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6-Deoxy-6-fluorogalactofuranosides: regioselective glycosylation, unexpected reactivity, and anti-leishmanial activity

Jeane Vaugenot,^a Abderrafek El Harras,^a Olivier Tasseau,^a Rémi Marchal,^a Laurent Legentil,^a Boris Le Guennic,^a Thierry Benvenegu,^a and Vincent Ferrières*^a

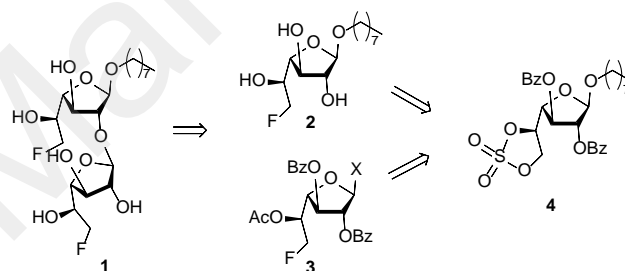
Selective glycosylation of the C-6 fluorinated galactofuranosyl acceptor **2** was studied with four galactofuranosyl donors. It was highlighted that this electron-withdrawing atom strongly impacted the behavior of the acceptor, thus leading to unprecedented glycosylation pathways. Competition between expected glycosylation of **2**, ring expansion of this acceptor and furanosylation, and intermolecular aglycon transfer was observed. Further investigation of the fluorinated synthetic compounds showed that the presence of fluorine atom contributed to increase the inhibition of the growth of *Leishmania tarentolae*, a non-pathogenic strain of *Leishmania*.

Introduction

The effects of fluorine atom, known to influence biological properties,¹⁻⁶ are mainly correlated with its physicochemical properties.⁷⁻⁹ Due to its size and to the presence of non-binding doublets, it can interestingly mimic hydroxyl group. However, its strong electronegativity is also responsible for changes in charge distribution along covalent links. As an example, the substitution of OH group at C-2 or C-5 of glycosyl entities was deeply studied by the Withers¹⁰ and Wong^{11,12} laboratories. The electron-withdrawing effect of fluorine at the proper position strengthens the anomeric bond, so that inhibiting properties were established. More recently, the impact of the presence of fluorine atoms on the carbohydrate conformation,^{13,14} even on glycosyl cation,¹⁵ and was studied. Moreover, fluorine-containing carbohydrates were used to improve immune response¹⁶ or as molecular tools to study interactions with lectins,¹⁷⁻¹⁹ or to trap the covalent glycosyl-enzyme intermediates.²⁰ Similar reactive species were observed thanks to the substitution of NHAc group by F atom.²¹ The contribution of this halogen has also been of great help in elucidating the ring contraction of galactopyranose (Galp) into the less stable galactofuranose (Galf) form in the corresponding nucleotide-sugars. Such rare behavior is now well documented and is catalyzed by UDP-Galp mutases.^{22,23} In order to elucidate this mechanism, the galactopyranose moiety of the natural substrate (UDP-Galp) was fluorinated at positions 2,^{24,25} 3,²⁵ and 4.²⁶ The 6-hydroxyl group of the pyranose form was also substituted by fluorine to study another family of important enzymes, the galactopyranosyl transferases.²⁷ More recently, substrates initially present in the furanose form were also prepared: the 2,2,3,3-tetra-fluoro-derivative, able to enhance affinity for the mutase and so to inhibit its activity,^{28,29} and the primary monofluoro-analog.³⁰ With this latter structural modulation, inhibition of both mutase and transferases, required in *Mycobacterium tuberculosis* for the biosynthesis of the natural polygalactofuranoside and the survival of the pathogen, was observed.^{30,31} As another consequence, weaker nucleophilicity of the vicinal OH-5 was anticipated, so that ring expansion was left aside, thus resulting in increased stability of UDP-6-F-Galf.

Alongside these studies, fluoro-derived furanosides were further used as substrates in transglycosylation reactions catalyzed by a furanosyl hydrolase.³² Several di- and trisaccharides were

isolated and their ability to induce production of TNF- α by murine macrophages was demonstrated, thus opening interesting opportunity in the field of immunostimulation. Amongst the oligofuranosides obtained, the disaccharide **1** (Sch. 1), characterized by the presence of a lipid chain on the reducing moiety, two fluorine atoms substituting both primary hydroxyls, and a β -(1 \rightarrow 2)-connection, showed promising activities. Moreover, in order to further demonstrate biological interests of furanosyl-containing derivatives,³³ we have also demonstrated that alkyl furanosides are able to inhibit the growth of *Leishmania*, a parasite infecting 1 to 2 million people annually.³⁴ Such simple monosaccharides indeed impair the parasite by rigidifying and so disturbing its membrane.³⁵



Sch. 1 Retrosynthetic scheme.

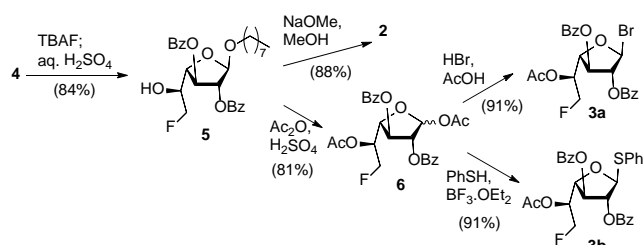
This study describes firstly the chemical approach towards **1** starting from the known fluorinated galactofuranosidic acceptor **2**.³⁶ Considering the 6-F function, we expected that electron-withdrawing property of the halogen atom, which dissipates with distance, may result in reactivity for OH-2 slightly better than the one of OH-3, but clearly improved with respect to that of OH-5. Therefore, it was envisaged not to use protecting groups, thus saving time-consuming manipulations. Moreover, this acceptor was a good model compound to study possible regioselective glycosylation, a research field explored in pyranose series^{37,38} but scarcely in the furanose one.^{39,40} Finally, the second partner of the coupling, donor **3**, was designed with participating benzoyl group on C-2 to ensure β -configuration. Since it is fluorinated at C-6, it was obtained from **4**,⁴¹ a building block useful to prepare **2**, thus making the strategy highly convergent. Secondly, leishmanicidal effect was also evaluated on *Leishmania tarentolae*, the non-pathogenic strain of *Leishmania* spp., for some synthesized neo-octyl digalactofuranosides.

Results and discussion

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The synthesis of acceptor **2** and donors **3** (Sch. 2) started from known building block **4** through a regioselective opening of the cyclic sulfate by fluoride anion to give **5** in 84% yield. While Zemplén debenzoylation afforded **2**, acido-catalyzed acetolysis gave **6** which was isolated as an anomeric mixture in 81% yield. Subsequent bromination and thioglycosylation gave donors **3a** and **3b**, respectively, both in 91% yields.



Sch. 2 Synthesis of studied acceptor **2** and donors **3**.

Regioselective glycosylation of **2** was then performed (Table 1). With brominated donor **3a** under activation by silver(I) trifluoromethanesulfonate (AgOTf), three products were chromatographically isolated. Mass spectrometry (MS) data suggested the presence of a disaccharide (**7**) and two monosaccharides (**8**, **9**) (entry 1). Compound **8** resulted from partial hydrolysis of donor **3a**. The second monosaccharide **9** was characterized by monoisotopic footprint ($m/z=567.2365$), ^1H NMR signals between 1 and 2 ppm, a primary carbon at 80.6 ppm with a coupling constant of 173 Hz, and three signals corresponding to carbonyl functions (170.1, 165.6 and 165.4 ppm). These are evidence of the presence of fluorine atom and of an aliphatic chain. Moreover, $\delta_{\text{C-1}}$ at 105.6 ppm attested a sugar residue in a furanose form. This was corroborated by a low $J_{\text{H1,H2}}$, also synonymous of a β configuration. It results from these analytical data that the peracetylated 6-fluorinated octyl galactofuranoside **9** was obtained during the coupling reaction. This suggests an apparent intermolecular transfer of aglycon from the acceptor **2** to the donor **3a**.

Considering now the structure of the disaccharide ($m/z=731.2847$), expected signals for the furanosidic entity ($\delta_{\text{C-1b}}=108.0$ ppm, $J_{\text{H1b,H2b}}=3.2$ Hz) allowed to identify the non-reducing moiety (b). The reducing residue (a) was characterized by HMBC thanks to chemical shift for C-1a at 98.4 ppm and a coupling constant $J_{\text{H1a,H2a}}$ of 3.6 Hz. Moreover, correlation between H-1b (5.07 ppm) and C-5b (68.5 ppm) gave evidence for a six-membered ring. Finally, a high chemical shift for C-2a (78.3 ppm) and a correlation between C-1b (108.3 ppm) and H-2a (3.89 ppm) led to the structure $\beta\text{-D-Galf-(1}\rightarrow\text{2)-}\alpha\text{-D-Galp}$ for **7**, thus revealing isomerization of the furanosidic acceptor.

On the basis of this result, subsequent attempt was performed in the presence of molecular sieves (entry 2) in

Table 1 Glycosylation of acceptor **2** by donor **3**.

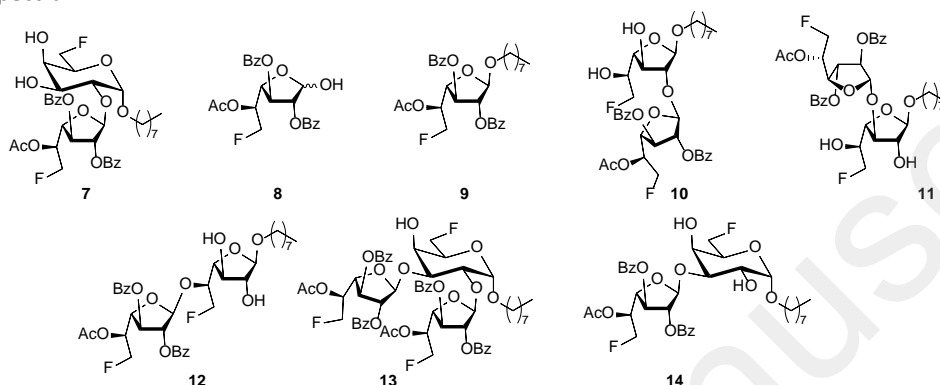
| | | | |
|--------------|------------|---|----------|
| Donor | + 2 | → | Products |
| (1.2 equiv.) | (1 equiv.) | | |

order to avoid ring expansion of the unprotected acceptor. Even if furanosides **8** and **9** were still isolated in non-negligible amounts, the desired disaccharides **10** and **11** were both isolated in 8% yields. For these compounds, the furanose form of the reducing moiety was clearly established thanks to high δ -values measured for C-1a (106.1 and 108.0 ppm), and $J_{\text{H1a,H2a}}$ lower than 1 Hz. Since glycosylation also shifts signal for the carbon centre involved in the new bond towards high fields, this resulted in sequences $\beta\text{-D-Galf-(1}\rightarrow\text{2)-}\beta\text{-D-Galf}$ (**10**) and $\beta\text{-D-Galf-(1}\rightarrow\text{3)-}\beta\text{-D-Galf}$ (**11**). Surprisingly, the analysis of this complex mixture underlined the presence of another disaccharide isolated in similar ratio, i.e. the $\beta\text{-D-Galf-(1}\rightarrow\text{5)-}\beta\text{-D-Galf}$ (**12**). This structure was deduced from characteristic data [$J_{\text{H1b,H2b}}$ near 1 Hz for H-1b, 107.9 and 106.4 ppm for C-1a and C-1b, respectively, and 75.6 ppm for C-5a, as well as correlation from HMBC spectrum between H-5a (4.33 ppm) and C-1b (106.4 ppm)]. As a consequence, all three hydroxyl groups in acceptor **2** appeared to have reacted to a similar extend.

