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Novel and facile synthesis of furanodictines A and B based on transformation of 2-acetamido-2-deoxy-D-glucose into 3,6-anhydro hexofuranoses

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ABSTRACT

A novel synthesis of furanodictines A [2-acetamido-3,6-anhydro-2-deoxy-5-*O*-isovaleryl-D-glucofuranose (**1**)] and B [2-acetamido-3,6-anhydro-2-deoxy-5-*O*-isovaleryl-D-mannofuranose (**2**)] is described starting from 2-acetamido-2-deoxy-D-glucose (GlcNAc). The synthetic protocol is based on deriving the epimeric bicyclic 3,6-anhydro sugars [2-acetamido-3,6-anhydro-2-deoxy-D-glucofuranose (**4**) and 2-acetamido-3,6-anhydro-2-deoxy-D-mannofuranose (**5**)] from GlcNAc. Reaction with borate upon heating led to a facile transformation of GlcNAc into the desired epimeric 3,6-anhydro sugars. The C5 hydroxyl group of the 3,6-anhydro compounds **4** and **5** was regioselectively esterified with the isovaleryl chloride to complete the synthesis of furanodictines A and B, respectively. The targets **1** and **2** were synthesized in only two steps requiring no protection/deprotection.

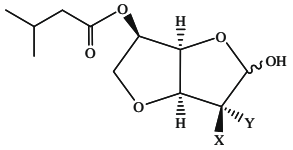
1. Introduction

Oshima and co-workers isolated the 3,6-anhydro amino sugar derivatives, furanodictines A (**1**) and B (**2**) from the metabolic extract of the fruiting body of the cellular slime mold *Dictyostelium discoideum* (Fig. 1).[1] Both these compounds display potent neuronal differentiation activity in rat PC-12 cells.[1,2] The absolute configurations of furanodictines A and B were confirmed by asymmetric syntheses of **1** and **2**, which possess a 3,6-anhydro hexofuranose carbon skeleton corresponding to **4** and **5**, respectively. Furanodictines A (**1**) and B (**2**) are the first examples of amino sugars with an interesting bicyclic bis-tetrahydrofurofuran structure. The structural complexity, coupled with the potent biological activity, makes **1** and **2** attractive targets for total synthesis.[3–5] Although total synthesis has been achieved, these synthetic procedures generally require multi-step pathways and are unsatisfactory for obtaining the target compounds in reasonable yield. There is an urgent need to prepare large quantities of such pharmacophore-containing compounds from easily available raw materials by simple methods. Here a simple synthetic strategy for **1** and **2** starting from readily available GlcNAc was designed and executed.

2. Results and discussion

2.1. Transformation of GlcNAc into hexofuranoses

The reaction was initially carried out at a concentration of GlcNAc (100 mM) in borate solution (pH 7.0) at 100 °C for 2 h. The reaction mixture was applied to a column of charcoal–Celite with a linear gradient of ethanol as shown in Figure 2. The chromatogram showed five fractions (F-1–F-5), numbered according to the order of elution. Each fraction was collected and analyzed separately. Fraction 1 contained GlcNAc and 2-acetamido-2-deoxy-D-mannose (ManNAc) in a proportion of 2:1, respectively, in a yield of 10%. Fraction 2 was not identified. Fractions 3, 4, and 5 were obtained in actual yields of 9.8%, 10.2%, and 36%, respectively, and identified as the respective unsaturated derivative **3** (F-5) and two epimeric 3,6-anhydro derivatives **4** (F-4) and **5** (F-3). In the



X = H, Y = NHAc: furanodictine A (**1**)
X = NHAc, Y = H: furanodictine B (**2**)

Figure 1. Structures of furanodictines A and B.

