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Synthetic Routes towards Fluorine-Containing Amino Sugars: Synthesis of Fluorinated Analogues of Tomosamine and 4-Amino-4-deoxyarabinose

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Dedicated to our colleague Professor Paul Kosma on the occasion of his 60th birthday

Keywords: Aldol reactions / Chiral auxiliaries / Carbohydrates / Fluorine

Fluorinated analogues of bioactive amino sugars are of high interest in medicinal chemistry. We developed a straightforward synthetic route towards this class of carbohydrates by applying a titanium-mediated aldol addition. Thus, two-carbon chain elongations of serine- and threonine-derived aldehydes with a chiral fluoroacetyl-oxazolidinone could be achieved in good yields and excellent diastereoselectivities to generate a fluorohydrin-containing carbon skeleton. A short deprotection sequence subsequently furnished the pyranoid forms of various 4-amino-2-fluoropentoses and -hexoses, respectively. The versatility of this strategy was demonstrated by the stereoselective synthesis of naturally abundant 4-amino-4-deoxyarabinose and 4-amino-4,6-dideoxygalactose (tomosamine).

Introduction

Amino-functionalized carbohydrates play various important roles in biological systems. To perform systematic studies for a better understanding of the biological function of these compounds, short and high-yielding synthetic routes for their preparation as well as sophisticated investigation strategies are essential. In this respect, fluorine substitution represents a valuable tool to probe the critical binding aspects of macromolecule complexes such as antigen–antibody adducts.[1] Various rare mono-, di-, and trideoxy (di)amino sugars can be found in the lipopolysaccharides (LPSs) of the outer cell wall of Gram-negative bacteria.[2] As these compounds are involved in immune response, pathogenicity, and adaptation mechanisms (e.g., antibiotics resistance),[3] it is highly desirable to understand their precise mode of interaction with biomolecules. Fluorinated analogues of perosamine[4] (4-amino-4,6-dideoxymannose) can be used to determine key hydrogen-bonding interactions between the O-antigens of both Inaba and Ogawa serotypes of *Vibrio cholerae*[5] and their respective antibodies. As fluorine substitution results in major electronic, but only minor steric changes,[6] the decrease or increase of affinity constants of fluorinated antigen fragments depicts the electronic environment of the binding interface. In the example at hand, decreasing K_D values were attributed to loss of hydrogen-donor ability and/or unfavorable hydrophobic effects.[7] Additionally, there is an interest in using these synthetic carbohydrate antigen fragments for the development of conjugate vaccines owing to their beneficial pharmacokinetic properties, such as enhanced metabolic stability[8] and immunogenicity.[9] Fluorinated analogues of sialic acids represent another promising application in medicinal chemistry as they are potential sialidase inhibitors and, therefore, may be used for the treatment of medical conditions such as viral infections, cancer, or diabetes.[10] Another advantage of fluorine is the possibility to perform facile NMR-based investigations.[11] The naturally 100% abundant isotope ^{19}F is an excellent nucleus for NMR experiments owing to its high sensitivity, large spectral dispersion, and the relative size of its coupling constants. Although fluorine chemistry has experienced a quantum leap within the past decade,[12] the most commonly used strategy for the preparation of fluorinated amino sugars remains F/OH substitution at a late stage with diethylaminosulfur trifluoride (DAST).[13] To the best of our knowledge, these classic carbohydrate chemistry approaches, which use nucleophilic substitutions accompanied by multiple protection/deprotection steps, suffer from considerable drawbacks such as expensive starting materials, low overall yields owing to lengthy linear synthetic routes, and/or limited scope. Hence, we were interested in developing a short and efficient general approach. Herein, we report our efforts towards the preparation of fluorinated amino sugars through stereoselective titanium-mediated aldol additions.

Results and Discussion

We started our reaction sequence by using the easily accessible serine- and threonine-derived amino aldehydes **1**, **3**,

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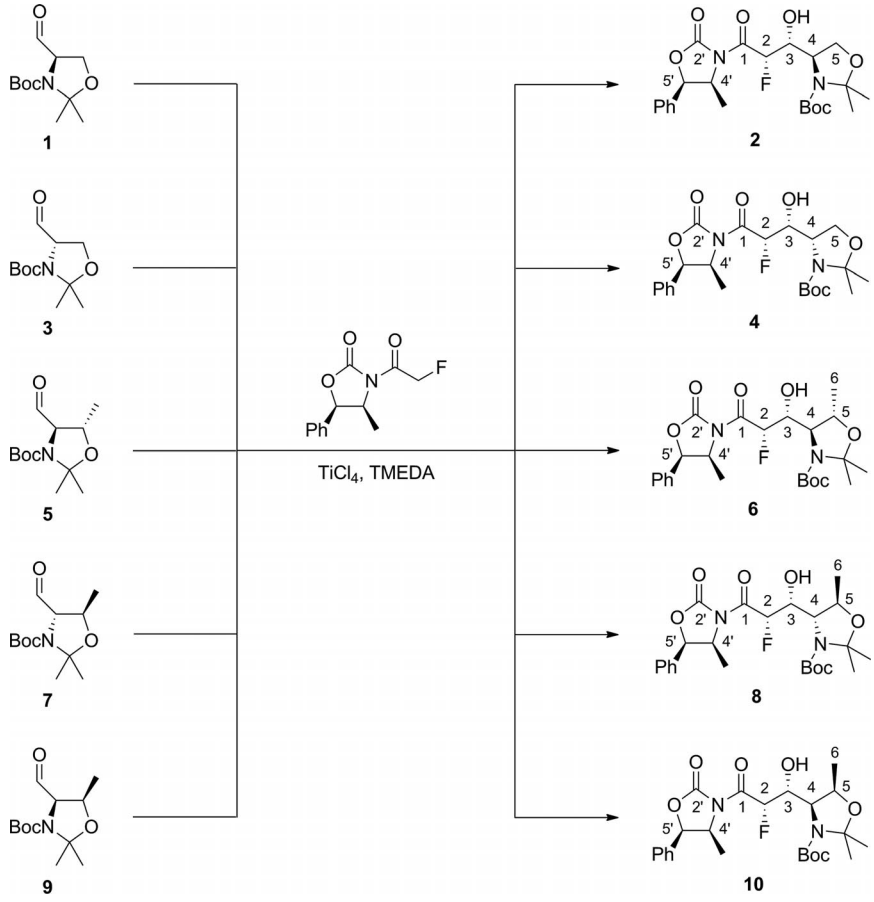


Scheme 1. Aldol additions of serine- and threonine-derived amino aldehydes to fluoroacetyl-ephedrine-oxazolidinone.

5, **7**, and **9** (Scheme 1), which were prepared from the matched, unnatural and mismatched, natural amino acids according to the protocol of Garner et al.[14] These aldehydes were subjected to a two-carbon chain-elongation step by applying a stereoselective Lewis acid mediated aldol addition.[15] As donor substrate, we used a chiral fluoroacetyl-oxazolidinone, which was prepared from commercially available ephedrine-oxazolidinone and fluoroacetyl chloride.[16] The best results for the chain-elongation reaction were achieved when $TiCl_4$ and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) were used for enolization. This result is in agreement with observations made by Evans et al.,[15a] who reported improvements to the selectivity of the addition reaction for "nonchelate" *syn*-aldol products upon the application of TMEDA to the reaction mixture. The results of the diastereoselective aldol additions are summarized in Table 1. The stereoselectivities obtained were excellent when matched (unnatural) D-amino acid derived aldehydes were used (Table 1, Entries 1, 3, and 5). As titanium is assumed to behave as a nonchelating metal in this reaction, the results may reflect the involvement of a nonchelating chairlike transition state as proposed by Pridgen et al.[15b]

Table 1. Diastereoselectivities of aldol reactions.

Entry	Compound	Yield (brsm)[a] [%]	*dr*[b]
1	**2**	66 (82)	17:1:1:1
2	**4**	68 (83)	8:2:1:1
3	**6**	55 (76)	32:2:1:0.5
4	**8**	44 (77)	15:3:1:1
5	**10**	47 (47)	20:1:0:0

[a] Yield based on recovered starting material. [b] Diastereomeric ratios of four possible diastereomers: C-2/C-3 *syn*, C-4′/C-2 *anti*; C-2/C-3 *syn*, C-4′/C-2 *syn*; C-2/C-3 *anti*, C-4′/C-2 *anti*; and C-2/C-3 *anti*, C-4′/C-2 *syn*; determined by chromatographic separation of the diastereomers, only the major diastereomer was characterized.

Although threonine derivatives generally furnished lower yields, they exhibited higher diastereomeric ratios (*dr*) than the respective serine derivatives, and mismatched-case aldol adducts also displayed acceptable selectivity. The yields obtained were satisfactory in general, although a small amount of product (3–5%) was lost owing to *tert*-butyloxycarbonyl (Boc) deprotection under the harsh conditions employed. We also investigated various other Lewis acids including different Li, B, Sn^{II}, and Sn^{IV} reagents, which all failed to furnish reasonable amounts of aldol adduct.

The diastereomeric ratios were determined by conventional column chromatographic separation. For **2**, **6**, **8**, and **10**, the major diastereomer could be obtained in pure form. Compound **4** was obtained as a mixture of two diastereomers, which were separated at a later stage of the synthesis. The relative ratios of minor diastereomers, which in

most cases could not be separated, were estimated from integrals of representative signals of NMR spectra of the respective product mixtures. Ultimately, extensive NMR investigations of the final products of the reaction sequence (vide infra) made the exact assignment of the stereochemistry of all isolated compounds possible. The pyranose ring system allows the assignment of the relative stereochemistry of the newly generated stereocenters in relation to that present in the chiral starting aldehyde by exhaustive analysis of the coupling constant pattern.