When **2** reacted with **3b** (entry 3) under the assistance of *N*-iodosuccinimide (NIS) and trimethylsilyl triflate (TMSOTf), a complex mixture was obtained from which the trisaccharide **13** ($m/z=1145.3971$) could be isolated. As previously, the furanose configuration for the non-reducing parts was unambiguously established. Otherwise, the acceptor also underwent a ring expansion leading to the $\beta\text{-D-Galf-(1}\rightarrow\text{2)-}[\beta\text{-D-Galf-(1}\rightarrow\text{3)]-\alpha\text{-D-Galp}$ skeleton for **13** ($\delta_{\text{C-1p}}=98.7$ ppm vs. $\delta_{\text{C-1f}}=107.3$ and 107.6 ppm). Decreasing the reaction temperature to -30 °C (entry 4) allowed synthesizing the same trisaccharide as well as the disaccharides **7** and **14**. Chemical shifts for **14** ($\delta_{\text{C-1a}}=98.5$ ppm, $\delta_{\text{C-1b}}=107.3$ ppm, $\delta_{\text{C-3a}}=78.0$ ppm) were characteristic for a $\beta\text{-D-Galf-(1}\rightarrow\text{3)-}\alpha\text{-D-Galp}$ arrangement, a regioisomer of **7**. In order to avoid the furanose-pyranose isomerization, attempts with lower amount of Lewis acid catalyst were performed at 0 or -50 °C (entries 5 and 6). Under these conditions, di- and trisaccharides were isolated in moderate overall 22% and 36% yields, respectively. Fortunately, no pyranosyl entity was detected. The desired $\beta\text{-D-Galf-(1}\rightarrow\text{2)-}\beta\text{-D-Galf}$ **10** and $\beta\text{-D-Galf-(1}\rightarrow\text{3)-}\beta\text{-D-Galf}$ **11**, as well as the $\beta\text{-D-Galf-(1}\rightarrow\text{5)-}\beta\text{-D-Galf}$ **12** were obtained. A mixture of trisaccharides **15** (MS found 1145.3969) was also synthesized.

| Entry | Donor | Promotor (equiv.) | T (°C) | Products (yield) ^[b] |
|------------------|-----------|-------------------------|--------|---|
| 1 | 3a | AgOTf (1) | 20 | 7 (8%), 8 (22%), 9 (45%) |
| 2 ^[a] | 3a | AgOTf (1) | 20 | 10 (8%), 11 (8%), 12 (11%), 8 (15%), 9 (20%) |
| 3 | 3b | NIS (2.3), TMSOTf (1.2) | 0 | 13 (11%) |
| 4 ^[c] | 3b | NIS (2.3), TMSOTf (1.2) | - 30 | 7 (6%), 14 (6%), 13 (11%) |
| 5 | 3b | NIS (2.3), TMSOTf (0.5) | 0 | 10 (7%), 11 (5%), 12 (1%), Trifuranosides 15 (9%) |
| 6 | 3b | NIS (2.3), TMSOTf (0.5) | - 50 | 10 (12%), 11 (5%), 12 (9%), Trifuranosides 15 (11%) |

^[a] The reaction was performed with molecular sieves. ^[b] Structures of isolated and characterized products. ^[c] Ratio was deduced from ¹H NMR spectra



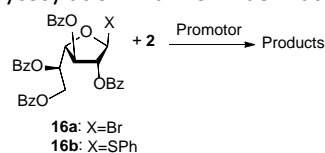
Considering the moderate yields of the reactions reported in Table 1, further glycosylations of acceptor **2** were performed using the non-fluorinated donors⁴² **16a** and **16b** (Table 2). These substrates afforded products in much more interesting overall 95% and 78% yields, respectively (entries 1 and 4). Once again, coupling with brominated donor mainly gave side-products resulting from hydrolysis (**18**, 43%) and apparent transglycosylation (**19**, 45%). Moreover, preservation of the five-membered ring size of the acceptor was better performed with thioglycoside **16b** (entry 4) than with **16a** (entry 1). Finally, the desired (1→2)- (**20**) and (1→3)- (**21**) disaccharides were obtained, still with the (1→5)-isomer (**22**). A mixture of trisaccharides **23** was also obtained (*m/z* 1473.4891) but exact structure could not be elucidated.

Even if far away from the electrophilic or nucleophilic centres, the fluorine atoms on the furanosyl donors and acceptor significantly impacted the progress of the reaction. Considering firstly the donors, this study clearly showed a lower reactivity of the fluoro-compounds **3** compared to the non-fluorinated donors **16**. Secondly, from the unprotected acceptor, ring expansion indicated a non-negligible nucleophilicity for OH-5, and hydrogen bonding cannot be excluded.

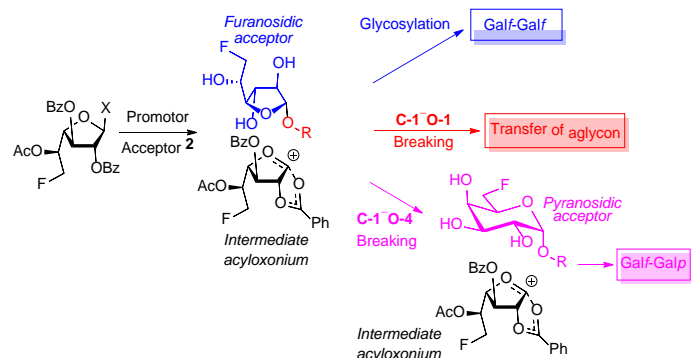
The transfer of the *O*-aglycon from the acceptor towards the donor constituted an unexpected second side-reaction. The stability of **2** was thus studied under glycosylation conditions but in the absence of donor. Even in the presence of a large amount of water (0.5 equiv.), neither the octanol release nor the formation of the thermodynamically more stable α -pyranosidic counterpart was observed. In other words, none of the electrophilic species, i.e. silver cation, iodonium ion, the Lewis acid TMSOTf, possibly the proton, may

induce transformation of the furanosidic acceptor **2**. That suggests that interactions with the activated donor (Sch. 3) induced competitive behaviour: glycosylation leading to GalF-GalF disaccharides, but also weakening of bonds involving the anomeric centre. The latter phenomenon resulted in transglycosylation when C-1-O-1 of the acceptor **2** was broken, or in GalF-Galp formation through C-1-O-4 cleavage and glycosylation.

Table 2 Glycosylation with non-fluorinated donors **16**.

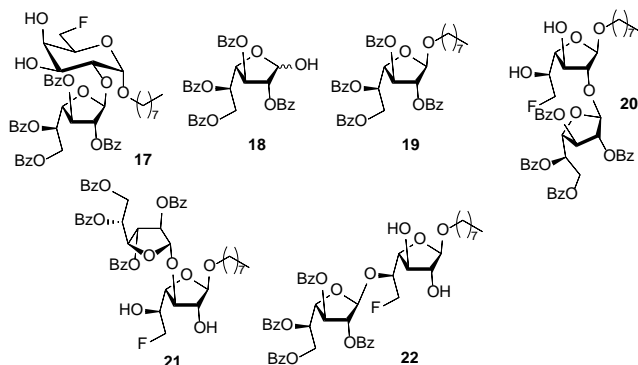


| Entry | Donor | Promotor (equiv.) | T (°C) | Products (yield) |
|-------|------------|-------------------|--------|---|
| 1 | 16a | AgOTf (1) | 20 | 17 (7%), 18 (43%), 19 (45%) |
| 2 | 16a | AgOTf (1) | 20 | 17 (42%), 19 (2%), 20 (7%), 21 (5%), 22 (10%) ^a |



| | | | | |
|----------------|------------|-------------------------|-----|--|
| 3 | 16a | AgOTf (1) | -50 | 18 (49%), 19 (8%), 20 (7%), 21 (4%), 22 (9%) ^a |
| 4 ^b | 16b | NIS (2.3), TMSOTf (0.5) | -50 | 20 (6%), 21 (5%), 22 (10%), 23 ^c (57%) ^d |

^[a] 20-22 ratio was estimated by ¹H NMR; ^[b] Non-separable mixture of di- and trisaccharides; ^[c] Exact structure of the trisaccharide could not be obtained; ^[d] Conversion yield calculated from acceptor **2**.

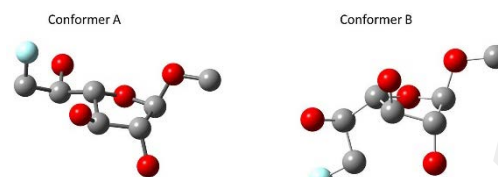


These experimental results from acceptor **2** also gave evidence that a non-negligible nucleophilicity remained for both OH-5 and O-1. The influence of fluorine atom on the acceptor reactivity was previously studied, but neither on glycosidic acceptors nor on furanosyl derivatives.⁴³ The O-1 (from **2**) reactivity observed herein, reminded us of the secondary reaction often observed during the glycosylation of a thioglycoside used as an acceptor with a brominated donor.⁴⁴ This is generally explained by the residual nucleophilicity of the Sulphur atom.

Sch. 3 Possible interactions that may explain experimental results.

A computational approach based on Density Functional Theory (see Computational details) was considered in order to decipher our observations. The methyl glycosides were used as model compounds in order to limit calculation time. Assuming first a kinetically controlled reaction, condensed Fukui functions were considered. They describe the electron density after adding or removing electrons, and thus are suitable for predicting where the most electrophilic and nucleophilic sites on a molecule are.⁴⁵ Since calculations depend on the overall conformation, and considering the flexibility of the furanose rings in solution,^{46, 47} two conformations of the methyl β -D-galactofuranoside, ⁴T₀ and ³T₂ for conformers **A** and **B**,

respectively, were optimized. Among several hypothetical starting structures that were optimized, only these two conformations were minima on the potential energy surface as confirmed by frequency calculations. They mainly differ by the



orientation of the C-4-C-5-C-6 side arm carrying the halogen atom (Fig. 1). They are almost iso-energetic with conformer **A** slightly more stable than conformer **B** by 0.03 eV at the B3LYP/6-311G(d) level of calculations, while the opposite is found with the M06-2X functional (see ESI).

Fig. 1 DFT optimized structures for the two conformers at the B3LYP/6-311G(d) level. Colors: Carbon: grey; Oxygen: red; Fluorine: blue.

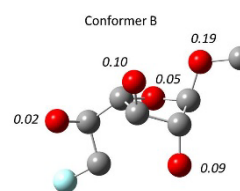
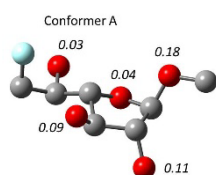
Furthermore, *f* values obtained for all oxygen atoms (Table 3) showed that nucleophilicity is significantly higher for O-1 than for all other oxygen atoms, whatever the population analysis scheme (Mulliken, Hirshfeld, Voronoi, or Bader) or the functional used. This result was quite relevant for supporting the transfer of the *O*-aglycon to the donor. Moreover, O-2 and O-3 appeared to have similar nucleophilicity, and (1→2)- and (1→3)-disaccharides were indeed isolated in very close proportions. Fukui values, however, appear to be inappropriate for explaining the observed reactivity of O-5. Nevertheless, the H-bond donating ability of OH-5 due to the vicinal fluorine atom,⁴⁸ whatever the solvent used, could increase the reactivity of O-5.

