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STEREOSELECTIVE SYNTHESIS OF 1,4-DIDEOXY-1,4-IMINO-L-LYXITOL AND 1,5-DIDEOXY-1,5-IMINO-D-RIBITOL

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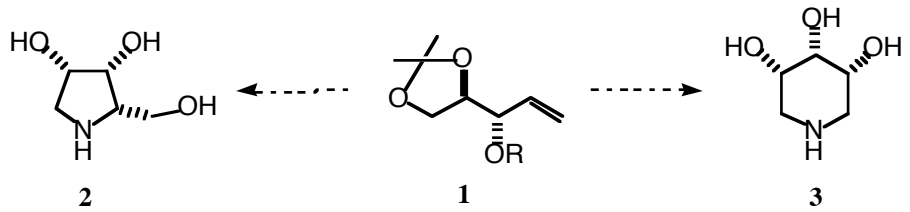
Abstract- 1,4-Dideoxy-1,4-imino-L-lyxitol (**2**) and 1,5-dideoxy-1,5-imino-D-ribitol (**3**) were prepared from allylic alcohol (**1**) derived from D-glucono-δ-lactone. Key transformation includes diastereoselective epoxidation of (**1**) with *m*-CPBA.

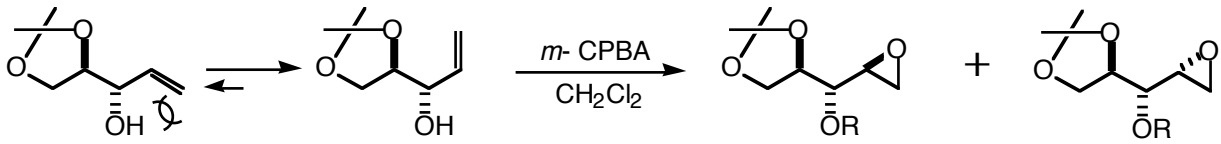
Interest in both natural and synthetic 1,4-dideoxy-1,4-iminopentitols has been increased by the findings that these type of compounds have potentials for type II diabetes, [1] cancers,[2] viral infection including HIV,[3] and hereditary lysosomal storage disease.[4] Because of their biological activities and diverse stereochemistry, many chemists have reported chiral synthesis of 1,4-dideoxy-1,4-imino derivatives of D-xylitol,[5] L-xylitol,[6] D-arabinitol,[7] L-arabinitol,[5a, 7a] D-ribitol,[8] L-ribitol,[9] and D-lyxitol[9a, 10] from carbohydrates. These methods, however, are limited to change stereochemistry of hydroxy group due to their fixed configuration. In this paper, we wish to report synthetic route for 1,4-dideoxy-1,4-imino-L-lyxitol (**2**) *via* stereoselective epoxidation of allylic alcohol (**1**) derived from D-glucono-δ-lactone. We



2 **1** **3**

also prepared 1,5-dideoxy-1,5-imino-D-ribitol (**3**) which will be expected a new glucosidase inhibitor because its C-3 epimer has inhibitory effect on sweet almond β-glucosidase.[11] As our chiral synthon we chose allylic alcohol (**1**) which supplies the complete C_5-unit and two chiral centers in final

polyhydroxylates (**2** and **3**). It also has allylic alcohol moiety which can be introduced necessary hydroxy group for compound (**2**) and (**3**) *via* diastereoselective epoxidation.



1 *anti* **4a** : R = H **5a** : R = MOM *syn* **4b** : R = H **5b** : R = MOM

Scheme 1

Table. Diastereoselective epoxidation of allylic alcohol (**1**) with *m*- CPBA

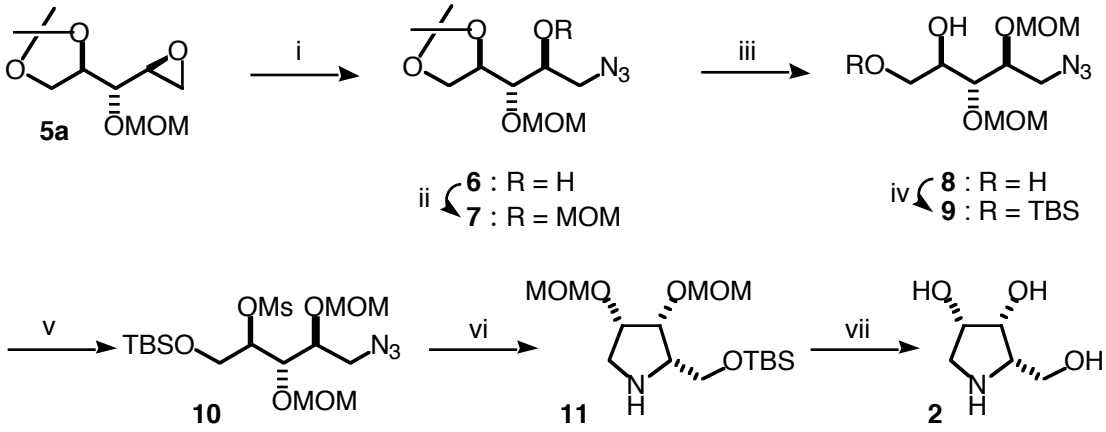
entry	temp (°C)	time (h)	yield (%)[a]	ratio (*anti* : *syn*)[b]
1	rt	5	96	1.3 : 1
2	0	24	87	1.8 : 1
3	-20	72	83	5 : 1
4	-40	72	52	5 : 1

