SUPPORTING INFORMATION

Strained Olefin Enables Triflic Anhydride Mediated Direct Dehydrative Glycosylation

Guohua Chen, [‡*a] *Qiang Yin,* [‡ab] *Jian Yin,* [c] *Xiangying Gu,* [ab] *Xiao Liu,* [ab] *Qidong You,* [a]

Yue-Lei Chen, [*b] *Bing Xiong,* [*b] *and Jingkang Shen* [*b]

[a] School of Pharmacy, China Pharmaceutical University, 24 Tongjiaxiang, Nanjing 210009, P. R. China.

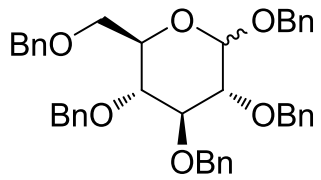
[b] Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, P. R. China.

[c] The Key Laboratory of Carbohydrate Chemistry and Biotechnology, Ministry of Education, School of Biotechnology, Jiangnan University, 1800 Lihu Avenue, Wuxi 214122, P. R. China.

E-mail: *chenyuelei@gmail.com*

Table of Contents

General. All solvents were dried and purified prior to use: Toluene was distilled from sodium, Et_2O and THF were distilled from potassium, and CH_2Cl_2 was distilled from CaH_2. All other commercially available reagents were used as received. Reactions at −78 °C were performed in a dry ice/acetone bath. All moisture sensitive reactions were performed under N_2 (ca. +1.1 bar) in heating-gun (500-600 °C)/vacuum dried glassware sealed with rubber septa. Flash chromatography was performed on silica gel (300-400 mesh ASTM), and monitored by thin layer chromatography (TLC) on HSGF-254 (10-40 μm) TLC plates. NMR data were collected on a *Varian* Mercury-300 High Performance Digital FT-NMR, a *Varian* Mercury-400 High Performance Digital FT-NMR, or a *Bruker* Ultrashield 500 NMR. Spectra from solutions in $CDCl_3$ (δC = 77.0 ppm) are calibrated relative to TMS (δH = 0.00 ppm). HRMS were carried out on a *Thermo Finnigan* MAT-95 spectrometer (for EI), or on a *Waters*, Q-Tof Ultima Global spectrometer (for ESI). Melting points were measured on an uncorrected SGW X-4 micro melting point apparatus. HPLC analysis was performed on a Gilson HPLC system (306 pump, UV/vis-156 Detector, 215 liquid handle) with a YMC-ODS column (4.6 x 50 mm, 5 μm). HPLC conditions: solvent A = H_2O containing 0.1% (v/v) TFA, solvent B = MeCN containing 0.1% (v/v) TFA; flow rate = 2.5 mL/min; Gradient (B%): 0-0.5 min (4% isostatic), 0.5-4.5 min (4% - 95%), 4.5-6.1 min (95% isostatic), 6.1-6.3 min (95% - 4%), 6.3-8.0 min (4% isostatic); peaks were identified at 254 nm and 214 nm. An Elementar Vario EL Cube analyzer was used for elemental analysis.



3

Reaction condition in scheme 2 and preparation of benzyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (3):

Glucosyl donor **1** [1] (100 mg, 0.185 mmol, 1 equiv) was dissolved in DCM (1 mL) and cooled to -78 ^{o}C, followed by addition of Tf_2O (0.05 mL, 0.28 mmol, 1.5 equiv) and *beta*-(-)-pinene (0.15 mL, 0.93 mmol, 5 equiv). The mixture was warmed to 0 ^{o}C, treated with BnOH (0.09 mL, 0.93 mmol, 5 equiv), slowly warmed to RT and stirred overnight at RT. The reaction was quenched with sat. aq. $NaHCO_3$. The phases were separated and the organic phase was washed with brine, dried with Na_2SO_4 and evaporated to dryness. The residue was purified with flash chromatography on silica gel (15:1, 60 - 90 ^{o}C petroleum ether - EtOAc) to afford product **3** (colorless oil, 36 mg, 0.057 mmol, 31%, *alpha*:*beta* =1:0.91). Representative NMR signals: 4.04 (t, J = 9.3 Hz, H-1, *alpha*-anomer); 3.50-3.44 (m,1 H, *beta*-anomer). NMR data was parallel to literature report. [2]

Reaction condition in Table 1, entry 1:

Tf_2O (0.05 mL, 0.28 mmol, 1.5 equiv) and *beta*-(-)-pinene (0.15 mL, 0.93 mmol, 5 equiv) were dissolved in DCM and cooled to -50 ^{o}C. A solution of glucosyl donor **1** [1] (100 mg, 0.185 mmol, 1 equiv) in DCM (1 mL) was added dropwise to above solution. The resulting clear solution was stirred at -45 ^{o}C for 45 min, treated with the acceptor (0.09 mL, 0.93 mmol, 5 equiv), slowly warmed to RT in ca. 2 h, and stirred at RT for 4 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the phases were separated. The organic phase was evaporated to dryness and the residue was purified with flash chromatography on silica gel (15:1, 60 - 90 ^{o}C petroleum ether - EtOAc) to afford product **3** [2]. The anomeric ratio was measured by NMR and indicated in Table 1, along with the yield.

Reaction conditions in Table 1, entry 2:

Glucosyl donor **1** [1] (100 mg, 0.185 mmol, 1 equiv) and Ph_2SO (105 mg, 0.518 mmol, 2.8 equiv) were dissolved in DCM (1 mL) and cooled to -78 ^{o}C, followed by addition of Tf_2O (0.05 mL, 0.26 mmol, 1.4

[1] J. Zeng, S. Vedachalam, S. Xiang, X. W. Liu, *Org. Lett.* **2011**, *13*, 42-45.

[2] X. Gu, L. Chen, X. Wang, X. Liu, Q. You, W. Xi, L. Gao, G. Chen, Y. L. Chen, B. Xiong, J. Shen, *J. Org. Chem.* **2014**, *79*, 1100-1110.

equiv). The mixture was warmed to -40 °C in 1 h, treated with 2-chloropyridine (0.08 mL, 0.93 mmol, 5 equiv) and BnOH (0.06 mL, 0.56 mmol, 3 equiv), stirred at -40 °C for 40 min, slowly warmed to RT in 1 h, and stirred at RT for 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the phases were separated. The organic phase was evaporated to dryness and the residue was purified with flash chromatography on silica gel (15:1, 60 - 90 °C petroleum ether - EtOAc) to afford product **3** [2]. The anomeric ratio was measured by NMR and indicated in Table 1, along with the yield.

