Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 16 (2005) 83–95

Synthesis of fully protected α-L-fucopyranosyl-(1→2)-β-D-galactopyranosides with a single free hydroxy group at position 2′, 3′ or 4′ using *O*-(2-naphthyl)methyl (NAP) ether as a temporary protecting group

Zoltán B. Szabó,[a] Anikó Borbás,[a] István Bajza[a] and András Lipták[a,b,*]

[a]*UD-HAS Research Group for Carbohydrates, PO Box 55, H-4010 Debrecen, Hungary*
[b]*Department of Biochemistry, Faculty of Sciences, University of Debrecen, Egyetem tér 1, H-4032 Debrecen, Hungary*

Received 13 October 2004; accepted 23 November 2004
Available online 21 December 2004

This article is dedicated to the memory of the outstanding chemist and excellent colleague Christian Pedersen

Abstract—Perbenzylated methyl α-L-fucopyranosyl-(1→2)-β-D-galactopyranosides having a single free OH group at position C-2′, C-3′ or C-4′ have been synthesized. Methyl 3,4,6-tri-*O*-benzyl-β-D-galactopyranoside was glycosylated either with phenyl 3,4-di-*O*-benzyl-2-*O*-(2-naphthyl)methyl-, phenyl 2,4-di-*O*-benzyl-3-*O*-(2-naphthyl)methyl- or phenyl 2,3-di-*O*-benzyl-4-*O*-(2-naphthyl)-methyl-1-thio-β-L-fucopyranoside. The 2-ONAP ether functioned well as a non-participating group. The yields of the glycosylation reactions, promoted by NIS/TfOH, were above 80% and the stereoselectivity was 8:1 to 10:1 in favour of the α-anomers. The 2-ONAP ether was obtained by (2-naphthyl)methylation, the 3-ONAP and the 4-ONAP ethers were prepared either by hydrogenolysis of the 3,4-*O*-(2-naphthyl)methylene acetals of β-L-fucopyranoside or by tin acetal-mediated alkylations. The latter procedure afforded higher yields. The ONAP ethers from the disaccharides were removed by oxidative cleavage with DDQ.

1. Introduction

Skp1 is a 21 kD protein, a subunit of the SCF-E3 ubiquitin ligases and other protein complexes in the nucleus and cytoplasm of yeast and mammalian cells.[1] In *Dictyostelium* it is partially modified by a complex, unusual pentasaccharide *O*-linked to hydroxyproline 143.[2,3] Since glycoproteins play extremely important biological roles, the biosynthesis of hundreds of glycoproteins are known. These investigations suggested that protein glycosylation occurred exclusively on extracellular or lumenal polypeptides. Today it is well known that a huge number of glycosylated proteins are located in the nuclear and cytoplasmic compartment in the cell.[4] It seems very probable that complex glycosylation can occur in these compartments,[5–7] too. Recently, structural investigations of the cytoplasmic protein called Skp1, isolated from the slime mould *Dictyostelium discoideum*, have unequivocally confirmed that complex *O*-glycosylation can take place in the cytoplasm of a eukaryote.[2] The pentasaccharide is linear, and the rough structure can be described by the following abbreviated form: Hex → Hex → Fuc → Hex → HexNAc. The attachment site was verified by Edman degradation and proved to be hydroxyproline. After methanolysis, the aminosugar HexNAc was identified as GlcNAc. Exoglycosidase digestion of glycopeptide Skp1 and MALDI-TOF MS analysis of the digestum suggested the following pentasaccharide structure: α-D-Galp-(1→6)-α-D-Galp-(1→?)-α-L-Fucp-(1→2)-β-D-Galp-(1→3)-β-D-GlcpNAc-(1 → Hy pro).[2] It is worth mentioning that in the meantime a β-D-Galp-(1→6)-β-D-Galp-(1→ structure was also proposed for the non-reducing disaccharide end, and the outer β-D-Galp-(1→6)-β-D-Galp-(1→?)-L-Fuc cap structure has not been found elsewhere. It is also interesting to note that the core trisaccharide, α-L-Fucp-(1→2)-β-D-Galp-(1→3)-β-D-GlcpNAc is equivalent to blood group H (type 1) expressed by mammalian cells.[5]

* Corresponding author. Tel.: +36 52 512900x2256; fax: +36 52 512913; e-mail: liptaka@tigris.klte.hu

0957-4166/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2004.11.056

The most delicate question connected with the structure of the pentasaccharide of Skp1 is the branching point of the α-L-Fucp residue. To help answering this question we decided to synthesize the partially protected three α-L-Fucp-(1→2)-β-D-Galp disaccharides carrying separately a free OH group at position 2′-, 3′- and 4′, which could be the building blocks for the preparation of the desired pentasaccharides.

2. Results and discussion

2.1. Preparation of the NAP ethers via (2-naphthyl)-methylene acetal derivatives

Since in the planned disaccharides the galactopyranoside unit has a β-anomeric configuration we selected methyl 3,4,6-tri-*O*-benzyl-β-D-galactopyranoside **1** (Fig. 1) as a model acceptor compound. For the synthesis of **1** a published procedure[8] was followed. To construct a 1,2-*cis*-L-fucopyranosyl glycosidic bond, a non-participating group at position two is necessary, which is a benzyl or a substituted benzyl in most cases. The real break-through in the syntheses of the α-L-fucopyranosyl unit-containing oligosaccharides occurred in 1975 when Lemieux[9] introduced the in situ anomerization reaction of a peracetylated α-glycosyl bromide into the more reactive β-anomer. This methodology worked successfully also in the case of 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide and the Lewis A blood-group antigenic determinant was synthesized. Nowadays, perbenzylated thio-glycosides compete with the Lemieux method and it is especially true for the synthesis of the α-L-fucopyranoside-containing oligosaccharides. Since the thioglycosides are more stable than the glycosyl bromides they have been used regularly over the last 5–6 years. We selected therefore the derivatives of phenyl 1-thio-β-L-fucopyranoside. In search of 2′-hydroxy-, 3′-hydroxy- and 4′-hydroxy otherwise fully protected α-L-fucopyranosyl-(1→2)-β-D-galactopyranoside derivatives in the literature only one report could be found when Hindsgaul and co-workers[10] synthesized octyl 2′-*O*-methyl-, 3′-*O*-methyl- and 4′-*O*-methyl-α-L-fucopyranosyl-(1→2)-β-D-galactopyranoside and octyl 2′,6′-dideoxy-α-L-*lyxo*-hexopyranosyl-,3′,6′-dideoxy-α-L-*xylo*-hexopyranosyl- and 4′,6′-dideoxy-α-L-*xylo*-hexopyranosyl-(1→2)-β-D-galactopyranoside disaccharides, which were used as substrates in enzymatic investigations. In that case the acceptor was octyl 3,4,6-tri-*O*-benzyl-β-D-galactopyranoside and ethyl 3,4-di-*O*-benzyl-2-*O*-(*p*-methoxy)benzyl-1-thio-β-L-, ethyl 3-*O*-acetyl-2,4-di-*O*-benzyl-1-thio-β-L- and ethyl 4-*O*-acetyl-2,3-di-*O*-benzyl-1-thio-β-L-fucopyranosides were used as the donors. The yields were 67%, 71% and 71%, respectively. These authors did not observe any formation of the β-anomers.

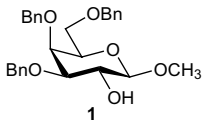
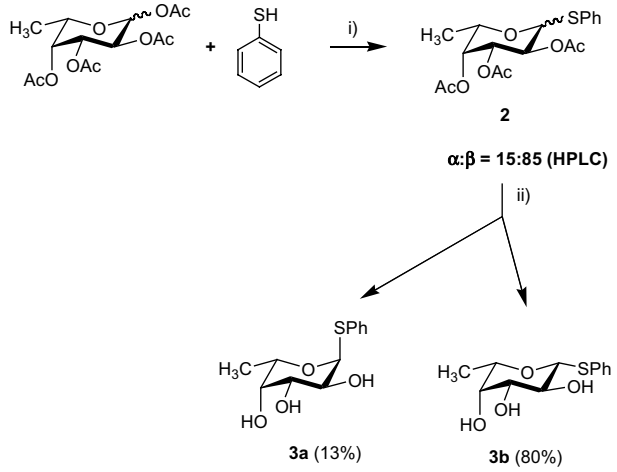


Figure 1. Structure of the acceptor used.[8]

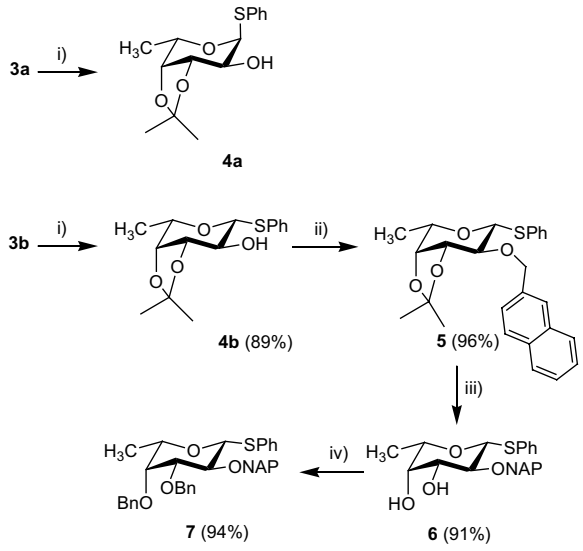
Recently, it was reported that the (2-naphthyl)methyl (NAP) ethers were excellent protecting groups in carbohydrate chemistry[11–14] and these ethers could be generated by the hydrogenolysis of dioxane[15,16] and dioxolane-type (2-naphthyl)methylene acetals.[15,17] To extend the use of the NAP ethers to the syntheses of fucose-containing oligosaccharides we decided to prepare phenyl 3,4-di-*O*-benzyl-2-*O*-(2-naphthyl)methyl-1-thio **7**, phenyl 2,4-di-*O*-benzyl-3-*O*-(2-naphthyl)methyl-1-thio **13** and phenyl 2,3-di-*O*-benzyl-4-*O*-(2-naphthyl)methyl-1-thio-β-L-fucopyranoside **14** and use them as glycosyl donors.

Treatment of peracetylated L-fucopyranose with thiophenol in the presence of $BF_3{\cdot}Et_2O$ has been described by Hasegawa and co-workers.[18] In our case the ratio of the α:β anomers **2** was 15:85, as determined by HPLC. Zemplén deacetylation of the anomeric mixture **2** resulted in the crystalline β-anomer **3b** obtained from an ethanol–hexane solvent system. The α-anomer **3a** was isolated as a syrup after chromatographic purification. The overall yield of the three steps was 80% for **3b** (Scheme 1).



Scheme 1. Preparation of phenyl 1-thio-α- and β-L-fucopyranosides. Reagents and conditions: (i) $BF_3{\cdot}Et_2O$, CH_2Cl_2, overnight, 0 °C; (ii) NaOMe, MeOH, rt.

