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-glucosidase3,4 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 patients9a and healthy consumers in food market to date.9b We have investigated O-glycosidation reactions of D-psicose10,11 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.
RESULTS AND DISCUSSION

Preparation of 1 has been improved two step-shorter than the previous route\textsuperscript{10} (Scheme 2). \(\text{D-Ribose derivative 2}\)\textsuperscript{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.\textsuperscript{13} Then, selective mono-benzoylation of the resultant D-psicose 4 gave 5 with a 3:1 ratio of anomeric isomers.

We first examined \(\text{N-glycosylation of uracil with 1 by Vorbrüggen method}\textsuperscript{14}\) (Table 1, entry 1). \(\text{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 \(\text{N}\text{-4-benzoylcytosine also gave N-glycosides 7 and 8 in 91\% and 72\% yields with a β/α-ratio of 8:1 and 7:1, respectively (entries 2 and 3).}\textsuperscript{15}\) 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 \(\text{S-psicofuranosidation (entries 4 and 5). This unsatisfied β-selectivity with thiol would arise from a size of glycosyl acceptor in primary thiol \textit{vs} pyrimidine nucleobase.}\textsuperscript{16}
Table 1. Glycosylation of pyrimidines and thiols with D-psicofuranosyl donor 1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Nucleophile</th>
<th>Product</th>
<th>Nuc</th>
<th>Temp. (°C)</th>
<th>Time</th>
<th>Yield (%)</th>
<th>β/α ratio</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>OTMS</td>
<td>6</td>
<td>N</td>
<td>rt</td>
<td>1 d</td>
<td>68</td>
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<td>Me</td>
<td>7</td>
<td>Me</td>
<td>rt</td>
<td>1 d</td>
<td>91</td>
<td>8:1</td>
</tr>
<tr>
<td>3</td>
<td>NHBz</td>
<td>8</td>
<td>N</td>
<td>rt</td>
<td>2 d</td>
<td>72</td>
<td>7:1</td>
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<tr>
<td>4</td>
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<td>9</td>
<td>N</td>
<td>–40 to –20</td>
<td>20 min</td>
<td>79</td>
<td>3:1</td>
</tr>
<tr>
<td>5</td>
<td>HSC_{12}H_{25}</td>
<td>10</td>
<td>N</td>
<td>–40 to –20</td>
<td>20 min</td>
<td>83</td>
<td>2:1</td>
</tr>
</tbody>
</table>

*a Nucleophile (1.5 equiv) and TMSOTf (1.0 equiv) were used in CH_{2}Cl_{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. 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 TBDPSCI to give 11 in 93% yield. Then, protection of C-3/4-diol as 3-pentylidene group, followed by the replacement of two O-TBDPS groups with O-benzyol 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.
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 N4-benzoylcytosine resulted in the similar β-selectivities described in Table 1 with 1, albeit rather slower reaction rate.20

\[
\begin{align*}
15 & \quad + \quad R-SH \\
\text{TMSOTf} & \quad \text{CH}_2\text{Cl}_2, \text{MS} 4 \, \text{Å} \\
\text{–40 to –20 °C, 1 h} & \quad 16 (R = \text{Ph}): 83\%, \beta:\alpha = 7:1 \\
& \quad 17 (R = \text{C}_{12}\text{H}_{25}): 72\%, \beta:\alpha = 7:1
\end{align*}
\]

**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 N4-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 CHCl₃ or H₂O as a solvent. ¹H NMR and ¹³C 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 CDCl₃ (77.0 ppm) or to MeCN (1.47 ppm) when D₂O was used, for ¹³C 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 CH₂Cl₂ was dried over P₂O₅, 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 CH₂Cl₂ (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. NaHCO₃ solution. The aqueous layer was extracted with CHCl₃ and the combined organic layers were washed with water and brine, dried (MgSO₄), 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$_2$Cl$_2$ (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$_3$N (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$_2$O, 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$_2$S$_2$O$_3$ 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$_2$SO$_4$, 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$_5$Na, 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. NaHCO₃ 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 Na₂SO₄ 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. Rᵋ = 0.44 (60% EtOAc in n-hexane). ¹H NMR (300 MHz, CDCl₃) 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, J₃,₄ = 5.9, J₄,₅ = 1.3 Hz, H-4), 4.68 (1H, d, J₃,₄ = 5.9 Hz, H-3), 4.61 (1H, dd, J₆ₐ,₆ₐ = 10.8, J₅,₆ₐ = 6.8 Hz, H-6a), 4.56−4.40 (1H, m, H-5), 4.37 (1H, dd, J₆ₐ,₆ₐ = 10.8, J₅,₆₆ = 6.4 Hz, H-6b), 4.02 (1H, br s, 2-OH), 3.79 (2H, br s, H-1), 2.44 (1H, br s, 1-OH), 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, J₃,₄ = 7.2 Hz, H-3), 4.74 (1H, dd, J₃,₄ = 7.2, J₄,₅ = 3.5 Hz, H-4), 4.56−4.40 (3H, m, H-5, 6a, 6b), 4.30 (1H, br s, 2-OH), 3.61 (2H, br s, H-1), 2.44 (1H, br s, 1-OH), 1.63 (3H, s), 1.41 (3H, s). ¹³C NMR (75 MHz, CDCl₃) 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 C₁₆H₂₀O₇Na, 347.1107; found, 347.1104.