On another hand, the process could also be governed by thermodynamic factors. We therefore evaluated the energy difference between products **7** [β -D-Galf-(1→2)- α -D-Galp] and **10** [β -D-Galf-(1→2)- α -D-Galf] in their methyl version, and using the same procedure as previously described. As expected, the pyranosyl-containing disaccharide **7** was significantly more stable than its difuranosyl isomer **10** ($\Delta E=0.47$ eV). Consequently, based on this computational inspection, it is not possible to decide between thermodynamic or kinetic control for the studied glycosylation reaction but both are convergent and could contribute to explain the main experimental results obtained, i.e. the ring expansion and the aglycon transfer.

Table 3 Calculated condensed atomic Fukui functions *f* for different atomic charges at the B3LYP/6-311G(d) level.

| | Conformation A | | | | Conformation B | | | |
|-----|-----------------------|-----------|---------|-------|-----------------------|-----------|---------|-------|
| | Mulliken ^a | Hirshfeld | Voronoi | Bader | Mulliken ^a | Hirshfeld | Voronoi | Bader |
| O-1 | 0.18 | 0.17 | 0.19 | 0.26 | 0.19 | 0.18 | 0.20 | 0.32 |

| | | | | | | | | |
|-----|------|------|------|-------|------|------|------|------|
| O-2 | 0.11 | 0.11 | 0.10 | 0.07 | 0.09 | 0.09 | 0.08 | 0.03 |
| O-3 | 0.09 | 0.09 | 0.08 | 0.10 | 0.10 | 0.10 | 0.10 | 0.12 |
| O-4 | 0.04 | 0.04 | 0.04 | -0.02 | 0.05 | 0.04 | 0.05 | 0.03 |
| O-5 | 0.03 | 0.03 | 0.03 | 0.02 | 0.02 | 0.02 | 0.02 | 0.01 |



Finally, debenzoylation under Zemplén conditions afforded pure difluorinated disaccharides **24-27** and a mixture of non-separable disaccharides **28-30** (Fig. 2). It is interesting to note that the difuranoside **24** presents the same NMR characteristics as the product previously obtained thanks to a biocatalyzed approach.³² The chemical approach also afforded new disaccharides **25-30** and thus complements well the chemoenzymatic synthesis.

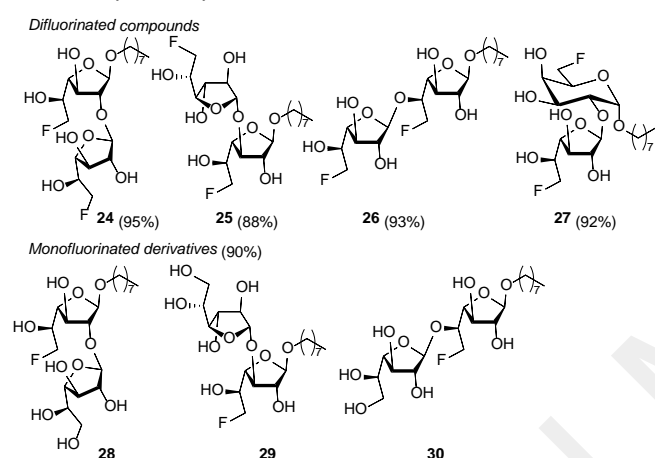


Fig. 2 Structures of deprotected compounds (yield of deacylation).

It was previously demonstrated that octyl galactofuranoside derivatives with polar substituent at C-6 position showed promising parasitostatic activities against the promastigote form of *Leishmania donovani*.³⁵ Therefore, the growth of *Leishmania tarentolae*, the non-pathogenic analog, was further investigated in the presence of the octyl 6-fluoro Galf **2** and the synthetic difuranosides **24**, **28-30**, **27**, and **26**. Their activities were compared to the ones of the non-fluorinated and 6-fluorinated octyl monogalactofuranosides, **GalfOct** and **2**, respectively. The minimum inhibition concentration (MIC), responsible for 99% of parasite growth inhibition, was calculated on *L. tarentolae* with increasing concentrations of the studied octyl glycosides. The reference **GalfOct** had a MIC value of 0.75 mM. While disaccharide **27**, bearing two fluorine atoms and a pyranosidic residue, did not show activity at a concentration of 1 mM, disaccharides **27** and **28-30**, characterized by the presence of non-fluorinated Galf non-reducing end, demonstrated similar activity as the **GalfOct** (0.75 mM). Lower MIC values were obtained for the disaccharides **26** (0.5 mM), **24** (0.25 mM) and the monosaccharide **2** (0.175 mM), all presenting an external 6-deoxy-6-fluoro Galf entity. These results highlighted the

beneficial effect of fluorination on furanosyl entities at the non-reducing end, provided that the carbohydrate linked to the alkyl chain is not in the pyranose form. The latter observation can be correlated to the absence of leishmanicidal activity of octyl galactopyranoside on the infectious parasite *Leishmania donovani*.³⁵

Experimental

General Experimental Details. Reagents were purchased from commercial sources and were used without further, except octyl galactofuranoside.⁴⁹ Dried dichloromethane was purchased sealed. All reactions were monitored by TLC on Silica Gel 60 F254, and spots were detected under 254 nm UV-light and/or by staining with orcinol solution. Column chromatography was performed on Silica Gel (25 or 50 μ m). NMR spectra were recorded at 400 MHz for ¹H and 100 MHz for ¹³C. Chemical shifts are given in δ units (ppm) and referenced to either CDCl₃ or CD₃OD. Coupling constants *J* were calculated in Hertz (Hz). Proton and carbon NMR peaks were unambiguously assigned by COSY (double quantum filtered with gradient pulse for selection), HSQC (gradient echo-antiecho selection and shape pulse) and HMBC (echo-antiecho gradient selection, magnitude mode) correlation experiments. For each isolated compound, the reducing end was quoted as “a”, and nonreducing entity as “b”. High Resolution Masses were recorded in positive mode using direct Electrospray ionization on a Bruker maXis 4G or a Thermo Fisher Q-Exactive spectrometer.

***n*-Octyl 2,3-di-*O*-benzoyl-6-deoxy-6-fluoro- β -D-galactofuranoside (**5**).** To a solution of **4**⁴¹ (550 mg, 0.98 mmol) in acetone (5.5 mL) was added a 1 M solution of TBAF in THF (1.5 mL, 1.5 mmol). After stirring at room temperature for 1 h and concentration under reduced pressure, the crude oil was diluted in THF (5.5 mL) before adding a solution of concentrated aqueous H₂SO₄ (152 μ L, 2.7 mmol) and H₂O (48.6 μ L, 2.7 mmol). The reaction media was stirred at room temperature for 20 min and then neutralized with Et₃N, concentrated under reduced pressure and partitioned between AcOEt (25 mL) and brine (7 mL). The organic layer was washed with aqueous saturated Na₂CO₃ solution and the aqueous layers extracted with AcOEt (3x5 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Flash chromatography (Chex/AcOEt gradient from 100:0 up to 50:50) afforded the desired product as a colorless oil (414 mg, 84%); R_f=0.3 (Chex/AcOEt 5:1); ¹H NMR (CDCl₃): 8.11-8.03 (m, 4H, H_{arom}), 7.63-7.55 (m, 2H, H_{arom}), 7.50-7.40 (m, 4H, H_{arom}), 5.59 (ddd,

$J_{3,4}=4.5$ Hz, $J_{2,3}=1.3$ Hz, $J_{1,3}=0.7$ Hz, 1H, H-3), 5.51 (d, $J_{2,3}=1.3$ Hz, 1H, H-2), 5.26 (s, 1H, H-1), 4.68-4.46 (m, 1H, H-6a), 4.40-4.27 (m, 1H, H-6b), 4.39-4.29 (m, H-4, H-5), 3.74 (dt, $^2J=9.5$ Hz, $^3J=6.8$ Hz, 1H, OCH₂), 3.53 (dt, $^2J=9.5$ Hz, $^3J=6.2$ Hz, 1H, OCH₂), 1.6 (m, 2H, OCH₂CH₂), 1.27 (m, 10H, 5 CH₂), 0.86 (t, $^3J=6.8$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 166.3 (CO), 165.5 (CO), 133.7, 130.1, 130.0, 129.2, 129.2, 128.7, 128.6 (C₆H₅), 105.8 (C-1), 83.8 (d, $J_{C6-F}=171.4$ Hz, C-6), 82.5 (d, $J_{C4-F}=5.2$ Hz, C-4), 81.5 (C-2), 78.0 (d, $J_{C3-F}=1.4$ Hz, C-3), 69.4 (d, $J_{C5-F}=20.4$ Hz, C-5), 67.8 (OCH₂), 32.0 (OCH₂CH₂), 29.5, 29.4, 27.1, 26.3, 22.8 (5 CH₂), 14.2 (CH₃); HRMS: Calcd for C₂₈H₃₆O₈FNa [M+Na]⁺ 523.2302; found 523.2301.

1,5-di-O-Acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-D-galactofuranose (6). To a solution of **6** (150 mg, 0.28 mmol) in dry CH₂Cl₂ (1.5 mL) were added acetic anhydride (170 μL, 1.8 mmol) and sulfuric acid (31.5 μL, 0.58 mmol). The mixture was stirred 6 h at room temperature and then neutralized with Et₃N. CH₂Cl₂ (10 mL) was added to the mixture and washed with aqueous saturated NaHCO₃ solution (3x6 mL) and aqueous saturated NaCl solution (2x7 mL, until pH 7). Organic layer was dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography (CHex/AcOEt gradient from 100:0 up to 60:40) afforded **6** (108 mg, 81%, α/β=16:84) as a colourless oil. Rf=0.5 (CHex/AcOEt 7:3); Data for **6β**: ¹H NMR (CDCl₃): 8.15-7.97 (m, 4H, H_{arom}), 7.69-7.55 (m, 2H, H_{arom}), 7.54-7.43 (m, 4H, H_{arom}), 6.45 (s, 1H, H-1), 5.59 (d, $J_{2,3}=1.4$ Hz, 1H, H-2), 5.58-5.50 (m, 2H, H-3, H-5), 4.78-4.69 (m, 1H, H-6a), 4.66-4.56 (m, 2H, H-6b, H-4), 2.18 (s, 3H, OCH₃), 2.04 (s, 3H, OCH₃); ¹³C NMR (CDCl₃): 170.1 (CO), 169.2 (CO), 165.5 (CO), 165.3 (CO), 134.0, 133.9, 130.1, 130.0, 129.0, 128.8, 128.7 (C₆H₅), 99.3 (C-1), 82.3 (d, $J_{C4-F}=5.1$ Hz, C-4), 81.1 (C-3), 80.9 (d, $J_{C6-F}=173.5$ Hz, C-6), 76.9 (C-2), 70.2 (d, $J_{C5-F}=20.9$ Hz, C-5), 21.2 (CH₃), 20.9 (CH₃); HRMS: Calcd for C₂₄H₂₃O₉FNa [M+Na]⁺ 497.1218; found 497.1221.