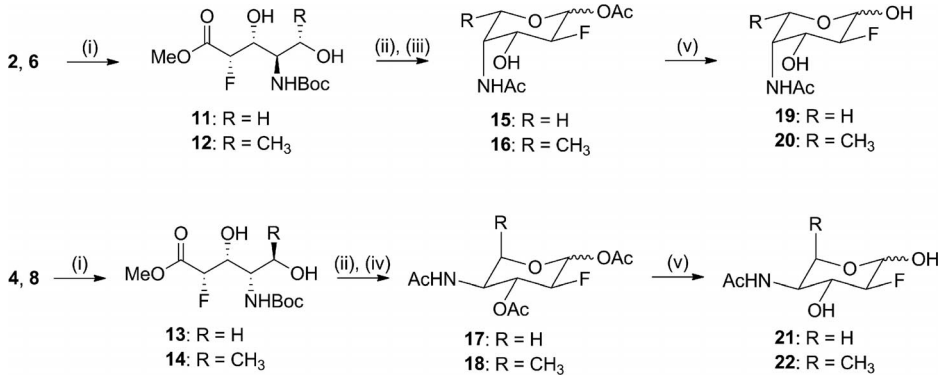
The deprotection of fluorohydrins **2**, **4**, **6**, and **8** was performed under acidic conditions. Unfortunately, the use of HCl leads to the formation of γ-lactams, which prompted us to develop a sequential deprotection sequence. After displacement of the chiral auxiliary with NaOMe, the acetonide protecting group was cleaved with acidic ion-exchange resin to leave the Boc protecting group intact and, therefore, prevent the risk of lactam formation (Scheme 2). Unfortunately, the D-*allo*-threonine derivative **10** resisted all attempts at selective acetonide cleavage, possibly owing to a shielding effect of the methyl group, which renders the isopropylidene protecting group particularly stable.

Subsequently, the reduction of **11**, **12**, **13**, and **14** with diisobutylaluminium hydride (DIBAL) was performed, followed by acetylation to overcome the inherent problem of imine formation during acidic Boc cleavage, which was subsequently performed under standard conditions with trifluoroacetic acid (TFA; Scheme 2).

In the case of D-amino acid derived compounds **15** and **16**, immediate acetyl migration from C-3-OAc to C-4-NH_2 (within free amine intermediates), driven by the *cis* alignments of the functional groups, occurred. However, we chose to prepare fully acetylated, L-amino acid derived compounds **17** and **18** as the migration did not occur in these cases owing to the *trans* alignments of C-3-OAc and C-4-NH_2. Additionally, slow autocatalytic C-3-OAc cleavage was observed within free amines.

Finally, Zemplén saponification[17] of **15**, **16**, **17**, and **18** could be successfully achieved to yield the target compounds **19**, **20**, **21**, and **22** (Figure 1). As they adopt rigid, chairlike conformations and their configurations at C-4 (and C-5) are determined by the starting materials, the configurations at C-2 and C-3 can be deduced by the magnitude of the respective $^3J_{H,H}$ NMR coupling constants (Table 2).

Interestingly, α-**22** adopts a $^1C_4$ chairlike conformation, whereas β-**22** adopts the respective $^4C_1$ conformation. However, both anomers of acetylated compound **18** feature a $^4C_1$ conformation in accordance with analogous ido-configured substances.[18] Compounds **19** and **20**, 4-amino-4-deoxyarabinose and 4-amino-4,6-dideoxygalactose[19] (tomosamine) derivatives, respectively, represent particularly inter-



Scheme 2. Deprotection sequence. Reagents and conditions: (i) (a) NaOMe/MeOH, –30 °C, 30 min; (b) DOWEX H^+, MeOH, room temp., 2–16 h, 35–59%, two steps. (ii) (a) DIBAL (1 M in toluene), THF, –78 °C, 1.5 h; (b) Ac_2O/pyridine, DMAP, room temp., 16 h; (iii) TFA/DCM, room temp., 1 h, 47–66%, two steps; (iv) TFA/DCM, room temp., 1 h, then Ac_2O, room temp., 1 h, 53–56%, two steps; (v) NaOMe/MeOH, room temp., 1 h, 89–100%.

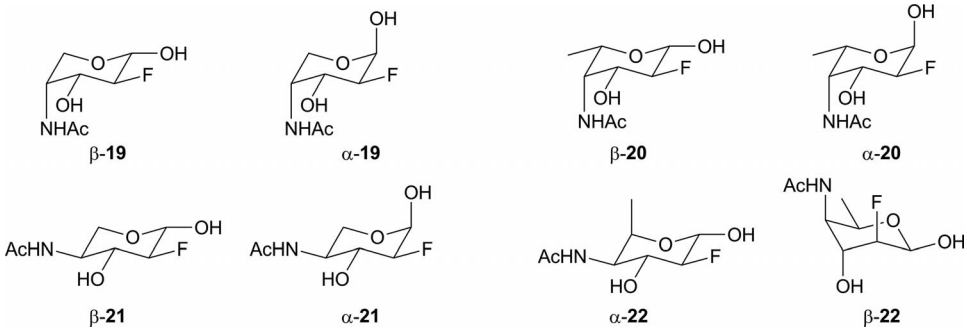


Figure 1. Conformations of α/β-anomers of final products.

Table 2. Characteristic $^3J_{H,H}$ coupling constants[Hz] of final products.

Compound	$^3J_{1\text{-H},2\text{-H}}$	$^3J_{2\text{-H},3\text{-H}}$	$^3J_{3\text{-H},4\text{-H}}$	$^3J_{4\text{-H},5\text{-H}}$
α-**19**	3.1	8.4	4.4	3.0, 4.5
β-**19**	7.2	9.2	4.9	2.2, 2.5
α-**20**	4.1	10.3	4.7	1.7
β-**20**	7.8	9.8	4.9	1.6
α-**21**	3.7	9.0	9.9	6.2, 10.1
β-**21**	7.8	8.8	10.0	5.2, 10.5
α-**22**	5.0	6.4	7.3	4.4
β-**22**	1.0	3.4	3.0	2.4

esting substances as their parent amino sugars are abundant in the LPS of Gram-negative bacteria and, hence, are associated with pathogenicity and survival of bacteria in hostile environments.

Conclusions

We have developed a new approach for the synthesis of fluorinated amino sugars by means of a stereoselective titanium-mediated aldol addition of protected serine- and threonine-derived aldehydes and fluoroacetyl-ephedrine-oxazolidinone to generate 4-amino-2-fluoropentoses and 6-deoxyhexoses within seven steps in overall yields of 16–23% (77–81% per step). Although aldol[15c,15d] (and Reformatsky)[20] type chain elongations of Garner's aldehyde have been thoroughly investigated in the past, to the best of our knowledge, there is no example of a (mono)fluoroacyl addition, which effectively makes protected amino/fluoro sugars accessible in one step and, therefore, delivers the desired mechanistic carbohydrate probes in a most simple way. The configurations of **19**, **20**, **21**, and **22** were proven by NMR techniques and, therefore, the proposed stereochemical outcome[15b] of the titanium-mediated aldol addition could be verified. These compounds are of interest for binding studies as well as the development of conjugate vaccines and antimicrobial agents. We are investigating the possibility of *anti*-selective aldol additions with our system to broaden the stereochemical scope of our approach.

Experimental Section

General Methods: NMR spectra were recorded with a Bruker Avance DPX 400 or 600 spectrometer; $CDCl_3$, D_2O, or CD_3OD were used for calibration. MS experiments were measured in the ESI mode with a Finnigan MAT 900 spectrometer. For chromatography, Merck silica gel 60 (0.004–0.063 mm) was used. For TLC monitoring, Merck plates (silica gel 60 F254) were used; the plates were stained by treatment with a solution of ninhydrin (0.3 g) in butanol (100 mL) and acetic acid (3 mL), followed by charring with a heat gun. All solvents were distilled before use. Optical rotations were measured with a Perkin–Elmer 341 polarimeter. Chemicals were purchased in reagent grade.

General Procedure for Aldol Reactions (Method A): A stirred solution of (4*S*,5*R*)-3-(2-fluoroacetyl)-4-methyl-5-phenyloxazolidin-2-one in dry dichloromethane (DCM) under argon was cooled to –78 °C, and $TiCl_4$ followed by TMEDA were added. The resulting dark-brown solution was stirred at –78 °C for 2 h, whereupon the aldehyde dissolved in dry DCM was added. The reaction mixture was warmed to –40 °C and was then allowed to slowly warm to 0 °C over 3 h. The reaction was quenched by the addition of saturated ammonium chloride solution, and the yellow precipitate formed was removed by filtration and rinsed with DCM. The phases of the filtrate were separated, and the aqueous phase was extracted three times with DCM. The combined organic extracts were dried with anhydrous $MgSO_4$ and filtered. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography to yield fluorohydrins **2**, **4**, **6**, **8**, and **10** as white crystalline solids.

General Procedure for Oxazolidinone/Acetonide Cleavage (Method B): A stirred solution of the fluorohydrin in dry methanol under argon was cooled to the temperature stated, and sodium methoxide was added. The resulting solution was stirred for 30 min, whereupon acidic ion-exchange resin was added. The reaction mixture was warmed to room temperature, and stirred for the time stated. Afterwards, the reaction mixture was filtered, and the solvents were evaporated to dryness. The crude product was purified by flash column chromatography.

General Procedure for DIBAL Reduction/Acetylation/Boc Cleavage (Method C): A stirred solution of the methyl ester in dry tetrahydrofuran (THF) under argon was cooled to –78 °C, and DIBAL (1 M in toluene) was added dropwise. The resulting solution was stirred at –78 °C for 1.5 h, whereupon the reaction was quenched by the addition of saturated potassium sodium tartrate solution and warmed to room temperature. The resulting biphasic mixture was diluted with ethyl acetate (EA) and stirred for 3 h. Afterwards the phases were separated, and the aqueous phase was extracted three times with EA. The combined organic extracts were dried with anhydrous $MgSO_4$ and filtered. After removal of the solvent under reduced pressure, the crude product was dissolved in pyridine/acetic anhydride (1:1) under argon, and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) was added. The resulting solution was stirred at room temperature overnight and then concentrated under reduced pressure and co-evaporated with toluene. The crude reaction product was redissolved in TFA/DCM (1:3) and stirred at ambient temperature for 1.5 h. The reaction mixture was then concentrated to dryness, and the crude product was redissolved in MeOH. The resulting solution was treated with basic ion-exchange resin whilst being stirred until pH = 6. After filtration and evaporation of the solvent, the crude product was further treated as stated.

General Procedure for Zemplén Saponification (Method D): To a solution of the acetylated fluoroamino sugar in dry MeOH under argon, a catalytic amount of NaOMe was added, and the resulting solution was stirred at room temperature for 1–2 h as judged by TLC (DCM/MeOH, 9:1). Then a small amount of acidic ion-exchange resin was added, and the reaction mixture was stirred at room temperature for an additional 10 min. After filtration, the solvent was evaporated to dryness, and the residue was redissolved in water and washed twice with ethyl acetate (EA), and the solvents were evaporated to dryness. The obtained products needed no further purification in general but can be purified by flash column chromatography (DCM/MeOH, 9:1) if necessary.

