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β-SELECTIVE D-PSICOFURANOSYLATION OF PYRIMIDINE BASES AND THIOLS

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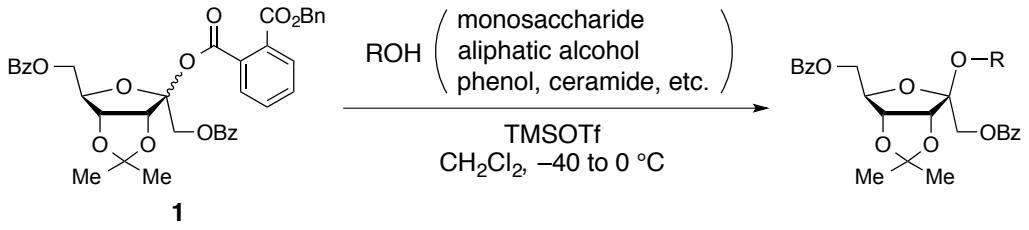
Abstract – *N*-Glycosidation of D-psicofuranosyl donor **1** with pyrimidine bases took place β-selectively in a β/α-ratio of 8:1 ~ 7:1. For *S*-glycosidation, 3,4-*O*-(3-pentylidene)-protected D-psicofuranosyl donor **15** was effective to increase β-selectivity up to 7:1.

INTRODUCTION

Rare sugars including L-glucose, L-ribose, D-allose, D-tagatose, and so on, attract many scientists by their unique properties.[1] D-Psicose is one of the D-hexuloses and is also categorized into rare sugar due to its rare occurrence in nature. D-Psicose and its analogs have shown a variety of biological activities regarding anti-oxidant,[2] inhibitors against α-glucosidase[3,4] and *N*-acetylglycosyltransferase,[5] and anti-tumor activities.[6] However, limited supply and expensive price restrict development of their use and research. In 1993, Izumori et al. have found the specific isomerase for the transformation of D-fructose to D-psicose.[7] After developing this finding, recent successful mass-production has provided large quantities of D-psicose commercially available.[8] Indeed, due to a specific property as a low-calorie sweetener, D-psicose attracts dietary patients[9a] and healthy consumers in food market to date.[9b] We have investigated *O*-glycosidation reactions of D-psicose[10,11] in which we reported the chemical synthesis of **1** from D-ribose,[10] and found an excellent β-selectivity of **1** as an efficient D-psicofuranosyl donor with wide-range of glycosyl acceptors, such as monosaccharide, aliphatic alcohol, phenol, ceramide, and so forth (Scheme 1).[11,12] In an extension of these studies, we report β-selective D-psicofuranosidation with pyrimidines and thiols, herein.

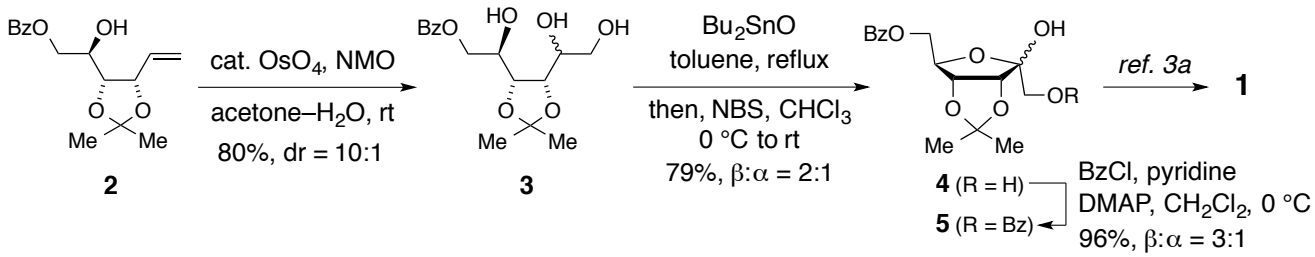
This paper is dedicated to Professor Kiyoshi Tomioka on the occasion of his 70th birthday.



Scheme 1. β-Selective *O*-glycosylation of D-psicofuranose

RESULTS AND DISCUSSION

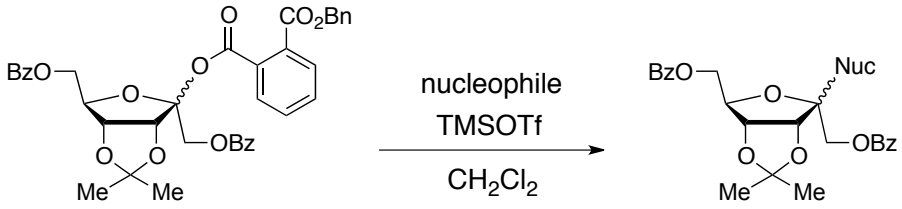
Preparation of **1** has been improved two step-shorter than the previous route[10] (Scheme 2). D-Ribose derivative **2**[10] was first dihydroxylated to a triol **3**, and one of the two secondary alcohols was oxidized selectively with the other intact under the conditions reported by Grindley et al.[13] Then, selective mono-benzoylation of the resultant D-psicose **4** gave **5** with a 3:1 ratio of anomeric isomers.



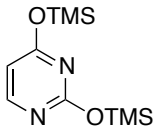
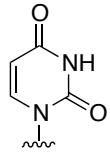
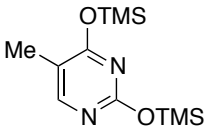
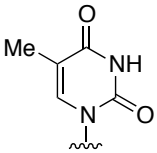
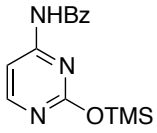
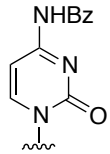
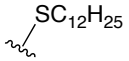
Scheme 2. Synthesis of glycosyl donor **1**

We first examined *N*-glycosylation of uracil with **1** by Vorbrüggen method[14] (Table 1, entry 1). *O*,*O'*-Bis(trimethylsilyl)uracil, generated in situ from uracil and *N*,*O*-bis-(trimethylsilyl)acetamide, was reacted with **1** using TMSOTf as a promoter to give 1-(D-psicofuranosyl)uracil **6** in 68% yield in a β/α-ratio of 7:1. *N*-Psicofuranosylation of thymine, and N^4-benzoylcytosine also gave *N*-glycosides **7** and **8** in 91% and 72% yields with a β/α-ratio of 8:1 and 7:1, respectively (entries 2 and 3).[15] On the other hand, poor selectivities (β/α = 3:1 ~ 2:1) were observed when thiophenol and 1-dodecanethiol were used as a glycosyl acceptor in *S*-psicofuranosidation (entries 4 and 5). This unsatisfied β-selectivity with thiol would arise from a size of glycosyl acceptor in primary thiol *vs* pyrimidine nucleobase.[16]

Table 1. Glycosylation of pyrimidines and thiols with D-psicofuranosyl donor **1**

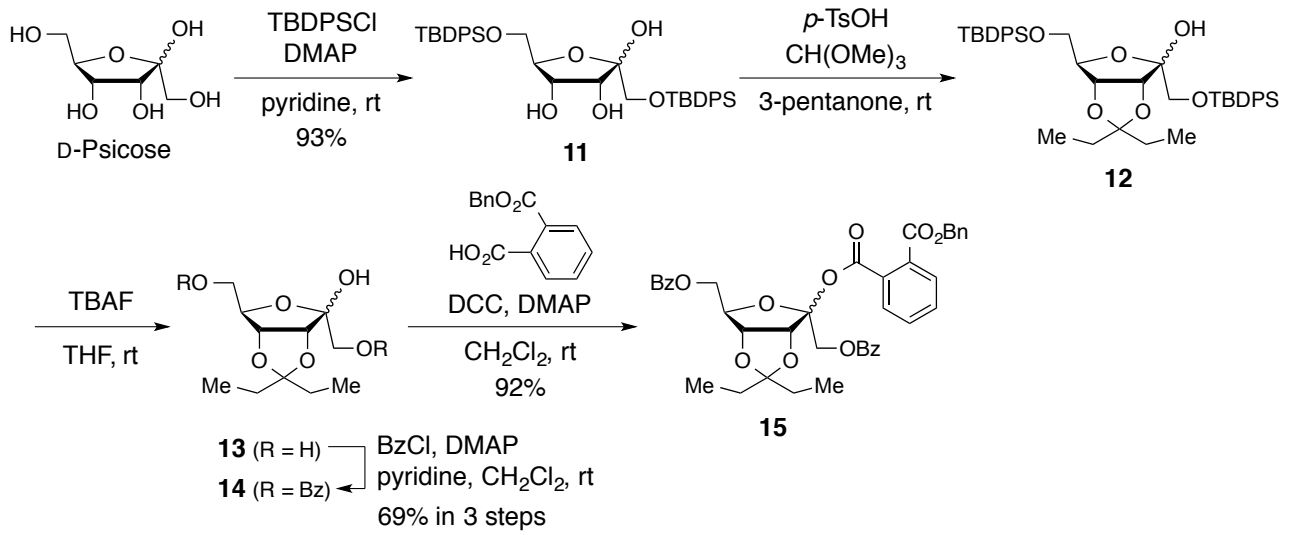


1 **6–10**

Entry[a]	Nucleophile	Product	Nuc	Temp. (°C)	Time	Yield (%)	β/α ratio
1		**6**		rt	1 d	68	7:1
2		**7**		rt	1 d	91	8:1
3		**8**		rt	2 d	72	7:1
4	HSPh	**9**		–40 to –20	20 min	79	3:1
5	$HSC_{12}H_{25}$	**10**		–40 to –20	20 min	83	2:1

