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Synthesis of 4-*O*-[3-(aryl)prop-2-ynyl]-Neu5Ac2en and its 4-*epi*-analogs modified at C-4 by Sonogashira coupling reaction

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Abstract—To explore new inhibitors of the sialidase of human parainfluenza virus type 1 (hPIV-1), a series of novel Neu5Ac2en derivatives were synthesized. Thus, 8,9-*O*-isopropylidene-4-*O*-2-propynyl-Neu5Ac2en methyl ester **8** was subjected to a Sonogashira coupling reaction with a variety of heteroaryl halides to produce a series of 4-*O*-(3-heteroaryl-2-propynyl) compound **9**. Treatment of **9** with 80% acetic acid followed by alkaline hydrolysis afforded deprotected Neu5Ac2en compounds. The 4-*epi*-analogs of this type of Neu5Ac2en were synthesized in a similar manner. Compound **5d** showed the most potent inhibitory activity (IC_{50} 1.2 μM) against hPIV-1 sialidase.

1. Introduction

Sialic acids (Neu5Ac) are characterized as sugar carboxylic acids with nine carbon atoms in a framework of sialic acid, which are often involved in important cell surface communications.[1] Modification of the functional groups on sialic acids may lead to changes in the steric and/or electronic properties of the molecules, which can be used to probe space and charge requirements of sialic acid-recognizing proteins.[2] Among the diverse array of compounds related to the sialic acid family, 5-acetamido-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-enonic acid (Neu5Ac2en) **1** is known as an inhibitor of sialidases from both bacterial and viral sources, occupying an important position in modern chemistry.[3] A variety of Neu5Ac2en analogs have been synthesized as competitive sialidase inhibitors. Among them, zanamivir **2** has been used as anti-influenza virus agent.[4] Human parainfluenza viruses (hPIVs), which are members of the *Paramyxoviridae* family, are important respiratory tract pathogens of infants, children, and young adults.[5] Four different types of hPIVs have been identified, all of which cause a spectrum of illnesses in the upper and lower respiratory tracts of children. At this time there are no effective vaccines or specific therapies to control parainfluenza virus infections.

We demonstrated that 4-*O*-thiocarbamoylmethyl-**3**[6] and the 4-*O*-ethyl-Neu5Ac2en derivative **4**[7] have potential inhibitory activities against the sialidase from hPIV-1. Small polyfunctionalized heterocyclic compounds play important roles in the discovery process.[8] As part of a program aimed at identifying new inhibitors against the hPIV-1 sialidase, we report herein the synthesis of a novel Neu5Ac2en **5** having heterocycles using the Sonogashira coupling reaction[9] as the key reaction and their evaluation as inhibitors of hPIV-1 HN sialidase activity. For further insight into the interaction of the sialidase with substituent at C-4 of Neu5Ac2en derivatives, the synthesis of the 4-*epi*-Neu5Ac2en derivatives **6** modified at C-4 of **5** was also described (Fig. 1).

2. Results and discussion

2.1. Synthesis of 5

Our initial focus was the synthesis of the products **5** using a Sonogashira coupling reaction starting from the 4-*O*-2-

Keywords: 4-*O*-(3-Heteroaryl-2-propynyl)Neu5Ac2en; Sonogashira coupling reaction; Sialidase inhibitor; Human parainfluenza virus type 1.
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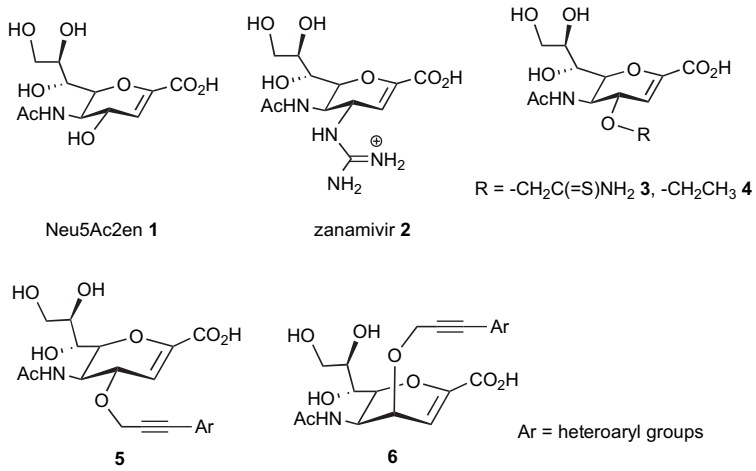
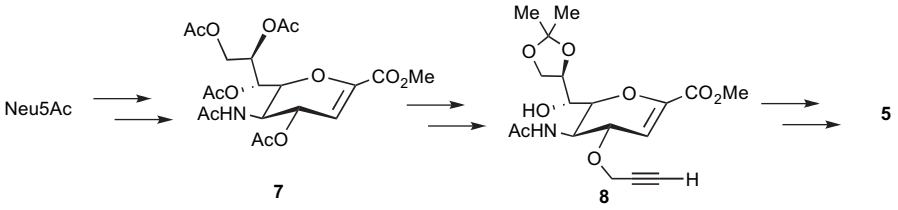


Figure 1.



Scheme 1.

propynyl-Neu5Ac2en derivative **8**,[7] which was prepared from Neu5Ac via **7** in seven steps (Scheme 1). Sonogashira coupling reactions were performed using $PdCl_2(PPh_3)_2$ (2 mol %), CuI (4 mol %), and Et_3N (3.0 equiv) in CH_3CN under the method A conditions in Table 1.[9]

When iodobenzene was used as an aryl halide, the corresponding product **9a** was obtained in 53% yield (Table 1, entry 1). When 2-iodopyridine, 3-iodopyridine, and 2-iodothiophene were used as heteroaryl halides under the same conditions, the products **9b–d** were obtained in 73, 93, and 83% yields, respectively (entries 2–4). However, the coupling reaction of **8** with 3-bromothiophene led to the recovery of **8** under the method A conditions (entry 5). The reaction of **8** with bromothiophene by the combination of $PdCl_2(CH_3CN)_2$ (5 mol %), $Cu(OAc)_2\cdot H_2O$ (5 mol %), PPh_3 (10 mol %), and *i*-Pr_2NH under the method B conditions[10] as an alternative procedure gave a poor yield of **9e** (entry 6). When iodothiophene as a heteroaryl halide was used in method A, **9e** was successfully obtained in 76% yield (entry 7). In sharp contrast with the result of entry 8, the coupling reaction of **8** with 2-bromo-1,3-thiazole under the method B conditions afforded **9f** in 59% yield (entry 9).

For the synthesis of **9g–j** having an additional substitution on the heteroaryl five-membered ring, compound **8** successfully underwent a Sonogashira coupling reaction with heteroaryl halides under the method A conditions to afford **9g–j** in 92, 55, 62, and 49% yields, respectively (Table 2).

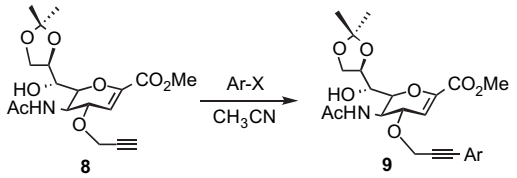
The removal of the isopropylidene group of **9a–j**, except for **9g**, with 80% acetic acid at 80 °C for 1 h gave the triols **10a–f** and **10h–j**, whose methyl ester group was hydrolyzed with 0.1 M KOH/MeOH (1:1) to give the target compounds **5a–f** and **5h–j** (Table 3). In the case of **9g**, decomposition of the starting material occurred with the treatment under acidic conditions. Compounds **5b**,**c** having a pyridyl group were isolated as potassium salts.

2.2. Synthesis of 6

We were interested in comparing the inhibitory activity against the hPIV-1 sialidase between Neu5Ac2en **5** and 4-*epi*-Neu5Ac2en derivatives **6** with an altered configuration of 4-hydroxy group of Neu5Ac2en. As outlined in Scheme 2, the synthesis of compound **13** as the key intermediate began with the known compound **11**.[11] Initially, the methyl ester of Neu5Ac, derived from Neu5Ac, was treated with acetic anhydride in the presence of concentrated sulfuric acid at 80 °C for 3 h to give in 96% yield an inseparable mixture of **11α** and **11β** with an α/β ratio of 1:8, which was employed in the subsequent step without further purification. Thus, Zemplen O-deacetylation of **11** with 0.1 M sodium methoxide in MeOH followed by subsequent protection by 2,2-dimethoxypropane and Amberlite 120 (H^+) in DMF afforded the 8,9-*O*-isopropylidene compound **12** in 58% yield as a single diastereomer after purification by silica gel column chromatography. The $J_{4,5}$ and $J_{3,4}$ values (4.1 and 5.7 Hz, respectively) of an ^1H NMR spectroscopic analysis of **12** demonstrated the H-4,5 and H-3,4 relationships. Installation of a propargyl group at the 4-hydroxyl group of **12** using sodium hydride (2.0 equiv) and propargyl bromide (1.3 equiv) in DMF gave the key intermediate **13** in 39% yield.

The synthesis of **14a–c** was performed using a Sonogashira coupling reaction in a manner similar to the preparation of **9**.