Acetalation of **3b** with 2,2-dimethoxypropane furnished the crystalline **4b**,[33] from an ether–hexane solvent mixture, with a yield of 89%. Naphthylmethylation of **4b** yielded the crystalline compound **5** (96%). Acid hydrolysis of the isopropylidene group from **5** afforded the likewise crystalline **6** with 91% yield. Benzylation of **6** proceeded, again, with high yield (94%) and the new compound **7**, the first required glycosyl donor, was crystalline (Scheme 2). The $[\alpha]_D$ values given in the literature for compounds **3b**[18] and **4b**[34] were different from the values measured in our laboratory. To solve this problem the C-1, H-1 coupling constants for compounds **3a**, **3b**, **4a** and **4b** (α and β pairs) were determined on a Bruker 360 MHz apparatus and the specific rotatory values



Scheme 2. Preparation of phenyl 3,4-di-*O*-benzyl-2-*O*-(2-naphthyl)-methyl-1-thio-β-L-fucopyranoside. Reagents and conditions: (i) 2,2-dimethoxypropane, pTSA, 48 h, rt; (ii) NaH, NAPBr, DMF, 2 h, rt; (iii) $HCl_{(aq)}$–MeOH, 2 h, 50 °C; (iv) NaH, BnBr, DMF, 3 h, rt.

were, where available, compared to that of D-enantiomers.

Our retrosynthetic analysis showed that the other two glycosyl donors **13** and **14** might be synthesized from the *exo*- **9*exo*** and *endo*-naphthyl **9*endo*** isomers of phenyl 3,4-*O*-(2-naphthyl)methylene-1-thio-β-L-fucopyranoside.

It is well documented that the direction of the hydrogenolysis of the dioxolane-type acetals is independent of the reagent, but rather depends on the configuration of the acetalic carbon atom: *equatorial* ethers are obtained from the *exo*-(alkyl,aryl)-acetals; the *endo*-isomers, on the other hand, react in an opposite way and *axial* ethers are produced. Up to now the dioxolane-type (2-naphthyl)methylene acetals of fucose derivatives have not been investigated, but the ring cleavage of the (2-naphthyl)methylene acetals of rhamnosides[17] followed the general rules.

Completion of the reaction of **3b** with two equivalents of 2-(dimethoxymethyl)naphthalene **8** (Fig. 2) in DMF required 7 days and three products could be detected. The compound with the highest chromatographic mobility proved to be the 3,4-*O*-(*exo*-2-naphthyl)methylene acetal **9*exo***, its isolated yield was 22%. Compound having the lowest mobility was the 3,4-*O*-(*endo*-2-naphthyl)methylene acetal **9*endo*** (25%, Scheme 3). The third product having a medium chromatographic mobility was a so-called mixed acetal: phenyl 2-*O*-*R*/*S*(methoxy-2′-naphthyl)methyl-3,4-*O*-(*endo*-2-naphthyl)-methylene-1-thio-β-L-fucopyranoside **10** (6%) which proved to be a single diastereomer, but its absolute configuration has not been determined. Replacement of DMF by CH_3CN in the transacetalization reaction considerably reduced the reaction time to several hours under reflux conditions, and the conversion was also higher. However, the separation of the **9*exo*** and **9*endo*** isomers still remained the bottleneck of this synthetic route because of their low stability on silica. Nevertheless, all three compounds were crystalline, and their ^{1}H and ^{13}C NMR spectra verified the postulated structures.

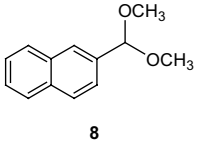


Figure 2. 2-(Dimethoxymethyl)-naphthalene used for the preparation of (2-naphthyl)methylene acetals of glycosides.

Hydrogenolysis of the acetals **9*exo*** and **9*endo*** proceeded smoothly and with complete stereoselectivity. The acetal ring cleavage required only AlH_3 ($LiAlH_4/AlCl_3$ = 3:1) and the reaction time was 15–20 min at room temperature. Compound **9*exo*** furnished the 3-*O*-NAP ether **11** (97%) and the **9*endo*** gave the 4-*O*-NAP ether **12** (98%). The structure of compound **10** was confirmed also by hydrogenolysis, and it produced compound **12** under cleavage conditions, showing that the cyclic acetal ring had the *endo* configuration. This reaction did not give any information about the absolute configuration of the mixed acetal at position 2.

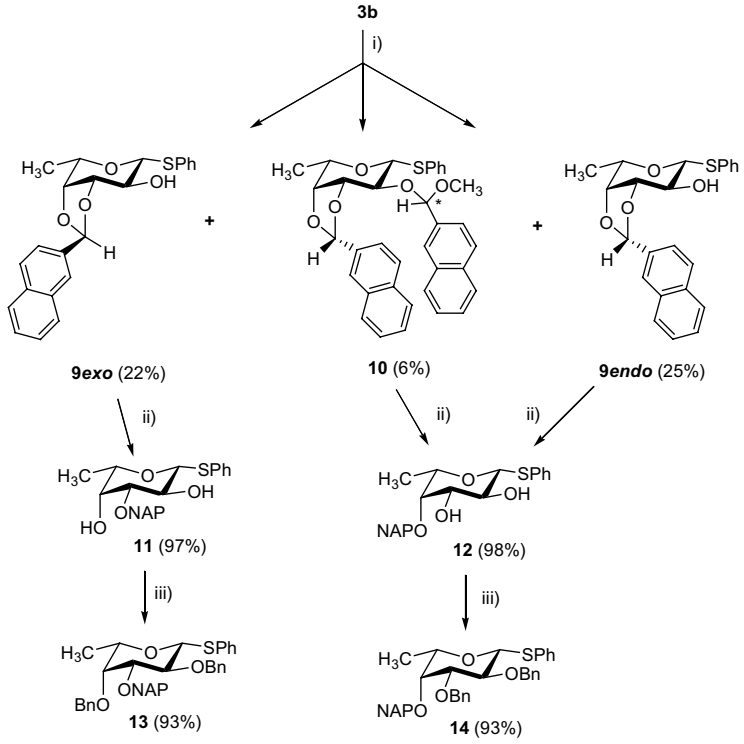
Since the chromatographic separation of compounds **11** and **12** can be easily achieved, hydrogenolysis of the acetal mixture **9*exo*/*endo***, **10** and separation of compounds **11** and **12** resulted in higher yields than the step-by-step isolation of the intermediates of the whole synthesis.

Benzylation of compound **11** yielded the fully protected second glycosyl donor **13**, similarly compound **12** gave the third glycosyl donor **14** under the same conditions. In both cases the yields were above 90%.

2.2. Preparation of the NAP ethers via stannylene derivatives

To shorten the synthesis and increase the yields during the preparation of compounds **13** and **14** our attention turned to the stannylene acetal method.[20–22]

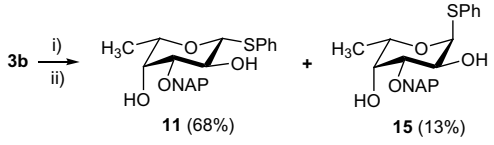
Selective acylation, alkylation or aralkylation of 1,2-, 1,3-diols or even polyols can be achieved by the so-called stannylenation. The procedure involves a stannylene formation step, when the appropriate diol is heated with Bu_2SnO, either under the azeotropic removal of water (in benzene or toluene), or in dry methanol, without the removal of water. The formed stannylene derivative is directly reacted with the alkylating agent in DMF in the presence of $Bu_4N^+Br^-$ or I^-, or caesium fluoride.[22] In the course of the alkylating step the more reactive oxygen atom of the tin acetal is alkylated, in the case of *cis*-diols it is the oxygen atom in *equatorial* position. Firstly, our thio-fucoside compounds were reacted with dibutyltin oxide in methanolic solution then with 2-(naphthyl)methyl bromide in DMF, but no aralkylated product was formed. On the other hand, when the



Scheme 3. Preparation and hydrogenolysis of 2-(naphthyl)methylene acetals of phenyl 1-thio-β-L-fucopyranoside. Reagents and conditions: (i) 2-naphthaldehyde-dimethylacetal, CSA, DMF, 7 days, rt; (ii) $LiAlH_4/AlCl_3$ (3:1), CH_2Cl_2/Et_2O (1:1), 15 min, rt; (iii) NaH, BnBr, DMF, 3 h, rt.

acetalization step was carried out in toluene, the aralkylation proceeded satisfactorily, indicating that the acetal formation was not successful in methanol. 2-(Naphthyl)methyl bromide was applied only most recently by Matta and co-workers[23] for the aralkylation of dibutyltin acetals.

Treatment of compound **3b** with Bu_2SnO and subsequent aralkylation with 2-(naphthyl)methyl bromide in DMF gave two products. The main and faster moving product proved to be the crystalline 3-*O*-NAP ether **11** (68%). The slower moving component was also crystalline and the NMR data gave the structure: phenyl 3-*O*-(2-naphthyl)methyl-1-thio-α-L-fucopyranoside **15**, showing that the β-anomer partly anomerized into the α-anomer, the yield was 13% (Scheme 4).



Scheme 4. 2-(Naphthyl)methylation of compound **3b** under tin-mediated conditions. Reagents and conditions: (i) Bu_2SnO, toluene, 3 h, reflux; (ii) NAPBr, CsF, DMF, 18 h, rt.

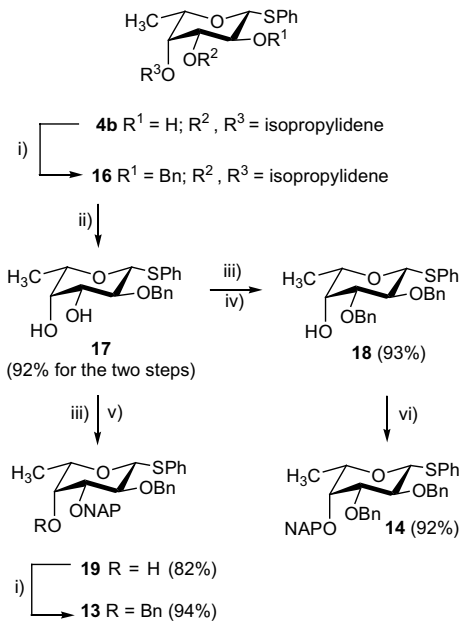
Compound **4b** was benzylated with 1.2 equiv of benzyl bromide in the presence of NaH and the crystalline **16** was treated with $HCl_{(aq)}$–MeOH at 50 °C for 2.5 h and crystalline **17** was isolated with 92% yield for the two steps. Compound **17** was stannylenated and the crude reaction product was benzylated with benzyl bromide in DMF to give the crystalline compound **18** (93%). Conventional (2-naphthyl)methylation of **18** proceeded with an excellent yield (92%) and furnished compound **14**.

The 2-*O*-benzyl ether **17** of phenyl β-L-fucopyranoside was naphthylmethylated under tin-mediated conditions to obtain **19** (82%), the benzylation of which resulted in compound **13** (94%, Scheme 5).

In summary all three planned glycosyl donors **7**, **13** and **14** were prepared, compound **13** and **14** were synthesized either by the reductive (AlH_3) hydrogenolysis of the diastereomeric dioxolane-type (2-naphthyl)methylene acetals or by tin-mediated regioselective alkylation. Both methods proceeded with excellent selectivity, the latter with very high yields.