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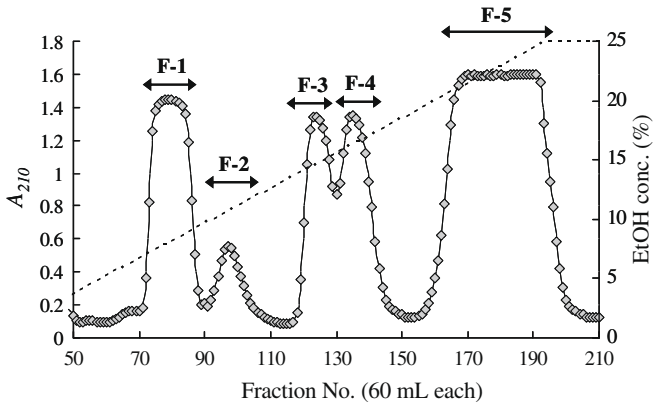


Figure 2. Charcoal–Celite chromatography of products formed from GlcNAc transformation. Dotted line, concentration of ethanol in gradient elution (%).

Morgan–Elson reaction, Chromogen I (2-acetamido-2,3-dideoxy-D-erythro-hex-2-enofuranose, **3**) is known to be the major chromogen formed by alkali treatment of GlcNAc under the conditions used by Kuhn and Kruger.[6,7] Sinay and co-workers have established that the major Chromogen I of the Morgan–Elson reaction is the structure **3**, which was derived in four steps from ManNAc.[8] Compound **3** was produced in preference to epimeric 3,6-anhydro forms **4** and **5**.[9] Derevitskaya et al. have reported that the epimeric **4** and **5** are formed in low yields during the alkaline degradation of GlcNAc, based on the Morgan–Elson reaction. Compounds **4** and **5** are formed in a 1:1 ratio during the entire course of the reaction. These results indicated that about two-thirds of the GlcNAc starting material is converted into a series of hexofuranose derivatives. The structures of these compounds were evaluated by ^{1}H and ^{13}C NMR analyses in D_2O solution, and were consistent with published data.[8,10] In addition, ESI-MS analysis was also carried out on each fraction. The same molecular ion at m/z 226 was obtained for **3**, **4,** and **5** arising from the $[M+Na]^+$ ion of GlcNAc with loss of mass corresponding to a water molecule. As a result, we established a facile transformation of GlcNAc into **4** and **5**, which is useful for the synthesis of furanodictines A and B.

2.2. Time–course analysis of GlcNAc transformation in borate solution

A time–course study of the GlcNAc transformation was carried out in borate solution with heating as described above. HPLC peaks corresponding to **3**, **4,** and **5** appeared at retention times of 8.5, 5.7, and 5.1 min, respectively (see Section 4). The time for maximum formation of **3**, **4,** and **5** was reached at ~2 h and their concentrations varied little upon further reaction (Fig. 3a). Compounds **3**, **4,** and **5** were obtained in a total analytical yield of about 80% and in a ratio of 4.7:1:1, respectively. Compound **3** formed in preference to **4** and **5**, which were produced in equal amount during the entire course of the reaction. GlcNAc and ManNAc were in part epimerized to each other during the reaction process.[11–13] When ManNAc was used instead of GlcNAc as a starting material, three products **3**, **4,** and **5** were generated in a similar ratio and yield (Fig. 3b). Little color was produced at pH 7, but browning occurred at pH values greater than 8. Indeed, as the pH of the reaction increased above 8 there was a significant deepening in this coloration accompanied by an increase in the proportion of unknown products other than the three hexofuranoses (data not shown). Thus, the 2-amino sugars rapidly decompose in alkaline solution upon heating to give a multitude of products followed by a browning reaction.[8] Proximity of the amino group to the anomeric center in 2-amino-sugars confers special properties, which are unusual in the carbohydrate

