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Synthesis of multiply fluorinated *N*-acetyl-D-glucosamine and D-galactosamine analogs via the corresponding deoxyfluorinated glucosazide and galactosazide thiodonors

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Abstract

Multiple fluorination of glycostructures has emerged as an attractive way of modulating their protein affinity, metabolic stability, and lipophilicity. Here we described the synthesis of a series of mono-, di- and trifluorinated *N*-acetyl-D-glucosamine and D-galactosamine analogs. The key intermediates were the corresponding multiply fluorinated glucosazide and galactosazide thiodonors prepared from deoxyfluorinated 1,6-anhydro-2-azido-β-D-hexopyranose precursors by ring-opening reaction with phenyl trimethylsilyl sulfide. Nucleophilic deoxyfluorination at C4 and C6 by reaction with DAST, thioglycoside hydrolysis and azide/acetamide transformation completed the synthesis.

Keywords

Fluorinated carbohydrates; deoxyfluorination; amino sugars; thioglycosides; hexosamine hemiacetals

Introduction

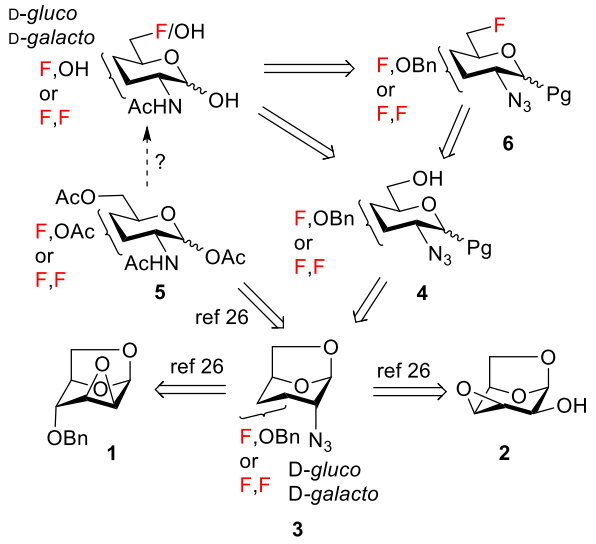
Fluorinated carbohydrates are versatile carbohydrate mimetics used to probe or manipulate recognition of carbohydrates by carbohydrate-binding proteins or carbohydrate-processing enzymes [1–7]. The introduction of additional fluorine atoms into a monofluorinated carbohydrate is an attractive way of modulating binding affinity and pharmacokinetic properties of fluorinated glycomimetics. Hydrophobic segments incorporating multiple C–F bonds could (1) reduce the desolvation penalty associated with binding of hydrophilic natural carbohydrates [8], and (2) create additional contacts with the binding cavity via electrostatic and dipolar interactions with C–F bonds [9,10], new intermolecular hydrogen bonds [11], or rearrangement of hydrogen bond-mediating water molecules [12]. Fluorination of sugars is also a promising strategy to improve unfavorable pharmacokinetic properties of natural carbohydrates such as low lipophilicity [13–16] and fast metabolic degradation [17–19]. Over the last few years, considerable effort has been expended on the synthesis of unprotected multiply-deoxyfluorinated monosaccharides, including a complete series of mono-, di-, and trifluorinated D-glucose [15], difluorinated [20] and tetrafluorinated [13] D-galactose, and 2,3,4-trifluoro analogs of D-mannose, D-galactose, D-allose, D-talose, and D-altrose [13,21].

Unprotected multiply-deoxyfluorinated *N*-acetyl-D-glucosamine (GlcNAc) and *N*-acetyl-D-galactosamine (GalNAc) have not yet been described except for 4,6-difluoro-GalNAc analog [22], although GlcNAc is the most abundant monosaccharide component of mammalian glycans [23], and GalNAc occurs in important glycan structures including T_N and T antigen [24] and their sialylated forms [25]. A complete series of O-protected monofluorinated [22,26–31] and several difluorinated [22,26,32,33] GlcNAc/GalNAc analogs have been prepared. Some acylated mono- and difluorinated analogs have potential in biomedical applications due to their ability to inhibit glycan and glycosaminoglycan biosynthesis [33–37]. Preparation of glycostructures comprising multifluorinated GlcNAc and GalNAc will be greatly facilitated if synthetic routes to the corresponding glycosyl donors are developed. Here we

describe the synthesis of a complete series of unprotected GlcNAc and GalNAc analogs systematically deoxyfluorinated at all non-anomeric hydroxyl positions. The key synthetic intermediates are multifluorinated glucosazide and galactosazide thioglycosides and hemiacetals, which are also valuable glycosyl donors for the installation of a 1,2-*cis*-linked multifluorinated GlcNAc and GalNAc moiety.