Procedure for the Preparation of Flouroacetyl Chloride: Ethyl fluoroacetate (13.6 mL, 141 mmol) was dissolved in EtOH/H_2O (9:1; 200 mL), and NaOH (6.72 g, 168 mmol) was added. A white precipitate slowly started to form, and after the mixture had been stirred at room temperature for 20 h, the solvent was removed under reduced pressure. The sodium fluoroacetate obtained was redis-

solved in HCl (3 M, 120 mL), and the aqueous solution was saturated with NaCl and then extracted four times with Et_2O (100 mL). The combined organic extracts were dried with anhydrous $MgSO_4$ and filtered, and the solvents were evaporated to dryness. The obtained fluoroacetic acid (10.4 g, 133 mmol, 95%) was essentially pure and was directly added to PCl_5 (30.6 g, 147 mmol) in a flask equipped with a reflux condenser under vigorous stirring and cooling (*Caution, strongly exothermic reaction!*). After the initial reaction subsided, the reaction mixture was heated at 80 °C for 1 h. Afterwards, the fluoroacetyl chloride was directly distilled from the reaction mixture by using a short distillation column (b.p. 70–71 °C); yield: 12 g (80%). The obtained fluoroacetyl chloride contained trace amounts of $POCl_3$ and was used directly without further purification.

(4*S*,5*R*)-3-(2-Fluoroacetyl)-4-methyl-5-phenyloxazolidin-2-one: A stirred solution of (4*S*,5*R*)-4-methyl-5-phenyloxazolidin-2-one (14.52 g, 81.94 mmol) in dry THF (300 mL) under argon was cooled to –78 °C, and BuLi (1.6 M in hexanes; 53.8 mL, 86.08 mmol) was added dropwise. The reaction mixture was stirred at –78 °C for 30 min, and then fluoroacetyl chloride (6.3 mL, 90.10 mmol) was added dropwise. After additional stirring for 10 min, the reaction mixture was warmed to 0 °C and quenched by the addition of water. After separation of the phases, the aqueous layer was extracted three times with Et_2O (100 mL). The combined organic extracts were washed with brine, dried with anhydrous $MgSO_4$, and filtered. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography eluted with hexanes (HE)/EA (3:1). Yield: 11.08 g (57%). $[\alpha]_D^{20}$ = –23.5 (*c* = 6.9, CH_2Cl_2). M.p. 87–89 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ = 0.96 (d, $^3J_{4\text{-H},CH_3}$ = 6.7 Hz, 3 H, CH_3), 4.80 (dq, $^3J_{4\text{-H},5\text{-H}}$ = 7.1 Hz, $^3J_{4\text{-H},CH_3}$ = 6.7 Hz, 1 H, 4-H), 5.43 (dd, $^2J_{2a'\text{-H},2b'\text{-H}}$ = 16.6 Hz, $^2J_{2'\text{-H},2a'\text{-F}}$ = 47.5 Hz, 1 H, 2a′-H), 5.47 (dd, $^2J_{2a'\text{-H},2b'\text{-H}}$ = 16.6 Hz, $^2J_{2'\text{-F},2b'\text{-H}}$ = 47.5 Hz, 1 H, 2b′-H), 5.79 (d, $^3J_{4\text{-H},5\text{-H}}$ = 7.1 Hz, 1 H, 5-H), 7.27–7.32 (m, 2 H, Ar H), 7.36–7.47 (m, 3 H, Ar H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C): δ = 14.7 (CH_3), 54.5 (C-4), 80.2 (d, $^1J_{2'\text{-F},C\text{-}2'}$ = 180.0 Hz, C-2′), 80.7 (C-5), 125.6, 128.9, 129.1 (Ar H), 132.7 (Ar Cq), 153.0 (C-2), 167.1, 167.4 (C-1′) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –229.89 ppm. HRMS (ESI): calcd. for $C_{12}H_{12}FNNaO_3$ [M + Na]$^+$ 260.0699; found 260.0709.

***tert*-Butyl (4*R*)-4-{(1*R*,2*S*)-2-Fluoro-1-hydroxy-3-[(4*S*,5*R*)-4-methyl-2-oxo-5-phenyloxazolidin-3-yl]-3-oxopropyl}-2,2-dimethyloxazolidine-3-carboxylate (2):** (4*S*,5*R*)-3-(2-Fluoroacetyl)-4-methyl-5-phenyloxazolidin-2-one (1.35 g, 5.67 mmol) in dry DCM (40 mL) was treated according to Method A with $TiCl_4$ (670 µL, 6.11 mmol), freshly distilled TMEDA (2.6 mL, 17.45 mmol), and aldehyde **1** (1 g, 4.36 mmol). Purification by silica gel chromatography was performed with HE/EA (2:1) as eluent. Yield: main diastereomers 1.18 g (58%, *dr* = 17:1); minor diastereomers 163 mg (8%, *dr* = 1:1). $[\alpha]_D^{20}$ = +4.6 (*c* = 7.1, CH_2Cl_2). M.p. 87–90 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ = 0.97 (d, $^3J_{4'\text{-H},CH_3}$ = 6.6 Hz, 3 H, CH_3), 1.51, 1.64 (2s, 15 H, 5 CCH_3), 3.97–4.23 (m, 2 H, 3-H, 5a-H), 4.28–4.37 (m, 2 H, 4-H, 5b-H), 4.78 (dq, $^3J_{4'\text{-H},5'\text{-H}}$ = 7.1 Hz, $^3J_{4'\text{-H},CH_3}$ = 6.6 Hz, 1 H, 4′-H), 4.90 (d, $^3J_{3\text{-OH},3\text{-H}}$ = 9.2 Hz, 1 H, OH), 5.76 (d, $^3J_{4'\text{-H},5'\text{-H}}$ = 7.1 Hz, 1 H, 5′-H), 6.16 (d, $^2J_{2\text{-F},2\text{-H}}$ = 47.8 Hz, 1 H, 2-H), 7.27–7.31 (m, 2 H, Ar H), 7.34–7.46 (m, 3 H, Ar H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C): δ = 14.2 (4′-CH_3), 23.9, 26.5, 28.4 (5 CCH_3), 55.5 (C-4′), 60.1 (C-4), 64.6 (C-5), 72.9 (d, $^2J_{2\text{-F},C\text{-}3}$ = 20.2 Hz, C-3), 80.3 (C-5′), 81.6 (Cq-Boc), 89.1 (d, $^1J_{2\text{-F},C\text{-}2}$ = 183.6 Hz, C-2), 94.7 (Cq-Isoprop), 125.6, 128.8, 129.0 (Ar), 132.7 (Ar Cq), 152.9 (C-2′), 167.3 (C-1) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –210.99 ppm. HRMS (ESI): calcd. for $C_{23}H_{31}FN_2NaO_7$ [M + Na]$^+$ 489.2013; found 489.2017.

***tert*-Butyl (4*S*)-4-{(1*S*,2*R*)-2-Fluoro-1-hydroxy-3-[(4*S*,5R)-4-methyl-2-oxo-5-phenyloxazolidin-3-yl]-3-oxopropyl}-2,2-dimethyloxazolidine-3-carboxylate (4):** (4*S*,5*R*)-3-(2-Fluoroacetyl)-4-methyl-5-phenyloxazolidin-2-one (1.35 g, 5.67 mmol) in dry DCM (40 mL) was treated according to Method A with $TiCl_4$ (670 µL, 6.11 mmol), freshly distilled TMEDA (2.6 mL, 17.45 mmol), and aldehyde **3** (1 g, 4.36 mmol). Purification by silica gel chromatography was performed with HE/EA (3:1) as eluent. Yield: main diastereomers (could not be separated at this stage) 1.24 g (61%, *dr* = 4:1); minor diastereomers 142 mg (7%, *dr* = 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C, main diastereomer): δ = 0.98 (d, $^3J_{4'\text{-H},CH_3}$ = 6.8 Hz, 3 H, CH_3), 1.50, 1.52, 1.61 (3 s, 15 H, 5 CCH_3), 4.03 (dd, $^3J_{4\text{-H},5a\text{-H}}$ = 6.0 Hz, $^2J_{5a\text{-H},5b\text{-H}}$ = 9.4 Hz, 1 H, 5a-H), 4.09–4.26 (m, 2 H, 3-H, 5b-H), 4.28–4.45 (m, 1 H, 4-H), 4.64 (d, $^3J_{3\text{-OH},3\text{-H}}$ = 7.1 Hz, 1 H, OH), 4.77 (dq, $^3J_{4'\text{-H},5'\text{-H}}$ = 6.7 Hz, $^3J_{4'\text{-H},CH_3}$ = 6.8 Hz, 1 H, 4′-H), 5.78 (d, $^3J_{4'\text{-H},5'\text{-H}}$ = 6.7 Hz, 1 H, 5′-H), 5.96 (d, $^2J_{2\text{-F},2\text{-H}}$ = 48.8 Hz, 1 H, 2-H), 7.27–7.46 (m, 5 H, Ar H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C): δ = 14.2 (4′-CH_3), 24.3, 27.3, 28.4 (5 CCH_3), 55.5 (C-4′), 58.3 (C-4), 64.4 (C-5), 73.9 (d, $^2J_{2\text{-F},C\text{-}3}$ = 18.9 Hz, C-3), 80.3 (C-5′), 81.8 (Cq-Boc), 89.4 (d, $^1J_{2\text{-F},C\text{-}2}$ = 185.8 Hz, C-2), 94.7 (Cq-Isoprop), 125.6, 128.8, 129.0 (Ar), 132.6 (Ar Cq), 152.9 (C-2′), 166.5 (d, $^2J_{2\text{-F},C\text{-}1}$ = 24.1 Hz, C-1) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –211.02 ppm. HRMS (ESI): calcd. for $C_{23}H_{31}FN_2NaO_7$ [M + Na]$^+$ 489.2013; found 489.2012.