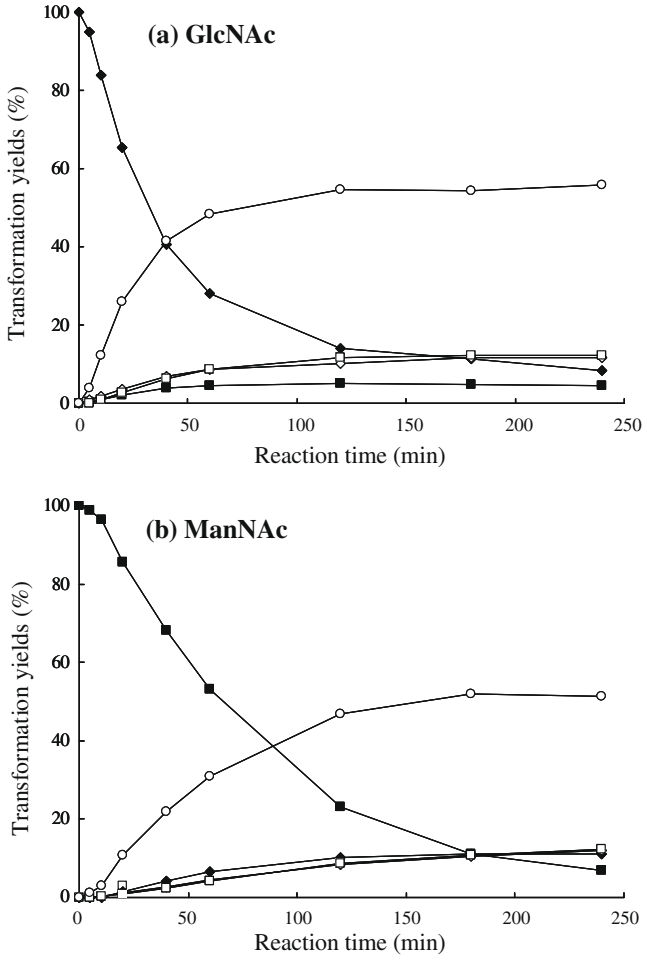


Figure 3. HPLC analyses of GlcNAc/ManNAc on transformation in borate solution (pH 7.0) upon heating. Time–course of products **3**, **4,** and **5** on transformation formed from GlcNAc/ManNAc. (a) GlcNAc. (b) ManNAc. Filled diamond, GlcNAc; filled square, ManNAc; open circle, **3**; open diamond, **4**; open square, **5**.

group.[11] In addition, when GlcNAc was boiled in water as a control experiment, three compounds **3**, **4,** and **5** were also produced, although in extremely low total yields (5%).

Each of the products **3**–**5** was reacted again under the same conditions and analyzed by HPLC. Whichever compound was chosen (i.e., **3**, **4,** or **5**), the same products were generated during the reaction. For example, starting with **4**, 85% of **4** was converted to **3**, **5**, GlcNAc and ManNAc after 120 min in a ratio of 4.4:1.0:0.7:0.3,

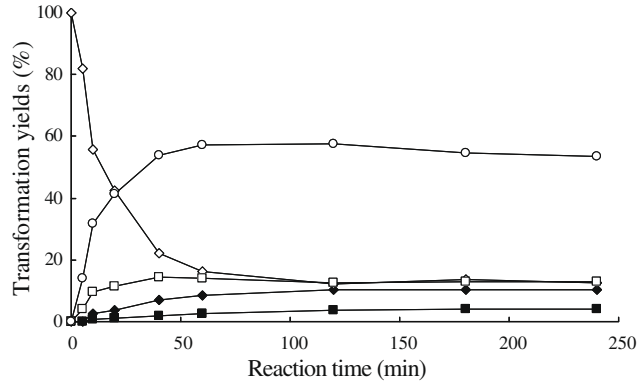
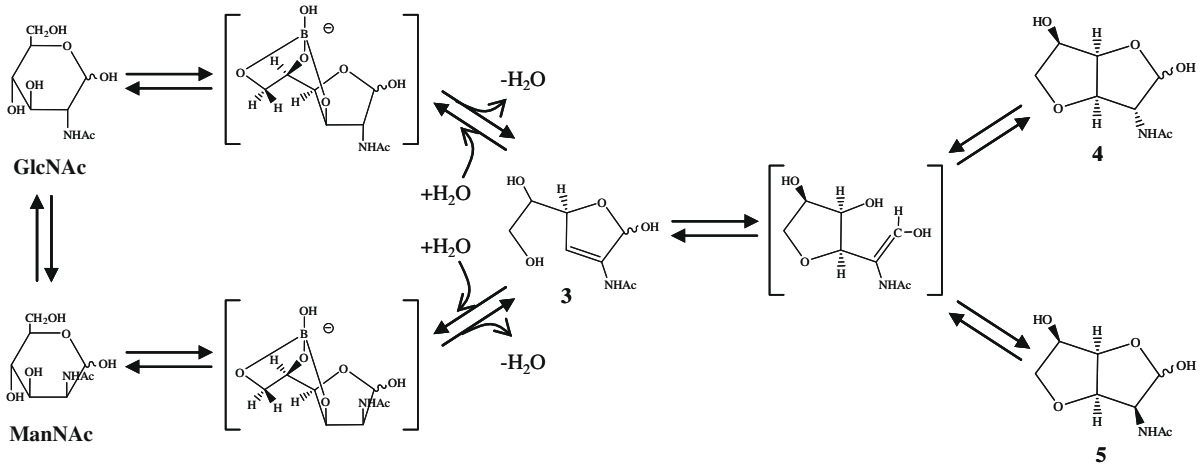