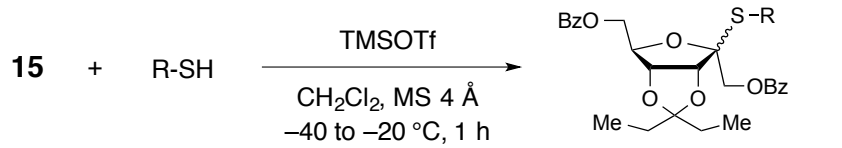
[a] Nucleophile (1.5 equiv) and TMSOTf (1.0 equiv) were used in CH_2Cl_2 (0.1 M).

The protecting group of 3,4-diol in **1** could play an important role for the facile formation of β-D-psicofuranoside. The acetonide group may prevent an access of the glycosyl acceptor from the α-side.[10,11] Based on this consideration, we used 3-pentylidene group in **15** as a larger glycosyl donor instead of acetonide. The synthesis from D-psicose is described in Scheme 3. First, primary alcohols of D-psicose were protected with TBDPSCl to give **11** in 93% yield. Then, protection of C-3/4-diol as 3-pentylidene group,[17] followed by the replacement of two *O*-TBDPS groups with *O*-benzoyl groups by desilylation and benzoylation processes gave psicofuranose **14** in 69% overall yield from **11** in three steps. Esterification of **14** with benzyl hydrogen phthalate by DCC provided **15** in 92% yield.[18]



Scheme 3. Synthesis of 3,4-*O*-(3-pentylidene)-protected glycosyl donor **15**

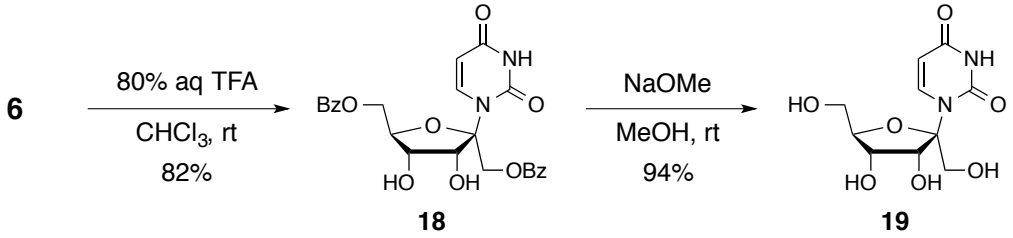
The glycosyl donor **15** was subjected to glycosidation with thiophenol. The thioglycoside **16** was obtained in 83% yield (Scheme 4).[19] The selectivity was improved to be 7:1 from 3:1 (β/α-ratio). β-Selectivity of the reaction with 1-dodecanethiol was also increased to 7:1 from 2:1. On the other hand, glycosidation employing **15** for uracil, thymine, and N^4-benzoylcytosine resulted in the similar β-selectivities described in Table 1 with **1**, albeit rather slower reaction rate.[20]



Scheme 4. *S*-Glycosidation of D-psicofuranosyl donor **15**

Deprotection of β-D-psicofuranoside was shown in Scheme 5. Treatment of uridine derivative **6** with aqueous trifluoroacetic acid (TFA) gave a diol **18** in 82% yield. Two *O*-benzoyl groups were removed under Zemplén's conditions to provide a psicouridine **19** in 94% yield.[21]

In conclusion, we have demonstrated β-selective *N*-psicofuranosylation of pyrimidine bases and *S*-psicofuranosylation of thiols. *N*-Glycosidation of **1** with uracil, thymine, and N^4-benzoylcytosine resulted in 8~7:1 ratio of β- and α-anomers. The modification of 3,4-*O*-protecting group to 3-pentylidene yielded increased the β-selectivities for *S*-glycosidation of psicofuranose **15** (β:α = 7:1). These results will be valuable for the synthesis of other *N*- and *S*-psicofuranoside derivatives.



Scheme 5. Deprotection of β-D-psicofuranoside **6**

EXPERIMENTAL

General information. Specific rotations were measured on a JASCO P-2200 or DIP-370 polarimeter using $CHCl_3$ or H_2O as a solvent. ^1H NMR and ^{13}C NMR spectra were measured on JEOL JNM-AL-300 (300 MHz and 75 MHz), Varian UNITY INOVA 400 NB (400 MHz) spectrometer, or Varian NMR System 500PS SN (500 MHz and 125 MHz). Chemical shifts (δ) are reported in parts per million (ppm) relative to the resonance of tetramethylsilane (0.00 ppm) for ^1H NMR spectra, and ppm relative to the resonance of the central peak of $CDCl_3$ (77.0 ppm) or to MeCN (1.47 ppm) when D_2O was used, for ^{13}C NMR spectra. IR spectra were recorded on a JASCO FT/IR-410 or Shimadzu IRAffinity-1 FT-IR spectrophotometer. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS 303HF spectrometer using fast atom bombardment (FAB) ionization in the dual focusing sector field mode or on a JEOL JMS-T100TD using electrospray ionization (ESI) or direct analysis in real time (DART) ionization in TOF mode. Silica gel (230–400 mesh) was used for flash column chromatography. Analytical thin-layer chromatography (TLC) was performed on glass pre-coated with silica gel (0.25 mm thickness). All moisture sensitive reactions were carried out under an argon atmosphere. THF was dried over sodium/benzophenone ketyl, and CH_2Cl_2 was dried over P_2O_5, and they were distilled prior to use.

General procedure for *N*-glycosidation:

A stirred solution of pyrimidine base (0.300 mmol) and *N,O*-bis(trimethylsilyl)acetamide (0.147 mL, 0.600 mmol) in MeCN (1.0 mL) was heated at reflux for 1 h. The reaction mixture was cooled to 0 °C and was added donor **1** or **15** (0.200 mmol) in CH_2Cl_2 (2.0 mL) and trimethylsilyl trifluoromethanesulfonate (TMSOTf, 36.2 μL, 0.200 mmol for **1** and 72.4 μL, 0.400 mmol for **15**). The reaction was stirred for the mentioned time at room temperature and quenched with satd. aq. $NaHCO_3$ solution. The aqueous layer was extracted with $CHCl_3$ and the combined organic layers were washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash column chromatography on silica gel eluted with EtOAc in *n*-hexane to give the desired *N*-glycoside.

General procedure for *S*-glycosidation:

The donor **1** or **15** (0.200 mmol) was azeotropically dried with toluene twice. Then, the above donor was

dissolved in CH_2Cl_2 (2.0 mL) and molecular sieves (MS) 4 Å (for **15** only, 100 mg) and thiol (0.300 mmol) were added to the solution. To this solution was added TMSOTf (36.2 μL, 0.200 mmol for **1** and 72.4 μL, 0.400 mmol for **15**) dropwise at –40 °C. The reaction mixture was warmed to –20 °C and stirred for the mentioned time. After completion of the reaction, the reaction mixture was quenched with Et_3N (0.1 or 0.2 mL) and warmed to room temperature. After filtration through a Celite pad and concentration under vacuum, the residue was purified by flash column chromatography on silica gel eluted with EtOAc in *n*-hexane to give the *S*-glycoside. Stereochemical assignments of anomeric position were performed by comparison with their structurally related β-D-psicofuranosides[10,11] (e.g., coupling constants of $J_{3,4}$ and $J_{4,5}$ values in ^{1}H NMR, chemical shifts of C2 in ^{13}C NMR, R_f values, etc.).