2.3. Synthesis of partially protected α-L-fucopyranosyl-(1→2)-β-D-galactopyranosides

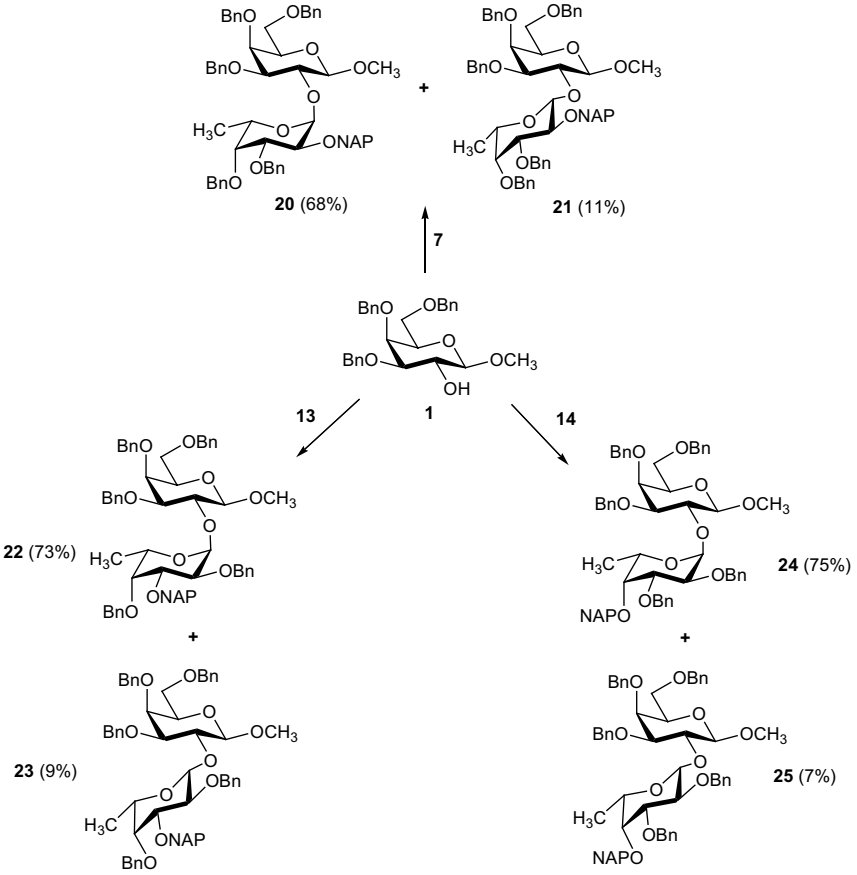
For the preparation of a 1,2-*cis*-fucopyranosyl bond a non-participating protecting group at 2-OH is necessary. Searching the literature for 2-*O*-alkyl 1-thio-fucopyranosyl derivatives the following compounds were found: methyl 1-thio-β-L-fucopyranoside with 2-*O*-benzyl,[19] 2-*O*-*p*-methoxy-benzyl,[24] ethyl 1-thio-β-L-fucopyranoside with 2-*O*-benzyl,[25] 2-*O*-*p*-chlorobenzyl,[26] 2-*O*-methyl,[27] 2-*O*-[2-(benzoylhydroxy)ethyl][28] and 2-*O*-[2-(trimethylsilyl)ethoxymethoxybenzyl],[29] *p*-tolyl 1-thio-β-L-fucopyranoside with a 2-*O*-benzyl,[30] phenyl 1-thio-β-L-fucopyranoside with 2-*O*-benzyl,[31] and *p*-(chloro)phenyl 1-thio-β-L-fucopyranoside with 2-*O*-benzyl[32] protecting groups.



Scheme 5. Synthesis of compounds **13** and **14** using the stannylene acetal method. Reagents and conditions: (i) NaH, BnBr, DMF, 2 h, rt; (ii) $HCl_{(aq)}$–MeOH, 2.5 h, 50 °C; (iii) Bu_2SnO, toluene, 3 h, reflux; (iv) BnBr, CsF, DMF, 18 h, rt; (v) NAPBr, CsF, DMF, 18 h, rt; (vi) NaH, NAPBr, DMF, 3 h, rt.

For our synthetic plans the 2′-OH, 3′-OH and 4′-OH derivatives of the α-L-fucopyranosyl-(1→2)-β-D-galactopyranoside might be prepared by using the glycosyl donors **7**, **13** and **14**. The 2-*O*-NAP ether of thio-fucosides for the preparation of the 1,2-*cis*-fucopyranosyl bond has not been used yet.

The selected aglycone, compound **1**,[8] was glycosylated with the donor **7**. The coupling reaction was achieved by NIS/TfOH promotor in dry dichloromethane at −30 °C and the major product **20** was obtained in a yield of 68%. Its structure was confirmed by ^1H, ^{13}C NMR spectra. A small amount of the β-anomer **21** was also detected in the reaction mixture and it was also isolated and characterized. Under similar conditions as above, coupling of compounds **1** and **13** resulted in 73% of the disaccharide **22**, and in this case the β-anomer **23** could also be isolated in pure form and the spectroscopic investigations verified their structures. The third coupling reaction between compounds **1** and **14** proceeded also smoothly and again both anomers were detected and isolated. The yield of the α-anomer **24** reached 75%, the β-anomer **25** was present in approx. 10% (Scheme 6). The ^1H–^1H COSY and HMQC experiments for compounds **7** and **20**–**25** were preformed on a Bruker 360 MHz spectrometer at 298 K. Comparing the



Scheme 6. Synthesis of L-fucopyranosyl-(1→2)-D-galactopyranoside derivatives. Conditions: 1.5 equiv of donor **7**, **13** and **14**, 2.25 equiv of NIS, 0.38 equiv of TfOH, CH_2Cl_2, −30 °C, 20 min.

Table 1. ^{1}H NMR chemical shifts (δ in ppm) and coupling constants (J in Hz) for compounds **7** and **20**–**25**

	Monosaccharide unit	H-1, $J_{1,2}$	H-2, $J_{2,3}$	H-3, $J_{3,4}$	H-4, $J_{4,5}$	H-5, $J_{5,6a}$	H-6a, $J_{gem.}$	H-6b, $J_{5,6b}$	OMe
7	β-L-Fuc	4.63d, 9.3	3.99t, 9.3	3.61dd, 2.8	3.63d, 2.8	3.53m, 6.4	1.27d, 6.4		—
20	β-D-Gal	4.40d, 7.7	4.23dd, 9.7	3.75dd, 2.7	3.96bd, 2.8	3.64–3.54m	3.64–3.54m	3.64–3.54m	3.46s
	α-L-Fuc	5.68d, 3.8	4.09dd, 10.2	3.97dd, 2.7	3.70bd, 2.8	4.31m, 6.5	1.12d, 6.5		—
21	β-D-Gal	4.26d, 7.6	4.21dd, 8.9	3.51dd, 2.8	3.89d, 2.9	3.60–3.52m	3.60–3.52m	3.60–3.52m	3.42s
	β-L-Fuc	4.85d, 7.7	3.83dd, 9.0	3.56dd, 3.0	3.60–3.52m	3.34d, 6.4	1.12d, 6.4		—
22	β-D-Gal	4.37d, 7.7	4.22dd, 9.7	3.73dd, 2.7	3.94bd, 2.8	3.64–3.54m	3.64–3.54m	3.64–3.54m	3.44s
	α-L-Fuc	5.66d, 3.7	4.08dd, 10.1	4.00dd, 2.7	3.71bd, 2.7	4.31bd, 6.5	1.14d, 6.5		—
23	β-D-Gal	4.39d, 7.6	4.33dd, 9.0	3.66dd, 3.0	4.03d, 3.0	3.75–3.65m	3.75–3.65m	3.75–3.65m	3.56s
	β-L-Fuc	4.96d, 7.6	3.94dd, 9.7	3.70dd, 2.9	3.75–3.65m	3.44d, 6.5	1.23d, 6.4		—
24	β-D-Gal	4.37d, 7.7	4.20dd, 9.7	3.73dd, 2.8	3.94bd, 2.9	3.62–3.55m	3.62–3.55m	3.62–3.55m	3.44s
	α-L-Fuc	5.66d, 3.8	4.08dd, 10.1	3.96dd, 2.7	3.73bd, 2.8	4.31bd, 6.5	1.14d, 6.5		—
25	β-D-Gal	4.36d, 7.6	4.30dd, 8.9	3.63[a]	4.00d, 2.7	3.72–3.56m	3.72–3.56m	3.72–3.56m	3.53s
	β-L-Fuc	4.94d, 7.6	3.91d, 8.0	3.63[a]	3.72–3.65m	3.41d, 6.4	1.21d, 6.3		—

[a] Overlap.

Table 2. ^{13}C NMR data (δ in ppm) for compounds **7** and **20**–**25**

	Monosaccharide unit	C-1	C-2	C-3	C-4	C-5	C-6	OMe
7	β-L-Fuc	87.8	77.4	84.8	76.9	74.9	17.6	—
20	β-D-Gal	102.8	72.9	83.9	71.8	73.2	68.8	56.4
	α-L-Fuc	97.3	75.5	79.5	77.7	66.3	16.4	—
21	β-D-Gal	104.5	77.2	81.4	73.5	73.3[a]	68.9	57.0
	β-L-Fuc	102.7	80.2	82.7	76.9[a]	70.0	16.8	—
22	β-D-Gal	102.8	72.8	83.9	71.9	73.1	68.7	56.4
	α-L-Fuc	97.3	75.6	79.5	77.8	66.2	16.4	—
23	β-D-Gal	104.4	77.1	81.5	73.3	73.5[a]	68.9	56.9
	β-L-Fuc	102.7	80.2	82.5	77.0[a]	70.0	16.8	—
24	β-D-Gal	102.9	72.8	83.9	71.9	73.2	68.8	56.4
	α-L-Fuc	97.4	75.7	79.7	77.5	66.3	16.5	—
25	β-D-Gal	104.5	77.3	81.7	73.5	73.5[a]	69.0	57.1
	β-L-Fuc	102.9	80.3	82.8	76.9[a]	70.1	17.0	—

[a] Interchangeable assignments.

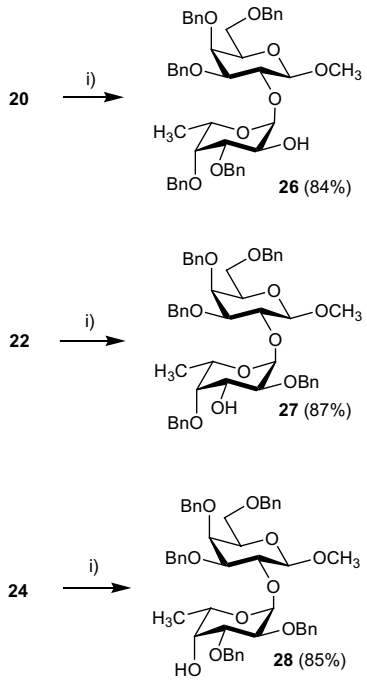
obtained data with the spectra of methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-galactopyranoside described by Watt et al[8]., it turned out that the (2-naphthyl)methylated carbon atoms resonated at higher fields than the benzylated ones. For the protons attached to the (2-naphthyl)methylated carbon a shift to the lower magnetic field was observed. These differences are not very large but they are characteristic and could only be observed in the case of the α-L-fucopyranosyl unit-containing disaccharides. The β-anomers did not show such a behaviour. The chemical shift data and the coupling constants of compounds **7** and **20**–**25** are collected in Tables 1 and 2.

Having our three target disaccharides **20**, **22** and **24**, the last steps were aimed at the removal of the NAP ethers and the regeneration of the OH-2′, OH-3′ and OH-4′. It was shown earlier that the NAP ethers could be hydrogenolyzed in the presence of benzyl ethers and esters[28] and they are less sensitive to acids than the *p*-methoxybenzyl ethers. The most important observation, however, is that the NAP ethers can easily be removed by DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) under conditions when the other usual protecting groups such as acetyl, pivaloyl, phthalimido, benzyl and benzylidene survive.[11,12,15]

Compounds **20**, **22** and **24** were treated, separately, with 1.5 equiv of DDQ in dichloromethane–methanol (4:1) at room temperature for 3 h. In each case complete conversion of the starting material was observed by TLC and the monohydroxy derivatives, OH-2′ **26** (84%), OH-3′ **27** (87%) and OH-4′ **28** (85%), were obtained and characterized (Scheme 7).