Results and discussion

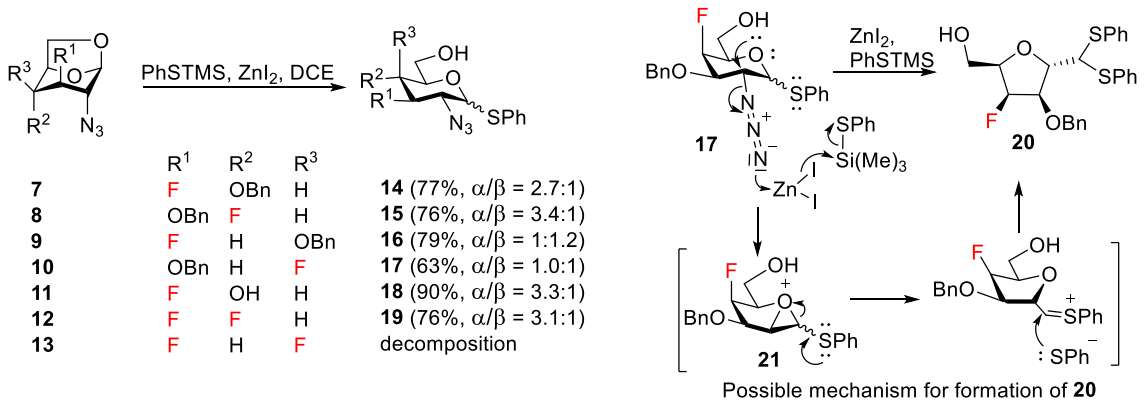
Our approach to the synthesis is summarized in Scheme 1. Challenging regio- and stereoselective introduction of fluorine at C3 and C4 of the pyranose ring, together with azide installation at C2, can be accomplished by nucleophilic fluorination and azidolysis starting from dianhydro derivatives **1** and **2** as we described previously [26]. The resulting intermediates **3** can be transformed into 2-azido-hexopyranosides **4** by cleavage of the internal acetal and protection of the anomeric position. Deoxyfluorination at C6 should then afford an intermediate **6**. Protecting-group manipulation of intermediates **4** and **6** should deliver the required fluoro analogs. The initially contemplated conversion of intermediates **3** into acetates **5** [26], followed by base-catalyzed O-deacetylation, led to substantial decomposition. These observations are consistent with recently reported instability of O-acylated GlcNAc under basic conditions due to elimination reactions of transient hemiacetal intermediates [38]. This instability of amino sugar hemiacetals underscores the requirement to both protect the anomeric position with a robust protecting group and to conduct final deprotection under neutral conditions. After initial experimentation with benzyl glycosides (Scheme 1, Pg = OBn), phenyl thioglycosides (Scheme 1, Pg = SPh), readily available from 1,6-anhydropyranoses [39] as we described earlier [40] were found to fulfill this requirement satisfactorily.



Scheme 1. Retrosynthetic analysis of the target fluoro analogs

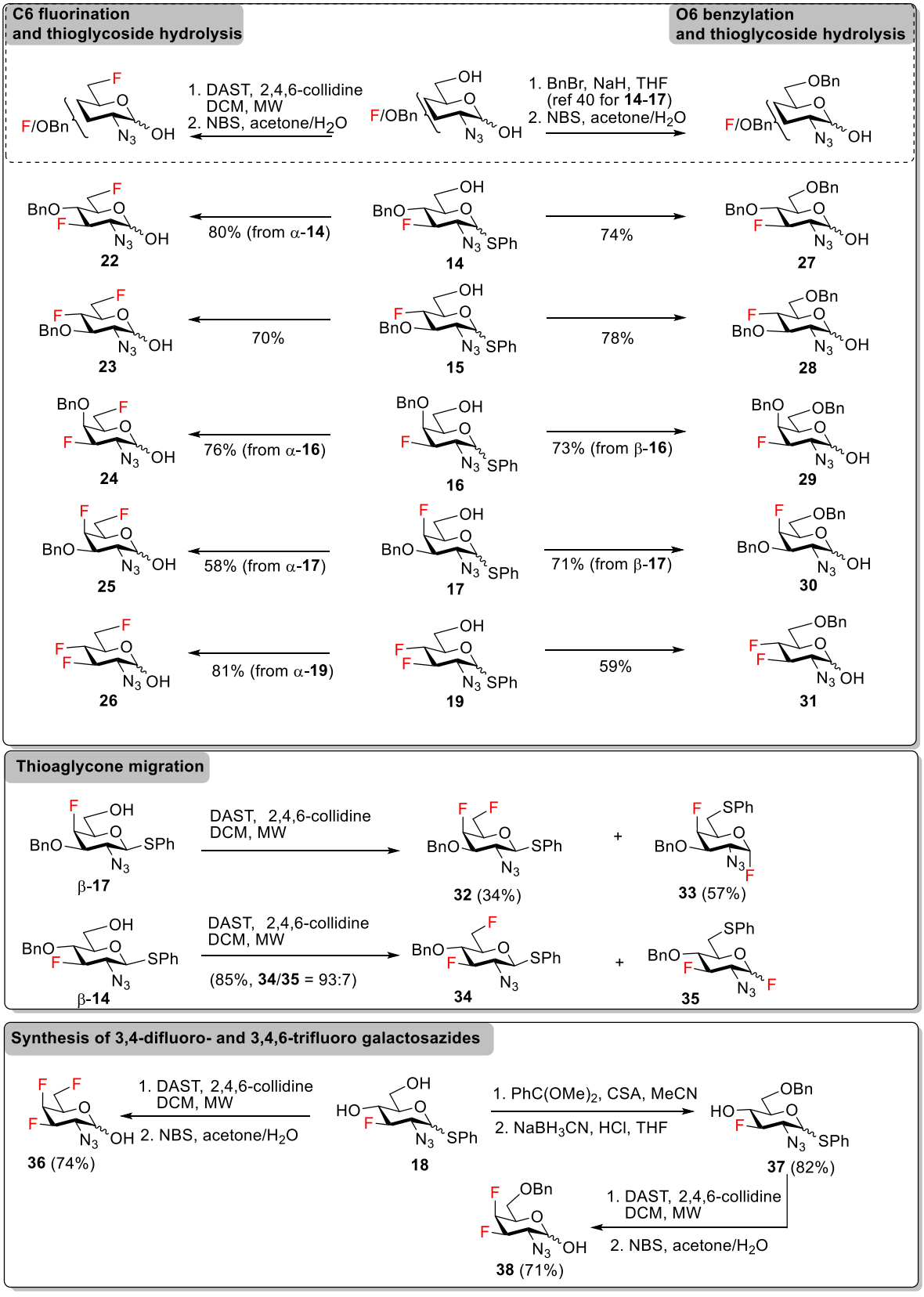