Reaction conditions in Table 1, entries 3-6:

Tf_2O (0.05 mL, 0.28 mmol, 1.5 equiv) and indicated acid scavenger (0.93 mmol, 5 equiv) were dissolved in DCM and cooled to -50 °C. A solution of glucosyl donor **1** [1](100 mg, 0.185 mmol, 1 equiv) in DCM (1 mL) was added dropwise to above solution. The resulting clear solution was stirred at -45 °C for 45 min, treated with the acceptor (0.09 mL, 0.93 mmol, 5 equiv), slowly warmed to RT in ca. 2 h, and stirred at RT for 4 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the phases were separated. In case that the formation of product **3** could be confirmed by TLC, the organic phase was evaporated to dryness and the residue was purified with flash chromatography on silica gel (15:1, 60 - 90 °C petroleum ether - EtOAc) to afford product **3** [2]. The anomeric ratio was measured by NMR and indicated in Table 1, along with the yield.

Reaction conditions in Table 1, entries 7-13:

Tf_2O (0.05 mL, 0.28 mmol, 1.5 equiv) and *beta*-(-)-pinene (0.15 mL, 0.93 mmol, 5 equiv) were dissolved in DCM and cooled to -50 °C. A solution of glucosyl donor **1** [1] (100 mg, 0.185 mmol, 1 equiv) in DCM (1 mL) was added dropwise to above solution. The resulting clear solution was stirred at -50 °C for 45 min, treated with the additive (0.185 mmol, 1 equiv) indicated in Table 1, stirred again at -50 °C for 45 min, treated with acceptor (0.09 mL, 0.93 mmol, 5 equiv), slowly warmed to RT in ca. 2 h, and stirred at RT for 4 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the phases were separated. In case that the formation of product **3** could be confirmed by TLC, the organic phase was evaporated to

dryness and the residue was purified with flash chromatography on silica gel (15:1, 60-90 ^{o}C petroleum ether-EtOAc) to afford product **3** [2]. The anomeric ratio was measured by NMR and indicated in Table 1, along with the yield.

General procedure A for reactions in scheme 3:

Tf_2O (0.05 mL, 0.28 mmol, 1.5 equiv) and *beta*-(-)-pinene (0.15 mL, 0.93 mmol, 5 equiv) were dissolved in DCM and cooled to -50 ^{o}C. A solution of donor **1**, **8**, or **9** [1] (100 mg, 0.185 mmol, 1 equiv) in DCM (1 mL) was added dropwise to above solution. The resulting clear solution was stirred at -45 ^{o}C for 45 min, treated with the acceptor (0.93 mmol, 5 equiv), slowly warmed to RT in ca. 2 h, and stirred at RT for 4-16 h (indicated below individually). The reaction was quenched with sat. aq. $NaHCO_3$ and the phases were separated. The organic phase was evaporated to dryness and the residue was purified with flash chromatography on silica gel (15:1, 60 - 90 ^{o}C petroleum ether - EtOAc) to afford product **11-18**.

General procedure B for reactions in scheme 5:

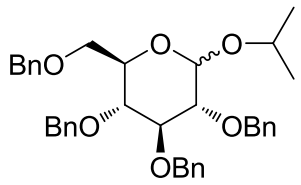
Tf_2O (0.04 mL, 0.23 mmol, 1.3 equiv) and *beta*-(-)-pinene (0.14 mL, 0.90 mmol, 5 equiv) were dissolved in DCM and cooled to -50 ^{o}C. A solution of donor **2**1, [3] **22**, [4] or **23** [5] (100 mg, 0.180 mmol, 1 equiv) in DCM (1 mL) was added dropwise to above solution. The resulting clear solution was stirred at -50 ^{o}C for 45 min, treated with the acceptor (0.90 mmol, 5 equiv), slowly warmed to RT in ca. 2 h, and stirred at RT for 4-16 h (indicated below individually). The reaction was quenched with sat. aq. $NaHCO_3$ and the phases were separated. The organic phase was evaporated to dryness and the residue was purified with flash chromatography on silica gel (15:1, 60 - 90 ^{o}C petroleum ether - EtOAc) to

[3] K. C. Nicolaou, H. J. Mitchell, N. F. Jain, T. Bando, R. Hughes, N. Winssinger, S. Natarajan, A. E. Koumbis, *Chem.-Eur. J.* **1999**, *5*, 2648-2667.

[4] S. R. Sanapala, S. S. Kulkarni, *Chemistry* **2014**, *20*, 3578-83.

[5] M. A. Nashed, L. Anderson, *Carbohydr. Res.* **1983**, *114*, 53-61.

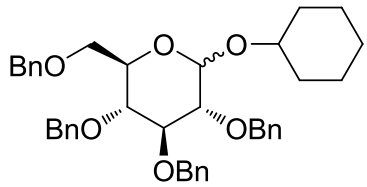
afford product **25-33**.



11

Isopropyl 2,3,4,6-tetra-*O*-benzyl- D-glucopyranoside (11):

From donor **1** [1] (100 mg, 0.185 mmol, 1 equiv) and isopropanol (0.07 mL, 0.93 mmol, 5 equiv), according to general procedure A, after 16 h of reaction, compound **11** was obtained (colorless liquid, 58 mg, 54%, *alpha*:*beta* = 1:0.52). Representative NMR signals: 4.87 (d, *J* = 3.7 Hz, H-1, *alpha*-anomer), 4.07 – 3.96 (m, C<u>H</u>$(CH_3)_2$, *beta*-anomer). NMR data was parallel to literature report.[6]



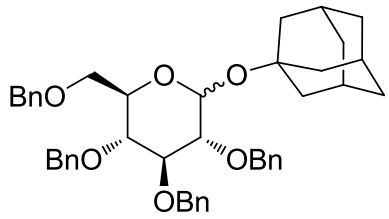
12

Cyclohexyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (12):

From donor **1** [1] (100 mg，0.185 mmol,1 equiv) and cyclohexanol (0.10 mL, 0.93 mmol, 5 equiv), according to general procedure A, after 16 h of reaction, compound **12** was obtained (colorless liquid, 84 mg, 73%, *alpha*:*beta* = 1:0.35). Representative NMR signals: 5.00 (d, *J* = 10.8 Hz, 1H, *beta*-anomer); 4.00 (t, *J* = 9.4 Hz, 1H, *alpha*-anomer). NMR data was parallel to literature report. [7]

[6] M. Mossotti, L. Panza, *J. Org. Chem.* **2011**, *76*, 9122-9126.

