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Carbohydrate Research 339 (2004) 1367–1372
Carbohydrate RESEARCH

Note

2β,3β-Difluorosialic acid derivatives structurally modified at the C-4 position: synthesis and biological evaluation as inhibitors of human parainfluenza virus type 1

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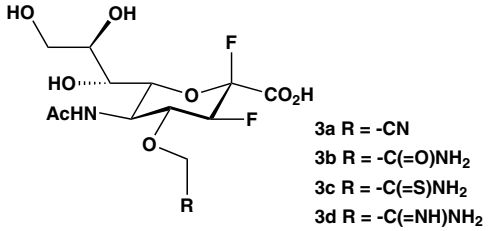
Received 31 October 2003; accepted 18 February 2004

Available online 2 April 2004

Abstract—A series of 4-*O*-substituted 2β,3β-difluorosialic acid derivatives (**3a**–**d**) has been synthesized. A key intermediate was synthesized efficiently by the electrophilic *syn*-addition of fluorine to the double bond of a glycal precursor using molecular fluorine or xenon difluoride in the presence of $BF_3{\cdot}OEt_2$. Among compounds **3a**–**d**, the 4-*O*-thiocarbamoylmethyl derivative **3c** showed the most potent inhibitory activity against sialidase of human parainfluenza virus type 1.

4-*O*-substituted analogues of 2β,3β-difluorosialic acid



Keywords: 2β,3β-difluorosialic acid derivative; Human parainfluenza virus type 1; Sialidase inhibitor

1. Introduction

N-Acetylneuraminic acid (Neu5Ac) and related sialic acids are biologically important compounds widely distributed in living systems in various forms.[1] Influenza sialidase, a key enzyme responsible for propagation of the influenza virus, is a target for drug design. A variety of 2-deoxy-2,3-didehydro-*N*-acetylneuraminic acid (Neu5Ac2en, **1**) analogues have been synthesized as competitive sialidase inhibitors.[2] Among them, 2,3-didehydro-2,4-dideoxy-4-guanidinyl-*N*-acetylneuraminic acid showed the most potent inhibitory activity against sialidase.[3] Human parainfluenza virus type 1 (hPIV-1) is an important pathogen causing upper and lower respiratory disease in infants and young children.[4] However, there are no known potential inhibitors of hPIV-1 infection. There has been considerable interest in the synthesis and properties of fluorinated carbohydrates related to their

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doi:10.1016/j.carres.2004.02.029

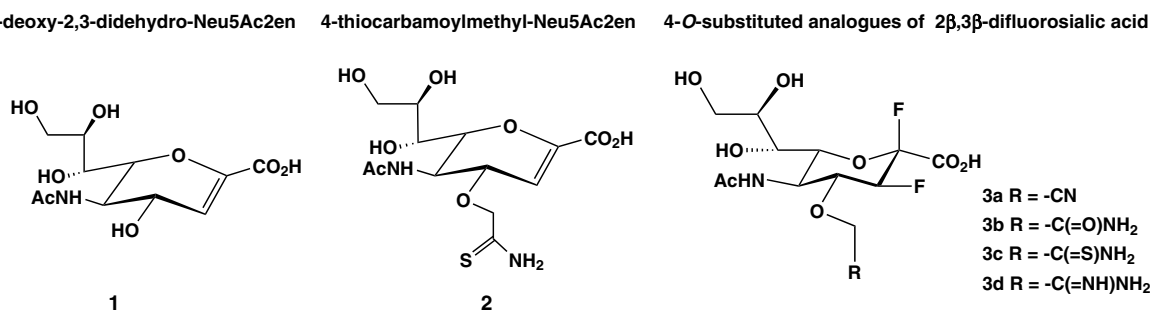
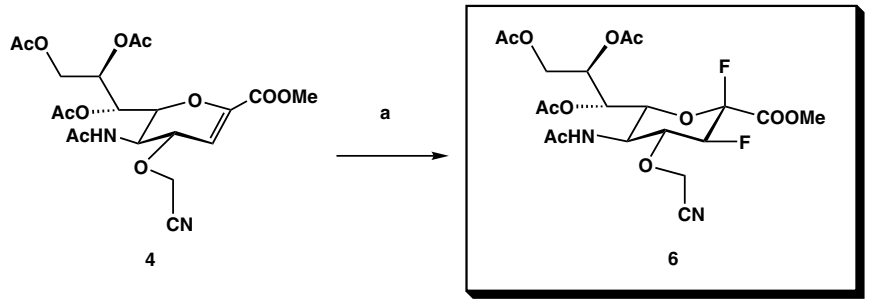


Figure 1. Neu5Ac derivatives.