Accordingly, the synthesis started from known fluorinated 1,6-anhydro-2-azido-hexopyranoses **7**–**13** (Scheme 2) [26,40]. Reaction of compounds **7**–**10** with phenyl trimethylsilyl sulfide (PhSTMS) and ZnI_2 delivered phenyl thioglycosides **14**–**17** [40]. 1,6-Anhydropyranoses **11** and **12** under these conditions produced the expected thioglycosides **18** and **19**, respectively. Difluorinated derivative **13** decomposed on reaction with PhSTMS/ZnI_2 system. Separation of anomers of the products **14**–**19** was attempted because of the risk of thiophenyl migration in the subsequent C6 deoxyfluorination, which would likely occur with the β-anomers of **14**–**19** [41]. Complete separation of the α-anomer by conventional silica gel column chromatography was possible for thioglycosides **14**, **16**, **17**, and **19**, while the products **15**, and **18** were obtainable as enriched α-anomers (α/β ≥ 3.3:1). Cleavage of the internal acetal with PhSTMS was accompanied by the formation of low quantities of side-products detectable by TLC and separable by careful chromatography except for the cleavage of **12** where the side products co-eluted with the fraction containing the β-anomer of the product. In the case of the cleavage of 1,6-anhydroderivative **10**, we were able to isolate one of the side-products in sufficient purity and quantity to be assigned the structure of *C*-furanoside **20** (Scheme 2). This compound resulted from pyranose ring contraction probably caused by intramolecular displacement of the C2 azide aided by coordination of ZnI_2. When the α-anomer of thioglycoside **17** was separately subjected to the reaction conditions, the by-product **20** started to form in trace amounts in accordance with the suggested mechanism. The ring contraction may involve formation of