Figure 4. Time–course of products **3**, **5**, GlcNAc, and ManNAc on transformation in borate solution (pH 7.0) upon heating formed from **4**. Filled diamond, GlcNAc; filled square, ManNAc; open circle, **3**; open diamond, **4**; open square, **5**.



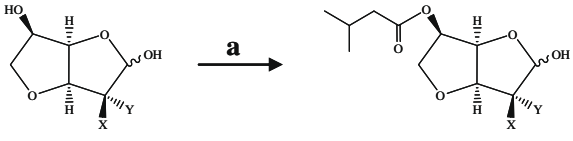
Scheme 1. Proposed mechanism of transformation of GlcNAc/ManNAc into **3**, **4**, and **5** in borate solution upon heating.

respectively, and their concentrations varied little after prolonged reaction (Fig. 4). These results suggest that the transformation of GlcNAc into **3**–**5** is a reversible reaction.

The present reaction is proposed to account for a series of hexofuranose transformations as shown in Scheme 1. Despite the complexity of the system, considerable attention has been focused on the reaction of borates with carbohydrates and boron.[14] Tridentate complexes with borate at 3-, 5-, and 6-hydroxyl groups of D-glucofuranose have been studied previously.[15] The formation of a borate complex from glucose might facilitate its conversion from the pyranose to the furanose form in borate solution upon heating. Indeed, formation of the complex facilitates abstraction of the 2-hydrogen substituent to give **3** followed by dehydration with one water molecule. The resulting **3** undergoes a ready epimerization to afford **4** and **5** in an equal amount, suggesting that they proceed through 2-enol as intermediate by consecutive electron displacement involving intramolecular attack of HO-6 at C-3 in **3**. Whichever compound was chosen (i.e., **3**–**5** or GlcNAc), the reaction profiles were indistinguishable in the equilibrium state. We therefore conclude that the GlcNAc transformation is a reversible reaction followed by consecutive dehydration and epimerization.

2.3. Syntheses of furanodictines A (1) and B (2)

The ability to generate large quantities of **4** and **5** facilitated the synthesis of furanodictines A and B. Compounds **4** and **5** were directly converted to furanodictines A (**1**) and B (**2**) as shown in Scheme 2. The C5 hydroxy group in **4** and **5** was regioselectively esterified with isovaleryl chloride in dry pyridine to complete the total synthesis of **1** and **2**, respectively. The target products **1** and **2** were purified by chromatography on silica gel and ODS column to give yields of 30% and 28%, respectively, based on the amount of **4** and **5**. The structures of these compounds were evaluated by ^{1}H and ^{13}C NMR analyses in $CDCl_3$ solution. In addition, HRESI-MS analysis of **1** and **2** showed molecular ions at *m/z* 310.12710 and 310.12707, respectively, arising from the $[M+Na]^+$ ions. Thus, the target products **1** and **2** were conveniently synthesized in only a two-step process. The spectral data of synthetic **1** and **2** were identical to those of the natural products.[1]



X = H, Y = NHAc (**4**) X = H, Y = NHAc: furanodictine A (**1**)
X = NHAc, Y = H (**5**) X = NHAc, Y = H: furanodictine B (**2**)

Scheme 2. Syntheses of furanodictines A and B. Reagents and conditions: (a) dry pyridine, isovaleryl chloride, 25 °C, 2 h, 30% (**1**), 28% (**2**).

3. Conclusions

In conclusion, a total synthesis of furanodictines A and B has been executed via a two-step process starting from readily available GlcNAc. Our process comprises a new synthetic strategy that does not necessitate protection/deprotection. As a result, a facile transformation of GlcNAc into **4** and **5** with a 3,6-anhydro hexofuranose carbon skeleton offers a promising approach towards the mass production of furanodictines A and B.