3. Conclusion

In the synthesis of the perbenzylated α-L-Fucp-(1→2)-β-D-Galp-(1→OMe) disaccharides carrying a single free OH group either at position C-2′, C-3′ or C-4′, all of the three possible regioisomers of phenyl di-*O*-benzyl-mono-*O*-(2-naphthyl)methyl-1-thio-β-L-fucopyranoside were used as glycosyl donors. For the easy preparation



Scheme 7. Deprotection of the NAP group from disaccharides **20**, **22**, **24**. Reagents and conditions: (i) DDQ, CH_2Cl_2/MeOH = 4:1, 3 h, rt.

of the regioisomeric *O*-NAP ethers different methods were presented. In each case the *O*-NAP group served successfully as a temporary protecting group and could be cleaved in the presence of benzyl groups. It also acted as a non-participating substituent and governed the formation of an 1,2-*cis*-fucopyranosyl interglycosidic bond at position C-2. The method presented for the preparation of the disaccharides can be utilized for the total synthesis of those pentasaccharides and oligosaccharides, that involve a non-terminal L-fucose unit.

4. Experimental

4.1. General methods

Optical rotations were measured at room temperature with a Perkin–Elmer 241 automatic polarimeter. Melting points were determined on a BÜCHI-B-540 apparatus and are uncorrected. TLC was performed on Kieselgel 60 F_{254} (Merck) with detection by charring with 50% aqueous sulfuric acid. Column chromatography was performed on Silica Gel 60 (E. Merck 0.062–0.200 mm). The organic solutions were dried over $MgSO_4$ and concentrated in vacuo. The ^1H (200 and 500 MHz) and ^{13}C (50.30, 125.76 MHz) spectra were recorded with Bruker WP-200SY, Bruker AC-200 and Bruker DRX-500 spectrometers for solutions in $CDCl_3$, or CD_3OD. The ^1H–^1H COSY and HMQC measurements for compounds **7** and **20**–**25** were performed on Bruker 360 MHz spectrometer at 298 K in $CDCl_3$. Internal references: TMS (0.00 ppm for ^1H), $CDCl_3$ (77.00 ppm for ^{13}C), CD_3OD (49.05 ppm for ^{13}C). The ratio of compounds **2a** and **2b** in the reaction mixture was determined by HPLC (Merck Hitachi) using a Purospher Si 3 μm column, a diode array detector (λ = 256 nm) with a flow rate of 0.5 mL/min. The composition of the eluent was hexane/EtOAc = 89:11, **2a** (R_f = 9.76 min), **2b** (R_f = 15.15 min).

4.2. General method A for performing aralkylation reactions (for compounds 5, 7, 13, 14, 16)

The starting material (10 mmol) was dissolved in dry DMF (15 mL) and cooled to 0 °C. NaH (12 mmol, 1.2 equiv, 60%, previously treated with hexane) was added carefully to the mixture and stirred for half an hour. Then the aralkylating agent (12 mmol, 1.2 equiv) was added to the mixture. Reactions usually reached completion within 2–3 h. The excess NaH was decomposed by the addition of some drops of MeOH and the solvent was evaporated in vacuo. The residue was dissolved in DCM and was extracted three times with water, then the organic layer was dried and the solvent was evaporated.

4.3. General method B for the hydrogenolysis of (2-naphthyl)methylene acetals of 1-thio fucosides (for compounds 11, 12)

To a solution of the starting acetal compound (6.0 mmol) in a mixture of dry DCM and dry Et_2O (20 mL and 10 mL), $LiAlH_4$ (27 mmol, 4.5 equiv) was added and the resulting mixture was cooled to 0 °C. Then a solution of anhydrous $AlCl_3$ (9.0 mmol, 1.5 equiv) in dry Et_2O (10 mL) was added dropwise to the mixture. Reactions usually reached completion within 15–20 min. The reaction mixture was diluted with Et_2O (200 mL) and the excess of $LiAlH_4$ was decomposed by the addition of a small amount of EtOAc and careful addition of water. The solution was decanted, poured into a separatory funnel and was extracted three times with water. The solution was then dried and evaporated, the crude product was purified either by crystallization or by column chromatography.

4.4. General method C for performing aralkylation reactions via a stannylene acetal (for compounds 11, 15, 18, 19)

A mixture of the starting material (3.0 mmol) and Bu_2SnO (3.9 mmol, 1.3 equiv) was suspended in dry toluene (25 mL) and was refluxed for three hours under a Dean–Stark apparatus. Then CsF (6.0 mmol, 2.0 equiv) was added to the solution and following another 10 min refluxing the solvent was evaporated to dryness in vacuo. The residue was redissolved in dry DMF (20 mL) and the aralkylating agent (6.0 mmol, 2.0 equiv) was added. Reactions usually took place within 16–18 h. Then the reaction mixture was diluted with DCM (250 mL), the precipitating salts were filtered through a Celite layer, and the filtrate was extracted with water and saturated NaCl solution, dried and evaporated.

4.5. General method D for fucosylation reactions (for compounds 20–25)

To a solution of the galactoside acceptor **1**[8] (0.50 mmol) and the appropriate fucoside donor (0.75 mmol,

1.5 equiv) in dry DCM (5 mL), 4 Å molecular sieves (0.5 g) were added and the mixture was stirred for 1 h at room temperature. Then the solution was cooled to −30 °C and a mixture of *N*-iodosuccinimide (0.253 g, 1.12 mmol, 2.25 equiv) and trifluoromethanesulfonic acid (16.5 μL, 0.19 mmol, 0.38 equiv) dissolved in 1:1 mixture of dry THF and dry DCM (1 mL) was added to promote the reaction. The colour of the solution turned into deep brown immediately after the addition of the promoter. The mixture was kept at −30 °C for 20 min when t.l.c. (DCM/acetone = 97:3) showed the disappearance of the acceptor. It was then neutralized with Et_3N and allowed to warm up. The mixture was filtered and the filtrate was diluted with DCM, washed twice with 5% $Na_2S_2O_3$ and once with satd. $NaHCO_3$ solutions. The organic layer was dried, evaporated and the syrupy residue was purified by column chromatography (DCM/acetone = 99:1 → 98:2) and the α and β isomers were separated.

4.6. General method E for the deprotection of (2-naphthyl)methyl ethers of glycosides by DDQ (for compounds 26–28)

The starting material (0.2 mmol) was dissolved in a mixture of DCM and MeOH (4:1, 2 mL) and freshly crystallized DDQ (0.3 mmol, 1.5 equiv) was added. Reactions reached completion within three hours (DCM/acetone = 97:3). The reaction mixture was neutralized by the addition of Et_3N and the solvents were evaporated. The residue was purified by column chromatography.

4.6.1. Phenyl 2,3,4-tri-*O*-acetyl-1-thio-α/β-L-fucopyranoside 2a and b. To a cooled (0 °C) solution of L-fucose (42.30 g, 0.258 mol) in dry pyridine (200 mL) acetic anhydride (200 mL) was added in four portions. The reaction reached completion within six hours (hexane/acetone = 1:1, R_f = 0.85). The solution was poured onto ice water, the aqueous phase was decanted and the syrupy residue was dissolved in dichloromethane. It was extracted with 0.5 M H_2SO_4 solution, then neutralized with aqueous $NaHCO_3$. The decanted aqueous phase was also extracted with DCM and washed as indicated previously. The organic phases were dried, evaporated and the residue was directly used for the next step. The syrupy residue (85.60 g) was dissolved in dry DCM (440 mL), thiophenol (32 mL, 0.314 mol, 1.2 equiv) was added and the mixture was cooled to 0 °C. Then $BF_3{\cdot}Et_2O$ (94.6 mL, 0.769 mol, 3.0 equiv) was poured to the solution in several portions and the resulting mixture was refrigerated. The reaction reached completion overnight (DCM/acetone = 96:4, $R_{f,a}$ = 0.77, $R_{f,b}$ = 0.68). The solution was diluted with DCM (500 mL), and the excess Lewis acid was decomposed by the addition of solid $NaHCO_3$ and aqueous $NaHCO_3$. When the evolution of CO_2 ceased the phases were separated in a separatory funnel. The organic layer was washed with 1 M NaOH (2 × 600 mL) solution, then with water, dried and evaporated. A small fraction of the syrupy mixture was purified by column chromatography and the separated **2a** and **2b** compounds (both syrups) were characterized by NMR. The mixture of **2a** and **2b** was directly used for the next step. **2a**: $[\alpha]_D$ = −246.3 (*c* 0.13, $CHCl_3$), [lit:[33] $[\alpha]_D$ = −225.0 (*c* 0.47, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ (ppm): 7.45–7.28 (5H, m, arom.), 5.94 (1H, d, $J_{1,2}$ = 5 Hz, *H*-1), 5.43 (3H, m, *H*-2,3,4), 4.62 (1H, dd, *H*-5), 2.18–2.04 (9H, 3s, 3 × CH_3CO), 1.15 (3H, d, $J_{5,6}$ = 7 Hz, CH_3); ^{13}C NMR δ (ppm): 170.44, 170.12, 169.82 (3 × CH_3*C*O), 133.18, 131.69, 129.00, 127.41 (6C, arom.), 85.52 (*C*-1), 70.85, 68.56, 68.07, 65.46 (*C*-2 to *C*-5), 20.76, 20.59, 20.52 (3 × *C*H_3CO), 15.77 (*C*-6). Anal. Calcd for $C_{18}H_{22}O_7S$: C, 56.53; H, 5.80; S, 8.38. Found: C, 56.62; H, 5.83; S, 8.29.

2b: $[\alpha]_D$ = −12.8 (*c* 0.24, $CHCl_3$), [lit:[18] $[\alpha]_D$ = −3.0 (*c* 0.90, CH_3OH)][†]; ^1H NMR ($CDCl_3$) δ (ppm): 7.55–7.32 (5H, m, arom.), 5.23 (2H, m), 5.06 (2H, dd), 4.73 (1H, d, $J_{1,2}$ = 10 Hz, *H*-1), 2.18–1.97 (9H, 3s, 3 × CH_3CO), 1.24 (3H, d, $J_{5,6}$ = 6 Hz, CH_3); ^{13}C NMR δ (ppm): 170.50, 170.00, 169.36 (3 × CH_3*C*O), 132.80, 132.23, 128.76, 127.84 (6C, arom.), 86.33 (*C*-1), 73.06, 72.33, 70.26, 67.29 (*C*-2 to *C*-5), 20.75, 20.50 (3C, 3 × *C*H_3CO), 16.36 (*C*-6). Anal. Calcd for $C_{18}H_{22}O_7S$: C, 56.53; H, 5.80; S, 8.38. Found: C, 56.59; H, 5.78; S, 8.31.

4.6.2. Phenyl 1-thio-α/β-L-fucopyranoside 3a and 3b. To a solution of phenyl 1-thio-2,3,4-tri-*O*-acetyl-L-fucopyranoside α and β mixture (93.77 g, **2a** and **2b**) in dry MeOH (900 mL) a catalytic amount of NaOMe was added and the mixture was stirred for overnight. After completion the solution was neutralized by AMBERLITE IR-120 H^+ ion exchange resin, filtered and the solvent was evaporated. The syrupy crude product (64.05 g) was dissolved in hot ethanol (645 mL) and allowed to cool down. Then hexane (∼1200 mL) was added to the solution, which allowed to crystallize the β-isomer **3b** as white needles. More product could be obtained from the mother liquor by crystallization and by column chromatography (DCM/EtOAc/MeOH = 5:4:1; $R_{f,a}$ = 0.47, $R_{f,b}$ = 0.36), the latter afforded also the α-anomer in pure form.