5-O-Acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranosyl bromide (3a). To a solution of **6** (300 mg, 0.63 mmol) in glacial acetic acid (2.2 mL) was added hydrogen bromide 30% in acetic acid (250 μL, 1.3 mmol). The mixture was left under agitation at room temperature for 3 h. CH₂Cl₂ (10 mL) was added and the mixture was washed with aqueous iced water (2x5 mL) and aqueous iced saturated NaHCO₃ solution (2x5 mL). The organic layer was dried over MgSO₄ and concentrated under reduced pressure to afford **3a** (340mg) in 91% yield as a beige solid. ¹H NMR (CDCl₃): 8.15-8.10 (m, 2H, H_{arom}), 8.08-8.04 (m, 2H, H_{arom}), 7.66-7.58 (m, 2H, H_{arom}), 7.52-7.45 (m, 4H, H_{arom}), 6.59 (d, $J_{1,2}=1$ Hz, 1H, H-1), 5.88 (d, $J_{1,2}=0.7$ Hz, 1H, H-2), 5.67 (dq, $J_{5,F}=17.2$ Hz, $J_{4,5}=4.9$ Hz, 1H, H-5), 5.53 (dt, $J_{3,4}=4.5$ Hz, $J_{2,3}=0.9$ Hz, 1H, H-3), 4.80 (td, $J_{3,4}=4.6$, 0.8 Hz, 1H, H-4), 4.67 (dt, $J_{6,F}=46.5$ Hz, $J_{6a,6b}=5.2$ Hz, 2H, H-6), 2.08 (s, 3H, OCH₃); ¹³C NMR (CDCl₃): 169.9 (CO), 165.5 (CO), 165.0 (CO), 134.0, 133.9, 130.1, 129.9, 128.7 (C₆H₅), 87.9 (C-1), 85.3 (C-2), 83.7 (d, $J_{C4-F}=5.2$ Hz, C-4), 80.8 (d, $J_{C6-F}=174.3$ Hz, C-6), 76.3 (C-3), 69.5 (d, $J_{C5-F}=21.1$ Hz, C-5), 20.7 (OCH₃); HRMS: Calcd for C₂₂H₂₀O₇FBr Na [M+Na]⁺ 517.0269; found 517.0260.

Thiophenyl 5-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranoside (3b). To a solution of **6** (40 mg, 0.08 mmol) in dry CH₂Cl₂ (0.20 mL) at -5 °C, were added thiophenol (13 μL, 0.12 mmol) and BF₃·Et₂O (10.6 μL, 0.095 mmol). The mixture was left stirring at room temperature for 2 h. CH₂Cl₂ (10 mL) was added and the

mixture was quickly washed with iced water (2x5 mL) and aqueous iced saturated NaHCO₃ solution (2x5 mL). The organic layer was dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography (CHex/AcOEt gradient from 100:0 up to 90:10) afforded **3b** (38 mg, 91%) of the desired product as white foam. ¹H NMR (CDCl₃): 8.14-8.00 (m, 4H, H_{arom}), 7.67-7.54 (m, 4H, H_{arom}), 7.53-7.42 (m, 4H, H_{arom}), 7.38-7.27 (m, 3H, H_{arom}), 5.77 (br s, 1H, H-1), 5.65 (d, $J_{2,3}=1.6$ Hz, 1H, H-2), 5.64-5.51 (m, 2H, H-5, H-3), 4.77 (t, $J=4.8$ Hz, 1H, H-4), 4.75-4.68 (m, 1H, H-6a), 4.65-4.55 (m, 1H, H-6b), 2.08 (s, 3H, OCH₃); ¹³C NMR (CDCl₃): 170.3 (CO), 165.6 (CO), 165.4 (CO), 133.9, 133.8, 133.3, 132.7, 130.2, 130.0, 129.2, 129.0, 129.0, 128.7, 128.7, 128.2 (C₆H₅), 91.3 (C-1), 82.2 (C-2), 81.2 (d, $J_{C6-F}=172.4$ Hz, C-6), 80.4 (d, $J_{C4-F}=5.2$ Hz, C-4), 77.4 (d, $J_{C3-F}=1$ Hz, C-3), 70.1 (d, $J_{C5-F}=20.9$ Hz, C-5), 20.9 (OCH₃); HRMS: Calcd for C₂₈H₂₅O₇FNa [M+Na]⁺ 547.1197; found 547.1198.

Glycosylation of acceptor 2 from brominated donors (A): To a solution of the acceptor **2** in dry acetonitrile (75 mM) was added a spoon of previously activated molecular sieves 4 Å. The mixture was left under agitation for 30 min. Donor and then AgOTf were added to the flask and the mixture was stirred at the desired temperature for 2 h. The reaction was quenched by adding Et₃N and silver salts were filtered over celite. Solvent was removed under reduced pressure. Flash chromatography (Chex/AcOEt 100:0 up to 0:100) afforded the different products. Yields are given in tables 1 and 2.

Glycosylation of acceptor 2 from thioglycosides (B): To a solution of the acceptor **2** in dry CH₂Cl₂ (0.2 M) were added NIS (2.3 equiv) and TMSOTf. The mixture was stirred for 10 min. In another flask, of the thiofuranosidic donor (1.2 equiv.) was dissolved in dry CH₂Cl₂ (0.2 M). The acceptor was put at the desired temperature and the donor solution was added. The mixture was then stirred for 2 h. The reaction was quenched with NaHCO₃ and solvent was removed under reduced pressure. Flash chromatography (Chex/AcOEt 100:0 up to 0:100) afforded the different products. Yields are given in tables 1 and 2.

Octyl 5-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranosyl-(1→2)-6-deoxy-6-fluoro-α-D-galactopyranoside (7): Compound **7** was obtained according to procedure A (table 1, entry 1) and procedure B (table 1, entry 4) and isolated as a white solid. Rf=0.2 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5. ¹H (CDCl₃): 8.10-8.03 (m, 4H, H_{arom}), 7.63-.57 (m, 2H, H_{arom}), 7.50-7.43 (m, 4H, H_{arom}), 3.73 (dt, $^2J=9.7$ Hz, $^3J=6.9$ Hz, 1H, OCH₂), 3.47 (dt, $^2J=9.7$ Hz, $^3J=6.6$ Hz, 1H, OCH₂), 2.08 (s, 3H, OCH₃), 1.65-1.48 (m, 2H, OCH₂CH₂), 1.36-1.12 (m, 10H, 5 CH₂), 0.86 (t, $^3J=7.2$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 170.1 (CO), 166.5 (CO), 165.7 (CO), 134.0, 133.9, 130.2, 130.1, 128.9, 128.8, 128.7, 128.6 (C₆H₅), 68.8 (OCH₂), 32.0 (OCH₂CH₂), 29.7, 29.5, 29.3, 26.4, 22.8 (5 CH₂), 20.9 (OCH₃), 14.2 (CH₃). HRMS: Calcd for C₃₆H₄₆O₁₂F₂Na [M+Na]⁺ 731.2849; found 731.2847.

5-O-Acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-α,β-D-galactofuranose (8): Compound **8** was obtained according to procedure A and isolated as a white solid (table 1, entries 1, 2). Rf=0.4 (CHex-AcOEt, 6-4); ¹H NMR (CDCl₃): 8.11-8.02 (m, 4H, H_{arom}), 7.63-7.56 (m, 2H, H_{arom}), 7.49-7.41 (m, 4H, H_{arom}), 5.65 (s, 1H, H-1), 5.61-5.45 (m, 3H, H-2, H-3, H-5), 4.69 (t, $J=4.7$ Hz, 1H, H-4), 4.67

(ddd, $J_{6a,6b}=46.7$ Hz, $J_{5,6}=5.1$ Hz, $J_{5,6}=1.7$ Hz, 2H, H-6), 2.08 (s, 3H, OCH₃); ¹³C NMR (CDCl₃): 170.2 (CO), 166.8 (CO), 166.6 (CO), 133.8, 130.1, 130.0, 129.1, 129.0, 128.7 (C₆H₅), 101.1 (C-1), 82.4 (C-2), 81.1 (d, $J_{C6-F}=176.3$ Hz, C-6), 80.8 (d, $J_{C4-F}=3.2$ Hz, C-4), 77.4 (C-3), 70.4 (d, $J_{C5-F}=20.7$ Hz, C-5), 20.9 (OCH₃). MS: Calcd for C₂₂H₂₁O₈FNa [M+Na]⁺ 455.4; found 454.9.

Octyl 5-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranoside (9): Compound **9** was obtained according to procedure A as a white solid (table 1, entries 1, 2). Rf=0.9 (CHex/AcOEt, 6:4) ¹H NMR (CDCl₃): 8.10-8.03 (m, 4H, H_{arom}), 7.62-7.56 (m, 2H, H_{arom}), 7.49-7.43 (m, 4H, H_{arom}), 5.57 (dq, $J_{5,6a}=16.9$ Hz, $J_{5,6b}=5.0$ Hz, 1H, H-5), 5.47-5.43 (m, 2H, H-2, H-3), 5.21 (s, 1H, H-1), 4.70 ($J=5.8$ Hz, 10.0 Hz, 46.6 Hz, 1H, H-6), 4.64 ($J=5.0$ Hz, 10.0 Hz, 46.6 Hz, 1H, H-6), 4.49 (t, $J=4.5$ Hz, H-4), 3.75 (dt, $^2J=9.4$ Hz, $^3J=7.2$ Hz, 1H, OCH₂), 3.53 (dt, $^2J=9.5$, $^3J=6.8$ Hz, 1H, OCH₂), 2.08 (s, 3H, OCH₃), 1.69-1.57 (m, 2H, OCH₂CH₂), 1.44-1.01 (10H, 5 CH₂), 0.86 (t, $^3J=6.5$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 170.1 (CO), 165.6 (CO), 165.4 (CO), 133.6, 133.5, 129.9, 129.9, 129.2, 129.1, 128.5, 128.5 (C₆H₅), 106.7 (C-1), 82.0 (C-2), 81.1 (d, $J_{C6-F}=173.2$ Hz, C-6), 80.2 (d, $J_{C4-F}=5.7$ Hz, C-4), 77.3 (C-3), 70.4 (d, $J_{C5-F}=20.7$ Hz, C-5) 67.7 (OCH₂), 31.8 (OCH₂CH₂), 29.5, 29.4, 29.3, 29.2, 22.7 (5 CH₂), 20.8 (OCH₃), 14.1 (CH₃). HRMS: Calcd for C₃₀H₃₇O₈FNa [M+Na]⁺ 567.2365; found 567.2365.

Octyl 5-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranosyl-(1→2)-6-deoxy-6-fluoro-β-D-galactofuranoside (10): Compound **10** was obtained according to procedure A (table 1, entry 2) and procedure B (table 1, entries 5, 6) and isolated as a white solid. Rf=0.3 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5. ¹H NMR (CDCl₃): 8.09-8.03 (m, 4H, H_{arom}), 7.64-7.57 (m, 2H, H_{arom}), 7.50-7.44 (m, 4H, H_{arom}), 3.73 (dt, $^2J=9.5$ Hz, $^3J=6.8$ Hz, 1H, OCH₂), 3.44 (dt, $^2J=9.7$ Hz, $^3J=6.6$ Hz, 1H, OCH₂), 2.08 (s, 3H, OCH₃), 1.62-1.54 (m, 2H, OCH₂CH₂), 1.35-1.17 (m, 10H, 5 CH₂), 0.88 (t, $^3J=7.3$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 170.1 (CO), 166.7 (CO), 166.6 (CO), 134.0, 133.9, 130.1, 130.0, 128.9, 128.8, 128.7, 128.7 (C₆H₅), 68.2 (OCH₂), 31.9 (OCH₂CH₂), 29.7, 29.4, 29.3, 26.2, 22.8 (5 CH₂), 20.9 (OCH₃), 14.2 (CH₃). HRMS: Calcd for C₃₆H₄₆O₁₂F₂Na [M+Na]⁺ 731.2849; found 731.2847.

