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Radiosynthesis of ^{18}F-labeled D-allose

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ABSTRACT

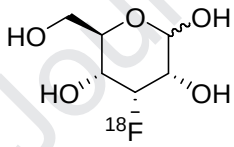
Rare sugars are defined as monosaccharides that exist in nature but are only present in limited quantities. D-Allose is a rare sugar that has been reported to have some unique physiological effects. The present study describes suitable synthetic procedures for novel rare sugars of D-allose that are ^{18}F-labeled at the C-3 and C-6 positions and the preparation of the appropriate labeling precursors. The goal is to facilitate in vivo, noninvasive positron emission tomography (PET) investigation of the behavior of rare sugar analogs of D-allose in organs. We found five precursors that were practical for labeling, three for 3-deoxy-3-[^{18}F]fluoro-D-allose ([^{18}F]3FDA) and two for 6-deoxy-6-[^{18}F]fluoro-D-allose ([^{18}F]6FDA). With manual operation synthesis, the highest radiochemical conversion rates were 75% for [^{18}F]3FDA with a precursor of 1,2,4,6-tetra-*O*-acetyl-3-*O*-trifluoromethanesulfonyl-β-D-glucopyranose and 69% for [^{18}F]6FDA with a precursor of 1,2,3,4-tetra-*O*-acetyl-6-*O*-trifluoromethanesulfonyl-β-D-allopyranose. Furthermore, the practical yields of [^{18}F]3FDA and [^{18}F]6FDA using an automated synthesizer were also investigated. Radiochemical yields of 67% and 49% were obtained for [^{18}F]3FDA and [^{18}F]6FDA,

respectively, in an automated synthesizer. As basic assessment of stability for use in PET scanning, high performance liquid chromatography analysis showed no decomposition of [^{18}F]3FDA and [^{18}F]6FDA after up to 6 h in rabbit blood plasma.

Keywords:

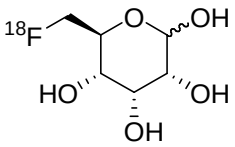
Rare sugar; 3-Deoxy-3-[^{18}F]fluoro-D-allose; 6-Deoxy-6-[^{18}F]fluoro-D-allose; Fluorine-18; Radiochemical synthesis; PET tracer

Graphical abstract:



3-Deoxy-3-[^{18}F]fluoro-D-allose

([^{18}F]3FDA)



6-Deoxy-6-[^{18}F]fluoro-D-allose

([^{18}F]6FDA)

1. Introduction

D-Allose is a rare sugar and an epimer of D-glucose at the C-3 position. Therapeutic applications of D-allose that have recently been the subject of research include protection of neurons from ischemic insult [1,2], a growth inhibitory effect on cancer cells [3–6], and enhancement of anticancer agents [7–10].

At the cell level, some of the mechanisms of those effects have been revealed. For example, the anticancer mechanism may include up-regulation of thioredoxin interacting protein [4] and down-regulation of glucose transporter type 1 [6], but other mechanisms are not known, particularly at the organ level.

Regarding sugar compounds, ^{18}F-labeled D-glucose at the C-2 position, 2-deoxy-2-[^{18}F]fluoro-D-glucose ([^{18}F]FDG), is widely applied for assessment of tumors [11–13], functional activity of tissue in organs such as the brain [14–16], and inflammation of the heart [17] or aortic wall [18], in conjunction with positron emission tomography (PET). This means that the labeled compound plays an important role in revealing the mechanisms of pathophysiological processes at the organ level.

^{18}F-labeled compounds at the different positions of C-3 (3-deoxy-3-[^{18}F]fluoro-D-glucose: [^{18}F]3FDG) [19] and C-6 (6-deoxy-6-[^{18}F]fluoro-D-glucose: [^{18}F]6FDG) [20], as D-glucose analogs, were also synthesized, and the characteristics of these compounds were demonstrated.

It is also of interest to label D-allose with radioisotopes to investigate their behavior in organs in vivo. In previous reports [21,22], 2-deoxy-2-[^{18}F]fluoro-D-allose was synthesized with electrophilic fluorination, and it was demonstrated that it can act as a PET tracer for tumor imaging with higher tumor to blood ratios and lower physiological uptake in the brain than [^{18}F]FDG.

D-glucose analogs have been labeled at different positions, and [^{18}F]3FDG [19] and [^{18}F]6FDG

[20] showed different behavior in organs from [^{18}F]FDG. Biodistribution of [^{18}F]3FDG on mouse, rat, and dog revealed to have smaller lumped-constant of brain and slower blood clearance than [^{18}F]FDG [23]. EMT6 tumor (mouse mammary gland tumor cells) imaging of [^{18}F]6FDG on mouse demonstrated that [^{18}F]6FDG is a potential tracer for glucose transport only unlike [^{18}F]FDG [24]. Difference of labeled position of [^{18}F]3FDG and [^{18}F]6FDG causes different properties from [^{18}F]FDG, thus, it would be of interest and importance to reveal the dependence of their behavior on the labeled position of the D-allose analog.

Along these lines, the present study aims to introduce ^{18}F radioisotopes at C-3 and C-6 to D-allose, namely, 3-deoxy-3-[^{18}F]fluoro-D-allose ([^{18}F]3FDA: [^{18}F]**1**) and 6-deoxy-6-[^{18}F]fluoro-D-allose ([^{18}F]6FDA: [^{18}F]**2**), respectively. [^{18}F]6FDA may be expected never to become 6-phosphate analog in vivo, and [^{18}F]3FDA might be expected to have similar properties with 3-deoxy-D-glucose which is a same compound with 3-deoxy-D-allose.

We designed some possible synthetic routes and assessed their merit by radiochemical conversions (RCCs) and length of reaction time using manual operation synthesis. After the best precursors were found, for future synthesis of [^{18}F]3FDA and [^{18}F]6FDA with sufficient quality, practical yields with these precursors were also investigated using an automated synthesizer. Because of the 109.8 min physical half-life of ^{18}F, it is desirable that labeling and hydrolytic deprotection reactions in automated synthesizers proceed within approximately 1–2 physical half-lives, with reasonable percent

yields of at least approximately 50%.

2. Results and discussion

2.1 Preparation of precursors and non-radioactive authentic standards

As possible synthetic routes, an S_N2 reaction of no-carrier-added [^{18}F]fluoride to triflate precursors with protecting groups on the non-reacting positions was adopted as the [^{18}F]fluorination reaction, and then the protecting groups were eliminated by a hydrolysis reaction. Five precursors were practical for labeling: 1,2:5,6-di-*O*-isopropylidene-3-*O*-trifluoromethanesulfonyl-α-D-glucofuranose (**3**), 1,2,4,6-tetra-*O*-acetyl-3-*O*-trifluoromethanesulfonyl-β-D-glucopyranose (**4a**), and 1,2,4,6-tetra-*O*-benzoyl-3-*O*-trifluoromethanesulfonyl-β-D-glucopyranose (**4b**) for [^{18}F]3FDA and 1,2,3,4-tetra-*O*-acetyl-6-*O*-trifluoromethanesulfonyl-β-D-allopyranose (**5a**), and 1,2,3,4-tetra-*O*-benzoyl-6-*O*-trifluoromethanesulfonyl-β-D-allopyranose (**5b**) for [^{18}F]6FDA.

In this context, pyranose-type precursors of [^{18}F]3FDA, **4a** and **4b**, were first prepared from 1,2,4,6-tetra-*O*-acetyl-β-D-glucopyranose (**6a**) [25] and 1,2,4,6-tetra-*O*-benzoyl-β-D-glucopyranose (**6b**) [26] with yields of 93% and 86%, respectively (Scheme 1). A furanose-type precursor of [^{18}F]3FDA, **3**, was prepared from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**14**) using a literature method [27]. In contrast, pyranose-type precursors of [^{18}F]6FDA, **5a** and **5b**, were prepared from D-allose (**7**) by a 4-step reaction with overall yields of 52% and 21%, respectively (Scheme 2).

For identification of radioactive compounds [^{18}F]3FDA, [^{18}F]6FDA, [^{18}F]**11a**, [^{18}F]**11b**, [^{18}F]**12a**, and [^{18}F]**12b**, non-radioactive authentic standards 3FDA, 6FDA, **11a**, **11b**, **12a**, and **12b** were also synthesized (Scheme 3).

2.2 Manual operation synthesis

The ^{18}F-labeling and hydrolytic deprotection procedure using manual operation synthesis is shown in Scheme 4. The total synthesis time of manual operation was approximately 1–2 hours. The RCCs using manual operation synthesis were determined by the ratio of photographic densities of ^{18}F-labeled compound TLC spots. The RCCs of [^{18}F]fluorination, RCCs of products [^{18}F]3FDA or [^{18}F]6FDA, and calculated efficiencies of hydrolytic deprotection reactions (calculated by dividing the RCCs of the product by those of [^{18}F]fluorination) are summarized in Table 1.

^{18}F-labeled intermediates [^{18}F]**13**, [^{18}F]**11a**, [^{18}F]**11b**, [^{18}F]**12a**, and [^{18}F]**12b** were derived from generated precursors, **3**, **4a**, **4b**, **5a**, and **5b** with 9%, 88%, 85%, 90% and 88% RCC, respectively. This means that pyranose type precursors **4a**, **4b**, **5a**, and **5b** had higher RCCs (85%–90%) than furanose-type ones did, (**3**, 9%). Regarding the hydrolytic deprotection reactions of acyl groups by NaOH, acetyl derivatives [^{18}F]**11a** and [^{18}F]**12a** proceeded to [^{18}F]3FDA and [^{18}F]6FDA with efficiencies of 85% and 77%, respectively. The hydrolytic deprotection efficiency of benzoyl derivatives, from [^{18}F]**11b** to [^{18}F]3FDA and [^{18}F]**12b** to [^{18}F]6FDA, were 38% and 30%, respectively. The results showed that the

efficiencies of deprotection with acyl groups by NaOH were higher than those with benzoyl derivatives. Acetyl groups were able to react with NaOH at room temperature in <5 min, while benzoyl groups needed 30 min for the deprotection reaction to complete. As a whole, **4a** and **5a** were found to be practical precursors for synthesis of [^{18}F]3FDA and [^{18}F]6FDA, respectively.

