at C-6 prior deprotection. Treatment of **27** with sulfur trioxide–trimethylamine complex in *N*,*N*-dimethylformamide followed by ion-exchange chromatography (Na^+ resin) afforded the sodium salt **28** in 89% yield. Comparison of the ^{1}H NMR spectra of **27** and **28** (Table 2), recorded strictly under the same conditions, showed the expected[20] downfield shift ($\Delta\delta \sim 0.4$–0.5 ppm) of the signals for Gal*p* H-6a and H-6b in the 6-O-sulfonated species. Final deprotection of **27** and **28** was achieved through catalytic hydrogenation (Pd/C) followed by hydrazinolysis[21] of the ester groups in methanol to give the target molecules **4** and **6** in 80% and 85% yields, respectively. The ^{1}H (Table 4) and ^{13}C NMR data (Table 5) of **4** and **6** confirmed the expected structures, and showed the additional couplings $^3J_{H,P} = 9.0$ Hz and $^2J_{C,P} = 5.0$ Hz in the signals for Xyl*p* H-2 and Xyl*p* C-2, respectively. For the sulfoform **6**, the expected downfield shifts $\Delta\delta \sim 0.4$–0.5 ppm in ^{1}H and $\Delta\delta \sim 6$ ppm in ^{13}C NMR data (Tables 4 and 5, respectively) were also observed. Conventional acetylation of **23** (or of minor isomer **25**) followed by delevulinoylation with hydrazine acetate gave crystalline **29** in 90% overall yield. This later was either transesterified with methanolic sodium methoxide to give the crystalline target molecule **3** in 92% yield, or sulfated at C-6 as described for the preparation of **28** to give **30** (90% yield), which was, in turn, saponified with aqueous sodium hydroxide in methanol to give the crystalline sulfoform **5** in 90% yield. The ^{1}H (Table 4) and ^{13}C NMR data (Table 5) of **3** and **5** were also in accord with the expected structure and showed the same features as those reported above for **4** and **6**.

Preparation of the target molecules **7**–**10** was then achieved as follows (Scheme 4). Condensation of 2,3,4,6-tetra-*O*-benzoyl-1-*O*-trichloroacetimidoyl-α-D-galactopyranose **31**[9] (1.25 equiv) with acceptor **22** (1 equiv) in dichloromethane, in the presence of trimethylsilyl triflate, gave **32** in 86% yield. Treatment of **32** with triethylamine–trihydrofluoride complex in tetrahydrofuran[22] gave smoothly the crystalline diol **33** in 90% yield. Selective levulinoylation of **33** at O-6 with levulinic acid, 1,3-dicyclohexylcarbodiimide and 4-dimethylaminopyridine in dichloromethane followed by subsequent benzoylation at O-4 gave **34** in 85% overall yield. A small amount (~5%) of the 4,6-dilevulinoylated derivative was easily removed by chromatography and recycled. Introduction of the trichloroacetimidoyl group at C-1 was then achieved as reported for the preparation of **19** to give **35** in 75% yield, the structure of which was deduced from its ^{1}H NMR spectrum (Table 2). Condensation of imidate **35** (1 equiv) with acceptor **13** (1.3 equiv),

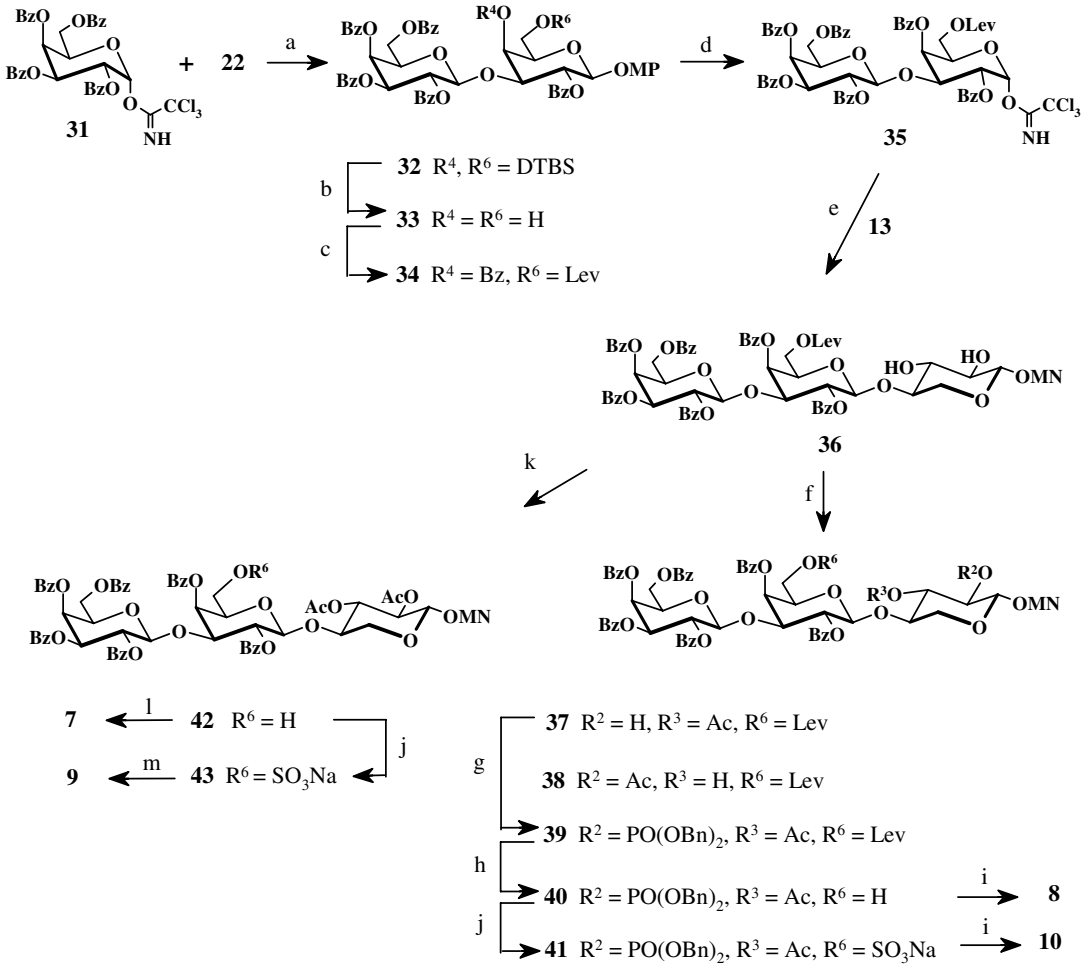


Scheme 3. Reagents and conditions: (a) donor (1 equiv), TMSOTf, 4 Å mol. sieves, CH_2Cl_2, 0 °C, 30 min; then 60% AcOH, 100 °C, 15 min; (b) Bu_2SnO, dioxane/benzene, reflux, 6 h; then Ac_2O, rt, 2 h; (c) $Ipr_2NP(OBn)_2$, 1-*H*-tetrazole, CH_2Cl_2, rt, 30 min; then *m*-CPBA, −10 °C, 30 min; (d) hydrazine acetate, pyridine, rt, 8 min; (e) H_2, Pd–C, 24 h; then hydrazine hydrate, MeOH, rt, 5 h; (f) $Me_3N{\cdot}SO_3$, DMF, 60 °C, 1 h; (g) Ac_2O, pyridine, rt, 4 h; (h) MeONa, MeOH/CH_2Cl_2, rt, 2 h; (i) 4 M NaOH, MeOH, rt, 4 h.