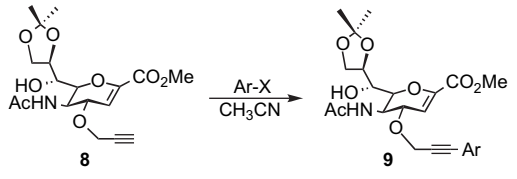
Table 1. Synthesis of **9a–f** by the Sonogashira coupling reaction

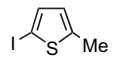
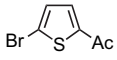
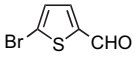
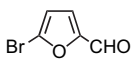


Entry	Ar–X	Condition[a]	Product	Yield (%)
1		A	**9a**	53
2		A	**9b**	73
3		A	**9c**	93
4		A	**9d**	83
5		A	N.R.[b]	
6		B	**9e**	5
7		A	**9e**	76
8		A	N.R.[b]	
9		B	**9f**	59

[a] Method A: RX (1.1 equiv), $Pd(PPh_3)_2Cl_2$ (2 mol %), CuI (4 mol %), Et_3N (3 equiv). Method B: RX (1.1 equiv), $PdCl_2(CH_3CN)_2$ (5 mol %), $Cu(OAc)_2 \cdot H_2O$ (5 mol %), PPh_3 (10 mol %), *i*-Pr_2NH (2 mL).
[b] N.R.: no reaction.

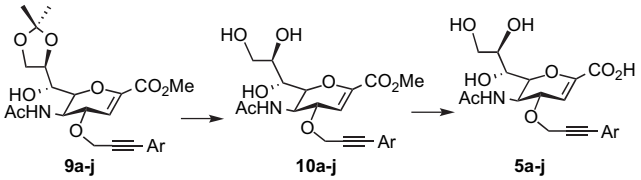
Table 2. Synthesis of **9g–j** by the Sonogashira coupling reaction

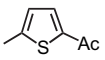
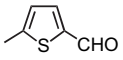
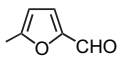


Entry	Ar–X	Condition[a]	Product	Yield (%)
1		A	**9g**	92
2		A	**9h**	55
3		A	**9i**	62
4		A	**9j**	49

[a] Method A: RX (1.1 equiv), $Pd(PPh_3)_2Cl_2$ (2 mol %), CuI (4 mol %), Et_3N (3 equiv).

Table 3. Synthesis of **5a–j**



Entry	Ar	Yield of **10** (%)	Yield of **5** (%)
1		**10a** (82)	**5a** (83)
2		**10b** (91)	**5b** (quant.)[a]
3		**10c** (83)	**5c** (quant.)[a]
4		**10d** (98)	**5d** (66)
5		**10e** (89)	**5e** (76)
6		**10f** (83)	**5f** (54)
7		**10h** (95)	**5h** (98)
8		**10i** (80)	**5i** (96)
9		**10j** (89)	**5j** (46)

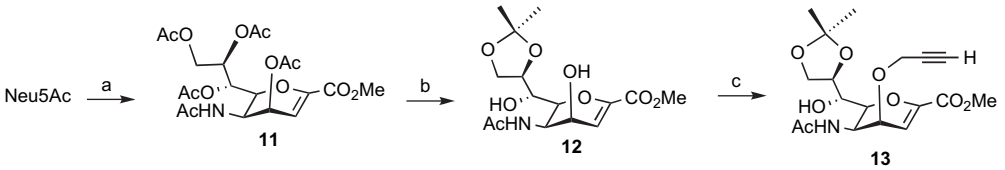
[a] The products were isolated as potassium salt.

The results are summarized in Table 4. When 2-iodothiophene and 3-iodothiophene were used as heteroaryl halides under $Pd(PPh_3)_2Cl_2$ (2 mol %), CuI (4 mol %), and Et_3N (3 equiv) in CH_3CN under the method A conditions, the corresponding products **14a**,**b** were obtained in 64 and 73% yield, respectively (Table 4, entries 1 and 2). In the case of using 2-bromo-1,3-thiazole as a heteroaryl halide, the combination of $PdCl_2(CH_3CN)_2$ (5 mol %), $Cu(OAc)_2 \cdot H_2O$ (5 mol %), PPh_3 (10 mol %), and *i*-Pr_2NH under the method B conditions gave **14c** in 48% yield (entry 3).

The deprotection of the isopropylidene group of **14a–c** with 80% acetic acid at 80 °C for 1 h afforded the triols **15a–c**, whose methyl ester group was hydrolyzed with 0.1 M KOH/MeOH (1:1) to give the target compounds **6a–c** (Table 5).

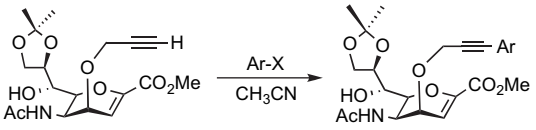
3. Biological evaluation

The behavior of synthesized compounds **5** and **6** toward hPIV-1 sialidase was assayed by a fluorometric assay using 4-methylumbelliferyl *N*-acetyl-α-neuraminic acid as our previously reported method.[6b] As may be seen in Table 6, interestingly, 2-thienyl-Neu5Ac2en **5d** exhibited the most potent inhibitory activity (IC_{50} 1.2 μM). Compounds **5e** and **5f** had almost the same inhibitory effects. In the previous study,[6b] 4-guanidino-Neu5Ac2en **2** had much lower inhibitory activity toward hPIV-1 sialidase than that of **1** (IC_{50}



Scheme 2. (a) (i) MeOH, Amberlite IR120 (H^+), rt, 15 h, quant.; (ii) Ac_2O, H_2SO_4, 80 °C, 3 h, 96% (**11α/11β**=1:8). (b) (i) NaOMe, MeOH, 0 °C, 1 h, quant.; (ii) 2,2-dimethoxypropane, DMF, Amberlite IR120 (H^+), rt, 12 h, 58%. (c) Propargyl bromide (1.3 equiv), NaH (2.0 equiv), DMF, 0 °C, 1 h, 39%.

Table 4. Synthesis of **14a–c** by the Sonogashira coupling reaction



Entry	Ar–X	Condition[a]	Product	Yield (%)
1		A	**14a**	64
2		A	**14b**	73
3		B	**14c**	48

[a] Method A: RX (1.1 equiv), $Pd(PPh_3)_2Cl_2$ (2 mol %), CuI (4 mol %), Et_3N (3 equiv). Method B: RX (1.1 equiv), $PdCl_2(CH_3CN)_2$ (5 mol %), $Cu(OAc)_2 \cdot H_2O$ (5 mol %), PPh_3 (10 mol %), *i*-Pr_2NH (2 mL).

30 μM). Compounds **6a–c** as 4-*epi*-analogs of **5** exhibited decreased sialidase inhibition compared with **5d**, and compound **5b** was practically inactive against sialidase.

4. Conclusion

We have synthesized the novel Neu5Ac2en compounds **5** and **6** to develop hPIV-1 sialidase inhibitors. Sonogashira coupling reactions of **8** and **14** with aryl or heteroaryl halides and subsequent deprotection provided the new Neu5Ac2en analogs **5** and **6**, respectively. The 2-thienyl-Neu5Ac2en **5d** showed the most potent inhibitory activity (IC_{50} 1.2 μM) against hPIV-1 sialidase.

Table 6. Inhibitory activities of **5a–f**

Entry	Compound	IC_{50} (μM)[a]
1	**5a**	15
2	**5b**	88
3	**5c**	14
4	**5d**	1.2
5	**5e**	2.5
6	**5f**	3.1

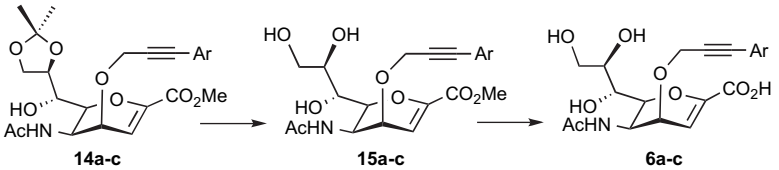
[a] Inhibitory activities were determined by the method according to Ref. 6b.

5. Experimental

5.1. General

All melting points are uncorrected. Optical rotations were measured with a JASCO P-1030 (Japan) digital polarimeter. IR spectra were recorded on a SHIMADZU IRPrestige-21 (Japan) spectrometer. ^1H NMR spectra were recorded with a JEOL ECA-500 (500 MHz) (Japan). ^{13}C NMR spectra were recorded with a JEOL ECA-500 (126 MHz) (Japan). Chemical shifts are expressed in parts per million relative to Me_4Si (δ=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 or thioglycerol matrix. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-700 (Japan) under FAB conditions. Column chromatography was

Table 5. Synthesis of **6a–c**



Entry	Ar	Yield of **15** (%)	Yield of **6** (%)
1		**15a** (68)	**6a** (60)
2		**15b** (79)	**6b** (99)
3		**15c** (53)	**6c** (94)

performed on Silica Gel 60 (70–230 mesh, Merck). Desalting was carried out with an ASAHI CHEMICAL Micro Acylizer G1. 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.

5.2. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(phenyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9a)

To a solution of **8** (80 mg, 0.21 mmol),[7] $PdCl_2(PPh_3)_2$ (2 mg, 0.004 mmol), and CuI (2 mg, 0.008 mmol) in CH_3CN (2 mL) were added Et_3N (64 mg, 0.63 mmol) and iodobenzene (47 mg, 0.23 mmol) under Ar. The mixture was stirred at room temperature for 6 h, and then concentrated in vacuo. The residue was purified by column chromatography using $CHCl_3$/MeOH (50:1 to 40:1, v/v) to give **6a** (51 mg, 53%) as an amorphous material. $[\alpha]_D^{24}$ +38 (*c* 0.80, $CHCl_3$). IR (neat) 3298, 1730, 1633 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.35, 1.39 (s, each 3H, Me_2C), 2.02 (s, 3H, Ac), 3.57 (dd, 1H, $J_{7,OH}$=4.6 Hz, $J_{7,8}$=7.5 Hz, H-7), 3.79 (s, 3H, OMe), 4.06–4.09 (m, 2H, H-6 and H-9a), 4.14–4.21 (m, 2H, H-5 and H-9b), 4.35–4.38 (m, 1H, H-8), 4.48 (dd, 1H, $J_{3,4}$=2.3 Hz, $J_{4,5}$=9.8 Hz, H-4), 4.46, 4.54 (d, each 1H, J_{gem}=16.0 Hz, $OCH_2C{\equiv}$), 4.63 (d, 1H, OH), 5.68 (d, 1H, $J_{5,NH}$=5.2 Hz, NH), 6.10 (d, 1H, H-3), 7.32–7.37 (m, 3H, Ar), 7.45–7.47 (m, 2H, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.3, 25.3, 27.1, 48.7, 52.5, 56.9, 67.4, 70.5, 72.7, 74.3, 77.6, 84.7, 87.3, 107.3, 109.3, 122.0, 128.6, 129.1, 131.9, 146.0, 162.3, 172.7. Positive ion FABMS (NBA): *m*/*z* 460 $[M+H]^+$, 482 $[M+Na]^+$. FAB HRMS calcd for $C_{24}H_{30}NO_8$ 460.1971, found 460.1992.