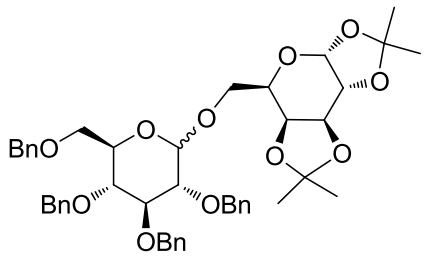
[7] H. Imagawa, A. Kinoshita, T. Fukuyama, H. Yamamoto, M. Nishizawa, *Tetrahedron Lett.* **2006**, *47*, 4729-4731.



13

Adamantyl 2,3,4,6-tetra-*O*-benzyl- D-glucopyranoside (13):

From donor **1** [1] (100 mg, 0.185 mmol, 1 equiv) and adamantol (0.141 g, 0.93 mmol, 5 equiv), according to general procedure A, after 16 h of reaction, compound **13** was obtained (colorless liquid, 52 mg, 42%, *alpha*:*beta* = 1:4). Representative NMR signals: 5.28 (d, *J* = 3.6 Hz, H-1, *alpha*-anomer); 4.91 (d, *J* = 11.0 Hz, 1H, PhC$\underline{H}_2$, *beta*-anomer). NMR data was parallel to literature report.[8]



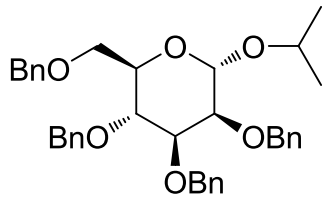
14

2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*alpha*-D-galactopyranose (14):

From donor **1** [1] (100 mg, 0.185 mmol, 1 equiv) and acceptor **10** (240 mg, 0.93 mmol, 5 equiv), according to general procedure A, after 16 h of reaction, compound **14** was obtained (colorless liquid, 78 mg, 54%, *alpha*:*beta* = 1.1:1). Representative NMR signals: 5.56 (d, *J* = 5.2 Hz, H-1', *beta*-anomer); 5.52 (d, *J* = 4.8 Hz, H-1', *alpha*-anomer). NMR data was parallel to literature report.[9]

[8] E. A. Mensah, J. M. Azzarelli, H. M. Nguyen, *J. Org. Chem.* **2009**, *74*, 1650-1657.

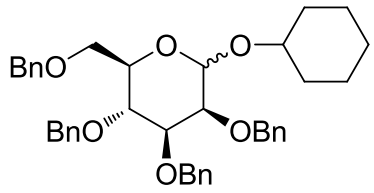
[9] D. J. Cox, A. J. Fairbanks, *Tetrahedron: Asymmetry* **2009**, *20*, 773-780.



15

Isopropyl 2,3,4,6-tetra-*O*-benzyl-*alpha*-D-mannopyranoside (15):

From donor **8** [1] (100 mg，0.185 mmol, 1 equiv) and isopropanol (0.07 mL, 0.93 mmol, 5 equiv), according to general procedure A, after 16 h of reaction, compound **15** was obtained (colorless liquid, 46 mg, 43%, *alpha*-only). NMR data was parallel to literature report.[10]



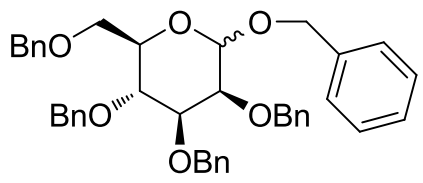
16

Cyclohexyl 2,3,4,6-tetra-*O*-benzyl-D-mannopyranoside (16):

From donor **8** [1] (100 mg，0.185 mmol, 1 equiv) and cyclohexanol (0.10 mL, 0.93 mmol, 5 equiv), according to general procedure A, after 16 h of reaction, compound **16** was obtained (colorless liquid, 53 mg, 46%, *alpha*:*beta* = 1:0.10). Representative NMR signals: 5.00(s, 1H, *alpha*-anomer), 4.42(d, *J* = 11.8 Hz, 1H, *beta*-anomer). NMR data was parallel to literature report.[11]

[10] G. Singh, H. Vankayalapati, *Tetrahedron: Asymmetry* **2000**, *11*, 125-138.

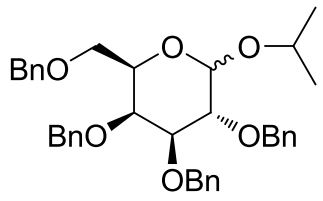
[11] K. Toshima, H. Nagai, K. Kasumi, K. Kawahara, S. Matsumura, *Tetrahedron* **2004**, *60*, 5331-5339.



17

Benzyl 2,3,4,6-tetra-*O*-benzyl-D-mannopyranoside (17):

From donor **8** [1] (100 mg, 0.185 mmol, 1 equiv) and BnOH (0.09 mL, 0.93 mmol, 5 equiv), according to general procedure A, after 7 h of reaction, compound *alpha*- **17** [12] (colorless liquid, 82 mg, 70%) and *beta*- **17** [13] (colorless liquid, 14 mg, 12%) were obtained (*alpha*:*beta* = 1:0.17). NMR data was parallel to literature report.



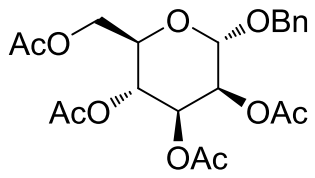
18

Isopropyl 2,3,4,6-tetra-*O*-benzyl- D-galactopyranoside (18):

From donor **9** [1] (100 mg, 0.185 mmol, 1 equiv) and isopropanol (0.07 mL, 0.93 mmol, 5 equiv), according to general procedure A, after 16 h of reaction, compound **18** was obtained (colorless liquid, 44 mg, 41%, *alpha*:*beta* = 1:0.90). Representative NMR signals: 4.96 (d, *J* = 3.2Hz, H-1, *alpha*-anomer), 3.79 (dd, *J* = 7.7, 9.7 Hz, H-2, *beta*-anomer).[8]

[12] Y. Wang, X. Zhang, P. Wang, *Org. Biomol. Chem*. **2010**, *8*, 4322-4328.