Octyl 5-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranosyl-(1→3)-6-deoxy-6-fluoro-β-D-galactofuranoside (11): Compound **11** was obtained according to procedure A (table 1, entry 2) and procedure B (table 1, entries 5, 6) and isolated as a white solid. Rf=0.2 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5. ¹H NMR (CDCl₃): 8.08-8.02 (m, 4H, H_{arom}), 7.63-7.56 (m, 2H, H_{arom}), 7.50-7.41 (m, 4H, H_{arom}), 3.63 (dt, $^2J=9.5$ Hz, $^3J=6.9$ Hz, 1H, OCH₂), 3.41 (dt, $^2J=9.6$ Hz, $^3J=6.6$ Hz, 1H, OCH₂), 2.08 (s, 3H, OCH₃), 1.59-1.47 (m, 2H, OCH₂CH₂), 1.35-1.15 (m, 10H, 5 CH₂), 0.86 (t, $^3J=7.1$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 170.2 (CO), 166.7 (CO), 166.6 (CO), 133.9, 133.8, 130.1, 130.0, 129.0, 128.9, 128.7, 128.6 (C₆H₅), 68.0 (OCH₂), 31.9 (OCH₂CH₂), 29.6, 29.4, 29.3, 26.1, 22.8 (5 CH₂), 20.9 (OCH₃), 14.2 (CH₃). HRMS: Calcd for C₃₆H₄₆O₁₂F₂Na [M+Na]⁺ 731.2849; found 731.2851.

Octyl 5-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranosyl-(1→5)-6-deoxy-6-fluoro-β-D-galactofuranoside (12): Compound **12** was obtained according to procedure A (table 1,

entry 2) and procedure B (table 1, entries 5, 6) and isolated as a white solid. Rf=0.3 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5. ¹H NMR (CDCl₃): 8.12-8.03 (m, 4H, H_{arom}), 7.63-7.55 (m, 2H, H_{arom}), 7.50-7.41 (m, 4H, H_{arom}), 3.66 (dt, $^2J=9.7$ Hz, $^3J=6.7$ Hz, 1H, OCH₂), 3.40 (dt, $^2J=9.6$ Hz, $^3J=6.5$ Hz, 1H, OCH₂), 2.08 (s, 3H, OCH₃), 1.58-1.49 (m, 2H, OCH₂CH₂), 1.34-1.19 (m, 10H, 5 CH₂), 0.88 (t, $^3J=6.7$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 170.2 (CO), 166.8 (CO), 166.4 (CO), 133.9, 133.8, 130.3, 130.0, 129.0, 128.9, 128.7, 128.6 (C₆H₅), 68.0 (OCH₂), 31.9 (OCH₂CH₂), 29.6, 29.4, 29.3, 26.2, 22.8 (5 CH₂), 20.9 (OCH₃), 14.2 (CH₃). HRMS: Calcd for C₃₆H₄₆O₁₂F₂Na [M+Na]⁺ 731.2849; found 731.2847.

Octyl 5-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranosyl-(1→3)-[5-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranosyl-(1→2)]-6-deoxy-6-fluoro-α-D-galactopyranoside (13): Trisaccharide **13** was obtained according to procedure B (table 1, entries 3, 4) and isolated as a white solid. Rf=0.6 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5. ¹H NMR (CDCl₃): 8.09-7.98 (m, 4H, H_{arom}), 7.96-7.88 (m, 3H, H_{arom}), 7.61-7.55 (m, 4H, H_{arom}), 7.55-7.40 (m, 5H, H_{arom}), 7.39-7.30 (m, 4H, H_{arom}) 3.70 (dt, $^2J=9.5$ Hz, $^3J=7.0$ Hz, 1H, OCH₂), 3.43 (dt, $^2J=9.7$ Hz, $^3J=6.7$ Hz, 1H, OCH₂), 2.08 (s, 3H, OCH₃), 2.02 (s, 3H, OCH₃), 1.62-1.50 (m, 2H, OCH₂CH₂), 1.32-1.13 (m, 10H, 5 CH₂), 0.86 (t, $^3J=6.7$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 170.2 (CO), 170.1 (CO), 166.7 (CO), 166.5 (CO), 166.4 (CO), 166.3 (CO), 133.9, 133.7, 133.6, 133.5, 130.2, 130.0, 130.0, 129.9, 129.2, 129.1, 129.1, 128.9, 128.8, 128.6, 128.5, 128.4 (C₆H₅), 68.9 (OCH₂), 32.0 (OCH₂CH₂), 29.7, 29.5, 29.3, 26.3, 22.8 (5 CH₂), 20.9, 20.9 (OCH₃), 14.2 (CH₃). HRMS: Calcd for C₅₈H₆₅O₁₉F₃Na [M+Na]⁺ 1145.3970; found 1145.3971.

Octyl 5-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactofuranosyl-(1→3)-6-deoxy-6-fluoro-α-D-galactopyranoside (14): Compound **14** was obtained according to procedure B (table 1, entry 4) and isolated as a white solid. Rf=0.5 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5. ¹H NMR (CDCl₃): 8.11-7.98 (m, 4H, H_{arom}), 7.63-7.52 (m, 2H, H_{arom}), 7.49-7.41 (m, 4H, H_{arom}), 3.75 (dt, $^2J=9.8$ Hz, $^3J=7.0$ Hz, 1H, OCH₂), 3.50 (dt, $^2J=9.7$ Hz, $^3J=6.6$ Hz, 1H, OCH₂), 2.08 (s, 3H, OCH₃), 1.67-1.60 (m, 2H, OCH₂CH₂), 1.38-1.10 (m, 10H, 5 CH₂), 0.88 (t, $^3J=7.0$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 170.1 (CO), 166.7 (CO), 166.6 (CO), 134.0, 133.9, 130.1, 130.0, 128.9, 128.8, 128.8, 128.7 (C₆H₅), 68.7 (OCH₂), 32.0 (OCH₂CH₂), 29.6, 29.5, 29.4, 26.3, 20.9 (5 CH₂), 20.9 (OCH₃), 14.2 (CH₃). HRMS: Calcd for C₃₆H₄₆O₁₂F₂Na [M+Na]⁺ 731.2849; found 731.2853.

Trifuranoside (15): Trisaccharide **15** was obtained according to procedure B (table 1, entries 5, 6) and isolated as a white solid. Rf=0.6 (CHex/AcOEt, 6:4). HRMS: Calcd for C₅₈H₆₅O₁₉F₃Na [M+Na]⁺ 1145.3964; found 1145.3969.

Octyl 2,3,5,6-tetra-O-benzoyl-β-D-galactofuranosyl-(1→2)-6-deoxy-6-fluoro-α-D-galactopyranoside (17): Disaccharide **17** was obtained according to procedure A (table 2, entry 1) and isolated as a white solid. Rf=0.2 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5. ¹H NMR (CDCl₃): 8.10-7.91 (m, 8H, H_{arom}), 7.59-7.49 (m, 4H, H_{arom}), 7.43-7.29 (m, 8H, H_{arom}), 3.68 (dt, $^2J=9.7$ Hz, $^3J=6.9$ Hz, 1H, OCH₂), 3.44 (dt, $^2J=9.7$ Hz, $^3J=6.6$ Hz, 1H, OCH₂), 1.57-1.49 (m, 2H, OCH₂CH₂), 1.32-1.13 (m, 10H, 5 CH₂), 0.85 (t, $^3J=6.3$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 166.5 (CO), 166.2 (CO), 165.7 (CO), 165.7 (CO), 133.9,

133.7, 133.5, 133.3, 130.1, 130.1, 130.0, 129.9, 129.6, 129.5, 129.0, 128.7, 128.6, 128.6, 128.5 (C₆H₅), 68.9 (OCH₂), 32.0 (OCH₂CH₂), 29.8, 29.5, 29.3, 26.3, 22.8 (5 CH₂), 14.2 (CH₃). HRMS: Calcd for C₄₈H₅₃O₁₄FNa [M+Na]⁺ 895.3312; found 895.3315.

2,3,5,6-tetra-O-benzoyl- α , β -D-galactofuranose (18): Compound **18** was obtained according to procedure A (table 2, entries 2, 3) and isolated as a white solid. Rf=0.6 (CHex/AcOEt, 6:4); ¹H NMR (CDCl₃): 8.11-7.88 (m, 8H, H_{arom}), 7.58-7.46 (m, 4H, H_{arom}), 7.44-7.27 (m, 8H, H_{arom}), 6.10 (t, J_{2 α -3 α} =5.1 Hz, 0.3H, H-3 α), 6.06 (dt, J_{4 β -5 β} =7.0 Hz, J_{5 β -6 β} =3.1 Hz, 0.7H, H-5 β), 5.98 (td, J_{4 α -5 α} =6.3 Hz, J_{5 α -6 α} =3.6 Hz, 0.3H, H-5 α), 5.85 (d, J_{1 α -2 α} =4.5 Hz, 0.3H, H-1 α), 5.72 (s, 0.7H, H-1 β), 5.66 (ddd, J_{3 β -4 β} =5.0 Hz, J_{2 β -3 β} =1.4 Hz, J_{1 β -3 β} =0.7 Hz, 0.7H, H-3 β), 5.56 (dd, J_{2 α -3 α} =5.4 Hz, J_{1 α -2 α} =4.4 Hz, 0.3H, H-2 α), 5.52 (dd, J_{2 β -3 β} =1.4 Hz, J_{1 β -2 β} =0.6 Hz, 0.7H, H-2 β), 4.87 (dd, J_{3 β -4 β} =5.0 Hz, J_{4 β -5 β} =4.0 Hz, 0.7H, H-4 β), 4.82-4.68 (m, 2H, H-6 α , H-6 β), 4.56 (dd, J_{4 β -5 β} =6.6 Hz, J_{3 α -4 α} =4.7 Hz, 0.3H, H-4 α); ¹³C NMR (CDCl₃): 166.4 (CO), 166.2 (CO), 166.2 (CO), 165.9 (5CO), 165.8 (CO), 165.8 (CO), 165.7 (CO), 165.6 (CO), 133.7, 133.6, 133.5, 133.4, 133.2, 130.1, 130.0, 129.8, 129.8, 129.5, 129.6, 129.6, 129.1, 128.9, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4 (C₆H₅), 101.2 (C-1 β), 96.2 (C-1 α), 82.8 (C-2 β), 81.8 (C-4 β), 79.5 (C-4 α), 77.8 (C-3 β), 77.7 (C-2 α), 76.0 (C-3 α), 72.4 (C-5 α), 70.7 (C-5 β), 63.7 (C-6 β), 63.3 (C-6 α); HRMS : Calcd for C₃₄ H₂₈ O₁₀ Na [M+Na]⁺ 619.1575; found 619.1576.