2.3 Automated synthesis

[^{18}F]3FDA and [^{18}F]6FDA were also synthesized from **4a** and **5a** using a commercially available automated synthesizer. Results for the synthesis of [^{18}F]3FDA and [^{18}F]6FDA by using NaOH hydrolytic deprotection with high performance liquid chromatography (HPLC) purification (method 1), NaOH hydrolytic deprotection with solid phase extraction (SPE) (method 2), or HCl hydrolytic deprotection with SPE purification (method 3) on the automated synthesizer are summarized in Table 2. The radiochemical yields value of method 2 (decay corrected based on [^{18}F]fluoride; 67% for [^{18}F]3FDA and 49% for [^{18}F]6FDA) was higher than that of method 1 (43% and 26%, respectively) or method 3 (44% and 31%). The radiochemical purity of method 1 (>99.9% for [^{18}F]3FDA and >99.9% for [^{18}F]6FDA) was somewhat higher than that of method 2 (98.6% and 99.0%, respectively) or method 3 (99.1% and 99.5%). Regarding total synthesis time, method 2 (41 min for [^{18}F]3FDA and 41 min for [^{18}F]6FDA) was somewhat shorter than method 1 (52 min and 57 min, respectively) or method 3 (58 min and 44 min). However, total synthesis time required for methods 1–3 was reasonably short considering the physical

half-life of ^{18}F radionuclide.

2.4 Test of stability in blood plasma

No decomposition was observed in blood plasma for 6 h, suggesting that both [^{18}F]3FDA and [^{18}F]6FDA were stable in blood plasma and meet the requirements for in vivo PET imaging.

3. Conclusion

Suitable synthetic procedures for [^{18}F]3FDA and [^{18}F]6FDA have been established. Therefore, [^{18}F]3FDA and [^{18}F]6FDA can allow assessment of the behavior of D-allose in organs in vivo using PET.

In addition, [^{18}F]3FDA and [^{18}F]6FDA were proven to be sufficiently stable in in vitro blood plasma. This property is practically important to simplify analysis of PET imaging data.

In the course of the present study, we also established synthetic methods for precursors **4a** and **5a**.

Limitation: Possible limitations may include the inability to detect differences between D-allose and D-allose analogs of [^{18}F]3FDA and [^{18}F]6FDA, This problem corresponds to a similar inability to distinguish between D-glucose and D-glucose analogs of [^{18}F]FDG. For example, it is reported that [^{18}F]FDG has different metabolic rates from D-glucose [28,29]. Differences of [^{18}F]3FDA and [^{18}F]6FDA

from D-allose could be clarified by the use of the natural substance and specific labeled D-allose by ^{11}C or ^{14}C [30].

4. Experimental

4.1 General methods

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (**14**) was obtained from Kanto Chemicals Co., Inc. D-Allose (**7**) was obtained from Nagara Science Co., Ltd. 1,2,4,6-Tetra-*O*-acetyl-β-D-glucopyranose (**6a**) [25] and 1,2,4,6-tetra-*O*-benzoyl-β-D-glucopyranose (**6b**) [26] were prepared from **14** by 4-step reactions using the literature method [25].

Non-radioactive compounds were identified by 1D ^{1}H and ^{13}C NMR, 2D ^{1}H-^{1}H COSY using a JNM-ECA600 (JEOL, Tokyo, Japan), and high-resolution FAB mass spectroscopy using a JMS-GCmate II (JEOL, Tokyo, Japan) with sodium doping.

Heparinized rabbit blood (New Zealand White) was obtained from Rockland Immunochemicals, Inc. (Limerick, PA, USA).

No-carrier-added [^{18}F]fluoride was produced by proton irradiation of ^{18}O-enriched water (Taiyo Nippon Sanso, Tokyo, Japan) using an HM-18 cyclotron (Sumitomo Heavy Industries, Tokyo, Japan), a BC168 Baby-cyclotron (The Japan Steel works, Ltd, Tokyo, Japan), and an HM-20 cyclotron (Sumitomo Heavy Industries). A Hybrid-type Synthesizer (JFE Engineering Corporation) or F100 (Sumitomo Heavy

Industries) was used as the automated synthesizer. The RCCs were determined by silica gel TLC (Merck 0.2 mm $60F_{254}$ on aluminum sheet). The ratio of ^{18}F-labeled compounds on TLC was determined by recording the scanning values of exposed BAS IP MS 2040 E imaging plate (GE Healthcare Japan, Tokyo, Japan) with an FLA-7000 imaging analyzer (Fujifilm, Tokyo, Japan).

*4.2 1,2:5,6-di-O-isopropylidene-3-O-trifluoromethanesulfonyl-α-D-glucofuranose (**3**)*

3 was prepared by a 1-step reaction using a literature method [27] as follows: **14** (1042 mg, 4 mmol) and pyridine (1249 μL, 15.5 mmol) were dissolved in CH_2Cl_2 (83 mL), and the mixture was cooled to −17 °C. Trifluoromethanesulfonic anhydride (808 μL, 4.8 mmol) was added to the solution, and the mixture was stirred for 4.5 h. The reaction mixture was poured to mixture of ice (20 g) and saturated aqueous $NaHCO_3$ (20 mL), and the mixture was extracted with CH_2Cl_2 (50 mL×2). The combined organic layer was dried over Na_2SO_4, and the mixture was filtered. The filtrate was concentrated under reduced pressure at <37 °C, and pyridine was azeotropically removed by toluene (100 mL×3). The residue was dissolved in hexane (160 mL), and supernatant was filtered. The filtrate was concentrated under reduced pressure at <37 °C, **3** (1548 mg, 99%) was obtained: colorless powder; mp 70 °C (dec., from hexane; lit. 70.0 °C from light petroleum [27]); ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.99 (d, 1H, *J*=4.1 Hz, H-1), 5.26 (d, 1H, *J*=2.1 Hz, H-3), 4.77 (d, 1H, *J*=4.1 Hz, H-2), 4.23-4.18 (m, 2H, H-4 and H-5), 4.15 (dd, 1H, *J*=8.9, 5.5 Hz, H-6a), 3.97 (dd, 1H, *J*=8.9, 4.1 Hz, H-6b), 1.52 (s, 3H, Me), 1.43 (s, 3H, Me),

1.34 (s, 3H, Me), 1.33 (s, 3H, Me).

*4.3 1,2,4,6-Tetra-O-acetyl-3-O-trifluoromethanesulfonyl-β-D-glucopyranose (**4a**)*

6a (699 mg, 2 mmol) and pyridine (645 μL, 8 mmol) were dissolved in CH_2Cl_2 (40 mL), and the mixture was cooled to −17 °C. Trifluoromethanesulfonic anhydride (673 μL, 4 mmol) was added to the solution, and the mixture was heated to room temperature (rt) and stirred for 30 min. After cooling to −17 °C, water (40 mL) was added to the reaction mixture, and the mixture was extracted with CH_2Cl_2 (40 mL×3). The combined organic layer was dried over Na_2SO_4, and the mixture was filtered. The filtrate was concentrated under reduced pressure, and pyridine was azeotropically removed by toluene (100 mL×3). The residue was separated by silica gel (48 g) flash column chromatography (eluent: hexane/AcOEt=3:1), and the separated fraction was concentrated under reduced pressure. After the residue was recrystallized from AcOEt (5 mL)-hexane (45 mL), **4a** (896 mg, 93%) was obtained: colorless needles; mp 87–88 °C (dec., from AcOEt-hexane); ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.71 (d, 1H, *J*=8.3 Hz, H-1), 5.323 (t, 1H, *J*=9.7 Hz, H-4), 5.318 (dd, 1H, *J*=9.7, 8.3 Hz, H-2), 5.05 (t, 1H, *J*=9.7 Hz, H-3), 4.28 (dd, 1H, *J*=12.6, 4.3 Hz, H-6a), 4.13 (dd, 1H, *J*=12.6, 2.3 Hz, H-6b), 3.82 (ddd, 1H, *J*=9.7, 4.3, 2.3 Hz, H-5), 2.13 (s, 3H, Ac), 2.12 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.10 (s, 3H, Ac); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.53, 168.94, 168.76, 168.68, 118.23 (q, *J*=319.3 Hz), 91.44, 84.07, 72.52, 69.15, 66.83, 61.11, 20.71, 20.67, 20.39, 20.33; HRMS (FAB): calculated 503.0447 for $C_{15}H_{19}O_{12}F_3S$ $[M+Na]^+$, found 503.0442; IR (KBr, cm^{-1}):

1755, 1210.

*4.4 1,2,4,6-Tetra-O-benzoyl-3-O-trifluoromethanesulfonyl-β-D-glucopyranose (**4b**)*

6b (596 mg, 1 mmol) and pyridine (193 μL, 2.4 mmol) were dissolved in CH_2Cl_2 (3 mL) and cooled to −17 °C. Trifluoromethanesulfonic anhydride (202 μL, 1.2 mmol) was added to the solution, and trhen the mixture was heated to rt and stirred for 1 h. After cooling to −17 °C, saturated aqueous $NaHCO_3$ (10 mL) was added to the reaction mixture, and the mixture was extracted with CH_2Cl_2 (20 mL×3). The combined organic layer was washed with water (10 mL) and dried over Na_2SO_4. The mixture was then filtered, and the filtrate was concentrated under reduced pressure, after which the pyridine was azeotropically removed by toluene (20 mL×4). The residue was recrystallized from i-PrOH (20 mL), yielding **4b** (626 mg, 86%): colorless powder; mp 130–131 °C (dec., from i-PrOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06–7.99 (m, 8H, Ph), 7.59 (t, 1H, *J*=7.6 Hz, Ph), 7.57–7.51 (m, 3H, Ph), 7.46–7.37 (m, 8H, Ph), 6.20 (d, 1H, *J*=8.2 Hz, H-1), 5.92 (dd, 1H, *J*=9.6, 8.2 Hz, H-2), 5.88 (t, 1H, *J*=9.6 Hz, H-4), 5.54 (t, 1H, *J*=9.6 Hz, H-3), 4.65 (dd, 1H, *J*=12.4, 3.5 Hz, H-6a), 4.46 (dd, 1H, *J*=12.4, 4.8 Hz, H-6b), 4.31 (ddd, 1H, *J*=9.6, 4.8, 3.5 Hz, H-5); ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.99, 164.64 (2C), 164.39, 134.08, 133.97, 133.85, 133.22, 130.25 (2C), 130.08 (2C), 129.99 (2C), 129.82 (2C), 129.32, 128.61 (4C), 128.55 (2C), 128.39 (2C), 128.21, 128.18, 128.04, 118.06 (q, J_F=320.8 Hz), 92.31, 84.06, 72.74, 69.85, 68.22, 62.25; HRMS (FAB): calculated 751.1073 for $C_{35}H_{27}O_{12}F_3S$ $[M+Na]^+$, found 751.1063; IR (KBr, cm^{-1}):

1737, 1267.