a transient oxiranium cation as suggested in Scheme 2 [42–45]. Analogous ring-contraction reactions have been described for substrates possessing a good C2 leaving group [42,46–50].



Scheme 2. Conversion of 1,6-anhydro derivatives into thioglycosides, and a possible mechanism for the formation of *C*-furanosides by ring contraction.

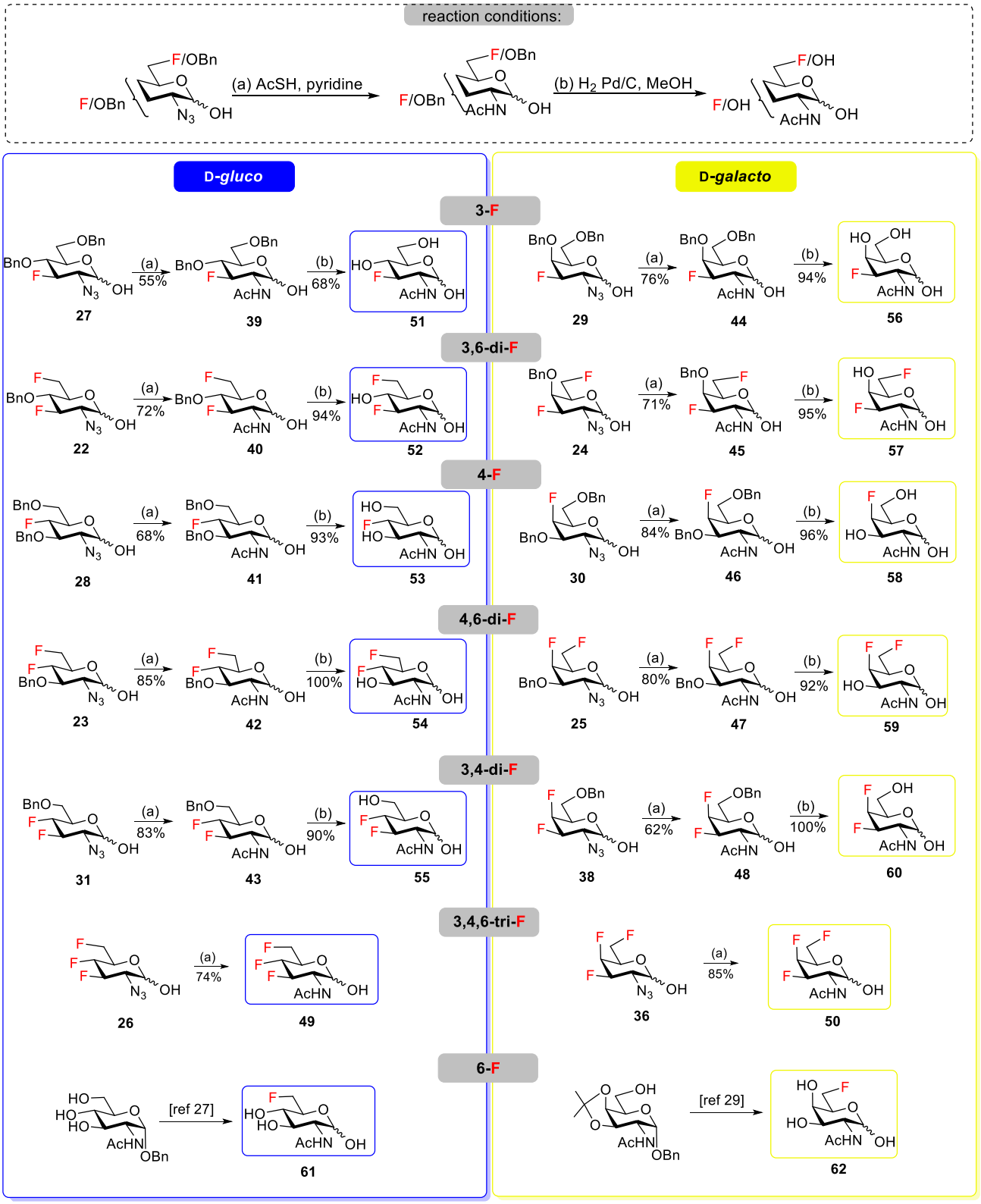
We initially considered converting thioglycosides **14**–**19** to benzyl glycosides because thioglycosides give glycosyl fluorides on reaction with diethylamino sulfurtrifluoride (DAST) [51], but our experiments revealed that DAST-mediated C6-deoxyfluorination of thioglycosides **14**–**17** and **19** proceeded satisfactorily under microwave irradiation, on condition that pure or substantially enriched α-anomers were subjected to reaction with DAST. Subsequent thioglycoside hydrolysis yielded hemiacetals **22**–**26** (Scheme 3). Reaction of β-thiogalactosides possessing an unprotected C6 hydroxyl with DAST was accompanied by migration of the anomeric thio-aglycone to C6 [41,52] as shown for β-thiogalactoside β-**17**, which mostly delivered migration product **33** (Scheme 3, see also the synthesis of compound **24** in the Supporting Information File 1). However, β-thioglucoside β-**14** yielded only 6% of migration product **35** together with main C6-fluoro product **34**, suggesting that starting fluorinated 2-azido-thioglucosides were significantly less prone to thiophenyl migration than 2-azido-thiogalactosides were. This was convenient because thioglucosides **15** and **18** (vide infra) were available for deoxyfluorination only as enriched anomeric mixtures $\alpha/\beta \geq 3.3:1$ and any traces of the migration products were removed in the subsequent thioaglycone hydrolysis. Thioglycosides **14**–**17** and **19** were also O6-benzylated [40] and then hydrolyzed to hemiacetals **27**–**31** (Scheme 3).



Scheme 3. Deoxyfluorination and O-benzylation of thioglycosides, hydrolysis to hemiacetals and thioaglycone migration

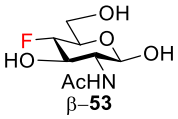
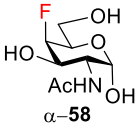
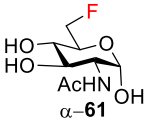
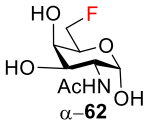
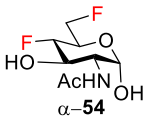
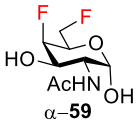
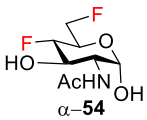
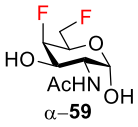
As the C3/C4 difluorinated thiogalactoside could not be accessed from compound **13** by reaction with PhSTMS/ZnI_2 (Scheme 2), it was necessary to obtain 3,4-difluoro and 3,4,6-trifluoro analogs of GalNAc from 3-fluoro-4,6-diol **18**. According to precedents in the literature [53], deoxyfluorination of the C4-hydroxyl group in compound **18** was expected to occur with inversion of configuration to give the desired *galacto*-configured 4-fluoro products. Accordingly, treatment of diol **18** with DAST resulted in deoxyfluorination of both hydroxyl groups to yield trifluoro galactosazide **36** after thioglycoside hydrolysis (Scheme 3). 4,6-O-Benzylidenation of diol **18** followed by regioselective opening of the benzylidene acetal produced compound **37**. Subsequent DAST deoxyfluorination delivered desired hemiacetal **38** after thioglycoside hydrolysis (Scheme 3). For both compounds **18** and **37**, deoxyfluorination of the C4 hydroxyl group occurred with inversion of configuration.