[a] Isolated yield . [b]Ratio determined by ^{1}H NMR (500 MHz).

1,4-Dideoxy-1,4-imino-L-lyxitol (2)

The allylic alcohol (**1**) required for the preparation of our target compounds (**2**) and (**3**) were easily sythesized from D-glucono-δ-lacton as described.[12] Initially, when the Sharpless epoxidation[13] of allylic alcohol (**1**) using L-(+)-diethyl tartrate as the chiral auxiliary reagent was investigated, however, satisfatory result was not observed, with the starting material being recovered. Treatment of allylic alcohol (**1**) with *m*-chloroperbenzoic acid (*m*-CPBA) at room temperature for 5 h afforded a diastereomeric mixture (*anti*/*syn*, 1.3/1) of epoxy alcohol (**4**) in 96% yield. Treatment of allylic alcohol (**1**) with *m*-CPBA at –20 °C gave epoxy alcohol (**4**) as a 5:1 mixture of *anti* and *syn* isomers in 83% yield. These were separated after protection of the hydroxy group with methoxymethyl (MOM) group to the MOM ether (**5a**); $[\alpha]_D$ = +6.13° (c 2.00, $CHCl_3$), and (**5b**); $[\alpha]_D$ = +54.10° (c 1.00, $CHCl_3$) in 90% yield. The major isomer (**4a**) was assigned as *anti* configuration by converting into the target compound (**3**) (*vide infra*). The *anti*-selectivity observed in the conversion **1** to **4a** may be rationalized that hydroxy group of more favorable **1** exerts a directive effect on epoxidation according to Henbest rule.[14] The treatment of epoxide (**5a**) with sodium azide in presence of ammonium chloride took place leading to regiospecific ring opening to give azide (**6**) in 88% yield. This azido group had a crucial role in the synthetic sequence it provide the means to occur intramolecular amination. The resulting hydroxy group of azide (**6**) was converted to its methoxy methyl ether (**7**). The terminal isopropylidene group was cleaved by treatment with 70% acetic acid aqueous solution to give the corresponding diol (**8**) in 92%

yield. The primary alcohol of diol (**8**) was protected with TBSCl, and resulting alcohol (**9**) was reacted with MsCl in THF to give mesylate (**10**) in quantitative yield. Hydrogenolysis of (**10**) in the presence of

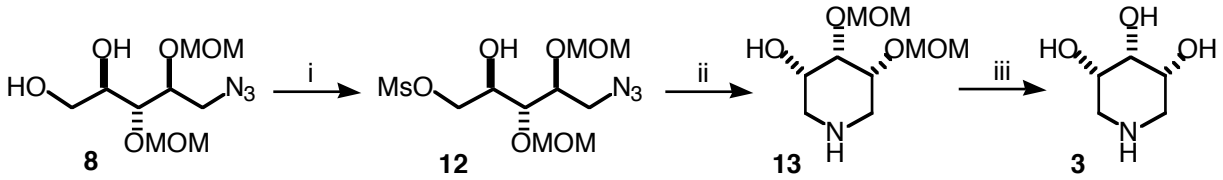


Scheme 2. i, NaN_3, NH_4Cl, MeOH/H_2O (8/1), reflux, 12 h; ii, MOMCl, *N*-ethyldiisopropylamine, CH_2Cl_2, 0 °C - rt, 12 h; iii, 70% AcOH, rt, 8 h; iv, TBDMSCl, Imidazole, DMF, rt, 10 min; v, MsCl, Et_3N, THF, 0 °C, 10 min; vi, H_2, 10% Pd/C, MeOH, 0.5 N NaOH, rt, 10 h; vii, Dowex 50W-X8, MeOH, reflux, 12 h.

palladium on charcoal and sodium hydroxide led to direct intramolecular nucleophilic amination to pyrrolidine ring (**11**) in 89% yield. The remaining acid sensitive groups were removed by treatment of compound (**11**) with Dowex 50W-X8 in 90% methanol to give the free base form of 1,4-dideoxy-1,4-imino-L-lyxitol (**2**) which was pure enough sample for HREIMS data without additional ion exchange chromatography.