6-*O*-Benzoyl-3,4-*O*-isopropylidene-D-allitol and 6-*O*-benzoyl-3,4-*O*-isopropylidene-D-altritol (3): To a mixed solution of alkene **2**[10] (4.90 g, 16.8 mmol) in acetone and water (2:1, 34 mL) were added osmium tetroxide solution (4 wt. % in H_2O, 1.02 mL, 0.167 mmol) and 4-methylmorpholine *N*-oxide (2.95 g, 25.2 mmol) at room temperature and the reaction was vigorously stirred for 3 days at room temperature. The reaction mixture was quenched with satd. aq. $Na_2S_2O_3$ solution (100 mL) and stirred for 30 min. The reaction mixture was extracted with EtOAc (4 × 150 mL) and combined organic layers were washed with 1 M HCl, water, and brine (50 mL each), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluted with 65% EtOAc in *n*-hexane to give triol **3** (4.36 g, 80%) as a 10:1 diastereomeric mixture. Colorless oil. R_f = 0.28 for major isomer and 0.13 for minor isomer (60% EtOAc in *n*-hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ (major): 8.07–8.03 (2H, m), 7.58–7.51 (1H, m), 7.45–7.38 (2H, m), 4.71 (1H, d, *J* = 11.9 Hz), 4.61 (1H, br s), 4.46 (1H, br s), 4.39 (1H, dd, *J* = 11.9, 5.7 Hz), 4.23–4.09 (3H, m), 3.93–3.81 (2H, m), 3.72–3.65 (1H, m), 3.06 (1H, br s), 1.38 (3H, s), 1.31 (3H, s); δ (minor): 8.08–8.04 (2H, m), 7.61–7.55 (1H, m), 7.48–7.42 (2H, m), 4.71 (1H, dd, *J* = 11.5, 2.1 Hz), 4.41 (1H, dd, *J* = 11.5, 6.2 Hz), 4.37–4.30 (1H, m), 4.25 (1H, dd, *J* = 6.1, 2.6 Hz), 4.21–4.14 (1H, m), 4.14 (1H, dd, *J* = 9.4, 6.1 Hz), 3.82 (1H, dd, *J* = 11.3, 5.6 Hz), 3.76–3.69 (1H, m), 3.53 (1H, br s), 2.96 (1H, d, *J* = 7.5 Hz), 2.39 (1H, br s), 1.50 (3H, s), 1.37 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ (major): 167.3, 133.2, 129.7, 129.7, 128.4, 109.2, 77.3, 76.8, 69.5, 68.5, 67.1, 64.3, 27.9, 25.4. IR (film): 3406, 2987, 1721, 1452 cm^{-1}. HRMS (FAB) *m*/*z*: $[M+Na]^+$ calcd for $C_{16}H_{22}O_7Na$, 349.1263; found, 349.1266.

6-*O*-Benzoyl-3,4-*O*-isopropylidene-D-psicofuranose (4): A mixture of triol **3** (4.36 g, 13.4 mmol) and di-*n*-butyltin(IV) oxide (3.50 g, 14.1 mmol) in toluene (168 mL) was heated at reflux overnight with Dean-Stark apparatus attached to the reaction vessel, then cooled to ambient temperature and evaporated. The residue was dissolved in $CHCl_3$ (168 mL) and was added *N*-bromosuccinimide (2.51 g, 14.1 mmol)

at 0 °C. The reaction was stirred for 1 h at room temperature and the reaction mixture was quenched with satd. aq. $NaHCO_3$ solution (100 mL). The aqueous layer was extracted with EtOAc (3 × 200 mL) and combined organic layers were washed with water and brine (100 mL each), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel eluted with 35% EtOAc in *n*-hexane to give furanose **4** (3.40 g, 79%) as a 2:1 mixture of β- and α-anomers. Colorless oil. R_f = 0.44 (60% EtOAc in *n*-hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ (β-anomer)[22]: 8.07–8.01 (2H, m), 7.60–7.53 (1H, m), 7.47–7.41 (2H, m), 4.86 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 1.3 Hz, H-4), 4.68 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.61 (1H, dd, $J_{6a,6b}$ = 10.8, $J_{5,6a}$ = 6.8 Hz, H-6a), 4.56–4.40 (1H, m, H-5), 4.37 (1H, dd, $J_{6a,6b}$ = 10.8, $J_{5,6b}$ = 6.4 Hz, H-6b), 4.02 (1H, br s, 2-O*H*), 3.79 (2H, br s, H-1), 2.44 (1H, br s, 1-O*H*), 1.49 (3H, s), 1.34 (3H, s); δ (α-anomer)[22]: 8.07–8.01 (2H, m), 7.60–7.53 (1H, m), 7.47–7.41 (2H, m), 4.82 (1H, d, $J_{3,4}$ = 7.2 Hz, H-3), 4.74 (1H, dd, $J_{3,4}$ = 7.2, $J_{4,5}$ = 3.5 Hz, H-4), 4.56–4.40 (3H, m, H-5, 6a, 6b), 4.30 (1H, br s, 2-O*H*), 3.61 (2H, br s, H-1), 2.44 (1H, br s, 1-O*H*), 1.63 (3H, s), 1.41 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ (β-anomer)[22]: 166.6, 133.2, 129.7, 128.4, 113.1, 106.7, 85.3, 84.0, 82.6, 65.6, 64.8, 26.3, 24.9; δ (α-anomer)[22]: 166.4, 133.3, 129.6, 128.5, 115.8, 103.1, 81.3, 80.7, 80.3, 65.4, 64.3, 26.5, 24.9. IR (film): 3443, 2939, 1725, 1602 cm^{-1}. HRMS (FAB) *m*/*z*: $[M+Na]^+$ calcd for $C_{16}H_{20}O_7Na$, 347.1107; found, 347.1104.

1,6-Di-*O*-benzoyl-3,4-*O*-isopropylidene-D-psicofuranose (5): To a solution of furanose **4** (735 mg, 2.27 mmol) in CH_2Cl_2 (20 mL) were added triethylamine (0.947 mL, 6.81 mmol) and benzoyl chloride (0.525 mL, 4.54 mmol) at 0 °C and the reaction was stirred for 20 min at the same temperature. The reaction mixture was quenched with MeOH (1 mL) and stirred for 10 min at room temperature, then added satd. aq. $NaHCO_3$ solution (20 mL). The aqueous layer was extracted with EtOAc (3 × 20 mL) and combined organic layers were dried over anhydrous Na_2SO_4 and evaporated. The residue was purified by flash column chromatography on silica gel eluted with 15% EtOAc in *n*-hexane to give furanose **5** (936 mg, 96%) as a 3:1 mixture of β- and α-anomers. The spectroscopic data showed the same value as those reported previously.[10]

1-(1,6-*O*-Benzoyl-3,4-*O*-isopropylidene-β- and α-D-psicofuranosyl)uracil (6β and 6α): According to the general procedure for the *N*-glycosidation, a mixture of compounds **6β** and **6α** was obtained from **1** and uracil in 68% yield in a 7:1 ratio. White solid. Eluent for column: 50% EtOAc in *n*-hexane. R_f = 0.37 (60% EtOAc in *n*-hexane). ^{1}H NMR (400 MHz, C_6D_6–$CDCl_3$, 5:2) δ (β-anomer)[22]: 9.07 (1H, br s, N*H*), 7.93–7.79 (4H, m), 7.31 (1H, d, $J_{5,6}$ = 8.2 Hz, H-6), 7.23–7.01 (6H, m), 5.38 (1H, d, $J_{3',4'}$ = 6.0 Hz, H-3'), 5.21 (1H, d, $J_{5,6}$ = 8.4 Hz, H-5), 5.10 (1H, d, $J_{1'a,1'b}$ = 12.1 Hz, H-1'a), 4.86 (1H, d, $J_{1'a,1'b}$ = 12.1 Hz, H-1'b), 4.43 (1H, ddd, $J_{5',6'b}$ = 3.3, $J_{5',6'a}$ = 2.7, $J_{4',5'}$ = 1.5 Hz, H-5'), 4.40 (1H, dd, $J_{3',4'}$ = 6.0, $J_{4',5'}$ = 1.5