To obtain the target fluoro analogs, the hemiacetals **22**–**31**, **36** and **38** were debenzylated and their azide group converted to an acetamide. Although palladium-catalyzed hydrogenolysis in ethanol/acetic anhydride appeared to be a logical deprotection step [26], the desired fluoro sugars were contaminated with varying quantities of unidentified by-products. However, clean debenzylation was achieved by first converting the azide to an acetamide on reaction with thioacetic acid [54–55]. Hence, the hemiacetals were reacted with thioacetic acid in pyridine to give acetamides **39**–**48** (Scheme 4) and the target trifluoro analogs **49** and **50**. Reversing the order of hemiacetal and azide/acetamide formation was not an option because NBS-promoted hydrolysis of 2-acetamido thioglycosides was sluggish and incomplete. Protecting the primary hydroxyl at C6 by O-benzylation (Scheme 3) was essential before treatment with thioacetic acid; otherwise, an O6-acetylated by-product was formed. Acetylation of the anomeric hydroxyl occurred only to a very limited degree upon reaction with AcSH in pyridine and traces of O1 acetates were removed by chromatography or recrystallization. Palladium-catalyzed hydrogenolytic debenzylation of **39**–**48** then yielded the target fluoro analogs **51**–**60**. To complete the series of fluorinated analogs for the purpose of comparing their NMR spectra, the known C6 monodeoxyfluorinated compounds **61** [27,28] and **62** [29] were prepared by published procedures [27,29].



Scheme 4. Synthesis of the target compounds by azide/acetamide conversion and debenzylation.

Table 1. The values [Hz] of selected coupling constants. Colored cells illustrate the trends discussed in the text

compound	$^{2}J_{C3-F4}$	$^{1}J_{C4-F4}$	$^{2}J_{C5-F4}$		$^{3}J_{H3-F4}$	$^{2}J_{H4-F4}$	$^{3}J_{H5-F4}$
 β–**53**	18.6	180.9	24.2		15.6	50.8	2.5
 α–**58**	19.1	180.1	18.1		28.9	50.5	30.3
	$^{4}J_{C3-F6}$	$^{3}J_{C4-F6}$	$^{2}J_{C5-F6}$	$^{1}J_{C6-F6}$	$^{3}J_{H5-F6}$	$^{2}J_{H6-F6}$	$^{2}J_{H6'-F6}$
 α–**61**	0.7	7	17.6	171.3	27.1	48.2	48.2
 α–**62**	1.1	2.5	13.0	166.8	14.6	46.4	48.1
	$^{3}J_{C2-F4}$	$^{2}J_{C3-F4}$	$^{1}J_{C4-F4}$	$^{2}J_{C5-F4}$	$^{3}J_{C4-F6}$	$^{2}J_{C5-F6}$	$^{1}J_{C6-F6}$
 α–**54**	8.0	18.5	181.2	23.7	7.4	18.2	172.5
 α–**59**	2.7	18.8	180.1	17.7	5.9	23.1	168.1
	$^{5}J_{H1-F4}$	$^{3}J_{H3-F4}$	$^{2}J_{H4-F4}$	$^{3}J_{H5-F4}$	$^{3}J_{H5-F6}$	$^{2}J_{H6-F6}$	$^{2}J_{H6'-F6}$
 α–**54**	3.3	14.8	50.6	4.1	26.6	48.1	47.5
 α–**59**		28.9	51.0	30.3	12.7	47.3	46.2

The magnitudes of the vicinal $^{3}J_{H-H}$, $^{3}J_{H-F}$, $^{3}J_{C-F}$, geminal $^{2}J_{H-F}$, $^{2}J_{C-F}$, and one-bond $^{1}J_{C-F}$ coupling constants confirmed the expected fluorination pattern and D-*gluco* or D-*galacto* configuration for all fluoro analogs **49**–**62**. The values of the coupling constants correlated with the $^{4}C_{1}$ conformation adopted by the target fluoro analogs in solution (Tables 1 and S1 in Supporting Information File 1). For example, the magnitude of the germinal fluorine-carbon coupling $^{2}J_{C5-F4}$ indicated an antiperiplanar ($^{2}J_{C5-F4}$ = 23.2–24.2 Hz, D-*gluco* configuration, F4 equatorial) or a gauche ($^{2}J_{C5-F4}$ = 17.5–18.1 Hz, D-*galacto* configuration, F4 axial) relationship between the C4–F and C5–O bonds [59]. Similarly, the values of $^{3}J_{H3/H5-F4}$ coupling

constants reflected an axial ($^3J_{H3/H5-F}$ = 25.5–30.3 Hz) or equatorial ($^3J_{H3-F4}$ = 14.8–16.8 Hz, $^3J_{H5-F4}$ = 2.5–4.8 Hz) position of the C4 fluorine substituent [60]. Moreover, evaluation of $^3J_{H5-F6}$ coupling constants revealed that 6-fluoro D-*gluco* analogs **49**, **52**, **54**, and **61** assumed preferentially *gauche,gauche* (*gg*) conformation of the exocyclic C5–C6 bond in solution ($^3J_{H5-F6}$ = 24.6‑27.1 Hz), whereas the corresponding D-*galacto*-configured analogs **50**, **57**, **59**, and **62** adopted *gauche,trans* (*gt*) or *trans,gauche* (*tg*) conformations to a significant degree ($^3J_{H5-F6}$ = 12.7‑14.6 Hz). These findings were in accordance with the previous reports by Giguère [13,15,46].

In summary, we have demonstrated that multiply deoxyfluorinated GlcNAc and GalNAc are accessible via the corresponding multifluorinated 1-thiophenyl gluco- and galactosazides. Installation of the thiophenyl aglycone permits C6 deoxyfluorination and circumvents the problems resulting from the low stability of amino sugar hemiacetals. The prepared polyfluorinated thiodonors and hemiacetals are valuable intermediates in oligosaccharide synthesis and their utility in glycosylation is currently being studied in our group.