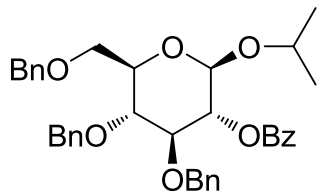
[13] W. Lu, L. Navidpour, S. D. Taylor, *Carbohydr. Res.* **2005**, *340*, 1213-1217.



20

Preparation of benzyl 2,3,4,6-tetra-*O*-acetyl-*alpha*-D- mannopyranoside (20):

Tf_2O (0.06 mL, 0.37 mmol, 1.3 equiv) and *beta*-(-)-pinene (0.23 mL, 1.43 mmol, 5 equiv) were dissolved in DCM and cooled to -50 ^oC. A solution of mannoyl donor **19** [14] (100 mg, 0.287 mmol, 1 equiv) in DCM (1 mL) was added dropwise to above solution. The resulting clear solution was stirred at -50 ^oC for 15 min, treated with the acceptor (0.15 mL, 1.43 mmol, 5 equiv), slowly warmed to RT in ca. 2 h, and stirred at RT for 16 h. The reaction was quenched with sat. aq. $NaHCO_3$ and the phases were separated. The organic phase was evaporated to dryness and the residue was purified with flash chromatography on silica gel (4:1, 60 - 90 ^oC petroleum ether - EtOAc) to afford product **20** (colorless oil, 16 mg , 13%, *alpha*-only). NMR data was parallel to literature report.[15]



25

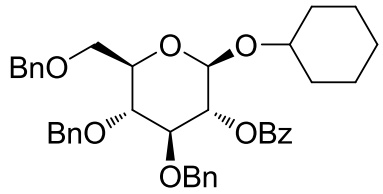
Isopropyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-*beta*-D-glucopyranoside (25):

From donor **21** [3] (100 mg, 0.180 mmol, 1 equiv) and isopropanol (0.07 mL, 0.90 mmol, 5 equiv), according to general procedure B, after 16 h of reaction, compound **25** was obtained (colorless liquid, 43 mg, 40%, *beta*-only). R_f 0.69 (6:1, 60 - 90 ^oC petroleum ether - EtOAc); $[\alpha]_D$ 76.50 (*c* 0.1 $CHCl_3$);

[14] W. J. Hennen, H. M. Sweers, Y. Wang, C. Wong, *J. Org. Chem.* **1988**, *53*, 4939-4945.

[15] M. Poláková, M. U. Roslund, F. S. Ekholm, T. Saloranta, R. Leino, *Eur. J. Org. Chem.* **2009**, *2009*, 870-888.

HPLC t_R 3.65 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.8 Hz, 2H, ArH), 7.57 (t, *J* = 7.3 Hz, 1H, ArH), 7.44 (t, *J* = 7.5 Hz,2H, ArH), 7.40 – 7.11 (m, 15H, ArH), 5.26 (d, *J* = 3.6 Hz, 1H, H-1), 5.09 (dd, *J* = 10.0, 3.6 Hz, 1H, H-2), 4.83 (d, *J* = 11.1 Hz, 3H, PhC$\underline{H}_2$), 4.67 (d, *J* = 12.1 Hz, 1H, PhC$\underline{H}_2$), 4.52 (d, *J* = 11.1 Hz, 2H, PhC$\underline{H}_2$), 4.18 (t, *J* = 10.0 Hz, 1H, H-3), 3.98 (d, *J* = 10.0 Hz, 1H, H-5), 3.90 – 3.75 (m, 3H, C$\underline{H}(CH_3)_2$, H-4, H-6), 3.69 (d, *J* = 10.6 Hz, 1H, H-6), 1.20 (d, *J* = 6.2 Hz, 3H, CH(C$\underline{H}_3)_2$), 1.02 (d, *J* = 6.0 Hz, 3H, CH(C$\underline{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.10 (Ph$\underline{C}$=O), 138.49, 138.27, 138.15, 133.24, 130.09, 129.84, 128.55, 128.52, 128.43, 128.15, 128.02, 127.94, 127.81, 127.70, 95.01 (C-1), 80.47 (C-3), 78.09 (C-4), 75.61 (Ph$\underline{C}H_2$), 75.33 (Ph$\underline{C}H_2$), 74.38 (C-2), 73.63 (Ph$\underline{C}H_2$), 71.01 ($\underline{C}H(CH_3)_2$) , 70.50 (C-5) , 68.61 (C-6), 23.43 (CH($\underline{C}H_3)_2$), 21.92 (CH($\underline{C}H_3)_2$); HRMS (ESI$^+$) calcd. For $C_{37}H_{40}O_7Na^+$ 619.2672, found 619.2689.

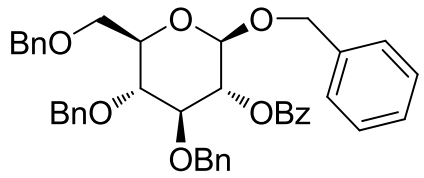


26

Cyclohexyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-*beta*-D-glucopyranoside (26):

From donor **21** [3] (100 mg, 0.180 mmol, 1 equiv) and cyclohexanol (0.09 mL, 0.90 mmol, 5 equiv), according to general procedure B, after 16 h of reaction, compound **26** [16] was obtained (colorless liquid, 74 mg, 65%, *beta*-only). R_f 0.76 (6:1, 60 - 90 ^{o}C petroleum ether - EtOAc); $[\alpha]_D$ 112.33 (*c* 0.1 $CHCl_3$); HPLC t_R 3.93 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.9 Hz, 2H, ArH), 7.57 (t, *J* = 7.3 Hz, 1H, ArH), 7.44 (t, *J* = 7.6 Hz, 2H, ArH), 7.39 – 7.10 (m, 15H, ArH), 5.30 (d, *J* = 3.6 Hz, 1H, H-1), 5.09 (dd, *J* = 9.9, 3.6 Hz, 1H, H-2), 4.83 (d, *J* = 11.0 Hz, 3H, PhC$\underline{H}_2$), 4.67 (d, *J* = 12.1 Hz, 1H, PhC$\underline{H}_2$), 4.52 (d, *J* = 11.5 Hz, 2H, PhC$\underline{H}_2$), 4.20 (t, *J* = 9.9 Hz, 1H, H-3), 4.01 (d, *J* = 9.7 Hz, 1H, H-5), 3.84 – 3.74 (m, 2H, H-4, H-6), 3.70 (d, *J* = 10.6 Hz, 1H, H-6), 3.56 (m, 1H, Cyclohexyl-C$\underline{H}$), 1.82 (s, 1H, Cyclohexyl-