5.3. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(2-pyridyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9b)

The reaction was carried out using **8** (80 mg, 0.21 mmol) and 2-iodopyridine (47 mg, 0.23 mmol) in a manner similar to the preparation of **9a**, to give **9b** (70 mg, 73%) as an amorphous material. IR (KBr) 3257, 1735, 1637 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.36, 1.41 (s, each 3H, Me_2C), 2.04 (s, 3H, Ac), 3.56–3.59 (m, 1H, H-7), 3.78 (s, 3H, OMe), 4.03 (d, 1H, J_{gem}=9.8 Hz, H-9a), 4.10–4.23 (m, 3H, H-5, H-6, and H-9b), 4.36–4.40 (m, 1H, H-8), 4.45, 4.56 (d, each 1H, J_{gem}=17.2 Hz, $OCH_2C{\equiv}$), 4.64 (dd, $J_{3,4}$=2.3 Hz, $J_{4,5}$=8.6 Hz, H-4), 4.80 (d, 1H, $J_{7,OH}$=4.0 Hz, OH), 6.04 (d, 1H, H-3), 6.79 (br, 1H, NH), 7.29 (m, 1H, Ar), 7.44 (d, 1H, *J*=7.5 Hz, Ar), 7.71 (dt, 1H, *J*=1.7, 7.5 Hz, Ar), 8.53 (d, 1H, *J*=4.6 Hz, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 22.8, 25.2, 26.9, 48.5, 52.3, 56.4, 67.1, 69.7, 72.3, 74.3, 77.7, 85.6, 86.3, 107.3, 109.0, 123.6, 126.8, 136.7, 142.0, 145.6, 149.6, 162.3, 173.3. Positive ion FABMS (NBA): *m*/*z* 461 $[M+H]^+$, 483 $[M+Na]^+$. FAB HRMS calcd for $C_{23}H_{29}N_2O_8$ 461.1924, found 461.1883.

5.4. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(3-pyridyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9c)

The reaction was carried out using **8** (117 mg, 0.31 mmol) and 3-iodopyridine (70 mg, 0.34 mmol) in a manner similar to the preparation of **9a**, to give **9c** (130 mg, 93%) as an amorphous material. $[\alpha]_D^{24}$ +28 (*c* 0.66, $CHCl_3$). IR (neat) 3298, 1729, 1632 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.35, 1.39 (s, each 3H, Me_2C), 2.04 (s, 3H, Ac), 3.57 (dd, 1H, $J_{7,OH}$=4.0 Hz, $J_{7,8}$=8.0 Hz, H-7), 3.79 (s, 3H, OMe), 4.06–4.17 (m, 3H, H-6, H-9a, and H-9b), 4.21–4.26 (m, 1H, H-5), 4.33–4.37 (m, 1H, H-8), 4.46–4.55 (m, 4H, H-4, OH, and $OCH_2C{\equiv}$), 5.74 (br, 1H, NH), 6.11 (d, 1H, $J_{3,4}$=2.9 Hz, H-3), 7.28 (dd, 1H, *J*=4.6, 7.5 Hz, Ar), 7.76 (dd, 1H, *J*=1.7, 7.5 Hz, Ar), 8.57 (br, 1H, Ar), 8.69 (br, 1H, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.4, 25.3, 27.1, 48.5, 52.6, 56.3, 67.3, 70.5, 72.9, 74.3, 77.5, 83.7, 88.2, 106.9, 109.3, 119.5, 123.2, 139.0, 146.2, 149.3, 152.5, 162.3, 172.4. Positive ion FABMS (NBA): *m*/*z* 461 $[M+H]^+$, 483 $[M+Na]^+$. FABHRMS calcd for $C_{23}H_{29}N_2O_8$ 461.1924, found 461.1880.

5.5. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(2-thienyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9d)

The reaction was carried out using **8** (139 mg, 0.36 mmol) and 2-iodothiophene (84 mg, 0.40 mmol) in a manner similar to the preparation of **9a**, to give **9d** (140 mg, 83%) as an amorphous material. $[\alpha]_D^{25}$ +27 (*c* 0.16, $CHCl_3$). IR (neat) 3290, 1728, 1674 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.35, 1.39 (s, each 3H, Me_2C), 2.04 (s, 3H, Ac), 3.55 (dd, 1H, $J_{7,OH}$=4.6 Hz, $J_{7,8}$=8.0 Hz, H-7), 3.79 (s, 3H, OMe), 4.06–4.09 (m, 2H, H-6 and H-9a), 4.14–4.20 (m, 2H, H-5 and H-9b), 4.34–4.38 (m, 1H, H-8), 4.46, 4.56 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C{\equiv}$), 4.46 (dd, 1H, $J_{3,4}$=2.9 Hz, $J_{4,5}$=8.6 Hz, H-4), 4.63 (d, 1H, OH), 5.64 (d, 1H, $J_{5,NH}$=6.9 Hz, NH), 6.07 (d, 1H, H-3), 7.00 (dd, 1H, *J*=3.5, 5.2 Hz, Ar), 7.27 (dd, 1H, *J*=1.2, 3.5 Hz, Ar), 7.31 (dd, 1H, *J*=1.2, 3.5 Hz, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.3, 25.3, 27.1, 48.7, 52.5, 56.9, 67.4, 70.4, 72.8, 74.3, 77.7, 80.6, 88.8, 107.1, 109.3, 121.7, 127.3, 128.2, 133.2, 146.0, 162.3, 172.8. Positive ion FABMS (NBA): *m*/*z* 466 $[M+H]^+$, 488 $[M+Na]^+$. FABHRMS calcd for $C_{22}H_{28}NO_8S$ 466.1536, found 466.1544.

5.6. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(3-thienyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9e)

The reaction was carried out using **8** (147 mg, 0.38 mmol) and 3-iodothiophene (88 mg, 0.42 mmol) in a manner similar to the preparation of **9a**, to give **9e** (136 mg, 76%) as an amorphous material. $[\alpha]_D^{24}$ +41 (*c* 0.32, $CHCl_3$). IR (neat) 3257, 1728, 1637 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.35, 1.39 (s, each 3H, Me_2C), 2.02 (s, 3H, Ac), 3.55 (dd, 1H, $J_{7,OH}$=4.6 Hz, $J_{7,8}$=8.0 Hz, H-7), 3.79 (s, 3H, OMe), 4.06–4.09 (m, 2H, H-6 and H-9a), 4.14–4.20 (m, 2H, H-5 and H-9b), 4.34–4.38 (m, 1H, H-8), 4.47 (dd, 1H, $J_{3,4}$=2.3 Hz, $J_{4,5}$=8.0 Hz, H-4), 4.43, 4.51 (d, each 1H, J_{gem}=16.1 Hz, $OCH_2C{\equiv}$), 4.63 (d, 1H, OH), 5.71 (d, 1H, $J_{5,NH}$=6.9 Hz, NH), 6.09 (d, 1H, H-3), 7.13 (d, 1H, *J*=5.2 Hz, Ar), 7.30 (dd, 1H, *J*=2.9, 5.2 Hz, Ar), 7.52 (d, 1H, *J*=2.9 Hz, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.3, 25.3, 27.1, 48.7, 52.5, 56.8, 67.4, 70.5, 72.7, 74.3, 77.6, 82.5, 84.5, 107.3, 109.3, 121.0, 125.9, 129.9, 130.0, 146.0, 162.3, 172.7. Positive ion FABMS (NBA): *m*/*z* 466 $[M+H]^+$, 488 $[M+Na]^+$. FABHRMS calcd for $C_{22}H_{28}NO_8S$ 466.1536, found 466.1482.

5.7. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(2-thiazolyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9f)

To a mixture of **8** (130 mg, 0.34 mmol), $PdCl_2(CH_3CN)_2$ (4 mg, 0.017 mmol), $Cu(OAc)_2$ (3 mg, 0.017 mmol), and PPh_3 (5 mg, 0.034 mmol) in CH_3CN (2 mL) were added *i*-Pr_2NEt (2 mL) and 2-bromo-1,3-thiazole (61 mg, 0.37 mmol) under Ar. The resulting mixture was stirred at 45 °C for 6 h, and then concentrated in vacuo. The residue was purified by column chromatography on silica gel using $CHCl_3$/MeOH (50:1 to 40:1, v/v) to give **9f** (95 mg, 59%) as an amorphous material. IR (neat) 3298, 1734, 1637 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.35, 1.39 (s, each 3H, Me_2C), 2.05 (s, 3H, Ac), 3.55 (dd, 1H, $J_{7,OH}$=4.6 Hz, $J_{7,8}$=8.0 Hz, H-7), 3.78 (s, 3H, OMe), 4.03–4.12 (m, 2H, H-6 and H-9a), 4.15–4.23 (m, 2H, H-5 and H-9b), 4.34–4.38 (m, 1H, H-8), 4.55 (dd, 1H, $J_{3,4}$=2.3 Hz, $J_{4,5}$=8.6 Hz, H-4), 4.48, 4.58 (d, each 1H, J_{gem}=17.2 Hz, $OCH_2C{\equiv}$), 4.67 (d, 1H, OH), 6.04 (d, 1H, H-3), 6.38 (d, 1H, $J_{5,NH}$=7.4 Hz, NH), 7.41 (d, 1H, J=3.5 Hz, Ar), 7.83 (d, 1H, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.1, 25.3, 27.1, 48.6, 52.5, 56.4, 67.3, 70.1, 72.9, 74.3, 77.7, 80.1, 90.2, 106.9, 109.2, 121.5, 143.6, 146.1, 147.7, 162.4, 173.1. Positive ion FABMS (NBA): *m*/*z* 467 $[M+H]^+$. FABHRMS calcd for $C_{21}H_{27}N_2O_8S$ 467.1488, found 467.1500.