Hz, H-4'), 4.04 (1H, dd, $J_{6'a,6'b}$ = 12.4, $J_{5',6'a}$ = 2.7 Hz, H-6'a), 3.75 (1H, dd, $J_{6'a,6'b}$ = 12.4, $J_{5',6'b}$ = 3.3 Hz, H-6'b), 1.46 (3H, s), 1.15 (3H, s); δ (α-anomer)[22]: 9.33 (1H, br s, N*H*), 8.01–7.90 (4H, m), 7.34 (1H, d, $J_{5,6}$ = 8.2 Hz, H-6), 7.23–7.01 (6H, m), 5.44 (1H, d, $J_{5,6}$ = 8.2 Hz, H-5), 4.94 (1H, d, $J_{3',4'}$ = 5.7 Hz, H-3'), 4.84 (1H, d, $J_{1'a,1'b}$ = 11.7 Hz, H-1'a), 4.80 (1H, d, $J_{1'a,1'b}$ = 11.7 Hz, H-1'b), 4.45 (1H, dd, $J_{3',4'}$ = 5.7, $J_{4',5'}$ = 4.2 Hz, H-4'), 4.27–4.19 (3H, m, H-5', 6'a, 6'b), 1.18 (3H, s), 1.11 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ (β-anomer)[22]: 165.7, 165.6, 162.6, 150.0, 140.3, 133.9, 133.3, 129.6, 129.3, 129.0, 128.8, 128.7, 128.5, 114.0, 101.1, 99.8, 86.7, 83.8, 81.8, 65.0, 64.6, 25.9, 24.4. IR (KBr): 3448, 1726, 1686 cm^{-1}. HRMS (FAB) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{26}N_2O_9Na$, 545.1536; found, 545.1530.

1-(1,6-*O*-Benzoyl-3,4-*O*-isopropylidene-β- and α-D-psicofuranosyl)thymine (7β and 7α): According to the general procedure for the *N*-glycosidation, a mixture of compounds **7β** and **7α** was obtained from **1** and thymine in 91% yield in a 8:1 ratio. White solid. Eluent for column: 60% EtOAc in *n*-hexane. R_f = 0.41 (60% EtOAc in *n*-hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ (β-anomer)[22]: 7.87–7.35 (11H, m), 5.54 (1H, d, $J_{3',4'}$ = 6.2 Hz, H-3'), 4.98 (1H, dd, $J_{3',4'}$ = 6.2, $J_{4',5'}$ = 1.3 Hz, H-4'), 4.96 (1H, d, $J_{1'a,1'b}$ = 12.1 Hz, H-1'a), 4.87 (1H, ddd, $J_{5',6'b}$ = 3.1, $J_{5',6'a}$ = 2.8, $J_{4',5'}$ = 1.3 Hz, H-5'), 4.76 (1H, dd, $J_{6'a,6'b}$ = 12.6, $J_{5',6'a}$ = 2.8 Hz, H-6'a), 4.70 (1H, d, $J_{1'a,1'b}$ = 12.1 Hz, H-1'b), 4.27 (1H, dd, $J_{6'a,6'b}$ = 12.6, $J_{5',6'b}$ = 3.1 Hz, H-6'b), 1.68 (3H, s), 1.61 (3H, s), 1.45 (3H, s); δ (α-anomer)[22]: 8.29 (1H, br s, N*H*), 8.06–7.90 (4H, m), 7.64–7.50 (3H, m), 7.48–7.33 (4H, m), 5.20 (1H, d, *J* = 5.4 Hz), 5.03–4.83 (3H, m), 4.59–4.44 (3H, m), 1.97 (3H, s), 1.43 (3H, s), 1.38 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ (β-anomer)[22]: 165.5, 163.0, 149.9, 136.3, 134.0, 133.2, 129.6, 129.5, 129.4, 128.9, 128.7, 128.5, 128.4, 109.3, 99.7, 86.7, 83.9, 81.4, 65.1, 64.4, 25.9, 24.5, 12.0. IR (KBr): 2963, 1686 cm^{-1}. HRMS (FAB) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{28}N_2O_9Na$, 559.1693; found, 559.1686.

***N*^{4}-Benzoyl-1-(1,6-*O*-benzoyl-3,4-*O*-isopropylidene-β- and α-D-psicofuranosyl)cytosine (8β and 8α):** According to the general procedure for the *N*-glycosidation, a mixture of compounds **8β** and **8α** was obtained from **1** and N^4-benzoylcytosine in 72% yield in a 7:1 ratio. White solid. Eluent for column: 60% EtOAc in *n*-hexane. R_f = 0.18 (60% EtOAc in *n*-hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ (β-anomer)[22]: 8.75 (1H, br s, N*H*), 8.09 (1H, d, $J_{5,6}$ = 7.7 Hz, H-6), 7.97–7.28 (16H, m), 5.56 (1H, d, $J_{3',4'}$ = 6.1 Hz, H-3'), 5.03 (1H, d, $J_{1'a,1'b}$ = 11.9 Hz, H-1'a), 4.96 (1H, dd, $J_{3',4'}$ = 6.1, $J_{4',5'}$ = 1.0 Hz, H-4'), 4.90 (1H, ddd, $J_{5',6'b}$ = 2.9, $J_{5',6'a}$ = 2.4, $J_{4',5'}$ = 1.0 Hz, H-5'), 4.90 (1H, d, $J_{1'a,1'b}$ = 11.9 Hz, H-1'b), 4.67 (1H, dd, $J_{6'a,6'b}$ = 12.7, $J_{5',6'a}$ = 2.4 Hz, H-6'a), 4.33 (1H, dd, $J_{6'a,6'b}$ = 12.7, $J_{5',6'b}$ = 2.9 Hz, H-6'b), 1.70 (3H, s), 1.45 (3H, s); δ (α-anomer)[22]: 8.69 (1H, br s, N*H*), 8.16 (1H, d, $J_{5,6}$ = 7.6 Hz, H-6), 7.94–7.10 (16H, m), 5.29 (1H, d, *J* = 5.6 Hz), 5.06–4.78 (3H, m), 4.54–4.37 (3H, m), 1.27 (3H, s), 1.26 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ (β-anomer)[22]: 165.6, 165.4, 162.2, 145.1, 133.3, 133.1, 133.0, 129.5, 129.4, 129.1, 128.9, 128.4,

128.4, 127.5, 113.8, 100.4, 86.4, 83.9, 81.7, 64.8, 64.6, 25.9, 24.4. IR (KBr): 3423, 1720 cm^{-1}. HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{34}H_{31}N_3O_9Na$, 648.1958; found, 648.1978.

Phenyl 1,6-*O*-benzoyl-3,4-*O*-isopropylidene-2-thio-β- and α-D-psicofuranoside (9β and 9α): According to the general procedure for the *S*-glycosidation, a mixture of compounds **9β** and **9α** was obtained from **1** and thiophenol in 79% yield in a 3:1 ratio. Colorless oil. Eluent for column: 15% EtOAc in *n*-hexane. R_f = 0.33 for **9β** and 0.29 for **9α** (20% EtOAc in *n*-hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ (β-anomer)[22]: 8.14–8.10 (4H, m), 7.62–7.54 (4H, m), 7.49–7.45 (4H, m), 7.31–7.27 (1H, m), 7.24–7.19 (2H, m), 4.98 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 2.6 Hz, H-4), 4.85 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.79 (1H, dd, $J_{6a,6b}$ = 11.4, $J_{5,6a}$ = 6.6 Hz, H-6a), 4.77 (1H, dd, $J_{6a,6b}$ = 11.4, $J_{5,6b}$ = 7.0 Hz, H-6b), 4.66 (1H, ddd, $J_{5,6b}$ = 7.0, $J_{5,6a}$ = 6.6, $J_{4,5}$ = 2.6 Hz, H-5), 4.52 (1H, d, $J_{1a,1b}$ = 11.5 Hz, H-1a), 4.27 (1H, d, $J_{1a,1b}$ = 11.5 Hz, H-1b), 1.50 (3H, s), 1.35 (3H, s); δ (α-anomer)[22]: 8.05–8.03 (2H, m), 8.00–7.97 (2H, m), 7.61–7.53 (4H, m), 7.42–7.32 (5H, m), 7.30–7.26 (2H, m), 5.07 (1H, d, $J_{3,4}$ = 7.7 Hz, H-3), 4.89 (1H, ddd, $J_{5,6b}$ = 6.0, $J_{4,5}$ = 5.9, $J_{5,6a}$ = 3.3 Hz, H-5), 4.78 (1H, dd, $J_{3,4}$ = 7.7, $J_{4,5}$ = 5.9 Hz, H-4), 4.68 (1H, dd, $J_{6a,6b}$ = 12.1, $J_{5,6a}$ = 3.3 Hz, H-6a), 4.56 (1H, dd, $J_{6a,6b}$ = 12.1, $J_{5,6b}$ = 6.0 Hz, H-6b), 4.48 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1a), 4.24 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1b), 1.73 (3H, s), 1.41 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ (β-anomer)[22]: 166.2, 165.7, 135.5 (2C), 133.2, 133.0, 129.82 (2C), 129.80 (3C), 129.7, 129.6, 129.1, 128.9 (2C), 128.42 (2C), 128.37 (2C), 114.1, 97.6, 86.2, 85.0, 83.0, 64.8, 62.8, 26.5, 25.3; δ (α-anomer)[22]: 166.1, 165.8, 136.3 (2C), 133.2 (2C), 130.3, 130.0, 129.8, 129.7, 129.59 (2C), 129.57, 128.9, 128.7 (2C), 128.45 (2C), 128.42, 128.37, 117.7, 95.8, 83.6, 81.2, 79.9, 66.1, 63.7, 25.9, 25.4. IR (film): 3063, 2990, 2940, 1721 cm^{-1}. HRMS (DART) *m/z*: $[M+NH_4]^+$ calcd for $C_{29}H_{32}NO_7S$, 538.1900; found, 538.1921.