*4.5 1,2,3,4-Tetra-O-acetyl-6-O-triphenylmethyl-β-D-allopyranose (**9a**)*

Triphenylmethyl chloride (15.336 g, 55 mmol) was added to D-allose (**7**) (9.021 g, 50 mmol), which was suspended in pyridine (100 mL), the mixture was stirred at 40 °C for 5 days. The reaction mixture was cooled to rt, and acetic anhydride (37.8 mL, 400 mmol) was added, after which the mixture was stirred at rt for 6 days. The reaction mixture was cooled to 0 °C, and water (100 mL) was added to the mixture, which was extracted with $CHCl_3$ (100 mL×3). The combined organic layer was dried over Na_2SO_4, and the mixture was filtered. The filtrate was concentrated under reduced pressure, and the pyridine was azeotropically removed by toluene (100 mL×4). The residue was separated by silica gel (50 g) column chromatography (eluent: CH_2Cl_2/AcOEt=9:1), and the separated fraction was concentrated under reduced pressure. After the residue was recrystallized from toluene, **9a** (18.426 g, 62%) was obtained: colorless prisms; mp 216–217 °C (from toluene); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43 (dd, 6H, *J*=7.8, 1.3 Hz, Ph), 7.28 (t, 6H, *J*=7.8 Hz, Ph), 7.22 (dt, 3H, *J*=7.8, 1.3 Hz, Ph), 6.01 (d, 1H, *J*=8.6 Hz, H-1), 5.71 (t, 1H, *J*=2.9 Hz, H-3), 5.23 (dd, 1H, *J*=10.2, 2.9 Hz, H-4), 5.08 (dd, 1H, *J*=8.6, 2.9 Hz, H-2), 4.06 (ddd, 1H, *J*=10.2, 3.7, 2.2 Hz, H-5), 3.39 (dd, 1H, *J*=10.6, 2.2 Hz, H-6a), 3.03 (dd, 1H, *J*=10.6, 3.7 Hz, H-6b), 2.16 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.03 (s, 3H, Ac), 1.75 (s, 3H, Ac); ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.87, 169.33, 169.12, 168.76, 143.58 (3C), 128.70 (6C), 127.79 (6C), 127.01 (3C), 90.36,

86.42, 72.36, 68.49, 68.32, 66.04, 61.54; HRMS (FAB): calculated 613.2050 for $C_{33}H_{34}O_{10}$ $[M+Na]^+$, found 613.2040; IR (KBr, cm^{-1}): 1757, 1221.

*4.6 1,2,3,4-Tetra-O-acetyl-β-D-allopyranose (**10a**)*

10% Pd/C (21.291 g) was suspended in 1,2-dichloroethane (360 mL), and **9a** (11.813 g, 20 mmol) was solved to the suspension. Then, 98% formic acid (40 mL) was added, and the mixture was stirred at rt for 3 h. Then, the reaction mixture was filtered by Celite and washed with $CHCl_3$. The combined filtrate was concentrated under reduced pressure, and the formic acid was azeotropically removed by toluene (40 mL×3). The residue was separated by silica gel (118.1 g) column chromatography (eluent: hexane/AcOEt=1:2), and after the separated fraction was concentrated under reduced pressure, **10a** (6.713 g, 96%) was obtained: colorless prisms; mp 122–123 °C (from MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.02 (d, 1H, *J*=8.6 Hz, H-1), 5.73 (t, 1H, *J*=3.0 Hz, H-3), 5.03 (dd, 1H, *J*=10.3, 3.0 Hz, H-4), 4.97 (dd, 1H, *J*=8.6, 3.0 Hz, H-2), 4.06 (ddd, 1H, *J*=10.3, 4.3, 2.3 Hz, H-5), 3.79 (ddd, 1H, *J*=12.6, 6.9, 2.3 Hz, H-6a), 3.59 (ddd, 1H, *J*=12.6. 6.9, 4.3 Hz, H-6b), 2.19 (t, 1H, *J*=6.9 Hz, OH), 2.17 (s, 3H, Ac), 2.13 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.02 (s, 3H, Ac); ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.88, 169.61, 169.41, 169.09, 90.10, 73.29, 68.45, 68.29, 65.77, 61.00, 20.93, 20.70, 20.60, 20.54; HRMS (FAB): calculated 317.0954 for $C_{14}H_{20}O_{10}$ $[M+Na]^+$, found 371.0949; IR (KBr, cm^{-1}): 3589, 3507, 1750, 1225.

*4.7 1,2,3,4-Tetra-O-acetyl-6-O-trifluoromethanesulfonyl-β-D-allopyranose (**5a**)*

10a (349 mg, 1 mmol) and 2,6-lutidine (463 μL, 4 mmol) were dissolved in CH_2Cl_2 (20 mL), and the mixture was cooled to 0 °C. Trifluoromethanesulfonic anhydride (337 μL, 2 mmol) was added to the solution, and the mixture was stirred at 0 °C for 1 h. Water (20 mL) was added to the reaction mixture, and the mixture was extracted with CH_2Cl_2 (20 mL×3). The combined organic layer was dried over Na_2SO_4, and the mixture was filtered. The filtrate was concentrated under reduced pressure, and the 2,6-lutidine was azeotropically removed by toluene (50 mL×4). The residue was separated by silica gel (24 g) flash column chromatography (eluent: hexane/AcOEt=2:1), and the separated fraction was concentrated under reduced pressure. After the residue was recrystallized from AcOEt (0.8 mL)-hexane (7.2 mL), **5a** (419 mg, 87%) was obtained: colorless needles; mp 81–82 °C (dec., from AcOEt-hexane); ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.02 (d, 1H, *J*=8.6 Hz, H-1), 5.76 (t, 1H, *J*=2.9 Hz, H-3), 5.00 (dd, 1H, *J*=8.6, 2.9 Hz, H-2), 4.96 (dd, 1H, *J*=10.3, 2.9 Hz, H-4), 4.59 (dd, 1H, *J*=11.2, 2.3 Hz, H-6a), 4.55 (dd, 1H, *J*=11.2, 4.4 Hz, H-6b), 4.31 (ddd, 1H, *J*=10.3, 4.4, 2.3 Hz, H-5), 2.18 (s, 3H, Ac), 2.13 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.03 (s, 3H, Ac); ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.64, 169.14, 168.89, 168.85, 118.41 (q, J_F=319.3 Hz), 89.88, 73.21, 70.23, 67.89, 67.77, 65.72, 20.79, 20.63, 20.48, 20.38; HRMS (FAB): calculated for 503.0447 $C_{15}H_{19}O_{12}F_3S$ $[M+Na]^+$, found 503.0442; IR (KBr, cm^{-1}): 1755, 1744, 1245, 1212.

*4.8 1,2,3,4-Tetra-O-benzoyl-β-D-allopyranose (**10b**)*

Triphenylmethyl chloride (1 g, 3.6 mmol) and $CHCl_3$ (6 mL) were added to **7** (540 mg, 3 mmol), which was suspended in pyridine (3 mL), and mixture was stirred at 40 °C for 3 days. The reaction mixture was cooled to rt, and benzoyl chloride (2.2 mL, 19 mmol) was added. The mixture was stirred at rt for 1 h and then cooled to 0 °C, after which ice (10 g) and iced water (20 mL) were added to the mixture. Then, the mixture was extracted with $CHCl_3$ (15 mL×3). The combined organic layer was washed with water (15 mL×2) and saturated aqueous $NaHCO_3$ (15 mL×1). The resulting organic layer was then dried over Na_2SO_4, and then the mixture was filtered. The filtrate was concentrated under reduced pressure, and the pyridine was azeotropically removed by toluene (50 mL×2). The residue was dissolved in dichloromethane (30 mL), and $FeCl_3 \cdot 6H_2O$ (1.6 g, 6 mmol) was added to the mixture, after which the mixture was stirred at rt for 1 day. Water (40 mL) and $CHCl_3$ (10 mL) were added to the reaction mixture, and the organic layer was separated and extracted with $CHCl_3$ (20 mL×2). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (20 mL×1), and the resulting organic layer was dried over Na_2SO_4. The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was separated by silica gel (90 g) column chromatography (eluent: hexane/AcOEt=3:1), and the separated fraction was concentrated under reduced pressure. After the residue was recrystallized from MeOH, **10b** (395 mg, 22%) was obtained: colorless prisms; mp 181–

182 °C (from MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.10 (d, 2H, *J*=7.6 Hz, Ph), 8.05 (d, 2H, *J*=7.6 Hz, Ph), 7.88 (d, 2H, *J*=7.6 Hz, Ph), 7.84 (d, 2H, *J*=7.6 Hz, Ph), 7.67 (t, 1H, *J*=7.6 Hz, Ph), 7.57–7.50 (m, 4H, Ph), 7.46 (t, 1H, *J*=7.6 Hz, Ph), 7.42 (t, 2H, *J*=7.6 Hz, Ph), 7.35 (t, 2H, *J*=7.6 Hz, Ph), 7.28 (t, 2H, *J*=7.6 Hz, Ph), 6.61 (d, 1H, *J*=8.9 Hz, H-1), 6.33 (t, 1H, *J*=2.8 Hz, H-3), 5.70 (dd, 1H, *J*=8.9, 2.8 Hz, H-2), 5.56 (dd, 1H, *J*=9.6, 2.8 Hz, H-4), 4.51 (ddd, 1H, *J*=9.6, 4.8, 2.1 Hz, H-5), 3.95 (ddd, 1H, *J*=12.4, 5.5, 2.1 Hz, H-6a), 3.76 (ddd, 1H, *J*=12.4, 5.5, 4.8 Hz, H-6b), 2.50 (t, 1H, *J*=5.5 Hz, OH); ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.34 (2C), 165.10, 164.82, 133.91, 133.70, 133.66, 133.45, 130.15 (2C), 129.87 (2C), 129.81 (4C), 129.29, 128.79 (3C), 128.72, 128.57 (2C), 128.54, 128.49 (2C), 128.40 (2C), 91.35, 74.12, 69.48, 68.91, 66.68, 61.25; HRMS (FAB): calculated 619.1580 for $C_{34}H_{28}O_{10}$ $[M+Na]^+$, found 619.1572; IR (KBr, cm^{-1}): 3491, 1733, 1267.