5.8. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(5′-methyl-2′-thienyl)-prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9g)

The reaction was carried out using **8** (144 mg, 0.38 mmol) and 2-iodo-5-methylthiophene (92 mg, 0.41 mmol) in a manner similar to the preparation of **9a**, to give **9g** (166 mg, 92%). $[\alpha]_D^{25}$ +49 (*c* 0.19, $CHCl_3$). IR (neat) 3196, 1732, 1653 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.34, 1.38 (s, each 3H, Me_2C), 2.02 (s, 3H, Ac), 2.45 (s, 3H, CMe), 3.53 (dd, 1H, $J_{7,8}$=7.5 Hz, $J_{7,OH}$=4.0 Hz, H-7), 3.76 (s, 3H, OMe), 4.02–4.07 (m, 2H, H-6 and H-9a), 4.11–4.06 (m, 2H, H-5 and H-9b), 4.34 (m, 1H, H-8), 4.42, 4.52 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C{\equiv}$), 4.44 (dd, 1H, $J_{3,4}$=2.3 Hz, $J_{4,5}$=8.6 Hz, H-4), 4.69 (d, 1H, OH), 5.82 (d, 1H, $J_{5,NH}$=6.9 Hz, NH), 6.05 (d, 1H, H-3), 6.63 (1H, J=2.9 Hz, Ar), 7.05 (d, 1H, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 15.5, 23.3, 25.3, 27.0, 48.6, 52.4, 57.0, 67.3, 70.2, 72.7, 74.2, 77.6, 81.0, 88.1, 107.4, 109.2, 119.1, 125.6, 133.5, 143.1, 145.8, 162.3, 172.9. Positive ion FABMS (NBA): *m*/*z* 480 $[M+H]^+$. FABHRMS calcd for $C_{23}H_{30}NO_8S$ 480.1515, found 480.1590.

5.9. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(5′-acetyl-2′-thienyl)-prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9h)

The reaction was carried out using **8** (128 mg, 0.33 mmol) and 2-acetyl-5-bromothiophene (74 mg, 0.36 mmol) in a manner similar to the preparation of **9a**, to give **9h** (93 mg, 55%). $[\alpha]_D^{23}$ +7.6 (*c* 0.21, $CHCl_3$). IR (neat) 3288, 1737, 1633 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.36, 1.40 (s, each 3H, Me_2C), 2.06 (s, 3H, NAc), 2.55 (s, 3H, CAc), 3.56 (dd, 1H, $J_{7,8}$=11.5 Hz, $J_{7,OH}$=4.6 Hz, H-7), 3.80 (s, 3H, OMe), 4.07–4.12 (m, 2H, H-6 and H-9a), 4.15–4.24 (m, 2H, H-5 and H-9b), 4.36 (ddd, 1H, $J_{8,9a}$=5.2 Hz, $J_{8,9b}$=8.0 Hz, H-8), 4.45 (dd, 1H, $J_{3,4}$=2.9 Hz, $J_{4,5}$=8.6 Hz, H-4), 4.46 (dd, 1H, OH), 4.48, 4.55 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C{\equiv}$), 5.57 (d, 1H, $J_{5,NH}$=6.9 Hz, NH), 6.08 (d, 1H, H-3), 7.23 (1H, J=4.0 Hz, Ar), 7.55 (d, 1H, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.2, 25.1, 26.7, 26.9, 48.2, 52.4, 56.2, 67.1, 70.2, 72.9, 74.0, 79.6, 91.9, 106.6, 109.1, 129.4, 131.9, 133.5, 145.2, 146.1, 162.0, 172.4, 190.0. Positive ion FABMS (NBA): *m*/*z* 508 $[M+H]^+$. FABHRMS calcd for $C_{23}H_{30}NO_9S$ 508.1641, found 508.1592.

5.10. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(5′-formyl-2′-thienyl)-prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9i)

The reaction was carried out using **8** (168 mg, 0.44 mmol) and 5-bromo-2-thiophenecarboxaldehyde (93 mg, 0.48 mmol) in a manner similar to the preparation of **9a**, to give **9i** (135 mg, 62%). IR (neat) 3273, 1732, 1653 cm^{-1}. $[\alpha]_D^{23}$ +43 (*c* 0.75, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 1.36, 1.39 (s, each 3H, Me_2C), 2.06 (s, 3H, NAc), 3.56 (d, 1H, $J_{7,8}$=13.8 Hz, H-7), 3.80 (s, 3H, OMe), 4.10–4.17 (m, 3H, H-6, H-9a, and H-9b), 4.23 (m, 1H, H-5), 4.35 (ddd, 1H, $J_{8,9a}$=5.7 Hz, $J_{8,9b}$=6.2 Hz, H-8), 4.45 (br, 1H, OH), 4.45 (dd, 1H, $J_{3,4}$=2.3 Hz, $J_{4,5}$=8.0 Hz, H-4), 4.48, 4.55 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C{\equiv}$), 5.59 (d, 1H, $J_{5,NH}$=6.9 Hz, NH), 6.08 (d, 1H, H-3), 7.32 (d, 1H, J=3.5 Hz, Ar), 7.65 (d, 1H, Ar), 9.87 (s, 1H, CHO). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.3, 25.1, 27.0, 48.2, 52.5, 56.1, 67.2, 70.3, 73.1, 74.1, 77.4, 79.4, 93.1, 106.6, 109.2, 130.9, 133.5, 135.7, 144.4, 146.2, 162.1, 172.4, 182.4. Positive ion FABMS (NBA): *m*/*z* 494 $[M+H]^+$, 516 $[M+Na]^+$. FABHRMS calcd for $C_{23}H_{28}NO_9S$ 494.1485, found 494.1483.

5.11. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(5′-formyl-2′-furyl)-prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (9j)

The reaction was carried out using **8** (137 mg, 0.36 mmol) and 5-bromo-2-furaldehyde (70 mg, 0.40 mmol) in a manner similar to the preparation of **9a**, to give **9j** (84 mg, 49%). $[\alpha]_D^{24}$ +27 (*c* 0.20, $CHCl_3$). IR (neat) 3290, 1728, 1634 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.30, 1.33 (s, each 3H, Me_2C), 2.04 (s, 3H, NAc), 3.54 (dd, 1H, $J_{7,8}$=11.5 Hz, $J_{7,OH}$=4.6 Hz, H-7), 4.04–4.12 (m, 3H, H-6, H-9a, and H-9b), 4.17 (m, 1H, H-5), 4.29 (ddd, 1H, $J_{8,9a}$=5.2 Hz, $J_{8,9b}$=6.3 Hz, H-8), 4.51 (dd, 1H, $J_{3,4}$=2.3 Hz, $J_{4,5}$=8.6 Hz, H-4), 4.44, 4.51 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C{\equiv}$), 4.62 (d, 1H, OH), 6.04 (d, 1H, H-3), 6.54 (d, 1H, $J_{5,NH}$=8.0 Hz, NH), 6.74 (d, 1H, J=3.5 Hz, Ar), 7.21 (d, 1H, Ar), 9.53 (s, 1H, CHO). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.0, 25.1, 26.8, 48.2, 52.3, 55.9, 66.9, 69.7, 73.1, 74.2, 75.8, 77.4, 92.7, 107.0, 108.9, 117.8, 122.0, 140.6, 145.8, 152.2, 162.2, 172.9, 177.1. Positive ion FABMS (NBA): *m*/*z* 478 $[M+H]^+$, 500 $[M+Na]^+$. FABHRMS calcd for $C_{23}H_{28}NO_{10}$ 478.1713, found 478.1706.

5.12. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(phenyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (10a)

A solution of **9a** (51 mg, 0.11 mmol) in 80% AcOH (3 mL) was stirred at 80 °C for 1 h, and then evaporated. The residue was purified by column chromatography on silica gel using $CHCl_3$/MeOH (9:1 to 6:1, v/v) to give **10a** (38 mg, 82%) as

an amorphous material. $[\alpha]_D^{25}$ +89 (*c* 0.18, CH_3OH). IR (neat) 3263, 1718, 1635 cm^{-1}. ^1H NMR (500 MHz, D_2O): δ 1.83 (s, 1H, Ac), 3.48–3.52 (m, 2H, H-7 and H-9a), 3.66 (s, 3H, OMe), 3.72 (d, 1H, J_{gem}=12.1 Hz, H-9b), 3.77 (m, 1H, H-8), 4.09 (dd, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.21 (d, 1H, H-6), 4.40 (d, each 1H, J_{gem}=16.1 Hz, $OCH_2C\equiv$), 4.53 (d, 1H, H-4), 6.12 (s, 1H, H-3), 7.26–7.30 (m, 3H, Ar), 7.37–7.39 (m, 2H, Ar). Positive ion FABMS (NBA): *m/z* 420 $[M+H]^+$, 442 $[M+Na]^+$. FABHRMS calcd for $C_{21}H_{26}NO_8$ 420.1658, found 420.1628.