4. Experimental

4.1. General methods

GlcNAc and isovaleryl chloride were purchased from Sigma–Aldrich (St. Louis, MO). All other reagents were of the highest quality commercially available and were used without further purification.

4.2. Analytical methods

HPLC analysis was carried out using a Unison UK-Amino column (4.6 × 250 mm, Imtakt) with a JASCO Intelligent system liquid chromatograph and detection at 210 nm. The bound material was eluted with 95% CH_3CN at a flow rate of 1.0 mL/min at 40 °C. The ESI-MS spectra were measured on a JMS-T100LC mass spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-LA 500 spectrometer at 25 °C. Chemical shifts are expressed in δ relative to sodium 3-(trimethylsilyl) propionate as an external standard.

4.3. Transformation of GlcNAc into hexofuranoses

GlcNAc (5.52 g, 25 mmol) dissolved in 0.4 M borate buffer (pH 7.0, 250 mL) was incubated for 2 h at 100 °C. The mixture was then loaded onto a charcoal–Celite column (4.5 × 100 cm) equilibrated with distilled water. Subsequently, the adsorbed portion was eluted with a linear gradient of 0–25% ethanol in a total volume of 10 L, followed by 25% ethanol, at a flow rate of 4.7 mL/min. Fractions (60 mL/tube) were collected during the elution of material from the column. The chromatogram identified five distinct peaks.