1-Dodecyl 1,6-*O*-benzoyl-3,4-*O*-isopropylidene-2-thio-β- and α-D-psicofuranoside (10β and 10α): According to the general procedure for the *S*-glycosidation, compounds **10β** and **10α** were obtained from **1** and 1-dodecanethiol in 56% and 27% yields, respectively. Eluent for column: 7% (**10β**) and 10% (**10α**) EtOAc in *n*-hexane. R_f = 0.52 for **10β** and 0.45 for **10α** (20% EtOAc in *n*-hexane). **10β**: Colorless oil. $[\alpha]^{17}_D$ –31.9 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.14–8.04 (4H, m), 7.63–7.53 (2H, m), 7.51–7.41 (4H, m), 4.96 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 2.2 Hz, H-4), 4.74 (1H, d, $J_{1a,1b}$ = 11.4 Hz, H-1a), 4.68 (1H, dd, $J_{6a,6b}$ = 10.7, $J_{5,6a}$ = 6.3 Hz, H-6a), 4.66 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.62 (1H, dd, $J_{6a,6b}$ = 10.7, $J_{5,6b}$ = 7.1 Hz, H-6b), 4.59 (1H, ddd, $J_{5,6b}$ = 7.1, $J_{5,6a}$ = 6.3, $J_{4,5}$ = 2.2 Hz, H-5), 4.53 (1H, d, $J_{1a,1b}$ = 11.4 Hz, H-1a), 2.73 (1H, dt, *J* = 11.8, 7.5 Hz, SC*H*H), 2.64 (1H, dt, *J* = 11.8, 7.6 Hz, SCH*H*), 1.53 (3H, s, OCC*H*$_3$), 1.52–1.45 (2H, m, SCH_2CH_2), 1.37 (3H, s, OCC*H*$_3$), 1.30–1.12 (18H, m), 0.88 (3H, t, *J* = 7.0 Hz, CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.1, 165.9, 133.2, 133.0, 130.1, 129.83 (2C), 129.75

(2C), 129.69, 128.4 (2C), 128.3 (2C), 113.9, 95.0, 86.5, 85.1, 83.3, 65.0, 63.2, 31.9, 29.61, 29.59, 29.50, 29.4, 29.3, 29.23, 29.20, 29.1, 28.0, 26.7, 25.4, 22.7, 14.1. IR (film): 2926, 2855, 1724 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{35}H_{48}O_7SNa$, 635.3018; found, 635.2991. **10α**: Colorless oil. R_f = 0.45 (20% EtOAc in *n*-hexane). $[\alpha]^{17}_D$ +53.3 (*c* 0.80, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ: 8.09–7.89 (4H, m), 7.62–7.48 (2H, m), 7.43–7.29 (4H, m), 5.01 (1H, d, $J_{3,4}$ = 7.6 Hz, H-3), 4.76 (1H, dd, $J_{3,4}$ = 7.6, $J_{4,5}$ = 5.1 Hz, H-4), 4.67 (1H, d, $J_{1a,1b}$ = 12.1 Hz, H-1a), 4.72–4.44 (3H, m, H-1b, 5, 6a), 4.51 (1H, dd, $J_{6a,6b}$ = 12.9, $J_{5,6b}$ = 5.9 Hz, H-6b), 2.78–2.58 (2H, m, SC*H*$_2$), 1.68 (3H, s, OCC*H*$_3$), 1.65–1.58 (2H, m, SCH_2CH_2), 1.38 (3H, s, OCC*H*$_3$), 1.44–1.21 (18H, m), 0.88 (3H, t, *J* = 6.8 Hz, CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.2, 165.9, 133.13, 133.07, 129.7, 129.62 (2C), 129.61 (2C), 129.5, 128.44 (2C), 128.38 (2C), 117.5, 94.2, 83.4, 81.1, 79.9, 66.2, 63.6, 31.9, 30.0, 29.64, 29.61, 29.58, 29.52, 29.3, 29.20, 29.17, 27.3, 25.7, 25.4, 22.7, 14.1. IR (film): 2926, 2855, 1724 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{35}H_{48}O_7SNa$, 635.3018; found, 635.3013.

1,6-Di-*O*-(*tert*-butyldiphenylsilyl)-D-psicofuranose (11): To a solution of D-psicose (1.00 g, 5.56 mmol) in pyridine (30 mL) were added *tert*-butyldiphenylchlorosilane (TBDPSCl; 4.34 mL, 16.7 mmol) and 4-(dimethylamino)pyridine (DMAP; 339 mg, 2.78 mmol) at room temperature and the reaction mixture was stirred at the same temperature for 24 h. The reaction mixture was quenched with 1 M HCl, extracted with EtOAc twice. Combined organic extracts were washed with water, satd. aq. $NaHCO_3$ solution, and brine. After drying over anhydrous $MgSO_4$ and evaporation of solvent, the residue was purified by flash column chromatography on silica gel eluted with 30% EtOAc in *n*-hexane to give silyl ether **11** (3.41 g, 93%). White amorphous solid. R_f = 0.36 (40% EtOAc in *n*-hexane). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.71–7.67 (2H, m), 7.67–7.63 (2H, m), 7.63–7.59 (4H, m), 7.43–7.37 (4H, m), 7.37–7.28 (8H, m), 4.22 (1H, br s, 2-O*H*), 4.25–4.16 (2H, m, H-4, 5), 4.03 (1H, dd, $J_{3,3\text{-OH}}$ = 7.6, $J_{3,4}$ = 5.6 Hz, H-3), 3.76 (1H, dd, $J_{6a,6b}$ = 11.0, $J_{5,6a}$ = 3.5 Hz, H-6a), 3.76 (2H, s, H-1), 3.69 (1H, dd, $J_{6a,6b}$ = 11.0, $J_{5,6b}$ = 4.7 Hz, H-6b), 3.07 (1H, d, $J_{3,3\text{-OH}}$ = 7.6 Hz, 3-O*H*), 2.84 (1H, d, $J_{4,4\text{-OH}}$ = 6.6 Hz, 4-O*H*), 1.06 (9H, s), 0.99 (9H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 135.54 (2C), 135.47 (6C), 132.9, 132.8, 132.6, 132.5, 129.87, 129.85, 129.81, 129.7, 127.79 (2C), 127.77 (2C), 127.75 (2C), 127.72 (2C), 102.8, 84.0, 72.5, 72.4, 66.7, 64.1, 26.8 (3C), 26.7 (3C), 19.2, 19.1. IR (KBr): 3449, 2932, 2869 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{38}H_{48}O_6Si_2Na$, 679.2887; found, 679.2895.