***tert*-Butyl (4*S*,5*S*)-4-{(1*R*,2*S*)-2-Fluoro-1-hydroxy-3-[(4*S*,5*R*)-4-methyl-2-oxo-5-phenyloxazolidin-3-yl]-3-oxopropyl}-2,2,5-trimethyloxazolidine-3-carboxylate (6):** (4*S*,5*R*)-3-(2-Fluoroacetyl)-4-methyl-5-phenyloxazolidin-2-one (0.76 g, 3.20 mmol) in dry DCM (25 mL) was treated according to Method A with $TiCl_4$ (400 µL, 3.65 mmol), freshly distilled TMEDA (1.5 mL, 9.94 mmol), and aldehyde **5** (0.60 g, 2.47 mmol). Purification by silica gel chromatography was performed with HE/EA (4:1) as eluent. Yield: main diastereomers 624 mg (53%, *dr* = 16:1); minor diastereomers 27 mg (2%, *dr* = 2:1). $[\alpha]_D^{20}$ = –4.8 (*c* = 9.3, CH_2Cl_2). M.p. 70–73 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ = 0.97 (d, $^3J_{4'\text{-H},4'\text{-}CH_3}$ = 6.6 Hz, 3 H, 4′-CH_3), 1.40 (d, $^3J_{5\text{-H},6\text{-H}}$ = 6.3 Hz, 3 H, 6-CH_3), 1.50, 1.51, 1.61 (3s, 9 H, 5 CCH_3), 3.91 (dd, $^3J_{3\text{-H},4\text{-H}}$ = 2.3 Hz, $^3J_{4\text{-H},5\text{-H}}$ = 6.8 Hz, 1 H, 4-H), 4.01–4.17 (m, 1 H, 3-H), 4.33–4.44 (m, 1 H, 5-H), 4.79 (dq, $^3J_{4'\text{-H},4'\text{-}CH_3}$ = 6.6 Hz, $^3J_{4'\text{-H},5'\text{-H}}$ = 7.1 Hz, 1 H, 4′-H), 5.78 (d, $^3J_{4'\text{-H},5'\text{-H}}$ = 7.1 Hz, 1 H, 5′-H), 6.08 (d, $^2J_{2\text{-F},2\text{-H}}$ = 48.3 Hz, 1 H, 2-H), 6.15 (br. s, 1 H, OH), 7.27–7.31 (m, 2 H, Ar H), 7.36–7.45 (m, 3 H, Ar H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C): δ = 14.2 (4′-CH_3), 19.5 (C-6), 26.4, 28.5, 28.6 (5 CCH_3), 55.7 (C-4′), 67.9 (C-4), 70.7 (d, $^2J_{2\text{-F},C\text{-}3}$ = 18.5 Hz, C-3), 71.9 (C-5), 80.5 (C-5′), 81.8 (Cq-Boc), 89.2 (d, $^1J_{2\text{-F},C\text{-}2}$ = 187.9 Hz, C-2), 94.7 (Cq-Isoprop), 125.7, 128.9, 129.1 (Ar), 132.8 (Ar Cq), 153.2 (C-2′), 167.2 (d, $^2J_{2\text{-F},C\text{-}1}$ = 24.7 Hz, C-1) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –210.78 ppm. HRMS (ESI): calcd. for $C_{24}H_{33}FN_2NaO_7$ [M + Na]$^+$ 503.2170; found 503.2160.

***tert*-Butyl (4*R*,5*R*)-4-{(1*R*,2*S*)-2-Fluoro-1-hydroxy-3-[(4*S*,5*R*)-4-methyl-2-oxo-5-phenyloxazolidin-3-yl]-3-oxopropyl}-2,2,5-trimethyloxazolidine-3-carboxylate (8):** (4*S*,5*R*)-3-(2-Fluoroacetyl)-4-methyl-5-phenyloxazolidin-2-one (1.92 g, 8.09 mmol) in dry DCM (60 mL) was treated according to Method A with $TiCl_4$ (950 µL, 8.66 mmol), freshly distilled TMEDA (3.8 mL, 25.18 mmol), and aldehyde **7** (1.516 g, 6.23 mmol). Purification by silica gel chromatography was performed with HE/EA (4:1) as eluent. Yield: main diastereomers 1.20 g (40%, *dr* = 5:1); minor diastereomers 120 mg (4%, *dr* = 1:1). $[\alpha]_D^{20}$ = –67.7 (*c* = 8.2, CH_2Cl_2). M.p. 164–167 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ = 0.98 (d, $^3J_{4'\text{-H},4'\text{-}CH_3}$ = 6.8 Hz, 3 H, 4′-CH_3), 1.41 (d, $^3J_{5\text{-H},6\text{-H}}$ = 6.3 Hz, 3 H, 6-CH_3), 1.49, 1.52, 1.64 (3s, 15 H, 5 CCH_3), 4.12–4.27 (m, 2 H,

3-H, 4-H), 4.39 (dq, $^3J_{4\text{-H},5\text{-H}}$ = 3.1 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 6.3 Hz, 1 H, 5-H), 4.78 (dq, $^3J_{4'\text{-H},4'\text{-CH}_3}$ = 6.8 Hz, $^3J_{4'\text{-H},5'\text{-H}}$ = 7.1 Hz, 1 H, 4′-H), 4.91 (br. s, 1 H, OH), 5.79 (d, $^3J_{4'\text{-H},5'\text{-H}}$ = 7.1 Hz, 1 H, 5′-H), 5.92 (dd, $^3J_{2\text{-H},3\text{-H}}$ = 1.3 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 48.5 Hz, 1 H, 2-H), 7.26–7.31 (m, 2 H, Ar H), 7.35–7.46 (m, 3 H, Ar H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C): δ = 14.6 (4′-CH_3), 21.8 (C-6), 28.1, 28.7, 29.4 (5 CCH_3), 55.9 (C-4′), 64.7 (C-4), 73.2 (C-5), 74.9 (C-3), 80.8 (C-5′), 82.2 (Cq-Boc), 89.3 (d, $^1J_{2\text{-F},C\text{-}2}$ = 184.3 Hz, C-2), 95.0 (Cq-Isoprop), 126.0, 129.2 (Ar), 133.0 (Ar Cq), 153.4 (C-2′), 166.3 (d, $^2J_{2\text{-F},C\text{-}1}$ = 24.1 Hz, C-1) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –209.80 ppm. HRMS (ESI): calcd for $C_{24}H_{33}FN_2NaO_7$ [M + Na]$^+$ 503.2170; found 503.2176.

***tert*-Butyl (4*R*,5*R*)-4-Formyl-2,2,5-trimethyloxazolidine-3-carboxylate (9):**[21] Aldehyde **7**[22] (1.5 g, 6.17 mmol) was dissolved in THF (120 mL), and LiOH (15 mg, 0.62 mmol) was added. The resulting solution was heated to reflux overnight and then concentrated to dryness. The crude product was redissolved in Et_2O (50 mL) and washed with water and brine. The organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The diastereomers were separated by flash column chromatography with HE/EA (19:1) as eluent. Yield: 495 mg (33%), 990 mg (66%) starting material.

***tert*-Butyl (4*S*,5*R*)-4-{(1*R*,2*S*)-2-Fluoro-1-hydroxy-3-[(4*S*,5*R*)-4-methyl-2-oxo-5-phenyloxazolidin-3-yl]-3-oxopropyl}-2,2,5-trimethyloxazolidine-3-carboxylate (10):** (4*S*,5*R*)-3-(2-Fluoroacetyl)-4-methyl-5-phenyloxazolidin-2-one (512 mg, 2.16 mmol) in dry DCM (20 mL) was treated according to Method A with $TiCl_4$ (260 μL, 2.37 mmol), freshly distilled TMEDA (1 mL, 6.63 mmol), and aldehyde **9** (404 mg, 1.66 mmol). Purification by silica gel chromatography was performed with HE/EA (4:1) as eluent. Yield: main diastereomers 374 mg (47%, *dr* = 20:1). $[\alpha]_D^{20}$ = –7.9 (*c* = 6.4, CH_2Cl_2). M.p. 80–83 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ = 0.98 (d, $^3J_{4'\text{-H},4'\text{-CH}_3}$ = 6.6 Hz, 3 H, 4′-CH_3), 1.46 (d, $^3J_{5\text{-H},6\text{-H}}$ = 6.6 Hz, 3 H, 6-CH_3), 1.51, 1.56, 1.66 (3s, 9 H, 5 CCH_3), 4.09–4.22 (m, 2 H, 3-H, 4-H), 4.31–4.40 (m, 1 H, 5-H), 4.62 (br. s, 1 H, OH), 4.77 (dq, $^3J_{4'\text{-H},4'\text{-CH}_3}$ = 6.6 Hz, $^3J_{4'\text{-H},5'\text{-H}}$ = 6.8 Hz, 1 H, 4′-H), 5.76 (d, $^3J_{4'\text{-H},5'\text{-H}}$ = 6.8 Hz, 1 H, 5′-H), 6.10 (d, $^2J_{2\text{-F},2\text{-H}}$ = 47.0 Hz, 1 H, 2-H), 7.27–7.31 (m, 2 H, Ar H), 7.35–7.45 (m, 3 H, Ar H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz, 25 °C): δ = 14.2 (4′-CH_3), 15.0 (C-6), 24.6, 26.7, 28.4 (5 CCH_3), 55.7 (C-4′), 62.8 (C-4), 70.1 (d, $^2J_{2\text{-F},C\text{-}3}$ = 19.4 Hz, C-3), 72.0 (C-5), 80.2 (C-5′), 81.4 (Cq-Boc), 89.9 (d, $^1J_{2\text{-F},C\text{-}2}$ = 184.3 Hz, C-2), 93.4 (Cq-Isoprop), 125.6, 128.8, 129.0 (Ar H), 132.7 (Ar Cq), 152.59 (C-2′), 154.46 (C=O Boc), 167.3 (d, $^2J_{2\text{-F},C\text{-}1}$ = 24.5 Hz, C-1) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –208.66 ppm. HRMS (ESI): calcd. for $C_{24}H_{33}FN_2NaO_7$ [M + Na]$^+$ 503.2170; found 503.2171.

Methyl (2*S*,3*R*,4*R*)-4-[(*tert*-Butoxycarbonyl)amino]-2-fluoro-3,5-dihydroxypentanoate (11): Fluorohydrin **2** (486 mg, 1.04 mmol) in dry MeOH (10 mL) was cooled to –25 °C and treated according to Method B with NaOMe (23 mg, 0.42 mmol) and then with acidic ion-exchange resin for 16 h. Purification by silica gel chromatography was performed with HE/EA (1:2) as eluent. Yield: 121 mg (41%). $[\alpha]_D^{20}$ = –17.2 (*c* = 4.7, CH_2Cl_2). M.p. 123–125 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ = 1.45 (s, 9 H, 3 CCH_3), 3.78–3.88 (m, 2 H, 4-H, 5a-H), 3.85 (s, 3 H, OCH_3), 4.06 (dd, $^3J_{4\text{-H},5\text{b-H}}$ = 3.0 Hz, $^2J_{5\text{a-H},5\text{b-H}}$ = 10.9 Hz, 1 H, 5b-H), 4.22 (m, 1 H, 3-H), 5.11 (dd, $^3J_{2\text{-H},3\text{-H}}$ = 1.8 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 47.5 Hz, 1 H, 2-H), 5.29 (br. s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C): δ = 28.3 (3 CCH_3), 52.5 (C-4), 52.7 (OCH_3), 62.4 (C-5), 71.6 (d, $^2J_{2\text{-F},C\text{-}3}$ = 19.8 Hz, C-3), 80.4 (Cq-Boc), 89.0 (d, $^1J_{2\text{-F},C\text{-}2}$ = 189.4 Hz, C-2), 156.0 (C=O Boc), 168.9 (d, $^2J_{2\text{-F},C\text{-}1}$ = 25.5 Hz, C-1) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –208.49 ppm. HRMS (ESI): calcd. for $C_{11}H_{20}FNNaO_6$ [M + Na]$^+$ 304.1172; found 304.1178.