Table 2. ^{1}H NMR data: carbohydrate ring protons for disaccharide derivatives **23**–**30** and **32**–**35**[a]

	H-1^{I} $J_{1,2}$	H-2^{I} $J_{2,3}$ $J_{2,P}$	H-3^{I} $J_{3,4}$	H-4^{I} $J_{4,5}$	H-5^{I}	H-6^{I}	H-1^{II} $J_{1,2}$	H-2^{II} $J_{2,3}$	H-3^{II} $J_{3,4}$	H-4^{II} $J_{4,5}$	H-5^{II}	H-6^{II}
23	5.09 6.5	3.78 8.5	3.84 8.5	3.88	3.88, 3.45		4.92 8.0	5.79 10.5	5.59 3.5	5.89 1.0	4.35	4.34, 4.30
24	5.24 6.0	3.85 7.0	5.25 7.0	4.05	4.05, 3.55		4.92 8.0	5.76 10.5	5.63 3.5	5.88 0.8	4.20	4.37, 4.25
25	5.07 7.5	5.16 9.0	3.90	3.90	3.90, 3.45		4.94 8.0	5.79 10.5	5.58 3.5	5.88 0.8	4.34	4.38, 4.25
26	5.14 7.5	4.68 9.0 9.0	5.40 9.0	4.11	4.08, 3.45		4.91 8.0	5.70 10.5	5.53 3.5	5.86 0.8	4.25	4.28, 4.22
27[b]	5.17 7.0	4.64 8.5 9.0	5.43 8.5	4.08	4.04, 3.45		4.93 8.0	5.77 10.5	5.56 3.5	5.84 0.8	4.05	3.85, 3.65
28[b]	5.23 7.0	4.58 8.5 9.0	5.38 9.0	4.11	4.08, 3.51		5.05 8.0	5.64 10.5	5.58 3.5	5.92 0.8	4.43	4.27, 4.17
29[b]	5.31 5.5	5.09 7.0	5.43 7.0	3.96	4.07, 3.53		4.95 8.0	5.82 10.5	5.56 3.5	5.83 0.8	4.08	3.83, 3.67
30[b]	5.21 7.0	5.11 8.5	5.29 8.5	4.10	4.08, 3.51		5.05 8.0	5.67 10.5	5.58 3.5	5.92 1.0	4.43	4.21, 4.18
32	5.13 8.0	5.76 10.5	3.94 3.5	4.85 0.8	3.38	4.20, 4.08	4.87 8.0	5.83 10.5	5.48 3.5	5.94 0.8	4.31	4.66, 4.36
33	4.89 8.0	5.80 10.5	4.01 3.5	4.24 1.0	3.66	3.98, 3.88	5.03 8.0	5.72 10.5	5.54 3.5	5.95 0.8	4.39	4.64, 4.53
34	5.0 8.0	5.81 10.5	4.28 3.5	5.87 0.8	4.08	4.34, 4.22	5.02 8.0	5.58 10.0	5.40 3.5	5.95 1.0	4.30	4.76, 4.72
35	6.70 3.5	5.71 10.5	4.60 3.5	5.92 0.8	4.38	4.31, 4.16	5.04 8.0	5.59 10.0	5.46 3.5	6.08 1.0	4.51	4.78, 4.71

[a] For solns in $CDCl_3$, unless otherwise stated.
[b] 3:1 CD_3OD–$CDCl_3$.



Scheme 4. Reagents and conditions: (a) **31** (1.25 equiv), TMSOTf, 4 Å mol. sieves, CH_2Cl_2, rt, 30 min; (b) $Et_3N{\cdot}3HF$, THF, 0 °C, 2 h; (c) LevOH, DCC, DMAP, CH_2Cl_2, rt, 2 h; then PhCOCl, pyridine, rt, 16 h; (d) CAN, toluene/MeCN/water, rt, 20 min; then CCl_3CN, DBU, CH_2Cl_2, rt, 30 min; (e) **13** (1.3 equiv), TMSOTf, 4 Å mol. sieves, 0 °C, 30 min; then 60% AcOH, 100 °C, 15 min; (f) Bu_2SnO, dioxane/benzene, reflux, 6 h; then Ac_2O, rt, 4 h; (g) $Ipr_2NP(OBn)_2$, 1-*H*-tetrazole, CH_2Cl_2, rt, 30 min; then *m*-CPBA, −10 °C, 20 min; (h) hydrazine acetate, pyridine, rt, 10 min; (i) H_2, Pd/C, 24 h; then hydrazine hydrate, MeOH, rt, 6 h; (j) $Me_3N{\cdot}SO_3$, DMF, 60 °C, 1 h; (k) Ac_2O, pyridine, rt, 15 h; then hydrazine acetate, pyridine, rt, 10 min; (l) MeONa, $MeOH/CH_2Cl_2$, rt, 2 h; (m) 4 M NaOH, MeOH, rt, 3 h.

followed by mild acid hydrolysis, as reported for the preparation of **23**, gave the common intermediate **36** in 74% overall yield. Access to target molecules was then achieved using a route similar to those reported above for the disaccharide derivatives **3**–**6**. Tin-mediated regioselective acetylation of **36**, as reported above, gave predominantly the 3-acetate **37** (69%) along with its 2-isomer **38** (16%). Phosphorylation of **37** gave **39** in 89% yield, which was delevulinoylated to afford **40** in 92% yield. The ^1H NMR data (Table 3) of **39** and **40** were in agreement with the expected structures and showed the additional $^2J_{H,P}$ couplings. Sulfation of **40** gave **41** in 90% yield, whose ^1H NMR spectrum (Table 3) showed the expected downfield shift ($\Delta\delta \sim 0.4$–0.5 ppm) for the signals of H-6a and H-6b in the sulfated species. Final deprotection of **40** and **41**, as reported for the preparation of **4** and **6**, gave the target molecules **8** and **10** in 88% and 78% yields, respectively. The ^1H (Table 4) and ^{13}C NMR data (Table 5) for **8** and **10** were in accord with the expected structures and showed the same relevant downfield shifts and additional couplings. Acetylation of **36** (or **38**) followed by delevulinoylation gave **42** in 90% overall yield. This later was either transesterified to give the crystalline target molecule **7** in 91% yield, or sulfated at C-6, as reported above, to give **43** in 91% yield, which was in turn saponified to afford the target molecule **9** in 84% yield. The ^1H (Table 4) and ^{13}C NMR data (Table 5) for **7** and **9** agreed with the expected structures, and also showed the relevant downfield shifts characteristic of sulfation at Gal*p* C-6 in the sulfated species. Target molecules **1**–**10** were submitted to tandem mass spectrometry in the negative-ion mode[23] (ESIMS), which confirmed the structures of these anionic molecules and allowed their structural verification.

In conclusion, we have reported a stereocontrolled and high-yielding divergent preparation of a set of sulfoforms

Table 3. ^{1}H NMR data: carbohydrate ring protons for trisaccharide derivatives **36**–**43**[a]

	36	**37**	**38**	**39**	**40**[b]	**41**[b]	**42**[b]	**43**[b]
H-1^{I}	4.99	5.06	4.98	5.06	5.08	5.15	5.17	5.05
$J_{1,2}$	6.5	7.0	6.5	7.0	7.0	7.0	6.5	6.5
H-2^{I}	3.66	3.90	5.08	4.61	4.56	4.52	5.02	5.03
$J_{2,3}$	8.0	8.5	9.0	9.0	8.5	8.5	8.0	8.0
$J_{2,P}$	—	—	—	9.0	9.0	9.0	—	—
H-3^{I}	3.71	5.05	3.75	5.29	5.29	5.28	5.26	5.19
$J_{3,4}$	8.0	8.0	8.0	9.0	8.5	8.5	8.0	8.0
H-4^{I}	4.12	4.18	4.10	4.17	4.18	4.04	4.21	4.22
H-5^{I}	4.01	3.96	3.90	4.02	3.92	3.88	3.86	3.90
	3.31	3.41	3.30	3.31	3.27	3.38	3.35	3.39
H-1^{II}	4.66	4.69	4.67	4.68	4.67	4.77	4.71	4.81
$J_{1,2}$	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
H-2^{II}	5.58	5.58	5.61	5.56	5.58	5.51	5.61	5.52
$J_{2,3}$	10.5	10.5	10.5	10.5	10.0	10.5	10.5	10.5
H-3^{II}	4.07	4.36	4.22	4.28	4.22	4.24	4.21	4.22
$J_{3,4}$	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
H-4^{II}	5.84	5.88	5.86	5.86	5.80	5.84	5.81	5.84
$J_{4,5}$	0.8	0.8	0.8	0.8	0.8	1.0	0.8	1.0
H-5^{II}	4.05	3.99	4.08	3.97	3.84	3.88	3.86	3.95
H-6^{II}	4.28	4.30	4.30	4.24	3.74	4.22	3.72	4.24
	4.15	4.22	4.21	4.16	3.57	3.96	3.59	3.92
H-1^{III}	4.84	5.02	4.96	4.95	4.96	5.08	4.98	5.10
$J_{1,2}$	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
H-2^{III}	5.54	5.56	5.56	5.51	5.56	5.50	5.58	5.54
$J_{2,3}$	10.5	10.5	10.5	10.5	10.5	10.0	10.0	10.0
H-3^{III}	5.38	5.40	5.41	5.38	5.40	5.43	5.41	5.47
$J_{3,4}$	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
H-4^{III}	5.86	5.91	5.88	5.90	5.84	5.91	5.84	5.92
$J_{4,5}$	0.8	0.8	0.8	1.0	1.0	0.8	0.8	0.8
H-5^{III}	4.20	4.22	4.27	4.25	4.25	4.31	4.26	4.31
H-6^{III}	4.68	4.76	4.71	4.74	4.64	4.68	4.64	4.66
	4.44	4.35	4.45	4.30	4.28	4.34	4.27	4.35

[a] For solns in $CDCl_3$, unless otherwise stated.
[b] 3:1 CD_3OD–$CDCl_3$.

and phosphoforms of oligosaccharide derivatives from the linkage region of proteoglycans. These molecules, each obtained in 100–200 mg amounts, will be useful in assessing the possible role of these unique substituents in the biosynthesis of PGs. Compounds **3**–**6** will be precious tools to study the substrate specificity of GalT-2, and **7**–**10** will serve not only to characterize unambiguously the transfer products, but also as potential substrates for GlcAT-1. All these molecules are currently being evaluated in biological assays, and the results of these studies will be reported elsewhere in due course.