Octyl 2,3,5,6-tetra-O-benzoyl- β -D-galactofuranoside (19): Monosaccharide **19** was obtained according to procedure A (table 2, entries 1-3) as a white solid. Rf=0.7 (CHex/AcOEt, 6:4); ¹H NMR (CDCl₃): 8.11-7.89 (m, 8H, H_{arom}), 7.60-7.49 (m, 4H, H_{arom}), 7.45-7.27 (m, 8H, H_{arom}), 6.08 (ddd, J_{5,6a}=7.0 Hz, J_{5,6b}=4.6 Hz, J_{4,5}=3.5 Hz, 1H, H-5), 5.64 (td, J_{3,4}=5.2 Hz, J_{2,3}=0.9 Hz, 1H, H-3), 5.47 (d, J_{2,3}=1.1 Hz, 1H, H-2), 5.31 (s, 1H, H-1), 4.82-4.71 (m, 2H, H-6), 4.65 (dd, J_{3,4}=5.2 Hz, J_{4,5}=3.5 Hz, 1H, H-4), 3.75 (dt, ²J=9.5 Hz, ³J=6.3 Hz, 1H, OCH₂), 3.54 (dt, ²J=9.5 Hz, ³J=6.3 Hz, 1H, OCH₂), 1.71-1.67 (m, 2H, OCH₂CH₂), 1.41-1.18 (m, 10H, 5 CH₂), 0.87 (t, ²J=6.3 Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 165.9 (CO), 165.6 (CO), 165.5 (CO), 165.3 (CO), 133.2, 133.1, 133.0, 132.9, 129.9, 129.8, 129.7, 129.5, 129.4, 129.3, 128.9, 128.8 (C₆H₅), 105.4, (C-1), 81.9 (C-2), 81.0 (C-4), 77.4 (C-3), 70.1 (C-5), 67.5 (OCH₂), 63.3 (C-6), 31.6 (OCH₂CH₂), 29.3, 29.2, 29.1, 26.0, 22.5 (5 CH₂), 13.9 (CH₃); HRMS : Calcd for C₄₂ H₄₄ O₁₀ Na [M+Na]⁺ 731.2827; found 731.2829.

Octyl 2,3,5,6-tetra-O-benzoyl- β -D-galactofuranosyl-(1 \rightarrow 2)-6-deoxy-6-fluoro- β -D-galactofuranoside (20): Disaccharide **20** was obtained according to procedure A (table 2, entries 2 and 3) and procedure B (table 2, entry 4) and isolated as a white solid. Rf=0.6 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5; ¹H NMR (CDCl₃): 8.12-7.96 (m, 6H, H_{arom}), 7.91-7.84 (m, 2H, H_{arom}), 7.60-7.48 (m, 4H, H_{arom}), 7.46-7.23 (m, 8H, H_{arom}), 3.70-3.60 (m, 1H, OCH₂), 3.45-3.31 (m, 1H, OCH₂), 1.58-1.49 (m, 2H, OCH₂CH₂), 1.33-1.19 (m, 10H, 5 CH₂), 0.91-0.83 (m, 3H, CH₃); ¹³C NMR (CDCl₃): 166.4-165.5 (CO), 133.8-128.3 (C₆H₅), 68.0 (OCH₂), 321.9 (OCH₂CH₂), 29.6-22.8 (5 CH₂), 14.2 (CH₃). HRMS: Calcd for C₄₈H₅₃O₁₄FNa [M+Na]⁺ 895.3312; found 895.3315.

Octyl 2,3,5,6-tetra-O-benzoyl- β -D-galactofuranosyl-(1 \rightarrow 3)-6-deoxy-6-fluoro- β -D-galactofuranoside (21): Disaccharide **21** was obtained according to procedure A (table 2, entries 2, 3) and

procedure B (table 2, entry 4) and isolated as a white solid. Rf=0.6 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5; ¹H NMR (CDCl₃): 8.12-7.96 (m, 6H, H_{arom}), 7.91-7.84 (m, 2H, H_{arom}), 7.60-7.48 (m, 4H, H_{arom}), 7.46-7.23 (m, 8H, H_{arom}), 3.70-3.60 (m, 1H, OCH₂), 3.45-3.31 (m, 1H, OCH₂), 1.58-1.49 (m, 2H, OCH₂CH₂), 1.33-1.19 (m, 10H, 5 CH₂), 0.91-0.83 (m, 3H, CH₃); ¹³C NMR (CDCl₃): 166.4-165.5 (CO), 133.8-128.3 (C₆H₅), 68.0 (OCH₂), 321.9 (OCH₂CH₂), 29.6-22.8 (5 CH₂), 14.2 (CH₃). HRMS: Calcd for C₄₈H₅₃O₁₄FNa [M+Na]⁺ 895.3312; found 895.3314.

Octyl 2,3,5,6-tetra-O-benzoyl- β -D-galactofuranosyl-(1 \rightarrow 5)-6-deoxy-6-fluoro- β -D-galactofuranoside (22): Disaccharide **22** was obtained according to procedure A (table 2, entries 2 and 3) and procedure B (table 2, entry 4) and isolated as a white solid. Rf=0.6 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5; ¹H NMR (CDCl₃): 8.12-7.96 (m, 6H, H_{arom}), 7.91-7.84 (m, 2H, H_{arom}), 7.60-7.48 (m, 4H, H_{arom}), 7.46-7.23 (m, 8H, H_{arom}), 3.70-3.60 (m, 1H, OCH₂), 3.45-3.31 (m, 1H, OCH₂), 1.58-1.49 (m, 2H, OCH₂CH₂), 1.33-1.19 (m, 10H, 5 CH₂), 0.91-0.83 (m, 3H, CH₃); ¹³C NMR (CDCl₃): 166.4-165.5 (CO), 133.8-128.3 (C₆H₅), 68.0 (OCH₂), 321.9 (OCH₂CH₂), 29.6-22.8 (5 CH₂), 14.2 (CH₃). HRMS: Calcd for C₄₈H₅₃O₁₄FNa [M+Na]⁺ 895.33116; found 895.3314.

Trifuranoside (23): Trisaccharide **23** was obtained according to procedure B (table 2, entry 4) and isolated as a white solid. Rf=0.6 (CHex/AcOEt, 6:4); NMR data in tables 4 and 5. HRMS: Calcd for C₈₂H₇₉O₂₃FNa [M+Na]⁺ 1473.4888; found 1473.4891.

General procedure for deacylation reaction (C): To a solution of the protected carbohydrate in dry CH₂Cl₂/MeOH (1/1) (0.07 M) was added MeONa 5.4M (0.2 equiv). The mixture was stirred for 24h at room temperature. Then the solution was neutralized by the addition of IR 120-H⁺ form resin. After filtration, the filtrate was evaporated under reduced pressure. The residual solid was suspended in water and freeze dried in order to co evaporate methyl esters.

Octyl 6-deoxy-6-fluoro- β -D-galactofuranosyl-(1 \rightarrow 2)-6-deoxy-6-fluoro- β -D-galactofuranoside (24): Disaccharide **24** was obtained according to procedure C and isolated as a white solid (6 mg, 95%). ¹H NMR (CD₃OD): 5.08 (d, J_{1,2}=1.9 Hz, 1H, H-1b), 4.98 (d, J_{1,2}=1.6 Hz, 1H, H-1a), 4.58-4.48 (m, 2H, H-6a, H-6b), 4.46-4.35 (m, 2H, H-6a, H-6b), 4.17 (dd, J_{3,4}=7.7 Hz, J_{2,3}=4.1 Hz, 1H, H-3a), 4.07 (dd, J_{3,4}=6.3 Hz, J_{2,3}=3.9 Hz, 1H, H-3b), 4.00 (dd, J_{2,3}=3.9 Hz, J_{1,2}=1.9 Hz, 1H, H-2b), 3.99 (dd, J_{2,3}=4.1 Hz, J_{1,2}=1.6 Hz, 1H, H-2a), 3.97-3.90 (m, 3H, H-4b, H-5b, H-5a), 3.85 (dd, J_{3,4}=7.7 Hz, J_{4,5}=3.2 Hz, 1H, H-4a), 3.68 (dt, ²J=9.6 Hz, ³J=6.7 Hz, 1H, OCH₂), 3.43 (dt, ²J=9.6 Hz, ³J=6.5 Hz, 1H, OCH₂), 1.64-4.55 (m, 2H, OCH₂CH₂), 1.41-1.25 (m, 10H, 5 CH₂), 0.91 (t, ³J=6.3 Hz, 3H, CH₃); ¹³C NMR (CD₃OD): 109.8 (C-1b), 108.0 (C-1a), 90.6 (C-2a), 85.2 (d, J_{C-F}=171.2 Hz, C-6b), 85.1 (d, J_{C-F}=169.9, C-6a), 83.6 (d, J_{C-F}=4.3 Hz, C-4b), 83. (C-2b), 81.8 (d, J_{C-F}=7.3 Hz, C-4a), 78.3 (C-3b), 77.2 (C-3a), 69.8 (d, J_{C-F}=20.0 Hz, C-5a, C-5b), 68.9 (OCH₂), 33.0, 30.8, 30.5, 30.4, 27.3, 23.7 (6 CH₂), 14.4 (CH₃). HRMS: Calcd for C₂₀H₃₆O₁₀F₂Na [M+Na]⁺ 481.2220; found 481.2222.

Octyl 6-deoxy-6-fluoro- β -D-galactofuranosyl-(1 \rightarrow 3)-6-deoxy-6-fluoro- β -D-galactofuranoside (25): Disaccharide **25** was obtained according to procedure C and isolated as a white solid (8 mg, 88%). ¹H NMR (CD₃OD): 5.06 (d, J_{1,2}=2.0 Hz, 1H, H-1b), 4.86 (d, J_{1,2}=1.6 Hz,

1H, H-1a), 4.56-4.46 (m, 2H, H-6a, H-6b), 4.43-4.34 (m, 2H, H-6a, H-6b), 4.15-4.10 (m, 1H, H-3a), 4.08 (dd, $J_{2,3}=3.2$ Hz, $J_{1,2}=1.6$ Hz, 1H, H-2a), 4.06-3.99 (m, 3H, H-3b, H-4a, H-5b), 4.00 (d, $J_{1,2}=2.1$ Hz, 1H, H-2b), 3.98-3.89 (m, 2H, H-4b, H-5a), 3.65 (dt, $^2J=9.7$ Hz, $^3J=6.7$ Hz, 1H, OCH₂), 3.41 (dt, $^2J=9.7$ Hz, $^3J=6.4$ Hz, 1H, OCH₂), 1.64-4.52 (m, 2H, OCH₂CH₂), 1.49-1.23 (m, 10H, 5 CH₂), 0.89 (t, $J=7.4$ Hz, 3H, CH₃); ¹³C NMR (CD₃OD): 109.3 (C-1a), 109.1 (C-1b), 85.2 (d, $J_{C-F}=169.6$ Hz, C-6a), 85.0 (d, $J_{C-F}=170.7$ Hz, C-6b), 84.2 (C-3a), 83.5 (d, $J_{C-F}=6.3$ Hz, C-4b), 83.0 (C-2b), 82.1 (d, $J_{C-F}=6.6$ Hz, H-4a), 81.6 (C-2a), 78.0 (C-3b), 67.8 (d, $J_{C-F}=18.3$ Hz, C-5b), 69.7 (d, $J_{C-F}=20.2$ Hz, C-5a), 68.7 (OCH₂), 32.8, 30.5, 30.3, 30.2, 27.0, 23.5, (6 CH₂), 14.4 (CH₃). HRMS: Calcd for C₂₀H₃₆O₁₀F₂Na [M+Na]⁺ 481.2220; found 481.2220.