Methyl (2*S*,3*R*,4*R*,5*S*)-4-[(*tert*-Butoxycarbonyl)amino]-2-fluoro-3,5-dihydroxyhexanoate (12): Fluorohydrin **6** (202 mg, 0.42 mmol) in dry MeOH (10 mL) was cooled to –30 °C and treated according to Method B with NaOMe (9 mg, 0.17 mmol) and then with acidic ion-exchange resin for 2.5 h. Purification by silica gel chromatography was performed with toluene (T)/EA (2:1) as eluent. Yield: 70 mg (56%). $[\alpha]_D^{20}$ = –10.8 (*c* = 7.1, CH_2Cl_2). M.p. 138–140 °C. ^{1}H NMR (MeOD, 600 MHz, 25 °C): δ = 1.15 [d, cf (conformers), $^3J_{5\text{-H},6\text{-H}}$ = 6.5 Hz, 3 H, 6-CH_3], 1.45 (s, 9 H, 3 CCH_3), 3.62 (dd, $^3J_{4\text{-H},5\text{-H}}$ = 1.5 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 10.4 Hz, 1 H, 4-H), 3.80 (s, 3 H, OCH_3), 4.04 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 1.2 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 10.4 Hz, $^3J_{2\text{-F},3\text{-H}}$ = 28.9 Hz, 1 H, 3-H), 4.20 (dq, $^3J_{4\text{-H},5\text{-H}}$ = 1.5 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 6.5 Hz, 1 H, 5-H), 5.06 (dd, cf, $^3J_{2\text{-H},3\text{-H}}$ = 1.2 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 47.8 Hz, 1 H, 2-H) ppm. ^{13}C NMR (MeOD, 150 MHz, 25 °C): δ = 20.4 (cf, 6-C), 28.7 (cf, 3 CCH_3), 52.7 (OCH_3), 56.4 (d, cf, $^3J_{2\text{-F},C\text{-}4}$ = 2.7 Hz, C-4), 65.7 (cf, C-5), 71.9 (d, $^2J_{2\text{-F},C\text{-}3}$ = 19.3 Hz, C-3), 80.4 (Cq-Boc), 90.3 (d, $^1J_{2\text{-F},C\text{-}2}$ = 188.5 Hz, C-2), 158.2 (C=O-Boc), 170.9 (d, cf, $^2J_{2\text{-F},C\text{-}1}$ = 25.2 Hz, C-1) ppm. ^{19}F NMR (MeOD, 565 MHz, 25 °C): δ = –211.85 (cf) ppm. HRMS (ESI): calcd. for $C_{12}H_{22}FNNaO_6$ [M + Na]$^+$ 318.1329; found 318.1327.

Methyl (2*S*,3*R*,4*S*)-4-[(*tert*-Butoxycarbonyl)amino]-2-fluoro-3,5-dihydroxypentanoate (13): Fluorohydrin **4** (788 mg, 1.69 mmol) in dry MeOH (20 mL) was cooled to –40 °C and treated according to Method B with NaOMe (18 mg, 0.34 mmol) and then with acidic ion-exchange resin for 4 h. Purification by silica gel chromatography was performed with HE/EA (1:1) as eluent. Yield: main diastereomer 165 mg (35%); minor diastereomer 33 mg (7%). $[\alpha]_D^{20}$ = –6.1 (*c* = 15.0, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ = 1.43 (s, 9 H, 3 CH_3), 3.24 (br. s, 1 H, 5-OH), 3.72–3.90 (m, 3 H, 4-H, 5a-H, 5b-H), 3.82 (s, 3 H, OCH_3), 4.30 (m, 1 H, 3-H), 5.06 (dd, $^3J_{2\text{-H},3\text{-H}}$ = 3.0 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 48.0 Hz, 1 H, 2-H), 5.36 (d, $^3J_{4\text{-NH},4\text{-H}}$ = 8.6 Hz, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C): δ = 28.7, 28.7 (3 CH_3), 53.1 (OCH_3), 53.7 (C-4), 63.3 (C-5), 70.7 (d, $^2J_{2\text{-F},C\text{-}3}$ = 19.1 Hz, C-3), 80.7 (Cq-Boc), 89.6 (d, $^1J_{2\text{-F},C\text{-}2}$ = 188.9 Hz, C-2), 157.0 (C=O-Boc), 168.6 (d, $^2J_{2\text{-F},C\text{-}1}$ = 24.6 Hz, C-1) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –206.97 ppm. HRMS (ESI): calcd. for $C_{11}H_{20}FNNaO_6$ [M + Na]$^+$ 304.1172; found 304.1177.

Methyl (2*S*,3*R*,4*S*,5*R*)-4-[(*tert*-Butoxycarbonyl)amino]-2-fluoro-3,5-dihydroxyhexanoate (14): Fluorohydrin **8** (200 mg, 0.42 mmol) in dry MeOH (10 mL) was cooled to –30 °C and treated according to Method B with NaOMe (11 mg, 0.20 mmol) and then with acidic ion-exchange resin for 2 h. Purification by silica gel chromatography was performed with T/EA (2:1) as eluent. Yield: 70 mg (57%). $[\alpha]_D^{20}$ = –15.0 (*c* = 13.9, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ = 1.23 (d, $^3J_{5\text{-H},6\text{-H}}$ = 6.2 Hz, 3 H, 6-CH_3), 1.44 (s, 9 H, 3 CCH_3), 2.71 (br. s, 1 H, 5-OH), 3.42 (br. s, 1 H, 3-OH), 3.71 (m, 1 H, 4-H), 3.83 (s, 3 H, OCH_3), 4.14 (m, 1 H, 5-H), 4.29 (m, 1 H, 3-H), 5.05 (dd, $^2J_{2\text{-F},2\text{-H}}$ = 47.8 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 3.0 Hz, 1 H, 2-H), 5.24 (d, $^3J_{4\text{-NH},4\text{-H}}$ = 9.60 Hz, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, 25 °C): δ = 20.6 (C-6), 28.5 (3 CCH_3), 52.9 (OCH_3), 55.8 (C-4), 69.6 (C-5), 73.4 (d, $^2J_{2\text{-F},C\text{-}3}$ = 19.1 Hz, C-3), 80.1 (Cq-Boc), 89.3 (d, $^1J_{2\text{-F},C\text{-}2}$ = 188.9 Hz, C-2), 157.3 (C=O-Boc), 168.3 (d, $^2J_{2\text{-F},C\text{-}1}$ = 23.8 Hz, C-1) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –207.49 ppm. HRMS (ESI): calcd. for $C_{12}H_{22}FNNaO_6$ [M + Na]$^+$ 318.1329; found 318.1336.

4-Acetamido-1-*O*-acetyl-2,4-dideoxy-2-fluoro-D-arabinose (15): Ester **11** (94 mg, 0.33 mmol) in dry THF (7 mL) was treated according to Method C with DIBAL (2 mL, 2 mmol). Purification by silica gel chromatography was performed with EE/MeOH (99:1) as eluent. Yield: 52 mg (mixture of anomers: α/β = 1:1; 66%). ^{1}H NMR (MeOD, 400 MHz, 25 °C): α-anomer: δ = 2.01 (s, 3 H,

NHAc), 2.13 (s, 3 H, OAc), 3.66 (ddd, $^2J_{5a\text{-}H,5b\text{-}H}$ = 12.3 Hz, $^3J_{4\text{-}H,5a\text{-}H}$ = 3.9 Hz, ^4J = 1.5 Hz, 1 H, 5a-H), 3.92 (dd, $^2J_{5a\text{-}H,5b\text{-}H}$ = 12.3 Hz, $^3J_{4\text{-}H,5b\text{-}H}$ = 2.8 Hz, 1 H, 5b-H), 4.19 (ddd, $^3J_{2\text{-}F,3\text{-}H}$ = 10.7 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 8.7 Hz, $^3J_{3\text{-}H,4\text{-}H}$ = 4.6 Hz, 1 H, 3-H), 4.33–4.38 (m, 1 H, 4-H), 4.67 (ddd, $^3J_{1\text{-}H,2\text{-}H}$ = 3.4 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 8.7 Hz, $^2J_{2\text{-}F,2\text{-}H}$ = 48.2 Hz, 1 H, 2-H), 6.21 (dd, $^3J_{1\text{-}H,2\text{-}H}$ = 3.4 Hz, $^3J_{2\text{-}F,1\text{-}H}$ = 5.1 Hz, 1 H, 1-H) ppm; β-anomer: δ = 2.00 (s, 3 H, NHAc), 2.11 (s, 3 H, OAc), 3.62 (dd, $^2J_{5a\text{-}H,5b\text{-}H}$ = 11.6 Hz, $^3J_{4\text{-}H,5a\text{-}H}$ = 3.0 Hz, 1 H, 5a-H), 3.87 (ddd, ^4J = 0.8 Hz, $^3J_{4\text{-}H,5b\text{-}H}$ = 5.7 Hz, $^2J_{5a\text{-}H,5b\text{-}H}$ = 11.6 Hz, 1 H, 5b-H), 4.05 (ddd, $^3J_{2\text{-}F,3\text{-}H}$ = 11.8 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 6.8 Hz, $^3J_{3\text{-}H,4\text{-}H}$ = 4.6 Hz, 1 H, 3-H), 4.25–4.30 (m, 1 H, 4-H), 4.51 (ddd, $^3J_{1\text{-}H,2\text{-}H}$ = 5.3 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 6.8 Hz, $^2J_{2\text{-}F,2\text{-}H}$ = 48.1 Hz, 1 H, 2-H), 5.74 (dd, $^3J_{1\text{-}H,2\text{-}H}$ = 5.3 Hz, $^3J_{2\text{-}F,1\text{-}H}$ = 7.1 Hz, 1 H, 1-H) ppm. ^{13}C NMR (MeOD, 100 MHz, 25 °C): α-anomer: δ = 21.1 (OAc), 22.9 (NHAc), 51.3 (d, $^3J_{2\text{-}F,C\text{-}4}$ = 6.6 Hz, C-4), 64.8 (C-5), 67.9 (d, $^2J_{2\text{-}F,C\text{-}3}$ = 20.5 Hz, C-3), 89.2 (d, $^1J_{2\text{-}F,C\text{-}2}$ = 186.8 Hz, C-2), 91.5 (d, $^2J_{2\text{-}F,C\text{-}1}$ = 20.7 Hz, C-1), 171.3 (CO OAc), 174.1 (CO NHAc) ppm; β-anomer: δ = 21.1 (OAc), 23.0 (NHAc), 50.0 (d, $^3J_{2\text{-}F,C\text{-}4}$ = 4.5 Hz, C-4), 64.3 (C-5), 69.6 (d, $^2J_{2\text{-}F,C\text{-}3}$ = 22.2 Hz, C-3), 90.5 (d, $^1J_{2\text{-}F,C\text{-}2}$ = 179.4 Hz, C-2), 93.4 (d, $^2J_{2\text{-}F,C\text{-}1}$ = 29.0 Hz, C-1), 171.3 (CO OAc), 174.4 (CO NHAc) ppm. ^{19}F NMR (MeOD, 565 MHz, 25 °C): δ = –201.19, –208.69 ppm. HRMS (ESI): calcd. for $C_9H_{14}FNNaO_5$ $[M + Na]^+$ 258.0754; found 258.0751.