Scheme 1. (a) 5% F_2/N_2, $CHCl_3$ (85%) or XeF_2, $BF_3{\cdot}OEt_2$, CH_2Cl_2–ether (74%).

potential as inhibitors or modifiers of cell surface glycoconjugates.[5] The synthesis and biological activities of such fluorinated sialic acids as *N*-acetyl-9-deoxy-9-fluoro-neuraminic acid,[6] *N*-acetyl-2-deoxy-2-α- and β-fluoro-neuraminic acids[7] and *N*-acetyl-3-fluoro-neuraminic acid[8] were reported. Recently, we demonstrated that 4-*O*-thiocarbamoylmethyl-Neu5Ac2en (**2**) had strong inhibitory activity toward hPIV-1 sialidase as compared with **1**.[9]

To explore the influence on binding to sialidase from hPIV-1, the hydroxyl group at C-4 in 2β,3β-difluorosialic acid[†] derivatives was changed to a cyanomethyl, carbamoylmethyl, thiocarbamoylmethyl, or amidinomethyl group via the key compound **6**. Here we describe the synthesis of novel 2β,3β-difluorosialic acid analogues **3** and their inhibition of hPIV-1 (Fig. 1).

2. Results and discussion

2.1. Chemical synthesis

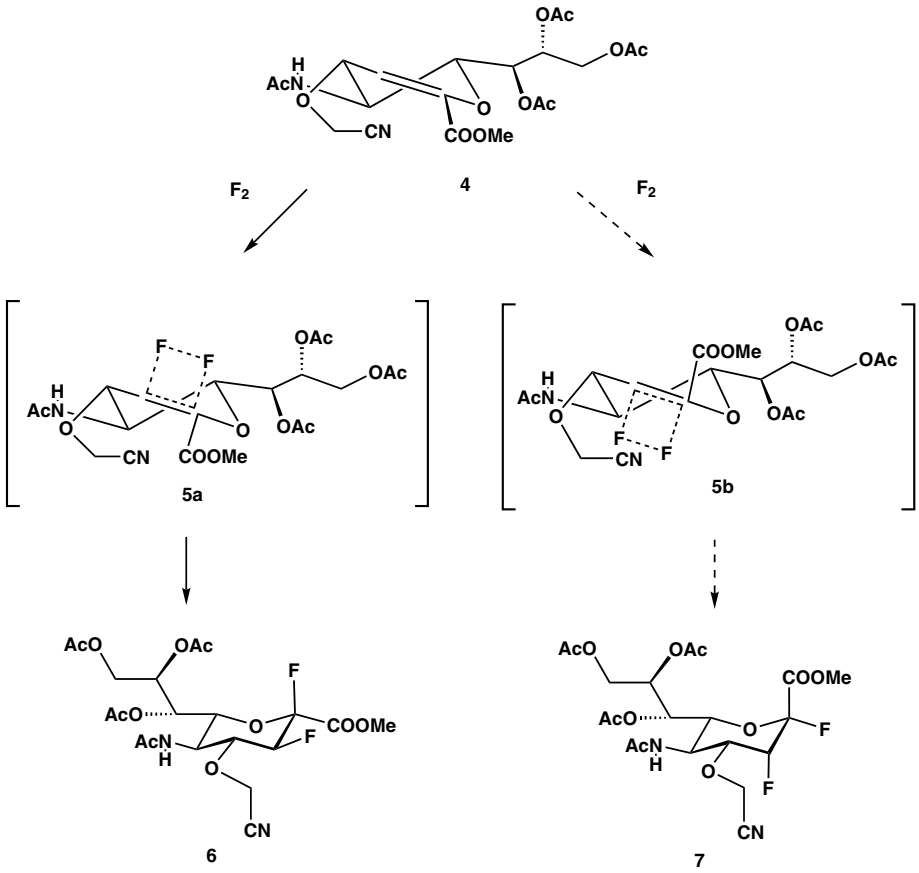
For the synthesis of **6** as a key intermediate in the production of 4-*O*-substituted analogues of 2β,3β-difluorosialic acid, compound **4**[10] was chosen as the starting material (Scheme 1).