3. Experimental

3.1. General methods

Melting points were determined in capillary tubes with a Büchi apparatus and are uncorrected. Optical rotations are measured at 20–25 °C with a Perkin–Elmer 341 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded at 25 °C with a Bruker DPX-250 spectrometer operating at 250 and 62.8 MHz, respectively, with Me_4Si as internal standard, unless otherwise stated. Assignments were based on homo- and heteronuclear correlations using the supplier's software. ^{31}P NMR spectra were recorded with a Bruker DPX 400 spectrometer operating at 162 MHz. Mass spectra were obtained on a Perkin–Elmer SCIEX API 300 spectrometer operating in the ion-spray (IS) mode or on a Micromass Quattro Ultima triple quadrupole spectrometer equipped with a Z-spray electrospray ionization source (ESIMS) operating in the negative mode. Flash-column chromatography was performed on Silica gel (E. Merck, 40–63 μm). Elemental analyses were performed by the Service Central de Microanalyse du CNRS (Vernaison, France).

3.2. 7-Methoxy-2-naphthyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside (12)

A mixture of 1,2,3,4-tetra-*O*-acetyl-β-D-xylopyranose **11**[12] (6.36 g, 20 mmol), 7-methoxy-2-naphtol (6.27 g, 36 mmol), and 4 Å powdered molecular sieves (2.0 g) in anhyd CH_2Cl_2 (80 mL) was stirred for 30 min under

Table 4. ^{1}H NMR data: carbohydrate ring protons for target molecules **1**–**10**[a]

	1[b]	**2**	**3**[b]	**4**	**5**	**6**	**7**[b]	**8**	**9**	**10**
H-1^{I}	4.95	5.23	5.03	5.23	5.04	5.24	5.02	5.23	5.04	5.25
$J_{1,2}$	7.5	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0
H-2^{I}	3.24	**3.98**[c]	3.30	**4.04**	3.51	**4.05**	3.28	**4.08**	3.52	**4.05**
$J_{2,3}$	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0
$J_{2,P}$	—	9.0	—	9.0	—	9.0	—	9.0	—	9.0
H-3^{I}	3.35	3.74	3.38	3.84	3.63	3.86	3.36	3.85	3.64	3.87
$J_{3,4}$	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0
H-4^{I}	3.36	3.69	3.63	3.92	3.80	3.95	3.62	3.95	3.80	3.95
H-5^{I}	3.78	3.96	3.96	4.10	4.05	4.08	3.92	4.10	4.08	4.10
	3.26	3.45	3.35	3.55	3.46	3.56	3.38	3.58	3.55	3.58
H-1^{II}			4.24	4.39	4.32	4.44	4.24	4.44	4.31	4.51
$J_{1,2}$			8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
H-2^{II}			3.40	3.44	3.44	3.48	3.41	3.50	3.48	3.53
$J_{2,3}$			10.5	10.0	10.0	10.0	10.0	10.0	10.5	10.0
H-3^{II}			3.29	3.54	3.53	3.58	3.56	3.74	3.75	3.72
$J_{3,4}$			3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
H-4^{II}			3.61	3.82	3.86	4.14	3.65	4.07	4.06	4.12
$J_{4,5}$			0.8	0.8	1.0	1.0	1.0	0.8	0.8	0.8
H-5^{II}			3.50	3.60	3.76	3.82	3.55	3.80	3.81	3.81
H-6^{II}			3.48	3.75	**4.12**	**4.14**	3.58	3.71	**4.13**	**4.14**
			3.42	3.61	**4.10**	**4.11**	3.43	3.60	**4.09**	**4.10**
H-1^{III}							4.31	4.47	4.37	4.49
$J_{1,2}$							8.0	8.0	8.0	8.0
H-2^{III}							3.38	3.52	3.44	3.56
$J_{2,3}$							10.0	10.0	10.5	10.5
H-3^{III}							3.27	3.60	3.60	3.58
$J_{3,4}$							3.5	3.5	3.5	3.5
H-4^{III}							3.68	3.81	3.82	3.84
$J_{4,5}$							1.0	0.8	1.0	1.0
H-5^{III}							3.51	3.69	3.66	3.68
H-6^{III}							3.52	3.71	3.72	3.74
							3.43	3.60	3.61	3.62

[a] For solns in D_2O at 25 °C (internal acetone, δ_H 2.225), unless otherwise stated.
[b] 1:1, $(CD_3)_2SO/D_2O$.
[c] Values in bold type reflect the location of phosphate and/or sulfate groups.

dry Ar, then cooled to 0 °C. A soln of Me_3SiOTf in toluene (1 M, 4 mL) was added, and the mixture was stirred for 2 h at 0 °C. Triethylamine (1 mL) was added, and the mixture was filtered, washed with cold water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. The residue was stirred with diethyl ether (100 mL) at 0 °C the solids were filtered off, and recrystallized from EtOH to give **12** (6.66 g, 77%), mp 154–155 °C; $[\alpha]_D^{22}$ −24 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 7.60–6.90 (m, 6H, aromatic H), 3.42 (s, 3H, OC*H*$_3$), 1.84, 1.82, 1.70 (3s, 9H, Ac); ISMS: *m*/*z* 455 [M+Na]$^+$. Anal. Calcd for $C_{22}H_{24}O_9$: C, 61.11; H, 5.59. Found: C, 61.01; H, 6.05.

3.3. 7-Methoxy-2-naphthyl β-D-xylopyranoside (1)

A solution of **12** (4.33 g, 10 mmol) in MeOH (30 mL) and CH_2Cl_2 (10 mL) was treated for 1 h with methanolic sodium methoxide (1 M, 1 mL), then was deionized with Amberlite IR-120 [H$^+$] resin, filtered and concentrated. Crystallization of the residue from EtOH gave **1** (2.88 g, 94%); mp 176–177 °C; $[\alpha]_D^{22}$ −30 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, 1:1, $(CD_3)_2SO/D_2O$): carbohydrate ring protons (see Table 4); δ 7.80–7.0 (m, 6H aromatic H), 3.84 (s, 3H, OC*H*$_3$); ^{13}C NMR (62.8 MHz, 1:1, $(CD_3)_2SO/D_2O$): see Table 5; ISMS: *m*/*z* 329 [M+Na]$^+$. Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.64; H, 5.97.

3.4. 7-Methoxy-2-naphthyl 2,3-*O*-isopropylidene- (13) and 3,4-*O*-isopropylidene-β-D-xylopyranoside (14)

2-Methoxypropene (0.8 mL, 8 mmol) was added in four portions, every 20 min, to a solution of **1** (920 mg, 3 mmol) and CSA (100 mg) in anhyd DMF (10 mL). Triethylamine (0.3 mL) was added, and the mixture was concentrated. Flash silica chromatography (4:3, petroleum ether/EtOAc, containing 0.2% of Et_3N) gave first **14** (239 mg, 23%); mp 183–184 °C; $[\alpha]_D^{22}$ −51 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 7.75–7.05 (m, 6H, aromatic H), 3.92 (s, 3H, OC*H*$_3$), 2.70 (d, 1H, $J = 3.0$ Hz, *H*O-2), 1.52, 1.50 (2s, 6H, $(CH_3)_2C$); ISMS: *m*/*z* 369 [M+Na]$^+$.

