Supporting Information

β-SELECTIVE D-PSICOFURANOSYLATION OF PYRIMIDINE BASES AND THIOLS

Atsushi Ueda,[1,2] * Yuri Nishimura,[1] Yui Makura,[2] Masakazu Tanaka,[2] and

Jun'ichi Uenishi[1,3]

[1] Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto 607-8412, Japan
[2] Graduate School of Biomedical Sciences, Nagasaki University, 1-14 Bunkyo-machi, Nagasaki 852-8521, Japan.
[3] Graduate School of Pharmaceutical Sciences, Osaka University, Suita, Osaka 565-0871, Japan.

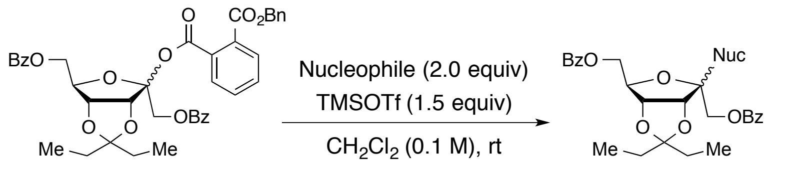
E-mail for A. Ueda: aueda@nagasaki-u.ac.jp

Table of Contents

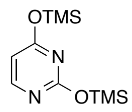
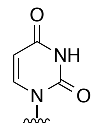
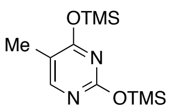
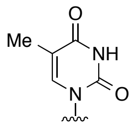
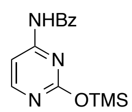
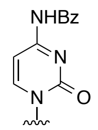
1. *N*-Glycosidation of D-psicofuranose **15** with pyrimidine bases ······ S2
2. Spectroscopic data of compounds **21** and **23** ······ S5
3. *O*-Glycosidation of D-psicofuranose **1** with 1-pentadecanol ······ S6

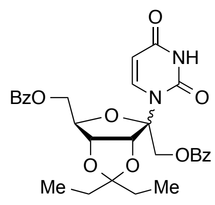
1. *N*-Glycosidation of D-psicofuranose 15 with pyrimidine bases

Table S1. *N*-Glycosidation of D-psicofuranose **15** with pyrimidine bases



15 **S-1–S-3**

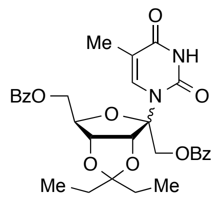
Entry	Nucleophile	Product	Nuc	Time (d)	Yield (%)	β/α ratio
1		**S-1**		1	57	8:1
2		**S-2**		1	46	9:1
3		**S-3**		2	56	8:1