Electrophilic addition of fluorine to glycal **4** using dilute F_2 (5% in N_2)[11] in $CHCl_3$ at −60 °C gave stereoselectively in a *syn* manner the 2β,3β-difluorosialic acid derivative **6** {FABMS: m/z 509 $(M+H)^+$} in 85% yield. The stereochemistry of **6** was supported by the ^1H NMR spectrum, which showed the H-3 signal at δ 4.93 as an octet ($J_{H\text{-}3,F3}$ 47.5, $J_{F\text{-}2,H\text{-}3}$ 21.3, $J_{H\text{-}3,H\text{-}4}$ 8.5 Hz). The reaction of xenon difluoride (XeF_2) with the glycal **4** in ether–CH_2Cl_2 using $BF_3{\cdot}OEt_2$ as a catalyst at room temperature[12] also proceeded stereoselectively to give **6** in 74% yield. The stereoselective formation of **6** in the reaction of glycal **4** with F_2 can be rationalized as follows (Scheme 2).

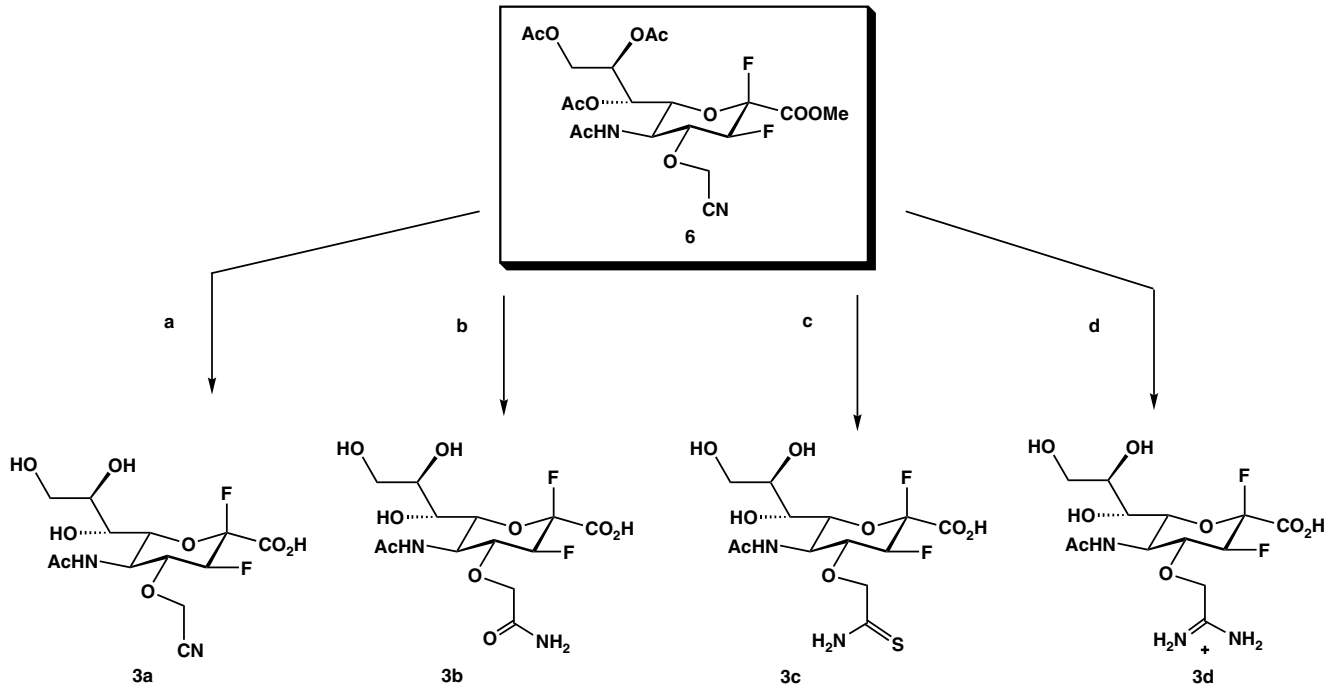
Fluorine would approach in *syn* manner to the double bond of **4** in two directions to give tight ion pairs (**5a** and **5b**) by way of four-centered transition states.[13] The attack of F_2 on the β-face of the double bond of **4** to produce **6** through **5a** would be the more favorable for steric reasons. In addition, the anomeric effect operates to produce the 2β-axial fluoro compound **6** stereoselectively (Scheme 3).