Table 5. ^{13}C NMR data (62.8 MHz) for target molecules **1**–**10**[a]

	1[b]	**2**	**3**[b]	**4**	**5**	**6**	**7**[b]	**8**	**9**	**10**
C-1^{I}	100.77	100.02	100.54	100.01	100.80	100.04	100.85	100.24	100.90	100.12
C-2^{I}	72.90	**75.30**[c]	72.93	**75.58**	72.93	**75.64**	72.88	**75.46**	72.55	**75.56**
$J_{C,P}$	—	5.0	—	5.0	—	5.0	—	5.0	—	5.0
C-3^{I}	76.50	75.80	74.36	74.11	74.02	74.03	74.26	74.29	74.10	74.28
C-4^{I}	69.17	69.10	75.90	75.94	77.17	75.57	76.01	75.89	77.30	75.49
C-5^{I}	65.60	64.79	63.41	62.74	63.20	62.70	63.29	62.80	63.20	62.72
C-1^{II}			102.12	101.72	102.11	101.21	100.49	101.37	101.80	100.86
C-2^{II}			69.66	70.80	70.68	70.59	68.91	69.93	69.69	69.68
C-3^{II}			72.71	72.86	72.83	72.91	82.65	82.39	82.91	82.13
C-4^{II}			67.97	68.96	68.48	68.46	67.29	68.68	68.11	68.18
C-5^{II}			75.38	75.43	74.10	74.03	75.10	75.20	74.01	72.69
C-6^{II}			60.28	61.37	**67.31**	**67.05**	60.17	61.31	**67.28**	**67.09**
C-1^{III}							104.87	104.51	104.50	104.52
C-2^{III}							70.99	71.21	71.19	71.28
C-3^{III}							72.69	72.70	72.75	72.62
C-4^{III}							67.86	68.77	68.75	68.74
C-5^{III}							75.06	75.20	75.18	75.20
C-6^{III}							60.52	61.11	61.04	61.05
Ar_C	157.49	157.56	157.50	157.62	157.57	157.62	157.43	157.63	157.65	157.63
	155.35	155.15	155.28	155.21	155.31	155.28	155.27	155.33	155.21	155.28
	135.24	135.48	135.24	135.49	135.48	135.51	135.19	135.50	135.48	135.51
	128.80	129.71	128.79	129.82	129.88	129.86	128.78	129.86	129.88	129.88
	128.70	129.52	128.68	129.58	129.58	129.56	128.65	129.62	129.58	129.52
	124.22	126.51	124.25	126.10	126.14	126.08	124.21	126.10	126.08	126.10
	116.30	126.17	116.31	125.52	125.40	125.62	116.31	125.91	125.82	125.72
	115.90	116.87	115.89	116.78	116.82	116.92	115.87	116.96	116.98	116.97
	109.36	110.90	109.42	110.81	110.61	110.73	109.37	110.89	110.56	110.68
	105.16	105.98	105.16	105.94	105.98	106.02	105.14	106.07	105.96	106.06
O*C*H$_3$	54.89	55.52	54.89	55.53	55.53	55.52	54.89	55.53	55.52	55.54

[a] For solns in D_2O at 25 °C (internal acetone, δ_C 30.45), unless otherwise stated.
[b] 1:1, $(CD_3)_2SO/D_2O$.
[c] Values in bold type reflect the location of phosphate and/or sulfate groups.

Anal. Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40. Found: C, 65.72; H, 6.45.

Next eluted was **13** (717 mg, 69%); mp 137–138 °C; $[\alpha]_D^{22}$ −41 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 7.70–7.0 (m, 6H, aromatic H), 3.92 (s, 3H, OC*H*$_3$), 2.43 (d, 1H, $J = 4.0$ Hz, *H*O-4), 1.54, 1.52 (2s, 6H, (C*H*$_3$)$_2$C); ISMS: *m*/*z* 369 $[M+Na]^+$. Anal. Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40. Found: C, 65.78; H, 6.51.

3.5. 7-Methoxy-2-naphthyl 2-*O*-dibenzyloxyphosphinyl-3,4-*O*-isopropylidene-β-D-xylopyranoside (15)

A solution of dibenzyl *N*,*N*-diisopropylphosphoramidite (245 mg, 0.7 mmol) in anhyd CH_2Cl_2 (1 mL) was added to a solution of **14** (160 mg, 0.46 mmol) and 1-*H*-tetrazole (0.4 M in MeCN, 2.5 mL) in anhyd CH_2Cl_2 (1 mL), and the mixture was stirred for 1 h, then was cooled to −10 °C. *m*-Chloroperbenzoic acid (225 mg, 1 mmol) was added in portions, and the mixture was stirred for 30 min, then was diluted with CH_2Cl_2 (30 mL), washed with aq 5% $Na_2S_2O_3$, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (3:2, petroleum ether/EtOAc) and crystallization of the residue from diethyl ether gave **15** (244 mg, 87%); mp 106–107 °C; $[\alpha]_D^{22}$ −15 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 7.70–7.0 (m, 16H, aromatic H), 5.14, 5.07 (2ABq, 4H, OC*H*$_2$Ph), 3.90 (s, 3H, OC*H*$_3$), 1.47, 1.43 (2s, 6H, (C*H*$_3$)$_2$C); ISMS: *m*/*z* 629 $[M+Na]^+$. Anal. Calcd for $C_{33}H_{35}O_9P$: C, 65.34; H, 5.81; P, 5.10. Found: C, 65.21; H, 5.92; P, 4.98.

3.6. 7-Methoxy-2-naphthyl 2-*O*-disodium phosphonato-β-D-xylopyranoside (2)

A mixture of **15** (200 mg, 0.33 mmol), Pd/C (10%, 100 mg) and AcOH (0.1 mL) in EtOAc/MeOH/H_2O (6:2:1, 9 mL) was stirred under H_2 for 24 h, then was filtered through a pad of Celite and concentrated. A suspension of the residue in water (5 mL) was treated with NaOH (1 M, 0.66 mL), concentrated, and eluted from a column (2 × 60 cm) of Sephadex LH-20 with water to give **2** (108 mg, 80%) as a white powder; $[\alpha]_D^{22}$ −17 (*c* 1.0, H_2O); ^1H NMR (250 MHz, D_2O): carbohydrate ring protons (see Table 4); δ 7.75–6.95 (m, 6H, aromatic H), 3.81 (s, 3H, OC*H*$_3$); ^{13}C NMR (62.8 MHz, D_2O, internal acetone): see Table 5; ESIMS:

m/*z* 385.1 $[M-2Na+H]^-$. Anal. Calcd for $C_{16}H_{17}NaO_9P$: C, 44.66; H, 3.98. Found: C, 44.38; H, 4.07.

3.7. 4-Methoxyphenyl 2,3,4-tri-*O*-benzoyl-6-*O*-trityl-β-D-galactopyranoside (17)

A mixture of 4-methoxyphenyl β-D-galactopyranoside **16**[14] (2.86 g, 10 mmol) and freshly recrystallized trityl chloride (1.95 g, 7 mmol) in anhyd pyridine (50 mL) was stirred for 6 h at 60 °C, then was cooled to rt. Benzoyl chloride (6.65 mL, 40 mmol) was added, and the mixture was stirred overnight. Methanol (5 mL) was added, and the mixture was diluted with CH_2Cl_2 (150 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Crystallization of the residue from EtOAc/petroleum ether gave **17** (7.58 g, 90%); mp 212–213 °C; $[\alpha]_D^{22}$ +98 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 8.0–6.80 (m, 34H, aromatic H), 3.75 (s, 3H, OCH_3); ISMS: *m*/*z* 864 $[M+Na]^+$. Anal. Calcd for $C_{53}H_{44}O_{10}$: C, 75.70; H, 5.27. Found: C, 75.55; H, 5.34.

3.8. 4-Methoxyphenyl 2,3,4-tri-*O*-benzoyl-6-*O*-levulinoyl-β-D-galactopyranoside (18)

A soln of **17** (3.36 g, 4 mmol) in anhyd CH_2Cl_2 (50 mL) was treated successively with $BF_3{\cdot}Et_2O$ (0.56 mL, 4.4 mmol) and anhyd MeOH (1.76 mL, 44 mmol) and the mixture was stirred for 30 min at rt, then was diluted with CH_2Cl_2 (50 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. A mixture of the residue, levulinic acid (0.51 g, 4.4 mmol) and DMAP (61 mg, 0.5 mmol) in anhyd CH_2Cl_2 (25 mL) was treated in portions with DCC (0.9 g, 4.4 mmol), and the mixture was stirred for 1 h at rt. The precipitated DCU was filtered off, washed with CH_2Cl_2, and the filtrate was washed with cold 0.1 M HCl, water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography of the residue (1:1, EtOAc/petroleum ether) gave **18** (2.33 g, 93%) as a colorless glass; $[\alpha]_D^{22}$ +142 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 8.10–6.80 (m, 19H, aromatic H), 3.76 (s, 3H, OCH_3), 2.74, 2.60 (2m, 4H, CH_2CO), 2.15 (s, 3H, $COCH_3$); ISMS: *m*/*z* 719 $[M+Na]^+$. Anal. Calcd for $C_{39}H_{36}O_{12}$: C, 67.23; H, 5.21. Found: C, 67.12; H, 5.35.