C<u>H</u>$_2$), 1.66 (d, *J* = 12.8 Hz, 2H, Cyclohexyl-C<u>H</u>$_2$), 1.59 – 1.53 (m, 1H, Cyclohexyl-C<u>H</u>$_2$), 1.49 – 1.35 (m, 2H, Cyclohexyl-C<u>H</u>$_2$), 1.21 (m, 4H, Cyclohexyl-C<u>H</u>$_2$); ^{13}C NMR(126 MHz, $CDCl_3$) δ 166.08 (Ph<u>C</u>=O), 138.52, 138.30, 138.20, 133.21, 130.12, 129.83, 128.54, 128.51, 128.42, 128.15, 127.99, 127.94, 127.90, 127.78, 127.69, 94.88 (C-1), 80.51 (C-3), 78.15 (C-4), 76.38 (Cyclohexyl-C1), 75.60 (Ph<u>C</u>H$_2$), 75.33 (Ph<u>C</u>H$_2$), 74.47 (C-2), 73.63(Ph<u>C</u>H$_2$), 70.56(C-5), 68.71(C-6), 33.48 (Cyclohexyl-<u>C</u>H$_2$), 31.65 (Cyclohexyl-<u>C</u>H$_2$), 25.68 (Cyclohexyl-<u>C</u>H$_2$), 24.07 (Cyclohexyl-<u>C</u>H$_2$), 23.69 (Cyclohexyl-<u>C</u>H$_2$); HRMS (ESI$^+$) calcd. For $C_{40}H_{44}O_7Na^+$ 659.2985, found 619.2969.



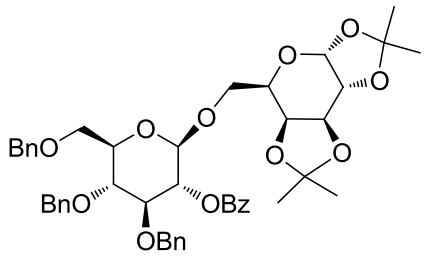
27

Benzyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-*beta*-D-glucopyranoside (27):

From donor **21** [3] (100 mg，0.180 mmol, 1 equiv) and BnOH (0.09 mL, 0.90 mmol, 5 equiv), according to general procedure B, after 16 h of reaction, compound **27** was obtained (colorless liquid, 67 mg, 58%, *beta*-only). R_f 0.62 (6:1, 60 - 90 ^{o}C petroleum ether - EtOAc); $[\alpha]_D$ -3.17 (*c* 0.1 $CHCl_3$); HPLC t_R 3.38 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.1 Hz, 2H, ArH), 7.57 (t, *J* = 7.4 Hz, 1H, ArH), 7.43 (t, *J* = 7.7 Hz, 2H, ArH), 7.39 – 7.06 (m, 20H, ArH), 5.37 (t, *J* = 8.0 Hz, 1H, H-2), 4.87 (d, *J* = 12.7 Hz, 1H, PhC<u>H</u>$_2$), 4.82 (d, *J* = 10.9 Hz, 1H, PhC<u>H</u>$_2$), 4.74 – 4.55 (m, 6H, PhC<u>H</u>$_2$), 4.54 (d, *J* = 8.0 Hz, 1H, H-1), 3.83 – 3.70 (m, 4H, H-3, H-4, H-6), 3.57 – 3.48 (m, 1H,H-5); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.33 (Ph<u>C</u>=O), 138.26, 138.09, 137.92, 137.32, 133.15, 130.10, 129.96, 128.52, 128.42, 128.35, 128.11, 128.08, 127.93, 127.89, 127.75, 127.69, 99.56 (C-1), 82.89 (C-3), 78.12 (C-4), 75.38 (C-5), 75.11 (2C, Ph<u>C</u>H$_2$), 73.87 (Ph<u>C</u>H$_2$), 73.67 (C-2), 70.20 (Ph<u>C</u>H$_2$), 68.92 (C-6)；HRMS (ESI$^+$) calcd. For

[16] M. Heuckendorff, H. D. Premathilake, P. Pornsuriyasak, A. Madsen, C. M. Pedersen, M. Bols, A. V. Demchenko, *Org. Lett.* **2013**, *15*, 4094-4097.

$C_{41}H_{44}O_7Na^+$ 667.2672, found 667.2658.

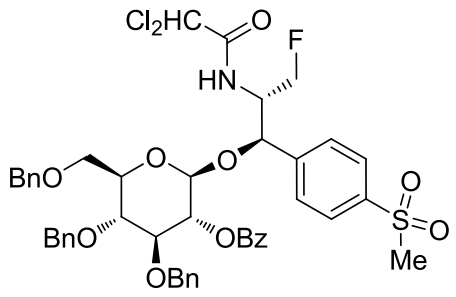


28

2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-*beta*-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*alpha*-D-galactopyranose (28):