Next, we studied the synthesis of target compounds **3a–d** from **6**. Hydrolysis of **6** with 0.1 M KOH–MeOH afforded the cyanomethyl compound **3a** {FABMS: m/z 369 $(M+H)^+$} in 62% yield, after purification by chromatography on silica gel and then Sephadex LH-20 columns, followed by lyophilization from H_2O suspension. Treatment of **6** with 0.1 M NaOMe–MeOH, with aqueous $NaHCO_3$ and then with 0.1 M KOH–MeOH (saponification) gave the carbamoylmethyl derivative **3b** {FABMS: m/z 409 $(M+Na)^+$} in 47% yield in three steps. Treatment of **6** with AcSH–pyridine[14] followed by hydrolysis gave the thiocarbarmoylmethyl derivative **3c** {FABMS: m/z 403 $(M+H)^+$} in 64% yield in two steps. When compound **6** was

[†] Strictly named as derivatives of 5-amino-3,5-dideoxy-3-fluoro-D-*erythro*-α-L-*gluco*-non-2-ulopyranosylonic acid fluoride, but assigned for convenience the trivial names used here.



Scheme 2. Proposed mechanism for fluorination of glycal 4 with F_2.



Scheme 3. (a) 0.1 M KOH–MeOH (62%); (b) (i) 0.1 M NaOMe–MeOH, (ii) aq $NaHCO_3$, (iii) 0.1 M KOH–MeOH (47% in three steps); (c) (i) AcSH, pyridine, (ii) 0.1 M KOH–MeOH (64% in two steps) (d) (i) 0.1 M NaOMe–MeOH, (ii) anhyd NH_4Cl, (iii) 0.1 M KOH–MeOH (64% in three steps).

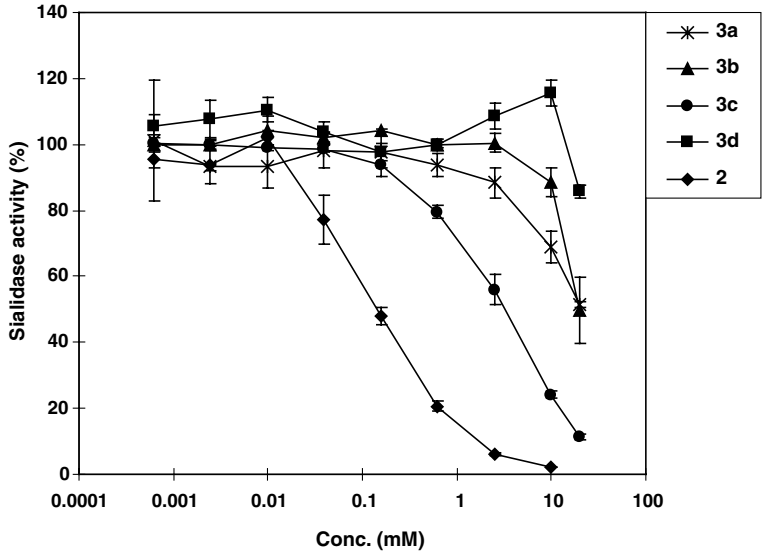


Figure 2. Inhibition of sialidase of hPIV-1 by 2β,3β-difluoro-sialic acids. Values are the mean ± S.D. of three measurements.

successively treated with 0.1 M NaOMe–MeOH, anhydrous NH_4Cl, and then 0.1 M KOH–MeOH, amidinomethyl compound **3d** {FABMS: m/z 386 $(M+H)^+$} was obtained in 64% yield in three steps.

2.2. Biological evaluation

The behavior of compounds **3a**–**d** newly synthesized in this study toward sialidase from hPIV-1 was compared to that of 4-*O*-thiocarbamoylmethyl-Neu5Ac2en (**2**) (Fig. 2 and Table 1).[9b] As may be seen from Table 1, the most effective compound against the sialidase was 4-*O*-thiocarbamoylmethyl-Neu5Ac (**3c**, IC_{50} 0.86 mM), although the degree of inhibition was less than that for **2** (IC_{50} 0.05 mM). The analogues of 2β,3β-difluorosialic acid (**3a** and **3b**) exhibited a decrease in the inhibition of sialidase compared with **3c**, and compound **3d** showed almost no inhibitory effect.

In conclusion, 2β,3β-difluorosialic acid derivatives having a cyanomethyl, carbamoylmethyl, thiocarbamoylmethyl, and amidinomethyl group at the C-4 position were synthesized via the key compound **6**. These compounds had weak inhibitory activity against hPIV-1. From this study, it is suggested that the expression of inhibitory activity of sialic acid derivatives against hPIV requires both the structural feature of a 2,3-double bond and the presence of a 4-*O*-thiocarbamoylmethyl group of sialic acid. The present findings should provide useful information for the development of anti-human parainfluenza virus compounds.