3.9. 2,3,4-Tri-*O*-benzoyl-6-*O*-levulinoyl-1-*O*-trichloroacetimidoyl-α-D-galactopyranoside (19)

A mixture of **18** (2.44 g, 3.5 mmol) and CAN (9.6 g, 17.5 mmol) in 1:1.5:1 toluene/MeCN/H_2O (70 mL) was stirred for 20 min at rt, then was diluted with EtOAc (150 mL), washed with water, brine, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (1:1, EtOAc/petroleum ether) gave the corresponding free hemiacetal as a yellow foam. A mixture of the above isolated hemiacetal, CCl_3CN (3 mL, 30 mmol), and DBU (0.11 mL, 0.72 mmol) in CH_2Cl_2 (15 mL) was stirred for 30 min at rt, then was concentrated. Flash silica chromatography (3:2, petroleum ether/EtOAc, containing 0.1% of Et_3N) gave **19** (1.78 g, 78%) as a white foam; $[\alpha]_D^{22}$ +167 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 8.64 (s, 1H, C=N*H*), 8.10–7.20 (m, 15H, Ph), 2.70, 2.52 (2m, 4H, CH_2CO), 2.12 (s, 3H, $COCH_3$); ISMS: *m*/*z* 745 $[M+Na]^+$ for ^{35}Cl. Anal. Calcd for $C_{33}H_{30}Cl_3NO_{11}$: C, 54.82; H, 4.18; N, 1.94. Found: C, 54.68; H, 4.27; N, 1.81.

3.10. 4-Methoxyphenyl 3,4-*O*-isopropylidene-6-*O*-(2-methoxy-2-propyl)-β-D-galactopyranoside (20)

A mixture of **16** (5.0 g, 17.5 mmol) and CSA (0.2 g) in 2,2-dimethoxypropane (80 mL) was stirred for 48 h at rt. Triethylamine (1.4 mL) was added, and the mixture was concentrated. Flash silica chromatography (12:1, CH_2Cl_2/acetone, containing 1% of Et_3N) gave **20** (5.23 g, 75%); mp 107–108 °C (from EtOAc/petroleum ether); $[\alpha]_D^{22}$ −29 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 6.95 (m, 4H, aromatic H), 3.78, 3.18 (2s, 6H, OCH_3), 2.54 (d, 1H, *J* 2.5 Hz, *H*O-2), 1.60, 1.42, 1.40 (3s, 12H, $(CH_3)_2C$); ISMS: *m*/*z* 421 $[M+Na]^+$. Anal. Calcd for $C_{20}H_{30}O_8$: C, 60.29; H, 7.59. Found: C, 60.12; H, 7.65.

Further elution with 5:1, CH_2Cl_2/acetone gave the corresponding 2,6-diol (1.15 g, 20%); mp 133–134 °C (from EtOAc/petroleum ether). This later was treated and purified as described above to give a second crop of **20** (1.05 g, 15%), raising the overall yield to 90%.

3.11. 4-Methoxyphenyl 2-*O*-benzoyl-3,4-*O*-isopropylidene-6-*O*-(2-methoxy-2-propyl)-β-D-galactopyranoside (21)

Benzoyl chloride (2.32 mL, 20 mmol) was added dropwise at 0 °C to a solution of **20** (5.08 g, 12.75 mmol) in anhyd pyridine (10 mL) and CH_2Cl_2 (30 mL), and the mixture was stirred at 0 °C for 1 h. Methanol (1 mL) was added, and the mixture was diluted with CH_2Cl_2 (100 mL), washed with cold water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Crystallization of the residue from EtOAc/petroleum ether gave **21** (6.05 g, 94%); mp 95–96 °C; $[\alpha]_D^{22}$ +10 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 8.10–6.80 (m, 9H, aromatic H), 3.73, 3.22 (2s, 6H, OCH_3), 1.66, 1.40, 1.38 (3s, 12H, $(CH_3)_2C$); ISMS: *m*/*z* 525 $[M+Na]^+$. Anal. Calcd for $C_{27}H_{34}O_9$: C, 64.53; H, 6.82. Found: C, 64.40; H, 6.90.

3.12. 4-Methoxyphenyl 2-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilylene-β-D-galactopyranoside (22)

A soln of **21** (6.0 g, 11.9 mmol) in 9:1, TFA/H_2O (20 mL) was stirred for 10 min at rt, then was diluted with water (20 mL), concentrated, and evaporated twice with water (10 mL). Crystallization of the residue from EtOH gave the intermediary triol (4.24 g, 91%); mp 176–177 °C.

Di-*tert*-butylsilyl ditriflate (4.4 mL, 13 mmol) was added at 0 °C to a suspension of the above isolated triol and *sym*-collidine (4.0 mL, 30 mmol) in anhyd CH_2Cl_2 (40 mL), and the mixture was stirred for 90 min at 0 °C. The clear solution was washed with water, cold 5% HCl, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (5:2, petroleum ether/EtOAc) gave **22** (5.06 g, 80% from **21**) as a white foam; $[\alpha]_D^{22}$ +4 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 1); δ 8.10–6.80 (m, 9H aromatic H), 3.75 (s, 3H, OCH_3), 2.77 (d, 1H, $J = 10.0$ Hz, *H*O-3), 1.16, 1.06 (2s, 18H, (CH_3)$_3$C); ISMS: *m*/*z* 553 $[M+Na]^+$. Anal. Calcd for $C_{28}H_{38}O_8Si$: C, 63.37; H, 7.22. Found: C, 63.21; H, 7.30.

3.13. 7-Methoxy-2-naphthyl *O*-(2,3,4-tri-*O*-benzoyl-6-*O*-levulinoyl-β-D-galactopyranosyl)-(1→3)-β-D-xylopyranoside (23)

A mixture of imidate **19** (1.74 g, 2.4 mmol), alcohol **13** (0.83 g, 2.4 mmol), and powdered 4 Å molecular sieves (0.5 g) in anhyd CH_2Cl_2 (40 mL) was stirred at 0 °C under dry Ar. A solution of Me_3SiOTf in toluene (1 M, 0.36 mL) was added, and the mixture was stirred for 30 min at 0 °C. Triethylamine (0.5 mL) was added, and the mixture was filtered, washed with satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. A soln of the residue in 60% AcOH (30 mL) was stirred at 100 °C for 15 min, then was cooled, concentrated, and evaporated twice with water. Flash silica chromatography (7:1, CH_2Cl_2/acetone) gave **23** (1.50 g, 71%) as a white foam; $[\alpha]_D^{22}$ +80 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.10–7.0 (m, 21H, aromatic H), 4.05 (br s, 1H, Xyl*p* *H*O-3), 3.03 (br s, 1H, Xyl*p* *H*O-2), 2.75, 2.60 (2m, 4H, CH_2CO), 2.15 (s, 3H, COCH_3); ISMS: *m*/*z* 901 $[M+Na]^+$. Anal. Calcd for $C_{48}H_{46}O_{16}$: C, 65.60; H, 5.27. Found: C, 65.48; H, 5.31.

3.14. 7-Methoxy-2-naphthyl *O*-(2,3,4-tri-*O*-benzoyl-6-*O*-levulinoyl-β-D-galactopyranosyl)-(1→3)-3-*O*- (24) and 2-*O*-acetyl-β-D-xylopyranoside (25)

A mixture of **23** (1.40 g, 1.6 mmol) and dibutyltin oxide (0.44 g, 1.76 mmol) in 1,4-dioxane (40 mL) and benzene (20 mL) was heated for 6 h under reflux with azeotropic removal of water. Solvents (40 mL) were then slowly distilled at atmospheric pressure, and the mixture was cooled to rt. A soln of Ac_2O (175 μL, 1.84 mmol) in benzene (1 mL) was added, and the mixture was stirred overnight, then was concentrated. Flash silica chromatography (3:2, toluene/EtOAc) gave first the 2-acetate **25** (266 mg, 18%) as a white foam; $[\alpha]_D^{22}$ +95 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.10–7.0 (m, 21H, aromatic H), 4.15 (d, 1H, $J = 2.5$ Hz, Xyl*p* *H*O–3), 3.91 (s, 3H, OCH_3), 2.75, 2.60 (2m, 4H, CH_2CO), 2.20, 2.12 (2s, 6H, COCH_3); ISMS: *m*/*z* 943 $[M+Na]^+$. Anal. Calcd for $C_{50}H_{48}O_{17}$: C, 65.21; H, 5.25. Found: C, 64.98; H, 5.21.

Next eluted was the 3-acetate **24** (1.05 g, 71%) isolated as a white foam; $[\alpha]_D^{22}$ +38 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.10–6.90 (m, 21H, aromatic H), 3.24 (d, 1H, $J = 8.5$ Hz, Xyl*p* *H*O–2), 3.91 (s, 3H, OCH_3), 2.74, 2.58 (2m, 4H, CH_2CO), 2.16, 2.14 (2s, 6H, COCH_3); ESIMS: *m*/*z* 943 $[M+Na]^+$. Anal. Calcd for $C_{50}H_{48}O_{17}$: C, 65.21; H, 5.25. Found: C, 65.12; H, 5.29.