4-Acetamido-1-*O*-acetyl-2,4,6-trideoxy-2-fluoro-L-galactose (16): Ester **12** (69 mg, 0.23 mmol) in dry THF (5 mL) was treated according to Method C with DIBAL (1.6 mL, 1.6 mmol). After final workup, the crude product was stirred in methanolic solution at room temperature for 1 h. Purification by silica gel chromatography was performed with EE/HE (4:1) as eluent. Yield: 27 mg (mixture of anomers: α/β = 2:3; 47%). ^{1}H NMR (MeOD, 600 MHz, 25 °C): α-anomer: δ = 1.08 (d, $^3J_{5\text{-}H,6\text{-}H}$ = 6.4 Hz, 3 H, 6-CH_3), 2.05 (s, 3 H, NHAc), 2.13 (s, 3 H, OAc), 4.21 (ddd, $^3J_{3\text{-}H,4\text{-}H}$ = 4.8 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 10.2 Hz, $^3J_{2\text{-}F,3\text{-}H}$ = 12.7 Hz, 1 H, 3-H), 4.22 (dq, $^3J_{4\text{-}H,5\text{-}H}$ = 2.0 Hz, $^3J_{5\text{-}H,6\text{-}H}$ = 6.4 Hz, 1 H, 5-H), 4.40 (m, 1 H, 4-H), 4.66 (ddd, $^3J_{1\text{-}H,2\text{-}H}$ = 4.2 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 10.2 Hz, $^2J_{2\text{-}F,2\text{-}H}$ = 48.6 Hz, 1 H, 2-H), 6.28 (d, $^3J_{1\text{-}H,2\text{-}H}$ = 4.2 Hz, 1 H, 1-H) ppm; β-anomer: δ = 1.13 (d, $^3J_{5\text{-}H,6\text{-}H}$ = 6.4 Hz, 3 H, 6-CH_3), 2.05 (s, 3 H, NHAc), 2.12 (s, 3 H, OAc), 3.92 (dq, $^3J_{4\text{-}H,5\text{-}H}$ = 1.7 Hz, $^3J_{5\text{-}H,6\text{-}H}$ = 6.4 Hz, 1 H, 5-H), 4.03 (ddd, $^3J_{3\text{-}H,4\text{-}H}$ = 5.1 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 9.7 Hz, $^3J_{2\text{-}F,3\text{-}H}$ = 14.9 Hz, 1 H, 3-H), 4.33 (m, 1 H, 4-H), 4.45 (ddd, $^3J_{1\text{-}H,2\text{-}H}$ = 8.0 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 9.7 Hz, $^2J_{2\text{-}F,2\text{-}H}$ = 51.6 Hz, 1 H, 2-H), 5.64 (dd, $^3J_{2\text{-}F,1\text{-}H}$ = 4.4 Hz, $^3J_{1\text{-}H,2\text{-}H}$ = 8.0 Hz, 1 H, 1-H) ppm. ^{13}C NMR (MeOD, 150 MHz, 25 °C): α-anomer: δ = 16.7 (C-6), 20.7 (OAc), 22.5 (NHAc), 55.3 (d, $^3J_{2\text{-}F,C\text{-}4}$ = 8.4 Hz, C-4), 68.4 (d, $^2J_{2\text{-}F,C\text{-}3}$ = 17.9 Hz, C-3), 69.1 (C-5), 88.8 (d, $^1J_{2\text{-}F,C\text{-}2}$ = 186.7 Hz, C-2), 90.8 (C-1), 171.0 (CO OAc), 174.7 (CO NHAc) ppm; β-anomer: δ = 16.6 (C-6), 20.7 (OAc), 22.4 (NHAc), 55.1 (d, $^3J_{2\text{-}F,C\text{-}4}$ = 8.7 Hz, C-4), 71.7 (d, $^2J_{2\text{-}F,C\text{-}3}$ = 17.6 Hz, C-3), 72.3 (C-5), 91.4 (d, $^1J_{2\text{-}F,C\text{-}2}$ = 159.9 Hz, C-2), 93.5 (d, $^2J_{2\text{-}F,C\text{-}1}$ = 25.0 Hz, C-1), 170.9 (CO OAc), 174.7 (CO NHAc) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –208.92, –210.42 ppm. HRMS (ESI): calcd. for $C_{10}H_{16}FNNaO_5$ $[M + Na]^+$ 72.0912; found 272.0908.

4-Acetamido-1,3-di-*O*-acetyl-2,4-dideoxy-2-fluoro-D-xylose (17): Ester **13** (88 mg, 0.31 mmol) in dry THF (7 mL) was treated according to Method C with DIBAL (1.9 mL, 1.9 mmol). The crude amino sugar was then dissolved in dry DCM (5 mL) and treated with Ac_2O (60 μL, 0.63 mmol) at room temperature for 1 h. After evaporation of the solvent, purification by silica gel chromatography was performed with HE/EA (1:4) as eluent. Yield: 49 mg (mixture of anomers: α/β = 1:7; 56%). ^{1}H NMR ($CDCl_3$, 600 MHz, 25 °C): α-anomer: δ = 1.93 (s, 3 H, NHAc), 2.13, 2.15 (2s, 6 H, 2 OAc), 3.50 (dd, $^2J_{5a\text{-}H,5b\text{-}H}$ = 11.4, $^3J_{4\text{-}H,5a\text{-}H}$ = 11.3 Hz, 1 H, 5a-H), 3.91 (ddd, ^4J = 1.5 Hz, $^3J_{4\text{-}H,5b\text{-}H}$ = 5.5 Hz, $^2J_{5a\text{-}H,5b\text{-}H}$ = 11.4 Hz, 1 H, 5b-H), 4.18 (m, 1 H, 4-H), 4.63 (ddd, $^3J_{1\text{-}H,2\text{-}H}$ = 3.9 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 9.3 Hz, $^2J_{2\text{-}F,2\text{-}H}$ = 48.5 Hz, 1 H, 2-H), 5.28 (ddd, $^3J_{2\text{-}H,3\text{-}H}$ = 9.3 Hz, $^3J_{3\text{-}H,4\text{-}H}$ = 10.4 Hz, $^3J_{2\text{-}F,3\text{-}H}$ = 11.3 Hz, 1 H, 3-H), 5.93 (d, $^3J_{4\text{-}NH,4\text{-}H}$ = 7.7 Hz, 1 H, NH), 6.32 (dd, $^3J_{2\text{-}F,1\text{-}H}$ = 1.3 Hz, $^3J_{1\text{-}H,2\text{-}H}$ = 3.9 Hz, 1 H, 1-H) ppm; β-anomer: δ = 1.95 (s, 3 H, NHAc), 2.12, 2.14 (2s, 6 H, 2 OAc), 3.38 (dd, $^3J_{4\text{-}H,5a\text{-}H}$ = 8.4 Hz, $^2J_{5a\text{-}H,5b\text{-}H}$ = 11.8 Hz, 1 H, 5a-H), 4.13 (dd, $^3J_{4\text{-}H,5b\text{-}H}$ = 4.7 Hz, $^2J_{5a\text{-}H,5b\text{-}H}$ = 11.8 Hz, 1 H, 5b-H), 4.18 (m, 1 H, 4-H), 4.43 (ddd, $^3J_{1\text{-}H,2\text{-}H}$ = 6.2 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 7.3 Hz, $^2J_{2\text{-}F,2\text{-}H}$ = 48.7 Hz, 1 H, 2-H), 5.08 (ddd, $^3J_{2\text{-}H,3\text{-}H}$ = 7.3 Hz, $^3J_{3\text{-}H,4\text{-}H}$ = 8.2 Hz, $^3J_{2\text{-}F,3\text{-}H}$ = 12.6 Hz, 1 H, 3-H), 5.78 (dd, $^3J_{2\text{-}F,1\text{-}H}$ = 5.9 Hz, $^3J_{1\text{-}H,2\text{-}H}$ = 6.2 Hz, 1 H, 1-H), 6.08 (d, $^3J_{4\text{-}NH,4\text{-}H}$ = 8.5 Hz, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz, 25 °C): α-anomer: δ = 20.8, 20.9 (2 OAc), 23.1 (NHAc), 49.5 (d, $^3J_{2\text{-}F,C\text{-}4}$ = 5.8 Hz, C-4), 62.0 (C-5), 70.3 (d, $^2J_{2\text{-}F,C\text{-}3}$ = 18.9 Hz, C-3), 86.2 (d, $^2J_{2\text{-}F,C\text{-}2}$ = 193.0 Hz, C-2), 89.0 (d, $^2J_{2\text{-}F,C\text{-}1}$ = 22.7 Hz, C-1), 168.9, 172.0 (2 CO OAc), 170.3 (CO NHAc) ppm; β-anomer: δ = 20.8, 20.8 (2 OAc), 23.1 (NHAc), 48.4 (d, $^3J_{2\text{-}F,C\text{-}4}$ = 4.4 Hz, C-4), 63.6 (C-5), 70.8 (d, $^2J_{2\text{-}F,C\text{-}3}$ = 21.1 Hz, C-3), 86.9 (d, $^1J_{2\text{-}F,C\text{-}2}$ = 186.5 Hz, C-2), 91.4 (d, $^2J_{2\text{-}F,C\text{-}1}$ = 26.0 Hz, C-1), 169.0, 171.0 (2 CO OAc), 170.3 (CO NHAc) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –201.08, –197.06 ppm. HRMS (ESI): calcd. for $C_{11}H_{16}FNNaO_6$ $[M + Na]^+$ 300.0859; found 300.0845.