Table 1. Inhibition (IC_{50}) of hPIV-1 sialidase by the synthesized compounds (**3a**–**d**)

Compound	IC_{50} (mM)
3a	6.6
3b	8.2
3c	0.86
3d	n.d.[a]
2	0.05

[a] Not determined.

3. Experimental

All melting points are uncorrected. Optical rotations were measured with a Jasco DIP-140 (Japan) digital polarimeter. IR spectra were recorded on a Jasco IR-810 (Japan) spectrometer. ^1H NMR spectra were recorded with a Jeol JNM-EX 270 (270 MHz) (Japan) instrument. Chemical shifts are expressed in ppm relative to Me_4Si ($\delta = 0$) in $CDCl_3$ and in D_2O referenced to HOD (4.85 ppm) as internal standards. Fast-atom-bombardment (FAB) mass spectra were obtained with a Jeol JMS-700 (Japan) mass spectrometer in the positive-ion mode using an NBA and thioglycerol matrix. High resolution mass spectra (HR-MS) were recorded on a Jeol JMS-700 (Japan) instrument under FAB conditions. Column chromatography was performed on Silica Gel 60 (70–230 mesh, Merck) and Sephadex LH-20 (Pharmacia). All reactions were monitored using TLC (Silica Gel $60F_{254}$, E. Merck, Germany) by charring after spraying 5% H_2SO_4 in MeOH and then heating.

3.1. Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-4-*O*-cyanomethyl-2,5-dideoxy-2β,3β-difluoro-β-D-*erythro*-L-*gluco*-2-nonulopyranosonate (6)

3.1.1. Reaction of glycal 4 with 5% F_2/N_2. To a solution of **4** (58 mg, 0.1 mmol) in $CHCl_3$ (100 mL) was bubbled 5% F_2/N_2 (0.8 mmol, 20 mL/min) at −60 °C. After stirring for 10 min at the same temperature, the mixture was washed with H_2O and the organic layer was dried ($MgSO_4$). After removal of the solvent, the residue was chromatographed on a column of silica gel with a mix-

ture of CH_2Cl_2 and MeOH (10:1, v/v) to give **6** (43 mg, 85%) as an amorphous powder, $[\alpha]_D$ +4.7 (*c* 1.0, $CHCl_3$); ν_{max} ($CHCl_3$): 1219, 1668, 1753 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.04 (s, 3H, AcNH), 2.10, 2.14, 2.18 (3s, 9H, Ac), 3.91 (s, 3H, MeO), 4.03 (dd, 1H, $J_{8,9a}$ 5.5, $J_{9a,9b}$ 12.5 Hz, H-9a), 4.15 (dd, 1H, $J_{8,9b}$ 2.5 Hz, H-9b), 4.40, 4.57 (d, each 1H, J_{gem} 16.5 Hz, $-OCH_2CN$), 4.42 (ddd, 1H, $J_{5,NH} = J_{4,5} = J_{5,6} = 10.5$ Hz, H-5), 4.44 (dd, 1H, $J_{6,7}$ 2 Hz, H-6), 4.93 (ddd, 1H, $J_{H\text{-}3,F3}$ 47.5, $J_{F\text{-}2,H\text{-}3}$ 21.3, $J_{H\text{-}3,H\text{-}4}$ 8.5 Hz, H-3), 5.17 (ddd, 1H, $J_{7,8}$ 7.5 Hz, H-8), 5.31 (dd, 1H, H-4), 5.40 (dd, 1H, H-7), 5.82 (d, 1H, NH); positive ion HR-FABMS (NBA) Anal. Calcd for $C_{20}H_{27}N_2O_{11}F_2$: *m*/*z* 509.1583 $[M+H]^+$. Found: 509.1563.

3.1.2. Reaction of glycal 4 with XeF_2–$BF_3{\cdot}OEt_2$. To solid XeF_2 (24 mg, 0.14 mmol) in a dry flask was added a solution of **4** (61 mg, 0.13 mmol) in a 1:1 solution (2 mL) of dry ether and dry CH_2Cl_2. To the stirred suspension, a solution of BF_3–etherate (4 mg, 0.03 mmol) in dry benzene (1 mL) was added dropwise for 5 min, and the mixture was stirred overnight. After washing with saturated aqueous $NaHCO_3$, the aqueous layer was extracted with ether, and the combined organic layer was washed with brine and dried ($MgSO_4$). Solvents were evaporated in vacuo and the residue was chromatographed on a column of silica gel. Elution with 10:1 CH_2Cl_2–MeOH gave **6** (49 mg, 74%).