3.15. 7-Methoxy-2-naphthyl *O*-(2,3,4-tri-*O*-benzoyl-6-*O*-levulinoyl-β-D-galactopyranosyl)-(1→3)-3-*O*-acetyl-2-*O*-dibenzyloxyphosphinyl-β-D-xylopyranoside (26)

Compound **24** (617 mg, 0.67 mmol) was treated as described for the preparation of **15**. Flash silica chromatography (2:1, toluene/EtOAc) gave **26** (724 mg, 91%) as a white foam; $[\alpha]_D^{22}$ +70 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.10–6.90 (m, 31H, aromatic H), 5.02 (2 ABq, 4H, CH_2Ph), 3.88 (s, 3H, OCH_3), 2.75, 2.58 (2m, 4H, CH_2CO), 2.16, 1.95 (2s, 6H, COCH_3). Anal. Calcd for $C_{64}H_{61}O_{20}P$: C, 65.08; H, 5.20; P, 2.62. Found: C, 65.01; H, 5.31; P, 2.41.

3.16. 7-Methoxy-2-naphthyl *O*-(2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-3-*O*-acetyl-2-*O*-dibenzyloxyphosphinyl-β-D-xylopyranoside (27)

A soln of **26** (0.69 g, 0.58 mmol) in pyridine (2 mL) was treated for 8 min at rt with 12:8:1 pyridine/AcOH/hydrazine hydrate (21 mL), then was diluted with CH_2Cl_2 (50 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (3:2, toluene/EtOAc) gave **27** (0.59 g, 93%) as a white foam; $[\alpha]_D^{22}$ +89 (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, 3:1, $CD_3OD/CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.05–6.95 (m, 31H, aromatic H), 5.04 (2ABq, 4H, CH_2Ph), 3.87 (s, 3H, OCH_3), 1.98 (s, 3H, COCH_3). Anal. Calcd for $C_{59}H_{55}O_{18}P$: C, 65.43; H, 5.12; P, 2.86. Found: C, 65.25; H, 5.18; P, 2.64.

3.17. 7-Methoxy-2-naphthyl *O*-(2,3,4-tri-*O*-benzoyl-6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-3-*O*-acetyl-2-*O*-dibenzyloxyphosphinyl-β-D-xylopyranoside (28)

A mixture of **27** (300 mg, 0.28 mmol) and sulfur trioxide–trimethylamine complex (66 mg, 0.5 mmol) in anhyd DMF (3 mL) was stirred for 1 h at 60 °C, then was cooled. Methanol (0.5 mL) was added, and the mixture was concentrated. Flash silica chromatography of the residue (15:1, CH_2Cl_2/MeOH, containing 0.5% of Et_3N) followed by elution from a column (1.5 × 25 cm) of Sephadex SP-C25 [Na^+] with 9:1, CH_2Cl_2/MeOH gave **28** (370 mg, 89%) as a colorless glass; $[\alpha]_D^{22}$ +70 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, 3:1, $CD_3OD/CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.0–6.90 (m, 31H, aromatic H), 4.99 (2ABq, 4H, C*H*$_2$Ph), 3.85 (s, 3H, OC*H*$_3$), 1.96 (s, 3H, COC*H*$_3$). Anal. Calcd for $C_{59}H_{54}O_{21}NaPS$: C, 59.80; H, 4.59. Found: C, 59.65; H, 5.12.

3.18. 7-Methoxy-2-naphthyl *O*-(2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2,3-di-*O*-acetyl-β-D-xylopyranoside (29)

Conventional acetylation (pyridine/acetic anhydride) of **23** (0.88 g, 1 mmol) gave quantitatively the corresponding diacetate. This later was treated as described for the preparation of **27** and the residue was crystallized from EtOAc/petroleum ether to give **29** (0.78 g, 90%); mp 115–116 °C; $[\alpha]_D^{22}$ +101 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, 3:1, $CD_3OD/CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.10–6.90 (m, 21H, aromatic H), 3.89 (s, 3H, OC*H*$_3$), 2.92 (t, 1H, *J* = 6.5 Hz, Gal*p* *H*O-6), 2.10, 2.08 (2s, 6H, COC*H*$_3$); ISMS: *m*/*z* 887 $[M+Na]^+$. Anal. Calcd for $C_{47}H_{44}O_{16}$: C, 65.27; H, 5.13. Found: C, 65.21; H, 5.20.

3.19. 7-Methoxy-2-naphthyl *O*-(2,3,4-tri-*O*-benzoyl-6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-2,3-di-*O*-acetyl-β-D-xylopyranoside (30)

Compound **29** (0.39 g, 0.45 mmol) was treated as described for the preparation of **28** to give **30** (0.39 g, 90%) as a white foam; $[\alpha]_D^{22}$ +69 (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, 3:1, $CD_3OD/CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.00–6.90 (m, 21H, aromatic H), 3.86 (s, 3H, OC*H*$_3$), 2.10, 2.04 (2s, 6H, COC*H*$_3$); ISMS: *m*/*z* 989 $[M+Na]^+$. Anal. Calcd for $C_{47}H_{43}O_{19}NaS$: C, 58.38; H, 4.48. Found: C, 58.10; H, 4.59.

3.20. 7-Methoxy-2-naphthyl *O*-(β-D-galactopyranosyl)-(1→3)-β-D-xylopyranoside (3)

A solution of **29** (345 mg, 0.4 mmol) in MeOH (10 mL) and CH_2Cl_2 (5 mL) was treated with methanolic sodium methoxide (1 M, 1 mL) for 2 h at rt, then was deionized with Amberlite IR-120 [H^+] resin, filtered, and concentrated. Crystallization of the residue from MeOH gave **3** (173 mg, 92%); mp 238–240 °C; $[\alpha]_D^{22}$ −27 (*c* 1.0, $(CH_3)_2SO$); ^{1}H NMR (250 MHz, 1:1, $(CD_3)_2SO/D_2O$): carbohydrate ring protons (see Table 4); δ 7.75–6.95 (m, 6H, aromatic H), 3.84 (s, 3H, OC*H*$_3$); ^{13}C NMR (62.8 MHz, 1:1, $(CD_3)_2SO/D_2O$): see Table 5; ISMS: *m*/*z* 491 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{28}O_{11}$: C, 56.41; H, 6.02. Found: C, 56.30; H, 6.12.

3.21. 7-Methoxy-2-naphthyl *O*-(β-D-galactopyranosyl)-(1→3)-2-*O*-disodium phosphonato-β-D-xylopyranoside (4)

A mixture of **27** (325 mg, 0.3 mmol) and Pd/C (10%, 0.1 g) in 12:2:1 EtOAc/MeOH/H_2O (15 mL) was stirred under H_2 for 24 h, then was filtered through a pad of Celite, and concentrated. A suspension of the residue in water (10 mL) was treated with NaOH (1 M, 0.6 mL), and concentrated. A mixture of the residue and hydrazine hydrate (2.5 mL) in MeOH (10 mL) was stirred for 5 h at rt, then was cooled to 0 °C. Acetone (20 mL) was carefully added, and the mixture was stirred for 30 min, then was concentrated. The resulting syrup was triturated with acetone (20 mL), the solids were filtered off, washed with acetone, and a solution of the residue in water (3 mL) was eluted from a column (2 × 60 cm) of Sephadex LH-20 with water to afford **4** (143 mg, 80%) as a white hygroscopic powder; $[\alpha]_D^{22}$ −41 (*c* 1.0, H_2O); ^{1}H NMR (250 MHz, D_2O): carbohydrate ring protons (see Table 4); δ 7.85–6.95 (m, 6H, aromatic H), 3.83 (s, 3H, OC*H*$_3$); ^{13}C NMR (62.8 MHz, D_2O): see Table 5; ESIMS: *m*/*z* 547.4 $[M-2Na+H]^-$. Anal. Calcd for $C_{22}H_{27}Na_2O_{14}P$: C, 44.60; H, 4.59. Found: C, 44.32; H, 4.71.

3.22. 7-Methoxy-2-naphthyl *O*-(6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→4)-β-D-xylopyranoside (5)

A mixture of **30** (387 mg, 0.4 mmol) and NaOH (4 M, 1.5 mL) in MeOH (12 mL) was stirred for 4 h at rt, then was diluted with water (10 mL). The pH of the solution was brought to ~3.5 with Amberlite IR-120 [H^+] resin (pH meter control), and the mixture was filtered, concentrated and dried. The residue was extracted with acetone (3 × 5 mL), then was taken up in water (2 mL) and eluted from a column (2 × 60 cm) of Sephadex LH-20 with water to give **5** (206 mg, 90%) as a white solid; mp 215–216 °C (from MeOH/H_2O); $[\alpha]_D^{22}$ −45 (*c* 1.0, H_2O); ^{1}H NMR (250 MHz, D_2O): carbohydrate ring protons (see Table 4); δ 7.80–6.90 (m, 6H, aromatic H), 3.77 (s, 3H, OC*H*$_3$); ^{13}C NMR (62.8 MHz, D_2O): see Table 5; ESIMS: *m*/*z* 547.2 $[M-Na]^-$. Anal. Calcd for $C_{22}H_{27}NaO_{14}S$: C, 46.32; H, 4.77. Found: C, 46.04; H, 4.92.