From donor **21** [3] (100 mg, 0.180 mmol, 1 equiv) and acceptor **10** (0.234 g, 0.90 mmol, 5 equiv), according to general procedure B, after 16 h of reaction, compound **28** [17] was obtained (colorless liquid, 52 mg, 36% *beta*-only). R_f 0.47 (4:1, 60 - 90 °C petroleum ether - EtOAc); $[\alpha]_D$ -11.17 (*c* 0.1 $CHCl_3$); HPLC t_R 3.31 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.1 Hz, 2H, ArH), 7.54 (t, J = 7.4 Hz, 1H, ArH), 7.41 (t, J = 7.7 Hz, 2H, ArH), 7.38 – 7.10 (m, 15H), 5.38 (d, *J* = 5.0 Hz, 1H, H-1), 5.28 (t, *J* = 8.5 Hz, 1H, H-2'), 4.81 (d, *J* = 11.0 Hz, 1H, PhC$\underline{H}_2$), 4.73 (d, *J* = 11.0 Hz, 1H, PhC$\underline{H}_2$), 4.69 – 4.62 (m, 3H, H-1', PhC$\underline{H}_2$), 4.58 (d, *J* = 12.0 Hz, 2H, PhC$\underline{H}_2$), 4.40 (dd, *J* = 8.0, 2.3 Hz, 1H, H-3), 4.18 (dd, *J* = 5.0, 2.3 Hz, 1H, H-2), 4.11 (dd, *J* = 8.0, 1.7 Hz, 1H, H-4), 4.01 (dd, *J* = 11.0, 5.2 Hz, 1H, H-4'), 3.86 – 3.67 (m, 6H, H-5, H-6, H-3', H-6'), 3.55 (m, 1H, H-5'), 1.38 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.22 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.18 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.17 (s, 3H, C(C$\underline{H}_3$)$_2$);.^{13}C NMR (126 MHz, $CDCl_3$) δ 165.40 (Ph$\underline{C}$=O), 138.31, 138.16, 138.01, 133.00, 130.24, 130.11, 128.55, 128.52, 128.37, 128.35, 128.14, 128.11, 127.99, 127.94, 127.74, 109.25, 108.51, 101.47 (C-1'), 96.30 (C-1), 82.97 (C-3'), 78.12 (C-4'), 75.46 (Ph$\underline{C}$H$_2$), 75.14 (Ph$\underline{C}$H$_2$, C-5'), 73.80 (C-2'), 73.69 (Ph$\underline{C}$H$_2$), 71.00 (C-4), 70.62 (C-2, C-3), 68.78 (C-6), 68.06 (C-6'), 67.32 (C-5), 26.04 (C($\underline{C}$H$_3$)$_2$), 25.81 (C($\underline{C}$H$_3$)$_2$), 25.00 (C($\underline{C}$H$_3$)$_2$), 24.31 (C($\underline{C}$H$_3$)$_2$);.HRMS (ESI$^+$) calcd. For $C_{46}H_{52}O_{12}Na^+$ 819.3356, found 819.3337.

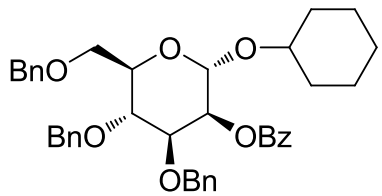
[17] Y. H. Lin, B. Ghosh, K. K. Mong, *Chem. Commun.* **2012**, *48*, 10910-2.



29

2,2-Dichloro-*N*-[(1*R*,2*S*)-3-fluoro-1-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-*beta*-D-glucopyranosyloxy)-1-(4-methanesulfonylphenyl)propan-2-yl]acetamide (29):

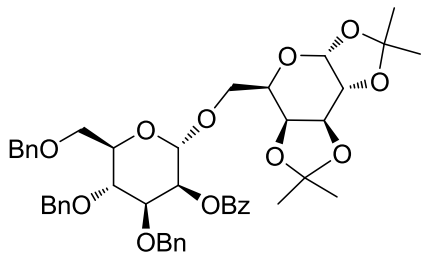
From donor **21** [3] (100 mg, 0.180 mmol, 1 equiv) and Florfenicol (0.323 g, 0.90 mmol, 5 equiv), according to general procedure B, after 16 h of reaction, compound **29** was obtained (colorless liquid, 88 mg, 55%, *beta*-only). R_f 0.25 (2:1, 60 - 90 ^oC petroleum ether - EtOAc); $[\alpha]_D$ 30.00 (c 0.1 $CHCl_3$); HPLC t_R 2.93 min; ^1H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.2 Hz, 2H, ArH), 7.66 (t, *J* = 7.4 Hz, 1H, ArH), 7.56 (d, *J* = 8.3 Hz, 2H, ArH), 7.49 (t, *J* = 7.8 Hz, 2H, ArH), 7.39 – 7.12 (m, 16H, ArH), 7.00 (d, *J* = 8.6 Hz, 1H, ArH), 5.77 (s, 1H, C<u>H</u>Cl_2), 5.38 – 5.33 (m, 1H, H-2), 5.16 (d, *J* = 3.0 Hz, 1H, C<u>H</u>), 4.84 (d, *J* = 10.8 Hz, 1H, PhC<u>H</u>$_2$), 4.74 (d, *J* = 11.3 Hz, 1H, PhC<u>H</u>$_2$), 4.68 – 4.57 (m, 4H, PhC<u>H</u>$_2$), 4.49-4.17(m, 4H, H-1, C<u>H</u>$_2$F, C<u>H</u>NHC=O), 3.84 – 3.71 (m, 4H, H-3, H-5, H-6), 3.48 (dd, *J* = 9.5, 2.6 Hz, 1H, H-4), 2.95 (s, 3H, C<u>H</u>$_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.51 (C=O), 164.32 (C=O), 143.16, 140.76, 138.00, 137.79, 137.67, 134.01, 129.95, 129.28, 128.79, 128.64, 128.62, 128.44, 128.15, 128.11, 128.07, 127.94, 127.89, 127.81, 127.71, 98.85 (C-1), 82.05 (C-3), 81.17 (Ph<u>C</u>H$_2$), 79.78 (Ph<u>C</u>H$_2$), 77.82 (C-5), 75.48 (C-4), 75.26(d, $J_{C\text{-}F}$ = 5.5Hz, <u>C</u>H$_2$F), 75.03 (<u>C</u>H), 73.79 (Ph<u>C</u>H$_2$), 73.71 (C-2), 68.54 (C-6), 66.07 (<u>C</u>HCl_2), 54.75 (d, $J_{C\text{-}C\text{-}F}$ = 23.0Hz, <u>C</u>HNHC=O), 44.47 (<u>C</u>H$_3$); HRMS (ESI^+) calcd. For $C_{46}H_{46}NO_{10}FSCl_2Na^+$ 916.2101, found 916.2122.