1,6-Di-O-benzoyl-3,4-O-isopropylidene-β-D-psicofuranose (5): To a solution of furanose 4 (735 mg, 2.27 mmol) in CH₂Cl₂ (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. NaHCO₃ solution (20 mL). The aqueous layer was extracted with EtOAc (3 × 20 mL) and combined organic layers were dried over anhydrous Na₂SO₄ 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. Rᵋ = 0.37 (60% EtOAc in n-hexane). ¹H NMR (400 MHz, C₆D₆–CDCl₃, 5:2) δ (β-anomer) 22: 9.07 (1H, br s, NH), 7.93−7.79 (4H, m), 7.31 (1H, d, J₅,₆ = 8.2 Hz, H-6), 7.23−7.01 (6H, m), 5.38 (1H, d, J₃',₄' = 6.0 Hz, H-3'), 5.21 (1H, d, J₅,₆ = 8.4 Hz, H-5), 5.10 (1H, d, J₁',₄',₅' = 12.1 Hz, H-1'a), 4.86 (1H, d, J₁',₄',₅' = 12.1 Hz, H-1'b), 4.43 (1H, ddd, J₅',₆' = 3.3, J₅',₆' = 2.7, J₆',₅' = 1.5 Hz, H-5'), 4.40 (1H, dd, J₅',₄' = 6.0, J₆',₅' = 1.5
Hz, H-4'), 4.04 (1H, dd, J_{6',6''} = 12.4, J_{5',6''} = 2.7 Hz, H-6'a), 3.75 (1H, dd, J_{6',6''} = 12.4, J_{5',6''} = 3.3 Hz, H-6'b), 1.46 (3H, s), 1.15 (3H, s); δ (α-anomer)\(^{22}\): 9.33 (1H, br s, NH), 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_{3',4'} = 11.7 Hz, H-1'a), 4.80 (1H, d, J_{3',4'} = 11.7 Hz, H-1'b), 1.46 (3H, s), 1.15 (3H, s); 13C 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\(_2\)O\(_9\)Na, 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_{3',4'} = 6.2, J_{4',5'} = 1.3 Hz, H-1'a), 4.76 (1H, dd, J_{6',6''} = 12.6, J_{5',6''} = 2.8 Hz, H-6'a), 4.70 (1H, d, J_{3',4'} = 12.1 Hz, H-1'b), 4.27 (1H, dd, J_{6',6''} = 12.6, J_{5',6''} = 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, NH), 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); 13C 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\(_2\)O\(_9\)Na, 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, NH), 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_{3',4'} = 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''} = 2.9, J_{5',6''} = 2.4, J_{4',5'} = 1.0 Hz, H-5'), 4.90 (1H, d, J_{3',4'} = 11.9 Hz, H-1'b), 4.67 (1H, dd, J_{6',6''} = 12.7, J_{5',6''} = 2.4 Hz, H-6'a), 4.33 (1H, d, J_{6',6''} = 12.7, J_{5',6''} = 2.9 Hz, H-6'b), 1.70 (3H, s), 1.45 (3H, s); δ (α-anomer)\(^{22}\): 8.69 (1H, br s, NH), 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). 13C 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\(_3\)O\(_9\)Na, 648.1958; found, 648.1978.

**Phenyl 1,6-\(O\)-benzoyl-3,4-\(O\)-isopropylidene-2-thio-\(\alpha\)-\(\beta\)-psicofuranoside (9\(\beta\) and 9\(\alpha\)):**
According to the general procedure for the S-glycosidation, a mixture of compounds 9\(\beta\) and 9\(\alpha\) 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 9\(\beta\) and 0.29 for 9\(\alpha\) (20% EtOAc in \(n\)-hexane). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (\(\beta\)-anomer): \(^2\) 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); \(\delta\) (\(\alpha\)-anomer): 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\(_3\)) \(\delta\) (\(\beta\)-anomer): 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; \(\delta\) (\(\alpha\)-anomer): 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+Na]\(^+\) calcd for C\(_{29}\)H\(_{32}\)NO\(_8\)S, 538.1900; found, 538.1921.