5.13. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2-pyridyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (10b)

The reaction was carried out using **9b** (70 mg, 0.15 mmol) in a manner similar to the preparation of **10a**, to give **10b** (58 mg, 91%) as an amorphous material. $[\alpha]_D^{25}$ +12 (*c* 0.19, CH_3OH). IR (neat) 3342, 1734, 1635 cm^{-1}. ^1H NMR (500 MHz, D_2O): δ 1.82 (s, 1H, Ac), 3.49–3.54 (m, 2H, H-7, H-9a), 3.64 (s, 3H, OMe), 3.72 (dd, 1H, $J_{8,9b}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.77 (ddd, 1H, $J_{8,9a}$=5.7 Hz, $J_{7,8}$=8.6 Hz, H-8), 4.07 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.20 (d, 1H, H-6), 4.40, 4.44 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C\equiv$), 4.50 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 6.07 (d, 1H, H-3), 7.28 (m, 1H, Ar), 7.42 (d, 1H, *J*=8.0 Hz, Ar), 7.69 (dt, 1H, *J*=1.7 Hz, Ar), 8.32 (d, 1H, *J*=4.6 Hz, Ar). Positive ion FABMS (NBA): *m/z* 421 $[M+H]^+$, 443 $[M+Na]^+$. FABHRMS calcd for $C_{20}H_{25}N_2O_8$ 421.1611, found 421.1585.

5.14. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(3-pyridyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (10c)

The reaction was carried out using **9c** (130 mg, 0.28 mmol) in a manner similar to the preparation of **10a**, to give **10c** (99 mg, 83%) as an amorphous material. $[\alpha]_D^{25}$ +40 (*c* 0.18, CH_3OH). IR (neat) 3298, 1734, 1637 cm^{-1}. ^1H NMR (500 MHz, D_2O): δ 1.85 (s, 1H, Ac), 3.50–3.53 (m, 2H, H-7, H-9a), 3.67 (s, 3H, OMe), 3.73 (dd, 1H, $J_{8,9b}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.78 (ddd, 1H, $J_{7,8}$=8.6 Hz, $J_{8,9b}$=5.7 Hz, H-8), 4.11 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.23 (d, 1H, H-6), 4.42, 4.46 (d, each 1H, J_{gem}=16.1 Hz, $OCH_2C\equiv$), 4.52 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 6.12 (d, 1H, H-3), 7.32 (dd, 1H, *J*=5.2, 7.2 Hz, Ar), 7.81 (d, 1H, *J*=8.1 Hz, Ar), 8.36 (br, 1H, Ar), 8.48 (br, 1H, Ar). Positive ion FABMS (NBA): *m/z* 421 $[M+H]^+$. FABHRMS calcd for $C_{20}H_{25}N_2O_8$ 421.1611, found 421.1585.

5.15. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2-thienyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (10d)

The reaction was carried out using **9d** (83 mg, 0.18 mmol) in a manner similar to the preparation of **10a**, to give **10d** (74 mg, 98%) as an amorphous material. $[\alpha]_D^{26}$ +33 (*c* 0.14, CH_3OH). IR (neat) 3265, 1734, 1624 cm^{-1}. ^1H NMR (500 MHz, D_2O): δ 1.99 (s, 1H, Ac), 3.51–3.57 (m, 2H, H-7 and H-9a), 3.70 (s, 3H, OMe), 3.78 (dd, 1H, $J_{8,9b}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.89 (m, 1H, H-8), 4.15 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.20 (d, 1H, H-6), 4.39, 4.46 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C\equiv$), 4.52 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 6.07 (d, 1H, H-3), 6.95 (dd, 1H, *J*=4.0, 5.2 Hz, Ar), 7.22 (d, 1H, Ar), 7.24 (d, 1H, Ar). Positive ion FABMS (NBA): *m/z* 426 $[M+H]^+$, 448 $[M+Na]^+$. FABHRMS calcd for $C_{19}H_{24}NO_8S$ 426.1223, found 426.1187.

5.16. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(3-thienyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (10e)

The reaction was carried out using **9e** (59 mg, 0.13 mmol) in a manner similar to the preparation of **10a**, to give **10e** (48 mg, 89%) as an amorphous material. $[\alpha]_D^{25}$ +30 (*c* 0.22, CH_3OH). IR (neat) 3313, 1734, 1624 cm^{-1}. ^1H NMR (500 MHz, D_2O): δ 1.85 (s, 1H, Ac), 3.51–3.57 (m, 2H, H-7 and H-9a), 3.67 (s, 3H, OMe), 3.73 (dd, 1H, $J_{8,9b}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.78 (m, 1H, H-8), 4.10 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.24 (d, 1H, H-6), 4.39, 4.43 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C\equiv$), 4.53 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 6.12 (d, 1H, H-3), 7.07 (d, 1H, *J*=4.6 Hz, Ar), 7.33 (m, 1H, Ar), 7.55 (d, 1H, *J*=2.9 Hz, Ar). Positive ion FABMS (NBA): *m/z* 426 $[M+H]^+$, 448 $[M+Na]^+$.

5.17. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2-thiazolyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (10f)

The reaction was carried out using **9f** (98 mg, 0.21 mmol) in a manner similar to the preparation of **10a**, to give **10f** (74 mg, 83%) as an amorphous material. $[\alpha]_D^{25}$ +52 (*c* 0.22, CH_3OH). IR (neat) 3392, 1734, 1624 cm^{-1}. ^1H NMR (500 MHz, D_2O): δ 1.90 (s, 1H, Ac), 3.56–3.59 (m, 2H, H-7 and H-9a), 3.72 (s, 3H, OMe), 3.79 (dd, 1H, $J_{8,9b}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.85 (m, 1H, H-8), 4.15 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.28 (d, 1H, H-6), 4.51, 4.54 (d, each 1H, J_{gem}=17.2 Hz, $OCH_2C\equiv$), 4.56 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 6.14 (d, 1H, H-3), 7.59 (d, 1H, *J*=2.9 Hz, Ar), 7.76 (d, 1H, *J*=3.4 Hz, Ar). Positive ion FABMS (NBA): *m/z* 427 $[M+H]^+$. FABHRMS calcd for $C_{18}H_{23}N_2O_8S$ 427.1175, found 427.1093.

5.18. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(5′-acetyl-2′-thienyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (10h)

The reaction was carried out using **9h** (40 mg, 0.079 mmol) in a manner similar to the preparation of **10a**, to give **10h** (35 mg, 95%). $[\alpha]_D^{25}$ +12 (*c* 0.12, CH_3OH). IR (neat) 3257, 1714, 1637 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.89 (s, 3H, NAc), 2.47 (s, 3H, CAc), 3.49–3.56 (m, 2H, H-7 and H-9a), 3.70 (s, 3H, OMe), 3.76 (dd, 1H, $J_{8,9b}$=2.9 Hz, J_{gem}=12.0 Hz, H-9b), 3.82 (ddd, 1H, $J_{7,8}$=9.2 Hz, $J_{8,9a}$=6.3 Hz, H-8), 4.10 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.24 (d, 1H, H-6), 4.43–4.50 (m, 2H, 3H, H-4 and $OCH_2C\equiv$), 6.10 (d, 1H, $J_{3,4}$=2.3 Hz, H-3), 7.22 (d, 1H, *J*=4.0 Hz, Ar), 7.68 (d, 1H, Ar). Positive ion FABMS (NBA): *m/z* 468 $[M+H]^+$, 490 $[M+Na]^+$.

5.19. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(5′-formyl-2′-thienyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (10i)

The reaction was carried out using **9i** (42 mg, 0.085 mmol) in a manner similar to the preparation of **10a**, to give **10i** (31 mg, 80%). $[\alpha]_D^{25}$ +53 (*c* 0.19, CH_3OH). IR (neat) 3265,

1734, 1624 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.89 (s, 3H, NAc), 3.23–3.59 (m, 2H, H-7 and H-9a), 3.71 (s, 3H, OMe), 3.76 (dd, 1H, $J_{8,9b}$=2.9 Hz, J_{gem}=12.0 Hz, H-9b), 3.81 (ddd, 1H, $J_{7,8}$=9.2 Hz, $J_{8,9b}$=6.3 Hz, H-8), 4.13 (dd, 1H, $J_{4,5}$=9.2 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.26 (d, 1H, H-6), 4.48, 4.51 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C\equiv$), 4.52 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 6.13 (d, 1H, H-3), 7.32 (d, 1H, J=3.5 Hz, Ar), 7.79 (d, 1H, Ar), 9.68 (s, 1H, CHO). Positive ion FABMS (NBA): m/z 454 $[M+H]^+$, 476 $[M+Na]^+$.

5.20. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(5′-formyl-2′-furyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (10j)

The reaction was carried out using **9j** (70 mg, 0.15 mmol) in a manner similar to the preparation of **10a**, to give **10j** (58 mg, 91%). IR (neat) 3246, 1734, 1616 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.91 (s, 3H, NAc), 3.54–3.59 (m, 2H, H-7 and H-9a), 3.71 (s, 3H, OMe), 3.76–3.83 (m, 2H, H-8 and H-9b), 4.11 (dd, 1H, $J_{4,5}$=9.8, $J_{5,6}$=10.9 Hz, H-5), 4.25 (d, 1H, H-6), 4.46–4.52 (m, 3H, H-4 and $OCH_2C\equiv$), 6.09 (d, 1H, $J_{3,4}$=2.9 Hz, H-3), 6.82 (d, 1H, J=3.4 Hz, Ar), 7.40 (d, 1H, Ar), 9.35 (s, 1H, CHO). Positive ion FABMS (NBA): m/z 438 $[M+H]^+$, 460 $[M+Na]^+$. FABHRMS calcd for $C_{20}H_{24}NO_{10}$ 438.1400, found 438.1353.