3.2. 5-Acetamido-4-*O*-cyanomethyl-2,5-dideoxy-2β,3β-difluoro-β-D-*erythro*-L-*gluco*-2-nonulopyranosonic acid (3a)

Compound **6** (49 mg, 0.096 mmol) was dissolved in a 1:1 solution of 0.1 M KOH in MeOH (4 mL). The mixture was stirred for 15 h at room temperature and neutralized with Amberlite IRC-50 (1.0 g). The precipitates were filtered off through Celite 545 and the filtrate was concentrated. The residue was chromatographed on silica gel using 6:6:1 $CHCl_3$–MeOH–H_2O to give **3a** (22 mg, 62%) as an amorphous powder after lyophilization from H_2O suspension. ^1H NMR (D_2O): δ 2.11 (s, 3H, AcNH), 3.59 (dd, 1H, $J_{7,8}$ 9.5, $J_{6,7}$ 0.7 Hz, H-7), 3.66 (dd, 1H, $J_{8,9a}$ 6.0, $J_{9a,9b}$ 12.0 Hz, H-9a), 3.80 (ddd, 1H, $J_{7,8}$ 9.5, $J_{8,9b}$ 2.5 Hz, H-8), 3.91 (dd, 1H, $J_{5,6}$ 10.0 Hz, H-6), 4.13 (m, 2H, H-4, H-5), 4.27, 4.39 (d, each 1H, J_{gem} 15.5 Hz, $-OCH_2CN$), 4.96 (ddd, 1H, $J_{H\text{-}3,F\text{-}3}$ 39.5, $J_{H\text{-}3,F\text{-}2}$ 21.5, $J_{H\text{-}3,H\text{-}4}$ 9.0 Hz, H-3); positive ion HR-FABMS (thioglycerol-NBA) Anal. Calcd for $C_{13}H_{19}N_2O_8F_2$: *m*/*z* 369.1109 $[M+H]^+$. Found: 369.1091.

3.3. 5-Acetamido-4-*O*-carbamoylmethyl-2,5-dideoxy-2β,3β-difluoro-β-D-*erythro*-L-*gluco*-2-nonulopyranosonic acid (3b)

Compound **6** (30 mg, 0.06 mmol) was dissolved in dry MeOH (3 mL), and 0.1 M NaOMe (3 mL) was added and the mixture at 0 °C under Ar. After being stirred for 12 h at room temperature, saturated aqueous $NaHCO_3$ (1 mL) was added and the mixture was stirred for 5 days at room temperature. The mixture was adjusted to pH 2 with Amberlite 120 (H^+), the resin was filtered through Celite 545, and the filtrate was subjected to gel filtration, and the aqueous solution was evaporated. The residue was dissolved in a solution of 0.1 M KOH in MeOH (1:1) (2 mL) at 0 °C and the mixture was stirred for 12 h at room temperature. The mixture was adjusted to pH 2 with Amberlite 120 (H^+), the resin was filtered through Celite 545, and the resulting aqueous solution was evaporated. The residue was purified by silica gel column chromatography using 6:6:1 $CHCl_3$–MeOH–H_2O to give **3b** (11 mg, 47%) after lyophilization from H_2O suspension. ^1H NMR (D_2O): δ 2.09 (s, 3H, AcNH), 3.57 (dd, 1H, $J_{6,7}$ 0.7, $J_{7,8}$ 9.5 Hz, H-7), 3.65 (dd, 1H, $J_{8,9a}$ 6.0, $J_{9a,9b}$ 12 Hz, H-9a), 3.79 (ddd, 1H, $J_{8,9b}$ 3.0 Hz, H-9b), 4.13–4.36 (m, 3H, H-4, H-5, H-6), 4.46, 4.51 (d, each 1H, J_{gem} 15.7 Hz, $-OCH_2CONH_2$), 4.97 (ddd, 1H, $J_{H\text{-}3,F\text{-}3}$ 48, $J_{H\text{-}3,F2}$ 21.5, $J_{H\text{-}3,H\text{-}4}$ 9.0 Hz, H-3); positive ion HR-FABMS (thioglycerol-NBA) Anal. Calcd for $C_{13}H_{20}N_2O_9F_2Na$: *m*/*z* 409.1035 $[M+Na]^+$. Found: 409.1063.