1,5-Dideoxy-1,5-imino-D-ribitol (3)

We next intended to apply compound (**8**) to 1,5-dideoxy-imino-D-ribitol (**3**). Immediately, the primary hydroxy group of diol (**8**) was selectively mesylated by reaction of diol (**8**) with methanesulfonyl chloride in methylene chloride at –40 °C for 10 min to give mesylate (**12**) in 82% yield. The cyclization of mesylate (**12**) was accomplished under the same reaction condition for compound (**11**) to afford the corresponding piperidine (**13**) in 92% yield. 1,5-Dideoxy-1,5-imino-D-ribitol (**3**) was easily obtained by



Scheme 3. i, MsCl, Et_3N, CH_2Cl_2, -40 °C, 20 min; ii, H_2, Pd/C, MeOH, 0.5 N NaOH, rt, 9 h; iii, Dowex 50W-X8, MeOH, reflux, 12 h.

treatment of **13** with Dowex 50W-X8 in 90% MeOH in quantitative yield without additional ion exchange chromatography too. The stereochemistry of compound (**3**) was determined from it's ^1H and ^{13}C NMR spectra based on the chemical shift values (δ_H: 2.58, 2.64, 3.57, and 3.76; δ_c: 42.8, 65.8, and 68.0). Both spectra revealed the compound (**3**) to be *meso* compound. Therefore, stereochemistry of compound (**4a**)

has been deduced to be *anti*- isomer from the absolute stereochemistry of compound (**3**). As anticipated, the *meso* compound (**3**) was inactive: $[\alpha]_D$ = 0.00° (c 2.50, H_2O). In summary, we have achieved stereoselective synthesis of 1,4-dideoxy-1,4-imino-L-lyxitol (**2**) and 1,5-dideoxy-1,5-imino-D-ribitol (**3**) from allylic alcohol (**1**). This synthetic tool can be easily approached to the synthesis of diverse 1,4-dideoxy-1,4-iminopentitols.

EXPERIMENTAL

General. Dowex 50W-X8 was purchased from Sigma Chemical Co**.** All non-aqueous reactions were carried out under N_2 atmosphere. THF was distilled from Na/benzophenone; methanol was distilled from Mg; DMF and methylene dichloride were distilled from CaH_2. Column chromatography was carried out using 230-400 mesh silica gel. Final solution before evaporation was dried over anhydrous Na_2SO_4. Mps were measured on a Thomas-Hoover capillary apparatus and are uncorrected. IR spectra were recorded on Hitachi 270-50. NMR spectra were conducted on a Bruker AW-500 spectrometer. The chemical shifts are reported in ppm relative to internal tetramethylsilane in $CDCl_3$. HREIMS were obtained on a JEOL JMS–700 mass spectrometer. Optical rotaions were measured on a JASCO DIP-1000 polarimeter and $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2g^{-1}.

(*3S,4R*)-4,5-*O*-Isopropylidene-1-pentene-3,4,5-triol (1). This compound was prepared from D-glucono-δ-lactone according to a reported procedure.[12] Colorless oil, 70% yield. $[\alpha]_D^{28}$ = +1.70° (c 1.20, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.37 (s, 3H), 1.45 (s, 3H), 2.21 (m, 1H), 3.91 (dd, *J* = 6.7, 8.3 Hz, 1H), 3.96 (dd, *J* = 6.6, 8.3 Hz, 1H), 4.12 (ddd, *J* = 4.5, 6.6, 6.6 Hz, 1H), 4.29 (br, 1H), 5.24 (m, 1H), 5.39 (m, 1H), 5.84 (ddd, *J* = 5.5, 10.6, 17.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 25.1, 26.5 , 64.8, 71.9, 78.1, 109.5, 116.9, 135.8. Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.97; H, 8.52.