S-1

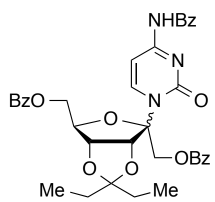
1-[1,6-*O*-Benzoyl-3,4-*O*-(3-pentylidene)-β- and α-D-psicofuranosyl]uracil (S-1β and S-1α): According to the general procedure for the *N*-glycosidation, a mixture of compounds **S-1β** and **S-1α** was obtained from **15** and uracil in 57% yield in a 8:1 ratio. Colorless syrup. Eluent for column: 40% EtOAc in *n*-hexane. R_f = 0.18 (40% EtOAc in *n*-hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ (β-anomer)[1]: 8.76 (1H, br s, N*H*), 7.90–7.86 (2H, m), 7.86–7.81 (2H, m), 7.67 (1H, d, $J_{5,6}$ = 8.3 Hz, H-6), 7.60–7.50 (2H, m), 7.46–7.35 (4H, m), 5.56 (1H, d, $J_{3',4'}$ = 6.4 Hz, H-3’), 5.47 (1H, dd, $J_{5,6}$ = 8.3, J = 1.9 Hz, H-5), 5.00 (1H, d, $J_{1'a,1'b}$ = 12.3 Hz, H-1’a), 4.92 (1H, dd, $J_{3',4'}$ = 6.4, $J_{4',5'}$ = 2.2 Hz, H-4’), 4.86 (1H, d, $J_{1'a,1'b}$ = 12.3 Hz, H-1’b), 4.85 (1H, ddd, $J_{5',6'b}$ = 3.7, $J_{5',6'a}$ = 2.7, $J_{4',5'}$ = 2.2 Hz, H-5’), 4.62 (1H, dd, $J_{6'a,6'b}$ = 12.7, $J_{5',6'a}$ = 2.7 Hz, H-6’a), 4.38 (1H, dd, $J_{6'a,6'b}$ = 12.7, $J_{5',6'b}$ = 3.7 Hz, H-6’b), 1.98–1.85 (2H, m), 1.75–1.65 (2H, m), 1.08 (3H, t, J = 7.5 Hz), 0.94 (3H, t, J = 7.5 Hz); δ (α-anomer)[1]: 8.98 (1H, br s, N*H*), 8.00–7.94 (2H, m), 7.94–7.90 (2H, m), 7.78 (1H, d, $J_{5,6}$ = 8.3 Hz, H-6), 7.60–7.50 (2H, m), 7.46–7.35 (4H, m), 5.77 (1H, d, $J_{5,6}$ = 8.3 Hz, H-5), 5.23 (1H, d, $J_{3',4'}$ = 6.0 Hz, H-3’), 4.90–4.82 (3H, m), 4.58–4.53 (2H, m), 4.49–4.43 (1H, m), 1.75–1.65

(4H, m), 0.90–0.82 (6H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ (β-anomer)[1]: 165.7, 165.6, 163.0, 150.1, 140.5, 133.8, 133.3, 129.5 (4C), 129.1 (2C), 128.7 (2C), 128.5 (2C), 118.7, 101.0, 99.8, 86.5, 84.4, 81.2, 64.45, 64.41, 28.6, 27.6, 8.6, 8.3. IR (film): 2978, 1715, 1683, 1452 cm^{-1}. HRMS (ESI) *m*/*z*: [M+Na]$^+$ calcd for $C_{29}H_{30}N_2O_9Na$, 573.1849; found, 573.1876.