3.4. 5-Acetamido-2,5-dideoxy-2β,3β-difluoro-4-*O*-thiocarbamoylmethyl-β-D-*erythro*-L-*gluco*-2-nonulopyranosonic acid (3c)

To a solution of **6** (50 mg, 0.1 mmol) in pyridine (1 mL) and CH_2Cl_2 (1 mL) was added thioacetic acid (61 mg, 0.1 mmol) at room temperature under Ar, and the mixture was stirred for 12 h. After removal of the solvent, the residue was chromatographed on silica gel using 2:1 EtOAc–hexane to give the thiocarbamoylmethyl compound (44 mg), which was redissolved in a solution of 0.1 M KOH in MeOH (1:1) (4 mL) at 0 °C and the mixture was stirred for 12 h at room temperature. The mixture was adjusted to pH 2 with Amberlite 120 (H^+), the resin was filtrated through Celite 545, the filtrate was desalted with LH-20 column, and the aqueous solution was evaporated. The residue was purified by silica gel column chromatography using 6:6:1 $CHCl_3$–MeOH–H_2O to give **3c** (21 mg, 64%) as an amorphous powder after lyophilization from H_2O suspension. ^1H NMR (D_2O): δ 2.09 (s, 3H, AcNH), 3.57 (dd, 1H, $J_{6,7}$ 0.7, $J_{7,8}$ 9.5 Hz, H-7), 3.64 (dd, 1H, $J_{8,9a}$ 6.5, $J_{9a,9b}$ 12 Hz, H-9a), 3.79 (dd, 1H, $J_{8,9b}$ 3.0 Hz, H-8), 3.86 (d, 1H, H-9b), 4.12–4.41 (m, 3H, H-4, H-5, H-6), 4.56–4.71 (d, each 1H, J_{gem} 18 Hz, $-OCH_2CSNH_2$), 4.94 (ddd, 1H, $J_{H\text{-}3,F\text{-}3}$ 48.0, $J_{H\text{-}3,F\text{-}2}$ 21.0, $J_{H\text{-}3,H\text{-}4}$ 9.0 Hz, H-3); positive ion HR-FABMS (thioglycerol-NBA) Anal. Calcd for $C_{13}H_{21}N_2O_8SF_2$: *m*/*z* 403.0987 $[M+H]^+$. Found: 403.0967.

3.5. 5-Acetamido-4-*O*-amidinomethyl-2,5-dideoxy-2β,3β-difluoro-β-D-*erythro*-L-*gluco*-2-nonulopyranosonic acid (3d)

Compound **6** (57 mg, 0.1 mmol) was dissolved in dry MeOH (10 mL) and 0.2 M NaOMe (3 mL) was added to

the mixture at 0 °C under Ar. After being stirred for 12 h at room temperature, anhydrous NH_4Cl (37.5 mg, 0.68 mmol) was added to the reaction mixture and the whole was heated at 50 °C for 2 h and evaporated. The residue was dissolved in H_2O, desalted with an LH-20 column, and the aqueous solution was concentrated to dryness. The residue was dissolved in a solution of 0.1 M KOH in MeOH (1:1) (2 mL) at 0 °C and the mixture was stirred for 12 h at room temperature. The mixture was adjusted to pH 2 with Amberlite 120 (H^+), the resin was filtered through Celite 545, the filtrate was subjected to gel filtration, and the aqueous solution was evaporated. The residue was purified by silica gel column chromatography using 6:6:1 $CHCl_3$–MeOH–H_2O to give **3d** (25 mg, 64%) as an amorphous powder after lyophilization from H_2O suspension. ^1H NMR (D_2O): δ 2.23 (s, 3H, AcNH), 3.72 (dd, 1H, $J_{6,7}$ 0.7, $J_{7,8}$ 9.5 Hz, H-7), 3.77 (dd, 1H, $J_{8,9a}$ 6.0, $J_{9a,9b}$ 11.5 Hz, H-9a), 3.88 (ddd, 1H, $J_{7,8}$ 9.5, $J_{8,9b}$ 0.5 Hz, H-8), 3.98 (dd, 1H, H-9b), 4.35–4.50 (m, 3H, H-4, H-5, H-6), 4.80, 4.88 (d, each 1H, J_{gem} 16.0 Hz, $-OCH_2C(NH)NH_2$), 5.10 (ddd, 1H, $J_{H\text{-}3,F\text{-}3}$ 48.0, $J_{H\text{-}3,F\text{-}2}$ 22.0, $J_{H\text{-}3,H\text{-}4}$ 9.5 Hz, H-3); positive ion HR-FABMS (NBA) Anal. Calcd for $C_{13}H_{22}N_3O_8F_2$: m/z 386.1375 $[M+H]^+$. Found: 386.1383.