**1-Dodecyl 1,6-\(O\)-benzoyl-3,4-\(O\)-isopropylidene-2-thio-\(\alpha\)-\(\beta\)-psicofuranoside (10\(\beta\) and 10\(\alpha\)):**
According to the general procedure for the S-glycosidation, compounds 10\(\beta\) and 10\(\alpha\) were obtained from 1 and 1-dodecanethiol in 56% and 27% yields, respectively. Eluent for column: 7% \(\alpha\) and 0.29 for 10\(\alpha\) (20% EtOAc in \(n\)-hexane). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 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, SCH\(_\beta\)), 2.64 (1H, dt, \(J = 11.8, 7.6\) Hz, SCH\(_\alpha\)), 1.53 (3H, s, OCCH\(_3\)), 1.52–1.45 (2H, m, SCH\(_2\)CH\(_2\)), 1.37 (3H, s, OCCH\(_3\)), 1.30–1.12 (18H, m), 0.88 (3H, t, \(J = 7.0\) Hz, CH\(_2\)CH\(_3\)). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): 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_{7}SNa, 635.3018; found, 635.2991. 10α: Colorless oil. R_f = 0.45 (20% EtOAc in n-hexane). [α]_D^{17} +53.3 (c 0.80, CHCl3). 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\_H2), 1.68 (3H, s, OCC\_H3), 1.65–1.58 (2H, m, SCH2\_C\_H2), 1.38 (3H, s, OCC\_H3), 1.44–1.21 (18H, m), 0.88 (3H, t, J = 6.8 Hz, CH2\_C\_H3). 13C 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_{7}SNa, 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-OH), 4.25–4.16 (2H, m, H-4, 5), 4.03 (1H, dd, J_{3,3-OH} = 7.6, J_{3,4} = 5.6 Hz, H-3), 3.76 (1H, dd, J_{6a,6b} = 11.0, J_{5,6b} = 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-OH} = 7.6 Hz, 3-OH), 2.84 (1H, d, J_{4,4-OH} = 6.6 Hz, 4-OH), 1.06 (9H, s), 0.99 (9H, s). 13C 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), 127.72 (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_{6}Si_{2}Na, 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). 1H 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). 13C 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$_2$Cl$_2$ (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$_2$Cl$_2$ and passed through a Celite pad (CH$_2$Cl$_2$). Combined organics were washed with 5% Na$_2$CO$_3$ 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$_2$O 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, $J_{1a,1b} = 12.0$ Hz, H-1), 5.26 (1H, d, $J_{1a,1b} = 12.0$ Hz, CH$_2$HPh), 5.22 (1H, d, $J_{1a,1b} = 12.0$ Hz, CH$_2$HPh), 4.99 (1H, d, $J_{1a,1b} = 11.3$ Hz, H-1a), 4.96 (1H, d, $J_{1a,1b} = 11.3$ Hz, H-1b), 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, 133.0 (2C), 133.0 (2C), 132.9 (2C), 132.0 (2C), 129.9 (2C), 129.8 (2C), 129.7 (2C), 129.6 (2C), 129.4 (2C), 128.5 (2C), 128.3 (2C), 128.2 (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]$^+$ calec 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): 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), 4.98 (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), 4.81 (1H, dd, $J_{6a,6b} = 11.4$, $J_{5,6a} = 6.7$ Hz, H-6a), 4.80 (1H, dd, $J_{6a,6b} = 11.4$, $J_{5,6b} = 7.3$ Hz, H-6b), 4.68 (1H, ddd, $J_{5,6b} = 7.3$, $J_{5,6b} = 6.7$, $J_{4,5} = 2.6$ Hz, H-5), 4.58 (1H, d, $J_{1a,1b} = 11.3$ Hz, H-1), 4.27 (1H, d, $J_{1a,1b} = 11.3$ Hz, H-1b), 1.81–1.69 (2H, m), 1.6 (2H, q, $J = 7.5$ Hz), 0.93 (3H, t, $J = 7.5$ Hz), 0.85 (3H, t, $J = 7.5$ Hz); δ (α-anomer): 8.07–8.04 (4H, m), 7.60–7.54 (4H, m), 7.45–7.39 (4H, 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-1), 1.70–1.58 (4H, m), 0.95–0.83 (6H, m). $^{13}$C NMR (125 MHz, CDCl$_3$) δ (β-anomer): 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): 166.2, 165.7, 136.3 (2C), 133.2, 133.1, 130.4, 130.0–128.3
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. Rf = 0.57 for 17β and 0.49 for 17α (20% EtOAc in n-hexane). 17β: Colorless syrup. [α]D 21 –21.5 (c 1.02, CHCl3). 1H NMR (500 MHz, CDCl3) δ: 8.14–8.05 (4H, m), 7.62–7.53 (2H, m), 7.50–7.42 (4H, m), 4.95 (1H, dd, J3,4 = 6.0, J4,5 = 2.2 Hz, H-4), 4.76 (1H, d, J1a,1b = 11.3 Hz, H-1a), 4.68 (1H, dd, J6a,6b = 10.9, J5,6a = 6.7 Hz, H-6a), 4.65 (1H, dd, J6a,6b = 10.9, J5,6b = 7.0 Hz, H-6b), 4.65 (1H, d, J3,4 = 6.0 Hz, H-3), 4.61 (1H, dd, J5,6b = 6.7, J4,5 = 2.2 Hz, H-5), 4.55 (1H, d, J1a,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). 13C NMR (125 MHz, CDCl3) 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 C37H52O7SNa, 663.3331; found, 663.3328.