30

Cyclohexyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-*alpha*-D-mannopyranoside (30):

From donor **22** [4] (100 mg, 0.180 mmol, 1 equiv) and cyclohexanol (0.09 mL, 0.90 mmol, 5 equiv), according to general procedure B, after 16 h of reaction, compound **30** [18] was obtained (colorless liquid, 44 mg 38%, *alpha*-only). R_f 0.87 (6:1, 60 - 90 ^oC petroleum ether - EtOAc); $[\alpha]_D$ 2.00 (*c* 0.1 $CHCl_3$); HPLC t_R 3.91 min; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 2H, ArH), 7.54 (t, *J* = 7.3 Hz, 1H, ArH), 7.42 – 7.08 (m, 17H, ArH), 5.57 (s, 1H, H-2), 5.11 (s, 1H,H-1), 4.90 – 4.71 (m, 3H, PhC$\underline{H}_2$), 4.62 – 4.49 (m, 3H, PhC$\underline{H}_2$), 4.14 (dd, *J* = 9.4 Hz, 2.8 Hz 1H, H-3), 4.08 (t, *J* = 9.4 Hz, 1H, H-4), 3.95(d, *J* = 9.4Hz, 1H, H-5), 3.91(dd, *J* = 10.3, 3.8Hz, 1H, H-6), 3.77 (d, *J* = 10.3 Hz, 1H, H-6), 3.65 (m, 1H, Cyclohexyl-C$\underline{H}$), 1.85 (s, 2H, Cyclohexyl-C$\underline{H}_2$), 1.70 (s, 2H, Cyclohexyl-C$\underline{H}_2$), 1.51 (s, 1H, Cyclohexyl-C$\underline{H}_2$), 1.44 – 1.16 (m, 5H, Cyclohexyl-C$\underline{H}_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.01 (Ph$\underline{C}$=O), 138.67, 138.55, 138.28, 133.20, 130.17, 130.10, 128.51, 128.47, 128.45, 128.42, 128.23, 128.17, 127.80, 127.70, 127.61, 127.58, 95.99 (C-1), 78.53 (C-3), 75.76 (Cyclohexyl-C1), 75.49 (Ph$\underline{C}H_2$), 74.71 (C-4), 73.53 (Ph$\underline{C}H_2$), 71.74 (C-5), 71.70 (Ph$\underline{C}H_2$), 69.88 (C-2), 69.32 (C-6), 33.37 (Cyclohexyl-$\underline{C}H_2$), 31.54 (Cyclohexyl-$\underline{C}H_2$), 25.74 (Cyclohexyl-$\underline{C}H_2$), 24.17 (Cyclohexyl-$\underline{C}H_2$), 23.92 (Cyclohexyl-$\underline{C}H_2$); HRMS (ESI^+) calcd. For $C_{40}H_{44}O_7Na^+$ 659.2985, found 619.3004.

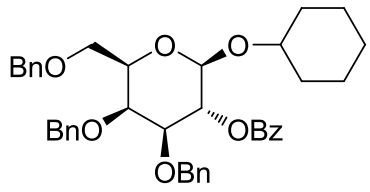


31

2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-*alpha*-D-mannopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*alpha*-D-galactopyranose (31):

[18] S. Anas, V. S. Sajisha, R. Rajan, R. T. Kumaran, K. V. Radhakrishnan, *Bull. Chem. Soc. Jpn.* **2007**, *80*, 553-560.

From donor **22** [4] (100 mg, 0.180 mmol, 1 equiv) and acceptor **10** (0.234 g, 0.90 mmol, 5 equiv), according to general procedure B, after 16 h of reaction, compound **31** [17] was obtained (colorless liquid, 52 mg, 36%, *alpha*-only). R_f 0.61 (4:1, 60 - 90 °C petroleum ether - EtOAc); $[\alpha]_D$ -28.00 (*c* 0.1 $CHCl_3$); HPLC t_R 3.52 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.8 Hz, 2H, ArH), 7.57 (t, *J* = 7.4 Hz, 1H, ArH), 7.21 (d, *J* = 7.2 Hz, 2H, ArH), 7.44 – 7.23 (m, 15H, ArH), 5.66 (s, 1H, H-2'), 5.52 (d, *J* = 5.0 Hz, 1H, H-1), 5.03 (s, 1H, H-1'), 4.91 – 4.75 (m, 3H, PhC$\underline{H}_2$), 4.62 (d, *J* = 8.0 Hz, 1H, H-3), 4.58 (dd, *J* = 14.7, 11.5 Hz, 3H, PhC$\underline{H}_2$), 4.32 (d, *J* = 5.0Hz, 1H, H-2), 4.24 (d, *J* = 8.0 Hz, 1H, H-4), 4.12 (m, 2H, H-3', H-4'), 4.00 – 3.86 (m, 3H, H-5, H-6'), 3.88 – 3.72 (m, 3H, H-6, H-5'), 1.55 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.45 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.37 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.36 (s, 3H, C(C$\underline{H}_3$)$_2$); ^{13}C NMR(126 MHz, $CDCl_3$) δ 165.65 (Ph$\underline{C}$=O), 138.47, 138.39, 138.06, 133.07, 129.95, 129.90, 128.36, 128.31, 128.28, 128.25, 128.00, 127.60, 127.52, 127.43, 109.37, 108.63, 97.93 (C-1'), 96.25 (C-1), 78.21 (C-3'), 75.24 (Ph$\underline{C}$H$_2$), 74.25 (C-4'), 73.39 (Ph$\underline{C}$H$_2$), 71.76 (C-5'), 71.59 (Ph$\underline{C}$H$_2$), 70.80 (C-4), 70.63 (C-2), 70.57 (C-3), 68.99 (C-2'), 68.89 (C-6'), 66.16 (C-6), 65.95 (C-5), 26.14 (C($\underline{C}$H$_3$)$_2$), 25.94 (C($\underline{C}$H$_3$)$_2$), 24.91 (C($\underline{C}$H$_3$)$_2$), 24.48 (C($\underline{C}$H$_3$)$_2$); HRMS (ESI$^+$) calcd. For $C_{46}H_{52}O_{12}Na^+$ 819.3356, found 819.3333.