Supporting Information

Supporting Information File 1: Experimental. Experimental procedures and spectral data.

Supporting Information File 2: Copies of NMR spectra. Copies of ^{1}H, ^{13}C, ^{19}F, and 2D NMR spectra for new compounds.

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References

1. Linclau, B.; Arda, A.; Reichardt, N. C.; Sollogoub, M.; Unione, L.; Vincent, S. P.; Jimenez-Barbero, J. *Chem. Soc. Rev.* **2020,** *49*, 3863–3888. https://doi.org/10.1039/C9CS00099B
2. Williams, S. J.; Withers, S. G. *Carbohydr. Res.* **2000,** *327*, 27–46. https://doi.org/10.1016/S0008-6215(00)00041-0
3. Namchuk, M.; Braun, C.; McCarter, J. D.; Withers, S. G. Fluorinated sugars as probes of glycosidase mechanisms. In *Biomedical Frontiers of Fluorine Chemistry*; Ojima, I.; McCarthy, J. R.; Welch, J. T., Eds.; ACS Symposium Series, Vol. 639; American Chemical Society: Washington DC 1996; pp 279–293.
4. Williams, D. A.; Pradhan, K.; Paul, A.; Olin, I. R.; Tuck, O. T.; Moulton, K. D.; Kulkarni, S. S.; Dube, D. H. *Chem. Sci.* **2020,** *11* (7), 1761–1774. https://doi.org/10.1039/C9SC05955E
5. Glaudemans, C. P. J.; Kováč, P.; Nashed, E. M. *Methods Enzymol.*, **1994,** *247*, 305–322. https://doi.org/10.1016/S0076-6879(94)47023-5
6. Valverde, P.; Quintana, J. I.; Santos, J. I.; Ardá, A.; Jiménez-Barbero, J. *ACS Omega* **2019,** *4*, 13618–13630. https://doi.org/10.1021/acsomega.9b01901
7. Gimeno, A.; Valverde, P.; Ardá, A.; Jiménez-Barbero, J. *Curr. Opin. Struct. Biol.* **2020,** *62*, 22–30. https://doi.org/10.1016/j.sbi.2019.11.004
8. Biffinger, J. C.; Kim, H. W.; DiMagno, S. G. *ChemBioChem* **2004,** *5*, 622–627. https://doi.org/10.1002/cbic.200300910
9. van Straaten, K. E.; Kuttiyatveetil, J. R. A.; Sevrain, C. M.; Villaume, S. A.; Jiménez-Barbero, J.; Linclau, B.; Vincent, S. P.; Sanders, D. A. R. *J. Am. Chem. Soc.* **2015,** *137*, 1230–1244. https://doi.org/10.1021/ja511204p
10. Dohi, H.; Périon, R.; Durka, M.; Bosco, M.; Roué, Y.; Moreau, F.; Grizot, S.; Ducruix, A.; Escaich, S.; Vincent, S. P. *Chem. Eur. J.* **2008,** *14*, 9530–9539. https://doi.org/10.1002/chem.200801279

11. Thanna, S.; Lindenberger, J. J.; Gaitonde, V. V.; Ronning, D. R.; Sucheck, S. J. *Org. Biomol. Chem.* **2015,** *13*, 7542–7550. https://doi.org/10.1039/C5OB00867K

12. Vermersch, P. S.; Tesmer, J. J. G.; Quiocho, F. A. *J. Mol. Biol.* **1992,** *226*, 923–929. https://doi.org/10.1016/0022-2836(92)91041-M

13. Denavit, V.; Lainé, D.; St-Gelais, J.; Johnson, P. A.; Giguère, D. *Nat. Commun.* **2018,** *9*, 4721. https://doi.org/10.1038/s41467-018-06901-y

14. St-Gelais, J.; Bouchard, M.; Denavit, V.; Giguère, D. *J. Org. Chem.* **2019,** *84*, 8509–8522. https://doi.org/10.1021/acs.joc.9b00795

15. St-Gelais, J.; Cote, E.; Laine, D.; Johnson, P. A.; Giguere, D. *Chem. Eur. J.* **2020,** *26*, 13499–13506. https://doi.org/10.1002/chem.202002825

16. Linclau, B.; Wang, Z.; Compain, G.; Paumelle, V.; Fontenelle, C. Q.; Wells, N.; Weymouth-Wilson, A. *Angew. Chem. Int. Ed.* **2016,** *55*, 674–678. https://doi.org/10.1002/anie.201509460

17. Johannes, M.; Reindl, M.; Gerlitzki, B.; Schmitt, E.; Hoffmann-Röder, A. *Beilstein J. Org. Chem.* **2015,** *11*, 155–161. https://doi.org/10.3762/bjoc.11.15

18. Sun, X.-L.; Kanie, Y.; Guo, C.-T.; Kanie, O.; Suzuki, Y.; Wong, C.-H. *Eur. J. Org. Chem.* **2000,** 2643–2653. https://doi.org/10.1002/1099-0690(200007)2000:14<2643::AID-EJOC2643>3.0.CO;2-1