17α: Colorless syrup. 1H NMR (500 MHz, CDCl3) δ: 8.05–7.94 (4H, m), 7.59–7.49 (2H, m), 7.42–7.30 (4H, m), 4.99 (1H, d, J3,4 = 7.7 Hz, H-3), 4.72 (1H, dd, J3,4 = 7.7, J4,5 = 6.0 Hz, H-4), 4.66 (1H, d, J1a,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, J6a,6b = 11.4, J5,6b = 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 C37H52O7SNa, 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 CHCl3 (8 mL) and 80% aq. trifluoroacetic acid (4.5 mL) was stirred overnight at room temperature. Satd. aq. NaHCO3 was added to the reaction mixture, which was extracted with CHCl3. The whole organic layer was washed with satd. aq. NaHCO3 solution, water, and brine, dried over MgSO4, 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. Rf = 0.37 for 18β and 0.23 for 18α (80% EtOAc in n-hexane). 18β: White solid. Mp 82–83 °C. [α]16D –159.1 (c 1.00, CHCl3). 1H NMR (500 MHz, CDCl3) δ: 9.20 (1H, br s, NH), 7.98–7.89 (2H, m), 7.89–7.82 (2H, m), 7.73 (1H, d, J5,6 = 8.3 Hz, H-6), 7.60–7.52 (2H, m), 7.47–7.36 (4H, m), 5.56 (1H, d, J5,6 = 8.3 Hz, H-5), 4.97 (1H, d, J3',4' = 3.0 Hz, H-3'), 4.87 (1H, d, J1'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’-OH), 4.36 (dd, $J_{6'a,6'b} = 11.6$, $J_{5',6'a} = 1.9$ Hz, 1H, H-6’b), 3.29 (1H, br s, 3’-OH).

$^{13}$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$_2$O$_9$Na, 505.1223; found, 505.1226.

$^{18}$α: $^1$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, $J_{4',5'} = 12.5$, $J_{6'a,6'b} = 4.8$, $J_{5',6'a} = 2.6$ Hz, H-5’), 3.15 (1H, d, $J = 9.7$ Hz, OH). HRMS (ESI) $m/z$: [M+Na$^+$] calcd for C$_{24}$H$_{22}$N$_2$O$_9$Na, 505.1223; found, 505.1230.

1-β-D-Psicofuranosyluracil (19): To a stirred solution of $^{18}$β (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$_2$O) 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. [α]$_{26}^D +2.7$ (c 1.00, H$_2$O). $^1$H NMR (500 MHz, CD$_3$OD) 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$_2$O) 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$_2$O$_7$Na, 297.0699; found, 297.0684.

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REFERENCES AND NOTES
4. A. Hossain, F. Yamaguchi, T. Matsuo, I. Tsukamoto, Y. Toyoda, M. Ogawa, Y. Nagata, and M.


16. Electronic character would also affect the selectivity, because O-psicofuranosidation of 1 with 1-pentadecanol gave the corresponding β-isomer exclusively.20


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.


22. Assignment was performed from the spectrum of anomeric mixture.