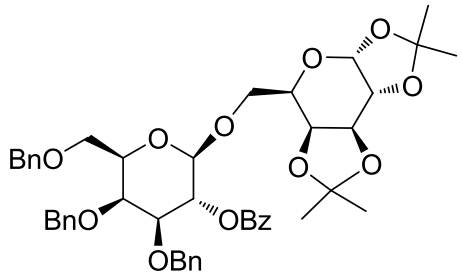


32

Cyclohexyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-*beta*-D-galactopyranoside (32):

From donor **23** [5] (100 mg, 0.180 mmol, 1 equiv) and cyclohexanol (0.09 mL, 0.90 mmol, 5 equiv), according to general procedure B, after 16 h of reaction, compound **32** [18] was obtained (colorless liquid, 49 mg, 43%, *beta*-only). R_f 0.57 (8:1, 60 - 90 °C petroleum ether - EtOAc); $[\alpha]_D$ 98.83 (*c* 0.1 $CHCl_3$); HPLC t_R 3.82 min; ^{1}H NMR (400 MHz, CDCl3) δ 8.07 (d, *J* = 7.5 Hz, 2H, ArH), 7.59 (t, *J* = 7.4 Hz, 1H, ArH), 7.47 (t, *J* = 7.6 Hz, 2H, ArH), 7.34 (m, 15H, ArH), 5.52 (dd, *J* = 10.4, 3.6 Hz, 1H, H-2), 5.36 (d, *J* = 3.6 Hz, 1H, H-1), 4.99 (d, *J* = 11.3 Hz, 1H, PhC$\underline{H}_2$), 4.74 (s, 2H, PhC$\underline{H}_2$), 4.63 (d, *J* = 11.3 Hz, 1H,

PhC$\underline{H}_2$), 4.51(d, *J* = 11.3 Hz, 1H, PhC$\underline{H}_2$), 4.44(d, *J* = 11.3 Hz, 1H, PhC$\underline{H}_2$), 4.16 (m, 2H, H-3, H-5), 4.10 (s, 1H, H-4), 3.67-3.55 (m, 2H, H-6), 3.50(m, 1H, Cyclohexyl-C$\underline{H}$), 1.84 (s, 1H, Cyclohexyl-C$\underline{H}_2$), 1.74 – 1.53 (m, 2H, Cyclohexyl-C$\underline{H}_2$), 1.41 (dd, *J* = 21.8, 11.3 Hz, 2H, Cyclohexyl-C$\underline{H}_2$), 1.33 – 1.08 (m, 5H, Cyclohexyl-C$\underline{H}_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.25 (Ph$\underline{C}$=O), 138.72, 138.49, 138.19, 133.04, 130.47, 129.84, 128.54, 128.46, 128.38, 127.90, 127.85, 127.70, 127.68, 127.63, 95.31 (C-1), 76.41 (Cyclohexyl-C1), 74.92(C-4), 74.82 (Ph$\underline{C}H_2$), 73.64 (Ph$\underline{C}H_2$), 72.77 (Ph$\underline{C}H_2$), 72.09 (C-2), 69.46 (C-5), 69.10 (C-6), 33.51 (Cyclohexyl-$\underline{C}H_2$), 31.76 (Cyclohexyl-$\underline{C}H_2$), 25.69 (Cyclohexyl-$\underline{C}H_2$), 24.14 (Cyclohexyl-$\underline{C}H_2$), 23.79 (Cyclohexyl-$\underline{C}H_2$); HRMS (ESI$^+$) calcd. For $C_{40}H_{44}O_7Na^+$ 659.2985, found 619.3000.



33

2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-*beta*-D-galactopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*alpha*-D-galactopyranose (33):

From donor **23** [5] (100 mg, 0.180 mmol, 1 equiv) and acceptor **10** (0.234 g, 0.90 mmol, 5 equiv), according to general procedure B, after 16 h of reaction, compound **33** [19] was obtained (colorless liquid, 50 mg, 35%, *beta*-only). R_f 0.55 (4:1, 60 - 90 °C petroleum ether - EtOAc); $[\alpha]_D$ 48.00 (*c* 0.1 $CHCl_3$); HPLC t_R 3.28 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 7.99 (m, 2H, ArH), 7.60 – 7.50 (m, 1H, ArH), 7.42 (t, *J* = 7.8 Hz, 2H, ArH), 7.38 – 7.21 (m, 15H, ArH), 5.57 (dd, *J* = 10.4, 3.8 Hz, 1H, H-2'), 5.44 (d, *J* = 5.0 Hz, 1H, H-1), 5.21 (d, *J* = 3.8 Hz, 1H, H-1'), 4.95 (d, *J* = 11.5 Hz, 1H, PhC$\underline{H}_2$), 4.72 – 4.65 (m, 2H, PhC$\underline{H}_2$), 4.60 (d, *J* = 11.5 Hz, 1H, PhC$\underline{H}_2$), 4.50 (d, *J* = 11.5 Hz, 1H, PhC$\underline{H}_2$), 4.44 (d, *J* = 11.5 Hz,

[19] Y. Zeng, Z. Wang, W. Dennis, X. Huang, *J. Org. Chem.* **2008**, 7952-7962.

1H, PhC$\underline{H}_2$), 4.41 (dd, *J* = 7.9, 2.4 Hz, 1H, H-3), 4.23 (dd, *J* = 5.0, 2.4 Hz, 1H, H-2), 4.15 – 4.04 (m, 4H, H-4, H-3', H-4', H-5'), 3.91 (m, 1.4 Hz, 1H, H-5), 3.79 (dd, *J* = 10.3, 6.8 Hz, 1H, H-6), 3.67 – 3.62 (m, 1H, H-6'), 3.62 – 3.54 (m, 2H, H-6, H-6'), 1.45 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.33 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.27 (s, 3H, C(C$\underline{H}_3$)$_2$), 0.98 (s, 3H, C(C$\underline{H}_3$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.97 (Ph$\underline{C}$=O), 138.64, 138.41, 138.04, 133.06, 130.33, 129.95, 128.57, 128.45, 128.38, 128.07, 127.91, 127.72, 127.68, 127.61, 109.28, 108.59, 97.15(C-1'), 96.33 (C-1), 74.95 (Ph$\underline{C}$H$_2$), 74.48 (C-4'), 73.65 (Ph$\underline{C}$H$_2$), 72.63 (Ph$\underline{C}$H$_2$), 71.60 (C-2'), 70.77 (C-4), 70.68 (C-2), 70.52 (C-3), 69.39 (C-6'), 68.69 (C-5'), 66.70 (C-6), 66.12 (C-5), 26.14 (C($\underline{C}$H$_3$)$_2$), 25.97 (C($\underline{C}$H$_3$)$_2$), 25.02 (C($\underline{C}$H$_3$)$_2$), 24.01 (C($\underline{C}$H$_3$)$_2$). The single of C-3' was overlapped by the solvent. HRMS (ESI$^+$) calcd. For $C_{46}H_{52}O_{12}Na^+$ 819.3356, found 819.3338.

-The End-