1,6-Di-*O*-benzoyl-3,4-*O*-(3-pentylidene)-D-psicofuranose (14): To triol **11** (2.40 g, 3.65 mmol) and trimethyl orthoformate (1.20 mL, 11.0 mmol) in 3-pentanone (12 mL) was added *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H_2O; 69.4 mg, 0.365 mmol) at room temperature and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was quenched by adding triethylamine (0.2 mL)

and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel eluted with 5% EtOAc in *n*-hexane to afford desired ketal **12** (R_f = 0.54 and 0.46 with 15% EtOAc in *n*-hexane) contaminated with its methyl glycoside **20** (R_f = 0.54 with 15% EtOAc in *n*-hexane). Fractions eluted with 7% EtOAc in *n*-hexane gave 2,3-*O*-(3-pentylidene) byproduct **21**[20] (~5%). The above product **12** was dissolved in THF (37 mL) and treated with tetrabutylammonium fluoride solution (1 M in THF, 14.6 mL, 14.6 mmol) at room temperature. The reaction mixture was stirred at room temperature for 1.5 h and quenched with $CaCO_3$ (3.0 g), Dowex 50W×8-400 (9.0 g), and MeOH[23] (21 mL) and further stirred at room temperature for 1 h. The resultant suspension was filtered through a Celite pad and concentrated under vacuum to give residue, which was passed through a short plug of silica gel eluted first with $CHCl_3$ (discarded) and then with 10% MeOH in EtOAc (collected). Removal of solvent provided a crude product **13** (contaminated with its methyl glycoside **22**), which was used for the next step without further purification. To a stirred solution of the above triol **13**, pyridine (8.86 mL, 110 mmol), and DMAP (224 mg, 1.83 mmol) in CH_2Cl_2 (37 mL) was added benzoyl chloride (4.24 mL, 36.5 mmol) dropwise at 0 °C, and the resultant mixture was stirred at 0 °C for 30 min. The reaction mixture was quenched by adding MeOH (8 mL) at 0 °C and stirred for 10 min at room temperature prior to the addition of water (10 mL). After removal of solvent, the residue was dissolved in EtOAc and 1 M HCl, and the aqueous layer was extracted with EtOAc twice. Combined organics were washed with water, satd. aq. $NaHCO_3$ solution, and brine. After drying over anhydrous $MgSO_4$ and concentration under vacuum, the residue was purified by flash column chromatography on silica gel (10% then 15% EtOAc in *n*-hexane) to afford benzoate **14** (1.15 g, 69% in 3 steps, α:β = 7:1) as a colorless oil. The methyl glycoside byproduct **23**[20] (~15%) was removed at this stage. **14**: R_f = 0.25 (20% EtOAc in *n*-hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ (β-anomer)[22]: 8.10–8.04 (4H, m), 7.59–7.51 (2H, m), 7.46–7.37 (4H, m), 4.87 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 1.5 Hz, H-4), 4.79 (1H, dd, $J_{6a,6b}$ = 11.4, $J_{5,6a}$ = 8.4 Hz, H-6a), 4.73 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.62 (1H, d, $J_{1a,1b}$ = 11.6 Hz, H-1a), 4.56 (1H, d, $J_{1a,1b}$ = 11.6 Hz, H-1b), 4.54 (1H, ddd, $J_{5,6a}$ = 8.4, $J_{5,6b}$ = 6.0, $J_{4,5}$ = 1.5 Hz, H-5), 4.32 (1H, dd, $J_{6a,6b}$ = 11.4, $J_{5,6b}$ = 6.0 Hz, H-6b), 4.20 (1H, s, OH), 1.80–1.66 (2H, m), 1.62 (2H, q, J = 7.5 Hz), 0.95 (3H, t, J = 7.5 Hz), 0.89 (3H, t, J = 7.5 Hz); δ (α-anomer)[22]: 8.04–8.00 (4H, m), 7.59–7.51 (2H, m), 7.46–7.37 (4H, m), 4.83–4.75 (2H, m), 4.56–4.45 (4H, m), 4.45 (1H, d, $J_{1a,1b}$ = 11.6 Hz, H-1a), 4.42 (1H, d, $J_{1a,1b}$ = 11.6 Hz, H-1b), 1.91–1.85 (2H, m), 1.71–1.66 (2H, m), 1.04 (3H, t, J = 7.5 Hz), 0.89 (3H, t, J = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ (β-anomer)[22]: 166.8, 166.5, 133.2, 133.1, 129.77 (2C), 129.76 (2C), 129.68, 129.63, 128.32 (2C), 128.26 (2C), 117.7, 106.1, 85.5, 85.0, 82.5, 65.92, 65.86, 29.4, 29.0, 8.3, 7.6; δ (α-anomer)[22]: 166.2, 165.9, 133.6–128.4 (12C), 120.8, 101.5, 81.2, 81.1, 79.9, 66.3, 64.1, 28.9, 28.7, 8.4, 7.9. IR (film): 3437, 2974, 2943, 1701 cm^{-1}. HRMS (DART) *m*/*z*: [M+H – H_2O]$^+$ calcd for $C_{25}H_{27}O_7$, 439.1757; found, 439.1764.

Benzyl [1,6-di-*O*-benzoyl-3,4-*O*-(3-pentylidene)-D-psicofuranosyl] phthalate (15): To a solution of alcohol **14** (235 mg, 0.515 mmol) and benzyl hydrogen phthalate (396 mg, 1.55 mmol) in CH_2Cl_2 (5 mL) were added *N*,*N'*-dicyclohexylcarbodiimide (319 mg, 1.55 mmol) and DMAP (62.8 mg, 0.515 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 24 h. The resultant suspension was diluted with CH_2Cl_2 and passed through a Celite pad (CH_2Cl_2). Combined organics were washed with 5% Na_2CO_3 aq and brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel eluted with 20% EtOAc in *n*-hexane to give the title compound **15** (330 mg, 92%, mostly β-anomer). Colorless syrup. R_f = 0.63 (10% Et_2O in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.09–8.03 (2H, m), 8.03–7.97 (2H, m), 7.83–7.76 (1H, m), 7.64–7.57 (1H, m), 7.56–7.49 (2H, m), 7.49–7.43 (2H, m), 7.42–7.27 (9H, m), 5.39 (1H, d, $J_{3,4}$ = 6.0 Hz, H-3), 5.31 (1H, d, J = 12.3 Hz, C*H*HPh), 5.26 (1H, d, J = 12.3 Hz, CH*H*Ph), 5.22 (1H, d, $J_{1a,1b}$ = 12.0 Hz, H-1a), 4.99 (1H, d, $J_{1a,1b}$ = 12.0 Hz, H-1b), 4.96 (1H, dd, $J_{3,4}$ = 6.0, $J_{4,5}$ = 1.9 Hz, H-4), 4.69 (1H, ddd, $J_{5,6a}$ = 7.0, $J_{5,6b}$ = 6.6, $J_{4,5}$ = 1.9 Hz, H-5), 4.42 (1H, dd, $J_{6a,6b}$ = 11.5, $J_{5,6a}$ = 7.0 Hz, H-6a), 4.37 (1H, dd, $J_{6a,6b}$ = 11.5, $J_{5,6b}$ = 6.6 Hz, H-6b), 1.88–1.72 (2H, m), 1.64 (2H, q, J = 7.5 Hz), 0.99 (3H, t, J = 7.5 Hz), 0.91 (3H, t, J = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.5, 166.2, 166.0, 165.8, 135.4, 133.05, 133.01, 132.98, 131.6, 130.9, 130.4, 129.9, 129.8 (2C), 129.7 (2C), 129.6, 129.4, 128.53, 128.51 (2C), 128.3 (5C), 128.20 (2C), 118.2, 112.5, 86.3, 84.9, 82.3, 67.4, 64.6, 63.2, 29.1, 28.9, 8.4, 7.8. IR (KBr): 2974, 2941, 1736, 1719 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{40}H_{38}O_{11}Na$, 717.2312; found, 717.2318.