4-Acetamido-1,3-di-*O*-acetyl-2,4,6-trideoxy-2-fluoro-D-idose (18): Ester **14** (66 mg, 0.22 mmol) in dry THF (6 mL) was treated according to Method C with DIBAL (1.4 mL, 1.4 mmol). The crude amino sugar was then dissolved in dry DCM (5 mL) and treated with Ac_2O (40 μL, 0.42 mmol) at room temperature for 1 h. After evaporation of the solvent, purification by silica gel chromatography was performed with HE/EA (1:2) as eluent. Yield: 33 mg (mixture of anomers: α/β = 2:3; 53%). ^{1}H NMR ($CDCl_3$, 600 MHz, 25 °C): α-anomer: δ = 1.19 (d, $^3J_{5\text{-}H,6\text{-}H}$ = 6.5 Hz, 3 H, 6-CH_3), 2.04 (s, 3 H, NHAc), 2.11, 2.12 (2s, 6 H, 2 OAc), 4.15 (m, 1 H, 4-H), 4.43 (dq, $^3J_{4\text{-}H,5\text{-}H}$ = 2.1 Hz, $^3J_{5\text{-}H,6\text{-}H}$ = 6.5 Hz, 1 H, 5-H), 4.45–4.47, 4.52–4.54 (m, 1 H, 2-H), 5.01–5.04 (m, 1 H, 3-H), 5.92 (d, $^3J_{4\text{-}NH,4\text{-}H}$ = 10.5 Hz, 1 H, NH), 6.15 (d, $^3J_{2\text{-}F,1\text{-}H}$ = 11.8 Hz, 1 H, 1-H) ppm; β-anomer: δ = 1.24 (d, $^3J_{5\text{-}H,6\text{-}H}$ = 6.3 Hz, 3 H, 6-CH_3), 2.03 (s, 3 H, NHAc), 2.13, 2.19 (2s, 6 H, 2 OAc), 4.15 (m, 1 H, 4-H), 4.23 (dq, $^3J_{4\text{-}H,5\text{-}H}$ = 2.3 Hz, $^3J_{5\text{-}H,6\text{-}H}$ = 6.3 Hz, 1 H, 5-H), 4.50–4.52, 4.58–4.60 (m, 1 H, 2-H), 5.19 (m, 1 H, 3-H), 5.91 (d, $^3J_{2\text{-}F,1\text{-}H}$ = 22.8 Hz, 1 H, 1-H), 6.01 (d, $^3J_{4\text{-}NH,4\text{-}H}$ = 9.2 Hz, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz, 25 °C): α-anomer: δ = 16.5 (C-6), 20.8, 21.0 (2 OAc), 23.3 (NHAc), 47.8 (C-4), 64.5 (C-5), 67.1 (d, $^2J_{2\text{-}F,C\text{-}3}$ = 27.7 Hz, C-3), 83.2 (d, $^1J_{2\text{-}F,C\text{-}2}$ = 171.6 Hz, C-2), 90.5 (d, $^2J_{2\text{-}F,C\text{-}1}$ = 35.3 Hz, C-1), 168.6, 169.2 (2 CO OAc), 170.2 (CO NHAc) ppm; β-anomer: δ = 16.5 (C-6), 20.9, 21.0 (2 OAc), 23.3 (NHAc), 47.9 (C-4), 68.8 (d, $^2J_{2\text{-}F,C\text{-}3}$ = 25.8 Hz, C-3), 71.4 (C-5), 84.4 (d, $^1J_{2\text{-}F,C\text{-}2}$ = 184.9 Hz, C-2), 90.4 (d, $^2J_{2\text{-}F,C\text{-}1}$ = 15.2 Hz, C-1), 168.8, 168.9 (2 CO OAc), 170.0 (CO NHAc) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –190.05, –208.98 ppm. HRMS (ESI): calcd. for $C_{12}H_{18}FNNaO_6$ $[M + Na]^+$ 314.1016; found 314.0998.

4-Acetamido-2,4-dideoxy-2-fluoro-D-arabinose (19): Acetylated sugar **15** (52 mg, 0.22 mmol) in dry MeOH (5 mL) was treated according to Method D. Purification by silica gel chromatography was performed with DCM/MeOH (9:1) as eluent. Yield: 38 mg (mixture of anomers: α/β = 1:2; 89%). $[\alpha]_D^{28}$ = –66.8 (c = 14.0, H_2O). ^{1}H NMR (D_2O, 600 MHz, 25 °C): α-anomer: δ = 2.06 (s, 3 H, NHAc), 3.42 (ddd, ^4J = 1.8 Hz, $^3J_{4\text{-}H,5a\text{-}H}$ = 4.5 Hz, $^2J_{5a\text{-}H,5b\text{-}H}$ = 12.2 Hz, 1 H, 5a-H), 4.06 (dd, $^3J_{4\text{-}H,5b\text{-}H}$ = 3.0 Hz, $^2J_{5a\text{-}H,5b\text{-}H}$ = 12.2 Hz, 1 H, 5b-H), 4.29 (ddd, $^3J_{3\text{-}H,4\text{-}H}$ = 4.4 Hz, $^3J_{2\text{-}H,3\text{-}H}$ = 8.4 Hz, $^3J_{2\text{-}F,3\text{-}H}$ = 10.4 Hz, 1 H, 3-H), 4.35 (m, 1 H, 4-H), 4.62

(ddd, $^3J_{1\text{-H},2\text{-H}}$ = 3.1 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 8.4 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 48.2 Hz, 1 H, 2-H), 5.39 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 3.1 Hz, $^3J_{2\text{-F},1\text{-H}}$ = 6.3 Hz, 1 H, 1-H) ppm; β-anomer: δ = 2.08 (s, 3 H, NHAc), 3.75 (dd, $^3J_{4\text{-H},5a\text{-H}}$ = 2.2 Hz, $^2J_{5a\text{-H},5b\text{-H}}$ = 12.7 Hz, 1 H, 5a-H), 3.87 (ddd, ^4J = 1.5 Hz, $^3J_{4\text{-H},5b\text{-H}}$ = 2.5 Hz, $^2J_{5a\text{-H},5b\text{-H}}$ = 12.7 Hz, 1 H, 5b-H), 4.15 (ddd, $^3J_{3\text{-H},4\text{-H}}$ = 4.9 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 9.2 Hz, $^3J_{2\text{-F},3\text{-H}}$ = 14.0 Hz, 1 H, 3-H), 4.32 (ddd, $^3J_{1\text{-H},2\text{-H}}$ = 7.2 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 9.2 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 50.5 Hz, 1 H, 2-H), 4.34 (m, 1 H, 4-H), 4.84 (dd, $^3J_{2\text{-F},1\text{-H}}$ = 3.9 Hz, $^3J_{1\text{-H},2\text{-H}}$ = 7.2 Hz, 1 H, 1-H) ppm. ^{13}C NMR (D_2O, 150 MHz, 25 °C): α-anomer: δ = 21.9 (CH_3), 49.1 (d, $^3J_{2\text{-F},C\text{-}4}$ = 4.8 Hz, C-4), 60.9 (C-5), 65.9 (d, $^2J_{2\text{-F},C\text{-}3}$ = 21.8 Hz, C-3), 88.7 (d, $^1J_{2\text{-F},C\text{-}2}$ = 185.1 Hz, C-2), 90.3 (d, $^2J_{2\text{-F},C\text{-}1}$ = 20.1 Hz, C-1), 174.6 (CO) ppm; β-anomer: δ = 21.9 (CH_3), 50.1 (d, $^3J_{2\text{-F},C\text{-}4}$ = 8.2 Hz, C-4), 64.5 (C-5), 69.4 (d, $^2J_{2\text{-F},C\text{-}3}$ = 17.2 Hz, C-3), 91.9 (d, $^1J_{2\text{-F},C\text{-}2}$ = 177.1 Hz, C-2), 94.2 (d, $^2J_{2\text{-F},C\text{-}1}$ = 24.1 Hz, C-1), 174.7 (CO) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –207.10, –203.18 ppm. HRMS (ESI): calcd. for $C_7H_{12}FNNaO_4$ $[M + Na]^+$ 216.0648; found 216.0644.