19. Axer, A.; Jumde, R. P.; Adam, S.; Faust, A.; Schäfers, M.; Fobker, M.; Koehnke, J.; Hirsch, A. K. H.; Gilmour, R. *Chem. Sci.* **2021**, *12*, 1286–1294. https://doi.org/10.1039/D0SC04297H

20. Malassis, J.; Vendeville, J.-B.; Nguyen, Q.-H.; Boujon, M.; Gaignard-Gaillard, Q.; Light, M.; Linclau, B. *Org. Biomol. Chem.* **2019,** *17*, 5331–5340. https://doi.org/10.1039/C9OB00707E

21. Bresciani, S.; Lebl, T.; Slawin, A. M. Z.; O'Hagan, D. *Chem. Commun.* **2010,** *46*, 5434-5436. https://doi.org/10.1039/C0CC01128B

22. Sharma, M.; Bernacki, R. J.; Paul, B.; Korytnyk, W. *Carbohydr. Res.* **1990,** *198* (2), 205–221. https://doi.org/10.1016/0008-6215(90)84293-4

23. Werz, D. B.; Ranzinger, R.; Herget, S.; Adibekian, A.; von der Lieth, C.-W.; Seeberger, P. H. *ACS Chem. Biol.* **2007,** *2*, 685–691. https://doi.org/10.1021/cb700178s

24. Sletmoen, M.; Gerken, T. A.; Stokke, B. T.; Burchell, J.; Brewer, C. F. *Glycobiology* **2018,** *28*, 437–442. https://doi.org/10.1093/glycob/cwy032

25. Fu, C.; Zhao, H.; Wang, Y.; Cai, H.; Xiao, Y.; Zeng, Y.; Chen, H. *HLA* **2016,** *88*, 275–286. https://doi.org/10.1111/tan.12900

26. Horník, S.; Šťastná, L. C.; Cuřínová, P.; Sýkora, J.; Káňová, K.; Hrstka, R.; Císařová, I.; Dračínský, M.; Karban, J. *Beilstein J. Org. Chem.* **2016,** *12*, 750–759. https://doi.org/10.3762/bjoc.12.75

27. Morrison, Z. A.; Nitz, M. *Carbohydr. Res.* **2020,** *495*, 108071. https://doi.org/10.1016/j.carres.2020.108071

28. Hough, L.; Penglis, A. A. E.; Richardson, A. C. *Can. J. Chem.* **1981,** *59*, 396–405. https://doi.org/10.1139/v81-061

29. Sharma, M.; Potti, G. G.; Simmons, O. D.; Korytnyk, W. *Carbohydr. Res.* **1987,** *162*, 41–51. https://doi.org/10.1016/0008-6215(87)80199-4

30. Wagner, S.; Mersch, C.; Hoffmann-Röder, A. *Chem. Eur. J.* **2010,** *16*, 7319–7330. https://doi.org/10.1002/chem.200903294

31. Mersch, C.; Wagner, S.; Hoffmann-Röder, A. *Synlett* **2009,** 2167–2171. https://doi.org/10.1055/s-0029-1217566

32. Johannes, M.; Oberbillig, T.; Hoffmann-Röder, A. *Org. Biomol. Chem.* **2011,** *9*, 5541–5546. https://doi.org/10.1039/C1OB05373F

33. Stephenson, E. L.; Zhang, P.; Ghorbani, S.; Wang, A.; Gu, J.; Keough, M. B.; Rawji, K. S.; Silva, C.; Yong, V. W.; Ling, C.-C. *ACS Central Science* **2019,** *5*, 1223–1234. https://doi.org/10.1021/acscentsci.9b00327

34. Barthel, S. R.; Antonopoulos, A.; Cedeno-Laurent, F.; Schaffer, L.; Hernandez, G.; Patil, S. A.; North, S. J.; Dell, A.; Matta, K. L.; Neelamegham, S.; Haslam, S. M.; Dimitroff, C. J. *J. Biol. Chem.* **2011,** *286*, 21717–21731. https://doi.org/10.1074/jbc.M110.194597

35. Nishimura, S.-I.; Hato, M.; Hyugaji, S.; Feng, F.; Amano, M. *Angew. Chem. Int. Ed.* **2012,** *51*, 3386-3390. https://doi.org/10.1002/anie.201108742

36. Wijk, X. M. v.; Lawrence, R.; Thijssen, V. L.; Broek, S. A. v. d.; Troost, R.; Scherpenzeel, M. v.; Naidu, N.; Oosterhof, A.; Griffioen, A. W.; Lefeber, D. J.; Delft, F. L. v.; Kuppevelt, T. H. v. *FASEB J.* **2015,** *29*, 2993–3002. https://doi.org/10.1096/fj.14-264226

37. Keough, M. B.; Rogers, J. A.; Zhang, P.; Jensen, S. K.; Stephenson, E. L.; Chen, T.; Hurlbert, M. G.; Lau, L. W.; Rawji, K. S.; Plemel, J. R.; Koch, M.; Ling, C.-C.; Yong, V. W. *Nat. Commun.* **2016,** *7*, 11312. https://doi.org/10.1038/ncomms11312

38. Qin, K.; Zhang, H.; Zhao, Z.; Chen, X. *J. Am. Chem. Soc.* **2020,** *142*, 9382–9388. https://doi.org/10.1021/jacs.0c02110