Phenyl 1,6-*O*-benzoyl-3,4-*O*-(3-pentylidene)-2-thio-β- and α-D-psicofuranoside (16β and 16α): According to the general procedure for the *S*-glycosidation, a mixture of compounds **16β** and **16α** was obtained from **15** and thiophenol in 83% yield in a 7:1 ratio. Colorless oil. Eluent for column: 8% EtOAc in *n*-hexane. R_f = 0.38 for **16β** and 0.36 for **16α** (20% EtOAc in *n*-hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ (β-anomer)[22]: 8.16–8.08 (4H, m), 7.62–7.54 (4H, m), 7.50–7.44 (4H, m), 7.30–7.26 (1H, m), 7.23–7.17 (2H, m), 4.99 (1H, dd, $J_{3,4}$ = 6.0, $J_{4,5}$ = 2.6 Hz, H-4), 4.85 (1H, d, $J_{3,4}$ = 6.0 Hz, H-3), 4.84 (1H, dd, $J_{6a,6b}$ = 11.4, $J_{5,6a}$ = 6.7 Hz, H-6a), 4.81 (1H, dd, $J_{6a,6b}$ = 11.4, $J_{5,6b}$ = 7.3 Hz, H-6b), 4.68 (1H, ddd, $J_{5,6b}$ = 7.3, $J_{5,6a}$ = 6.7, $J_{4,5}$ = 2.6 Hz, H-5), 4.58 (1H, d, $J_{1a,1b}$ = 11.3 Hz, H-1a), 4.27 (1H, d, $J_{1a,1b}$ = 11.3 Hz, H-1b), 1.81–1.69 (2H, m), 1.61 (2H, q, J = 7.5 Hz), 0.93 (3H, t, J = 7.4 Hz), 0.85 (3H, t, J = 7.5 Hz); δ (α-anomer)[22]: 8.07–8.04 (2H, m), 8.00–7.97 (2H, m), 7.63–7.18 (11H, m), 5.05 (1H, d, $J_{3,4}$ = 7.6 Hz, H-3), 4.83–4.66 (3H, m, H-4, 5, 6a), 4.55 (1H, dd, $J_{6a,6b}$ = 12.1, $J_{5,6b}$ = 6.4 Hz, H-6b), 4.48 (1H, d, $J_{1a,1b}$ = 12.0 Hz, H-1a), 4.21 (1H, d, $J_{1a,1b}$ = 12.0 Hz, H-1b), 1.70–1.58 (4H, m), 0.95–0.83 (6H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ (β-anomer)[22]: 166.2, 165.6, 135.4 (2C), 133.2, 133.0, 130.0, 129.81 (2C), 129.79 (2C), 129.69, 129.61, 129.0, 128.9 (2C), 128.41 (2C), 128.37 (2C), 118.4, 98.0, 86.4, 85.6, 83.1, 65.1, 62.7, 29.2, 29.1, 8.3, 7.8; δ (α-anomer)[22]: 166.2, 165.7, 136.3 (2C), 133.2, 133.1, 130.4, 130.0–128.3

(13C), 122.1, 95.9, 83.9, 81.3, 79.6, 66.4, 63.8, 29.0, 28.9, 8.3, 7.8. IR (film): 2974, 1734 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+K]^+$ calcd for $C_{31}H_{32}O_7SK$, 587.1506; found, 587.1477.

1-Dodecyl 1,6-*O*-benzoyl-3,4-*O*-(3-pentylidene)-2-thio-β- and α-D-psicofuranoside (17β and 17α): According to the general procedure for the *S*-glycosidation, compounds **17β** and **17α** were obtained from **15** and 1-dodecanethiol in 63% and 9% yields, respectively. Eluent for column: 4% (**17β**) and 5% (**17α**) EtOAc in *n*-hexane. R_f = 0.57 for **17β** and 0.49 for **17α** (20% EtOAc in *n*-hexane). **17β**: Colorless syrup. $[\alpha]^{21}_D$ –21.5 (*c* 1.02, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.14–8.05 (4H, m), 7.62–7.53 (2H, m), 7.50–7.42 (4H, m), 4.95 (1H, dd, $J_{3,4}$ = 6.0, $J_{4,5}$ = 2.2 Hz, H-4), 4.76 (1H, d, $J_{1a,1b}$ = 11.3 Hz, H-1a), 4.68 (1H, dd, $J_{6a,6b}$ = 10.9, $J_{5,6a}$ = 6.7 Hz, H-6a), 4.65 (1H, dd, $J_{6a,6b}$ = 10.9, $J_{5,6b}$ = 7.0 Hz, H-6b), 4.65 (1H, d, $J_{3,4}$ = 6.0 Hz, H-3), 4.61 (1H, ddd, $J_{5,6b}$ = 7.0, $J_{5,6a}$ = 6.7, $J_{4,5}$ = 2.2 Hz, H-5), 4.55 (1H, d, $J_{1a,1b}$ = 11.3 Hz, H-1b), 2.73 (1H, dt, *J* = 11.7, 7.6 Hz), 2.64 (1H, dt, *J* = 11.7, 7.6 Hz), 1.84–1.69 (2H, m), 1.67–1.60 (2H, m), 1.53–1.43 (2H, m), 1.33–1.09 (18H, m), 0.96 (3H, t, *J* = 7.4 Hz), 0.88 (3H × 2, t, *J* = 7.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.2, 165.9, 133.2, 133.0, 130.1, 129.80 (2C), 129.76 (2C), 129.73, 128.38 (2C), 128.32 (2C), 118.1, 95.3, 86.6, 85.5, 83.4, 65.3, 63.3, 31.9, 29.61, 29.59, 29.49, 29.45, 29.32, 29.30, 29.22 (2C), 29.19, 29.12, 27.9, 22.7, 14.1, 8.3, 7.8. IR (film): 2926, 1724, 1452 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{37}H_{52}O_7SNa$, 663.3331; found, 663.3328. **17α**: Colorless syrup. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.05–7.94 (4H, m), 7.59–7.49 (2H, m), 7.42–7.30 (4H, m), 4.99 (1H, d, $J_{3,4}$ = 7.7 Hz, H-3), 4.72 (1H, dd, $J_{3,4}$ = 7.7, $J_{4,5}$ = 6.0 Hz, H-4), 4.66 (1H, d, $J_{1a,1b}$ = 12.0 Hz, H-1a), 4.64–4.57 (2H, m, H-1b, 6a), 4.57–4.53 (1H, m, H-5), 4.51 (1H, dd, $J_{6a,6b}$ = 11.4, $J_{5,6b}$ = 5.2 Hz, H-6b), 2.72–2.60 (2H, m), 1.95 (2H, q, *J* = 7.5 Hz), 1.70–1.58 (4H, m), 1.42–1.35 (2H, m), 1.32–1.23 (16H, m), 1.05 (3H, t, *J* = 7.5 Hz), 0.88 (3H, t, *J* = 7.7 Hz), 0.88 (3H, t, *J* = 6.6 Hz). HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{37}H_{52}O_7SNa$, 663.3331; found, 663.3358.

1-(1,6-*O*-Benzoyl-β- and α-D-psicofuranosyl)uracil (18β and 18α): A mixed solution of **6** (659 mg, 1.26 mmol) in $CHCl_3$ (8 mL) and 80% aq. trifluoroacetic acid (4.5 mL) was stirred overnight at room temperature. Satd. aq. $NaHCO_3$ was added to the reaction mixture, which was extracted with $CHCl_3$. The whole organic layer was washed with satd. aq. $NaHCO_3$ solution, water, and brine, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel eluted with 70% (for **18β**) to 90% (for **18α**) EtOAc in *n*-hexane to give **18β** (497 mg, 82%) along with **18α**. R_f = 0.37 for **18β** and 0.23 for **18α** (80% EtOAc in *n*-hexane). **18β**: White solid. Mp 82–83 °C. $[\alpha]^{16}_D$ –159.1 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.20 (1H, br s, N*H*), 7.98–7.89 (2H, m), 7.89–7.82 (2H, m), 7.73 (1H, d, $J_{5,6}$ = 8.3 Hz, H-6), 7.60–7.52 (2H, m), 7.47–7.36 (4H, m), 5.56 (1H, d, $J_{5,6}$ = 8.3 Hz, H-5), 4.97 (1H, d, $J_{3',4'}$ = 3.0 Hz, H-3'), 4.87 (1H, d, $J_{1'a,1'b}$ = 12.3 Hz, H-1'a), 4.81 (1H, dd,