5.21. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(phenyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonic acid (5a)

A solution of **10a** (20 mg, 0.048 mmol) in 0.1 M KOH/MeOH (1:1) (2 mL) was stirred at room temperature overnight, and then adjusted to pH 2–3. The resin was filtered off and the filtrate was evaporated. The residue was purified by column chromatography on silica gel using $CHCl_3$/MeOH/H_2O (65:35:5, v/v/v), and then desalted with an AC Micro Acylizer G1. The resulting aqueous solution was concentrated to give **5a** (16 mg, 83%) after lyophilization. $[\alpha]_D^{25}$ +22 (c 0.22, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.89 (s, 3H, Ac), 3.53–3.57 (m, 2H, H-7 and H-9a), 3.78 (dd, 1H, $J_{8,9b}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.85 (ddd, 1H, $J_{7,8}$=9.2 Hz, $J_{8,9a}$=6.3 Hz, H-8), 4.11 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.19 (d, 1H, H-6), 4.43, 4.47 (d, each 1H, J_{gem}=16.1 Hz, $OCH_2C\equiv$), 4.52 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 5.79 (d, 1H, H-3), 7.30–7.36 (m, 3H, Ar), 7.43–7.45 (m, 2H, Ar). Positive ion FABMS (NBA): m/z 428 $[M+Na]^+$.

5.22. Potassium 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2-pyridyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (5b)

A solution of **10b** (58 mg, 0.138 mmol) in 0.1 M KOH/MeOH (1:1) (2 mL) was stirred at room temperature overnight, and then evaporated. The residue was purified by column chromatography on silica gel with $CHCl_3$/MeOH/H_2O (65:35:5, v/v), and then desalted with an AC Micro Acylizer G1 to give **5b** (60 mg, 99%) after lyophilization. $[\alpha]_D^{25}$ +17 (c 0.15, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.86 (s, 3H, Ac), 3.51 (d, 1H, $J_{7,8}$=9.2 Hz, H-7), 3.53 (dd, 1H, $J_{8,9a}$=6.3 Hz, J_{gem}=12.0 Hz, H-9a), 3.78 (dd, 1H, $J_{8,9b}$=2.3 Hz, H-9b), 3.84 (m, 1H, H-8), 4.12 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.19 (d, 1H, H-6), 4.47, 4.51 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C\equiv$), 4.54 (d, 1H, H-4), 5.77 (s, 1H, H-3), 7.35 (dd, 1H, J=5.2, 7.5 Hz, Ar), 7.53 (d, 1H, J=8.0 Hz, Ar), 7.77 (dd, 1H, Ar), 8.40 (d, 1H, Ar). Positive ion FABMS (NBA): m/z 445 $[M+H]^+$, 467 $[M+K]^+$. FABHRMS calcd for $C_{19}H_{22}N_2O_8K$ 445.1013, found 445.1023.

5.23. Potassium 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(3-pyridyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonate (5c)

The reaction was carried out using **10c** (38 mg, 0.099 mmol) in a manner similar to the preparation of **5b**, to give **5c** (39 mg, 99%). $[\alpha]_D^{25}$ +22 (c 0.26, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.88 (s, 3H, Ac), 3.51 (d, 1H, $J_{7,8}$=9.2 Hz, H-7), 3.53 (dd, 1H, $J_{8,9a}$=6.3 Hz, J_{gem}=12.1 Hz, H-9a), 3.78 (dd, 1H, $J_{8,9b}$=2.9 Hz, H-9b), 3.84 (ddd, 1H, H-8), 4.11 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.18 (d, 1H, H-6), 4.45, 4.49 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C\equiv$), 4.52 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 5.77 (d, 1H, H-3), 7.35 (dd, 1H, J=5.2, 8.0 Hz, Ar), 7.85 (m, 1H, Ar), 8.39 (dd, 1H, J=1.8 Hz, Ar), 8.53 (d, 1H, Ar). Positive ion FABMS (NBA): m/z 467 $[M+K]^+$. FABHRMS calcd for $C_{19}H_{22}N_2O_8K$ 445.1013, found 445.1046.

5.24. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2-thienyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonic acid (5d)

The reaction was carried out using **10d** (41 mg, 0.099 mmol) in a manner similar to the preparation of **5a**, to give **5d** (26 mg, 66%). $[\alpha]_D^{25}$ +23 (c 0.15, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.89 (s, 3H, Ac), 3.53–3.56 (m, 2H, H-7 and H-9a), 3.76 (dd, 1H, $J_{8,9b}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.84 (ddd, 1H, $J_{7,8}$=8.6 Hz, $J_{8,9a}$=5.7 Hz, H-8), 4.08 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.18, (d, 1H, H-6), 4.42, 4.46 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C\equiv$), 4.49 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 5.75 (d, 1H, H-3), 6.97 (dd, 1H, J=3.4, 5.2 Hz, Ar), 7.25 (d, 1H, Ar), 7.37 (d, 1H, Ar). Positive ion FABMS (NBA): m/z 412 $[M+H]^+$, 434 $[M+Na]^+$. FABHRMS calcd for $C_{18}H_{22}NO_8S$ 412.1066, found 412.1003.

5.25. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(3-pyridyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonic acid (5e)

The reaction was carried out using **10e** (22 mg, 0.052 mmol) in a manner similar to the preparation of **5a**, to give **5e** (16 mg, 76%). $[\alpha]_D^{25}$ +25 (c 0.11, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.90 (s, 3H, Ac), 3.53–3.57 (m, 2H, H-7 and H-9a), 3.79 (dd, 1H, $J_{8,9a}$=2.9 Hz, J_{gem}=12.1 Hz, H-9b), 3.86 (m, 1H, H-8), 4.11 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.20 (d, 1H, H-6), 4.42, 4.46 (d, each 1H, J_{gem}=16.0 Hz, $OCH_2C\equiv$), 4.53 (dd, 1H, $J_{3,4}$=1.7 Hz, H-4), 5.78 (d, 1H, H-3), 7.12 (d, 1H, J=5.2 Hz, Ar), 7.37 (m, 1H, Ar), 7.59 (d, 1H, J=2.3 Hz, Ar). Positive ion FABMS (NBA): m/z 412 $[M+H]^+$. FABHRMS calcd for $C_{18}H_{22}NO_8S$ 412.1066, found 412.1122.

5.26. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2-thiazolyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonic acid (5f)

The reaction was carried out using **10f** (74 mg, 0.17 mmol) in a manner similar to the preparation of **5a**, to give **5f**

(39 mg, 54%). $[\alpha]_D^{25}$ +8.1 (*c* 0.10, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.82 (s, 3H, Ac), 3.46–3.50 (m, 2H, H-7 and H-9a), 3.72 (dd, 1H, $J_{8,9a}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.79 (m, 1H, H-8), 4.06 (dd, 1H, $J_{4,5}$=9.2 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.15 (d, 1H, H-6), 4.47, 4.48 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C\equiv$), 4.70 (m, 1H, H-4), 5.77 (d, 1H, $J_{3,4}$=2.3 Hz, H-3), 7.52 (d, 1H, *J*=3.4 Hz, Ar), 7.70 (d, 1H, Ar). Positive ion FABMS (NBA): *m*/*z* 413 $[M+H]^+$. FABHRMS calcd for $C_{17}H_{21}N_2O_8S$ 413.1019, found 413.1005.

5.27. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(5′-acetyl-2′-thienyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonic acid (5h)

The reaction was carried out using **10h** (16 mg, 0.039 mmol) in a manner similar to the preparation of **5a**, to give **5h** (15 mg, 98%). ^1H NMR (500 MHz, D_2O): δ 1.90 (s, 3H, Ac), 2.50 (s, 3H, Ac), 3.51–3.57 (m, 2H, H-7 and H-9a), 3.78 (dd, 1H, $J_{8,9b}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.84 (ddd, 1H, $J_{7,8}$=9.2 Hz, $J_{8,9a}$=6.3 Hz, H-8), 4.10 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.19 (d, 1H, H-6), 4.43–4.51 (m, 3H, H-4, $OCH_2C\equiv$), 5.75 (d, 1H, $J_{3,4}$=2.3 Hz, H-3), 7.25 (d, 1H, *J*=4.0 Hz, Ar), 7.37 (d, 1H, Ar). Positive ion FABMS (NBA): *m*/*z* 476 $[M+Na]^+$. FABHRMS calcd for $C_{20}H_{23}NO_9SNa$ 476.0992, found 476.1044.

5.28. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(5′-formyl-2′-thienyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonic acid (5i)

The reaction was carried out using **10i** (18 mg, 0.04 mmol) in a manner similar to the preparation of **5a**, to give **5i** (17 mg, 96%). ^1H NMR (500 MHz, D_2O): δ 1.92 (s, 3H, Ac), 3.54 (d, 1H, $J_{7,8}$=9.2 Hz, H-7), 3.55 (dd, 1H, $J_{8,9a}$=6.3 Hz, J_{gem}=12.0 Hz, H-9a), 3.79 (dd, 1H, $J_{8,9b}$=2.9 Hz, H-9b), 3.86 (ddd, 1H, H-8), 4.11 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.20 (d, 1H, H-6), 4.47–4.55 (m, 3H, H-4, $OCH_2C\equiv$), 5.76 (d, 1H, $J_{3,4}$=2.3 Hz, H-3), 7.34 (d, 1H, *J*=4.0 Hz, Ar), 7.81 (d, 1H, Ar), 9.69 (s, 1H, CHO). Positive ion FABMS (NBA): *m*/*z* 462 $[M+Na]^+$.