Octyl 6-deoxy-6-fluoro-β-D-galactofuranosyl-(1→5)-6-deoxy-6-fluoro-β-D-galactofuranoside (26): Disaccharide **26** was obtained according to procedure C and isolated as a white solid (6 mg, 93%). ¹H NMR (CD₃OD): 5.17 (s, 1H, H-1b), 4.83 (d, $J_{1,2}=1.7$ Hz, H-1a), 4.70-4.61 (m, 1H, H-6a), 4.61-4.46 (m, 2H, H-6a, H-6b), 4.46-4.41 (m, 1H, H-6a), 4.21-4.10 (m, 1H, H-5a), 4.13 (dd, $J_{3,4}=4.5$ Hz, $J_{4,5}=3.4$ Hz, 1H, H-4b), 4.05-3.98 (m, 3H, H-3a, H-3b, H-5b), 3.97-3.90 (m, 3H, H-2a, H-4a, H-2b), 3.69-3.60 (m, 1H, OCH₂), 3.46-3.36 (m, 1H, OCH₂), 1.61-1.50 (m, 2H, OCH₂CH₂), 1.38-1.20 (m, 10H, 5 CH₂), 0.87 (t, $^3J=5.4$ Hz, 3H, CH₃); ¹³C NMR (CD₃OD): 109.1 (C-1a, C-1b), 85.2 (d, $J_{C-F}=6.4$ Hz, C-4b), 85.1 (d, $J_{C-F}=167.5$ Hz, C-6b), 84.1 (d, $J_{C-F}=168.9$ Hz, C-6a), 83.0 (C-2a, C-2b), 82.9 (d, $J_{C-F}=7.2$ Hz, C-4a), 78.2 (C-3a), 77.6 (C-3b), 74.6 (d, $J_{C-F}=17.5$ Hz, C-5a), 70.5 (d, $J_{C-F}=19.9$ Hz, C-5b), 69.9 (OCH₂), 32.7, 30.3, 30.2, 30.1, 26.9, 23.4 (6 CH₂), 14.4 (CH₃); HRMS : Calcd for C₂₀H₃₆O₁₀F₂Na [M+Na]⁺ 481.2220; found 481.2220.

Octyl 6-deoxy-6-fluoro-β-D-galactopyranosyl-(1→2)-6-deoxy-6-fluoro-β-D-galactofuranoside (27): Disaccharide **27** was obtained according to procedure C and isolated as a white solid (4 mg, 92%). ¹H NMR (CD₃OD): 5.06 (d, $J_{1,2}=1.7$ Hz, 1H, H-1b), 4.99 (d, $J_{1,2}=3.8$ Hz, 1H, H-1a), 4.65-4.35 (m, 4H, H-6a, H-6b), 4.08 (dd, $J_{2,3}=3.8$ Hz, $J_{1,2}=1.8$ Hz, 1H, H-2b), 4.03-4.01 (m, 1H, H-5b), 4.01-3.92 (m, 1H, H-5a), 3.99 (dd, $J_{2,3}=3.8$ Hz, $J_{2,3}=3.1$ Hz, 1H, H-3b), 3.97 (dd, $J_{3,4}=3.1$ Hz, $J_{4,5}=2.1$ Hz, 1H, H-4b), 3.92 (dd, $J_{3,4}=3.4$ Hz, $J_{4,5}=1.3$ Hz, 1H, H-4a), 3.87 (dd, $J_{2,3}=10.0$ Hz, $J_{3,4}=3.4$ Hz, 1H, H-3a), 3.77 (dd, $J_{2,3}=10.0$ Hz, $J_{1,2}=3.7$ Hz, 1H, H-2a), 3.69 (dt, $^2J=9.6$ Hz, $^3J=6.9$ Hz, 1H, OCH₂), 3.45 (dt, $^2J=9.6$ Hz, $^3J=6.4$ Hz, 1H, OCH₂), 1.67-1.56 (m, 2H, OCH₂CH₂), 1.43-1.28 (10H, 5 CH₂), 0.91 (t, $^3J=6.7$ Hz, 3H, CH₃); ¹³C NMR (CDCl₃): 110.9 (C-1b), 99.7 (C-1a), 84.3 (d, $J_{C-F}=170.6$ Hz, C-6a), 84.0 (d, $J_{C-F}=5.6$ Hz, C-4b), 83.6 (d, $J_{C-F}=167.2$ Hz, C-6b), 81.8 (C-2b), 77.9 (C-3b), 77.6 (C-2a), 70.2 (d, $J_{C-F}=21$ Hz, H-5b), 70.2 (d, $J_{C-F}=6.2$ Hz, C-4a), 69.6 (d, $J_{C-F}=16.9$ Hz, C-5a), 69.5 (C-3a), 69.1 (OCH₂), 32.7, 30.3, 30.2, 30.1, 23.4 (5 CH₂), 14.4 (CH₃). HRMS: Calcd for C₂₀H₃₆O₁₀F₂ Na [M+Na]⁺ 481.2220; found 481.2213.

Disaccharides 28, 29 and 30 were deacylated according to procedure C. Purification gave a mixture of the three compounds (15 mg, 90%, ratio 30:26:44 for 25/26/27). NMR assignment for each disaccharide yielded to the following data: HRMS : Calcd for C₂₀H₃₇O₁₀FNa [M+Na]⁺ 479.2263; found 479.2262; **Octyl β-D-galactofuranosyl-(1→2)-6-deoxy-6-fluoro-β-D-galactofuranoside (28):** ¹H NMR (CD₃OD): 5.07 (d, $J_{1,2}=1.6$ Hz, H-1b), 4.99 (d, $J_{1,2}=1.4$ Hz, H-1a), 4.54-4.47 (m, 1H, H-6a), 4.41-4.34 (m, 1H, H-6a), 4.13 (dd, $J_{3,4}=3.5$ Hz, $J_{2,3}=1.6$ Hz, H-3a), 4.05-4.02 (m, 1H, H-3b), 4.01-3.96 (m, 2H, H-2a, H-2b), 3.96-3.92 (m, 2H, H-5a, H-4b), 3.86 (dd, $J_{4,5}=7.3$ Hz,

$J_{3,4}=3.1$ Hz, H-4a), 3.76-3.70 (m, 1H, H-5b), 3.68-3.58 (m, 3H, H-6b, OCH₂), 3.45-3.35 (m, 1H, OCH₂), 1.60-1.50 (m, 2H, OCH₂CH₂), 1.37-1.19 (m, 10H, 5 CH₂), 0.86 (t, $^3J=6.7$ Hz, 3H, CH₃); ¹³C NMR (CD₃OD): 108.0 (C-1b), 106.5 (C-1a), 88.5 (C-2a), 84.1 (d, $J_{C-F}=169.2$ Hz, C-6a), 83.9 (C-3b), 81.5 (C-2b), 80.9 (d, $J_{C-F}=6.2$ Hz, C-4a), 77.3 (C-3b), 75.7 (C-3a), 71.0 (C-5b), 68.5 (d, $J_{C-F}=19.9$ Hz, C-5a), 67.9 (OCH₂), 63.4 (C-6b), 31.7, 29.4, 29.2, 29.1, 25.9, 22.4 (5 CH₂), 13.5 (CH₃); **Octyl β-D-galactofuranosyl-(1→3)-6-deoxy-6-fluoro-β-D-galactofuranoside (29):** ¹H NMR (CD₃OD): 5.07 (d, $J_{1,2}=1.6$ Hz, H-1b), 4.86 (d, $J_{1,2}=1.6$ Hz, H-1a), 4.54-4.47 (m, 1H, H-6a), 4.41-4.34 (m, 1H, H-6a), 4.17-4.13 (m, 1H, H-3a), 4.07 (dd, $J_{2,3}=3.2$ Hz, $J_{1,2}=1.6$ Hz, H-2a), 4.09-4.05 (m, 1H, H-5a), 4.03-3.98 (m, 3H, H-4a, H-2b, H-3b), 3.98-3.92 (m, 1H, H-4b), 3.76-3.70 (m, 1H, H-5b), 3.68-3.58 (m, 3H, H-6b, OCH₂), 3.45-3.35 (m, 1H, OCH₂), 1.60-1.50 (m, 2H, OCH₂CH₂), 1.37-1.19 (m, 10H, 5 CH₂), 0.86 (t, $^3J=6.7$ Hz, 3H, CH₃); ¹³C NMR (CD₃OD): 108.1 (C-1a), 107.6 (C-1b), 84.1 (d, $J_{C-F}=169.2$ Hz, C-6a), 83.9 (C-4b), 82.4 (C-3a), 81.5 (C-2b), 80.9 (d, $J_{C-F}=6.6$ Hz, C-4a), 80.1 (C-2a), 77.3 (C-3b), 70.9 (C-5b), 68.3 (d, $J_{C-F}=19.7$ Hz, C-5a), 67.8 (OCH₂), 63.1 (C-6b), 31.7, 29.4, 29.2, 29.1, 25.9, 22.4 (5 CH₂), 13.5 (CH₃); **Octyl β-D-galactofuranosyl-(1→5)-6-deoxy-6-fluoro-β-D-galactofuranoside (30):** ¹H NMR (CD₃OD): 5.16 (s, 1H, H-1b), 4.83 (d, $J_{1,2}=1.7$ Hz, H-1a), 4.66-4.63 (m, 1H, H-6a), 4.54-4.47 (m, 1H, H-6a), 4.20-4.12 (m, 2H, H-4b, H-5a), 4.05-3.98 (m, 3H, H-2b, H-3b, H-3a), 3.96-3.92 (m, 2H, H-2a, H-4a), 3.76-3.70 (m, 1H, H-5b), 3.68-3.58 (m, 3H, H-6b, OCH₂), 3.45-3.35 (m, 1H, OCH₂), 1.60-1.50 (m, 2H, OCH₂CH₂), 1.37-1.19 (m, 10H, 5 CH₂), 0.86 (t, $^3J=6.7$ Hz, 3H, CH₃); ¹³C NMR (CD₃OD): 108.0 (C-1a), 107.8 (d, $J_{C-F}=2.4$ Hz, C-1b), 84.4 (C-4b), 83.6 (d, $J_{C-F}=170.1$ Hz, C-6a), 81.9 (C-2a), 81.7 (d, $J_{C-F}=7.2$ Hz, C-4a), 80.8 (C-2b), 77.8 (C-3b), 77.3 (C-3a), 73.2 (d, $J_{C-F}=18.6$ Hz, C-5a), 71.0 (C-5b), 68.9 (OCH₂), 62.8 (C-6b), 31.7, 29.4, 29.2, 29.1, 25.9, 22.4 (5 CH₂), 13.5 (CH₃).

Computational details: All DFT calculations were carried out with the Gaussian16 (version A.03) program,⁵⁰ tightening self-consistent field convergence thresholds (10⁻¹⁰ au). For all calculations, the hybrid B3LYP functional^{51, 52} has been used. The 6-311G(2d,p) atomic basis set has been employed for geometry and frequency calculations. Solvent effects (solvent=acetonitrile) were included according to the Polarizable Continuum Model.⁵³ Fukui and condensed Fukui functions⁵⁴ have been calculated *via* Finite Difference method and are given for various atomic charges (Mulliken, Hirshfeld, Voronoi, Bader).

Microtiter test based evaluation of minimum inhibitory concentration (MIC) against *Leishmania tarentolae*:⁵⁵

Preparation of *Leishmania tarentolae* cultures: Amplification of *Leishmania tarentolae* (ATCC®30267) in its promastigote phase was carried out by culture in modified M199 medium supplemented with 10% inactivated fetal calf serum, 40 μM HEPES, 100 μM adenine, 5 μM hemin, 1 μM biotin, 3 μM biopterin and 1 μM penicillin/streptomycin pH 7.4 at 27 °C for 6 days, until they reached stationary phase.

Preparation of different concentrations of octyl glycofuranosides: Different amounts of octyl glycofuranosides were dissolved in M199 medium supplemented as above in order to obtain a total volume of 1 mL with the following concentrations in furanosides: 0, 50, 100, 250, 500 and 750 μmol.L⁻¹. Each tube was then supplemented with 10 μL of the *L. tarentolae* culture. In parallel, an equal number of

tubes without inoculum was prepared to serve as blanks. All samples were finally incubated for 3 days at 27 °C.