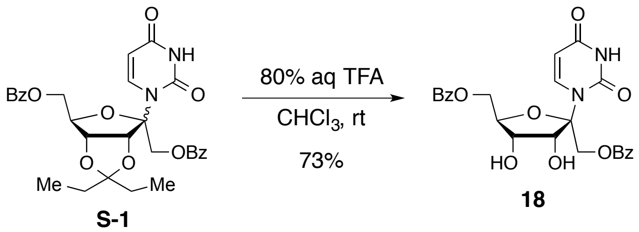
S-2

1-[1,6-*O*-Benzoyl-3,4-*O*-(3-pentylidene)-β- and α-D-psicofuranosyl]thymine (S-2β and S-2α): According to the general procedure for the *N*-glycosidation, a mixture of compounds **S-2β** and **S-2α** was obtained from **15** and thymine in 46% yield in a 9:1 ratio. Colorless syrup. Eluent for column: 40% EtOAc in *n*-hexane. R_f = 0.16 (40% EtOAc in *n*-hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ (β-anomer)[1]: 8.39–8.23 (1H, m, N*H*), 7.89–7.79 (4H, m), 7.63–7.49 (2H, m), 7.43 (1H, d, *J* = 1.2 Hz, H-6), 7.47–7.32 (4H, m), 5.62 (1H, d, $J_{3',4'}$ = 6.4 Hz, H-3'), 5.01 (1H, d, $J_{1'a,1'b}$ = 12.2 Hz, H-1'a), 4.95 (1H, dd, $J_{3',4'}$ = 6.4, $J_{4',5'}$ = 1.9 Hz, H-4'), 4.85 (1H, ddd, $J_{5',6'b}$ = 3.9, $J_{5',6'a}$ = 2.3, $J_{4',5'}$ = 1.9 Hz, H-5'), 4.82 (1H, d, $J_{1'a,1'b}$ = 12.2 Hz, H-1'b), 4.73 (1H, dd, $J_{6'a,6'b}$ = 12.6, $J_{5',6'a}$ = 2.3 Hz, H-6'a), 4.28 (1H, dd, $J_{6'a,6'b}$ = 12.6, $J_{5',6'b}$ = 3.9 Hz, H-6'b), 1.95–1.85 (2H, m), 1.77–1.61 (2H, m), 1.58 (3H, d, *J* = 1.2 Hz, 5-CH_3), 1.07 (3H, t, *J* = 7.5 Hz), 0.94 (3H, t, *J* = 7.5 Hz); δ (α-anomer)[1]: 8.62–8.49 (1H, m, N*H*), 8.01–7.96 (2H, m), 7.96–7.90 (2H, m), 7.63–7.49 (2H, m), 7.47–7.32 (5H, m), 5.23 (1H, d, $J_{3',4'}$ = 6.0 Hz, H-3'), 4.91 (1H, d, $J_{1'a,1'b}$ = 11.5 Hz, H-1'a), 4.88–4.81 (2H, m), 4.58–4.52 (2H, m), 4.50–4.44 (1H, m), 1.96 (3H, d, *J* = 1.2 Hz, 5-CH_3), 1.77–1.61 (4H, m), 0.90–0.81 (6H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ (β-anomer)[1]: 165.54, 165.50, 163.3, 150.1, 136.5, 133.9, 133.3, 129.5 (2C), 129.3, 129.0 (2C), 128.9, 128.7 (2C), 128.4 (2C), 118.5, 109.3, 99.9, 86.4, 84.6, 81.3, 64.6, 64.4, 28.6, 27.6, 12.0, 8.6, 8.2. IR (film): 2978, 1722, 1717, 1674 cm^{-1}. HRMS (ESI) *m*/*z*: [M+Na]$^+$ calcd for $C_{30}H_{32}N_2O_9Na$, 587.2027; found, 587.2006.