Fractions corresponding to each of the five peaks, F-1 to F-5, were pooled, concentrated, and lyophilized. F-1 (fractions 73–86) contained 520 mg as a mixture of GlcNAc and ManNAc in a ratio of 2:1, respectively. F-3 (fractions 121–128) was obtained as 2-acetamido-3,6-anhydro-2-deoxy-D-mannofuranose (**5**, 495 mg, 9.8%), which was crystallized from ethanol;[9] α-anomer, mp 169–170 °C; $[\alpha]_D^{27}$ +151.5 (*c* 1.0, water); HRESIMS: *m/z* 226.06938 $[M+Na]^+$ (calcd for $C_8H_{13}N_1Na_1O_5$, 226.06914); ^1H NMR (D_2O, 500 MHz, the spectrum was measured after 2 h) α-anomer: δ 5.53 (d, 1H, $J_{1,2}$ = 5.5 Hz, H-1), 4.70 (t, 1H, $J_{3,4}$ = 5.5, $J_{4,5}$ = 5.5 Hz, H-4), 4.65–4.62 (1H, H-3), 4.42–4.38 (1H, H-5), 4.35 (t, 1H, $J_{1,2}$ = 5.5, $J_{2,3}$ = 5.5 Hz, H-2), 3.96–3.89 (2H, H-6b, H-6a), 2.07 (s, 3H, C*H*$_3$CONH–); β-anomer: δ 5.31 (d, 1H, $J_{1,2}$ = 6.0 Hz, H-1), 4.81 (t, 1H, $J_{3,4}$ = 4.6, $J_{4,5}$ = 4.6 Hz, H-4), 4.65–4.62 (1H, H-3), 4.42–4.38 (1H, H-5), 4.25 (t, 1H, $J_{1,2}$ = 6.0, $J_{2,3}$ = 6.0 Hz, H-2), 4.02 (dd, 1H, $J_{5,6b}$ = 6.7, $J_{6a,6b}$ = 8.4 Hz, H-6b), 3.55 (t, 1H, $J_{5,6a}$ = 8.4, $J_{6a,6b}$ = 8.4 Hz, H-6a), 2.05 (s, 3H, C*H*$_3$CONH–); ^{13}C NMR (D_2O, 125 MHz) α-anomer: δ 177.0 (CH$_3$*C*ONH–), 98.3 (C-1), 84.7 (C-4), 83.0 (C-3), 73.95 (C-5), 73.5 (C-6), 57.5 (C-2), 24.4 (*C*H$_3$CONH–); β-anomer: δ 177.2 (CH$_3$*C*ONH–), 103.7 (C-1), 83.5 (C-4), 82.7 (C-3), 74.3 (C-5), 73.90 (C-6), 61.8 (C-2), 24.5 (*C*H$_3$CONH–). F-4 (fractions 132 ∼ 139) was obtained as 2-acetamido-3,6-anhydro-2-deoxy-D-glucofuranose (**4**, 516 mg, 10.2%), which was crystallized from ethyl acetate. Compound **4** was a mixture of two anomers (α/β = 2/1); m.p. 124–125 °C; $[\alpha]_D^{27}$ +104.5 (*c* 1.0, water); HRESIMS: *m/z* 226.07013 $[M+Na]^+$ (calcd for $C_8H_{13}N_1Na_1O_5$, 226.06914); ^1H NMR (D_2O, 500 MHz) α-anomer: δ 5.62 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 4.76 (t, 1H, $J_{3,4}$ = 5.0, $J_{4,5}$ = 5.0 Hz, H-4), 4.66 (t, 1H, $J_{2,3}$ = 5.0, $J_{3,4}$ = 5.0 Hz, H-3), 4.33–4.29 (1H, H-5), 4.27 (t, 1H, $J_{1,2}$ = 5.0, $J_{2,3}$ = 5.0 Hz, H-2), 4.00 (dd, 1H, $J_{5,6b}$ = 6.5, $J_{6a,6b}$ = 8.5 Hz, H-6b), 3.66 (t, 1H, $J_{5,6a}$ = 8.5, $J_{6a,6b}$ = 8.5 Hz, H-6a), 2.06 (s, 3H, C*H*$_3$CONH–); β-anomer: δ 5.44 (1H, H-1), 4.79 (t, 1H, $J_{3,4}$ = 5.0, $J_{4,5}$ = 5.0 Hz, H-4), 4.52 (d, 1H, $J_{3,4}$ = 5.0 Hz, H-3), 4.33–4.29 (1H, H-5), 4.18 (1H, H-2), 3.96 (t, 1H, $J_{5,6b}$ = 8.0, $J_{6a,6b}$ = 8.0 Hz, H-6b), 3.88 (t, 1H, $J_{5,6a}$ = 8.0, $J_{6a,6b}$ = 8.0 Hz, H-6a), 2.02 (s, 3H, C*H*$_3$CONH–); ^{13}C NMR (D_2O, 125 MHz) α-anomer: δ 177.1 (CH$_3$*C*ONH–), 100.4 (C-1), 88.5 (C-3), 81.7 (C-4), 73.0 (C-5, C-6), 61.5 (C-2), 24.56 (*C*H$_3$CONH–); β-anomer: δ 176.8 (CH$_3$*C*ONH–), 105.2 (C-1), 88.6 (C-3), 85.6 (C-4), 73.8 (C-6), 73.5 (C-5), 64.7 (C-2), 24.60 (*C*H$_3$CONH–). F-5 (fractions 162–197) was obtained as Chromogen I (**3**) in the form of a syrupy liquid (1.8 g, 36%). Compound **3** was a mixture of two anomers (α/β = 1.6/1); $[\alpha]_D^{27}$ +14.8 (*c* 1.0, water); HRESIMS: *m/z* 226.06893 $[M+Na]^+$ (calcd for $C_8H_{13}N_1Na_1O_5$, 226.06914); ^1H NMR (D_2O, 500 MHz) α-anomer: δ 6.16 (1H, H-3), 6.04 (1H, H-1), 5.06 (1H, H-4), 3.83–3.57 (3H, H-5, H-6b, H-6a), 2.13 (s, 3H, C*H*$_3$CONH–); β-anomer: δ 6.21 (1H, H-3), 5.99 (1H, H-1), 4.83 (1H, H-4), 3.83–3.57 (3H, H-5, H-6b, H-6a), 2.13 (s, 3H, C*H*$_3$CONH–); ^{13}C NMR (D_2O, 125 MHz) α-anomer: δ 176.1 (CH$_3$*C*ONH–), 137.0 (C-2), 112.0 (C-3), 102.2 (C-1), 87.5 (C-4), 76.2 (C-5), 65.2 (C-6), 25.4 (*C*H$_3$CONH–); β-anomer: δ 176.1 (CH$_3$*C*ONH–), 136.5 (C-2), 112.7 (C-3), 102.0 (C-1), 87.2 (C-4), 76.5 (C-5), 65.1 (C-6), 25.4 (*C*H$_3$CONH–).