3.23. 7-Methoxy-2-naphthyl *O*-(6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→4)-2-*O*-disodium phosphonato-β-D-xylopyranoside (6)

A mixture of **28** (320 mg, 0.27 mmol) and Pd/C (10%, 100 mg) in 12:2:1 EtOAc/MeOH/H_2O (15 mL) was stirred for 24 h under H_2, then was filtered and concentrated. The pH of a solution of the residue in 9:1, MeOH/H_2O was brought to ~8 with aq NaOH (pH meter control), and the mixture was concentrated. A suspension of the residue in MeOH (10 mL) was treated with hydrazine hydrate (3 mL) for 5 h at rt, then was cooled to 0 °C. Acetone (30 mL) was carefully added, and the mixture was concentrated. The residue was extracted with acetone (3 × 5 mL), then taken up in water (2 mL) and eluted from a column (2 × 60 cm) of Sephadex LH-20 with water to give **6** (160 mg, 85%) as a white powder; $[\alpha]_D^{22}$ −45 (*c* 1.0, H_2O); ^{1}H NMR (250 MHz, D_2O): carbohydrate ring protons (see Table 4); δ 7.85–6.90 (m, 6H, aromatic H), 3.82 (s, 3H, OC*H*$_3$); ^{13}C NMR (62.8 MHz, D_2O): see Table 5; ESIMS: *m*/*z* 649.2 $[M-2Na+H]^-$. Anal. Calcd for $C_{22}H_{26}Na_3O_{17}PS$: C, 38.05; H, 3.75. Found: C, 37.78; H, 3.93.

3.24. 4-Methoxyphenyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilylene-β-D-galactopyranoside (32)

A mixture of 2,3,4,6-tetra-*O*-benzoyl-1-*O*-trichloroacetimidoyl-α-D-galactopyranose **31**[10] (4.45 g, 6 mmol), alcohol **22** (2.55 g, 4.80 mmol), and 4 Å powdered molecular sieves (1.0 g) in anhyd CH_2Cl_2 (40 mL) was stirred for 30 min under dry Ar. A solution of Me_3SiOTf in toluene (1 M, 0.9 mL) was added, and the mixture was stirred for 30 min at rt. Triethylamine (0.7 mL) was added, and the mixture was filtered and concentrated. Flash silica chromatography (11:1, toluene/EtOAc, containing 0.2% of Et_3N) gave **32** (4.59 g, 86%) as a white foam; $[\alpha]_D^{22}$ +90 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.10–6.70 (m, 29H, aromatic H), 3.75 (s, 3H, OC*H*$_3$), 1.12, 1.09 (2s, 18H, (C*H*$_3$)$_3$C); ISMS: *m*/*z* 553 $[M+Na]^+$. Anal. Calcd for $C_{62}H_{64}O_{17}Si$: C, 67.13; H, 5.82. Found: C, 67.02; H, 5.80.

3.25. 4-Methoxyphenyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2-*O*-benzoyl-β-D-galactopyranoside (33)

A mixture of **32** (4.44 g, 4 mmol) and $Et_3N{\cdot}3HF$ (1.63 mL, 10 mmol) in anhyd THF (50 mL) was stirred for 2 h at 0 °C, then was concentrated to ~10 mL, diluted with CH_2Cl_2 (200 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Crystallization of the residue from EtOH gave **33** (3.50 g, 90%); mp 230–232°C; $[\alpha]_D^{22}$ +13 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.10–6.70 (m, 29H, aromatic H), 3.68 (s, 3H, OC*H*$_3$), 3.15 (br s, 1H, *H*O-4), 2.20 (t, 1H, *J* = 6.0 Hz, *H*O-6); ISMS: *m*/*z* 991 $[M+Na]^+$. Anal. Calcd for $C_{54}H_{48}O_{17}$: C, 66.94; H, 4.99. Found: C, 66.82; H, 5.06.

3.26. 4-Methoxyphenyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-6-*O*-levulinoyl-β-D-galactopyranoside (34)

A soln of **33** (3.39 g, 3.5 mmol), levulinic acid (0.49 g, 4.2 mmol) and DMAP (0.12 g, 1 mmol) in anhyd CH_2Cl_2 (50 mL) was treated in portions with DCC (0.87 g, 4.2 mmol), and the mixture was stirred for 2 h at rt, then was treated as described for the preparation of **18**. A mixture of the residue and benzoyl chloride (0.84 mL, 7 mmol) in anhyd pyridine (30 mL) was stirred overnight at rt. Methanol (0.5 mL) was added, and the mixture was diluted with CH_2Cl_2 (100 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (3:1, toluene/EtOAc) gave **34** (3.49 g, 85%) as a white foam; $[\alpha]_D^{22}$ +111 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.15–6.70 (m, 34H, aromatic H), 3.72 (s, 3H, OC*H*$_3$), 2.75, 2.60 (2m, 4H, C*H*$_2$CO), 2.17 (s, 3H, COC*H*$_3$); ISMS: *m*/*z* 1194 $[M+Na]^+$. Anal. Calcd for $C_{66}H_{58}O_{20}$: C, 67.69; H, 4.99. Found: C, 67.51; H, 5.02.

3.27. *O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-6-*O*-levulinoyl-1-*O*-trichloroacetimidoyl-α-D-galactopyranose (35)

Compound **34** (3.27 g, 2.8 mmol) was treated as described for the preparation of **19**. Flash silica chromatography (4:1, toluene/EtOAc, containing 0.1% of Et_3N) gave **35** (2.54 g, 75%) as a colorless glass; $[\alpha]_D^{22}$ +123 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 2); δ 8.54 (s, 1H, C=N*H*), 8.15–6.90 (m, 30H, Ph), 2.70, 2.54 (2m, 4H, C*H*$_2$CO), 2.15 (s, 3H, COC*H*$_3$); ISMS: *m*/*z* 1225 $[M+NH_4]^+$ for ^{35}Cl. Anal. Calcd for $C_{61}H_{51}Cl_3NO_{19}$: C, 60.63; H, 4.25; N, 1.16. Found: C, 60.38; H, 4.31; N, 1.06.

3.28. 7-Methoxy-2-naphthyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2,3,4-tri-*O*-benzoyl-6-*O*-levulinoyl-β-D-galactopyranosyl)-(1→3)-β-D-xylopyranoside (36)

A mixture of imidate **35** (846 mg, 0.7 mmol) and alcohol **13** (324 mg, 0.93 mmol) was treated as described for the preparation of **23** to give **36** (702 mg, 74%) as a white foam; $[\alpha]_D^{22}$ +73 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 3); δ

8.15–6.95 (m, 36H, aromatic H), 4.10 (d, 1H, $J = 4.0$ Hz, Xyl*p* *H*O-3), 3.88 (s, 3H, OCH_3), 3.08 (br s, 1H, Xyl*p* *H*O-2), 2.78, 2.64 (2m, 4H, CH_2CO), 2.20 (s, 3H, COCH_3); ISMS: *m*/*z* 1376 $[M+Na]^+$. Anal. Calcd for $C_{75}H_{68}O_{24}$: C, 66.56; H, 5.06. Found: C, 66.42; H, 5.12.

3.29. 7-Methoxy-2-naphthyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2,3,4-tri-*O*-benzoyl-6-*O*-levulinoyl-β-D-galactopyranosyl)-(1→3)-3-*O*- (37) and 2-*O*-acetyl-β-D-xylopyranoside (38)

A mixture of **36** (676 mg, 0.5 mmol) and dibutyltin oxide (136 mg, 0.55 mmol) was treated as described for the preparation of **24**. Flash silica chromatography (3:2, toluene/EtOAc) gave first **38** (112 mg, 16%) as a colorless glass; $[\alpha]_D^{22}$ +79 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 3); δ 8.20–6.85 (m, 36H, aromatic H), 4.15 (d, 1H, $J = 4.0$ Hz, Xyl*p* *H*O-3), 3.87 (s, 3H, OCH_3), 2.75, 2.58 (2m, 4H, CH_2CO), 2.20, 2.06 (2s, 6H, COCH_3); ISMS: *m*/*z* 1418 $[M+Na]^+$. Anal. Calcd for $C_{77}H_{70}O_{25}$: C, 66.28; H, 5.06. Found: C, 66.08; H, 5.11.