$J_{4',OH}$ = 5.2, $J_{3',4'}$ = 3.0 Hz, H-4'), 4.77 (1H, d, $J_{1'a,1'b}$ = 12.3 Hz, H-1'b), 4.74 (1H, dd, $J_{6'a,6'b}$ = 11.6, $J_{5',6'a}$ = 3.5 Hz, H-6'a), 4.73–4.71 (1H, m, H-5'), 4.55 (1H, d, $J_{4',OH}$ = 5.2 Hz, 4'-O*H*), 4.36 (dd, $J_{6'a,6'b}$ = 11.6, $J_{5',6'b}$ = 1.9 Hz, 1H, H-6'b), 3.29 (1H, br s, 3'-O*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 165.8, 165.7, 163.2, 151.7, 141.0, 133.7, 133.4, 129.6 (2C), 129.2 (2C), 129.1, 129.0, 128.6 (2C), 128.5 (2C), 101.7, 98.4, 84.5, 77.7, 73.4, 64.6, 63.7. IR (KBr): 3437 (br), 2951, 2922, 1717, 1684 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{24}H_{22}N_2O_9Na$, 505.1223; found, 505.1226. **18α**: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.25 (1H, br s, N*H*), 7.99–7.94 (2H, m), 7.92–7.88 (2H, m), 7.82 (1H, d, $J_{5,6}$ = 8.3 Hz, H-6), 7.59–7.49 (2H, m), 7.43–7.38 (2H, m), 7.36–7.31 (2H, m), 5.81 (1H, d, $J_{5,6}$ = 8.3 Hz, H-5), 4.87–4.82 (1H, m), 4.80 (1H, dd, $J_{6'a,6'b}$ = 12.5, $J_{5',6'a}$ = 2.6 Hz, H-6'a), 4.69 (1H, d, $J_{1'a,1'b}$ = 11.6 Hz, H-1'a), 4.64 (1H, d, $J_{1'a,1'b}$ = 11.6 Hz, H-1'b), 4.46 (1H, dd, $J_{6'a,6'b}$ = 12.5, $J_{5',6'b}$ = 4.9 Hz, H-6'b), 4.42–4.32 (2H, m), 4.25 (1H, ddd, $J_{4',5'}$ = 9.1, $J_{5',6'b}$ = 4.8, $J_{5',6'a}$ = 2.6 Hz, H-5'), 3.15 (1H, d, *J* = 9.7 Hz, O*H*). HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{24}H_{22}N_2O_9Na$, 505.1223; found, 505.1230.

1-β-D-Psicofuranosyluracil (19): To a stirred solution of **18β** (51.5 mg, 0.107 mmol) in MeOH (2 mL) was added NaOMe (5 M in MeOH, 21.4 μL, 0.107 mmol) at room temperature and the reaction was stirred for 1 h at the same temperature. The crude product was purified by Amberlite FPC3500 column (H_2O) and lyophilized to give **19** (27.6 mg) in 94% yield. White solid. R_f = 0.28 (30% MeOH in $CHCl_3$). Mp 96–99 °C. $[\alpha]^{26}_D$ +2.7 (*c* 1.00, H_2O). ^{1}H NMR (500 MHz, CD_3OD) δ: 8.11 (1H, d, $J_{5,6}$ = 8.3 Hz, H-6), 5.61 (1H, d, $J_{5,6}$ = 8.3 Hz, H-5), 4.73 (1H, d, $J_{3',4'}$ = 5.0 Hz, H-3'), 4.59 (1H, br s, N*H*), 4.20 (1H, d, $J_{1'a,1'b}$ = 12.2 Hz, H-1'a), 4.14 (1H, ddd, $J_{4',5'}$ = 6.1, $J_{5',6'b}$ = 4.4, $J_{5',6'a}$ = 3.1 Hz, H-5'), 4.09 (1H, dd, $J_{4',5'}$ = 6.1, $J_{3',4'}$ = 5.0 Hz, H-4'), 3.93 (1H, d, $J_{1'a,1'b}$ = 12.2 Hz, H-1'b), 3.81 (1H, dd, $J_{6'a,6'b}$ = 12.3, $J_{5',6'a}$ = 3.1 Hz, H-6'a), 3.65 (1H, dd, $J_{6'a,6'b}$ = 12.4, $J_{5',6'b}$ = 4.4 Hz, H-6'b). ^{13}C NMR (125 MHz, D_2O) δ: 167.4, 152.0, 143.9, 100.9, 99.9, 84.8, 76.0, 70.6, 62.4, 61.1. IR (KBr): 3449, 1686, 1655 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{10}H_{14}N_2O_7Na$, 297.0699; found, 297.0684.

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REFERENCES AND NOTES

1. T. B. Granström, G. Takata, M. Tokuda, and K. Izumori, *J. Biosci. Bioeng.*, 2004, **97**, 89.
2. Y. Sun, S. Hayakawa, M. Ogawa, and K. Izumori, *Food Control*, 2007, **18**, 220.
3. T. Matsuo and K. Izumori, *Tech. Bull. Fac. Agr. Kagawa Univ.*, 2006, **58**, 27.
4. A. Hossain, F. Yamaguchi, T. Matsuo, I. Tsukamoto, Y. Toyoda, M. Ogawa, Y. Nagata, and M.

Tokuda, *Pharmacol. Ther.*, 2015, **155**, 49.

5. (a) M. Baráth, C.-H. Lin, I. Tvaroška, and J. Hirsch, *Chemical Papers*, 2015, **69**, 348; (b) M. Bella, S. Yan, S. Šesták, S. Kozmon, C.-H. Lin, J. Mucha, and M. Koóš, *Eur. J. Org. Chem.*, 2017, 6179.
6. W. Schroeder and H. Hoeksema, *J. Am. Chem. Soc.*, 1959, **81**, 1767.
7. K. Izumori, A. R. Khan, H. Okaya, and T. Tsumura, *Biosci., Biotechnol., Biochem.*, 1993, **57**, 1037.
8. (a) H. Itoh, T. Sato, and K. Izumori, *J. Ferment. Bioeng.*, 1995, **80**, 101; (b) K. Takeshita, A. Suga, G. Takada, and K. Izumori, *J. Biosci. Bioeng.*, 2000, **90**, 453.
9. (a) T. Matsuo, H. Suzuki, M. Hashiguchi, and K. Izumori, *J. Nutr. Sci. Vitaminol.*, 2002, **48**, 77; (b) N. Hayashi, T. Yamada, S. Takamine, T. Iida, K. Okuma, and M. Tokuda, *J. Funct. Foods*, 2014, **11**, 152.
10. J. Uenishi and A. Ueda, *Tetrahedron: Asymmetry,* 2008, **19**, 2210.
11. (a) A. Ueda, T. Yamashita, and J. Uenishi, *Carbohydr. Res.*, 2010, **345**, 1722; (b) A. Ueda, T. Yamashita, and J. Uenishi, *Heterocycles*, 2010, **81**, 1711; (c) S. Kamitori, A. Ueda, Y. Tahara, H. Yoshida, T. Ishii, and J. Uenishi, *Carbohydr. Res.*, 2011, **346**, 1182; (d) J. Uenishi and A. Ueda, *Heterocycles*, 2009, **77**, 1297.
12. Yamanoi et al. has studied stereochemistry of *O*-psicofuranosylation. (a) T. Yamanoi, T. Ishiyama, Y. Oda, S. Matsuda, and M. Watanabe, *Heterocycles*, 2010, **81**, 1141; (b) T. Yamanoi, Y. Oda, T. Ishiyama, and M. Watanabe, *Heterocycles*, 2016, **93**, 55.
13. X. Kong and B. Grindley, *J. Carbohydr. Chem.*, 1993, **12**, 557.
14. H. Vorbrüggen and K. Krolikiewicz, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 421.
15. Chattopadhyaya et al. reported the synthesis of oxetane-nucleosides *via N*-psicofuranosidation of nucleobases with varied anomeric selectivities. M. Bogucka, P. Naus, W. Pathmasiri, J. Barman, and J. Chattopadhyaya, *Org. Biomol. Chem.*, 2005, **3**, 4362.
16. Electronic character would also affect the selectivity, because *O*-psicofuranosidation of **1** with 1-pentadecanol gave the corresponding β-isomer exclusively.[20]
17. Protection of 2,3-diol using 3-pentylidene group in ribose; see, S. Hirano, S. Ichikawa, and A. Matsuda, *J. Org. Chem.*, 2007, **72**, 9936.
18. K. S. Kim, Y. J. Lee, H. Y. Kim, S. S. Kang, and S. Y. Kwon, *Org. Biomol. Chem.*, 2004, **2**, 2408.
19. The reaction in the absence of MS 4 Å also gave the same β/α ratio of 7:1 with decreased yield.
20. For details, see the Supporting Information.
21. G. Zemplén and E. Pacsu, *Ber. Dtsch. Chem. Ges.*, 1929, **62**, 1613.
22. Assignment was performed from the spectrum of anomeric mixture.
23. Y. Kaburagi and Y. Kishi, *Org. Lett.*, 2007, **9**, 723.