1,2-Anhydro-4,5-isopropylidene-D-ribitol (4). To a solution of *m*-chloroperbenzoic acid (*m*-CPBA, 57 – 86%) (9.74 g, 3.95 mol) in CH_2Cl_2 (40 mL) was added a solution of **1** (2.50 g, 15.80 mmol) in CH_2Cl_2 (20 mL) at –20 °C. The reaction mixture was stirred for 72 h at the same temperature, then was quenched with saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (100 mL × 2). The combined organic layers were washed with brine, dried, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane-EtOAc (6:1) as eluent to give mixture of **4** (*anti*/*syn* , 5/1) (1.58 g, 83%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.37 (s, 3H), 1.43 (s, 3H), 2.20 (s, 1H), 2.80 (m, 1H), 2.86 (m, 1H), 3.21 (m, 1H), 3.53 (m, 1H: *anti*) and 3.85 (m, 1H: *syn*), 4.00 (m, 1H), 4.11 (m, 2H).

1,2-Anhydro-4,5-isopropylidene-3-methoxymethyl-D-ribitol (5a) and (5b). To an ice-cooled solution of **4** (1.32 g, 7.67 mmol) in CH_2Cl_2 (40 mL) was added *N*-ethyldiisopropylamine (2.67 mL, 15.34 mmol). After being stirred for 5 min, MOMCl (1.17 mL, 15.34 mmol) was added and then the reaction mixture was stirred at rt for 12 h. The reaction mixture was quenched with saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (100 mL × 2). The combined organic layers were dried, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane-EtOAc (10:1) as eluent to give the compounds (**5a**) (1.25 g, 75%) and (**5b**) (0.26 g, 15%), respectively, as a colorless oil. **5a**; $[\alpha]_D^{29}$ = +6.13° (c 2.00, $CHCl_3$). IR (neat) ν_{max}: 2996, 1156, 1074, 1032. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.36 (s, 3H), 1.40 (s, 3H), 2.66 (dd, *J* = 2.7, 4.9 Hz, 1H), 2.85 (dd, *J* = 4.5, 4.6 Hz, 1H), 3.05 (ddd, *J* = 2.7, 4.5, 6.8 Hz, 1H), 3.32 (t, *J* = 6.8 Hz, 1H), 3.40 (s, 3H), 3.93 (dd, *J* = 5.7, 8.1 Hz, 1H), 4.11–4.19 (m, 2H), 4.68 (d, *J* = 6.6 Hz, 1H), 4.90 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 25.6, 26.9, 44.6, 53.1, 56.2, 67.2, 75.9, 78.9, 96.4, 109.9. Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.15; H, 8.52. **5b**; $[\alpha]_D^{20}$ = +54.10° (c, 1.00, $CHCl_3$). IR (neat) ν_{max}: 3000, 1158, 1080, 1032. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.36 (s, 3H), 1.40 (s, 3H), 2.66 (dd, *J* = 2.7, 4.9 Hz, 1H), 2.86 (t, *J* = 4.7 Hz, 1H), 3.05 (m, 1H), 3.32 (t, *J* = 6.7 Hz, 1H), 3.40 (s, 3H), 3.93 (dd, *J* = 5.6, 8.1 Hz, 1H), 4.12–4.18 (m, 2H), 4.68 (d, *J* = 6.6 Hz, 1H), 4.90 (d, *J* = 6.6 Hz, 1H). Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.38; H, 8.45.

1-Azido-4,5-*O*-isoprpylidene-3-methoxymethyl-1-deoxy-D-ribitol (6). To a mixed solution of **5a** (1.51 g, 6.90 mmol) in MeOH/H_2O (8/1, 23 mL) were added NaN_3 (2.24 g, 34.50 mmol) and NH_4Cl (0.81 g, 15.18 mmol). The reaction mixture was refluxed for 12 h, then was quenched with H_2O. The organic layer was separated, and the aqueous layer was extracted with EtOAc (70 mL × 3). The combined organic layers were washed with brine, dried, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane-EtOAc (8:1) as eluent to give the compound (**6**) (1.59 g, 88%) as a colorless oil. $[\alpha]_D^{29}$ = -4.70° (c 3.00, $CHCl_3$). IR (neat) ν_{max}: 3450, 2996, 2962, 2944, 2112 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.36 (s, 3H), 1.42 (s, 3H), 3.01(br, 1H), 3.40-3.47 (m, 5H), 3.66 (dd, *J* = 3.6, 6.4 Hz, 1H), 3.88 (m, 1H), 3.92 (dd, *J* = 6.4, 8.5 Hz, 1H), 4.11 (dd, *J* = 6.4, 8.4 Hz, 1H), 4.18 (dd, *J* = 6.4, 12.7 Hz, 1H), 4.71 (d, *J* = 6.7 Hz, 1H), 4.74 (d, *J* = 6.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 25.6, 26.8, 53.8, 56.5, 67.0, 71.6, 76.2, 79.5, 98.4, 109.8. Anal. Calcd for $C_{10}H_{19}N_3O_5$: C, 45.97; H, 7.33; N, 16.08. Found: C, 45.70; H, 7.42; N, 16.24.