S-3

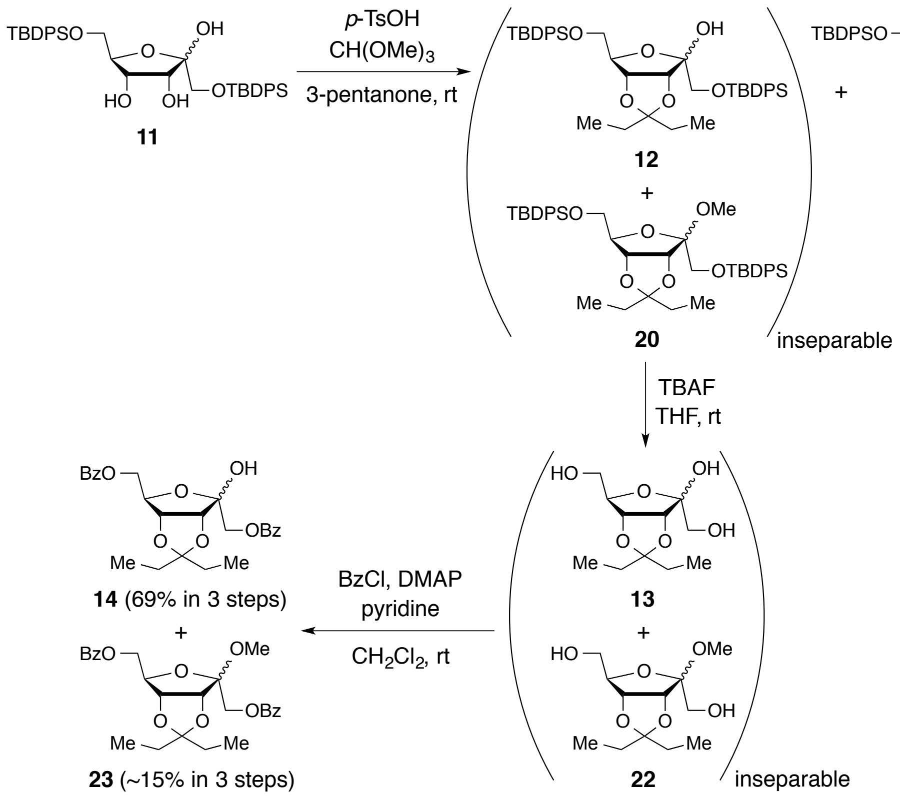
***N*^{4}-Benzoyl-1-[1,6-*O*-benzoyl-3,4-*O*-(3-pentylidene)-β- and α-D-psicofuranosyl]cytosine (S-3β and S-3α):** According to the general procedure for the *N*-glycosidation, a mixture of compounds **S-3β** and **S-3α** was obtained from **15** and *N*^{4}-benzoylcytosine in 56% yield in a 8:1 ratio. Colorless syrup. Eluent for column: 60% EtOAc in *n*-hexane. R_f = 0.26 (70% EtOAc in *n*-hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ (β-anomer)[1]: 8.47 (1H, br s, N*H*), 8.10 (1H, d, $J_{5,6}$ = 7.4 Hz, H-6), 7.87–7.83 (2H, m), 7.81 (1H, d, $J_{5,6}$ = 7.4 Hz, H-5), 7.77–7.71 (2H, m), 7.65–7.58 (1H, m), 7.57–7.48 (3H, m), 7.44–7.35 (4H, m), 7.35–7.28 (3H, m), 5.65 (1H, d, $J_{3',4'}$ = 6.4 Hz, H-3'), 5.10 (1H, d, $J_{1'a,1'b}$ = 12.1 Hz, H-1'a), 5.05 (1H, d, $J_{1'a,1'b}$ = 12.1 Hz, H-1'b), 4.93 (1H, dd, $J_{3',4'}$ = 6.4, $J_{4',5'}$ = 2.1 Hz, H-4'), 4.88 (1H, ddd, $J_{5',6'b}$ = 3.5, $J_{5',6'a}$ = 2.3, $J_{4',5'}$ = 2.1 Hz, H-5'), 4.68 (1H, dd, $J_{6'a,6'b}$ = 12.7, $J_{5',6'a}$ = 2.3 Hz, H-6'a), 4.33 (1H, dd, $J_{6'a,6'b}$ = 12.7, $J_{5',6'b}$ = 3.5 Hz, H-6'b), 2.01–1.89 (2H, m), 1.81–1.67 (2H, m), 1.11 (3H, t, J = 7.5 Hz), 0.95 (3H, t, J = 7.5 Hz); δ (α-anomer)[1]: 8.77 (br s, N*H*), 8.23 (1H, d, $J_{5,6}$ = 7.6 Hz, H-5), 7.99–7.95 (2H, m), 7.95–7.23 (14H, m), 5.41 (1H, d, $J_{3',4'}$ = 5.8 Hz, H-3'), 5.05 (1H, d, $J_{1'a,1'b}$ = 11.5 Hz, H-1'a), 4.99 (1H, d, $J_{1'a,1'b}$ = 11.5 Hz, H-1'b), 4.90–4.86 (1H, m), 4.60–4.55 (2H, m), 4.47 (1H, dd, $J_{6'a,6'b}$ = 12.7, $J_{5',6'b}$ = 7.4 Hz, H-6'b), 1.81–1.67 (2H, m), 1.66–1.55 (2H, m), 0.87 (3H, t, J = 7.7 Hz), 0.77 (3H, t, J = 7.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ (β-anomer)[1]: 165.6, 165.5, 162.3, 154.8, 145.4, 133.3, 133.1, 133.0, 129.44 (2C), 129.41, 129.2 (2C), 128.9 (3C), 128.44 (2C), 128.40 (3C), 127.5 (3C), 118.5, 100.5, 95.7, 86.1, 84.6, 81.2, 64.7, 64.1, 28.6, 27.7, 8.6, 8.2. IR (KBr): 3310, 1719 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{36}H_{35}N_3O_9Na$, 676.2272; found, 676.2271.



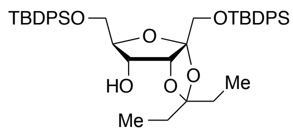
Scheme S1. Deprotection of **S-1** to diol **18**

Compounds **18β** and **18α** were also obtained from **S-1** under the similar condition described for the synthesis of **18** from **6** (73% yield for **18β**).