*4.9 1,2,3,4-Tetra-O-benzoyl-6-O-trifluoromethanesulfonyl-β-D-allopyranose (**5b**)*

10b (1194 mg, 2 mmol) and 2,6-lutidine (927 μL, 8 mmol) were dissolved in CH_2Cl_2 (40 mL), and the mixture was cooled to 0 °C. Trifluoromethanesulfonic anhydride (673 μL, 4 mmol) was added to the solution and stirred at 0 °C for 1 h. Water (40 mL) was added to the reaction mixture, and the mixture was extracted with CH_2Cl_2 (40 mL×3). The combined organic layer was dried over Na_2SO_4, and the mixture was filtered. The filtrate was concentrated under reduced pressure, and the 2,6-lutidine was azeotropically removed by toluene (100 mL×4). The residue was separated by silica gel (72.9 g) flash

column chromatography (eluent: CH_2Cl_2), and the separated fraction was concentrated under reduced pressure. After the residue was recrystallized from CH_2Cl_2 (4 mL)-hexane (16 mL), **5b** (1398 mg, 96%) was obtained: colorless powder; mp 102–104 °C (dec., from CH_2Cl_2-hexane); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (dd, 2H, *J*=8.3, 1.2 Hz, Ph), 8.05 (dd, 2H, *J*=8.3, 1.2 Hz, Ph), 7.87 (dd, 2H, *J*=8.3, 1.2 Hz, Ph), 7.84 (dd, 2H, *J*=8.3, 1.2 Hz, Ph), 7.67, (tt, 1H, *J*=7.5, 1.2 Hz, Ph), 7.59–7.52 (m, 4H, Ph), 7.46 (tt, 1H, *J*=7.5, 1.2 Hz, Ph), 7.44 (dd, 2H, *J*=8.3, 7.5 Hz, Ph), 7.37 (dd, 2H, *J*=8.3, 7.5 Hz, Ph), 7.28 (dd, 2H, *J*=8.3, 7.5 Hz, Ph), 6.63 (d, 1H, *J*=8.5 Hz, H-1), 6.36 (t, 1H, *J*=3.0 Hz, H-3), 5.72 (dd, 1H, *J*=8.5, 3.0 Hz, H-2), 5.51 (dd, 1H, *J*=10.3, 3.0 Hz, H-4), 4.76 (ddd, 1H, *J*=10.3, 5.1, 2.3 Hz, H-5), 4.75 (dd, 1H, *J*=11.4, 2.3 Hz, H-6a), 4.69 (dd, 1H, *J*=11.4, 5.1 Hz, H-6b); ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.14, 164.81, 164.66, 164.63, 134.00, 133.86, 133.83, 133.54, 130.17 (2C), 129.82 (4C), 129.80 (2C), 129.02, 128.86 (2C), 128.65, 128.62 (2C), 128.57 (2C), 128.42 (2C), 128.38 (2C), 118.50 (q, J_F=320.1 Hz), 91.04, 73.34, 71.05, 68.90, 68.48, 66.46; HRMS (FAB): calculated 751.1073 for $C_{35}H_{27}O_{12}F_3S$ $[M+Na]^+$, found 751.1063; IR (KBr, cm^{-1}): 1731, 1261.

*4.10 1,2,4,6-Tetra-O-acetyl-3-deoxy-3-fluoro-β-D-allopyranose (**11a**)*

6a (697 mg, 2 mmol) was dissolved in CH_2Cl_2 (6 mL) and cooled to −17 °C, and then (diethylamino)sulfur trifluoride (1585 μL, 12 mmol) was added to the solution at −17 °C. The mixture was heated to rt and stirred for 14 days. The reaction mixture was cooled to −17 °C again, and saturated

aqueous $NaHCO_3$ (10 mL) was added to the mixture. The mixture was heated to rt and stirred for 2 h. The reaction mixture was extracted with $CHCl_3$ (30 mL×3), and the combined organic layer was dried over Na_2SO_4. The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was separated by silica gel (35 g) column chromatography (eluent: hexane/AcOEt=1:1), and after the separated fraction was concentrated under reduced pressure, **11a** (106 mg, 15%) was obtained: colorless prisms; mp 86–87 °C (from MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.02 (d, 1H, *J*=8.6 Hz, H-1), 5.15 (dt, 1H, J_F=53.6 Hz, *J*=2.1 Hz, H-3), 4.94 (ddd, 1H, J_F=27.0 Hz, *J*=10.2, 2.1 Hz, H-4), 4.93 (ddd, 1H, J_F=27.4 Hz, *J*=8.6, 2.1 Hz, H-2), 4.33 (dd, 1H, *J*=12.4, 4.1 Hz, H-6a), 4.23 (ddd, 1H, *J*=10.2, 4.1, 1.9 Hz, H-5), 4.18 (dd, 1H, *J*=12.4, 1.9 Hz, H-6b), 2.133 (s, 3H, Ac), 2.128 (s, 3H, Ac), 2.121 (s, 3H, Ac), 2.09 (s, 3H, Ac); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.65, 169.45, 169.38, 168.99, 89.73 (d, J_F=4.3 Hz), 87.58 (d, J_F=183.5 Hz), 70.39 (d, J_F=2.9 Hz), 68.99 (d, J_F=17.3 Hz), 66.40 (d, J_F=17.4 Hz), 61.71, 20.88, 20.74, 20.63 (2C); HRMS (FAB): calculated 373.0911 for $C_{14}H_{19}O_9F$ $[M+Na]^+$, found 373.0906; IR (KBr, cm^{-1}): 1764, 1747, 1737, 1243, 1234, 1209.

*4.11 1,2,4,6-Tetra-O-benzoyl-3-deoxy-3-fluoro-β-D-allopyranose (**11b**)*

6b (596 mg, 1 mmol) was dissolved in CH_2Cl_2 (3 mL) and cooled to −17 °C, and (diethylamino)sulfur trifluoride (528 μL, 4 mmol) was added to the solution at −17 °C. The mixture was heated to rt and stirred for 9 days. Then, the reaction mixture was cooled to −17 °C again, and saturated

aqueous $NaHCO_3$ (10 mL) was added. The resulting mixture was heated to rt and stirred for 2 h. The reaction mixture was then extracted with $CHCl_3$ (20 mL×3), and the combined organic layer was dried over Na_2SO_4. The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was separated by silica gel (18 g) column chromatography (eluent: hexane/AcOEt=9:1), and after the separated fraction was concentrated under reduced pressure, **11b** (304 mg, 51%) was obtained: colorless powder; mp 151–152 °C (from MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.10–8.00 (m, 8H, Ph), 7.59 (t, 1H, *J*=7.6 Hz, Ph), 7.57–7.52 (m, 3H, Ph), 7.46–7.38 (m, 8H, Ph), 6.55 (d, 1H, *J*=8.2 Hz, H-1), 5.55 (ddd, 1H, J_F=27.5 Hz, *J*=8.2, 2.1 Hz, H-2), 5.51 (dt, 1H, J_F=51.5 Hz, *J*=2.1 Hz, H-3), 5.48 (ddd, 1H, J_F=28.8 Hz, *J*=10.3, 2.1 Hz, H-4), 4.74–4.68 (m, 2H, H-5 and H-6a), 4.52 (dd, 1H, *J*=12.4, 4.8 Hz, H-6b); ^{13}C NMR (150 MHz, $CDCl_3$): δ 166.09, 165.08, 165.01, 164.67, 133.78 (2C), 133.68, 133.15, 130.13 (2C), 129.97 (4C), 129.79 (2C), 129.52, 128.72, 128.69, 128.57 (2C), 128.51 (3C), 128.48 (2C), 128.37 (2C), 90.67 (d, J_F=2.9 Hz), 88.04 (d, J_F=185.0 Hz), 70.75 (d, J_F=2.9 Hz), 69.50 (d, J_F=15.9 Hz), 67.66 (d, J_F=17.3 Hz), 62.82; HRMS (FAB): calculated 621.1537 for $C_{34}H_{27}O_9F$ $[M+Na]^+$, found 621.1530; IR (KBr, cm^{-1}): 1728, 1272.

*4.12 3-Deoxy-3-fluoro-D-allose (3FDA: **1**)*

11b (121 mg, 0.2 mmol) was dissolved in 1,4-dioxane (20 mL), and 0.2 mol/L aqueous NaOH (10 mL) was added to the solution. The mixture was stirred at rt for 2 h, and then 0.2 mol/L aqueous HCl

(12 mL) was added. The resulting mixture was concentrated under reduced pressure, and then 3FDA (27 mg, 75%) was separated by preparative HPLC (Column: Nakarai Cosmosil Sugar-D, 20 mmI.D.×20+250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 10 mL/min) with RI-2031 refractive index detector (JASCO, Tokyo, Japan).

β-Pyranose form (ca. 90% equilibrium ratio in D_2O) of 3FDA (3-deoxy-3-fluoro-β-D-allopyranose): ^{1}H NMR (600 MHz, D_2O): δ 4.87 (dt, 1H, J_F=53.5 Hz, J=2.1 Hz, H-3), 4.77 (d, 1H, J=8.3 Hz, H-1), 3.74 (dd, 1H, J=12.3, 2.0 Hz, H-6a), 3.66 (ddd, 1H, J=10.1, 5.4, 2.0 Hz, H-5), 3.60 (ddd, 1H, J_F=29.1 Hz, J=10.1, 2.1 Hz, H-4), 3.57 (dd, 1H, J=12.3, 5.4 Hz, H-6b), 3.37 (ddd, 1H, J_F=30.1 Hz, J=8.3, 2.1 Hz, H-2); ^{13}C NMR (150 MHz, D_2O): δ 93.58, 93.38 (d, J_F=173.4 Hz), 73.74, 70.39 (d, J_F=15.8 Hz), 65.86 (d, J_F=17.4 Hz), 60.82.