4.4. Syntheses of furanodictines A (1) and B (2)

Compound **4** (150 mg, 0.74 mmol) was dissolved in dry pyridine (5.0 mL) at 0 °C. Isovaleryl chloride (90 μL, 0.74 mmol) was added to the solution, and then the mixture was stirred magnetically for 2 h at room temperature. The reaction was terminated by adding crushed ice. After three extractions with $CHCl_3$, the organic layer was washed with saturated sodium bicarbonate solution, water and brine, and then dried over anhydrous sodium sulfate before being concentrated. The reaction products were dissolved in 1.0 mL of $CHCl_3$/MeOH = 27:1 and then loaded onto a Silica Gel 60 N column (2.0 × 40 cm). The column was developed with the same solvent at a flow rate of 10 mL/min and a fraction size of 15 mL/tube. An aliquot from fractions 36–50 was concentrated and dissolved in 1.0 mL of H_2O and then loaded onto a ODS column (1.5 × 30 cm). The bound compound was eluted with a linear gradient of 0–30% MeOH in a total volume of 1.2 L at a flow rate of 2.0 mL/min, and a fraction size of 15 mL/tube. Fractions 70–76 were pooled and concentrated. Furanodictine A (**1**) was obtained in a total yield of 30% (64 mg) as a colorless oil. Compound **1** was a mixture of two anomers (α/β = 6.8/1); R_f = 0.20 (EtOAc); $[\alpha]_D^{25}$ +116.3 (*c* 0.8, $CHCl_3$); HRESIMS: *m/z* 310.12710 $[M+Na]^+$ (calcd for $C_{13}H_{21}N_1Na_1O_6$, 310.12666); ^1H NMR ($CDCl_3$, 500 MHz) α-anomer: δ 6.40 (d, 1H, $J_{NH,2}$ = 7.5 Hz, NH), 5.50 (d, 1H, $J_{1,2}$ = 4.5 Hz, H-1), 4.95 (ddd, 1H, $J_{4,5}$ = 5.5, $J_{5,6a}$ = 8.0, $J_{5,6b}$ = 6.0 Hz, H-5), 4.84 (t, 1H, $J_{3,4}$ = 5.5, $J_{4,5}$ = 5.5 Hz, H-4), 4.52 (dd, 1H, $J_{2,3}$ = 4.0, $J_{3,4}$ = 5.5 Hz, H-3), 4.33 (m, 1H, H-2), 4.01 (dd, 1H, $J_{5,6b}$ = 6.0, $J_{6a,6b}$ = 9.0 Hz, H-6b), 3.77 (dd, 1H, $J_{5,6a}$ = 8.0, $J_{6a,6b}$ = 9.0 Hz, H-6a), 2.25–2.17 (2H, C*H*$_2$), 2.10–2.02 (1H, C*H*), 1.99 (s, 3H, C*H*$_3$CONH–), 0.92 (d, 6H, C*H*$_3$); β-anomer: δ 5.50 (br s, 1H, N*H*), 5.22 (br s, 1H, H-1), 5.04 (ddd, 1H, $J_{4,5}$ = 5.0, $J_{5,6a}$ = 6.0, $J_{5,6b}$ = 4.5 Hz, H-5), 4.87 (t, 1H, $J_{3,4}$ = 5.0, $J_{4,5}$ = 5.0 Hz, H-4), 4.38 (1H, H-3), 4.17 (m, 1H, H-2), 4.09 (dd, 1H, $J_{5,6b}$ = 4.5, $J_{6a,6b}$ = 9.5 Hz, H-6b), 3.89 (dd, 1H, $J_{5,6a}$ = 6.0, $J_{6a,6b}$ = 9.5 Hz, H-6a), 2.25–2.17 (2H, C*H*$_2$), 2.10–2.02 (1H, C*H*), 1.96 (s, 