Determination of MICs: A 50 µL aliquot from a 0.0125% (w/v) solution of resazurin (1.25 mg of resazurin in 10 mL of a 0.1 M phosphate buffer saline solution) was added to each sample after filtration (0.2 µm). After developing for 4 h at 37 °C and 100 rpm, each sample (400 µL) was centrifuged (5000 rpm, 5 min). The supernatant (200 µL) was then pipetted and added to the identified wells of a 96-well microplate. The plate had a set of controls: a column with octyl galactofuranoside as a positive control (in serial dilution), a column with all solutions with the exception of the test compound, and a column with all solutions with the exception of *L. tarentolae*. The absorbance of each well at 602 nm was then measured in 96-well microtiter plate reader. The MIC of the sample without bacterial inoculum was then calculated as the concentration where 99% of the bacteria growth is inhibited.

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Table 4 ^1H NMR (CDCl_3) data [δ (J, Hz)].

| | Unit c | | | | | | | Unit b | | | | | | | Unit a | | | | | | |
|------------------------------|--------|---------------|-----------------------|---------------|---------------|-----------|------|---------------|---------------|---------------|---------------|-----------------------|--------------------------------|--------------------------------|---------------|-----------------------|--|------------------------|---------------------------------|--------------------------|------|
| | H-1 | H-2 | H-3 | H-4 | H-5 | H-6 | H-6' | H-1 | H-2 | H-3 | H-4 | H-5 | H-6 | H-6' | H-1 | H-2 | H-3 | H-4 | H-5 | H-6 | H-6' |
| 7 | | | | | | | | 5.37 (1.0) | 5.46 (3.3) | 5.60 (7.0) | 4.72- 4.48 | 5.45- 5.37 | 4.72-4.48 | 5.07 (3.6) | 3.89 (9.0) | 4.16- 4.06 | 4.16- 4.06 | 4.16- 4.06 | | 4.72-4.48 | |
| 8β | | | | | | | | | | | | | | | 5.65 (<1) | 5.61-5.45 (4.7) | 4.69 (4.7) | 5.61- 5.45 | | 4.67 (1.7, 5.1, 46.7) | |
| 9 | | | | | | | | | | | | | | | 5.25 (<1) | 5.47-5.43 | 4.49 (4.5) | 5.57 (16.9, 5.0) | 4.64 (5.0, 10.0, 46.6) | 4.70 (5.8, 46.6) | |
| 10 | | | | | | | | 5.46 (<1) | 5.42 (1.5) | 5.50 (5.0) | 4.53 (4.8) | 5.58- 5.53 | 4.64 (5.1, 9.6, 46.4) | 4.70 (5.4, 9.7, 46.6) | 5.14 (0.7) | 4.17 (1.9) | 4.24 (3.9, 10.1) | 4.13- 4.10 | 4.09- 4.02 | 4.51 (5.4, 46.8) | |
| 11 | | | | | | | | 5.45 (<1) | 5.46 | 5.53- 5.47 | 4.50 (4.8) | 5.53- 5.47 | 4.78-4.53 | 4.97 (1.1) | 4.28 (ls) | 4.24 (2.3, 4.9) | 4.17-4.12 | | 4.50 (5.4, 47.4) | | |
| 12 | | | | | | | | 5.56 (<1) | 5.53-5.48 | 4.75 (4.9) | 5.53- 5.48 | 4.82-4.56 | 4.94 (<1) | 4.08- 4.02 | 4.00- 3.94 | 4.15 (2.7, 3.8) | 4.33 (2.7, 4.4, 7.1, 14.0) | 4.82-4.56 | | | |
| 13 | 5.53 | 4.49- 4.47 | 5.44 (5.4, 1.3) | 4.55- 4.50 | 5.57- 5.50 | 4.75-4.55 | 5.81 | 5.58 (1.2) | 5.49- 5.47 | 4.55- 4.50 | 5.57- 5.50 | 4.75-4.55 | 5.03 (3.7) | 4.12 (3.4) | 4.26 (9.9) | 4.12-4.07 | 4.75-4.55 | | | | |
| 14 | | | | | | | | 5.68 (0.6) | 5.58 (2.2) | 5.54 (5.2) | 4.49 | 5.50- 5.42 | 4.80-4.50 | 4.97 (3.7) | 4.16- 4.02 | 3.96 (3.3, 9.7) | 4.16-4.02 | 4.80-4.50 | | | |
| 17 | | | | | | | | 5.46 (<1) | 5.48 (2.5) | 5.75 (6.2) | 4.75 | 5.97 (6.8, 4.1) | 4.78-4.64 | 5.07 (3.6) | 3.95 (9.6) | 4.16-4.03 | 4.69-4.56 | | | | |
| 18α | | | | | | | | | | | | | | 5.85 (4.5) | 5.56 (5.4) | 6.10 (5.1) | 4.56 (6.7) | 5.98 (3.6) | 4.82-4.68 | | |
| 18β | | | | | | | | | | | | | | 5.72 (<1) | 5.52 (1.4) | 5.66 (5.0) | 4.87 (4.0) | 6.14- 6.04 | 4.82-4.68 | | |
| 19 | | | | | | | | | | | | | | 5.33 | 5.49 (1.0) | 5.65 (5.2) | 4.67 (3.5) | 6.10 (7.0) | 4.83-4.71 | | |

| | | | | | | | | | | | | |
|----|------|-------|-------|-------|-------|-----------|------|-------|-------|-----------|-----------|-----------|
| 20 | 5.52 | 5.43 | 5.68 | 4.71- | 6.08- | 4.84-4.67 | 5.18 | 4.19 | 4.32- | 4.12-4.09 | 4.44-4.42 | |
| | | (1.3) | (5.3) | 4.67 | 5.99 | | (<1) | (2.0) | 4.27 | | 4.57-4.53 | |
| 21 | 5.54 | 5.48 | 5.66- | 4.67- | 6.08- | 4.84-4.67 | 4.98 | 4.37- | 4.31- | 4.20- | 4.12- | 4.43-4.38 |
| | | (1.4) | 5.64 | 4.60 | 5.99 | | | 4.23 | 4.27 | 4.17 | 4.09 | 4.54-4.50 |
| 22 | 5.61 | 5.41 | 5.65 | 4.99- | 6.08- | 4.84-4.67 | 4.95 | 3.95 | 4.12- | 4.15 | 4.34- | 4.84-4.69 |
| | | (1.4) | (5.2) | 4.95 | 5.99 | | | | 4.09 | | 4.23 | |

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Table 5. ^{13}C NMR data [δ ($J_{\text{C-F}}$, Hz)].

| | Unit c | | | | | | Unit b | | | | | | Unit a | | | | | |
|------------------------------|--------|------|------|---------------|----------------|-------------------------|----------------|------|------|---------------|----------------|-------------------------|--------|------|------|---------------|----------------|-----------------|
| | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 |
| 7 | | | | | | | 108.3 | 83.6 | 75.9 | 78.6 (6.3) | 68.8 (21.1) | 80.5 (173.9) | 98.5 | 78.3 | 68.6 | 68.9 (4.9) | 68.5 (24.3) | 83.2 (164.5) |
| 8β | | | | | | | | | | | | | 101.1 | 82.4 | 77.4 | 80.8 (3.2) | 70.6 (20.7) | 81.4 (176.3) |
| 9 | | | | | | | | | | | | | 106.7 | 82.0 | 77.3 | 80.2 (5.7) | 70.4 (20.7) | 81.1 (173.2) |
| 10 | | | | | | | 105.7 | 82.2 | 76.2 | 80.9 (4.6) | 70.1 (21.1) | 80.8 (173.6) | 106.1 | 86.1 | 76.2 | 84.7 (5.2) | 69.7 (20.6) | 83.7 (170.7) |
| 11 | | | | | | | 106.2 | 82.1 | 76.9 | 80.7 (5.2) | 70.1 (20.9) | 80.7 (173.9) | 108.4 | 79.8 | 84.3 | 81.5 (6.2) | 69.4 (19.9) | 84.3 (169.9) |
| 12 | | | | | | | 106.4 (5.6) | 82.0 | 77.1 | 81.0 (7.9) | 70.2 (21.1) | 81.3 (172.8) | 107.9 | 79.0 | 78.4 | 85.2 (3.9) | 75.6 (19.0) | 83.6 (170.8) |
| 13 | 107.6 | 82.3 | 77.2 | 81.7 (5.0) | 70.3 (20.5) | 81.1 or 80.6 (173.4) | 107.2 | 81.4 | 77.2 | 80.3 (4.4) | 70.3 (20.5) | 80.6 or 81.1 (173.4) | 98.7 | 75.4 | 74.9 | 69.7 (6.4) | 68.0 (22.5) | 88.6 (168.9) |
| 14 | | | | | | | 107.3 | 82.3 | 76.8 | 80.7 (5.0) | 70.1 (20.2) | 80.8 (173.6) | 98.5 | 68.5 | 78.0 | 69.2 (6.5) | 68.6 (21.0) | 82.5 (167.5) |
| 17 | | | | | | | 108.5 | 83.6 | 76.8 | 80.8 | 70.3 | 63.5 | 98.5 | 78.2 | 68.4 | 68.7 (5.6) | 68.4 (22.8) | 82.9 (167.1) |
| 18α | | | | | | | | | | | | | 96.2 | 77.7 | 76.0 | 79.5 | 72.4 | 63.3 |
| 18β | | | | | | | | | | | | | 101.2 | 82.8 | 77.8 | 81.8 | 70.7 | 63.7 |
| 19 | | | | | | | | | | | | | 106.4 | 81.9 | 77.4 | 81.0 | 70.1 | 63.3 |
| 20 | | | | | | | 105.9 | 82.6 | 77.5 | 82.1 | 70.3 | 63.3 | 106.0 | 86.2 | 76.2 | 84.6 (6.7) | 69.7 (20.9) | 83.7 (172.6) |
| 21 | | | | | | | 105.8 | 82.3 | 77.2 | 82.1 | 70.5 | 63.4 | 108.5 | 79.7 | 83.4 | 81.2 (5.8) | 69.2 (20.3) | 84.0 (169.3) |
| 22 | | | | | | | 106.4 (3.5) | 82.4 | 77.8 | 82.5 | 70.6 | 63.5 | 108.0 | 79.3 | 78.4 | 85.1 (2.7) | 75.3 (19.2) | 83.6 (171.4) |

Conclusions

Synthesis of fluor-containing oligofuranosides was performed from a C-6-fluorinated and O-2, O-3, O-5 unprotected glycofuranoside **2**, and four different furanosyl donors. This study highlighted the significant impact of the fluorine atom on both the donor and the acceptor reactivity. The presence of fluorine at C-6 decreased the reactivity of the donor with respect to the standard perbenzoylated galactofuranosyl one. Moreover, regioselective glycosylation of the fluorinated acceptor followed different pathways yielding to (i) the three difuranosides (and trisaccharides), (ii) isomers characterized by a pyranosyl moiety originated from the starting furanosidic acceptor, and (iii) a monofuranoside resulting from the transfer of the aglycon from the acceptor to the donor. Best results in terms of the desired regioselective glycosylation of **2** were obtained with the non-fluorinated thiogalactofuranoside **16b**. Interestingly, DFT calculations of Fukui indexes f helped to explain the remained nucleophilicity of O-1, and so the transfer of the O-alkyl chain from the fluorinated acceptor to the donor. On another hand, the presence of fluorine atoms in octyl mono- or digalactofuranosides contributed to the growth inhibition of *Leishmania tarentolae* and MIC values were improved by a magnitude of 3-4 compared to the non-fluorinated **GalfOct** used as a reference.

Conflicts of interest

There are no conflicts to declare.

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