2. Spectroscopic data of compounds 21 and 23

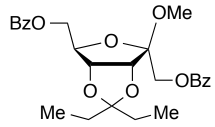


Scheme S2. Detailed synthesis of **14**



21

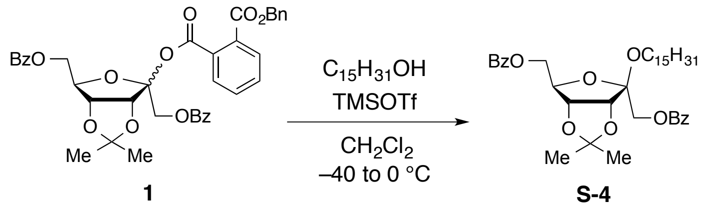
1,6-Di-*O*-benzoyl-2,3-*O*-(3-pentylidene)-α-D-psicofuranose (21): Colorless syrup. R_f = 0.31 (15% EtOAc in *n*-hexane). $[\alpha]^{26}_{D}$ +18.9 (*c* 0.89, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ: 7.72–7.60 (8H, m), 7.45–7.29 (12H, m), 4.57 (1H, d, $J_{3,4}$ = 4.5 Hz, H-3), 4.08 (1H, ddd, $J_{4,OH}$ = 9.7, $J_{4,5}$ = 8.8, $J_{3,4}$ = 4.5 Hz, H-4), 4.01 (1H, ddd, $J_{4,5}$ = 8.8, $J_{5,6b}$ = 4.4, $J_{5,6a}$ = 3.5 Hz, H-5), 3.86 (1H, dd, $J_{6a,6b}$ = 11.3, $J_{5,6a}$ = 3.5 Hz, H-6a), 3.82 (1H, dd, $J_{6a,6b}$ = 11.3, $J_{5,6b}$ = 4.4 Hz, H-6b), 3.77 (1H, d, $J_{1a,1b}$ = 11.2 Hz, H-1a), 3.73 (1H, d, $J_{1a,1b}$ = 11.2 Hz, H-1b), 2.28 (1H, d, $J_{4,OH}$ = 9.7 Hz, OH), 1.86–1.75 (2H, m), 1.69–1.60 (2H, m), 1.03 (9H, s), 0.99 (3H, t, J = 7.5 Hz), 0.97 (9H, s), 0.84 (3H, t, J = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 135.6 (4C), 133.2, 133.1, 132.8, 132.6, 129.80 (2C), 129.78 (2C), 129.63 (2C), 129.59 (2C), 127.79 (2C), 127.75 (2C), 127.65 (2C), 127.63 (2C), 117.0, 112.8, 82.0, 79.9, 72.8, 64.6, 63.5, 29.7, 29.5, 26.83 (3C), 26.76 (3C), 19.2, 19.1, 8.5, 8.2. IR (KBr): 3489, 2932, 2859 cm^{-1}. HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd for $C_{43}H_{56}O_6Si_2Na$, 747.3513; found, 747.3504.