5.29. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(5′-formyl-2′-furyl)prop-2-ynyl]-D-*glycero*-D-*galacto*-non-2-enonic acid (5j)

The reaction was carried out using **11j** (20 mg, 0.046 mmol) in a manner similar to the preparation of **5a**, to give **5j** (9 mg, 46%). ^1H NMR (500 MHz, D_2O): δ 1.90 (s, 3H, Ac), 3.52 (d, 1H, $J_{7,8}$=9.2 Hz, H-7), 3.54 (dd, 1H, $J_{8,9a}$=6.3 Hz, J_{gem}=12.0 Hz, H-9a), 3.78 (dd, 1H, $J_{8,9b}$=2.9 Hz, H-9b), 3.84 (ddd, 1H, H-8), 4.11 (dd, 1H, $J_{4,5}$=8.6 Hz, $J_{5,6}$=10.9 Hz, H-5), 4.18 (d, 1H, H-6), 4.50 (dd, 1H, $J_{3,4}$=2.3 Hz, H-4), 4.51 (d, each 1H, J_{gem}=17.2 Hz, $OCH_2C\equiv$), 5.74 (d, 1H, H-3), 6.85 (d, 1H, *J*=3.5 Hz, Ar), 7.43 (d, 1H, Ar), 9.37 (s, 1H, CHO). Positive ion FABMS (NBA): *m*/*z* 424 $[M+H]^+$.

5.30. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*talo*-non-2-enonate (12)

To a solution of compound **11** (3.02 g, 6.38 mmol)[11a] in MeOH (20 mL) was added a solution of NaOMe (0.035 g, 0.64 mmol) in MeOH (10 mL) at 0 °C, and the mixture was stirred for 2 h at the same temperature. The reaction mixture was treated with Amberlite IRC-50 (5 g) and the suspension was filtered and the filtrate was evaporated in vacuo. The resulting residue was dissolved in 2,2-dimethoxypropane (20 mL) and DMF (5 mL) containing Amberlite IRA 120 (H^+) (3 g), and the mixture was stirred for 12 h at room temperature, filtered, and concentrated in vacuo. Purification of the residue by column chromatography on silica gel with AcOEt yielded **12** (1.28 g, 58%). $[\alpha]_D^{24}$ −105 (*c* 1.63, CH_3OH). ^1H NMR (500 MHz, $CDCl_3$): δ 1.35, 1.40 (s, each 3H, Me_2C), 2.10 (s, 3H, NAc), 2.74 (br, 1H, OH-4), 3.50 (dd, 1H, $J_{7,OH}$=4.0 Hz, $J_{7,8}$=8.7 Hz, H-7), 3.78 (s, 3H, OMe), 3.93 (d, 1H, $J_{5,6}$=11.5 Hz, H-6), 4.09–4.18 (m, 3H, H-5, H-9a, and H-9b), 4.25 (ddd, 1H, $J_{3,4}$=5.7 Hz, $J_{4,5}$=4.1 Hz, $J_{4,OH}$=5.7 Hz, H-4), 4.41 (ddd, 1H, $J_{8,9a}$=5.2 Hz, $J_{8,9b}$=6.3 Hz, H-8), 4.85 (d, 1H, OH-7), 6.11 (d, 1H, H-3), 6.53 (d, 1H, $J_{5,NH}$=7.5 Hz, NH). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.1, 25.2, 27.0, 47.7, 52.5, 61.2, 67.2, 69.6, 73.2, 74.1, 107.4, 109.1, 146.4, 162.5, 172.5. Positive ion FABMS (NBA): *m*/*z* 346 $[M+H]^+$. FABHRMS calcd for $C_{15}H_{24}NO_8$ 346.1502, found 346.1465.

5.31. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-(prop-2-ynyl)-D-*glycero*-D-*talo*-non-2-enonate (13)

Sodium hydride (31 mg, 1.3 mmol) at 0 °C under Ar was added to a solution of **12** (350 mg, 1.0 mmol). Propargyl bromide (244 mg, 2.0 mmol) in DMF (5 mL) was added, and the mixture was stirred for 1 h. After the addition of MeOH (1 mL), the solvent was concentrated and dried. The residue was chromatographed on silica gel using 50:1 $CHCl_3$/MeOH to give **13** (151 mg, 39%). $[\alpha]_D^{24}$ −103 (*c* 0.29, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 1.31, 1.35 (s, each 3H, Me_2C), 2.05 (s, 3H, NAc), 2.52 (t, 1H, *J*=2.3 Hz, C≡CH), 3.44 (dd, 1H, $J_{7,OH}$=3.5 Hz, $J_{7,8}$=8.0 Hz, H-7), 3.73 (s, 3H, OMe), 3.96 (d, 1H, $J_{5,6}$=10.9 Hz, H-6), 4.05 (dd, 1H, $J_{8,9a}$=5.2 Hz, J_{gem}=9.2 Hz, H-9a), 4.10–4.21 (m, 4H, H-4, H-5, H-9b, and $OCH_2C\equiv C$), 4.30 (dd, 1H, J_{gem}=16.1 Hz, $OCH_2C\equiv$), 4.33 (ddd, 1H, $J_{8,9b}$=2.3 Hz, H-8), 4.73 (d, 1H, OH), 6.12 (d, 1H, $J_{3,4}$=5.2 Hz, H-3), 6.40 (d, 1H, $J_{5,NH}$=8.0 Hz, NH). Positive ion FABMS (NBA): *m*/*z* 384 $[M+H]^+$, 406 $[M+Na]^+$. FABHRMS calcd for $C_{18}H_{26}NO_8$ 384.1658, found 384.1681.

5.32. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(2′-thienyl)prop-2-ynyl]-D-*glycero*-D-*talo*-non-2-enonate (14a)

The reaction was carried out using **13** (83 mg, 0.22 mmol) and 2-iodothiophene (56 mg, 0.26 mmol) in a manner similar to the preparation of **9a**, to give **14a** (64 mg, 64%). ^1H NMR (500 MHz, $CDCl_3$): δ 1.37, 1.41 (s, each 3H, Me_2C), 2.07 (s, 3H, NAc), 3.51 (d, 1H, $J_{7,8}$=8.0 Hz, H-7), 3.79 (s, 3H, OMe), 4.04 (d, 1H, $J_{5,6}$=11.5 Hz, H-6), 4.11 (dd, 1H, $J_{8,9a}$=5.2 Hz, J_{gem}=8.6 Hz, H-9a), 4.18 (d, 1H, $J_{8,9b}$=6.3 Hz, H-9b), 4.20–4.24 (m, 1H, H-4), 4.25–4.27 (m, 1H, H-5), 4.39–4.43 (m, 1H, H-8), 4.46, 4.59 (d, each 1H, J_{gem}=16.1 Hz, OCH_2C), 4.77 (br, 1H, OH), 6.22 (d, 1H, $J_{3,4}$=5.2 Hz, H-3), 6.39 (d, 1H, $J_{5,NH}$=8.0 Hz, NH), 6.99 (dd, 1H, *J*=4.0, 5.2 Hz, Ar), 7.24 (d, 1H, Ar), 7.30 (d, 1H, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.1, 25.2, 26.9, 46.6, 52.3, 56.3, 66.8, 67.1, 69.5, 73.8, 74.2, 80.8, 87.9, 103.7, 108.9,

121.5, 127.0, 127.9, 132.8, 147.1, 162.3, 172.2. Positive ion FABMS (NBA): *m/z* 466 $[M+H]^+$. FABHRMS calcd for $C_{22}H_{28}NO_8S$ 466.1536, found 466.1482.

5.33. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(3′-thienyl)prop-2-ynyl]-D-*glycero*-D-*talo*-non-2-enonate (14b)

The reaction was carried out using **13** (101 mg, 0.26 mmol) and 3-iodothiophene (67 mg, 0.32 mmol) in a manner similar to the preparation of **9a**, to give **14b** (89 mg, 73%). $[\alpha]_D^{24}$ −107 (*c* 0.22, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 1.35, 1.40 (s, each 3H, Me_2C), 2.05 (s, 3H, NAc), 3.50 (dd, 1H, $J_{7,8}$=7.4 Hz, $J_{7,OH}$=2.3 Hz, H-7), 3.77 (s, 3H, OMe), 4.02 (d, 1H, $J_{5,6}$=10.9 Hz, H-6), 4.10 (dd, 1H, $J_{8,9a}$=5.2 Hz, J_{gem}=8.6 Hz, H-9a), 4.26 (dd, 1H, $J_{4,5}$=4.0 Hz, H-4), 4.15–4.23 (m, 1H, H-5 and H-9b), 4.39 (m, 1H, H-8), 4.42, 4.54 (d, each 1H, J_{gem}=16.0 Hz, $OCH_2C{\equiv}$), 4.78 (d, 1H, OH), 6.23 (d, 1H, $J_{3,4}$=5.7 Hz, H-3), 6.42 (d, 1H, $J_{5,NH}$=8.0 Hz, NH), 7.10 (dd, 1H, *J*=1.2, 5.2 Hz, Ar), 7.28 (d, 1H, *J*=2.9 Hz, Ar), 7.48 (d, 1H, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.3, 25.3, 27.1, 46.8, 52.5, 56.5, 66.9, 67.3, 69.7, 73.9, 74.3, 82.8, 83.8, 104.0, 109.1, 120.9, 125.8, 129.8, 129.9, 147.2, 162.5, 172.4. Positive ion FABMS (NBA): *m/z* 466 $[M+H]^+$. FABHRMS calcd for $C_{22}H_{28}NO_8S$ 466.1536, found 466.1482.