1-Azido-2,3-*O*-dimethoxymethyl-4,5-*O*-isopropylidene-1-deoxy-D-ribitol (7). To an ice-cooled solution of **6** (1.59 g, 6.07 mmol) in CH_2Cl_2 (35 mL) was added *N*-ethyldiisopropylamine (2.11 mL, 12.14 mmol). After being stirred for 5 min, MOMCl (0.92 mL, 12.14 mmol) was added and then the reaction mixture

was stirred at rt for 12 h. The reaction mixture was quenched with saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (60 mL × 2). The combined organic layers were washed with brine, dried, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane-EtOAc (15:1) as eluent to give the compound (**7**) (1.82 g, 87%) as a colorless oil. $[\alpha]_D^{29}$ = +3.35° (c 2.50, $CHCl_3$). IR (neat) ν_{max}: 2996, 2962, 2944, 2109 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 1.35 (s, 3H), 1.40 (s, 3H), 3.40 (s, 3H), 3.43 (s, 3H), 3.50 (d, *J* = 6.3 Hz, 2H), 3.78 (dd, *J* = 6.3, 3.2 Hz, 1H), 3.88 (m, 1H), 3.98 (m, 1H), 4.08 (dd, *J* = 8.2, 6.4 Hz, 1H), 4.20 (dd, *J* = 6.4, 12.7 Hz, 1H), 4.75 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 2.3, 26.6, 51.4, 56.1, 56.2, 66.6, 75.1, 76.6, 76.8, 77.1, 77.3, 78.3, 97.4, 98.2, 109.0. Anal. Calcd for $C_{12}H_{23}N_3O_6$: C, 47.20; H, 7.59; N, 13.76. Found: C, 47.38; H, 7.76; N, 13.82.

1-Azido-2,3-*O*-dimethoxymethyl-1-deoxy-D-ribitol (8). A solution of **7** (1.80 g, 5.90 mmol) in 70% AcOH (20 mL) was stirred at rt for 8 h. The reaction mixture was quenched with saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with EtOAc (80 mL × 3). The combined organic layers were washed with brine, dried, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane-EtOAc (1:1) as eluent to give the compound (**8**) (1.31 g, 92%) as a colorless oil. $[\alpha]_D^{30}$ = -0.54° (c 1.50, $CHCl_3$). IR (neat) ν_{max}: 3438, 2930, 2104 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.69 (br, 1H), 3.39-3.62 (m, 9H), 3.70-3.77 (m, 4H), 4.00 (m, 1H), 4.68-4.81 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 52.2, 56.6, 56.7, 63.4, 71.1, 77.6, 78.8, 98.2, 98.9. Anal. Calcd for $C_9H_{19}N_6O_3$: C, 39.26; H, 10.62; N, 15.26. Found: C, 39.45; H, 10.70; N, 15.41.

1-Azido-2,3-*O*-dimethoxymethyl-5-*O*-*tert*-butyldimethylsilyl-1-deoxy-D-ribitol (9). To a solution of **8** (0.60 g, 2.26 mmol) in DMF (15 mL) were added imidazole (0.38 g, 5.65 mmol) and TBDMSCl (0.85 g, 5.65 mmol) at rt. After being stirred for 10 min, the reaction mixture was quenched with saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with EtOAc (50 mL × 3). The combined organic layers were washed with brine, dried, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane-EtOAc (10:1) as eluent to give the compound (**9**) (0.81 g, 95%) as a colorless oil. $[\alpha]_D^{26}$ = +0.22° (c 2.00, $CHCl_3$). IR (neat) ν_{max}: 3488, 2932, 2858, 2103 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: -0.99 (s, 6H), 0.82 (s, 9H), 2.88 (d, *J* = 5.9 Hz, 1H), 3.31 (s, 3H), 3.34 (s, 3H), 3.47 (m, 2H), 3.62 (m, 3H), 3.72 (dd, *J* = 9.84, 3.62 Hz, 1H), 3.93 (m, 1H), 4.61 (m, 2H), 4.69 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: –5.0, -5.0, 18.7, 26.3, 52.5, 56.5, 56.6, 64.0, 71.0, 77.2, 79.5, 98.1, 98.8. Anal. Calcd for $C_{15}H_{33}N_3O_6Si$: C, 47.47; H, 8.76; N, 11.07. Found: C, 47.61; H, 8.88; N, 11.21.