39. Wang, L.-X.; Sakairi, N.; Kuzuhara, H. *J. Chem. Soc., Perkin Trans. 1* **1990,** 1677–1682. https://doi.org/10.1039/P19900001677

40. Kurfiřt, M.; Červenková Šťastná, L.; Dračínský, M.; Müllerová, M.; Hamala, V.; Cuřínová, P.; Karban, J. *J. Org. Chem.* **2019,** *84* (10), 6405–6431. https://doi.org/10.1021/acs.joc.9b00705

41. Lin, P.-C.; Adak, A. K.; Ueng, S.-H.; Huang, L.-D.; Huang, K.-T.; Ho, J.-a. A.; Lin, C.-C. *J. Org. Chem.* **2009,** *74*, 4041–4048. https://doi.org/10.1021/jo900516r

42. Dax, K.; Albert, M.; Hammond, D.; Illaszewicz, C.; Purkarthofer, T.; Tscherner, M.; Weber, H., Rearrangements in the Course of Fluorination by Diethylaminosulfur Trifluoride at C-2 of Glycopyranosides: Some New Parameters. In *Timely Research Perspectives in Carbohydrate Chemistry*; Schmid, W.; Stütz, A. E., Eds.; Springer Vienna: Vienna, 2002; pp 77–98.

43. Karban, J.; Císařová, I.; Strašák, T.; Šťastná, L. C.; Sýkora, J. *Org. Biomol. Chem.* **2012,** *10*, 394-403. https://doi.org/10.1039/C1OB06336G

44. Lainé, D.; Denavit, V.; Lessard, O.; Carrier, L.; Fecteau, C.-É.; Johnson, P. A.; Giguère, D. *Beilstein J. Org. Chem.* **2020,** *16*, 2880–2887. https://doi.org/10.3762/bjoc.16.237

45. Quiquempoix, L.; Wang, Z.; Graton, J.; Latchem, P. G.; Light, M.; Le Questel, J.-Y.; Linclau, B. *J. Org. Chem.* **2019,** *84*, 5899–5906. https://doi.org/10.1021/acs.joc.9b00310

46. Baer, H. H.; Mateo, F. H.; Siemsen, L. *Carbohydr. Res.* **1989,** *187* 67–92. https://doi.org/10.1016/0008-6215(89)80056-4

47. Popsavin, V.; Benedeković, G.; Popsavin, M.; Divjaković, V.; Armbruster, T. *Tetrahedron* **2004,** *60* 5225–5235. https://doi.org/10.1016/j.tet.2004.04.040

48. Chen, S. Y.; Joullie, M. M. *J. Org. Chem.* **1984,** *49* (10), 1769–1772. https://doi.org/10.1021/jo00184a020

49. Vera-Ayoso, Y.; Borrachero, P.; Cabrera-Escribano, F.; Gómez-Guillén, M. *Tetrahedron: Asymmetry* **2005,** *16*, 889–897. https://doi.org/10.1016/j.tetasy.2004.12.024

50. Vera-Ayoso, Y.; Borrachero, P.; Cabrera-Escribano, F.; Carmona, A. T.; Gómez-Guillén, M. *Tetrahedron: Asymmetry* **2004,** *15*, 429–444. https://doi.org/10.1016/j.tetasy.2003.11.034

51. Suzuki, K.; Ito, Y.; Kanie, O. *Carbohydr. Res.* **2012,** *359*, 81–91. https://doi.org/10.1016/j.carres.2012.07.003

52. Herczeg, M.; Mező, E.; Eszenyi, D.; Lázár, L.; Csávás, M.; Bereczki, I.; Antus, S.; Borbás, A. *Eur. J. Org. Chem.* **2013,** 5570–5573. https://doi.org/10.1002/ejoc.201300681

53. Card, P. J.; Reddy, G. S. *J. Org. Chem.* **1983,** *48*, 4734–4743. https://doi.org/10.1021/jo00172a054

54. Kolakowski, R. V.; Shangguan, N.; Sauers, R. R.; Williams, L. J., Mechanism of Thio Acid/Azide Amidation. *J. Am. Chem. Soc.* **2006,** *128*, 5695–5702. https://doi.org/10.1021/ja057533y

55. Dhakal, B.; Crich, D. *J. Am. Chem. Soc.* **2018,** *140*, 15008–15015. https://doi.org/10.1021/jacs.8b09654

56. Hamala, V.; Červenková Šťastná, L.; Kurfiřt, M.; Cuřínová, P.; Dračínský, M.; Karban, J. *Org. Biomol. Chem.* **2020,** *18*, 5427–5434. https://doi.org/10.1039/D0OB01065K

57. Sharma, M.; Bernacki, R. J.; Hillman, M. J.; Korytnyk, W. *Carbohydr. Res.* **1993,** *240*, 85–93. https://doi.org/10.1016/0008-6215(93)84174-5

58. Berkin, A.; Szarek, W. A.; Kisilevsky, R. *Carbohydr. Res*. **2000**, *326*, 250–263. https://doi.org/10.1016/S0008-6215(00)00049-5

59. Wray, V. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1598–1605. https://doi.org/10.1039/P29760001598

60. Phillips, L.; Wray, V. *J. Chem. Soc. B.* **1971**, 1618–1624. https://doi.org/10.1039/J29710001618