5.34. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-[3-(2′-thiazolyl)prop-2-ynyl]-D-*glycero*-D-*talo*-non-2-enonate (14c)

The reaction was carried out using **13** (151 mg, 0.39 mmol) and 2-bromothiazole (71 mg, 0.43 mmol) in a manner similar to the preparation of **9f**, to give **14c** (70 mg, 48%). $[\alpha]_D^{24}$ −101 (*c* 0.22, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 1.35, 1.39 (s, each 3H, Me_2C), 2.08 (s, 3H, NAc), 3.49 (dd, 1H, $J_{7,8}$=8.0 Hz, $J_{7,OH}$=4.0 Hz, H-7), 3.77 (s, 3H, OMe), 4.03 (d, 1H, $J_{5,6}$=11.5 Hz, H-6), 4.10 (dd, 1H, $J_{8,9a}$=5.2 Hz, J_{gem}=8.6 Hz, H-9a), 4.15 (dd, 1H, $J_{8,9b}$=6.3 Hz, H-9b), 4.20–4.25 (m, 1H, H-4), 4.27 (m, 1H, H-5), 4.39 (m, 1H, H-8), 4.48, 4.60 (d, each 1H, J_{gem}=16.0 Hz, $OCH_2C{\equiv}$), 4.75 (d, 1H, OH), 6.19 (d, 1H, $J_{3,4}$=5.7 Hz, H-3), 6.40 (d, 1H, $J_{5,NH}$=8.0 Hz, NH), 7.40 (d, 1H, *J*=3.5 Hz, Ar), 7.83 (d, 1H, Ar). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.3, 25.3, 27.1, 46.7, 52.6, 55.9, 67.2, 67.3, 69.7, 73.9, 74.3, 80.4, 88.9, 103.2, 109.2, 121.4, 143.8, 147.4, 147.7, 162.3, 172.4. Positive ion FABMS (NBA): *m/z* 467 $[M+H]^+$. FABHRMS calcd for $C_{21}H_{27}N_2O_8S$ 467.1488, found 467.1439.

5.35. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2′-thienyl)prop-2-ynyl]-D-*glycero*-D-*talo*-non-2-enonate (15a)

The reaction was carried out using **14a** (41 mg, 0.088 mmol) in a manner similar to the preparation of **10a**, to give **15a** (25 mg, 68%). $[\alpha]_D^{24}$ −200 (*c* 1.20, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.99 (s, 3H, NAc), 3.56 (d, 1H, $J_{7,8}$=9.2 Hz, H-7), 3.59 (dd, 1H, $J_{8,9a}$=5.7 Hz, J_{gem}=12.0 Hz, H-9a), 3.69 (s, 3H, OMe), 3.80 (d, 1H, H-9b), 3.87 (m, 1H, H-8), 4.14–4.26 (m, 3H, H-4, H-5, and H-6), 4.42 (d, each 1H, J_{gem}=16.6 Hz, $OCH_2C{\equiv}$), 6.17 (d, 1H, $J_{3,4}$=5.2 Hz, H-3), 6.92 (dd, 1H, *J*=2.3, 5.2 Hz, Ar), 7.19 (d, 1H, Ar), 7.29 (d, 1H, Ar). Positive ion FABMS (NBA): *m/z* 426 $[M+H]^+$. FABHRMS calcd for $C_{19}H_{24}NO_8S$ 426.1223, found 426.1279.

5.36. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(3′-thienyl)prop-2-ynyl]-D-*glycero*-D-*talo*-non-2-enonate (15b)

The reaction was carried out using **14b** (73 mg, 0.157 mmol) in a manner similar to the preparation of **10a**, to give **15b** (53 mg, 79%). $[\alpha]_D^{24}$ −214 (*c* 0.74, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.83 (s, 3H, NAc), 3.48 (d, 1H, $J_{7,8}$=9.8 Hz, H-7), 3.51 (dd, 1H, $J_{8,9a}$=5.8 Hz, J_{gem}=12.0 Hz, H-9a), 3.57 (s, 3H, OMe), 3.72 (d, 1H, H-9a), 3.79 (br, 1H, H-8), 4.00 (d, 1H, $J_{5,6}$=3.5 Hz, H-6), 4.08 (d, 1H, $J_{4,5}$=11.5 Hz, H-5), 4.16 (dd, 1H, $J_{3,4}$=4.6 Hz, H-4), 4.23, 4.30 (d, each 1H, J_{gem}=17.2 Hz, $OCH_2C{\equiv}$), 6.02 (d, 1H, H-3), 6.91 (d, 1H, *J*=4.6 Hz, Ar), 7.10 (br, 1H, Ar), 7.32 (br, 1H, Ar). Positive ion FABMS (NBA): *m/z* 426 $[M+H]^+$. FABHRMS calcd for $C_{19}H_{24}NO_8S$ 426.1223, found 426.1135.

5.37. Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2′-thiazolyl)prop-2-ynyl]-D-*glycero*-D-*talo*-non-2-enonate (15c)

The reaction was carried out using **14c** (41 mg, 0.088 mmol) in a manner similar to the preparation of **10a**, to give **15c** (20 mg, 53%). $[\alpha]_D^{24}$ −30 (*c* 1.07, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.92 (s, 3H, NAc), 3.59–3.62 (m, 2H, H-7 and H-9a), 3.74 (s, 3H, OMe), 3.82 (dd, 1H, $J_{8,9a}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.89 (m, 1H, H-8), 4,22–4.31 (m, 3H, H-4, H-5, and H-6), 4.56 (d, each 1H, J_{gem}=17.2 Hz, $OCH_2C{\equiv}$), 6.29 (d, 1H, $J_{3,4}$=5.8 Hz, H-3), 7.60 (d, 1H, *J*=3.5 Hz, Ar), 7.77 (d, 1H, Ar). Positive ion FABMS (NBA): *m/z* 427 $[M+H]^+$. FAB HRMS calcd for $C_{18}H_{23}N_2O_8S$ 427.1175, found 427.1209.

5.38. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2′-thienyl)prop-2-ynyl]-D-*glycero*-D-*talo*-non-2-enonic acid (6a)

The reaction was carried out using **15a** (25 mg, 0.059 mmol) in a manner similar to the preparation of **5a**, to give **6a** (15 mg, 60%). $[\alpha]_D^{24}$ −174 (*c* 0.17, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.90 (s, 3H, Ac), 3.55 (d, 1H, $J_{7,8}$=9.8 Hz, H-7), 3.58 (dd, 1H, $J_{8,9a}$=6.3, 12.0 Hz, H-9a), 3.81 (dd, 1H, $J_{8,9b}$=2.3 Hz, H-9b), 3.90 (ddd, 1H, H-8), 4.17 (d, 1H, $J_{5,6}$=12.1 Hz, H-6), 4.22–4.27 (m, 2H, H-4 and H-5), 4.49 (d, each 1H, J_{gem}=17.2 Hz, $OCH_2C{\equiv}$), 5.99 (d, $J_{3,4}$=5.2 Hz, H-3), 6.99 (dd, 1H, *J*=4.0, 5.2 Hz, Ar), 7.26 (d, 1H, Ar), 7.39 (d, 1H, Ar). Positive ion FABMS (NBA): *m/z* 412 $[M+H]^+$. FABHRMS calcd for $C_{18}H_{22}NO_8S$ 412.1066, found 412.1081.

5.39. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(3′-thienyl)prop-2-ynyl]-D-*glycero*-D-*talo*-non-2-enonic acid (6b)

The reaction was carried out using **15b** (35 mg, 0.082 mmol) in a manner similar to the preparation of **5a**, to give **6b** (34 mg, 99%). $[\alpha]_D^{24}$ −169 (*c* 0.22, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.86 (s, 3H, NAc), 3.53–3.58 (m, 2H,

H-7 and H-9a), 3.78 (dd, 1H, $J_{8,9b}$=2.3 Hz, J_{gem}=12.0 Hz, H-9b), 3.89 (ddd, 1H, $J_{7,8}$=8.6 Hz, H-8), 4.14 (d, 1H, $J_{5,6}$=11.5 Hz, H-6), 4.18–4.21 (m, 2H, H-4 and H-5), 4.42 (d, each 1H, J_{gem}=17.2 Hz, $OCH_2C{\equiv}$), 5.92 (d, $J_{3,4}$= 5.7 Hz, H-3), 7.08 (d, 1H, J=3.5 Hz, Ar), 7.35 (m, 1H, Ar), 7.55 (d, 1H, J=2.3 Hz, Ar). Positive ion FABMS (NBA): *m/z* 412 $[M+H]^+$. FABHRMS calcd for $C_{18}H_{22}NO_8S$ 412.1066, found 412.1012.

5.40. 5-Acetamido-2,6-anhydro-3,5-dideoxy-4-*O*-[3-(2′-thiazolyl)prop-2-ynyl]-D-*glycero*-D-*talo*-non-2-enonic acid (6c)

The reaction was carried out using **15c** (20 mg, 0.047 mmol) in a manner similar to the preparation of **5a**, to give **6c** (18 mg, 94%). $[\alpha]_D^{24}$ −191 (*c* 0.15, CH_3OH). ^1H NMR (500 MHz, D_2O): δ 1.86 (s, 3H, NAc), 3.55 (d, 1H, $J_{7,8}$= 9.8 Hz, H-7), 3.58 (dd, 1H, $J_{8,9a}$=6.8 Hz, J_{gem}=12.0 Hz, H-9a), 3.81 (dd, 1H, $J_{8,9b}$=2.9 Hz, H-9b), 3.90 (ddd, 1H, H-8), 4.18 (d, 1H, $J_{5,6}$=12.6 Hz, H-6), 4.24–4.27 (m, 2H, H-4 and H-5), 4.56 (dd, each 1H, J_{gem}=16.6 Hz, $OCH_2C{\equiv}$), 5.96 (d, 1H, $J_{3,4}$=5.2 Hz, H-3), 7.60 (d, 1H, J=3.4 Hz, Ar), 7.77 (d, 1H, Ar). Positive ion FABMS (NBA): *m/z* 413 $[M+H]^+$. FABHRMS calcd for $C_{17}H_{21}N_2O_8S$ 413.1019, found 413.1005.

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