3H, C*H*$_3$CONH–), 0.92 (d, 6H, C*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) α-anomer: δ 172.6 (C′-1), 170.8 (CH$_3$*C*ONH–), 98.0 (C-1), 86.9 (C-3), 77.7 (C-4), 72.2 (C-5), 68.6 (C-6), 58.6 (C-2), 42.9 (C′-2), 25.6 (C′-3), 23.0 (*C*H$_3$CONH–), 22.3 (C′-4, C′-5); β-anomer: δ 172.8 (C′-1), 170.6 (CH$_3$*C*ONH–), 103.4 (C-1), 86.5 (C-3), 81.6 (C-4), 73.1 (C-5), 70.6 (C-6), 61.2 (C-2), 42.8 (C′-2), 25.4 (C′-3), 22.9 (*C*H$_3$CONH–), 22.3 (C′-4, C′-5). Furanodictine B (**2**) was obtained in a similar manner with a total yield of 28% (59 mg) as a colorless oil from compound **5** and isovaleryl chloride. Compound **2** was a mixture of two anomers (α/β = 1/2.5); R_f = 0.21 (EtOAc); $[\alpha]_D^{25}$ +103.9 (*c* 0.8, $CHCl_3$); HRESIMS: *m/z* 310.12707 $[M+Na]^+$ (calcd for $C_{13}H_{21}N_1Na_1O_6$, 310.12666); ^1H NMR ($CDCl_3$, 500 MHz) α-anomer: δ 6.16 (d, 1H, $J_{NH,2}$ = 7.5 Hz, N*H*), 5.17 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1), 5.10 (td, 1H, $J_{4,5}$ = 5.0, $J_{5,6a}$ = 5.5, $J_{5,6b}$ = 5.5 Hz, H-5), 4.90 (t, 1H, $J_{3,4}$ = 5.0, $J_{4,5}$ = 5.0 Hz, H-4), 4.55 (dd, 1H, $J_{2,3}$ = 6.5, $J_{3,4}$ = 5.0 Hz, H-3), 4.15 (m, 1H, H-2), 4.00 (dd, 1H, $J_{5,6b}$ = 5.5, $J_{6a,6b}$ = 9.5 Hz, H-6b), 3.76 (dd, 1H, $J_{5,6a}$ = 5.5, $J_{6a,6b}$ = 9.5 Hz, H-6a), 2.25–2.16 (2H, C*H*$_2$), 2.09–2.01 (1H, C*H*), 1.98 (s, 3H, C*H*$_3$CONH–), 0.92–0.90 (6H, C*H*$_3$); β-anomer: δ6.16 (d, 1H, $J_{NH,2}$ = 7.5 Hz, N*H*), 5.32 (br s, 1H, H-1), 5.04 (td, 1H, $J_{4,5}$ = 5.5, $J_{5,6a}$ = 6.5, $J_{5,6b}$ = 6.5 Hz, H-5), 4.86 (dd, 1H, $J_{3,4}$ = 5.0, $J_{4,5}$ = 5.5 Hz, H-4), 4.47 (1H, H-3), 4.37 (m, 1H, H-2), 4.03 (dd, 1H, $J_{5,6b}$ = 6.5, $J_{6a,6b}$ = 9.0 Hz, H-6b), 3.92 (dd, 1H, $J_{5,6a}$ = 6.5, $J_{6a,6b}$ = 9.0 Hz, H-6a), 2.25–2.16 (2H, C*H*$_2$), 2.09–2.01 (1H, C*H*), 1.99 (s, 3H, C*H*$_3$CONH–), 0.92–0.90 (6H, C*H*$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) α-anomer: δ 172.2 (C′-1), 171.0 (CH$_3$*C*ONH–), 103.5 (C-1), 80.3 (C-3), 79.6 (C-4), 72.8 (C-5), 70.7 (C-6), 58.9 (C-2), 42.9 (C′-2), 25.6 (C′-3), 23.1 (*C*H$_3$CONH–), 22.3 (C′-4, C′-5); β-anomer: δ 172.3 (C′-1), 170.3 (CH$_3$*C*ONH–), 96.4 (C-1), 80.7 (C-3), 80.6 (C-4), 73.4 (C-5), 69.7 (C-6), 54.6 (C-2), 42.8 (C′-2), 25.5 (C′-3), 23.0 (*C*H$_3$CONH–), 22.3 (C′-4, C′-5).

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