Overall yield for **3b** including all purification steps: 53.24 g (80%); mp: 91–93 °C; $[\alpha]_D$ = −8.3 (*c* 0.13, MeOH), [lit:[18] 91–92 °C; $[\alpha]_D$ = +68.0 (*c* 0.6, MeOH)]; ^1H NMR (CD_3OD) δ (ppm): 7.55–7.28 (5H, m, arom.), 4.55 (1H, d, $J_{1,2}$ = 9 Hz, *H*-1), 3.70–3.45 (4H, m, *H*-2,3,4,5), 1.27 (3H, d, $J_{5,6}$ = 7 Hz, CH_3); ^{13}C NMR δ (ppm): 135.99, 132.21, 129.87, 128.08 (6C, arom.), 89.97 (*C*-1, $J_{C\text{-}1,H\text{-}1}$ = 155.13 Hz), 76.48, 75.97, 73.08, 70.84 (*C*-2 to *C*-5), 17.06 (*C*H_3). Anal. Calcd for $C_{12}H_{16}O_4S$: C, 56.23; H, 6.29; S, 12.51. Found: C, 56.17; H, 6.28; S, 12.58.

Overall yield for the α-isomer: 8.65 g (13%), syrup, $[\alpha]_D$ = +258.1 (*c* 0.32, MeOH); ^1H NMR (CD_3OD) δ (ppm): 7.53–7.27 (5H, m, arom.), 5.26 (1H, d, $J_{1,2}$ = 5 Hz, *H*-1), 4.03–3.70 (4H, m, *H*-2,3,4,5), 1.25 (1H, d, $J_{5,6}$ = 6 Hz, CH_3); ^{13}C NMR δ (ppm): 136.18, 132.82, 129.85, 128.24 (6C, arom.), 92.89 (*C*-1, $J_{C\text{-}1,H\text{-}1}$ =

[†] The $[\alpha]_D$ value for phenyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-fucopyranoside is +11.9 (*c* 1.0, $CHCl_3$).[34]

166.74 Hz), 87.03, 83.54, 78.35, 67.80 (*C*-2 to *C*-5), 19.79 (CH_3). Anal. Calcd for $C_{12}H_{16}O_4S$: C, 56.23; H, 6.29; S, 12.51. Found: C, 56.26; H, 6.31; S, 12.57.

4.6.3. Phenyl 3,4-*O*-isopropylidene-1-thio-α-L-fucopyranoside 4a. The title compound was prepared from **3a** similarly to **4b (4.6.4.)**. Mp: 73–75 °C; $[\alpha]_D = -295.0$ (*c* 0.14, $CHCl_3$), [lit:[35] mp: 72–74 °C; $[\alpha]_D = -278.0$ (*c* 1.1, MeOH)]; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.50 (2H, d, arom.), 7.33–7.23 (3H, m, arom.), 5.54 (1H, d, $J_{1,2} = 3.4$ Hz, *H*-1), 4.56 (1H, dd), 4.18–4.05 (3H, m), 2.44 (1H, s, O*H*), 1.43, 1.36 (6H, 2s, $2 \times CH_3$), 1.35 (3H, d, $J_{5,6} = 6.8$ Hz, $3 \times H$-6); ^{13}C NMR δ (ppm): 134.16, 131.38, 129.04, 127.30, 109.44 ($C_{acetalic}$), 88.31 (*C*-1, $J_{C\text{-}1,H\text{-}1} = 169.79$ Hz), 76.26, 75.75, 70.02, 65.41 (*C*-2 to *C*-5), 27.89, 25.92 ($2 \times CH_3$, Isp), 16.09 (*C*-6). Anal. Calcd for $C_{15}H_{20}O_4S$: C, 60.79; H, 6.80; S, 10.82. Found: C, 60.87; H, 6.81; S, 10.76.

4.6.4. Phenyl 3,4-*O*-isopropylidene-1-thio-β-L-fucopyranoside 4b. Compound **3b** (10.00 g, 39 mmol) was suspended in dimethoxypropane (35 mL) and a catalytic amount of *p*-toluenesulfonic acid were added, which was followed by the immediate clarification of the mixture. After two days t.l.c. showed a conversion above 95% (hexane/EtOAc = 6:4, $R_f = 0.60$). The solution was neutralized with some drops of Et_3N, and was evaporated. The crude product (11.44 g) was a colourless syrup, which was dissolved in diethyl ether and by the addition of hexane the crystalline product appeared as white needles. The mother liquor could be purified by column chromatography with hexane/EtOAc = 7:3 as eluent. After crystallization and chromatographic purification the yield is 10.34 g (89%), mp: 86–87 °C; $[\alpha]_D = -7.0$ (*c* 0.63, $CHCl_3$), [lit:[35] mp: 82–83 °C; $[\alpha]_D = +35.1$ (*c* 1.0, MeOH)][‡]; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.60–7.30 (5H, m, arom.), 4.43 (1H, d, $J_{1,2} = 10$ Hz, *H*-1), 4.05 (2H, m), 3.89 (1H, dd), 3.57 (1H, m), 2.88 (1H, s, O*H*), 1.43 (3H, d, $J_{5,6} = 7$ Hz, $3 \times H$-6), 1.43, 1.36 (6H, 2s, $2 \times CH_3$); ^{13}C NMR δ (ppm): 132.48, 132.12, 128.84, 127.84 (6C, arom.), 109.78 ($C_{acetalic}$), 87.65 (*C*-1, $J_{C\text{-}1,H\text{-}1} = 153.33$ Hz), 79.04, 76.18, 72.63, 71.17 (*C*-2 to *C*-5), 25.48, 23.72 ($2 \times CH_3$, Isp), 14.31 (*C*-6). Anal. Calcd for $C_{15}H_{20}O_4S$: C, 60.79; H, 6.80; S, 10.82. Found: C, 60.85; H, 6.82; S, 10.78.

4.6.5. Phenyl 3,4-*O*-isopropylidene-2-*O*-(2-naphthyl)-methyl-1-thio-β-L-fucopyranoside 5. Compound **4** (4.00 g, 13.5 mmol) was reacted with NAPBr according to General method A, to give **5** in two hours (t.l.c, hexane/EtOAc = 8:2, $R_f = 0.38$). Yield: 5.63 g (96%), mp: 132–134 °C (from EtOH), $[\alpha]_D = -11.5$ (*c* 0.27, $CHCl_3$); ^{1}H NMR ($CDCl_3$) (ppm): 7.90–7.75 (4H, m, arom.), 7.65–7.40 (5H, m, arom.), 7.38–7.23 (3H, m, arom.), 5.05–4.80 (2H, $2 \times$ d, $J_{gem.} \sim 11$ Hz, CH_2), 4.63 (1H, d, $J_{1,2} = 9$ Hz, *H*-1), 4.28 (1H, t, $J = 6$ Hz), 4.06 (1H, dd), 3.84 (1H, m), 3.59 (1H, m), 1.43 (3H, d, $J_{5,6} = 7$ Hz, $3 \times H$-6), 1.41, 1.40 (6H, $2 \times$ s, $2 \times CH_3$); ^{13}C NMR δ (ppm): 135.40, 133.76, 133.20, 133.03, 132.05, 128.68, 127.94, 127.60, 127.28, 126.97, 126.28, 125.89, 125.76 (16C, arom.), 109.63 ($C_{acetalic}$), 86.07 (*C*-1), 79.81, 78.00, 76.37, 72.36 (*C*-2 to *C*-5), 73.40 (CH_2), 27.79, 26.32 ($2 \times CH_3$, Isp), 16.82 (*C*-6). Anal. Calcd for $C_{26}H_{28}O_4S$: C, 71.53; H, 6.46; S, 7.34. Found: C, 71.42; H, 6.43; S, 7.38.

4.6.6. Phenyl 2-*O*-(2-naphthyl)methyl-1-thio-β-L-fucopyranoside 6. To a solution of **5** (4.56 g, 10 mmol) in methanol (20 mL) cc. $HCl_{(aq)}$/water = 1:3 mixture (0.7 mL cc. HCl + 2.1 mL H_2O) was added and the solution was kept at 50 °C for two hours. According to t.l.c. (DCM/EtOAc = 9:1, $R_f = 0.24$) the conversion was above 95%. The mixture was neutralized with Et_3N, evaporated in vacuo, and was co-evaporated once with toluene. The crude product was recrystallized from EtOAc–hexane solvent system, the mother liquor was purified by chromatography. Yield: 3.79 g (91%), mp: 133–134 °C, $[\alpha]_D = -27.0$ (*c* 0.21, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 7.90–7.75 (4H, m, arom.), 7.60–7.40 (5H, m, arom.), 7.37–7.25 (3H, m, arom.), 5.62–4.87 (2H, $2 \times$ d, $J_{gem.} \sim 11$ Hz, CH_2), 4.65 (1H, d, $J_{1,2} = 9$ Hz, *H*-1), 3.75–3.50 (4H, m, H-2,3,4,5), 2.50 (2H, s, $2 \times$ O*H*), 1.34 (3H, d, $J_{5,6} = 7$ Hz, CH_3); ^{13}C NMR δ (ppm): 135.44, 134.03, 133.07, 131.64, 128.92, 128.41, 127.94, 127.67, 127.40, 127.13, 126.15, 126.05 (16C, arom.), 87.37 (*C*-1), 77.89, 75.28, 74.42, 71.67 (*C*-2 to *C*-5), 75.22 (CH_2), 16.57 (*C*-6). Anal. Calcd for $C_{23}H_{24}O_4S$: C, 69.67; H, 6.10; S, 8.09. Found: C, 69.80; H, 6.07; S, 8.13.

4.6.7. Phenyl 3,4-di-*O*-benzyl-2-*O*-(2-naphthyl)methyl-1-thio-β-L-fucopyranoside 7. Compound **6** (3.10 g, 7.8 mmol) was reacted with double amounts of BnBr according to General method A. The reaction reached completion in three hours (hexane/EtOAc = 8:2, $R_f = 0.48$). The crude product (a pale yellowish syrup) was purified by column chromatography (hexane/EtOAc = 8:2 → 7:3). Yield: 4.16 g (94%). The product can be crystallized from EtOAc–hexane system, mp: 81.5–82.5 °C, $[\alpha]_D = -19.9$ (*c* 0.45, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 7.90–7.23 (22H, m, arom.), 5.13–4.68 (7H, m, $3 \times CH_2$, *H*-1); ^{13}C NMR δ (ppm): 138.97, 138.61, 136.18, 134.63, 133.54, 133.26, 131.72, 128.98, 128.63, 128.40, 128.19, 127.88, 127.76, 127.69, 127.18, 126.68 (28C, arom.), 75.79, 74.85, 73.05 ($3 \times CH_2$). Anal. Calcd for $C_{36}H_{36}O_4S$: C, 76.57; H, 6.43; S, 5.68. Found: C, 76.44; H, 6.48; S, 5.74.