α-Pyranose form (ca. 10% equilibrium ratio in D_2O) of 3FDA (3-deoxy-3-fluoro-α-D-allopyranose): ^{1}H NMR (600 MHz, D_2O): δ 5.08 (d, 1H, J=4.4 Hz, H-1), 4.85 (dt, 1H, J_F=54.4 Hz, J=2.4 Hz, H-3), 3.86 (ddd, 1H, J=10.5, 5.0, 2.2 Hz, H-5), 3.73 (dd, 1H, J=12.2, 5.0 Hz, H-6a), 3.68 (dd, 1H, J=12.2, 2.2 Hz, H-6b), 3.67 (ddd, 1H, J_F=28.1 Hz, J=4.4, 2.4 Hz, H-2), 3.67–3.56 (m, overlapped with peak of β-pyranose form according to ^{1}H-^{1}H COSY, H-4); ^{13}C NMR (150 MHz, D_2O): δ 92.59 (d, J_F=176.3 Hz), 91.29, 66.723 (d, J_F=15.9 Hz), 66.718, 65.12 (d, J_F=18.8 Hz), 60.49.

HRMS (FAB): calculated 205.0488 for $C_6H_{11}O_5F$ $[M+Na]^+$, found 205.0484.

*4.13 1,2,3,4-Tetra-O-acetyl-6-deoxy-6-fluoro-β-D-allopyranose (**12a**)*

10a (2.704 g, 7.75 mmol) was dissolved in CH_2Cl_2 (23.3 mL) and cooled to −17 °C, and (diethylamino)sulfur trifluoride (5 g, 31 mmol) was added to the solution at −17 °C. The mixture was heated to rt and stirred for 20 h. The reaction mixture was cooled to −17 °C again, and saturated aqueous $NaHCO_3$ (100 mL) was added. The resulting mixture was heated to rt and stirred for 1 h. The reaction mixture was then extracted with $CHCl_3$ (50 mL×3), and the combined organic layer was dried over Na_2SO_4. The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was separated by silica gel (135.8 g) column chromatography (eluent: hexane/AcOEt=1:2), and after the separated fraction was concentrated under reduced pressure, **12a** (574 mg, 21%) was obtained: colorless prisms; mp 119–120 °C (from MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.02 (d, 1H, *J*=8.6 Hz, H-1), 5.75 (t, 1H, *J*=2.9 Hz, H-3), 5.04 (dd, 1H, *J*=10.3, 2.9 Hz, H-4), 5.00 (dd, 1H, *J*=8.6, 2.9 Hz, H-2), 4.56 (ddd, 1H, J_F=47.5 Hz, *J*=10.6, 2.0 Hz, H-6a), 4.47 (ddd, 1H, J_F=46.9 Hz, *J*=10.6, 3.6 Hz, H-6b), 4.19 (dddd, 1H, J_F=24.9 Hz, *J*=10.3, 3.6, 2.0 Hz, H-5), 2.17 (s, 3H, Ac), 2.13 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.02 (s, 3H, Ac); ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.79, 169.32, 168.99, 168.95, 90.00, 80.93 (d, J_F=174.9 Hz), 71.72 (d, J_F=18.8 Hz), 68.16, 68.02, 65.30 (d, J_F=7.3 Hz), 20.90, 20.66, 20.51 (2C); HRMS (FAB): calculated 373.0911 for $C_{14}H_{19}O_9F$ $[M+Na]^+$, found 373.0906; IR (KBr, cm^{-1}): 1755, 1222.

*4.14 1,2,3,4-Tetra-O-benzoyl-6-deoxy-6-fluoro-β-D-allopyranose (**12b**)*

10b (418 mg, 0.7 mmol) was dissolved in CH_2Cl_2 (1.4 mL) and cooled to −17 °C, and (diethylamino) sulfur trifluoride (370 μL, 2.8 mmol) was added to the solution at −17 °C. The mixture was heated to rt and stirred for 1 day. The reaction mixture was then cooled to −17 °C again, and saturated aqueous $NaHCO_3$ (10 mL) was added. The resulting mixture was heated to rt and stirred for 2 h. The reaction mixture was then extracted with $CHCl_3$ (20 mL×3), and the combined organic layer was dried over Na_2SO_4. The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was separated by silica gel (21 g) column chromatography (eluent: hexane/AcOEt=9:1), and after the separated fraction was concentrated under reduced pressure, **12b** (137 mg, 33%) was obtained: colorless powder; mp 119–120 °C (from MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (d, 2H, *J*=7.6 Hz, Ph), 8.06 (d, 2H, *J*=7.6 Hz, Ph), 7.89 (d, 2H, *J*=7.6 Hz, Ph), 7.84 (d, 2H, *J*=7.6 Hz, Ph), 7.66 (t, 1H, *J*=7.6 Hz, Ph), 7.58–7.51 (m, 4H, Ph), 7.46 (t, 1H, *J*=7.6 Hz, Ph), 7.43 (t, 2H, *J*=7.6 Hz, Ph), 7.36 (t, 2H, *J*=7.6 Hz, Ph), 7.28 (t, 2H, *J*=7.6 Hz, Ph), 6.63 (d, 1H, *J*=8.3 Hz, H-1), 6.35 (t, 1H, *J*=2.8 Hz, H-3), 5.73 (dd, 1H, *J*=8.3, 2.8 Hz, H-2), 5.58 (dd, 1H, *J*=10.3, 2.8 Hz, H-4), 4.710 (dd, 1H, J_F=47.4 Hz, *J*=4.1 Hz, H-6a), 4.707 (dd, 1H, J_F=49.4 Hz, *J*=2.1 Hz, H-6b), 4.60 (dddd, 1H, J_F=21.3 Hz, *J*=10.3, 4.1, 2.1 Hz, H-5); ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.21, 164.99, 164.72, 164.67, 133.90, 133.71, 133.60, 133.45, 130.19 (2C), 129.80 (6C), 129.22, 128.78 (4C), 128.55 (2C), 128.52, 128.48 (2C), 128.40 (2C), 91.23, 81.13 (d, J_F=176.3 Hz), 72.51 (d, J_F=18.8 Hz), 69.15, 68.65, 66.10 (d, J_F=7.2 Hz); HRMS (FAB) calculated 621.1537 for $C_{34}H_{27}O_9F$ $[M+Na]^+$, found 621.1529; IR (KBr, cm^{-1}): 1734, 1263.

*4.15 6-Deoxy-6-fluoro-D-allose (6FDA: **2**)*

12b (60 mg, 0.1 mmol) was dissolved in 1,4-dioxane (2.6 mL), and then 0.6 mol/L aqueous NaOH (1 mL) was added to the solution. The mixture was stirred at rt for 1.5 h, and then 1 mol/L aqueous. CH_3CO_2H (1.2 mL) was added to the reaction mixture. The mixture was concentrated under reduced pressure, after which the CH_3CO_2H was azeotropically removed by water (5 mL×2). The resulting residue was dissolved in water (5 mL), and the mixture was filtered by a syringe filter (pore size: 0.45 μm). The filtrate was concentrated under reduced pressure, and 6FDA (7.7 mg, 42%) was purified by preparative HPLC (Column: Nakarai Cosmosil $5C_{18}$-PAQ, 20 mmI.D.×50+250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 10 mL/min) with an RI-2031 refractive index detector (JASCO, Tokyo, Japan).

β-Pyranose form (ca. 83% equilibrium ratio in D_2O) of 6FDA (6-deoxy-6-fluoro-β-D-allopyranose): ^{1}H NMR (600 MHz, D_2O): δ 4.81 (d, 1H, *J*=8.2 Hz, H-1), 4.60 (ddd, 1H, J_F=47.5 Hz, *J*=11.0, 2.0 Hz, H-6a), 4.56 (ddd, 1H, J_F=47.5 Hz, *J*=11.0, 4.1 Hz, H-6b), 4.09 (t, 1H, *J*=2.8 Hz, H-3), 3.64 (dd, 1H, *J*=10.3, 2.8 Hz, H-4), 3.82 (dddd, 1H, J_F=27.5 Hz, *J*=10.3, 4.1, 2.0 Hz, H-5), 3.32 (dd, 1H, *J*=8.2, 2.8 Hz, H-2); ^{13}C NMR (150 MHz, D_2O): δ 93.65, 82.89 (d, J_F=167.6 Hz), 72.25 (d, J_F=17.3 Hz), 71.17, 71.07, 65.75 (d, J_F=5.8).

α-Pyranose form (ca. 17% equilibrium ratio in D_2O) of 6FDA (6-deoxy-6-fluoro-α-D-allopyranose): ^{1}H NMR (600 MHz, D_2O): δ 5.06 (d, 1H, *J*=4.1 Hz, H-1), 4.60 (ddd, 1H, J_F=47.5 Hz, *J*=11.0, 2.0 Hz, H-6a),

4.56 (ddd, 1H, J_F=47.5 Hz, J=11.0, 4.1Hz, H-6b), 4.09 (t, 1H, J=2.8 Hz, H-3), 4.00 (dddd, 1H, J_F=21.3 Hz, J=10.3, 4.1, 2.0 Hz, H-5), 3.64 (dd, 1H, J=10.3, 2.8 Hz, H-4), 3.61 (t, 1H, J=2.8 Hz, H-2); ^{13}C NMR (150 MHz, D_2O): δ 93.06, 82.89 (d, J_F=167.6 Hz), 71.61, 66.97, 65.93 (d, J_F=17.3 Hz), 65.19 (d, J_F=5.8 Hz).

HRMS (FAB): calculated 205.0488 for $C_6H_{11}O_5F$ $[M+Na]^+$, found 205.0485.