4-Acetamido-2,4,6-trideoxy-2-fluoro-D-galactose (20): Acetylated sugar **16** (20 mg, 0.08 mmol) in dry MeOH (mL) was treated according to Method D. Yield: 16 mg (mixture of anomers: α/β = 1:2; 96%). $[\alpha]_D^{20}$ = –66.7 (*c* = 4.7, H_2O). ^{1}H NMR (D_2O, 600 MHz, 25 °C): α-anomer: δ = 1.11 (d, $^3J_{5\text{-H},6\text{-H}}$ = 6.5 Hz, 3 H, 6-CH_3), 2.11 (s, 3 H, NHAc), 4.30 (ddd, $^3J_{3\text{-H},4\text{-H}}$ = 4.7 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 10.3 Hz, $^3J_{2\text{-F},3\text{-H}}$ = 13.2 Hz, 1 H, 3-H), 4.35 (m, 1 H, 4-H), 4.42 (dq, $^3J_{4\text{-H},5\text{-H}}$ = 1.7 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 6.5 Hz, 1 H, 5-H), 4.58 (ddd, $^3J_{1\text{-H},2\text{-H}}$ = 4.1 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 10.3 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 49.0 Hz, 1 H, 2-H), 5.44 (d, $^3J_{1\text{-H},2\text{-H}}$ = 4.1 Hz, 1 H, 1-H) ppm; β-anomer: δ = 1.16 (d, $^3J_{5\text{-H},6\text{-H}}$ = 6.4 Hz, 3 H, 6-CH_3), 2.12 (s, 3 H, NHAc), 3.99 (dq, $^3J_{4\text{-H},5\text{-H}}$ = 1.6 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 6.4 Hz, 1 H, 5-H), 4.14 (ddd, $^3J_{3\text{-H},4\text{-H}}$ = 4.9 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 9.8 Hz, $^3J_{2\text{-F},3\text{-H}}$ = 14.8 Hz, 1 H, 3-H), 4.24 (ddd, $^3J_{1\text{-H},2\text{-H}}$ = 7.8 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 9.8 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 51.0 Hz, 1 H, 2-H), 4.31 (m, 1 H, 4-H), 4.86 (dd, $^3J_{2\text{-F},1\text{-H}}$ = 3.6 Hz, $^3J_{1\text{-H},2\text{-H}}$ = 7.8 Hz, 1 H, 1-H) ppm. ^{13}C NMR (D_2O, 150 MHz, 25 °C): α-anomer: δ = 15.4 (C-6), 21.8 (NHAc), 54.3 (d, $^3J_{2\text{-F},C\text{-}4}$ = 8.3 Hz, C-4), 65.0 (C-5), 66.7 (d, $^2J_{2\text{-F},C\text{-}3}$ = 17.9 Hz, C-3), 88.8 (d, $^1J_{2\text{-F},C\text{-}2}$ = 183.3 Hz, C-2), 89.8 (d, $^2J_{2\text{-F},C\text{-}1}$ = 21.1 Hz, C-1), 175.5 (CO NHAc) ppm; β-anomer: δ = 15.4 (C-6), 21.8 (NHAc), 54.0 (d, $^3J_{2\text{-F},C\text{-}4}$ = 8.8 Hz, C-4), 70.1 (d, $^2J_{2\text{-F},C\text{-}3}$ = 17.5 Hz, C-3), 70.1 (C-5), 92.2 (d, $^1J_{2\text{-F},C\text{-}2}$ = 180.6 Hz, C-2), 93.9 (d, $^2J_{2\text{-F},C\text{-}1}$ = 23.6 Hz, C-1), 175.5 (CO NHAc) ppm. ^{19}F NMR (D_2O, 565 MHz, 25 °C): δ = –206.13, –206.34 ppm. HRMS (ESI): calcd. for $C_8H_{14}FNNaO_4$ $[M + Na]^+$ 230.0805; found 230.0804.

4-Acetamido-2,4-dideoxy-2-fluoro-D-xylose (21): Acetylated sugar **17** (32 mg, 0.12 mmol) in dry MeOH (3 mL) was treated according to Method D. Yield: 22 mg (mixture of anomers: α/β = 2:3; 100%). $[\alpha]_D^{20}$ = –45.9 (*c* = 8.5, H_2O). ^{1}H NMR (D_2O, 600 MHz, 25 °C): α-anomer: δ = 1.94 (s, 3 H, NHAc), 3.59 (ddd, ^4J = 1.8 Hz, $^3J_{4\text{-H},5a\text{-H}}$ = 6.2 Hz, $^2J_{5a\text{-H},5b\text{-H}}$ = 11.4 Hz, 1 H, 5a-H), 3.62 (dd, $^3J_{4\text{-H},5b\text{-H}}$ = 10.1 Hz, $^2J_{5a\text{-H},5b\text{-H}}$ = 11.4 Hz, 1 H, 5b-H), 3.86 (ddd, $^3J_{4\text{-H},5a\text{-H}}$ = 6.2 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 9.9 Hz, $^3J_{4\text{-H},5b\text{-H}}$ = 10.1 Hz, 1 H, 4-H), 3.94 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 9.0 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 9.9 Hz, $^3J_{2\text{-F},3\text{-H}}$ = 12.4 Hz, 1 H, 3-H), 4.41 (ddd, $^3J_{1\text{-H},2\text{-H}}$ = 3.7 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 9.0 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 48.9 Hz, 1 H, 2-H), 5.35 (d, $^3J_{1\text{-H},2\text{-H}}$ = 3.7 Hz, 1 H, 1-H) ppm; β-anomer: δ = 1.94 (s, 3 H, NHAc), 3.26 (dd, $^3J_{4\text{-H},5a\text{-H}}$ = 10.5 Hz, $^2J_{5a\text{-H},5b\text{-H}}$ = 11.4 Hz, 1 H, 5a-H), 3.78 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 8.8 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 10.0 Hz, $^3J_{2\text{-F},3\text{-H}}$ = 14.3 Hz, 1 H, 3-H), 3.83 (dd, $^3J_{4\text{-H},5b\text{-H}}$ = 5.2 Hz, $^2J_{5a\text{-H},5b\text{-H}}$ = 11.4 Hz, 1 H, 5b-H), 3.87 (ddd, $^3J_{4\text{-H},5b\text{-H}}$ = 5.2 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 10.0 Hz, $^3J_{4\text{-H},5a\text{-H}}$ = 10.5 Hz, 1 H, 4-H), 4.08 (ddd, $^3J_{1\text{-H},2\text{-H}}$ = 7.8 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 8.8 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 51.0 Hz, 1 H, 2-H), 4.75 (dd, $^3J_{2\text{-F},1\text{-H}}$ = 2.8 Hz, $^3J_{1\text{-H},2\text{-H}}$ = 7.8 Hz, 1 H, 1-H) ppm. ^{13}C NMR (D_2O, 150 MHz, 25 °C): α-anomer: δ = 21.9 (NHAc), 50.5 (d, $^3J_{2\text{-F},C\text{-}4}$ = 7.3 Hz, C-4), 59.1 (C-5), 68.4 (d, $^2J_{2\text{-F},C\text{-}3}$ = 18.7 Hz, C-3), 90.0 (d, $^2J_{2\text{-F},C\text{-}1}$ = 21.1 Hz, C-1), 90.6 (d, $^1J_{2\text{-F},C\text{-}2}$ = 184.9 Hz, C-2), 174.6 (CO NHAc) ppm; β-anomer: δ = 21.9 (NHAc), 50.7 (d, $^3J_{2\text{-F},C\text{-}4}$ = 7.9 Hz, C-4), 63.3 (C-5), 71.5 (d, $^2J_{2\text{-F},C\text{-}3}$ = 18.4 Hz, C-3), 93.3 (d, $^1J_{2\text{-F},C\text{-}2}$ = 182.6 Hz, C-2), 94.2 (d, $^2J_{2\text{-F},C\text{-}1}$ = 23.3 Hz, C-1), 174.7 (CO NHAc) ppm. ^{19}F NMR ($CDCl_3$, 565 MHz, 25 °C): δ = –199.71, –199.04 ppm. HRMS (ESI): calcd. for $C_7H_{12}FNNaO_4$ $[M + Na]^+$ 216.0648; found 216.0636.

4-Acetamido-2,4,6-trideoxy-2-fluoro-D-idose (22): Acetylated sugar **18** (19 mg, 0.07 mmol) in dry MeOH (2 mL) was treated according to Method D. Yield: 13 mg (mixture of anomers: α/β = 1:2; 97%). $[\alpha]_D^{20}$ = +18.3 (*c* = 5.9, H_2O). ^{1}H NMR (D_2O, 600 MHz, 25 °C): α-anomer: δ = 1.19 (d, $^3J_{5\text{-H},6\text{-H}}$ = 6.9 Hz, 3 H, 6-CH_3), 2.02 (s, 3 H, NHAc), 3.95 (dd, $^3J_{4\text{-H},5\text{-H}}$ = 4.4 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 7.3 Hz, 1 H, 4-H), 4.02 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 6.4 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 7.3 Hz, $^3J_{2\text{-F},3\text{-H}}$ = 12.1 Hz, 1 H, 3-H), 4.29 (ddd, $^3J_{1\text{-H},2\text{-H}}$ = 5.0 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 6.4 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 48.7 Hz, 1 H, 2-H), 4.40 (dq, $^3J_{4\text{-H},5\text{-H}}$ = 4.4 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 6.9 Hz, 1 H, 5-H), 5.17 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 5.0 Hz, $^3J_{2\text{-F},1\text{-H}}$ = 8.1 Hz, 1 H, 1-H) ppm; β-anomer: δ = 1.17 (d, $^3J_{5\text{-H},6\text{-H}}$ = 6.6 Hz, 3 H, 6-CH_3), 2.04 (s, 3 H, NHAc), 3.82 (dddd, ^4J = 0.6 Hz, $^4J_{2\text{-F},4\text{-H}}$ = 0.9 Hz, $^3J_{4\text{-H},5\text{-H}}$ = 2.4 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 3.0 Hz, 1 H, 4-H), 4.14 (ddd, $^3J_{3\text{-H},4\text{-H}}$ = 3.0 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 3.4 Hz, $^3J_{2\text{-F},3\text{-H}}$ = 6.7 Hz, 1 H, 3-H), 4.24 (dq, $^3J_{4\text{-H},5\text{-H}}$ = 2.4 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 6.6 Hz, 1 H, 5-H), 4.45 (dddd, $^3J_{1\text{-H},2\text{-H}}$ = 1.0 Hz, ^4J = 1.0 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 3.4 Hz, $^2J_{2\text{-F},2\text{-H}}$ = 46.0 Hz, 1 H, 2-H), 5.09 (ddd, ^4J = 0.5 Hz, $^3J_{1\text{-H},2\text{-H}}$ = 1.0 Hz, $^3J_{2\text{-F},1\text{-H}}$ = 23.2 Hz, 1 H, 1-H) ppm. ^{13}C NMR (D_2O, 150 MHz, 25 °C): α-anomer: δ = 13.9 (C-6), 21.7 (NHAc), 52.0 (d, $^3J_{2\text{-F},C\text{-}4}$ = 3.9 Hz, C-4), 65.5 (C-5), 67.2 (d, $^2J_{2\text{-F},C\text{-}3}$ = 21.5 Hz, C-3), 90.3 (d, $^2J_{2\text{-F},C\text{-}1}$ = 28.6 Hz, C-1), 90.9 (d, $^1J_{2\text{-F},C\text{-}2}$ = 177.1 Hz, C-2), 174.4 (CO NHAc) ppm; β-anomer: δ = 15.8 (C-6), 21.7 (NHAc), 50.4 (C-4), 67.3 (d, $^2J_{2\text{-F},C\text{-}3}$ = 24.0 Hz, C-3), 68.9 (C-5), 87.8 (d, $^1J_{2\text{-F},C\text{-}2}$ = 179.9 Hz, C-2), 91.2 (d, $^2J_{2\text{-F},C\text{-}1}$ = 15.9 Hz, C-1), 174.3 (CO NHAc) ppm. ^{19}F NMR (D_2O, 565 MHz, 25 °C): δ = –194.82, –211.86 ppm. HRMS (ESI): calcd. for $C_8H_{14}FNNaO_4$ $[M + Na]^+$ 230.0805; found 230.0796.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra of all key intermediates and final products.

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