4.6.8. Preparation of 2-(dimethoxymethyl)naphthalene 8. To a solution of 2-naphthaldehyde (15.6 g, 0.10 mol) in dry methanol (30 mL) trimethyl-orthoformate (15.6 mL, 0.15 mol, 1.5 equiv) and a catalytic amount (~45 mg) of *p*-toluene-sulfonic acid were added. The overnight reaction reached a conversion greater than 95% and a product of higher mobility formed (t.l.c: hexane/EtOAc = 8:2, $R_f = 0.67$). The mixture was diluted with DCM (500 mL) and was washed with satd. $NaHCO_3$ solution and water. The organic layer was dried and evaporated. Yield: 19.6 g, orange-coloured

[‡] The $[\alpha]_D$ value for phenyl 3,4-*O*-isopropylidene-1-thio-β-D-fucopyranoside is +7.6.[36]

liquid, which was pure enough for transacetalization reactions. Vacuum distillation (bp 141–143 °C/2 mmHg; d 1.10 g cm^{-3}) of the crude product afforded a colourless liquid. ^1H NMR ($CDCl_3$) δ (ppm): 7.93–7.77 (4H, arom.), 7.54 (1H, dd, arom.), 7.50–7.42 (2H, arom.), 5.53 (1H, s, $H_{acetalic}$), 3.34 (6H, s, $2\times OCH_3$); ^{13}C NMR δ (ppm) 135.39, 133.31, 132.90, 128.20, 127.97, 127.57, 126.12, 126.00, 124.28 (10C, arom.), 103.05 ($C_{acetalic}$), 52.60 (OCH_3).

4.6.9. Phenyl 3,4-*O*-*exo*/*endo*-(2-naphthyl)methylene-1-thio-β-L-fucopyranoside 9*exo* and 9*endo*. To a solution of **3b** (10.00 g, 39 mmol) in dry DMF (15 mL) **8** (15.8 mL, 78 mmol, 2.0 equiv) and a catalytic amount of 10-camphorsulfonic acid (CSA) were added. After seven days t.l.c. (DCM/acetone = 97:3, $R_{f,exo} = 0.58$, $R_{f,10} = 0.47$, $R_{f,endo} = 0.40$) showed an acceptable conversion of the starting material (~80%), the *exo* and *endo* isomers were formed approx. in a 1:1 ratio, compound **10** (see **4.6.10.**) was formed in a small quantity. The mixture was neutralized with Et_3N, diluted with DCM (700 mL) and washed with satd. $NaHCO_3$ and water. The organic layer was dried, evaporated and the resulting crude product was purified by column chromatography (DCM/acetone = 98:2 → 97:3). Complete separation of the *exo* and *endo* isomers could not be achieved due to **10**, thus the non-homogeneous fractions were collected and purified further. The material in the unique fractions could be recrystallized from EtOAc–hexane solvent mixture, the mother liquors were purified further. Yield for **9*exo***: 3.30 g (22%), mp: 143–144 °C, $[\alpha]_D = -16.7$ (*c* 0.32, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.95–7.80 (4H, arom.), 7.65–7.44 (5H, arom.), 7.40–7.32 (3H, arom.), 6.30 (1H, s, $H_{acetalic}$), 4.53 (2H, m), 4.09 (1H, dd), 3.82 (2H, m), 2.81 (1H, s, O*H*), 1.50 (3H, d, $J_{5,6} = 7$ Hz, $3\times H$-6); ^{13}C NMR δ (ppm): 136.14, 133.64, 132.83, 132.62, 132.10, 129.03, 128.28, 128.06, 127.65, 126.39, 126.22, 125.53, 123.85 (16C, arom.), 103.31 ($C_{acetalic}$), 87.92 (*C*-1), 80.07, 76.21, 72.95, 69.07 (*C*-2 to *C*-5), 17.07 (*C*-6). Anal. Calcd for $C_{23}H_{22}O_4S$: C, 70.03; H, 5.62; S, 8.13. Found: C, 69.92; H, 5.66; S, 8.09.

Yield for **9*endo***: 3.86 g (25%), mp: 147–148 °C, $[\alpha]_D = +18.1$ (*c* 0.27, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.96–7.72 (4H, m, arom.), 7.61–7.40 (5H, m, arom.), 7.36–7.26 (3H, m, arom.), 6.08 (1H, s, $H_{acetalic}$), 4.50 (1H, d, $J_{1,2} = 10$ Hz, *H*-1), 4.22 (1H, t, $J = 6$ Hz), 4.11 (1H, dd), 3.92 (1H, m), 3.63 (1H, dd), 3.30 (1H, s, O*H*), 1.52 (3H, d, $J_{5,6} = 7$ Hz, $3\times H$-6); ^{13}C NMR δ (ppm): 134.72, 133.77, 132.83, 131.75, 128.81, 128.25, 127.88, 127.60, 126.42, 126.32, 126.08, 123.80 (16C, arom.), 104.50 ($C_{acetalic}$), 87.43 (*C*-1), 78.80 (2C), 72.45, 71.44 (*C*-2 to *C*-5), 16.82 (*C*-6). Anal. Calcd for $C_{23}H_{22}O_4S$: C, 70.03; H, 5.62; S, 8.13. Found: C, 69.90; H, 5.68; S, 8.17.

4.6.10. Phenyl 2-*O*-*R*/*S*(methoxy-2′-naphthyl)methyl-3,4-*O*-(*endo*-2-naphthyl)methylene 1-thio-β-L-fucopyranoside 10. The title compound was isolated in the course of the preparation of compounds **9*exo*** and **9*endo*** (DCM/acetone = 97:3, $R_f = 0.47$). Yield: 1.37 g (6%), mp: 147–152 °C, $[\alpha]_D = -63.9$ (*c* 0.37, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 6.40 (1H, s, $H_{acetalic}$), 6.05 (1H, s, $H_{acetalic}$), 2.80 (3H, s, OCH_3). Anal. Calcd for $C_{35}H_{32}O_5S$: C, 74.44; H, 5.71; S, 5.68. Found: C, 74.61; H, 5.75; S, 5.60.

4.6.11. Phenyl 3-*O*-(2-naphthyl)methyl-1-thio-β-L-fucopyranoside 11. Compound **9*exo*** (2.36 g, 6 mmol) was reacted according to General method B. The yield after chromatographic purification (DCM/EtOAc = 85:15, $R_f = 0.44$): 2.30 g (97%), mp: 113–115 °C (EtOAc–hexane), $[\alpha]_D = +26.3$ (*c* 0.32, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.85–7.80 (4H, m, arom.), 7.58–7.56 (2H, dd, arom.), 7.51–7.47 (3H, m, arom.), 7.33–7.26 (3H, m, arom.), 4.90 (2H, dd, CH_2), 4.48 (1H, d, $J_{1,2} = 10$ Hz, *H*-1), 3.81 (1H, m), 3.58 (1H, dd), 3.5 (1H, dd), 2.40 (2H, s, $2\times OH$), 1.38 (3H, d, $J_{5,6} = 6$ Hz, CH_3); ^{13}C NMR δ (ppm): 135.09, 133.18, 132.52, 128.91, 128.47, 127.87, 127.71 126.82, 126.25, 126.10, 125.71 (16C, arom.), 88.45 (*C*-1), 81.54, 74.60, 69.39, 68.76 (*C*-2 to *C*-5), 72.15 (CH_2), 16.70 (*C*-6). Anal. Calcd for $C_{23}H_{24}O_4S$: C, 69.67; H, 6.10; S, 8.09. Found: C, 69.81; H, 6.07; S, 8.06.

4.6.12. Phenyl 4-*O*-(2-naphthyl)methyl-1-thio-β-L-fucopyranoside 12. Compound **9*endo*** (2.36 g, 6 mmol) was reacted according to General method B. The yield after chromatographic purification (DCM/EtOAc = 85:15, $R_f = 0.24$): 2.33 g (98%), amorphous solid, could not be recrystallized from solvents generally used, mp: 134–137 °C, $[\alpha]_D = +3.4$ (*c* 0.89, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.85 (4-H, m, arom.), 7.65–7.45 (5H, m, arom.), 7.28 (3H, dd, arom.), 4.93 (2H, s, CH_2), 4.50 (1H, d, $J_{1,2} = 9$ Hz, *H*-1), 3.80–3.55 (4H, m, *H*-2,3,4,5), 2.67 (2H, s, $2\times OH$), 1.37 (3H, d, $J_{5,6} = 7$ Hz, CH_3); ^{13}C NMR δ (ppm): 135.72, 133.17, 132.91, 132.77, 132.02, 128.81, 128.11, 127.84, 127.66, 127.56, 126.29, 126.10, 125.88, 125.72 (16C, arom.), 88.27 (*C*-1), 79.14, 75.68, 74.98, 69.93 (*C*-2 to *C*-5), 75.56 (CH_2), 17.26 (*C*-6). Anal. Calcd for $C_{23}H_{24}O_4S$: C, 69.67; H, 6.10; S, 8.09. Found: C, 69.76; H, 6.13; S, 8.14.

4.6.13. Phenyl 2,4-di-*O*-benzyl-3-*O*-(2-naphthyl)methyl-1-thio-β-L-fucopyranoside 13. Compound **11** (1.77 g, 4.5 mmol) was reacted with double amounts of BnBr according to General method A. The reaction reached completion in three hours (hexane/EtOAc = 8:2, $R_f = 0.46$). Yield after chromatography (hexane/EtOAc = 8:2 → 7:3): 2.36 g (93%), mp: 84–86 °C, decomp. (Et_2O–hexane), $[\alpha]_D = -20.4$ (*c* 0.72, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.88–7.12 (22H, m, arom.), 5.13–4.69 (6H, m, $3\times CH_2$), 4.64 (1H, d, $J_{1,2} = 10$ Hz, *H*-1), 3.99 (1H), 3.67 (2H, m), 3.54 (1H, m), 1.30 (3H, d, $J_{5,6} = 6$ Hz, CH_3); ^{13}C NMR δ (ppm) 138.71, 138.40, 135.79, 134.34, 133.22, 132.94, 131.48, 128.71, 128.30, 128.15, 127.89, 127.67, 127.45, 126.91, 126.26, 126.11, 125.90, 125.63 (28C, arom.), 87.52 (*C*-1), 84.28, 77.12, 76.68, 74.59 (*C*-2 to *C*-5), 75.51, 74.59, 72.85 ($3\times CH_2$), 17.27 (*C*-6). Anal. Calcd for $C_{36}H_{36}O_4S$: C, 76.57; H, 6.43; S, 5.68. Found: C, 76.48; H, 6.47; S, 5.74.

4.6.14. Phenyl 2,3-di-*O*-benzyl-4-*O*-(2-naphthyl)methyl-1-thio-β-L-fucopyranoside 14. Compound **12** (3.32 g,

8.4 mmol) was reacted with double amounts of BnBr according to General method A. The reaction took place in three hours (hexane/EtOAc = 8:2, $R_f = 0.46$). Yield after chromatography (hexane/EtOAc = 8:2 → 7:3): 3.45 g (93%), mp: 83–85 °C, decomp. (Et_2O–hexane), $[\alpha]_D = -21.5$ (*c* 0.53, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.92–7.80 (4H, m, arom.) 7.72–7.20 (18H, arom.), 5.22 (1H, d, CH*H*), 4.96–4.75 (5H, m, $2.5 \times CH_2$), 4.68 (1H, d, $J_{1,2} = 9$ Hz, *H*-1), 4.04 (1H, t, $J = 9$ Hz), 3.75–3.53 (3H, m), 1.34 (3H, d, $J_{5,6} = 6$ Hz, CH_3); ^{13}C NMR δ (ppm): 138.30, 136.12, 134.36, 133.12, 132.88, 131.40, 128.68, 128.39, 128.27, 127.80, 127.64, 127.51, 126.89, 126.50, 126.21, 125.94, 125.72 (28C, arom.), 87.59 (*C*-1), 84.53, 77.16, 76.45, 74.56 (*C*-2 to *C*-5), 75.50, 74.56, 72.89 ($3 \times CH_2$), 17.33 (*C*-6). Anal. Calcd for $C_{36}H_{36}O_4S$: C, 76.57; H, 6.43; S, 5.68. Found: C, 76.65; H, 6.45; S, 5.65.