Acknowledgements

The authors thank Marukin Chuyu Co., Ltd. (Kyoto, Japan) for the generous gift of Neu5Ac. This work was supported in part by a Grant-in-Aid for Scientific Research (No. 13672223) from the Ministry of Education, Science, Sports and Culture of Japan.

References

1. Schauer, R.; Kelm, S.; Reuter, G.; Roggentin, P.; Shaw, L. Biochemistry and role of sialic acids. In *Biology of the Sialic Acids*; Rosenberg, A., Ed.; Plenum: New York, 1995; p 7.
2. Wilson, J. C.; Thomson, R. J.; Dyason, J. C.; Florio, P.; Quelch, K. J.; Abo, S.; von Itzstein, M. *Tetrahedron: Asymmetry* **2000**, *11*, 53–73, and references cited therein.
3. von Itzstein, M.; Wu, W.-Y.; Kok, G. B.; Pegg, M. S.; Dyason, J. C.; Jin, B.; Phan, T. V.; Smythe, M. L.; White, H. F.; Oliver, S. W.; Colman, P. M.; Varghese, J. N.; Ryan, D. M.; Woods, J. M.; Bethell, R. C.; Hotham, V. J.; Cameron, J. M.; Penn, C. R. *Nature* **1993**, *363*, 418–423.
4. (a) Collins, P. L.; Chanock, R. M.; McIntosh, K. Parainfluenza viruses. In *Fields Virology*; Fields, B. N., Knipe, D. M., Howley, P. M., Eds.; Lippincott-Raven: Philadelphia, 1996; pp 1205–1241; (b) Murphy, B. R. Parainfluenza viruses. In *Infectious Diseases*; Gorbach, S. L., Bartlett, J. G., Blacklow, N. R., Eds.; W.B. Saunders Company: Philadelphia, 1998; pp 2125–2131.
5. (a) Tsuchiya, T. *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 91–277; (b) Miethchen, R., Defaye, J., Eds. **2000**, *327*, 1–218.
6. (a) Sharma, M.; Korytnyk, W. *J. Carbohydr. Chem.* **1982/1983**, *1*, 311–315; (b) Sharma, M.; Petrie, C. R., III; Korytnyk, W. *Carbohydr. Res.* **1988**, *175*, 25–34; (c) Liu, J. L.-C.; Shen, G.-J.; Ichikawa, Y.; Rutan, J. F.; Zapata, G.; Vann, W. F.; Wong, C.-H. *J. Am. Chem. Soc.* **1992**, *114*, 3901–3910.
7. Sharma, M.; Eby, R. *Carbohydr. Res.* **1984**, *127*, 201–210.
8. (a) Nakajima, T.; Hori, H.; Ohrui, H.; Meguro, H.; Ido, T. *Agric. Biol. Chem.* **1988**, *52*, 1209–1215; (b) Hagiwara, T.; Kijima-Suda, I.; Ido, T.; Ohrui, H.; Tomita, K. *Carbohydr. Res.* **1994**, *263*, 167–172.
9. (a) Ikeda, K.; Sano, Kimihiko; Ito, M.; Saito, M.; Hidari, K.; Suzuki, T.; Suzuki, Y.; Tanaka, K. *Carbohydr. Res.* **2001**, *330*, 31–41; (b) Suzuki, T.; Ikeda, K.; Koyama, N.; Hosokawa, C.; Kogure, T.; Takahashi, T.; Hidari, K.; Miyamoto, D.; Tanaka, K.; Suzuki, Y. *Glycoconjugate J.* **2001**, *18*, 331–337.
10. Ikeda, K.; Konishi, K.; Sano, K.; Tanaka, K. *Chem. Pharm. Bull.* **2000**, *48*, 163–165.
11. Ido, T.; Wan, C.-N.; Fowler, J. S.; Wolf, A. P. *J. Org. Chem.* **1977**, *42*, 2341–2342.
12. Korytnyk, W.; Valentekovic-Horvath, S.; Petrie, C. R., III. *Tetrahedron* **1982**, *38*, 2547–2550.
13. Satyamurthy, N.; Bida, G. T.; Padgett, H. C.; Barrio, J. R. *J. Carbohydr. Chem.* **1985**, *4*, 489–512.
14. Elosson, M.; Salvador, L. A.; Kihlberg, J. *Tetrahedron* **1997**, *53*, 369–390.