*4.16 General procedures for synthesis of 3-deoxy-3-[^{18}F]fluoro-D-allose ([^{18}F]3FDA: [^{18}F]**1**) and 6-deoxy-6-[^{18}F]fluoro-D-allose ([^{18}F]6FDA: [^{18}F]**2**) from **4a** and **5a**, respectively, by manual operation synthesis*

In total, 50–60 MBq of no-carrier-added [^{18}F]fluoride in water (ca. 1 mL) was adsorbed to a Waters Sep-Pak Accell Plus QMA Plus Light Cartridge, which was activated by 1 mol/L aqueous K_2CO_3 (10 mL) and water (30 mL). The [^{18}F]fluoride was desorbed by a mixture of K_2CO_3 (17 μmol), cryptand 222 (34 μmol), water (0.2 mL), and CH_3CN (0.7 mL). The eluent was concentrated by heating to 85 °C with N_2 flowing. CH_3CN (1 mL) was added to the residue and azeotropically dried by heating to 85 °C with N_2 flowing. A CH_3CN (1 mL) solution of **4a** (20 mg, 42 μmol) or **5a** (20 mg, 42 μmol) was added to the residue and stirred at 85 °C for 5 min, and 1,2,4,6-tetra-*O*-acetyl-3-deoxy-3-[^{18}F]fluoro-β-D-allopyranose ([^{18}F]**11a**) or 1,2,3,4-tetra-*O*-acetyl-6-deoxy-6-[^{18}F]fluoro-β-D-allopyranose ([^{18}F]**12a**) was obtained at 88% or 90%

RCC, respectively, determined by silica gel TLC (R_f 0.60 for [^{18}F]**11a**, 0.58 for [^{18}F]**12a**, eluent: hexane/AcOEt=1:1), determined using authentic non-radioactive samples of **11a** or **12a**. After concentration by heating to 85 °C with N_2 flowing and cooling to rt, the residue was dissolved in tetrahydrofuran (1 mL), and then 0.3 mol/L aqueous NaOH (1 mL) was added to the solution, the mixture was shaken, and it stood at rt for 5 min. Then 1 mol/L aqueous CH_3CO_2H (0.5 mL) was added to the reaction mixture, and [^{18}F]3FDA or [^{18}F]6FDA was obtained at 75% or 69% RCC, respectively, as determined by silica gel TLC (R_f 0.38 for [^{18}F]3FDA, 0.38 for [^{18}F]6FDA, eluent: $CHCl_3$/MeOH=2:1) using authentic non-radioactive samples of 3FDA or 6FDA. After concentration by heating to 85 °C with N_2 flowing, [^{18}F]3FDA or [^{18}F]6FDA was separated by semi-preparative HPLC (Column: Nakarai Cosmosil Sugar-D, 10 mmI.D.×20+250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 2 mL/min, retention time: 13.9 min for [^{18}F]3FDA, 11.1 min for [^{18}F]6FDA) with PD1A radio-detector (UNIVERSAL GIKEN, Kanagawa, Japan).

*4.17 General procedures for synthesis of [^{18}F]3FDA and [^{18}F]6FDA from **4b** and **5b**, respectively, by manual operation synthesis*

In total, 50–60 MBq of no-carrier-added [^{18}F]fluoride in water (ca. 1 mL) was adsorbed to a Waters Sep-Pak Accell Plus QMA Plus Light Cartridge, which was activated by 1 mol/L aqueous K_2CO_3 (10 mL) and water (30 mL). The [^{18}F]Fluoride was desorbed by a mixture of K_2CO_3 (17 μmol), cryptand

222 (34 μmol), water (0.2 mL), and CH_3CN (0.7 mL). The eluent was concentrated by heating to 85 °C with N_2 flowing. CH_3CN (1 mL) was added to the residue and azeotropically dried by heating to 85 °C with N_2 flowing. After a CH_3CN (3 mL) solution of **4b** (30 mg, 42 μmol) or **5b** (30 mg, 42 μmol) was added to the residue and the mixture was stirred at 85 °C for 5 min, 1,2,4,6-tetra-*O*-benzoyl-3-deoxy-3-[^{18}F]fluoro-β-D-allopyranose ([^{18}F]**11b**) or 1,2,3,4-tetra-*O*-benzoyl-6-deoxy-6-[^{18}F]fluoro-β-D-allopyranose ([^{18}F]**12b**) was obtained at 85% or 88% RCC, respectively, as determined by silica gel TLC (R_f 0.39 for [^{18}F]**11b**, 0.36 for [^{18}F]**12b**, eluent: toluene/AcOEt=9:1) using authentic non-radioactive samples **11b** or **12b**. After concentration by heating to 85 °C with N_2 flowing and cooling to rt, the residue was dissolved in tetrahydrofuran (1 mL), and 0.3 mol/L aqueous NaOH (1 mL) was added to the solution, after which the mixture was shaken, and it stood at rt for 30 min. Then, after 1 mol/L aqueous CH_3CO_2H (0.5 mL) was added to the reaction mixture, [^{18}F]3FDA or [^{18}F]6FDA was obtained at 33% or 26% RCC, respectively which was determined by silica gel TLC (R_f 0.38 for [^{18}F]3FDA, 0.39 for [^{18}F]6FDA, eluent: $CHCl_3$/MeOH=2:1) using authentic non-radioactive samples 3FDA or 6FDA. After concentration by heating to 85 °C with N_2 flowing, [^{18}F]3FDA or [^{18}F]6FDA was separated by semi-preparative HPLC (Column: Nakarai Cosmosil Sugar-D, 10 mmI.D.×20+250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 2 mL/min, retention time: 13.9 min for [^{18}F]3FDA, 11.1 min for [^{18}F]6FDA) with a PD1A radio-detector (UNIVERSAL GIKEN, Kanagawa, Japan).

*4.18 Synthesis of [^{18}F]3FDA from **3** by manual operation synthesis*

In total, 50–60 MBq of no-carrier-added [^{18}F]fluoride in water (ca. 1 mL) was adsorbed to a Waters Sep-Pak Accell Plus QMA Plus Light Cartridge, which was activated by 1 mol/L aqueous K_2CO_3 (10 mL) and water (30 mL). [^{18}F]Fluoride was desorbed by a mixture of K_2CO_3 (17 μmol), cryptand 222 (34 μmol), water (0.2 mL), and CH_3CN (0.7 mL). The eluent was concentrated by heating to 85 °C with N_2 flowing. CH_3CN (1 mL) was added to the residue and azeotropically dried by heating to 85 °C with N_2 flowing. A CH_3CN (1 mL) solution of **3** (16.3 mg, 42 μmol) was added to the residue and the mixture was stirred at 85 °C for 1 h, assumed 1,2:5,6-di-*O*-isopropylidene-3-deoxy-3-[^{18}F]fluoro-α-D-allofuranose ([^{18}F]**13**) was obtained at 9% RCC by silica gel TLC (R_f 0.62, eluent: hexane/AcOEt=1:1). After concentration by heating to 85 °C with N_2 flowing, 1 mol/L aqueous HCl (1 mL) was added to the residue, and the mixture was stirred at 85 °C for 50 min. [^{18}F]3FDA was obtained at 4% RCC, determined by silica gel TLC (R_f 0.39, eluent: $CHCl_3$/MeOH=2:1) using authentic non-radioactive sample **1**. After concentration by heating to 85 °C with N_2 flowing, [^{18}F]3FDA was separated by semi-preparative HPLC (Column: Nakarai Cosmosil Sugar-D, 10 mmI.D.×20+250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 2 mL/min, retention time: 13.9 min) with a PD1A radio-detector (UNIVERSAL GIKEN, Kanagawa, Japan).

*4.19 General procedures for synthesis of [^{18}F]3FDA and [^{18}F]6FDA from **4a** and **5a**, respectively, using an automated synthesizer (Hybrid-type Synthesizer) with NaOH hydrolytic deprotection and HPLC separation (method 1)*

No-carrier-added [^{18}F]fluoride in [^{18}O]H_2O (ca. 1 mL) was adsorbed to Waters Sep-Pak Accell Plus QMA Plus Light Cartridge which was activated by 1 mol/L aqueous K_2CO_3 (10 mL) and water (30 mL). [^{18}F]Fluoride was desorbed by mixture of K_2CO_3 (17 μmol), cryptand 222 (34 μmol), water (0.2 mL), and CH_3CN (0.7 mL). The eluent was concentrated under reduced pressure by heating to 140 °C with N_2 flowing. CH_3CN (1 mL) was added to the residue and azeotropically dried under reduced pressure by heating to 140 °C with N_2 flowing. CH_3CN (1 mL) solution of **4a** or **5a** (20 mg) respectively was added to the residue and stood at 85 °C for 5 min. After concentration under reduced pressure by heating to 85 °C with N_2 flowing, the residue was cooled to rt. 0.3 mol/L aqueous NaOH (1 mL) was added to the residue and the reaction mixture was stood at rt for 5 min. Then 1 mol/L aqueous CH_3CO_2H (0.5 mL) was added to the reaction mixture. The reaction mixture was separated by semi-preparative HPLC (column: Nakarai Cosmosil 5C_{18}-MS-II, 10 mmI.D.×250 mm, eluent: H_2O, flow rate: 2.5 mL/min). After concentration under reduced pressure, water (8 mL) was added to the residue and the solution was filtered with sterilization filter (Merck Vented Millex GS, pore size: 0.22 μm, 25 mmI.D.), [^{18}F]3FDA or [^{18}F]6FDA was obtained.

[^{18}F]3FDA was synthesized from [^{18}F]fluoride (2.7 GBq) and **4a** (20 mg, 42 μmol) as a colorless

aqueous solution (844 MBq, 43% (decay corrected)); retention time of semi-preparative HPLC: 6.5 min; radiochemical purity: >99.9% (by HPLC analysis, column: Nakarai Cosmosil Sugar-D, 4.6 mmI.D.×250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 1.0 mL/min, retention time: 5.9 min); pH: 7 (by test paper); cryptand 222: <40 ppm (by spot test using iodoplatinate reagent); total synthesis time: 52 min.

[^{18}F]6FDA was synthesized from [^{18}F]fluoride (2.3 GBq) and **5a** (20 mg, 42 μmol) as a colorless aqueous solution (424 MBq, 26% (decay corrected)); retention time of semi-preparative HPLC: 6.7 min; radiochemical purity: >99.9% (by HPLC analysis, column: Nakarai Cosmosil Sugar-D, 4.6 mmI.D.×250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 1.0 mL/min, retention time: 4.9 min); pH: 7 (by test paper); cryptand 222: <40 ppm (by spot test using iodoplatinate reagent); total synthesis time: 57 min.