4.6.15. Phenyl 3-*O*-(2-naphthyl)methyl-α/β-L-fucopyranoside 11 and 15. Compound **3b** (0.85 g, 3.3 mmol) was reacted with NAPBr according to General method C. The crude product was purified and the isomers were separated by chromatography (DCM/EtOAc = 85:15; $R_{f,\mathbf{15}} = 0.25$). Yield for **11**(β): 0.89 g (68%), mp: 114–116 °C. The $[\alpha]_D$ value and NMR data were the same to that of compound **11** obtained according to General method B. Yield for **15**(α): 0.165 g (13%), mp: 122.5–124.0 °C, $[\alpha]_D = -105.5$ (*c* 0.80, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.90–7.80 (4H, m, arom.), 7.56–7.44 (5H, m, arom.), 7.37–7.24 (3H, m, arom.), 5.66 (1H, d, $J_{1,2} = 6$ Hz, *H*-1), 4.91 (2H, s, $2 \times CH_2$), 4.46–4.30 (2H, m), 3.93 (1H, dd), 3.62 (1H, dd), 2.45 (2H, s, $2 \times OH$), 1.32 (3H, d, $J_{5,6} = 7$ Hz, CH_3); ^{13}C NMR δ (ppm): 134.92, 134.21, 133.18, 131.52, 128.96, 128.55, 127.88, 127.72, 127.24, 126.77, 126.31, 126.17, 125.59 (16C, arom.), 90.10 (*C*-1), 79.42, 69.29, 67.98, 67.18 (*C*-2 to *C*-5), 72.16 (CH_2), 16.10 (*C*-6). Anal. Calcd for $C_{23}H_{24}O_4S$: C, 69.67; H, 6.10; S, 8.09. Found: C, 69.56; H, 6.12; S, 8.06.

4.6.16. Phenyl 2-*O*-benzyl-3,4-*O*-isopropylidene-1-thio-β-L-fucopyranoside 16. Compound **4b** (4.32 g, 14.6 mmol) was benzylated with BnBr according to General method A. A small amount of the crude product was purified and characterized and the rest (~5.5 g) was used directly for the next step, (t.l.c: hexane/EtOAc = 8:2, $R_f = 0.41$). mp: 95–98 °C, $[\alpha]_D = -8.5$ (*c* 0.78, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.60–7.52 (2H, m, arom.), 7.47–7.25 (8H, m, arom.), 4.83 (1H, d, $J_{gem.} = 11$ Hz CH*H*), 4.67 (1H, d, $J_{gem.} = 11$ Hz, C*H*H), 4.60 (1H, d, $J_{1,2} = 10$ Hz, *H*-1), 4.24 (1H, t, $J = 6$ Hz), 4.05 (1H, dd), 3.83 (1H, m), 3.51 (1H, dd), 1.42, 1.37 (6H, $2 \times CH_3$), 1.40 (3H, d, $J_{5,6} = 6$ Hz, CH_3); ^{13}C NMR δ (ppm): 137.92, 133.74, 132.06, 128.70, 128.22, 128.17, 127.65, 127.31 (12C, arom.), 109.64 ($C_{acetalic}$), 86.05 (C-1), 79.78, 78.06, 76.38, 72.34 (*C*-2 to *C*-5), 73.40 (CH_2), 27.84, 26.35 ($2 \times CH_3$), 16.85 (*C*-6). Anal. Calcd for $C_{22}H_{26}O_4S$: C, 68.37; H, 6.78; S, 8.29. Found: C, 68.50; H, 6.74; S, 8.36.

4.6.17. Phenyl 2-*O*-benzyl-1-thio-β-L-fucopyranoside 17. Crude compound **16** (5.5 g) was dissolved in MeOH (30 mL), $HCl_{(aq)}$/water = 1:3 (4 mL) solution was added and the mixture was kept at 50 °C for 2.5 h. The solvent was evaporated in vacuo and co-evaporated once with toluene. The product was recrystallized from MeOH, the mother liquor was purified by column chromatography (DCM/acetone = 85:15; $R_f = 0.51$). Yield from **4b**: 4.73 g (92%), mp: 110.5–111.0 °C, $[\alpha]_D = -10.9$ (*c* 0.27, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.60–7.55 (2H, dd, arom.), 7.45–7.27 (8H, m, arom.), 4.97 (1H, d, $J_{gem.} = 11$ Hz, CH*H*), 4.73 (1H, d, $J_{gem.} = 11$ Hz, C*H*H), 4.62 (1H, d, $J_{1,2} = 9$ Hz, *H*-1), 3.77–3.48 (4H, m, *H*-2,3,4,5), 2.51 (2H, s, $2 \times OH$), 1.36 (3H, d, $J_{5,6} = 6$ Hz, CH_3); ^{13}C NMR δ (ppm): 138.06, 134.00, 131.63, 128.89, 128.56, 128.24, 128.04, 127.39 (12C, arom.), 87.38 (*C*-1), 78.04, 75.28, 74.41, 71.68 (*C*-2 to *C*-5), 75.22 (CH_2), 16.59 (*C*-6). Anal. Calcd for $C_{19}H_{22}O_4S$: C, 65.87; H, 6.40; S, 9.25. Found: C, 65.98; H, 6.42; S, 9.17.

4.6.18. Phenyl 2,3-di-*O*-benzyl-1-thio-β-L-fucopyranoside 18. Compound **17** (0.72 g, 2.0 mmol) was benzylated according to General method C. The reaction took place within 16 h (hexane/EtOAc = 7:3, $R_f = 0.42$). The crude product was chromatographed in hexane/EtOAc = 65:35 eluent. Yield: 0.78 g (89%), mp: 95–96 °C (EtOAc–hexane), $[\alpha]_D = 0.0$ (*c* 0.41, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.60 (2H, m, arom.), 7.46–7.25 (13H, m, arom.), 4.89–4.68 (4H, m, $2 \times CH_2$), 4.63 (1H, d, $J_{1,2} = 10$ Hz, *H*-1), 3.85–3.53 (4H, m, *H*-2,3,4,5), 2.32 (1H, s, O*H*), 1.39 (3H, d, $J_{5,6} = 6$ Hz, CH_3); ^{13}C NMR δ (ppm): 138.17, 137.63, 133.93, 131.85, 128.79, 128.48, 128.30, 128.20, 127.94, 127.83, 127.74, 127.29, 126.90 (18C, arom.), 87.47 (*C*-1), 82.81, 76.78, 74.14, 69.30 (*C*-2 to *C*-5), 75.62, 72.06 ($2 \times CH_2$), 16.70 (*C*-6). Anal. Calcd for $C_{26}H_{28}O_4S$: C, 71.53; H, 6.46; S, 7.34. Found: C, 71.69; H, 6.42; S, 7.31.

4.6.19. Phenyl 2-*O*-benzyl-3-*O*-(2-naphthyl)methyl-1-thio-β-L-fucopyranoside 19. Compound **17** (0.42 g, 1.2 mmol) was 2-(naphthyl)methylated according to General method C. The reaction took place within 18 h (t.l.c: hexane/EtOAc = 7:3, $R_f = 0.36$). The crude product was purified by column chromatography (hexane/EtOAc = 65:35). Yield: 0.47 g (82%), syrup, $[\alpha]_D = -7.8$ (*c* 0.56, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 7.90–7.26 (17H, m, arom.), 4.91–4.80 (4H, m, $2 \times CH_2$), 4.65 (1H, d, $J_{1,2} = 10$ Hz, *H*-1), 3.90–3.50 (4H, m, *H*-2,3,4,5), 2.38 (1H, s, O*H*), 1.40 (3H, d, $J_{5,6} = 7$ Hz, CH_3); ^{13}C NMR δ (ppm): 138.18, 135.05, 133.93, 133.09, 132.96, 131.75, 128.74, 128.26, 128.13, 127.79, 127.67, 127.60, 127.22, 126.61, 126.12, 125.98, 125.66 (22C, arom.), 87.45 (*C*-1), 82.60, 76.80, 74.11, 69.32 (*C*-2 to *C*-5), 75.58, 72.04 ($2 \times CH_2$), 16.65 (*C*-6). Anal. Calcd for $C_{30}H_{27}O_4S$: C, 74.51; H, 5.63; S, 6.63. Found: C, 74.40; H, 5.60; S, 6.67.

4.6.20. Methyl 3,4-di-*O*-benzyl-2-*O*-(2-naphthyl)methyl-α- and -β-L-fucopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside 20 and 21. The title compound was prepared according to General method D using **7** as the donor. T.l.c: DCM/acetone = 97:3; $R_{f,\alpha,\mathbf{20}} = 0.65$; $R_{f,\beta,\mathbf{21}} = 0.57$. Yield for **20**: 0.316 g (68%), syrup, $[\alpha]_D = -45.6$ (*c* 0.37, $CHCl_3$). Anal. Calcd for $C_{59}H_{62}O_{10}$: C, 76.11; H, 6.71. Found: C, 76.18; H,

6.68. Yield for **21**: 0.051 g (11%), mp: 148–150 °C, $[\alpha]_D = -29.41$ (*c* 0.15, $CHCl_3$). Anal. Calcd for $C_{59}H_{62}O_{10}$: C, 76.11; H, 6.71. Found: C, 76.09; H, 6.73.

4.6.21. Methyl 2,4-di-*O*-benzyl-3-*O*-(2-naphthyl)methyl-α- and -β-fucopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside 22 and 23. The title compound was prepared according to General method D using **13** as the donor. $R_{f,\alpha,\mathbf{22}} = 0.61$; $R_{f,\beta,\mathbf{23}} = 0.54$. Yield for **22**: 0.340 g (73%), syrup, $[\alpha]_D = -57.9$ (*c* 0.17, $CHCl_3$). Anal. Calcd for $C_{59}H_{62}O_{10}$: C, 76.11; H, 6.71. Found: C, 76.18; H, 6.70. Yield for **23**: 0.042 g (9%), mp: 151–153 °C, $[\alpha]_D = -27.7$ (*c* 0.10, $CHCl_3$). Anal. Calcd for $C_{59}H_{62}O_{10}$: C, 76.11; H, 6.71. Found: C, 76.15; H, 6.70.

4.6.22. Methyl 2,3-di-*O*-benzyl-4-*O*-(2-naphthyl)methyl-α- and -β-L-fucopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside 24 and 25. The title compound was prepared according to General method D using **14** as the donor. $R_{f,\alpha,\mathbf{24}} = 0.68$; $R_{f,\beta,\mathbf{25}} = 0.59$. Yield for **24**: 0.354 g (75%), syrup, $[\alpha]_D = -46.8$ (*c* 0.68, $CHCl_3$). Anal. Calcd for $C_{59}H_{62}O_{10}$: C, 76.11; H, 6.71. Found: C, 76.04; H, 6.74. Yield for **25**: 0.033 g (7%), mp: 171–173 °C, $[\alpha]_D = -14.28$ (*c* 0.11, $CHCl_3$). Anal. Calcd for $C_{59}H_{62}O_{10}$: C, 76.11; H, 6.71. Found: C, 76.05; H, 6.68.