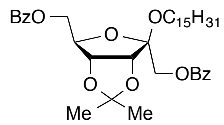
23

Methyl 1,6-di-*O*-benzoyl-3,4-*O*-(3-pentylidene)-β-D-psicofuranoside (23): Colorless oil. R_f = 0.45 (20% EtOAc in *n*-hexane). $[\alpha]^{26}_{D}$ +29.7 (*c* 1.04, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.06–7.97 (4H, m), 7.59–7.52 (2H, m), 7.43–7.35 (4H, m), 4.85 (1H, d, $J_{3,4}$ = 7.5 Hz, H-3), 4.75 (1H, dd, $J_{3,4}$ = 7.5, $J_{4,5}$ = 5.0 Hz, H-4), 4.57 (1H, dd, $J_{6a,6b}$ = 12.0, $J_{5,6a}$ = 3.7 Hz, H-6a), 4.56 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1a), 4.48 (1H, dd, $J_{6a,6b}$ = 12.0, $J_{5,6b}$ = 5.0 Hz, H-6b), 4.40 (1H, ddd, $J_{4,5}$ = $J_{5,6b}$ = 5.0, $J_{5,6a}$ = 3.7 Hz, H-5), 4.38 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1b), 3.48 (3H, s), 1.89 (2H, q, J = 7.5 Hz), 1.71–1.58 (2H, m), 1.00 (3H, t, J = 7.5 Hz), 0.90 (3H, t, J = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.2, 165.9, 133.2, 133.1, 129.7 (2C), 129.64, 129.60 (2C), 129.57, 128.41 (2C), 128.38 (2C), 121.0, 103.5, 83.2, 81.1, 80.2, 64.0, 62.9, 49.4, 29.2, 29.0, 8.4, 8.2. IR (film): 2972, 2943, 1719 cm^{-1}. HRMS (DART) *m/z*: $[M+NH_4]^+$ calcd for $C_{26}H_{34}NO_8$, 488.2284; found, 488.2293.

3. *O*-Glycosidation of D-psicofuranose 1 with 1-pentadecanol



Scheme S3. *O*-Glycosidation of **1** with 1-pentadecanol



S-4

1-Pentadecyl 1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-psicofuranoside (S-4): A mixture of **1** (103 mg, 0.154 mmol) and 1-pentadecanol (52.7 mg, 0.231 mmol) was predried azeotropically by coevaporation with dry toluene three times, which was further dried under reduced pressure over the presence of P_4O_{10}. The above mixture was dissolved in dry CH_2Cl_2 (3 mL), to which was added trimethylsilyl trifluoromethanesulfonate (41.8 μL, 0.231 mmol) at −40 °C. The reaction was gradually warmed to 0 °C over 45 min. The reaction mixture was quenched with satd. aq. $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layers were washed with water and brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluted with 5% EtOAc in *n*-hexane to give **S-4** (88.2 mg, 89%) as a colorless oil. R_f = 0.77 (30% EtOAc in *n*-hexane). $[\alpha]^{23}_{D}$ −10.5 (*c* 1.05, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 8.10–8.06 (4H, m), 7.61–7.55 (2H, m), 7.48–7.43 (4H, m), 4.85 (1H, dd, $J_{3,4}$ = 5.9, $J_{4,5}$ = 1.5 Hz, H-4), 4.73 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1a), 4.72 (1H, d, $J_{3,4}$ = 5.9 Hz, H-3), 4.54 (1H, ddd, $J_{5,6b}$ = 7.3, $J_{5,6a}$ = 6.8, $J_{4,5}$ = 1.5 Hz, H-5), 4.44 (1H, dd, $J_{6a,6b}$ = 11.0, $J_{5,6a}$ = 6.8 Hz, H-6a), 4.44 (1H, d, $J_{1a,1b}$ = 11.9 Hz, H-1b), 4.36 (1H, dd, $J_{6a,6b}$ = 11.0, $J_{5,6b}$ = 7.3 Hz, H-6b), 3.60 (1H, dt, *J* = 9.0, 6.4 Hz), 3.47 (1H, dt, *J* = 9.0, 7.0 Hz), 1.52 (3H, s), 1.50–1.42 (2H, m), 1.35 (3H, s), 1.25–1.14 (24H, m), 0.88 (3H, t, *J* = 6.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.0, 165.8, 133.1, 133.0, 129.9, 129.7, 129.7, 128.3, 128.3, 113.1, 108.9, 85.4, 84.0, 82.4, 65.2, 61.4, 59.7, 31.8, 29.6, 29.6, 29.5, 29.4, 29.3, 26.5, 26.1, 25.1, 22.6, 14.1. IR (film): 2925, 2853, 1726, 1602, 1452 cm^{-1}. MS (FAB) *m*/*z*: 661 $[M+Na]^+$. HRMS (FAB) *m*/*z*: calcd for $C_{38}H_{54}O_8Na$, 661.3716; found, 661.3710.

NOTE

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