1-Azido-2,3-*O*-dimethoxymethyl-4-*O*-methanesulfonyl-5-*O*-*tert*-butyldimethylsilyl-1-deoxy-D-ribitol (10). To a solution of **9** (0.61 g, 1.61 mmol) in THF (8 mL) were added Et_3N (0.45 mL, 3.22 mmol) and MsCl (0.25 mL, 3.22 mmol) at 0°C. After being stirred for 10 min, the reaction mixture was quenched with saturated sat. $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine, dried, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane-EtOAc (12:1) as eluent to give the compound (**10**) (0.64 g, 98%) as a colorless oil. $[\alpha]_D^{30}$ = +1.53° (c 1.30, $CHCl_3$). IR (neat) ν_{max}: 2950, 2105 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 0.01 (s, 6H), 0.81 (s, 9H), 3.00 (s, 3H), 3.33 (s, 3H), 3.34 (s, 3H), 3.48 (m, 2H), 3.78 (m, 2H), 3.91 (m, 2H), 4.67 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: -4.8, 19.0, 26.5, 39.4, 52.5, 56.8, 57.0, 62.7, 77.1, 77.3, 82.8, 98.3, 98.7. Anal. Calcd for $C_{16}H_{35}N_3O_8SSi$: C, 42.00; H, 7.71; N, 9.18. Found: C, 42.19; H7.95; N, 9.30.

3,4-*O*-Dimethoxymethyl-6-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy–1,4-imino-L-lyxitol (11). To a solution of **10** (0.58 g, 1.27 mmol) in MeOH (4 mL) was hydrogenated over 10% palladium on charcoal (60 mg) at atmospheric pressure for 8 h. Subsequently, 0.5N NaOH (1 mL) was added to the residue, and the reaction mixture was stirred at rt for 2 h. The reaction mixture was filtered, and then the filtrate was quenched with H_2O and added CH_2Cl_2/isopropyl alcohol (IPA). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2/IPA (2/1) (20 mL × 5). The combined layers were dried and, concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with CH_2Cl_2-IPA (6:1) as eluent to give the compound (**11**) (0.38 g, 89%) as a colorless oil. $[\alpha]_D^{25}$ = +3.55° (c 2.00, $CHCl_3$). IR (neat) ν_{max}: 3300, 2950 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: -0.01 (s, 6H), 0.84 (s, 9H), 2.33 (br, 1H), 2.82 (dd, *J* = 11.9, 3.0 Hz, 1H), 3.28 (m, 1H), 3.30-3.34 (m, 7H), 3.66 (dd, *J* = 9.9, 6.4 Hz, 1H), 3.72 (dd, *J* = 7.1, 9.9 Hz, 1H), 4.05 (dd, *J* = 1.5, 4.4 Hz, 1H), 4.08 (m, 1H), 4.62 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: -5.4, -5.3, 18.3, 25.9, 50.9, 55.5, 55.6, 61.7, 62.2, 80.9, 81.3, 95.7, 96.3. Anal. Calcd for $C_{15}H_{33}NO_5Si$: C, 53.70; H, 9.91; N, 4.17. Found: C, 53.95; H, 10.04; N, 4.40.

1,4-Dideoxy-1,4-imino-L-lyxitol (2) and its hydrochloride salt. To a solution of compound (**11**) (0.20 g, 0.60 mmol) in 90% MeOH (3 mL) was added Dowex 50W-X8 resin (0.10 g). After refluxing for 12 h, the reaction mixture was filtered, washed with MeOH (50 mL). The remaining residue was eluted with 3N NH_4OH. The ammoniacal solution was evaporated, then co-evaporated with toluene to give compound (**2**) (75 mg, 95%) as a crystal. mp 137-139 °C (H_2O/EtOH). ^1H NMR (500 MHz, D_2O) δ: 3.16 (d, *J* = 12.7 Hz, 1H), 3.60 (dd, *J* = 12.8, 4.8 Hz, 1H), 3.75 (m, 1H), 3.94 (dd, *J* = 11.7, 7.5 Hz, 1H), 4.05 (dd, *J* = 11.7, 5.7 Hz, 1H), 4.37 (m, 1H), 4.43 (m, 1H). ^{13}C NMR (125 MHz, D_2O) δ: 49.5, 57.6, 60.8, 74.5, 74.7.

HREIMS: [M^+] 133.0746 (calcd 133.0739 for $C_5H_{11}O_3N$), m/z (rel. int.): 133 (2), 116 (11), 102 (100), 84 (16), 73 (21), 60 (22), 55 (54).