*4.20 General procedures for synthesis of [^{18}F]3FDA and [^{18}F]6FDA from **4a** and **5a**, respectively, by using automated synthesizer (Hybrid-type Synthesizer) with NaOH hydrolytic deprotection and SPE separation (method 2)*

No-carrier-added [^{18}F]fluoride in [^{18}O]H_2O (ca. 1 mL) was adsorbed to a Waters Sep-Pak Accell Plus QMA Plus Light Cartridge, which was activated by 1 mol/L aqueous K_2CO_3 (10 mL) and water (30 mL). [^{18}F]Fluoride was desorbed by a mixture of K_2CO_3 (17 μmol), cryptand 222 (34 μmol), water (0.2 mL), and CH_3CN (0.7 mL). The eluent was concentrated under reduced pressure by heating to 140 °C with N_2 flowing. CH_3CN (1 mL) was added to the residue and azeotropically dried under reduced

pressure by heating to 140 °C with N_2 flowing. A CH_3CN (1 mL) solution of **4a** or **5a** (20 mg) was added to the residue and stood at 85 °C for 5 min. After concentration under reduced pressure by heating to 85 °C with N_2 flowing, the residue was cooled to rt, 0.3 mol/L aqueous NaOH (1 mL) was added to the residue, and the reaction mixture stood at rt for 5 min. Then, water (2 mL) was added to the reaction mixture. The reaction mixture was passed through three sequential SPE cartridges (S*PURE Maxi-Clean IC-H Plus 1.5 mL, Waters Sep-Pak PS-2 Plus Short Cartridge, and Waters Sep-Pak Alumina N Plus Long Cartridge), which were activated by 10 mL ethanol for disinfection (76.9–81.4 vol%; Japanese Pharmacopoeia,) and water (40 mL) and sequentially passed through a sterilization filter (Merck Vented Millex GS, pore size: 0.22 μm, 25 mmI.D.). Then, after the SPE cartridges and sterilization filter were washed with water (10 mL), [^{18}F]3FDA or [^{18}F]6FDA was obtained.

[^{18}F]3FDA was synthesized from [^{18}F]fluoride (2.2 GBq) and **4a** (20 mg, 42 μmol) as a colorless aqueous solution (1,137 MBq, 67% (decay corrected)); radiochemical purity: 98.6% (by HPLC analysis, column: Nakarai Cosmosil Sugar-D, 4.6 mmI.D.×250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 1.0 mL/min, retention time: 5.8 min); pH: 7 (by test paper); cryptand 222: <40 ppm (by spot test using iodoplatinate reagent); Al^{3+}: <2 ppm (by test paper); total synthesis time: 41 min.

[^{18}F]6FDA was synthesized from [^{18}F]fluoride (2.7 GBq) and **5a** (20 mg, 42 μmol) as a colorless aqueous solution (1,035 MBq, 49% (decay corrected)); radiochemical purity: 99.0% (by HPLC analysis, column: Nakarai Cosmosil Sugar-D, 4.6 mmI.D.×250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 1.0

mL/min, retention time: 4.9 min); pH: 7 (by test paper); cryptand 222: <40 ppm (by spot test using iodoplatinate reagent); Al^{3+}: <2 ppm (by test paper); total synthesis time: 41 min.

*4.21 General procedures for synthesis of [^{18}F]3FDA and [^{18}F]6FDA from **4a** and **5a**, respectively, using automated synthesizer (F100) with HCl hydrolytic deprotection and SPE separation (method 3)*

No-carrier-added [^{18}F]fluoride in [^{18}O]H_2O (ca. 4.5 mL) was adsorbed to a Waters Sep-Pak Accell Plus QMA Plus Light Cartridge, which was activated by 1 mol/L aqueous K_2CO_3 (10 mL) and water (30 mL). [^{18}F]Fluoride was desorbed by an aqueous solution (0.6 mL) of K_2CO_3 (22 μmol), and a CH_3CN solution (1 mL) of cryptand 222 (35 μmol) was added to the mixture. The mixture was concentrated under reduced pressure by heating. A CH_3CN solution (1.5 mL) of **4a** or **5a** (20 mg) was added to the residue and stirred at 90 °C for 5 min. After concentration under reduced pressure by heating, 1 mol/L aqueous HCl (2 mL) was added to the residue, and the reaction mixture was stirred at 135 °C for 5 min. After cooling to rt, the reaction mixture was passed through four sequential SPE cartridges (S*PURE Maxi-Clean IC-H Plus 0.5 mL, Bio-Rad AG 11A8 resin, Waters Sep-Pak C18 Plus Short Cartridge, and Waters Sep-Pak Alumina N Plus Long Cartridge), which were activated by 10 mL ethanol for disinfection (76.9–81.4 vol%, Japanese Pharmacopoeia) and water (40 mL) and sequentially passed through a sterilization filter (Merck Vented Millex GS, pore size: 0.22 μm, 25 mmI.D.). Then, after the SPE cartridges and sterilization filter were washed with water (8 mL), [^{18}F]3FDA or [^{18}F]6FDA was

obtained.

[^{18}F]3FDA was synthesized from [^{18}F]fluoride (22.2 GBq) and **4a** (20 mg, 42 μmol) as a colorless aqueous solution (6,790 MBq, 44% (decay corrected)); radiochemical purity: 99.1% (by HPLC analysis, column: Bio-Rad Aminex HPX-87H, 7.8 mmI.D.×300 mm, eluent: H_2O, flow rate: 0.8 mL/min, retention time: 7.5 min); pH: 7 (by test paper); total synthesis time: 58 min.

[^{18}F]6FDA was synthesized from [^{18}F]fluoride (22.4 GBq) and **5a** (20 mg, 42 μmol) as a colorless aqueous solution (5,270 MBq, 31% (decay corrected)); radiochemical purity: 99.5% (by HPLC analysis, column: Bio-Rad Aminex HPX-87H, 7.8 mmI.D.×300 mm, eluent: H_2O, flow rate: 0.8 mL/min, retention time: 7.8 min); pH: 7 (by test paper); total synthesis time: 44 min.

4.22 Evaluation for stability of [^{18}F]3FDA and [^{18}F]6FDA in rabbit blood plasma

Plasma of heparinized rabbit blood (New Zealand White) was separated by centrifugation. The stability of [^{18}F]3FDA and [^{18}F]6FDA in blood plasma was measured by HPLC (Column: Nakarai Cosmosil Sugar-D, 10 mmI.D.×20+250 mm, eluent: CH_3CN/H_2O=3:1, flow rate: 2 mL/min) with a radio-detector (Perkin-Elmer Radiomatic 150TR with SolarScint solid scintillator containing 400 μL heterogeneous flow cells) from 5 min to 6 h after mixing. No decomposition of [^{18}F]3FDA or [^{18}F]6FDA was observed up to 6 h.

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Conflict of Interest

Hiroyuki Yamamoto, Kenji Wada, Testuro Tago, Masanobu Ibaraki, Toshibumi Kinoshita, Yuka Yamamoto, Yoshihiro Nishiyama and Nobuyuki Kudomi declare no conflict of interest. Jun Toyohara receives a research grant from Sumitomo Heavy Industries (Tokyo, Japan).

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Table 1. Radiochemical conversions (RCCs) and efficiencies of 3-deoxy-3-[^{18}F]fluoro-D-allose ([^{18}F]3FDA) and 6-deoxy-6-[^{18}F]fluoro-D-allose ([^{18}F]6FDA) synthesis by manual operation.

Product	Precursor	RCC of [^{18}F]fluorination (%)	Deprotection efficiency (%)	RCC of product (%)
[^{18}F]3FDA	**3**	9	44	4
	4a	88	85	75
	4b	85	38	33
[^{18}F]6FDA	**5a**	90	77	69
	5b	88	30	26

Table 2. Results of [^{18}F]3FDA and [^{18}F]6FDA synthesis using automated synthesizer.

Product	Precursor	Method	Deprotection reagent	Separation	Percent yield (%, decay corrected)	Radiochemical purity (%)	Total synthesis time (min)
[^{18}F]3FDA	**4a**	1	NaOH	HPLC	43	>99.9	52
		2	NaOH	SPE	67	98.6	41
		3	HCl	SPE	44	99.1	58
[^{18}F]6FDA	**5a**	1	NaOH	HPLC	26	>99.9	55
		2	NaOH	SPE	49	99.0	41
		3	HCl	SPE	31	99.5	44

Captions to Schemes

Scheme 1. Preparation of precursors **4a** and **4b**. Reagents and conditions: (a) trifluoromethanesulfonic anhydride (Tf_2O), pyridine, CH_2Cl_2, room temperature (rt), 30 min and 93% yield for **4a**, 1 h and 86% yield for **4b**.

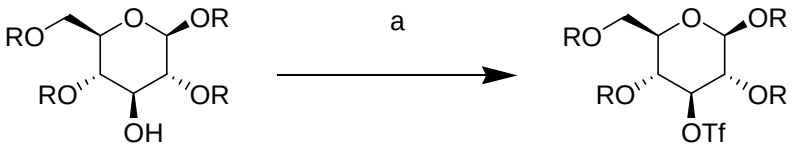
Scheme 2. Preparation of precursors **5a** and **5b**. Reagents and conditions: (a) triphenylmethyl chloride (TrCl), pyridine, 40 °C, 3-5 days; (b) acetic anhydride (Ac_2O), pyridine, rt, 6 days and 62% yield for **9a** from **7**, or benzoyl chloride (BzCl), pyridine, rt, 3 days for **9b**; (c) 10% Pd/C, HCO_2H, $ClCH_2CH_2Cl$, rt, 3 h and 96% yield for **10a**, or $FeCl_3 \bullet 6H_2O$, CH_2Cl_2, rt, 1 day and 22% yield for **10b** from **7**; (d) trifluoromethanesulfonic anhydride (Tf_2O), 2,6-lutidine, CH_2Cl_2, 0 °C, 1 h and 87% yield for **5a**, 1 h and 96% yield for **5b**.

Scheme 3. Preparation of non-radioactive authentic samples 3FDA, 6FDA, **11a**, **11b**, **12a**, and **12b**. Reagents and conditions: (a) Et_2NSF_3, CH_2Cl_2, rt, 14 days and 15% yield for **11a**, 9 days and 51% yield for **11b**, 20 h and 21% yield for **12a**, 1 day and 33% yield for **12b**; (b) NaOH, H_2O, 1,4-dioxane, rt, 2 h and 75% yield for 3FDA from **11b**, 1.5 h and 42% yield for 6FDA from **12b**.