4.6.23. Methyl 3,4-di-*O*-benzyl-α-L-fucopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside 26. Disaccharide **20** was treated with DDQ according to General method E. T.l.c: DCM/acetone = 97:3; $R_f = 0.33$. Yield: 0.133 g (84%), syrup, $[\alpha]_D = -59.7$ (*c* 0.23, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 7.35–7.22 (25H, m, arom.), 5.41 (1H, d, $J_{1',2'} = 4.3$ Hz, *H*-1′), 4.92 (1H, d, $J_{gem.} = 12$ Hz, CH*H*), 4.84 (1H, d, $J_{gem.} = 12$ Hz, CH*H*), 4.70–4.60 (5H, m, $2.5 \times CH_2$), 4.54 (1H, d, $J_{gem.} = 12$ Hz, CH*H*), 4.44 (2H, dd, CH_2), 4.25 (1H, d, $J_{1,2} = 7.7$ Hz, *H*-1), 4.15 (2H, m), 4.04 (1H, t, $J = 8.7$ Hz), 3.94 (1H, s), 3.68 (2H, m), 3.62–3.52 (4H, m), 3.45 (3H, s, OCH_3), 2.28 (1H, s, O*H*), 1.14 (3H, d, $J_{5',6'} = 6$ Hz, *H*-6′); ^{13}C NMR δ (ppm): 138.63, 138.53, 138.36, 137.76, 137.41, 128.40, 128.38, 128.31, 128.09, 127.86, 127.81, 127.77, 127.49, 127.44 (25C, arom.), 103.11, 99.60, 83.10, 80.33, 76.86, 75.00, 74.51, 74.32, 73.54, 73.25, 72.33, 72.19, 72.11, 69.14, 68.70, 66.80, 56.55 (OCH_3), 16.58 (*C*-6′). Anal. Calcd for $C_{48}H_{54}O_{10}$: C, 72.89; H, 6.88. Found: C, 72.99; H, 6.86.

4.6.24. Methyl 2,4-di-*O*-benzyl-α-L-fucopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside 27. Disaccharide **22** was treated with DDQ according to General method E. $R_f = 0.29$. Yield: 0.138 g (87%), syrup, $[\alpha]_D = -85.8$ (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 7.35–7.18 (23H, m, arom.), 7.05 (2H, m, arom.), 5.63 (1H, d, $J_{1',2'} = 3.4$ Hz, *H*-1′), 4.81 (2H, t, $J_{gem.} = 12.3$ Hz, CH_2), 4.76 (1H, d, $J_{gem.} = 12$ Hz, CH*H*), 4.65 (1H, d, $J_{gem.} = 12$ Hz, CH*H*), 4.55–4.41 (6H, m, $3 \times CH_2$), 4.34 (2H, m), 4.16 (2H, m), 4.04 (1H, dd), 3.98 (1H, d, $J = 2.6$ Hz), 3.72 (1H, dd), 3.68 (1H, dd), 3.65–3.55 (4H, m), 3.46 (3H, s, OCH_3), 2.00 (1H, s, O*H*), 1.16 (3H, d, $J_{5',6'} = 6.8$ Hz, *H*-6′); ^{13}C NMR δ (ppm): 138.58, 138.35, 137.93, 137.85, 137.76, 128.41, 128.35, 128.22, 128.11, 128.08, 127.92, 127.82, 127.64, 127.54, 127.49, 127.30, 126.14, (25C, arom.) 102.93, 96.67, 84.07, 79.65, 76.04, 75.22, 74.34, 73.58, 73.07, 71.67, 71.45, 70.97, 70.43, 68.68, 66.22, 56.53 (OCH_3), 16.39 (*C*-6′). Anal. Calcd for $C_{48}H_{54}O_{10}$: C, 72.89; H, 6.88. Found: C, 72.77; H, 6.90.

4.6.25. Methyl 2,3-di-*O*-benzyl-α-L-fucopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside 28. Disaccharide **24** was treated with DDQ according to General method E. $R_f = 0.32$. Yield: 0.134 g (85%), syrup, $[\alpha]_D = -57.4$ (*c* 0.39, $CHCl_3$); ^{1}H NMR δ (ppm): 7.36–7.20 (20H, m, arom.), 7.16–7.07 (3H, m, arom.), 7.03–6.98 (2H, m, arom.), 5.61 (1H, d, $J_{1',2'} = 3.4$ Hz, *H*-1′), 4.82 (1H, d, $J_{gem.} = 12$ Hz, CH*H*), 4.76 (2H, d, $J_{gem.} = 12$ Hz, CH_2), 4.68 (1H, d, $J_{gem.} = 12$ Hz, CH*H*), 4.59 (1H, d, $J_{gem.} = 12.8$ Hz, CH*H*), 4.53 (2H, d, $J_{gem.} = 11.1$ Hz, CH*H*), 4.48–4.40 (3H, m), 4.36 (2H, d, $J = 7.7$ Hz), 4.20 (1H, t, $J = 8.4$ Hz), 3.95 (1H, s), 3.86 (2H, m), 3.78 (1H, dd), 3.71 (1H, dd), 3.64–3.55 (3H, m), 3.48 (3H, s, OCH_3), 2.06 (1H, s, O*H*), 1.25 (3H, d, $J_{5',6'} = 6.8$ Hz, *H*-6′); ^{13}C NMR δ (ppm): 138.40, 138.26, 138.04, 137.81, 128.43, 128.40, 128.14, 128.04, 127.93, 127.83, 127.74, 127.70, 127.60, 127.50, 127.32, 126.30 (25C, arom.), 102.86, 97.21, 83.97, 78.20, 74.85, 74.34, 73.62, 73.21, 72.40, 71.92, 71.22, 70.33, 68.79, 65.12, 56.45 (OCH_3), 15.90 (*C*-6′). Anal. Calcd for $C_{48}H_{54}O_{10}$: C, 72.89; H, 6.88. Found: C, 72.81; H, 6.85.

Acknowledgements

This work was supported by the Hungarian Research Fund (OTKA T038066 A.B. and T035128 I.B.).

References

1. Bai, C.; Sen, P.; Hofmann, K.; Ma, L.; Goebl, M.; Harper, J. W.; Elledge, S. J. *Cell* **1996**, *86*, 263–274.
2. Teng-umnuay, P.; Morris, H. R.; Dell, A.; Panico, M.; Paxton, T.; West, C. M. *J. Biol. Chem.* **1998**, *273*, 18242–18249.
3. van der Wel, H.; Morris, H. R.; Panico, M.; Paxton, T.; North, S. J.; Dell, A.; Thomson, J. M.; West, C. M. *J. Biol. Chem.* **2001**, *276*, 33952–33963.
4. Sassi, S.; Sweetinburgh, M.; Erogul, J.; Zhang, P.; Teng-umnuay, P.; West, C. M. *Glycobiology* **2001**, *11*, 283–295.
5. Dell, A. *Aust. J. Chem.* **2002**, *55*, 27–37.
6. Comer, F. I.; Hart, G. W. *J. Biol. Chem.* **2000**, *275*, 29179–29182.
7. Wells, L.; Vosseller, K.; Hart, G. W. *Science* **2001**, *291*, 2376–2378.
8. Watt, D. K.; Brasch, D. J.; Larsen, D. S.; Melton, L. D.; Simpson, J. *Carbohydr. Res.* **1996**, *285*, 1–15.
9. Lemieux, R. U.; Driguez, H. *J. Am. Chem. Soc.* **1975**, *97*, 4063–4068.
10. Mukherjee, A.; Palcic, M. M.; Hindsgaul, O. *Carbohydr. Res.* **2000**, *326*, 1–21.
11. Xia, J.; Abbas, S. A.; Locke, R. D.; Piskorz, C. F.; Alderfer, J. L.; Matta, K. L. *Tetrahedron Lett.* **2000**, *41*, 169–173.
12. Liao, W.; Locke, R. D.; Matta, K. L. *Chem. Commun.* **2000**, 369–370.

13. Csávás, M.; Borbás, A.; Szilágyi, L.; Lipták, A. *Synlett* **2002**, 887–890.
14. Csávás, M.; Borbás, A.; Jánossy, L.; Lipták, A. *Tetrahedron Lett.* **2003**, *44*, 631–635.
15. Lipták, A.; Borbás, A.; Jánossy, L.; Szilágyi, L. *Tetrahedron Lett.* **2000**, *41*, 4949–4953.
16. Borbás, A.; Szabó, Z. B.; Szilágyi, L.; Bényei, A.; Lipták, A. *Tetrahedron* **2002**, *58*, 5723–5732.
17. Borbás, A.; Szabó, Z. B.; Szilágyi, L.; Bényei, A.; Lipták, A. *Carbohydr. Res.* **2002**, *337*, 1941–1951.
18. Komba, S.; Ishida, H.; Kiso, M.; Hasegawa, A. *Bioorg. Med. Chem.* **1996**, *4*, 1833–1848.
19. Sato, S.; Mori, M.; Ito, Y.; Ogawa, T. *Carbohydr. Res.* **1986**, *155*, C6–C10.
20. David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643–663.
21. David, S. Selective O-Substitution and Oxidation Using Stannylene Acetals and Stannyl Ethers. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker: New York, 1997; pp 69–83.
22. Grindley, T. B. *Adv. Carbohydr. Chem. Biochem.* **1998**, *53*, 17–142.
23. Xia, J.; Piskorz, C. F.; Alderfer, J. L.; Locke, R. D.; Matta, K. L. *Tetrahedron Lett.* **2000**, *41*, 2773–2776.
24. Jain, R. K.; Locke, R. D.; Matta, K. L. *Carbohydr. Res.* **1991**, *212*, C1–C3.
25. Kallin, E.; Lönn, H.; Norberg, T. *Glycoconjugate J.* **1988**, *5*, 3–8.
26. Nilsson, S.; Lönn, H.; Norberg, T. *Glycoconjugate J.* **1989**, *6*, 21–34.
27. Veeneman, G. H.; van Boom, J. H. *Tetrahedron Lett.* **1990**, *31*, 275–278.
28. Heskamp, B. M.; van der Marel, G. A.; van Boom, J. H. *J. Carbohydr. Chem.* **1995**, *14*, 1265–1277.
29. Jobron, L.; Hindsgaul, O. *J. Am. Chem. Soc.* **1999**, *121*, 5835–5836.
30. Zhang, Z.; Ollmann, I. R.; Ye, X. S.; Wischnat, R.; Baasov, T.; Wong, C. H. *J. Am. Chem. Soc.* **1999**, *121*, 734–753.
31. Roy, R.; Park, W. K. C.; Srivastava, O. P.; Foxall, C. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1399–1402.
32. Gaunt, M. J.; Yu, J.; Spencer, J. B. *J. Org. Chem.* **1998**, *63*, 4172–4173.
33. Paquette, L. A.; Barriault, L.; Pissarnitski, D.; Johnston, J. N. *J. Am. Chem. Soc.* **2000**, *122*, 619–631.
34. Paulsen, H.; Rutz, V.; Brockhausen, I. *Liebigs Ann. Chem.* **1992**, 747–758.
35. Carpintero, M.; Jaramillo, C.; Fernandez-Mayoralas, A. *Eur. J. Org. Chem.* **2000**, *7*, 1285–1296.
36. Stick, R. V.; Tilbrook, D. M. G.; Williams, S. J. *Aust. J. Chem.* **1999**, *52*, 895–904.