To the free base was added conc. HCl. The mixture was evaporated, then co-evaporated with toluene. The crystalline residue was recrystallized from methanol/ether to afford compound (**2**) as its hydro chloride salt. Spectra data were consistent with those reported,[15] $[\alpha]_D^{25}$ = -18.30° (c 0.60, H_2O) {lit.,[16] $[\alpha]_D$ = -17.20° (c 0.40, H_2O)}.

1-Azido-2,3-*O*-dimethoxymethyl-5-*O*-methanesulfonyl-1-deoxy-D-ribitol (12). To a solution of **8** (0.60 g, 2.26 mmol) in CH_2Cl_2 (10 mL) were added Et_3N (0.47 mL, 3.39 mmol) and MsCl (0.26 mL, 3.39 mmol) at -40°C. After being stirred for 20 min, the reaction mixture was quenched with saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The combined organic layers were washed with brine, dried, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with hexane-EtOAc (2:1) as eluent to give the compound (**12**) (0.63 g, 82%) as a colorless oil. $[\alpha]_D^{23}$ = +13.39° (c 1.30, $CHCl_3$). IR (neat) ν_{max}: 3450, 2940, 2110 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 3.09 (s, 3H), 3.14 (s, 1H), 3.44 (s, 6H), 3.47 (dd, *J* = 13.1, 4.8 Hz, 1H), 3.62 (dd, *J* = 13.1, 3.6 Hz, 1H), 3.79 (dd, *J* = 6.3, 4.5 Hz, 1H), 3.89 (m, 1H), 4.13 (ddd, *J* = 3.2, 4.5, 7.4 Hz, 1H), 4.31 (dd, *J* = 11.0, 7.4 Hz, 1H), 4.43 (dd, *J* = 11.0, 3.2 Hz, 1H), 4.73 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 38.6, 52.4, 57.2, 57.3, 70.3, 71.9, 77.3, 80.9, 97.8, 99.0. Anal. Calcd for $C_{10}H_{21}N_3O_8S$: C, 34.98; H, 6.16; N, 12.24. Found: C, 34.57; H, 6.40; N, 12.53.

3,4-*O*-Dimethoxymethyl-1,5-dideoxy-1,5-imino-D-ribitol (13). To a solution of **12** (0.55 g, 1.60 mmol) in MeOH (6 mL) was hydrogenated over 10% palladium on charcoal (60 mg) at atmospheric pressure for 5 h. Subsequently, 0.5 N NaOH (1 mL) was added to the residue, and then the reaction mixture was stirred at rt for 4 h. The reaction mixture was filtered, and then the filtrate was quenched with H_2O and added CH_2Cl_2/IPA. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2/IPA (2/1) (30 mL × 5). The combined layers were dried, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel with CH_2Cl_2-IPA (3:1) to give the compound (**13**) (0.32 g, 92%) as a colorless oil. $[\alpha]_D^{25}$ = -4.38° (c 0.77, CH_3OH). IR (neat) ν_{max}: 3400, 3300, 2936, 1152, 1108, 1038 cm^{-1}. ^1H NMR (500 MHz, CD_3OD) δ: 2.69-2.86 (m, 4H), 3.31 (m, 1H), 3.39 (m, 6H), 3.65 (m, 2H), 4.70 (m, 4H). ^{13}C NMR (125 MHz, CD_3OD) δ: 56.2, 56.2, 56.3, 70.5, 75.9, 76.0, 96.9, 97.9, 98.1. Anal. Calcd for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61; N, 4.10. Found: C, 67.15; H, 5.90; N, 4.36.

1,5-Dideoxy-1,5-imino-D-ribitol (3). To a solution of compound (**13**) (0.20 g, 0.91 mmol) in 90% MeOH (4 mL) was added Dowex 50W-X8 resin (0.12 g). The reaction mixture was refluxed for 12 h. The

reaction mixture was filtered, washed with MeOH (50 mL). The remaining residue was eluted with 3 N NH_4OH. The ammoniacal solution was evaporated, then co-evaporated with toluene to give compound (**3**) (0.10 g, 92%) as crystal. mp 156-158 °C. $[\alpha]_D^{25}$ = 0.00° (c 2.50, H_2O). ^1H NMR (500 MHz, D_2O) δ: 2.58 (m, 2H), 2.64 (m, 2H), 3.57 (m, 2H), 3.76 (t, *J* = 2.7 Hz, 1H). ^{13}C NMR (125 MHz, D_2O) δ: 42.8, 65.8, 68.0. HREIMS: [M^+] 133.0742 (calcd 133.0739 for $C_5H_{11}O_3N$), m/z (rel. int.): 133 (39), 115 (38), 98 (19), 86 (19), 73 (100), 60 (46), 55 (11). Anal. Calcd for $C_5H_{11}NO_3$: C, 45.10; H, 8.33; N, 10.52. Found: C, 45.39; H, 8.67; N, 10.65.