Scheme 4. Preparation of [^{18}F]3FDA and [^{18}F]6FDA. Reagents and conditions: (a) [^{18}F]KF, K_2CO_3,

cryptand 222, CH_3CN, 85 °C, 5 min for **4a**, **4b**, **5a**, and **5b**, or 1 h for **3**; (b) HCl, H_2O, 85 °C, 50 min; (c) NaOH, H_2O, tetrahydrofuran, rt, 5 min for **4a** and **5a**, or 30 min for **4b** and **5b**.

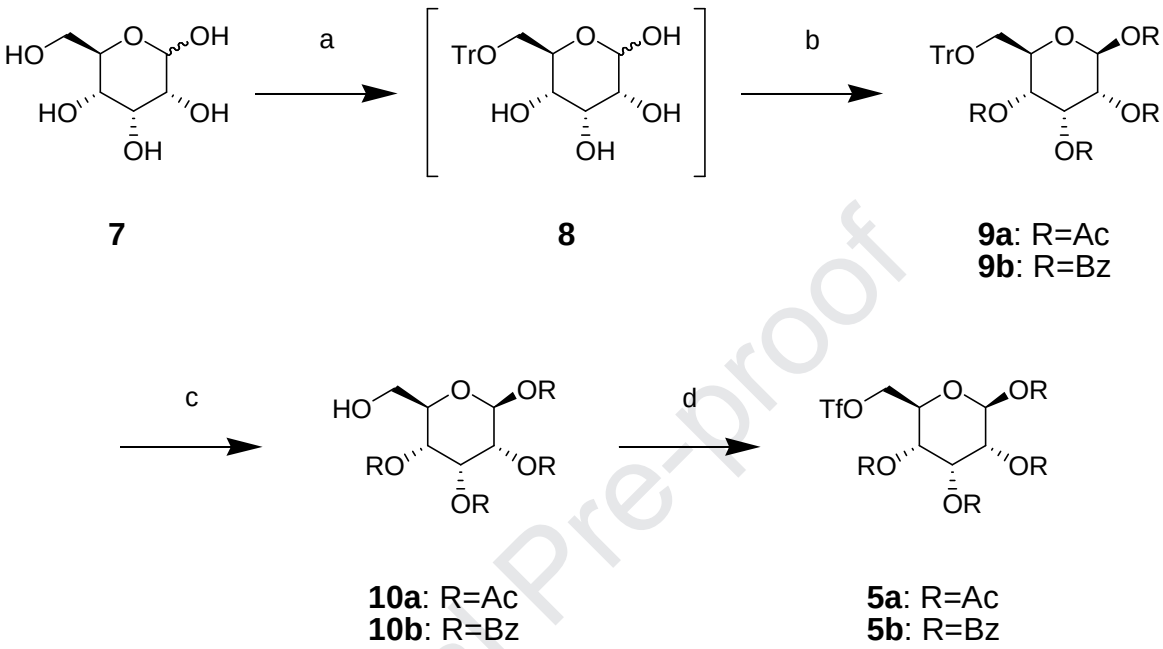
Scheme 1.



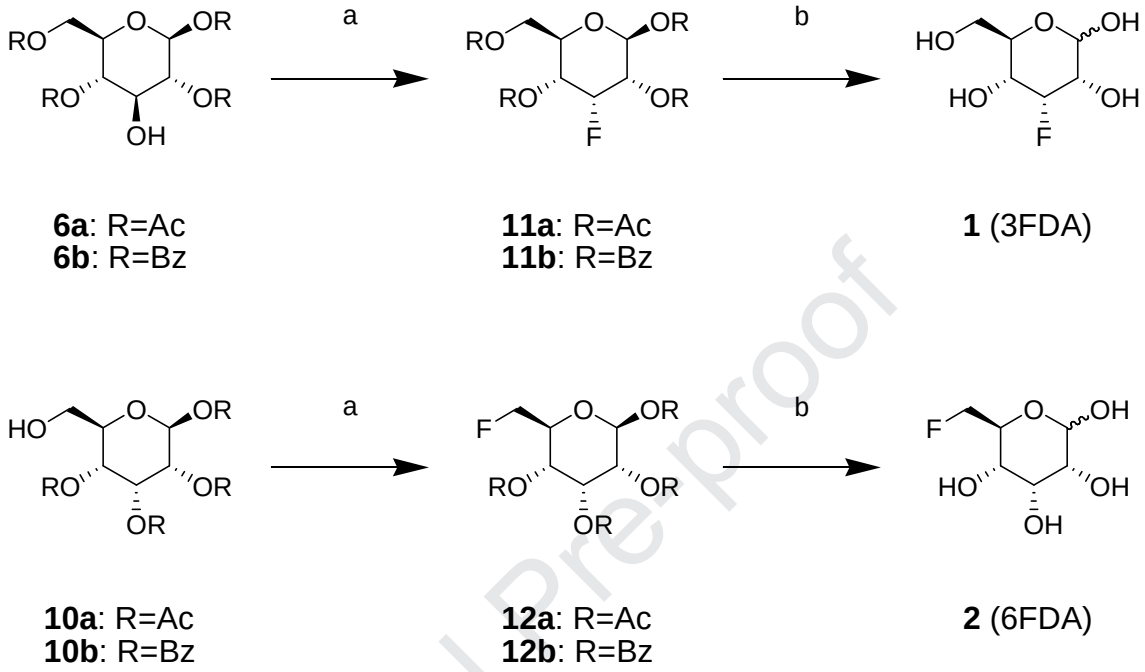
6a: R=Ac
6b: R=Bz

4a: R=Ac
4b: R=Bz

Scheme 2.



Scheme 3.



6a: R=Ac
6b: R=Bz

11a: R=Ac
11b: R=Bz

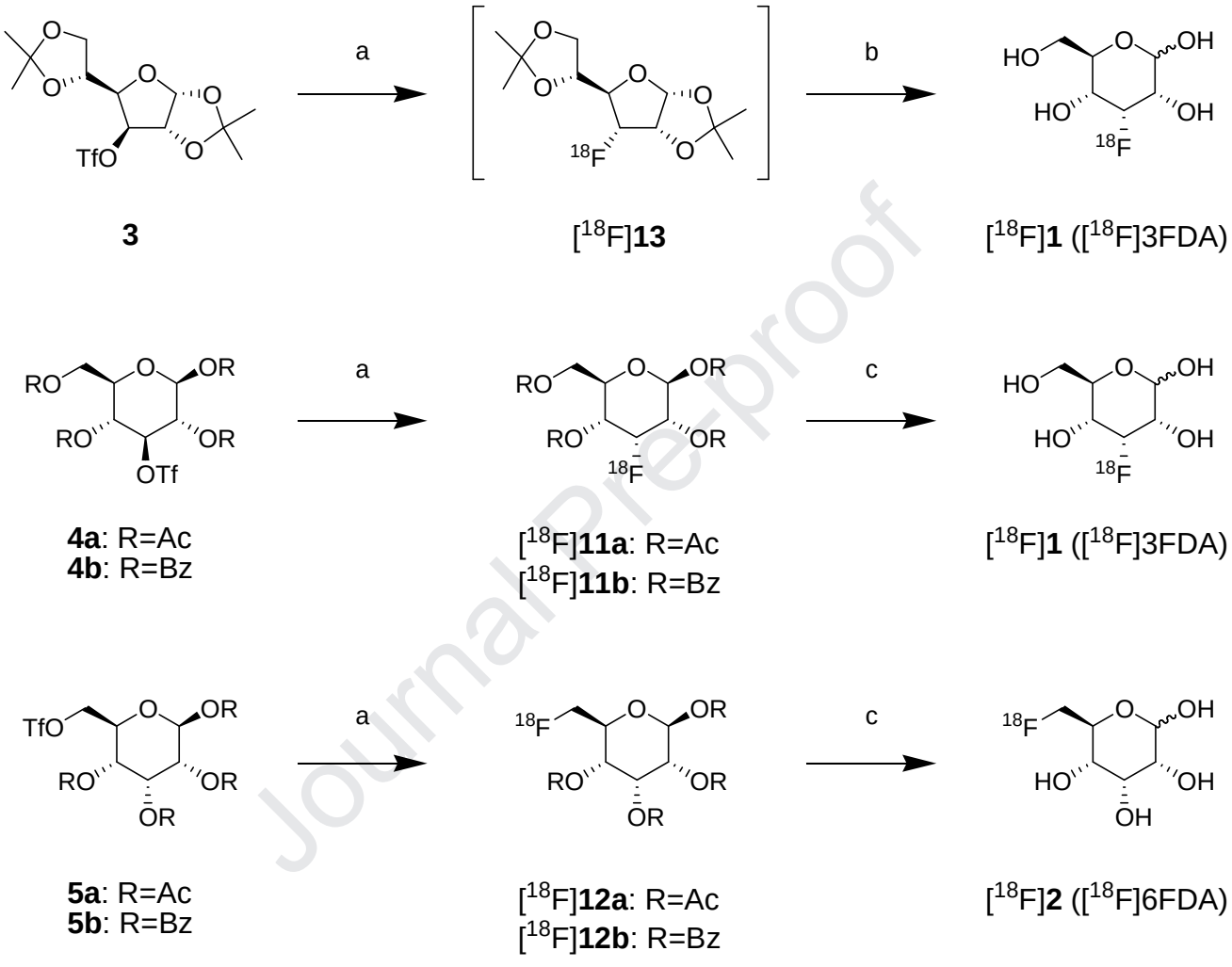
1 (3FDA)

10a: R=Ac
10b: R=Bz

12a: R=Ac
12b: R=Bz

2 (6FDA)

Scheme 4.



Highlights:

- 3-Deoxy-3-[^{18}F]fluoro-D-allose was synthesized for the first time from three precursors.
- 6-Deoxy-6-[^{18}F]fluoro-D-allose was synthesized for the first time from two precursors.
- Pyranose-type precursors protected by acetyl groups provided the highest radiochemical conversions.
- 3-Deoxy-3-[^{18}F]fluoro-D-allose and 6-deoxy-6-[^{18}F]fluoro-D-allose were also synthesized using an automated synthesizer.

Declaration of interests

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☒The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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