Next eluted was **37** (482 mg, 69%) isolated as a white foam; $[\alpha]_D^{22}$ +45 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 3); δ 8.20–6.90 (m, 36H, aromatic H), 3.92 (s, 3H, OCH_3), 3.21 (d, 1H, $J = 9.0$ Hz, Xyl*p* *H*O-2), 2.74, 2.58 (2d, 4H, CH_2CO), 2.16, 2.07 (2s, 6H, COCH_3); ISMS: *m*/*z* 1418 $[M+Na]^+$. Anal. Calcd for $C_{77}H_{70}O_{25}$: C, 66.28; H, 5.06. Found: C, 66.19; H, 5.14.

3.30. 7-Methoxy-2-naphthyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2,3,4-tri-*O*-benzoyl-6-*O*-levulinoyl-β-D-galactopyranosyl)-(1→3)-3-*O*-acetyl-2-*O*-dibenzyloxyphosphinyl-β-D-xylopyranoside (39)

Compound **37** (765 mg, 0.55 mmol) was treated as described for the preparation of **26** to give **39** (816 mg, 89%) as a white foam; $[\alpha]_D^{22}$ +73 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): carbohydrate ring protons (see Table 3); δ 8.20–6.95 (m, 46H, aromatic H), 4.95 (2ABq, 4H, CH_2Ph), 3.87 (s, 3H, OCH_3), 2.75, 2.60 (2m, 4H, CH_2CO), 2.18, 1.94 (2s, 6H, COCH_3). Anal. Calcd for $C_{91}H_{83}O_{28}P$: C, 66.02; H, 5.05; P, 1.87. Found: C, 65.80; H, 5.15; P, 1.69.

3.31. 7-Methoxy-2-naphthyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-3-*O*-acetyl-2-*O*-dibenzyloxyphosphinyl-β-D-xylopyranoside (40)

Compound **39** (0.75 g, 0.45 mmol) was treated as described for the preparation of **27** to give **40** (645 mg, 92%) as a white foam; $[\alpha]_D^{22}$ +70 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, 3:1, $CD_3OD/CDCl_3$): carbohydrate ring protons (see Table 3); δ 8.20–6.90 (m, 46H, aromatic H), 4.96 (2ABq, 4H, CH_2Ph), 3.87 (s, 3H, OCH_3), 1.96 (s, 3H, COCH_3). Anal. Calcd for $C_{86}H_{77}O_{26}P$: C, 66.31; H, 4.98. Found: C, 66.23; H, 5.07.

3.32. 7-Methoxy-2-naphthyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2,3,4-tri-*O*-benzoyl-6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-3-*O*-acetyl-2-*O*-dibenzyloxyphosphinyl-β-D-xylopyranoside (41)

Compound **40** (0.33 g, 0.21 mmol) was treated as described for the preparation of **28** to give **41** (317 mg, 90%) as a white powder; $[\alpha]_D^{22}$ +71 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, 3:1, $CD_3OD/CDCl_3$): carbohydrate ring protons (see Table 3); δ 8.15–6.85 (m, 46H, aromatic H), 4.93 (2ABq, 4H, CH_2Ph), 3.85 (s, 3H, OCH_3), 1.86 (s, 3H, COCH_3); ISMS: *m*/*z* 1682 $[M+Na]^+$. Anal. Calcd for $C_{86}H_{76}O_{39}NaPS$: C, 62.24; H, 4.62. Found: C, 62.02; H, 4.79.

3.33. 7-Methoxy-2-naphthyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2,3-di-*O*-acetyl-β-D-xylopyranoside (42)

Compound **36** (0.42 g, 0.3 mmol) was treated as described for the preparation of **29** to give **42** (362 mg, 90%) as a colorless glass; $[\alpha]_D^{22}$ +66 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, 3:1, $CD_3OD/CDCl_3$): carbohydrate ring protons (see Table 3); δ 8.20–6.85 (m, 36H, aromatic H), 3.88 (s, 3H, OCH_3), 2.02, 2.00 (2s, 6H, COCH_3); ISMS: *m*/*z* 1362 $[M+Na]^+$. Anal. Calcd for $C_{74}H_{66}O_{24}$: C, 66.36; H, 4.97. Found: C, 66.25; H, 5.05.

3.34. 7-Methoxy-2-naphthyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2,3,4-tri-*O*-benzoyl-6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-2,3-di-*O*-acetyl-β-D-xylopyranoside (43)

Compound **42** (0.34 g, 0.25 mmol) was treated as described for the preparation of **28** to give **43** (328 mg, 91%) as a white powder; $[\alpha]_D^{22}$ +66 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, 3:1, $CD_3OD/CDCl_3$): carbohydrate ring protons (see Table 3); δ 8.20–6.90 (m, 36H, aromatic H), 3.86 (s, 3H, OCH_3), 2.01, 1.98 (2s, 6H, COCH_3); ISMS: *m*/*z* 1464 $[M+Na]^+$. Anal. Calcd for $C_{74}H_{65}O_{27}NaS$: C, 61.66; H, 4.55. Found: C, 61.49; H, 4.63.

3.35. 7-Methoxy-2-naphthyl *O*-(β-D-galactopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-xylopyranoside (7)

Compound **42** (550 mg, 0.39 mmol) was treated as described for the preparation of **3**. Crystallization of the

residue from MeOH gave **7** (225 mg, 91%); mp 176–178 °C; $[\alpha]_D^{22}$ −7 (*c* 1.0, $(CH_3)_2SO$); ^1H NMR (250 MHz, 1:1, $(CD_3)_2SO/D_2O$): carbohydrate ring protons (see Table 4); δ 7.70–6.90 (m, 6H, aromatic H), 3.81 (s, 3H, OCH_3); ^{13}C NMR (62.8 MHz, 1:1, $(CD_3)_2SO/_2O$): see Table 5; ESIMS: *m*/*z* 630.5 $[M]^-$. Anal. Calcd for $C_{28}H_{38}O_{16}$: C, 53.33; H, 6.07. Found: C, 53.17; H, 6.12.

3.36. 7-Methoxy-2-naphthyl *O*-(β-D-galactopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-2-*O*-disodium phosphonato-β-D-xylopyranoside (8)

Compound **40** (400 mg, 0.24 mmol) was treated as described for the preparation of **4** to give **8** (160 mg, 88%) as a white powder; $[\alpha]_D^{22}$ −29 (*c* 1.0, H_2O); ^1H NMR (250 MHz, D_2O): carbohydrate ring protons (see Table 4); δ 7.80–6.95 (m, 6H, aromatic H), 3.82 (s, 3H, OCH_3); ^{13}C NMR (62.8 MHz, D_2O): see Table 5; ^{31}P NMR (162 MHz, D_2O); δ 3.85 (s); ESIMS: *m*/*z* 709.5 $[M-2Na+H]^-$. Anal. Calcd for $C_{28}H_{37}Na_2O_{19}P$: C, 44.57; H, 4.94. Found: C, 44.28; H, 5.07.

3.37. 7-Methoxy-2-naphthyl *O*-(6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-xylopyranoside (9)

Compound **43** (340 mg, 0.23 mmol) was treated as described for the preparation of **5** to give **9** (145 mg, 84%) as a white powder; $[\alpha]_D^{22}$ −27 (*c* 1.0, H_2O); ^1H NMR (250 MHz, D_2O): carbohydrate ring protons (see Table 4); δ 7.85–6.90 (m, 6H, aromatic H), 3.81 (s, 3H, OCH_3); ^{13}C NMR (62.8 MHz, D_2O): see Table 5; ESIMS: *m*/*z* 709.5 $[M-Na]^-$. Anal. Calcd for $C_{28}H_{37}NaO_{19}S$: C, 45.90; H, 5.09. Found: C, 45.63; H, 5.21.

3.38. 7-Methoxy-2-naphthyl *O*-(6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-2-*O*-disodium phosphonato-β-D-xylopyranoside (10)

Compound **41** (300 mg, 0.18 mmol) was treated as described for the preparation of **6** to give **10** (121 mg, 78%) as a white powder; $[\alpha]_D^{22}$ −25 (*c* 1.0, H_2O); ^1H NMR (250 MHz, D_2O): carbohydrate ring protons (see Table 4); δ 7.80–6.95 (m, 6H, aromatic H), 3.83 (s, 3H, OCH_3); ^{13}C NMR (62.8 MHz, D_2O): see Table 5; ESIMS: *m*/*z* 811.6 $[M-2Na+H]^-$. Anal. Calcd for $C_{28}H_{36}Na_3O_{22}PS$: C, 39.26; H, 4.24. Found: C, 38.98; H, 4.37.

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