To the free base was added conc. HCl. The mixture was evaporated, then co-evaporated with toluene. The crystalline residue was recrystallized from methanol/ether to afford compound (**3**) as its hydrochloride salt. Spectra data were consistent with those reported,[17] $[\alpha]_D^{25}$ = 0.00° (c 2.50, H_2O).

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REFFERENCES

1. B. L. Rhinehart, K. M. Robinson, P. S. Liu, A. J. Payne, M. E. Wheatley, and S. R. Wagner, *J. Pharmacol. Exptl. Therapeur.* **1987**, *241*, 915.
2. R. J. Bernacki and W. Korytnyk, *Cancer Metastasis Rev.*, **1985**, *4*, 81.
3. (a) R. A. Gruters, J. J. Neefjes, M. Tersmette, R. E. Y. de Goede, A. Tulp, H. G. Huisman, F. Miedema, and H. L. Ploegh, *Nature*, **1987**, *330*, 74. (b) L. Ratner, *AIDS Res. Hum. Retroviruses*, **1992**, *8*, 165.
4. (a) I. Cenci di Bello, P. Dorling, and B. Winchester, *Biochem. J.*, **1983**, *215*, 693. (b) F. M. Platt, G. R. Neises, R. A. Dwek, and T. D. Butters, *J. Biol. Chem.*, **1994**, *269*, 8362.
5. (a) D. W. C. Jones, R. J. Nash, E. A. Bell, and J. M. Williams, *Tetrahedron Lett.*, **1985**, *26*, 3125. (b) J. G. Buchanan, K. W. Lumbard, R. J. Sturgeon, D. K. Thompson, and R. H. Wightman, *J. Chem. Soc., Perkin Trans.* 1, **1990**, 699.
6. (a) A. Hosaka, S. Ichikawa, H. Shindo, and T. Sato, *Bull. Chem. Soc. Jpn.*, **1989**, *62*, 797. (b) N. Ikota, *Chem. Pharm. Bull.*, **1989**, *37*, 3399. (c) Q. Meng and M. Hesse, *Helv. Chim. Acta*, **1991**, *74*, 445.
7. (a) G. W. J. Fleet and P. W. Smith, *Tetrahedron*, **1986**, *42*, 5685. (b) T. Ziegler, A. Straub, and F. Effenberger, *Angew. Chem., Int. Ed. Engl.*, **1988**, *27*, 716. (c) G. W. J. Fleet and D. R. Witty, *Tetrahedron: Asymmtry,* **1990**, *1*, 119.
8. G. W. J. Fleet and J. C. Son, *Tetrahedron*, **1988**, *44*, 2637.
9. (a) H. Setoi, H, Kayakiri, H. Takeno, and M, Hashimoto, *Chem. Pharm. Bull.*, **1987**, *35*, 3995. (b) G. W. J. Fleet, J. C. Son, D. St. C. Green, I. Cenci di Bello, and B. Winchester, *Tetrahedron*, **1988**, *44*, 2649.
10. (a) G. N. Austin, P. D. Baird, G. W. J. Fleet, J. M. Peach, P. W. Smith, and D. J. Watkin, *Tetrahedron*, **1987**, *43*, 3095. (b) S.-Y. Han, P. A. Liddell, and M. M. Joullié, *Synth. Commun.*, **1988**, *18*, 275.
11. M. P. Dale, H. E. Ensley, K. Kern, K. A. R. Sastry, and L. D. Byers, *Biochemistry*, **1985**, *24*, 3530.
12. (a) A. V. R. Rao, E. R. Reddy, B. V. Joshi, and J. S. Yadav, *Tetrahedron Lett.*, **1987**, *28*, 6497. (b) A. Fürstner, *Tetrahedron Lett.*, **1990**, *31,* 3735.
13. T. Katsuki, A. W. M. Lee, P. Ma, V. S. Martin, S. Masamune, K. B. Sharpless, D. Tuddenham, and F. J. Walker, *J. Org. Chem.*, **1982**, *47*, 1373.
14. H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.,* **1957**, 1958.

15. A. Dureault, C. Greck, and J.-C. Depezay, *J. Carbohydr. Chem.*, **1990**, *9*, 121.
16. D. K. Thompson, C. N. Hubert, and R. H. Wightman, *Tetrahedron*, **1993**, *49*, 3827.
17. D.-K. Kim, G. Kim, and Y.-W. Kim, *J. Chem. Soc., Perkin Trans. 1*, **1996**. 803.